Phase 1 Study of SCH 900105, an Anti-Hepatocyte Growth Factor Monoclonal Antibody, as a Single Agent in Combination with Erlotinib in Patients with Advanced Solid Tumors


Abstract

Background: SCH 900105 is a humanized monoclonal antibody (mAb) targeting hepatocyte growth factor (HGF). HGF has been implicated in many forms of cancer and is thought to be an important therapeutic target for patients with advanced solid tumors.

Methods: In Study 1, single-agent SCH 900105 was evaluated in the setting of monotherapy in Phase 1 dose escalation and expansion cohorts (1–20mg/kg SC every 21 days, 150 mg/d erlotinib). In Study 2, combination arm of SCH 900105 (20mg/kg SC) + erlotinib was evaluated in Phase 1 and Phase 2 expanded cohorts.

Results: 51 healthy volunteers and 109 patients were enrolled. Individual dose levels were evaluable in 27–73% of patients (n=3–5). In Study 1, 20 mg/kg SCH 900105 induced significantly greater reduction in plasma HGF compared to normal donors. Additionally, consistent reduction in HGF was seen in pancreatic adenocarcinoma patients receiving 505 mg/kg (n=3).

Conclusions: SCH 900105 administered IV over 60 min at doses of 2, 5, 10 or 20 mg/kg resulted in significant decreases in plasma HGF levels tested (2, 5, 10 or 20 mg/kg) in combination with erlotinib (20 mg/kg SCH 900105 & 150 mg/d erlotinib) in stable disease or better of 2 or more cycles.

Keywords: SCH 900105, mAb, anti-HGF, Phase 1, combination therapy, metastatic disease, solid tumors.

Abstract #2525

Targeting the HGF/Met Signaling Pathway

• HGF is the ligand regulated for the Met receptor tyrosine kinase.

• Dysregulated HGF/ Met signaling has emerged as a crucial feature of cancer metastasis.

• High HGF levels suggest poor prognosis in a wide variety of human tumors.

• SCH 900105 administered IV over 60 min at doses of 2, 5, 10 or 20 mg/kg resulted in significant decreases in plasma HGF levels tested (2, 5, 10 or 20 mg/kg) in combination with erlotinib (20 mg/kg SCH 900105 & 150 mg/d erlotinib) in stable disease or better of 2 or more cycles.

Introduction

HGF/cMet signaling has emerged as a crucial feature of cancer metastasis. High HGF levels suggest poor prognosis in a wide variety of human tumors. Monoclonal antibodies (mAbs) targeting HGF have been extensively pursued as a potential therapeutic strategy. Results from the phase 1 study of SCH 900105, an anti-HGF mAb, in combination with erlotinib are described.

Study Design

• To determine safety, tolerability, dose-finding, PK, PD, and immunogenicity of SCH 900105 (SCH) measured using decrease in plasma HGF, pharmacokinetics (PK) and immunology.

• SCH 900105 administered IV over 60 min at doses of 2, 5, 10, or 20 mg/kg in patients with metastatic solid tumors (N=3–5).

Results - Safety and Activity

• The average baseline HGF levels in study patients are 6-fold higher versus normal donors (p < 0.0001).

• HGF levels tested (2, 5, 10 or 20 mg/kg) in combination with erlotinib (20 mg/kg SCH 900105 & 150 mg/d erlotinib) were 2.2- fold higher versus normal donors (p < 0.0001).

• SCH 900105 administered IV over 60 min at doses of 2, 5, 10 or 20 mg/kg resulted in significant decreases in plasma HGF levels tested (2, 5, 10 or 20 mg/kg) in combination with erlotinib (20 mg/kg SCH 900105 & 150 mg/d erlotinib) in stable disease or better of 2 or more cycles.

Results - Pharmacokinetics

• SCH 900105 administered IV over 60 min at doses of 2, 5, 10, or 20 mg/kg resulted in significant decreases in plasma HGF levels tested (2, 5, 10 or 20 mg/kg) in combination with erlotinib (20 mg/kg SCH 900105 & 150 mg/d erlotinib) in stable disease or better of 2 or more cycles.

Conclusions

• SCH 900105 administered IV over 60 min at doses of 2, 5, 10, or 20 mg/kg resulted in significant decreases in plasma HGF levels tested (2, 5, 10 or 20 mg/kg) in combination with erlotinib (20 mg/kg SCH 900105 & 150 mg/d erlotinib) in stable disease or better of 2 or more cycles.

• These results support further evaluation of SCH 900105 in combination with erlotinib in the clinic.