56
S1

VOLUME 56 SUPPLEMENT 1 FEBRUARY 2024
ISSN 1590-8658

# Digestive and Liver Disease

*An International Journal of Gastroenterology and Hepatology*

Abstracts of the 56th A.I.S.F. - Italian Association for the Study of the Liver - Annual Meeting 2024
Rome, March 14th-15th, 2024

Publication of this abstract supplement has been supported by A.I.S.F. - Italian Association for the Study of the Liver

Digestive and Liver Disease Vol. 56/S1 (2024) S1–S100
ELSEVIER

DIGESTIVE AND LIVER DISEASE
*An International Journal of Gastroenterology and Hepatology*
Volume 56, No. S1 (2024)

# Editorial Board



ELSEVIER

Amsterdam • Boston • London • New York • Oxford • Paris • Philadelphia • San Diego • St. Louis

*(Editorial Board continued)*

# Digestive and Liver Disease

## Contents

**Vol. 54 No. S1 (February 2024)**

*Index Medicus (MEDLINE), Current Contents/Clinical Practice,*
*Science Citation Index and EMBASE/Excerpta Medica*
*Sociedad Iberoamericana de Información Científica (SIIC)*

*Associato alla Unione Stampa Periodica Italiana*

**S1** Oral communications: 56th Annual Meeting of the Italian Association for the Study of the Liver – A.I.S.F. (Rome, March 14th-15th, 2024)

**S21** Thursday Posters: 56th Annual Meeting of the Italian Association for the Study of the Liver – A.I.S.F. (Rome, March 14th-15th, 2024)

**S61** Friday Posters: 56th Annual Meeting of the Italian Association for the Study of the Liver – A.I.S.F. (Rome, March 14th-15th, 2024)

**S99** A.I.S.F. 2024: Abstracts Evaluation Procedure

Digestive and Liver Disease 56 (2024) S1–S20

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

# Oral communications: 56th Annual Meeting of the Italian Association for the Study of the Liver – A.I.S.F. (Rome, March 14th-15th, 2024)

## OC-01

### Improving Predictive Accuracy in Primary Biliary Cholangitis: A New Genetic Risk Score

A. Gerussi [1,2], C. Cappadona [3,4], D.P. Bernasconi [5], L. Cristoferi [1,2,5], M.G. Valsecchi [5], M. Carbone [1,2], P. Invernizzi [1,2,*], R. Asselta [3,4,*], on behalf of the Italian PBC Genetic Study Group

[1] *Division of Gastroenterology, Center for Autoimmune Liver Diseases, Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy*
[2] *European Reference Network on Hepatological Diseases (ERN RARE-LIVER), IRCSS Fondazione San Gerardo dei Tintori, Monza, Italy*
[3] *Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20072 Pieve Emanuele, Milan, Italy*
[4] *IRCCS Humanitas Research Hospital, Via Manzoni 56, 20089 Rozzano, Milan, Italy*
[5] *Bicocca Bioinformatics Biostatistics and Bioimaging Centre - B4, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy*

* These authors contributed equally.

**Introduction and Aim:** Genetic variants influence Primary Biliary Cholangitis (PBC) risk. We established and tested an accurate Polygenic Risk Score (PRS) using these variants.
**Materials and Methods:** Data from two Italian cohorts (OldIT 444 cases, 901 controls; NewIT 255 cases, 579 controls) were analyzed. The latest international genome-wide meta-analysis provided effect size estimates. The PRS together with HLA status and sex were included in an integrated risk model.
**Results:** Starting from 46 non-HLA genes, 22 variants were selected. PBC patients in the OldIT cohort showed higher risk score than controls: -0.014 (interquartile range, IQR, -0.023, 0.005) vs -0.022 (IQR -0.030, -0.013) ($P<2.2 \times 10^{-16}$). For genetic-based prediction, the area under the curve (AUC) was 0.72; adding sex increased AUC to 0.82. Validation in the NewIT cohort confirmed the model accuracy (0.71 without sex, 0.81 with sex). Individuals in the top group, representing the highest 25%, had a PBC risk approximately 14 times higher than that of the reference group (lowest 25%; $P<10^{-6}$).
**Conclusions:** We set up a PRS consisting of variants that, combined with sex and HLA factors, demonstrated a great capacity to precisely distinguish between PBC cases and controls, also pinpointing individuals of heightened risk who warrant tailored, vigilant monitoring.

doi: 10.1016/j.dld.2024.01.002

## OC-02

### Analysis of HBV integration in mitochondrial DNA of HepAD38 cells by the high-throughput HBV integration sequencing and RNASeq approaches

C. Musolino [1], D. Lombardo [2], V. Chines [5], G. Raffa [2], D. Giosa [3], R. Aiese Cigliano [4], M. Aguennouz [2], G. Raimondo [2], T. Pollicino [2]

[1] *Department of Human Pathology, University Hospital G. Martino Messina, Messina*
[2] *Department of Clinical and Experimental Medicine, University Hospital G. Martino Messina, Messina*
[3] *Department of ChiBioFarAm, University of Messina, Messina*
[4] *Sequentia Biotech Sl, Barcelona, Spain*
[5] *University Hospital G. Martino Messina, Messina*

**Introduction:** Hepatitis B virus (HBV) infection is a leading cause of hepatocellular carcinoma (HCC) worldwide. The integration of HBV DNA into the host genome is one of the carcinogenic mechanisms of HBV. It has been recently demonstrated that mitochondrial DNA (mtDNA) can be a target of HBV, suggesting a new potential mechanism by which HBV integration may contribute to liver damage and HCC development.
**Aim:** (1) To conduct a deeper investigation of HBV integration in mtDNA of HepAD38 cell line, which derives from HepG2 cells and supports tetracycline (Tet)-off inducible HBV replication; (2) to evaluate mitochondrial function in HBV-replicating HepAD38 cells.
**Methods:** We used a high-throughput HBV integration sequencing (HBIS) approach and RNASeq to investigated HBV integration in mitochondria isolate from HepAD38 cells after Tet removal for 7 days. Moreover, at the same time point we analysed mitochondrial function of HepAD38 cells using the Seahorse XFp analyzer.
**Results:** After 7 days Tet removal, mean amounts of HBV DNA and HBV RNA in HepAD38 cells were $1.1 \times 10^3 \pm 6.0 \times 10^2$ and $1.0 \times 10 \pm 5.9 \times 10^{-1}$ copies/cell, respectively; while mean amounts of HBV DNA and HBsAg in the cell supernatants were $2 \times 106 \pm 2.7 \times 10^4$ copies/mL and $4.1 \times 10^3 \pm 7.2 \times 10^2$ IU/mL, respectively. At the same

time point, HBIS led us to detect a mean amount of 81± 11.9 HBV integration sites in mtDNA from HBV-replicating HepAD38. In particular, HBV integration sites were detected at high frequency in COX1, RNR2, and ND2 mitochondrial genes. In addition, RNASeq analysis ledus to detect large amount (mean±S.D.: 635± 143.7) of HBV-mitochondria chimeric transcripts in HBV-induced HepAD38 cells. These transcripts contained - at higher frequency - sequences corresponding COX1, RNR2, ND2, ND4, and ND6 mitochondrial genes. The analysis of mitochondrial function showed that, compared to HepAD38 cells without HBV replication and viral integration, HBV replicating HepAD38 cells had a 2-fold reduction of basal respiration, of ATPlinked respiration, and of maximal respiration.
**Conclusions:** (1) HBV may integrate into mtDNA of HBV replicating HepAD38 cells; (2) The site of HBV insertion into mtDNA may be transcriptionally active; (3) HBV replication and viral integration into mtDNA may induce mitochondrial dysfunction

doi: 10.1016/j.dld.2024.01.003

## OC-03

### Non-selective beta-blockers lower the risk of first decompensation in patients with cirrhosis and enduring clinically significant portal hypertension after etiological treatment

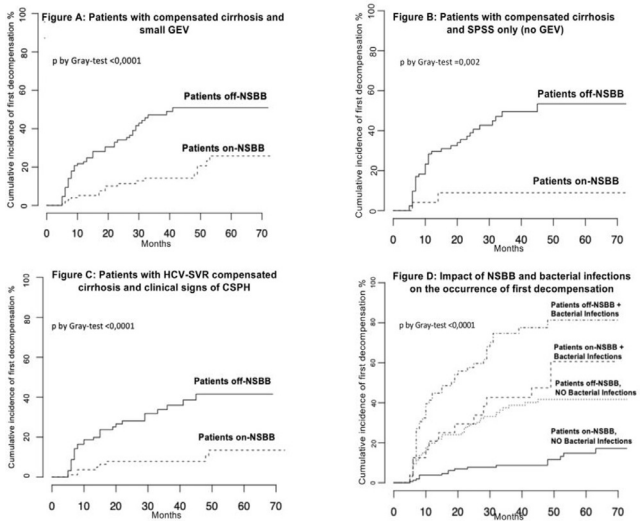
L. Turco [1], M.G. Taru [2,3], G. Vitale [1], F. Mirici Cappa [1], S. Berardi [1], A. Baldan [1], R. Di Donato [1], P. Pianta [1], V. Vero [1], L. Vizioli [1], M.C. Morelli [1], F. Piscaglia [3]

[1] *Internal Medicine Unit for the Treatment of Severe Organ Failure, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy*
[2] *Hepatology Department, Regional Institute of Gastroenterology and Hepatology "Octavian Fodor", Cluj-Napoca, Romania; Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*
[3] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy*

**Background and aim:** Non-selective beta-blockers (NSBB) can lower the risk of first decompensation in patients with cirrhosis and clinically significant portal hypertension (CSPH) (identified by a hepatic venous pressure gradient ³10 mmHg) with ongoing active etiological factor. Our aim was to examine the effect of NSBB on the risk of first decompensation in patients with cirrhosis and enduring CSPH after etiological treatment.
**Methods:** Single-center retrospective analysis of patients with compensated cirrhosis with enduring clinical evidence of CSPH (gastroesophageal varices -GEV- and/or spontaneous portosystemic collaterals- SPSS) after two years from etiological treatment. Primary endpoint was first decompensation (occurrence of variceal bleeding, ascites or hepatic encephalopathy) in patients on-NSBB vs off-NSBB.
**Results:** Final cohort included 406 patients. Baseline characteristics of patients on-NSBB (n=187) and off-NSBB (n=219) were comparable, except for signs of PH that were more pronounced in the on-NSBB group. During a mean follow-up of 32 months, 127 (31%) patients decompensated, with ascites being the most common (77%) decompensating event. Decompensation rates were significantly lower in patients on-NSBB (16% vs 44%, p<0,0001). The benefit of NSBB on decompensation was maintained in patients with small GEV (17% vs 43%, p<0,0001) (Figure A), in those with SPSS only (8% vs 43%, p=0,002) (Figure B) and in each different etiology, including HCV-cured cirrhosis (9% vs 32%, p<0,0001) (Figure C).

At Cox regression analysis, Hemoglobin, Child-Pugh, MELD-Na, diabetes and bacterial infections were independent predictors of decompensation, while NSBB-use had a protective effect (HR 0,32, 95% CI 0,20-0,49; p<0,0001).

Bacterial infections were the strongest trigger factor for decompensation (HR 2,43, 95% CI 1,65-3,58; p<0,0001). NSBB-use was independently associated with lower rate of bacterial infections (HR 0,36, 95% CI 0,22-0,58; p<0,0001), mitigating the risk of first decompensation (Figure D).
**Conclusion:** NSBB decrease the risk of first decompensation in patients with cirrhosis and enduring CSPH after etiological treatment.




doi: 10.1016/j.dld.2024.01.004

## OC-04

### Clinical impact of contrast-enhanced ultrasound on indeterminate or non-characterizable liver nodules on CT/MRI: subanalysis from a prospective multicenter trial

F. Piscaglia [1,2], Y. Kono [3], S.R. Wilson [4], A. Medellin [4], S.K. Rodgers [5,6], P.S. Sidhu [7], A. Kamaya [8], D. Fetzer [9], V. Planz [10], A. Berzigotti [11], L. Finch [12], C.E. Wessner [13], K. Bradigan [14], C.M. Kuon Yeng Escalante [14], T. Siu Xiao [14], J.R. Eisenbrey [14], F. Forsberg [14], A. Lyshchik [14]

[1] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy*
[2] *Department of Medical and Surgical Sciences, University of Bologna, Italy*
[3] *University of California, San Diego, San Diego CA, United States*
[4] *University of Calgary, Calgary, Canada*
[5] *Einstein Medical Center, Philadelphia PA, United States*
[6] *Thomas Jefferson University Hospital, Philadelphia, PA, United States*
[7] *Department of Imaging Sciences, School of Biomedical Engineering and Imaging Sciences, Faculty of Life Sciences and Medicine, King's College London. Department of Radiology, King's College Hospital, London, UK*
[8] *Stanford University, Stanford CA, United States*
[9] *UT Southwestern Medical Center, Dallas, TX, United States*
[10] *Vanderbilt University, Nashville, TN, United States*
[11] *Department of Visceral Surgery and Medicine, Bern University Hospital, University of Bern, Bern, Switzerland*
[12] *Swedish Medical Center, Seattle, WA, United States*

[13] *Division of Biostatistics, Department of Pharmacology, Physiology, and Cancer Biology, Sidney Kimmel Medical College, Philadelphia, PA, United States*
[14] *Thomas Jefferson University Hospital, Philadelphia, PA, United States*

**Introduction:** The present retrospective study of prospectively collected cases aimed to investigate the clinical utility of CEUS for HCC diagnosis in cases where liver lesions were indeterminate at intermediate risk (corresponding to LR3 class) or non-characterizable (LR-NC class) on computed tomography (CT) or magnetic resonance imaging (MRI), conditions for which AASLD and EASL guidelines recommend CEUS despite the lack of prospective studies.
**Methods:** A prospective international multicenter validation study for CEUS Liver Imaging Reporting and Data System (LI-RADS) enrolled 646 patients with at least one (<5cm) lesion at risk for HCC between January 2018 and August 2021. CEUS was performed using Sonovue/Lumason (Bracco Diagnostic) within 4 weeks of CT/MRI. Tissue histology or 12 months follow-up CT/MRI imaging results were used as the reference standard in the respective preferential order. The current study focused on the diagnostic performance of CEUS for HCC diagnosis in masses classified as LR-3 or LR-NC.
**Results:** Within the original dataset, 75 nodules were classified as LR-3 (n=54) or non-characterizable (LR-NC, n=21) on CT/MRI. Among LR-3, 25.9% (14/54) were confirmed as HCC, 72.2% (39/54) non-malignant, and 1.9% (1/54) non-hepatocellular malignancy. CEUS LR-1 and LR-2 lesions (13.0%, 7/54) were confirmed as non-malignant, while all LR-5 (13.0%, 7/54) as HCC. Accordingly, the use of CEUS LI-RADS following LR-3 CT/MRI classification resulted in a conclusive diagnosis in 30.7% of previously indeterminate cases. Of 21 nodules initially classified as LR-NC on CT/MRI, final diagnosis was 52.4% HCC (11/21), 42.8% non-malignant nodules (9/21), and 4.8% other malignancies (LR-M) (1/21). CEUS LR-1 (n=1), LR-5 (n=6) and LR-M (n=2) were confirmed as benign, HCC, and other malignancies, respectively. Accordingly, CEUS LI-RADS showed a clinical impact of 42.9% of previously indeerminate cases.
**Conclusion:** CEUS LI-RADS demonstrated high clinical impact in liver nodules with indeterminate CT/MRI characterization, validating the recommendations for its use in this setting.

doi: 10.1016/j.dld.2024.01.005

## OC-05

### Growth differentiation factor 15 performance as a novel non-invasive circulating biomarker of liver damage in paediatric non-alcoholic fatty liver disease

A. Mosca [1], M.R. Braghini [2], G. Andolina [2], D. Comparcola [1], A. Alterio [1], M.R. Sartorelli [1], L. Monti [3], G. Maggiore [1], A. Alisi [2], N. Panera [2]

[1] *Hepatology Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy*
[2] *Research Unit of Genetics of Complex Phenotypes, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy*
[3] *Department of Radiology, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy*

**Introduction:** To date, non-alcoholic fatty liver disease is considered the most common chronic hepatopathy worldwide. NAFLD spectrum is comprehensive of simple fatty liver (FLT) that may progress to non-alcoholic fatty steatohepatitis (NASH) even in the presence or absence of fibrosis. Several circulating factors, such as the recent growth differentiation factor 15 (GDF15), have been investigated as promising biomarkers of liver fibrosis. However, studies investigating whether plasma levels of GDF15 might be associated with fibrosis in children with NAFLD are still poor.
**Aim:** Here, we evaluated the ability of GDF15 plasma levels as surrogate biomarkers of liver damage in children affected by liver biopsy-proven NAFLD,
**Materials and Methods:** The study was performed on available samples of 124 adolescents (mean age 13.36 years ± 3.36), 77 (62%) males, who underwent liver biopsy for NAFLD between 2014 to 2021, and 24 healthy controls evaluated at the Hepatology Unit of the "Bambino Gesù" Children's Hospital. Plasma levels of GDF15 were assessed by a commercially available enzyme-linked immunosorbent assay (ELISA) assay.
**Results:** Our results revealed that children with NAFLD exhibited higher median levels of circulating GDF15 ($p<0.0001$) than control subjects. GDF15 plasma levels in the NAFLD population correlated positively with steatosis ($r=0.25$, $p=0.015$), fibrosis ($r=0.42$, $p=0.001$), and inflammation ($r=0.25$, $p=0.008$) but not with ballooning. Moreover, circulating levels of GDF15 correlated with other metabolic parameters, and insulin resistance was measured as a homeostasis model assessment of insulin resistance ($r=0.41$, $p=0.0001$). Of note at multivariate regression analysis, after adjusting for body mass index, age, and gender, only the correlation of GDF15 levels with fibrosis and metabolic parameters was confirmed.
**Conclusions:** In conclusion, our results suggest that plasma levels of GDF15 could be potential biomarkers for NAFLD-related fibrosis in adolescents, although further studies are needed to better define its relationship with fibrosis and insulin resistance.

doi: 10.1016/j.dld.2024.01.006

## OC-06

### Longer transplant-free and liver-related event-free survival in obeticholic acid-treated patients with primary biliary cholangitis compared to external controls from two large real-world cohorts

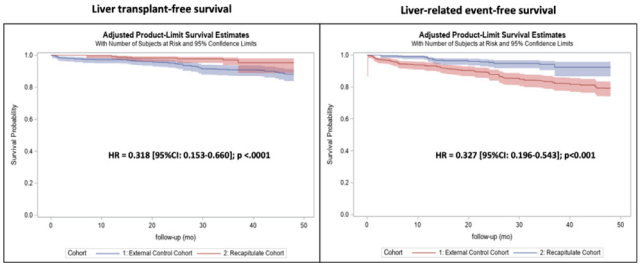
F. Terracciani [1,*], A. De Vincentis [1,*], D. D'Amato [2], P. Invernizzi [3], A. Morgando [2], E. Vanni [2], M. Viganò [4], D. Alvaro [5], R. Venere [5], A. Lleo [6], F. Colapietro [6], E. Degasperi [7], R. Viganò [8], E.G. Giannini [9], S. Labanca [9], V. Feletti [10], A. Mussetto [10], R. Cozzolongo [11], F. Losito [11], M. Pompili [12], F.R. Ponziani [12], G.A. Niro [13], R. Cotugno [13], P. Pozzoni [14], L. Chessa [15], G. Cuccorese [16], V. Pace Palitti [17], M. Russello [18], M. Cannavò [18], E. Frazzetto [19], G. Bertino [19], M. Marzioni [20], N. Terreni [21], T. Zolfino [22], C. Saitta [23], A. Pellicelli [24], B. Coco [25], M. Brunetto [25], N. Cazzagon [26], A. Floreani [26], L. Muratori [27], F. Rosina [28], M. Di Stefano [29], G. Scifo [29], L. Baiocchi [30], G. Grassi [30], R. Sacco [31], A. Izzi [32], S.L. Crocè [33], C. Fiorini [34], F. Marra [34], A. Galli [34], L. Simone [35], O. Morelli [36], L. Abenavoli [37], F. Pizzolante [38], N. De Matthaeis [38], M. Scaravaglio [3], G. Gimignani [39], V. Boano [40], G.F. Manfredi [41], M. Marignani [42], S. Fanella [42], M. Giacchetto [43], A. Castellaneta [44], G. Poggi [45], V. Buzzanca [20], P. Scivetti [46], A. Tortora [12], S. Casella [47], V. Bellia [48], B.F. Omazzi [49], G. Alagna [50], C. Ricci [51], P. Poisa [51], C. Rigamonti [41], V. Calvaruso [43], C. Corpechot [52], F. Carrat [53], G. Hirschfield [54], A. Gulamhusein [54], C. Levy [55], A. Tananka [56], A. J Montano-Loza [57], M. Londono [58], J. E Eaton [59], G. N Dalekos [60], N. Gatselis [60], N. Abbas [61], P. Trivedi [61], D. Thorburn [62], A. Bonder [63], A. van der Meer [64], E. Zigmond [65], A. E Kremer [66], T. Bruns [67], O. Chazouilleres [52], B. E Hansen [68,69,70,^], M. Carbone [3,^], U. Vespasiani-Gentilucci [1,^]

[1] *Internal Medicine and Hepatology, University Campus Bio-Medico of Rome*

[2] Department of Medical Sciences, Division of Gastroenterology and Hepatology, a.O. Città Della Salute e Della Scienza Di Torino, University of Turin
[3] Division of Gastroenterology and Center for Autoimmune Liver Diseases, San Gerardo Hospital, Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy
[4] Division of Hepatology, Ospedale San Giuseppe, Università Di Milano
[5] Department of Translation and Precision Medicine, Sapienza University of Rome, Rome, Italy
[6] Humanitas University, Rozzano (Milan), Italy, Division of Internal Medicine and Hepatology, Humanitas Clinical Research Center Ircss
[7] Division of Gastroenterology and Hepatology, Foundation Irccs Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[8] Hepatology and Gastroenterology, Asst GOM Niguarda
[9] Gastroenterology Unit, Department of Internal Medicine, University of Genoa, IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[10] Gastroenterology Unit, Santa Maria Delle Croci Hospital, Ravenna, Italy
[11] Gastroenterology Unit, National Institute of Gastroenterology "S De Bellis" Reseach Hospital, Castellana Grotte (Bari), Italy
[12] Internal Medicine and Hepatology Unit, Policlinico Gemelli, Sapienza University, Rome, Italy
[13] Gastroenterology Unit, Fondazione Casa Sollievo Della Sofferenza Irccs, San Giovanni Rotondo (Foggia), Italy
[14] Hepatology Unit, Alessandro Manzoni Hospital, Lecco, Italy
[15] Liver Unit, University Hospital of Cagliari, Cagliari, Italy
[16] Internal Medicine Ospedale "R.Dimiccoli", Barletta, Italy
[17] Hepatology Unit, Santo Spirito Hospital, Pescara, Italy
[18] Liver Unit, Arnas Garibaldi, Catania, Italy
[19] Gastroenterology and Hepatology Unit, University Hospital Policlinico Vittorio Emanuele, Catania, Italy
[20] Clinic of Gastroenterology and Hepatology, Università Politecnica delle Marche, Ancona, Italy
[21] Hepatology Unit, Valduce Hospital, Como
[22] Department of Gastroenterology AO G. Brotzu, Cagliari, Italy
[23] Division of Medicine and Hepatology, University Hospital of Messina "Policlinico G. Martino", Messina, Italy
[24] Hepatology Unit, San Camillo Forlanini Hospital, Rome, Italy
[25] Hepatology Unit, University Hospital of Pisa, Italy
[26] Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy
[27] DIMEC Università di Bologna, Policlinico di Sant'Orsola, Bologna, Italy
[28] Medical Team Torino, Torino, Italy
[29] Department of Infectious Diseases, Umberto I Hospital, Siracusa, Italy
[30] Liver and Transplant Unit, Tor Vergata University Hospital, Rome, Italy
[31] Gastroenterology Unit, Ospedali Riuniti, Foggia, Italy
[32] Department of Infectious Diseases, D. Cotugno Hospital, Napoli, Italy
[33] Liver Clinic, Trieste University Hospital, Trieste, Italy
[34] Internal Medicine and Hepatology Unit, Department of Experimental and Clinical Medicine, University of Firenze, Firenze, Italy
[35] Azienda Ospedaliero-Universitaria Di Ferrara, Ferrara, Italy
[36] Clinic of Gastroenterology and Hepatology, Department of Medicine, Universita' degli Studi di Perugia, Perugia, Italy
[37] Department of Health Sciences, University "Magna Graecia" of Catanzaro, Italy
[38] Uoc of Gastroenterology, Gastroenterological, Endocrine- Metabolic and Nephro-Urological Sciences Department, Fondazione Policlinico Universitario A.Gemelli Irccs, Università Cattolica Del Sacro Cuore, Rome, Italy
[39] Unit of Internal Medicine, San Paolo Hospital, Civitavecchia, Italy
[40] Department of Gastroenterology and Endoscopy, Cardinal Massaia Hospital, Asti, Italy
[41] Department of Internal Medicine, Università Del Piemonte Orientale, Novara, Italy
[42] Digestive and Liver Disease Department, School of Medicine and Psychology University "Sapienza", Azienda Ospedaliera S. Andrea, Rome, Italy
[43] Department of Gastroenterology and Hepatology, University of Palermo, Palermo, Italy
[44] Gastroenterology Unit, Policlinico Di Bari Hospital, Bari, Italy
[45] Oncology Unit, Istituto Di Cura Città Di Pavia, Pavia, Italy
[46] Internal Medicine Unit, Azienda Sanitaria Locale Di Biella, Biella, Italy
[47] Hepatology Unit, Spedali Civili Gardone Val Trompia, Brescia, Italy
[48] Hepatology Unit, Valtellina e Alto Lario Hospital, Sondrio, Italy
[49] Gastroenterology Unit, Guido Salvini Hospital, Rho, Italy
[50] UOC Medicina Interna, Ospedale SS Annunziata, Sassari, Italy
[51] Internal Medicine, Spedali Civili, Brescia, Italy
[52] Reference Center for Inflammatory Biliary Diseases and Autoimmune Hepatitis, European Reference Network on Hepatological Diseases (ERN Rare-Liver), Saint-Antoine Hospital, Assistance Publique - Hôpitaux de Paris, Inserm UMR_S938, Saint-Antoine Research Center, Sorbonne University, Paris, France
[53] Public Health Unit, Saint-Antoine Hospital, Assistance Publique - Hôpitaux de Paris, Pierre Louis Institute of Epidemiology and Public Health, Sorbonne University, Paris, France
[54] Toronto Centre for Liver Disease, University Health Network, University of Toronto, Toronto, Canada
[55] Schiff Center for Liver Diseases, Division of Digestive Health and Liver Diseases, University of Miami, Miami, Florida, USA
[56] Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan
[57] Division of Gastroenterology and Liver Unit, University of Alberta, Edmonton, Canada
[58] Liver Unit, Hospital Clínic, University of Barcelona, The August Pi i Sunyer Biomedical Research Institute, Biomedical Research Networking Center in Hepatic and Digestive Diseases, European Reference Network on Hepatological Diseases (ERN Rare-Liver), Barcelona, Spain
[59] Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, USA
[60] Department of Medicine and Research Laboratory of Internal Medicine, National Expertise Center of Greece in Autoimmune Liver Diseases, European Reference Network on Hepatological Diseases (ERN Rare-Liver), General University Hospital, Larissa, Greece
[61] Birmingham Biomedical Research Centre, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom
[62] University College London Institute for Liver and Digestive Health, Royal Free Hospital, London, United Kingdom
[63] Department of Medicine, Division of Gastroenterology, Beth Israel Deaconess Medical Center, Boston, USA
[64] Department of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands
[65] The Research Center for Digestive Tract and Liver Diseases, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[66] Department of Gastroenterology and Hepatology, University Hospital Zürich, Zürich, Switzerland
[67] Department of Medicine III, University Hospital RWTH Aachen, Aachen, Germany
[68] Department of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands
[69] Toronto Centre for Liver Disease, University Health Network, University of Toronto, Toronto, Canada
[70] IHPME University of Toronto, Toronto, Ontario, Canada

* co-first authors
^ co-last authors

**Background:** Obeticholic acid (OCA) stands as the sole approved second-line treatment for primary biliary cholangitis (PBC) patients unresponsive to ursodeoxycholic acid (UDCA). Preliminary studies suggested OCA's efficacy in reducing PBC decompensation and increasing survival. However, these studies face limitations, either due to heterogeneous cohorts (OCA registrative trial Vs real-world controls) or reliance on administrative data.
**Aim:** To compare transplant-free and liver-related event (LRE)-free survival between two large real-world cohorts of OCA-treated and untreated PBC patients.
**Methods:** The Italian RECAPITULATE is a multicenter real-world cohort of OCA-treated PBC patients enrolled from across Italy. An external control cohort of OCA-untreated PBC patients was derived from the GLOBAL-PBC dataset. Controls met OCA prescription criteria in Italy (ALP≥1.5/ULN and/or 1<bilirubin<2 mg/dl after ≥1 year of UDCA treatment), and a random visit in which eligibility criteria were met represented the index date. LRE (ascites with-/-out spontaneous bacterial peritonitis, hepatic encephalopathy, and upper gastrointestinal bleeding), liver transplant and liver-related death were tracked during follow-up. Weighted Cox regression method (using propensity scores) was applied for the external control group, incorporating age, ALP, AST, bilirubin, UDCA duration, cirrhosis and age at OCA start as baseline confounders.
**Results:** The study included 437 RECAPITULATE patients (female: 88%; cirrhotics: 34%; on UDCA: 98%), and 831 GLOBAL-PBC controls (female: 91%; cirrhotics: 15%; on UDCA: 74%). RECAPITULATE's median follow-up was 30 months, and time was censored accordingly in the control cohort. Liver transplant/liver-related death and LRE were 4 and 16 in the RECAPITULATE cohort, and 58 and 107 in GLOBAL-PBC controls, respectively. In the weighted Cox regression analyses, patients in the RECAPITULATE cohort showed reduced risk of liver transplant/liver-related death [HR 0.318 (0.153-0.660); p<0.0001] and LRE [HR 0.327 (0.196-0.543); p<0.001] with respect to GLOBAL-PBC controls (Figure 1).
**Conclusion:** In the comparison between two real-world cohorts, OCA-treated PBC patients show a longer transplant-free and LRE-free survival with respect to propensity-matched untreated controls.




doi: 10.1016/j.dld.2024.01.007

## OC-07

### End-procedural complete haemodynamic response may not be essential for the clinical success of TIPS in patients with cirrhosis

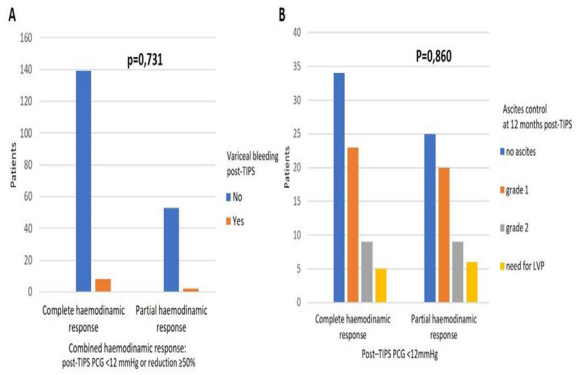
D. Roccarina [1], M. Rosi [1], D. Saltini [2], V. Adotti [1], M. Senzolo [3], S. Nardelli [4], T. Guasconi [2], S. Gitto [1], L. Biribin [3], S. Gioia [4], F. Indulti [2], C. Campani [1], P. Burra [3], O. Riggio [4], F. Marra [1,5], F. Schepis [2], F. Vizzutti [1]

[1] *Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy*
[2] *Division of Gastroenterology, Modena Hospital, University of Modena and Reggio Emilia, Modena, Italy*
[3] *Gastroenterology, Multivisceral Transplant Unit, Department of Surgical and Gastroenterological Sciences, University of Padua, Padua, Italy*
[4] *Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy*
[5] *Center for Research, High Education and Transfer DENOThe, University of Florence, Florence, Italy*

**Background:** Transjugular intrahepatic portosystemic shunt (TIPS) is a well-established treatment for variceal bleeding (VB) and refractory ascites (RA) in cirrhosis. Immediate post-TIPS complete haemodynamic response (CHR), defined as a post-TIPS porto-caval gradient (PCG) <12 mmHg in VB and RA, or 50% PCG reduction in VB, is used to define a treatment success. TIPS underdilation reduces post-derivative complications, although with this strategy CHR is not always achieved, raising concerns on control of portal hypertensive complications and survival.
**Aim:** We compared ascites control, bleeding recurrence and mortality rate among patients achieving CHR or partial haemodynamic response (PHR) after TIPS.
**Methods:** We retrospectively analysed a series of cirrhotic patients who consecutively received TIPS for RA or secondary prophylaxis of VB at four referral Italian Centers from 2007 to 2021.
**Results:** 415 patients, median age 61(15), 28% females were enrolled. TIPS was indicated in 51% for VB and in 49% for RA. Fifty-percent received underdilated TIPS (<8mm). Overall, a CHR was achieved in 65%, with a median post-TIPS PCG/% of PGC reduction of 8(4) mmHg/60(19)%. In PHR, post-TIPS PCG/% of PGC reduction was 15(4) mmHg/36(14)%. Non-significant differences were observed in rebleeding rate (5% vs 4%, p=0.73, in CHR vs PHR, respectively) (Fig.1A). The grade of ascites or the need for large volume paracentesis at 3, 6, 12 months did not significantly differ (p=0.76, 0.77, 0.86, respectively) between CHR and PHR (Fig.1B). The median overall survival was 24(34) months. Regardless of TIPS indication, survival was not significant different between CHR and PHR (Fig.2). Advanced age, disease severity before TIPS and eventual development of HCC resulted as predictors of mortality.

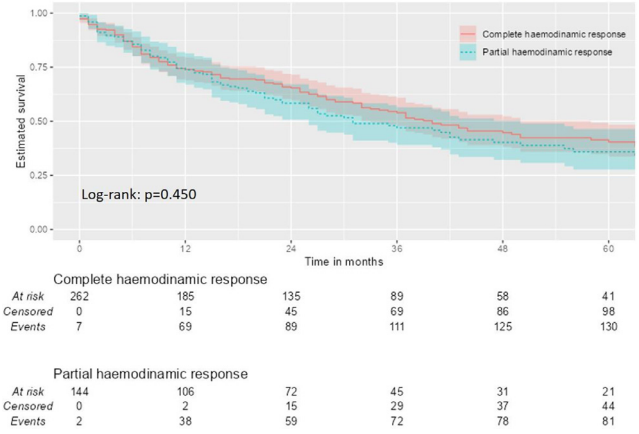
**Conclusions:** CHR immediately after TIPS may not be essential to define the clinical success, with a substantial reduction in PCG exerting a pivotal role. Further studies are needed to identify a minimal threshold for PCG reduction.

Figure 1. Barr charts of bleeding recurrence (A) and ascites (B) control post-TIPS in complete and partial haemodynamic responses (Contingency tables, Chi-square test)




**Abbreviations:** TIPS, transjugular intrahepatic portosystemic shunt; PCG, porto-caval gradient; LVP, large volume paracentesis.

Figure 2. Kaplan Meier Survival Plot in complete and partial haemodynamic responses




doi: 10.1016/j.dld.2024.01.008

## OC-08

### CiThroModel improves the prediction of venous thromboembolism in hospitalized patients with cirrhosis

A Zanetto [1], F. Pelizzaro [1], E. Campello [2], C. Bulato [2], M. Gambato [1], G. Germani [1], F.P. Russo [1], P. Burra [1], P. Simioni [2], M. Senzolo [1]

[1] *Gastroenterology and Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padova University Hospital, Padova, Italy*
[2] *General Internal Medicine Unit and Thrombotic and Hemorrhagic Disease Unit, Department of Medicine, Padova University Hospital, Padova, Italy*

**Introduction:** The incidence and risk factors for venous thromboembolism (VTE) in hospitalized patients with cirrhosis are poorly understood.
**Aim:** We investigated the incidence, risk factors, and clinical impact of VTE in a prospective cohort of patients with cirrhosis.
**Materials and Methods:** Patients were recruited at hospital admission and prospectively followed during hospitalization for development of VTE. Patients receiving anticoagulation and those with cancer were not eligible. Associations with baseline characteristics and 3-months mortality were explored. Hazard ratios (HR) and 95% CIs were calculated using Cox regression.
**Results:** We included 461 patients (median age 61 years old; 67% male; 52% with alcohol-related cirrhosis). Ascites ± hepatic encephalopathy were the most common reasons for admission. The median MELD score was 18 (12-24); 11% of patients were Child-Pugh A, 41% were Child-Pugh B, and 48% were Child-Pugh C. During hospitalization, 28 (6.1%) patients experienced VTE. Multivariate analysis showed that Child-Pugh C vs. A/B (HR: 5.25; 95% CI: 1.75-15.73), reduced mobility (HR: 4.21; 95% CI: 1.83-9.67), and bacterial infections (HR: 2.35; 95% CI: 1.06-5.12) were independent predictors of VTE. A predictive model (CirrhosisThrombosisModel) based on these variables accurately identified patients at risk (sensitivity 96.3%, specificity 66.7%) (Table). The AUROC of CiThroModel was significantly higher compared with the Padua prediction score (0.842 [0.784-0.899] vs. 0.753 [0.669-0.837]; p=0.04). Regarding 3-month mortality, a multivariate Cox regression model including Child-Pugh stage, AKI, infections, and VTE showed that Child-Pugh stage was the only independent predictor of death.
**Conclusion:** Hospitalized patients with cirrhosis are at risk of VTE. Reduced mobility, Child-Pugh stage C, and bacterial infections are independently associated with the risk of developing VTE, thus allowing risk stratification. The CiThroModel can be used to identify the patients at higher risk and guide thromboprophylaxis. Whether VTE in cirrhosis is independently linked to mortality requires further investigation.

**Table. The CiTrhoModel: independent predictors of VTE based on multivariate analysis.**

| Variable | β coefficient | HR (95% CI) | p | Points |
|---|---|---|---|---|
| Child-Pugh | | | | |
| A/B | 0 | - | - | 0 |
| C | 1.867 | 6.47 (2.23-18.8) | <0.001 | 4 |
| Bacterial infections | | | | |
| No | 0 | - | - | 0 |
| Yes | 0.933 | 2.54 (1.15-5.61) | 0.02 | 2 |
| Reduced mobility | | | | |
| No | 0 | - | - | 0 |
| Yes | 1.439 | 4.21 (1.84-9.67) | <0.001 | 3 |

Legend: VTE: venous thromboembolism. Simplified version of CiTrhoModel: the cumulative score is calculated by adding the individual points obtained for each variable. A cut-off value of 5 differentiates between patients at high vs. low risk of VTE.

doi: 10.1016/j.dld.2024.01.009

## OC-09

### Decoding human Intrahepatic Cholangiocarcinoma Metabolism: Unveiling the Impact of SLC2A3 on Aggressiveness and Prognosis

M.A. Polidoro [1], B. Franceschini [1], F. Milana [2], C. Soldani [1], R. Carriero [3], A. Aghemo [4,5], M. Donadon [6,7], G. Torzilli [3,4], R. Pastorelli [8], L. Brunelli [8], A. Lleo [4,5]

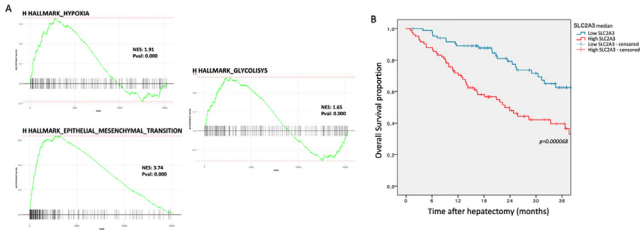
[1] *Hepatobiliary Immunopathology Laboratory, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy*
[2] *Division of Hepatobiliary and General Surgery, Department of Surgery, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy*
[3] *Bioinformatics Unit, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy*
[4] *Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI), Italy*
[5] *Division of Internal Medicine and Hepatology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy*

[6] Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy
[7] Department of General Surgery, University Maggiore Hospital, Novara, Italy
[8] Laboratory of Metabolites and Proteins in translational research, IRCCS Istituto di ricerche farmacologiche Mario Negri, Milano, Italy

**Background and Aims:** Intrahepatic Cholangiocarcinoma (iCCA) is a cancer of the biliary epithelium with a poor prognosis and limited therapies. Understanding iCCA pathophysiology is crucial for developing effective treatments. In this scenario, tumor metabolism reprogramming, a cancer hallmark, is of interest due to its impact on tumor aggressiveness and therapy resistance. Herein, we investigated the role of upregulated glycolysis in iCCA and its interplay with aggressiveness and prognosis.
**Method:** Normal cholangiocytes (n=5) and iCCA cells (n=25) were isolated from patients resected at the Division of Hepatobiliary and General Surgery, Humanitas Clinical Institute. iCCA cell supernatants were analyzed by mass spectrometry-based targeted and untargeted metabolomic approaches. RNAseq and RT-PCR analyses were carried out to identify altered metabolic pathways in iCCA. An iCCA cell line (HuH28) was cultured under hypoxic conditions and migration assay was performed. RNAseq and clinical data of iCCA patients were obtained from a public dataset (OEP001105).
**Results:** The metabolomic analysis revealed that i**CCA** primary cells displayed elevated mitochondrial activity compared to normal cholangiocytes, with increased glutamine and glucose uptake. Moreover, RNAseq analysis unveiled changes in the glycolytic pathway, along with upregulation in hypoxia and epithelial-to-mesenchymal transition (EMT) pathways in iCCA cells (Fig. 1A).

To better elucidate the role of glycolysis, we analyzed the expression by RT-PCR of two main glucose transporters, observing a down-regulation of SLC2A1 and a significant upregulation of SLC2A3 in iCCA cells, compared to cholangiocytes. Moreover, glucose uptake assays showed a positive correlation between glucose intake and SLC2A3 expression, underscoring its role in mediating glucose metabolism in iCCA cells, than SLC2A1.

To gain insights into the interplay between hypoxia and glycolysis, HuH28 cells were cultured under hypoxic conditions, showing increased migratory ability and upregulation of SLC2A3 and N-CAD expression, compared to normoxia. We further explored the link between glycolysis and EMT, demonstrating a correlation between SLC2A3 expression and EMT markers, as ZEB1 and N-CAD, in iCCA cells. To elucidate the impact of SLC2A3 on iCCA prognosis, patients (n=151) from public RNAseq dataset were divided into low- and high-SLC2A3 expressions based on the median value. Notably, high-SLC2A3 patients displayed significantly poorer survival outcomes than low-expressing SLC2A3 patients (Fig. 1B).
**Conclusion:** This study revealed the significant upregulation of SLC2A3 in iCCA and its association with hypoxia and EMT, unveiling the interplay between metabolic reprogramming and tumor aggressiveness in iCCA. These findings emphasize the therapeutic potential of targeting SLC2A3, offering a promising avenue for intervention in iCCA.




doi: 10.1016/j.dld.2024.01.010

## OC-10

### Virological and clinical outcomes of patients with HDV-related compensated cirrhosis treated with Bulevirtide monotherapy for 96 weeks: a retrospective multicenter european study (SAVE-D)

M.P. Anolli [1], E. Degasperi [1], M. Jachs [2], T. Reiberger [2], V. De Ledinghen [3], S. Metivier [4], G. D'Offizi [5], F. di Maria [5], C. Schramm [6], H. Schmidt [6], C. Zöllner [7], F. Tacke [7], C. Dietz-Fricke [8], H. Wedemeyer [8], M. Papatheodoridi [9], G. Papatheodoridis [9], F. Van Bömmel [10], M.R. Brunetto [11], G. Verucchi [12], A. Ciancio [13], F. Zoulim [14], A. Mangia [15], M.N. Hilleret [16], U. Merle [17], T.A. Santantonio [18], N. Coppola [19], A. Pellicelli [20], B. Roche [21], X. Causse [22], L. D'Alteroche [23], J. Dumortier [24], N. Ganne [25], F. Heluwaert [26], I. Ollivier [27], A. Loglio [28], M. Viganò [29], A. Federico [30], F. Pileri [31], M. Maracci [32], M. Tonnini [33], J.P. Arpurt [34], K.I. Barange [35], E. Billaud [36], S. Pol [37], A. Gervais [38], A. Minello [39], I. Rosa [40], M. Puoti [41], P. Lampertico [1,42]

[1] Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[2] Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria
[3] Hepatology Department, Haut-Lévêque Hospital, Bordeaux, France
[4] Hepatology Unit, CHU Rangueil, 31059, Toulouse, France
[5] Division of Infectious Diseases - Hepatology, Department of Transplantation and General Surgery, Istituto Nazionale per le Malattie Infettive "L. Spallanzani" IRCCS, Rome Italy
[6] Department of Gastroenterology, Hepatology and Transplant Medicine, Medical Faculty, University of Duisburg-Essen, Essen, Germany
[7] Department of Hepatology and Gastroenterology, Charité Universitätsmedizin Berlin, Berlin, Germany
[8] Department of Gastroenterology, Hepatology, Infectious Diseases and Endocrinology at Hannover Medical School, Hannover, Germany
[9] Department of Gastroenterology, General Hospital of Athens "Laiko", Medical School of National & Kapodistrian University of Athens, Greece
[10] Division of Hepatology, Department of Medicine II, Leipzig University Medical Center, Laboratory for Clinical and Experimental Hepatology, Leipzig, Germany
[11] Department of Clinical and Experimental Medicine, University of Pisa and Hepatology Unit, University Hospital of Pisa, Pisa, Italy
[12] Department of Medical and Surgical Sciences, Unit of Infectious Diseases, "Alma Mater Studiorum" University of Bologna, S. Orsola-Malpighi Hospital, Bologna, Italy
[13] Department of Medical Sciences, University of Turin, Gastroenterology Division of Città della Salute e della Scienza of Turin, University Hospital, Turin, Italy
[14] Lyon Hepatology Institute, Université Claude Bernard Lyon 1; Hospices Civils de Lyon; INSERM Unit 1052 - CRCL; Lyon, France
[15] Liver Unit, Fondazione IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Italy
[16] Service d'hépato-gastro-entérologie, CHU Grenoble-Alpes, Grenoble, France
[17] Department of Internal Medicine IV, Gastroenterology & Hepatology, Heidelberg University Hospital, Heidelberg, Germany
[18] Department of Medical and Surgical Sciences, Infectious Diseases Unit, University of Foggia, Foggia, Italy
[19] Department of Mental Health and Public Medicine - Infectious Diseases Unit, University of Campania Luigi Vanvitelli, Naples, Italy
[20] Liver Unit, San Camillo Hospital, Department of Transplantation and General Surgery, Rome, Italy

[21] Hepato-Biliary Center, AP-HP Hôpital Universitaire Paul Brousse, Paris-Saclay University, Research INSERM-Paris Saclay Unit 1193, Villejuif, France
[22] Hôpital de la Source Orleans, France
[23] Service d'Hépato-Gastroentérologie CHU de Tours, France
[24] Department of Digestive Diseases, Hospices Civils de Lyon, Edouard Herriot hospital, France; Claude Bernard Lyon 1 University, France
[25] AP-HP, Avicenne Hospital, Hepatology Department, F-93000 Bobigny, France
[26] Centre Hospitalier Annecy Genevois, 74000 Annecy, France
[27] Department of Hepatogastroenterology, CHU de Caen Normandie, Caen, France
[28] Gastroenterology, Hepatology and Transplantation Division, ASST Papa Giovanni XXIII, Bergamo, Italy
[29] Division of Hepatology, Ospedale San Giuseppe, Italy
[30] Division of Hepatogastroenterology, Department of Precision Medicine, Università della Campania "Luigi Vanvitelli", Naples, Italy
[31] Division of Internal Medicine and Center for Hemochromatosis, University of Modena and Reggio Emilia, Modena, Italy
[32] Institute of Infectious Diseases and Public Health, Università Politecnica delle Marche, Ancona, Italy
[33] Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
[34] Department of Gastroenterology, CH d'Avignon, Avignon, France
[35] Department of Gastroenterology, Toulouse University Hospital, Toulouse, France
[36] Université de Nantes, INSERM UIC 1413, Department of Infectious Diseases, CHU Hôtel Dieu, Nantes, France
[37] Université Paris Cité; Assistance Publique des Hôpitaux de Paris, Hôpital Cochin, Hepatology/Addictology department, Paris, France
[38] Assistance Publique des Hôpitaux de Paris, Hôpital Bichat Claude Bernard, Service des Maladies Infectieuses et Tropicales, Paris, France
[39] CHU Dijon, Service d'Hépato-gastroentérologie et oncologie digestive, Inserm EPICAD LNC-UMR1231, Université de Bourgogne-Franche Comté, Dijon, France
[40] Service d'hépatogastroentérologie, Centre Hospitalier Intercommunal, Créteil
[41] School of Medicine and Surgery University of Milano Bicocca
[42] CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

**Background:** Bulevirtide (BLV) received EMA approval for treatment of chronic compensated hepatitis due to Delta virus (HDV) infection, however real-life data in large cohorts of patients with cirrhosis are lacking.
**Methods:** Consecutive HDV patients with cirrhosis starting BLV 2 mg/day since September 2019 were included in a retrospective multicenter real-life European study (SAVE-D). Patients' characteristics before and during BLV treatment were collected. Virological, biochemical, combined responses, adverse events and liver-related events (HCC, decompensation, liver transplant) were assessed.
**Results:** 215 patients with HDV compensated (CPT-A) cirrhosis receiving BLV monotherapy for a median of 72 (24-120) weeks were included: at BLV start, age was 49 (18-81) years, 60% men, ALT 78 (23-1,074) U/L, liver stiffness measurement (LSM) 18.3 (6.4-75.0) kPa, platelets 91 (17-454) x $10^3$/$mm^3$, 54% with varices, 8% HIV-positive, 6% with previous ascites, 6% with active HCC, 91% on NUC, median HDV RNA 5.5 (1.5-8.5) log IU/mL and HBsAg 3.7 (0.8-4.7) log IU/mL. Virological responses and HDV-RNA undetectability at W24, W48, W72, W96 were 54%, 68%, 68%, 77% and 18%, 32%, 41% and 46%, respectively. Biochemical and combined responses were 54%, 63%, 60%, 57%, and 34%, 48%, 48%, and 50%, respectively. Patients with <1 log HDV-RNA decline vs. baseline declined from 21% at W24 to 8% at W96. AST, GGT, albumin, IgG and LSM values significantly improved throughout treatment. Bile acids significantly increased, 9% patients reported mild and transient pruritus, 3% injection site reactions. The W96 cumulative risks of de-novo HCC (n=7) and decompensation (n=6) were 3.8% (95% CI 2-7%) and 3.2% (95% CI 1-6%), respectively. 7 patients underwent liver transplantation and 4 died of BLV-unrelated causes.
**Conclusions:** BLV 2 mg/day monotherapy up to 96 weeks was safe and effective in patients with HDV-related compensated cirrhosis. Virological and clinical responses increased over time and liver-related events were few.

doi: 10.1016/j.dld.2024.01.011

## OC-11

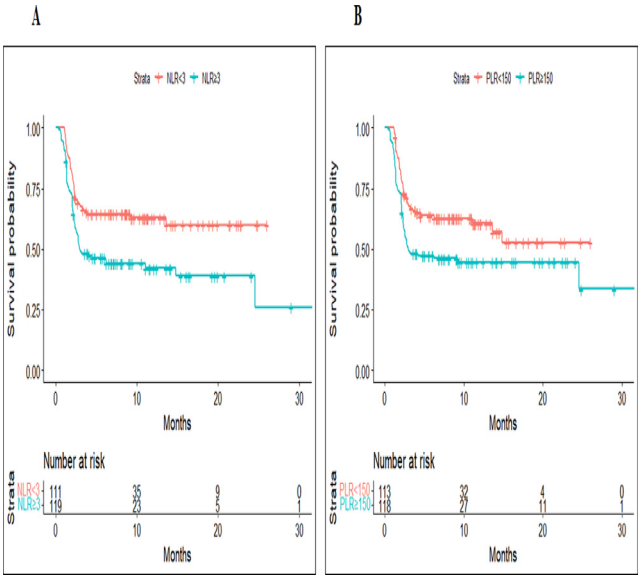
### Identification of factors associated with primary refractoriness to atezolizumab plus bevacizumab in patients with advanced hepatocellular carcinoma

G.F. Manfredi [1,2], C.A.M. Fulgenzi [2], A. D'Alessio [2,3], C. Celsa [2,4,5], B. Stefanini [2,6], J. Cheon [7], C. Ang [8], T.U. Marron [8], A. Saeed [9], B. Wietharn [9], T. Pressiani [10], M. Pinter [11], B. Scheiner [11], Yi-Hsiang Huang [12], S. Phen [13], A. Rafeh Naqash [14], F. Piscaglia [6], R. Po-Ting Lin [15,16], C. -yen Lin [15,16], A. Dalbeni [17], C. Vivaldi [18], G. Masi [18], R. Thimme [19], A. Vogel [20], M. Schönlein [21], J. von Felden [22], K. Schulze [22], H. Wege [22], P.R. Galle [23], M. Kudo [24], L. Rimassa [10,25], A. Singal [13], R. Sharma [2], A. Cortellini [1,26], H. Jae Chon [7], M. Burlone [27], M. Pirisi [1,27], D.J. Pinato [2,3]

[1] Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy
[2] Department of Surgery & Cancer, Imperial College London, Hammersmith Hospital, Du Cane Road, London, UK
[3] Division of Oncology, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[4] Section of Gastroenterology & Hepatology, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, PROMISE, University of Palermo, Palermo, Italy
[5] Department of Surgical, Oncological and Oral Sciences (Di.Chir.On.S.), University of Palermo, Palermo, Italy
[6] Department of Medical and Surgical Sciences, University of Bologna, Italy
[7] Medical Oncology, Department of Internal Medicine, CHA Bundang Medical Center, CHA University, Seongnam, Republic of Korea
[8] Department of Medicine, Division of Hematology/Oncology, Tisch Cancer Institute, Mount Sinai Hospital, New York, NY, USA
[9] Department of Medicine, Division of Medical Oncology, Kansas University Cancer Center, Kansas City, KS, USA
[10] Medical Oncology and Hematology Unit, Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Via A. Manzoni 56, 20089 Rozzano, Milan, Italy
[11] Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria
[12] Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; Institute of Clinical Medicine, National Yang Ming Chiao Tung University School of Medicine, Taipei, Taiwan

[13] Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, USA
[14] Medical Oncology/TSET Phase 1 Program, Stephenson Cancer Center, University of Oklahoma, Oklahoma City, USA
[15] Department of Gastroenterology and Hepatology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan
[16] College of Medicine, Chang Gung University, Taoyuan, Taiwan
[17] University of Verona, Department of Medicine General Medicine C Unit & Liver Unit
[18] Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy; Unit of Medical Oncology 2, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy
[19] Department of Medicine II (Gastroenterology, Hepatology, Endocrinology and Infectious Diseases), Freiburg University Medical Center, Faculty of Medicine, University of Freiburg, Freiburg, Germany
[20] Toronto General Hospital, UHN, Toronto, ON M5G 2C4, Canada; Princess Margaret Cancer Centre, Toronto, ON, Canada; Hannover Medical School, Hannover, Germany
[21] Department of Oncology, Hematology and Bone Marrow Transplantation with Section of Pneumology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[22] I. Department of Medicine, University Medical Center Hamburg-Eppendorf, Germany
[23] University Medical Center Mainz, I. Dept. of Internal Medicine, Mainz, Germany
[24] Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka-Sayama, Japan
[25] Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20072 Pieve Emanuele, Milan, Italy
[26] Medical Oncology, Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy
[27] Division of Internal Medicine, AOU Maggiore della Carità, Novara, Italy

**Introduction:** Atezolizumab plus bevacizumab (A+B) is not universally efficacious in patients with advanced hepatocellular carcinoma. Primary refractoriness to A+B is associated with dismal prognosis. Mechanisms underscoring lack of response are poorly understood.
**Methods:** From a multinational (24 centers) dataset, we identified 591 patients with Child-Pugh grade (CP) A who received first-line A+B. We stratified the cohort in "primary progressors (PP), patients with progressive disease at the first radiological assessment after therapy start and "responders" (RE), patients with partial/complete response. Baseline characteristics of the groups, comprising neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were compared. Clinical factors associated with patients' response to therapy were used to stratify OS and PFS.
**Results:** Median OS was 16.8 months (95% CI 14.7-18.9), median PFS 8.2 months (95% CI 6.9-9.4). Considering the characteristics of PP (N=171) and RE (N=125), no differences between the groups were underlined regarding sex, age, liver disease aetiology, CP, macrovascular invasion, metastatic disease, albumin-bilirubin grade. The PP group had higher tumour burden based on BCLC stage (A+B 20.8%, C 79.2% vs A+B 31%, C 69% p=0.047), higher NLR and PLR (medians 3.7 vs 2.6, $p < 0.001$; 168.6 vs 135.4, p =0.008, respectively). NLR $\geq$ 3 was associated with shorter OS (12.9 months vs 24.2 months, $p < 0.001$) and PFS (11.0 months vs 3 months, p=0.006 respectively, Panel A). PLR > 150 predicted for shorter OS and PFS compared with PLR < 150 (14.1 months vs 21.6 months, p=0.01; 3 months vs 13.4 months, p=0.004 respectively, Panel B). No significant difference was found among patients with BCLC A+B vs C, both for OS-PFS.
**Conclusion:** Higher levels of systemic inflammation were associated with primary refractoriness to A+B, shorter PFS and OS regardless the disease stage. Modulation of the systemic inflammatory status might augment responsiveness to A+B in this prognostically disadvantaged population.




doi: 10.1016/j.dld.2024.01.012

## OC-12

### Validating and expanding Baveno VII criteria of recompensation in patients with decompensated cirrhosis

M. Tonon, R. Gagliardi, G. Zilio, S. Incicco, V. Calvino, A. Accetta, N. Zeni, C.G. Gambino, A. Barone, P. Angeli, S. Piano

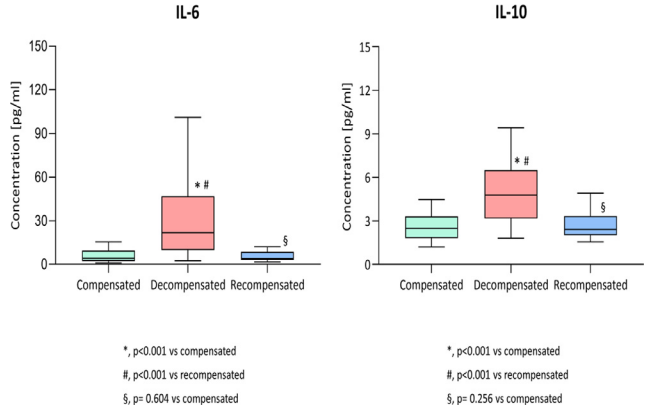
*Unit of Internal Medicine and Hepatology, Department of Medicine, University and Hospital of Padova, Padova, Italy*

**Background and aims:** Baveno-VII consensus defines recompensation in cirrhotic patients achieving: 1) removal/suppression/cure of cirrhosis's etiology of cirrhosis; 2) resolution of ascites (off diuretics), hepatic encephalopathy (off lactulose/rifaximin) and bleeding for>12 months; c) stable improvement of liver function. This study aims to evaluate the incidence and prognostic impact of recompensation in patients with decompensated cirrhosis.
**Methods:** Outpatients with cirrhosis and curable etiologies (alcohol, HCV, HBV) were consecutively included and followed up (median time=35 months). Demographic, clinical, laboratory and endoscopic data were collected at enrolment and follow-up visits. Recompensation, defined by Baveno VII criteria, was assessed. Considering the subjectivity of treatment withdrawal, we evaluated expanded recompensation criteria for patients meeting all criteria, but still on decompensation treatment (diuretics/lactulose/rifaximin). Recompensation was considered a time-varying covariate in survival analysis. In 160 patients (62 compensated, 60 decompensated, 38 recompensated), plasma samples were analyzed for inflammatory cytokines (IL-6,IL-10,IL1beta).
**Results:** 691 patients were enrolled (mean age 57±11 years, men 72.5%; alcohol=55%). Among decompensated patients (n=525), 298 achieved an effective etiological treatment and 22 (4.2%) achieved recompensation (Baveno-VII criteria), while 115 patients achieved expanded recompensation criteria (22.3%). MELD score was the only independent predictor of recompensation (aHR=0.90;p=0.002).

In multivariable analysis (adjusted for age, sex, MELD, albumin, varices and further decompensation), mortality risk showed no significant difference between patients achieving recompensation and compensated patients (aHR=2.53; p=0.107), while decompensated patients had the highest risk (aHR=4.74;p<0.001). Mortality risk showed no significant difference between patients meeting expanded recompensation criteria and Baveno-VII criteria (HR=1.02; p=0.961).

IL-6 and IL-10 were significantly higher in decompensated patients than in compensated ones (Figure). Following recompensation, inflammatory cytokines significantly decreased and no difference was found vs compensated patients.

**Conclusions:** Baveno-VII criteria identify cirrhotic patients with a prognosis similar to compensated patients, but<5% achieve recompensation. Expanding the criteria to include patients on medical treatment for decompensation identifies patients at low risk of mortality.




doi: 10.1016/j.dld.2024.01.013

## OC-13

### Role of rare and common variants in the diagnosis of adults with cryptogenic liver and lipid disorders

L. Ronzoni [1], S. Pelusi [1], V. Moretti [1], F. Malvestiti [2], H.E. Torghabehei [3], J. Rondena [1], G. Periti [1], C. Bianco [1], M. De Filippo [3], D. Prati [1], L. Valenti [1,2,3]

[1] *Precisione Medicine Lab, Biological Resource Center and Department of Transfusion Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milano, Milan, Italy*
[2] *Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy*
[3] *Omic Sciences Lab, Scientific Direction, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milano, Milan, Italy*

**Background:** Chronic liver diseases (CLD) remain undiagnosed in up to 30% of adult patients despite extensive clinical and instrumental workup. Genetic analysis may help in providing a diagnosis, but they are not yet widely clinically available.

**Aim:** To evaluate the clinical utility of genetic analysis in diagnosis CLD in adult patients.

**Materials and Methods:** A total of 70 unrelated adult patients with liver and lipid disorders with suspected genetic contribution were evaluated; four clinical subgroups were considered: cholestasis, hyperferritinemia, dyslipidemia, and steatotic liver disease (SLD). For each patient we detected the presence of rare variants, through a Next-generation Sequencing Customized Targeted Panel (TS), including 82 liver and lipid metabolism-related genes, and evaluated the contribution of common risk variants, as captured by poligenic risk score (PRS), to the individual susceptibility to SLD.

**Results:** A total of 82 clinically relevant rare variants was detected in 54 patients, allowing to establish a clinical diagnosis of a Mendelian disorder in 20 patients (29%). Younger patients were more likely to be diagnosed (OR 0.97; 95% CI: 0.94-1; p= 0.09). Increased SLD-PRS values were detected in 18 patients (26%), 15 of whom (83%) had a SLD phenotype. A positive impact of age and a negative one of family history on high SLD-PRS was detected (p=0.02 and p=0.015, respectively), as well as of clinical phenotype, with SLD being associated with an increased risk (OR 3.58; 95% CI: 1.15-11.18; p=0.003). The presence of a high SLD-PRS could increase the diagnostic uptake of a significant fraction in SLD subgroup and in the overall cohort (+29%, p 0.001 and +15%, p 0.0001, respectively) (Fig.1).

**Discussion:** TS is a useful genetic test for the diagnosis of selected adult patients with CLD. The complementary evaluation of common variants, as capture by PRS, may significantly increase the diagnostic uptake for patients with SLD.

doi: 10.1016/j.dld.2024.01.014

## OC-14

### Underdilation strategy for TIPS placement reduces incidence of overt hepatic encephalopathy without affecting clinical efficacy and survival: results of a multicenter prospective Italian study

D. Saltini [1], S. Nardelli [2], V. Addotti [3], L. Biribin [4], T. Guasconi [1], S. Gioia [2], C. Caporali [5], M. Bianchini [1], M. Rosi [3], D. Roccarina [3], L. Ridola [2], F. Casari [5], F. Prampolini [5], F. Indulti [1], B. Cuffari [1], L. Ragozzino [3], N. De Maria [1], A. Colecchia [1], M. Senzolo [4], M. Merli [2], F. Marra [3], O. Riggio [2], F. Vizzutti [3], F. Schepis [1]

[1] *Division of Gastroenterology, Azienda Ospedaliero-Universitaria of Modena, University of Modena and Reggio Emilia, Modena, Italy*
[2] *Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy*
[3] *Internal Medicine and Liver Unit, University Hospital Careggi, Department of Experimental and Clinical Medicine, University of Florence, Italy*
[4] *Multivisceral Transplant Unit-Gastroenterology, Department of Surgery, Oncology, and Gastroenterology, Padua University Hospital, Padua, Italy*
[5] *Division of Radiology, Azienda Ospedaliero-Universitaria of Modena, University of Modena and Reggio Emilia, Modena, Italy*

**Introduction:** Transjugular intrahepatic portosystemic shunt (TIPS) is a well-established treatment for portal hypertension complications in patients with cirrhosis. Overt hepatic encephalopathy (OHE) is the most feared complication of TIPS, significantly impacting the patient's quality of life and care giver burden. TIPS underdilation to <8 mm is a promising approach to reduce the incidence of this complication.

**Aims:** To compare the probability of OHE between patients with underdilated TIPS and those with TIPS dilated to ≥8 mm. The secondary objective was to evaluate the recurrence of ascites/bleeding and the 2-year mortality rate.

**Materials and Methods:** This was a prospective multicenter observational study conducted at four referral Centers participating in the Italian-TIPS-Registry. Consecutive patients who received TIPS from April 2012 to March 2022 were included. Competitive risk analysis was conducted for primary and secondary outcomes.

**Results:** Out of 574 enrolled patients, 284 (49%) received TIPS underdilated to <8mm. The 1-year incidence of OHE was significantly higher in ≥8mm group compared to the underdilated group (55%

vs. 35%; p<0.001), regardless of TIPS indication. Multivariable analysis identified older age, elevated INR, low sodium, and history of previous OHE as independent predictors of OHE; conversely, underdilated TIPS exerted a significant protective role (sHR 0.51; p<0.001). No significant difference in TIPS dysfunction rate was observed. Clinical efficacy was unaffected by the underdilation approach, as demonstrated by the lack of significant differences in recurrence of ascites requiring large-volume paracentesis or rebleeding between groups. Regardless of TIPS indication, the 2-year mortality rates did not significantly differ between the underdilated and ≥8 mm groups (26% vs. 30%; p=0.4).
**Conclusion:** The study confirms that the TIPS underdilation strategy significantly reduces the burden of OHE while maintaining clinical efficacy, and does not negatively impact mortality when compared to the standard dilation strategy.

doi: 10.1016/j.dld.2024.01.015

## OC-15

### Radiomics-based prognostication in primary sclerosing cholangitis: a proof-of-concept study

L. Cristoferi [1], C. Maino [2], D.P. Bernasconi [3], A. Savino [1,4], I. Ripamonti [1,4], M. Scaravaglio [1,4], E. Pesatori [1], O. Falco [1], D. D'Amato [1], A. Gerussi [1,4], F. Gallivanone [5], C. Alberzoni [2], M.G. Valsecchi [3], R. Corso [2], P. Invernizzi [1,4], D. Ippolito [2,4], E. De Bernardi [4], M. Carbone [1,4]

[1] *Division of Gastroenterology, Centre for Autoimmune Liver Diseases, European Reference Network on Hepatological Diseases (ERN RARE-LIVER), Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy*
[2] *Department of Diagnostic Radiology, San Gerardo Hospital, IRCCS San Gerardo dei Tintori, Monza, Italy*
[3] *Bicocca Bioinformatics Biostatistics and Bioimaging Centre-B4, School of Medicine and Surgery, University of Milan-Bicocca. Monza, Italy*
[4] *Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy*
[5] *Institute of Molecular Bioimaging and physiology, National Research Council (IBFM-CNR), Milan, Italy*

**Introduction:** Magnetic resonance imaging (MRI) in primary sclerosing cholangitis (PSC) risk assessment generally relies on qualitative analysis, leading to interpretation variability. Radiomics emerges as a promising field for developing quantitative radiological biomarkers for PSC monitoring and risk stratification.
**Aim:** This study aims to identify and validate radiomic features from MRI images to identify patients at higher-risk of developing poor outcome.
**Methods:** This is a prospective, observational study (Jan 2019 - Dec-2022) recruiting 100 PSC patients undergoing routine gadoxetate disodium-enhanced MRI with standardized protocol. From PyRadiomics implemented in Python both morphological and radiomics features were extracted by five selected MRI sequences. Patients were categorized into high-risk groups based on the Mayo risk score (MRS)>0 and the liver stiffness measurement (LSM)>9.6kPa. Predictive features from a training cohort of 58 patients were validated in 42 additional PSC patients, followed by survival analysis in the combined 100-patient cohort.
**Results:** One-hundred patients were analysed. Among the 58 patients of the training cohort 15 (25.0%) and 17 (30.0%) were defined at high-risk by MRS and LSM. One-hundred and seven radiomic features were extracted from each of the 5 MRI sequences selected. GLRLM-Run Entropy in T2WI with fat saturation significantly correlates with estimates of clinical outcomes with an OR of 4.04 (CI 3.63-4.71, p=0.0002) for MRS and 2.93 (CI 1.71-3.43, p=0.009) for LSM (Table). Its prognostic potential was confirmed on observed clinical events by univariate Cox analysis (HR per 0.1 of increase 1.478 95% CI 1.175;1.860) showing an excellent predicting performance (C-index = 0.85).
**Conclusions:** This study highlights the potential of a unique, quantitative radiomic feature for monitoring and risk-stratify PSC patients. Its quantitative nature, and extraction using free, globally available software makes it a promising candidate in radiological biomarkers' field in PSC. Additional research with wider cohorts and longer follow-up is required to confirm these findings.

doi: 10.1016/j.dld.2024.01.016

## OC-16

### Circulating mitochondrial bioenergetic profile reflects the hepatic one and represents a non-invasive biomarker of disease severity in MASLD genetically predisposed individuals

E. Paolini [1,2], M. Longo [1], M. Meroni [1], P. Podini [3], A. Quattrini [3], A.L. Fracanzani [1,4], P. Dongiovanni [1]

[1] *Medicine and Metabolic Diseases, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Department of Pharmacological and Biomolecular Sciences, Università Degli Studi di Milano, Milan, Italy*
[3] *Experimental Neuropathology Unit, Institute of Experimental Neurology (INSPE), Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy*
[4] *Department of Pathophysiology and Transplantation, Università Degli Studi di Milano, Milan, Italy*

**Introduction:** Mitochondrial dysfunction is a key player in Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) onset and progression. The co-presence of loss-of-function mutations in PNPLA3, TM6SF2 and MBOAT7 genes impacts on mitochondrial morphology and function in in vitro models. Conversely, the restore of MBOAT7 and/or TM6SF2 activity in knock-out HepG2 cells decreased the number of misshapen-dysfunctional mitochondria and improved OXPHOS capacity.
**Aims:** To translate our in vitro findings into a clinical perspective and discover novel non-invasive biomarkers, we assessed mitochondrial activity in 41 MASLD patients stratified according to GG-PNPLA3, TT-MBOAT7 and TT-TM6SF2 genotype, of whom frozen liver biopsies and peripheral blood mononuclear cells (PBMCs) were available.
**Method:** $H_2O_2$, ROS, mitochondrial complexes activities were measured by enzymatic assays, the oxygen consumption rate (OCR) by Seahorse.
**Results:** According to our in vitro results, liver biopsies and PBMCs of GG-PNPLA3, TT-MBOAT7 and TT-TM6SF2 carriers, alone and especially combined (number of risk variants, NRV=3), showed higher $H_2O_2$ and ROS than MASLD patients with no variants. Consistently, the activity of mitochondrial complexes I, III, citrate and ATP synthase was lower in biopsies and PBMCs of GG-PNPLA3, TT-MBOAT7 and TT-TM6SF2 individuals, showing the sharpest effect in their co-presence ($^{*}p<0.05$, $^{**}p<0.001$, $^{***}p<0.0001$ vs NRV=0). Finally, biopsies and PBMCs of NRV=3 subjects exhibited OCR depletion yielded by complex I/IV and II/IV activities compared to NRV=0 at Seahorse ($^{***}p<0.0001$). At multivariate analysis adjusted for age, gender, BMI, diabetes and MASLD severity, NRV=3 was associated with reduced OCR in hepatic biopsies ($\beta$=-21.24) and PBMCs ($\beta$=-20.08) (p<0.0001). Finally, at nominal logistic analysis, adjusted for NRV=3, OCR predicted MASH-fibrosis with AUC of 0.81 and 0.86 in biopsies and PBMCs, respectively.
**Conclusion:** PBMCs mitochondrial activity is impaired in NRV=3 carriers and completely reflects the hepatic one. Therefore, PBMCs bioenergetic profile could represent a potential non-invasive

biomarker of disease severity in MASLD genetically predisposed individuals.

doi: 10.1016/j.dld.2024.01.017

## OC-17

### Prognostic role of ELF test compared to liver biopsy in patients with metabolic dysfunction-associated steatotic liver disease (MASLD)

A. Liguori [1,2], F. D'Ambrosio [3], N. Viceconti [2], F. Termite [2], L. Petrucci [2], R. Beschi [1], M. Orienti [3], S. Galletti [3], S. Cardinali [3], L. Riccardi [1,2], M. Garcovich [1,2], F. Pizzolante [1,2], N. De Matthaeis [1,2], M.A. Zocco [1,2], M.E. Ainora [1,2], M.C. Giustiniani [2,4], G. Marrone [1,2], M. Biolato [1,2], Cefalo C [2], F.M. Vecchio [2,4], A. Grieco [1,2], A. Urbani [2,3], M. Sanguinetti [2,3], A. Gasbarrini [1,2], L. Miele [1,2]

[1] *Department of Traslational Medicine and Surgery, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy*
[2] *Università Cattolica del Sacro Cuore, Rome, Italy*
[3] *Department of Laboratory and Infectious Sciences, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy*
[4] *Department of Women, children and public health sciences, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy*

**Introduction:** Liver fibrosis is the strongest predictor of liver-related events (LRE) in patients with MASLD. The enhanced liver fibrosis (ELF) score is a composite of direct fibrosis biomarkers that reflect extracellular matrix turnover. ELF test shows high diagnostic accuracy for advanced liver fibrosis in patients with MASLD but its utility as a prognostic biomarker is still unclear.
**Aim:** The aim of our study is to compare the prognostic effectiveness of ELF, FIB4 and liver histology in patients with MASLD.
**Materials and Methods:** We retrospectively enrolled 289 patients with MASLD. ELF score was determined using a serum sample collected at baseline. FIB4 computation and liver biopsy were performed at baseline. The primary outcome was a composite endpoint of all-cause mortality, hepatocellular carcinoma, liver transplantation or cirrhosis complications (ascites, variceal bleeding, hepatic encephalopathy, MELD≥15). Considering existing literature cut-offs, subjects were stratified accordingly to ELF (≤9.8, 9.8-11.3, ≥11.3), FIB-4 (<1.3, 1.3-2·67, >2.67) and histology (F0-2, F3, F4) to assess risk of occurrence of primary outcome.
**Results:** We included data of 289 patients (30.4% female, median age 50y [IQR 39-58]). After a median follow-up of 41 months [IQR 21-68], the composite endpoint was observed in 11.8% of patients. There was a stepwise increase in the incidence of primary outcome according with ELF ≤9.8 (0.5%), 9.8-11.2 (14.5%), ≥11.3 (69.7%). Survival curves for pairwise comparisons between groups showed significant differences according to pre-defined histological and NITs stratification ($p<0.05$). At multivariate Cox regression analysis, ELF and liver histology were significant predictors of the primary outcome after adjusting for gender, diabetes, age, BMI. (ELF >11.2vs<9.8 HR 135.4 [95%CI 15.9-1149.0 $p<0.01$], 9.8-11.2vs<9.8 HR 22.5 [95%CI 2.7-183.9 $p<0.01$]) (F4vs0-2 HR 216.6 [95%CI 23.5-1999.2 $p<0.01$], F3vs0-2 HR 5.44 [95%CI 1.0-30.9 $p=0.05$]).
**Conclusions:** ELF, a simple non-invasive blood test, performed as well as histologically assessed fibrosis in predicting clinical outcomes and should be considered as alternative to liver biopsy for prognostic assessment in patients with MASLD.

doi: 10.1016/j.dld.2024.01.018

## OC-18

### Hepatocellular carcinoma incidence and risk stratification in patients with metabolic dysfunction-associated steatotic liver disease on long-term follow-up

G.P. Caviglia [1], S. Pelusi [2], A. Liguori [3], M. Guariglia [1], C. Rosso [1], A. Armandi [1,4], K. GJini [1], N. Viceconti [3], M.L. Abate [1], L. Miele [3,5], L. Valenti [2,6], E. Bugianesi [1,7]

[1] *Department of Medical Sciences, University of Turin, 10126 Turin, Italy*
[2] *Precision Medicine, Department of Transfusion Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[3] *Dipartimento Universitario Medicina e Chirurgia Traslazionale, Università Cattolica del Sacro Cuore, Rome, Italy*
[4] *Metabolic Liver Disease Research Program, I. Department of Medicine, University Medical Center of the Johannes Gutenberg-University, 55131 Mainz, Germany*
[5] *Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Gemelli IRCCS, Rome, Italy*
[6] *Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*
[7] *Gastroenterology Unit, Città della Salute e della Scienza—Molinette Hospital, 10126, Turin, Italy*

**Background:** Metabolic dysfunction-associated steatotic liver disease (MASLD) is projected to become the leading cause of hepatocellular carcinoma (HCC) worldwide. The identification of novel tools able to stratify the risk of HCC is an unmet medical need.
**Aim:** To investigate the performance of non-invasive tests (NITs) and protein induced by vitamin K absence or antagonist-II (PIVKA-II) for HCC risk stratification in MASLD patients on long-term follow-up (FU).
**Materials and Methods:** We retrospectively enrolled 366 MASLD patients (age: 58, 49–66 years; males: 198 [54.1%]; T2DM: 168, [45.9%]) with significant liver fibrosis (LSM≥8kPa or F≥2 at liver biopsy); 279 (76.2%) had compensated advanced chronic liver disease (cACLD) (LSM≥10kPa or F≥3 at liver biopsy). NITS (i.e. APRI, FIB-4, and NFS) were calculated at baseline. Serum PIVKA-II was measured by CLEIA (Lumipulse®G600II, Fujirebio).
**Results:** During 2.9 (IQR 1.0–4.3) years of FU, 19/366 (5.2%) patients developed HCC (1.49 per 100 person/years). Notably, all the 19 HCC occurred in cACLD patients (n=279) (2.06 per 100 person/years). Most patients had early-stage HCC (BCLC=0/A, n=14). In the whole cohort (n=366), NFS showed the best performance for HCC prediction (C-index=0.81), followed by FIB-4 (C-index=0.78), and by APRI (C-index=0.71); the accuracy of serum PIVKA-II was C-index=0.76. In patients with cACLD (n=279), the predictive performance of NITs was C-index=0.77 for NFS, C-index=0.75 for FIB-4, and C-index=0.68 for APRI, while PIVKA-II showed C-index=0.74. Remarkably, in cACLD patients the combination of NFS+PIVKA-II significantly improved the accuracy for HCC prediction (C-index=0.84), allowing patients to be stratified into 3 risk categories with different HCC incidence: low-risk (0/52; 0%), medium-risk (9/190; 4.7%), and high-risk (10/37; 27.0%) ($p<0.001$).
**Conclusion:** In MASLD patients with significant fibrosis, NFS showed appropriate performance for HCC prediction. However, in patients with more advanced liver disease, serum PIVKA-II may be a useful diagnostic complement to improve HCC prediction and risk stratification.

doi: 10.1016/j.dld.2024.01.019

## OC-19

### Intrahepatic cholangiocarcinoma-derived organoids for disease modelling and drug screening

S. De Siervi [1], S. Conti Nibali [1], S. Mantovani [2], B. Oliviero [2], M.U. Mondelli [2,3], M. Maggi [1], F. Arena [1], I. Samarati [1], V. Cavalloro [4,5], D. Ronchi [6], S. Collina [7], C. Arrigoni [1], M.G. Lolicato [1], C. Turato [1]

[1] *Department of Molecular Medicine, University of Pavia, Pavia, Italy*
[2] *Division of Clinical Immunology and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy*
[3] *Department of Internal Medicine and Therapeutics, University of Pavia, Italy*
[4] *Department of Earth and Environmental Sciences, University of Pavia, Pavia, Italy*
[5] *National Biodiversity Future Center, Piazza Marina 61, 90133 Palermo, Italy*
[6] *Department of Electrical, Computer and Biomedical Engineering, University of Pavia, Pavia, Italy*
[7] *Department of Drug Sciences, University of Pavia, Pavia, Italy*

**Background and Aim:** Intrahepatic cholangiocarcinoma (iCCA) is characterized by a very poor outcome and reliable predictive biomarkers as well as validated therapeutic strategies are urgently needed. In this regard, accurate in vitro models are necessary to better understand the molecular and cellular processes underlying iCCA progression and provide high-throughput experimental techniques to define the efficacy of treatments.

The aim of this study was to treat iCCA patient-derived organoids with different therapeutic agents, screening drugs/molecules which experimentally interfere with the viability of tumour cells, in order to identify possible substances that would be effective against iCCA.

**Methods:** To develop organoids, we minced tumor biopsies and shortly digested in small cell clusters that are seeded into Matrigel. After characterization using immunofluorescence and qPCR techniques, iCCA-derived organoids were treated with a different dosage of each selected compound for 72h, before measuring cell viability. We also studied possible molecular processes which are potential targets of these substances.

**Results:** We developed and characterized a biobank of human iCCA-derived organoids, evaluating the morphological characteristics and revealing the presence of typical CCA markers (EpCaM, CK19, CK7, Ki67). Subsequently, as an initial screening, for each patient-derived organoid culture, we tested their sensitivity to five anti-cancer compounds, including drugs in clinical use or development. In particular, we started to analyze three small molecules targeting the Voltage Dependence Anion Selective Channel isoform 1 (VDAC1), showing a significant dose-dependent decrease of viability in tumor cells. In addition, we studied the effect of a natural-derived metabolite Usnic Acid, which potentially acts through mTOR and MAPK phosphorilation, underlying a reduction of cell viability at high concentration. We also treated iCCA-organoids with L-Asparaginase with no relevant effects in the tested experimental setting.

