TPS4589 General Poster Session (Board #34A), Mon, 8:00 AM-11:45 AM

A phase II study of cabozantinib (XL184) in patients with advanced/metastatic urothelial carcinoma.

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Background: Accumulating evidence supports MET as a therapeutic target in urothelial carcinoma. Activated MET can promote angiogenesis and tumor growth by upregulating VEGF and may play a role in urothelial carcinoma pathogenesis. Cabozantinib inhibits primarily VEGFR2 and MET pathways. Cabozantinib has been approved by the FDA for the treatment of progressive metastatic medullary thyroid cancer, is in Phase 3 trials for metastatic castration-resistant prostate cancer and has demonstrated clinical activity in multiple solid tumors. We previously reported that shed MET levels in serum and urine of patients with urothelial carcinoma correlate with stage, presence of visceral metastases and urinary source and that cabozantinib is effective in reversing HGF-driven urothelial carcinoma cell growth and invasion. These data support the evaluation of cabozantinib in patients with metastatic urothelial carcinoma. **Methods:** This is a phase II study of oral cabozantinib 60mg daily given continuously in 28-day cycles. There are three study cohorts: [1] metastatic urothelial carcinoma [2] bone only metastatic urothelial carcinoma [3] metastatic non-urothelial carcinoma of the bladder, urethra, ureter, or renal pelvis. A maximum of 55 subjects will be enrolled. Up to 45 patients will be accrued to cohort 1.The remainder will be enrolled on exploratory cohorts 2 & 3. A two-stage single-arm phase II design will be employed. The primary objective is to determine the objective response rate in patients with metastatic urothelial carcinoma who have progressed on prior chemotherapy. Secondary objectives include progression free survival, safety and toxicity, and overall survival. Exploratory objectives include tumor tissue Met expression, shed MET levels in serum and urine, immune subsets, genetic biomarkers, molecular markers of angiogenesis and circulating tumor cells, correlation with clinical response parameters. Finally we will explore treatment evaluation with FDG and NaF PET/CT compared to standard imaging. This study is supported by the Cancer Therapy Evaluation Program (CTEP). NCT01688999 Clinical trial information: NCT01688999.