First-in-Human Phase I Study of MP0250, a First-in-Class DARPin Drug Candidate Targeting VEGF and HGF, in Patients With Advanced Solid Tumors

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PURPOSE
A first-in-human study was performed with MP0250, a DARPin drug candidate. MP0250 specifically inhibits both vascular endothelial growth factor (VEGF) and hepatocyte growth factor (HGF) with the aim of disrupting the tumor microenvironment.

PATIENTS AND METHODS
A multicenter, open-label, repeated-dose, phase I study was conducted to assess the safety, tolerability, and pharmacokinetics of MP0250 in 45 patients with advanced solid tumors. In the dose-escalation part, 24 patients received MP0250 as a 3-hour infusion once every 2 weeks at five different dose levels (0.5-12 mg/kg). Once the maximum tolerated dose (MTD) was established, 21 patients were treated with a 1-hour infusion (n = 13, 8 mg/kg, once every 2 weeks and n = 8, 12 mg/kg, once every 3 weeks) of MP0250 in the dose confirmation cohorts.

RESULTS
In the dose-escalation cohort, patients treated with 12 mg/kg MP0250 once every 2 weeks experienced dose-limiting toxicities. Therefore, MTD was 8 mg/kg once every 2 weeks or 12 mg/kg once every 3 weeks. The most common adverse events (AEs) were hypertension (69%), proteinuria (51%), and diarrhea and nausea (both 36%); hypoalbuminemia was reported in 24% of patients. Most AEs were consistent with inhibition of the VEGF and HGF pathways. Exposure was dose-proportional and sustained throughout the dosing period for all patients (up to 15 months). The half-life was about 2 weeks. Signs of single-agent antitumor activity were observed: 1 unconfirmed partial response with a time to progression of 23 weeks and 24 patients with stable disease, with the longest duration of 72 weeks and a median duration of 18 weeks.

CONCLUSION
MP0250 is a first-in-class DARPin drug candidate with suitable tolerability and appropriate pharmacokinetic properties for further development in combination with other anticancer therapies.

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