Advanced systemic therapy for hepatocellular carcinoma

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Primary liver cancer is sixt most common cancer and third leading cancer related cause of death in the world according to GLOBOCAN 2022. Hepatocellular carcinoma (HCC) accounts for 75–85% of primary liver cancer cases (1). Curative treatment can be offered to patients in early stages of the disease. However, the majority of patients is diagnosed at an advanced stage and they can be only offered systemic therapy in case of perserved liver function, good performance status and absence of significant comorbidities (2). For over a decade, receptor tyrosine inhibitors, including sorafenib and later lenvatinib, have been the only first-line options (3,4). The turning point in patient management was in 2020, when a phase III IMbrave trial started a new era in immune checkpoint inhibitor therapy. In this landmark study, the combination ob anti-PD-L1 monoclonal atibody atezolizumab and anti-vascular endothelial growth factor bevacizumab showed superiority to sorafenib in terms of overall survival (OS) and several other clinical endopoints (5). Himalaya study was another succesful phase III study comparing dual immunotherapy with durvalumab and tremelimumab to sorafenib. This combination also showed superior efficacy in terms of OS. Durvalumab in monotherapy was noninferior to sorafenib. (6) Other promising first line combination studies (LEAP-002, COSMIC-312, CARES-310) showed promising results but none showed significat advantage over control regimens (7,8,9). On basis of IMbrave 150 study, several studies evaluating triple drug regimens are being conducted.

Regorafenib, cabozantinib and ramucirumab are drugs of choice in second line setting, as well as immunotherapy with nivolumab/ipilimumab or pembrolizumab for patients who are immunotherapy-naive. (10,11,12,13,14)

There has been an immense progress in field of advanced HCC in recent years, however there is still a significat procentage of patients with advanced HCC who suffer from therapeutic resistance and disease progression so future studies and precise personalized medicine is needed. (15)

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