ECOG 3805 Phase III Randomized Study of Chemohormonal Therapy Versus Androgen Ablation Therapy in Patients With Extensive Metastatic Prostate Cancer [CHAARTED]

Alternate Title
Androgen Ablation Therapy With or Without Chemotherapy in Treating Patients With Metastatic Prostate Cancer

Basic Trial Information

<table>
<thead>
<tr>
<th>Phase</th>
<th>Type</th>
<th>Status</th>
<th>Age</th>
<th>Sponsor</th>
<th>Protocol IDs</th>
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<tbody>
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<td>Phase III</td>
<td>Treatment</td>
<td>Active</td>
<td>18 and over</td>
<td>NCI</td>
<td>ECOG-E3805 NCT00309985</td>
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Special Category: CTSU trial

Objectives

Primary

1. Evaluate the ability of early chemotherapy to improve overall survival of patients commencing androgen deprivation for metastatic prostate cancer.

Secondary

1. Determine whether early chemotherapy can increase the time to clinical progression (radiographic or symptomatic deterioration due to disease) over hormonal therapy alone.
2. Determine whether early chemotherapy can increase the time to development of hormone-refractory disease over hormonal therapy alone.
3. Determine whether early chemotherapy can increase the time to serological progression over hormonal therapy alone.
4. Determine rates of biochemical response at 6 months and 12 months in the chemohormonal arm versus the hormonal therapy alone arm.
5. Determine the frequency of adverse events and the tolerability of chemotherapy combined with hormonal therapy versus hormonal therapy alone.
6. Determine whether the postulated clinically meaningful increase in disease control is associated with an alteration in overall quality of life using the Functional Assessment of Cancer Therapy-Prostate questionnaire.
7. Determine the ability of prostate-specific antigen changes to be a surrogate for clinical benefit from therapy and overall survival.

Tertiary

1. Determine whether there are proteins differentially translated from the genome in hormone-sensitive prostate cancer, prostate cancer that has responded to hormonal therapy, and hormone-refractory prostate cancer.
2. Determine the frequency of polymorphisms of enzymes involved in steroid metabolism and other carcinogenic processes.

3. Determine whether the amount and frequency of certain carcinogenic proteins such as CXCR4 and manganese superoxide dismutase can be correlated with a poor prognosis.

Entry Criteria

Disease Characteristics:

- Histologically or cytologically confirmed prostate cancer
- Extensive metastatic disease meeting any of the following criteria:
  - Visceral metastases (extranodal)
  - Bone metastases
    - At least 4 bone lesions
    - At least 1 bone lesion must be outside of the vertebral column or pelvis
- On androgen deprivation therapy for < 90 days
  - Prostate-specific antigen (PSA) level may not have risen > 50% from its lowest point between the start of androgen deprivation therapy and study entry

Prior/Concurrent Therapy:

- See Disease Characteristics
- At least 4 weeks since prior major surgery and recovered
- Prior adjuvant or neoadjuvant hormonal therapy allowed provided the following are true:
  - At least 12 months since prior therapy with no evidence of disease, defined as 1 of the following:
    - PSA < 0.1 ng/dL after prostatectomy plus hormonal therapy
    - PSA < 0.5 ng/dL and has not doubled above nadir after radiotherapy plus hormonal therapy
  - No more than 24 months of prior therapy
  - Last depot injection must have expired by the 24-month mark
- Prior palliative radiotherapy allowed if commenced within 30 days before starting androgen deprivation
- Anti-androgen therapy allowed as single-agent therapy ≤ 7 days before medial castration to prevent flare
- No prior chemotherapy in adjuvant or neoadjuvant setting
- More than 30 days (or 6 half-lives) (whichever is longer) since prior participation in another clinical trial
- Concurrent participation in nontherapeutic trials allowed
- Concurrent antiandrogen therapy (e.g., bicalutamide or flutamide) allowed, but not as sole hormonal therapy
- No concurrent 5-alpha reductase inhibitors

Patient Characteristics:

- ECOG performance status (PS) 0-2
  - PS 2 eligible only if decline in PS is due to metastatic prostate cancer
- Absolute neutrophil count ≥ 1,500/mm³
- Platelet count ≥ 100,000/mm³
- Bilirubin ≤ normal
- ALT ≤ 2.0 times upper limit of normal (ULN)
- Creatinine clearance ≥ 30 mL/min
- PT and INR ≤ 1.5 times ULN (unless on therapeutic anticoagulation)
- PTT ≤ 1.5 times ULN (unless on therapeutic anticoagulation)
- No prior malignancy in the past 5 years except for basal cell or squamous cell carcinoma of the skin
Other malignancies that are considered to have low potential to progress (e.g., grade 2, T1a transitional cell carcinoma) may be allowed

- No peripheral neuropathy > grade 1
- No history of severe hypersensitivity reaction to docetaxel or other drugs formulated with polysorbate 80
- No active cardiac disease, including the following:
  - Active angina
  - Symptomatic congestive heart failure
  - Myocardial infarction within the past 6 months
- Fertile patients must use effective contraception

**Expected Enrollment**

568

A total of 568 patients will be accrued for this study.

**Outcomes**

*Primary Outcome(s)*

Overall survival

*Secondary Outcome(s)*

Prostate-specific antigen (PSA) response  
Change in PSA over time  
Time to hormone refractory disease  
Time to clinical progression  
Time to PSA progression  
Toxicity

**Outline**

This is a randomized, multicenter study. Patients are stratified according to age (≥ 70 vs < 70), ECOG performance status (0-1 vs 2), planned combined blockade for > 30 days (yes vs no), duration of prior adjuvant hormonal therapy (> 12 months vs ≤ 12 months), and concurrent bisphosphonate use (yes vs no). Patients are randomized to 1 of 2 treatment arms.

- **Arm I:** Patients receive androgen deprivation therapy (including luteinizing hormone-releasing hormone [LHRH] agonist therapy, LHRH antagonist therapy, or surgical castration). Patients also receive docetaxel IV over 1 hour on day 1. Treatment with docetaxel repeats every 21 days for up to 6 courses in the absence of disease progression or unacceptable toxicity.

- **Arm II:** Patients receive androgen deprivation therapy (as in arm I) alone.

Quality of life is assessed at baseline and at weeks 12, 24, 36, and 48.

After completion of study treatment, patients are followed every 3 months for 10 years.

**Trial Contact Information**

**Trial Lead Organizations**

Eastern Cooperative Oncology Group

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