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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.

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Involvement of the potassium channel ERG1 in cholangiocarcinoma

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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.

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TKIs treatment for HCC before Liver transplantation: an ELITA/ELTR collaborative study

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