Varlitinib demonstrates potent antitumour efficacy in patient-derived gastric cancer xenograft models.

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INTRODUCTION

• Gastric Cancer is the 5th most common cancer worldwide, with 952,000 cases diagnosed in 2012, constituting 7% of all cancer diagnoses. Progress for gastric cancer is poor, with the overall survival

METHODS

• Patient-derived gastric cancer xenografts were established with 25% 1023G1. Varlitinib was orally administrated at 25 mg/kg, 50 mg/kg or 100 mg/kg twice daily as indicated in each experiment.

ACKNOWLEDGEMENTS

• Varlitinib has demonstrated potent anti-tumour growth effects as monotherapy in two patient-derived gastric cancer xenograft models (GC22-088B and GC11-0414) selected for high-expression levels but not amplification of HER proteins.

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RESULTS

• In vivo Potency of Varlitinib

• Bioluminescent signal was monitored in real-time for 14 days after treatment with Varlitinib (50 mg/kg BID), and Varlitinib at 100 mg/kg BID, or Vehicle. The mean tumour growth inhibition was 82% and 98% for the 50 mg/kg and 100 mg/kg BID doses, respectively. The in vivo efficacy of Varlitinib was also demonstrated in a second GC PDX model GC11-0414 (A). The tumour growth inhibitory effect of Varlitinib was also observed in a third GC PDX model GC11-0414 (B).

• Tumour growth inhibition is observed in both GC PDX models after 14 days of treatment with Varlitinib at 50 mg/kg BID.

• The PDX model results correlate well with the clinical biomarker data.

• In vivo Mechanism of Action of Varlitinib

CONCLUSIONS

• Varlitinib demonstrates potent antitumour growth effects as monotherapy in two patient-derived gastric cancer xenograft models (GC22-088B and GC11-0414) selected for high-expression levels but not amplification of HER proteins.

• ASLAN has also conducted a paired biopsy study in 23 gastric cancer patients (co-expressing HER1 and HER2) who were dosed with Varlitinib monotherapy for 28 days. The clinical samples demonstrated decrease in MARK signaling (*85% of patients), reduction of Rb (*70% of patients) as a proliferation marker and an increase in TUNEL (*60% of patients).

• The PDX model results correlate well with the clinical biomarker data.

• Based on the anti-tumour efficacy data, ASLAN will initiate a Phase 2 clinical trial in gastric cancer in 2016, selecting for patients with HER1/HER2 co-expression without HER2 amplification.