Phase II Clinical Trial of Abiraterone Acetate Without Exogenous Glucocorticoids in Men With Castration-resistant Prostate Cancer With Correlative Assessment of Hormone Intermediates.

This study is ongoing, but not recruiting participants.

Sponsor:
Dana-Farber Cancer Institute

Collaborator:
Janssen Research & Development, LLC

Information provided by (Responsible Party):
Mary-Ellen Taplin, MD, Dana-Farber Cancer Institute

ClinicalTrials.gov Identifier:
NCT02025010

First received: December 13, 2013
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History of Changes

Purpose

This study is comparing the safety and effectiveness of **abiraterone** acetate alone, followed by the addition of **prednisone** (when the participant's disease worsens or the physician feels it would lessen symptoms of toxicity) versus the current approved treatment regimen which involves the concomitant use of **prednisone** in conjunction with **abiraterone** acetate. Additionally, this study is also examining why participants stop responding to treatment with **abiraterone** acetate by evaluating blood and tissue.

Condition	Intervention	Phase
Castration-resistant Prostate Cancer	Drug: **abiraterone** acetate Drug: **prednisone** Procedure: pre-treatment and progression tumor biopsies Genetic: assessment of serum corticosteroid intermediates and ACTH	Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Phase II Clinical Trial of **Abiraterone** Acetate Without Exogenous Glucocorticoids in Men With Castration-resistant Prostate Cancer With Correlative Assessment of Hormone Intermediates.

Resource links provided by NLM:

Genetics Home Reference related topics: prostate cancer

MedlinePlus related topics: Biopsy Cancer Health Checkup Hormones Prostate Cancer Steroids

Drug Information available for: Prednisone Abiraterone acetate

U.S. FDA Resources

Further study details as provided by Dana-Farber Cancer Institute:

Primary Outcome Measures:

- The proportion of participants requiring the addition of **prednisone** to manage symptoms of persistent or severe mineralocorticoid excess (Hypertension and Hypokalemia). [Time Frame: 2 Years] [Designated as safety issue: No]

Secondary Outcome Measures:

- Assessment of safety and tolerability associated with AA monotherapy and the addition of **prednisone** to AA. [Time Frame: 2 Years] [Designated as safety issue: Yes]
- The proportion of participants requiring the addition of **prednisone** to manage symptoms of severe fatigue. [Time Frame: 2 years] [Designated as safety issue: No]
- Assessment of changes in serum concentrations of corticosteroid intermediates between baseline and subsequent assessment visits. [Time Frame: 2 Years] [Designated as safety issue: Yes]
- Assessment of changes in serum concentrations of ACTH between baseline and subsequent assessment visits. [Time Frame: 2 Years] [Designated as safety issue: No]
- Assessment of changes in serum concentrations of androgen (including testosterone, DHT and androgen precursors) between baseline and subsequent assessment visits. [Time Frame: 2 Years] [Designated as safety issue: No]
- Assessment of changes in BMI and hemoglobin-A1c between baseline and subsequent assessment visits. [Time Frame: 2 Years] [Designated as safety issue: Yes]
- Assessment of PSA response and duration of PSA response to AA monotherapy. [Time Frame: 2 Years] [Designated as safety issue: Yes]
- Assessment of PSA response and duration of PSA response to addition of **prednisone** to AA at time of PSA progression on AA monotherapy. [Time Frame: 2 Years] [Designated as safety issue: No]
- Assessment of the response of measurable disease and time to progression of measurable disease to AA monotherapy. [Time Frame: 2 Years] [Designated as safety issue: No]
- Assessment of response of measurable disease and time to progression of measurable disease to addition of **prednisone** to AA at time of PSA progression on AA monotherapy. [Time Frame: 2 Years] [Designated as safety issue: No]