**Conclusion:** We developed and characterized a well-defined iCCA in vitro model that allowed us to investigate the effect of different anti-cancer substances as new possible therapy strategies.

doi: 10.1016/j.dld.2024.01.020

## OC-20

### Novel insights into the effect of SGLT-2 inhibitor empagliflozin on hepatic damage in diabetic obese Zucker rats

C. Pirozzi [1], S. Melini [1], F. Comella [1], A. Aragón Herrera [2], A. Lama [1], Y. Farrag [3], G. Mattace Raso [1], O. Gualillo [3], F. Lago Paz [2], R. Meli [1]

[1] *Department of Pharmacy, University of Naples Federico II, Naples, Italy*
[2] *Cellular and Molecular Cardiology Unit and Department of Cardiology, Institute of Biomedical Research of Santiago de Compostela (IDIS-SERGAS), Santiago de Compostela, Spain*
[3] *SERGAS (Servizo Galego de Saude) and NEIRID Lab (Neuroendocrine Interactions in Rheumatology and Inflammatory Diseases), Research Laboratory 9, IDIS (Instituto de Investigación Sanitaria de Santiago), Santiago University Clinical Hospital, Santiago de Compostela, Spain*

**Introduction and Aim/Methods:** Sodium-glucose cotransporter 2 inhibitor empagliflozin (EMPA) have emerged as an effective pharmacological tool for patients with type 2 diabetes mellitus, cardiovascular disease and/or other metabolic disturbances. However, the alternative mechanisms implicated in its beneficial effects are still unknown. Our study aimed to evaluate the impact of a 6-week-EMPA treatment on hepatic dysfunction observed in diabetic obese Zucker Diabetic Fatty (ZDF) rats. Glucose and lipid metabolism as well as inflammatory and pro-fibrotic markers were evaluated in the liver of ZDF mice by Western blot and Real-Time PCR analysis.

**Results:** Firstly, EMPA induced the insulin signaling pathway and contextually counteracted hepatic gluconeogenesis, The increased phosphorylation of AMPK by EMPA ran in tandem with the improvement of hepatic lipid metabolism altered in ZDF rats. Indeed, EMPA treatment modulated the gene expression of key mediators of fatty acid metabolism in the liver of ZDF rats, reducing the cluster of differentiation (CD)36, a key marker of steatosis together with FOXO-1. Moreover, EMPA increased the transcription of the nuclear receptor PPAR-gamma and its coactivator PGC1-alpha, as well as the fatty acid binding protein (FABP)1, which contributes to clean hepatic free fatty acids. EMPA also improved hepatic mitochondrial functions compromised in diabetic rats, increasing the expression of UCP2 and the mitochondrial transporter ABCG1. Finally, we showed EMPA beneficial effect against hepatic inflammation and fibrosis mainly associated with insulin resistance and hyperglycemia characterizing ZDF model. Specifically, EMPA markedly reduced the hepatic mRNAs of different inflammatory and pro-fibrotic mediators. Notably, the hepatic expression of SGLT-2 did not change between EMPA-treated and untreated animals, suggesting the involvement of other converging mechanisms beyond the pharmacologically established one.

**Conclusions:** Taken together, we shed light on the hepatoprotective effect of EMPA in counteracting insulin resistance and other metabolic and inflammatory alterations due to diabetes and its related comorbidities.

doi: 10.1016/j.dld.2024.01.021

## OC-21

### Relationship of non-invasive measures with histological response in patients with nonalcoholic steatohepatitis and fibrosis: 52-week data from the Phase 3 MAESTRO-NASH trial

A. Mangia [1], R. Loomba [2], JM. Schattenberg [3], R. Taub [4], D. Labriola [4], M. Noureddin [5], V. Ratziu [6], S.A. Harrison [7]

[1] *Epatologia IRCCS "Casa Sollievo della Sofferenza" San giovanni Rotondo, Italy*
[2] *University of California San Diego, CA, US*
[3] *Metabolic Liver Research Program, Department of Medicine, University Medical Center, Mainz, Germany*
[4] *Madrigal Pharmaceuticals, Conshohocken, PA, US*
[5] *Houston Research Institute, Houston, TX, US*
[6] *Pitie–Salpetriere Hospital, Institute of Cardiometabolism and Nutrition, Sorbonne Universite, Paris, France*
[7] *University of Oxford, Oxford, United Kingdom and Pinnacle Clinical Research, San Antonio, TX, US*

**Introduction:** MAESTRO-NASH (NCT03900429) is an ongoing 54-month, randomized, double-blind, placebo-controlled Phase 3 trial evaluating the efficacy of resmetirom in patients with biopsy-confirmed nonalcoholic steatohepatitis (NASH) and fibrosis. 966 patients were randomized 1:1:1 to resmetirom 80mg, 100mg, or placebo administered once daily. Histologic endpoints were assessed after 52 weeks. Dual primary endpoints were achieved with both resmetirom 80mg and 100mg: NASH resolution with no worsening of fibrosis (NR) or ≥1-stage reduction in fibrosis with no worsening of NAS (FR).

Adults with ≥3 metabolic risk factors, liver stiffness ≥8.5 kPa, hepatic fat ≥8%, biopsy-confirmed NASH with F1B-F3 fibrosis, and NAS ≥4 were eligible to participate in MAESTRO-NASH.

**Aim:** To assess the relationship of non-invasive measures with histological response (NR and/or FR) in the resmetirom 80mg, resmetirom 100mg, and placebo groups.

**Results:** Patients with biopsy-confirmed NASH with fibrosis had high metabolic risk. Among patients treated with resmetirom 80mg or 100mg who achieved a ≥30% reduction from baseline in MRI-PDFF, NR was observed in 28% and 38% and FR in 17% and 18% more patients than placebo. A ≥30% PDFF response was observed in 96%, 88%, and 92% of resmetirom 100mg NR, FR, and NR and/or FR responders. Half of resmetirom ≥30% PDFF responders without NR or FR showed ≥2-point NAS reduction. On biopsy, NR correlated ($r^2$) with FR (=0.30). Additional correlates ($r^2$) of NR and FR at resmetirom 100mg included reduction in PDFF (0.39, 0.23); ALT (0.20, 0.24); and liver volume (0.25, 0.18).

**Conclusions:** Achievement of NASH resolution and fibrosis reduction was associated with a ≥30% reduction from baseline in MRI-PDFF - at both resmetirom doses (80 and 100mg). Additional analyses are ongoing.

doi: 10.1016/j.dld.2024.01.022

## OC-22

### A Markov model unveiling the impact of Resmetirom on the natural history of MASLD patients with baseline significant or severe liver fibrosis

G. Pennisi [1,*], G. Di Maria [2,*], C. Celsa [1], M. Enea [2], M. Vaccaro [3], C. Ciccioli [1], G. Infantino [1], A. Tulone [1], V. Di Marco [1], C. Cammà [1,#], S. Petta [1,#]

[1] *Section of Gastroenterology and Hepatology, Dipartimento Di Promozione Della Salute, Materno Infantile, Medicina Interna e Specialistica Di Eccellenza (PROMISE), University of Palermo, Italy*
[2] *Dipartimento Di Promozione Della Salute, Materno Infantile, Medicina Interna e Specialistica Di Eccellenza (PROMISE), University of Palermo, Italy*
[3] *Dipartimento di Scienze Economiche, Aziendali e Statistiche, University of Palermo, 90133 Palermo, Italy*

* These authors equally contribute to this paper.
# These authors equally contribute to this paper.

**Background & Aim:** The MAESTRO Phase 3 trial reported that 52-week treatment of Resmetirom is effective in improving fibrosis and MASH in patients with metabolic-dysfunction associated steatotic liver disease (MASLD) with F2 or F3 fibrosis, while data on the impact on 5-year and long-term clinical outcomes are still lacking. Moreover, data about the full spectrum of the natural history of MASLD patients with F2 or F3 fibrosis are scarce and fragmentary. We simulated the transition probabilities of disease progression in MASLD patients with F2 or F3 fibrosis, and the effect of Resmetirom treatment on clinical outcomes.

**Methods:** Data from 40 studies and individual sources on MASLD subjects formed transition matrices for fibrosis stages and complications, defined as cirrhosis development (CD), hepatocellular carcinoma (HCC) and liver decompensation (LD). Markov models were developed to depict the F2 and F3 fibrosis stage progression towards the complications and to evaluate the effect of 52-week Resmetirom treatment on the natural history.

**Results:** We estimated the 5-year and lifetime probability of untreated or Resmetirom-treated MASLD patients with baseline F2 fibrosis of developing cirrhosis (11% and 39.5% in untreated; 8.8% and 37.2% in treated), LD (0.9% and 11.9% in untreated; 0.7% and 11% in treated), and HCC (0.8% and 7.2% in untreated; 0.5% and 6.8% in treated). Similarly, we estimated the 5-year and lifetime probability of untreated or resmetirom-treated MASLD patients with baseline F3 fibrosis of developing cirrhosis (27.7% and 52.6% in untreated; 22.9% and 48.7% in treated), LD (2.8% and 17.3% in untreated; 2.2% and 15.6% in treated), and HCC (2.8% and 10.4% in untreated; 2.1% and 9.8% in treated). Sensitivity analyses considering changes in transition probabilities, treatment efficacy and treatment duration are ongoing.

**Conclusions:** Resmetirom decreases the 5-year and lifetime Markov-model estimated risk of cirrhosis development, LD and HCC in patients with MASLD and F2 or F3 fibrosis.

doi: 10.1016/j.dld.2024.01.023

## OC-23

### 1-Piperidine propionic acid is effective in reducing HCC development and fatty acid accumulation in experimental liver carcinogenesis

P. Guerra [1], G. Villano [4], M.G. Ruvoletto [1], A. Biasiolo [1], S. Quarta [1], S. Cagnin [1], A. Martini [1], C.R. Gordillo [3], C. Gil-Pitarch [3], I. Gonzalez Recio [3], S. Cannito [2], E. Trevellin [1], M. Guido [1], R. Vettor [1], M. Parola [2], P. Angeli [1], M.L. Martínez-Chantar [3], P. Pontisso [1]

[1] *Dept. of Medicine, University of Padova, Italy*
[2] *Unit of Experimental Medicine and Clinical Pathology, Dept. of Clinical and Biological Sciences, University of Torino, Italy*
[3] *Liver Disease and Liver Metabolism Laboratory, CIC bioGUNE-BRTA (Basque Research & Technology Alliance), Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Derio, Bizkaia, Spain*
[4] *Department of Surgical, Oncological and Gastroenterological Sciences – DISCOG, University of Padova, Italy*

**Introduction:** hepatocellular carcinoma (HCC) and metabolic dysfunction-associated steatotic liver disease (MASLD) are two major problems in modern hepatology since their incidence is increasing and specific treatments are lacking. Protease-activated receptor 2 (PAR2) is a member of G protein-coupled receptors and has been associated with lipid metabolism dysregulation and cancer progression, becoming an interesting therapeutic target. Recent results indicate that PAR2 is activated by SerpinB3, a serin-protease inhibitor involved in fibrosis and oncogenesis and is inhibited by the small molecule 1-Piperidine propionic Acid (1-PPA).
**Aim:** this study aims to investigate the effect of 1-PPA in steatosis progression and HCC development.
**Method:** in a mouse model of liver carcinogenesis, wild-type (BC/WT), knocked-out (BC/KO) and transgenic (C57/TG) mice for SerpinB3 were injected with diethylnitrosamine (DEN) and fed with CDAA diet in the presence or absence of 1-PPA for 26 weeks. Human preadipocytes were cultured in vitro with different concentrations of SerpinB3 (SB3) and 1-PPA. Primary hepatocytes extracted from C57 wild-type mice were treated with different steatogenic conditions (oleic acid, methionine-choline deficient (MCD) and SB3), different concentrations of 1-PPA and/or an inhibitor of VLDL formation/export: lomitapide.
**Results:** the presence of SerpinB3 in mice was associated with larger liver tumours, showing high steatosis content and this effect was reverted by 1-PPA. Mice treated with 1-PPA showed liver reduction of ER stress-related genes and in primary hepatocytes, this compound determined a reduction of ROS accumulation. Proteomic analysis revealed that 1-PPA determined a reduction in lipid metabolism and cancer-development-associated pathways. Human preadipocytes treated with SerpinB3 showed increased production of pro-adipogenic C/EBP-beta which was inhibited by administration of 1-PPA. Primary hepatocytes treated with steatogenic conditions and 1-PPA showed a reduction in lipid body accumulation, compared to controls. Simultaneous treatment with lomitapide erased the effect of 1-PPA, suggesting the involvement of VLDL formation/export in the mechanism of 1-PPA-associated lipid reduction. In agreement, 1-PPA treatment in mice was associated with higher levels of triglycerides in serum.
**Conclusion:** PAR2 inhibition by 1-PPA leads to reduced liver cancer development, associated with lower lipid accumulation, favoured, at least in part by an increased VLDL secretion.

doi: 10.1016/j.dld.2024.01.024

## OC-24

### Eliminating HCV infection from prisons in sicily: the SINTESI project ☆

L. Di Marco [1,6], F. Cartabellotta [2,6], F. Santangelo [6], F. Scalici [3], R. Insinna [3], T. Prestileo [4,6], M.G. Minissale [2,6], V. Calvaruso [5,6], A. Craxì [6], V. Di Marco [5,6], on behalf the SIcilian Network for Therapy, Epidemiology and Screening In Hepatology (SINTESI)

[1] *Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy*
[2] *Department of Medicine Buccheri -La Ferla Hospital, Palermo, Italy*
[3] *Medical Area of the "Pagliarelli-Lorusso" Prison, Palermo, Italy*
[4] *UOSD Infectious Pathologies of Vulnerable Populations, ARNAS-Civico Hospital, Palermo, Italy*
[5] *Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Italy*
[6] *SIcilian Network for Therapy, Epidemiology and Screening In Hepatology (SINTESI), Italy*

☆ The project was approved by the Regional Department of Health and the Regional Department of Prisons and was funded by HCV STAT (Simplification and Test and Treat Strategies toward HCV Elimination) program of Gilead Sciences

**Background:** In all countries HCV among prisoners has a higher prevalence than in the general population. Specific models of screening and linkage to care are needed to improve the care cascade.
**Methods:** The SIcilian Network for Therapy, Epidemiology and Screening In Hepatology (SINTESI) run an HCV point-of-care project in all 23 prisons of Sicily.All prisoners received information on HCV screening and the possibility of receiving treatment with Direct Acting Antiviral (DAA) while incarcerated. HCV status was assessed by screening all subjects for anti-HCV by rapid oral test (OraQuick HCV) and immediate reflex testing for HCV-RNA (GeneXpert-HCV Viral Load, Cepheid). HCV RNA positive subjects received DAA therapy within 72 hours of screening. All prisoners signed an informed consent to use personal data. Chi-square test was used to analyze differences between groups
**Result:** Among 5,912 prisoners (98% of prison population) informed of the screening project, 4,911 (83%) accepted to undergo HCV testing. The mean age was 42 years (range 18-86) and 95.8% was males. Non-Italian origin accounted for 12.2% of prisoners (3.7% other EU countries, 7.5% Africa, 0.6% Asia and 0.2% South America). Overall, 245 subjects (5%) testes anti HCV positive, with a prevalence of 4.9% among males and 6.7% among females (p=0.25). We evaluated the risk of drug addiction in subjects with HCV infection in a prison. A prevalence of 25% (25/99) was found among PWUDs on opioid substitution, as compared to 2.9% (30/1,040) in non-PWUDs ($p<0.0001$). Among 245 anti HCV positive prisoners, 20 refused to be tested for HCV-RNA, 100 tested negative (80 had a history of viral clearance under previous DAA treatment while 20 did not report previous therapy for HCV) and 125 were HCV-RNA positive. Twelve of the latter refused treatment, while 113 started a cycle of DAAs while incarcerated. Among 56 subjects assessable for SVR, 55 (98%) obtained HCV clearance.
**Conclusions:** In Sicily, HCV infection is 4 times more common among people in prison than in the general population mostly due to parenteral drug use. Half of the prisoners with a positive screening were unaware of their HCV status and only 32% had received DAAs previously. A one-shot HCV test-and-treat point-of-care approach is highly effective in this setting.

doi: 10.1016/j.dld.2024.01.025

## OC-25

### Burden of Hepatitis D Virus infection in Italy: interim results from a prospective multicentre nationwide study

G.P. Caviglia [1], P. Colombatto [2], B. Coco [2], A. Loglio [3], M. Viganò [3], S. Fagiuoli [3,4], A. Olivero [1], E. Dileo [1], G. Troshina [1], A. Ciancio [1], M. Milella [5], A. Saracino [5], C.F. Magni [6], S. Antinori [7], G. Rizzardini [6], M. Quaranta [8], S. Taurian [8], G. Cariti [8], V. Cossiga [9], F. Morisco [9], S. Cretella [10], G. Verucchi [10], G. Cologni [11], M. Rizzi [11], G.G. Di Costanzo [12], M.P. Anolli [13], P. Lampertico [13,14], V. Di Marco [15], C. Cosentino [16], A. Marrone [16], T.A. Santantonio [17], E. Biliotti [18], A.R. Garbuglia [18], G. D'Offizi [18], N. Capoluongo [19], N. Cuomo [20], A. Perrella [19], A. Izzi [19], E. Fornasiere [21], P. Toniutto [21], R. Cotugno [22], M. Barone [23], R. Cozzolongo [24], E.M. Cela [25], G.A. Niro [22], R. Rapetti [26], M. Pirisi [26], R. Viganò [27], L.S. Belli [27], M. Puoti [28], E. Teti [29], M. Andreoni [29], N. Coppola [30], M. Feasi [31], E. Pontali [31], M. Cipullo [32], A. Federico [32], L. Rapisarda [33], E. Siciliano [34], E. Bracciamà [34], A. Risicato [34], G. Bertino [35], M. Distefano [36], M.R. Brunetto [2], M. Rizzetto [1]

[1] *Department of Medical Sciences, University of Torino, Turin, Italy*
[2] *Department of Clinical and Experimental Medicine, Hepatology and Liver Physiopathology Laboratory and Internal Medicine Unit, University of Pisa, Pisa, Italy*
[3] *Division of Gastroenterology, Hepatology and Transplantation, ASST Papa Giovanni XXIII, Bergamo, Italy*
[4] *Gastroenterology, Department of Medicine, University of Milan Bicocca, Milan, Italy*
[5] *Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Ionian Area, University of Bari "Aldo Moro," Bari, Italy*
[6] *Division of Infectious Diseases, ASST-FBF-Sacco, Milan, Italy*
[7] *Dipartimento di Scienze Biomediche e Cliniche, Università degli Studi di Milano, Milan, Italy*
[8] *Infectious Diseases Unit, "Amedeo di Savoia" Hospital, Turin, Italy*
[9] *Department of Clinical Medicine and Surgery, Liver and Biliary Diseases Unit, University of Naples "Federico II", Naples, Italy*
[10] *Infectious Diseases Unit, Department of Medical and Surgical Sciences, University of Bologna, Italy*
[11] *SC Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy*
[12] *Hepatology Unit, AORN A. Cardarelli, Naples, Italy*
[13] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[14] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*
[15] *Section of Gastroenterology and Hepatology, Dipartimento Di Promozione Della Salute, Materno Infantile, Medicina Interna e Specialistica Di Eccellenza (PROMISE), University of Palermo, Italy*
[16] *Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy*
[17] *Department of Medical and Surgical Sciences, Infectious Diseases Unit, University of Foggia, Foggia, Italy*
[18] *Infectious Diseases and Hepatology Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy*
[19] *UOC di malattie infettive emergenti e ad alta contagiosità, Ospedale Cotugno, Naples, Italy*
[20] *UOC Microbiologie e Virologia, Ospedale Cotugno, Naples, Italy*
[21] *Hepatology and Liver Transplant Unit, Azienda Sanitaria Universitaria Integrata di Udine, Udine, Italy*
[22] *Gastroenterology Unit, Fondazione Casa Sollievo Della Sofferenza IRCCS, San Giovanni Rotondo, Italy*
[23] *Gastroenterology Unit, Department of Precision and Regenerative Medicine—Jonian Area—(DiMePRe-J), University of Bari "Aldo Moro", Policlinic University Hospital, Bari, Italy*
[24] *Gastroenterology Unit, IRCCS "S. De Bellis", Castellana Grotte, Italy*
[25] *Gastroenterology Unit, Riuniti Polyclinic of Foggia, Foggia, Italy*
[26] *Internal Medicine, Azienda Ospedaliero-Universitaria "Maggiore Della Carità", Novara, Italy; Department of Translational Medicine (DiMeT), Università del Piemonte Orientale, Novara, Italy*
[27] *Hepatology and Gastroenterology Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy*
[28] *Division of Infectious Diseases, ASST Grande Ospedale Metropilitano Niguarda; Department of Medicine, University of Milan Bicocca, Milan, Italy*
[29] *Infectious Disease Unit, Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy*
[30] *Infectious Diseases Unit, Department of Mental Health and Public Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy*
[31] *Department of Infectious Diseases, Galliera Hospital, Genoa, Italy*
[32] *Department of Precision Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy*
[33] *Hepatology Unit, University Hospital Policlinico "G. Rodolico - San Marco", Department Biomedical and Biotechnological Sciences (BIOMETC), Section of Pharmacology, University of Catania, Catania, Italy*
[34] *Hepatology Unit, University Hospital Policlinico "G. Rodolico - San Marco", Catania, Italy*
[35] *Hepatology Unit, University Hospital Policlinico "G. Rodolico - San Marco", Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy*
[36] *UOSD Hepatology, Ospedale Umberto I°, ASP 8 Siracusa, Italy*

**Introduction:** Although compulsory hepatitis B virus (HBV) vaccination greatly reduced new hepatitis D virus (HDV) disease in native Italians, migratory flows from HDV endemic areas are increasingly reconstituting the reservoir of this infection in Italy.
**Aim:** To report the preliminary results of a survey on the epidemiologic, virologic and clinical features of contemporary HDV cases in Italy.
**Materials and Methods:** Consecutive patients positive for hepatitis B surface antigen (HBsAg) and antibodies to HDV (anti-HD) referred to 27 third-level Italian Centers were prospectively enrolled from August 2022 to October 2023.
**Results:** A total of 497 patients positive for anti-HD were recruited; median age was 56 (IQR 45–62) years and most patients were male (62.2%). Native Italians were 298 (60.0%). Among patients born abroad, the majority (n=166; 86.5%) were from Eastern Europe, followed by Africa (n=19; 9.9%) and Asia (n=4; 2.1%). Native Italians were older (median age 60, IQR 56–64, years vs. 44, IQR 37–51 years in patients born abroad; $p<0.001$) and had a more advanced liver disease (cirrhosis: 64.2% vs 51.1%; p=0.005; HCC: 14.5% vs 1.6%; $p<0.001$; liver stiffness: 12.0, IQR 7.9–18.5 kPa vs 9.2, IQR 6.3–14.4 kPa, p=0.001) compared to patients born abroad. One-hundred-thirty-three patients underwent centralized serum HDV-RNA assessment (RoboGene®v2) and HDV genotyping (direct sequencing). Overall, 103 (77.4%) patients were HDV-RNA-positive (median 5.26, IQR 4.03–6.04 Log IU/mL). The prevalent genotype was HDV-1 (n=100); 3 patients were infected with HDV-5. HDV-RNA correlated with ALT values ($r_s$=0.303, 95%CI 0.105–0.484; p=0.004) and HDV-RNA-positivity was significantly associated with liver cirrhosis (OR=3.03, 95%CI 1.14–8.07; p=0.027).
**Conclusions:** In Italy, patients born abroad accounted for nearly half of the overall HDV infections collected in the past year. Most patients had advanced liver disease with high levels of serum HDV-RNA. These preliminary findings confirm that HDV infection in migrants represents an increasing medical alert in Italy.

This research was supported by Gilead Sciences, Inc (study ID: IN-IT-980-6382).

doi: 10.1016/j.dld.2024.01.026

## OC-26

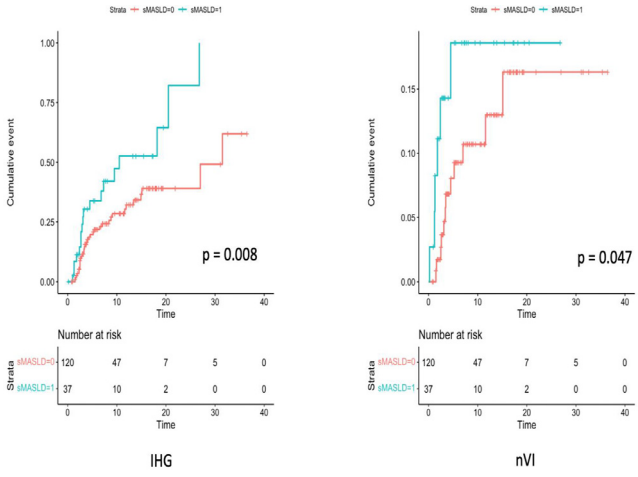
### The impact of etiology on patterns of progression of advanced HCC

B. Stefanini [1,2], F. Piscaglia [2,3], A. Dalbeni [4,5], C. Vivaldi [6], P. Federico [7], A. Palloni [8], C. Soldà [9], B. Stefanini [11], I. Garajova [12], L. Ielasi [13], S. De Lorenzo [14], G. Masi [6], S. Lonardi [10], G. Brandi [2,8], B. Daniele [7], F. Trevisani [2,11], G. Svegliati-Baroni [15], C. Campani [16], R. Chen [2], F. Tovoli [2,3]

[1] *Department of Surgery & Cancer, Imperial College London, Hammersmith Hospital, Du Cane Road, W120HS London, UK*
[2] *Department of Medical and Surgical Sciences, University of Bologna*
[3] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna 40138, Italy*
[4] *Unit of General Medicine C, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[5] *Liver Unit, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[6] *Unit of Medical Oncology 2, Azienda Ospedaliero- Universitaria Pisana, Pisa, Italy*
[7] *Medical Oncology Unit, Ospedale del Mare, Napoli, Italy*
[8] *Oncology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[9] *Oncology Unit 1, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy*
[10] *Oncology Unit 3, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy*
[11] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[12] *Medical Oncology Unit, University Hospital of Parma, Parma, Italy*
[13] *Medical Oncology Unit, "Degli Infermi" Hospital, AUSL della Romagna, Faenza*
[14] *Oncology Unit, Azienda USL Bologna, Bologna, Italy*
[15] *Liver Injury and Transplant Unit, Polytechnic University of Marche, Ancona, Italy*
[16] *Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze, Firenze, Italy*

**Background and aim:** Atezolizumab/bevacizumab (A+B) is the recommended first-line treatment for HCC, irrespective of the etiology of the underlying liver disease. Preclinical models showed that only intrahepatic HCC arising in mice with MASLD was less responsive to A+B, while subcutaneous tumours had a decent response, likely related to a higher proportion of exhausted T-cells being recruited in the intrahepatic lesions. Since HCC can progress with different patterns, we aimed to verify whether MASLD etiology had an impact on the pattern of progression to A+B.
**Methods:** Multicenter study including consecutive patients with non-resectable HCC patients from the ARTE database. Patterns of progression were defined as proposed by Reig et al: intrahepatic/extrahepatic growth of pre-existing lesions (IHG and EHG, respectively) new intrahepatic/extrahepatic lesions (NIHL, NEHL), new vascular invasion (NVI). A Kaplan-Meier survival analysis was performed to verify whether MASLD patients were at increased risk of specific patterns of progression.
**Results:** A total of 157 patients were included. Single-etiology MASLD was the cause of HCC in 37 patients (23.6%). MASLD patients were similar to controls in terms of macrovascular invasion, AFP>400, Child-Pugh Class, ALBI grade, and ECOG. Median OS of MASLD-HCC patients was similar to non-MASLD group (20.6 months vs 18.4, p = 0.277), whereas PFS was longer for non-metabolic HCC (11.9 vs 7.3 months, p = 0.02).

HCC patients with MASLD had an increased risk of progressing both for IHG (HR 2.14 CI 95% 1.2-3.8, p = 0.008) NVI (HR 1.88 CI 95% 1.03-5.02, p = 0.047) (figure 1). Conversely, the risk of developing progression due to EHG or NEHL was similar across the etiology groups
**Conclusion:** Patients with MASLD-HCC were more likely to develop an intrahepatic progression than non-MASLD patients, confirming preclinical data and suggesting biologic differences between tumors arising from different etiologies with potential implications on HCC clinical management.




doi: 10.1016/j.dld.2024.01.027

## OC-27

### The IMPROVEMENT project: first report of the global liver transplant activity ☆

A.W. Avolio [1], M.M. Pascale [1], P. Burra [2], S. Bhoori [3], N. De Maria [4], F. Donato [5], S. Fagiuoli [6], A. Galeota Lanza [7], V. Giannelli [8], S Ginanni Corradini [9], I. Lenci [10], B. Magro [11], S. Martini [12], S. Petruccelli [13], F. Piscaglia [14], M. Pompili [1], M. Rendina [15], G.L. Svegliati Baroni [16], P. Violi [17], L. Barbier [18], F. Braun [19], I. Boin [20], L. Caccamo [5], O. Cicarelli [21], U. Cillo [2], A. Carraro [17], M. Cescon [14], L. De Carlis [22], R De Carlis [22], P. De Simone [13], M. De Santibanes [23], F. Deng [24], F. Di Benedetto [4], G.M. Ettorre [8], H. Fernandez [25], M. Gastaca [26], S. Gruttadauria [11,27], Z. Guo [28], J. Hammond [29], Q Lai [9], M. Lesurtel [30], L. Llado [31], P. Martins [32], V. Mazzaferro [3], G. Mejia [33], S. Nadalin [34], G. Oniscu [35], M. Patel [36], T. Perera [37], D. Pinelli [6], W. Polak [38], C. Quintini [39], M. Ravaioli [13], M. Rela [40], R. Romagnoli [12], E Salame [41], G. Subash [42], F. Tandoi [15], I. Takashi [43], T. Timucin [44], G. Tisone [10], G. Vennarecci [7], M. Vivarelli [16], A. Vorasittha [45], K. Zieniewicz [46], V. Agopian [47]

[1] *Fondazione Policlinico "A. Gemelli" IRCCS, Rome, Italy*
[2] *Transplant Center, Padua, Italy*
[3] *Istituto Nazionale Tumori, Milan, Italy*
[4] *Transplant Center, Modena, Italy*
[5] *Ospedale Maggiore Policlinico, Milan, Italy*
[6] *Transplant Center, Bergamo, Italy, Transplant Center*
[7] *AORN Cardarelli, Naples, Italy*
[8] *Transplant Center, POIT, Rome, Italy*
[9] *Umberto I, Rome, Italy*
[10] *Transplant Center, PTV; Rome, Italy*
[11] *Transplant Center, ISMETT, Palermo, Italy*
[12] *Ospedale Molinette, Turin, Italy*

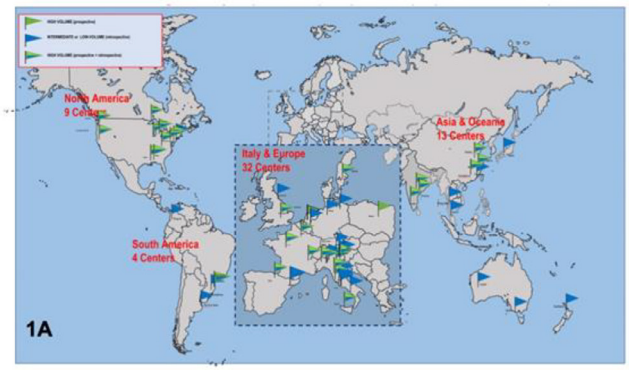
[13] Transplant Center, Pisa, Italy
[14] Ospedale Sant'Orsola, Bologna, Italy
[15] Transplant Center, Policlinico di Bari, Bari, Italy
[16] Transplant Center, Ancona, Italy
[17] Transplant Center, Verona, Italy
[18] Auckland Transplant Institute, Auckland, Australia
[19] University Schleswig-Holstein, Kiel, Germany
[20] Hospital de Clinicas, Campinas, Brazil
[21] Saint-Luc Univ Catholique, Brussels, Belgium
[22] Ospedale Metropolitano Niguarda, Milan, Italy
[23] Hospital Italiano, Buenos Aires, Argentina
[24] Transplant Center, Foshan, China
[25] Baylo-Scott, Dallas, Tx, United States
[26] Transplant Center, Bilbao, Spain
[27] University of Catania, Italy
[28] Sun Yet- First University, Guangzhou, China
[29] Transplant Center, Newcastle, United Kingdom
[30] Hopital Beaujon, Paris, France
[31] Universitat Internacional de Catalunya, Barcelona, Spain
[32] University of Massachusetts, Worcester, Ma, United States
[33] Fundation Cardioinfantil, Bogota, Colombia
[34] Transplant Center, Tubingen, Germany
[35] Karolinska Institutet, Stockholm, Sweden
[36] Southwestern Medical Center, Dallas, Tx, United States
[37] Queen Elisabeth Hospital, Birmingham, United Kingdom
[38] Erasmus MC, Rotterdam, Netherlands
[39] Transplant Center, Cleveland, Ohio, United States
[40] Rela Transplant Institute, Chennai, India
[41] Transplant Center, Tours, France
[42] Transplant Center, New Delhi, India
[43] Transplant Center, Kyoto, Japan
[44] Mayo Clinic, Rochester, Fl, United States
[45] Transplant Center, Bangkok, Thailand
[46] Transplant Center, Warsaw, Poland
[47] UCLA, Los Angeles, Ca, United States

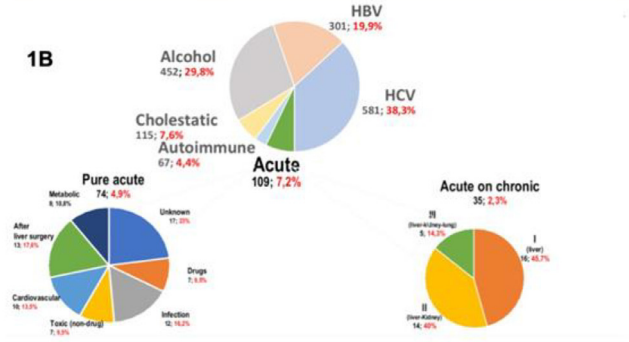
☆ The IMPROVEMENT project (ClinicalTrial.gov NCT05289609) was designed by a steering committee from 5 continents to develop predictive models of 90-day/1-yr allograft failure after liver transplant (LT).

**Methods:** Three LT types are included according to the donor: standard Deceased Brain Donors (DBDs); Deceased Cardiac Donors (DCDs); high-risk DBDs; Living donors (LDs). The data collection (retrospective/completed or prospective/ongoing includes [high volume (>65 LTs/yr) and intermediate-volume (≤65 LTs/yr)]. Each Center enrolled a fixed number of LT to minimize Center-volume bias.

**Results:** The retrospective data consists of 3,884 LT from 2017 to 2019. There were 2958 (76.2%) standard DBDs, 797 (20.5%) DCD & amp; high-risk DBDs, 129 (3.3%) LDs. We stratified the cases into 5 geographical areas (Fig. 1A): Italy (N=1,766); Europe except-Italy (N=936); Asia-Oceania (N=496); North-America (N=377); South-America (N=309). Among the 53 LT centers of the retrospective cohort, there were 27 high-volume centers and 26 intermediate-volume centers). Italy and Asia had the larger adoption of machine perfusion, while DCDs were prevalent in Europe and North-America. Extended Criteria Donors (ECD) were mainly performed in Italy and North-America. Italy shows the highest donor age followed by Europe except Italy, North-America, South-America and Asia-Oceania. The mean recipient age was similar in all the areas, with a prevalence of hepatocarcinoma in Italy **(Fig. 1B).** The differences in the prevalence of other indications are summarised **(Fig. 1C).**

**Conclusions:** The analysis of IMPROVEMENT data depicts a screenshot of global liver transplant activity, never done before. Differences are due to epidemiological and logistic factors. The prospective data (ongoing) will provide more accurate information.




1C

| | | | | | |
|---|---|---|---|---|---|
| DCD | 3,8% | 16,2% | 5,8% | 7,9% | 0% |
| ECD | 44,6% | 36,6% | 16,2% | 45,1% | 6,2% |
| Machine Perfusion | 6,3% | 2% | 5,8% | 4% | 0% |
| Transplant Indication / Co-indication | | | | | |
| HCC | 48,2% | 32,6% | 33,8% | 11,7% | 25,1% |
| Alcoholic Disease | 27,8% | 31,2% | 16,4% | 37,1% | 12,3% |
| Cholestatic Disease | 3,9% | 10,8% | 2,7% | 7,4% | 3,6% |
| Autoimmune Disease | 6,2% | 6,3% | 2,9% | 3,4% | 6,3% |
| Viral Disease | 38,2% | 16,4% | 46,3% | 17,3% | 16,2% |
| HCV | 20% | 11,2% | 6,8% | 15,9% | 16,4% |
| HBV | 17,1% | 6% | 20,2% | 1,8% | 0% |
| Other | 5,1% | 1,9% | 0,4% | 0% | 0% |
| Donor Age [median (SD)] | 58,3 (48,4-68,4) | 56,3 (42,2-71,4) | 39,4 (24,6-46,3) | 54,4 (38,4-58,3) | 51,2 (28,6-56,4) |
| Recipient Age [median (SD)] | 57,3 (51,2-61,8) | 58,3 (52,4-63,2) | 57,4 (46,5-62,3) | 58,6 (54,4-62,8) | 58,4 (54,2-62,7) |

*= except Italy; DCD= Deceased Cardiac Donor; ECD= Extended Criteria Donor;
HBV= Hepatitis B Virus; HCV= Hepatitis C Virus; SD= Standard Deviation

doi: 10.1016/j.dld.2024.01.028

## OC-28

### Transjugular intrahepatic portosystemic shunt after liver transplantation: is patient selection the key to success?

F. Leonardi [1], B. Magro [2], L. Maruzzelli [3], L. Pasulo [1], P. Marra [4], I. Petridis [2], D. Pinelli [5], R. Miraglia [3], S. Fagiuoli [1,6], S. Gruttadauria [2,7]

[1] Gastroenterology and Transplant Hepatology, Papa Giovanni XXIII Hospital, Bergamo, Italy
[2] Department for the Treatment and Study of Abdominal Diseases and Abdominal Transplantation, IRCCS ISMETT, UPMC Italy (University of Pittsburgh Medical Center Italy), Palermo, Italy
[3] Radiology Unit, Diagnostic and Therapeutic Services, IRCCS ISMETT, UPMC Italy, Palermo, Italy
[4] Department of Diagnostic Radiology, Papa Giovanni XXIII Hospital, Bergamo, Italy

[5] Department of Surgery, Papa Giovanni XXIII Hospital, Bergamo, Italy
[6] Department of Medicine and Surgery, University of Milano Bicocca, Milano, Italy
[7] Department of Surgery and Medical and Surgical Specialties, UPMC, University of Catania, Catania, Italy

**Introduction:** Transjugular intrahepatic portosystemic shunt (TIPS) placement after liver transplantation (LT) has been reported in a limited number of studies, with controversial results. Prognosis of these patients is still unclear. This study aims at evaluating both long-term graft-/patient-survival and which patients could eventually benefit from this procedure in the post-LT setting
**Methods:** Patients who underwent TIPS for post-LT portal hypertension- or venous-related complications in our two Italian Transplant Centers were retrospectively evaluated. Clinical success was defined according with "SIR Quality Improvement Guidelines for TIPS". Patients' follow-up was until death or June 30th 2023.
**Results:** Between 2002 and 2021, 74 patients underwent TIPS insertion after LT. Patients were more frequently males (77.0%), with a median age at LT of 52 years (range 18-69) and predominantly viral etiology (74.3%). TIPS was performed after a median time of 11 months (0.6-154) following LT. More frequent indications were: Refractory Ascites (44.6%), Sinusoidal Obstruction Syndrome-related ascites (31.1%), high-risk Gastroesophageal Varices (9.5%) and Portal Vein Thrombosis (6.8%). Recurrence of cirrhosis at the time of TIPS was documented in 30 patients (40.5%). Mean pre-TIPS MELD-score was 13.4±4.4; mean Porto-Systemic pressure Gradient was 15.2±5.4 mmHg pre-TIPS and 6.9±2.9 mmHg post-TIPS. Clinical success was achieved in 57 patients (77.0%). During the follow-up, 26 patients (35.1%) developed at least one episode of encephalopathy; shunt stenosis/occlusion was recorded in 19 patients (25.7%). Median follow up was 47.9 months (0.13-262). Graft- and patient-survival rates at 1, 3 and 5 years post-TIPS were 72.8%, 51.4%, 39.6% and 76.8%, 62.6%, 50.1% respectively. Graft-survival rates were significantly better in patients with age at TIPS <65 years, a time OLT-TIPS <12 months, a pre-TIPS MELD<15 and in patients without cirrhosis recurrence and a pre-TIPS SOS-related refractory ascites.
**Conclusions:** Patients undergoing TIPS insertion after LT showed a 5-year graft-survival post-TIPS of nearly 40%; patient selection can improve survival rate to 65%.

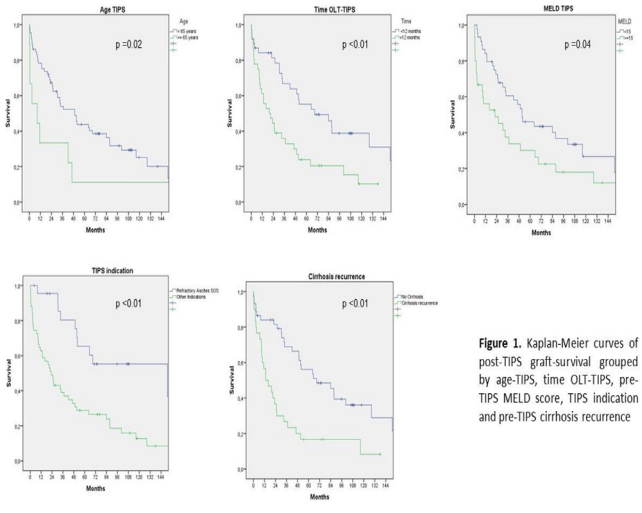



**Figure 1.** Kaplan-Meier curves of post-TIPS graft-survival grouped by age-TIPS, time OLT-TIPS, pre-TIPS MELD score, TIPS indication and pre-TIPS cirrhosis recurrence

doi: 10.1016/j.dld.2024.01.029

## OC-29

### Induced regulatory T cells via cyclin-dependent kinase inhibition from patients with primary biliary cholangitis are suppressive and stable in an IFN enriched environment and are epigenetically different from natural regulatory T cells

V. Ronca [1,2,3,4,5], K. Kayani [1,2], S.P. Davies [1,2], M. Arai [4], Y. Nakamura [4], N. Okamoto [4], N. Mikami [4], N. Ohkura [4], J. White [4], N. Richardson [1], P. Invernizzi [3,5], S. Sakaguchi [4], Y.H. Oo [1,2,5]

[1] Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK
[2] NIHR Birmingham Biomedical Research Centre, University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[3] Division of Gastroenterology, Center for Autoimmune Liver Diseases, Department of Medicine and Surgery, University of Milano Bicocca, 20900 Monza, Italy
[4] Laboratory of Experimental Immunology, WPI Immunology Frontier Research Center, Osaka University, Suita, Japan
[5] European Reference Network on Hepatological Diseases (ERN RARE-LIVER), Birmingham, UK

**Background and Aims:** Dysfunction in regulatory T cells (Tregs) in primary biliary cholangitis (PBC) is well-documented. Studies using murine models have indicated the efficacy of Treg-based cell therapies in restoring liver tolerance in PBC. These therapies are effective when using Tregs from healthy animals, but not from PBC models, underscoring the impaired functionality of PBC-derived Tregs. Our research introduces a novel protocol aimed at generating stable and functional induced Tregs through the epigenetic modification of CD4+ T cells from the peripheral blood of PBC patients. The objective of our study is to assess the functionality and stability of our induced Tregs in comparison to natural Tregs from PBC patients, employing an ex-vivo wedge perfusion model.
**Method:** CD4+ T cells were magnetically enriched from peripheral blood mononuclear cells (PBMCs) of PBC patients. CD4+T cells were activated through TCR stimulation by CD3+ activator beads and cultured in presence of AS2863619 (4-[1-(2-methyl-1H-benzimidazol-5-yl)-1H-imidazo[4,5-c] pyridin-2-yl]-1,2,5-oxadiazol-3-amine dihydrochloride) and IL-2. FoxP3, CTLA4 and Helios expression was assessed in SF-iTregs via flow cytometry and by bisulphite sequencing pre- and post-activation in presence of Th1 polarising cytokines. The functionality of Tregs and SF-iTregs was investigated by in vitro suppression assays using CellTrace Violet dye-labelled effector T-cells, CD3 activator beads and IL-2. For the all three cell populations, nTreg, Tnaive, SF-iTregs, Foxp3 gene locus for STAT5 binding, H3K27ac, and chromatin status was characterized by Chromatin immunoprecipitation followed by sequencing (ChIP-seq) and assay for transposase-accessible Chromatin using sequencing (ATAC-seq). After labelling the cells with cell-tracker red, they were perfused under constant pressure in a liver wedge from a discarded donor liver for 12 hours.
**Results:** The chemical inhibition of cyclin-dependent kinase 8/19 and the deprivation of CD28 signal induced DNA hypomethylation in Treg signature genes. We obtained a 100-fold increase in the cell number and the product was suppressive and pure (>90% FOXP3 expressing cells). The SFiTregs were found to be more stable compared with nTreg when cultured for 6 days in Th1 polorising conditions. ATAC-seq and ChIP-seq confirmed that Treg specific epigenetic changes in the SF-iTregs were comparable to nTreg at the baseline. However, differentially accesible regions of SF-iTregs differ significantly when compared to nTreg. Furthemore, the cells were retained in the liver parenchyma significantly more than healthy and PBC controls when infused in a ex-vivo liver wedge.

**Conclusion:** We applied a novel technique to generate abundant, functional regulatory T cells from peripheral T CD4+ cells in patients with PBC. This approach would allow us to overcome the potential limit of using autologous ex-vivo expanded Tregs based therapy and generate a more stable product to infuse in the inflamed environment typical of the liver of PBC patients.

doi: 10.1016/j.dld.2024.01.030

## OC-30

### Real-life experience of long-term albumin treatment for the management of ascites in patients with decompensated cirrhosis accross Italy

E. Pompili [1,2], G. Iannone [1,2], C. De Venuto [1,2], S. Piano [3], A. Lombardo [4], D. Bitetto [5], S. Gioia [6], G. Zaccherini [1,2], R. Gagliardi [3], V. Calvaruso [4], M. Tonon [3], M. Baldassarre [1,2], G. Tedesco [2], S. Nardelli [6], P. Toniutto [5], V. Di Marco [4], P. Angeli [3], P. Caraceni [1,2]

[1] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[2] *Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, Bologna, Italy*
[3] *Unit of Internal Medicine and Hepatology, Department of Medicine - DIMED, University and Hospital of Padova, Padova, Italy*
[4] *UOC di Gastroenterologia, Dipartimento di Promozione della Salute, Materno Infantile, Medicina Interna e Specialistica (PROMISE), University of Palermo, Palermo, Italy*
[5] *Hepatology and Liver Transplantation Unit, University Academic Hospital, Udine, Italy*
[6] *Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy*

**Background and Aims:** Long-term albumin (LTA) has become standard of care for patients with decompensated cirrhosis in many Italian hepatological centres. This study aimed to address several issues related to patients and treatment still undefined in real-life practice.

**Methods:** This multicenter retrospective observational study included patients with cirrhosis and ascites receiving LTA (at least one month) between 01/2016 and 02/2022. Data on patient characteristics, albumin treatment, clinical courses and outcomes were collected.

**Results:** 312 patients, the majority with alcoholic cirrhosis, were included in 5 Italian centers. At baseline, median Child-Pugh was 8, MELD 15 and MELD-Na 18. In 55% of patients, ascites was grade 2, in 36% grade 3 and in 28% refractory, while 47% had paracentesis in the previous 6 months. Median LTA was about 10 months with a median dose of 40 g/week. Albumin was infused in territorial services in 44% of cases and only 1% discontinued due to logistic reasons. Ascites resolved to grade 0-1 in 34% of patients within the first 3 months and 61% at the end of treatment. Among patients receiving paracenteses prior LTA, about 40% had no paracentesis at 6 months. Factors independently associated with ascites resolution were grade 2 ascites and INR at baseline, albumin dose, serum albumin of 38 g/l at 1 month and no paracentesis in the previous 6 months. Interestingly, 75 patients, including some with refractory ascites, discontinued LTA due to clinical improvement. No adverse events were reported.

**Conclusions:** LTA is feasible, safe and very effective in treating ascites, with almost 25% of patients being able to stop treatment for ascites resolution. Patients with uncomplicated ascites appear the best candidates to LTA, although those with refractory ascites may also benefit of treatment. Confirming previous data, on-treatment serum albumin concentration close to 40 g/l predicts a better response.

doi: 10.1016/j.dld.2024.01.031

Digestive and Liver Disease 56 (2024) S21–S60

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

# Thursday Posters: 56th Annual Meeting of the Italian Association for the Study of the Liver – A.I.S.F. (Rome, March 14th-15th, 2024)

## T-1

### Biochemical response to obeticholic acid drives liver stiffness variation over time and the risk of liver-related events in patients with primary biliary cholangitis

A. De Vincentis [1], F. Terracciani [1], D. D'Amato [2], M. Scaravaglio [3], P. Invernizzi [3], E. Vanni [2], D. Campion [2], A. Floreani [4], N. Cazzagon [4], D. Alvaro [5], R. Venere [5], E.G. Giannini [6], S. Labanca [6], A. Lleo [7], F. Colapietro [7], E. Degasperi [8], M. Viganò [9], E. Pesatori [9], S. Fagiuoli [9], M. Marzioni [10], V. Buzzanca [10], R. Viganò [11], F. D'Amico [11], A. Galli [12], A. Curto [12], F. Marra [12], P. Begini [13], L. Baiocchi [14], P. Carnì [14], L. Muratori [15], B. Coco [16], M. Brunetto [16], F. Pizzolante [17], N. De Matthaeis [17], E. Falbo [18], L. Surace [18], A. Mattalia [19], D. Ieluzzi [20], F. Salomone [21], G. Delle Monache [22], R. Tatonetti [22], I. Cavalli [23], V. Cossiga [24], F. Morisco [24], V. Valiani [25], P. Gatti [25], V. Boccaccio [25], D. Angrisani [26], G. Vettori [27], B. Cuffari [28], A. Moretti [29], A. Rocco [30], G. Nardone [30], P. Scivetti [31], M. Costanzo [31], V. Boano [32], G.F. Manfredi [33], L. Simone [34], V. Pace Palitti [35], M. Russello [36], M. Cannavò [36], E. Frazzetto [37], G. Bertino [37], M. Di Stefano [38], A. Izzi [39], F. Cerini [40], L. Chessa [41], M. Miglianti [41], V. Feletti [42], A. Mussetto [42], R. Cozzolongo [43], F. Losito [43], G.A. Niro [44], R. Cotugno [44], R. Sacco [45], C. Ricci [46], P. Poise [46], L. Cadamuro [47], A. Castellaneta [48], F. Squeo [48], N. Terreni [49], N. Bina [49], P. Pozzoni [50], S. Casella [51], F. Zani [51], O. Morelli [52], G. Cuccorese [53], C. Saitta [54], T. Zolfino [55], C. Rigamonti [33], V. Calvaruso [47], M. Carbone [3], U. Vespasiani-Gentilucci [1]

[1] *Internal Medicine and Hepatology, University Campus Bio-Medico of Rome, Rome, Italy*
[2] *Gastroenterology Unit, Cittaì€ della salute e della scienza, Turin, Italy*
[3] *Division of Gastroenterology, Centre for Autoimmune Liver Diseases, Department of Medicine and Surgery, University of Milano-Bicocca, European Reference Network on Hepatological Diseases (ERN RARE-LIVER), San Gerardo Hospital, Monza, Italy*
[4] *Gastroenterology Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy*
[5] *Department of Translation and Precision Medicine, Sapienza University of Rome, Rome, Italy*
[6] *Gastroenterology Unit, Department of Internal Medicine, University of Genoa, IRCCS Ospedale Policlinico San Martino, Genoa, Italy*
[7] *Internal Medicine and Hepatology, Humanitas Clinical and Research Center IRCCS, Humanitas University, Milan, Italy*
[8] *Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico – Division of Gastroenterology and Hepatology – CRC "A.M. and A. Migliavacca" Center for Liver Disease, Milan, Italy*
[9] *Hepatology and Liver Transplant Unit, Papa Giovanni XXIII Hospital, Bergamo, Italy*
[10] *Clinic of Gastroenterology and Hepatology, Universitaì€ Politecnica delle Marche, Ancona, Italy*
[11] *Hepatology Unit, Niguarda Hospital, Milan, Italy*
[12] *Internal Medicine and Hepatology Unit, Department of Experimental and Clinical Medicine, University of Firenze, Firenze, Italy*
[13] *Digestive and Liver Disease Department, School of Medicine and Psychology University "Sapienza", Azienda Ospedaliera S. Andrea, Rome, Italy*
[14] *Hepatology Unit, University of Rome "Tor Vergata", Rome, Italy*
[15] *DIMEC Universitaì€ di Bologna, Policlinico di Sant'Orsola, Bologna, Italy*
[16] *Hepatology Unit, University Hospital of Pisa, Italy*
[17] *UOC of Gastroenterology, Gastroenterological, Endocrine-Metabolic and Nephro-Urological Sciences Department, Fondazione Policlinico Universitario A.Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy*
[18] *Azienda Sanitaria Provinciale di Catanzaro, Presidio Ospedaliero "Giovanni Paolo II" Lamezia Terme (CZ)*
[19] *Division of Gastroenterology, Santa Croce e Carle General Hospital, Cuneo, Italy*
[20] *USD Liver Unit, Azienda Ospedaliera Universitaria Integrata di Verona*
[21] *Ospedale di Acireale, Azienda Sanitaria Provinciale di Catania, Catania, Italy*
[22] *Ospedale di Penne, Pescara*
[23] *Division of Internal Medicine, Cremona Hospital*
[24] *Department of Clinical Medicine and Surgery, Gastroenterology Unit, University of Naples "Federico II"*
[25] *Internal Medicin Unit, Perrino Hospital, Brindisi, Italy*
[26] *AORN Cardarelli di Napoli*
[27] *Gastroenterology and Endoscopy Unit, Santa Chiara Hospital, Trento 38014, Italy*
[28] *Division of Gastroenterology, Azienda Ospedaliero-Universitaria di Modena and University of Modena and Reggio Emilia, Modena, Italy*
[29] *UOC GASTROENTEROLOGIA, Ambulatorio di Epatologia, P.O. San Filippo Neri*
[30] *Gastroenterology and Hepatology, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy*

[31] *Internal Medicine Unit, Azienda Sanitaria Locale di Biella, Biella, Italy*
[32] *Department of Gastroenterology and Endoscopy, Cardinal Massaia Hospital, Asti, Italy*
[33] *Dipartimento di Medicina Traslazionale, Università del Piemonte Orientale, Novara, Italy and Division of Internal Medicine, AOU Maggiore della Carità, Novara, Italy*
[34] *Azienda Ospedaliero-Universitaria Di Ferrara, Ferrara, Italy*
[35] *Hepatology Unit, Santo Spirito Hospital, Pescara, Italy*
[36] *Liver Unit, Arnas Garibaldi, Catania, Italy*
[37] *Gastroenterology and Hepatology Unit, University Hospital Policlinico Vittorio Emanuele, Catania, Italy*
[38] *Department of Infectious Diseases, Umberto I Hospital, Siracusa, Italy*
[39] *Department of Infectious Diseases, D. Cotugno Hospital, Napoli, Italy*
[40] *Hepatology Unit, San Giuseppe Hospital, Milan, Italy*
[41] *Liver Unit, University Hospital of Cagliari, Cagliari, Italy*
[42] *Gastroenterology Unit, Santa Maria Delle Croci Hospital, Ravenna, Italy*
[43] *Gastroenterology Unit, National Institute of Gastroenterology "S de Bellis" Reseach Hospital, Castellana Grotte, Bari, Italy*
[44] *Gastroenterology Unit, Fondazione Casa Sollievo Della Sofferenza IRCCS, San Giovanni Rotondo, Foggia, Italy*
[45] *Gastroenterology Unit, Ospedali Riuniti, Foggia, Italy*
[46] *Internal Medicine, Spedali Civili, Brescia, Italy*
[47] *Gastroenterology and Hepatology Unit, University of Palermo, Palermo, Italy*
[48] *Gastroenterology Unit, Policlinico di Bari Hospital, Bari, Italy*
[49] *Hepatology Unit, Valduce Hospital, Como, Italy*
[50] *Hepatology Unit, Alessandro Manzoni Hospital, Lecco, Italy*
[51] *Hepatology Unit, Spedali Civili Gardone Val Trompia, Brescia, Italy*
[52] *Clinic of Gastroenterology and Hepatology, Department of Medicine, Universita' degli Studi di Perugia, Perugia, Italy*
[53] *Internal Medicine Ospedale "R.Dimiccoli", Barletta, Italy*
[54] *Division of Medicine and Hepatology, University Hospital of Messina "Policlinico G. Martino", Messina, Italy*
[55] *Department of Gastroenterology, Brotzu Hospital, Cagliari, Italy*

**Introduction:** In PBC, the prognostic value of alkaline phosphatase, bilirubin and liver stiffness measurements(LSM) has been well established. However, the significance of their variation during treatment with obeticholic acid (OCA) has never been investigated.
**Aim:** To describe on-treatment trajectories of LSM based on biochemical response to OCA, and to evaluate associated risk of liver-related events (LRE) in a large cohort of OCA-treated PBC patients.
**Materials and Methods:** We used data from the Italian RECAPITULATE cohort, including OCA-treated PBC patients from centers belonging to the Italian PBC Registry and/or the CLEO/AIGO PBC study groups. Subjects with <6 months' observation and cirrhotics in Child-Pugh B-C classes were excluded. Biochemical response was evaluated through POISE criteria. Linear mixed models were used to describe on-treatment variation of LSM, while Cox-models to assess the impact on LRE. Joint models were applied to estimate the association between LSM changes and LRE, defined as the occurrence of liver-related death, liver transplantation, or hepatic decompensation.
**Results:** 631 PBC patients (median age 58, women 89%, cirrhosis 27%) accounted for 29 LRE during 19,164 patient-months (median follow-up, 30 months). A sub-cohort of 243 patients with at least two LSMs (total, 656 LSMs) was also analysed. POISE response rates were 42% and 58% at 1 and 3 years, respectively. LSM progressively increased in POISE non-responders (slope +0.44 KPa/year, 95%CI 0.04,0.85), while decreasing over time in responders (slope -0.45 KPa/year 95%CI -0.75,-0.13; p interaction<0.001). Patients attaining 1year-POISE response showed a significantly reduced incidence of LRE during follow-up (HR 0.22, 95%CI 0.08,0.59). Any increase in LSM was associated with an increased risk of LRE, with an overall HR per 10% increase in LSM/year of 1.39 (95%CI 1.18,1.67).
**Conclusions:** In patients with PBC, biochemical response to OCA translates into a reduction of LSM and of LRE during follow-up, while non-response is associated with increased LSM and risk of LRE.

doi: 10.1016/j.dld.2024.01.033

## T-2

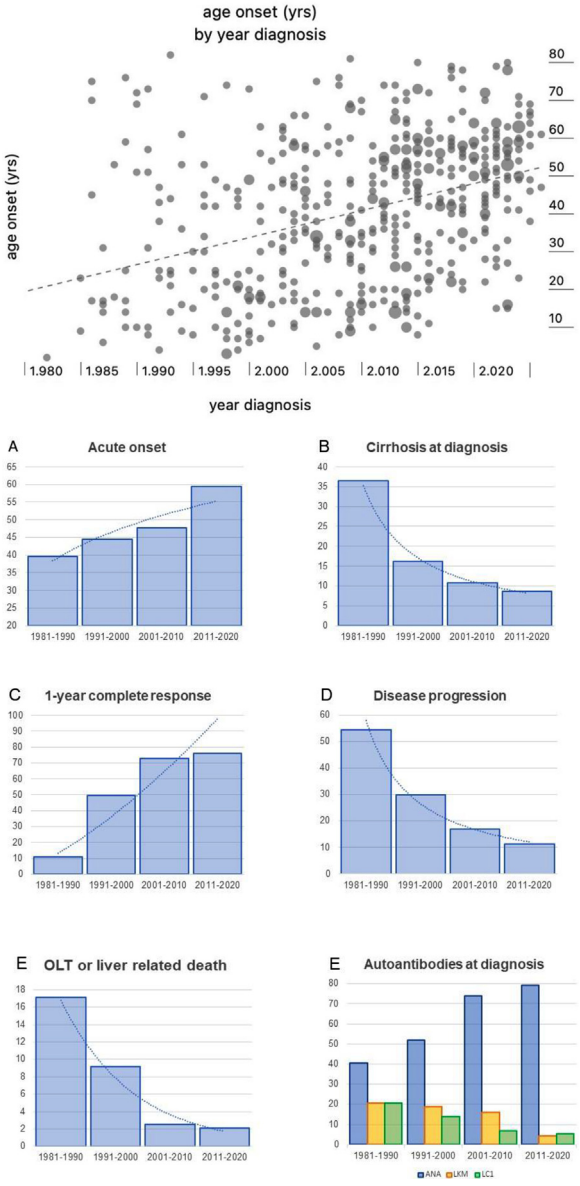
### Autoimmune hepatitis in Italy, changing epidemiology or increased awareness? Evidence from a 40-years referral-centre study

M. Ferronato [1,2], M. Lenzi [1,2,3], L. Muratori [1,2,3]

[1] *DIMEC Università di Bologna*
[2] *IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy*
[3] *European Reference Network for Hepatological Disease (ERN RARE-LIVER)*

**Background:** Autoimmune hepatitis (AIH) is a chronic inflammatory disease of the liver with clinically heterogeneous presentations, ranging from asymptomatic detection of altered liver function tests to acute icteric hepatitis.
**Aim:** To describe the changing presentation of AIH, its clinical and immunological modification and prognosis during the last 40 years in Italy.
**Methods:** Single-centre, tertiary-care retrospective study on 507 consecutive Italian patients with AIH. The cohort has been divided in four subgroups according to the year of diagnosis: 1981-1990, 1991-2000, 2001-2010 and 2011-2020. Clinical, laboratory, histological and immunological features at diagnosis have been collected; response to treatment and clinical outcomes have been assessed. Acute presentation is defined as transaminase > 10-fold the upper limit and/or a bilirubin >5 mg/dL. Complete response is defined as normalization of transaminases and IgG after 12 months of standard treatment. Clinical progression is defined as development of cirrhosis in non-cirrhotic patients and hepatic decompensation or hepatocellular carcinoma in compensated cirrhosis.
**Results:** Median age at diagnosis increased across decades (24, 31, 39, 52 years, p<0.001). Female sex remained predominant (p=0.487). Acute onset became the most common presentation (39.6%, 44.4%, 47.7%, 59.5%, p=0.019), while cirrhosis at diagnosis became less frequent (36.5%, 16.3%, 10.8%, 8.7%, p<0.001). Complete response rates rose (11.1%, 49.4%, 72.7%, 76.2%, p<0.001) and clinical progression during follow-up decreased (54.3%, 29.9%, 16.9%, 11.2%, p<0.001). Anti-nuclear antibodies positivity increased (40.7%, 52.0%, 73.7%, 79.3%, p <0.001), while IgG levels/upper limit progressively decreased (1.546, 1.515, 1.252, 1.120, p <0.001). Liver-related death and liver transplantation reduced (17.1%, 9.2%, 2.5%, 2.1%, p<0.001).
**Conclusions:** In the new millennium the most common onset of AIH in Italy is acute hepatitis in a 50-year or older female non-cirrhotic patient, very likely to respond completely to standard

treatment and less at risk to progress to cirrhosis and its complications.




doi: 10.1016/j.dld.2024.01.034

## T-3

### Targeting Hedgehog signaling pathway by a natural compound: a promising approach for anti-cancer therapeutic development in Intrahepatic Cholangiocarcinoma

S. Paradiso [1], G. Carpino [1], D. Quaglio [2], F. Ghirga [2], C. Di Meo [2], L. Paoletti [2], T. De Luca [3], M. Franchitto [4], L. Di Marcotullio [5], P. Infante [3], E. Gaudio [1], D. Alvaro [3], V. Cardinale [3]

[1] *Department of Anatomical, Histological, Forensic Medicine and Orthopedics Sciences, Sapienza University of Rome, Italy*
[2] *Department of Chemistry and Technologies of Drugs, Sapienza University of Rome, Italy*
[3] *Department of Translational and Precision Medicine, Sapienza University of Rome, Italy*
[4] *Department of Medical-Surgical Sciences and Translation Medicine, Sant'Andrea Hospital, Sapienza University of Rome, Italy*
[5] *Department of Molecular Medicine, Sapienza University of Rome, Italy*

**Introduction:** Intrahepatic cholangiocarcinoma (**iCCA**) constitutes a rare and aggressive cancer that emerge in the biliary tree bearing a fatal prognosis (5-years relative survival rate). iCCA is characterized by intertumoral clinical-pathological and molecular heterogeneity, leading to a new histological classification approved by WHO (*ICD-O-3.2*), into small and large bile duct iCCA. The molecular pathogenesis of iCCA embroils multiple molecular networks: among them, **Hedgehog** (Hh) pathway plays a key role in many aspects of iCCA, such as tumor proliferation, survival, migration, and epithelial-mesenchymal transition. Evidence on the pathogenetic role of Hh in iCCA entails the chance of targeting this cascade for therapeutic purposes in iCCA.
**Aim:** The main purpose of this study is to test a new natural compound, named Glabrescione B (GlaB) able to selectively inhibit Gli1 (Hh downstream transcriptional factor), *in vitro* in established and primary cell lines.
**Materials and Methods Results:** The dose-response effect of free GlaB and hyaluronic acid (HA)-encapsulated GlaB (HA-GlaB) has been assessed by Trypan Blue Exclusion Test. The target protein expression levels have been analysed by Western blot. The cell migratory activity has been evaluated by Wound healing assay. Cell death has been explored by Flow cytometry analyses. All experiments have been conducted in N.3 experimental replicates.
**Results:** Our research illustrates a decrease in iCCA cell rate proliferation, migration and a Gli1 levels reduction in a dose- and time-dependent manner after both free GlaB and HA-GlaB treatments ($p<0.05$), leading to a considerable reduction of proliferation and invasiveness in cancer cells. Eventually, flow cytometry preliminary data shows cell death, as a consequence of drug administration compared to controls.
**Conclusion:** These data shed a light on a novel and putative natural therapeutic compound for the treatment of iCCA.

doi: 10.1016/j.dld.2024.01.035

## T-4

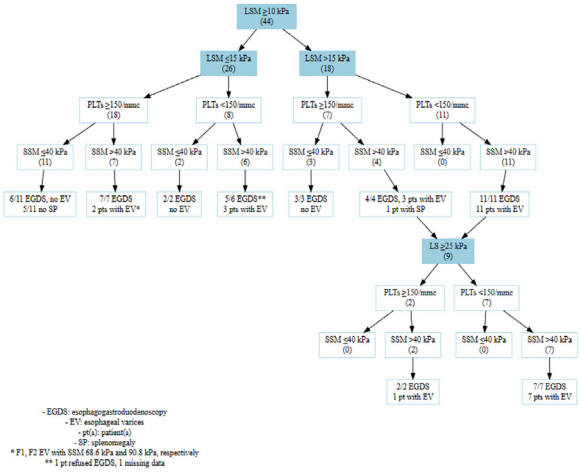
### Spleen stiffness measurement improves non-invasive prediction of clinically significant portal hypertension in primary biliary cholangitis

G.F. Manfredi [1,2], I. Ergenç [3,4], M.G. Cittone [1], R. Bertetto [1], C. De Benedittis [1], H. Basri Yapici [5], M. Pirisi [1], Y. Yilmaz [3,6], C. Rigamonti [1]

[1] *Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy and Division of Internal Medicine, AOU Maggiore della Carità, Novara, Italy*
[2] *Department Department of Surgery & Cancer, Imperial College London, Hammersmith Hospital, Du Cane Road, London, UK*
[3] *Department of Gastroenterology, School of Medicine, Marmara University, Istanbul, Turkey*
[4] *Department of Hepatology, King's College Hospital NHS Foundation Trust, London, UK*
[5] *Department of Internal Medicine, School of Medicine, Marmara University, Istanbul, Turkey*
[6] *Department of Gastroenterology, School of Medicine, Recep Tayyip ErdoÄŸan University, Rize, Turkey*

**Introduction:** Primary biliary cholangitis (PBC) may lead to clinically significant portal hypertension (CSPH) even in a pre-cirrhotic stage. According to Baveno VII criteria (BVIIc), CSPH in compensated advanced chronic liver disease can be ruled-out or ruled-in by coupling liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) with platelets (PLTs).

Algorithms combining BVIIc with spleen stiffness measurement (SSM) have showed to improve diagnostic performance for CSPH compared with BVIIc alone.
**Aim:** To evaluate the accuracy of SSM-based algorithms in PBC.
**Methods:** Multicentric study of 214 PBC patients (122 from Novara, 92 from Istanbul) who underwent VCTE (LSM, SSM). Esophagogastroduodenoscopy was performed according to Baveno VI guidelines. To rule-out CSPH, two of LSM ≤15 kPa, PLTs ≥150/mmc and SSM ≤40 kPa had to be present. To rule-in CSPH, two of LS ≥25 kPa, PLTs <150/mmc and SSM >40 kPa had to be present.
**Results:** Among the 214 patients (95% women, median age 56 years, median disease duration 31 months, 13% cirrhotic): median LSM was 6.4 kPa (IQR 5.1-9.1), being ≥10 kPa in 44/214, ≥25 kPa in 9/214. Median SSM was 22.4 kPa (IQR 18.6-29.7), resulting >40 kPa in 34/214. In 23/44 patients with LSM ≥10 kPa CSPH could be ruled-out: 11/23 patients fulfilled 3 criteria (no esophageal varices, EV, were present); 12/23 patients fulfilled 2 criteria including 2 patients with EV (both with SSM >40 kPa: 68.8 and 90 kPa). In 9/44 patients CSPH could be ruled-in: 7/9 patients fulfilled 3 criteria and all of them had EV, 2/9 patients fulfilled 2 criteria (1 had varices). All the remaining 10 patients not fulfilling rule-in or rule-out criteria had SSM >40 kPa, with 6 showing EV and 5 splenomegaly.
**Conclusions:** SSM improved BVIIc performance in PBC patients. SSM cut-off >40 kPa identified CSPH with 100% sensitivity regardless LSM and PLTs.




doi: 10.1016/j.dld.2024.01.036

## T-5

### Hepatic sarcoidosis:an Italian multicenter study

C. Della Corte [1], F. Malinverno [2], D. D'Amato [2], R. Reati [1], I. Arena [1], M. Campigotto [3], V. Cardinale [4], A. Cespiati [5], E. Degasperi [6], P. Del Poggio [7], E. Durante [8], A. Federico [9], G. Galati [10], G. Germani [11], G. Giannini [12], R. Marin [13], A. Martini [14], C. Mazzarelli [15], F. Mirici [16], G. Missale [17], E. Morana [18], M. Morelli [19], L. Pasulo [20], M. Piras [21], G. Perricone [22], G. Pieri [12], N. Pugliese [23], R. Rapetti [24], M. Rendina [25], S. Sciarrone [26], L. Simone [27], L. Surace [28], S. Strona [29], G. Svegliati B [30], F. Terracciani [10], M. Viganò [31], G. Manes [1], M. Carbone [2]

[1] *U.O. Gastroenterologia ASST Rhodense, Rho, MI*
[2] *U.O. Gastroenterologia Ospedale San Gerardo Monza*
[3] *U.O. Gastroenterologia Ospedali Riuniti Trieste*
[4] *U.O. Epatogastroenterologia Policlinico Umberto I Roma*
[5] *U.O.Medicina Interna e Malattie Metaboliche, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano*
[6] *U.O. Gastroenterologia ed Epatologia Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano*
[7] *U.O. Gastroenterologia ed Endoscopia Policlinico San Marco Zingonia (BG)*
[8] *U.O.C. Medicina Infettivologica e dei Trapianti, AORN dei Colli Monaldi, Napoli*
[9] *U.O. Epatogastroenterologia Azienda Ospedaliera Universitaria L. Vanvitelli Napoli*
[10] *Campus Biomedico, Roma*
[11] *UOSD Trapianto Multiviscerale Dipartimento di Scienze Chirurgiche, Oncologiche e Gastroenterologiche Azienda Ospedaliera-Università di Padova*
[12] *Clinica Gastroenterologica IRCCS Ospedale Policlinico San Martino Genova*
[13] *U.O. Gastroenterologia ed Endoscopia digestiva Ospedale di Dolo (VE)*
[14] *U.O. Medicina Interna Azienda Ospedaliera Università di Padova*
[15] *U.O. Epatologia e Gastroenterologia Azienda Ospedaliera Ospedale Niguarda Ca' Granda (Milano)*
[16] *Centro Trapianti Bologna*
[17] *U.O. Malattie Infettive ed Epatologia Azienda Ospedaliero-Universitaria di Parma*
[18] *SSD Gastroenterologia ed Endoscopia Digestiva, Ospedale Umberto Parini, Aosta*
[19] *Dipartimento delle insufficienze d'organo e dei trapianti Policlinico S. Orsola-Malpighi (Bologna)*

[20] *U.S.C. Gastroenterologia Epatologia e Trapiantologia Dipartimento di Medicina Specialistica e dei Trapianti ASST Papa Giovanni XXIII, Bergamo*
[21] *SSD Coordinamento Trapianti Fegato - Cagliari*
[22] *U.O. Epatologia e Gastroenterologia e S.C. Liver Unit – ASST Grande Ospedale Metropolitano Niguarda*
[23] *U.O. Gastroenterologia Humanitas Research Hospital (Milano)*
[24] *SCDU Medicina Interna AOU Maggiore della Carità di Novara*
[25] *U.O. Gastroenterologia Universitaria Policlinico di Bari*
[26] *U.O. Gastroenterologia ed Endoscopia Digestiva Ospedale di San Bonifacio (VR)*
[27] *U.O. Gastroenterologia ed Endoscopia Digestiva Ospedale di Ferrara*
[28] *Centro medicina del viaggiatore e delle Migrazioni Azienda Sanitaria Provinciale Di Catanzaro*
[29] *U.O. Gastroenterologia ASL Torino*
[30] *U.O. Danno Epatico e Trapianti Ospedali Riuniti Ancona*
[31] *U.O. Epatologia Ospedale San Giuseppe Milano*

**Introduction:** Sarcoidosis is a systemic granulomatous disease involving the liver in about 10-20% of cases. In absence of high-quality data on the management of hepatic sarcoidosis (HS), it is still experienced-based.
**Aim:** To collect and analyze data on the Italian real-world experience in HS management.
**Methods, Results:** Thirty-six AISF-affiliated hepatologic centers received questionnaires, thirty-three of them reported managing 78 patients with HS. Eighteen centers subsequently transmitted demographic and clinical data belonging to 11 Italian regions. Statistical analyses were performed with R Studio. 55 patients were included, median age at diagnosis was 52(44.8-57.3).Female patients were 33 (60%) and 45 (82%) patients were Caucasian.

