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posters

P – 118 Tepotinib (MSC2156119J) monotherapy in patients with MET-positive advanced hepatocellular carcinoma with Child-Pugh Class A liver function who have failed sorafenib treatment: phase Ib/II trial

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Introduction: The incidence of hepatocellular carcinoma (HCC) is increasing in Western countries. Patients with HCC have a poor prognosis and no active therapy is available for use after failure of sorafenib, the only approved systemic treatment. Thus, there is a high unmet need for new therapies. c-Met/hepatocyte growth factor (HGF) activation/overexpression is associated with poor prognosis in patients with HCC. The highly selective c-Met inhibitor tepotinib (MSC2156119J) has shown promising antitumor activity in solid tumors in a phase I trial. Studies have demonstrated that HGF/c-Met-expressing primary liver explants are sensitive to tepotinib, and HGF/c-Met signaling inhibition has efficacy in patients with Met-overexpressing advanced HCC. A phase Ib/II trial comparing tepotinib with sorafenib in Asian patients with advanced HCC is ongoing. We are conducting a multicenter, single-arm, nonrandomized phase Ib/II study to evaluate tepotinib in patients with MET+ advanced HCC pretreated with sorafenib (clinicaltrials.gov: NCT02115373).

Methods: For the phase Ib part of the study, eligible criteria are as follows: adults with confirmed, advanced HCC and Child-Pugh Class A liver function; life expectancy >3 months; ECOG PS 0 or 1; pretreatment tumor biopsy after sorafenib failure and <28 days before tepotinib initiation; pretreated with sorafenib for ≥4 weeks and discontinued ≥14 days prior to day 1 of tepotinib treatment. For the phase II part, only patients with moderate (2+) or strong (3+) MET protein overexpression in the majority of tumor cells, as determined by immunohistochemistry, will be eligible. Key exclusion criteria include prior systemic therapy for HCC other than sorafenib and prior therapy with an agent targeting the HGF/c-Met pathway. Patients are currently being enrolled in Europe and recruitment will be expanded to include the USA in future. Up to 18 patients will be enrolled to the phase Ib expansion part (3 + 3 design; tepotinib 300 mg or 500 mg p.o./day; 21-day cycle). The primary objective is to determine the recommended phase II dose (RP2D) of tepotinib for sorafenib-pretreated HCC based on the occurrence of dose-limiting toxicity (DLT) during the first cycle of tepotinib. Tepotinib therapy in both parts will be continued until disease progression, intolerable toxicity, or withdrawal of consent. Planned enrollment to the phase II part is 48 patients, who will receive tepotinib at the RP2D. The primary objective of this part of the trial is to investigate the antitumor activity of tepotinib by determining investigator-assessed progression-free survival (PFS) status at 12 weeks (phase II). Secondary objectives include pharmacokinetics, antitumor activity, biochemical response, safety, and tolerability. Patient-reported outcomes will also be assessed. To date, 4 patients have been treated with tepotinib 300 mg/day (median age: 65.5 years; male/female: 2/2; ECOG PS 0/1: 3/1; histologic grade 1/2/ ≥ 3: 1/0/3; distant metastases present: n = 3); all 4 patients were evaluable for the safety analysis. Enrollment to the first dose cohort (300 mg) has been completed, and the trial will move ahead with the next dose level.