Enrollment:	60
Study Start Date:	December 2013
Estimated Study Completion Date:	June 2018
Estimated Primary Completion Date:	December 2017 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: **abiraterone** acetate • Pre-treatment and progression tumor biopsies. • Four 250 mg tablets (1,000 mg) of **abiraterone** acetate (AA) taken orally on 28 day cycles. • For participants who experience symptoms of persistent or severe hypertension or hypokalemia, **prednisone** 5 mg by mouth twice daily. • For participations who tolerate AA monotherapy without the addition of **prednisone** to manage symptoms of persistent or severe mineralocorticoid excess, **prednisone** 5 mg by mouth twice daily will be added at PSA progression. • Participants will undergo assessment of serum corticosteroid intermediates and ACTH at baseline and subsequent treatment visits for correlation with symptoms of mineralocorticoid excess.	Drug: **abiraterone** acetate Daily four 250 mg tablets (1,000 mg) of AA taken orally for 28 day cycles. No food should be consumed for at least two hours before the dose and for at least one hour after the dose. The tablets should be swallowed whole with water. Tablets should not be crushed or chewed. Other Name: JNJ21208 Drug: **prednisone** Take with food 5 mg Oral Twice daily Other Name: exogenous glucocorticoids Procedure: pre-treatment and progression tumor biopsies Participants will undergo pre-treatment and progression tumor biopsies. After the progression biopsy is performed, protocol therapy will be discontinued. Participants who stop protocol therapy before receiving four cycles of AA will not be asked to undergo the second biopsy. Genetic: assessment of serum corticosteroid intermediates and ACTH •Participants will undergo assessment of serum corticosteroid intermediates and ACTH at baseline and subsequent treatment visits for correlation with symptoms of mineralocorticoid excess.

Detailed Description:

- Participants will be treated with abiraterone acetate (AA) in 28-day cycles. Participants will be monitored (weekly for the first two cycles, then on Day 1 of each subsequent cycle) for symptoms of persistent or severe mineralocorticoid excess (including hypertension, hypokalemia). For participants who experience symptoms of persistent or severe hypertension or hypokalemia as detailed in the above schema, prednisone 5 mg by mouth twice daily will be added. We will monitor for other symptoms of AA toxicity to include fluid retention and fatigue.
- For participations who tolerate AA monotherapy without the addition of prednisone to manage symptoms of persistent or severe mineralocorticoid excess, prednisone 5 mg by mouth twice daily will be added at Prostate Specific Antigen (PSA) progression. Participants will be continued on study until symptomatic or radiographic progression or taken off study for another reason as detailed in protocol.
- Participants will undergo pre-treatment and progression tumor biopsies. Participants will also undergo pre-treatment and progression tumor biopsies for assessment of possible mechanisms of AA resistance. After the progression biopsy is performed, protocol therapy will be discontinued. Participants who stop protocol therapy before receiving four cycles of AA will not be asked to undergo the second biopsy.

- Correlative Studies: Participants will undergo assessment of serum corticosteroid intermediates and Adrenocorticotropic hormone (ACTH) at baseline and subsequent treatment visits for correlation with symptoms of mineralocorticoid excess.

Eligibility

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Genders Eligible for Study:	Male
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Participants must meet the following criteria on screening examination to be eligible to participate in the study:
- Be a male ≥ 18 years of age.
- Participants must have histologically or cytologically confirmed adenocarcinoma of the prostate without >50% neuroendocrine differentiation or small cell histology.
- Participants must have progressive disease as defined by one or more of the following:
- Castrate resistant disease as defined by Prostate cancer working Group (PCWG).[30] Participants must have a rise in PSA on two successive determinations at least one week apart and PSA levels ≥ 2 ng/ml (only the screening PSA needs to be ≥ 2 ng/ml) and testosterone levels < 50 ng/dL.
- Soft tissue progression defined by Response Evaluation Criteria In Solid Tumors (RECIST) 1.1.
- Bone disease progression defined by Prostate Cancer Clinical Trials Working Group 2 (PCWG2) with two or more new lesions on bone scan. [30]
- Castration-resistant prostate cancer (CRPC) with metastatic disease with at least one site of metastatic disease must be amenable to needle biopsy. Soft tissue biopsy sites include: lymph node or visceral metastases. Bone sites include lumbar vertebrae, pelvic bones and long bones. Excluded sites are thoracic, cervical vertebrae, skull and rib lesions. Biopsy site will be selected with guidance of interventional radiologist determining best site to optimize balance of obtaining useful tissue for analysis and minimizing risk.
- Participants without orchiectomy must be maintained on Luteinizing hormone-releasing hormone (LHRH) agonist/antagonist therapy.
- Participants may have had any number of previous hormonal therapies (antiandrogens including enzalutamide, steroids, estrogens, finasteride, dutasteride, ketoconazole) provided these were discontinued ≥ 4 weeks before starting the trial.
- Participants may have had up to two previous cytotoxic therapeutic regimens provided these were discontinued ≥ 4 weeks before starting the trial.
- At least a 4 week interval from previous prostate cancer treatment other than LHRH agonist/antagonist therapy or bisphosphonates to the start of protocol therapy.
- Participants receiving bisphosphonates therapy can be maintained on this therapy. If participants have not started bisphosphonates, it is recommended that they start treatment after the first biopsy.
- Eastern Cooperative Oncology Group (ECOG) performance status < 2 (Karnofsky >60%, see Appendix A).

