Cancer Research Consortium of West Michigan
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FAST FACTS

EA8153 - Cabazitaxel with Abiraterone versus Abiraterone alone Randomized Trial for Extensive Disease following Docetaxel: the CHAARTED2 Trial

Eligibility Criteria

1. Age ≥ 18 years.
2. Histologically confirmed diagnosis of prostate cancer (adenocarcinoma of the prostate).
3. Previous chemotherapy with at least 3 cycles of docetaxel for hormone-sensitive metastatic prostate cancer.
4. Metastatic disease as evidenced by the presence of soft tissue and/or bone metastases on imaging studies (CT/MRI of abdomen/pelvis, bone scintigraphy or NaF PET/CT).
5. Ability to swallow abiraterone acetate tablets as a whole.
6. All patients must be receiving standard of care androgen deprivation treatment (surgical castration versus LHRH agonist or antagonist treatment); subjects receiving LHRH agonist or antagonist must continue treatment throughout the time on this study.
7. Patients must have castrate serum level of testosterone of < 50 ng/dL (< 1.73 nmol/L), confirmed ≤ 4 weeks prior to randomization.
8. Patients must have progressive disease while receiving androgen deprivation therapy defined by any one of the following as per the Prostate Cancer Clinical Trials Working Group 3 (PCWG3) criteria for PSA, measurable disease or non-measurable (bone) disease [23] during
    a. treatment with ADT:PSA: At least two consecutive rises in serum PSA, obtained at a minimum of 1- week intervals, with the final value ≥ 1.0 ng/mL, confirmed ≤ 4 weeks prior to randomization

    OR

    b. Measurable disease (by RECIST 1.1): > 20% increase in the sum of the longest diameters of all measurable lesions or the development of new measurable lesions. The short axis of a target lymph node must be more that 15 mm to be assessed for change in size.

    OR

    c. Non-measurable (bone) disease: The appearance of two or more new areas of uptake on bone scan (or NaF PET/CT) consistent with metastatic disease compared to previous imaging during castration therapy. The increased uptake of pre-existing lesions on bone scan will not be taken to constitute progression, and ambiguous results must be confirmed by other imaging modalities (e.g. X-ray, CT or MRI).
9. Patients may or may not have been treated previously with a nonsteroidal antiandrogen, such as flutamide, bicalutamide or nilutamide. For patients previously treated with an antiandrogen, they must be off treatment for at least 4 weeks (for flutamide) or 6 weeks (for bicalutamide or nilutamide) prior to registration and must have shown PSA progression after discontinuing the anti-androgen.
10. Patients must have an ECOG performance status of 0, 1, or 2.
11. Adequate hematologic and renal function as evidenced by the following baseline laboratory values ≤ 4 weeks prior to randomization:
    a. ANC ≥ 1500/mm3

