Overall EA8153 Study Objective
To examine whether a second course of chemohormononal therapy, cabazitaxel and abiraterone acetate (abiraterone), can delay disease progression in patients with metastatic castration-resistant prostate cancer (CRPC).

Arm A†
Androgen deprivation†
Abiraterone acetate 1000 mg PO qd
+ Cabazitaxel 25 mg/m² IV on d 1 q 21 d for up to 6 cycles
+ Prednisone

Arm B†
Androgen deprivation†
Abiraterone acetate 1000 mg PO qd
+ Prednisone

Accrual goal = 210 patients.
Cycle = 21 days.
All treatments will be given on an outpatient basis.
†Randomization 1:1 between the 2 arms.
††All patients will continue androgen deprivation as per standard of care and receive prednisone 5 mg PO bid.
‡ADT with either LHRH agonist or antagonist or surgical castration with bilateral orchiectomy.
ADT = androgen deprivation therapy; CRPC = castration-resistant prostate cancer; LHRH = luteinizing hormone-releasing hormone.

Stratification Factors:
• ECOG performance status 0 vs 1-2
• Time from initiation of ADT to development of CRPC ≤ 12 vs > 12 mo
• Visceral metastases (non-bone, non-lymph node) status yes vs no

Radiographic or symptomatic progression

EA8153 Cabazitaxel With Abiraterone Versus Abiraterone Alone Randomized Trial for Extensive Disease Following Docetaxel: The CHAARTED2 Trial
**Study Objectives**

**Primary Objective**
- Assess whether the addition of 6 cycles of cabazitaxel to abiraterone in patients with CRPC who have previously received docetaxel and androgen deprivation therapy (ADT) for metastatic hormone-sensitive prostate cancer (HSPC) can improve progression-free survival (PFS), compared to abiraterone alone.

**Secondary Objectives**
- Assess whether the addition of cabazitaxel can increase the percentage of change in prostate-specific antigen (PSA) from baseline to week 12 of treatment as well as the maximum decline in PSA that occurs at any point after treatment.
- Assess whether the addition of cabazitaxel can prolong time to PSA progression.

**Exploratory Objectives**
- Analyze whether the addition of cabazitaxel can prolong radiographic or clinical PFS in patients with circulating tumor cells (CTCs) positive for androgen-receptor splice variant 7 messenger RNA (AR-V7) at baseline.
- Examine changes in AR-V7 status due to the addition of cabazitaxel.
- Examine the impact of cabazitaxel on future development of AR-V7 positivity at the time of disease progression.

**Imaging Objectives**
- Compare the changes in total tumor burden from baseline to week 12 as assessed with 18F-sodium fluoride (NaF) PET/CT between the 2 arms.
- Correlate total tumor burden at baseline as assessed with NaF PET/CT with the PFS.
- Correlate heterogeneity of response from baseline to week 12 as assessed with NaF PET/CT with the PFS.

**Exploratory Tobacco Use Objectives**
Refer to Protocol Section 2.3.3 for list of objectives.

**Eligibility Criteria**

**Main Inclusion Criteria**
- ≥ 18 years of age with histologically confirmed diagnosis of prostate cancer (adenocarcinoma of the prostate).
- Previous chemotherapy with ≥ 3 cycles of docetaxel for hormone-sensitive metastatic prostate cancer.

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.
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)

Ability to swallow abiraterone tablets as a whole

Receiving standard-of-care ADT (surgical castration vs luteinizing hormone–releasing hormone [LHRH] agonist or antagonist treatment); patients receiving LHRH agonist or antagonist must continue treatment throughout study

Castrate serum level of testosterone of < 50 ng/dL (< 1.73 nmol/L) confirmed ≤ 4 weeks prior to randomization

Progressive disease while receiving ADT, defined by the Prostate Cancer Clinical Trials Working Group 3 (PCWG3) criteria for PSA, measurable disease, or nonmeasurable (bone) disease during treatment with ADT

May or may not have been treated previously with a nonsteroidal antiandrogen, such as flutamide, bicalutamide, or nilutamide. Previous treatment with an antiandrogen must be completed at least 4 weeks (flutamide) or 6 weeks (bicalutamide or nilutamide) prior to registration and must have shown PSA progression after discontinuing the antiandrogen

ECOG performance status of 0-2

Adequate hematologic and renal function ≤ 4 weeks prior to randomization

Resected or irradiated brain metastases or treatment with stereotactic radiation therapy is allowed, provided that treatment with steroids exceeding 10 mg of prednisone daily or equivalent is not required

Use of effective contraception or abstinence

NaF PET/CT optional sub-study: ability to lie still for imaging; weight ≤ 300 lbs; metastatic disease confined predominantly to bone

Main Exclusion Criteria

Prior chemotherapy or androgen receptor–directed therapy for CRPC (eg, docetaxel, cabazitaxel, mitoxantrone, abiraterone, ketoconazole, or enzalutamide); previous treatment with radium-223, sipuleucel-T, or other immunotherapy-based treatment is allowed

(Continued)
**Eligibility Criteria**

*Main Exclusion Criteria*

- Pure small cell or other variant (non-adenocarcinoma) prostate cancer histology for which treatment with abiraterone would not be considered appropriate
- Receiving other therapeutic investigational agents or receiving concurrent anticancer therapy other than standard ADT. Concurrent treatment with agents to prevent skeletal-related events (ie, zoledronic acid or denosumab) is allowed if initiated prior to study registration
- Medical condition for which prednisone (corticosteroid) is contraindicated
- Chronic liver disease or abnormal liver function at baseline
- Active infection requiring treatment with antibiotics
- History of adrenal insufficiency or hypoaldosteronism
- Myocardial infarction or arterial thrombotic event ≤ 6 months of randomization, heart failure of NYHA class II or higher, uncontrolled angina, severe uncontrolled ventricular arrhythmia
- External beam radiation therapy ≤ 2 weeks of registration
- Prior history of allergic reactions to granulocyte colony-stimulating factor (G-CSF), docetaxel, and/or medications formulated with polysorbate 80
- History of a second active malignancy
- Life expectancy of < 12 months at screening
- Grade ≥ 2 neuropathy
- Uncontrolled hypertension

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.*