

Randomized trial of enzalutamide (Arm A) versus bicalutamide (Arm B) in combination with androgen deprivation (ADT) in metastatic hormone sensitive prostate cancer (mHSPC): A Prostate Cancer Clinical Trials Consortium Trial.

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Background: The addition of abiraterone or docetaxel has overall survival (OS) benefit in mHSPC. The clinical outcomes with early enzalutamide in mHSPC are unknown. We compared the combination of enzalutamide (Arm A) or bicalutamide (Arm B) each with LHRH analogue therapy in mHSPC.

Methods: The primary endpoint was PSA nadir ≤ 4 ng/ml after 7 months of therapy, as an accepted surrogate for overall survival (OS) outcomes. Secondary endpoints were toxicities, biochemical and radiologic progression free survival (PFS), and OS. Stratification was by presence of bone pain (yes/no) and race; (AA or other). PSA was monitored monthly for first 7 months and then every 3 months. Metastatic site biopsies were mandatory pretherapy and optional post therapy.

Results: 71 men ; 29 AA, 41 Caucasian and 1 Asian were enrolled. The median age was 67 years (range 46-87 years) and median baseline PSA was 56.3 ng/ml in Arm A (4.2- 10,431 ng/ml) and 60 (4.9-12,030 ng/ml) in Arm B. 26 pts (39%) had bone pain and 37(52%) had extensive disease. Predominant grade 3+ adverse events on Arm A were: Hypertension (13%), infection (7%), and syncope (7%) and on Arm B were: Hypertension (21%), Fatigue (7%), and Hematuria (7%). No seizures were noted. PSA nadir ≤ 4 ng/ml at month 7 was achieved in 29/31 (94%) pts in arm A and 16/24 (67%) pts in arm B. 53% on arm A and 43% on Arm B continue to maintain PSA ≤ 4 ng/ml. 4 (11%) deaths have occurred on enzalutamide as compared to 13 (37.1%) deaths on Arm B. Among AA patients, PSA response rate at Month 7 was 100% on Arm A and 46% on Arm B. 53 (75%) biopsy samples had tumor tissue available. TMPRSS-ERG fusion gene and CXCR4 expression and androgen biosynthetic enzyme levels were determined in metastatic biopsies. Patients with low copy number of ERG had an increased 7-month PSA remission rate, (19/20 or 95%) as compared to high ERG copy number (14/20 or 70%).

Conclusions: Enzalutamide improved likelihood of PSA remission in mHSPC and follow up is ongoing. High ERG copy number was associated with lower likelihood of PSA remission. Early enzalutamide use in mHSPC improved PSA remission rates and has the potential to subsequently improve PFS and OS outcomes This is the first report of a randomized trial comparing the addition of enzalutamide or bicalutamide to ADT in mHSPC.