Most patients (45%) reported systemic symptoms (asthenia, fever) and a cholestatic pattern of liver enzymes elevation (Table1). Males had a significantly higher level of GGT (p 0.02) and bilirubin (p<0.01) at presentation. Figure1 shows radiological findings. In coexistence with HS, mainly pulmonary (43%) and lymphatic (36%) involvement were reported. Patients with only HS were 6 (10.9%).Clinically-significant-portal-hypertension (CSPH) at diagnosis was detected in 8(14.5%) patients according to LSM≥25Kpa or varices, only one of them had histological cirrhosis. BMI was significantly higher in patients with CSPH(p 0.01). Twenty-six patients were treated with first-line steroid therapy (48%), 11(20%) patients with steroid+ ursodeoxycholic-acid (UDCA), 6(11%) patients with UDCA only, 11 (20%) with combination of different agents, including anti-metabolites. Median alkaline-phosphatase (ALP) decrease was 56,3% in 12 months, independently from the medical treatment used (p>0.09). Seventeen (31%) patients received treatment adjustment with a second line agent. None of the patients underwent liver transplantation or developed hepatocellular carcinoma. One patient died during follow-up owing to liver-related complications.
**Conclusion:** HS is a rare entity with a heterogeneus clinical presentation and management. HS has an intrinsic risk of CSPH not only explained by the presence of cirrhosis, that is higher in patients with higher BMI; these findings need further investigations. Drug choice doesn't have an impact on ALP decrease, but UDCA are associated to a better GPT-reduction. A multicentric, prospective, national cohort study is eeded to further study this disease.

| | level | Overall |
|---|---|---|
| n | | 55 |
| REGIONE (%) | Calabria | 1 (1.8) |
| | Campania | 3 (5.5) |
| | Emilia Romagna | 10 (18.2) |
| | Friuli VG | 4 (7.3) |
| | Lazio | 5 (9.1) |
| | Liguria | 3 (5.5) |
| | Lombardia | 20 (36.4) |
| | Marche | 1 (1.8) |
| | Piemonte | 1 (1.8) |
| | Valle d'Aosta | 1 (1.8) |
| | Veneto | 6 (10.9) |
| age_diagnosis (median [IQR]) | | 52.58 [44.18, 57.30] |
| sex (%) | F | 33 (60.0) |
| | M | 22 (40.0) |
| extrahepatic_sarcoidosis (%) | lung | 18 (32.7) |
| | lung, lymphatic | 5 (9.1) |
| | lung, other | 6 (10.9) |
| | lymphatic | 20 (36.4) |
| | no | 6 (10.9) |
| etnia (%) | afro-american | 3 (5.5) |
| | asian | 3 (5.5) |
| | caucasian | 45 (81.8) |
| | middle eastern | 4 (7.3) |
| fumo _diagnosi (%) | no | 37 (74.0) |
| | previous | 9 (18.0) |
| | yes | 4 (8.0) |
| alcol_diagnosi (%) | no | 49 (89.1) |
| | yes | 6 (10.9) |
| BMI_diagnosi (median [IQR]) | | 26.00 [22.00, 29.00] |
| BMI (%) | normal weight | 22 (44.0) |
| | obesity | 9 (18.0) |
| | overweight | 19 (38.0) |
| BMI_25 (%) | < 25 | 22 (44.0) |
| | ≥ 25 | 28 (56.0) |
| Clinical_presentation (%) | abdominal symptoms | 3 (5.5) |
| | asymptomatic | 16 (29.1) |
| | pulmonary symptoms | 3 (5.5) |
| | systemic symptoms | 25 (45.5) |
| | systemic, abdominal symptoms | 7 (12.7) |
| | systemic, pumonary symptoms | 1 (1.8) |
| AST_0 (median [IQR]) | | 36.00 [23.00, 50.00] |
| ALT_0 (median [IQR]) | | 41.00 [22.50, 68.25] |
| ALP_0 (median [IQR]) | | 190.00 [112.00, 258.75] |
| GGT_0 (median [IQR]) | | 168.50 [84.25, 318.00] |
| Tbil_0 (median [IQR]) | | 0.90 [0.52, 1.20] |
| ACE_0 (median [IQR]) | | 91.00 [60.75, 145.82] |

doi: 10.1016/j.dld.2024.01.037

## T-6

### Does HLA-G play a role in PBC?

M. Miglianti [1,4], R. Littera [2,4], S. Mocci [7], C. Sanna [7], A. Mascia [3], M. Serra [3], M. Conti [5], C. Balestrieri [5], G. Serra [5], F. Pes [5], T. Zolfino [6], A. Perra [3], L. Chessa [1,4,5]

[1] *Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Italy*
[2] *Medical Genetics, R. Binaghi Hospital, Sardegna, Italy*
[3] *Section of Pathology, Oncology and Molecular Pathology Unit, Department of Biochemical Sciences, University of Cagliari, Cagliari, Italy*
[4] *AART-ODV (Association for the Advancement of Research on Transplatation)*
[5] *Liver Unit, University Hospital, Cagliari, Italy*
[6] *Division of Gastroenterology, ARNAS S. Michele Hospital, Cagliari, Italy*
[7] *Medical Genetics, Department of Medical Science and Public Health, University of Cagliari, Cagliari, Italy*

**Introduction:** Primary biliary cholangitis (PBC) is a rare autoimmune cholestatic liver disease. PBC has a mosaic pathogenesis, environmental factors probably interact with immunogenetic and epigenetic risk, favouring the development of the disease. The human leukocyte antigen-G (HLA-G) is one of the most significant tolerogenic system due to its immunosuppressive effects on all types of immune cells. Our previous studies have demonstrated that type 1 autoimmune hepatitis (AIH-1) patients had sHLA-G levels significantly lower than those in the control group, and lower levels are associated with a more severe disease. HLA has been extensively studied in PBC, however, to the best of our knowledge, the immunomodulatory effects of HLA-G expression and its role in PBC have not been investigated.
**Aim:** In this study we investigated the role of soluble HLA-G (sHLA-G) and whereas it could affect onset and therapy response in PBC patients.
**Materials and Methods:** A cohort of 166 Sardinian PBC patients was compared to two groups, 180 healthy individuals and 205 AIH-1 patients. Soluble HLA-G levels were measured in patients and in healthy controls at the time of enrolment.
**Results:** Reduced levels of sHLA-G were more frequently present in patients of our PBC group when compared to the other two groups, suggesting disease predisposition for those patients showing those characteristics [PBC 16.3 (3.5 – 29.1) U/mL vs Controls 24.3 (5.7 – 42.3) U/mL and vs AIH-1 24.3 (0.6 – 48) U/mL; P = 0.002]. Soluble HLA-G levels are significantly related to the therapy response, in fact among PBC patients those who do not reach an adequate therapy response have significantly lower sHLA-G levels compared to those with adequate response [15.53 (6.29 – 24.77) U/mL vs 25.58 (0.0 – 60.9) U/mL respectively; P = 0.010]
**Conclusion:** Reduced levels of sHLA-G are involved in PBC onset and in therapy response.

doi: 10.1016/j.dld.2024.01.038

## T-7

### Autoimmune hepatitis cholestatic variant syndromes recurrence following liver transplantation affects graft and patient survival in an international multicentre cohort

V. Ronca [1], A. Parente [2], M. Ebadi [2], B.E. Hansen [3], G. Hirschfield [3], S. Elwir [4], M. Alsaed [4], P. Milkiewicz [5], M.K. Janik [5], H.U. Marschall [6], M.A. Burza [6], C. Efe [7], Ali Rıza Calıs Kan [8], M. Harputluoglu [8], G. Kabaçam [9], D. Terrabuio [10], F. de Quadros Onofrio [3], N. Selzner [3], A. Bonder [11], A. Parés [12], L. Llovet [12], M. Akyıldız [13], C. Arikan [14], M.P. Manns [15], R. Taubert [15], A.L. Weber [15], T.D. Schiano [16], B. Haydel [16], P. Czubkowski [17], P. Socha [17], N. Ołdak [17], N. Akamatsu [18], A. Tanaka [19], C. Levy [20], E.F. Martin [20], A. Goel [21], M. Sedki [21], I. Jankowska [22], T. Ikegami [23], M. Rodriguez [24], M. Sterneck [24], C. Weiler-Normann [24], C. Schramm [24], M.F. Donato [25], A. Lohse [26], R.J. Andrade [27], V.R. Patwardhan [11], B. van Hoek [28], M. Biewenga [28], A.E. Kremer [29,30], Y. Ueda [31], M. Deneau [32], M. Pedersen [33], M.J. Mayo [33], A. Floreani [34], P. Burra [34], M.F. Secchi [35], B. Terziroli Beretta-Piccoli [36], M. Sciveres [37], G. Maggiore [38], S.M. Jafri [39], D. Debray [40], M. Girard [40], F. Lacaille [41], E. Lytvyak [1], A.L. Mason [1], M. Heneghan [42], A.J. Montano-Loza [2], Y. Htun Oo [43], on behalf of the International Autoimmune Hepatitis Group (IAIHG)

[1] *Division of Gastroenterology and Liver Unit, University of Alberta, Edmonton, AB, Canada*
[2] *Center for Liver Research & NIHR Birmingham BRC, University of Birmingham & University Hospital Birmingham NHS Foundation Trust, Institute of Immunology and Immunotherapy, University of Birmingham, UK*
[3] *Toronto Center for Liver Disease, University Health Network, University of Toronto, Toronto, Canada*
[4] *Baylor University Medical Center, Dallas, USA*
[5] *Liver and Internal Medicine Unit, Medical University of Warsaw, Poland*
[6] *Sahlgrenska University Hospital, Gothenburg, Sweden*
[7] *Department of Gastroenterology, Harran University Hospital, S¸anlıurfa, Turkey*
[8] *Department of Gastroenterology, Inönü University School of Medicine, Malatya, Turkey*
[9] *Clinic of Gastroenterology and Liver Transplantation, Guven Hospital Ankara, Turkey*
[10] *Department of Gastroenterology - University of São Paulo School of Medicine, São Paulo, Brazil*
[11] *Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA*
[12] *Liver Unit, Hospital Cliníc, University of Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain*
[13] *Koç University School of Medicine, Department of Gastroenterology and Liver Transplantation Center, Istanbul, Turkey*
[14] *Koc University School of Medicine, Pediatric Gastroenterology and Hepatology, Organ Transplantation Center, Koc University Research Center for Translational Medicine (KUTTAM), Istanbul, Turkey*

[15] European Reference Network on Hepatological Diseases (ERN RARE-LIVER), Department Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany
[16] Recanati/Miller Transplantation Institute/Division of Liver Diseases, Mount Sinai Medical Center, New York, USA
[17] Department of Gastroenterology, Hepatology, Nutritional Disorders and Pediatrics, The Children's Memorial Health Institute, Warsaw, Poland
[18] University of Tokyo, Japan
[19] Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan
[20] University of Miami Miller School of Medicine, Miami, USA
[21] Stanford University, Stanford, USA
[22] Children's Memorial Health Institute, Warsaw, Poland
[23] Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
[24] UKE Hamburg, Hamburg, Germany
[25] Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Liver Tranplant Hepatology Unit, Division of Gastroenterology and Hepatology, Milan, Italy
[26] University Medical Center, Hamburg, Germany
[27] Gastroenterology Service -IBIMA. University Hospital and CIBERehd, University of Málaga, Spain
[28] Leiden University Medical Center, Leiden, Netherlands
[29] Department of Medicine, University Hospital Erlangen and Friedrich-Alexander- University Erlangen-Nürnberg, Erlangen, Germany
[30] Department of Gastroenterology and Hepatology, University Hospital Zürich, University of Zürich, Zürich, Switzerland
[31] Department of Gastroenterology and Hepatology, Graduate School of Medicine, Kyoto University, Kyoto, Japan
[32] University of Utah, Salt Lake City, USA
[33] University of Texas Southwestern Medical Center, Dallas, USA
[34] Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy
[35] University of Padova, Padova, Italy
[36] Epatocentro Ticino & Università della Svizzera Italiana, Lugano, Switzerland
[37] UPMC Pediatric Liver Center, Palermo, Italy
[38] Hepatogastroenterology, Nutrition and Liver Transplant IRCCS Bambino Gesù Pediatric Hospital, Rome, Italy
[39] Henry Ford Health System, Detroit, Michigan, USA
[40] Pediatric Liver Unit, French National Reference Center for Rare Diseases BA and Genetic Cholestasis, Hôpital Necker, Université de Paris, Paris, France
[41] Gastroenterology-Hepatology-Nutrition Unit, Hôpital Necker-Enfants malades, Paris, France
[42] King's College Hospital NHS Foundation Trust, London, UK
[43] Center for Liver and Gastro Research & National Institute of Health Research Birmingham Biomedical Research Centre, University of Birmingham, Centre for Rare Disease and ERN Rare Liver Centre, Liver Transplant and Hepatobiliary Unit, University Hospital Birmingham NHS Foundation Trust, UK

**Background:** A significant proportion of patients with variant syndromes (VS), namely AIH/PBC or AIH/PSC require liver transplantation (LT), despite treatment. The frequency of disease recurrence and the effect on graft survival is yet to be clarified. The aim of this international, multicentric, retrospective study is to evaluate risk factors associated with recurrence and the impact of the disease recurrence after liver transplant (LT) on graft and patient survival.
**Methods:** We evaluated 172 patients undergone LT for VS in 33 centres in North America, South America, Europe and Asia. Clinical data before and after LT, biochemical data within the first 12 months after LT, and immunosuppression after LT were analysed to identify patients with a higher risk of recurrence of autoimmune disease based on histological and radiological diagnosis. Cumulative probabilities of graft and overall survival after LT were calculated using semi-Markov model.
**Results:** VS recurred after LT in 23% and 33% of patients after 5 and 10 years, respectively. An increased ALP and ALT at 12 months after LT (HR, 1.60; 95% CI, 1.13-2.25; $p<0.01$, HR, 1.25; 95% CI, 1.01-1.53; $p= 0.03$) and acute rejection (HR 3.58; 95% CI, 1.60-7.73; $p<0.01$) were found associated with a higher risk of VS syndrome recurrence, whilst the use of predniso(lo)ne was associated with a reduced risk (HR 0.30, 95% CI 0.14-0.64, $p<0.01$). After adjusting for ALT and ALP at 12- months, the use of predniso(lo)ne were found independently and negatively associated with recurrent disease. The recurrence of VS was found significantly associated with graft loss and patients' survival at the multivariate Cox regression analysis with time-dependent covariate. The 5-, 10- year probability of graft survival was 68% and 41% in patients with recurrent VS compared to 83% and 60% in patients without recurrent disease (p-value, $p = 0.01$). The overall survival was significantly reduced in patients with recurrent disease ($p = 0.01$), with event probability at 5- and 10- years of 75% and 49% vs 84% and 60% in patients without recurrence.
**Conclusion:** VS recurrence after LT is frequent and is associated with elevation of liver enzymes within the first year after LT and rejection episodes. VS recurrence negatively impacts graft and patient survival. Strategies are warranted to prevent VS recurrence or mitigate its negative effects.

doi: 10.1016/j.dld.2024.01.039

## T-8

### Impact of maralixibat on cholestatic pruritus in young adults aged 16 years and older with Alagille syndrome

G. Hirschfield [1], D. Mogul [2], A. Soglian [2], M. Baek [2], P. Vig [2], B.M. Kamath [3]

[1] University of Toronto, Toronto Centre for Liver Disease, University Health Network, Toronto, Ontario, Canada
[2] Mirum Pharmaceuticals, Inc., Foster City, California, United States
[3] The Hospital for Sick Children and the University of Toronto, Division of Gastroenterology, Hepatology and Nutrition, Toronto, Ontario, Canada

**Introduction:** Data in ALGS has primarily focused on pediatric patients, however adults with ALGS who survive with their native liver may require treatment for cholestasis and pruritus.
**Aim:** We report on the efficacy and safety of MRX, an IBAT inhibitor, in young adults aged ≥16 years with ALGS transitioning to adult care.
**Methods & Results:** Participants received ≥1 dose of MRX ≥16 years of age within the MRX ALGS clinical development program. Pruritus [ItchRO (Obs)] and serum bile acids (sBA) were assessed at Baseline, before and after 16 years, and at study end. 14 individuals were included; 11 began treatment at <16 years of age and 3 patients began MRX ≥16 years. Baseline mean (SE) pruritus score was 2.5 (0.21), and significantly decreased to 0.8 (delta = -1.7; $p = 0.002$); pruritus response was durable with no significant change before and after age 16 years (delta = -0.2; $p = 0.2$), or to end of therapy (delta = 0.2; $p = 3$) in individuals that started MRX <16 years old. Baseline mean sBA was 130 µmol/L, significantly decreased to 52 µmol/L (delta = -79; $p = 0.03$) prior to 16 years; no significant change before and after age 16 years (delta = -7; $p = 0.3$), or to end of therapy (delta = 3; $p = 0.4$) was observed. Three individuals that started MRX ≥16 years had improvements in pruritus from Baseline (delta = -2.8, -0.6, and -1.0). One patient had a large decrease in sBA (delta = -112 µmol/L) and two

had small increases in sBA (delta = 8 and 11 µmol/L). MRX was generally well tolerated with the same safety profile previously reported.
**Conclusions:** MRX was effective, durable, and well tolerated in ALGS patients ≥16 years, providing critical data for patients who transition to adulthood while on therapy.

doi: 10.1016/j.dld.2024.01.040

## T-9

### Optimizing AI Performance for Autoimmune Hepatitis Guidelines: A Case Study on Enhanced GPT Model Accuracy

M. Giuffrè [1,4], F. Masutti [2], M. Gulotta [1], G. De Monte [1], L. Fusaro [1], F. Orbosuè [1], L.S. Crocè [1,2,3]

[1] *DSM Università di Trieste UCO Clinica Patologie del Fegato, Trieste Italia*
[2] *Azienda Sanitaria Universitaria Giuliano Isontina-ASUGI Trieste Italia*
[3] *Fondazione Italiana fegato-FIF Trieste Italia, Department of Internal Medicine (Digestive Diseases)*
[4] *Yale School of Medicine, Yale University, Connecticut, United States*

**Background:** The application of Artificial Intelligence (AI) in healthcare, particularly via Generative Pre-trained Transformers (GPTs), presents great promise but also significant challenges, such as errors and misconceptions in output. This case study on autoimmune hepatitis (AIH) guidelines, derived from the European Association for the Study of the Liver (EASL), examines these issues and evaluates how different formatting and instructional strategies affect the performance of specialized GPT models. Our goal is to improve the dependability and functionality of GPTs in the interpretation of intricate medical guidelines.
**Methods:** A series of experiments were conducted utilizing custom GPT models based on 10 queries related to the European guidelines for AIH. These experiments varied in their approach: including or omitting supplemental guideline documents, presenting guidelines in PDF and .docx formats, offering directives versus not, working with structured versus unstructured texts, and transforming tabular data (initially image-based in the guidelines) into text lists. Each query was repeated five times under each set of conditions to assess the models' consistency.
**Results:** The baseline performance of the custom GPTs without supplementary guideline material was 40%. This figure rose to 55% with the addition of guidelines in PDF format, and to 72% in a .docx format. When guidelines were coupled with instructions, accuracy rose markedly to 80%, compared to 65% without. Notably, GPTs performed better with unstructured text, achieving 78% accuracy against 65% with structured text. Converting tables to lists improved accuracy to 82%, up from 73% without such conversion. The largest gain in accuracy was observed when all optimized conditions were combined—guidelines, unstructured text, and list conversion—reaching an 88% peak in accuracy.
**Discussion:** The findings highlight the critical role of format, instructional context, and data organization in the efficient deployment of custom GPT models for medical guidelines. The marked increase in accuracy with specific adaptations indicates an encouraging path for improving AI applications in healthcare. These results emphasize AI's potential, especially when fine-tuned, to reliably interpret and apply complex medical information.

doi: 10.1016/j.dld.2024.01.041

## T-10

### Cholestasis impacts on performance of non invasive tests for ruling out high-risk esophageal varices in patients with primary biliary cholangitis and compensated advanced chronic liver disease

V. Calvaruso, C. Celsa, L. Cristoferi, M. Scaravaglio, L. Capodicasa, G. Di Maria, L. Cadamuro, A. Gerussi, F. Malinverno, P. Lampertico, N. Cazzagon, M. Marzioni, U. Vespasiani Gentilucci, P. Andreone, A. Lleo De Nalda, C. Rigamonti, M. Viganò, E.G. Giannini, M. Russello, E. Vanni, F. Cerini, G. Missale, M. Brunetto, G. Niro, G. Vettori, A. Castellaneta, V. Cardinale, D. Alvaro, A. Mega, V. Pace Palitti, F. Bellanti, V. Di Marco, P. Invernizzi, C. Cammà, M. Carbone

*Italian PBC registry*

**Introduction:** Non-invasive tests (NITs) to identify patients with Primary Biliary Cholangitis (PBC) and compensated Advanced Chronic Liver Disease (cACLD) who can avoid esophagogastroduodenoscopy (EGDS) are lacking. Aims of this study were to evaluate the diagnostic performance of NITs to rule out high-risk esophageal varices (HRV) in patients with PBC-related cACLD and to assess the influence of cholestasis on the NITs performance.
**Method:** Data of patients with cACLD from 24 centres participating to "Italian PBC registry", were captured. All PBC patients who performed an EGD for evaluation of signs of portal hypertension were analyzed. Outcome was the presence of HRV at index EGD. RESIST criteria (platelets - PLT $>120\times10^9$/L and serum albumin >3.6 g/dL) were compared with elastography-based criteria (Baveno VI, Expanded Baveno VI, and Baveno VII) in patients with Alkaline Phosphatase (ALP) < or ³ 1.67 ULN. Decision curve analysis (DCA) of NITs were calculated.
**Result:** The cohort consisted of 250 patients. At EGDS, 137 patients (54.8%) had no varices, 79 (31.6%) had low-risk varices and 34 (13.6%) had HRV. Liver stiffness by Fibroscan was available in 186 patients (74.%). Overall, the proportion of correctly spared endoscopies for HRV was 61.1%, 54.1%, 31.4% and 18.2% for RESIST, Expanded Baveno VI, Baveno VI and Baveno VII criteria, respectively. and RESIST criteria were associated with the lowest rate of missing HRV (2.9%). In patients with ALP ³ 1.67 ULN (101, 40.4%) the rate of missing HRV for Baveno VI and Expandend Baveno VI criteria were 23.8 and 18.9% respectively. In the same category of patients RESIST criteria false negative rate was 6%. DCA demonstrates the highest net benefit of RESIST criteria compared to elastography-based criteria for ruling out HRV both in patients with ALP < or ³ 1.67 ULN (Figure 1).
**Conclusion:** Cholestasis impacts on NITs ability to rule out HRV in patients with PBC and cACLD. Biochemical-based RESIST criteria demonstrates the highest net benefit compared to elastography-based criteria for ruling out HRV.

doi: 10.1016/j.dld.2024.01.042

## T-11

### Fatigue is not influenced by chronotype and is reported to be mainly muscular in patients with primary biliary cholangitis

E.N. Lynch [1,2], P. Rossi [1], T. Innocenti [1,2], G. Dragoni [1,3], M.R. Biagini [1,3], P. Forte [3], A. Galli [1,3]

[1] *Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy*
[2] *Department of Medical Biotechnologies, University of Siena, Siena, Italy*
[3] *Clinical Gastroenterology Unit, "Careggi" University Hospital, Florence, Italy*

**Introduction:** Fatigue is considered one of the most frequent and debilitating symptoms in primary biliary cholangitis (PBC), affecting over 50% of PBC patients. The pathophysiology of fatigue and the role of contributing factors are still largely unknown.
**Aim:** The aim of the study was to assess whether patient chronotype was associated with fatigue in PBC. In addition, we evaluated the impact on fatigue of environmental and liver disease characteristics and whether fatigue was perceived by patients as mainly muscular or mental.
**Materials and Methods:** All noncirrhotic PBC patients attending our tertiary referral centre were asked to complete the main questionnaires on fatigue, sleepiness, and chronotype (PBC-40, Fatigue Impact Scale [FIS], Epworth Sleepiness Scale [ESS], Morningness-Eveningness Questionnaire [MEQ] between January 2023 and June 2023. Patients were also questioned on environmental factors (employment, sleep quality, nighttime light exposure) and as to whether fatigue was perceived as mainly muscular or mental. Clinical data of patients who responded was obtained from clinical records.
**Results:** Of a total of 69 patients, 34 agreed to participate in the study. Most patients reported mainly muscular fatigue rather than mental (64% vs 36%). Chronotype did not differ among fatigue and sleepiness severity score groups (PBC-40 Fatigue p=0.62; FIS p=0.24; ESS p=0.46), as shown in **Table 1**. Nighttime light exposure significantly affected fatigue and sleepiness (PBC-40 p=0.01; FIS p=0.01; ESS p=0.05). No other environmental factor or disease characteristic was found to be associated with fatigue or sleepiness.
**Conclusions:** Chronotype does not appear to have an impact on fatigue in patients with PBC, although nighttime light exposure significantly worsens daytime sleepiness and fatigue, and therefore should be avoided. PBC patients report mainly muscular rather than mental fatigue.

| MEQ | PBC-40 Fatigue | p |
|---|---|---|
| <53 | 20.75 | 0.59 |
| 53-64 | 20.26 | |
| >64 | 21.03 | |
| **MEQ** | **FIS** | **p** |
| <53 | 56.28 | 0.60 |
| 53-64 | 55.45 | |
| >64 | 57.07 | |
| **MEQ** | **ESS** | **p** |
| <53 | 7.06 | 0.23 |
| 53-64 | 6.77 | |
| >64 | 6.86 | |

*Table 1 Assessment of the impact of chronotype on fatigue*

doi: 10.1016/j.dld.2024.01.043

## T-12

### Liver steatosis assessed by CAP in patients with primary biliary cholangitis

F. Bueti [1], C. Pitrone [1], R. Filomia [1], M.S. Franzè [2], G. Caccamo [1], S. Maimone [1], I. Cacciola [1,2], G. Raimondo [1,2], C. Saitta [1,2]

[1] *Department of Medical Sciences, Unit of Medicine and Hepatology, University Hospital of Messina, Messina, Italy*
[2] *Department of Clinical and Experimental Medicine, Unit of Medicine and Hepatology, University of Messina, Messina, Italy*

**Introduction:** Primary biliary cholangitis (PBC) is a chronic inflammatory autoimmune cholestatic liver disease frequently associated with hyperlipidaemia. However, the impact of steatosis on the liver disease in PBC patients has not been studied so far.
**Aim:** To investigate liver steatosis [assessed by controlled attenuation parameter (CAP)] and its relationship with liver stiffness (LS) [evaluated by transient elastography (TE)] in patients with PBC.

**Materials and Methods:** All patients with PBC admitted to the Unit of Medicine and Hepatology of the University Hospital of Messina in 2023 underwent contemporaneous LS and CAP measurements. Demographic, anthropometric, biochemical, ultrasonographic data, and treatment information were collected from all patients. The Spearman's rank test was used for analyzing the correlation between CAP values and all the recorded variables. Uni- and stepwise multivariate analyses were performed for identifying factors independently associated with higher liver stiffness values.
**Results:** Seventy-four patients (68 females, 6 males; mean age 61.3 ± 11.3 years) under ursodeoxycholic acid treatment for at least twelve (range 12-233) months were included in the analysis, and 14 of them (18.9%) had cirrhosis. Mean liver stiffness was 9.1 ± 6.9 kPa, mean CAP values were 228.5 ± 55.7 dB/m. Ultrasonographic signs of steatosis were present in 70/74 (94.6%) patients, mean BMI was 25.7 ± 4.2 Kg/m$^2$. The Spearman's rank test showed significant correlation between CAP values and BMI ($p < 0.05$), IgM levels ($p < 0.05$), and liver stiffness ($p= 0.01$). Multivariate analysis showed that higher gamma-globulin levels ($p= 0.002$, OR 4.73), larger spleen diameter ($p= 0.004$, OR 1.02), and higher CAP values ($p= 0.02$, OR 3.11) were independently associated with higher liver stiffness values.
**Conclusions:** Liver steatosis is highly prevalent in patients with PBC and appears to impact on liver stiffness.

doi: 10.1016/j.dld.2024.01.044

## T-13

### Pathways sustaining HDV activity act independently from the size of HBV resevoir and are fueled by an abundant expression of HBsAg from integrated HBV-DNA

R. Salpini [1], S. D'Anna [2], L. Piermatteo [1], E. Teti [3], A. Di Lorenzo [3], G. Brancaccio [4], G. Torre [1], V. Malagnino [3], M. Iannetta [3], F. Ceccherini-Silberstein [1], C. Pasquazzi [5], U. Cillo [6], A. Vitale [6], E. Gringeri [6], M. Magrofuoco [6], M. Pacenti [7], L. Baiocchi [8], S. Francioso [8], I. Lenci [8], A.M. Geretti [3], M.L. Abate [9], A. Olivero [9], G.B. Gaeta [10], L. Sarmati [3], M. Rizzetto [9], G.P. Caviglia [9], V. Svicher [1]

[1] *Department of Biology, University of Rome Tor Vergata, Rome, Italy*
[2] *Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy*
[3] *Department of Systems Medicine, Infectious Disease Clinic, University of Rome Tor Vergata, Rome, Italy*
[4] *Infectious Diseases Unit, Department of Molecular Medicine, University of Padova, Padova, Italy*
[5] *Sant'Andrea Hospital, Rome, Italy*
[6] *Hepatobiliary Surgery and Liver Transplantation Unit, Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy*
[7] *Microbiology and Virology Unit, Padova University Hospital, Padova, Italy*
[8] *Hepatology Unit, Policlinico Tor Vergata, Rome, Italy*
[9] *Department of Medical Sciences, University of Turin, Turin, Italy*
[10] *Infectious Disease Unit, University L. Vanvitelli, Naples, Italy*

**Background & Aims:** HDV exploits HBV surface glycoproteins (HBsAg) for viral morphogenesis and infectivity. Here, we investigate HBV-HDV replicative activity and their interplay by analysing liver biopsies from chronically HBV/HDV infected (CHD) patients.
**Method:** Liver tissue was analysed from 25 HBeAg-negative CHD patients. Intrahepatic covalently-closed circular DNA (cccDNA), pregenomic HBV-RNA (pgRNA) and HDV-RNA were quantified by droplet-digital-PCR (ddPCR). ddPCR assays were set-up to quantify total HBs transcripts and to distinguish those deriving from cccDNA and integrated HBV-DNA (Grudda,2022).
**Results:** Patients had high serum HDV-RNA and HBsAg levels (median [IQR]: 6.3[3.8-7.7] logIU/mL and 14,460[5,207-21,118] IU/mL, respectively) and low HBV viremia (serum HBV-DNA detectable in 48% with median [IQR]: 50[34-214] IU/ml). Median (IQR) ALT was 72(52-102) U/L, half of patients had fibrosis score>F5.

Median (IQR) intrahepatic HDV-RNA was 787(1-2913) copies/1000cells, positively correlated with serum HDV-RNA (Rho=0.63, P=0.05).

Regarding HBV intrahepatic reservoir, median (IQR) cccDNA and pgRNA were 3(0.1-24) and 8(1-147) copies/1000cells, respectively. Despite a limited HBV reservoir, we observed an abundant production of HBs transcripts (median [IQR] total HBsRNAs: 6,028[409-19,137] copies/1000 cells), positively correlated with serum HBsAg (Rho=0.54; P=0.04).

Notably, 99% of HBs transcripts derived from integrated HBV-DNA, with a limited contribution of cccDNA transcriptional activity, supporting HBV-DNA integration as the main HBsAg source in HBeAg-negative CHD.

Finally, intrahepatic HDV-RNA levels did not differ according to HBV reservoir size (median[IQR]: 787[1-5,495] and 880[1-3,338] copies/1000cells in cccDNA<3 and >3copies/1000cells, p=0.9), while markers of HBV activity were significantly lower in patients with more restricted HBV reservoir (median[IQR]: 1[1-10] vs 147[9-406] copies/1000cells for pgRNA and 0.3[0.2-1] vs 73[7-243] copies/1000cells for cccDNA-derived HBs transcripts in cccDNA<3 vs >3copies/1000cells, p<0.01 for both).
**Conclusion:** Pathways sustaining HDV activity act independently from the extent of intrahepatic HBV reservoir and are fueled by an abundant production of HBs transcripts, mainly derived from integrated HBV-DNA. These issues are crucial for deciphering mechanisms underlying HDV persistence, that could jeopardise anti-HDV therapeutic strategies success.

doi: 10.1016/j.dld.2024.01.045

## T-14

### Parenchymal renal cell carcinoma is associated with occult hepatitis B virus infection

D. Lombardo [1], M. Rossanese [2], C. Musolino [2], G. Raffa [1], G. Caminiti [1], C. Saitta [1], G. Mucciardi [3], M. Chiappetta [1], M. Martini [2], A. Ieni [2], V. Ficarra [1], G. Raimondo [1], T. Pollicino [1]

[1] *Department of Clinical and Experimental Medicine, University Hospital G. Martino Messina, Messina*
[2] *Department of Human Pathology, University Hospital G. Martino Messina, Messina*
[3] *University Hospital G. Martino Messina, Messina*

**Introduction:** Evidence exists of a significant association between chronic kidney disease and hepatitis B virus (HBV) infection, even in cases with occult HBV infection (OBI), which is the long-lasting persistence of HBV genomes in HBsAg-negative individuals. Furthermore, a higher prevalence of renal cell carcinoma (RCC) was reported in HBsAg-positive subjects, but no data are available on RCC in OBI subjects.
**Aims:** of this study were (1) to evaluate the prevalence of OBI in patients with RCC and (2) to investigate the molecular virological features of HBV in tumour and non-tumour kidney tissues
**Methods:** We prospectively enrolled all consecutive patients who underwent nephrectomy for malignant renal tumours at the Urology Unit of the Messina University Hospital from April 2019 to May 2021. In analogy, patients who received nephrectomy for kidney benign tumours were enrolled as control group (CG). Tumour and adjacent non-tumour tissues were collected at the end of surgery. Each specimen was divided in two parts, one for histology and the

other immediately frozen and stored for molecular analyses. Serum samples were collected and stored at -80°C from each case. DNA extracted from the tissues and paired serum samples were tested for OBI by a very sensitive nested-PCR.
**Results:** A total of 83 HBsAg-negative patients (54 RCC, 29 CG) were included in the study. All the patients had no clinical, biochemical or ecografic evidence of liver disease. OBI was detected in 19/54 (35.2%) RCC patients, in 1/29 (3.4%) CG patients (P=0.001), and in any of the sera collected from RCC and CG patients. Thirty-six/54 RCC cases had clear cell renal cell carcinoma (ccRCC) and 18/54 had papillary or chromophobe RCC. OBI was detected in 9/36 (25%) RCC and in 10/18 (55.5%) non-ccRCC cases (P=0.03). Further molecular analyses showed the presence of the replicative intermediate HBV cccDNA minichromosome in renal tissues from OBI cases
**Conclusions:** OBI is significantly associated with RCC, and particularly with the non-ccRCC histotype. The detection of replication competent HBV cccDNA both in tumour and non-tumour kidney tissues suggests that HBV may potentially replicate in renal cells

doi: 10.1016/j.dld.2024.01.046

## T-15

### Bulevirtide monotherapy prevents liver decompensation and reduces mortality in patients with HDV-related cirrhosis: a case control study with propensity score weighted analysis

E. Degasperi [1], A. De Silvestri [2], M.P. Anolli [1], D. Sambarino [1], M. Borghi [1], R. Perbellini [1], F. Facchetti [1], R. Soffredini [1], S. Monico [1], V. De Ledinghen [3], S. Metivier [4], M. Jachs [5], T. Reiberger [5], G. D'Offizi [6], C. Dietz-Fricke [7], G. Papatheodoridis [8], M.R. Brunetto [9], G. Verucchi [10], A. Ciancio [11], F. Zoulim [12], A. Mangia [13], M.N. Hilleret [14], T. A Santantonio [15], N. Coppola [16], A. Pellicelli [17], B. Roche [18], X. Causse [19], L. D'Alteroche [20], J. Dumortier [21], N. Ganne [22], F. Heluwaert [23], I. Ollivier [24], A. Loglio [25], M. Viganò [26], A. Federico [27], F. Pileri [28], M. Maracci [29], M. Tonnini [30], J.P. Arpurt [31], K. Barange [32], E. Billaud [33], S. Pol [34], A. Gervais [35], A. Minello [36], I. Rosa [37], M. Puoti [38], P. Lampertico [1,39]

[1] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Clinical Epidemiology and Biometry Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy*
[3] *Hepatology Department, Haut-Lévêque Hospital, Bordeaux, France*
[4] *Hepatology Unit, CHU Rangueil, 31059, Toulouse, France*
[5] *Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria*
[6] *Division of Infectious Diseases - Hepatology, Department of Transplantation and General Surgery, Istituto Nazionale per le Malattie Infettive "L. Spallanzani" IRCCS, Rome Italy*
[7] *Department of Gastroenterology, Hepatology Infectious Diseases and Endocrinology at Hannover Medical School, Hannover, Germany*
[8] *Department of Gastroenterology, General Hospital of Athens "Laiko", Medical School of National & Kapodistrian University of Athens, Greece*
[9] *Department of Clinical and Experimental Medicine, University of Pisa and Hepatology Unit, University Hospital of Pisa, Pisa, Italy*
[10] *Department of Medical and Surgical Sciences, Unit of Infectious Diseases, "Alma Mater Studiorum" University of Bologna, S. Orsola-Malpighi Hospital, Bologna, Italy*
[11] *Department of Medical Sciences, University of Turin, Gastroenterology Division of Città della Salute e della Scienza of Turin, University Hospital, Turin, Italy*
[12] *Hepatology Department, Université Claude Bernard Lyon 1; Hospices Civils de Lyon; INSERM Unit 1052 - CRCL; Lyon, France*
[13] *Liver Unit, Fondazione IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Italy*
[14] *Service d'hépato-gastro-entérologie, CHU Grenoble-Alpes, Grenoble, France*
[15] *Department of Medical and Surgical Sciences, Infectious Diseases Unit, University of Foggia, Foggia, Italy*
[16] *Department of Mental Health and Public Medicine - Infectious Diseases Unit, University of Campania Luigi Vanvitelli, Naples, Italy*
[17] *Liver Unit, San Camillo Hospital, Department of Transplantation and General Surgery, Rome, Italy*
[18] *Hepato-Biliary Center, AP-HP Hôpital Universitaire Paul Brousse, Paris-Saclay University, Research INSERM-Paris Saclay Unit 1193, Villejuif, France*
[19] *Hôpital de la Source Orleans, France*
[20] *Service d'Hépato-Gastroentérologie CHU de Tours, France*
[21] *Department of Digestive Diseases, Hospices Civils de Lyon, Edouard Herriot hospital, France; Claude Bernard Lyon 1 University, France*
[22] *AP-HP, Avicenne Hospital, Hepatology Department, F-93000 Bobigny, France*
[23] *Centre Hospitalier Annecy Genevois, 74000, Annecy, France*
[24] *Department of Hepatogastroenterology, CHU de Caen Normandie, Caen, France*
[25] *Gastroenterology, Hepatology and Transplantation Division, ASST Papa Giovanni XXIII, Bergamo, Italy*
[26] *Division of Hepatology, Ospedale San Giuseppe, Italy*
[27] *Division of Hepatogastroenterology, Department of Precision Medicine, Università della Campania "Luigi Vanvitelli", Naples, Italy*
[28] *Division of Internal Medicine and Center for Hemochromatosis, University of Modena and Reggio Emilia, Modena, Italy*
[29] *Institute of Infectious Diseases and Public Health, Università Politecnica delle Marche, Ancona, Italy*
[30] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[31] *Department of Gastroenterology, CH d'Avignon, Avignon, France*
[32] *Department of Gastroenterology, Toulouse University Hospital, Toulouse, France*
[33] *Université de Nantes, INSERM UIC 1413, Department of Infectious Diseases, CHU Hôtel Dieu, Nantes, France*
[34] *Université Paris Cité; Assistance Publique des Hôpitaux de Paris, Hôpital Cochin, Hepatology/Addictology department, Paris, France*
[35] *Assistance Publique des Hôpitaux de Paris, Hôpital Bichat Claude Bernard, Service des Maladies Infectieuses et Tropicales, Paris, France*
[36] *CHU Dijon, Service d'Hépato-gastroentérologie et oncologie digestive, Inserm EPICAD LNC-UMR1231, Université de Bourgogne-Franche Comté, Dijon, France*
[37] *Service d'hépatogastroentérologie, Centre Hospitalier Intercommunal, Créteil*
[38] *School of Medicine and Surgery University of Milano Bicocca*
[39] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

**Background and aim:** Bulevirtide (BLV) monotherapy yields high rates of virological and biochemical response in hepatitis Delta (HDV) cirrhotic patients, however clinical benefits on hard outcomes remain unknown.
**Methods:** Patients with HDV-related cirrhosis treated with BLV monotherapy in a retrospective multicenter European study (SAVED) were compared with untreated HDV cirrhotic patients enrolled in a previous cohort study (Romeo, Gastroenterology 2009). Liver-related events (LRE: HCC, decompensation) and overall mortality were compared by inverse probability treatment weighting (IPTW) analysis.
**Results:** The BLV-treated cohort included 176 patients (median follow-up: 15 [2-46] months): at BLV start, median age was 50

(19-82) years, 59% men, ALT 77 (23-1,074) U/L, albumin 3.9 (2.8-4.9) g/dL, 100% CPT score A, 55% with varices. The untreated cohort included 140 patients (median follow-up: 91 [3-359] months): at study entry, median age was 40 (18-66) years, 78% men, ALT 102 (11-3,054) U/L, albumin 4.0 (2.0-5.2) g/dL, 94% CPT score A, 46% with varices. Overall, the 2-year cumulative probabilities of LRE were 6.9% (95% CI 3-11%) in the BLV-treated cohort *vs.* 15.7% (95% CI 9-22%) in untreated patients (p=0.02): 4.9% *vs.* 6.7% for de-novo HCC (p=0.45) and 2.0% *vs.* 9.1% for decompensation (p=0.01), respectively. The 2-year probability of overall mortality was 1.2% (95% CI 0.3-3%) *vs.* 3% (95% CI 0.5-6%) in BLV-treated *vs.* untreated patients (p=0.13). By IPTW analysis adjusted for confounding baseline factors and competing mortality risks, the BLV-treated cohort had a significantly decreased risk of all-type liver-related events (HR 0.38; 95% CI 0.24-0.60, p<0.0001), decompensation (HR 0.15; 95% CI 0.06-0.36, p<0.0001) and mortality (HR 0.27; 95% CI 0.08-0.93, p=0.04) compared to untreated patients. Conversely, the HCC risk was similar (HR 0.76; 95% CI 0.42-1.40, p=0.38).
**Conclusions:** In HDV cirrhotic patients, a 2-year course of BLV monotherapy resulted in lower risks of decompensation and mortality, but did not impact HCC risk.

doi: 10.1016/j.dld.2024.01.047

## T-16

### Kinetics of the three HBsAg forms along with HDV-RNA predict virological and biochemical responses in chronic hepatitis delta patients treated with bulevirtide for 48 weeks

S. D'Anna [1], R. Salpini [2], E. Degasperi [3], L. Duca [1], M.P. Anolli [3], L. Piermatteo [2], D. Sambarino [3], M. Borghi [3], F. Facchetti [3], F. Ceccherini-Silberstein [1], R. Perbellini [3], P. Lampertico [3,4], V. Svicher [1,2]

[1] *Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy*
[2] *Department of Biology, University of Rome Tor Vergata, Rome, Italy*
[3] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[4] *Department of Pathophysiology and Transplantation, CRC "A. M. and A. Migliavacca" Center for Liver Disease, University of Milan, Milan, Italy*

**Introduction & Aim:** HDV exploits HBV surface protein (HBsAg) for releasing of progeny and entry into hepatocytes. HBsAg consists of three different proteins: Large-HBsAg (L-HBs), Middle-HBsAg (M-HBs) and small-HBsAg (S-HBs). L-HBs is predominantly present in virions and mediates binding to NTCP receptor. Here, we investigate the kinetics of HBs-forms under bulevirtide-treatment (BLV).
**Method:** 28 consecutive patients with HDV-related compensated cirrhosis starting BLV-monotherapy were enrolled in this retrospective/longitudinal study, all under effective NUC-treatment at entry. L-HBs, M-HBs and S-HBs were quantified by *ad-hoc* ELISAs in baseline and week 48 (W48) samples (Beacle). HDV-RNA was quantified by Robogene. Virological response was defined as HDV-RNA undetectable or >2log decline compared to baseline, biochemical response as ALT normalization.
**Results:** At baseline, median(IQR) age was 53(40-63) years, liver stiffness 19.4(15.4-32.9) kPa, ALT 106(77-147) U/l, serum HDV-RNA 5.4(4.4-6.0) logIU/ml and HBsAg levels 3.7(3.4-4.9) logIU/ml. Pre-treatment median(IQR) levels of S-HBs, M-HBs and L-HBs were 3999(1482-7184), 1032(305-2222) and 6(2-14) ng/ml, respectively. At W48, serum HDV-RNA declined by 3.1(1.8-3.7) logIU/ml while virological and biochemical responses were observed in 71% and 75% of patients, respectively. S-HBs, M-HBs and L-HBs decreased of >10% respect to baseline in 57%, 54% and 39% of patients with a median (IQR) decline of 1095(839-2403), 145(39-350) and 10(4-15) ng/ml, respectively.

HDV-RNA<5logIU/ml at baseline was associated with HDV-RNA<100IU/ml at W48 (75% with vs 25% without, P=0.02). A similar correlation was observed for L-HBs<9 ng/ml at baseline (62.5% with vs 25% without, P=0.05). Notably, the combination of pre-treatment L-HBs<9ng/ml + HDV-RNA<5logIU/ml was the best predictor for achieving HDV-RNA<100IU/ml (PPV:87.5 % and NPV:70%; P=0.01). This combination showed also the best diagnostic accuracy for predicting HDV-RNA<100IU/ml plus ALT normalization (PPV:75%; NPV:75%; P=0.03).
**Conclusion:** Quantification of L-HBs along with serum HDV-RNA may reflect the burden of circulating infectious virions, possibly providing a new tool to identify patients more likely to respond to BLV-monotherapy.

doi: 10.1016/j.dld.2024.01.048

## T-17

### Baseline predictors of virological and biochemical responses in HDV compensated cirrhotic patients treated with Bulevirtide monotherapy (HEP4Di study)

E. Degasperi [1], M.P. Anolli [1], G. D'Offizi [2], M.R. Brunetto [3], G. Verucchi [4], A. Ciancio [5], A. Mangia [6], T.A. Santantonio [7], N. Coppola [8], A. Pellicelli [9], A. Loglio [10], M. Viganò [11], A. Federico [12], F. Pileri [13], M. Maracci [14], M. Tonnini [15], M. Puoti [16], P. Lampertico [1,17]

[1] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Division of Infectious Diseases - Hepatology, Department of Transplantation and General Surgery, Istituto Nazionale per le Malattie Infettive "L. Spallanzani" IRCCS, Rome Italy*
[3] *Department of Clinical and Experimental Medicine, University of Pisa and Hepatology Unit, University Hospital of Pisa, Pisa, Italy*
[4] *Department of Medical and Surgical Sciences, Unit of Infectious Diseases, "Alma Mater Studiorum" University of Bologna, S. Orsola-Malpighi Hospital, Bologna, Italy*
[5] *Department of Medical Sciences, University of Turin, Gastroenterology Division of Città della Salute e della Scienza of Turin, University Hospital, Turin, Italy*
[6] *Liver Unit, Fondazione IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo, Italy*
[7] *Department of Medical and Surgical Sciences, Infectious Diseases Unit, University of Foggia, Foggia, Italy*
[8] *Department of Mental Health and Public Medicine - Infectious Diseases Unit, University of Campania Luigi Vanvitelli, Naples, Italy*
[9] *Liver Unit, San Camillo Hospital, Department of Transplantation and General Surgery, Rome, Italy*
[10] *Gastroenterology, Hepatology and Transplantation Division, ASST Papa Giovanni XXIII, Bergamo, Italy*
[11] *Division of Hepatology, Ospedale San Giuseppe, Italy*
[12] *Division of Hepatogastroenterology, Department of Precision Medicine, Università della Campania "Luigi Vanvitelli", Naples, Italy*
[13] *Division of Internal Medicine and Center for Hemochromatosis, University of Modena and Reggio Emilia, Modena, Italy*
[14] *Institute of Infectious Diseases and Public Health, Università Politecnica delle Marche, Ancona, Italy*
[15] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[16] *School of Medicine and Surgery University of Milano Bicocca*
[17] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

**Background:** Bulevirtide (BLV) has received EMA approval for treatment of compensated chronic hepatitis Delta (CHD), however predictors of response are still unknown.
**Methods:** Consecutive CHD patients with cirrhosis treated with BLV 2 mg/day monotherapy were enrolled in a retrospective multicenter Italian real-life study (HEP4Di). Features at BLV start and on-treatment were collected. Virological response (HDV RNA undetectable or ≥ 2-log decline *vs.* baseline), biochemical response (ALT <40 U/L) and combined response (biochemical + virological) were assessed. HDV RNA was quantified locally.
**Results:** 97 CHD patients with cirrhosis receiving BLV monotherapy up to 96 weeks were included: at BLV start, median age was 52 (29-77) years, 53% males, 100% CPT score A, 52% with varices, 19% with previous ascites, 11% with active HCC, 97% on NUC. Median ALT were 80 (26-1,074) U/L, liver stiffness measurement (LSM) 17.4 (6.4-68.1) kPa, platelets 83 (17-330) x$10^3$/$mm^3$, HBsAg 3.7 (0.8-4.5) Log IU/mL and HDV RNA 5.1 (1.2-7.6) Log IU/mL. At BLV treatment weeks (W) W24, W48, W72 and W96, rates of virological response were 53%, 70%, 75% and 80%, respectively, and HDV RNA was undetectable in 16%, 15%, 38% and 33% patients. Biochemical response and combined response were achieved by 65%, 74%, 81% 67% and 38%, 59%, 63%, 67%, respectively. By univariate logistic regression analysis, baseline viremia was the only predictor of virological response: indeed, HDV RNA levels <5 LogIU/mL predicted HDV RNA <1000 IU/mL (OR 3.33, 95% CI 1.19-9.26, p=0.02) and <100 IU/mL (OR 7.30, 95% CI 2.49-21.41, p=0.0003) at week 24, while HDV RNA levels <5 LogIU/mL were associated with HDV RNA undetectability at week 48 (OR 2.77, 95% CI 1.05-7.29, p=0.04). Conversely, none of the baseline features predicted biochemical or combined response.
**Conclusions:** In CHD patients with compensated cirrhosis receiving BLV monotherapy, baseline viremia is the only factor associated with virological response.

doi: 10.1016/j.dld.2024.01.049

## T-18

### Quantification of plasma HDV RNA in untreated and Bulevirtide-treated patients with CHD: a comparison between Robogene 2.0, Eurobioplex and Altostar

M.P. Anolli [1], S. Uceda Renteria [2], E. Degasperi [1], F. Facchetti [1], D. Sambarino [1], M. Borghi [1], R. Perbellini [1], R. Soffredini [1], S. Monico [1], F. Ceriotti [2], P. Lampertico [1,3]

[1] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Virology Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[3] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

**Background and Aim:** Accurate HDV-RNA quantification is crucial for diagnosis and management of chronic hepatitis Delta, yet variability between assays exist. We compared three methods to quantify HDV-RNA in untreated and Bulevirtide (BLV)-treated CHD patients.
**Methods:** Frozen plasma from untreated and BLV–treated CHD patients were tested in a single-center retrospective study: Robogene HDV-RNA Quantification Kit 2.0 (Roboscreen GmbH; LOD 6 IU/mL on 7500 Fast Real-Time PCR System [Applied Byosystem]), EurobioPlex HDV PCR quantitative (Eurobio Scientific, LOD 100 IU/m) on CFX96$^{TM}$ real-time PCR detection system [Bio-Rad]) and AltoStar HDV RT-PCR Kit 1.5 (Altona Diagnostics; RUO test, estimated LOD <10 IU/mL).
**Results:** Overall, 429 plasma samples from 130 CHD (69 untreated and 61 BLV-treated) patients were studied. Median HDV-RNA were higher with Robogene than EurobioPlex [3.78 (0.70-7.99) *vs.* 4.69 (2.00-8.19) Log IU/mL, p<0.0001]. Compared to Robogene 2.0, EurobioPlex reported similar HDV-RNA (Δ ± 0.5 Log) in 66 (28%) patients but higher >0.5 Log in 160 (69%). Viremia was lower with Robogene than AltoStar [3.32 (0.70-7.37) *vs.* 3.91 (0.19-7.54) Log IU/mL, p<0.0001]. AltoStar reported HDV-RNA levels >0.5 Log in 127 (52%). Virological response at week 24 (Robogene *vs.* Eurobio and AltoStar) and 48 (Robogene *vs.* AltoStar) did not differ. HDV-RNA undetectability rates at week 24 were 11% *vs.* 33% with Robogene *vs.* EurobioPlex, and 11% *vs.* 3% Robogene *vs.* AltoStar. At week 48, 18% *vs.* 4% Robogene *vs.* AltoStar. 47 on-treatment samples were analyzed with the three tests: HDV-RNA levels were 3.04 (0.70-6.20) IU m/l *vs.* 3.62 (2.00-7.12) *vs.* 3.37 (0.28-6.45) IU/mL with Robogene *vs.* EurobioPlex *vs.* AltoStar, respectively (p=0.36). At week 72 HDV-RNA was undetectable in 42%, 83% and 25% of patients, respectively.
**Conclusions:** HDV-RNA levels quantified by EurobioPlex and Altostar were 1 and 0.5 logs higher than Robogene 2.0, respectively. HDV-RNA undetectability rates during BLV differed according to the method.

doi: 10.1016/j.dld.2024.01.050

## T-19

### Hepatitis B surface antigen positive donors for liver recipients with hepatocellular carcinoma: a single centre experience

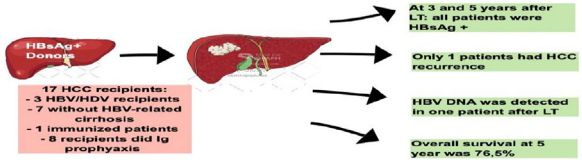
B. Magro [1], A. Lombardo [2], D. Pagano [1], V. Di Marco [2], C. Cammà [2], S. Gruttadauria [1,3]

[1] *Department for the Treatment and Study of Abdominal Diseases and Abdominal Transplantation, IRCCS - ISMETT (Istituto di Ricovero e Cura a Carattere Scientifico - Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione), UPMC (University of Pittsburgh Medical Center)*
[2] *Section of Gastroenterology and Hepatology, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, PROMISE, University of Palermo, Palermo, Italy*
[3] *Department of Surgery and Medical and Surgical Specialties, University of Catania, Catania, Italy*

**Introduction:** Due to the severe shortage of the donor pool, the use of hepatitis B surface antigen-positive donors is a possible strategy to increase the donor pool, but there are few data about the outcomes in liver recipients with hepatocellular carcinoma (HCC) and their recurrence rate.
**Aim: The** aim of this study is to evaluate the impact of HBsAg poisitive donors in liver recipients transplanted for HCC
**Methods:** Patients undergoing liver transplantation (LT) between January, 2004, and November 2022, were retrospectively evaluated. 17 patients (1,5%) with HCC, received the graft from hepatitis B surface antigen positive (HBsAg)-positive deceased donors
**Results:** All patients were male and Milan IN. Median time of follow up was 63±5 months. Median MELD was 16. Seven (41%) recipients had not an HBV-related liver disease. Only one patient before LT had hepatitis B surface antibody. Three patients had an HBV/HDV cirrhosis. In all recipients HBV DNA was suppressed at the time of LT. Eight (47%) patients did a prophylaxis with HBV-specific immunoglobulins after LT.

At 1 – 3 and 5 year in all the recipients, hepatitis B surface antigen positivity was recorded. Only one patient developed hepatitis B surface antibodies but was immunized before LT.

HBV DNA was detected in one patient at 1 and 3 years, but they were responsive to antiviral treatment. Only one patient had HCC recurrence. Overall survival at 1-3 and 5 year was 76,5%.
**Conclusions: We** suggest that the use of HBsAg positive donors is safe and in our cohort of HCC transplanted patients, only one experienced HCC recurrence. Moreover, it would be fundamental to immunize all patients before LT.




doi: 10.1016/j.dld.2024.01.051

## T-20

### Improvement of non-invasive fibrosis tests in HDV cirrhotic patients with clinically significant portal hypertension responding to Bulevirtide monotherapy

E. Degasperi [1], M.P. Anolli [1], S. Uceda Renteria [2], D. Sambarino [1], M. Borghi [1], R. Perbellini [1], F. Facchetti [1], S. Monico [1], M. Fraquelli [3], A. Costantino [3], F. Ceriotti [2], P. Lampertico [1,4]

[1] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Virology Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[3] *Division of Gastroenterology and Endoscopy, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[4] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

**Background and aim:** Non-invasive fibrosis tests (NITs) showed significant improvement following antiviral treatment in HBV or HCV-infected patients, whereas data in chronic hepatitis Delta under Bulevirtide (BLV) treatment are lacking.
**Methods:** Consecutive HDV cirrhotic patients with clinically significant portal hypertension (CSPH) according to Baveno VII criteria with a virological response (≥ 2 Log HDV RNA decline *vs.* baseline) to BLV monotherapy 2 mg/day up to 96 weeks were enrolled in this single-center study. AST to Platelet Ratio Index (APRI), Fibrosis-4 (FIB-4) Index and liver stiffness-spleen size-to-platelet ratio score (LSPS) were calculated from clinical variables recorded on-therapy. Liver (LSM) and spleen (SSM) stiffness measurement performed by transient elastography (Fibroscan®) and point shear-wave elastography (ElastPQ) were assessed every 24 weeks.
**Results:** 46 HDV cirrhotic patients with a virological response to BLV were included: pre-treatment, median age was 52 (30-77) years, 59% males, ALT 98 (30-1,074) U/L, platelets 78 (17-217) x$10^3$/$mm^3$, 54% with varices, spleen 15 (9-25) cm, CPT-A 100%, HDV RNA 5.2 (2.4-6.9) Log IU/mL. During BLV monotherapy, serological NIT significantly improved at all timepoints, APRI from baseline 3.5 (0.6-16.5) to 1.2 (0.3-4.5) at week 96 (p<0.001), and FIB-4 from 6.1 (1.3-28.1) to 4.1 (1.2-9.0) (p=0.003). LSM decreased from baseline 17.2 (6.4-68.1) to 13.8 (5.4-54.3) kPa at week 48 (p=0.001) and LSPS from baseline 4.1 (0.5-23.7) to 3.8 (0.3-14.3) at week 48 (p=0.001), whereas no other significant changes were observed throughout weeks 48 and 96. Conversely, other NITs did not significantly modify (baseline *vs.* week 96): liver ElastPQ 14.3 (4.2-35.2) *vs.* 10.9 (7.0-22.3) kPa (p=0.54); SSM 50.3 (19.7-100) *vs.* 47.9 (21.2-97.9) kPa (p=0.69), Spleen ElastPQ 36.9 (12.8-114) *vs.* 30.6 (17.4-51.8) kPa (p=0.31).
**Conclusions:** In HDV compensated cirrhotic patients with CSPH and a virological response to BLV monotherapy, long-term treatment led to a significant improvement of serological fibrosis NITs, liver stiffness and LSPS.

doi: 10.1016/j.dld.2024.01.052

## T-21

### Bulevirtide progressively improves liver function in liver transplant candidates with advanced HDV cirrhosis and severe portal hypertension

A. Loglio [1], M. Viganò [1,2], L. Goisis [3], E. Farina [1], M.E.G. Arosio [3,4], P. Marra [5,6], C. Farina [4,6], S. Fagiuoli [1,2]

[1] *Gastroenterology, Hepatology and Transplantation Division, ASST Papa Giovanni XXIII, Bergamo, Italy*
[2] *Gastroenterology, Department of Medicine, University of Milano Bicocca, Milan, Italy*
[3] *Biobank, ASST Papa Giovanni XXIII, Bergamo, Italy*
[4] *Microbiology and Virology Laboratory, ASST Papa Giovanni XXIII, Bergamo, Italy*
[5] *Radiology Department, ASST Papa Giovanni XXIII, Bergamo, Italy*
[6] *University of Milano Bicocca, Milan, Italy*

**Introduction:** Chronic Hepatitis Delta (CHD) is the most severe viral hepatitis, remaining a prevalent indication for liver transplantation (LT). Bulevirtide (BLV) treatment has been approved for compensated CHD but data in patients with most advanced liver disease are lacking.
**Aim:** To describe BLV efficacy and safety in CHD patients in the LT waiting-list.
**Material and Methods:** All consecutive CHD patients indicated for LT due to advanced cirrhosis at the LT Centre of Bergamo who started BLV were included in this prospective study. HDV-RNA was quantified by Robogene 2.0 (LLQ 6 IU/mL).
**Results:** All three Caucasian non-HCC patients with neither HCV/HIV infections nor alcohol use [2 male, 39 (31-43) years, CPT B8 (B7-B9), MELD 17 (14-18), qHBsAg 4,320 (2,336-6,124) IU/mL, HDV RNA 55,238 (27-355,260) IU/mL, AFP 9 (1-10) ng/mL] were on effective ETV treatment. All patients had severe portal hypertension [platelets 27 (26-38)*$10^3$/mmc, spleen 21 (17-26) cm, liver and spleen stiffness 25 (17-30) and 44 (28-45) kPa] with esophageal varices, previously band-ligated in 2. During the median 16 (16-24) weeks of BLV treatment no adverse events occurred, all patients achieved virological response (≥ 2 $Log_{10}$ HDV-RNA decline) including two with undetectable HDV-RNA. CPT and MELD remained stable [B8 (B7-B8) and 16 (14-17)], there was an improvement in quality of life (EQ-5D-3L and VAS) and on LFTs compared to baseline [ALT 35 (30-50) *vs* 61 (35-79) U/L, AST 41 (32-74) *vs* 67 (35-105) U/L, bilirubin 2.5 (2.6-3.1) *vs* 2.5 (2.5-4.7) mg/dL, albumin 3.4 (3.2-3.7) *vs* 3.3 (3.2-3.4) g/dL, PCHE 3,051 (2,232-6,081) *vs* 2,498 (2,250-5,336) U/L, INR 1.6 (1.4-1.8) *vs* 1.7 (1.4-1.9)] and an asymptomatic increase of biliary acids: 112 (102-138) vs 55 (22-69) µmol/L.
**Conclusions:** BLV use in most advanced CHD cirrhotic patients is safe and showed a virological response and a progressive biochemical and clinical improvement postponing the need for LT.

doi: 10.1016/j.dld.2024.01.053

## T-22

### Lessons from HCV screening 1969-1989: moving to reflex HCV testing and multiparametric US of the liver for the goal of microelimination

E. Garlatti Costa [1], D. Little [2], D. Villalta [3], S. Lalla [4], R. Maso [4], M. Da Re [3], G. Basaglia [5], S. Grazioli [1]

[1] *Department of Internal Medicine, Pordenone, Italy*
[2] *Office of Chief Medical Officer, Pordenone, Italy*
[3] *Department of Immunology and Allergology, Pordenone, Italy*
[4] *Screening Unit, Pordenone, Italy*
[5] *Department of Microbiology and Virology, Pordenone, Italy*

**Introduction:** WHO has launched a global programme to achieve HCV elimination targets for 2030. However, the HCV care plan can fail because of difficulties in linkage to care and loss to follow-up after the first visit.
**Aim:** To evaluate the feasibility of an innovative model based on reflex HCV testing and a multiparametric US (mpUS) for patients screened from the 1969-1989 birth-cohort.
**Materials and methods:** All subjects were screened with reflex HCV testing. Viremic patients were alerted from the Screening Team and scheduled for secondary level biochemical tests and a hepatological evaluation including: mpUS, measurement of 2D-SWE, UGAP (LOGIQ E10), detection focal liver lesions (FLL) and characterization of FLL with CEUS. All patients were examined by a sonographer-hepatologist.
**Results:** Between April 2023 and November 2023, 21.891 subjects were tested and 23 patients (0.1%) (50% females, 46% non-Italian) with chronic hepatitis C emerged. HBV-HIV co-infections were not detected. Co-factors: alcohol (23%), metabolic (19%). 73% of patients were unaware of infection. Median 2D-SWE values 6.0 (2.8-15.3) kPa and median UGAP values 0.67 (≥S1). B-mode US revealed: steatosis in 12 pts, liver cirrhosis in one patient. US Doppler showed a case of portal hypertension. FLL were consistent with typical hemangiomas in 4 patients; simple cysts in 2 patients. CEUS identified atypical hemangioma in one patient and steatosis sparing areas in another. Adopting mpUS and reflex HCV testing, 46 Hospital visits were avoided. All patients started DAAs simultaneously with the first visit that included a mpUS. A follow-up ultrasound for HCC surveillance was scheduled for patients with cirrhosis, F3 and SLD with diabetes.
**Conclusions:** Our “One-stop-shop” model is an effective solution for microelimination. Laboratories should abandon the two-step diagnostic algorithm for HCV infection. Hepatologists should improve ultrasound skills and utilize mpUS as a new tool for patients with liver disease.

doi: 10.1016/j.dld.2024.01.054

## T-23

### Liver-related outcomes in patients with HCV compensated liver cirrhosis after SVR: results from 5-years of follow-up

F. Morisco [1], A. Federico [2], M. Marignani [3], F.L. Lombardo [4], V. Cossiga [1], A. De Conte [1], M. Romeo [2], M. Cipullo [2], P. Begini [3], F. Gioli [3], T. Stroffolini [5]

[1] *Department of Clinical Medicine and Surgery, Departmental Program “Diseases of the liver and biliary system”, University of Naples “Federico II”, Naples, Italy*
[2] *Hepato-Gastroenterology Unit, University of Campania Luigi Vanvitelli, Naples, Italy*
[3] *Department of Digestive and Liver Disease, S. Andrea University Hospital, Rome, Italy*
[4] *National Center for Disease Prevention and Health Promotion, Italian National Institute of Health, 00161 Rome, Italy*
[5] *Department of Tropical and Infectious Diseases, Policlinico Umberto I, Rome, Italy*

**Background and Aim:** In cirrhotic patients with HCV infection, the clinical challenge for physicians after achieving sustained virological response (SVR) is to identify the subset of patients at-risk of liver-related event (LRE). The aim is to evaluate incidence of and risk factors for LRE in a cohort of advanced chronic liver disease (ACLD) patients treated with DAA, during a 5-years follow-up after SVR.
**Methods:** A prospective multicenter study was conducted in 3 Italian centers. Consecutive patients with HCV-ACLD starting DAA-therapy between September 2014 and June 2018 were enrolled. Patients were followed for a mean period of 4.6 years after achieving SVR12. The at-risk-period for each subject was defined by the time from the SVR12 until the end of follow-up or the onset of event. Cumulative and separate analysis were made according to the development of LRE.
**Results:** A total of 575 ACLD patients achieving SVR12 were followed-up for 5 years. The male/female ratio was 1.1 and the mean age was 64.1±12 years. Nearly all subjects (94.4%) belonged to the Child-Pugh A stage. The mean liver stiffness (LSM) at baseline was 19.2 kPa. Overall, 98 (17%) patients developed any type of event and the mortality rate was of 8.8% (33% for liver-related cause). The HCC was the most frequent LRE (7.1%), followed by ascites (5%). The incidence rate was 1.6 (95%CI 1.2-2.2) per 100 person/year for both HCC and liver decompensation. Among pre-treatment variables, LSM≥ 20 kPa (HR 13.5; 95%CI 5.2-35.3) was the only independent predictor of liver decompensation, while liver stiffness≥20 kPa (HR 9.2; 95%CI 4.0-21.3) and male sex (HR 3.6 95% CI 1.6-8.0) both were independent predictors of HCC development.
**Conclusions:** This is the first study with a long-term follow-up of 5 years after SVR. HCC is confirmed as the most frequent LRE and LSM≥20 kPa as strong basal predictor of LRE

doi: 10.1016/j.dld.2024.01.055

## T-24

### Prevalence and Characterization of Resistance Profiles of “Unusual” HCV Subtypes in Italy within the Italian Resistance Network Vironet C

O. El Khalili [1], C. Chenwi [1,2], V.C. Di Maio [3], M. Alkhatib [1], E. Teti [4], A. Bertoli [1,5], S. Paolucci [6], C. Caudai [7], T. Pollicino [8], N. Coppola [9], B. Bruzzone [10], L. Monno [11], S. Khan [1], C. Minichini [9], G. Torre [1,5], L. Bresciani [12], G. Parruti [13], V. Pace Palitti [14], V. Micheli [15], A.P. Callegaro [16], S. Galli [17], V. Di Marco [18], T. Mulas [4], B. Rossetti [19], A.L. Zignego [20], A. Pieri [14], F. Novazzi [6], M. Milana [21], L. Carioti [1], M. Ciotti [5], I. Lenci [21], L. Ansaldo [4], A. Pellicelli [22], A. Moretti [23], F. Morisco [24], R. Gulminetti [25], S. Novati [25], M. Lichtner [26], C. Mastroianni [27], F. Di Lorenzo [28], P. Andreone [29], S. Marenco [30], G. Taliani [31], H. Hasson [32], L.A. Nicolini [33], C.F. Magni [34], C. Paternoster [35], A. Licata [36], S. Babudieri [37], V. Malagnino [4], S. Francioso [21], E. Degasperi [38], G. Quartini [39], C. Pasquazzi [12], N. Iapadre [40], R. Cozzolongo [41], V. Sangiovanni [42], R. Schiavo [43], A. Soria [44], D. Tacconi [45], P.L. Blanc [46], P. Lampertico [38], F. Baldanti [6], G. Raimondo [8], L. Baiocchi [21], M. Andreoni [4], C.F. Perno [2,3], M Puoti [47], L. Sarmati [4], A. Craxì [18], M. Zazzi [48], F. Ceccherini-Silberstein [1], for HCV Virology Italian Resistance Network Vironet C

[1] Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy
[2] Chantal Biya International Reference Centre for Research on HIV and AIDS Prevention and Management (CIRCB)
[3] Unit of Microbiology and Diagnostic Immunology, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
[4] Infectious Diseases, University Hospital of Rome Tor Vergata, Rome, Italy
[5] Microbiology and Virology Unit, University Hospital of Rome Tor Vergata, Rome, Italy
[6] Molecular Virology Unit, Microbiology and Virology department, IRCCS Policlinic Foundation San Matteo, Pavia, Italy
[7] Department of Innovative Experimental Translational and Clinical Research, University of Siena, Siena, Italy
[8] Department of Clinical and Experimental Medicine, University Hospital of Messina, Messina, Italy
[9] Infectious Diseases Unit, University of Campania L. Vanvitelli, Naples, Italy
[10] Hygiene Unit, IRCCS AOU San Martino-IST, Genoa, Italy
[11] Clinic of Infectious Diseases, University of Bari, Bari, Italy
[12] Infectious Diseases, Sant'Andrea Hospital "La Sapienza", Rome, Italy
[13] Infectious Disease Unit, Pescara General Hospital, Pescara, Italy
[14] Internal Medicine Unit, Pescara General Hospital, Pescara, Italy
[15] Clinical Microbiology, Virology and Bioemergencies Diagnosis, L. Sacco University Hospital, Milan, Italy
[16] Department of Laboratory Medicine, ASST Papa Giovanni XXIII, Bergamo, Italy
[17] UOC of Microbiology, IRCCS Policlinico di Sant'Orsola- Bologna, Italy
[18] Gastroenterology, "P. Giaccone" University Hospital, Palermo, Italy
[19] Infectious Diseases, Ospedale della Misericordia, Grosseto, Italy
[20] Department of Internal Medicine, University of Florence
[21] Hepatology Unit, University Hospital of Rome Tor Vergata, Rome, Italy
[22] Hepatology Unit, San Camillo Forlanini Hospital, Rome, Italy
[23] A.C.O. San Filippo Neri, Gastroenterology, Rome, Italy
[24] Department of Clinical Medicine and Surgery, University "Federico II" of Naples, Naples, Italy
[25] Infectious Diseases Unit -Fondazione IRCCS Policlinico San Matteo - University of Pavia, Pavia, Italy
[26] Infectious Diseases Unit, Sapienza University, Polo Pontino, Latina, Italy
[27] Department of Public Health and Infectious Diseases, Policlinico Umberto I, Sapienza University of Rome, Rome, Italy
[28] Infectious Diseases Unit, ARNAS Civico-Di Cristina-Benefratelli, Palermo, Italy
[29] Department of Medical and Surgical Sciences, Maternal-Infantile and Adult Sciences, University of Modena and Reggio Emilia, Modena, Italy
[30] Division of Hepatology, University of Genoa-AOU IRCCS San Martino-IST, Genoa, Italy
[31] Department of Clinical Medicine, Clinic of Tropical Medicine, Sapienza University of Rome, Rome, Italy
[32] Division of Infectious Diseases, IRCCS, Ospedale San Raffaele, Milan, Italy
[33] Department of Health Sciences (DISSAL), University of Genoa; Genoa, Italy
[34] Division of Infectious Diseases, ASST Fatebenefratelli Sacco, Milan, Italy
[35] Infectious Disease Unit, Ospedale di Trento, Trento, Italy
[36] Internal Medicine and Hepatology, PROMISE, University of Palermo, Palermo, Italy
[37] Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy
[38] Division of Gastroenterology and Hepatology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[39] Hepatology Unit, Santa Maria Hospital, Terni, Italy
[40] Infectious Diseases Unit, "S Salvatore" Hospital, L'Aquila, Italy
[41] Division of Gastroenterology, National Institute of Gastroenterology S De Bellis, Castellana Grotte, Bari, Italy
[42] Hospital Cotugno, Naples, Italy
[43] Hospital "Guglielmo da Saliceto" Piacenza, Italy
[44] Clinic of Infectious Diseases, IRCCS San Gerardo dei Tintori, Monza, Italy
[45] Department of Specialized and Internal Medicine, Infectious Diseases Unit, San Donato Hospital, Arezzo, Italy
[46] Infectious Diseases, Ospedale S. Maria Annunziata, Firenze, Italy
[47] Division of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy
[48] Department of Medical Biotechnology, University of Siena, Siena, Italy

**Background:** Recent data showed that "unusual" hepatitis C virus (HCV) subtypes harbor amino-acid residues in NS5A that may confer resistance to direct-acting-antivirals (DAAs) and have lower response to treatment, compared to the most prevalent subtypes. We aimed to characterize prevalence and resistance profiles of HCV unusual-subtypes in Italy.
**Methods:** Clinical and virological data of unusual-subtypes (defined as non-1a/b genotype (GT)1, non-2a/b GT2, non-3a GT3, non-4a/d GT4) were analyzed within VIRONET-C. The prevalence of resistance-associated-substitutions (RASs) and substitutions at resistance-associated-positions (PRASs) was evaluated.
**Results:** Out of 3579 individuals with an available NS3±NS5A±NS5B sequence, 304 (9%; median age 70 years; 58% males) were infected with unusual-subtypes (GT1e/g/i/l=1/4/1/2; GT2c/j=262/3; GT3b/g/h/k=2/1/9/1; GT4c/i/l/m/n/o/r/v=1/1/1/1/3/7/3/1). Subtype distribution varied according to ethnicity: GT2c-GT3h were most prevalent in Italians (90-100%), other unusual-GT3 in Asians (75%), and unusual-GT1-GT4 in Africans (77%). 214 individuals (70%) were DAA-naïve (105 with known outcome after DAA-treatment, 2 failures), while 92 were DAA-failures (30%; Figure1). Patients infected with unusual-GT3-subtypes were more prone to failure (85%, 11/13), followed by GT4 (44%, 8/18), GT2 (26%, 69/265) and GT1 (25%, 2/8; p=0.0001). All failures except three (2 with GT4n, 1 with GT2c) displayed at least one RAS/PRAS in at least one protein (Figure2). Number and type of RAS/PRASs varied by GT/subtype/treatment-exposure. NS5A-RAS/PRASs were most prevalent (93%), followed by NS5B-RAS/PRASs (53%), and NS3-RAS/PRASs (17.2%, even if in GT3 at 71%, p=0.005). NS5A-RASs at position 93 (C/H/F/S) were more prevalent at failure (odds ratio =13, p=0.0001) and detected in GT1e/g, GT3h/k and GT4o/v. Few patients had NS3-RASs only at failure (GT3h: 80R±158V; GT2c: 56Y/H±168V/A and GT4o: 168H/K) and only one GT4o had NS5B-S282C at failure.
**Conclusions:** In our setting, HCV unusual-subtypes were frequent, predominated by GT2c in Italians, and with failure rates highest within GT3. Most DAA-failures carried complex NS5A-RAS patterns. These results advise for closer surveillance and deeper characterization of the impact of unusual-subtypes on DAA-efficacy.

doi: 10.1016/j.dld.2024.01.056

## T-25

### Safety of direct-acting antivirals for Hepatitis C infection and direct oral anticoagulants co-administration: an Italian multicentric study

V. Rosato [1], M. Dallio [2], A. Federico [2], A. Spinetti [3], A. Ciancio [4], M. Milella [5], P. Colombatto [6], M. Brunetto [6], G. D'Adamo [7], E. Rosselli Del Turco [8], P. Gallo [9], A. Falcomatà [9], U. Vespasiani-Gentilucci [9], S. De Nicola [10], N. Pugliese [10], A. Aghemo [10], R. D'Ambrosio [11], P. Lampertico [11,12], A.G. Soria [13], E. Colella [13], D. Mastrocinque [1], E. Claar [1]

[1] *Liver Unit, Ospedale Evangelico Betania, Napoli, Italy*
[2] *Hepatogastroenterology Division, Department of Precision Medicine, University of Campania "Luigi Vanvitelli", 80138 Naples, Italy*
[3] *Division of Infectious and Tropical Diseases, Department of Clinical and Experimental Sciences, University of Brescia and ASST Spedali Civili, 25123, Brescia, Italy*
[4] *Gastro-Hepatoloy Unit, Department of Medical Sciences, University of Turin, 10126, Turin, Italy*
[5] *Clinic of Infectious Diseases, University of Bari, University Hospital Policlinico, Bari, Italy*
[6] *Hepatology Unit and Laboratory of Molecular Genetics and Pathology of Hepatitis Viruses, Reference Center of the Tuscany Region for Chronic Liver Disease and Cancer, University Hospital of Pisa, Via Paradisa 2, 56124, Pisa, Italy*
[7] *UOC General Medicine, Nocera, Salerno, Italy*
[8] *Infectious Disease Unit, Policlinico Sant'Orsola-Malpighi, IRCCS Sant'Orsola, Via Massarenti, 11 - 40138, Bologna, Italy*
[9] *Clinical Medicine and Hepatology Unit, Campus Bio-Medico University, 00128, Rome, Italy*
[10] *Division of Internal Medicine and Hepatology, Department of Gastroenterology, IRCCS Humanitas Research Hospital, Rozzano, Italy*
[11] *ivision of Gatroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy*
[12] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*
[13] *Department of Infectious Diseases, IRCCS San Gerardo dei Tintori, 20900, Monza, Italy*

**Introduction:** Direct oral anticoagulants (DOAC) are generally recommended for the management of thrombosis and atrial fibrillation. As substrates of cytochrome P450 (CYP) 3A4 and/or P-glycoprotein, they are implicated in potential co-medication drug-drug interactions. NS5A/NS5B inhibitors are hepatitis C direct-acting agents (DAAs) that exert a mild inhibition of p-glycoprotein without effects on CYP3A4, but, theoretically, may lead to an increased risk of bleeding. We retrospectively evaluated the risk of vascular adverse events (bleeding and thrombosis) among HCV patients under DOAC/DAAs therapy.
**Methods:** Patients receiving sofosbuvir-based HCV regimens and DOAC concomitantly between may 2017 and April 2023 in 12 Italian medical centers were consecutively enrolled. Baseline characteristics, especially on bleeding risk and liver function, were collected. In order to compare the occurrence of vascular events rate, a cohort of patients that switched to warfarin during antiviral treatment, matched by demographic characteristics (age and sex) in a ratio of 1:1, was enrolled
**Results:** Of 104 total patients, 38(36,5%) were cirrhotic. Sofosbuvir/velpatasvir (78,8%) was the most commonly prescribed DAAs and rivaroxaban (35,6%) most frequent DOAC, followed by apixaban (26,9%), dabigatran(19,2%) and edoxaban (18,3%). Only four minor bleeding events occurred during concomitant DOAC/DAAs treatment, but none caused DAA or DOAC discontinuation. In comparison with 104 matched warfarin patients, no significant differences were found in the rate of clinically relevant bleeding even if a single major bleeding-event leading to anticoagulation and DAAs discontinuation was reported (table). The antiplatelet therapy was only risk factors associated to bleeding events at univariate analysis, hazard ration (HR) 13,3, CI 95% 1,6-10. Moreover, the antiplatelet therapy, evaluated by LOGIT binomial analysis with demographic characteristics, remained statistically associated to bleeding events, leading to a HR of 20,8, CI 95% 1,5-28,6.
**Conclusions:** The concomitant use of NS5A/NS5B inhibitors with DOAC showed a good safety with the same bleeding risk of patients switched to Warfarin. These findings support the use of DOAC during sofosbuvir-based HCV treatment.

**Table.** Characteristics of pts receiving concomitant DAAs for HCV and DOAC or warfarin.

| | DOAC | Warfarin | p-value |
|---|---|---|---|
| N. of pts | 104 | 104 | |
| Age | 80 (71-83) | 78 (69-81) | 0,079 |
| Male | 47 (45,2) | 46 (44,2) | 0,889 |
| Indication for anticoagulation | | | 0,610 |
| Atrial Fibrillation | 79 (76) | 83 (79,8) | |
| Thrombosis | 14 (13,5) | 14 (13,5) | |
| Other | 11 (10,6) | 7 (6,7) | |
| Antiplatelet therapy | 9 (8,7) | 14 (13,5) | 0,269 |
| Hypertension | 67(64,4) | 68 (65,4) | 0,884 |
| Cirrhosis | 38 (36,5) | 33 (31,7) | 0,465 |
| Decompensation | 2 (1,9) | 1 (1) | 0,138 |
| Esophageal varices | 13 (12,6) | 9 (8,7) | 0,356 |
| DAAs treatment | | | 0,460 |
| SOF/VEL | 81(78,6) | 86 (82,7) | |
| SOF/LDV | 22 (21,4) | 18 (17,3) | |
| Creatinine at baseline (mg/dl) | 0,91 (0,79-1,1) | 0,9 (0,77-1,08) | 0,873 |
| Platelets ($10^3$/ml) | 177(132-226) | 174 (142-199) | 0,244 |
| INR | **1,1 (1-1,2)** | **2,1 (1,53-2,56)** | **<0,001** |
| Bilirubin, mg/dl | 0,8 (0,5-1) | 0,9 (0,7-1) | 0,389 |
| Albumin, g/dl | 4 (3,7-4,3) | 3,9 (3,5-4,1) | 0,061 |
| Liver stiffness median, kPa | 9,2 (6,1 – 16,8) | 9,3 (7,1 – 14,7) | 0,979 |
| HAS BLED score >3 | 38 (36,5) | 32 (30,8) | 0,379 |
| SVR 12 | 103 (99) | 103 (99) | 1 |
| Clinical relevant bleeding | 4 | 5 | 0,316 |
| Major bleeding | 0 (0) | 1 (1) | |
| Non-major bleeding | 4 (3,8) | 4 (3,8) | |
| DOAC discontinuation | 0 (0) | 1 (1) | 0,316 |

Median (IQR) for continuous variables and *n* (percentage) for categorical variables.
DAAs: direct antiviral agents; DOAC: direct oral anticoagulants; INR: International normalized Ratio; LDV: Ledipasvir; SOF: Sofosbuvir; SVR 12: Sustained Virological Response at week 12; VEL: Velpatasvir

doi: 10.1016/j.dld.2024.01.057

## T-26

### Concomitant use of proton pump inhibitors and Sofosbuvir/Velpatasvir: evidence from randomized clinical trials and real-world data

R. Esteban [1], S. Flamm [2], M. Buti [1], J. Turnes [3], L. Ni [4], C. Hernández [5], A. Mangia [6]

[1] *Hospital Vall Hebron, Barcelona, Spain*
[2] *NorthwesternUniversity Feinberg School of Medicine, Chicago, United States*
[3] *Complejo Hospitalario Universitario de Pontevedra, Gastroenterology and Hepatology Department, Pontevedra, Spain*
[4] *Gilead Sciences, Biostatistics Virology, Foster City, United States*
[5] *Gilead Sciences, Global Medical Affairs, Madrid, Spain*
[6] *IRCCS Casa Sollievo della Sofferenza, UOSD Epatologia, San Giovanni Rotondo, Italy*

**Background:** Literature and product labels suggest velpatasvir bioavailability may be reduced when administered concomitantly with a proton pump inhibitor (PPI), based mainly on pharmacokinetic studies. We aimed to determine the clinical relationship between PPI use and sustained virologic response rates (SVR) in patients treated with sofosbuvir/velpatasvir (SOF/VEL) for chronic hepatitis C virus infection.
**Method:** Retrospective, descriptive analysis of available data of patients treated with 12weeks SOF/VEL with and without concomitant PPIs, from Phase 2/3 randomized controlled studies (RCTs) and real-world data (RWD) studies.

