肝細胞癌的最新治療

New treatment of hepatocellular carcinoma

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Hepatocellular carcinoma (HCC) ranks the second leading cause of cancer death for men, and the sixth for women, globally. Despite the advances in surveillance and HBV vaccination, a large number of cases are still at an unresectable, advanced stage and require systemic treatment. Sorafenib, a multi-kinase inhibitor that inhibits tumor-cell proliferation and angiogenesis, has been applied in patients with advanced HCC for a decade. However, the efficacy of sorafenib is not satisfactory; and the median time to progression ranges from 2.8 to 5.5 months. Recently, several clinical trials for the first or second lines of advanced HCC treatment had achieved positive results. Regorafenib is an oral multikinase inhibitor that blocks the activity of protein kinases involved in angiogenesis, oncogenesis, and the tumor microenvironment. It has a distinct molecular target profile and more potent pharmacologic activity than sorafenib in preclinical studies. The RESORCE trial shows that regorafenib improved overall survival with a hazard ratio of 0.63 (95%CI 0.50–0.79; P<0.001) and a median survival of 10.6 months versus 7.8 months with placebo in patients with HCC that progressed on sorafenib treatment. Sorafenib regorafenib sequential treatment can extend the survival to 26 months in selected patients with advanced HCC. Lenvatinib is a multitargeted TKI of the VEGFRs 1, 2, and 3, FGFRs 1–4, PDGFR α, RET, and KIT signaling networks. The phase 3 clinical trial of lenvatinib (RELFECT study) disclosed a comparable mOS of lenvatinib with sorafenib (13.6mo vs 12.3mo), but lenvatinib had a significant longer progression-free survival than sorafenib (7.4m vs 3.7m). Cabozantinib (XL184) also achieves its primary end-point to prolong OS in patients experienced first line or 2nd line systemic treatment (mOS 10.2m for cabozantinib, 8.0m for placebo). Most recently, Lilly announces ramucirumab phase 3 REACH-2 study in second-line HCC patients whose AFP levels were ≥400 ng/ml) met overall survival endpoint. Apart from targeted therapy, immune checkpoint inhibitors (ICI), mainly anti-PD-1 treatment have been demonstrated their positive responses in patients failed to sorafenib treatment. The 2018 EASL guideline has adopted these new agents as the treatment option for patients with advanced HCC. Combination therapy with ICI and targeted therapy may even provide higher treatment response according to current early phase studies. In

conclusion, multiple systemic treatments are available for patients with advanced HCC.