TPS5095 General Poster Session (Board #42F), Mon, 8:00 AM-11:45 AM

A phase I study of cabozantinib (Cabo) plus docetaxel (D) and prednisone (P) in metastatic castrate resistant prostate cancer (mCRPC).

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Background: In mCRPC, two randomized trials demonstrated an overall survival (OS) benefit with the chemotherapeutic agent D. However, the survival improvement is modest and new strategies are needed to enhance clinical response. D-based combinations have been evaluated as one alternative strategy. Cabo targets multiple tyrosine kinases including c-Met, vascular endothelial growth factor receptor 2 (VEGFR2) and RET. Cabo has shown activity in mCRPC, with resolution of bone lesions on bone scan, regression of soft tissue/visceral disease, and reductions in circulating tumor cells and bone biomarkers (Smith, et al, J Clin Oncol 30, 2012 [suppl; abstr 4513]). We hypothesize the addition of Cabo to D and P, in patients (pts) with mCRPC, will have an acceptable toxicity profile and could lead to improved survival by targeting different cellular pathways simultaneously. This combination therapy may represent a safe and effective strategy to improve the outcome of mCRPC pts treated with D-based chemotherapy. **Methods:** This is a phase I trial to determine the safety profile and the recommended phase II dose of Cabo in combination with D and P. Pts receive a fixed dose of D (75 mg/m2 IV day 1 of each 21 day cycle) and P (5 mg po q12 hours) in combination with Cabo at three escalating doses: dose level 1 is 20 mg, level 2 is 40 mg, and level 3 is 60 mg (all po qdaily). Using a standard 3 + 3 design, three patients will initially be treated at each dose level until the maximum tolerated dose (MTD) has been defined. An expansion cohort will then be enrolled at the MTD. The accrual ceiling for the study, including both the dose escalation and the expansion phases, is set at 24 pts. Secondary objectives include assessments of pharmacokinetics of each agent, evaluation of antitumor activity of the combination therapy, and assessment of changes in molecular biomarkers for receptor tyrosine kinase and angiogenesis pathways, as well as biomarkers for bone metabolism. Restaging with bone and CT scan will be undertaken every 3 cycles. Enrollment at dose level 1 has been completed without dose-limiting toxicity. Accrual is ongoing at the second dose level. Clinical trial information: NCT01683994.