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Phase II and Biomarker Study of the Dual MET/VEGFR2 Inhibitor Foretinib in Patients With Papillary Renal Cell Carcinoma.

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Abstract

PURPOSE Foretinib is an oral multikinase inhibitor targeting MET, VEGF, RON, AXL, and TIE-2 receptors. Activating mutations or amplifications in MET have been described in patients with papillary renal cell carcinoma (PRCC). We aimed to evaluate the efficacy and safety of foretinib in patients with PRCC. PATIENTS AND METHODS Patients were enrolled onto the study in two cohorts with different dosing schedules of foretinib: cohort A, 240 mg once per day on days 1 through 5 every 14 days (intermittent arm); cohort B, 80 mg daily (daily dosing arm). Patients were stratified on the basis of MET pathway activation (germline or somatic MET mutation, MET [7q31] amplification, or gain of chromosome 7). The primary end point was overall response rate (ORR). Results Overall, 74 patients were enrolled, with 37 in each dosing cohort. ORR by Response Evaluation Criteria in Solid Tumors (RECIST) 1.0 was 13.5%, median progression-free survival was 9.3 months, and median overall survival was not reached. The presence of a germline MET mutation was highly predictive of a response (five of 10 v five of 57 patients with and without germline MET mutations, respectively). The most frequent adverse events of any grade associated with foretinib were fatigue, hypertension, gastrointestinal toxicities, and nonfatal pulmonary emboli. CONCLUSION Foretinib demonstrated activity in patients with advanced PRCC with a manageable toxicity profile and a high response rate in patients with germline MET mutations.

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