A phase IA, open-label, dose-escalating study of PTK787/ZK 222584 administered orally on a continuous dosing schedule in patients with advanced cancer

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PTK787/ZK 222584 (PTK/ZK) offers a novel approach to inhibit tumour angiogenesis.; This study characterized the safety, tolerability, biological activity and pharmacokinetic profile of PTK/ZK, while determining the optimum dose. Seventy-one patients with advanced cancer were enrolled to receive once daily dosing. Pharmacokinetic, dynamic contrast enhanced magnetic resonance imaging and safety assessments were performed, along with measurement of soluble markers. Patients were treated until they had unacceptable toxicity and/or disease progression.; Twenty-nine patients were assessable for maximum tolerated dose (MTD) determination, but no MTD was established; only two patients experienced dose limiting toxicities. PTK/ZK was well tolerated with only nine patients experiencing serious adverse events suspected to be PTK/ZK related, but no objective tumour response was observed; 34% had stable disease and 48% had progressive disease. In addition, PTK/ZK was rapidly absorbed with a maximum concentration occurring 2 hours post-dosing. Vascular endothelial growth factor and basic fibroblastic growth factor were good predictors of best tumour response, as was the MRI bidirectional transfer constant on day 2 of treatment.; An MTD was not reached in this study but, based on these data and findings from other studies, 1200 mg was found to be the optimum dose of PTK/ZK for patients with advanced cancer.
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