

## 443PD | PHARMACODYNAMIC (PD) – PHARMACOKINETIC (PK) STUDY OF FICLATUZUMAB(F), A MONOCLONAL ANTIBODY (MAB) DIRECTED TO THE HEPATOCYTE GROWTH FACTOR (HGF), IN PATIENTS (PTS) WITH ADVANCED SOLID TUMORS WHO HAVE LIVER METASTASES (METS)

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### Background

F is a humanized IgG1 mAb directed to HGF that inhibits activation of the c-Met receptor, with potential anti-tumor activity. This study was to define the optimal dose using PD and PK assessments.

### Methods

Pts with solid tumors and liver mets, with phospho (p)-Met expression were sequentially enrolled into 2, 10, or 20 mg/kg (RP2D, defined in a previous study), of F given IV every 2 wks and were evaluated every 8 wks for response using RECIST 1.1. Target pathway modulation was assessed by measuring the following PD markers by IHC in biopsies of liver mets: p-Met, p-Akt, p-ERK, p-S6K, HGF, and c-Met; Ki67 and cleaved caspase-3; and CD31. PD-evaluable pts had measurable p-Met at Cycle 1 Day 1 pre-dose and at least one post-dose timepoint. Serum was collected to measure F, anti-drug antibody (ADA), s-Met, HGF, and HGF/F complex levels by ELISA.

### Results

Nineteen pts received F: 15 male/4 female; median age 60 years; ECOG PS 0/1 (8/11 pts). The most frequent TEAEs, mostly Grade 1 to 3, were asthenia, edema, hepatic pain (32% each), cough (26%). There were no DLTs or ADA. Serum albumin decreased to below normal for most pts at EOT and recovered at the follow up visit. Best overall response was SD (5/18 pts) and disease progression (13/18 pts), and median duration of treatment was 6 wks (range 2-59). PK analysis revealed dose-proportional drug exposure with a low systemic clearance leading to a terminal half-life of 7.4 to 10.0 days, and a low volume of distribution approximating the plasma volume. F treatment increased the total serum HGF and HGF/F complex levels. Increasing dose of F resulted in progressive decreases in p-Met and p-AKT. At RP2D, the majority of pts experienced  $\geq 25\%$  decrease from baseline in p-Met, p-ERK, p-Akt, Ki67 and CD31.

### Conclusions

Ficlatuzumab(F) is well tolerated in this population. The PK of F in this study was consistent with that reported previously. Increase in post-dose serum HGF and HGF/F complex levels indicates target engagement. At RP2D, a majority of pts experienced decreases in key cell signaling PD markers. This study supports the selection of 20 mg/kg F dose as RP2D.

### Disclosure

All authors have declared no conflicts of interest.

**Session Info:** Poster Discussion, [ ] Developmental therapeutics

**Day/Date:** Sunday, September 30, 2012

**Session Time:** 1:00 PM - 2:00 PM

**Room:** Hall H