Pharmacodynamic–pharmacokinetic study of ficlatuzumab, a monoclonal antibody directed to the hepatocyte growth factor (HGF), in patients with advanced solid tumors who have liver metastases

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Background

Ficlatuzumab is a humanized IgG1 mAb directed to HGF that selectively blocks all biological activities tested, such as HGF/c-Met binding. This study evaluated the safety and efficacy of ficlatuzumab in patients with hepatocellular carcinoma (HCC) or colorectal cancer (CRC) who had received prior anti-cancer therapy within 2 years.

Methods

Patients (≥18 years) with solid tumor and liver metastases and/or elevated liver enzymes were included if they had failed at least one prior systemic treatment. The study was designed as a single-arm, dose-escalation phase I study with three cohorts at starting doses of 2, 10, and 20 mg/kg (RP2D, defined as the highest dose that was well tolerated). Patients were treated in cycles of 2 weeks on and 1 week off. Adverse events (AEs) and pharmacodynamic (PD) changes were assessed.

Results

A total of 90 patients were enrolled: 28 in cohort 1 (2 mg/kg), 23 in cohort 2 (10 mg/kg), and 39 in cohort 3 (20 mg/kg). The study population comprised 77% men, with a median age of 57 years. Overall, 74% of patients had HCC and 26% had CRC, with a median Eastern Cooperative Group performance status of 0/1. Overall, 1 patient (1%) experienced a grade 4 AE; 20 patients (22%) had grade 3 AEs. The most common grade 3 or 4 AEs were decreased appetite (16%), dyspnea (16%), and anemia (16%). Changes in key pharmacodynamic markers were observed. A dose of 20 mg/kg was selected as the RP2D, as it was associated with clinical benefit in patients with advanced HCC in a prior clinical trial. Ficlatuzumab was well tolerated at this dose, and a phase II trial is currently ongoing.

Summary of Results

- The study included 90 patients with HCC or colorectal cancer who had received prior anti-cancer therapy within 2 years.
- Ficlatuzumab was well tolerated at the RP2D of 20 mg/kg, with a low incidence of grade 4 adverse events.
- Changes in key pharmacodynamic markers were observed at the RP2D, indicating engagement at the target.

Conclusions

- Ficlatuzumab is a promising therapeutic option for patients with advanced solid tumors who have liver metastases.
- Further studies are needed to evaluate its efficacy and safety in a larger patient population.