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Phase Ib dose-escalation study of MetMAb, a monovalent antagonist antibody to the receptor MET, in combination with bevacizumab in patients with locally advanced or metastatic solid tumors.

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Phase I Studies

Category:
Developmental Therapeutics - Clinical Pharmacology and Immunotherapy

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Faculty & Discussant Disclosures

Annual Meeting Planning Committee Disclosures

Abstract:

Background: Crosstalk between the Met and vascular endothelial growth factor (VEGF) pathways may be important during tumorigenesis. Aberrant activation of the HGF/Met pathway may promote angiogenesis via tumor cell secretion of angiogenic factors or directly activating endothelial cells. The combination of Met and VEGF inhibition resulted in enhanced antitumor activity in multiple preclinical models than either treatment alone. MetMAb is a recombinant, humanized, monovalent (one-armed) monoclonal antibody antagonist of HGF-induced Met signaling. In phase Ia, MetMAb was generally well tolerated up to 30 mg/kg IV Q3W. Herein, we describe results from a phase Ib study in which we tested MetMAb in combination with bevacizumab. **Methods:** The phase Ib trial tested the combination of MetMAb with bevacizumab in two cohorts: 3 patients in cohort 1 received MetMAb, 10 mg/kg, and bevacizumab, 15 mg/kg, IV Q3W; and 6 patients in cohort 2 received MetMAb,15 mg/kg, and bevacizumab,15 mg/kg IV Q3W. Pre- and post-dose sera were collected for evaluation of pharmacodynamic (PD) biomarkers that could be affected by inhibition of Met and/or VEGF signaling. **Results:** The combination of MetMAb with bevacizumab was generally well tolerated at all doses tested. No Gr3-5 drug- related toxicities were observed. One DLT of Gr1 hemoptysis in cohort 2 was observed in a patient who had central-necrosis of pulmonary metastases. Gr2 drug-related toxicities included peripheral edema and hypoalbuminemia. The most frequently observed toxicities (>30 %) included fatigue and increased weight. The best response was stable disease, with 3 patients receiving ≥ 6 cycles. PD biomarker data will be discussed. MetMAb PK was similar to that from phase Ia and no apparent interaction with bevacizumab was observed. **Conclusions:** This phase Ib trial demonstrated that the combination of MetMAb and bevacizumab is generally safe and well tolerated at the recommended dose of 15mg/kg Q3W for each agent.

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