

[] 8970 | CABOZANTINIB (XL184) AT 40 MG IN PATIENTS WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER (MCRPC): RESULTS OF A PHASE 2 NON-RANDOMIZED EXPANSION COHORT (NRE)

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Background

Cabozantinib (cabo) inhibits MET & VEGFR2. In a phase 2 NRE cohort of patients (pts) with mCRPC, cabo at 100 mg daily was associated with high rates of bone scan resolution, pain relief & overall disease control, independent of PSA changes. We now report the activity & safety of cabo 40 mg daily.

Methods

Docetaxel (D)-pretreated (≥ 225 mg/m) CRPC pts with bone metastasis were required to have progressed within 6 months of last dose of D. Tumor response was assessed q6 wks. Bone scan response used computer-aided assessment of bone scan lesion area (BSLA). Diffusion Weighted MRI was performed in some pts. Pain intensity (worst pain over the past 24 hrs; BPI scale 0-10) & interference with sleep & daily activity were prospectively assessed using an IVR system (7 day intervals). Analgesic use was collected by diary. Bone turnover markers & circulating tumor cells (CTCs) were assessed.

Results

51 pts were enrolled. Among 30 pts who had ≥ 6 wks f/u, the median age was 66 yrs. 20% received cabazitaxel, 70% abiraterone, & 20% had visceral disease. 47% (14/30) had pain (BPI ≥ 4) at baseline (bsl) of which 86% (12/14) were using narcotics. Median bsl CTC count was 17 & 73% had ≥ 5 . Median f/u was 84 days (range, 44-141). 55% (11/20 pts) with a f/u bone scan showed BSLA reduction (range, 1-70%). Increases in Apparent Diffusion Coefficient (suggestive of tumor necrosis) & enhancement reduction were observed in bone & soft tissue metastases. 10/14 pts (71%) evaluable for pain response had a $\geq 30\%$ reduction from bsl; 7/12 (58%) pts decreased narcotics. Sleep & daily activity improved in pts with pain relief. Among pts with elevated bsl serum levels of CTx, NTx & bALP, 57%, 60% & 33% respectively, had declines $\geq 30\%$. In 22 pts with CTCs ≥ 5 , 59% had a decrease of $\geq 30\%$ at wks 6 or 12, & 23% converted to < 5 CTCs. 5 (17%) pts required a dose reduction. The most common Gr 3/4 AEs were hypertension (13%), decreased appetite (7%), & back pain (7%).

Conclusions

Cabo 40 mg was well tolerated & demonstrated bone scan resolution, substantial pain relief with a narcotic sparing effect, & reductions in bone turnover markers & CTCs in heavily pretreated mCRPC pts. MRI results are consistent with an anti-tumor effect.

Disclosure

M.R. Smith: Consultant to Exelixis.

O.A. Sartor: Consultant for Exelixis.

All other authors have declared no conflicts of interest.

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