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Immunotherapy for Hepatocellular Carcinoma and Its New Development

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Abstract:

In a recent pilot clinical trial, 37 patients with HCC or HCV infection were injected with 15 mg/kg of the CTLA-4-blocking antibody tremelimumab for 90 days, to test the anti-tumour and antiviral effect of this antibody. In addition to demonstrating the safety of such approach in patients, a 17.6% partial response rate and a 76.4% disease control rate was achieved. A significant drop in viral load was also observed. Another phase I clinical trial of tremelimumab with percutaneous Radiofrequency Ablation (RFA) or trans-arterial therapy is ongoing (NCT01853618).

The anti-PD-1 antibody based therapy is even more promising than a CTLA-4 blockade. Nivolumab was the first immune drug approved as a second-line treatment for patients with HCC by FDA in September 2017. In the CheckMate040 study, 48 patients with HCC had received nivolumab 0.1-10 mg/kg intravenously for 2 years. The Objective Remission Rate (ORR) was 15%; median Overall Survival (OS) was 15.1 months and the 9 months OS rate was 67%. In a dose-expansion study of nivolumab, 174 patients with HCC received nivolumab 3 mg/kg intravenously. The ORR was 20% and tumor burden was reduced In 68 patients (39%). Besides, in 80 HCC patients treated with nivolumab only, the ORR was 23%; Disease Control Rate (DCR) was 63%; and 40% of patients had stable disease over than 6 months. However, in the group of sorafenib-experienced patients that received nivolumab, 91% (166/182) of patients progressed on sorafenib treatment. The ORR was 16%-19%. Most recently, the efficacy and safety of anti-PD1 therapy of advanced HCC was evaluated on 11 cases, no related adverse effects were noted; the disease control rate reached 81.8% comparing to an objective response of 63.6%, this clinical trial proved promising application of PD-1 in HCC. There are more clinical trials on other immune checkpoint blockade (Figure 2). Greten summarised clinical data of the therapies based on PD-1/PD-L1 blockade under study for the treatment of hepatocellular carcinoma.

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