**Results:** 546 patients using PPIs were identified, 87 from RCTs and 459 from RWD. The overall control group of patients without PPI use was 5,201; 2,517 in RCTs and 2,684 in RWD. In RCT, patients receiving PPI and SOF/VEL were male (79%), mean age of 57 years (26–78), GT3 in 56% and cirrhotic in 35%. Most patients participating in RCT (66%, 57/87) continuously used PPI during the 12-week SOF/VEL course, omeprazole being the most used PPI (68%). SVR12 in PPI users was 97% (84/87), comparable to the reported by non-PPI users (97%). SVR12 in GT3 patients was 96% (47/49), in F4 was 94% (30/32). In GT3 plus F4 patients, SVR12 was 96% (23/24). Three patients did not achieve SVR12 in PPI-users: 2 patients relapsed (relapse rate 2%) and one patient with history of diabetes discontinued SOF/VEL after 7 days due to hyperglycemia. In RWD, patients receiving PPI and SOF/VEL were male (54%), mean age of 61 years, 25% GT3, 29% cirrhotic. Overall SVR12 in PPI users was 99% (454/459), comparable to the reported by non-PPI users (99%).
**Conclusion:** In RCTs and RWD, SOF/VEL for 12 weeks was effective in patients with concomitant PPI use. These data support the use of SOF/VEL according to labeled recommendations with respect to co-administration of PPIs and other acid reducing agents

doi: 10.1016/j.dld.2024.01.058

## T-27

### Prevalence of HCV infection in a nursing home: the unknown submerged population

G. Di Pasquale [1], P. Gallo [1], V. Flagiello [1], A. De Vincentis [2], F. Terracciani [1], A. Picardi [1], U. Vespasiani Gentilucci [1], R. Antonelli Incalzi [2]

[1] *Clinical Medicine and Hepatology Unit, Campus Bio-Medico University, Rome, Italy*
[2] *Internal Medicine Unit, Campus Bio-Medico University, Rome, Italy*

**Introduction:** Despite the therapeutic success achieved with direct-acting antiviral agents, a substantial number of individuals with undiagnosed HCV infection, referred to as the “submerged" population, persists, especially in Nursing Homes. The aim of this study is to assess the prevalence of HCV infection among patients residing in the Italian Hospital Group Nursing Home in Guidonia Montecelio (Rome).
**Methods:** The investigation encompassed Psychiatric, Extensive and Intensive, Alzheimer, and Geriatric Units. Collected data included patients’ sociodemographic information, blood test results, and risk factors for HCV infection. Anti-HCV testing utilized the Advanced Quality Rapid capillary test, followed by confirmation through a serum test. Positive anti-HCV results underwent further testing with an HCV-RNA test. Descriptive statistics and logistic regressions were employed to assess risk factors for anti-HCV positivity.
**Results:** As detailed in Table 1, the study comprised 434 patients. Anti-HCV positivity (both capillary and serum) was detected in 13 patients (3%), yielding an infection prevalence of 2.3%. Positive patients were predominantly male and younger compared to anti-HCV negative patients. The highest prevalence was observed in the psychiatric unit (6 out of 13 patients, 46%). As showed in Table 2, logistic regression analysis identified age, sex, hepatitis B virus (HBV) infection, dementia, smoking, and injection drug use as significantly associated with anti-HCV positivity. Subsequent multivariate analysis confirmed only HBV infection and smoking as independently associated with positivity.
**Conclusions:** Our findings reveal a 2.3% prevalence of HCV infection (3% anti-HCV positivity) among residents of the Nursing Home. Anti-HCV positivity was negatively associated with age and positively with dementia. The highest prevalence occurred in psychiatric patients, who face a notably higher risk of HCV infection and are younger than the general Nursing Home population. These initial data suggest that institutionalized patients, particularly those in psychiatric care, should be included in screening programs for HCV infection within the submerged populations.

| Characteristics | Overall | Anti HCV-test | | p |
|---|---|---|---|---|
| | | Negative | Positive | |
| N | 434 | 421 (97%) | 13 (3%) | |
| Age | 75 (61-83) | 75 (62-83) | 61 (57-64) | 0.006 |
| Sex | M 207 (48%)<br>F 227 (52%) | M 197 (47%)<br>F 224 (53%) | M 10 (77%)<br>F 3 (23%) | 0.063 |
| ALT (U/l) | 15 (11-20) | 15 (11-20) | 32.5 (24.2-40.8) | 0.206 |
| AST (U/l) | 16 (13-20.5) | 16 (13-20) | 23 (19.5-26.5) | 0.350 |
| GGT (U/l) | 16 (12-24.8) | 16 (11.8-24) | 27.5 (26.2-28.8) | 0.118 |
| Platelets/ µL | 230 (181-301) | 229 (181-299) | 241 (155-336) | 0.977 |
| HBV infection | 9 (2%) | 6 (1,5%) | 3 (23%) | < 0.001 |
| Surgery | 133 (31%) | 128 (30%) | 5 (38%) | 0.753 |
| ADL Index | | | | 0.555 |
| Dementia | 236 (54%) | 234 (56%) | 2 (15%) | 0.010 |
| Smoke | 71 (16%) | 64 (15%) | 7 (54%) | < 0.001 |
| Alcohol | 4 (1%) | 4 (1%) | 0 (0%) | 1 |
| Injection drug use | 9 (2%) | 7 (2%) | 2 (15%) | 0.015 |
| Psychiatric Unit | 115 (26%) | 109 (26%) | 6 (46%) | 0.190 |
| Alzheimer Unit | 52 (12%) | 51 (12%) | 1 (8%) | 0.960 |
| Extensive and Intensive Unit | 37 (9%) | 36 (9%) | 1 (8%) | 1 |
| Geriatric1 Unit | 116 (27%) | 114 (27%) | 2 (15%) | 0.535 |
| Geriatric2 Unit | 114 (26%) | 111 (26%) | 3 (23%) | 1 |

*Table 1. General characteristics of study population, in IHG Nursing Home*

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| Variable | OR | 95% CI | p | OR | 95% CI | p |
| Age | 0.96 | 0.93-0.99 | 0.01 | 0.99 | 0.94-1.04 | 0.53 |
| Sex | 0.26 | 0.06-0.88 | 0.04 | 0.76 | 0.14-3.46 | 0.73 |
| ALT | 1.02 | 0.95-1.05 | 0.24 | | | |
| AST | 1.04 | 0.89-1.13 | 0.50 | | | |
| Gamma-GT | 1.01 | 0.92-1.05 | 0.64 | | | |
| Platelets | 0.99 | 0.99-1 | 0.80 | | | |
| HBV infection | 20.75 | 3.95-91.7 | < 0.001 | 13.7 | 1.82-94.8 | 0.008 |
| Surgery | 1.43 | 0.42-4.37 | 0.54 | | | |
| ADL Index | 1.18 | 0.93-1.5 | 0.16 | | | |
| Dementia | 0.14 | 0.02-0.55 | 0.01 | 0.26 | 0.03-1.37 | 0.13 |
| Smoke | 6.50 | 2.09-22.8 | < 0.001 | 6.23 | 1.12-40.5 | 0.04 |
| Alcohol | 2.04 | 1.4-8.3 | 0.99 | | | |
| Injection drug use | 10.5 | 1.59-51.09 | 0.005 | 2.66 | 0.21-21.9 | 0.39 |
| Psychiatric Unit vs Alzheimer Unit | 0.35 | 0.01-2.15 | 0.34 | | | |
| Psychiatric Unit vs Extensive and Intensive Unit | 0.50 | 0.02-3.09 | 0.53 | | | |
| Psychiatric Unit vs Geriatric1 Unit | 0.318 | 0.04-1.42 | 0.16 | | | |
| Psychiatric Unit vs Geriatric2 Unit | 0.49 | 0.10-1.91 | 0.32 | | | |
| Psychiatric Unit vs all the others togheter | 2.45 | 0.77-7.54 | 0.11 | 0.45 | 0.08-2.32 | 0.35 |

*Table 2. Logistic regression for the association of different variables with anti HCV positivity*

doi: 10.1016/j.dld.2024.01.059

## T-28

### Pilot, open, randomized, multicenter trial for the comparison of hypothermic versus normothermic ex-situ liver preservation in DCD liver transplantation with extended ischemia time (DCDNet trial)

J. Bronzoni, D. Pezzati, P. Carrai, S. Petruccelli, C. Martinelli, P.G. Vacca, E. Balzano, G. Catalano, S. Palladino, G. Tincani, D. Ghinolfi

*Azienda Ospedaliero Universitaria Pisana, Pisa, Italy*

**Introduction:** In Italy, 20 minutes of continuous, flat-line electrocardiogram are required for death declaration, which significantly increases the risks of complications after DCD liver transplantation. Despite prolonged warm ischemia time, Italian centers reported good outcomes in DCD liver transplantation by combining normothermic regional (NRP) and end-ischemic machine perfusion. However, there are no studies in this particular setting comparing the two main ex-situ preservation techniques: dual-hypothermic oxygenated machine perfusion (D-HOPE) versus normothermic machine perfusion (NMP).

**Methods:** DCDs donors offered to our center were retrieved after a period of NRP. Graft eligibility to transplantation was assessed on NRP parameters.

Grafts were then transported to our center and randomized to NMP or D-HOPE and transplanted after a variable period.

**Results:** Between January 2021 to November 2023, 29 liver grafts were procured and transplanted, being 13 assigned to DHOPE and 16 to NMP group. Median donor age was 62 and 57 years (p=0.12) in D-HOPE and NMP group, respectively, being 11 (38%) grafts older than 80 years. 90-day graft survival was 84% versus 100% (p=0.12) in D-HOPE and NMP group respectively.

No differences in terms of post-reperfusion syndrome rate (31% versus 31%, p=0.97), early allograft dysfunction rate (31% versus 19%, p=0.56), ICU stay (6,1 versus 4,7 days, p=0.57), hospital stay (15,9 versus 15,5 days, p=0.92) were noted in the D-HOPE and NMP group, respectively.

There were 5 cases of biliary complications in NMP group (2 ischemic cholangiopathy, 1 anastomotic stricture and 2 leakages) vs 2 (2 anastomotic strictures) in D-HOPE group (p=0.3).

**Conclusions:** The sequential use of NRP and end-ischemic machine perfusion is a safe method to perform DCD liver transplants with extended warm ischemia time without donor age limits. No major differences between D-HOPE and NMP have been showed. Further data are needed to draw definitive conclusions.

doi: 10.1016/j.dld.2024.01.060

## T-29

### Acute-on-chronic liver failure in severe acute alcoholic hepatitis: impact on management, prognostication, and urgency of liver transplantation

G. Perricone [1], C. Mazzarelli [1], R. Viganò [1], P. Prandoni [2], M. Vangeli [1], F. Aprile [1], M. Cucco [1], C. Becchetti [1], R. Stigiliano [1], L. Cesarini [1], A. Airoldi [1], M. Scaravaglio [3], G. Monti [4], A. Lauterio [5,6], L.S. Belli [1]

[1] *Hepatology and Gastroenterology Unit, ASST GOM Niguarda, Milan, Italy*
[2] *Department of Mental Health and Addiction Services, Niguarda Hospital, Milan, Italy*
[3] *Division of Gastroenterology and Center for Autoimmune Liver Diseases, San Gerardo Hospital and Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy*
[4] *Department of Anesthesiology, GOM Niguarda, Milan, Italy*
[5] *Department of General Surgery and Transplantation, GOM Niguarda, Milan, Italy*
[6] *School of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy*

**Introduction:** A better identification of factors predicting the course, outcome, and need for urgent liver transplantation in patients with severe acute alcoholic hepatitis (SAAH) is needed. Acute-on-chronic liver failure (ACLF) can occur in SAAH, and its impact on management, prognostication, and need for urgent liver transplantation in SAAH should be clarified.

**Aim:** To describe the impact of ACLF on management, prognostication, and need for urgent liver transplantation in SAAH.

**Materials and Methods:** Patients with SAAH referred to our center between April 2016 and May 2023, with those non-responders to medical treatment (MT) being evaluated for LT.

**Results:** One hundred patients were included, with a median Maddrey Discriminant Function of 72 and a median MELD-Na score of 28. At presentation, 52 patients had ACLF grade 0-1, and 48 ACLF grade 2-3 (31 grade 2, 17 grade 3) (see *Figure 1*). In the latter group, circulatory failure was present in 3 (6.25%), and respiratory failure in 4 (8.3%). SAAH was the only precipitant factor in 50 (96%) and 36 (75%) patients with ACLF grade 0-1 and ACLF grade 2-3, respectively, with infection being an associated factor in 1 (2%) and 8 (17%), and GI bleeding in 1 (2%) and 5 (10%), respectively.

Non-response to MT was significantly higher in patients with ACLF grade 2-3 (39/48, 81%) than in those with ACLF grade 0-1 (14/52, 27%). ACLF grade 2-3 was associated with a corresponding higher need of early LT (ACLF grade 2-3: 14/48, 29% vs ACLF grade 0-1: 3/52, 5.7%; p = 0.004).

ACLF status at presentation (ACLF grade 2-3 vs ACLF grade 0-1) resulted a better predictor of outcome (death or LT) than MELD-Na (>= or <30) (4.42 [2.67; 7.33] vs 2.50 [1.51; 4.12]).

**Conclusions:** ACLF is a frequent presentation of SAAH. Severe ACLF predicts non-response to MT, indicating the urgency of liver transplantation.

doi: 10.1016/j.dld.2024.01.061

## T-30

### The equitable benefit approach (EBA): a single ethical framework to guide the assessment of medical and psychosocial factors in liver transplant candidacy

L. Craxì [1], P.M. Cottone [2], D. Sacchini [3], P. Burra [4], P. Toniutto [5]

[1] *Department of Biomedicine, Neuroscience and Advanced Diagnostics, University of Palermo, Palermo, Italy*
[2] *A.R.N.A.S. Hospital Civico - Di Cristina – Benfratelli, Regional Transplant Center Sicilia, Palermo, Italy*
[3] *Institute of Bioethics, A. Gemelli School of Medicine, University Cattolica del Sacro Cuore, Rome, Italy*
[4] *Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy*
[5] *Hepatology and Liver Transplantation Unit, Department of Medicine, University of Udine, Udine, Italy*

Liver transplantation (LT) raises ethical issues because organ scarcity implies the need for equitable access and maximum benefit from transplantation through non-discriminatory eligibility criteria and allocation systems. Patient selection and LT prioritization criteria are mainly based on medical factors. However, psychosocial, and behavioral variables are having an increasing impact on the process of patient selection and on survival after LT. Ethical concerns regarding the inclusion of non-medical factors in the selection of LT candidates are related to their potential impact on health equity issues, discrimination, and stigma. Thus, there is a need to provide ethical guidance in the assessment of LT candidacy, considering both medical and psychosocial aspects in a single framework. The aim of this paper is to present the ethical foundations of a framework proposed by the multidisciplinary group of clinical experts in LT (CELT group) of the Italian Association for the Study of the Liver (AISF). First, the updated selection and prioritization criteria for LT based on pure medical factors are presented. Then, a specific ethical framework, called Equitable Benefit Approach (EBA), is presented to provide ethical guidance in LT candidacy and prioritization. EBA clarifies the overarching goals of LT and illustrates and ranks the principles that should guide allocation decisions in LT, distinguishing between substantive and procedural principles. It also integrates medical and psychosocial criteria into a single operational algorithm to guide the selection process, prioritization, and post LT follow-up. Finally, potential strategies for implementing this proposed approach in clinical practice are presented.

doi: 10.1016/j.dld.2024.01.062

## T-31

### Hepatofugal portal flow is highly predictive of acute-on-chronic liver failure: a new hemodynamic patho-physiological hypothesis

L. De Marco [1], R. Stupia [1], M. Bevilacqua [1], F. Cattazzo [1], M. Zoncapé [1], V. Paon [2], D. Ieluzzi [2], A. Dalbeni [1], D. Sacerdoti [2]

[1] *General Medicine C, Department of Medicine, University of Verona, Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy*
[2] *Liver Unit, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy*

**Introduction:** Acute-on-chronic liver failure (ACLF) is a severe complication of advanced liver disease. A significant number of ACLF patients have not clear precipitating factors.
**Aim:** The aim of the study was to investigate the role of alterations in porto-hepatic hemodynamics, especially non-forward portal flow (NFPF), in ACLF and liver-related mortality.
**Materials and Methods:** 233 cirrhotic patients were included in the study with a median follow-up of 24 months. Color-Doppler ultrasound was used to assess portal vein patency, flow direction and significant porto-systemic collaterals (> 8 mm). Patients with active cancer, both at baseline and during follow-up, severe non liver-related comorbidities and liver-unrelated death were excluded. ACLF and liver-related mortality were recorded during follow-up.
**Results:** Fifty-six patients (24%) developed ACLF; 24 (10,3%) had baseline NFPF. In survival analysis, NFPF, but not portal vein thrombosis, was independently associated with ACLF development (HR 2.85 95% C.I. [1.49-5.42], p=0.001) and liver-related mortality (HR 2.24 95% C.I. [1.16-4.28], p=0.015), even after adjustment for liver disease severity scores, baseline portal vein thrombosis, age and etiology of liver disease.
**Conclusions:** NFPF was independently associated with ACLF development and liver-related mortality, regardless of etiology, severity disease scores and portal vein thrombosis. Although there is no specific measure to reverse NFPF, patients with NFPF should receive prompt intensive management and urgent prioritization for liver transplantation.

doi: 10.1016/j.dld.2024.01.063

## T-32

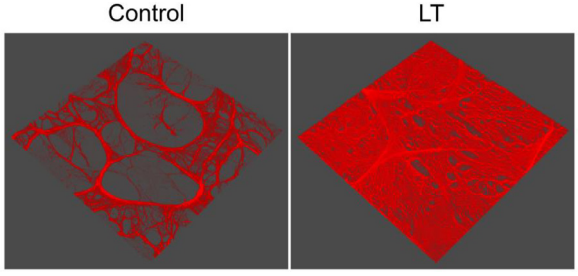
### Oxidative stress-induced fibrinogen modifications in liver transplant recipients: unraveling a novel potential mechanism for cardiovascular risk

S. Gitto [1,#], C. Fiorillo [2,#], F.R. Argento [2], E. Fini [2], S. Borghi [2], M. Falcini [1], D. Roccarina [1], R. La Delfa [1], L. Lillo [1], P. Forte [3], D. Ghinolfi [4], P. De Simone [4], F. Chiesi [5], F. Marra [1,*], M. Becatti [2,*‡], MEDITRA research group

[1] *Internal Medicine and Liver Unit, University Hospital Careggi, Department of Experimental and Clinical Medicine, University of Florence, Italy*
[2] *Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Firenze, 50134 Firenze, Italy*
[3] *Gastroenterology Unit, University Hospital Careggi, Florence, Italy, Unit of Clinical Nutrition, Careggi University Hospital, Department of Experimental and Clinical Medicine, University of Florence, Italy*
[4] *Hepatobiliary Surgery and Liver Transplantation, University of Pisa Medical School Hospital, Pisa, Italy*
[5] *Department of Neuroscience, Psychology, Drug, and Child's Health (NEUROFARBA), Section of Psychology, University of Florence, Italy*

# Sharing first authorship
* Sharing last authorship
‡ MEDITRA research group: A. Ingravallo[1], F. Vizzutti[1], S. Aspite[1], G. Laffi[1], E. Lynch[3], S. Petruccelli[4], P. Carrai[4], S. Palladino[4], F. Sofi[6], L. Stefani[7], A. Amedei[8], S. Baldi[8], C. Lau[9].

**Introduction & Aims:** Atherosclerotic cardiovascular events represent major cause of non–graft-related death after liver transplant. Since in many conditions of chronic inflammation fibrinogen oxidation has a chief role in favouring thrombosis, our aim was to analyze reactive oxygen species-induced structural and functional fibrinogen modifications as possible mechanism of post-transplant thrombosis.
**Methods:** We conducted a 1:1 case-control study enrolling clinically stable liver transplant recipients and non-transplanted matched controls. Assessment of reactive oxygen species production in leukocytes, lipid peroxidation, glutathione content, plasma antioxidant capacity, fibrinogen oxidation, fibrinogen structure and 3D fibrin determination and fibrinogen functional analysis, were conducted. We then verified the correlations between fibrin degradation rate and all the cohort variables.
**Results:** We enrolled 40 patients (cases), mostly males with mean age of 62 years and 40 controls. Cases showed a significant increase in reactive oxygen species and lipid peroxidation than controls (1.83 *vs* 0.35 Malondialdehyde nmol/ml, p<0.001). Fibrinogen from controls showed $\alpha$-helix secondary structure with minima at 208 nm and 222 nm, while decreased negative peak in the 215 nm to 225 nm region was observed in cases. Control fibrin gel had large pores and tick fibers in comparison with cases (see Figure). Fibrinogen from cases displayed a reduced ability to polymerize into fibrin. In cases, Lag phase value resulted increased (6.8 vs 3.4, p<0.001). Receiving a graft with steatosis and smoking habit were associated to high fibrin degradation rate ($t = 2.04$, $p = .049$; Cohen's $d = .68$ and $t = 1.91$, $p = .032$; Cohen's $d = .79$, respectively).
**Conclusions:** We firstly described reactive oxygen species-induced structural and functional fibrinogen modifications in transplant recipients as possible explanation for their higher cardiovascular risk in comparison to general population.




doi: 10.1016/j.dld.2024.01.064

## T-33

### "Early" vs "standard" liver transplantation in patients with severe alcoholic hepatitis

R. Viganò [1], A. Panariello [2], G. Perricone [1], C. Mazzarelli [1], C. Becchetti [1], M. Vangeli [1], L. Cesarini [1], R. Stigliano [1], F. Aprile [1], M. Cucco [1], M. Lucà [3], G. Despinzieri [4], E. Roselli [5], L.G. De Carlis [6,7], A. Airoldi [1], L.S. Belli [1]

[1] *Hepatology and Gastroenterology Unit, ASST GOM Niguarda, Milan, Italy;*
[2] *Department of Mental Health and Addiction Services, Niguarda Hospital, Milan, Italy;*
[3] *Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy*
[4] *Division of Gastroenterology and Center for Autoimmune Liver Diseases, San Gerardo Hospital and Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy*
[5] *Department of Anesthesiology, GOM Niguarda, Milan, Italy*
[6] *Department of General Surgery and Transplantation, GOM Niguarda, Milan, Italy*
[7] *School of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy*

**Introduction:** Liver transplantation (LT) is an established therapeutic option for a subgroup of highly selected patients with alcoholic-hepatitis non-responder to medical treatment (MT). While some patients have a rapidly progressive disease leading to an early-LT, others initially improve with MT but need to be evaluated for a standard-LT in the following months for persisting decompensation.
**Aim:** To describe the features of early-LT versus standard-LT for severe alcoholic hepatitis.
**Materials and Methods:** One hundred consecutive patients with severe-AH referred to our center since April 2016, with those non responder to medical treatment being evaluated for LT.
**Results:** Fifty-three patients were non-responder to MT and 17 underwent early-LT within 27 days from admission. Of the 47 responder patients, 14 were subsequently listed with 13 being transplanted after a median of 166 days for persisting decompensation despite initial clinical improvement, Fig.1. Patients receiving standard-LT had lower MELD-Na scores at presentation compared to early-LT (27 vs 34; p=0.008) and a lower prevalence of ACLF-grade 2-3 (23% vs 82.4%; p=0.002). After multivariate analysis patients with MELD-Na≥30 at index hospitalization were 5.88(95%CI:2.31-16.41) times more likely to be non-responders to MT than those with a MELD-Na < 30, while those with ACLF grade 2-3 were 12.56 (95%CI:4.95-35.04) times more likely to be non-responders as compared to those with ACLF grade 0-1. (Fig.). Overall, 15 LT recipients (50%) suffered from depression and 10 (33%) received antidepressants post-LT. Three patients in all (10%) relapsed into any alcohol consumption. Twenty-nine (97%) are currently alive after a median follow-up of 32.2 months from LT.
**Conclusions:** Patients with SAH have different patterns of progression. Of those transplanted, 57% received an early-LT and 43% a standard LT. Overall, the transplant benefit was huge and relapse into alcohol consumption acceptable, 10%. Treatment of psychiatric comorbidities proved valuable to mitigate the risk of relapse.

doi: 10.1016/j.dld.2024.01.065

## T-34

### Preoperative aortic regurgitation and early graft survival in liver transplant recipients

M. Biolato [1], F. Canale [2], E. Vernole [1], F. Ferri [2], G. Marrone [1], S. Parisse [2], L. Miele [1], L.I. Birtolo [2], A. Liguori [1], M. Mancone [2], A.W. Avolio [1], S. Ginanni Corradini [2], M. Pompili [1], A. Gasbarrini [1], M. Rossi [2], S. Agnes [1], Q. Lai [2]

[1] *Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Catholic University of Sacred Heart, Rome, Italy*
[2] *Azienda Ospedaliera Universitaria Policlinico Umberto I, Sapienza University of Rome, Italy*

**Introduction:** Cardiovascular events are the leading cause of early mortality after Liver Transplantation (LT). LT candidates undergo Doppler echocardiogram as part of the cardiac assessment before waitlist registration.
**Aim:** To identify echocardiographic parameters able to predict early graft loss.
**Materials and Methods:** Retrospective bi-center (Policlinico Umberto I and Policlinico Gemelli, both in Rome) observational study (period 2005-2020) including adult patients transplanted with a diagnosis of liver cirrhosis, with or without hepatocellular carcinoma. Echocardiographic examinations performed in peripheral centers or over 12 months from LT were excluded. Multivariable logistic regression analyses were performed.
**Results:** 481 patients were included. The population was stratified according to degree of liver dysfunction: MELD 6-29 Group (n=421, 87.5%), and MELD ≥30 Group (n=60, 12.5%). 43 (8.9%) graft losses were reported within the first 90 days after LT; in 9 (1.9%) patients graft loss was caused by a technical issue (hepatic arterial thrombosis=6, severe bleeding=3). No case of graft loss was directly correlated with heart failure. Patients with MELD ≥30 had a smaller median left ventricular mass (P=0.03), smaller median left atrial diameter (P=0.03), higher median ejection fraction (P=0.004), lower percentage of patients with mitral (P<0.001) and tricuspidal regurgitation (P=0.002), and lower median sPAP (P=0.004).

Aortic regurgitation was the only independent risk factor for graft loss (OR=2.58, 95%CI=1.12-5.93; P=0.03), and it's predictive value was confirmed in three sub-analysis: MELD ≥30 patients (OR=11.50, 95%CI=1.06-124.54; P=0.04), excluding surgical technique-related graft losses (OR=3.03; 95%CI=1.16-7.93; P=0.02), excluding the 8 (1.7%) cases of moderate aortic regurgitation OR=2.42 (95%CI=1.03-5.67; P=0.04). No relevant differences were observed when ejection fraction was estimated according to the presence or not of aortic regurgitation.
**Conclusions:** In LT patients, aortic regurgitation is an independent predictor of early graft survival, even in case of mild form and with a concomitant valid ejection fraction.

doi: 10.1016/j.dld.2024.01.066

## T-35

### Ex situ liver resection for intrahepatic cholangiocarcinoma: survival analysis and comparison to systemic chemotherapy

E. Nieddu [1], I. Billato [1,2], C. Peluso [1], A. Furlanetto [1], S. Lazzari [1], F.E. D'Amico [1], U. Cillo [1], E. Gringeri [1]

[1] *Department of Surgical, Oncological and Gastroenterological Sciences, Hepato-bilio-pancreatic Surgery and Liver Transplant Unit, University of Padova, Padova, Italy*
[2] *Department of Biology, University of Padova, Padova, Italy*

Surgical resection is the standard treatment for intrahepatic cholangiocarcinoma (iCCA). Systemic chemotherapy is the standard of care for patients not eligible for surgery. Ex situ liver resection is a surgical technique that could be an efficient treatment, increasing the number of patients eligible for surgery.

This retrospective study aims to evaluate long-term outcomes in terms of overall survival (OS) and progression-free survival (PFS) and the related prognostic factors in patients affected by iCCA treated with ex situ resection or chemotherapy.

Two populations of patients with iCCA, treated with surgical resection or chemotherapy were compared. OS and PFS were analyzed using survival analysis with the Kaplan-Meier estimator. OS was also analyzed using the Cox model. The non-parametric Log-rank test was used to evaluate the effect of individual covariates on survival. A total of 59 patients were included: 13 patients underwent ex situ resection and 46 patients were treated with chemotherapy. The surgical population had a survival benefit and a longer PFS compared to chemotherapy population: 1-year survival was 84.6% vs 52.2%, with a median OS of 46.1 vs 12.7 months and a median PFS of 23.08 vs 8.03 months, respectively. The other variables that influence patients' survival were the stage of disease, patient's age, Ca19-9 level, and liver function. The stage of disease, the treatment, performance status (PS), Ca19-9 level, and liver function tests, were significant in Cox's regression analysis.

Ex situ surgery seems to provide a longer survival and a lower progression probability compared to chemotherapy, even if it is technically challenging and burdened with high morbidity and mortality. Patients should be carefully selected, with good PS, low stage of disease, low Ca19-9 level, and good liver function. Ex situ surgery, deserves to be considered in high-volume hepatobiliary centers, with expertise in resective hepatic surgery and transplant surgery.

doi: 10.1016/j.dld.2024.01.067

## T-36

### Detection of coronary artery disease in liver transplant recipients: does stress echocardiography still have a role?

M. Saracco [1], C. Manuli [1], R. Lasco [1], G.P. Caviglia [1], B. Lavezzo [2], D. Cocchis [3], M. Giorgi [4], A. Ottobrelli [1], R. Romagnoli [3], S. Martini [1]

[1] *Gastrohepatology Unit, AOU Città della Salute e della Scienza di Torino*
[2] *Anesthesia and Intensive Care Unit 2, AOU Città della Salute e della Scienza di Torino*
[3] *General Surgery 2U and Liver Transplant Center, AOU Città della Salute e della Scienza di Torino*
[4] *Cardiology Unit, AOU Città della Salute e della Scienza di Torino*

**Background:** Asymptomatic coronary artery disease (CAD) has been reported up to 25% among liver transplant (LT) candidates, however cardiovascular pre-LT work-up is not yet standardized. We aimed to assess the efficacy of the protocol used in a high-volume LT center.

**Methods:** We enrolled all adult cirrhotic patients who underwent first-LT between 01/2015-12/2021 in our Center. Follow-up was closed on 30/06/2023. Per protocol, 3 minor (age 60-64years, arterial hypertension, non-insulin diabetes, BMI≥30Kg/m$^2$, CAD family history, active smoking) or 1 major cardiovascular-risk-factors (insulin-treated diabetes, age>64years, stroke, MAFLD) led to echostress test (EchoS). Coronary angiography (CATH) was performed in patients with CAD history/symptoms, positive/doubtful non-invasive tests or cardiology indication.

**Results:** 803 patients were included: median age 58 years, 77% male, BMI 25.4 Kg/m$^2$, 57.9% HCC.

Cardiovascular-risk-factors: 15.6% CAD family history, 24.9% 60-64 years, 26.4% arterial hypertension, 23.3% diabetics, 10.5% BMI≥30Kg/m$^2$, 25.9% active smokers, 1.6% previous CAD; 19.6%≥65 years, 1.9% previous stroke, 7.6% MAFLD.

372/803(46.3%) underwent pre-LT EchoS (42% dobutamine), 7/372(1.9%) tested positive. Overall, CATH was performed in 41/803 patients (5.1%, 9/41 with revascularization) and echoS positivity was confirmed in 3/7(43%).

*Post-LT:*

After a median follow-up of 51 months[IQR 32-74], 88.5% patients survived.

At 2 years, 12(1.5%) ischemic events were recorded (8 within 1 year, 4 within 2 years); all patients survived. 11/12(92%) underwent pre-LT EchoS, 11/11 tested negative. At univariate-analysis, ischemic event predictors were: MAFLD (p=0.022), age≥60 years(p=0.027), diabetes(p=0.026), previous CAD(p=0.043). At multivariate-analysis, MAFLD (p=0.026,HR=4.528) and previous CAD (p=0.049,HR=8.066) remained significant.

**Conclusion:** In our Italian multiregional cohort of 803 patients, pre-LT EchoS was performed in almost half of them, and <2% tested positive (57% false positive). All patients with ischemic events within 2 years after LT who underwent pre-LT EchoS, tested negative. After multidisciplinary team discussion, starting from January 2022 we implemented in our pre-LT work-up coronary CT instead of EchoS in patients with at least 1 major CV-RF.

doi: 10.1016/j.dld.2024.01.068

## T-37

### Perfusate cytokines concentrations during liver grafts ex-situ normothermic perfusion (DCDNet Study)

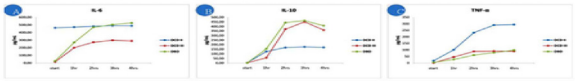
P.G. Vacca [1], D. Pezzati [1], J. Bronzoni [1], C. Martinelli [1], S. Petruccelli [1], P. Carrai [1], M. Franzini [2], E. Balzano [1], G. Tincani [1], G. Catalano [1], S. Palladino [1], M. Masini [2], M.I. Rotondo [3], S. Babboni [4], S. Del Turco [4], R. Morganti [5], D. Campani [3], V. De Tata [2], G. Biancofiore [6], G. Basta [4], A. Paolicchi [2], D. Ghinolfi [1]

[1] *Division of Hepatic Surgery and Liver Transplantation, University of Pisa Hospital, Pisa, Italy*
[2] *Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa Hospital, Pisa, Italy*
[3] *Division of Pathology, University of Pisa Hospital, Pisa, Italy*
[4] *Institute of Clinical Physiology, National Research Council, Pisa, Italy*
[5] *Division of Statistic, University of Pisa Hospital, Pisa, Italy*
[6] *Division of Transplant Anesthesia, University of Pisa Hospital, Pisa, Italy*

**Introduction:** Liver graft reperfusion after ischemia induces the activation of an immune cascade characterized by the release of pro and anti-inflammatory cytokines. However, cytokines liver release kinetics is unclear.

**Aim:** of the study is to evaluate the release of the cytokine after machine reperfusion of liver grafts in normothermic conditions (NMP) and to correlate with graft characteristics and clinical outcomes.
**Methods:** From September 2020 to May 2022, cytokines (IL-6, IL-10, TNF-$\alpha$) perfusate concentrations of transplanted liver grafts preserved under normothermic conditions was analyzed at commencing ex-situ perfusion and hourly thereafter. Cytokines absolute values and release ratios after 2 hours were correlated to donor-related factors and postoperative clinical endpoints (90-days graft- and patient-survival, transaminases peak value, postoperative vasopressors requirement, hospital stay, incidence of post-reperfusion syndrome, post-liver transplant acute kidney injury and early allograft dysfunction).
**Results:** Thirty liver grafts (16 DBD, 7 type-II and 7 type-III DCD) were evaluated. Cytokines concentrations during NMP showed significantly higher levels of IL-6 in type-II DCD at commencing perfusion compared to DBD and type-III DCD ($p<0.05$) with an increasing trendline during perfusion of DBD grafts **(Figure 1A).** IL-10 and TNF-$\alpha$ kinetics were similar in DBD and type-III DCD **(Figure 1B; Figure 1C)**. IL-6 and IL-10 release ratio was higher in older donors ($p=0.012$) and in DCD ($p=0.041$), respectively, while TNF-alpha release ratio increased in donors requiring high doses of vasopressors ($p<0.001$). At univariate analysis, a higher IL-10 release ratio during NMP was associated with a more severe risk of acute kidney injury after liver transplantation ($p=0.023$).
**Conclusions:** This is the first study comparing cytokines concentrations during NMP in different liver donor types. Cytokine trends during NMP differ according to donor type (DBD, type-II and type III DCD) and cytokine measured. A higher IL-10 release ratio is correlated with a more severe post liver transplant acute kidney injury.

Fig 1. IL-6,IL-10 and TNF-α perfusate levels during NMP in different donors type (DBD, type II DCD and type III, DCD III)



doi: 10.1016/j.dld.2024.01.069

## T-38

### Impact of pre-transplant cardiac risk factor burden on post-transplant events in liver transplant recipients

R. Lasco [1], C. Manuli [1], M. Saracco [1], B. Lavezzo [3], A. Ottobrelli [1], D. Cocchis [2], R. Romagnoli [2], S. Martini [1]

[1] *Gastrohepatology Unit, Aou Città Della Salute e Della Scienza Di Torino, Turin, Italy*
[2] *General Surgery 2U and Liver Transplant Center, Aou Città Della Salute e Della Scienza Di Torino, Turin, Italy*
[3] *Anesthesia and Intensive Care Unit 2, Aou Città Della Salute e Della Scienza Di Torino, Turin, Italy*

**Background:** Liver transplant (LT) recipients are getting older resulting in increase of comorbidities, alongside with metabolic dysfunction-associated steatotic liver disease (MASLD) as etiology of cirrhosis. We aimed to analyze the pre-LT cardiovascular burden and the incidence of major post-LT events (MACE) in our Italian multiregional LT cohort.
**Methods:** We included all adult patients who underwent first LT from 01/2015 to 06/2022 in our LT center. Follow-up was closed on 30/06/2023. In the first era (A: 2015-2018) multivessel coronary-artery-disease (CAD) contraindicated LT. Post-LT MACE (heart ischemia, de-novo arrhythmia, heart failure) were recorded.
**Results:** 852 patients were enrolled, 429 in the first era (A) and 423 in the second one (B).

Comparing B vs A era:

**Pre-LT:** median age 59 [IQR 54-65] vs 58 years [53-62] ($p<0.01$); age≥65 years: 25.8% vs 13.9%($p<0.01$); MASLD: 9.7% vs 5.8% ($p=0.04$); arterial hypertension: 30.9% vs 24.2% ($p=0.03$); previous CAD: 2.4% vs 0.7% ($p=0.05$); CAD stenting during pre-LT work-up: 2.8% vs 0% ($p=0.001$).

**Post-LT**: MACE within 1 year: 5.2% vs 5.6%, ($p=0.88$) (most frequently arrhythmias: 77.3% vs 58.3% ($p=0.22$); during the second year 0.9% vs 0.5%, $p=0.45$ (most frequently ischemic heart disease: 75% vs 50%, $p=0.99$).

At univariate analysis, MACE predictors were male sex ($p=0.02$), age >55 ($p=0.01$), diabetes ($p=0.03$), arterial hypertension ($p<0.01$) and previous CAD ($p<0.01$); LT era and CAD revascularization during LT-workup did not impact on MACE ($p=0.94$ and $p=0.12$). At multivariate analysis, male sex ($p=0.045$, HR=2.39), age>55 years ($p=0.048$, HR=2.01), arterial hypertension ($p=0.043$, HR=1.73) and CAD history ($p=0.041$, HR=3.01) remained significant.

Post-LT survival at 1 and 2 years of era-B vs era-A was: 96% vs 95%% and 94% vs 93%, respectively ($p=0.247$).
**Discussion:** In our cohort, despite the increase of pre-transplant cardiac risk factors in recent years**,** post-LT MACE incidence and mortality remained stable, suggesting the efficacy and the strong necessity of careful pre-LT cardiac work-up.

Table 1. Patients' characteristics, cardiovascular risk factors and post-LT cardiovascular events: A era (from January 2015 to December 2018) vs B era (from January 2019 to June 2022)

| | A ERA (01/2015-12/2018) (n = 429) | B ERA (01/2019-06/2022) (n = 423) | P value |
|---|---|---|---|
| **Patients' characteristics** | | | |
| Age at LT, years | 58 [53-62] | 59 [54-65] | **0.0008** |
| ≥ 65 years | 60, 13.9% | 109, 25.8% | **0.0001** |
| Gender, male | 342, 79.7% | 317, 74.9% | 0.10 |
| Body mass index (BMI), kg/m² | 25 [23-28] | 25 [23-28] | 0.80 |
| 25-29.9 kg/m² | 198, 46.2% | 170, 40.2% | **0.08** |
| ≥ 30 kg/m² | 40, 9.3% | 53, 12.5% | 0.15 |
| Primary etiology of liver cirrhosis | | | |
| Viral hepatitis | 249, 58.0% | 191, 45.1% | **0.0001** |
| Alcoholic | 90, 20.9% | 110, 26.0% | 0.09 |
| MASLD | 25, 5.8% | 41, 9.7% | **0.04** |
| MELD at LT | 13 [9-17] | 13 [9-18] | **0.009** |
| Hepatocellular carcinoma (HCC) | 253, 58.5% | 239, 56.5% | 0.58 |
| **Cardiovascular risk factors** | | | |
| Family history of cardiovascular disease | 67, 15.6% | 63, 14.9% | 0.77 |
| Diabetes mellitus | 91, 21.2% | 110, 26.0% | 0.10 |
| > 1 year | 79/91, 86.8% | 96/110, 87.3% | 0.99 |
| Insulin-dependent | 50/91, 54.9% | 58/110, 52.7% | 0.77 |
| Arterial hypertension | 104, 24.2% | 131, 30.9% | **0.03** |
| History of stroke or transient ischemic attack | 7, 1.6% | 9, 2.1% | 0.60 |
| Previous known coronary artery disease treated with coronary stenting or bypass | 3, 0.7% | 10, 2.4% | 0.05 |
| Pre-LT coronary revascularization in patients without previous CAD | 0, 0% | 12 (2.9%) | **<0.01** |
| Smoke | 269, 62.7% | 250, 59.6% | 0.29 |
| Active | 111, 25.9% | 110, 26.0% | 0.12 |
| Previous | 158, 36.8% | 140, 33.1% | 0.28 |
| **Post-LT** | | | |
| Median follow-up, months | 71 [59-83] | 30 [19-39] | <0.001 |
| 1-year survival | 95% | 96% | 0.247 |
| 2-year survival | 93% | 94% | |
| Major cardiovascular events within 1 year | 24, 5.6% | 22, 5.2% | 0.88 |
| Arrhythmias | 14/24, 58.3% | 17/22, 77.3% | 0.22 |
| Ischemic disease | 5/24, 20.8% | 3/22, 13.6% | 0.70 |
| Heart failure | 5/24, 20.8% | 2/22, 9.1% | 0.42 |
| Major cardiovascular events between 1 and 2 years | 2, 0.5% | 4, 0.9% | 0.45 |
| Ischemic heart disease | 1/2, 50% | 3/4, 75% | 0.99 |

Numerical variables: median [Q1-Q3]; categorical variables: number (prevalence, %). LT: liver transplant; CAD: coronary artery disease.

doi: 10.1016/j.dld.2024.01.070

## T-39

### Real-life assessment of long-term adverse events related to immunosuppression after liver transplantation: data from a cohort of patients followed-up in a non-transplant centre

E.N. Lynch [1,2], M. Baldini [1], S. Petruccelli [3], T. Innocenti [1,2], G. Dragoni [1,4], P. Forte [4], D. Ghinolfi [3], A. Galli [1,4]

[1] *Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy*
[2] *Department of Medical Biotechnologies, University of Siena, Siena, Italy*
[3] *Hepatobiliary Surgery and Liver Transplantation, University of Pisa Medical School Hospital, Pisa, Italy*
[4] *Clinical Gastroenterology Unit, "Careggi" University Hospital, Florence, Italy*

**Introduction:** Long-term exposure to immunosuppressive drugs and their cumulative adverse effects, including metabolic syndrome, cardiovascular events, and cancer, contribute to morbidity

in liver transplant (LT) recipients. Minimisation of immunosuppression is a clinical mainstay, although its possible real-life beneficial effect has not yet been thoroughly investigated.
**Aim:** The aim of the study was to assess the impact of cumulative exposure to immunosuppressants (cyclosporine [CS], tacrolimus [TC], mycophenolate mofetil [MMF], and everolimus [EVL]) on post-LT dyslipidaemia, diabetes mellitus [DM], and hypertension, on major cardiovascular events, and on malignancy (non-hepatocellular cancer [HCC] and non-melanoma skin cancer [NMSC]).
**Materials and Methods:** All liver transplant recipients transplanted between January 1990 and June 2022 and followed-up at our clinic were retrospectively included in our study. Indications for combined EVL-TC therapy or EVL monotherapy were LT for HCC or moderate kidney impairment. Cumulative exposure to CS, TC, EVL and MMF was estimated by multiplying the time of exposure (years) by median values of trough levels or daily dosage in milligrams for MMF.
**Results:** A total of 236 patients were included in the study. The median duration of follow-up was 9 (4-14) years. Pre-LT smoking was the only factor associated with cardiovascular events (OR 3.6, p=0.04 – **Table 1).** Exposure to EVL vs no exposure was independently associated with dyslipidaemia (OR 2.4, p=0.04), regardless total exposure load. High exposure to EVL (>75° percentile) was independently associated with NMSC (OR 4.3, p=0.03). Prevalence of DM was higher in patients treated with TC (30.9% vs 17.2%, p=0.03).
**Conclusions:** Pre-LT smoking is associated with increased risk of cardiovascular events. Exposure to EVL and TC is linked to higher prevalence of dyslipidaemia and DM, respectively. These adverse effects appear to be manageable as they do not lead to increased cardiovascular risk. NMSC were more frequent in patients highly exposed to EVL.

| | Cardiovascular disease | | | | Univariate analysis | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|---|
| | Y | | N | | | | | |
| | n/median | %/IQR | n/median | %/IQR | p-value | OR | CI | p-value |
| **Age (years)** | 56 | 51-63 | 52 | 45-57 | 0.001 | 1.060 | 0.002-1.120 | **0.042** |
| **Post-LT hypertension** | 32 | 23.7 | 103 | 76.3 | 0.017 | 1.434 | 0.518-3.972 | 0.488 |
| **Post-LT diabetes** | 17 | 29.8 | 40 | 70.2 | 0.016 | 0.986 | 0.347-2.807 | 0.979 |
| **Post-LT dyslipidaemia** | 21 | 28 | 54 | 72 | 0.012 | 1.1468 | 0.570-3.783 | 0.426 |
| **Pre-LT smoking** | 23 | 23.3 | 76 | 76.8 | 0.064 | 3.630 | 1.092-12.065 | **0.035** |
| **Pre LT AUD** | 12 | 31.6 | 26 | 68.4 | 0.031 | 1.112 | 0.393-3.142 | 0.842 |
| **eEVL exposure >75° percentile** | 14 | 28.6 | 35 | 71.4 | 0.239 | | | |
| **eTC exposure >75° percentile** | 16 | 22.2 | 56 | 77.8 | 0.211 | | | |
| **eEVL exposure** | 24.8 | 16.0-33.0 | 20.0 | 9.3-39.7 | 0.530 | | | |
| **eTC exposure** | 37.5 | 20.3-56.7 | 27.2 | 14.0-43.4 | 0.114 | | | |

***Table 1*** *Multivariate analysis for cardiovascular disease. Abbreviations: Y=yes; N=no; IQR=inter-quartile range; OR=odds ratio; LT=liver transplantation; AUD=alcohol use disorder; e=estimated; EVL=everolimus; TC=tacrolimus*

doi: 10.1016/j.dld.2024.01.071

## T-40

### Impact of first microbial infection on outcomes in natural history and trajectories in cirrhosis

M. Bucci [1], F. Pelizzaro [2], A. Ferrarese [1], M. Pellone [1], A. Cattelan [3], L. Sasset [3], G. Germani [1], F.P. Russo [1], M. Gambato [1], A. Zanetto [1], P. Burra [1], M. Senzolo [1]

[1] *Multivisceral Transplant Unit, Padua University-Hospital, Padua, Italy*
[2] *Department of gastroenterology, Padua University-Hospital, Padua, Italy*
[3] *Department of infective and tropical disease, Padua University-Hospital, Padua, Italy*

**Introduction:** Microbial infections are frequent complications in cirrhosis, resulting as a common trigger of acute-on-chronic liver failure (ACLF). However, data about impact on long-term are conflicting.
**Aims:** To prospectively evaluate epidemiology of microbial infections, their severity and impact on outcome of decompensated cirrhotics admitted at a Hepatology Unit.
**Material and methods:** All adult patients admitted at Multivisceral Transplant Unit, Padua, between January 2017 and December 2022 with diagnosis of microbial infection were consecutively enrolled, analysing severity and source of infection. Outcome was assessed both during the first hospitalisation and within 1-yr, prospectively collecting further episodes of acute decompensation (AD) or ACLF, or death / liver transplantation.
**Results:** 236 admissions with infections in 165 patients were evaluated. Patients were predominantly male (67.9%) with median age of 57.4 years; the prevalent aetiology of cirrhosis was alcohol (47.3%). The most common source of infection was bloodstream (28%), followed by pneumonia and spontaneous bacterial peritonitis. Out of 140 culture-positive infections (59% of total infections), gram positive and multidrug resistant strains were 52% and 43%, respectively. Only 47/165 (28%) patients were infected at admission, 42% presenting with ACLF, whereas remainder developed nosocomial infection. MELD score and qSOFA ≥2 were associated with ACLF development at multivariate analysis. Overall, 38/165 (23%) died during first hospitalisation and 29/165 (17.5%) died of sepsis. Among survivors after first hospitalisation (n. 127), 43 (33%) experienced another microbial infection within a year. A further episode of ACLF occurred in 22% patients, with cumulative mortality significantly higher than those who developed a further episode of AD (51% vs. 20%).
**Conclusion:** Microbial infection is associated with high in-hospital mortality, especially when ACLF occurs. One third of survivors are affected by further infections and experience further admissions for AD or ACLF. The latter condition is associated with detrimental survival.

doi: 10.1016/j.dld.2024.01.072

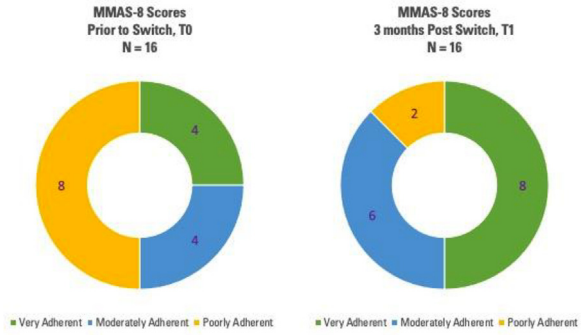
## T-41

### Patient voice on adherence and satisfaction following switch in therapy to trientine tetrahydrochloride for Wilson disease; the ASTRA study

M. Zuin [1], N. Cazzagon [2], A. Civolani [3], A. Crosignani [4], E. Bonavita [2], F. Tedone [5], S. Lopatriello [5], P.M. Battezzati [4,6]

[1] *University of Milan, Milan, Italy*
[2] *Department of Surgical, Oncological and Gastroenterological Sciences; University of Padua, UOC Gastroenterology, Padova, Italy*
[3] *UOC Gastroenterology, Azienda Ospedaliero-Universitaria di Cagliari, Cagliari, Italy*
[4] *ASST Santi Paolo e Carlo, RARE-LIVER ERN, Polo universitario San Paolo, Milan, Italy*
[5] *Helaglobe srl, Florence, Italy*
[6] *Department of Health Sciences, Università degli Studi di Milano, Milan, Italy*

**Introduction:** Wilson disease (WD) is an inherited disorder of copper transport resulting in copper accumulation predominantly affecting liver and brain. Lifelong treatment, separate from meals combined with side effects may all potentially negatively impact adherence to therapy leading to poorer outcomes. No prior study has reported adherence and satisfaction in WD patients following a change in therapy.
**Methods:** An Italian multicenter, prospective observational study of WD adults switching therapy to trientine tetrahydrochloride (TETA4). Demographic data, 24-hour urinary copper excretion (UCE), posology and pill count at each visit were collected. Patient reported outcomes (Morisky Medication Adherence Scale; MMAS-8), satisfaction score (Patient Experiences and Satisfaction with Medication questionnaire; PESaM) and quality of life (QoL) questionnaire (SF36) were collected at two-time points; baseline (T0) and first visit (3 months) after switching to TETA4 (T1).
**Results:** 25 patients enrolled. Median (IQR) age and time from diagnosis was 43 (30,52) and 24 (14,30) years, respectively. 8/25 had co-morbidities. Pre-switch therapies were, zinc (13), penicillamine (6), trientine dihydrochloride (4) and combination trientine/zinc (2). Median (range) UCE for zinc treated patients prior to switch 94 (19, 422) mcg/day with 6/13 suggesting non-adherence (UCE >100mcg/day). Median (range) UCE was 118 (26, 757) compared with at first follow up of 222 (21, 610) mcg/day in 12 patients receiving chelation (± zinc). Mean (range) of pills of TETA4 prescribed was 4 (2-6). At T1, based on returned pills, 16/23 were adherent, 6/23 moderately and 1/23 non-adherent. Change in MMAS-8 scores are shown in figure. PESaM questionnaires (24/25) showed improvement in two domains and SF36 questionnaires response showed an overall QoL improvement between T1 and T0.
**Conclusions:** Switching to trientine tetrahydrochloride from existing WD therapy improved treatment adherence and overall QoL. Patient satisfaction with TETA4 improved through perceived ease of use and fewer reported adverse events. Long-term follow-up to assess continued adherence and QoL are needed.




doi: 10.1016/j.dld.2024.01.073

## T-42

### Systolic and diastolic dysfunction in advanced liver disease: does cirrhotic cardiomyopathy really exist?

M. Bevilacqua [1,2], S. Romano [1], R. Villani [3], R. Lombardi [4], F. Cattazzo [1], R. Stupia [1], A. Cespiati [4], F. Cinque [4], D. Ieluzzi [2], V. Paon [2], A.L. Fracanzani [4], G. Serviddio [3], A. Dalbeni [1,2], D. Sacerdoti [2]

[1] *Division of General Medicine C, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy*
[2] *Division of Liver Unit, Department of Medicine, University and Azienda Ospedaliera UniversitariaIntegrata of Verona, Verona, Italy*
[3] *Centro C.U.R.E, Dept. of Medical and Surgical Sciences, University of Foggia, Italy*
[4] *SC-Medicina Indirizzo Metabolico, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, Department of Pathophysiology and Transplantation, University of Milan, Italy*

**Introduction:** Cirrhotic cardiomyopathy (CCM) has been increasingly recognized as a clinically significant comorbidity of chronic advanced liver disease (cALD), mainly because its association with an higher risk for both cardiovascular and liver-related events. Recently, a revised definition of CCM proposed systolic dysfunction (SD, as defined as impaired left-ventricle global longitudinal strain LV-GLS> -18% or hyper-contractility, LV-GLS < -22%), or relevant diastolic dysfunction (DD) as diagnostic criteria. However, the prevalence of CCM is not well defined and there is a lack of knowledge about risk factors of the three different phenotypes of CCM.
**Methods:** Cirrhotic patients of any aetiology and Child-Pugh (CP) class and without previous significant heart diseases were evaluated in three different centres. A complete standard Color- and Tissue-Doppler echocardiography was performed; LV-GLS was obtained.

**Results:** 62 subjects (50 males, median age 62 years, 24 CP A, 21B, 17 C) were evaluated. Age, sex, etiology of liver disease and metabolic risk factors were equally distributed among CP classes. DD and impaired LV-GLS were found in 7 (11.1%) and 11 (17.7%) subjects, respectively; in multivariate analysis, only age (OR 1.13,95%IC [1.02-1.26], p=0.023) and body mass index (OR 1.19,95%IC [1.01-1.40], p=0.039) were independent risk factors. An increasingly number of patients with advanced cirrhosis showed cardiac hyper-contractility (LV-GLS < -22%: 9.1% CP A, 57.1%CP B, 72.2% CP C, p<0.001), that was independently related alternatively to only CP score (OR 1.57, 95%IC [1.18-2.08], p=0.002) or MELD score (OR 1.19, 95%IC [1.06-1.35], p=0.005).
**Conclusion:** Our data are consistent with a high prevalence of cardiac hyper-contractility in cALD CP C. Both DD and SD, quite infrequent in our cohort, were found to be associated withclassical liver-unrelated metabolic risk factors, raising the question on the real patho-physiology of CCM.

doi: 10.1016/j.dld.2024.01.074

## T-43

### Preliminary evidence of the anti-steatotic effect of Abelmoschus esculentus extracts in in vitro models of MASLD

D. Gabbia, I. Zanotto, Y. Frion-Herrera, S. De Martin

*Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Padova, Italy*

**Introduction:** *Abelmoschus esculentus*, traditionally known as Okra, has been used as medicinal food since times, due to its positive effect on lipid profile, glycemic control, and chronic inflammation in diabetic patients, probably due to its antioxidant activity and polyphenol content.
**Aim:** assess the anti-steatotic effect of three Okra extracts in an in vitro model of MASLD.
**Materials and Methods:** The cytotoxic effect of 3 Okra extracts obtained from different extraction methods from seeds (OSE_M, obtained by maceration) and fruits (OFE and OFE_M, obtained by ultrasound-assisted extraction and maceration, respectively) was excluded by crystal violet assay on HepG2 cells. Their effect on the uptake and accumulation of fatty acids in HepG2 treated with palmitic/oleic acid (PA/OA1:1, 0.1 mM) was assessed after 24-treatment (0.5, 2 and 5 mg/mL of extract). The expression of pERK and PLIN2, proteins known to be involved in MASLD pathogenesis, was assessed in HepG2 cell lysates by means of Western blot.
**Results:** The 3 extracts have no effect on HepG2 cell viability after 48 and 72 hours. They significantly reduced the presence of lipid droplets in PA/OA-treated steatotic HepG2 cells in a dose dependent manner. Accordingly, after 24h-treatment at the highest concentration, they significantly reduced the expression of PLIN2 (p<0.05), a lipid droplet scaffolding protein promoting obesity, insulin resistance, or adipose inflammation, and of pERK, a downstream mediator of leptin signaling controlling food intake, body weight and thermogenic sympathetic outflow in steatotic HepG2 cells.
**Conclusions:** Okra extracts obtained from seeds and fruits caused a significant reduction of FA accumulation in hepatocytes due to a modulation of pERK and PLIN2 expression. They deserve further investigation of their possible use as food supplement in MASLD patients.

doi: 10.1016/j.dld.2024.01.075

## T-44

### Alcoholic aetiology and severity of liver disease is correlated with worse Stanford Integrated Psychosocial Assessment for Transplant (SIPAT) in liver transplant candidates (LT) and correlates with post-transplant adherence

E. Zanatta [1], S. Messerotti Benvenuti [2], A. Zanetto [1], F. Pellizzaro [1], E. Patron [2], F.P. Russo [1], M. Gambato [1], G. Germani [1], A. Ferrarese [1], F. Battermann [3], F. Buccheri [3], C. Cavalli [3], R. Schiavo [3], S. Pasquato [3], P. Feltracco [4], U. Cillo [5], P. Burra [1], M. Senzolo [1]

[1] *Multivisceral Transplant Unit-Gastroenterology, Department of Surgery, Oncology and Gastroenterology, Padua University Hospital, Padua, Italy*
[2] *Department of General Psychology, University of Padua, Padua, Italy*
[3] *Unitá Operativa Complessa (UOC) Hospital Psychology, Padua University Hospital, Padua, Italy*
[4] *Department of Medicine, UO Anesthesia and Intensive Care, University of Padua, Italy*
[5] *Hepatobiliary Surgery and Liver Transplant Unit, Department of Surgery, Oncology and Gastroenterology, University of Padua, Italy*

**Introduction:** the SIPAT is a validated interview tool to assess psychosocial well-being in candidates for organ transplantation. Adherence to immunosuppression and clinical follow-up is essential to obtain maximum survival benefit. ALD can decrease candidacy for LT and post-transplant compliance with physicians' prescriptions.
**Material and methods:** we retrospectively analysed (2019-2022), 163 candidates for liver transplantation, 134 finally enrolled, with median (DS) age 57,8 yrs (9,5), MELD score 13,9 (6,3), ALD aetiology 50%, clinical significant portal hypertension 78%. All patients underwent administration of SIPAT during evaluation for LT. Correlations between final admission to the waiting list for LT, clinical characteristics, SIPAT, outcome of those transplanted and evaluation of adherence to immunosuppression by the analysis of the Medication Level Variability Index (MLVI) were performed.
**Results:** During evaluation for LT, 77/134 (57%) were considered at high risk according to SIPAT lever ≥ 21, which significantly correlated with MELD score, ALD aetiology (70%), presence of encephalopathy (28%) and age. 85 patients were listed for LT, and 51 were transplanted; amongst those, 25/51 (49%) showed an MLVI higher than 1.8, suggestive of non-adherence to immunosuppression. In these patients, 68% had a SIPAT score ≥ 21 prior LT. During follow-up, there was only a single recidivism of alcohol abuse (2%).
**Conclusions:** Patients with worse psychosocial characteristics also have higher MELD scores, thus to be prioritised for LT, but possibly less adherence to medical prescriptions after transplantation. This specific subset of patients could be submitted to early psychological pre-habilitation before LT.

doi: 10.1016/j.dld.2024.01.076

## T-45

### Cost analysis of Wilson's disease in Italy: a retrospective cohort study

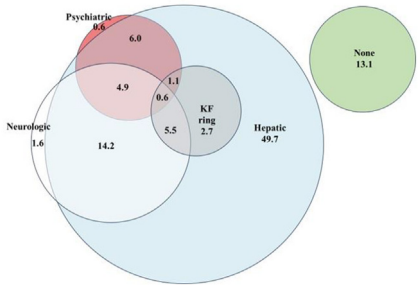
F.S. Mennini [1], N. Cazzagon [2], G. Loudianos [3], M. Zuin [4], P.M. Battezzati [4], G. Maggiore [5], A. Grieco [6], P. Sciattella [1], M. Scortichini [1], E. Baglione [2], M. Senzolo [2], S. Mazza [3], C. Della Corte [5], A. Tortora [6], F. Di Dato [7], M. Matarazzo [7], R. Iorio [7]

[1] *Economic Evaluation and Health Technology Assessment, Centre for Economic and International Studies, Faculty of Economics, University of Rome Tor Vergata, Rome, Italy*
[2] *Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy*
[3] *Clinica Pediatrica e Malattie Rare, Ospedale Regionale per le Microcitemie, Cagliari, Italy*
[4] *Department of Gastroenterology and Hepatology, ASST Santi Paolo e Carlo, Milan, Italy*
[5] *Hepatogastroenterology, Nutrition Digestive Endoscopy and Liver Transplant Unit, IRCCS Pediatric Hospital Bambino Gesù, Rome, Italy*
[6] *Department of Gastroenterological, Endocrine and Metabolic Sciences, Fondazione Policlinico Universitario Gemelli, Catholic University of the Sacred Heart, Rome, Italy*
[7] *Department of Translational Medical Science, Section of Pediatrics, University of Naples Federico II, Naples, Italy*

**Introduction:** Wilson's disease (WD) is an autosomal recessive disease, causing abnormal copper metabolism. It is characterized by a defective elimination of copper, leading to its progressive accumulation and toxicity in the liver, brain, and other organs. Early diagnoses and adequate pharmacological treatment allow a patients' life expectancy similar to the general population.
**Aim:** To describe the demographic and clinical characteristics of WD patients and estimate the economic burden of the disease in Italy using real-world data.
**Methods:** A retrospective multicenter cohort study was conducted involving six national reference centers for WD management in Italy. All patients with a visit for WD between 1/1/2019 and 12/31/2020 were enrolled. Demographic and clinical information at the time of enrolment (baseline) and resource consumption data in the following 12 months were collected, including pharmacological treatment, outpatient visits, diagnostic and laboratory tests, and hospital care. The Ethics Committees of centers approved the study.
**Results:** A total of 243 patients were enrolled, including 60 (24.7%) children and adolescents and 183 adults (75.3%). At baseline, the clinical manifestations of adult population were heterogeneous (figure-1). The mean age at diagnosis was 7.5 years and 15 years respectively. The first-line treatment was d-penicillamine for 61% of patients, followed by zinc acetate (26%), zinc sulfate (9%), and trientine dihydrochloride (4%). At the end of the study-period, 46% of patients were on zinc acetate, followed by penicillamine (26%), trientine tetrahydrochloride (21%), and zinc sulfate (8%). From the diagnosis-date, the percentage of switchers was 10% for pediatric patients (up to 3 switches) and 68.9% for adults (up to 5 switches).

The average annual expenditure per patient was €2,535 for pediatric patients and €10,004 for adults, for these latter costs progressively increase with the number of reported clinical manifestations, ranging from €3,326 to €13,995.
**Conclusions:** The economic burden of WD increases according to the different manifestations of disease.

**Figure 1: Percentage distribution of WD clinical manifestations in the adult population**




doi: 10.1016/j.dld.2024.01.077

## T-46

### The presence of sarcopenia at baseline seems to affect the fibrosis amelioration in patients with metabolic dysfunction associated steatotic liver disease

F. Santomenna [1,2], A. Cespiati [1,2], M. Carlomagno [2], G. Oberti [1], E.A. Pulixi [1], J. Currà [1,2], D. Smith [1,2], R. Lombardi [1,2], E. Fatta [1], C. Bertelli [1], G. Pisano [1], A.L. Fracanzani [1,2]

[1] *SC Medicina ad Indirizzo Metabolico, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico of Milan, Italy*
[2] *Department of Pathophysiology and Transplantation, University of Milan, Italy*

**Introduction:** Sarcopenia, defined as the loss of muscle mass, is linked to metabolic comorbidities, connecting to steatotic liver disease and cardiovascular damage (CVD). The impact of sarcopenia on liver and CVD progression over time is not well understood.
**Aim:** To evaluate the impact of baseline sarcopenia on liver and CVD progression after 5 years in non-cirrhotic metabolic dysfunction-associated liver disease (MASLD) patients.
**Methods:** 178 patients (62% male, mean age 51±10 years) were enrolled. Sarcopenia was defined as skeletal muscle mass/height$^2$ $\leq$ 10.7/7.5 kg/m$^2$ in men/women by bioimpedance analysis. CVD was assessed by carotid plaques or increased intima-media thickness (cIMT) > 0.9 mm at ultrasound, liver fibrosis by liver stiffness measurement (LSM) at Fibroscan and severity of steatosis (grade 2 -3) at ultrasound. After 5 years, liver disease and CVD severity were reassessed.
**Results:** At baseline 45% were sarcopenic, 35% obese, 39% hypertensive, 25% dyslipidemic, 12% diabetic, sarcopenic patients compared to non-sarcopenic were more prevalently males (p=0.04), had lower BMI (26.5 vs 30.8, p<0.001), lower waist circumference (97 vs 105, p<0.001), greater LSM (5.4 vs 4.9 p=0.01), but similar prevalence of carotid plaques (p=0.88). At 5 yrs of follow-up, despite life-style modification, sarcopenic patients maintained lower BMI (26.5 vs 30.8, p<0.001) with no differences in deltaBMI (p=0.10), showed less improvement in low-density lipoprotein (LDL) (9.7 vs 27.9, p=0.04) despite of lipid-lowering lipid drugs use, a less improvement in LSM (0.1 vs 0.7, p=0.04), with no differences in carotid plaques (p=0.97) and increased cIMT (p=0.88). At multivariate analysis, deltaLSM remained associated with sarcopenia (OR 1.86, p=0.04), irrespective of confounders.
**Conclusions:** Baseline sarcopenia seems to be related to less improvement in liver damage. Despite lower visceral adiposity, sarcopenic patients had greater LSM values, with the same extent of CV damage. SLD patients should be screened for sarcopenia to prevent liver disease progression.

doi: 10.1016/j.dld.2024.01.078

## T-47

### The effect of metabolic dysfunction-associated steatotic liver disease on liver fibrosis progression and regression in virus-related liver disease: a multicenter longitudinal study

F. Cinque [1,2], J. Milic [3], S. Renzetti [4], F. Motta [5], J. Bischoff [6], A. Desilani [7], J. Conti [7], F. Medioli [7], M. Del Monte [7], D. Kablawi [1,2], W. Elgretli [8], S. Calza [9], C. Mussini [3], J. Rockstroh [6], G. Guaraldi [3], G. Sebastiani [1,2,8]

[1] *Division of Gastroenterology and Hepatology, McGill University Health Centre, Montreal, Canada*
[2] *Chronic Viral Illness Service, Division of Infectious Diseases, Department of Medicine, McGill University Health Centre, Montreal, Canada*
[3] *Modena HIV Metabolic Clinic, University of Modena and Reggio Emilia, Modena, Italy*
[4] *Department of Medical-Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy*
[5] *Department of Physics, Informatics and Mathematics, University of Modena and Reggio Emilia, Modena, Italy*
[6] *Department of Internal Medicine I, Venusberg Campus 1, University Hospital Bonn, Bonn Germany*
[7] *Infectious Diseases Clinic, Azienda Ospedaliero-Universitaria, Policlinico of Modena, Modena, Italy*
[8] *Division of Experimental Medicine, McGill University, Montreal, Canada*
[9] *Unit of Biostatistics and Bioinformatics, Department of Molecular and Translational Medicine, University of Brescia, Brescia*

**Background:** Metabolic dysfunction-associated steatotic liver disease (MASLD) is a new positive, widely supported and not stigmatizing definition of hepatic steatosis, not requiring the exclusion of secondary causes of liver diseases, such as HIV and viral hepatitis. Liver fibrosis is a dynamic process recognized as the main predictor of liver disease progression and mortality. We aimed to investigate the effect of MASLD on liver fibrosis progression and regression in virus-related liver disease.
**Methods:** We included consecutive people with HIV, with and without coinfection with HCV and HBV, and with at least two transient elastography examinations with controlled attenuation parameters (CAP) from three prospective cohorts in Canada, Italy and Germany. MASLD was defined as the presence of hepatic steatosis (CAP >248 dB/m) and at least one metabolic abnormality, according to a recent multi-society Delphi consensus statement. Fibrosis progression was defined as development of significant liver fibrosis, defined as liver stiffness measurement (LSM) >8 kPa, or transition to cirrhosis, defined as LSM >13 kPa, for those with LSM >8 but <13 kPa at baseline. Fibrosis regression was defined as transition to no liver fibrosis, defined as LSM <8 kPa, or to significant liver fibrosis for those with cirrhosis at baseline. Weight gain was defined as a 5% body mass index increase in two consecutive visits. A continuous-time multi-state Markov model was used to describe transition across fibrosis stages. Cox regression model was used to identify predictors for liver fibrosis progression.
**Results:** 1183 patients were included (median age 53 years, 77% males, median duration since HIV diagnosis 18 years, 25% HIV/HCV coinfected and 4% HIV/HBV coinfected). The baseline prevalence of MASLD, significant liver fibrosis and cirrhosis was 47%, 14% and 6% respectively. During a median follow-up period of 2.5 (1.9-3.5) years, two to six annual LSM were performed. The incidence rate of fibrosis progression and of fibrosis regression was 3.4 per 100 persons-year and 1.2 per 100 person-years, respectively. In Markov model, weight gain predicted fibrosis progression and prevented its regression (see table). On multivariable Cox regression analysis, predictors of fibrosis progression were MASLD (adjusted hazard ratio 2.50, 95% CI 1.06-5.89; p=0.036) and weight gain (adjusted hazard ratio 2.65, 95% CI 1.32-5.26; p=0.006), after adjusting for male sex, age, nadir CD4 cell count, coinfection with HBV and HCV and exposure to different classes of antiretroviral regimens.
**Conclusion:** MASLD and weight gain are the main drivers of liver fibrosis progression in people with HIV, independently of HCV and HBV coinfection and antiretroviral exposure. In the global effort for liver fibrosis screening in at-risk populations, metabolic health should be prioritized in people with HIV.

doi: 10.1016/j.dld.2024.01.079

## T-48

### RESIST-NASH: a regional network for identification and referral of masld patients at risk for liver fibrosis

G. Pennisi [1], S. Buscemi [2], G. Bertino [3], L. Frittitta [4], F. Purrello [5], G. Raimondo [6], F. Cartabellotta [7], M. Russello [8], G. Malizia [9], A. Carroccio [2,10], A. Tuttolomondo [11], S. Camilleri [12], G. Magrì [13], A. Licata [14], A.B. Cefalù [2], M. Di Stefano [15], C. Giordano [16], C. Iaria [17], I. Scalisi [18], T. Prestileo [19], M.L. Arpi [20], V. Di Marco [1], C. Cammà [1], S. Petta [1]

[1] *Section of Gastroenterology and Hepatology, Dipartimento Di Promozione Della Salute, Materno Infantile, Medicina Interna e Specialistica Di Eccellenza (PROMISE), University of Palermo, Italy*
[2] *Dipartimento di Promozione della Salute, Materno-Infantile, Medicina Interna e Specialistica di Eccellenza (PROMISE), University of Palermo, I-90100 Palermo, Italy*
[3] *Gastroenterology and Hepatology Unit, University Hospital Policlinico Vittorio Emanuele, Catania, Italy*
[4] *Diabetes and Obesity Center, Garibaldi Hospital, Catania, Italy*
[5] *Department of Clinical and Experimental Medicine, Internal Medicine, Garibaldi-Nesima Hospital, University of Catania, 95122 Catania, Italy*
[6] *Division of Medicine and Hepatology, University Hospital of Messina, Italy; Department of Clinical and Experimental Medicine, University of Messina, Italy*
[7] *UOC Medicina Interna, Ospedale Buccheri La Ferla, Palermo, Italy*
[8] *Liver Unit, Azienda di Rilievo Nazionale ed Alta Specializzazione (ARNAS) Garibaldi-Nesima, Catania, Italy*
[9] *Gastroenterology Unit, Azienda Ospedaliera Ospedali Riuniti Villa Sofia-Cervello, Palermo, Italy*
[10] *Unit of Internal Medicine, "V. Cervello" Hospital, Ospedali Riuniti "Villa Sofia-Cervello", 90120, Palermo, Italy*
[11] *Internal Medicine and Stroke Care Ward, Department of Health Promotion, Maternal and Infant Care, Internal Medicine and Medical Specialities (ProMISE) "G. D'Alessandro", University of Palermo, Piazza delle Cliniche n.2, 90127, Palermo, Italy*
[12] *Gastroenterology and Endoscopy Unit, "S. Elia- Raimondi" Hospital, Caltanissetta, Italy*
[13] *Division of Gastroenterology, Ospedale di Acireale, Azienda Sanitaria Provinciale di Catania, Italy*
[14] *Medicina Interna ed Epatologia, Dipartimento di Promozione della Salute, Materno-Infantile, di Medicina Interna e Specialistica "G. D'Alessandro", PROMISE, University of Palermo, Via del Vespro 141, 90127, Palermo, Italy*
[15] *Infectious Diseases Unit Umberto Primo Hospital, Siracuse, Italy*
[16] *Section of Endocrinology and Diabetology, Health Promotion, Department of Health Promotion, Mother and Childcare, Internal Medicine and Medical Specialties "G. D'Alessandro", PROMISE, University of Palermo, 90127, Palermo, Italy*
[17] *Infectious Diseases Unit, ARNAS Civico-Di Cristina-Benfratelli Hospital, 90127, Palermo, Italy*
[18] *UOC Medicina Interna, Ospedale di Mazzara del Vallo, ASP, Trapani, Italy*

[19] *Infectious Diseases Unit, Arnas Civico Hospital, Palermo, Italy*
[20] *University of Catania, Department of Clinical and Experimental Medicine, Endocrinology Unit, Garibaldi-Nesima Hospital, Catania, 95122, Italy*

**Background/Aims:** The epidemic of metabolic-dysfunction associated steatotic liver disease (MASLD) and its related hepatic and extrahepatic complications, mostly observed in patients with advanced liver fibrosis, raise concerns about the lack of standardized approaches for case finding and linkage to care. The overall goal is the building of a regional network -RESIST-NASH- using standardized models for identification and referral of MASLD patients at risk for liver fibrosis.
**Methods:** Networking Sicilian specialists in gastroenterology, internal medicine and diabetology. Building a web-based platform for the standardized recording of data about patients with MASLD and/or metabolic risk factors. Automatical elaboration of the FIB-4 score, and according to Italian AISF/SID/SIO guidelines, only patients with a FIB-4 >1.3 are further evaluated by performing FibroScan and by recording further data. The platform allows a direct booking of FibroScan test and of hepatological evaluation across centers. Follow-up visits recording clinical events are also allowed.
**Results:** From 1st April 2023 to 31th October 2023 thirty-eight centers were activated across the Sicily, and twenty-one actively recruited patients with MASLD and/or metabolic risk factors. Nine FibroScan devices were available across the Sicily and shared among centers. Data on 1,424 patients were recorded. Mean age was 58.9 years, 55.2% were male, 47.6% obese, 45.9% were affected by diabetes. Fifty-six percent of patients had a FIB-4 <1.3 and were not worthy of further assessment, while 31.7% were at intermediate risk (FIB-4 1.3-2.67) and 12.3% at high risk (FIB-4 >2.67) of advanced liver fibrosis. Elaboration of data of liver stiffness measurement in patients with at risk FIB-4 and characteristics of this population are ongoing.
**Conclusion:** RESIST-NASH network can allow a systematic approach to patients with NAFLD and/or with metabolic comorbidities, leading to the correct identification and early referral of patients with liver disease worthy of a specialistic follow-up and management.

doi: 10.1016/j.dld.2024.01.080

## T-49

### Chrononutrition as a dietary strategy to reduce hepatic steatotis in patients with metabolic dysfunction-associated steatotic liver disease

G. Castelnuovo [1], N. Perez-Diaz-del-Campo [1], A. Armandi [1,2], G.P. Caviglia [1], C. Rosso [1], M. Guariglia [1], I. Poggiolini [1], F. Bioletto [1], F. Saba [1], A. Olivero [1], M.L. Abate [1], D.G. Ribaldone [1,3], G.M. Saracco [1,2], S. Bo [1], E. Bugianesi [1,3]

[1] *Department of Medical Sciences, University of Turin, Turin, Italy*
[2] *I. Department of Medicine, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany*
[3] *Gastroenterology Unit, Città della Salute e della Scienza – Molinette Hospital, Turin, Italy*

**Introduction & Aim:** Late chronotype, the individual's aptitude to perform daily activities late in the day, has been associated with metabolic dysfunction-associated steatotic liver disease (MASLD). We aimed to investigate the potential association between chronotype, dietary pattern and hepatic steatosis in individuals with MASLD.
**Methods:** 68 patients with MASLD were randomized to a 6-month mediterranean or low-carbohydrate diet, both with calorie restriction, or to a control diet without calorie restriction. Hepatic steatosis was assessed with the controlled attenuation parameter (CAP)(Fibroscan®530,Echosens). The chronotype (MSFsc) was defined by the Munich Chronotype Questionnaire as the mid-sleep on free days (MSF) corrected for sleep debt on working days. To perform the analyses, we defined early, intermediate and late chronotype by splitting the MSFsc into tertiles, evaluating the effect of tertile one versus two+three. Macronutrients (%) intake were calculated from the 3-day food records. Leptin and adiponectin levels were measured by Bioplex (LuminexR).
**Results:** After the intervention, both early and intermediate+late chronotype groups showed a reduction in body mass index (BMI) (both $p<0.001$), CAP ($p=0.017$vs.$p<0.001$), ALT ($p=0.042$vs.$p=0.035$), leptin (both $p<0.001$) and increased adiponectin levels ($p=0.001$vs.$p<0.001$). While early chronotype group showed improved glucose levels ($p=0.027$), intermediate+late group had significantly lower AST and insulin levels ($p=0.018$;$p=0.009$,respectively), as well as MSF and energy intake ($p=0.006$;$p=0.004$,respectively), whereas an increase in protein intake was observed ($p=0.003$). Moreover, 18 patients improved their CAP levels ≥15%, of which 16 (88.8%) were from the intermediate+late group. At multivariate logistic analysis intermediate+late group (OR=9.1; $p=0.015$) and BMI reduction (OR=0.5; $p=0.006$) were significantly and independently associated with CAP improvement.
**Conclusion:** In patients with MASLD and circadian preference towards eveningness, calorie reduction along with earlier sleep may be associated with improved hepatic steatosis. Nonetheless, further studies are needed to elucidate the relationship between chronotype and liver status.

*This research has been supported by the University of Torino, grant number ROSC_RILO_21_01.*

doi: 10.1016/j.dld.2024.01.081

## T-50

### The glucokinase regulator gene (GCKR) rs780094 C>T single nucleotide polymorphism affect diet response in overweight/obese subjects with metabolic-dysfunction associated steatotic liver disease

E. Dileo [1], C. Rosso [1], F. Saba [1], G. Castelnuovo [1], G.P. Caviglia [1], A. Armandi [1,2], M. Tatoli [1], NDDC Perez [1], M. Guariglia [1], M.L. Abate [1], A. Olivero [1], M. Parasiliti-Caprino [1], S. Bo [1], E. Bugianesi [1]

[1] *Department of Medical Sciences, University of Torino, Torino, Italy*
[2] *Department of Internal Medicine I, University Medical Center of the Johannes Gutenberg University, Mainz, Germany*

**Background & aims:** The glucokinase regulator gene (GCKR) rs780094 C>T single nucleotide polymorphism (SNP), involved in the regulation of glucose metabolism, has been associated with obesity and hepatic steatosis in patients with metabolic-dysfunction associated steatotic liver disease (MASLD). We explored its potential impact on diet response in a group of overweight/obese MASLD patients.
**Methods:** We analyzed 73 subjects (mean age 51±12y; male, N=50) with MASLD who underwent a calorie-restricted diet for 6 months. At baseline (t0) and after 6-months diet (t6) we collected blood samples and anthropometrical measurements. *GCKR* rs780094 C>T genotyping was performed by allelic discrimination assay. Hepatic steatosis was determined by controlled attenuation parameter (CAP, Fibroscan®).
**Results:** Overall, 44 (60.3%) patients were obese, 15 (20.5%) had type 2 diabetes and 28 (38.4%) had arterial hypertension. The prevalence of the *GCKR* rs780094 genotypes was 20.5% (CC), 41.1%

(CT) and 38.4% (TT). After 6 months of diet, all patients significantly improved BMI (t0=30.5 kg/m$^2$ *vs.* t6=29.5 kg/m$^2$, p<0.001) and CAP (308 dB/m *vs.* 274 dB/m, p<0.001). Specifically, a 15% of CAP improvement was observed in 20 subjects (27.4%). CAP and HOMA-IR significantly decreased in patients carrying the *GCKR* rs780094 TT risk omozygosis compared to those with the CC/CT variants (p=0.045 and p=0.048, respectively). At multivariate logistic regression analysis adjusted for age, gender, weight, HOMA-IR and energy intake, 15% of CAP decrease after diet was associated with *GCKR* TT genotype (OR=4.04, 95% CI=1.13-14.45, p=0.032).
**Conclusion:** Overweight/obese patients with MASLD carrying the GCKR rs780094 TT genotype are more likely to improve liver steatosis following a calorie-restricted diet.

*Funded by the University of Turin, g.n. ROSC_RILO_23_01.*

doi: 10.1016/j.dld.2024.01.082

## T-51

### Clinical outcomes of metabolic liver disease versus non-alcoholic fatty liver disease: a meta-analysis of observational studies

G. Pennisi [1,*], G. Infantino [1,*], C. Celsa [1,*], G. Di Maria [1], M. Enea [2], M. Vaccaro [2], R. Cannella [3], C. Ciccioli [1], C. La Mantia [1], A. Mantovani [4], F. Mercurio [1], H. Tilg [5], G. Targher [4,6], V. Di Marco [1], C. Cammà [1,°], S. Petta [1,°]

[1] *Section of Gastroenterology and Hepatology, Dipartimento Di Promozione Della Salute, Materno Infantile, Medicina Interna e Specialistica Di Eccellenza (PROMISE), University of Palermo, Italy*
[2] *Dipartimento di Scienze Economiche, Aziendali e Statistiche, University of Palermo, Italy*
[3] *Department of Biomedicine, Neuroscience and Advanced Diagnostics (BiND), University of Palermo, Italy*
[4] *Department of Medicine, Section of Endocrinology, Diabetes, and Metabolism, University of Verona, Verona, Italy*
[5] *Department of Internal Medicine I, Gastroenterology, Hepatology, Endocrinology & Metabolism, Medical University Innsbruck, Austria*
[6] *Metabolic Diseases Research Unit, IRCCS Sacro Cuore Don Calabria Hospital, Negrar di Valpolicella, Italy*

∗ These authors equally contributed to the study.
° These authors equally contributed to the study.

**Background & Aim:** The recent terminology change from non-alcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease (MAFLD) and then metabolic dysfunction-associated steatotic liver disease (MASLD) highlights the link between hepatic steatosis and metabolic dysfunction, taking out the stigmata of alcohol. We examined the comparative effects of NAFLD and MAFLD definitions on the risk of overall and cardiovascular (CV) mortality, liver-related events (LRE), nonfatal CV events (CVE), chronic kidney disease (CKD) and extra-hepatic cancers (EHC).
**Methods:** We systematically searched four large electronic databases for cohort studies (published through August 2023) that simultaneously used NAFLD and MAFLD definitions for examining the risk of mortality and adverse cardiovascular, renal, or oncological outcomes associated with both definitions. In total, 21 eligible cohort studies were identified.
**Results:** Compared with those with NAFLD, MAFLD individuals had significantly higher rates of overall mortality (random-effect OR 1.12, C.I. 1.04-1.21, p=0.004) and cardiovascular mortality (OR 1.15, C.I. 1.04-1.26, p=0.004), and a marginal trend towards higher rates of CKD (OR 1.06, C.I. 1.00-1.12, p=0.058) and EHC events (OR 1.11, C.I. 1.00-1.23, p=0.052). We found no significant differences in LRE and nonfatal CVE between MAFLD and NAFLD. Meta-regression analyses identified male sex and metabolic comorbidities as the strongest risk factors related to the risk of adverse clinical outcomes in MAFLD compared to NAFLD.
**Conclusions:** Individuals with MAFLD have significantly higher rates of overall and cardiovascular mortality and marginally higher rates of CKD and EHC events than those with NAFLD, possibly due to the less favorable metabolic risk profile of MAFLD.

doi: 10.1016/j.dld.2024.01.083

## T-52

### Semaglutide for type 2 diabetes control in metabolic dysfunction-associated steatotic liver disease (MASLD): a two-way effect?

