A TRANSLATIONAL PHASE 2 STUDY OF CABOZANTINIB IN MEN WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER WITH VISCERAL METASTASES WITH CHARACTERIZATION OF CIRCULATING TUMOR CELLS AND LARGE ONCOSOMES

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Aim: Cabozantinib (XL184) is a potent multi-targeted tyrosine kinase inhibitor (TKI) that is under active investigation in several malignancies including prostate cancer (PC). The mechanism of action in PC has not been well characterized at this time. While considerable attention has been given to the impact of this agent on Tc-bone scans, less is known about its activity in men with visceral metastases.

Methods: This study was designed as a single arm phase 2 study of cabozantinib 60 mg daily for men with visceral disease. The primary endpoint of this study is clinical benefit rate at 12 weeks (CBR12) which included stable disease and radiographic response. PSA was not used as an endpoint. Beyond standard clinical assessments, blood and urine were collected for circulating tumor cell (CTC) assessments using CellSearch (CS) and NanoVelcro (NV) chips and large oncosome selection. Biopsies before treatment and at progression are being collected when possible. Circulating tumor cell RNA and large oncosome content were profiled at baseline and 2 weeks for all patients.

Results: Eight pts. have been treated of the anticipated 40 patient cohort. 13% had pulmonary metastatic lesion; 88% had hepatic metastases; 88% had concurrent osseous metastases. CBR12 was 83% at the time of this report. Two patients discontinued treatment without evidence of progression due to grade 3 toxicity (diarrhea, corneal defect). Discordant responses were noted between visceral metastases and bone scans. Other grade 3 toxicities included hypertension, hand-foot syndrome, and GGT. CTC numbers by NV and CS declined within 2 weeks and increased at progression. Updated results of CTC and oncosome analysis will be presented including alterations in MET and SCHLAP1 expression.

Conclusions: Cabozantinib is a TKI with activity in PC even in men with visceral metastasis who are typically considered to have more aggressive disease. The activity in the viscera appears to be lower than that seen in osseous metastases. Further understanding of the biology of cabozantinib based on CTC, oncosomes, and tissue studies will refine our use of this active agent.

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