

TYPE OF CANCER: Metastatic Prostate Cancer
TYPE OF TRIAL: Phase III
TRIAL SPONSOR: Cougar Biotechnology, Inc

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STUDY SUMMARY

A Phase 3, Randomized, Double-blind, Placebo-Controlled Study of Abiraterone Acetate (CB7630) Plus Prednisone in Asymptomatic or Mildly Symptomatic Patients with Metastatic Castration-Resistant Prostate Cancer

TREATMENT OVERVIEW

- Patients will be randomized to receive either Abiraterone acetate 1000mg orally daily or Placebo orally daily with Prednisone 5mg orally twice daily
- Patient should be seen by the physician at least every 28 days
- Patients may continue to participate in the study unless they experience unacceptable toxicity or disease progression.

PRETREATMENT ASSESMENT

- Informed consent (signed)
- Medical history
- Demographics
- Prior prostate therapies
- BPI-SF, analgesic usage
- Physical Examination
- Vital signs
- ECOG Performance Status
- 12 Lead ECG
- Cardiac Imaging (MUGA/ ECHO)
- Prior/ Concomitant medications
- Adverse events
- CBC
- Coagulation Factors PT/PTT (INR)
- Serum chemistry, electrolytes
- Fasting glucose
- Serum lipids
- PSA
- Serum testosterone
- Urinalysis (dipstick)
- Tumor Evaluation [CT / MRI / Chest X-ray/Other imaging procedure]

- Bone Scan

ENTRANCE CRITERIA FOR PARTICIPATION IN TRIAL

Inclusion Criteria

1. Willing and able to provide written informed consent
2. Written Authorization for Use and Release of Health and Research Study Information has been obtained
3. Male aged 18 years and above
4. Histologically or cytologically confirmed adenocarcinoma of the prostate
5. Metastatic disease documented by positive bone scan or metastatic lesions other than liver or visceral metastasis on CT, MRI. If lymph node metastasis is the only evidence of metastasis, it must be ≥ 2 cm in diameter
6. Prostate cancer progression documented by PSA according to PCWG2 or radiographic progression according to modified RECIST criteria
7. Asymptomatic or mildly symptomatic from prostate cancer. A score of 0-1 on BPI-SF Question #3 (worst pain in last 24 hours) will be considered asymptomatic, and a score of 2-3 will be considered mildly symptomatic.
8. Surgically or medically castrated, with testosterone levels of < 50 ng/dL (< 2.0 nM). If the patient is being treated with LHRH agonists (patient who have not undergone orchiectomy), this therapy must have been initiated at least 4 weeks prior to Cycle 1 Day 1 and must be continued throughout the study.
9. Previous anti-androgen therapy and progression after withdrawal. Patients who received combined androgen blockade with an anti-androgen must have shown PSA progression after discontinuing the anti-androgen prior to enrollment (≥ 4 weeks since last flutamide, ≥ 6 weeks since last bicalutamide or nilutamide).
10. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
11. Hemoglobin ≥ 10.0 g/dL independent of transfusion
12. Platelet count $\geq 100,000/\mu\text{L}$
13. Serum albumin ≥ 3.5 g/dL
14. Serum creatinine < 1.5 x ULN or a calculated creatinine clearance ≥ 60 mL/min
15. Serum potassium ≥ 3.5 mmol/L
16. Liver function:
 - a. Serum bilirubin < 1.5 x ULN (except for patients with documented Gilbert's disease)
 - b. AST or ALT < 2.5 x ULN
17. Able to swallow the study drug whole as a tablet
18. Life expectancy of at least 6 months
19. Patients who have partners of childbearing potential must be willing to use a method of birth control with adequate barrier protection as determined to be acceptable by the principal investigator and sponsor during the study and for 13 weeks after last study drug administration.

Exclusion Criteria

1. Active infection or other medical condition that would make prednisone/prednisolone (corticosteroid) use contraindicated

2. Any chronic medical condition requiring a higher dose of corticosteroid than 5mg prednisone/prednisolone bid.
3. Pathological finding consistent with small cell carcinoma of the prostate
4. Liver or visceral organ metastasis
5. Known brain metastasis
6. Use of opiate analgesics for cancer-related pain, including codeine and dextropropoxyphene, currently or anytime within 4 weeks of Cycle 1 Day 1
7. Prior cytotoxic chemotherapy or biologic therapy for the treatment of CRPC
8. Radiation therapy for treatment of the primary tumor within 6 weeks of Cycle 1, Day 1
9. Radiation or radionuclide therapy for treatment of metastatic CRPC
10. Previously treated with ketoconazole for prostate cancer for greater than 7 days
11. Prior systemic treatment with an azole drug (e.g. fluconazole, itraconazole) within 4 weeks of Cycle 1, Day 1
12. Prior flutamide (Eulexin) treatment within 4 weeks of Cycle 1, Day 1 (patients whose PSA did not decline for three or more months in response to antiandrogen given as a second line or later intervention will require only a two week washout prior to Cycle 1, Day 1)
13. Bicalutamide (Casodex), nilutamide (Nilandron) within 6 weeks of Cycle 1 Day 1 (patients whose PSA did not decline for three or more months in response to antiandrogen given as a second line or later intervention will require only a two week washout prior to Cycle 1, Day 1)
14. Uncontrolled hypertension (systolic BP \geq 160 mmHg or diastolic BP \geq 95 mmHg). Patients with a history of hypertension are allowed provided blood pressure is controlled by anti-hypertensive treatment
15. Active or symptomatic viral hepatitis or chronic liver disease
16. History of pituitary or adrenal dysfunction
17. Clinically significant heart disease as evidenced by myocardial infarction, or arterial thrombotic events in the past 6 months, severe or unstable angina, or New York Heart Association (NYHA) Class II-IV heart disease or cardiac ejection fraction measurement of $<$ 50% at baseline
18. Atrial Fibrillation, or other cardiac arrhythmia requiring therapy
19. Other malignancy, except non-melanoma skin cancer, with a \geq 30% probability of recurrence within 24 months
20. Administration of an investigational therapeutic within 30 days of Cycle 1, Day 1
21. Any condition which, in the opinion of the investigator, would preclude participation in this trial.