G. Petralli [1], A. Salvati [2], S. Cappelli [3], L. Surace [2], G. Ricco [2], P. Colombatto [2], A. Solini [1], M.R. Brunetto [2,3]

[1] *Department of Surgical Medical, Molecular and Critical Area Pathology, University of Pisa, Pisa, Italy*
[2] *Hepatology Unit and Laboratory of Molecular Genetics and Pathology of Hepatitis Viruses, Reference Center of the Tuscany Region for Chronic Liver Disease and Cancer, University Hospital of Pisa, Pisa, Italy*
[3] *Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy*

**Introduction and Aim:** Therapeutic options for MASLD burden in T2D patients are scanty. GLP1-receptor agonists (GLP1-ra) are clearly indicated for T2D treatment and Semaglutide was shown to induce the steatohepatitis resolution at high daily dosage. In consecutive MASLD- GLP1-ra naïve diabetic patients we studied the impact on liver disease of Semaglutide introduction for glycemic control indication using non-invasive surrogate markers of liver steatosis and fibro-inflammation.
**Methods:** In 62 consecutive overweight/obese T2D pts with MASLD (age 61.4 ± 11.3yrs, females 32%, BMI 31.4 ± 5.0kg/m2), anthropometric, bio-humoral and transient elastography (TE) data were collected before (t0) and after 6.4 (6.1-6.6) months (t1) from the 1$^{st}$ injective/oral Semaglutide prescription. GIP, GLP1, Glucagon, Insulin, AST, ALT and GGT were measured in t0-t1 serum samples. FibroScan CAP and liver stiffness (LS) were used as non-invasive markers of liver steatosis and fibro-inflammation involvement (proxy), respectively.
**Results:** BMI (-1.4 ± 0.2kg/m$^2$), Waist Circumference (-3 ± 1cm), AST (-10 ± 3UI/L), ALT (-18 ± 5UI/L) GGT (-33 ± 15UI/L), glycol-metabolic parameters [fasting glucose (-40 ± 6mg/dl) and glycated hemoglobin (-12 ± 1mmol/mol)], CAP (-25 ± 8dB/m), and LS (-0.8 ± 0.4kPa) t0-t1 reductions were significant (p<0.006), while GLP1 (+95.9pM, p<0.0001) increased. Variations of serum ALT and GGT levels associated with glycated hemoglobin reduction (r=0.340, p=0.0196 and r=0.368, p=0.0210, respectively), but not with change in serum concentration of incretin hormones. CAP declined in association with BMI decline (r=0.391, p=0.0035) and GLP1 increase (r=-0.415, p=0.0251). In a multivariate model adjusted for all above mentioned variations, only the GLP1 increase was associated with CAP reduction (p=0.0468).
**Conclusion:** Semaglutide treatment for T2D in MASLD pts associates with a significant decline of non-invasive liver steatosis and fibro-inflammation proxy. While glycemic optimization correlated with a reduction of transaminases, an independent effect of GLP1 increase was associated with a reduction of the steatosis index.

doi: 10.1016/j.dld.2024.01.084

## T-53

### Non-invasive assessment of hepatic steatosis by ultrasound-derived fat fraction (UDFF) in individuals at high-risk for metabolic dysfunction-associated steatotic liver disease

F. Tavaglione [1,2], V. Flagiello [1], F. Terracciani [1,2], P. Gallo [1,2], E. Capparelli [1], C. Spiezia [3], A. De Vincentis [4,5], A. Palermo [6,7], S. Scriccia [8], G. Galati [2], N. Napoli [6,7], S.J. Daniels [9], J.E. Blau [10], B. Carlsson [11], Y.M. Khazrai [3,12], R. Antonelli Incalzi [4,5], A. Picardi [1,2], U. Vespasiani-Gentilucci [1,2]

[1] *Research Unit of Clinical Medicine and Hepatology, Department of Medicine and Surgery, Università Campus Bio-Medico di Roma, Rome, Italy*
[2] *Operative Unit of Clinical Medicine and Hepatology, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy*
[3] *Research Unit of Food Science and Human Nutrition, Department of Science and Technology for Sustainable Development and One Health, Università Campus Bio-Medico di Roma, Roma, Italy*
[4] *Research Unit of Internal Medicine, Department of Medicine and Surgery, Università Campus Bio-Medico di Roma, Rome, Italy*
[5] *Operative Unit of Internal Medicine, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy*
[6] *Research Unit of Metabolic Bone and Thyroid Disorders, Department of Medicine and Surgery, Università Campus Bio-Medico di Roma, Rome, Italy*
[7] *Operative Unit of Metabolic Bone and Thyroid Disorders, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy*
[8] *Check-up Center, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy*
[9] *Research and Early Development, Cardiovascular, Renal and Metabolism, BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK*
[10] *Research and Early Development, Cardiovascular, Renal and Metabolism, BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, Maryland*
[11] *Translational Science and Experimental Medicine, Research and Early Development, Cardiovascular, Renal and Metabolism, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden*
[12] *Operative Research Unit of Nutrition and Prevention, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy*

**Introduction:** Given the increasing number of individuals developing metabolic dysfunction-associated steatotic liver disease (MASLD) and the low rate of those with progressive liver disease, there is a pressing need to conceive simple and affordable biomarkers to assess MASLD in general population settings.
**Aims:** To investigate the performance of the recently developed ultrasound-derived fat fraction (UDFF) for hepatic steatosis in high-risk individuals.
**Materials and methods:** A total of 302 individuals with obesity, type 2 diabetes, or clinical history of hepatic steatosis was included in the analyses. Clinical, laboratory, and imaging data were collected using standardized procedures during a single screening visit in Rome, Italy. Hepatic steatosis was defined either by controlled attenuation parameter (CAP) $\geq$263 dB/m or ultrasound-based Hamaguchi's score $\geq$2. UDFF performance for hepatic steatosis was estimated by the area under the receiver operating characteristic curve (AUC).
**Results:** Overall, median (IQR) UDFF was 12% (7-20). UDFF was positively correlated with CAP ($\rho$=0.73, p<0.0001) and Hamaguchi's score ($\rho$=0.79, p<0.0001). Independent predictors of UDFF were circulating triglycerides, alanine aminotransferase (ALT), and ultrasound-measured visceral adipose tissue (VAT). UDFF AUC was 0.89 (0.85-0.93) and 0.92 (0.88-0.95) for CAP- and ultrasound-diagnosed hepatic steatosis, respectively. UDFF AUC for hepatic steatosis was higher than those of fatty liver index (FLI), hepatic steatosis index (HSI), and ALT (p<0.0001). Lower age, ALT, and VAT were associated with discordance between UDFF and ultrasound.
**Conclusions:** UDFF may be a simple and accurate tool to detect hepatic steatosis and to monitor changes in hepatic fat content over time or in response to therapeutic interventions beyond clinical trial settings.

doi: 10.1016/j.dld.2024.01.085

## T-54

### Improvement of insulin resistance indicators in subjects with metabolic syndrome under treatment with Gliflozins: possible role in the control of the natural history of MASLD

R. Citarrella [1], R. Chianetta [1], M. Soresi [1], D. Nikolic [2], L. Mirarchi [3], S. Amodeo [3], A. Licata [1], L. Giannitrapani [1]

[1] *Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy*
[2] *Interdisciplinary Department of Medicine, University of Bari, Bari, Italy*
[3] *Department of Internal Medicine, National Relevance and High Specialization Hospital Trust ARNAS Civico Di Cristina Benfratelli, Palermo, Italy*

**Introduction:** Metabolic syndrome (MetS) includes a set of interrelated metabolic alterations that contribute to increasing the risk not only of cardiovascular disease (CVD) but also of metabolic dysfunction associated steatotic liver disease (MASLD).
**Aim:** The objective of the study was to evaluate the reduction of insulin resistance indicators, CVD and MASLD risk parameters and to demonstrate the superiority of glycemic control in the group treated with SGLT-2 inhibitors (i-SGLT-2) versus the group not treated with the intervention.
**Materials and methods:** Sixty patients suffering from type 2 diabetes were enrolled. A single fixed oral dose of SGLT-2 inhibitor was added to the patients in Group A (n 30) already treated with Metformin 2-3 g, Dapagliflozin 10 mg daily. Group B (n 30) patients continued therapy with Metformin 2-3 g and Gliclazide 60 mg daily. Both groups were studied at baseline and after six months; at each time the following were measured: weight, height, BMI, waist circumference (WC), HbA1c, fasting blood sugar, insulinemia, cholesterol, triglycerides, creatininemia, AST/ALT, gamma-GT. VAI (Visceral Adiposity Index), HOMA-IR and HOMA-beta (Homeostatic Model Assessment), FLI (Fatty Liver Index), eGDR (estimated Glucose Disposal Rate).
**Results:** Only in group A an improvement in both the anthropometric parameters and the lipid profile was documented. Regarding the indicators of insulin resistance, a statistically significant improvement in HOMA-IR, FLI and eGDR was observed in group A. Both the HOMA-beta index and the VAI index had no statistically significant changes, although for both models a trend of improvement was found in group A vs B.
**Conclusions:** The objective was achieved exclusively in the group treated with Gliflozins, demonstrating a reduction in insulin resistance indicators and at the same time in CVD and MASLD risk parameters thus hypothesizing the use of this category of drugs in the prevention of liver damage in subjects with MetS.

doi: 10.1016/j.dld.2024.01.086

## T-55

### Association between severity of liver and cardiovascular damage in patients with metabolic dysfunction-associated steatotic liver disease (MASLD) according to cardiovascular risk categories

J. Currà [1,2], A. Cespiati [1,2], E.A. Pulixi [1], R. Lombardi [1,2], G. Oberti [1], C. Bertelli [1], E. Fatta [1], G. Pisano [1], F. Santomenna [1,2], D. Smith [1,2], F. Cinque [1,2], A.L. Fracanzani [1,2]

[1] *SC Medicina ad Indirizzo Metabolico, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Department of Pathophysiology and Transplantation, University of Milan, Italy*

**Background:** In 2023, the nomenclature of non-alcoholic fatty liver disease (NAFLD) was replaced by the more inclusive terminology of metabolic dysfunction-associated steatotic liver disease (MASLD), characterized by hepatic steatosis with at least one cardiometabolic risk factor. MASLD encompasses different disease severities ranging from steatosis, steatohepatitis (MASH), fibrosis, cirrhosis, and hepatocellular carcinoma. In 2021, the European Society of Cardiology (ESC) redefine CV risk and identified three risk categories (low, high, and very high).
**Aim:** To evaluate, in a cohort of MASLD patients without a history of previous CV events, the severity of liver damage and metabolic comorbidities according to the ESC 2021 CV risk.
**Methods:** 287 MASLD patients, fully characterized for metabolic, liver, and CV features, were divided into 3 groups according to the degree of CV risk. Liver fibrosis was assessed by liver stiffness measurement (LSM) and confirmed by histology in 30. CV damage was defined by the presence of carotid plaques or carotid intima-media thickness (cIMT) $\geq$ 0.9 mm by ultrasound. Epicardial fat thickness (EFT) was evaluated by echocardiography.
**Results:** with rising CV risk a significant increase in BMI (29±4.8 vs 31±4.4 kg/m2, p<0.001), obesity (33% vs 58%, p<0.001), liver fibrosis (4.7± 2.0 vs 5.2± 2.2 kPa, p=0.02), EFT (7.3±2.8 vs 8.3±3.0 mm, p=0.04), diabetes (7 vs 23%, p=0.004) and hypertension (39 vs 63%, p=0.003) was observed, as expected, carotid plaques and cIMT progressively increased from low to high-very high CV risk (p<0.001, and p=0.0003, respectively). At multivariate analysis, adjusted for age, sex, and all metabolic parameters, LSM was independently associated with the highest CV risk (OR 1.2, 95% C.I. 1.01-1.31).
**Conclusion:** The association between cardiometabolic factors and liver fibrosis severity exposes patients with MASLD to increased CV risk and should be well evaluated in all patients, thus making integrated management mandatory to reduce CV and liver disease progression.

doi: 10.1016/j.dld.2024.01.087

## T-56

### Identification of key predictors of significant weight loss in metabolic dysfunction-associated steatotic liver disease (MASLD) patients: a multicentre study

I. Arcari [1], N. Pugliese [1,2], S. Rocchetto [3], R. Lombardi [4,5], G. Pennisi [6], M. Sagasta [1,7], M. Soleri [1], D. De Deo [1], F. Cerini [3], A. Cespiati [4,5], S. De Nicola [1,2], D. Polverini [1], F. Colapietro [1,2], C. Masetti [1,2], A.L. Fracanzani [4,5], S. Petta [6,8], M. Viganò [3], A. Aghemo [1,2]

[1] *Department of Biomedical Sciences, Humanitas University, Milan, Italy*
[2] *Division of Internal Medicine and Hepatology, Department of Gastroenterology. IRCCS Humanitas Research Hospital, Via Manzoni 56, 20089, Rozzano, Milan, Italy*
[3] *Hepatology Division San Giuseppe Hospital, MultiMedica IRCCS, Università degli Studi di Milano, Via San Vittore 12, 20123, Milan, Italy*
[4] *Unit of Internal Medicine and Metabolic Disease, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, 20122, Milan, Italy*
[5] *Department of Pathophysiology and Transplantation, Università degli Studi di Milano, 20133, Milan, Italy*
[6] *Section of Gastroenterology and Hepatology, PROMISE, University of Palermo, Palermo, Italy*
[7] *Division of Gastroenterology, Maggiore Hospital and IRCCS Foundation, Milano, Italy*
[8] *Sezione di Gastroenterologia e Epatologia, Di. Bi.M.I.S., Università di Palermo, Piazza delle Cliniche 2, Palermo, 90127, Italy*

**Background and aim:** Significant weight loss is the only proven therapy for patients with metabolic dysfunction-associated steatotic liver disease (MASLD). This study aimed to identify factors that predict significant weight loss - exceeding 7% of the initial weight - in MASLD outpatients.
**Methods:** We included all MASLD patients referred to four Italian tertiary liver centres between January 2019 and December 2021. They received advice on lifestyle changes according to current guidelines, with reassessment of anthropometric measures after 18 to 24 months.
**Results:** After evaluating 908 patients meeting the inclusion criteria, the majority were found to be male (518/908, 57%) with a mean age of 61.7 ± 13.31 years and a mean baseline body mass index (BMI) of 30.31 ± 4.49 kg/m2. Over a mean follow-up period of 21.88 ± 6 months, only 166 (18.3%) patients achieved significant weight loss. Unadjusted regression analysis revealed significant correlations between dyslipidaemia, baseline BMI $\geq$ 30kg/m2, and the use of GLP-1 (glucagon-like peptide 1) agonists with significant weight loss (p<0.05). Multivariate regression analysis identified only BMI $\geq$ 30 kg/m2 (OR = 1.96, 95% CI: 1.37-2.8) and dyslipidaemia (OR = 0.6, 95% CI: 0.44-0.88) as independent predictors of significant weight loss.
**Conclusions:** A baseline BMI $\geq$ 30 kg/m2 and the absence of dyslipidemia emerged as significant predictors of achieving substantial weight loss in MASLD patients. These findings highlight the need for personalized interventions to improve the effectiveness of weight management strategies in MASLD.

doi: 10.1016/j.dld.2024.01.088

## T-57

### Exploring occupational toxicant exposures in patients with metabolic dysfunction-associated steatotic liver disease: a prospective pilot study

F. Tovoli [1,2], B. Stefanini [1], D. Mandrioli [3], S. Mattioli [4], A. Vornoli [3], D. Sgargi [3], F. Manservisi [3], F. Piscaglia [1,2], S. Curti [1], L. Bolondi [1]

[1] *Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy*
[2] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[3] *Cesare Maltoni Cancer Research Center, Ramazzini Institute, Bologna, Italy*
[4] *Department of Environmental and Prevention Sciences, University of Ferrara, Ferrara, Italy*

**Background:** Metabolic dysfunction-associated steatotic liver disease (MASLD) has been traditionally associated with insulin resistance and obesity. Recently, pollutants have been shown to contribute to the development of MASLD. Given the global burden of MASLD, understanding whether pollutants are merely associated with steatosis or contribute to its progression to advanced chronic liver disease (ACLD) and hepatocellular carcinoma (HCC) is critical. Workers exposed to occupational toxicants represent an ideal population for assessing the potentially hazardous consequences of professional exposure. Confirming a link between occupational exposure and ACLD/HCC may provide further elements in understanding MASLD and contribute to preventive strategies for exposed workers.
**Aim:** This study aimed to assess the prevalence of self-reported occupational exposure to toxicants in patients with MASLD.
**Methods:** This hospital-based prospective pilot study included 201 patients with MASLD. Data on workplace toxicant exposure were collected systematically using a structured questionnaire. Subsequently, patients with ACLD and/or HCC (n=55) were compared to controls (n=146). Logistic regression analysis and propensity score models were used to investigate the associations between self-reported occupational exposure and ACLD and/or HCC.
**Results:** Patients with ACLD/HCC reported exposure to metals, halogenated refrigerants, pain/resins, and fuel emissions more often than the controls. After controlling for confounders, durations of 21–30 years and >30 years of occupational exposure to toxicants showed odds ratios (ORs) of 2.31 (95% confidence interval [CI]: 1.09–4.88, p=0.029) and 4.47 (95% CI: 2.57–7.78, p<0.001), respectively.
**Conclusions:** In this pilot study, patients with MASLD complications were more likely to report workplace toxicant exposure. Our results warrant future multicentre confirmatory studies, as implementing prevention policies may reduce the risk of life-threatening diseases among exposed populations.

doi: 10.1016/j.dld.2024.01.089

## T-58

### Psychopathology and coping strategies in MASLD-related compensated advanced chronic liver disease

E. Maggio, A. Liguori, L.A. Antuofermo, G. Marrone, M. Biolato, M. Pompili, A. Grieco, A. Gasbarrini, R. Calia, L. Miele

*Fondazione Policlinico Universitario A. Gemelli IRCCS - Università Cattolica del Sacro Cuore, Rome, Italy*

**Introduction:** Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is characterized by a variety of symptoms known to have a negative impact on patients' health-related quality of life. In particular, depression and anxiety symptoms are associated to progression of chronic liver diseases.
**Aim:** The aim is to investigate the association between psychopathology (depression, anxiety, worry, emotional dysregulation), coping strategies and Compensated Advanced Chronic Liver disease (cACLD) in MASLD patients.
**Materials and methods:** This is a cross-sectional study conducted at MASLD clinic. We recruited 98 patients with MASLD stratified in cACLD and no-cACLD groups according to Baveno VII guidelines. Each patient underwent a psychological interview and the administration of validated questionnaires: BDI-II (depression), STAI-Y (state and trait anxiety), DERS (identify/regulate emotions), Brief-COPE (coping strategies) and PSWQ (worry). According to cACLD diagnosis, descriptive analyses on the sample and Student's t tests for all the scales and subscales of psychological testing were performed.
**Results:** Among the 98 patients (67.3% men; mean age 54 years) 27/98 (27.6%) had cACLD, 35/98 (35.7%) reach the clinical cut-off for depression, 15/98 (15.3%) for state and trait anxiety, 15/98 (15.3%) for emotional dysregulation, and 58/98 (59.2%) for uncontrollable and excessive worry. cACLD group has higher prevalence and severity of depression, somatic-affective component of depression, state/trait anxiety than no-cACLD group. cACLD group has higher DERS-Awareness (tendency to acknowledge emotions) ($p < .01$) but lower DERS-Strategies (difficulties in regulating emotions) ($p < .05$) than non-cACLD group. cACLD group has problem-focused coping strategies.
**Conclusions:** Patients with cACLD show more psychopathology than patients without cACLD. They also have more emotional awareness but, on the other hand, limited access to emotion regulation strategies. It would be important to plan psychological support for patients to better cope with the disease and to reinforce coping strategies related to steatosis.

doi: 10.1016/j.dld.2024.01.090

## T-59

### Evaluation of ChatGPT as a counselling tool for Italian-speaking MASLD patients: assessment of accuracy, completeness and comprehensiveness

N. Pugliese [1,2], D. Polverini [1,2], R. Lombardi [3], G. Pennisi [4], F. Ravaioli [5], A. Armandi [6], E. Buzzetti [7], A. Dalbeni [8], A. Liguori [9], A. Mantovani [10], R. Villani [11], L. Valenti [12,13], L. Miele [9,14], S. Petta [4], G. Sebastiani [15], C. Hassan [2,16], A. Aghemo [1,2]

[1] *Division of Internal Medicine and Hepatology, Department of Gastroenterology, IRCCS Humanitas Research Hospital, Rozzano, MI, Italy*
[2] *Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, MI, Italy*
[3] *Unit of Internal Medicine and Metabolic Disease, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, Italy; Department of Pathophysiology and Transplantation, University of Milan, Italy*
[4] *Section of Gastroenterology and Hepatology, PROMISE, University of Palermo, Palermo, Italy*
[5] *Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy*
[6] *Division of Gastroenterology and Hepatology, Department of Medical Sciences, University of Turin, Corso Dogliotti 14, 10126, Turin, Italy*
[7] *Internal Medicine and Centre for Hemochromatosis and Hereditary Liver Diseases, ERN-EuroBloodNet Center for Iron Disorders, Azienda Ospedaliero-Universitaria di Modena-Policlinico, Modena, Italy. Department of Medical and Surgical Sciences, Università degli Studi di Modena e Reggio Emilia, Modena, Italy*
[8] *Division of General Medicine C, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, University of Verona, Verona, Italy; Liver Unit, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, University of Verona, Verona, Italy*
[9] *DiSMeC - Department of Scienze Mediche e Chirurgiche, Fondazione Policlinico Gemelli IRCCS, Rome, Italy*
[10] *Section of Endocrinology, Diabetes and Metabolism, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Piazzale Stefani, 1, 37126, Verona, Italy*
[11] *C.U.R.E. (University Center for Liver Disease Research and Treatment), Liver Unit, Department of Medical and Surgical Sciences, University of Foggia, Foggia, Italy*
[12] *Precision Medicine Lab, Biological Resource Center - Department of Transfusion Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[13] *Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy*
[14] *Department of Medicina e Chirurgia Traslazionale, Università Cattolica Del Sacro Cuore, Rome, Italy*
[15] *Division of Gastroenterology and Hepatology, McGill University Health Centre, Montreal, Canada*
[16] *Division of Gastroenterology and Digestive Endoscopy, Humanitas Research Hospital-IRCCS, Rozzano, MI*

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a significant global public health concern and is expected to become the leading indication for liver transplantation in the coming decades. Chatbots, which utilize artificial intelligence (AI) to simulate conversations with users, could provide counselling and support to English-speaking patients with MASLD. In a recent study, we showed that while ChatGPT 3.5 is complete and comprehensive in answering MASLD-related questions, its accuracy is still suboptimal. Whether language plays a role in modifying these findings is unclear.

We evaluated the accuracy, completeness and comprehensiveness of ChatGPT 3.5 in answering 15 pre-set questions about MASLD in Italian. The questions were grouped into three domains: specialist referral, physical activity, and dietary composition. ChatGPT responses were rated on a 6-point accuracy scale, a 3-point completeness scale, and a 3-point comprehensibility scale by 13 native Italian MASLD experts.

The mean scores for accuracy and completeness were 4.57 ± 0.42 and 2.53 ± 0.51 respectively, with a mean score of 2.91 ± 0.07 for comprehensiveness. The physical activity domain received the highest mean score, with 4.82 ± 0.22 and 2.35 ± 0.11 for accuracy and completeness respectively. The mean Kendall's coefficient of concordance for accuracy, completeness and comprehensiveness across all 15 questions was 0.524, 0.623 and 0.73 respectively. Age and academic role of the evaluators did not affect the scores. The scores were not significantly different from those reported in our previous study focusing on the English language.

In conclusion we have shown that language does not affect the ability of ChatGPT to provide complete and understandable counselling for MASLD patients, however its accuracy remains suboptimal in certain domains. To ensure the trustworthiness of medical information provided by AI, the collaboration between healthcare professionals, patient associations and medical literature databases needs to be further improved.

doi: 10.1016/j.dld.2024.01.091

## T-60

### Significant decrease of hepatic steatosis is associated with decreased PAI-I levels in overweight/obese subjects with Metabolic-dysfunction Associated Steatotic Liver Disease

C. Rosso [1], K. Gjini [1], F. Saba [1], G. Castelnuovo [1], A. Armandi [1,2], G.P. Caviglia [1], N. Perez-Diaz-Del-Campo [1], E. Dileo [1], M. Scalici [1], M. Guariglia [1], M.L. Abate [1], A. Olivero [1], M. Parasiliti-Caprino [1], S. Bo [1], E. Bugianesi [1]

[1] *Division of Gastroenterology and Hepatology, Department of Medical Sciences, University of Turin, Italy*
[2] *Metabolic Liver Disease Research Program, University Medical Center of the Johannes Gutenberg, University of Mainz, Germany*

**Background & Aims:** Obese/overweight patients with metabolic-dysfunction associated steatotic liver disease (MASLD) are at higher risk of developing cardiovascular (CVD) events. Plasminogen activator inhibitor (PAI-1) plays a key regulatory role in fibrinolysis and is predictive of CVD events. We aimed to analyze PAI-1 levels and cardiovascular (CVD) risk in overweight/obese subjects with MASLD, and to assess their association with hepatic steatosis improvement.

**Methods:** We analyzed 73 subjects (mean age 51±12y; male, N=50) with MASLD who underwent a restricted calories diet for 6 months. At baseline (t0) and after 6-months diet (t6) we collected blood samples and anthropometrical measurements. PAI-1 was measured by Luminex®. 10 years CVD risk was calculated by Framingham (FRM) score. For all the metabolic parameters, we calculated the variation from t6 to t0 (Δ). Hepatic steatosis was determined by CAP (Fibroscan®). 20% of CAP improvement was considered as clinical endpoint.

**Results:** At baseline, PAI-1 levels significantly correlated with fasting insulin (r=0.51, p<0.001), CAP (r=0.46, p<0.001), liver stiffness (r=0.29, p=0.013) and FRM score (r=0.24, p=0.037). The FRM score significantly correlated with waist circumference (r=0.27, p=0.023), fasting glucose (r=0.40, p<0.001), fasting total cholesterol (r=0.24, p=0.040), CAP (r=0.33, p=0.005) and liver stiffness (r=0.38, p<0.001). After 6 months diet, the FRM score decreased by 14% (p=0.002) independent by the established clinical endpoint. Conversely, PAI-1 levels improved by 20% only in patients who ameliorated CAP by 20% (p=0.008). At multivariable logistic

regression analysis adjusted for age, gender, Δenergy intake and Δweight loss, 20% of CAP decrease after diet was associated with a significant reduction of FRM and PAI-1 (OR=6.9, p=0.029 and OR=3.9,p=0.05).
**Conclusion:** The decrease in PAI-1 levels and FRM score obtained after a 20% decrease in hepatic steatosis suggests that this threshold of steatosis improvement is necessary to significantly reduce the cardiovascular risk in MASLD patients.

Funded by the University of Turin, g.n.ROSC_RILO_23_01

doi: 10.1016/j.dld.2024.01.092

## T-61

### Repeated measurements and data integration to monitor and study MASLD patients experiencing weight loss

P. Torre, L. Schiavo, B.M. Motta, M. Aquino, F. Belladonna, M. Masarone, M. Persico

*Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, Baronissi, SA, Italy*

**Introduction:** MASLD is a multifactorial disease for which there are no approved pharmacological therapies and for which lifestyle changes still represent the most effective remedy. Nutritional studies could be essential to increase knowledge and assess causality in the field of MASLD.
**Aim:** Our aim is to monitor patients diagnosed with MASLD who attend a weight-loss program at our Hepatology Unit, through repeated measurements of clinical parameters, transient elastography (TE), controlled attenuation parameter (CAP), and blood tests. The interaction between genetics and TE/CAP is also considered.
**Patients and Methods:** Overweight or obese MASLD patients, aged ≥ 18, without decompensated cirrhosis or active cancer, were proposed to start a low-glycemic index, nutritionist-guided diet. Weight, BMI, TE/CAP, and blood tests recorded at baseline were compared with the same measurements obtained after 6 months. Weight loss was categorized into classes of weight change compared to baseline (<5%, 5%–10%, >10%). A genetic risk score (GRS) was calculated for each patient and related to changes in TE/CAP
**Results:**Among the 131 patients who underwent the first nutritional visit, 50 attended the 6-months control visit to date. At this time-point, as we previously observed in earlier follow-up visits, a significant difference compared to baseline was found in weight, BMI, and CAP (respectively -7.47 kg [-8.10%], -2.67 Kg/m$^2$, and -45.88 dB/m; all p<0.0001). The latter improved proportionally to the extent of weight loss; mean liver stiffness, on the contrary, remained almost unchanged, but it decreased in the >10% weight reduction class. Patients with high GRS experienced a greater decrease in TE/CAP values after 6 months of diet. Liver biochemistry also improved.
**Conclusions:** Diet-induced weight loss has beneficial effects on MASLD, and liver disease improves proportionally to its extent. Genetics appear to modulate change in liver disease severity in patients on diet. Weight loss data represent the backbone of our ongoing studies on changes in metabolomics and gut microbiota for these patients, aimed at further investigate the pathophysiology of the disease.

doi: 10.1016/j.dld.2024.01.093

## T-62

### Response to a 6-month personalized dietary intervention in patients with metabolic dysfunction-associated steatotic liver disease

N. Perez-Diaz-del-Campo [1], G. Castelnuovo [1], C. Rosso [1], G.P. Caviglia [1], E. Dileo [1], M. Guariglia [1], A. Armandi [1,2], I. Poggiolini [1], F. Saba [1], A. Olivero [1], M.L. Abate [1], G.M. Saracco [1,3], F. Bioletto [1], S. Bo [1], E. Bugianesi [1,3]

[1] *Department of Medical Sciences, University of Turin, 10126, Turin, Italy*
[2] *Metabolic Liver Disease Research Program, I. Department of Medicine, University Medical Center of the Johannes Gutenberg-University, 55131, Mainz, Germany*
[3] *Gastroenterology Unit, Città della Salute e della Scienza—Molinette Hospital, 10126, Turin, Italy*

**Introduction and aim:** Lifestyle modification with weight loss is so far the cornerstone of approaches to metabolic dysfunction-associated steatotic liver disease (MASLD); however, it has been shown that each individual's response to diet may differ depending on their background. In this study, we aimed to study the impact of a 6-month dietary intervention on the improvement of liver steatosis in patients with MASLD.
**Methods:** 87 patients with MASLD were randomly assigned to one of the three dietary arms: low-carbohydrate diet, Mediterranean diet and control diet. Subjects were evaluated at baseline and after 6 months. *PNPLA3*-rs738409 SNP was genotyped in all patients. Liver steatosis was evaluated by Controlled Attenuation Parameter (CAP)(Fibroscan®530, Echosens).
**Results:** Overall, median age was 51 years (IQR 42;61), 69% of patients were male and 17% diabetic. Weight, systolic and diastolic blood pressure significantly decreased after the intervention ($P$<0.001, $P$=0.003 and P=0.017, respectively), as well as hepatic transaminases (AST, $P$=0.002, ALT $P$<0.001 and GGT $P$=0.014), CAP, glucose and insulin levels ($P$<0.001, $P$=0.005, $P$=0.005, respectively). 23 patients decreased ≥ 15% their CAP values after the 6-month intervention, showing a significant improvement in weight (P<0.001), waist circumference ($P$=0.003), systolic blood pressure ($P$<0.001) and GGT ($P$=0.030). Furthermore, a logistic regression adjusted by weight-loss, sex, *PNPLA3*-rs738409 and diet showed that weight-loss was significant and independently associated with the improvement of CAP, while a trend for CG/GG *PNPLA3*-rs738409 towards improved steatosis was observed.
**Conclusion:** Weight loss and carrying the CG/GG PNPLA3-rs738409 genotype appear to be significant factors in the improvement of hepatic steatosis in patients with MASLD. However, more studies considering the individual response to nutritional treatment are needed to accurately understand precision nutrition.
*This research has been supported by the University of Torino, grant number ROSC_RILO_21_01.*

doi: 10.1016/j.dld.2024.01.094

## T-63

### First and further liver decompensation in patients with metabolic-dysfunction associated steatotic liver disease: what clinical impact?

G. Pennisi [1], M. Viganò [2], A.L. Fracanzani [3], L. Miele [4], E. Bugianesi [5], R. D'Ambrosio [6], F. Ravaioli [7], F. Schepis [7], F. Marra [8], A. Aghemo [9], G. Svegliati-Baroni [10], M. Masarone [11], L. Valenti [12], A. Armandi [5], C. Ciccioli [1], F. Cerini [2], A. Colecchia [13], A. Gasbarrini [4], G. Infantino [1], A. Liguori [4], S. Pelusi [12], D. Saltini [7], P. Lampertico [6], M. Persico [14], N. Pugliese [9], A. Tulone [1], V. Di Marco [1], C. Cammà [1], S. Petta [1]

[1] *Section of Gastroenterology and Hepatology, Dipartimento Di Promozione Della Salute, Materno Infantile, Medicina Interna e Specialistica Di Eccellenza (PROMISE), University of Palermo, Italy*
[2] *Hepatology Unit, Ospedale San Giuseppe, University of Milan, Milan, Italy*
[3] *Department of Pathophysiology and Transplantation, Ca' Granda IRCCS Foundation, Policlinico Hospital, University of Milan, Italy*
[4] *Department of Medical and Surgical Sciences, A. Gemelli University Policlinic Foundation IRCCS, 00168, Rome, Italy*
[5] *Division of Gastroenterology, Department of Medical Sciences, University of Torino, Torino, Italy*
[6] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[7] *Division of Gastroenterology, Azienda Ospedaliero-Universitaria di Modena and University of Modena and Reggio Emilia, Modena, Italy*
[8] *Dipartimento di Medicina Sperimentale e Clinica, University of Florence, Italy; Research Center DENOTHE, University of Florence, Italy*
[9] *Division of Internal Medicine and Hepatology, Department of Gastroenterology, IRCCS Humanitas Research Hospital, 20089, Rozzano, Italy*
[10] *Liver Injury and Transplant Unit, Università Politecnica delle Marche, 60121, Ancona, Italy*
[11] *Internal Medicine and Hepatology Unit, Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, Salerno, Italy*
[12] *Translational Medicine, Department of Transfusion Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico IRCCS, Milan, Italy*
[13] *Gastroenterology Unit, Department of Specialistic Medicines, University of Modena & Reggio Emilia, University Hospital of Modena and Reggio Emilia, Largo del Pozzo 71, 41125, Modena, Italy*
[14] *Department of General Surgery, Endocrinology, Orthopaedics, and Rehabilitations, Federico II University Medical School, Naples, Italy*

**Background/Aims:** We investigated the incidence of first and further decompensation and their impact on mortality in patients with compensated advanced chronic liver disease (cACLD) due to metabolic-dysfunction associated steatotic liver disease (MASLD).
**Methods:** Data from Italian patients at the first diagnosis of MASLD-related cACLD (that is, F3-F4 fibrosis at histology and/or liver stiffness measurement >10 KPa) were retrospectively reviewed and analyzed. The cumulative incidence of first decompensation, further decompensation (development or recurrence of a second decompensating event), and death was assessed. Clinical events of first decompensation were discriminated as acute or non-acute according to a recent, not yet validated, proposal of decompensated cirrhosis classification.
**Results:** 1,140 patients with MAFLD-related cACLD were enrolled (56.7% males, mean age 43 years, 56.3% obese, 64.5% diabetic). In a mean follow-up of 108 months 844 patients did not develop decompensation and 6.3% of them died; among the 296 patients (25.9%) who experienced first decompensation the raw rate of mortality was 25.9% ($p<0.001$). First decompensation was acute in 48.9% and non-acute in 51.1% of cases. Overall, in this group the mortality rate was slightly higher, but not statistically significant, in patients with further decompensation compared to those without (40.3% vs 35.3%, $p=0.38$). After patient stratification for the type of first decompensation, further decompensation increased the risk of mortality in patients with non-acute first decompensation (46.8% vs 36.7% in those without further decompensation), but not in those with acute first decompensation (33.8% vs 33.7% in those without further decompensation). The present analysis will be refined by including data about 4,000 other patients from international cohorts and by considering hepatic and extrahepatic competing risks.
**Conclusion:** In MAFLD-related cACLD with non-acute first decompensation, a significant increase in mortality is associated to the development of further decompensation.

doi: 10.1016/j.dld.2024.01.095

## T-64

### Steatotic liver in renal transplant recipients does not correlate with CVD, a retrospective cohort study

C. Secondulfo [1], P. Torre [2], L. Sangiovanni [2], F. Belladonna [2], M. Masarone [2], G. Bilancio [1], M. Persico [2]

[1] *Nephrology Unit, Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, Baronissi SA, Italy*
[2] *Internal Medicine and Hepatology Division, Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, Baronissi SA, Italy*

**Introduction:** Non-Alcoholic Fatty liver Disease (recently "renamed" as Metabolic Associated Steatotic Liver Disease - MASLD) is among the main causes of chronic liver disease in developed countries and is continuously growing. Chronic Kidney Disease (CKD) has a global prevalence of between 8-16%, also in this case the prevalence has been significantly increasing in recent years, with an increase of approximately 29% from 1990 to 2017. The simultaneous and parallel increase in the global burden of these pathologies is not surprising: both recognize common triggering causes, including obesity, diabetes mellitus, hypertension, dyslipidemia and metabolic syndrome, the prevalence of which conditions has gradually increased over time. The prevalence of CKD in patients with NAFLD/MASLD is between 4 and 40%. The severity of liver disease has been related to the progression of CKD which in turn can aggravate NAFLD by altering the intestinal barrier and microbiota, with the accumulation of uremic toxins and the modification of metabolism of glucocorticoids. To date, there is little data regarding the prevalence of steatosis in renal transplant recipients and how these alterations can modify the outcome of the renal transplant, and particularly the occurrence of CVD.
**Aims:** Investigate the prevalence of steatosis in a population of kidney transplant patients. Evaluate if there is an association between prevalence of CVD and steatosis and its severity in these patients.
**Patients and Methods:** 200 patients, followed-up in the Nephrology Unit of Salerno University Hospital, were enrolled after an informed consent. Demographical, clinical and laboratory data have been collected for each patient, as well as abdominal ultrasonography (US). Patients with steatosis underwent liver stiffness measurement and controlled attenuation parameter (CAP). Also, any history of active or inactive CVD was collected (myocardial infarction, angina, stroke). Data were analyzed with parametric and non-parametric tests when indicated, significance was given when a $p<0.05$ in a two-tailed analysis was reached.
**Results:** Of the 200 kidney transplant patients, 69% were males, the mean age was 56.8 yrs. The median time of the kidney transplant was 15.88 years (range ±7,5). Steatosis was present at the

US in 45.5% of the patients, with a median CAP of 219 (208-237.5) and LS of 5.0 (4.3-5.2). Of those with steatosis, 11.1% (8 pts) had a significant fibrosis (>8 Kpascal). The mean BMI was 26.9±4.8 overall, with 28.5±5.2 vs 25.5±3.9 kg/m$^2$ in patients with steatosis vs those without (p:0.0001). Metabolic syndrome was present in 30.8% of patients with steatosis vs 11.0% of those without (p:0.001). The prevalence of CVD among the overall population was of 14.5% with no differences between patients with and without steatosis (14.3 vs 14.7%). At a logistic binary regression CVD was correlated only with age and sex, but not with steatosis, BMI, LS, CAP and MS.
**Conclusions:** In a cohort of kidney transplant recipients, the prevalence of liver steatosis, as well as overweight and metabolic syndrome was higher than that of the general population. However, previous, or actual CVD did not seem to be correlated with the presence of metabolic steatosis and its causes.

doi: 10.1016/j.dld.2024.01.096

## T-65

### PNPLA3 p.I148M variant affects lipid droplets number and size in patient-derived liver organoids

E. Casirati [1], A. Cherubini [1], L. Cerami [1], D. Prati [1], D. Dondossola [3], L. Valenti [1,2]

[1] *Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico; Transfusion Medicine and Hematology*
[2] *Università Degli Studi di Milano; Department of Pathophysiology and Transplantation,*
[3] *Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Hbp Surgery and Liver Transplantation Unit*

**Introduction and aims:** *PNPLA3* rs738409 C>G p.I148M variant is the main genetic determinant of metabolic associated steatotic liver disease (MASLD). To this day, this association still lacks a molecular characterization, due to the lack of comprehensive human models. To overcome this gap in knowledge, we generated patient-derived human liver organoids (HLOs) and studied lipid accumulation across different *PNPLA3* genotypes.
**Materials and methods:** We generated HLOs from 49 surgical specimens (14 I/I, 24 I/M and 11 M/M for PNPLA3 p.I148M). HLOs were differentiated toward a hepatocyte-like phenotype (Hep-HLO) and exposed to 300 µM Palmitic and Oleic fatty acids (FAs) for 72h. Lipid droplets (LDs) average size and number (normalized for nuclei) were quantified by NileRed staining and compared between PNPLA3 Hep-HLOs (n=3 for each genotype).
**Results:** As a propaedeutic step, we ascertained that Hep-HLO retain *PNPLA3* expression before evaluating its genotype impact on LDs. Untreated organoids displayed LDs average sizes of 0.51±0.26 µm$^2$ (I/I), 0.51±0.23 µm$^2$ (I/M) and 1.31±1.41 µm$^2$ (M/M). While FAs did not impact on average LD size, M/M Hep-HLOs displayed larger LDs (p=0.002 of I/I vs M/M, p=0.0002 for I/M vs MM). Conversely, LDs number were 7.28±5.16, 21.17±12.40 and 53.14±60.2 in I/I, I/M, M/M respectively, and increased to 18.61±9.31, 47.68±30.16 and 81.46±54.59 upon exposure to FAs (Table 1). After ANOVA testing, 23.9% of variability in LDs number can be attributed to genotype and 6.9% to FAs (p<0.0001 for both).
**Conclusions:** Regardless of FA treatment, M/M Hep-HLOs show increased LDs size when compared to I/M and I/I. Conversely, LDs number showed direct correlation with the number of mutated alleles, suggesting that the p.I148M substitution promotes the formation of new LDs, which was exacerbated by exposure to FAs. We are now developing siRNAs specific for silencing *PNPLA3* rs738409 transcripts to examine the impact on LD phenotypes.

doi: 10.1016/j.dld.2024.01.097

## T-66

### Telomere length exhibits a strong association with non-alcoholic fatty liver disease progression in children

M.R. Braghini [1], S.D. Bianco [2], M. Bianchi [1], A. Mosca [3], S. Veraldi [1], P. Francalanci [4], T. Mazza [2], A. Alisi [1]

[1] *Research Unit of Genetics of Complex Phenotypes, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy*
[2] *Bioinformatics Laboratory, Fondazione IRCCS Casa Sollievo della Sofferenza*
[3] *Hepatology Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy*
[4] *Molecular Pathology Research Unit, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy*

**Introduction:** Non-alcoholic fatty liver disease (NAFLD), globally estimated as the most frequent chronic liver disease, ranges from simple fatty liver (FL) to NASH. Since NASH-related liver damage represents the driving force of liver fibrosis that can lead to cirrhosis, several studies have been conducted to prevent this serious complication. Previous studies demonstrated that telomere length (TL) assessed in leukocytes and liver may be an independent risk factor for advanced fibrosis in adult patients with NAFLD. However, data from studies on children appears to be controversial.
**Aim:** Hence this study points to explore the association of TL with the different features of disease in children with NAFLD.
**Material and Methods:** We enrolled 212 children with biopsy-proven NAFLD and 31 with a healthy liver evaluated at the Hepatology Unit of the "Bambino Gesù" Children's Hospital. TL was evaluated in leukocytes following a quantitative real-time polymerase chain reaction (qRT-PCR) method and was reported as both TL kilobases (TLkb) and telomere over Single copy gene (T/S) ratio.
**Results:** Our results revealed that children with NAFLD exhibited a significantly lower log-TLkb and log-T/S ratio than children with healthy liver, and the comparison between FL and NASH showed that the reduction of TLkb and T/S ratios were mainly ascribable to NASH group (4.91 vs 3.56; p<0.001 and 0.75 vs 0.43; p<0.001). From univariate regression analysis, it has emerged that there was no association between log-TL and anthropometrical or biochemical parameters. On the contrary, multiple linear regression demonstrated that fibrosis negatively impacts log-TL (p<0.0001). Finally, interestingly we observed a trimodal distribution of log-TL corresponding to F=0, F=1, and F=2.
**Conclusions:** In conclusion, our study demonstrated that there was a strong relationship between TL and NAFLD-related features, mainly with fibrosis. Further studies are needed to clarify the causal liaison between fibrosis progression and TL.

doi: 10.1016/j.dld.2024.01.098

## T-67

### Unravelling the role of mitochondrial dysfunction in the switching towards progressive MASLD by exploiting an AMLN diet-fed mouse model

E. Paolini [1,2], M. Meroni [1], M. Longo [1], M. Battistin [3], M. Ripolone [4], L. Napoli [4], S. Gatti [3], P. Dongiovanni [1]

[1] *Medicine and Metabolic Diseases, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Department of Pharmacological and Biomolecular Sciences, Università Degli Studi di Milano, Milan, Italy*
[3] *Center for Preclinical Research, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy*
[4] *Neuromuscular and Rare Diseases Unit, Department of Neuroscience, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy*

**Background:** Mitochondrial maladaptation is a key event in the transition from Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) to Steatohepatitis (MASH) up to fibrosis/cirrhosis. However, it remains to be defined how mitochondrial alterations evolve as the disease progresses.
**Aims:** We exploited a mice model fed high fat-high fructose diet (Amylin liver NASH (AMLN) diet) that resemble human MASLD to investigate the role of mitochondrial dysfunction in boosting severe disease.
**Method:** C57Bl/6 male mice were fed AMLN or standard diet for 14-22-28 weeks (Taconic-Biosciences), to feature simple steatosis, MASH, and fibrosis, respectively. Mitochondrial morphology and activity were assessed by TEM and Seahorse assays, respectively whereas mitobiogenesis and OXPHOS complexes by Western Blot.
**Results:** Mice fed AMLN diet recapitulated the human MASLD spectrum encompassing hepatic fat accumulation with a mixed micro/macro pattern, inflammation, and collagen deposition. TEM showed progressive morphologic dysfunction of mitochondria which appeared normo-shaped with rare misshapen ones in AMLN-steatosis and completely swollen in AMLN-MASH. In the fibrosis group we observed aberrant organelles with disorganized cristae and matrix loss. Mitochondrial derangement was paralleled by progressive fragmentation of endoplasmic reticulum, apoptotic nuclei and autophagic bodies. The mitophagy pathway was reduced in AMLN model and particularly in AMLN-fibrosis thus explaining the accumulation of damaged mitochondria. Furthermore, the citrate synthase and mitochondrial complexes activities alongside OXPHOS protein levels and ATP production were lowered across the disease, especially in the presence of MASH-fibrosis. The failed activity was paralleled by oxidative stress, lactate production and release of cell-free circulating mitochondrial-DNA, which reflects hepatic mitochondrial impairment. Consistently, the Seahorse assay showed a progressive reduction of oxygen consumption rate in primary hepatocytes isolated from mice fed AMLN diet.
**Conclusion:** By exploiting the AMLN mice model, we demonstrated that alterations in mitochondrial morphology, lifecycle and activity feature all disease stages, thus fostering the switching to MASH and fibrosis.

doi: 10.1016/j.dld.2024.01.099

## T-68

### Tiny but powerful: platelets behaviour in metabolic dysfunction-associated steatotic liver disease and its evolution to liver cirrhosis

M. Zoncapè [1,2], M. Castelli [1], D. Sacerdoti [2], P. Minuz [1], A. Dalbeni [1,2]

[1] *Division of General Medicine C, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy*
[2] *Liver Unit, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy*

**Introduction:** Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD), affects 30% globally, potentially leading to cirrhosis. Metabolic dysfunction-Associated Steatohepatitis (MASH) often involves platelets. Platelet roles in MASLD progression remain underexplored.
**Aim:** Our aim was to verify the possible platelet contributions to MASLD/MASH genesis and in MASLD-related cirrhosis, compared to healthy subjects, investigating the activation state of platelets *in vitro* and *in vivo*.
**Materials and Methods:** Patients with metabolic liver cirrhosis (Child-Pugh classes A/B), MASLD/MASH, and healthy volunteers without metabolic alterations were examined. Patients were diagnosed trough abdominal ultrasounds, TC, RM and liver biopsy, Fibroscan and other non-invasive test and scores were also used.

Microfluidic analysis assessed platelet adhesion on collagen, indicating pre-activation states and in vitro activation levels.

Urinary 11-dehydro-thromboxane-B2 (11-TXB2) measured in vivo thromboxane A2 synthesis, indirectly assessing platelet activation in vivo.

Platelet interaction with coagulation factors, specifically Factor VIII (FVIII) and von Willebrand Factor (vWF) activity, was explored through cross-mixing experiments.
**Results:** Among 66 participants, platelet count was significantly lower in cirrhotic patients compared to controls ($p<0.001$). However, no differences were observed in platelet distribution width, mean platelet volume, or immature reticulate fraction among the three cohorts.

*In vitro* adhesion on collagen was higher in MASLD/MASH and cirrhosis ($p<0.01$) compared to controls.

11-TXB2 levels were significantly elevated in cirrhotic patients compared to controls ($p<0.001$).

Higher levels of FVIII and vWF were observed in the platelet-poor plasma (PPP) of cirrhotic patients. Cross-mixing experiments indicated that elevated FVIII and vWF levels in cirrhotic patients were associated with these factors in PPP rather than a direct contribution from washed platelets.
**Conclusions:** MASLD/MASH showed normal platelet counts, but increased adhesion, suggesting pro-inflammatory and pro-fibrotic roles.

In contrast, cirrhotic patients displayed reduced platelet count, but increased adhesion function. They also exhibit significantly higher 11-TXB2 levels compared to controls, suggesting higher in-vivo platelet activation.

doi: 10.1016/j.dld.2024.01.100

## T-69

### New steps forward in learning about the use of DGAT1 and DGAT2 inhibitors for MASLD management: limits and benefits for their single or combined application

M. Longo [1], E. Paolini [1,2], M. Meroni [1], B. Rota [1], A.L. Fracanzani [1,3], P. Dongiovanni [1]

[1] *Medicine and Metabolic Diseases, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Department of Pharmacological and Biomolecular Sciences, Università Degli Studi di Milano, Milan, Italy*
[3] *Department of Pathophysiology and Transplantation, Università Degli Studi di Milano, Milan, Italy*

**Background:** Lack of approved pharmacological interventions for metabolic dysfunction-associated steatotic liver disease (MASLD) remains a challenge for both clinicians and researchers. Blocking DGAT1 and DGAT2 enzymes (i-DGAT1, i-DGAT2), involved in triglycerides (TG) synthesis, has shown a certain efficacy in reducing fat accumulation in clinical trials. However, their potential synergism and effects in MASLD progressive forms has been poorly explored.
**Aim:** To investigate i-DGAT1 and i-DGAT2 efficacy, alone or combined (i-DGAT1/2), on:1) fat accumulation and hepatocellular damage in a human hepatoma cell line (HepG2);2) hepatic stellate cells (HSCs) activation, mediating fibrogenesis, by exploiting immortalized human LX2 cells.
**Methods:** Steatotic and MASH conditions were reproduced by exposing HepG2 cells to palmitic/oleic acids (PAOA;167 µM) for 24 hours (steatotic medium), or to PAOA, LPS (5 µM), fructose and glucose (22.5 mM) for 5 consecutive days (MASH medium). LX2 cells were treated with conditioned steatotic and MASH media for 24 hours.
**Results:** i-DGAT1 and i-DGAT2 administration reduced lipid content and TG synthesis in HepG2 cells exposed to steatotic medium, showing the greatest efficacy when supplemented together. Markers of endoplasmic reticulum stress (ATF4, XBP1), oxidative damage (ROS, MDA) and inflammation (TNF$\alpha$,IL6) were slightly decreased after i-DGAT1 or i-DGAT2 supplementation. Conversely, i-DGAT1/2 combination improved hepatocellular injury and enhanced the TCA activity, ATP synthase and total ATP production, thus resulting the best strategy for counteracting cell damage and rescuing mitochondrial bioenergetics. In HepG2 cells exposed to MASH medium, in which hepatocellular damage was exacerbated compared to that induced by steatotic one, only the i-DGAT1/2 co-administration resulted effective in ameliorating TG synthesis, oxidative stress, and inflammation, with a parallel improvement of energetic balance. Finally, LX2 cells, challenged with steatotic/MASH media, showed less proliferative, contractile and migration capacity in response to i-DGAT1/2 drugs.
**Conclusions:** The combined use of i-DGAT1/2 opens new perspectives for the treatment of MASLD and its severe manifestations.

doi: 10.1016/j.dld.2024.01.101

## T-70

### Gender-related differences of hepatic lipid metabolism and mitochondrial function in genetically epileptic rats: effect of early lipopolysaccharide exposure

S. Melini [1], C. Pirozzi [1], G. Trinchese [2], A. Lama [1], F. Del Piano [3], F. Comella [1], F. Cimmino [2], N. Opallo [1], C.M.P. Mollica [2], G. Mattace Raso [1], R. Meli [1]

[1] *Department of Pharmacy, University of Naples Federico II, Naples, Italy*
[2] *Department of Biology, University of Naples Federico II, Naples, Italy*
[3] *Department of Veterinary Medicine and Animal Productions, University of Naples Federico II, Naples, Italy*

**Background:** Epilepsy is a non-communicable neurological disease characterized by abnormal electrical brain activity with conceivable peripheral implications. Among all, *in vivo* studies supported the crucial role of peripheral and brain inflammation in the relationship between seizure predisposition and NAFLD. Otherwise, severe early-life infections leading to sepsis may result in hepatic and neuro-inflammation that can aggravate epilepsy. Indeed, hepatic damage progression is associated with increased odds for hospital admissions for epilepsy.
**Aims and Methods:** Here, we examined the effect of early LPS challenge (1 mg/kg, *i.p.* at PND3) in inducing hepatic damage in a genetic model of young adult WAG/Rij epileptic rats (PND45). The gender-related differences on hepatic lipid dysmetabolism was evaluated and associated to mitochondrial oxidative damage and enzyme activities by Real-Time PCR and polarographic/spectrofluorimetric analyses, respectively.
**Results:** Both male and female epileptic rats, exposed to LPS, showed higher serum levels of hepatic enzymes, as well as increased cholesterol and triglycerides. Early LPS challenge induced a major inflammatory and immune response in male epileptic rats than females in both serum and liver, as demonstrated by increased pro-inflammatory cytokine levels and hepatic immune cell recruitment. Conversely, LPS-insulted females showed a marked alteration in hepatic metabolic and lipid profile, and the reduction of mitochondrial fatty acid oxidation (FAO) (decreased carnitine palmitoyltransferase activity, as rate-limiting enzyme of FAO). Interestingly, the two different gender-related mechanisms of LPS-induced liver injury converge in oxidative damage of mitochondria with intensified ROS production in both sexes, that notably induced a compensatory increase in antioxidant defense (mitochondrial superoxide dismutase activity) only in females. Moreover, LPS-challenged male rats showed an altered hepatic glutathione redox status (GSH/GSSG ratio) rather than females.
**Conclusions:** Our study translationally points out that early postnatal infections can predispose epileptic patients to develop or exacerbate hepatic disorders in a sex-dependent manner.

doi: 10.1016/j.dld.2024.01.102

## T-71

### Characterization by polygenic risk score of a dysmetabolic population of Southern Italy

B.M. Motta, M. Masarone, P. Torre, M. Aquino, F. Belladonna, M. Persico

*Internal Medicine and Hepatology Division, Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana", University of Salerno, 84081, Baronissi, SA, Italy*

**Background and Aims:** Non-alcoholic fatty liver disease (NAFLD) is the leading cause of liver diseases, ranging from simple steatosis to non-alcoholic steatohepatitis, and the susceptibility to develop NAFLD is highly variable and influenced by environmental and genetic factors. The gold standard for diagnosis and staging of NAFLD is liver biopsy, however, it is an invasive procedure, subject to sampling errors and inter-observer variability. Several non-invasive methods aim at diagnosing hepatic steatosis and predicting significant/advanced fibrosis. GWAS studies identified genetic risk factors, and genetic risk scores (GRS) were developed for risk stratification. NAFLD susceptibility is associated with four genetic variants: *PNPLA3* rs738409, *TM6SF2* rs58542926, rs641738 close to *MBOAT7* locus, *GCKR* rs1260326. Our aim was to evaluate how these variants and a polygenic risk score correlate with liver steatosis and biochemical phenotypes in our dysmetabolic population of Southern Italy.
**Methods:** We enrolled 109 patients attending our Hepatology Unit department, which were genotyped for rs738409, rs58542926, rs641738, rs1260326 by TaqMan 5′â€ nuclease assays. We calculated a weighted polygenic risk score (PRS) by multiplying the effect size (beta-coefficient) on steatosis by respective risk alleles and summing the products. Anthropometric data and blood test results were collected.
**Results:** In our population we evaluated the effect of the 4 variants on the risk of developing more severe liver disease by a weighted PRS, which increased from simple steatosis to NASH/NASH-cirrhosis subjects (Figure 1A p=0.02).We also recorded and biochemical data and evaluated the effect of the 4 variants together by PRS (Fgure 1B). ALT ($p = 0.01$), AST ($p = 0.002$), total cholesterol, and triglycerides levels increase proportionally with PRS, while LDL levels decrease ($p = N.S$).
**Conclusion:** This study shows that in our population, the polygenic risk score correlates with biochemical and clinical parameters, identifying the most dysmetabolic subjects.

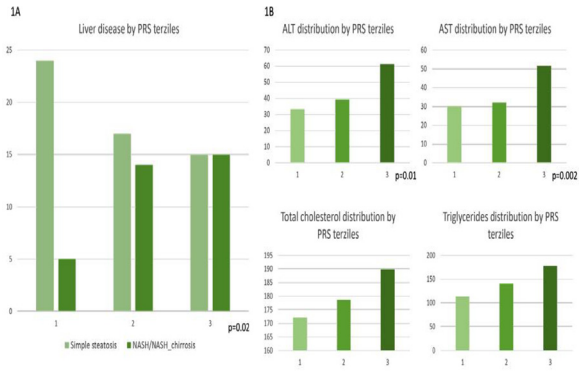



Figure 1. Characterization of dysmetabolic population. A) Liver disease severity distribution by PRS. Chi-Square test. B) Biochemical parameters stratified by PRS. One-way ANOVA test.

doi: 10.1016/j.dld.2024.01.103

## T-72

### Non-psychedelic doses of psilocybin as a novel therapeutic approach for MASLD

S. De Martin [1], D. Gabbia [1], M. Colognesi [1], A. Rinaldi [2], L. Cascione [2], I. Zanotto [1], K. Sayaf [3], S. Comai [1], A. Mattarei [1], M. Banzato [1], G. Pasut [1], F. Folli [4], L. Centofanti [4], S. Traversa [5], M. Pappagallo [5], P.L. Manfredi [5]

[1] *Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Padova, Italy*
[2] *Genomic Facility, IOR Institute of Oncology Research, Università della Svizzera Italiana, Bellinzona, CH*
[3] *Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy*
[4] *Department of Health Science, Università degli Studi di Milano, Milan, Italy*
[5] *Relmada Therapeutics Inc., USA*

**Introduction:** The serotonin receptor (5-HT2AR) agonist psilocybin, an alkaloid of *Psilocybe* mushrooms, reduced obesity in animal models. However, the effect of psilocybin in MASLD, a condition often associated to obesity, has not been evaluated so far.
**Aim:** to assess the effects and mechanism of non-psychedelic doses of psilocybin in mice with high-fat-high-fructose diet (HFHFD)-induced MASLD.
**Materials and Methods:** Psilocybin was tested *in vivo* on C57BL/6 male mice fed with HFHFD for 17 weeks. One group (n=10) received daily 0.05 mg/Kg*bw psilocybin and the other (n=10) received vehicle by oral gavage. Standard diet-fed mice (n=10) were used as controls. Body weight and food intake were assessed weekly. Fasting glucose and triglycerides were measured before sacrifice. Liver histology was assessed by H&E and ORO staining. Blood immunophenotyping was performed by FACS. RNA sequencing was performed to assess alteration of the global transcriptomic landscape of liver and muscle. The expression of proteins involved in insulin signaling was assessed by western blot.
**Results:** In MASLD mice psilocybin, without effects on food intake, reduced liver steatosis, body weight by 12% and restored the levels of plasma and liver triglycerides of standard-diet fed mice. A significant decrease of fasting glucose ($p<0.001$) and AUC was observed in the OGTT. Psilocybin restored the hepatic expression of genes involved in lipid localization and catabolic processes and the protein expression of insulin receptor and IRS-1 altered by MASLD ($p<0.05$), as well as the phenotype of circulating NK cells, by reverting the increase of PD-1 expressing exhausted NK cells of MASLD mice ($p<0.01$).
**Conclusion:** Oral 0.05 mg/Kg*bw psilocybin significantly reduced hepatic steatosis, blood glucose levels and body weight in MASLD mice, by exerting a pleiotropic action on lipid hepatic metabolism and glycemic control. Psilocybin at low non-psychedelic doses may be a novel candidate therapy for MASLD and associated metabolic disorders.

doi: 10.1016/j.dld.2024.01.104

Digestive and Liver Disease 56 (2024) S61–S98

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

# Friday Posters: 56th Annual Meeting of the Italian Association for the Study of the Liver – A.I.S.F. (Rome, March 14th-15th, 2024)

## F-01

### MAIT cells play a role in liver tissue repair via growth factor secretion

K. Sayaf[1], I. Tasin[1], H.D. Akther[2,3], L.C. Garner[3], N. Ramamurthy[2], C.P. Hackstein[4], F.P. Russo[1], P. Klenerman[2,3,5]

[1] *Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy*
[2] *Peter Medawar Building for Pathogen Research, South Parks Road, Oxford, UK*
[3] *Translational Gastroenterology Unit, Nuffield Department of Medicine, University of Oxford, Oxford, UK*
[4] *Center for Infection Prevention, Technical University of Munich, Freising, Germany*
[5] *NIHR Biomedical Research Centre, John Radcliffe Hospital, Oxford, UK*

**Introduction:** MAIT cells (Mucosa-Associated Invariant T cells) are highly enriched in the human liver, representing about 20-50% of intrahepatic CD8+ T cells. These cells express transcriptional signatures associated with tissue repair both in vitro and in vivo, even though the direct mediators of MAIT cell-directed tissue repair in human tissues have not been defined. The aim of our study is to identify such factors and their in vivo relevance, especially in liver injury and regeneration.
**Methods:** Peripheral blood PBMCs and isolated MAIT cells from healthy donors were stimulated via their TCR, with cytokines, or with both stimuli for 72h. The concentration of growth factors in these culture supernatants was quantified using LEGENDplex. MAIT cell supernatants with or without blocking antibodies were used in wound-healing assays with Caco-2 (epithelial cells) and HHL12 (hepatocytes) cell monolayers to functionally validate the importance of specific factors in tissue repair. Published single-cell RNA-seq datasets were explored to address in vivo expression of identified factors.
**Results:** PBMCs and activated MAIT cells produced GM-CSF, VEGF, PDGF-AA and M-CSF. Interestingly, we found that VEGF production by MAIT cells was significantly higher than conventional naïve, central memory, and effector memory T cells. In an in vitro wound healing assay, supernatants of activated sorted MAIT cells accelerated wound closure, an effect that could be blocked by anti-VEGFR2. Interrogation of a scRNA-seq data from a human experimental model showed that MAIT cell expression of VEGF in vivo was detectable in regenerating liver tissue.
**Conclusions:** Our data showed that stimulation of MAIT cells leads to the production of growth factors. We highlighted a key role for VEGF-VEGFR2 signalling in MAIT cell-mediated tissue repair and potentially in the unparalleled ability of the liver to undergo regeneration following injury.

doi: 10.1016/j.dld.2024.01.106

## F-02

### Prevalence and clinical outcomes of different forms of renal dysfunction in patients hospitalized for decompensated cirrhosis: focus on acute kidney disease. A prospective observational study

F. Frigo, M. Tizzani, A. Calleri, E. Bertoldi, D. Campion, A. Ottobrelli, A. Marzano, G.M. Saracco, C. Alessandria

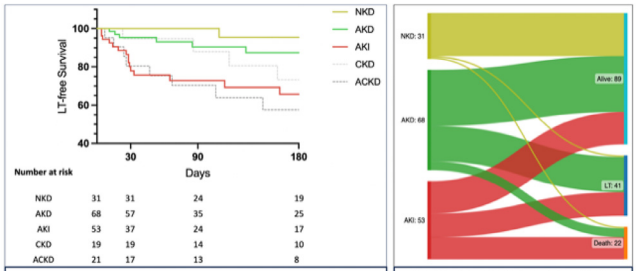
*Division of Gastroenterology and Hepatology, A.O.U. Città della Salute e della Scienza di Torino, University of Turin, Turin, Italy*

**Introduction:** in patients hospitalized for decompensated cirrhosis renal dysfunction is very common. In this setting, acute kidney disease (AKD) has been suggested to impact significantly on prognosis, but data are scant.
**Aims:** to assess prevalence and clinical outcomes of AKD compared to patients with no kidney disease (NKD) and acute kidney injury (AKI).
**Methods:** all patients hospitalized in a 16-month period for decompensated cirrhosis were prospectively evaluated. Patients were classified according to their renal function as per International Club of Ascites definitions and then followed-up until death or liver transplant (LT).
**Results:** 268 patients were screened, 192 enrolled. The most frequent etiology of cirrhosis and cause of hospitalization were alcohol (50%) and ascites (62%), respectively. Renal function was categorized as follows: 16% NKD, 35% AKD, 28% AKI, 10% chronic kidney disease (CKD), 11% acute-on-chronic kidney disease (ACKD). Median serum creatinine was: 0.82, 1.0, 1.71, 1.77, 3.13 mg/dL, respectively. Median follow-up was 3.6 months (IQR 1.3-8.4). Overall, 51 patients (27%) were transplanted and 46 (24%) died.

Among 85 patients with follow-up $\geq$ 3 months, the incidence of new-onset CKD was 5% for NKD, 20% for AKD and 25% for AKI (AKD vs NKD, p=0.11; AKD vs AKI, p=0.68; NKD vs AKI, p=0.06).

The 1 and 6-month LT-free survival was respectively 100% and 96% in NKD, 95% and 87% in AKD, 78% and 66% in AKI. Survival of AKD patients was then similar to those with NKD (p=0.2 for both time-points) and significantly different if compared with AKI (p=0.006 and p=0.003, respectively).

**Conclusions:** AKD is very common among patients hospitalized for decompensated cirrhosis. Unlike the few data currently available in the literature, our study suggests that AKD is not clinically meaningful, being associated with a short- and medium-term survival similar to that of NKD and significantly better if compared with AKI.




*Panel A:* six-month LT-free survival according to renal function

*Panel B:* six-month Sankey diagram for the evolution of patients with NKD, AKD and AKI

doi: 10.1016/j.dld.2024.01.107

## F-03

### Whole blood thrombin generation improves the understanding of cirrhotic coagulopathy and predicts clinical outcomes in patients with cirrhosis: a prospective cohort study

A. Zanetto [1], E. Campello [2], C. Bulato [2], R. Willems [3,4,5], J. Konings [3], M. Roest [3], S. Gavasso [2], G. Nuozzi [2], S. Toffanin [2], P. Zanaga [1], P. Burra [1], F.P. Russo [1], B. de Laat [3], P. Simioni [2,3], M. Senzolo [1]

[1] *Gastroenterology and Multivisceral Transplant Unit, Department of Surgery, Oncology and Gastroenterology, Padova University Hospital, Padova, Italy*
[2] *General Internal Medicine Unit, Thrombotic and Hemorrhagic Disease Unit and Hemophilia Center, Department of Medicine, Padova University Hospital, Padova, Italy*
[3] *Department of Functional Coagulation, Synapse Research Institute, Maastricht, The Netherlands*
[4] *Department of Internal Medicine, Section Vascular Medicine, Maastricht University Medical Center, Maastricht, the Netherlands*
[5] *CARIM, School for Cardiovascular Diseases, Maastricht, the Netherlands*

**Introduction:** Patients with cirrhosis have an increased thrombin generation (TG) in platelet-poor plasma (PPP). By reflecting the contribution of circulating blood cells, whole blood (WB) TG may allow a more physiological assessment of coagulation, thus improving our understanding of cirrhotic coagulopathy and its clinical implications.

**Aims:** We conducted a prospective study to 1) compare WB-TG vs. PPP-TG in cirrhosis; 2) assess whether WB-TG could predict hepatic decompensation, further decompensation/ACLF, bleeding unrelated to portal hypertension and venous thrombosis.

Material and methods: Assessment of coagulation included routine tests, factor VIII, natural anticoagulants, PPP-TG and WB-TG (with and without thrombomodulin [TM]). Twenty-five healthy subjects were included as controls. All patients were prospectively followed for up to 1 year.

**Results:** We included 183 patients (Child-Pugh A/B/C 71/50/62). In compensated cirrhosis, both PPP-TG and WB-TG indicated an increased TG capacity, as reflected by an endogenous thrombin potential (ETP) significantly higher than controls; in decompensated cirrhosis, PPP-TG indicated a hyper-coagulable state with increased ETP and higher peak height, whereas WB-TG revealed a progressive impairment of TG kinetics and total capacity, resulting in a profound hypo-coagulable state in Child-Pugh C. Median duration of follow-up was 11 months in compensated and 8 months in decompensated patients. In compensated cirrhosis, patients who experienced 1st decompensation had a significantly higher WB-TG than those who did not, whereas in decompensated cirrhosis WB-TG was comparable in patients with vs. without further decompensation/ACLF during follow-up. In decompensated patients, WB-TG was more severely compromised in patients who experienced bleeding complications, whereas no association was found with thrombosis.

**Conclusions:** In compensated cirrhosis, a more pronounced hypercoagulable state, as assessed by WB-TG, indicated a higher risk of decompensation, suggesting that hyper-coagulability may be responsible for cirrhosis progression. In decompensated cirrhosis, contrary to PPP-TG that indicates hypercoagulability, WB-TG reveals a significant hypo-coagulable state, which was associated with bleeding complications.

doi: 10.1016/j.dld.2024.01.108

## F-04

### Prospective 5-Year Follow-up Study of Spleen Stiffness Measurement with a Spleen-Dedicated Module (SSM@100Hz) for Predicting Hepatic Decompensation in cACLD: Competitive Risk Analysis

L. Colecchia [1,*], F. Ravaioli [1,*], E. Dajti [1], A. Vestito [1], A. Gobbato [1], F. Lami [2], M. Renzulli [1], M. Serenari [1], S. Ferri [1], F. Tovoli [1], D. Festi [1], A. Colecchia [2,°], G. Marasco [1,#]

[1] *Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy*
[2] *Gastroenterology Unit, Department of Specialistic Medicines, University of Modena & Reggio Emilia, University Hospital of Modena and Reggio Emilia, Largo del Pozzo 71, 41125, Modena, Italy*

[*] LC and FR contributed equally to this abstract and shared co-first authorship.
[#] AC and GM contributed equally to this abstract and shared the co-last authorship.

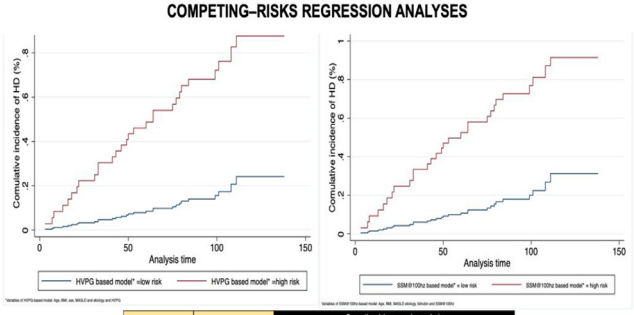
**Background & aims:** Liver and spleen stiffness measurements using FibroScan® (SSM@50Hz) have been endorsed by the Baveno VII consensus to assess clinically significant portal hypertension (CSPH), which is the main driver of hepatic decompensation (HD) in patients with compensated advanced chronic liver disease (cACLD). A new, dedicated 100Hz module for spleen stiffness measurement (SSM@100hz) seems to increase the clinical applicability of this technique, but there is currently no data available about its diagnostic performance for CSPH and its complications. The aim of our 5-years prospective study was to evaluate the role of the SSM@100hz module compared to HVPG in predicting HD in a group of patients with cACLD.

**Methods:** In this prospective study, we included patients with cACLD who underwent paired laboratory tests, liver stiffness measurement (LSM), hepatic venous pressure gradient measurement (HVPG), and SSM@100Hz. We used univariate and multivariate competing-risks regression analyses to evaluate the outcome, taking liver transplantation or death into account as competitive events.

**Result:** In this study, 69 patients were enrolled and followed until either HD or a competitive event occurred. During a me-

dian follow-up of 69 [31-105] months, 34 patients developed HD. Among the HD events, 17/69 (24.6%), 13/69 (18.8%), and 28/69 (40.6%) patients developed variceal bleeding, hepatic encephalopathy, and ascites, respectively. The results of univariate analysis revealed that SSM median value (SSM@100hz), male sex, metabolic etiology, presence of esophageal varices, bilirubin levels, and combined Baveno VII single cut-off rule-in criteria (by SSM@100hz) were independent predictors of HD (as per **Table 1**). Further multivariate analysis was conducted, and two models were developed. The first model revealed that age, lower BMI, a higher SSM@100hz value, higher bilirubin values, and MASLD were independent predictive factors of HD. The second model revealed that younger age, lower BMI, male sex, MASLD, and a higher HVPG value were predictors of HD. The two models showed comparable accuracy (AUROC 0.869 and 0.868).

**Conclusions:** The SSM@100Hz dedicated module is an accurate predictor of hepatic decompensation and can be useful to rule out the risk of complications at 5 years in patients with compensated cirrhosis.




| Variables | Characteristic of patients | | Competing-risks regression analysis | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Univariate analysis | | Multivariate HVPG-based model | | Multivariate SSM100hz-based model | |
| | No decompensation (N (IN.%)) | Decompensation (N (IN.%)) | Hazard Ratio (95% CI) | p-value | Hazard Ratio. (95% CI) | p-value | Hazard Ratio (95% CI) | p-value |
| Age | 59.4 (50.4-71.5) | 60.0 (49.1-68.7) | 0.995 (0.980 - 1.031) | 0.772 | 0.954 (0.918 - 0.991) | 0.015 | 0.955 (0.918 - 0.994) | 0.024 |
| BMI (kg/m2) | 25.7 (23.0-27.2) | 24.4 (22.1-30.0) | 1.0567 (0.888 - 1.256) | 0.534 | 0.75 (0.604 - 0.931) | 0.008 | 0.794 (0.663 - 0.951) | 0.012 |
| Sex | | | 5.471 (1.373 - 21.795) | 0.016 | 7.178 (1.359 - 37.91) | 0.02 | | |
| Female | 13 (37.1%) | 4 (11.8%) | | | | | | |
| Male | 22 (62.9%) | 30 (88.2%) | | | | | | |
| Aetiology | | | | | | | | |
| MASLD | | | 25.703 (5.317 - 124.252) | <0.001 | 20.911 (3.639 - 77.547) | <0.001 | 18.997 (4.486 - 80.449) | <0.001 |
| Non metabolic etiology | 28 (80.0%) | 18 (52.9%) | | | | | | |
| Metabolic etiology | 7 (20.0%) | 16 (47.1%) | | | | | | |
| Viral etiology | | | 1.1369 (0.478 - 3.926) | 0.559 | | | | |
| Non viral etiology | 7 (20.0%) | 4 (11.8%) | | | | | | |
| Viral etiology | 28 (80.0%) | 30 (88.2%) | | | | | | |
| ALD | | | 0.323 (0.187 - 1.481) | 0.216 | | | | |
| Non alcoholic etiology | 26 (74.3%) | 29 (85.3%) | | | | | | |
| Alcoholic etiology | 9 (25.7%) | 5 (14.7%) | | | | | | |
| Esophageal Varices | | | 2.564 (1.483 - 3.738) | <0.001 | | | | |
| Absent | 18 (51.4%) | 8 (23.5%) | | | | | | |
| F1-F2 | 17 (48.6%) | 19 (55.9%) | | | | | | |
| F3 | 0 (0.0%) | 7 (20.6%) | | | | | | |
| Bilirubin | 0.7 (0.6-1.1) | 1.1 (0.8-1.7) | 1.161 (1.075 - 1.253) | <0.001 | | | 1.233 (1.138 - 1.371) | <0.001 |
| Albumin | 4.0 (3.8-4.2) | 3.8 (3.3-4.0) | 0.816 (0.495 - 1.343) | 0.424 | | | | |
| INR | 1.2 (1.1-1.3) | 1.2 (1.1-1.3) | 1.119 (0.163 - 7.668) | 0.909 | | | | |
| PLT | 151.0 (115.0-193.0) | 82.5 (58.0-115.0) | 0.992 (0.984 - 1) | 0.060 | | | | |
| LSM median (kPa) | 23.4 (16.4-32.5) | 26.8 (17.3-36.3) | 1.018 (0.989 - 1.049) | 0.228 | | | | |
| SSM@100Hz median (kPa) | 47.4 (36.3-56.6) | 61.6 (43.4-80.8) | 1.025 (1.001 - 1.042) | 0.002 | | | 1.05 (1.029 - 1.073) | <0.001 |
| HVPG (mmHg) | 11.0 (10.0-14.0) | 13.5 (9.0-17.0) | 1.067 (0.997 - 1.165) | 0.060 | 1.142 (1.016 - 1.288) | 0.024 | | |
| Note. | | | | | AUROC = 0.869 | | AUROC = 0.868 | |
| Competing-risks events: Liver Transplantation and/or Death (n=3). | | | | | AIC = 157.512 | | AIC = 164.089 | |
| | | | | | BIC = 161.69 | | BIC = 170.241 | |

doi: 10.1016/j.dld.2024.01.109

## F-05

### External Validation of the ExPeCT TIPS Prediction Model in a North American Cohort

R.X. Wang [1], F. Vizzutti [2], C. Celsa [3], F. Schepis [4], D.E. Kaplan [5], V. Adotti [2], M. Rosi [2], F. Marra [2], N. Mahmud [5]

[1] *Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA*
[2] *Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy*
[3] *Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, PROMISE, Gastroenterology and Hepatology Unit, University of Palermo, Palermo, Italy*
[4] *Division of Gastroenterology, Modena Hospital, University of Modena and Reggio Emilia, Modena, Italy*
[5] *Division of Gastroenterology and Hepatology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA*

**Background:** Transjugular intrahepatic portosystemic shunt (TIPS) mortality prediction models assist in patient selection for TIPS implantation. The Elderly Patients Calculator TIPS (ExPeCT) score is a new model derived from an Italian cohort. We sought to validate the ExPeCT model in a large North American (NA) cohort.

**Methods:** This was a retrospective cohort study of cirrhotic patients in the Veterans Health Administration who received TIPS from 2008 to 2022. Patients were divided into younger (<70 years) and older (≥70) subcohorts to evaluate overall and older adult ExPeCT scores. Discrimination of ExPeCT, Model for End-Stage Liver Disease Sodium (MELD-Na), and Freiburg index of post-TIPS survival (FIPS) scores was evaluated using Harrell's C index. Calibration of prediction models was evaluated by joint hypothesis testing.

**Results:** 1,221 patients were included in the younger cohort and 178 patients in the older cohort. In the younger cohort, the overall ExPeCT model had the highest discrimination (Harrell's C: 0.622). In the older cohort, the older adult ExPeCT score had the lowest discrimination (Harrell's C: 0.562). Both ExPeCT models tended to overestimate post-TIPS mortality at 6, 12, 24, and 36 months ($p<0.05$). The observed differences in discrimination and calibration may stem from underlying differences in the NA cohort compared to the Italian in terms of male predominance, medical comorbidities, HCV-related cirrhosis, among other uncaptured patient characteristics. Moreover, data related to TIPS placement and function, such as stent diameters and pre/post-procedural pressure gradients, which may impact mortality were unavailable in our dataset. In fact, in the Italian derivation cohort, 60% of older adults had received undersized TIPS.

