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Titel des Beitrags: Phase II Results of Dovitinib (TKI258) in Patients with Metastatic Renal Cell Cancer.

Abstract: Fibroblast growth factor (FGF) signaling regulates tumor growth and vascularization and partly mediates antiangiogenic escape from VEGF receptor (VEGFR) inhibitors. Dovitinib (TKI258) is a tyrosine kinase inhibitor (TKI) that inhibits FGF receptor (FGFR), VEGFR, and platelet-derived growth factor receptor, which are known drivers of antiangiogenic escape, angiogenesis, and tumor growth in renal cell carcinoma (RCC). Patients with advanced or metastatic RCC were treated with oral dovitinib 500 mg/day (5-days-on/2-days-off schedule). The study population was enriched for patients previously treated with a VEGFR TKI and an mTOR inhibitor. Of 67 patients enrolled, 55 patients (82.1%) were previously treated with >= 1 VEGFR TKI and >= 1 mTOR inhibitor (per-protocol efficacy set). The 8-week overall response rate and disease control rate in this population were 1.8% and 52.7%, respectively. Disease control rate during the entire study period was 56.4% (50.9% >= 4 months). Median progression-free survival and overall survival in the entire population were 3.7 and 11.8 months, respectively. Pharmacodynamic analyses demonstrated dovitinib-induced inhibition of VEGFR (as determined by increased levels of placental growth
factor and decreased levels of soluble VEGFR2) and FGFR (as determined by increased FGF23 serum measures). The most frequently reported treatment-related adverse events of all grades included nausea (65.7%), diarrhea (62.7%), vomiting (61.2%), decreased appetite (47.8%), and fatigue (32.8%). Dovitinib was shown to be an effective and tolerable therapy for patients with metastatic RCC who had progressed following treatment with VEGFR TKIs and mTOR inhibitors. Clin Cancer Res; 20(11); 3012-22. ©2014 AACR.