[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

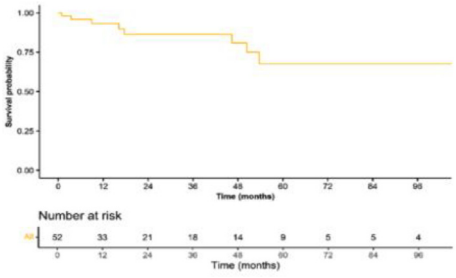
F-46

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]