**Conclusion:** The overall ExPeCT score represents a useful risk stratifying tool in patients <70 years of age undergoing TIPS. Refitting/addition of other parameters may improve the performance of the older adult ExPeCT model in risk stratifying NA older patients for TIPS placement.

| Younger Age Cohort (n=1,221) | | | | | |
|---|---|---|---|---|---|
| | 6 Month Survival | 12 Month Survival | 24 Month Survival | 36 Month Survival | Overall Discrimination (Harrell's C) |
| **FIPS** | | | | | |
| Discrimination (AUC) | 0.657 | 0.631 | 0.618 | 0.611 | 0.602 |
| Intercept (95% CI) | -0.01 (-0.15, 0.13) | -0.05 (-0.17, 0.07) | -0.04 (-0.14, 0.06) | 0.02 (-0.08, 0.12) | |
| Slope (95% CI) | 0.81 (0.63, 0.98) | 0.58 (0.43, 0.72) | 0.43 (0.31, 0.56) | 0.34 (0.23, 0.46) | |
| Joint Test (p-value) | p=0.09 | p<0.001 | p<0.001 | p<0.001 | |
| **MELD-Na** | | | | | |
| Discrimination (AUC) | 0.576 | 0.575 | 0.567 | 0.570 | 0.580 |
| Intercept (95% CI) | 0.09 (-0.04, 0.22) | 0.05 (-0.06, 0.15) | -0.004 (-0.09, 0.08) | -0.01 (-0.09, 0.07) | |
| Slope (95% CI) | 1.32 (0.62, 2.02) | 1.31 (0.74, 1.88) | 1.29 (0.80, 1.78) | 1.32 (0.85, 1.79) | |
| Joint Test (p-value) | p=0.27 | p=0.40 | p=0.51 | p=0.40 | |
| **ExPeCT Score** | | | | | |
| Discrimination (AUC) | 0.656 | 0.662 | 0.646 | 0.637 | 0.622 |
| Intercept (95% CI) | 44.9 (44.7, 45.1) | 42.8 (42.7, 43.0) | 28.3 (28.2, 28.5) | 1.28 (1.17, 1.38) | |
| Slope (95% CI) | 0.45 (0.33, 0.57) | 0.47 (0.35, 0.59) | 0.43 (0.32, 0.54) | 0.38 (0.28, 0.49) | |
| Joint Test (p-value) | p<0.001 | p<0.001 | p<0.001 | p<0.001 | |
| **Older Age Cohort (n=178)** | | | | | |
| | 6 Month Survival | 12 Month Survival | 24 Month Survival | 36 Month Survival | Overall Discrimination (Harrell's C) |
| **FIPS** | | | | | |
| Discrimination (AUC) | 0.620 | 0.585 | 0.573 | 0.562 | 0.577 |
| Intercept (95% CI) | -0.11 (-0.41, 0.19) | -0.12 (-0.38, 0.14) | -0.05 (-0.29, 0.19) | 0.08 (-0.17, 0.33) | |
| Slope (95% CI) | 0.92 (0.39, 1.45) | 0.53 (0.10, 0.96) | 0.33 (-0.04, 0.70) | 0.24 (-0.12, 0.59) | |
| Joint Test (p-value) | p=0.76 | p=0.08 | p<0.01 | p<0.001 | |
| **MELD-Na** | | | | | |
| Discrimination (AUC) | 0.561 | 0.592 | 0.584 | 0.562 | 0.585 |
| Intercept (95% CI) | -0.05 (-0.34, 0.24) | -0.03 (-0.27, 0.20) | -0.03 (-0.26, 0.19) | 0.03 (-0.20, 0.25) | |
| Slope (95% CI) | 1.03 (0.18, 1.89) | 1.32 (0.63, 2.01) | 0.91 (0.28-1.54) | 0.66 (0.01-1.31) | |
| Joint Test (p-value) | p=0.93 | p=0.64 | p=0.91 | p=0.59 | |
| **ExPeCT Score** | | | | | |
| Discrimination (AUC) | 0.608 | 0.566 | 0.564 | 0.535 | 0.562 |
| Intercept (95% CI) | 0.07 (-0.27, 0.41) | 0.02 (-0.25, 0.29) | 0.08 (-0.17, 0.33) | 0.19 (-0.06, 0.44) | |
| Slope (95% CI) | 0.49 (0.13, 0.84) | 0.47 (0.12, 0.82) | 0.37 (0.03, 0.71) | 0.27 (-0.07, 0.61) | |
| Joint Test (p-value) | p=0.01 | p=0.01 | p=0.001 | p<0.001 | |

**Table 1.** Discrimination and Calibration of Prediction Scores

| Factor | VHA Cohort Age <70 (n=1221) | VHA Cohort Age >70 (n=178) | P-value* | FIPS Training Cohort (n=1496) | ExPeCT Derivation Cohort Age <70 (n=312) | ExPeCT Derivation Cohort Age >70 (n=99) | P-value* |
|---|---|---|---|---|---|---|---|
| Age, mean (SD) | 59.3 (7.0) | 73.1 (3.0) | <0.001 | 57.9 (12.1) | 59.0 (5.6) | 74.0 (3.3) | |
| Male Sex | 1194 (97.8%) | 174 (97.8%) | 0.98 | | 288 (73.1%) | 69 (69.7%) | 0.60 |
| Race | | | 0.19 | | | | |
| Asian | 12 (1.0%) | 1 (0.6%) | | | | | |
| Black | 78 (6.4%) | 6 (3.4%) | | | | | |
| Hispanic | 97 (7.9%) | 19 (10.7%) | | | | | |
| Other | 130 (10.6%) | 13 (7.3%) | | | | | |
| White | 904 (74.0%) | 139 (78.1%) | | | | | |
| BMI, mean (SD) | 28.9 (6.3) | 28.2 (4.8) | 0.19 | | | | |
| Etiology of Liver Disease | | | <0.001 | | | | |
| MASLD | 157 (12.9%) | 59 (33.1%) | | 38 (2.5%) | 56 (17.9%) | 17 (17.2%) | 0.50 |
| Alcholic Related Liver Disease (ALD) | 571 (46.8%) | 82 (46.1%) | | 967 (64.6%) | 130 (41.7%) | 18 (18.2%) | <0.001 |
| Hepatitis C Virus (HCV) | 98 (8.0%) | 10 (5.6%) | | 131 (8.8%) | 57 (18.3%) | 38 (38.4%) | <0.001 |
| Hepatitis B Virus | 11 (0.9%) | 4 (2.2%) | | 43 (2.9%) | 13 (4.2%) | 3 (3.0%) | 0.53 |
| ALD + HCV | 352 (28.8%) | 16 (9.0%) | | | 15 (4.8%) | 3 (3.0%) | 0.63 |
| Other | 32 (2.6%) | 7 (3.9%) | | 317 (21.2%) | 40 (12.8%) | 19 (19.2%) | |
| Diabetes | 790 (64.7%) | 130 (73.0%) | 0.03 | | 35 (11.2%) | 13 (13.1%) | 0.68 |
| Coronary Artery Disease | 259 (21.2%) | 72 (40.4%) | <0.001 | | | | |
| Heart Failure | 144 (11.8%) | 39 (21.9%) | <0.001 | | | | |
| Atrial Fibrillation | 75 (6.1%) | 30 (16.9%) | <0.001 | | | | |
| Prior Cirrhosis Decompensation | 1150 (94.2%) | 168 (94.4%) | 0.92 | | | | |
| Prior Hepatic Encephalopathy | 406 (33.3%) | 47 (26.4%) | 0.07 | 195 (13.0%) | 60 (19.2%) | 8 (8.1%) | 0.02 |
| Prior Varices | 856 (70.1%) | 117 (65.7%) | 0.24 | | | | |
| Prior Ascites | 842 (69.0%) | 119 (66.9%) | 0.57 | 1131 (75.6%) | | | |
| MELD-Na, mean (SD) | 14.7 (6.6) | 13.2 (6.0) | 0.01 | 16.0 (6.0) | 13.9 (4.4) | 13.5 (4.6) | 0.48 |
| CTP Score, mean (SD) | 6.8 (1.3) | 6.4 (1.1) | <0.001 | 8.0 (2.0) | 7.6 (1.4) | 7.3 (1.3) | 0.08 |
| CTP Class | | | <0.001 | | | | 0.02 |
| Class A | 544 (44.6%) | 109 (61.2%) | | 250 (16.7%) | 62 (19.8%) | 26 (26.3%) | |
| Class B | 628 (51.4%) | 67 (37.6%) | | 974 (65.1%) | 222 (71.3%) | 70 (70.7%) | |
| Class C | 49 (4.0%) | 2 (1.1%) | | 272 (18.2%) | 28 (9.0%) | 3 (3.0%) | |
| Sodium, mean (SD) | 135.2 (4.7) | 137.1 (4.3) | 0.02 | 135.0 (5.0) | 136 (5) | 137 (5) | 0.07 |
| Creatinine, mean (SD) | 1.2 (0.8) | 1.30 (0.6) | 0.12 | 1.4 (0.2) | 1.04 (0.46) | 1.19 (0.53) | 0.02 |
| Albumin, mean (SD) | 2.9 (0.60) | 3.1 (0.6) | 0.02 | 3.0 (0.7) | 3.32 (0.58) | 3.36 (0.56) | 0.56 |
| Total Bilirubin, mean (SD) | 2.1 (2.3) | 1.5 (1.1) | <0.001 | 1.8 (2.1) | 1.41 (0.81) | 1.27 (0.75) | 0.11 |
| INR, mean (SD) | 1.4 (0.9) | 1.3 (0.2) | 0.10 | 1.2 (0.2) | 1.32 (0.2) | 1.26 (0.18) | 0.01 |
| Platelets, mean (SD) | 122.1 (69.9) | 120.4 (59.7) | 0.75 | 143.0 (90.0) | 107 (63) | 98 (46) | 0.19 |
| Mortality at 6 months | 247 (20.2%) | 47 (26.4%) | 0.06 | 318 (21.3%) | | | |
| Mortality at 12 months | 363 (29.7%) | 69 (38.9%) | 0.02 | | 37 (12%)* | 19 (19%)* | |
| Mortality at 24 months | 508 (41.6%) | 91 (51.1%) | 0.02 | | 44 (14%)* | 30 (30%)* | |
| Mortality at 36 months | 605 (49.5%) | 104 (58.4%) | 0.03 | | 65 (21%)* | 41 (41%)* | |

**Table 2.** Demographic Description of Younger and Older Cohort
*Comparison between VHA Cohort <70 and >70 years of age
*Comparison between ExPeCT Cohort <70 and >70 years of age
*Liver related mortality

doi: 10.1016/j.dld.2024.01.110

## F-06

### Underdilated neoadjuvant-TIPS in patients with cirrhosis and portal hypertension candidates to operative interventions

D. Saltini [1], T. Guasconi [1], A. Ingravallo [2], F. Indulti [1], C. Caporali [3], S. Gitto [2], M. Falcini [2], M. Bianchini [1], B. Cuffari [1], M. Scoppettuolo [1], R. Spadaccini [1], F. Prampolini [3], F. Casari [3], N. De Maria [1], F. Marra [2], A. Colecchia [1], F. Vizzutti [2], F. Schepis [1]

[1] *Division of Gastroenterology, Azienda Ospedaliero-Universitaria of Modena, University of Modena and Reggio Emilia, Modena, Italy*
[2] *Internal Medicine and Liver Unit, University Hospital Careggi, Department of Experimental and Clinical Medicine, University of Florence, Italy*
[3] *Division of Radiology, Azienda Ospedaliero-Universitaria of Modena, University of Modena and Reggio Emilia, Modena, Italy*

**Introduction:** Clinically significant portal hypertension (CSPH) often excluded patients with cirrhosis from operative procedures due to high complications rates. Neoadjuvant-transjugular intrahepatic-portosystemic shunt (Neo-TIPS) can enable surgery and improve post-operative outcomes, but concerns about shunt-related complications limit its use. The underdilation-TIPS strategy, using a stent-graft dilated to diameters <8mm, has been shown to reduce complications while maintaining effectiveness.
**Aims:** The objective of this study was to assess the safety and effectiveness of the underdilation strategy in patients with cirrhosis candidates to Neo-TIPS for CSPH or its complications.
**Materials and Methods:** A retrospective study on a prospective database encompassing 315 patients who underwent TIPS was conducted at two Italian referral centers. The rate of surgery access following underdilated Neo-TIPS, the incidence of intra-operative and peri-operative complications, the risk of shunt-related complications, and the 6-month and 1-year survival rates were analyzed.
**Results:** Thirty-six consecutive patients were included in the study, with a mean age of 63±10 years and a mean MELD-score of 12±3 at the time of TIPS placement. Twelve patients (33%) had refractory ascites, while 9 patients (25%) had a history of variceal bleeding. Abdominal surgery was the main indication (78%) and in 28 patients the intervention was prompted by a diagnosis of resectable cancer. The average TIPS dilation diameter was 6±1mm. After Neo-TIPS, 92% of patients successfully underwent scheduled interventions, within a median time of 43 days. No major intra-operative complications were recorded. Twelve patients (36%) experienced peri-operative complications, two of which resulted in death. The 6-month and 1-year survival rates were 83% and 70%, respectively. Over a median follow-up of 18-months, episodic overt hepatic encephalopathy and heart failure were evident in 22% and 8% of patients, respectively.
**Conclusion:** Underdilation Neo-TIPS strategy exhibited a safe profile and a high success rate in patients with cirrhosis associated to CSPH or its complications.

doi: 10.1016/j.dld.2024.01.111

## F-07

### Changes in mean arterial pressure are inadequate to guide treatment with terlipressin and albumin in patients with hepatorenal syndrome - acute kidney injury

V. Calvino, A. Barone, M. Tonon, C.G. Gambino, S. Incicco, R. Gagliardi, N. Zeni, P. Angeli, S.S. Piano

*Unit of Internal Medicine and Hepatology, Department of Medicine, University and Hospital of Padova, Padova, Italy*

**Background:** Terlipressin and albumin are the first-line treatment of hepatorenal syndrome(HRS-AKI). Terlipressin is titrated according to changes in serum creatinine(SCr) on day-3. An increase in mean arterial pressure(MAP) was associated with resolution of HRS-AKI, leading some experts to suggest titration of terlipressin according to MAP changes. However, the optimal MAP targets remain unclear.
**Aim:** to evaluate the association between MAP changes on day-3 and response to treatment with terlipressin and albumin in patients with HRS-AKI.
**Methods:** Patients with cirrhosis and HRS-AKI treated with terlipressin and albumin as continuous infusion were identified. Clinical and biochemical data were collected at day-0 and day-3. We followed patients until death, liver transplantation or up to 90 days. The primary endpoint was response to treatment (i.e.SCr<133 umol/l). Secondary endpoints were early response(i.e.reduction of SCr>25% vs Day-0 on Day-3), 90-day survival.
**Results:** We enrolled 108 patients (mean age=59±9 years; male=70%; MELD=29±7; alcohol-cirrhosis=58%). On Day-3 most of patients had an increase in MAP (delta MAP=5.6±11.5 mmHg;p<0.001). Response to treatment was found in 56 patients (52%). Delta MAP on Day-3 was not significantly different between responders and non-responders (7.8vs4.4 mmHg;p=0.218). Delta MAP on Day-3 was not significantly different between early responders and non-responders (5.3 vs 6.0 mmHg;p=0.751). Responders had lower baseline SCr (2.91vs2.51 µmol/L;p=0.016) and higher rate of precipitating factors of HRS-AKI (61vs38%;p=0.007). In multivariable analysis (adjusted for age, precipitating factors, baseline-SCr and ACLF grade) delta MAP on Day-3 was not significantly associated with response to treatment (sHR=1.00;p=0.870). Lower baseline SCr (sHR=0.75;p=0.012) and precipitating factors of HRS-AKI (sHR=1.89;p=0.014) were independent predictors of response. Ninety-day survival was significantly higher in responders than in non-responders (sHR=0.45;p=0.004).
**Conclusion:** Delta MAP on Day-3 was not associated with response to treatment with terlipressin and albumin. Considering the risk of adverse events, terlipressin should not be titrated according to MAP changes during treatment.

doi: 10.1016/j.dld.2024.01.112

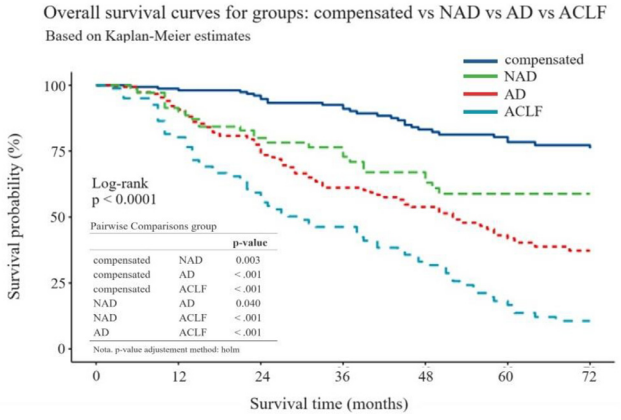
## F-08

### Role of infections and therapies in the development of the different stages of hepatic decompensation

M. Vicardi [1,2], A. Dalbeni [2,3], D. Sacerdoti [2,3]

[1] *Section of Innovation Biomedicine-Oncology Area, Department of Engineering for Innovation Medicine (DIMI), University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[2] *Liver Unit, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[3] *Unit of General Medicine C, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*

**Background and Aims:** new definitions of hepatic decompensation have recently emerged to avoid oversimplification. Non-acute decompensation (NAD) has been proposed as distinct entity from both acute decompensation (AD) and ACLF, based on progressive development of symptoms. The purpose of our study was to evaluate prognostic differences between the groups and explore the impact of bacterial infections and home therapies on hepatic decompensation.
**Methods:** from 2017 to 2022, we retrospectively enrolled 456 cirrhotic patients at the Verona Liver Unit (70.6% male, mean age 63.7 years). We collected data on comorbidities, home therapies, and laboratory tests at enrollment. Liver decompensations and infectious events developed over the years were used to stratify patients into compensated, AD, NAD and ACLF groups using the proposed definitions by D'Amico et al. These groups were analyzed to generate Kaplan-Meier mortality curves and conduct univariate and multivariate analyses to identify any influencing factors.
**Results:** among the 456 patients, 70 developed NAD, 151 AD and 81 ACLF, while 154 remained compensated. Mortality curves showed a significant difference between all groups ($p < 0.0001$). Differences were shown in etiology, comorbidities, and therapies. In the multivariate multistep, MDR colonizations were significantly associated with both AD (OR 3.20, $p = 0.001$) and ACLF (OR 2.55, $p = 0.014$). NOACs, on the other hand, were associated with prevention of NAD (OR 0.52; p=0.033) and AD (OR 0.49, p=0.016). In addition, UTI and sepsis were the only infections that remained independently associated with ACLF rather than AD (OR 2.28, p=0.050 and OR 2.21, p=0.037, respectively).
**Conclusions:** NAD should be considered as a new distinct entity in the history of decompensation. NOACs seem to prevent decompensation events. Not only do infections such as UTIs and sepsis play a crucial role in decompensated cirrhosis, but MDR colonizations may also have a significant impact on these conditions.




doi: 10.1016/j.dld.2024.01.113

## F-09

### Long-term albumin administration improves survival in outpatients with decompensated cirrhosis and diabetes: post-hoc analysis of the ANSWER Trial

G. Zaccherini [1,2], C. De Venuto [1,2], M. Baldassarre [1,2], E. Pompili [1,2], G. Iannone [1,2], O. Riggio [3], P. Angeli [4], C. Alessandria [5], S. Neri [6], F.G. Foschi [7], F. Levantesi [8], A. Airoldi [9], L. Simone [10], G. Svegliati-Baroni [11], S. Fagiuoli [12], G. Laffi [13], R. Cozzolongo [14], V. Di Marco [15], V. Sangiovanni [16], F. Morisco [17], P. Toniutto [18], A. Tortora [19], R. De Marco [20], S. Nardelli [3], S. Piano [4], C. Elia [5], P. Caraceni [1,2], M. Bernardi [2], for the ANSWER Study Investigators

[1] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy*
[2] *Department of Medical and Surgical Sciences, University of Bologna, Italy*
[3] *Department of Clinical Medicine, Sapienza University of Rome, Rome, Italy*
[4] *Unit of Internal Medicine and Hepatology, Department of Medicine, University of Padua, Padua, Italy*
[5] *Division of Gastroenterology and Hepatology, Città della Salute e della Scienza Hospital, Turin, Italy*
[6] *Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy*
[7] *Internal Medicine, Hospital of Faenza, Azienda Unità Sanitaria Locale of Romagna, Faenza, Italy*
[8] *Internal Medicine, Hospital of Bentivoglio, AUSL of Bologna, Bologna, Italy*
[9] *Liver Unit, Department of Hepatology and Gastroenterology, Niguarda Hospital, Milan, Italy*
[10] *Gastroenterology Unit, University Hospital, Ferrara, Italy*
[11] *Department of Gastroenterology, Polytechnic University of Marche, Ancona, Italy*
[12] *Gastroenterology and Transplant Hepatology, Papa Giovanni XXIII Hospital, Bergamo, Italy*
[13] *Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy*
[14] *Division of Gastroenterology, National Institute of Gastroenterology S. De Bellis, Castellana Grotte, Bari, Italy*
[15] *Unit of Gastroenterology and Hepatology, Biomedical Department of Internal and Specialistic Medicine, University of Palermo, Palermo, Italy*
[16] *Azienda Ospedaliera di Rilievo Nazionale dei Colli, Cotugno Hospital of Naples, Naples, Italy*
[17] *Gastroenterology Unit, Department of Clinical Medicine and Surgery, Federico II University of Naples, Naples, Italy*
[18] *Internal Medicine, Department of Medical Area, University of Udine, Udine, Italy*
[19] *Gastroenterology, Gemelli Foundation, Catholic University, Rome, Italy*
[20] *Gastroenterology Unit, Hospital of Cosenza, Cosenza, Italy*

**Introduction:** Type 2 diabetes mellitus (DM) is a frequent comorbidity in patients with liver cirrhosis, and represents an independent risk factor for bacterial infections, the occurrence of cirrhosis-related complications, and mortality. Apart from DM control, treatment strategies protecting patients from these risks still are an unmet need.
**Aims:** To determine whether long-term human albumin (HA) administration improves survival in outpatients with decompensated cirrhosis and DM.
**Methods:** We performed a post-hoc analysis of the ANSWER trial, that randomized 431 patients with cirrhosis and uncomplicated ascites to receive either the standard medical treatment (SMT) or the SMT plus HA up to 18 months, extrapolating the subgroup of

patients with insulin-treated DM. Overall survival rates during a follow-up of 18 months were determined.
**Results:** Eighty-five (19.7%) patients presented insulin-treated DM at baseline (50 in the SMT and 35 in the SMT+HA arm respectively). At baseline, diabetic patients who received long-term HA did not significantly differ from those randomized to SMT, as regards age, etiology of cirrhosis, body mass index (BMI), Child-Pugh class, and MELD score. During the follow-up, 39 patients ended the study prematurely (17 of them for medically uncontrolled ascites requiring at least 3 paracenteses per month, 14 in the SMT and 3 in the SMT+HA arm), and 16 died (12 in the SMT and 4 in the SMT+HA arm, respectively). Among the latter, 13 patients died for liver-related causes (10 [83%] in the SMT and 3 [75%] in SMT+HA arm, respectively). 18-month overall survival improved significantly in the patients enrolled in the SMT+HA arm (86% [95%CI: 66-95] vs 57% [95%CI: 35-74], log-rank p=0.016) with a 72% risk reduction for mortality (Hazard Ratio 0.27 [95%CI 0.09 – 0.85], p=0.025).
**Conclusions:** Long-term HA administration appears a beneficial therapeutic intervention that improves survival in insulin-treated diabetic outpatients with decompensated cirrhosis and ascites.

doi: 10.1016/j.dld.2024.01.114

## F-10

### The role of 2D-Shearwave elastography in non invasive portal hypertension diagnosis

F. Bronte [1], A. Affronti [1], F. Gambino [1], G. Mogavero [2], G. Bronte [3,4], M.G. Bavetta [5], G. Malizia [1]

[1] *Gastroenterology Unit - Ospedali Riuniti Villa Sofia – V. Cervello*
[2] *EndoscopyUnit – GastroenterologyUnit - Ospedali Riuniti Villa Sofia – V. Cervello*
[3] *Clinic of Laboratory and Precision Medicine, National Institute of Health and Sciences on Ageing (IRCCS INRCA), Ancona, Italy*
[4] *Department of Clinical and Molecular Sciences (DISCLIMO), Università Politecnica Delle Marche, Ancona, Italy*
[5] *EpatoOncology Unit - Ospedali Riuniti Villa Sofia – V. Cervello*

**Introduction and Objective:** The gold standard for the diagnosis of clinicallysignificant portal hypertension isrepresented by HVPG and Upper Gastrointestinalendoscopy is able to indirectlyassess the degree of portalhypertension through the evaluation of esophageal and/or gastric varices. Over the last 20 years, the introduction of non invasive tests (NITs) such asFibroscan has made it possibleto select patients with significantportal hypertension and therefore identify patients eligiblefor endoscopy. The BAVENO VII consensus identifies patientswho could benefit from endoscopy as those patientswith LSM $\geq$ 20 kPa assessed by TE and platelet count $\leq$ 150 $\times$ 109L. Moreover identifiesvalues of spleen stiffness to rulein and rule out portalhypertension such as SSM >50 kPa and SSM <21 kPa,respectively. Point-shear waveelastography and 2D-shear waveelastography have beenproposed as possible tools to non-invasively assess portalhypertension, but validation of the best cut-off is needed. Aim of this study is the evaluation of the role of 2D-Shear wave in non invasive diagnosis of portalhypertension.
**Methods:** From April 2022 to October 2023 we evaluated one hundred patients with chronichepatitis and cirrhosis (50 chronic hepatitis and 50 cirrhosis) whose baseline characteristics are presented in TABLE 1. All patients underwentabdominal ultrasound, liver and spleen stiffness (LS and SS) and liver and spleen 2D-shear wave(L2D-S and S2D-S); FIB-4 and the APRI score were alsocalculated. All cirrhotic patientsunderwent endoscopy to evaluate portal hypertension.
**Results:** The prevalence of varices in cirrhotic patients was50%. We found a statisticallysignificant correlation betwen LS and SS (p<0,001) and L2D-S and S2D-S (p<0,001) and the presence of varices, this was true also for APRI and FIB-4 (p<0,001), independently fromage, sex and BMI. We evaluated also the diagnostic performance for each individual test (Table 2), with an optimal cut-off 13.1 kPa and 12.5 kPa for LS and L2D-S (sensitivity 0.83 and 0.79, specificity 0.72 and 0.77, PPV 0.50 and 0.54, NPV 0.93 and 0.92 and AUROC 0.84 and 0.83 respectively), 45 kPa and 25 kPa for SS and S2D-S (sensitivity 0.77 and 0.91, specificity 0.89 and 0.66, PPV 0.69 and 0.47, NPV 0.92 and 0.96 and AUROC 0.88 and 0.80 respectively), 2.82 for FIB-4 (sensitivity 0.84, specificity 0.74, PPV 0.52, NPV 0.93 AUROC 0.80), 0.64 for APRI (sensitivity 0.72, specificity 0.70, PPV 0.44, NPV 0.88 AUROC 0.74). Each single test showed a low PPV for the prediction of oesophagealvarices (OV), however, when we combined the tests together wefound that the combination of LS and S2D-S showed a higher PPV for predicting OV (PPV 0.73; NPV 0.99).
**Conclusion:** We foundthat the combination of twotests (Liver stiffness and Spleen stiffness 2D-Shear wave) increases the probability of findingoesophageal varices and therefore can be useful for the non-invasive identification of patients with clinicallysignificant portalhypertension.

**Table 1**.

Patients characteristics

| | Chronic Hepatitis (50, 50%) | Cirrhosis (50, 50%) | p |
|---|---|---|---|
| Sex (male %) | 33 (66%) | 33 (66%) | 1** |
| Age y (mean ± SD) | 60,68 ± 11,63 | 65,46 ± 11,33 | 0,06* |
| BMI (Kg/m^2 means ± SD) | | | |
| Etiology<br>Viral<br>Metabolic<br>Autoimmune | 26 (52%)<br>15 (30%)<br>9 (18%) | 23 (46%)<br>24 (48%)<br>3 (6%) | 0,072** |
| AST U/l (mean ± SD) | 53,81 ± 119,44 | 41,48 ± 32,04 | 0,409* |
| ALT U/l (mean ± SD) | 65,50 ± 173,33 | 34,94 ± 29,11 | 0,607* |
| PLT mmc (mean ± SD) | 217875 ± 82284 | 145040 ± 111323 | **<0,001*** |
| APRI | 0,98 ± 2,41 | 1,61 ± 3,38 | **0,002*** |
| FIB-4 | 2,38 ± 2,66 | 5,83 ± 11,12 | **<0,001*** |
| Portal vein diameter (mm) | 10,82 ± 1,84 | 13,52 ± 2,71 | **<0,001*** |
| Spleen diameter (cm) | 10,61 ± 1,65 | 14,17 ± 2,60 | **<0,001*** |
| Spleen volume (cm²) | 38,89 ± 7,92 | 39,8 ± 59,24 | **<0,001*** |
| Liver Stiffness (Fibroscan ®) | 8,78 ± 10,73 | 25,38 ± 19,71 | **<0,001*** |
| Spleen Stiffness (Fibroscan ®) | 22,87 ± 14,05 | 46,83 ± 21,82 | **<0,001*** |
| Liver Stiffness (2-D Shearewave) | 7,74 ± 4,85 | 25,38 ± 19,71 | **<0,001*** |
| Spleen Stiffness (2-D Shearewave) | 31,54 ± 54,7 | 37,13 ± 57,74 | **<0,001*** |
| Oesophageal Varices<br>Absent<br>Present | 50 (100%)<br>0 (0%) | 25 (50%)<br>25 (50%) | **<0,001*** |

*Mann-Whitney U-Test
**Chi-Square Test

doi: 10.1016/j.dld.2024.01.115

## F-11

### Accuracy of a dedicated 100 Hz vibration-controlled spleen stiffness measurement for the detection of esophageal varices in naïve patients with compensated advanced chronic liver disease: interim results from a multicentric cohort

A. Armandi [1,2], T. Sanavia [3], E. Vanderschueren [4], G. Semmler [5], A. Liguori [6], S. Petta [7], M. Michel [2], M.M. Werner [2], T. Merizian [2], C. Labenz [2], M. Jachs [5], M. Mandorfer [5], W. Laleman [4], L. Miele [6], T. Reiberger [5], J.M. Schattenberg [2]

[1] *Division of Gastroenterology and Hepatology, Department of Medical Sciences, University of Turin, Italy*
[2] *Metabolic Liver Disease Research Program, University Medical Center of the Johannes Gutenberg-University, Mainz, Germany*

[3] Computational Biomedicine Unit, Department of Medical Sciences, University of Turin, Turin, Italy
[4] Department of Gastroenterology and Hepatology, Section of Liver and Biliopancreatic disorders, University Hospitals Leuven, KU LEUVEN, Leuven, Belgium
[5] Division of Gastroenterology and Hepatology, Department of Medicine III, Medical University of Vienna, Vienna, Austria
[6] Dipartimento di Scienze Mediche e Chirurgiche (DiSMeC), Fondazione Policlinico Gemelli IRCCS, Università Cattolica del S. Cuore, Rome, Italy
[7] Section of Gastroenterology and Hepatology, Dipartimento Di Promozione Della Salute, Materno Infantile, Medicina Interna e Specialistica Di Eccellenza (PROMISE), University of Palermo, Italy

**Introduction:** Clinically significant portal hypertension (CSPH) marks a critical step in the natural history of compensated advanced chronic liver disease (cACLD) and may lead to esophageal varices (EV). The Baveno VI criteria suggest liver stiffness measurement (LSM) and platelet count (PLT) for non-invasive identification of cACLD patients not requiring screening gastroscopy.
**Aim:** We investigated the accuracy of the novel 100 Hz vibration-controlled transient elastography-based spleen stiffness measurement (SSM) exam for the identification of EV in cACLD patients.
**Materials and Methods:** Retrospective study of Mainz, Vienna, Leuven, Rome and Palermo. Patients with cACLD of any etiology (LSM≥10kPa or histological F4 fibrosis), but without previous decompensation (bleeding, encephalopathy, ascites) were included. SSM and LSM were obtained using Fibroscan F630 ≤1 month within screening gastroscopy. Prediction performance between different SSM cut-offs with respect to the Baveno criteria (LSM>20kPa and/or PLT<150 G/L) were compared by logistic regression with 10-fold cross-validation, adjusted for age, gender, BMI, transaminases, INR, albumin, and bilirubin. Backward feature selection based on likelihood ratio test was applied to identify significant confounders. Performance was calculated by balanced accuracy (BA), specificity (SP) and sensitivity (SE). Wilcoxon test was used to evaluate significant performance improvement of SSM cut-offs with respect to Baveno criteria, or to signifcant confounders.
**Results:** 343 cACLD patients with a median age of 59 years (60.3% male) and NAFLD as the main etiology (51.3%) were included. 137 had EV with 49 high-risk EV (HR-EV), while median SSM, LSM and PLT were 40.5kPa, 21kPa and 139 G/L, respectively. The figure shows BAs at different SSM cut-offs, compared to Baveno (red line). The best overall performance with all-type EV was at SSM=60 kPa (BA=0.72, SP=0.86, SE=0.58); Baveno: BA=0.66, SP=0.86, SE=0.39. Comparing HR-EV vs. absence of EV, the best cut-off was at 50kPa (BA=0.71, SP=0.95, SE=0.47; Baveno: BA=0.56, SP=0.92, SE=0.29). These SSM thresholds significantly improved BA when significant confounders were considered.
**Conclusions:** The novel spleen-dedicated 100 Hz SSM is associated with presence of EV in cACLD patients. In both all-type EV and HR-EV, SSM showed better accuracy than the Baveno LSM-PLT criteria, achieving a better trade-off between SP and SE.

doi: 10.1016/j.dld.2024.01.116

## F-12

### Episodic overt hepatic encephalopathy after transjugular intrahepatic portosystemic shunt does not increase mortality in patients with cirrhosis

S. Nardelli [1], O. Riggio [1], F. Marra [2], S. Gioia [1], D. Saltini [3], D. Bellafante [1], V. Adotti [2], T. Guasconi [3], L. Ridola [1], M. Rosi [2], C. Caporali [4], F. Fanelli [5], D. Roccarina [2], M. Bianchini [3], F. Indulti [3], A. Spagnoli [6], M. Merli [1], F. Vizzutti [2], F. Schepis [3]

[1] Department of Translational and Precision Medicine, Sapienza University of Rome, Italy
[2] Department of Experimental and Clinical Medicine, University of Florence, Italy
[3] Division of Gastroenterology, Modena Hospital, University of Modena and Reggio Emilia, Modena, Italy
[4] Department of Radiology, Modena Hospital, University of Modena and Reggio Emilia, Modena, Italy
[5] Interventional Radiology Unit, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy
[6] Department of Public Health and Infectious Diseases, Sapienza University of Rome

**Background and Aims:** In patients with cirrhosis, transjugular intrahepatic portosystemic shunt (TIPS) is indicated for the prophylaxis of variceal re-bleeding and treatment of refractory ascites. Overt hepatic encephalopathy (OHE) is a major complication after TIPS, given its high incidence and possibility of refractoriness to medical treatment. Nevertheless, the impact of post-TIPS OHE on mortality has not been investigated in a large population.
**Methods:** We designed a multicenter non-inferiority observational study to evaluate the mortality rate at 30 months in patients with and without OHE after TIPS. We analyzed a database of 614 patients submitted to TIPS in three Italian centers and estimated the cumulative incidence of OHE and mortality with competitive risk analyses, setting the non-inferiority limit at 0.12.
**Results:** During a median follow-up of 30 months (IQR 12-30), 293 patients developed at least one episode of OHE. Twenty-seven (9.2%) of them experienced recurrent/persistent OHE. Patients with OHE, compared to those without, were older [64(57-71) vs 59(50-67) years, p<0.001], had lower albumin [3.1(2.8-3.5) vs 3.25(2.9-3.6) g/dl, p=0.023], and had a higher prevalence of pre-TIPS OHE (15.4% vs. 9.0%, p=0.023). Child-Pugh and MELD scores were similar between the two groups. The 30-month difference in mortality between patients with and without post-TIPS OHE was 0.03(95% CI: -0.042 - 0.102). Multivariable analysis showed that age [sHR 1.04 (1.02 -1.05), p<0.001] and MELD [sHR 1.09 (1.05;1.13), p<0.001], but not post-TIPS OHE, were associated with a higher mortality rate. Similar results were obtained when patients undergoing TIPS for variceal re-bleeding prophylaxis (n=356) or refractory ascites (n=258) were analyzed separately. The proportion of patients with persistent OHE after TIPS was significantly higher in the group of patients who died.
**Conclusion:** Episodic OHE after TIPS does not increase mortality in patients undergoing TIPS, regardless of the indication.

doi: 10.1016/j.dld.2024.01.117

## F-13

### Predictors of clinical trajectories in patients surviving an acute decompensation of cirrhosis

C. Gambino, A. Accetta, R. Buono, S. Incicco, R. Gagliardi, N. Zeni, M. Tonon, V. Calvino, A. Barone, P. Angeli, S. Piano

*Unit of Internal Medicine and Hepatology (UIMH), Department of Medicine, University of Padova, Padova, Italy*

**Background:** three different clinical trajectories have been described in patients surviving an acute decompensation of cirrhosis, namely stable decompensated cirrhosis (SDC), unstable decompensated cirrhosis (UDC) and pre-ACLF. The identification of these patients could be crucial in their clinical management, however, predicting the clinical course at time of discharge is challenging.
**Aim:** To investigate predictors of clinical course after discharge for AD and 180-day mortality.

**Methods:** clinical, laboratory and pharmacological data at admission, during hospitalization and at discharge were collected from consecutive patients surviving an AD of cirrhosis at our Unit. Patients were followed up until transplant, death, or 180 days.
**Results:** We included 360 patients (age=62±12; male=66%; alcoholic etiology=55%; MELD=16[12-22]). At 90-day after discharge, 195 (54%) patients were identified as SDC, 115 (32%) as UDC and 50 (14%) as pre-ACLF. Sixteen (22%) patients underwent LT. At discharge, pre-ACLF patients showed, if compared to SDC and UDC patients, higher serum creatinine (1.29vs0.83vs0.85mg/dl; p<0.001), INR (1.59vs1.39vs1.38; p=0.027), neutrophils (3.82vs2.92vs2.97 × 10^9/l; p=0.033), MELD (19vs14vs14; p<0.001). We couldn't find any difference between SDC and UDC patients at discharge. At 180-days after discharge, mortality rate was higher in pre-ACLF respect to UDC and SDC (38% vs 16% vs 2%; p<0.0001), and 30 (8.3%) patients underwent LT. In a multivariable model (adjusted for age, gender, aetiology, presence of varices, AKI or HE during hospitalization, serum creatinine, INR, bilirubin, CRP at discharge, and clinical trajectory) higher levels of CRP (HR=1.02; p=0.021), UDC (HR=9,98; p=0.009) and pre-ACLF (HR=31.4; p<0.001) were independent predictors of 180-day mortality.
**Conclusion:** Our study is one of the first external confirmation of the clinical trajectories after AD of cirrhosis showed in PREDICT cohort. Pre-ACLF patients showed worse liver and kidney function, and higher systemic inflammation at discharge. We were unable to distinguish SDC from UDC at discharge. Future trials and more raffinate biomarkers could be help in answering this question.

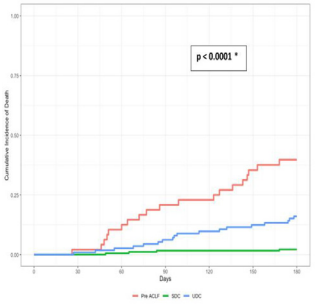



**Figure 1. Cumulative incidence of death at 180-day by clinical course.** *pre-ACLF vs UDC vs SDC ACLF, Acute-on-chronic liver failure; SDC, Stable decompensated cirrhosis; UDC, Unstable decompensated cirrhosis.

| | sHR (95% CI) | P-value |
|---|---|---|
| Age | 1.01 (0.97 – 1.04) | 0.701 |
| Sex (F) | 0.98 (0.37 – 2.60) | 0.970 |
| Etiology | | |
| Alcohol | 1.10 (0.38 – 3.18) | 0.861 |
| Autoimmune | 1.52 (0.24 – 9.75) | 0.660 |
| NASH | 1.78 (0.66 – 4.79) | 0.261 |
| HCV | 0.45 (0.15 – 1.34) | 0.151 |
| HBV | 1.01 (0.15 – 6.73) | 0.918 |
| Other | 0.61 (0.11 – 3.39) | 0.571 |
| Varices | 0.73 (0.28 – 1.91) | 0.523 |
| HE | 0.84 (0.37 – 1.88) | 0.660 |
| AKI | 1.69 (0.70 – 4.08) | 0.241 |
| Serum Creatinine at discharge | 1.00 (0.69 – 1.44) | 0.999 |
| INR at discharge | 0.98 (0.94 – 1.02) | 0.390 |
| Serum Albumin at discharge | 0.99 (0.93 – 1.05) | 0.660 |
| Bilirubin at discharge | 1.05 (0.97 – 1.13) | 0.240 |
| CRP at discharge | 1.02 (1.00 – 1.05) | 0.021 |
| Clinical trajectory | | |
| UDC (vs SDC) | 9.98 (1.76 – 56) | 0.009 |
| Pre-ACLF (vs SDC) | 31.4 (4.71 – 209) | <0.001 |

**Table 1. Multivariable analysis of 180-day mortality.** NASH, Non-Alcoholic steatohepatitis; HCV, Hepatitis C virus; HBV, Hepatitis B virus; HE, Hepatic Encephalopathy; AKI, Acute Kidney Injury; INR, International Normalized Ratio; CRP, C-reactive Protein; SDC, Stable decompensated cirrhosis; UDC, Unstable decompensated cirrhosis; ACLF, Acute-on-chronic liver failure.

doi: 10.1016/j.dld.2024.01.118

## F-14

### Transjugular intrahepatic portosystemic shunt (TIPS) in patients with vascular liver disorders: a comparative study

C. Becchetti [1], G. Perricone [1], M. Solcia [2], F. Morelli [2], A. Alfonsi [2], F. Barbosa [2], P.M. Brambillasca [2], C. Gallo [1,3], M. Vangeli [1], C. Mazzarelli [1], R. Viganò [1], F. Aprile [1], M. Cucco [1], R. Stigliano [1], L. Cesarini [1], A.G. Rampoldi [2], L.S. Belli [1], A. Airoldi [1]

[1] *Hepatology and Gastroenterology Unit, ASST GOM Niguarda, Milan, Italy*
[2] *Interventional Radiology Unit, ASST GOM Niguarda, Milan, Italy*
[3] *Division of Gastroenterology, Fondazione IRCCS San Gerardo dei Tintori, University of Milano-Bicocca School of Medicine, Milan, Italy*

**Introduction:** Vascular liver disorders (VLD) are an heterogenous groups of liver diseases ultimately leading to portal hypertension (PH) defined non-cirrhotic as opposed to what develops in patients with cirrhosis. Despite the different pathophysiological pattern, the current management of PH is the same in both conditions. Nevertheless, data on the use of transjugular intrahepatic portosystemic shunt (TIPS) in patients with VLD are scant.
**Aim:** to compare patients with VLD vs. cirrhosis undergoing TIPS for PH complications.
**Materials and Methods:** we included consecutive patients undergoing TIPS at our center from February 2014 to October 2022. Patients with previous LT or portal vein thrombosis without liver disease were excluded. Clinical variables were collected. The main outcome was 1-year LT free survival. Descriptive statistic and Kaplan Meier estimator were adopted for the analysis.
**Results:** Overall, 245 TIPS were placed during the study period. 20 patients did not meet the inclusion criteria. Therefore, 225 patients were considered, of them 29 (13%), 16 (10%) male, 49 years-old (IQR 35-51) had VLD, mainly porto-sinusoidal vascular disorder (16 [55%]) and Budd-Chiari syndrome (8 [28%]). Patients with VLD were younger than those with cirrhosis (49 vs. 59, p<0.001), but no difference concerning sex, hepatic venous pressure gradient (HVPG) pre-TIPS or post-TIPS was found (p>0.05). Ascites was more frequent as indication among patients with cirrhosis (42% vs 7%, p<0.001), while cavernoma was successfully recanalized more frequently in patients with VLD (30% vs. 4%, p<0.001). Hepatic encephalopathy was the main post-TIPS complication without difference among the two groups. Overall, after 1-year, 36 patients died (0.4% VLD vs. 16% cirrhosis, p=0.048), whereas 37 (0.4% vs. 12%, p=0.038) underwent LT. LT-free survival was higher for patients with VLD vs. those with cirrhosis (log-rank 0.014).
**Conclusions:** TIPS for PH complications in patients with VLD ensures an excellent prognosis, although with high complexity.

doi: 10.1016/j.dld.2024.01.119

## F-15

### Safety and Effectiveness of anticoagulation in patients with cirrhosis listed for liver transplantation: a single center observational study

R. Caccia [1], G. Tosetti [1], M. Primignani [1], M. Lucà [1], S. Stella [2], P. Lampertico [1,2,3]

[1] *Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, SC Gastroenterologia ed Epatologia, Milano, Italia*
[2] *Epidemiology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano*
[3] *CRC "A.M. e A. Migliavacca" per lo Studio e la Cura delle Malattie del Fegato, Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, Università degli Studi di Milano, Milano, Italia*

**Introduction:** Anticoagulation (AC) is safe in patients with cirrhosis and appears to decrease decompensation and increase survival. However, no data on safety and effectiveness of AC in patients listed for OLT are available.
**Aims:** We evaluated safety and effectiveness of AC in terms of decompensation, delisting and mortality in patients listed for OLT and anticoagulated, compared with patients not anticoagulated. Secondary aim was PVT outcome.
**Material and methods:** Retrospective data of consecutive patients followed at our Center (2017-2021), from listing until OLT, delisting or death were collected. Univariate and multivariate logistic regression models (adjusted for age, Child-Pugh class and time in list) were fitted to evaluate the effect of AC on bleeding, de-novo/further decompensation, delisting for improvement, OLT and death.
**Results:** 251 patients listed for OLT, 165 Child-Pugh class B/C, 34 AC (13.5%), mainly for Portal Vein Thrombosis (PVT) (85%). AC pa-

tients were more likely CP class B/C (85% vs 63%, p=0.002). AC included LMWH (67%), fondaparinux (18%), VKA (12%) and DOAC (3%). The bleeding rate was similar in AC and non-AC patients, either for total (23.5% vs. 20.7%; p=0.711), severe (8.8% vs. 9.7%; p=0.823) or portal hypertensive bleedings (2.9% vs. 1.8%; p=0.686).

Overall, there was no difference in the rate of de-novo decompensation (14.7% vs 9.7%; p=0.398); in CP class B/C patients there was no difference on further decompensation rate (48.3% vs 41.9%; p=0.617), but AC patients had significantly more delisting for improvement (10.3% vs 2.2%; p=0.034) and less deaths in list (0.0% vs 13.2%; p=0.038). PVT regressed in 13 (45%, 10 total and 3 partial regression), was stable in 12 (14%) and worsened in 4 (14%). No patients were delisted for PVT worsening.

**Conclusions:** In cirrhotic patients listed for OLT, requiring AC for PVT, AC was safe and associated with higher delisting and improved survival in list.

doi: 10.1016/j.dld.2024.01.120

## F-16

### Long-term therapy with intravenous human albumin increase survival in patients with decompensated cirrhosis and refractory ascites

A. Lombardo, L. Capodicasa, D. Alaimo, F. Mercurio, A. Zimbardo, F. Simone, N. Alessi, C. Celsa, G. Pennisi, G. Cabibbo, S. Petta, C. Cammà, V. Calvaruso, V. Di Marco

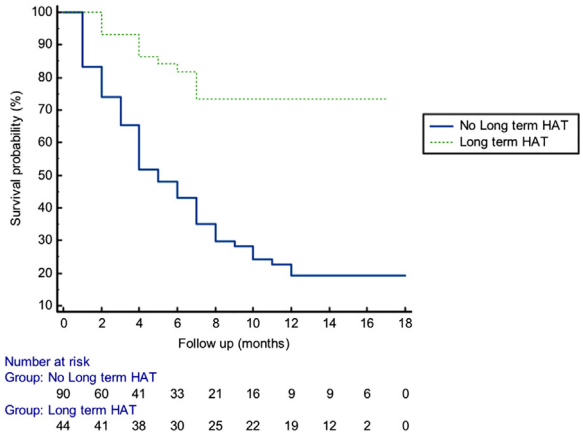
*Section of Gastroenterology and Hepatology, Dipartimento Di Promozione Della Salute, Materno Infantile, Medicina Interna e Specialistica Di Eccellenza (PROMISE), University of Palermo, Palermo, Italy*

**Background:** Refractory ascites in cirrhosis is associated with 50% survival at six months. The benefit of long-term human albumin therapy (HAT) was proven by ANSWER study in decompensated cirrhosis and have become best practice in Italian Liver Units.

**Methods:** We reported data of an observational study including 134 patients with cirrhosis and refractory ascites undergoing large-volume paracenteses (LVP) in the Day Hospital of our Liver Unit. The group I included 90 patients, observed from January 2019 and April 2022, who received HAT only during LVP. The group II of 44 patients, observed from May 2022 and November 2023, received HAT during LVP and long-term (40 grams/week).

**Results:** The mean age of patients was 68 years and 70% were male, the mean of MELD-score was 14, of serum albumin 32 g/L and sodium 136 mmol/L. The etiology was MASH in 38 patients, alcohol in 26, HCV in 3, HBV in 12, autoimmune in 2, while 10 patients had a cryptogenic cirrhosis and 15 had a mixed etiology. Twenty-nine patients had HCC and 17 had portal thrombosis. There were no significant clinical differences between the 2 groups at baseline. During the first year of follow-up, 10 patients received liver transplant and in 17 patients was placed a TIPS; 74 patients (82%) of group I and 19 patients (45%) of group II needed at least one hospitalization for complications (p< 0.001). In group I all patients undergoing LVP, while in group II 12 patients (27%) no longer performed LVP (p< 0.001). Finally, 65 patients (71%) of group I and 11 patients (26%) of group II died (p<0.001 by log rank test) **(figure 1)**

**Conclusions:** Long-term human albumin therapy treatment can significantly improve prognosis and reduce mortality in patients with refractory ascites. It is a well-tolerated treatment with no complications or contraindications.




doi: 10.1016/j.dld.2024.01.121

## F-17

### Efficacy and safety of lusutrombopag in a real-world Italian series of cirrhotic patients with severe thrombocytopenia undergoing invasive procedures: the Reality study

P. Gallo [1], A. De Vincentis [1], V. Pace-Palitti [2], M. Russello [3], A. Vignone [4], D. Alvaro [4], R. Tortora [5], M. Biolato [6], M. Pompili [6], V. Calvaruso [7], M. Veneziano [7], M. Tizzani [8], A. Caneglias [8], F. Frigo [8], M. Gesualdo [8], A. Marzano [8], V. Rosato [9], E. Claar [9], R. Villani [10], A. Izzi [11], R. Cozzolongo [12], A. Airoldi [13], C. Mazzarelli [13], M. Distefano [14], C. Iegri [15], S. Fagiuoli [15], V. Messina [16], E. Ragone [17], R. Sacco [10], P. Cacciatore [2], F. Masutti [18], S.L. Crocé [18], A. Moretti [19], F. Terracciani [1], A. Falcomatà [1], A. Picardi [1], U. Vespasiani-Gentilucci [1]

[1] *Fondazione Policlinico Campus Biomedico, Rome, Italy*
[2] *ASL Pescara, Pescara, Italy*
[3] *Arnas Garibaldi, Catania, Italy*
[4] *Sapienza University of Rome, Rome, Italy*
[5] *AORN Cardarelli, Naples, Italy*
[6] *Fondazione Policlinico Universitario Gemelli, Rome, Italy*
[7] *University of Palermo, Palermo, Italy*
[8] *Città della salute e della scienza, Torino, Italy*
[9] *Betania Hospital, Naples, Italy*
[10] *University of Foggia, Foggia, Italy*
[11] *D. Cotugno Hospital, Naples, Italy*
[12] *"S de Bellis" Research Hospital, Castellana Grotte, Bari, Italy*
[13] *ASST GOM Niguarda, Milano, Italy*
[14] *Umberto I Hospital, Siracusa, Italy*
[15] *ASST Papà Giovanni XXIII, Bergamo, Italy*
[16] *S. Anna and S. Sebastiano Hospital, Caserta, Italy*
[17] *Monaldi Hospital, Naples, Italy*
[18] *A.S.U. Giuliano Isontina, University of Trieste, Italy*
[19] *San Filippo Neri Hospital, Rome, Italy*

**Background and Aims:** Severe thrombocytopenia [platelet count (PLTs) <50,000/μL] poses challenges in management of patients with chronic liver disease (CLD). Recently, thrombopoietin receptor agonists, such as lusutrombopag, have been developed to obviate the need for platelet transfusions. Existing real-world data are limited to sporadic reports or administrative databases. We aimed to assess the first post-marketing real-world European cohort of cirrhotic patients treated with lusotrombopag to verify the efficacy and safety of the drug.

**Method:** In the REAL-world lusutrombopag treatment in Italy (REALITY) study, we collected data from consecutive cirrhotic pa-

tients receiving lusotrombopag before invasive procedures between March 2021 and March 2023 from 19 Italian hepatologic centers, mostly affiliated with the "Club Epatologi Ospedalieri" (CLEO). Efficacy, defined as the ability of lusutrombopag to raise PLTs to ≥50,000/μL and avoid transfusions, as well as treatment-related adverse events, were recorded and analyzed.
**Results:** 73 patients were enrolled (Table 1). Twelve patients (16%) had a previous medical history of portal vein thrombosis. Chronic viral hepatitis was the most common cause of CLD (55%), and endoscopic band ligation (38%) was the most common procedure performed (27%). Lusutrombopag induced a significant increase in PLTs [from 37,000 (33,000-44,000/μL) to 58,000 (49,000-82,000), p<0.001]. The efficacy of lusotrombopag was 74%. Logistic regression analysis (Table 2) identified baseline platelet value as the only independent factor associated with the response (OR 1.13, CI 95% 1.04-1.26, p 0.01) and with an adequate discriminative ability (AUROC of 0.78). Notably, we identified the baseline PLTs ≤29,000/μL as the threshold for identifying patients unlikely to respond to the drug (sensitivity 91%). Finally, de novo portal vein thrombosis was observed in 4 patients (5%).
**Conclusion:** In this initial real-world European series of CLD, lusutrombopag demonstrated efficacy and safety consistent with findings from registrative trials. According to our results, patients with baseline platelets ≤29,000/μL are unlikely to respond to the drug.

doi: 10.1016/j.dld.2024.01.122

## F-18

### Mild overt hepatic encephalopathy (HE) - more than meets the eye

D. Erminelli [1], C. Mangini [1], L. Zarantonello [1], P. Angeli [1], S. Montagnese [1,2]

[1] *Department of Medicine, University of Padova, Padova, Italy*
[2] *Chronobiology Section, Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK*

**Introduction:** The diagnosis of covert/mild overt HE remains a matter of debate.
**Aim:** To assess the impact of a qualitative approach to clinical HE diagnosis and to describe the features of patients being diagnosed with covert HE on abnormalities in either the Psychometric Hepatic Encephalopathy Score (PHES) or the electroencephalogram (EEG).
**Methods:** 411 patients evaluated in our dedicated HE clinic (2009-2023) [71% males, 60±10 years, MELD=14.4±5.9] were included. Patients were qualified as unimpaired (clinically normal with both PHES and EEG normal), covert HE (clinically normal but PHES and/or EEG abnormal) or overt HE, based on the semi-quantitative modification of Conn's criteria (Vilstrup et al., J Hep 2014). Patients were also classified as having/not having overt HE based on qualitative clinical impression, prior to formal assessment.
**Results:** 137 (33%) patients were unimpaired, 174(42%) had covert HE and 100(25%) overt HE; on qualitative assessment, 122(30%) were qualified as having overt HE. 30% of the 100 patients with overt HE were missed and 17% unimpaired/covert HE were erroneously qualified as having overt HE. Across the HE spectrum, patients with an abnormal EEG were older (61.5±9.1 vs 58.1±10.3, p<0.001), had higher MELD (15.8±6.1 vs 12.8±5.2, p<0.001) and higher ammonia levels (76.2±43.6 vs 54.9±41.6μmol/l, p<0.001). Patients with an abnormal PHES score were older (60.8±9.3 vs 58.9±10.0, p<0.05), had lower educational attainment (9.0±3.3 vs 10.6±4.1 years, p<0.0001), had higher MELD (15.7±6.4 vs 13.4±5.3, p<0.001) and higher ammonia levels (70.9±48.1 vs 59.7±38.9 μmol/l, p<0.05). Amongst patients with covert HE diagnosed on one abnormal test only, those with abnormal PHES have lower educational attainment compared to those with abnormal EEG (8.2±3.1 vs 10.2±4.1 years, p<0.002).
**Conclusions:** Qualitative clinical evaluation of mild HE is unreliable. The EEG and PHES work well in this context, with both being affected by age and PHES also by educational attainment.

doi: 10.1016/j.dld.2024.01.123

## F-19

### Liver Frailty Index predicts poor outcomes in patients hospitalized for acute decompensation of cirrhosis

R. Gagliardi, S. Incicco, M. Tonon, V. Calvino, N. Zeni, C.G. Gambino, A. Accetta, V. Santori, P. Angeli, S. Piano

*Unit of Internal Medicine and Hepatology, Department of Medicine, University and Hospital of Padova, Padova, Italy*

**Background and aims:** Physical frailty is common in patients with cirrhosis and has been associated with poor outcomes. Liver Frailty Index (LFI) is a standardized tool to assess frailty in cirrhotic patients on liver transplant waiting list. However, there is a paucity of data on the prognostic value of LFI in patients hospitalized for acute decompensation (AD) of cirrhosis. We evaluated LFI in patients hospitalized for AD and its association with complications during hospitalization and 90-day survival.
**Patients and Methods:** Cirrhotic patients admitted for AD between 2019 and 2022 were enrolled. LFI was measured at the time of hospital admission and complications (hepatic encephalopathy [HE], sepsis, organ failures, ACLF) during hospitalization were recorded. Patients were followed up until death, liver transplant or 90 days.
**Results:** We enrolled 161 patients (mean age=64+10 years, male=71%, MELD-Na=20+7). The majority of patients had alcohol-related cirrhosis (57%). Median LFI was 6.1. LFI showed a weak, but significant, correlation with age ($r$=0.185; p=0.019), MELD-Na ($r$=0.218; p=0.006) and C-Reactive Protein ($r$=0.214; p=0.013).

LFI was significantly higher in patients developing HE, sepsis, organ failures and ACLF than in those who did not (Figure 1). Patients transferred to the ICU had significantly higher LFI than those who did not.

LFI was significantly higher in patients who died than in those who survived during hospitalization (median=6.54 vs 5.99; p<0.001) and at 90 days (6.51 vs 5.57; p<0.001). In multivariable analysis (adjusted for age, gender, MELD-Na, HE and infections), LFI was an independent risk factor of 90-day mortality (HR=2.18; p<0.001), along with MELD-Na (HR=1.11; p<0.001).
**Conclusions:** In patients with cirrhosis hospitalized for AD, LFI identifies those at higher risk of worse outcomes and can be used for assessing frailty in these patients.

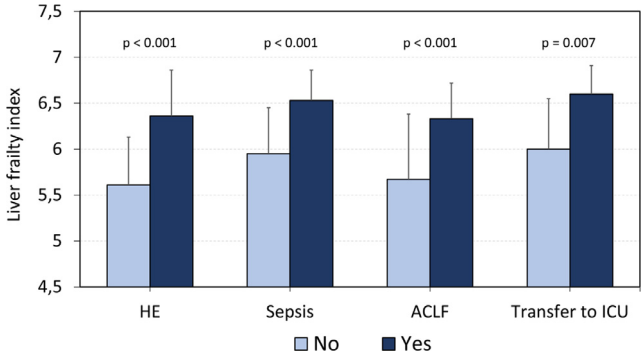



**Figure 1** Liver Frailty Index in patients developing or not complications during hospital stay.

doi: 10.1016/j.dld.2024.01.124

## F-20

### Placement of a trans-jugular intrahepatic portosystemic shunt (TIPS) modifies the expression of soluble mediators by circulating monocytes

M. Pastore [1], F. Vizzutti [1], D. Roccarina [1], N. Navari [1], B. Piombanti [1], M. Rosi [1], V. Adotti [1], M.P. Piccinni [1], L. Lombardelli [1], F. Logiodice [1], G. Bagni [1], A. Arcangeli [1], F. Fanelli [2], F. Marra [1]

[1] *Department of Experimental and Clinical Medicine, University of Florence, Italy*
[2] *Azienda Ospedaliero-Universitaria Careggi, Florence, Italy*

**Background/aims:** Decompensated cirrhosis is characterized by an imbalance in the innate immune system, leading to low-grade systemic inflammation. Inflammatory cytokines secreted by monocytes and macrophages have been implicated in the pathogenesis of portal hypertension and its complications. Trans- jugular intrahepatic portosystemic shunt (TIPS) is currently used for the treatment of complications of portal hypertension, but whether portosystemic derivation results in changes in the biology of inflammatory cell is currently unknown. Here we investigated the levels of different soluble factors in peripheral blood monocytes and plasma collected from different vascular districts, in a group of patients undergoing TIPS for a complication of cirrhosis.
**Method:** Fifteen patients with complications of portal hypertension referred to our Unit for TIPS placement were enrolled. During the TIPS procedure, blood from the portal (PV) and jugular veins (JV) was drawn, and at 4 weeks post-TIPS placement a sample from a peripheral vein was repeated. Monocytes were isolated from peripheral blood mononuclear cells by adherence to plastic after Ficoll-Hypaque purification and stimulated with LPS (1 µg/ml) for 8 and 24 hours. Gene expression was evaluated by Real-Time PCR. In a subset of patients, quantitative analysis of cytokines in plasma and conditioned medium of monocytes was performed using multiplex assay. Pro-angiogenic effects were evaluated by HUVEC cell migration assay and endothelial tube formation assay.
**Results:** In unstimulated conditions, gene expression of interlukin-1beta, interleukin-6 and interleukin-10 was significantly higher in monocytes collected from the PV that in those from either the JV pre-TIPS or the peripheral vein post-TIPS. In addition, LPS-mediated increase in mRNA for these cytokines was higher in monocytes collected in the PV. Similar changes were found when plasma- or monocyte-secreted cytokines at the protein level were analyzed in a subset of patients. These modifications were not a general feature of monocytes isolated from the PV, because basal and stimulated expression of interlukin-8, another cytokine, did not change comparing the different vascular districts. Release of vascular-endothelial growth factor (VEGF) by monocytes and in plasma was significant lower in the peripheral vein after TIPS than in portal vein pre-TIPS. Conditioned medium from monocytes collected in different districts was used in angiogenic assays. Medium from PV monocytes was significantly more effective in inducing endothelial cell migration or vascular tube formation, two indicators of angiogenesis.
**Conclusion:** In cirrhotic patients, monocyte expression of different cytokines involved in the regulation of the inflammatory response is in general higher in the portal circulation and tends to change after reduction of portal pressure by TIPS placement. Expression of VEGF is increased in the portal circulation and is associated with an increased proangiogenic effect in vitro.

doi: 10.1016/j.dld.2024.01.125

## F-21

### Assessment of sarcopenia and outcome with ultrasound-based measurements in patients with liver cirrhosis

V. Flagiello [1], P. Gallo [1], A. De Vincentis [2], F. Tavaglione [1], F. Terracciani [1], G. Di Pasquale [1], A. Picardi [1], U. Vespasiani Gentilucci [1]

[1] *Clinical Medicine and Hepatology Unit, Campus Bio-Medico University, Rome, Italy*
[2] *Internal Medicine Unit, Campus Bio-Medico University, Rome, Italy*

**Introduction:** Sarcopenia is a prevalent complication in individuals with chronic liver disease (CLD), typically diagnosed through operational definitions based on low muscle mass. Recently, muscle ultrasound-based measurements have garnered attention due to their enhanced feasibility; however, only a limited number of studies assessing this approach have been reported.
**Aim:** In a cohort of CLD patients, our objective was to validate ultrasound-derived measurements for assessing low muscle mass compared to bioelectrical impedance analysis (BIA) and to evaluate the correlation of these techniques with outcomes.
**Materials and Methods:** The study included consecutive adult outpatients attending our Hepato-Oncology Unit. Low muscle mass and strength were defined, following EWGSOP 2019 criteria, using BIA (Sergi's equation) and handgrip strength. Ultrasound was performed to measure muscle thickness and derive indices using different techniques.
**Results:** 88 patients were included (see Table 1). Logistic regression analysis (see Table 2) identified the average compression index (p 0.03), average feather index (p 0.002), and ultrasound psoas to height ratio (p 0.016) as significantly associated with low muscle mass defined by BIA. These indices exhibited adequate discriminative ability, with AUROCs of 0.71 (0.57-0.854), 0.81 (0.69-0.931), and 0.75 (0.63-0.862), respectively (see Figure 1). Additionally, Bland-Altman analysis indicated at least suboptimal agreement for all indices. Finally, Cox regression analyses identified the ileo-psoas index [HR 1.5(1.01-2.23), p 0.046], ultrasound psoas muscle index [HR 1.57(1.07-2.31), p 0.021], as well as low muscle strength [HR 1.82(1.18-2.79), p 0.006] as associated with a higher rate of mortality.
**Conclusions:** Our findings demonstrate a statistically significant association between certain ultrasonographic indices and low muscle mass defined by BIA, showcasing adequate discriminative ability and a valuable predictive role for outcomes. If these results are confirmed in larger external series, ultrasound could serve as a fea-

sible and cost-effective tool for assessing sarcopenia and predicting outcomes in CLD patients.

| | | |
|---|---|---|
| Average age (mean; SD) | 73 (±7) | |
| Average BMI (mean; SD) | 27 (±10) | |
| Sex [n (%)] | F= 19 (22) | |
| | M= 69 (78) | |
| Aetiology [n (%)] | Viral | 35 (40) |
| | Metabolic | 21 (24) |
| | Alcoholic | 10 (11) |
| | Alcoholic/Metabolic | 10 (11) |
| | Other causes | 12 (14) |
| Diabetes mellitus [n (%)] | Yes=45 (51) | |
| Active HCC [n (%)] | 54 (61) | |
| Child-Pugh [n (%)] | A= 70 (80) | |
| | B= 16 (18) | |
| | C= 2 (2) | |

Table 1

| Indices for sarcopenia evaluation | Odds Ratio (OR) (95% CI) p value |
|---|---|
| Average compression index | 0.43 (0.19, 0.87), 0.03 |
| Average feather index | 0.3 (0.13, 0.61), <0.002 |
| Ileo-Psoas index | 1.17 (0.6, 2.09), >0.614 |
| Ultrasound Psoas to height ratio | 0.35 (0.14, 0.77), 0.016 |
| Ultrasound Psoas muscle index | 1.08 (0.56, 1.91), 0.792 |
| Mean diaphragm excursion | 1.19 (0.64, 2.22), 0.581 |
| Diaphragm thickness expiration | 0.38 (0.02, 1.37), 0.497 |
| Diaphragm thickness inspiration | 0.04 (0, 0.82), 0.071 |
| Handgrip strength | 0.3 (0.12, 0.66), <0.006 |

Table 2

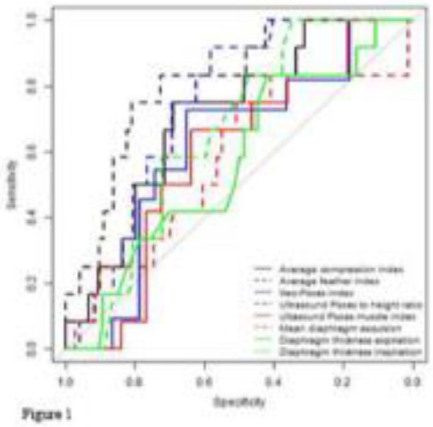


Figure 1

doi: 10.1016/j.dld.2024.01.126

## F-22

### Clinical predictors of liver and diabetes outcomes in cirrhotic patients with type 2 diabetes

C. Grisanti [1,2], C. Asero [1,2], A. Licata [3], G. Russo [2,3,4], A. Giandalia [2,3,4], C. Pitrone [1], R. Filomia [1], G. Caccamo [1], C. Saitta [1,2], R. Chianetta [3], A. Rizzo [3], R. Citarella [3], L. Giannitrapani [3], A.R. Caspanello [1,2], G. Raimondo [1,2], I. Cacciola [1,2]

[1] *Internal Medicine and Hepatology Unit; University Hospital of Messina*
[2] *Department of Clinical and Experimental Medicine, University of Messina, Italy*
[3] *Internal Medicine & Hepatology Unit, University Hospital of Palermo, PROMISE, University of Palermo, Italy*
[4] *Internal Medicine and Diabetology Unit*

**Background:** Type 2 Diabetes (T2D) and cirrhosis are chronic conditions often associated. Our aim was to assess clinical predictors of long-term liver- and diabetes-related outcomes in cirrhosis with T2D.
**Methods:** All T2D-cirrhotics attending the Liver Units of the University Hospitals of Messina and Palermo (Jan to Dec 2022), with 5 years follow-up at the time of evaluation, being Child-Pugh A class without hepatocarcinoma (HCC) were enrolled. Clinical and laboratory data, HCC onset, liver decompensation (LD) and T2D vascular complications were recorded at baseline and follow-up.
**Results:** One-hundred-fifty-five patients (54.2% men, age 73 years old), median follow-up of 108 months and median T2D duration of 180 months were enrolled. Diagnosis of liver cirrhosis was virus related in 62% of patients, metabolic related in 22%, alcohol-related in 5% and other etiologies in 11%. At last evaluation, 24,5% patients showed LD: 15% had ascites, 7% hepatic encephalopathy and 2% gastrointestinal bleeding; 13 (8,38) patients presented with LD and HCC, 12(7,74%) only HCC. Considering T2D complications, 39 patients (25%) developed only microvascular disease, 22(15%) only macrovascular complications and 37(24%) both. Stepwise regression model showed that LD was associated to higher liver stiffness values ($p = 0.009$) and alcohol intake ($p = 0.027$); HCC to male gender ($p = 0.018$), etiology of liver disease ($p = 0.039$), BMI ($p = 0.012$), cirrhosis ($p = 0.040$) and T2D duration ($p = 0.001$). Microvascular disease was associated to higher HbA1c($p = 0.015$) and creatinine values($p = 0.043$), hypoalbuminemia($p = 0.050$) and hypertension ($p = 0.047$); macrovascular disease was related to hypergammaglobulinemia ($p = 0.017$).
**Conclusions:** In our cohort liver disease progression was related to higher liver stiffness values, etiology of cirrhosis, T2D duration and BMI. T2D vascular complications were associated to higher HbA1c, hypergammaglobulin and creatinine values, hypertension, hypoalbuminemia. Metformin showed a protective role against microvascular disease.

doi: 10.1016/j.dld.2024.01.127

## F-23

### Safety and efficacy of direct oral anticoagulants in cirrhotic and non-cirrhotic patients with splanchnic vein thrombosis: preliminary results from sapient study

L. Giuli [1], R. Talerico [1], S. Betti [2], F. Bartolomei [2], A. Gasbarrini [1,3], V. De Stefano [2], R. Pola [1], E. Rossi [2], M. Pallozzi [1], B.E. Annicchiarico [1], M. Pompili [1], F.R. Ponziani [1,3], F. Santopaolo [1]

[1] *Department of Internal Medicine, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy*
[2] *Section of Hematology, Catholic University, Fondazione Policlinico "A. Gemelli" IRCCS, Rome, Italy*
[3] *Translational Medicine and Surgery Department, Catholic University, Rome, Italy*

**Introduction:** Splanchnic vein thrombosis (SVT) is a potentially life-threatening disease that can occur in cirrhotic and non-cirrhotic patients. Anticoagulation with heparins and vitamin K antagonists (VKA) is the mainstay of treatment. Recent studies have suggested that DOACs may offer a viable alternative in these set-

tings, however, data on the safety and efficacy of DOACs are still limited, especially in cirrhotic patients.
**Aim:** To prospectively define the incidence of recurrence thrombosis and bleeding events during therapy with DOACs in patients with diagnosed SVT.
**Materials and Methods Results:** We conducted a prospective, single-center, observational study. Consecutive cirrhotic and non-cirrhotic patients with either recent (< 6 months) or chronic SVT who started DOACs were enrolled between March to October 2023. At 1 and 3 month patients were evaluated for clinical manifestation of venous thromboembolism and bleeding. At 3 month a CT scan was performed to assess recurrence of SVT. Of the 39 patients enrolled (mean age 58, 53% males, 38% cirrhotic), 17 had a recent SVT (43.5%). Of the 22 patients with chronic SVT, 17 (77%) had a cavernous transformation. Among the 15 cirrhotic patients, 87% were Child A and 13% Child B. 21 patients (54%) started rivaroxaban,16 apixaban (41%) and 2 edoxaban (5%). All patients had a previous treatment with heparins or VKA. Cirrhotic patients had more frequently recent thrombosis (p=0,02), varices (P=0,0003) and previous episodes of variceal bleeding (P=0,002). Cirrhotic patients had lower mean level of platelets (p=0,0002) and higher mean level of bilirubin (P=0,01). No thrombotic or major bleeding events occurred at 3 month follow-up. Concerning recanalization, 22 patients (56,4%) presented stability and 17 regression of SVT. Regression of thrombosis was significantly more frequent in recent SVT (p=0,0009).
**Conclusions:** DOACs appears as a potential alternative to standard anticoagulation for the treatment of SVT in cirrhotic and non cirrhotic patients.

doi: 10.1016/j.dld.2024.01.128

## F-24

### Liver Transplant in ACLF and ALD: an effective option with limited access? Preliminary results of a single center experience

F. Ideo [1], C. Iegri [1], M. Vigano' [1], E. Farina [1], A. Merisio [2], G. Carioli [3], M.G. Luca' [1], L. Pasulo [1], M. Triolo [1], F. Leonardi [1], F. Poggi [1], D. Pinelli [4], F. Neri [4], M. Colledan [4], S. Fagiuoli [1]

[1] *Gastroenterology Hepatology and Transplantation Unit, ASST Papa Giovanni XXIII, Bergamo, Italy*
[2] *Department of Clinical Psychology, ASST Papa Giovanni XXIII, Bergamo, Italy*
[3] *FROM Research Foudation, ASST Papa Giovanni XXIII, Bergamo, Italy*
[4] *Department of Organ Failure and Transplantation, ASST Papa Giovanni XXIII, Bergamo, Italy*

**Background:** OLT is an effective option in ACLF, AH and sAH. However, is still unclear how many patients with a potential indication, can eventually access this option.
**Aims:** to evaluate the real access rate of waitlisting for liver transplant and the rate of recurrence of alcohol use disorder (AUD) after OLT in pts with ACLF and ALD.
**Materials and methods:** We retrospectively analyzed 62 patients with ACLF and ALD admitted at our center from Jan16 to Jan23. The following scores were used to assess patient status at baseline and during fup: MELD-Na, Maddrey DF, GAHS, ABIC, Lille, Child-Pugh, CLIF-ACLF, CLIF-SOFA. Alcohol relapse after OLT was defined by the presence of signs/biochemical alterations associated with heavy alcohol use.
**Results:** The clinical characteristics of the population are summarized in Table 1. 57 pts (92%) were potentially transplantable for age. 19 pts (31.6 %) were waitlisted or experienced a change in UNOS priority after the development of ACLF. 3 patients (4.8%) were already waitlisted maintaining an unmodified UNOS status after ACLF development.40 pts (66.6%) were never waitlisted: the most common reasons for ineligibility are shown in Table 2. Overall 20 pts were transplanted. Among them, the prevalence of AUD was relevant (7 pts-35%). During follow-up, 6 recipients (30%) experienced alcohol misuse after a median time of 1019 d [410-1564 d]; 2 pts (10%) developed ALD and died of liver failure.
**Conclusions:** OLT represents an effective option in pts with ACLF and ALD. However, the access to waitlist is very limited mostly because of multiple active substances abuse and inadequate psychosocial profile. The recurrence of alcohol abuse was more frequent in pts without AUD at admission. The involvement of addiction center specialists in post-LT follow-up might be enforced as a potentially protective action against alcohol abuse.

| | Total (n=40) |
|---|---|
| Age – n (%) | 5 (12.5) |
| Active abuse – n (%) | 13 (33%) |
| Comorbidity profile – n (%) | 6 (15) |
| Non-treatable infections – n (%) | 3 (7) |
| Inadequate psychosocial profile – n (%) | 10 (25) |
| Cancer diagnosis up to 5y prior – n (%) | 1 (2.5) |
| Surgical contraindications – n (%) | 1 (2.5) |
| Global frailty – n (%) | 1 (2.5) |

doi: 10.1016/j.dld.2024.01.129

## F-25

### Impact of acute on chronic liver failure (aclf) superimposed to alcoholic cirrhosis: a single centre experience

F. Ideo [1], C. Iegri [1], E. Farina [1], M Vigano' [1], G. Carioli [2], M.G. Luca' [1], L. Pasulo [1], M. Triolo [1], F. Leonardi [1], A. Loglio [1], D. Pinelli [3], M. Colledan [3], S. Fagiuoli [1,4]

[1] *Gastroenterology Hepatology and Transplantation Unit, ASST Papa Giovanni XXIII, Bergamo, Italy*
[2] *FROM Research Foundation, ASST Papa Giovanni XXIII, Bergamo, Italy*
[3] *Department of Organ Failure and Transplantation, ASST Papa Giovanni XXIII, Italy*
[4] *Gastroenterology, Department of Medicine, University of Milan Bicocca, Milan, Italy*

**Background:** Patients with ACLF superimposed to alcoholic cirrhosis (AC) represent a peculiar subpopulation characterized by hampered access to OLT, potentially risk of graft failure due to alcohol use relapse and increased susceptibility to infections. Aims: To assess the evolution of ACLF superimposed to alcoholic cirrhosis (AC), need for critical care, transplantation and survival rates.
**Materials and methods:** The clinical data of 62 patients with ACLF and AC admitted at our center from Jan16 to Jan23, were retrospectively analyzed. The following scores were adopted to assess patient status: MELD-Na, Maddrey DF, GAHS, ABIC, Lille, Child-Pugh, CLIF-ACLF, CLIF-SOFA. Patient's eligibility for transplantation were routinely evaluated by a multidisciplinary team.
**Results:** the clinical characteristics of the population are summarized in **Table 1**. The majority of patient (54 - 87%) presented with an identifiable trigger, with bacterial infections being the most common, followed by acute alcoholic hepatitis. 6 pts (9.6%) presented with both infection and AH. ACLF grades at presentations were: 34% ACLF-1, 37% ACLF-2, 29% ACLF-3.29 pts (47%) showed a rapid and positive response to the first line treatment, while 14

(23%) remained stable and 19 (30%) worsened. 20 pts (32%) were admitted at ICU/HDCU with the following median scores: CLIF-ACLF score 61 [52-65]; CLIF-SOFA 13 [IQR 12-14]; Meld 29 [26-35]. Seven pts (37%) needed continuous renal replacement therapy (RRT); 14 pts (74%) needed major vasopressor support; 10 patients underwent orotracheal intubation (OI) both for lung failure (7 pts-37%) or severe HE (3 pts-15%).20 patients (32%) were transplanted, with the following condition severity at the time of OLT: 33% no ACLF, 6% ACLF-1, 28% ACLF-2, 33% ACLF-3. 29 patients died during follow-up (47%), 7 of which after OLT (35%). No deaths were observed in waitlisted patients while 2 recipients (10%) died in the immediate post-operative period. OLT-free survival at 1 year was very poor (20%), while overall survival (OS) at 1 and 5 years in transplanted patients was 90% and close to 60%.

**Conclusions:** OLT represents an effective therapeutic option in patients with ACLF and alcoholic cirrhosis, with most patients showing an improvement in survival after OLT despite the severity of the condition at the time of transplantation. However, OLT is not a viable option in most of such patients due to the presence of severe psychosocial contraindications, frequently associated with AUD.

| | Total (62) |
|---|---|
| Age – median (IQR) | 55 (48.0–64.0) |
| Male – n (%) | 50 (81) |
| Viral hepatitis – n (%) | 15 (24) |
| Cardiovascular comorbidities - n (%): | 25 (40) |
| Obesity - n (%) | 12 (23) |
| Psychiatric comorbidities - n (%) | 13 (21) |
| Active smoking - n (%) | 24 (39) |
| Drug abuse history - n (%) | 11 (18) |
| AUD - n (%) | 34 (55) |
| Alcohol abuse duration (years) – median (IQR) | 24 (16.5-30.0) |
| Alcohol intake (units/day) – median (IQR) | 8.0 (5.0–15.0) |
| Active HCC – n (%) | 3 (5) |
| Acute alcoholic hepatitis – n (%) | 24 (39) |
| Severe acute alcoholic hepatitis (if AH) – n (%) | 21 (88) |
| Maddrey score – median (IQR) | 67.7 (39.9–94.4) |
| ABIC score – median (IQR) | 8.6 (7.2–10.2) |
| Child-Pugh score – median (IQR) | 11.0 (10.0–12.0) |
| MELD score - median (IQR) | 29.0 (25.0-34.0) |
| CLIF-ACLF score – median (IQR) | 50.0 (40.0-58.0) |
| CLIF-SOFA score – median (IQR) | 10.0 (9.0-12.0) |
| ACLF grade – n (%)<br>- ACLF-1<br>- ACLF-2<br>- ACLF-3 | <br>21(34)<br>23(37)<br>18 (29) |

doi: 10.1016/j.dld.2024.01.130

## F-26

### Role of P-shear wave hepatic elastography in prediction of high-risk varices in patients affected by compensated advanced chronic liver disease

N. Reggidori, M.L. Lazzari, F. Conti, F.G. Foschi

*Department of Internal Medicine, Ospedale di Faenza, Faenza, Italy*

**Introduction:** Liver cirrhosis is frequently complicated by clinically significant portal hypertension (CSPH) and esophageal varices (EV). Screening and treatment of EV is crucial for preventing variceal bleeding and was usually done through upper endoscopy. Baveno VI consensus recommended levels of liver stiffness (measured by Fibroscan) and platelets that could exclude CSPH, avoiding endoscopy. Reliability of liver stiffness measurement (LSM) by Shear-wave elastography (SWE) in this setting is still a matter of debate.
**Aim:** To evaluate the correlation between LSM (measured by SWE) and the presence of high-risk varices (HrV). To confirm the efficacy of Baveno VI criteria in excluding HrV even when LSM was obtained by SWE.
**Material and Methods Results:** We retrospectively analyzed 86 patients with compensated advanced chronic liver disease with an available upper endoscopy and a LSM by SWE within 12 months. Liver stiffness was calculated by using the ElastPQ software on Philips iU22 ultrasound machine. Patients with already-treated varices, portal vein thrombosis, splenectomy or HCC were excluded. High-risk varices were present in 13 (15,1%) of patients. Multivariate analysis identified platelet levels below $150 \times 10^9$/l and LSM as predictors of HrV; Youden test predicted a SWE $<$ 14 kPa as best cut-off for ruling-out high-risk varices. The copresence of platelets above $150 \times 10^9$/l and SWE $<$ 14 kPa (BAVENO-ElastPQ) identified a subset of patients (26, 30.2%) without HrV with sensitivity of 100%.
**Conclusions:** In patients with compensated advanced chronic liver disease, platelets above $150 \times 10^9$/l and LSM (calculated with SWE) $<$ 14 kPa could identify a subset of patients at very low probability of having HrV in whom upper endoscopy may be safely avoided.

doi: 10.1016/j.dld.2024.01.131

## F-27

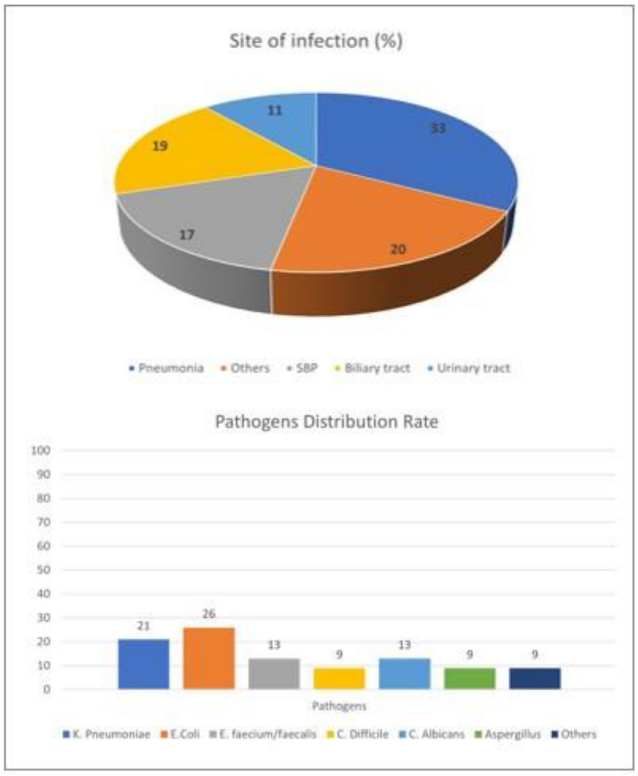
### Bacterial and Fungal Infections in ACLF: prevalence and impact on patient morbidity and mortality

C. Iegri [1], F. Ideo [1], A. Tebaldi [2], M. Vigano' [1], E. Farina [1], G. Carioli [3], M.G. Luca' [1], L. Pasulo [1], M. Triolo [1], F. Leonardi [1], A. Mangia [1], D. Pinelli [4], S. Camagni [4], A. Amaduzzi [4], M. Colledan [4], S. Fagiuoli [1,5]

[1] *Gastroenterology Hepatology and Transplantation Unit, ASST Papa Giovanni XXIII, Bergamo*
[2] *Department of Infectious Disease, ASST Papa Giovanni XXIII, Bergamo*
[3] *Bergamo Hospital Research Foundation (FROM), ASST Papa Giovanni XXIII*
[4] *Department of Organ Failure and Transplantation, ASST Papa Giovanni XXIII*
[5] *Gastroenterology, Department of Medicine, University of Milan Bicocca, Milan*

**Background:** In pts with ALD and ACLF a clear characterization of bacterial (BI) and fungal infections (FI) and their impact on survival is still lacking.
**Aims:** to define prevalence and characteristics of BI/FI and their influence on survival and liver transplant need in a population with ACLF and alcoholic cirrhosis(AC).
**Materials and methods:** 62 pts with ACLF and AC were consecutively admitted at our center from Jan 2016 to Jan 2023. Data on BI and FI were recorded at diagnosis and during hospitalization.
**Results:** 36 patients at admission (58% of the whole population) presented with FI (5-13.9%) or BI (31- 86.1%). In 6 cases (16.6%) infections coexisted with AH. The distribution of the infection site and identified pathogens is shown in **Figure 1**. FI were severe, with 2 cases of Aspergillus pneumonia and 3 invasive Candidiasis. Also pts with a suspicious BI were treated. Piperacillina/tazobactam was the most frequent first-line empirical treatment (31 pts -56.5%).A switch to targeted therapy was necessary in 18 pts (58%);antifungal therapy was always targeted. A severe ACLF (grade II or III) was more frequent in infected patients (group A) compared to the others (group B - 72% vs 50%; p=0.07). At OLT, 8 (61.5%) among gA had an ACLF grade 2 or 3 (vs 3- 42.8% gB; p = 0.42).29 pts (46.7%) died, 20 in gA (55.6%) and 9 in gB (34.6%; p=0.10; OR gA/gB 2.36).

