



Presentation Abstract

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Presentation Title: Final results from the Phase I study of MetMab, a monovalent antagonist antibody to the receptor Met, dosed as single agent and in combination with bevacizumab in patients with advanced solid malignancies

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Location: Room W414 C/D, Orange County Convention Center

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Abstract Body: Background: The receptor tyrosine kinase Met and/or its ligand, hepatocyte growth factor (HGF), are frequently over-expressed in cancers. Aberrant Met activation can enhance invasion, proliferation, and survival and may promote angiogenesis. MetMab was uniquely engineered as a recombinant, humanized, monovalent monoclonal antibody to act as an antagonist of HGF-induced Met signaling.

Materials and Methods: This 3+3 dose-escalation study consisted of three phases: 1) dose-escalation evaluating 1, 4, 10, 15, 20 and 30 mg/kg IV Q3W; 2) expansion at 15mg/kg IV Q3W; and 3) combination testing MetMab, at 10 and 15mg/kg IV Q3W, plus bevacizumab (15mg/kg Q3W). Pre- and post- dose serum was collected for evaluation of pharmacodynamic biomarkers that could be affected by inhibition of Met and/or VEGF signaling.

Results: 43 patients were treated in this study (21 in escalation, 13 in expansion, and 9 in combination). MetMab has a half-life of approximately 11 days, and there were no apparent PK interactions with bevacizumab. MetMab was generally well tolerated, both alone and in combination. The most frequent treatment-related adverse events included: fatigue, peripheral edema and hypoalbuminemia. In patients treated with the combination, no Grade 3-5 treatment-related adverse events were reported; a Grade 1, and dose-limiting adverse event of hemoptysis was reported in a patient who had central-necrosis of pulmonary metastases. A patient with gastric carcinoma achieved a complete response after 4 cycles of single-agent MetMab; this patient came off study after 10 cycles with a sustained complete response.

Conclusions: MetMab, when administered as a single-agent, or in combination with bevacizumab was generally safe and well tolerated. A Phase II trial testing MetMab in combination with bevacizumab and paclitaxel in patients with triple negative breast cancer is currently ongoing, while a Phase III trial testing MetMab in combination with erlotinib in advanced NSCLC patients is planned.

CME Designation: CME-Designated