   b. Hgb ≥ 9.0 gr/dL
   c. Platelets ≥ 100,000/mm3
   d. Creatinine < 2.0 mg/dL
12. Patients must be informed of the experimental nature of the study and its potential risks, and must sign an IRB-approved written informed consent form indicating such an understanding.
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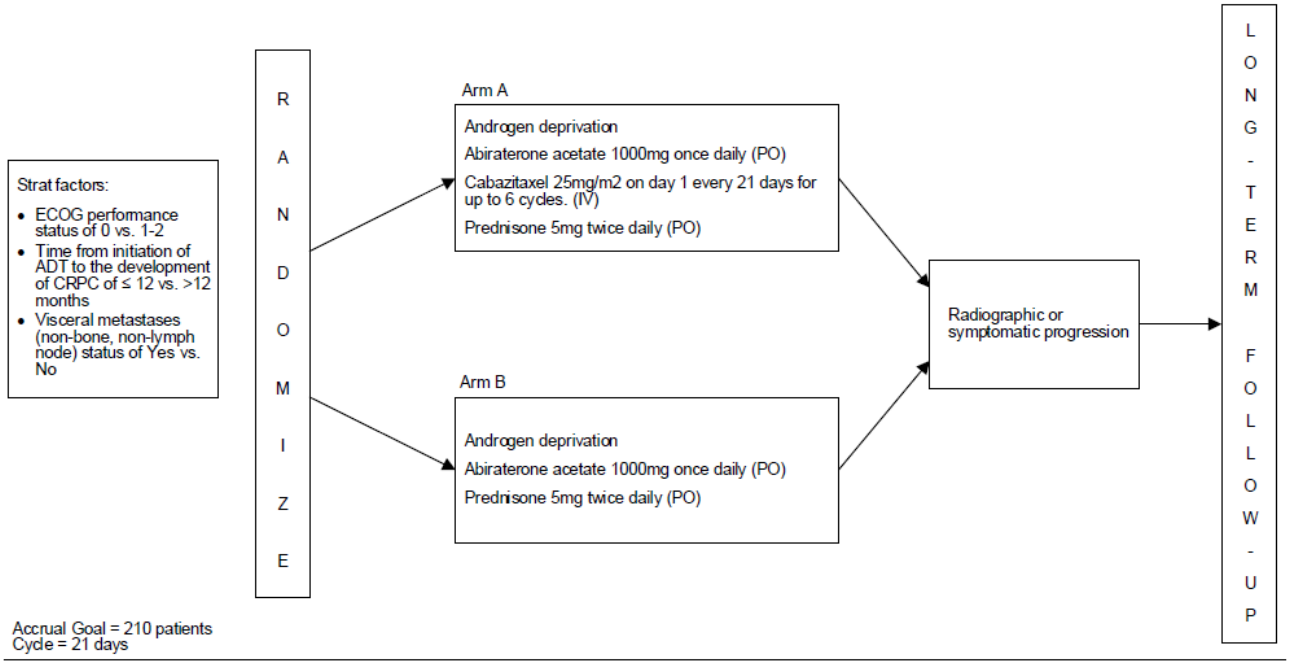
14. Sexually active males must use an accepted and effective method of double barrier contraception (vasectomy must be combined with a physical barrier method) or abstain from sexual intercourse for the duration of their participation in the study and for 26 weeks after the last dose of study drug.

Exclusion Criteria

1. Any prior chemotherapy or AR-directed therapy for CRPC, (e.g. docetaxel, cabazitaxel, mitoxantrone, abiraterone acetate, ketoconazole, or enzalutamide). Previous treatment with radium-223, sipuleucel-T, or other immunotherapy-based treatment is allowed.
2. Pure small cell or other variant (non-adenocarcinoma) prostate cancer histology for which treatment with abiraterone would not be considered appropriate.
3. Patients may not be receiving other therapeutic investigational agents or be receiving concurrent anticancer therapy other than standard androgen deprivation therapy. Concurrent treatment with agents to prevent skeletal-related events (such as zoledronic acid or denosumab) will be allowed as long as it was initiated prior to study registration.
4. Any medical condition for which prednisone (corticosteroid) is contraindicated.
5. Chronic liver disease or abnormal liver function at baseline:
   a. If total bilirubin is > ULN (NOTE: in subjects with Gilbert's syndrome, if total bilirubin is > ULN, measure direct and indirect bilirubin and if direct bilirubin is within normal range, subject may be eligible) or
   b. Alanine (ALT) or aspartate (AST) aminotransferase > 1.5xULN.
6. Active infection requiring treatment with antibiotics.
7. History of adrenal insufficiency or hypoaldosteronism.
8. Myocardial infarction or arterial thrombotic event ≤ 6 months of randomization, heart failure of New York Heart Association Class II or higher, uncontrolled angina, severe uncontrolled ventricular arrhythmia.
9. External beam radiation therapy ≤ 2 weeks of registration.
10. Prior history of allergic reactions to G-CSF.
11. Prior history of allergic reactions to docetaxel and/or to medications formulated with polysorbate 80.
12. History of active malignancy. Patients with a history of cancer that has been adequately treated and are free of disease recurrence for 3 years or more are allowed to participate. Patients with non-melanoma skin cancers or carcinoma in situ of the bladder that have been adequately excised are eligible to participate.
13. Life expectancy of < 12 months at screening.
14. Grade ≥ 2 neuropathy.
15. Uncontrolled hypertension (systolic BP ≥ 160 mmHg or diastolic BP ≥ 100 mmHg). Patients with a history of hypertension are allowed to enroll provided blood pressure is controlled with anti-hypertensive treatment.

2

Schema



Accrual Goal = 210 patients
Cycle = 21 days

1. All patients will continue androgen depravation as per standard of care.
2. All patients will receive Prednisone 5mg twice daily
3. Randomization 1:1 between the two arms