The OLT free survival was 48 days in gA vs 56 days in gB; p=0.20. None of the pts with MDRO/FIs before transplant had a recurrence of the same pathogen after OLT.
**Conclusions:** our study suggests the tendency to a worse outcome in infected patients. The prevalence of combined MDRO plus FI was high (30.5%). Among the recipients with MDRO/fungal before surgery, none showed a recurrence of the same pathogens.




doi: 10.1016/j.dld.2024.01.132

## F-28

### Performance evaluation of hepatic venous pressure gradient (HVPG) score as predictor tool of liver-related events in patients with advanced chronic liver disease

M. Capasso, M.R. Attanasio, V. Cossiga, F.M. Cutolo, F. Mazzitelli, A. De Conte, M. Guarino, F. Morisco

*Department of Clinical Medicine and Surgery, Diseases of the Liver and Biliary System Unit, University of Naples "Federico II", Naples, Italy*

**Background and Aim:** Clinically significant portal hypertension (CSPH) in patients with advanced chronic liver disease (ACLD) is associated with increasing risk of liver-related events (LRE). Several scores have been developed as non-invasive tests to assess portal hypertension (PH); the novel hepatic venous pressure gradient (HVPG) score showed good sensibility in CSPH prediction. The aim is to evaluate the ability of HVPG-score in predicting PH and LRE in a cohort of ACLD patients.
**Methods:** A retrospective study was conducted at the University of Naples "Federico II". All patients, referred from 2012 to 2022, with compensated ACLD who underwent esophagogastroduodenoscopy (EGD) for portal hypertension assessment were enrolled. Exclusion criteria were patients <18 years-old, liver transplantation, HCC patients, NSBB treatment, PVT. During the follow-up, any LRE (decompensation, HCC and death) was registered.
**Results:** Overall, 156 ACLD subjects were recruited (57.7% males, mean age 62 yrs). Nearly all patients (93%) were Child-Pugh A and mean liver stiffness (LSM) was 23.3kPa (IQR 14-29). Seventy-six patients (48.7%) showed endoscopic signs of PH and have higher LSM (27±13.7 vs 20.1±10.1kPa, p=0.0007), HVPG-score (14.54±1.44 vs 12.53±2.18mmHg, p <0.001), and spleen diameter (157.8±31.8 versus 129.2±20.7mm, p<0.0001) than patients without signs of PH, while platelets ($86*10^3$/cc vs $139*10^3$/cc, p<0.0001) and platelets/spleen diameter ratio (590.5±316.5 vs 1130.3±604.1, p<0.0001) were lower. The median follow-up was 47 months; patients with endoscopic signs of PH had higher incidence of LRE than those without (p=0.0002). The cumulative-incidence-rate of the first LRE was 46.7% (73 events) and showed a positive correlation with HVPG-score (Pearson-coefficient r=0.3). Moreover, HVPG-score was significantly higher in patients who experienced more than one decompensation event (14.9±0.9 vs. 13.5±1.6, p<0.0001).
**Conclusions:** HVPG-score is a simple tool for non-invasive prediction of PH and could be used to stratify the risk of LRE in ACLD patients, but it needs to be validated in larger cohorts

doi: 10.1016/j.dld.2024.01.133

## F-29

### Material deprivation is associated with liver stiffness measurement and liver-related events in people with HIV

F. Cinque [1,2], C. Long [1,2], D. Kablawi [1,2], D.H. Kim [1,2], T.F. Tadjo [1,2], W. Elgretli [3], L.R. Ballesteros [1,2], A. Lupu [1,2], M. Nudo [1,2], B. Lebouchel [2], N. Kronfli [2], J. Cox [2,4], C. Costiniuk [2], A. De Pokomandy [2], J.P. Routy [2], M. Klein [2,4], F. Lamonde [5], R. Agnihotram [5], S. Saeed [6], G. Sebastiani [1,2,4]

[1] *Division of Gastroenterology and Hepatology, McGill University Health Centre, Montreal, Canada*
[2] *Chronic Viral Illness Service, Division of Infectious Diseases, Department of Medicine, McGill University Health Centre, Montreal, Canada*
[3] *Division of Experimental Medicine, McGill University, Montreal, Canada*
[4] *Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Canada*
[5] *Research Institute, McGill University Health Centre, Montreal, Canada*
[6] *Department of Public Health Sciences, Queens University, Kingston, Canada*

**Introduction:** Socioeconomic status drives health disparities in people with HIV (PWH). The effect of material deprivation on hepatic outcomes in PWH has not been assessed.
**Aim:** to evaluate the association between material deprivation and liver fibrosis, metabolic dysfunction-associated steatotic liver disease (MASLD) and clinical outcomes in PWH.
**Methods:** We included consecutive PWH from the LIVEr disease in HIV (LIVEHIV) cohort with available Fibroscan. MASLD was defined as presence of hepatic steatosis by controlled attenuation parameter (CAP)>248 dB/m and at least one metabolic abnormality. Significant liver fibrosis was defined as liver stiffness measurement (LSM)>8. Socioeconomic status was assessed by the Pamplon Material Deprivation Index (MDI). PWH with MDI quintiles 4 and 5 were classified as "deprived" while PWH with MDI quintiles 1 and 2 as "privileged". Multivariable linear regression analysis investigated associations of MDI with LSM and CAP. Incidence of liver outcomes (ascites, variceal bleeding, hepatic encephalopathy, hepatocellular carcinoma, liver transplantation), extrahepatic outcomes (cancer, cardiovascular disease) and overall mortality were evaluated through survival analysis.

**Results:** Among the 768 PWH included (median age 54 years, 76% male, 25% HBV coinfected, 10% HCV coinfected, 23% with significant liver fibrosis and 33% with MASLD), 40% were materially privileged while 47% were materially deprived. At baseline, materially deprived PWH were more frequently female and of Black ethnicity and had higher prevalence of metabolic comorbidities. After adjustments, material deprivation was associated with increased LSM at baseline ($\beta$=1.858, 95% CI 0.53-3.17; p=0.006) but not with CAP ($\beta$=6.469, 95% CI -5.55-18.49; p=0.291). During a median follow-up of 3.8 years incidence of liver-related events was higher in PWH materially deprived compared to PWH materially privileged (Figure), while there was no difference in extrahepatic events or overall mortality.
**Conclusions:** Material deprivation, reflecting socioeconomic status, is associated with liver fibrosis and liver-related events in PWH. Future strategies should assess whether improved material security improves liver outcomes.

doi: 10.1016/j.dld.2024.01.134

## F-30

### Emerging metabolic and alcoholic etiologies in liver cirrhosis are related to high rate of recurrence after first episode of decompensation

C. Masetti [1], S. De Nicola [1], N. Pugliese [1,2], F. Colapietro [1,2], R. Ceriani [1], I. Bianchi [1], M. Ormas [1], A. Lleo [1,2], A. Aghemo [1,2]

[1] *Division of Internal Medicine and Hepatology, Department of Gastroenterology, Humanitas Research Hospital IRCCS, Milan, Italy*
[2] *Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy*

**Introduction:** First decompensation event in patients with cirrhosis is associated with worse clinical outcomes and requires prompt referral to transplantation. Little is known about impact of etiology of liver disease in type of decompensation, survival and occurrence of further events.
**Material and methods:** We consecutively analyzed data from patients admitted to ER from January 2019 to December 2022 for the first episode of decompensation, defined as ascites, hepatic encephalopathy, jaundice and upper digestive bleeding. Patients with previous or active HCC were excluded. We collected baseline features and survival rates, occurrence of further decompensation, transplantation and TIPS placement rates during follow-up.
**Results:** We included 105 patients, 70 males (66.6%), with median age of 65 years (range 35-94). Among them 65 (61.9%) were unaware of underlying liver disease. The majority of patients (58, 55.2%) had alcoholic liver disease (ALD), followed by metabolic (17, 16%) and viral etiologies (11, 10%). Ascites was the most frequent event (60.9%), followed by jaundice (19%) and digestive bleeding (14.3%). Median survival was 17 months. After first decompensation only 32 patients (30%) didn't experience further liver events, 7 (6.6%) underwent liver transplantation and in 5 patients (4.7%) TIPS was placed. 53 patients died during the follow-up period. A lower rate of further decompensation, even if not statistically significant, was observed in ALD (45%) when compared to other etiologies (79% in metabolic liver disease, p=0.36).
**Conclusions:** During last decades, active control of viral infections has deeply changed natural history of cirrhosis, with alcohol and metabolic disease progressively emerging as major causes of liver disease. Impressively, in our cohort, more than half of patients were unaware of their condition. First decompensation still significantly impacts on survival: therefore, more efforts are needed to increase specialist referral to improve early diagnosis and prevent decompensation.

doi: 10.1016/j.dld.2024.01.135

## F-31

### Emerging role of Spleen Stiffness Measurement in prediction of clinically significant portal hypertension: a single center experience

M. Capasso, S. Albano, F. Mazzitelli, F. Capozzi, L. Ranieri, A. Rutigliano, M. Guarino, V. Cossiga, F. Morisco

*Department of Clinical Medicine and Surgery, Diseases of the Liver and Biliary System Unit, University of Naples "Federico II", Naples, Italy*

**Background and Aim:** According to Baveno-VII, non-invasive-based criteria are useful to rule in or out clinically significant portal hypertension (CSPH). LSM≥25 kPa is highly predictive for CSPH, while LSM≤15kPa plus PLT $\geq 150^{*}10^{9}$/L exclude CSPH. Spleen Stiffness Measurement (SSM)<40kPa could identify patients with low probability of CSPH. The study aims to explore the utility of SSM in predicting CSPH and its added value compared to LSM and PLT.
**Methods:** All retrospective ACLD patients, referred to University of Naples "Federico II", with at least LSM≥10kPa who underwent esophagogastroduodenoscopy for PH assessment and SSM were enrolled. Exclusion criteria were PLT>$150^{*}10^{9}$/L, liver transplantation, HCC and PVT. The population was divided in: group A includes patients with LSM≥25kPa, group B LSM≥15 and <25kPa and group C LSM≥10 and <15kPa.
**Results:** Sixty-nine patients (41 male, mean age 62.7±14.8yrs) were recruited. The main etiology was virus-related (30 patients, 43.4%) followed by metabolic (13 patients, 18.8%) and alcoholic (12 patients, 17.4%). Most of patients (n=55, 79.7%) were Child A. Mean LSM and SSM was 24.7±12.9kPa and 59.8±23.5kPa. The groups were composed by 25 (A), 27 (B) and 17 (C) patients. Eighteen out of 25 patients (69.2%) of group A had endoscopic signs of PH and almost all of them (17/18, 94.4%) had SSM≥40kPa. Although in group B a lower rate of endoscopic signs of PH was found (14/27, 51.8%), SSM>40kPa identified all these patients showing higher accuracy (100%). Finally, in group C, in which according to Baveno-VII pre-test probability of CSPH is low, 5/17 (29.4%) had endoscopic signs of PH and, among them 60% (3/5) had SSM≥40kPa. Indeed, SSM demonstrated a better positive correlation with endoscopic signs of PH (Pearson coefficient r=0.4) then LSM (r=0.3).
**Conclusion:** SSM has a higher diagnostic performance then LSM and PLT assessment in predicting CSPH in patients with ACLD, improving the algorithm proposed by Baveno-VII

doi: 10.1016/j.dld.2024.01.136

## F-32

### Characteristics and outcomes of immunotherapy-related liver injury in patients with hepatocellular carcinoma compared to patients with advanced solid tumours

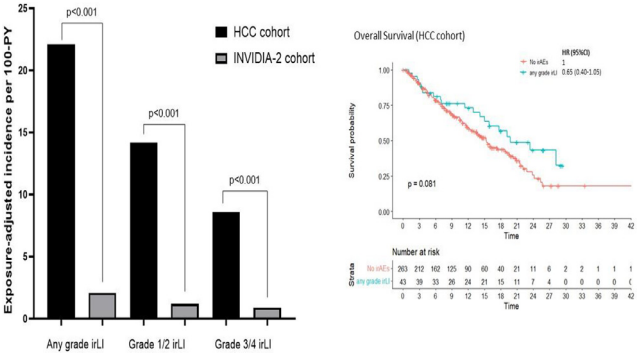
C. Celsa [1,2], G. Cabibbo [1], C. AM Fulgenzi [2,3], B. Scheiner [2,4], A. d'Alessio [2,5], G. F Manfredi [2,5], N. Nishida [6], C. Ang [7], T.U. Marron [7], A. Saeed [8], B. Wietharn [8], M. Pinter [4], J. Cheon [9], Yi-Hsiang Huang [10], Pei-Chang Lee [11], S. Phen [12], A. Gampa [13], A. Pillai [13], C. Vivaldi [14], F. Salani [14,15], G. Masi [14], N. Roehlen [16], R. Thimme [16], A. Vogel [17], M. Schönlein [18], J. von Felden [19], K. Schulze [19], H. Wege [19], P.R. Galle [20], M. Kudo [6], L. Rimassa [21,22], A.G. Singal [12], P. El Tomb [23], S. Ulahannan [23], A. Parisi [24], H. Jae Chon [9], Wei-Fan Hsu [25],

B. Stefanini [2,26], E. Verzoni [27], R. Giusti [28], A. Veccia [29], A. Catino [30], G. Aprile [31], P.F. Guglielmini [32], M. Di Napoli [33], P. Ermacora [34], L. Antonuzzo [35], E. Rossi [36], F. Verderame [37], F. Zustovich [38], C. Ficorella [39], F.R. Di Pietro [40], N. Battelli [41], G. Negrini [42], F. Grossi [43], R. Bordonaro [44], S. Pipitone [45], M. Banzi [46], S. Ricciardi [47], L. Laera [48], A. Russo [49], U. De Giorgi [50], L. Cavanna [51], M. Sorarù [52], V. Montesarchio [53], P. Bordi [54], L. Brunetti [3], C. Pinto [46], M. Bersanelli [54], A. Cortellini [2,3], C. Cammà [1], D.J. Pinato [2,5]

[1] *Gastroenterology and Hepatology Unit, Department of Health Promotion, Mother & Child Care, Internal Medicine & Medical Specialties, University of Palermo, Italy*
[2] *Department of Surgery & Cancer, Imperial College London, Hammersmith Hospital, Du Cane Road, W120HS, London, UK*
[3] *Operative Research Unit of Oncology, Fondazione Policlinico Universitario Campus Bio-Medico, Via Alvaro del Portillo, 200 - 00128, Roma, Italy*
[4] *Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria*
[5] *Division of Oncology, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy*
[6] *Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan*
[7] *Department of Medicine, Division of Hematology/Oncology, Tisch Cancer Institute, Mount Sinai Hospital, New York, NY, USA*
[8] *Department of Medicine, Division of Medical Oncology, Kansas University Cancer Center, Kansas City, Kansas, USA*
[9] *Medical Oncology, Department of Internal Medicine, CHA Bundang Medical Center, CHA University, Seongnam, Korea*
[10] *Healthcare and Services Center, Taipei Veterans General Hospital, Taipei, Taiwan; Division of Gastroenterology and Hepatology, Taipei Veterans General Hospital, Taipei, Taiwan; Institute of Clinical Medicine, Faculty of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[11] *Division of Gastroenterology and Hepatology, Taipei Veterans General Hospital, Taipei, Taiwan; Faculty of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan*
[12] *Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA*
[13] *Section of Gastroenterology, Hepatology & Nutrition, the University of Chicago Medicine 5841 S. Maryland Ave, 60637 Chicago, IL, USA*
[14] *Unit of Medical Oncology 2, Azienda Ospedaliero- Universitaria Pisana, Pisa, Italy*
[15] *Scuola Superiore Sant'Anna Pisa, interdisciplinary research center "Health Science", Pisa, Italy*
[16] *Department of Medicine II (Gastroenterology, Hepatology, Endocrinology and Infectious Diseases), Freiburg University Medical Center, Faculty of Medicine, University of Freiburg, Freiburg, Germany*
[17] *Hannover Medical School, Hannover, Germany*
[18] *Department of Oncology, Hematology and Bone Marrow Transplantation with Section of Pneumology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*
[19] *Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*
[20] *University Medical Center Mainz, Department of Internal Medicine I, Mainz, Germany*
[21] *Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20072 Pieve Emanuele, Milan, Italy*
[22] *Medical Oncology and Hematology Unit, Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Via Manzoni 56, 20089, Rozzano, Milan, Italy*
[23] *Medical Oncology/TSET Phase 1 Program, Stephenson Cancer Center, University of Oklahoma, Oklahoma City*
[24] *Department of Oncology, Università Politecnica delle Marche, Azienda Ospedaliero-Universitaria delle Marche, 60126, Ancona, Italy*
[25] *Center for Digestive Medicine, Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan*
[26] *Department of Medical and Surgical Sciences, University of Bologna*
[27] *SS. Oncologia Genitourinaria, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy*
[28] *Medical Oncology Unit, Sant'Andrea Hospital, Roma, Italy*
[29] *Medical Oncology, Santa Chiara Hospital, Trento, Italy*
[30] *Medical Thoracic Oncology Unit, IRCCS Istituto Tumori "Giovanni Paolo II", Bari, Italy*
[31] *Department of Oncology, San Bortolo General Hospital, Vicenza, Italy*
[32] *SC Oncologia, AO SS Antonio e Biagio e C. Arrigo, Alessandria, Italy*
[33] *UC Oncologia Medica Uro-Ginecologica, Istituto Nazionale Tumori "Fondazione G. Pascale", IRCCS, Napoli, Italy*
[34] *Dipartimento di Oncologia, Presidio Ospedaliero Universitario Santa Maria della Misericordia, Azienda sanitaria universitaria integrata Friuli Centrale, Udine, Italy*
[35] *Medical Oncology Unit, University Hospital Careggi, Firenze, Italy*
[36] *Medical Oncology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy*
[37] *Oncology Department, Ospedali Riuniti Villa Sofia Cervello, Palermo, Italy*
[38] *UOC Oncologia di Belluno, Dipartimento di Oncologia Clinica, AULSS 1 Dolomiti, Ospedale S.Martino, Belluno, Italy*
[39] *Department of Biotechnological and Applied Clinical Sciences, St Salvatore Hospital, University of L'Aquila, L'Aquila, Italy*
[40] *U.O.C. Oncologia, Istituto Dermopatico dell'Immacolata IDI-IRCCS, Roma, Italy*
[41] *UOC Oncologia, Ospedale Generale Provinciale di Macerata, ASUR Marche Area Vasta 3, Macerata, Italy*
[42] *Medical Oncology Unit, Papa Giovanni XXIII Hospital, Bergamo, Italy*
[43] *Medical Oncology Department, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[44] *Medical Oncology Unit, ARNAS Garibaldi, Catania, Italy*
[45] *Medical Oncology Unit, University Hospital of Modena e Reggio Emilia, Italy*
[46] *Medical Oncology Unit, AUSL-IRCCS of Reggio Emilia, Reggio Emilia, Italy*
[47] *Medical Oncology, San Camillo Forlanini Hospital, Roma, Italy*
[48] *Medical Oncology, Ospedale Generale Regionale F Miulli, Acquaviva delle Fonti, Puglia, Italy*
[49] *Dipartimento di Discipline Chirurgiche, Oncologiche e Stomatologiche, Università degli Studi di Palermo, Palermo, Italy*
[50] *Department of Medical Oncology, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy*
[51] *Oncologia Medica, ASL di Piacenza, Piacenza, Italy*
[52] *Medical Oncology, Camposampiero Hospital, AULSS 6 Euganea, Padova, Italy*
[53] *UOC Oncologia, Ospedale Monaldi, Azienda Ospedaliera Specialistica dei Colli, Napoli, Italy*
[54] *Medical Oncology Unit, Medicine and Surgery Department, University of Parma, Parma, Italy*

**Introduction:** Immune-related liver injury (irLI) is commonly observed in patients with cancer treated with immune checkpoint inhibitors (ICIs). In this comparative study, we aimed to compare incidence, clinical characteristics and outcomes of irLI between patients receiving ICIs for HCC versus other solid tumour indications. **Materials and Methods:** Two separate cohorts were included: 375 patients with advanced/unresectable HCC, Child-Pugh A class treated with first-line Atezolizumab+Bevacizumab from AB-real study and a non-HCC cohort, including 459 patients treated with first-line ICI therapy from INVIDIa-2 multicentre study. IrLI was defined as treatmentâ€ related increase of transaminases levels after exclusion of alternative aetiologies of liver injury. Incidence of irLI was adjusted for the duration of treatment exposure.

**Results:** In HCC patients, incidence of any-grade irLI was 11.4% over a median treatment exposure of 4.4 months (95%CI 3.7-5.2), compared to 2.6% in INVIDIa-2 cohort over a median treatment exposure of 12.4 months(95%CI 11.1-14.0). Exposure-adjusted incidence of any-grade irLI was 22.1 per 100-Patient-years (PY) in HCC patients and 2.1 per 100-PY in non-HCC patients (p<0.001), with median time-to-irLI of 1.4 in HCC and 4.7 months in non-HCC patients, respectively. Among patients who developed irLI, systemic corticosteroids were administered in 16.3% of HCC and in 75.0% of non-HCC patients (p<0.001) and irLI resolution was observed in 72.1% and 58.3%, respectively (p=0.362). In HCC patients, rates of hepatic decompensation and treatment discontinuation due to irLI were 7%. In both cohorts, no fatal irLI events occurred. Development of grade 1-2 irLI was associated with improved overall survival in HCC patients only (HR 0.53, 95%CI 0.29-0.96).
**Conclusions:** Despite higher incidence and earlier onset in patients with HCC, IrLI is characterised by high rates of remission, low requirement for corticosteroid therapy and low risk of decompensation compared to other solid tumours. Hepatotoxicity leads to discontinuation in 7% of patients with HCC and does not negatively affect oncological outcomes.




doi: 10.1016/j.dld.2024.01.137

## F-33

### Can AtezoBev be a safe and effective option for treating hepatocellular carcinoma in patients with Child-Pugh B cirrhosis? A retrospective multicenter real-world study

L. Stella [1,2,*], M. Pallozzi [1,*], L. Cerrito [1], A. Gasbarrini [1,2], M. Pompili [1,2], F. Marra [3], C. Campani [3], E. Pellegrini [4], F. Piscaglia [5], F. Tovoli [5], C. Hollande [6], S. Sidali [6], M. Bouattour [6,*], F.R. Ponziani [1,2,*]

[1] *Internal Medicine and Gastroenterology - Hepatology Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, 00168, Italy*
[2] *Department of Translational Medicine and Surgery, Catholic University, Rome, 00168, Italy*
[3] *Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy*
[4] *Medical Oncology Unit, Careggi University Hospital, Florence, Italy*
[5] *Division of Internal Medicine, IRCCS Azienda Ospedaliero-Universitaria di Bologna, via Albertoni 15, Italy*
[6] *Service d'Hépatologie, Hôpital Beaujon UMR 1149 Inserm - Université de Paris, Clichy, France*

[*] These authors contributed equally to this work

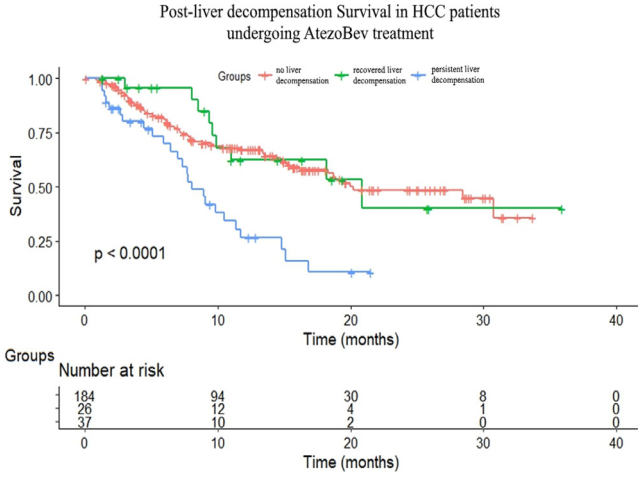
**Introduction and Aim:** Initial management of unresectable hepatocellular carcinoma (HCC) involves the use of atezolizumab plus bevacizumab (AtezoBev). There is a lack of research examining the influence of hepatic decompensation on patients during treatment and its impact on survival.
**Material and Method:** Between 2018 and 2023, 247 patients diagnosed with unresectable HCC and eligible for AtezoBev treatment were enrolled. Liver function was graded for all patients, comparing Child Pugh A (CPA, 59.5%) to Child Pugh B (CPB, 17.4%) and non-cirrhotic (NC, 23.1%).

A survival analysis assessed median overall survival (mOS), progression-free survival (PFS), and time-to-progression (TTP), while radiological response was evaluated using RECIST v1.1. Treatment-related adverse events (trAEs) graded according to CTCAE v5.0 were collected to evaluate AtezoBev safety.

We defined time-to-decompensation (TTD) as the interval from treatment start to the occurrence of events associated with the loss of liver function or worsening of portal hypertension. Its role in assessing the safety of treatment in cirrhotic patients was evaluated. Then, mOS was assessed in patients who experienced decompensation compared to those who didn't modify liver function.
**Results:** AtezoBev demonstrated significantly better mOS (20.2 vs. 9.8 months, p < 0.0001) and PFS (12.9 vs. 8.3 months, p < 0.017) in CPA patients compared to CPB patients. However, there were no differences in TTP (16.3 vs 12.3 months, p = 0.14), overall response rate (ORR, 24.4% vs 18.6%, p = 0.46), and disease control rate (DCR, 56.4% vs. 55.8%, p = 0.93) between the two groups.

The incidence of treatment-related adverse events (trAEs) remained consistent across subgroups, except for portal hypertension-related events, which were more frequent in the CPB group.

Indeed, CPB patients experienced a higher incidence of liver decompensation events (50% vs. 27.8%, p = 0.006), resulting in a TTD of 9.1 months. In contrast, CPA patients didn't reach a 50% occurrence rate of decompensation events during the follow-up period. Among patients who experienced liver decompensation (35% CPB, 65% CPA), those who regained previous liver function (31% CPB, 69% CPA) achieved a mOS comparable to those who didn't undergo liver decompensation (20.9 months vs 20.2 months, p = 0.77). However, persistent loss of liver function (38% CPB, 62% CPA) resulted in a poorer prognosis (mOS 8.1 months).
**Conclusion:** AtezoBev demonstrated efficacy and safety in both CPA and CPB subgroups. Liver decompensation had a higher incidence in CPB groups, but patients who recover from a liver decompensation related event showed a mOS comparable to those who didn't suffer from it. Considering this, access to AtezoBev in routine practice should be considered for CPB patients under close monitoring. Additionally, TTD could serve as a novel safety outcome for cirrhotic patients undergoing systemic treatment.




doi: 10.1016/j.dld.2024.01.138

## F-34

### Sorafenib as a second-line treatment after failure of atezolizumab-bevacizumab

F. Tovoli [1,2], M. Boe [1], C. Vivaldi [3], P. Federico [4], A. Palloni [5], A. Dalbeni [6,7], C. Soldà [8], B. Stefanini [1], I. Garajova [9], L. Ielasi [10], S. De Lorenzo [11], A. Granito [1,2], B. Stefanini [1], G. Masi [3], S. Lonardi [4], G. Brandi [1,5], B. Daniele [4], A. Auriemma [12], L. Lani [1,13], G. Svegliati-Baroni [14], C. Campani [15], F. Piscaglia [1,2], on behalf of the ARTE study group

[1] *Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy*
[2] *Unit of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[3] *Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy*
[4] *Medical Oncology Unit, Ospedale del Mare, Napoli, Italy*
[5] *Oncology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[6] *Unit of General Medicine C, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[7] *Liver Unit, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[8] *Oncology Unit 1, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy*
[9] *Medical Oncology Unit, University Hospital of Parma, Parma, Italy*
[10] *Department of Internal Medicine, Ospedale degli Infermi di Faenza, Faenza, Italy*
[11] *Oncology Unit, Azienda USL Bologna, Bologna, Italy*
[12] *Section of Innovation Biomedicine-Oncology Area, Department of Engineering for Innovation Medicine (DIMI), University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[13] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[14] *Liver Injury and Transplant Unit, Polytechnic University of Marche, Ancona, Italy*
[15] *Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze, Firenze, Italy*

**Introduction:** Patients receiving atezolizumab/bevacizumab (AB) for HCC may have a primary resistance to this combination. Another relevant proportion of patients will develop secondary resistance and, eventually, experience progressive disease. Randomized clinical trials (RCTs) trying to identify second-line treatments are undergoing. If such trials are unavailable or patients are non-eligible, sorafenib is often prescribed based on European approval and reimbursement policies. However, evidence supporting these policies is lacking, as no RCTs explored sorafenib in this setting.
**Aim:** To assess the efficacy of sorafenib in patients who permanently stopped AB.
**Methods:** The ARTE database collects prospectively enrolled patients treated with AB in a real-life setting(March 2022-November 2023). We analysed the outcome of patients who received sorafenib as second-line treatment. Moreover, we performed a case-control matching with historical controls who had received sorafenib as a frontline treatment before AB had become available in clinical practice. Patients were matched 4:1, based on known predictors of overall survival (OS) in sorafenib-treated patients (Child-Pugh class, AFP>400ng/ml, macrovascular invasion, extrahepatic spread, ECOG-PS>0).
**Results:** Amongst the 157 patients included in the ARTE database, 130 (67.4%) permanently discontinued AB. Of them, 57 received a second-line treatment. Sorafenib was prescribed in 29 patients. The disease control rate (DCR) was 17.2%, with no objective responses. The median PFS and OS were 3.2 and 7.9 months. Compared with historical controls, patients who received sorafenib as a second-line therapy had worse DCR (17.1 vs 47.4%, $p<0.01$) and PFS. A trend toward a worse OS was also noted (Figure)
**Conclusions:** In the post-AB setting, we found a suboptimal efficacy outcome of sorafenib. The very low DCR suggests that resistance to AB might select tumour cells that are able to escape the therapeutic targets of sorafenib. Enrollment of these patients in RCTs is strongly recommended to identify better therapeutic strategies.

doi: 10.1016/j.dld.2024.01.139

## F-35

### Treatment of hepatocellular carcinoma according to multiparametric therapeutic hierarchy approach: a prospective multicenter validation study

L. Canova [1,2], M. Iavarone [1], E. Alimenti [1], B. Antonelli [3], A.M. Ierardi [4], S. Crespi [4], M. Viganò [5], G. Cabibbo [6], A. Vitale [7], A. Sangiovanni [1], P. Lampertico [1,8]

[1] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Università degli Studi di Milano, Milan, Italy*
[3] *General and Liver Transplant Surgery Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[4] *Radiology Department, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[5] *Gastroenterology Hepatology and Transplantation Unit, ASST Papa Giovanni XXIII, 24127, Bergamo, Italy*
[6] *Gastroenterology and Hepatology Unit, Department of Health Promotion, Mother & Child Care, Internal Medicine & Medical Specialties, University of Palermo, Italy*
[7] *Hepatobiliary Surgery and Liver Transplantation Unit, Azienda Ospedale-Università di Padova, Padova, Italy*
[8] *CRC 'A. M. and A. Migliavacca' Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

**Background and aim:** Treatment strategy of hepatocellular carcinoma (HCC) is a complex decision-making process that should consider several variables in clinical practice. Recently, a "multiparametric therapeutic approach" has been proposed (Vitale A, Cabibbo G *et al* Lancet Oncol 2023). In this approach, the feasibility of all treatments is evaluated systematically in a hierarchical order, to match each patient with the optimal therapy. The aim of the study is to validate the reliability of the new multi-parametric decisional framework (MPDF) and the impact of the different variables included in the framework on the final treatment decision in clinical practice.
**Methods:** This is a prospective ongoing study with a first monocentric phase (A) and a second multicentric validation phase (B). Primary endpoints are: 1) adherence to MPDF for treatment allocation and 2) identification of the relative weight of variables involved in this multiparametric evaluation to predict treatment decision, while secondary endpoints are overall survival (OS) and radiological response after treatment. The study includes all consecutive patients with HCC managed in each center from September 1st, 2023. The disease is staged according to Barcelona Clinic Liver Cancer (BCLC) classification, while patient's characterization is conducted by Charlson Comorbidity Index (CCI), modified CCI (mCCI), Liver Frailty Index (LFI), Child-Pugh (CPT) and ALBI scores, MELD and skeletal muscle mass index (SMI) by CT-evaluation. Each pa-

tient is allocated to treatment according to MPDF, BCLC 2022 was used as benchmark of treatment allocation.
**Results:** As of November 1st, 2023, 48 patients were recruited into phase A of the study [median age 70 (52-87) years, 81% male, 37% HCV-Ab positive, 27% first diagnosis/treatment of HCC]. Thirteen (27%) patients were classified as BCLC 0, 17 (35%) as BCLC A, 6 (12.5%) as BCLC B, 6 (12.5%) as BCLC C and 6 (12.5%) as BCLC D. The median CCI was 8 (4-13), the median LFI was 4.15 (2.99-4.81) which corresponds to a pre-frail condition. Thirty-nine (81%) patients were in CPT class A, 7 (15%) in B and 2 (4%) in C, while 32 (67%) were classified ALBI grade 1 and 16 (33%) ALBI grade 2, and finally the median MELD score was 8.5 (6-22). Forty-four (92%) patients received treatment through a multidisciplinary team (MDT). According to the MPDF, 9 (19%) patients were allocated to liver transplant, 5 (10%) to laparoscopic surgical resection, 10 (21%) to microwave thermal ablation (MWTA), 7 (15%) to transarterial treatments (4 TACE and 3 TARE), 3 (6%) to other locoregional therapies (2 MWTA+TACE and 1 electrochemotherapy), 6 (13%) to systemic treatment and 5 (10%) to palliative care only. In 4 cases, the MDT decided for follow-up at 3 months and subsequent reassessment. The reason why each therapy was excluded for each patient is shown in Table 1. The treatment allocation was coherent to the BCLC 2022 treatment allocation system in the 69.2% for BCLC 0, 82.4% for BCLC A, 83.3% for BCLC B, 66.7% for BCLC C and 100% for BCLC D.
**Conclusions:** Preliminary data of our ongoing prospective study suggest that personalized approach for HCC treatment by MPDF is feasible in clinical practice and might help ensuring a customized approach in a standardized framework. Updated data will be presented at the meeting.

**Table 1.** Principal reason to exclude treatment allocation according to multi-parametric decisional framework.

| | |
|---|---|
| **Liver Transplant** | |
| Comorbidities | 11 (29.7%) |
| Extrahepatic extension of HCC | 6 (16.2%) |
| Beyond LT criteria | 5 (13.5%) |
| AFP>1000 | 1 (2.7%) |
| Unfeasible | 1 (2.7%) |
| Small benefit | 13 (35.1%) |
| **VLS Surgery** | |
| Frailty | 1 (3.1%) |
| Comorbidities | 14 (43.8%) |
| Extrahepatic extension of HCC | 6 (18.7%) |
| Multifocal HCC | 2 (6.3%) |
| CSPH | 4 (12.5%) |
| Liver disfunction | 2 (6.2%) |
| Limited liver volume remnant | 2 (6.3%) |
| Technical complexity | 1 (3.1%) |
| **Open Surgery** | |
| Frailty | 1 (3.1%) |
| Comorbidities | 13 (40.6%) |
| Extrahepatic extension of HCC | 6 (18.7%) |
| Multifocal HCC | 2 (6.3%) |
| CSPH | 3 (9.4%) |
| Liver disfunction | 5 (15.6%) |
| Limited liver volume remnant | 2 (6.3%) |
| **MWTA** | |
| Extrahepatic extension of HCC | 6 (30%) |
| > 3cm HCC | 4 (20%) |
| > 3 nodules of HCC | 2 (10%) |
| Critical location of HCC | 1 (5%) |
| Liver disfunction | 3 (15%) |
| Technical complexity | 2 (20%) |
| **VLS MWTA** | |
| ECOG PS > 2 | 1 (5.3%) |
| Extrahepatic extension of HCC | 6 (31.6%) |
| > 5cm HCC | 3 (15.8%) |
| > 3 nodules of HCC | 2 (10.5%) |
| Critical location of HCC | 2 (10.5%) |
| Liver disfunction | 3 (15.8%) |
| Technical complexity | 2 (10.5%) |
| **TACE** | |
| Extrahepatic extension of HCC | 6 (50%) |
| > 5 cm HCC | 1 (8.3%) |
| Multinodular and bilobar HCC | 2 (16.7%) |
| Liver disfunction | 3 (25%) |
| **TARE** | |
| Extrahepatic extension of HCC | 6 (54.5%) |
| Multinodular and bilobar HCC | 2 (18.2%) |
| Liver disfunction | 3 (27.3%) |
| **Systemic Therapy** | |
| ECOG PS>2 | 1 (25%) |
| Liver disfunction | 3 (75%) |

(*continued on next column*)

HCC, hepatocellular carcinoma; AFP, alpha fetoprotein; CSPH, clinically significant portal hypertension; VLS, videolaparoscopic; MWTA, microwave thermal ablation; ECOG PS, Eastern Cooperative Oncology Group Performance Status; TACE, transarterial chemoembolization; TARE, transarterial radioembolization

doi: 10.1016/j.dld.2024.01.140

## F-36

### Competitive Risk Analysis of Spleen Stiffness Measurement with a Spleen-Dedicated Module (SSM@100Hz) for Predicting de-novo HCC Occurrence in cACLD Patients: A Prospective 5-Year Follow-up Study

F. Ravaioli [1,*], L. Colecchia [1,*], E. Dajti [1], A. Vestito [1], A. Gobbato [1], F. Lami [2], M. Renzulli [1], M. Serenari [1], L. Di Marco [2], A. Pivetti [2], F. Tovoli [1], S. Ferri [1], D. Festi [1], A. Colecchia [2,°], G. Marasco [1,#]

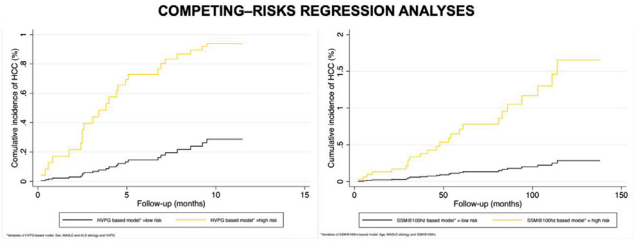
[1] *Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna, Italy*
[2] *Gastroenterology Unit, Department of Specialistic Medicines, University of Modena & Reggio Emilia, University Hospital of Modena and Reggio Emilia, Largo del Pozzo 71, 41125, Modena, Italy*

* FR and LC contributed equally to this abstract and share co-first authorship.
# AC and GM contributed equally to this abstract and share the co-last authorship.

**Background and Aims:** Hepatocellular carcinoma (HCC) impact significantly the survival of patients with liver disease, and it has been shown that portal hypertension (PH) is a major contributor to its development. Notably, clinically significant portal hypertension (CSPH), as identified by HVPG, can predict the occurrence of HCC. To explore the potential of spleen stiffness measurement (SSM) as a predictor of HCC occurrence, particularly with the use of a new spleen-dedicated module (SSM@100hz), we conducted a prospective study. Our investigation was aimed to determine whether SSM@100hz could identify HCC occurrence in individuals with compensated advanced chronic liver disease (cACLD).
**Methods:** We conducted a prospective study on patients who underwent paired laboratory exams, hepatic venous pressure gradient measurement (HVPG), liver stiffness measurement (LSM), and SSM@100hz. Patients were followed as per the current international guidelines for HCC screening, and we assessed the occurrence of HCC or other complications related to liver disease. We used competing-risks regression analysis to account for liver transplantation or death as competitive events.
**Results:** We enrolled 69 patients with a median follow-up of 68 months until HCC or a competitive event occurrence. **Table 1** re-

ports the characteristics of patients included and shows how HCC occurrence at competitive univariate statistical analysis was associated with a higher body mass index (BMI), SSM median value (SSM@100hz), HVPG, metabolic etiology, and combined Baveno VII single cut-off rule-in criteria (by SSM@100hz). Furthermore, we developed two competing risk models: one based on SSM@100Hz and the other based on HVPG. **Figure 1** demonstrates that both models can effectively predict the risk of HCC occurrence over time ($p < 0.001$ for both models).

**Conclusions:** SSM@100hz, mirroring portal hypertension, can predict the de novo HCC occurrence in patients with cACLD with a median follow-up time of 5 years.




| Variables | Characteristic of patients | | Competing-risks regression analysis | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Univariate analysis | | Multivariate SSM@100hz based model | | Multivariate based model | HVPG |
| | No HCC (n=66; 85%) | HCC occurrence (n=24; 30%) | Hazard Ratio (95% CI) | p-value | Hazard Ratio, (95% CI) | p-value | Hazard Ratio (95% CI) | p-value |
| Age | 62.9 (50.4-70.3) | 56.4 (48.1-66.3) | 0.979 (0.942 - 1.018) | 0.292 | 0.947 (0.906 - 0.991) | 0.018 | | |
| BMI (kg/m2) | 25.0 (24.2-26.6) | 30.0 (28.0-31.8) | 1.722 (1.331 - 2.227) | <0.001 | | | | |
| Sex | | | 2.644 (0.861 - 8.121) | 0.087 | | | 10.296 (1.824 - 58.1) | 0.008 |
| Female | 14 (31.1%) | 3 (12.5%) | | | | | | |
| Male | 31 (68.9%) | 21 (87.5%) | | | | | | |
| Aetiology | | | | | | | | |
| MASLD | | | 5.234 ( 2.259 - 12.149) | <0.001 | 20.911 (5.639 - 77.547) | <0.001 | 18.261 (4.092 - 72.999) | <0.001 |
| Non metabolic etiology | 38 (84.4%) | 8 (33.3%) | | | | | | |
| Metabolic etiology | 7 (15.6%) | 16 (66.7%) | | | | | | |
| Viral etiology | | | 1.134 (0.399 - 3.22) | 0.812 | | | | |
| Non viral etiology | 7 (15.6%) | 4 (16.7%) | | | | | | |
| Viral etiology | 38 (84.4%) | 20 (83.3%) | | | | | | |
| ALD | | | 0.609 (0.228 - 1.633) | 0.325 | | | 0.223 (0.061 - 0.811) | 0.023 |
| Non alcoholic etiology | 35 (77.8%) | 20 (83.3%) | | | | | | |
| Alcoholic etiology | 10 (22.2%) | 4 (16.7%) | | | | | | |
| Esophageal Varices | | | 1.118 (0.596 - 2.098) | 0.727 | | | | |
| Absent | 17 (37.8%) | 9 (37.5%) | | | | | | |
| F1-F2 | 22 (48.9%) | 14 (58.3%) | | | | | | |
| F3 | 6 (13.3%) | 1 (4.2%) | | | | | | |
| Bilirubin | 0.9 (0.6-1.6) | 0.9 (0.6-1.1) | 0.900 (0.737 - 1.266) | 0.809 | | | | |
| Albumin | 4.0 (3.5-4.1) | 3.8 (3.5-4.2) | 0.967 (0.686 - 2.4023) | 0.402 | | | | |
| INR | 1.2 (1.1-1.3) | 1.2 (1.1-1.3) | 0.710 (0.1667 - 3.1897) | 0.661 | | | | |
| PLT | 98.0 (70.0-143.0) | 100.0 (81.0-126.0) | 0.994 ( 985 - 1.003) | 0.198 | | | | |
| LSM median (kPa) | 20.4 (16.8-34.1) | 26.6 (17.6-35.3) | 1.02 (0.989 - 1.051) | 0.799 | | | | |
| SSM@100Hz median (kPa) | 53.6 (36.8-66.7) | 90.4 (40.4-79.9) | 1.022 (1.003 - 1.042) | 0.025 | 1.04 (1.013 - 1.068) | 0.003 | | |
| HVPG (mmHg) | 11.0 (9.0-14.0) | 13.5 (10.0-17.0) | 1.137 (1.047 - 1.235) | 0.002 | | | 1.171 (1.021 - 1.344) | 0.024 |
| Note: | | | | | AUROC = 0.752 | | AUROC = 0.731 | |
| Competing-risks events: Liver Transplantation and/or Death (n=5) | | | | | AIC = 54.423 | | AIC = 54.877 | |
| | | | | | BIC = 100.66 | | BIC = 103.19 | |

doi: 10.1016/j.dld.2024.01.141

## F-37

### A modified Charlson Comorbidity Index to improve management of patients with hepatocellular carcinoma: a step towards precision medicine

E. Alimenti [1], M. Iavarone [1], L. Canova [1,2], E. Fracas [2], B. Antonelli [3], A.M. Ierardi [4], S. Crespi [4], A. Zefelippo [3], A. Sangiovanni [1], P. Lampertico [1,5]

[1] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Università degli Studi di Milano, Milan, Italy*
[3] *General and Liver Transplant Surgery Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[4] *Radiology Department, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[5] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

**Background & aims:** Patients with hepatocellular carcinoma (HCC) frequently have comorbidities that limit access to treatments and might increase mortality. The Charlson comorbidity index (CCI) assigns a numeric score to 17 diseases according to their effect on mortality. In patients with cirrhosis and HCC, these variables might be excluded from the CCI (modified CCI, mCCI). Aim of the study was to evaluate the performance of CCI and mCCI for HCC patients' characterization.

**Methods:** We used data from our retrospective monocentric study of patients with first HCC diagnosis. We evaluated the performance of CCI and mCCI in dissecting our population and predicting overall survival (OS). As secondary end-point, the impact of mCCI on adherence to Barcelona Clinic Liver Cancer (BCLC) staging and treatment allocation was evaluated.

**Results:** The **study included** 385 patients (289 males, 68 years median age, 78% Child Pugh (CPT) A, 66% viral etiology) with HCC (271 BCLC 0/A, 64 B, 40 C and 10 D). According to CCI, 94% of our patients were "high-risk" (CCI≥5), 5.7% "intermediate-risk" (CCI 3-4) and 0.3% "low-risk" (CCI 0-2). These cutoffs were applied to mCCI: 21% "high-risk", 48% "intermediate-risk", and 31% "low-risk". Patients' mCCI correlated with CCI (Kendall's $\tau$=0.47; p-value< 0.0001). Overall, patients belonging to a "high" or "intermediate-risk" mCCI classes had a shorter OS as compared to "low-risk" patients (median OS 37 vs 49 vs 67 months, p-value=0.007). This was confirmed in BCLC 0/A (p-value=0.002). Moreover, "high-risk" mCCI class, worse CPT class, presence of varices, BCLC stage and AFP>200 ng/mL were independently associated to mortality [HR1.36 (95%CI 1.09-1.70, p-value=0.006; HR1.62 (95%CI 1.14-2.30), p-value=0.007; HR1.58 (95%CI 1.11-2.24), p-value=0.01; HR1.96 (95%CI 1.66-2.31) p-value<0.001; HR1.80 (1.17-2.79) p-value=0.008]. mCCI was also an independent predictor of mortality in BCLC 0/A, with higher tumor burden and worse CPT. No differences were observed in adherence to BCLC2022 algorithm and access to treatment among the mCCI risk classes.

**Conclusions:** mCCI better stratified patients with HCC as compared to CCI and independently predicted mortality. Implementation of a multiparametric therapeutic approach to treatment allocation including evaluation of comorbidities and frailty is warranted.

doi: 10.1016/j.dld.2024.01.142

## F-38

### Improved handling of BCLC 2022 update in the management of hepatocellular carcinoma in clinical practice

E. Alimenti [1], M. Iavarone [1], L. Canova [1,2], M. Bruccoleri [1], B. Antonelli [3], A.M. Ierardi [4], S. Sangiovanni [1], P. Lampertico [1,5]

[1] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Università degli Studi di Milano, Milan, Italy*
[3] *General and Liver Transplant Surgery Unit, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[4] *Radiology Department, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[5] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

**Introduction:** In 2022 the BCLC staging and treatment algorithm for hepatocellular carcinoma (HCC) management has been updated, granting for higher flexibility and customized management with a multidisciplinary decision process in the choice of the therapeutic strategy for HCC patients as compared to the 2018 version.

**Aim:** To evaluate the ability to adhere to BCLC 2022 in daily clinical practice as compared to the BCLC 2018 and the impact on patients' overall survival (OS).

**Methods:** We retrospectively evaluated data of 806 prospectively enrolled (year 2006 to 2022) patients with de novo HCC (Table 1) in different stages according to BCLC: 571 0-A, 133 B, 85 C and 17. First line treatment allocations were discussed by a multidisciplinary team (MTD), following updated recommendations and guidelines. All patients were followed until death or end of follow-up.

**Results:** Overall, the adherence to BCLC increased from 50% for the BCLC 2018 to 68% for the BCLC 2022 (p<0.001) considering all stages of HCC: 48% vs 71% stage 0/A (p<0.001), 50% vs 61% stage B (p=0.06), 59% vs 59% stage C (p=NS), 74% vs 74% for stage

D (p=NS). Among BCLC 0/A patients, 131 (32%) were treated with TACE, which is the second choice of treatment according to BCLC 2022, while among BCLC B patients, 5 (6%) underwent LT and 10 (12%) were treated with systemic therapy, which are now considered treatment options for this stage in selected patients. The expected survival rate following the BCLC 2018 recommendations remains unchanged by adhering to the BCLC 2022 update [74.5% vs 75.2% at year 2 (p=NS) and 41.4% vs 44.6% at year 5 (p=NS), respectively]. Finally, the rate of "upward stage migration" was similar by BCLC 2022 or BCLC 2018 (12% vs 14%, p=ns), while the rate of "downward stage migration" was lower with the new one (19% vs 36%, p<0.001). Overall, the 2-year survival rate of patients treated outside the BCLC 2022 recommendations did not significantly differ from those treated according to the updated algorithm (76% vs 74.5%, p=NS). In BCLC B and BCLC C, an upward stage migration was associated to higher rates of 2-year survival (93.5% vs 60.6%, p=0.002 for BCLC B and 36.9% vs 27.4%, p=0.01 for BCLC C), while there was no difference for stage 0/A between those treated outside and those treated according to the BCLC 2022.

**Conclusions:** The BCLC 2022 updated version of HCC staging and treatment system allowed a greater adherence to the algorithm in clinical practice, mainly in the early stages, without adversely affecting the survival of patients. In the intermediate and advanced stages, the access to more radical treatment could offer a survival benefit.

**Table 1**. Characteristics of patients included in the study.

| Variable | Included patients |
|---|---|
| | N=806 |
| **Age, years*** | 68 (60-74) |
| **Born males** | 602 (75%) |
| **Etiology** | |
| HCV | 470 (58%) |
| HBV | 76 (9%) |
| HCV+HBV | 22 (3%) |
| HDV | 19 (2%) |
| Mixed | 36 (4%) |
| Non-viral | 183 (24%) |
| **Child-Pugh Class** | |
| A | 603/776 (78%) |
| B | 161/776 (21%) |
| C | 12/776 (1%) |
| **MELD*** | 9 (7-10) |
| **Varices** | 257/782 (33%) |
| **BCLC** | |
| 0 | 187 (23%) |
| A | 384 (48%) |
| B | 133 (16%) |
| C | 85 (11%) |
| D | 17 (2%) |
| **Number of nodules** | |
| 1 | 487/802 (61%) |
| 2-3 | 213/802 (26%) |
| >3 | 102/802 (13%) |
| **Largest nodule's size (cm)*** | 2.5 (1.6-4.0) |
| **First line treatment** | |
| Liver transplantation | 39 (5%) |
| Resection | 142 (17%) |
| Radiofrequency ablation | 284 (35%) |
| Transarterial chemoembolization | 210 (26%) |
| Tyrosine-kinase inhibitors | 61 (8%) |
| Immunotherapy | 6 (1%) |
| Transarterial radioembolization | 6 (1%) |
| Combined therapy | 25 (3%) |
| Best supportive care | 33 (4%) |

Data are expressed as number (percentage), unless otherwise specified; *median (IQR)

doi: 10.1016/j.dld.2024.01.143

## F-39

### Impact of clonal hematopoiesis of indeterminate potential on hepatocellular carcinoma in individuals with steatotic liver disease

A. Marchetti [1,2], S. Pelusi [3], A. Marella [1], F. Malvestiti [4], A. Ricchiuti [1,2], L. Ronzoni [3], M. Lionetti [2], C. Bianco [3], A. Cherubini [3], S. Margarita [3], E. Bugianesi [5], L. Miele [6], U. Vespasiani-Gentilucci [7], P. Dongiovanni [8], A. Federico [9], G. Soardo [10], R. D'Ambrosio [11], S. Petta [12], F.P. Russo [13], M.V. McCain [14], H.L. Reeves [14], D. Prati [3], N. Bolli [1,2], L. Valenti [3,4,15]

[1] *Department of Oncology and Hemato-Oncology, Università degli Studi di Milano, Milan, Italy*
[2] *Hematology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[3] *Transfusion Medicine Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, 20122 Milan, Italy*
[4] *Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy*
[5] *Department of Medical Sciences, Division of Gastroenterology, University of Turin, Turin, Italy*
[6] *Dipartimento Universitario Medicina e Chirurgia Traslazionale, Università Cattolica del Sacro Cuore, Rome, Italy; Area Medicina Interna, Gastroenterologia e Oncologia Medica, Fondazione Policlinico A. Gemelli IRCCS, Rome, Italy*
[7] *Clinical Medicine and Hepatology Unit, Department of Medicine and Surgery, Campus Bio-Medico University of Rome, Rome, Italy*
[8] *Medicine and Metabolic Diseases, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[9] *Department of Precision Medicine, University of Campania "Luigi Vanvitelli", Naples, Italy*
[10] *Clinica Medica, Department of Medicine, European Excellence Center for Arterial Hypertension, University of Udine, Udine, Italy*
[11] *Gastroenterology and Hepatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[12] *Section of Gastroenterology, Di.Bi.M.I.S Policlinico Paolo Giaccone Hospital, University of Palermo, Italy*
[13] *Department of Surgery, Oncology and Gastroenterology, University Hospital Padua, Padua Italy*
[14] *Newcastle University Translational Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom*
[15] *Biological Resource Center Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*

**Introduction:** Clonal hematopoiesis of indeterminate potential (CHIP), defined as the presence of somatic mutations in hematopoietic stem cells with a variant allele frequency (VAF) ≥2% in genes involved in hematologic cancers, has been linked to MASLD and severe liver disease.

**Aim:** to examine whether CHIP is associated with MASLD-related HCC and its major clinical determinants.

**Methods:** patients with MASLD-related HCC (n=179), patients with advanced fibrosis without HCC (n=263), individuals with simple SLD (n=38) and healthy individuals (n=50) were enrolled. Age, sex, presence of type 2 diabetes (T2D), advanced liver fibrosis, AST and ALT levels were available.

DNA was sequenced by the HiSeq 4000/NextSeq2000 platforms (Illumina). Somatic mutations were identified accepting a minimum variant coverage of 20, a minimum alternative allele count of 3 and a VAF between 0.02 and 0.46. Only somatic and variants associated to malignancy or CHIP were included.

**Results:** CHIP-defining lesions were identified in 92 out of 530 participants (17.3%).

CHIP was found in 43 (24.0%) patients with HCC, 41 (15.6%) with advanced fibrosis without HCC, and in 8 (9.1%) without advanced fibrosis (p=0.006).

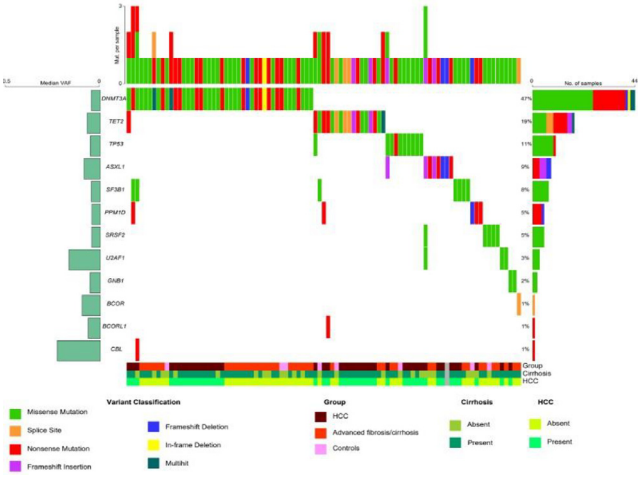
CHIP prevalence was age-dependent, with a spike after the age of 65.

The most frequently mutated gene was *DNMT3A*, followed by *TET2*, *TP53* and *ASXL1* **(Figure 1).**

CHIP was associated to HCC independently of sex, diabetes, polygenic risk score of SLD and cirrhosis (OR 1.81, 95%CI 1.10-2.98; p=0.018) but association was lost when correcting for age.

*TET2* mutations were enriched in HCC and the association between HCC and *TET2* remained significant when correcting for age, gender, diabetes, polygenic risk of SLD and cirrhosis (OR 4.35, 95%CI 1.18-16.01; p=0.029).

**Conclusion:** we suggest a possible role of CHIP in the progression of SLD and *TET2* mutations showed the strongest enrichment in HCC. Further studies are needed to clarify how CHIP can contribute to hepatic carcinogenesis.




doi: 10.1016/j.dld.2024.01.144

## F-40

### Characteristics and management of hepatocellular carcinoma (HCC) in Sicily: first results of the HCC Sicily Multidisciplinary Network

C. Celsa [1,2], G. Cabibbo [1], R. Ciccia [1], G. Di Maria [1], D. Pagano [3], R. Miraglia [3], L. Maruzzelli [3], M.G. Bavetta [4], M.R. Barcellona [4], C. Cocuzza [5], M. Tavarelli [5], R. F [6], C. Pitrone [6], G. Malizia [7], G. Bertino [8], F. Salomone [9], M. Distefano [10], M. Mitra [11], F. Cartabellotta [12], L. Giannitrapani [13], D. Giuffrida [14], M. Spada [15], G. Alaimo [16], D. Sambataro [17], G. Sportato [18], M.V. Grassini [1], R. Cannella [19], M. Antonucci [19], F. D'Amato [20], L. Capodicasa [1], A. Grova [1], S. Rao [1], M. Salvato [1], G. Cusimano [1], V. Gaudioso [1], A. Sparacino [1], F. Mercurio [1], M. Rizzo [3], V. Picciotto [4], R. Montenegro [5], S. Arena [6], C. Saitta [6], M. Russello [5], G. Fusco [4], V. Di Marco [1], S. Gruttadauria [3,21], C. Cammà [1]

[1] *Gastroenterology & Hepatology Unit, Department of Health Promotion, Mother & Child Care, Internal Medicine & Medical Specialties (PROMISE), University of Palermo, Palermo, Italy*
[2] *Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital, London, United Kingdom*
[3] *Department for the Treatment and Study of Abdominal Diseases and Abdominal Transplantation, Istituto di Ricovero e Cura a Carattere Scientifico-Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione (IRCCS-ISMETT), University of Pittsburgh Medical Center (UPMC), Palermo, Italy*
[4] *Unit of Hepatic Oncology, Division of Internal Medicine 2, Azienda Ospedaliera Ospedali Riuniti Villa Sofia-Cervello, Palermo, Italy*
[5] *Liver Unit, ARNAS Garibaldi-Nesima, Catania, Italy*
[6] *Department of Clinical and Experimental Medicine, University Hospital "G. Martino", Messina, Italy*
[7] *Gastroenterology Unit, Azienda Ospedaliera Ospedali Riuniti Villa Sofia-Cervello, Palermo, Italy*
[8] *Gastroenterology and Hepatology Unit, University Hospital Policlinico Vittorio Emanuele, Catania, Italy*
[9] *Division of Gastroenterology, Ospedale di Acireale, Azienda Sanitaria Provinciale di Catania, Catania, Italy*
[10] *UOC Malattie Infettive, Ospedale Umberto I di Siracusa, ASP Siracusa, Siracusa, Italy*
[11] *Medicina Interna 1, ARNAS Civico-Di Cristina-Benfratelli, Palermo, Italy*
[12] *Department of Internal Medicine, Ospedale Buccheri La Ferla, Palermo, Italy*
[13] *Unit of Internal Medicine, Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy*
[14] *Department of Oncology, Istituto Oncologico del Mediterraneo, Catania, Italy*
[15] *Medical Oncology Unit, Fondazione Istituto Giglio, Cefalù, Palermo, Italy*
[16] *UOC Medicina Interna, Ospedale di Agrigento, ASP Agrigento, Italy*
[17] *Medical Oncology Unit, Umberto I Hospital, Enna, Italy*
[18] *Infectious Disease Unit, S. Elia-Raimondi Hospital, Caltanissetta, Italy*
[19] *Department of Biomedicine, Neuroscience and Advanced Diagnostics (BiND), University of Palermo, Italy*
[20] *Azienda Ospedaliera Ospedali Riuniti Villa Sofia Cervello, Palermo, Italy*
[21] *Department of General Surgery and Medical-Surgical Specialties, University of Catania, Italy*

**Introduction:** Hepatocellular carcinoma (HCC) is constantly increasing in incidence, representing the third cause of cancer death worldwide. Multidisciplinary networks have shown to be effective in improving patient outcomes.

**Aim:** To describe the characteristics and management of HCC in Sicily (Italy).

**Materials & Methods:** HCC-Sicily-Network is a region-wide observational cohort initiated in November 2021, aiming to include all patients with HCC managed in a real-life situation by a multidisciplinary network. Up to November 2023, 1422 patients were included from 15 centres. In this first phase of the study, we reported clinical, biological, radiological and therapeutic characteristics of 546 patients who received active treatments before study enrolment.

**Results:** Median age was 72 years, 77.3% were men, median BMI was 24 kg/m2. HCC was diagnosed by surveillance programs in 52.4% of cases and diagnosed by liver biopsy in 10.1%. Cirrhosis was present in 88.3% of cases, with median MELD 8(IQR 7–10), Child-Pugh A in 56.8%, ALBI grade 1 in 46.5% and grade 3 in 2.5%, grade ≥2 esophageal varices in 22.2%. Etiologies were at least HCV infection in 60.3%, metabolic syndrome in 18.3%, alcohol in 10.3%, HBV in 10.4%. HCC was diagnosed as single nodule in 70.3%, 2 nodules in 15.4%, ≥3 nodules in 14.3%, with median AFP levels 4.5 ng/ml (IQR 2.3–34.5), portal thrombosis in 7.3% and extrahepatic disease in 6.2%. BCLC stages 0, A, B and C were 27.9%, 44.9%, 11.6%, and 15.6%, respectively. Treatment modalities were liver transplant in 4.6%, surgical resection in 28.9%, ablation in 39.2%, intra-arterial treatments in 60.8% and systemic treatment in 15.6%.

**Conclusion:** The first analysis of the HCC-Sicily-Network provides real-life data on clinical characteristics and therapeutic management of HCC patients in Sicily before the institution of the network. These will serve as benchmark for the second prospective study phase to assess if the institution of this network model is effective in improving patient outcomes.

doi: 10.1016/j.dld.2024.01.145

## F-41

### A multi-center comparative study of Atezolizumab plus Bevacivumab and Lenvatinib as primary systemic therapy for unresectable hepatocellular carcinoma (HCC): focus on thrombotic and hemorrhagic adverse events

M. Tizzani [1,2], C. Mazzarelli [3], M. Burlone [4], P. Carucci [1], G.P. Caviglia [5], C. Lisi [1,2], C. Canalis [1,2], L. Cesarini [3], M. Pirisi [6], A. Acquaviva [7], E. Rolle [1], P. Pochettino [8], K. Bencardino [9], F. Villa [9], M. Angiolillo [2,10], M. Scaldaferri [10], E. Castellana [10], F. Cattel [10], M. Airoldi [8], G.M. Saracco [1,2], S. Gaia [1]

[1] *Division of Gastroenterology and Hepatology, AOU Città della salute e della scienza, Turin*
[2] *University of Turin, Turin, Italy*
[3] *Hepatology and gastroenterology ASST GOM Niguarda*
[4] *AOU Maggiore della Carità-Novara, Medicina Interna 1*
[5] *Department of Medical Sciences, University of Turin, Turin*
[6] *Università del Piemonte Orientale, dipartimento di Medicina Traslazionale*
[7] *Medicina Interna, Ospedale S. Andrea, Vercelli*
[8] *Division of Medical Oncology 2, AOU Città della salute e della scienza, Turin*
[9] *Oncology ASST GOM Niguarda*
[10] *Division of Hospital Pharmacy, Città della salute e della scienza, Turin*

**Aims:** To compare efficacy and safety of Lenvatinib (Len) and Atezolizumab/Bevacivumab (AB), mainly focusing on thrombotic and hemorrhagic adverse events.
**Methods:** Demographic, clinical and radiologic data of all consecutive patients who received Len or AB in 3 northern Italian centers were collected. All patients were followed EASL guidelines for HCC systemic therapy.
**Results:** Overall 173 patients receiving AB (n=65) or Len (n=108) were enrolled. Baseline charateristics were similar for demographic and clinical features, low-risk esophageal varices (39%), and anticoagulant therapy (21%). Anti-aggregant therapy was more frequent in Lev-group (27.8%) compared to AB (12.3%), *p=0.022*. Viral aetiology was higher in AB-group (66.7%) vs Len-group (48.1%), (*p=0.050*). Median follow-up was longer in Lev-group (11.3 months, IQR5.7-21.4) *vs* AB (6.8 months, IQR4.1-11.1), *p<0.001*.

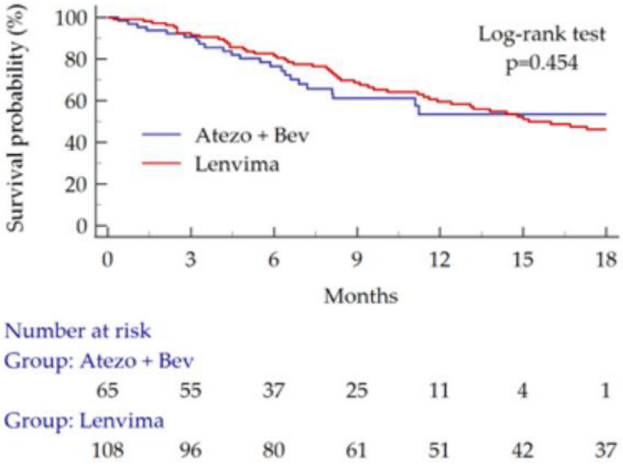
Mean overall survival (OS) was similar: 18.8 months (95%CI 16.2-21.6), (*p=0.454*). OS was related to radiological response at 3 months in both groups (*p<0.001*). Baseline AFP was associated to higher mortality only in Len-group (*p<0,001*).

Disease-control-rate at 3, 6 and 12 months was similar in Lev-group *vs* AB-group: 77% *vs* 66%, 64% *vs* 56% and 48% *vs* 37%, respectively (*p=ns*).

Thrombotic events were uncommon: 5/108 (4.6%) in Len-group [2 acute coronary syndrome, 1 portal vein thrombosis (PVT), 1 Pulmonary-embolism, 1 transitory-ischemic attack] *vs* 3/65 (4.6%) in AB-group (3PVT), (*p=0.561*). No thrombotic events occurred in patients with anticoagulants. Overall the use of anti-platelets didn't reduce the thrombotic risk (HR=1.69, p=0.481) nor increased the hemorrhagic risk (HR=1.08,*p=0.870*).

Mild and/or severe hemorrhagic events occurred in 15/108 (13.9%) in Lev-group and in 10/65 (15,3%) in AB-group (*p=0.421*): anticoagulants use increased hemorrhagic events (HR2.61,*p=0.02*).

Hospitalization for any reason occurred in 1/108 patient receiving Len and in 20/65 patients receiving AB, four of them related to hemorrhagic events.
**Conclusion:** AB or Lev had comparable OS and disease-control-rate. In both group thrombotic events were uncommon: therapy with anticoagulants avoided thrombotic events, but increased the hemorrhagic risks.




doi: 10.1016/j.dld.2024.01.146

## F-42

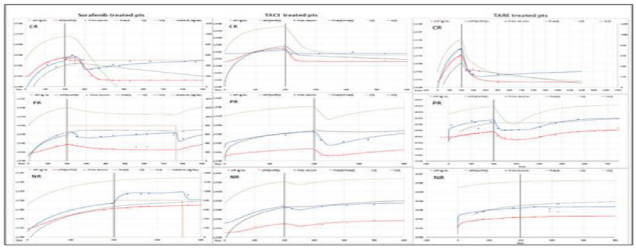
### Modeling cancer cells and tumor vasculature dynamics by serum biomarkers in HCC patients with different response to TKIs, TACE and TARE suggests a synergistic effect of systemic and endovascular treatments

F. Damone [1], P. Colombatto [1], G. Ricco [1], F. Oliveri [1], L. Civitano [1], V. Romagnoli [1], D. Cavallone [1], C.O. Demirtas [2], P. Boraschi [3], P. Scalise [3], L. Crocetti [4], E. Bozzi [4], B. Coco [1], A. Salvati [1], L. Surace [1], G. Boni [5], F. Bonino [6], M.R. Brunetto [1,6,7]

[1] *Hepatology Unit, Pisa University Hospital, Pisa, Italy*
[2] *Gastroenterology Department, Marmara University Istanbul, Turkey*
[3] *Radiodiagnostic Unit, Pisa University Hospital, Pisa, Italy*
[4] *Interventional Radiology Unit, Pisa University Hospital, Pisa, Italy*
[5] *Nuclear Medicine Unit, Pisa University Hospital, Pisa, Italy*
[6] *Biostructure and Bio-imaging Institute of National Research Council of Italy*
[7] *Department of Clinical and Experimental Medicine, Pisa University, Pisa, Italy*

**Introduction:** Tyrosine-kinase inhibitors (TKI), trans-arterial chemo-embolization (TACE) and trans-arterial radio-embolization (TARE) are used in patients (pts) with unresectable hepatocellular carcinoma (HCC). Previously, we proposed a physic-mathematical model to study cancer cells and tumor vasculature dynamics (doi:10.3390/cancers13092064) by serum $\alpha$-fetoprotein(AFP) and protein induced by vitamin K absence-II(PIVKA-II) kinetics integrated with digital imaging. We here quantified by the model TKIs, TACE and TARE therapeutic effects in patients with complete (CR), partial (PR) and no (NR) response.
**Patients and methods:** Ten pts (2-F/8-M;median age:65y; stage:1-BCLC-B/9-BCLC-C) received TKIs (1 regorafenib, 9 sorafenib), eight (5-F/3-M;77y; stage:8-BCLC-B) TACE (doxorubicin+DC-beads) and seven (1-F/6-M; 70y; stage:7-BCLC-B)TARE (Yttrium-90). AFP and

PIVKA-II were tested by commercial assays (Abbott, Fujirebio). HCC volume/densitometry were measured by CT scans (GE Advantage Workstation 4.6).
**Results:** Median HCC volume was greater in TKIvsTARE and TACE pts (42.1vs29.9vs9.7 $cm^3$/p=0.065). Changes of AFP and PIVKA-II serum values in 10-TKI (4-CR/4-PR/2-NR), 7-TARE (3-CR/3-PR/1-NR) and 8-TACE (2-CR/5-PR/1-NR) pts were fitted into the model. Anti-angiogenesis and anti-proliferative effectiveness were higher in CR vs non-CR (30.0 vs 10.0/p=0.023;10.0 vs 1.0/p=0.043), and in TKI vs TARE and TACE (median:40.0 vs 18.0 vs 3.0/p=0.015;4.0 vs 1.0 vs 0.5/p=0.013). TACE and TARE, however, reached maximal therapeutic effect earlier (<1.0 vs 4.6-99.9 days), due to the higher drug uptake coefficient (median:0.0005 and 0.00035 vs 0.0000075/p<0.001). Accordingly, AFP and PIVKA-II reduction occurred immediately after TACE and TARE, with AFP half-life comparable to its natural decay (0.10-0.16 $day^{-1}$). By contrast, AFP decline after TKI was delayed, and an early spike of PIVKA-II levels occurred in most responders, suggesting that PIVKA-II production rate by neoplastic cells increases transiently with slow ischemia onset.
**Conclusions:** The antiangiogenetic and antiproliferative effectiveness of TKI, TARE and TACE, computed by modeling AFP and PIVKA-II decline, correlates with treatments efficacy. Their different modes of action are captured by the model, suggesting a synergic effects of TKIs and endovascular treatments. Future trials could assess whether model tailored schedules increase therapeutic efficacy.



doi: 10.1016/j.dld.2024.01.147

## F-43

### Comparative analysis of subclassification models in patients with intermediate stage hepatocellular carcinoma (BCLC B) receiving systemic therapy

L. Ielasi [1], B. Stefanini [2,3], F. Conti [1], M. Tonnini [2,3], R. Tortora [4], G. Magini [5], R. Sacco [6,7], T. Pressiani [8], F. Trevisani [2,9], F.G. Foschi [1], F. Piscaglia [2,3], A. Granito [2,3], F. Tovoli [2,3]

[1] *Department of Internal Medicine, Ospedale degli Infermi di Faenza, Faenza, Italy*
[2] *Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy*
[3] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[4] *Liver Unit, Department of Transplantation, Cardarelli Hospital, Naples, Italy*
[5] *Department of Gastroenterology and Transplant Hepatology, Papa Giovanni XXIII Hospital, Bergamo, Italy*
[6] *Gastroenterology Unit, Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy*
[7] *Gastroenterology and Digestive Endoscopy Unit, Foggia University Hospital, Foggia, Italy*
[8] *Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy*
[9] *Semeiotica Medica, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*

**Introduction:** Intermediate stage hepatocellular carcinoma (BCLC B HCC) is a heterogeneous group of patients that could be addressed to a wide spectrum of treatments and, consequently, survival significantly varies among patients. In the last decades, several subclassification systems have been proposed to stratify patients' prognosis. We analyzed and compared these systems (Bolondi, Yamakado, Kinki, Wang, Lee, and Kim criteria) in patients undergoing systemic therapy.
**Materials and Methods:** We considered 171 patients with BCLC B HCC treated with sorafenib as first-line systemic therapy in six different Italian centers from 2010 to 2021 and retrospectively applied criteria of six different subclassification systems.
**Results:** Except for Yamakado criteria, all the subclassification systems showed a statistically significant correlation to overall survival (OS). In the postestimation analysis Bolondi criteria (OS of subgroup 22.5, 11.9 and 6.6 mo, respectively; C-index 0.586; AIC 1338; BIC 1344) and Wang criteria (OS of subgroups 20.6, 11.9 and 7.0, respectively; C-index 0.607; AIC 1337; BIC 1344) presented the best accuracy. Further analyses on these two subclassification systems implemented with the prognostic factor of alpha-fetoprotein (AFP) >400 ng/ml have shown an increase of accuracy for both systems (C-index 0.599 and 0.624, respectively).
**Conclusions:** Intermediate stage subclassification systems maintain their predictive value also in the setting of systemic therapy. Bolondi and Wang criteria showed the highest accuracy. AFP >400 ng/ml enhance the performance of these systems.

doi: 10.1016/j.dld.2024.01.148

## F-44

### Efficacy and safety of atezolizumab/bevacizumab for hepatocellular carcinoma in a real-life prospective cohort: data from a multicenter collaborative study

F. Tovoli [1,2], C. Vivaldi [3], P. Federico [4], B. Stefanini [1], A. Palloni [5], A. Dalbeni [6], C. Soldà [7], L. Lani [1], I. Garajova [8], S. Tamberi [9], S. De Lorenzo [10], A. Granito [1,2], D.P. Pallotta [1], G. Masi [3], S. Lonardi [7], G. Brandi [1,5], B. Daniele [4], D. Sacerdoti [6], B. Stefanini [1,11], G. Svegliati-Baroni [12], C. Campani [13], E. Pellegrini [14], F. Piscaglia [1,2], on behalf of the ARTE study group

[1] *Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy*
[2] *Unit of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[3] *Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa*
[4] *Medical Oncology Unit, Ospedale del Mare, Napoli, Italy*
[5] *Oncology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[6] *Liver Unit, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[7] *Oncology Unit 1, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy*
[8] *Medical Oncology Unit, University Hospital of Parma, Parma, Italy*
[9] *Medical Oncology Unit, "Degli Infermi" Hospital, AUSL della Romagna, Faenza*
[10] *Oncology Unit, Azienda USL Bologna, Bologna, Italy*

[11] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[12] *Gastroenterology Unit, Polytechnic University of Marche, Ancona, Italy*
[13] *Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze, Firenze, Italy*
[14] *SOD Oncologia Medica, AOU Careggi Firenze, Firenze, Italy*

**Introduction:** Atezolizumab/bevacizumab (AB) is the current standard of care for patients with unresectable hepatocellular carcinoma. Most efficacy and safety data derived from clinical trials, while only a few real clinical practice studies have been published.
**Aim:** To provide real-life clinical data of HCC patients treated with AB.
**Methods:** The ARTE study group prospectively collects data of patients who started AB outside of clinical trials. We evaluated clinical data and outcomes of HCC patients included in the ARTE database (March 2022-November 2023).
**Results:** Data from 157 patients from 12 centres were collected. Most patients had advanced HCC (59.9%). Twenty-seven (17.1%) patients had ≥1 condition(s) outside of the IMbrave-150 enrolling criteria (thrombocytopenia<70.000/mmc [n=8], concurrent/recent neoplasia [n=6], concurrent anticoagulation [n=6], arrhythmia [n=5], HIV infection [n=4], chronic heart failure [n=2]). HCV was the most commonly reported aetiology (43.9%), followed by MASLD (31.8%), ALD (23.6%), and HBV (14.0%). Forty-four (28%) patients reported multiple etiologies. The prevalence of performance status (PS)>0, macrovascular invasion (MVI), extrahepatic spread, and alpha-fetoprotein (AFP)>400 ng/ml was 38.2, 37.6, 38.2, and 29.9%, respectively. Nineteen (12.1%) patients received surgical (n=3), percutaneous (n=3), trans-arterial treatments (n=4), or non-liver-directed radiotherapy (n=9) after the start of AB. The median overall and progression-free survivals were 19.8 (95% CI 15.8-23.8) and 10.5 months (6.3-14.7), respectively. MVI, AFP>400 ng/ml, ALBI grade>1, and platelet-to-lymphocyte ratio>210 were independent negative prognostic factors. Progression due to new extrahepatic lesions/macrovascular invasion led to worse outcomes.

The most common treatment-related adverse events (AEs) included fatigue (42.3%), hypertension (28.2%), anorexia (18.6%), and diarrhoea (17.2%). The most common treatment-related Grade 3-4 AEs were hypertension (7.0%), digestive non-variceal bleeding (3.8%), increased aminotransferases (3.2%), and variceal bleeding (2.5%).
**Conclusions:** these real-life data confirm previous efficacy and safety information of AB. Multiple HCC etiologies, comorbidities, and combinations with locoregional treatments are common in clinical practice and warrant dedicated studies.

doi: 10.1016/j.dld.2024.01.149

## F-45

### Involvement of the potassium channel ERG1 in cholangiocarcinoma

J. Iorio, G. Alla Viligiardi, M. Pastore, C. Duranti, R. Colasurdo, C. Capitani, T. Lottini, A. Arcangeli, C. Raggi, F. Marra

*Department of Experimental and Clinical Medicine, Section of Internal Medicine, University of Florence, Florence, Italy*

**Background and Aim:** Due to the lack of proper biomarkers and potentially effective treatments, the management of cholangiocarcinoma (CCA) is still challenging. Ion channels have been proven to be novel biomarkers and new targets for cancer therapy, due to their easy druggability. The voltage-gated K+ channel hERG1 exerts pleiotropic effects in cancer cells. This study explored the role of hERG1 in the biology of intrahepatic CCA (iCCA).
**Methods:** Validation of h*ERG1* in iCCA tissues was performed in TCGA database. In vitro experiments were conducted to estimate the impact of h*ERG1 inhibition* on cell function in iCCA cell lines (HUCCT1, CCLP1, CCA4).
**Results:** A significant difference in h*ERG1* gene expression was observed between iCCA and normal tissue samples. Similarly, iCCA cell lines showed significantly higher protein content of hERG1 compared to normal cholangiocytes (NHC3).

