Background: XL647 is a novel, orally available, small-molecule inhibitor of multiple receptor tyrosine kinases, including vascular endothelial growth factor receptor 2 (VEGFR2), platelet-derived growth factor receptor (PDGFR), and ii oncoprotein kinase-1 (c-Met).

Methods: Patients with advanced solid malignancies were enrolled in successive cohorts based on prior exposure to EGFR inhibitors and irinotecan and were evaluable for safety (n = 13) and pharmacokinetics (n = 15).

Key inclusion criteria were any solid malignancy, prior treatment with irinotecan, and irinotecan exposure within 120 days of XL647 initiation.

Key exclusion criteria included patients with brain metastases, uncontrolled intercurrent illness, or any condition that would contraindicate XL647 therapy.

Key end points were overall response rate (ORR), disease control rate (DCR), median duration of response (mDOR), and median progression-free survival (mPFS).

Results: Eleven patients met all eligibility and safety criteria. Of these, eight (73%) achieved a partial response (PR), and three (27%) achieved stable disease (SD). Two patients (18%) had a decrease in target lesions/lesion burial. The best ORR was 8, with one PR and seven SD, as well as a decrease in target lesions (n = 2) or disease stabilization (n = 1).

The mPFS was 6.9 months (95% CI: 3.6–11.7; 10 patients evaluable for this end point). The mPFS for the ORR ≥ PR ≥ SD group was 6.3 months (95% CI: 2.0–11.4; 11 patients evaluable for this end point).

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Pharmacokinetic assessments were performed by tandem mass spectrometry, and urinalysis was performed to assess drug excretion.

Conclusions: XL647 demonstrated an acceptable safety profile and clinical activity in patients with advanced solid malignancies. The ORR and DCR were higher than those expected for a program that targets multiple receptor tyrosine kinases, including VEGFR2, PDGFR, and c-Met.

Methods:

A series of 23 patients were enrolled in this phase I study. Patients were treated with daily oral administration of XL647 for up to 56 days. Treatment cycles were 21 days in length, with a 7-day washout period between cycles.

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