GASTROINTESTINAL (NONCOLORECTAL) CANCER

Preliminary efficacy, safety, pharmacokinetics, pharmacodynamics, and quality of life study of pegylated recombinant human arginase 1 in patients with advanced hepatocellular carcinoma.

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Abstract Disclosures

Abstract

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Background: This study was designed to evaluate the efficacy, safety profile, pharmacokinetics/pharmacodynamics (PK/PD) and quality of life (QoL) of pegylated recombinant human arginase 1(Peg-rhAgr1) in patients with advanced hepatocellular carcinoma (HCC).**Methods:** Advanced HCC patients were given weekly doses of Peg-rhAgr1 (1600 U/kg). Tumour response was assessed every 8 weeks using RECIST 1.1 and modified RECIST criteria. **Results:** A total of 20 patients were recruited, of whom 15 were deemed evaluable for treatment efficacy. Eighteen patients (90%) were hepatitis-B carriers. Median age was 61.5 (range 30-75). Overall DCR was 13%, with 2 of the 15 patients achieving stable disease for >8 weeks. Median progression-free survival (PFS) was 1.7 (95% CI: 1.67-1.73) months, with a median overall survival (OS) of all 20 enrolled patients being 5.2 (95% CI: 3.3-12.0) months. PFS was significantly prolonged in patients with adequate arginine depletion (ADD) over >2 months versus those who had ≤2 months of ADD (6.4 versus 1.7 months; p=0.01). The majority of adverse events (AEs) were grade 1 and 2 non-hematological toxicities. Transient liver dysfunctions (25%) were the most commonly reported serious AEs and likely due to disease progression. Pharmacokinetic and pharmacodynamic data show that Peg-rhAgr1 induced rapid and sustained arginine depletion. The overall quality of life of the enrolled patients was well preserved.**Conclusions:** Peg-rhAgr1 is well tolerated with a good toxicity profile in patients with advanced HCC. A weekly dose of 1600U/kg is sufficient to induce ADD. Significantly longer PFS times were recorded for patients who had ADD for >2 months. Clinical trial information: NCT01092091.