Treatment with E4031, a selective hERG1 inhibitor, showed a limited impact on cell growth, but a substantial reduction of the invasive capabilities of iCCA cells. Immunoprecipitation assays and immunofluorescence revealed the formation of an active macromolecular complex with $\beta 1$ integrin responsible for VEGF-A activation through AKT signaling. Treatment with a bispecific antibody (scDb: single-chain Diabody) that binds the hERG1-$\beta 1$ complex, negatively impacted the invasiveness of iCCA cells as well as expression of genes regulating epithelial to mesenchymal transition. In vitro co-treatment with scDb and cisplatin-gemcitabine, significantly reduced growth of iCCA cells.
**Conclusion:** This study indicates that h*ERG1* may be relevant in promoting the malignant characteristics of iCCA.

doi: 10.1016/j.dld.2024.01.150

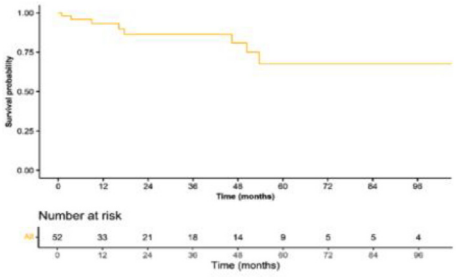
## F-46

### TKIs treatment for HCC before Liver transplantation: an ELITA/ELTR collaborative study

C. Mazzarelli [1], S. Bhoori [2], S. Grandi [2], S Gruttadauria [3], I. Petridis [3], J.I. Herrero [4], F. Rotellar [4], A. Shcherba [5], C. den Hoed [6], W. Polak [6], D. Patrono [7], R. Romagnoli [7], A. Ottobrelli [7], M De Giorgio [8], A Loglio [8], S. Fagiouli [8], M. Colledan [8], O. Detry [9], J. Dewailde [9], P Toniutto [10], U. Baccarani [10], M.F. Donato [11], L. Caccamo [11], M. Vivarelli [12], G. Svegliati-Baroni [12], G. Conte [12], A. Dalbeni [16], D. Sarcedoti [16], A. Carraro [16], R. Viganò [1], G. Perricone [1], L. De Carlis [15], T.M. Manzia [13], G. Tisone [13], A. Grieco [14], A. Avolio [14], V. Mazzaferro [2], L.S. Belli [1]

[1] *Hepatology and Gastroenterology ASST GOM Niguarda*
[2] *Istituto Nazionale dei Tumori, Milano, Italy*
[3] *ISMETT, Palermo, Italy*
[4] *University of Navarra, Pamplona, Spain*
[5] *RSP Center for Organ and Tissue Transplantation, Minsk Division of Liver transplantation and HPB surgery, Minsk, Belarus*
[6] *Erasmus University Medical Center, Department of Gastroenterology and Hepatology, Rotterdam, Netherlands*
[7] *Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, General surgery 2U, Torino, Italy*
[8] *ASST Papa Giovanni XXIII Hospital, Hepatology, Bergamo, Italy*
[9] *C hu De Liége, Dpt of Abdominal Surgery and Transplantation, Luik, Belgium*
[10] *Hospital Santa Maria della Misericordia, Udine, Italy*
[11] *Policlinico of Milan, Gastroenterology and Hepatology, Milano, Italy*
[12] *Marche Polytechnic University, epato-Pancreato-Biliary and Transplant Surgery, Department of Experimental and Clinical Medicine, Ancona, Italy*
[13] *Hospital Tor Vergata Roma, Department of Surgery Science, Roma, Italy*
[14] *Catholic University of the Sacred Heart, department of surgery, Milano, Italy*
[15] *Transplant Surgery, ASST GOM Niguarda, Milan, Italy*
[16] *General Medicine C, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy*

**Background and Aims:** Recent advances in systemic treatments for hepatocellular carcinoma (HCC) have driven the discussion on their possible role for downstaging advanced HCC prior to liver transplantation (LT) or for bridging to LT to prevent tumor progression and reduce the dropout risk. The aim of this study was to evaluate the outcome of patients treated with TKIs before LT.
**Method:** an online survey was sent to all centers affiliated to the ELITA/ELTR network between June and December 2022. Demographic and clinical data were retrospectively collected.
**Results:** Fifty-two patients, median age 60.5 years, receiving a LT between December 2006 and September 2022 were enrolled. Thirty patients (57.6%) were treated with TKI with a downstaging purpose, while 22 (42.3%) received TKI as a bridging treatment to LT. 34 patients (65%) received sorafenib, 15 lenvatinib (28%) and 3 patients (3%) a sequential therapy with sorafenib-regorafenib. Forty-eight patients (92%) received at least one locoregional treatment before LT. Only 12 patients (23%) were in Milan criteria at treatment start time. Twenty-nine patients were Milan-in at listing (55.7%). Nine patients had neoplastic portal vein thrombosis (17.3%). The five-year survival was 70% (Figure 1). After a median time of 7.7 months (5-12.7), 7 patients (13%) experienced HCC recurrence. The only factor associated with HCC recurrence was AFP (p 0.02) at LT-We observed only a single recurrence in one of the patients with neoplastic thrombosis. Twelve patients (23%) experienced vascular or early bleeding complications after LT. The type of TKIs or the time from the last dose to LT didn't influence the risk of post-LT complications.
**Conclusions:** This is the largest collected series of patients receiving TKIs pre-LT as downstaging/bridging therapy, with a very favourable long-term outcome (70 % at 5 years) even in patients with neoplastic vein thrombosis.




doi: 10.1016/j.dld.2024.01.151

## F-47

### Management of portal hypertension in patients receiving atezolizumab-bevacizumab for hepatocellular carcinoma

F. Tovoli [1,2], E. Franceschini [1], C. Vivaldi [3], P. Federico [4], A. Palloni [5], A. Dalbeni [6], C. Soldà [7], B. Stefanini [1], I. Garajova [8], L. Ielasi [9], S. De Lorenzo [10], A. Granito [1,2], R. Chen [1], G. Masi [3], S. Lonardi [7], G. Brandi [1,5], B. Daniele [4], D. Sacerdoti [6], L. Lani [1,11], G. Svegliati-Baroni [12], C. Campani [13], F. Piscaglia [1,2], on behalf of the ARTE study group

[1] *Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy*
[2] *Unit of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[3] *Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa*
[4] *Medical Oncology Unit, Ospedale del Mare, Napoli, Italy*
[5] *Oncology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[6] *Liver Unit, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[7] *Oncology Unit 1, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy*
[8] *Medical Oncology Unit, University Hospital of Parma, Parma, Italy*
[9] *Department of Internal Medicine, Ospedale degli Infermi di Faenza, Faenza, Italy*
[10] *Oncology Unit, Azienda USL Bologna, Bologna, Italy*
[11] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[12] *Liver Injury and Transplant Unit, Polytechnic University of Marche, Ancona, Italy*
[13] *Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze, Firenze, Italy*

**Introduction:** Guidelines recommend atezolizumab/bevacizumab (AB) as a frontline therapy for patients with unresectable hepatocellular carcinoma (HCC). Bevacizumab may increase the risk of bleeding. Patients with cirrhosis should undergo an upper digestive endoscopy (EGDS) prior to the start of AB. Moreover, patients with neoplastic portal vein invasion (nPVT) may develop portal hypertension even in the absence of cirrhosis.
**Aim:** To report the prevalence and esophageal varices in patients undergoing AB for unresectable HCC, identify risk factors associated to the presence of varices, describe prophylaxis, and report the prevalence of variceal bleeding.
**Methods:** The ARTE database includes prospectively-collected data from patients treated with AB in a real-life setting. We evaluated clinical data and outcome of HCC patients included in this database (March 2022-November 2023).
**Results:** Data of 157 patients from 12 centres were collected (median follow-up 8.9 months). Most patients (n=114, 72.4%) had liver cirrhosis. Overall, 117 patients (74.5%) had received an EGDS <6 months before starting AB. Amongst them, 34 (29.1%) had esophageal varices. Prophylaxis of bleeding was performed as followed: non-selective beta-blockers (NSBB) [n=17, 50.0%], elastic band ligation (EBL) [n=2, 5.9%], NSBB+EBL (n=3, 8.8%). Twelve patients (35.3%) did not receive prophylaxis for absolute or relative contraindications. There was no significant difference in the management between hepatology and oncology centres (p=0.662). The presence of varices was independently predicted by platelet count<150.000/mmc (OR 4.7, 95% CI 1.8-12.2, p=0.001) and alcoholic etiology (OR 4.2, 95% CI 1.6-11.0, p=0.004). Neither ALBI grade>1 (OR 1.6, 95% CI 0.6-4.22) or nPVT of the main portal trunk (OR 2.0, 95% C 0.74-9.6) reached the full statistical significance. Variceal bleeding occurred in 4 patients (2.6%; G3: n=1; G4:n=2; G5:n=1).
**Conclusions:** Variceal bleeding under AB remains a rare occurrence, but with severe consequences. EGDS should be strongly recommended for patients with low platelet count and/or alcoholic etiology.

doi: 10.1016/j.dld.2024.01.152

## F-48

### Application of Machine Learning Model-3P to Predict Portal Hypertension in Patient with Hepatocellular Carcinoma

F. Berardi [1,2], M. Soleri [1,2], A. Bertazzoni [1,2], F. Fortunato [1,2], R. Ceriani [1], F. Colapietro [1,2], N. Pugliese [1,2], C. Masetti [1], V. Pedicini [3], D. Poretti [3], L. Rimassa [4], T. Comito [5], G. Torzilli [6], A. LLeo [1,2], A. Aghemo [1,2], S. De Nicola [2]

[1] Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, 20072, Milan, Italy
[2] Division of Internal Medicine and Hepatology, Department of Gastroenterology, Humanitas Research Hospital IRCCS, 20089, Milan, Italy
[3] Department of Interventional Radiology, Humanitas University, Humanitas Research Hospital IRCCS, 20089, Rozzano, Italy
[4] Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20072, Pieve Emanuele (Milan), Italy; Medical Oncology and Hematology Unit, Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Via Manzoni 56, 20089, Rozzano, Milan, Italy
[5] Department of Radiosurgery and Radiotherapy, Istituto Clinico Humanitas Cancer Center and Research Hospital IRCCS, 20089, Milan, Italy
[6] Division of Hepatobiliary Surgery, Department of General Surgery, Humanitas Research Hospiral IRCSS, 20089, Milan, Italy

The occurrence of decompensation due to portal hypertension (PH) in patients with hepatocellular carcinoma (HCC) could preclude the access to treatment. To date, non-invasive methods to predicts PH failed their application in HCC patients. Reiniš, J(JHep,2023) proposed a new non-invasive method developed through machine learning models, called the 3P model, using as reference the invasive measurement of hepatic venous pressure gradient. The model considers three laboratory parameters (platelet count, bilirubin, international normalized ratio) and held promising results in predicting the presence of PH in cACLD (compensated advanced chronic liver disease). The aim of our study is to verify reliability of 3P model in a cohort of patients with HCC.

We retrospectively included all consecutive patients discussed in multidisciplinary HCC team consultation from 2018 to 2022 at our Academic Hospital. 3P score was calculated using the original formula and cut-off (0.332) and compared with baseline endoscopy.

Data from 240 cACLD patients with HCC were collected. 146 patients performed endoscopy at baseline and were included in statistical analysis. Main etiology of cirrhosis was viral infection (64/146,44%) followed by metabolic disease (44/146,30%). The HCC stage was classified using the Barcelona clinic liver cancer (BCLC) system: BCLC-0 22 patients (15.7%), BCLC-A 76(52.5%), BCLC-B 46(31.51%), BCLC-C 2(1.37%). A total of 42 patients (28.77%) had varices at endoscopy. Applying the 3P score with 0.332 cutoff in our cohort we obtained a sensitivity of 40% and specificity of 89% (AUC 0.65). Based on our data, another cut-off (0.15) was calculated for prediction of presence of varices at endoscopy reaching a sensitivity of 80% and specificity of 44%, with a negative predictive value of 83.7%.

3P model could be a rapid and non-invasive model to predict the absence of severe PH at diagnosis of HCC. More data are necessary to validate our proposed cut off in HCC setting.

doi: 10.1016/j.dld.2024.01.153

## F-49

### Off-label use of nivolumab beyond first-line in advanced hepatocellular carcinoma: a report of two international experiences

F. Frigo [1], P. Carucci [1], N. Ben Khaled [4], G.P. Caviglia [1], E. Rolle [1], E.N. De Toni [4], P. Pochettino [2], I. Piseddu [4], M. Scaldaferri [3], F. Cattel [3], E. Castellana [3], A. De Giorgi [1], G.M. Saracco [1], S. Gaia [1]

[1] Gastrohepatology Departement, A.O.U. Città della Salute e della Scienza di Torino, Torino, Italy
[2] Oncology Departement, A.O.U. Città della Salute e della Scienza di Torino, Torino, Italy
[3] Pharmacology Departement, A.O.U. Città della Salute e della Scienza di Torino, Torino, Italy
[4] Department of Medicine II, University Hospital, LMU Munich, Munich, Germany

Investigational use of nivolumab as first-line therapy for the treatment of hepatocellular carcinoma (HCC) yielded promising results but not enough to be introduced in guidelines. Limited data exists on its use beyond first-line.

**Aims:** to evaluate the efficacy and safety of nivolumab as monotherapy beyond first-line in patients with HCC

**Methods:** we analyzed data from consecutive HCC patients, ineligible for any other therapy, receiving off-label nivolumab at two referral centers in Italy and Germany between May-2016 and October-2023.

Measured outcomes were overall survival (OS), progression-free survival (PFS), disease-control-rate (DCR), biological response (BR), defined as an ≥25% decrease in alpha-fetoprotein (AFP) level after 3 months of therapy, and adverse events.

**Results:** 30 patients were enrolled (Italy n=24, Germany n=6). Patient characteristics were as follows: median age 65 (range 30-82) years, Child-Pugh A-B 80%-20%, BCLC B-C 13%-87%. One patient received nivolumab as I-line, 19 as II-line, 8 as III-line, and 2 as IV-line.

Median OS was 9.1 (95%CI 6.4-14.2) months and median PFS was 3.5 (95%CI 2.8-6.4) months. At 3 months, DCR was 27% (8/30) and BR was obtained in 23% (7/30) of patients. Two patients achieving complete radiologic response.

Median OS in patients with radiological disease control at 3 months was 27.7 (95%CI 4.7-41.2) months compared to 7.3 (95%CI 4.0-9.1) months in patients with disease progression (p<0.001). Median OS in patients with BR was 38.0 (95%CI 23.5-41.2) months compared to 7.8 (95%CI 3.6-12.1) months in patients without BR (p<0.001).

At baseline, better performance status, presence of metastatic lymphnodes, AFP≥400 µg/L, and lower disease burden were associated with longer OS (all p<0.05).

Grade 3-4 adverse events occurred in 10 patients (33%).

**Conclusion:** nivolumab could represent a valuable option in patients without other alternatives, showing an OS greater than 6 months in 77% of patients and an acceptable safety profile. Radiological response at 3 months and BR predict a significantly longer survival.

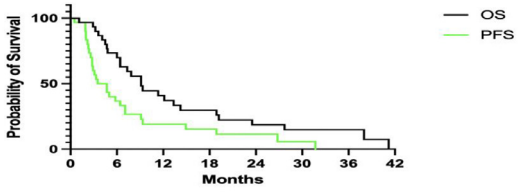
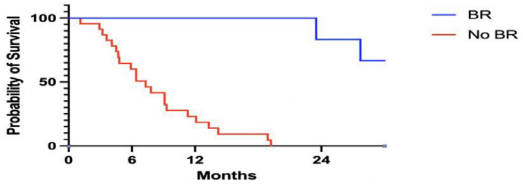



*Fig.1*: Overall and progression free survival




| Number at risk | | | | |
|---|---|---|---|---|
| *BR* | 7 | 7 | 7 | 6 |
| *No BR* | 23 | 14 | 6 | 0 |

*Fig. 2:* Survival per biological response

doi: 10.1016/j.dld.2024.01.154

## F-50

### ASAP score may predict HCC recurrence after complete radiological response to locoregional treatments

L. Canova [1,2], M. Iavarone [1], E. Alimenti [1], R. Perbellini [1], U. Renteria [3], R. D'Ambrosio [1], E. Degasperi [1], F. Facchetti [1], A.M. Ierardi [4], S. Sangiovanni [1], A. Ceriotti [3], P. Lampertico [1,5]

[1] *Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Università degli Studi di Milano, Milan, Italy*
[3] *Clinical Laboratory, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[4] *Radiology Department, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[5] *CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

**Background & Aims:** Alpha fetoprotein (AFP) and prothrombin induced by vitamin K absence/antagonist II (PIVKA-II) are biomarkers for hepatocellular carcinoma (HCC), which have been extensively in the diagnosis of HCC, while their use in the prognosis prediction remains poorly assessed. Recently, a new algorithm (ASAP) - including age, gender, AFP and PIVKA-II - has been validated as an alternative to GALAD for prediction of HCC development with a cut-off of 0.52. The identification of predictors of HCC recurrence after curative treatment has always been relevant to patients' management, and now may have further utility with the arrival of adjuvant therapies.

The aim of our study was to evaluate the predictive role of AFP and PIVKA-II alone or combined in the ASAP score for HCC recurrence in patients who achieved a complete response (CR) after locoregional treatment.

**Methods:** In this single-center, observational ongoing study, we have enrolled 156 consecutive patients with first diagnosis of HCC treated by ablation (MWTA) or chemoembolization (TACE). CR was evaluated by CT-scan 1 month after treatment, afterwards patients were evaluated every three months by CT-scan, clinical and biochemical features until recurrence, death or last follow up. PIVKA-II and AFP levels were measured at the day of treatment by Fujirebio assays, Japan.

**Results:** 81 (52%) patients with HCC who achieved CR after the first treatment were included: median age 66 (40-87); 83% men, 57% HCV-positive, 91% Child-Pugh A, 85% BCLC 0/A, 53% MWTA. The day of treatment, the median AFP was 6.3 ng/mL (1.3-3,537), median PIVKA-II was 112 (16-5,090) mAU/mL, median ASAP score was 0.405 (-3.44-6.64; 47% with ASAP value $>$ 0.52). During follow up, HCC recurred in 47 (58%) patients [median time to recurrence was 298 (41-1256) days after achieving CR]. PIVKA-II [HR 2.53 (95%CI 1.47-4.35), p=0.001] and age [HR 1.03 (95%CI 1.00-1.07), p=0.013] were the only independent predictors of overall HCC recurrence by a multivariable model for single variables only, while the ASAP score [HR 1.31 (95%CI 1.12-1.52), p$<$0.001] was the only independent predictor of recurrence in a multivariable model including only scores and algorithms. PIVKA-II [HR 2.14 (95%CI 1.09-4.18), p=0.026] was the only independent predictor of early recurrence in the first multivariable model, while platelet to lymphocyte ratio [PLR; HR 1.02 (95%CI 1.00-1.04)] and ASAP score [HR 1.30 (95%CI 1.03-1.64)] were independent predictors of early recurrence according to the second model. Adopting the ASAP cut-off of 0.52, the algorithm independently predicted HCC recurrence [HR 3.54 (95%CI 1.86-9.75), p$<$0.001], but did not predict HCC early recurrence [HR 1.95 (95%CI 0.87-4.34), p=0.103].

**Conclusions:** The ASAP algorithm may accurately predict HCC recurrence and early recurrence after complete radiological response, deserving further studies to refine the model.

doi: 10.1016/j.dld.2024.01.155

## F-51

### The synergic effect of metformin with atezolizumab/ bevacizumab in masld hcc patients: a retrospective study from arte multicentric Italian dataset

A. Dalbeni [1,2], M. Vicardi [2,3], L.A. Natola [1,2], A. Auriemma [3], B. Stefanini [4], C. Vivaldi [5], P. Federico [6], A. Palloni [7], C. Soldà [8], L. Lani [4], I. Garajova [9], S. Tamberi [10], S. De Lorenzo [11], F. Piscaglia [4,12], M. Milella [3], G. Masi [5], S. Lonardi [8], G. Brandi [4,7], B. Daniele [6], F. Trevisani [4,13], G. Svegliati-Baroni [14], F. Marra [15], F. Tovoli [4], D. Sacerdoti [2], on behalf of the ARTE study group

[1] *Unit of General Medicine C, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[2] *Liver Unit, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[3] *Section of Innovation Biomedicine-Oncology Area, Department of Engineering for Innovation Medicine (DIMI), University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[4] *Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy*
[5] *Unit of Medical Oncology 2, Azienda Ospedaliero- Universitaria Pisana, Pisa, Italy*
[6] *Medical Oncology Unit, Ospedale del Mare, Napoli, Italy*
[7] *Oncology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[8] *Oncology Unit 1, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy*
[9] *Medical Oncology Unit, University Hospital of Parma, Parma, Italy*
[10] *Medical Oncology Unit, "Degli Infermi" Hospital, AUSL della Romagna, Faenza*
[11] *Oncology Unit, Azienda USL Bologna, Bologna, Italy*
[12] *Unit of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[13] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[14] *Gastroenterology Unit, Polytechnic University of Marche, Ancona, Italy*
[15] *Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze, Firenze, Italy*

**Background:** The standard treatment of advanced HCC is immune checkpoint inhibitor (ICI) therapy. Metabolic dysfunction-associated steatotic liver disease (MASLD) appears to adversely affect the efficacy of ICI. Recently, the antidiabetic drug metformin has garnered attention for its possible antitumor and immunomodulatory properties, such as reduction of proinflammatory cytokines and CD8+ T cells activation during immunotherapy. The aim of our study was to investigate the role of metformin in patients treated with atezolizumab/bevacizumab (A+B).

**Patients and Methods:** 159 HCC patients (82% males, mean age 64.5) treated with A+B were enrolled from ARTE dataset. Clinical and radiological factors associated with patients' response to therapy were used to stratify objective response rate (ORR), overall survival (OS) and progression free survival (PFS) by Kaplan- Meier methodology, followed by Log-rank test in multivariate analysis.

**Results:** 53.3% patients had MASLD, with 31.9% being diabetic. No differences in OS, PFS and ORR were documented among the dif-

ferent etiologies. Considering 31 ORR patients, no differences between the two groups were underlined regarding sex, age, liver disease etiology. In the multistep multivariate model, diabetes was the only condition remained independently associate to ORR (OR 3.0, 95%CI 1.0-8.3; p=0.030). When diabetic patients were stratified based on antidiabetic treatments, those on metformin had a 12 months survival of 62% [44%-88%, 95% CI] vs insulin treatment with 21% [6%-72%, 95% CI], p<0.05.
**Conclusion:** Despite any clear difference in terms of ORR, OS and PFS between different etiologies, diabetic patients treated with metformin exhibited a better ORR and PFS, suggesting a potential immunological combination role of metformin with A+B treatment.

doi: 10.1016/j.dld.2024.01.156

## F-52

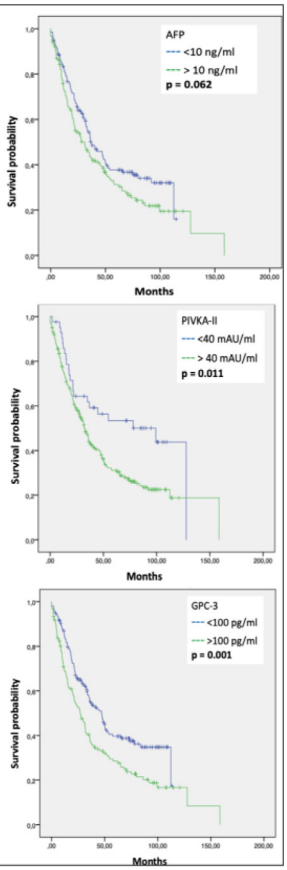
### The levels of AFP, PIVKA and GPC-3 serum biomarkers at diagnosis correlate with HCC clinical-pathological features and with overall survival

F. Damone [1,2], G.P. Caviglia [3], P. Colombatto [1], G. Ricco [1], F. Oliveri [1], S. Gaia [4], V. Romagnoli [1], D. Cavallone [1], E. Rolle [4], B. Coco [1], A. Salvati [1], L. Surace [1], P. Carucci [4], F. Bonino [5], M.R. Brunetto [1,5,6]

[1] *Hepatology Unit, Pisa University Hospital, Italy*
[2] *Gastroenterology Unit, Pisa University Hospital, Italy*
[3] *Department of Medical Sciences, University of Turin, Turin, Italy*
[4] *Unit of Gastroenterology, Città della Salute e della Scienza - Molinette Hospital, Turin, Italy*
[5] *Biostructure and Bio-imaging Institute of National Research Council of Italy*
[6] *Department of Clinical and Experimental Medicine, Pisa University, Pisa, Italy*

**Background:** Serum biomarkers role in the management of hepatocellular carcinoma (HCC) patients (pts) is debated. Aim of the study was to assess whether alpha-fetoprotein (AFP), protein induced by vitamin K absence-II (PIVKA) and glypican-3 (GPC-3) serum levels correlate with HCC pathological features and overall survival (OS).
**Material & Methods:** We retrospectively enrolled 293 pts from two tertiary referral centers (Pisa n=129 and Turin n=164): with a newly diagnosed HCC and available serum samples. AFP, PIVKA and GPC-3 were measured at diagnosis by commercial assays (Abbott, Fujirebio; pathologic cut-off values: 10 ng/ml, 40 mAU/ml and 100 pg/ml, respectively. Statistics used: $X^2$, Spearman test, Cox regression analysis.
**Results:** Figure 1a summarizes the main characteristics of study cohort**.** Out of 293 pts, 272 (92%) showed at least one elevated biomarker at diagnosis: PIVKA in 250 (85%), AFP in 153 (52%) and GPC-3 in 137 (47%). PIVKA was the only elevated biomarker in 86 (29%), AFP in 7 (2%) and GPC-3 in 3 (1%). Their serum levels directly correlate with the diameter of the largest lesion (AFP:p<0.001/rs=0.219;PIVKA: p<0.001/rs=0.447;GPC-3:p=0.009/rs=0.152).AFP levels correlated more with GPC-3 than PIVKA levels (p<0.001/rs=0.396 and p<0.001/rs=0.269). Higher levels of AFP and GPC-3 were found in HCV pts (median: 21.0vs6.1/p<0.001; median: 116.0vs82.8/p=0.018,respectively), in BCLC-C stage (median: 221.0vs7.9/p=0.046; median: 186.0vs85.0/p=0.027) and in pts with OS<12 months (median: 29.3vs9.0/p=0.049; median: 171.0vs85.0/p=0.002). PIVKA levels (p<0.001), single HCC (p<0.001), AST (p=0.002) and HBV active infection (p=0.021) were independently associated with OS. The survival curves according to baseline biomarker cut-offs are showed in figure 1b.
**Conclusions:** At diagnosis 92 % of pts showed elevated levels of at least one of the three HCC. PIVKA was the prevailing biomarker and independently associated with OS. AFP and GPC-3 are less prevalent and associated with more advanced disease and worst prognosis in the first 12 months.

| Variable | Category | N(%) or median (range) |
|---|---|---|
| Age at diagnosis | years | 69.4 (44.2-88.9) |
| Gender | Female | 63 (21.5) |
| | Male | 230 (78.5) |
| Etiology | HCV | 158 (54.2) |
| | HBV | 40 (13.4) |
| | Alcol | 26 (9.1) |
| | MAFLD | 61 (21.2) |
| | Other | 8 (3.1) |
| Child-Pugh Score | A | 270 (92.0) |
| | B | 22 (7.5) |
| | C | 1 (0.5) |
| Number of Lesion | Monofocal | 126 (43.0) |
| | Multifocal | 167 (57.0) |
| PVT | No | 257 (87.7) |
| | Yes | 36 (12.3) |
| Portal Hypertension | No | 172 (58.7 |
| | Yes | 121 (41.3) |
| BCLC Stage | 0 | 24 (8.2) |
| | A | 121 (41.0) |
| | B | 85 (29.0) |
| | C | 57 (23.8) |
| | D | 6 (2.0) |
| HCC diameter | cm | 3.20 (0.70-13.00) |




doi: 10.1016/j.dld.2024.01.157

## F-53

### Yttrium-90 Radioembolization in hepatocellular treatment beyond the BCLC guidelines: a single center experience

D. Costantino [1], C. Zavaglia [1], L. Cesarini [1], M. Fazio [1,6], G. Cabrini [2], S. Capitanio [2], C. Carbonini [3], D. Zanni [3], A. Rampoldi [4], M. Solcia [4], F. Morelli [4], P. Brambillasca [4], A. Alfonsi [4], A. Vanzulli [5], C. Sgrazzutti [5], I. Vicentin [5], L. Belli [1], C. Mazzarelli [1]

[1] *Hepatology and Gastroenterology, ASST GOM Niguarda, Milan, Italy*
[2] *Nuclear Medicine, ASST GOM Niguarda, Milan, Italy*
[3] *Medical Physics Department, ASST GOM Niguarda, Milan, Italy*
[4] *Interventional Radiology Unit, ASST GOM Niguarda, Milan, Italy*
[5] *Radiology, ASST GOM Niguarda, Milan, Italy*
[6] *Internal Medicine Residency Program, School of medicine, University of Insubria, Varese and Como*

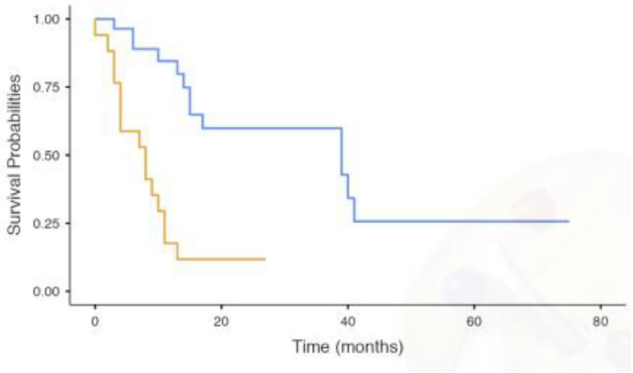
**Background:** Yttrium-90 Radioembolization (TARE) delivers microspheres loaded with a radioactive isotope (Y90) to a target lesion to promote radiation injury. This study was designed to evaluate the results of TARE in patients with intermediate and advanced HCC.
**Materials and Methods:** From September 2015 to February 2023, 56 patients were considered eligible for TARE after a multidisciplinary discussion at Niguarda Hospital. 10 were excluded after 99mTC albumin-macroaggregated test. Tumor response was as-

sessed according to modified Response Evaluation Criteria in Solid Tumor.

**Results:** Forty-six patients, with a mean age of 63.3 years, all Child-Pugh A. 82% were stage C according to BCLC, with 42% having PV3 and 31% PV2. Objective response rate (ORR) and disease control rate (DCR) were observed in 27 (58.6%) and 30 (65%) patients respectively. After TARE, 8 patients (17.3%) received curative treatment (resection or liver transplantation), 10 patients (21.7%) locoregional treatment, 12 patients (18.8%) were started on systemic treatment and 16 patients (35%) were referred to palliative care services. After a median follow-up of 344 days, 29 patients died (63%), 18 of them from HCC recurrence. Overall median survival (OS) was 14 months (range 11–40). The presence of PVT per se (p=0.3) did not affect survival, while patients with PVT 3 showed a significant trend for lower survival (p=0.068) when compared to patients with no or with limited thrombosis (PVT1 and PVT2). Tumor control rate significantly affected the patient outcome: treatment responders (CR and PR) had significantly better survival compared to non-responders (39 vs. 8 months, p <0.001) (Figure 1).

In univariate analysis, factors influencing OS were compensated liver function according to ALBI score (p 0.015), absence of portal hypertension (p 0,021), tumor size < 8 cm (p 0.05), and treatment response (p 0,001). After multivariate analysis, only treatment response (p 0-001 HR 6,64) and absence of portal hypertension (p=0.065 HR 2,65) resulted independently associated with survival. Since responders were significantly associated with better OS, the identification of factors that predict tumor response is important in clinical settings. Univariate analysis revealed that tumor size (<0.016) and PVT 3 (p = 0.013) were the only 2 factors associated with response failure.

**Conclusion:** TARE is a safe and effective option in patients with intermediate and advanced HCC, especially in those with size tumor <8 cm and limited tumor portal vein thrombosis (PV1 e PV2).




doi: 10.1016/j.dld.2024.01.158

## F-54

### The impact of metabolic risk factors on gender differences in HCC development and treatment allocation

D. Smith [1,2], A. Cespiati [1,2], C. Bertelli [1], R. Lombardi [1,2], A.L. Fracanzani [1,2]

[1] *SC Medicina ad Indirizzo Metabolico IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico di Milano*
[2] *Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti dell'Università degli studi di Milano*

**Introduction:** Liver's susceptibility to sexual hormones leads to gender differences in hepatocellular carcinoma (HCC). Metabolic comorbidities like obesity and diabetes, act as pro-oncogenic factors. Despite higher obesity rates in women, men with obesity face an increased HCC risk. The mechanism of this phenomenon is not fully understood. This study examines gender-based differences in HCC features and staging linked to metabolic comorbidities.

**Methods:** A retrospective evaluation was conducted, evaluating 126 patients (2014-2020) utilizing the Barcelona Clinic Liver Cancer (BCLC) system for staging and treatment decisions. A platelet count <150,000mm³ estimated portal hypertension in 65% of cases. Treatment distribution included 14% undergoing surgery, 74% receiving locoregional therapy, 3% systemic therapy, and 8% best supportive care.

**Results:** HCC prevalence was higher in men (78% vs. 22%), with men experiencing onset at a significantly younger age (67±11 vs. 74±11, p=0.04). Hepatitis C virus (HCV) was the primary etiology in both genders (41% in men vs. 70% in women, p=0.03). Men also presented with more lesions at onset (52% vs. 80%, p=0.03), were more diabetic (43% vs. 20%, p=0.04) and obese (64% vs. 38%, p=0.09). Metabolic comorbidities correlated with higher percentages of thrombocytopenia (71% vs. 56%, p=0.03) and hyperbilirubinemia (36% vs. 15%, p=0.04), regardless of gender. In multivariate analysis, the coexistence of metabolic risk factors strongly correlated with male gender (OR 10.8, p=0.04), low platelet levels (OR 6.7, p=0.03), and high bilirubin levels (OR 4.95, p=0.04), independently of age. However, multifocality at onset appeared to correlate with male gender (OR 10.5, p=0.04).

**Conclusion:** Our study establishes a robust association between metabolic risk factors and male gender, contributing to more severe liver disease and access to less curative treatments. Increased vigilance and early intervention for metabolic comorbidities are crucial for reducing disease progression risk and facilitating more curative HCC treatments.

doi: 10.1016/j.dld.2024.01.159

## F-55

### Serum ammonia predicts mortality in patients with hepatocellular carcinoma

P. Guerra [1], S. Cagnin [1], A.R. Caspanello [2], E. Libralesso [1], M. Tonon [1], C. Gambino [1], S. Piano [1], P. Pontisso [1], A. Martini [1], P. Angeli [1]

[1] *Dept. of Medicine, Unit of Hepatology and Interna Medicine, University of Padova, Italy*
[2] *Dept. of Clinical and Experimental Medicine, Unit of Medicine and Hepatology, University of Messina, Italy*

**Introduction:** ammonia levels have been recently associated with decompensation and liver-related death in patients with cirrhosis. Hepatocellular carcinoma (HCC) displays an alteration of ammonia metabolism, but its prognostic significance remains controversial. The present study aims to investigate the serum ammonia levels in relation to clinical outcomes in patients with HCC.

**Method:** 171 cirrhotic patients with HCC and available ammonia levels at presentation were evaluated in the Outpatient clinic (CMP) of the Padua Teaching Hospital and followed up until death and/or liver transplantation. Demographic, clinical, and laboratory data were collected. Patients were divided into two groups: altered-ammonia (AMMULN-ABNORM, n=20) or normal-ammonia (AMMULN-NORM, n=151). The median follow-up time was 22 months (range 11-43).

**Results:** the two groups of patients did not differ in age, aetiology of liver disease, Child-Pugh and MELD score, while patients in the AMMULN-ABNORM group presented a significantly higher ALBI grade. In addition, they were more frequently male (90% vs 74%; p=0.004) and presented at HCC diagnosis a signifi-

cantly higher frequency of diabetes (70% vs 30%; p<0.0001), portosystemic shunt (81% vs. 41%; p<0.0001) and previous episodes of hepatic encephalopathy (45% vs 31%; p=0.04). At HCC diagnosis, patients in the AMMULN-ABNORM group had higher BCLC stage (p=0.01) and nodule numbers (p=0.006). However, no differences were observed in AFP levels, frequency of metastasis, neoplastic thrombosis or nodule dimensions. Patients in the AMMULN-ABNORM group had lower overall survival at Kaplan-Meier curves (15 vs. 37 months; p=0.002). In Multivariate Cox Regression Analysis, abnormal ammonia levels were an independent predictor of mortality (aHR=2.37; p=0.008), together with BCLC stage (aHR=1.29; p<0.0001), ALBI grade (1.79; p=0.004), alpha-fetoprotein (aHR=1.000; p=0.003) and age (aHR=1.04; p<0.0001).
**Conclusions:** In patients with HCC, abnormal ammonia levels may be considered a negative prognostic indicator in a clinical setting, since they are independently associated with mortality.

doi: 10.1016/j.dld.2024.01.160

## F-56

### Do ACE inhibitors have a role in preventing drug-related proteinuria in advanced HCC patients?

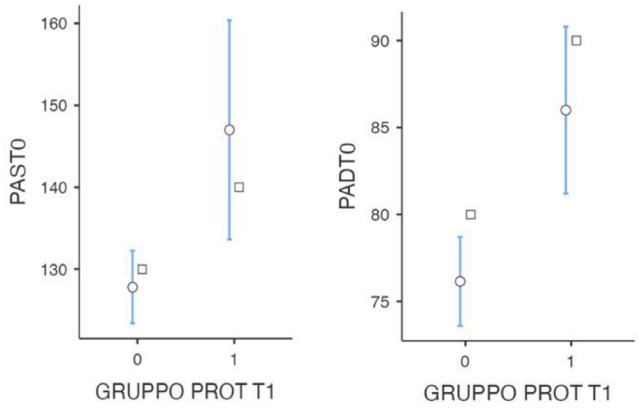
B. Stefanini [1,2], L. Ielasi [3], L.A. Natola [4,5], M. Milella [5], D. Sacerdoti [5], A. Auriemma [6], F.G. Foschi [3], F. Tovoli [2,3,4,5,6,7], F. Piscaglia [2,3,4,5,6,7], A. Dalbeni [4,5]

[1] *Department of Surgery & Cancer, Imperial College London, Hammersmith Hospital, Du Cane Road, W120HS, London, UK*
[2] *Department of Medical and Surgical Sciences, University of Bologna*
[3] *Department of Internal Medicine, Ospedale per gli Infermi di Faenza, 48018, Faenza, Italy*
[4] *Section of General Medicine C, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, 37134, Verona, Italy*
[5] *Liver Unit, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, 37134, Verona, Italy*
[6] *Section of Innovation Biomedicine-Oncology Area, Department of Engineering for Innovation Medicine (DIMI), University of Verona and University and Hospital Trust (AOUI) of Verona, 37134, Verona, Italy*
[7] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, 40138, Italy*

**Background and aim:** Both tyrosine-kinase inhibitors (TKI) and Atezolizumab/Bevacizumab (A+B) are used as systemic treatment for hepatocellular carcinoma (HCC). Hypertension and proteinuria are among most common side effects caused by these drugs and can lead to treatment discontinuation. Since Angiotensin-Converting Enzyme (ACE) inhibitors are known to reduce proteinuria, we aimed to verify if they had a protective role on proteinuria development
**Method:** We retrospectively included consecutive patients receiving systemic therapy as standard of care for non-resectable HCC from 3 different Italian centers and verified prevalence of proteinuria within 3 months from the start of treatment.

Differences between basal characteristics of the group were analyzed using a Mann-Whitney test or $X^2$. A regression analysis was performed to find potential predictors of proteinuria.
**Results:** A total of 151 patients were analyzed (54 receiving A+B, 97 receiving TKI). Significant proteinuria developed in 29 (19.2%) of the patients without differences between treatment regimen, history of hypertension or anti-hypertensive drug between the two groups. Only serum creatinine, systolic and diastolic blood pressure at the beginning of the treatment were significantly different (p = 0.023, p = 0.014, respectively).

Only a basal creatinine serum level and elevated systolic blood pressure (OR 1.14, p = 0.048) among who developed proteinuria were independently associated to the outcome.
**Conclusion:** Previous use of ACE inhibitors does not prevent proteinuria, however a scarce control of blood pressure at the beginning of systemic treatment is independently associated with its occurrence. An aggressive initial approach to lower systemic blood pressure seems justifiable.




doi: 10.1016/j.dld.2024.01.161

## F-57

### Aetiology of hepatocellular carcinoma and response to immunotherapy: is the problem inherent in the classification of non-viral disease?

F. Tovoli [1,2], R. Chen [1], C. Vivaldi [3], P. Federico [4], A. Palloni [5], L.A. Natola [6], C. Soldà [7], B. Stefanini [1], I. Garajova [8], L. Ielasi [9], S. De Lorenzo [10], A. Granito [1,2], G. Monaco [1], G. Masi [3], S. Lonardi [7], G. Brandi [1,5], B. Daniele [4], A. Dalbeni [6], L. Lani [1,11], G. Svegliati-Baroni [12], C. Campani [13], F. Piscaglia [1,2], on behalf of the ARTE study group

[1] *Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy*
[2] *Unit of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[3] *Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa*
[4] *Medical Oncology Unit, Ospedale del Mare, Napoli, Italy*
[5] *Oncology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[6] *Liver Unit, Medicine Department, University of Verona and University and Hospital Trust (AOUI) of Verona, Verona, Italy*
[7] *Oncology Unit 1, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy*
[8] *Medical Oncology Unit, University Hospital of Parma, Parma, Italy*
[9] *Department of Internal Medicine, Ospedale degli Infermi di Faenza, Faenza, Italy*
[10] *Oncology Unit, Azienda USL Bologna, Bologna, Italy*
[11] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy*
[12] *Gastroenterology Unit, Polytechnic University of Marche, Ancona, Italy*
[13] *Dipartimento di Medicina Sperimentale e Clinica, Università di Firenze, Firenze, Italy*

**Introduction:** Preclinical studies and post-hoc analyses of randomized clinical trials hint at a possible impaired efficacy of im-

mune checkpoint inhibitors in patients with non-viral hepatocellular carcinoma (HCC) in general and metabolic dysfunction-associated steatotic liver disease (MASLD) in specific. The heterogeneity of non-viral aetiologies and the possibility of multiple concurrent aetiologies may justify seemingly discordant data.
**Aim:** To explore and compare the objective response rate [ORR], disease control rate [DCR], progression-free survival [PFS], and overall survival [OS] of HCC patients treated with atezolizumab/bevacizumab (AB), stratified according to different criteria for non-viral etiologies and MASLD.
**Methods:** The ARTE database (March 2022-November 2023) prospectively enrolled patients treated with AB in a real-life setting. Three different classifications of HCC aetiologies were explored: 1) viral vs non-viral; 2) MASLD (either single-etiology or combined with other etiologies, for instance, HCV) vs non-MASLD; 3) single-etiology MASLD (sMASLD) vs non-sMASLD. ORR, DCR, PFS and OS comparisons were performed using univariable analyses and multivariable models, including other predictors of outcome.
**Results:** Data of 157 patients from 12 centres were collected. The ORR, DCR, median PFS and OS in the study population were 19.7%, 62.4%, 19.8 (95% CI 15.8-23.8) and 10.5 months (6.3-14.7), respectively. Stratification according to the viral vs non-viral etiologies did not capture differences in the main outcome measures (Figure). Conversely, patients with sMASLD had shorter PFS and a trend toward a lower DCR than controls but without differences in OS.
**Conclusions:** Viral and non-viral aetiologies had no significant differences in their response to AB. Patients with sMASLD had a shorter PFS than controls, but this difference did not translate into impaired survival. Based on current evidence, aetiology alone should not preclude patients from receiving immune-oncology drugs. A longer follow-up might help understand possible confounding effects from second-line therapies on the interpretation of OS.

doi: 10.1016/j.dld.2024.01.162

## F-58

### Exploring the role of aMAP and Toronto score: beyond diagnosis to prognosis

A. Cespiati [1,2], D. Smith [1,2], C. Bertelli [1], R. Lombardi [1,2], A.L. Fracanzani [1,2]

[1] *SC Medicina ad Indirizzo Metabolico, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Department of Pathophysiology and Transplantation, University of Milan, Italy*

**Background and Aims:** early identification of HCC is crucial for optimal curative treatment. aMAP and Toronto scores, validated for the first occurrence of HCC, lack validation for predicting early HCC recurrence after therapies. The early recurrence of HCC after treatment is a negative prognostic factor and it is related to both treatment and patient features.
**Aim:** to assess aMAP and Toronto scores' accuracy in predicting early HCC recurrence after locoregional treatment.
**Method:** 126 patients with HCC (mean age 69±11 years, 77% males) from 2014 to 2020 were enrolled. Early recurrence was defined as HCC recurrence within 2 years after the first treatment.
**Results:** cirrhosis etiologies were viral in 55%, alcohol-related in 22%, metabolic in 19%, iron overload-related in 4%. Even in non-metabolic cirrhosis, 59% had diabetes or obesity. At HCC diagnosis, 41% had more than one lesion, 12% underwent surgical resection, 77% locoregional treatment, 3% systemic therapy, and 8% best supportive care. Focusing on 96 locoregionally treated patients, 60% experienced early HCC recurrence. For the prediction of early recurrence, the accuracy of aMAP and Toronto scores were low (AUROC 0.63 for both). To optimize sensibility and sensitivity of the scores an aMAP > 74 and a Toronto score > 250 should be used (sensibility/specificity 54%/75% for aMAP score and 65%/63% for Toronto score). In patients with metabolic comorbidities, the accuracy of both scores for early recurrence decreased (AUROC of aMAP 0.40 vs 0.62 in metabolic and non-metabolic patients, respectively; AUROC of Toronto 0.50 vs 0.76, respectively).
**Conclusion:** aMAP and Toronto scores lacked accuracy in predicting early HCC recurrence after locoregional therapies. The presence of diabetes and obesity negatively affected both scores. Given the management implications of early HCC recurrence, there is a need to develop and validate specific scores for the assessment of early recurrence, considering diabetes and obesity presence.

doi: 10.1016/j.dld.2024.01.163

## F-59

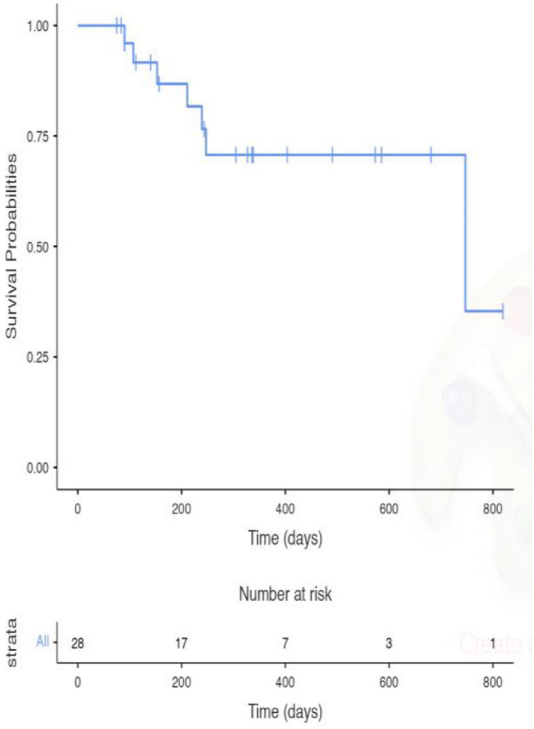
### Stereotactic body radiation therapy (SBRT) for HCC treatment: a single institution experience

C. Mazzarelli [1], D. Sibio [2], L. Cesarini [1], M.T. Patel [2], C. De Mattia [3], R. Viganò [1], G. Perricone [1], F. Aprile [1], M. Cucco [1], C. Becchetti [1], D. Costantino [1], M. Fazio [1,6], K. Bencardino [4], F. Villa [4], C. Sgrazzutti [5], I. Vicentin [5], M.F. Palazzi [2], L. Belli [1]

[1] *Hepatology and Gastroenterology, ASST GOM Niguarda, Milan, Italy*
[2] *Radiotherapy Unit, ASST GOM Niguarda, Milan, Italy*
[3] *Department of Medical Physics, ASST GOM Niguarda, Milan, Italy*
[4] *Oncology Unit, ASST GOM Niguarda, Milan, Italy*
[5] *Radiology, ASST GOM Niguarda, Milan, Italy*
[6] *Internal medicine residency program, school of medicine, University of Insubria, Varese and Como*

**Background and Aims:** Stereotactic body radiation therapy (SBRT) has an evolving role in the management of hepatocellular carcinoma (HCC), largely due to recent advances in imaging technology. SRBT is often the treatment choice, particularly for those who are not eligible for other locoregional treatment or because they are too frail. The aim of this study was to evaluate the efficacy and safety of SRBT in a consecutive series of Western patients treated at Niguarda Hospital.
**Methods:** SBRT was considered either when other locoregional therapies were not feasible for technical issues or in patients with multiple comorbidities. Response to treatment was evaluated according to mRecist criteria. Secondary endpoint was overall survival (OS).
**Results:** 30 consecutive patients, with a median age of 78.5 years (61-89), treated between June 2021 and June 2023 received SRBT without any significant adverse events or liver disease complications. All patients were cirrhotic (83.4% Child A/16.6% Child B7). The median size volum was 13 mm (10 mm-33 mm) and the median dose delivered was 50 Gy fractioned in 5 or 7 sessions. 23% of patients received at least a previous locoregional treatment for HCC. The overall response rate (Complete response + Partial response) was 76% (23/30 pts) and the disease control rate was 83% (25/30 pts). 8 patients experienced a tumor progression (evidence of new lesions or extrahepatic localizations). The median follow-up was 244 days (90-820), with a 2-year survival of 70%. **(Figure 1).**
**Conclusions:** Stereotactic body radiation therapy is a safe and effective therapeutic option for HCC lesions unsuitable to standard

loco-regional therapies, with acceptable local control rates and low treatment-related toxicity.




doi: 10.1016/j.dld.2024.01.164

## F-60

### CXCL3 is a target of miR-30e-3p and predicts tumor escape in sorafenib-treated HCC patients

C. Vianello [1,2], I. Leoni [1,2], G. Galvani [1,2], E. Monti [1,2], S. Marinelli [3], G. Marisi [4], A. Casadei Gardini [5], G.F. Foschi [6], C. Giovannini [1,7], M. Ravaioli [7,8], M. Cescon [7,8], F. Vasuri [9], M. Negrini [10], F. Piscaglia [3,7], C. Stefanelli [2], L. Gramantieri [3], F. Fornari [1,2]

[1] *Centre for Applied Biomedical Research - CRBA, University of Bologna, IRCCS Azienda Ospedaliero-Universitaria di Bologna, 40138, Bologna, Italy*
[2] *Department for Life Quality Studies, University of Bologna, 47921, Rimini, Italy*
[3] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, 40138, Bologna, Italy*
[4] *Biosciences Laboratory, Istituto di Ricovero e Cura a Carattere Scientifico di Natura Pubblica, Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori", 47014, Meldola, Italy*
[5] *Department of Oncology, Vita-Salute San Raffaele University, IRCCS San Raffaele Scientific Institute Hospital, 20132, Milan, Italy*
[6] *Department of Internal Medicine, Degli Infermi Hospital, AUSL Romagna, 48018, Faenza, Italy*
[7] *Department of Medical and Surgical Sciences, Bologna University, 40138, Bologna, Italy*
[8] *Hepato-biliary Surgery and Transplant Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, 40138, Bologna, Italy*
[9] *Pathology Unit, IRCCS Azienda-Ospedaliero Universitaria di Bologna, 40138, Bologna, Italy*
[10] *Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, 44100, Ferrara, Italy di Bologna, 40138, Bologna Italy*

**Introduction:** Possible curative options for hepatocellular carcinoma (HCC) are limited to a minority of patients who are diagnosed at an early stage. Immunotherapy and TKIs (sorafenib and lenvatinib) represent the first-line treatments in HCC. Despite immunotherapy has revolutionized HCC treatment, only a minority of patients respond to systemic treatments. The identification of biomarkers of drug response or tumor escape is still an unmet clinical need. MicroRNAs and chemokines play pivotal roles in tumor progression and drug resistance of HCC. We previously reported miR-30e-3p as a candidate for tumor escape in patients undergoing sorafenib treatment.
**Aims:** The aims of this study are to investigate CXCL3 regulation by miR-30e-3p, and to analyze its role in sorafenib resistance, and as a biomarker of tumor escape.
**Materials and Methods:** Serum and tissue miR-30e-3p and CXCL3 levels were analyzed by microarray and qPCR analysis in HCC patients and DEN-HCC rats. Functional analysis was used to assess CXCL3 targeting by miR-30e-3p in HCC cell lines. The contribution of CXLC3 to sorafenib response was evaluated in the DEN-HCC rat model. ELISA assay evaluated serum CXCL3 levels in sorafenib-treated HCC patients.
**Results:** CXCL3 was upregulated in human and rat HCCs and showed a direct correlation with CXCR2 and a negative one with miR-30e-3p. Functional analyses demonstrated CXCL3 targeting by miR-30e-3p in HCC cell lines, as confirmed by a luciferase reporter assay. Higher CXCL3 tissue levels associated with sorafenib resistance in the HCC rat model. In line, a negative correlation was detected between CXCL3 and apoptotic markers and positive one with tumor size in sorafenib-treated rats. Higher CXCL3 serum levels were observed in non-responder patients at the two-month follow-up.
**Conclusion:** CXCL3 is a novel target of miR-30e-3p in HCC and is involved in sorafenib resistance. CXCL3 is a promising circulating biomarker of early tumor escape in sorafenib-treated HCCs.

doi: 10.1016/j.dld.2024.01.165

## F-61

### Immunosuppressive contribution of tumor-infiltrating B cell subsets in human intrahepatic cholangiocarcinoma and their role in immunotherapy response

G. Milardi [1], B. Franceschini [1], C. Camisaschi [2], G. Costa [3], C. Soldani [1], P. Uva [4], D. Cangelosi [4], R. Carriero [5], G. Lodetti-Zangrandi [1], I. Malenica [6], M. Erreni [7], T. Pressiani [8], B. Cassani [9,10], G. Torzilli [3,11], L. Rimassa [8,11], A. Lleo [11,12]

[1] *Hepatobiliary Immunopathology Lab, IRCCS Humanitas Research Hospital, Rozzano, MI, Italy*
[2] *Flow Cytometry Core, IRCCS Humanitas Research Hospital, Rozzano, MI, Italy*
[3] *Division of Hepatobiliary and General Surgery, IRCCS Humanitas Research Hospital, Rozzano, MI, Italy*
[4] *Clinical Bioinformatics, IRCCS Istituto Giannina Gaslini, Genoa GE, Italy*
[5] *Bioinformatics Unit, Humanitas Research Hospital, Rozzano, MI, Italy*
[6] *Laboratory of Translational Immunology, IRCCS Humanitas Research Hospital, Rozzano, MI, Italy*
[7] *Multiscale ImmunoImaging Unit (mIIu), IRCCS Humanitas Research Hospital, Rozzano, MI, Italy*
[8] *Medical Oncology and Hematology Unit, IRCCS Humanitas Research Hospital, Rozzano, MI, Italy*
[9] *IRCCS Humanitas Research Hospital, Rozzano, MI, Italy*
[10] *Department of Medical Biotechnologies and Translational Medicine, Università Degli Studi di Milano, Milan MI, Italy*

[11] Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Italy
[12] Division of Internal Medicine and Hepatology, Department of Gastroenterology, IRCCS Humanitas Research Hospital, Rozzano, MI, Italy

**Background and Aim:** intrahepatic cholangiocarcinoma (iCCA) is a heterogeneous biliary tract cancer whose incidence rateincreased over the past decades. Due to the aggressive evolution of the disease, there is an urgent need for diagnostic and therapeutic alternatives. The immune infiltrate is a key component of the tumor microenvironment (TME), but remains poorly characterized, limiting the development of successful immunotherapies. Aspects related to T cells are undergoing extensive studies, while the effect exerted by B lymphocytes in iCCA development and progression is still controversial.
**Methods:** we characterized the B-cell compartment of tumor, tumor-free tissue and circulating counterpart of iCCA patients, performing high-dimensional single-cell technologies. We further carried out gene expression analysis and cellular assays to define B cell properties, investigating whether and how liver TME impacts B cell biology.
**Results:** results from single-cell RNA-sequencing of CD20+ cells in six iCCA patients identified four main subclusters and revealed a down-regulation of B cell activation/inflammatory genes in tumor compared to non-malignant tissue; suggesting an immunosuppressive condition of B cells in the TME. Multicolor flow cytometry analysis of B lymphocytes isolated from iCCA patients ($n$=19) highlighted a higher frequency of naïve B cells with respect to memory B in the tissue samples. Gene expression analysis and multiplex beads arrays showed higher expression levels and production of immunoregulatory cytokines within the tumor compared to non-tumoral tissue. A lower level of immunoglobulins was also detected in iCCA plasma samples. This may be caused by tumor and stromal cells that affect B cell skewing and activation state.

Immunohistochemical analyses highlighted that B cells, when infiltrate the tissues, create cellular aggregates similar to tertiary lymphoid structures (TLS). TLS density outside the tumor area positively correlated with better disease-free survival.

Circulating Bs from iCCA patients ($n$=19) treated with chemoimmunotherapy (gem-cis plus durvalumab) underwent phenotypic and functional variations. Responder patients showed a higher frequency of transitional and naïve B cells, more activated than the non-responder group, where we found an increase of memory B and plasmablasts.
**Conclusion:** the results sustain the heterogeneity of the B cell population within the TME and peripheral blood of iCCA patients, with a potential contribution to immunosuppressive function in the tumor burden. Findings from these cohorts also provide important insights into the role of B cells in response to chemoimmunotherapy. A deeper analysis of B cell subsets and crosstalk with other cells of the iCCA milieu will be exploitable for improving the therapy's effectiveness and developing new ones.

doi: 10.1016/j.dld.2024.01.166

## F-62

### The OSM/OSMR$\beta$ signalling axis in the development of MASLD-related hepatocellular carcinoma

J. Nurcis [1], S. Sutti [2], B. Foglia [1], A. Provera [2], C. Vecchio [2], C. Rosso [3], M. Maggiora [1], G. Caviglia [3], E. Bugianesi [3], E. Albano [2], M. Parola [1], S. Cannito [1]

[1] Dept. Clinical and Biological Sciences, Unit of Experimental Medicine & Clinical Pathology, University of Torino, Italy
[2] Dept. Health Sciences and Interdisciplinary Research Center for Autoimmune Diseases, University Amedeo Avogadro of East Piedmont, Novara, Italy
[3] Dept. Medical Sciences, University of Torino, Italy

**Introduction:** Metabolic dysfunction-associated steatotic liver disease (MASLD) is a spectrum of chronic liver disease that ranges from simple steatosis to metabolic-associated steatohepatitis (MASH) and it is emerging as the most rapidly raising cause of hepatocellular carcinoma (HCC) development. Oncostatin M (OSM) is a pleiotropic cytokine belonging to the IL-6 family suggested to promote different aspects related to tumor development and progression.
**Aim:** The aim of the study is to investigate the potential role of OSM in modulating the tumor microenvironment by affecting crucial events related to HCC progression.
**Materials and Methods:** In this study we have employed: I) mice genetically manipulated to delete OSMR$\beta$ in hepatocytes (OSMR$\beta$-/- mice) as well as control WT littermates, submitted to the experimental DEN/CDAA MASH-related protocol of liver carcinogenesis; II) cohort of MASLD patients carrying or not HCC.
**Results:** In OSMR$\beta$-/- mice the induction and progression of MASH-related liver tumors, as compared to WT mice, is characterized by: i) a significant decrease in tumor masses; ii) a significant reduction of angiogenic switch; iii) an impairment in proliferation indexes; iv) a significant decrease of immunosuppressive microenvironment. A homologous immunosuppressive trend was observed in a small cohort of human MASH-related HCC patients. Moreover, Multiplex Immunoassay analyses revealed a significant increase of a subset of cytokines that can be found in the immunosuppressive tumor microenvironment (including IL1$\beta$, CCL2, IL8, CXCL13). Of interest, transcript levels of these cytokines and chemokines correlated with OSM expression in MASLD patients and were significantly reduced in OSMR$\beta$-/- mice vs WT mice
**Conclusions:** These results indicate that OSM may play a crucial role in the progression of MASH-associated HCC by contributing to the formation of an immunosuppressive tumor microenvironment able to favor evasion of cancer cells from the control of immune system.

doi: 10.1016/j.dld.2024.01.167

## F-63

### Role of ganglioside GD2 in the stem-like compartment of intrahepatic cholangiocarcinoma

A. Mannini [1], M. Pastore [1], M. Correnti [2], T. Lottini [1], B. Piombanti [1], I. Tusa [3], E. Rovida [3], C. Coulouarn [4], J.B. Andersen [5], M. Lewinska [5], C. Campani [1], V.L. Battula [6], Y. Bin [6], M. Aureli [7], E.V. Carsana [7], C. Peraldo Neia [8], P. Ostano [8], L. Di Tommaso [9], F. Marra [1], C. Raggi [1]

[1] Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy
[2] Department of Biomedical Sciences for Health, University of Milan, Milan, Italy
[3] Department of Experimental and Clinical Biomedical Sciences 'Mario Serio', University of Florence, Florence, Italy
[4] Univ Rennes, Inserm, Inra, Institut NUMECAN (Nutrition Metabolisms and Cancer) - UMR_S 1241, UMR_A 1341, F35000, Rennes, France
[5] Biotech Research and Innovation Centre, University of Copenhagen, Copenhagen, Denmark
[6] Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
[7] Department of Medical Biotechnology and Translational Medicine, University of Milan, Italy

[8] *Fondazione Edo ed Elvo Tempia Valenta, Biella, Italy*
[9] *Humanitas Research Hospital -IRCCS, Pathology Unit, Rozzano, Italy*

**Background and Aims:** Due to the lack of proper biomarkers and potentially effective treatments, the management of cholangiocarcinoma (CCA) is still challenging. Ion channels have been proven to be novel biomarkers and new targets for cancer therapy, due to their easy druggability. The voltage-gated K+ channel hERG1 exerts pleiotropic effects in cancer cells. This study explored the role of hERG1 in the biology of intrahepatic CCA (iCCA).
**Method:** Validation of hERG1 in iCCA tissues was performed in TCGA database. In vitro experiments were conducted to estimate the impact of hERG1 inhibition on cell function in iCCA cell lines (HUCCT1, CCLP1, CCA4).
**Results:** A significant difference in hERG1 gene expression was observed between iCCA and normal tissue samples. Similarly, iCCA cell lines showed significantly higher protein content of hERG1 compared to normal cholangiocytes (NHC3). Treatment with E4031, a selective hERG1 inhibitor, showed a limited impact on cell growth, but a substantial reduction of the invasive capabilities of iCCA cells. Immunoprecipitation assays and immunofluorescence revealed the formation of an active macromolecular complex with $\beta 1$ integrin responsible for VEGF-A activation through AKT signaling. Treatment with a bispecific antibody (scDb: single-chain Diabody) that binds the hERG1-$\beta 1$ complex, negatively impacted the invasiveness of iCCA cells as well as expression of genes regulating epithelial to mesenchymal transition. In vitro co-treatment with scDb and cisplatin-gemcitabine, significantly reduced growth of iCCA cells.
**Conclusion:** This study indicates that hERG1 may be relevant in promoting the malignant characteristics of iCCA.

doi: 10.1016/j.dld.2024.01.168

## F-64

### Targeting RuvBL1 reduces mTOR-driven NASH-HCC progression in conditional PTEN-KO mice

A. Guida [1], I. Simeone [2], D. Papini [2], S. Polvani [2], G. Dragoni [2], E. Ceni [2], L. Picariello [2], A. Galli [2], T. Mello [2]

[1] *GenOMeC Doctorate, University of Siena, Siena, Italy*
[2] *Department of Clinical and Experimental Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy*

**Introduction:** RuvBL1 belongs to the highly conserved AAA+ ATPases. It is deregulated in various human cancers and its expression correlates with a worse prognosis in HCC patients. We previously found that RuvBL1 haploinsufficiency impairs the PI3K/Akt/mTOR pathway in liver.
**Aim:** Given the relevance of mTOR pathway hyperactivation in HCC, we hypothesized that RuvBL1 genetic targeting could reduce mTOR-driven hepatocarcinogenesis.
**Material and Methods Results:** $Pten^{hep-/-}$ and $Ruvbl1^{hep+/-}$ mice were crossed to generate $Pten^{hep-/-}Ruvbl1^{hep+/-}$ mice. NASH was assessed by histology at 12 weeks of age. Metabolic and inflammatory markers were evaluated by qPCR and IHC. mTOR pathway was analysed by WB of liver lysates. PPARalpha activity was evaluated by luciferase reporter assay. RuvBL1 interactome was evaluated by MS proteomics of RuvBL1-IP. HCC development was assessed by macroscopic tumour count and by histology. AML-12 PTEN KO cells were generated by CRISPR-Cas9 genome editing.

$Pten^{hep-/-}Ruvbl1^{hep+/-}$ developed significantly less steatosis, fibrosis, and inflammation compared to $Pten^{hep-/-}$ mice. The mTOR-driven lipogenic targets were similarly expressed in the two mice models. However, *Ppara* and its target CPT1 was increased in $Pten^{hep-/-}Ruvbl1^{hep+/-}$. The spontaneous and insulin-induced accumulation of lipid droplets in PTEN KO AML-12 cells was completely abrogated by RuvBL1 inhibition with CB-6644. Inhibition of RuvBL1 activity by CB-6644 increased PPARalpha transcriptional activity in AML-12 WT and PTEN KO. Analysis of RuvBL1-IP in AML-12 revealed that RuvBL1 interacts with members of the lysosomal AMPK complex. Furthermore, p-AMPK and p-RAPTOR were increased in $Pten^{hep-/-}Ruvbl1^{hep+/-}$ compared to $Pten^{hep-/-}$ mice. Finally, $Pten^{hep-/-}Ruvbl1^{hep+/-}$ mice aged to 15 months showed better survival than $Pten^{hep-/-}$ which developed significantly more HCC and of higher grade. qPCR analysis showed a significant upregulation of key lipolytic genes, such as *Cpt1a, Acadl, Acadvl* and *Ppara,* in $Pten^{hep-/-}Ruvbl1^{hep+/-}$ at 15 months of age.
**Conclusion:** RuvBL1 targeting reduces mTOR hyperactivation hampering NASH-HCC progression in $Pten^{hep-/-}$ mice, likely promoting the switch from mTOR-driven lipogenesis to AMPK-induced fatty acid catabolism

doi: 10.1016/j.dld.2024.01.169

## F-65

### MiR-22 regulates HIF-1A pathway and tumor progression and represents a possible biomarker of sorafenib response in hepatocellular carcinoma

G. Galvani [1,2], I. Leoni [1,2], E. Monti [1,2], C. Vianello [1,2], S. Marinelli [3], G. Marisi [4], A. Casadei Gardini [5], G.F. Foschi [6], C. Giovannini [1,7], M. Baldassarre [8], M. Ravaioli [7,9], M. Cescon [7,9], F. Vasuri [10], M. Domenicali [7], M. Negrini [11], F. Piscaglia [3,7], C. Stefanelli [2], L. Gramantieri [3], F. Fornari [1,2]

[1] *Centre for Applied Biomedical Research - CRBA, University of Bologna, IRCCS Azienda Ospedaliero-Universitaria di Bologna, 40138, Bologna, Italy*
[2] *Department for Life Quality Studies, University of Bologna, 47921, Rimini, Italy*
[3] *Division of Internal Medicine, Hepatobiliary and Immunoallergic Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, 40138, Bologna, Italy*
[4] *Biosciences Laboratory, Istituto di Ricovero e Cura a Carattere Scientifico di Natura Pubblica, Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori", 47014, Meldola, Italy*
[5] *Department of Oncology, Vita-Salute San Raffaele University, IRCCS San Raffaele Scientific Institute Hospital, 20132, Milan, Italy*
[6] *Department of Internal Medicine, Degli Infermi Hospital, AUSL Romagna, 48018, Faenza, Italy*
[7] *Department of Medical and Surgical Sciences, Bologna University, 40138, Bologna, Italy*
[8] *Unit of Semeiotics, Liver and Alcohol-related diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, 40138, Bologna, Italy*
[9] *Hepato-biliary Surgery and Transplant Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, 40138, Bologna, Italy*
[10] *Pathology Unit, IRCCS Azienda-Ospedaliero Universitaria di Bologna, 40138, Bologna, Italy*
[11] *Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, 44100, Ferrara, Italy di Bologna, 40138, Bologna Italy*

**Introduction:** Hepatocellular carcinoma (HCC) represents the third leading cause of cancer mortality worldwide with approximately 40% of patients diagnosed at advanced stages. Immunotherapy and tyrosine-kinase inhibitors sorafenib and lenvatinib represent the first-line treatments in HCC. Despite immunotherapy has revolutionized HCC management, advanced stages are characterized by limited response and early onset of drug-resistance. The identifica-

tion of biomarkers of treatment response or tumor escape is still an unmet clinical need.
**Aims:** The aims of this study are to investigate miR-22 contribution to HCC tumorigenesis and sorafenib response, and to analyze its role as a biomarker of drug response.
**Materials and Methods:** Serum and tissue miR-22 levels were analyzed by qPCR in HCC patients and DEN-HCC rats. Proliferation and apoptosis assays and live imaging analysis evaluated miR-22 influence on HCC phenotype in vitro. A xenograft mouse model was used to determine the role of miR-22 on HCC tumorigenesis. Functional analysis elucidated the regulation of HIF-1A pathway following miR-22 modulation in different settings.
**Results:** MiR-22 was downregulated in human and rat HCCs and associated with microvascular invasion, tumor grade, and a worse overall survival. In vitro assays revealed that miR-22 inhibits cell growth in normoxic and hypoxic conditions and blocked HIF-1A pathway in HCC cells. Regarding *in vivo* tumorigenesis, miR-22 silencing gave rise to bigger and more vascularized tumor masses in xenograft mice. Lower miR-22 tissue levels associated with sorafenib resistance and correlated with apoptotic markers in the rat model while serum levels showed the opposite. In sorafenib-treated patients, a positive correlation between circulating miR-22 levels and days of treatment was observed. In line, lower miR-22 basal levels were detected in non-responder HCCs.
**Conclusion:** Low miR-22 levels favor HCC tumorigenesis and associate with a poor prognosis. MiR-22 influences sorafenib sensitivity and deserves attention as a possible biomarker of treatment response.

doi: 10.1016/j.dld.2024.01.170

## F-66

### Liposomal doxorubicin targeted with the Fab' of atezolizumab exerts an immunomodulatory effect in in vitro models of hepatocellular carcinoma

I. Zanotto, D. Gabbia, A. Grigoletto, M. Toffanin, V. Mazzucco, A. De Rossi, G. Pasut, S. De Martin

*Dept. of Pharmaceutical and Pharmacological Sciences, University of Padova, Padova, Italy*

**Introduction:** PD-L1, one of the most studied immune checkpoints, represents a key pharmacological target for HCC therapy. Atezolizumab, a monoclonal antibody inhibiting PD-L1 and restoring T-cell–mediated antitumor activity, is approved for advanced HCC therapy in combination with bevacizumab. Liposomal doxorubicin (DXR) targeted with the Fab' of atezolizumab (SIL treatment) reduced tumor growth in preclinical models of HCC.
**Aim:** unravel the effect of PD-L1 targeted liposomal DXR on the immune phenotype of tumor associated macrophages and liver cancer cells, and on their invasiveness, using untargeted liposomal DXR as a control (SL treatment), in 2D and 3D cellular HCC models.
**Materials and Methods:** The effect of SIL and SL treatments on PD-L1 expression was evaluated in HepG2 2D cultures and spheroids treated with INF-gamma to induce its overexpression. Both liposomal formulations were tested to assess the effect on macrophage polarization, clonogenicity and invasiveness on HepG2 spheroids co-cultured with THP-1 monocytic cells. The effect of SL and SIL on the epithelial-to-mesenchymal transition (EMT) of HepG2 cells was evaluated on the epithelial marker Eâ€'cadherin and the mesenchymal marker Vimentin by immunocytochemistry.
**Results:** Only SIL significantly decreased the INF-gamma-induced PD-L1 overexpression in HepG2 2D cultures and spheroids ($p<0.01$ and $p<0.001$ respectively), showing immunomodulatory activity. In THP-1/HepG2 spheroids, SL and SIL decreased clonogenicity and invasiveness of HepG2 cells ($p<0.0001$) and pro-tumoral CD163-expressing macrophages ($p<0.0001$). Only SIL caused a significant downregulation of PD-L1 expression ($p<0.01$). Accordingly, they significantly increased E-cadherin expression and decreased Vimentin one, downregulated and upregulated by TNF-$\alpha$, respectively, at variance to SL ($p< 0.001$). Furthermore, SIL downregulated PD-L1 expression also in the TNF-$\alpha$ model ($p<0.001$ vs SL).
**Conclusion:** PD-L1-targeted liposomal DXR enhances the cytotoxic effect of liposomal doxorubicin and plays an immunomodulatory activity by decreasing PD-L1 expression and prompting macrophage polarization towards an antitumoral phenotype, showing promising results in preclinical models of HCC.

doi: 10.1016/j.dld.2024.01.171

## F-67

### RUVBL1 correlates with chaperones expression in HCC and its activity is required for HSF1-mediated stress response

T. Mello [1], A. Guida [1,2], I. Simeone [1], D. Papini [1], F. Vannucci [1], G. Defazio [1], S. Polvani [1], E. Ceni [1], G. Dragoni [1], T. Innocenti [1,2], L. Picariello [1], A. Galli [1]

[1] *Dept. of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy*
[2] *GenOMeC Doctorate, University of Siena, Siena, Italy*

RuvBL1 is an AAA+ ATPase involved in multiple cellular activities including proliferation, chromatin remodeling, gene expression and translation. High RuvBL1 expression correlates with a worse prognosis in HCC and other human tumors. Emerging data suggests that RuvBL1 might exert co-chaperone functions.

Aim of this study is to investigate the relations between RuvBL1 and molecular chaperones in HCC.

Gene expression analysis of the human HCC samples in the TCGA_LIHC cohort shows that RuvBL1 significantly correlates with the expression of dozens of HSPs family members, with all the TCP-1 ring complex (TRiC) genes and with the transcription factor HSF1. Combining gene expression data from the LIHC_TCGA with publicly available CHIP-seq dataset (CHIP-Atlas and HSF1base) we identified a subset of potential common targets of RuvBL1 and HSF1, which includes several HSPs and all the TRiC genes. Reactome analysis revealed that regulation of cytosolic and mitochondrial translation were among the top enriched pathway regulated by shared RUVBL1 and HSF1 targets. The expression of selected shared targets was evaluated by qPCR in AML-12 and Huh7 cells treated with the RUVBL1/2 ATPase inhibitor CB6644 under basal and stressed conditions. The Heat Shock (HS)- or mitochondrial UPR (mtUPR)-induced expression of HSP90AA1(Hsp90alpha), HSPE1(Hsp10), HSPH1(Hsp110) was abrogated by treatment with CB6644. HSPA8 (Hsp70a8) was induced by mtUPR but not by HS, HSPA4(Hsp70a4) and all the TRiC genes were not induced by either stresses but were nonetheless downregulated by CB6644. HSF1 transcriptional activity, measured in AML-12 clones stably expressing a HSE-Nanoluc reporter, was readily induced by HS or mtUPR and completely abrogated by CB6644. Finally, proximity ligation assay revealed a close interaction of RuvBL1 and Hsf1 proteins in the nucleus of Huh7 cells.

In conclusion, RUVBL1 and HSF1 appears to coordinate the expression of several chaperone genes involved in cytosolic and mitochondrial translation. Targeting RuvBL1/2 activity impairs HSF1-mediated stress-response.

doi: 10.1016/j.dld.2024.01.172

## F-68

### Expression of deiodinases-3 in HCC as predictor of poor tumor differentiation

V. Cossiga [1], C. Luongo [2], R. Montalti [3], G. Pontillo [1], M. Guarino [1], G. Rompianesi [4], M.A. De Stefano [2], M.C. Giglio [4], M. Capasso [1], A. De Conte [1], L. Ranieri [1], R. Troisi [4], D. Salvatore [2], F. Morisco [1]

[1] *Department of Clinical Medicine and Surgery, Diseases of the liver and biliary system Unit, University of Naples "Federico II", Naples, Italy*
[2] *Department of Clinical Medicine and Surgery, Endocrinology Unit, University of Naples Federico II, Naples, Italy*
[3] *Department of Public Health, University "Federico II", Naples, Italy*
[4] *Department of Clinical Medicine and Surgery, Division of Hepato-Bilio-Pancreatic, Minimally Invasive and Robotic Surgery, Federico II University Hospital, Naples, Italy*

**Background/Aim:** The complex signalling pathways of thyroid hormones (TH) has been recently involved in the liver diseases pathogenesis. Particularly, it has been proven that the expression of deiodinases type-1 and 3 (D1-3) changes during liver injury, but their role is still poorly understood in hepatocarcinogenesis process. We aimed to evaluate the role of TH signalling pathway in liver carcinogenesis.
**Methods:** In this prospective study, 49 patients underwent liver surgery for HCC in cirrhosis (31 cases) or for other non-neoplastic indication in non-cirrhotic context (18 controls). We evaluated genes and protein expression of the main TH metabolism factors (D1, Monocarboxylate transporter-MCT8, Thyroid receptors-TR alpha and beta, Kruppel-like factor-KLF-9 and TH-responsive SPOT-14 gene), with RT-PCR and Western blot analysis in HCC, cirrhotic tissue and healthy liver samples.
**Results:** RT-PCR analysis showed a progressive statistically significant decrease of D1 (p=0.003), MCT-8 (p=0.001), and TR$\beta$ (p=0.04) mRNA expression from healthy liver to HCC. The expression of KLF9, involved in cell differentiation and proliferation, decreased accordingly (p=0.01). Similarly, the expression of SPOT14 decreased in relation to reduced TH activation (p=0.009). Western Blot analysis showed a decreased expression of D1 protein in all cirrhotic samples (p=0.01), while D3 increased in 50% of HCC (p=0.02). Among HCC patients, D3 expression was associated with poor tumor differentiation compared to D3 negative HCC subjects (p=0.007). Furthermore, a shorter Progression Free Survival was observed in D3 positive patients (19.2 months vs 47.2 months), even if not statistically significant
**Conclusions:** These preliminary data showed that D3 expression could define a more severe phenotype of HCC with poor tumor differentiation. Moreover, the signalling pathway of TH is dysregulated in HCC, with intrahepatic hypothyroidism. However, these results need to be confirmed in large cohorts

doi: 10.1016/j.dld.2024.01.173

Digestive and Liver Disease 56 (2024) S99

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

# A.I.S.F. 2024: Abstracts Evaluation Procedure

Thanks to experts evaluating all the abstracts according to predetermined Clinical and Experimental categories.

The experts for the 2024 Annual Meeting are listed below:

**Category A. "EXPERIMENTAL VIRAL HEPATITIS"**
*C. Ferrari, Parma - T. Pollicino, Messina - P. Pontisso, Padua - V. Svicher, Rome*

**Category B. "HEPATITIS B & DELTA CLINICAL"**
*B. Coco, Pisa - V. Di Marco, Palermo, - A. Marzano, Turin - G. Taliani, Rome*

**Category C. "HEPATITIS C CLINICAL"**
*A. Mangia, S.G. Rotondo (FG) - F. Morisco, Naples - M. Viganò, Milan - A.L. Zignego, Florence*

**Category D. "NAFLD & ALD EXPERIMENTAL"**
*A. Alisi, Rome - P. Dongiovanni, Milan - A. Federico, Naples - L. Valenti, Milan*

**Category E. "NAFLD & ALD CLINICAL"**
*E. Bugianesi, Turin - A. Fracanzani, Milan - G. Marchesini, Bologna - L. Miele, Rome - S. Petta, Palermo - F. Salomone, Catania*

**Category F. "AUTOIMMUNE HEPATITIS & BILIARY DISEASE"**
*M. Carbone, Milan - V. Cardinale, Rome - A. Floreani, Padua - C. Rigamonti, Novara*

**Category H. "EXPERIMENTAL LIVER DAMAGE, FIBROSIS, CIRRHOSIS & PORTAL HYPERTENSION"**
*M. Fraquelli, Milan - F. Marra, Florence - M. Parola, Turin - G. Svegliati-Baroni, Ancona*

**Category I. "FIBROSIS, CIRRHOSIS & PORTAL HYPERTENSION CLINICAL"**
*P. Caraceni, Bologna - S. Montagnese, Padua - S. Piano, Padua - F. Schepis, Modena - M. Senzolo, Padua - G. Tosetti, Milan - L. Turco, Bologna*

**Category L. "HEPATOCELLULAR CARCINOMA EXPERIMENTAL"**
*G. Missale, Parma - F. Farinati, Padua - E. Villa Modena*

**Category M. "HEPATOCELLULAR CARCINOMA CLINICAL"**
*A. Aghemo, Rozzano (MI) - A. Cucchetti, Bologna - M. Iavarone, Milan - F. Piscaglia, Bologna - F. Trevisani, Bologna - A. Vitale, Padua*

**Category N. "LIVER FAILURE, HEPATOBILIARY SURGERY & TRANSPLANTATION"**
*L. Baiocchi, Rome - P. Burra, Padua - M.F. Donato, Milan - S. Ginanni Corradini – E. Gringeri, Padua - L. Pasulo, Bergamo*

**Category O. "MISCELLANEOUS: GENETIC, PEDIATRIC, NUTRACEUTICALS, DILI, OTHER"**
*G. Germani, Padua - A. Lleo, Rozzano (MI) - F.P. Russo, Padua - A. Zocco, Rome*

https://doi.org/10.1016/j.dld.2024.01.174
1590-8658