Participants must have normal organ and marrow function as defined below:

- Platelets > 50,000/microliter (mcL)
- Serum potassium ≥ 3.5 mmol/L (independent of potassium supplementation)
- Serum albumin ≥ 3.0 g/dL
- Aspartate transaminase (AST), Alanine transaminase (ALT), and total bilirubin ≤ 1.5 x Institutional Upper Limit of Normal (ULN).
- Partial thromboplastin time (PTT) ≤ 60, International Normalized Ratio (INR) ≤ 1.5 Institutional ULN unless on warfarin therapy (investigator would need to determine if safe for participant to stop warfarin prior to biopsy)
- Controlled blood pressure (systolic blood pressure < 140 and diastolic blood pressure <90) on no more than three anti-hypertensive agents. Drug formulations containing two or more anti-hypertensive agents will be counted based on the number of active agents in each formulation.
- EKG showing a normal QTc interval (QTc < 450 msec).
- Left ventricular ejection fraction ≥ 50%.
- Have signed an informed consent document indicating that the subjects understands the purpose of and procedures required for the study and are willing to participate in the study.
- Be willing/able to adhere to the prohibitions and restrictions specified in this protocol.
- Written Authorization for Use and Release of Health and Research Study Information (US sites only) has been obtained.
- Able to swallow the study drug whole as a tablet.
- Willing to take AA on an empty stomach; no food should be consumed at least two hours before and for at least one hour after the dose AA is taken.
- Participants 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 PI during the treatment period and for 1 week after last dose of AA.

Exclusion Criteria:

- Participants who exhibit any of the following conditions at screening will not be eligible for admission into the study.
- Uncontrolled illness including, but not limited to ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements or would make prednisone/prednisolone (corticosteroid) use contraindicated.
- 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 III or IV heart disease or cardiac ejection fraction measurement of < 50 % at baseline.
- Thromboembolism within 6 months of Cycle 1, Day 1.
- Severe hepatic impairment (Child-Pugh Class C).
- History of pituitary or adrenal dysfunction.
- Poorly controlled diabetes.
- History of gastrointestinal disorders (medical disorders or extensive surgery) which may interfere with the absorption of the study drug.
- Have a pre-existing condition that warrants long-term corticosteroid use.
- Individuals with a history of a different malignancy are ineligible except for the following circumstances: 1) individuals with a history of other malignancies are eligible if they have been disease-free for at least 5 years and are deemed by the investigator to be at low risk for recurrence of that malignancy, or 2) individuals with the following cancers are eligible if diagnosed and treated within the past 5 years: superficial bladder cancer, basal cell or squamous cell carcinoma of the skin.
- Known brain metastasis.
- Prior therapy with AA.
- Have known allergies, hypersensitivity, or intolerance to AA or prednisone or their excipients.
- Surgery or local prostatic intervention within 30 days of the first dose. In addition, any clinically relevant issues from the surgery must have resolved prior to Cycle 1, Day 1.
- Major surgery or radiation therapy within 4 weeks of Cycle 1, Day 1.
- Strontium-89 or samarium-153 therapy within 4 weeks of Cycle 1, Day 1.
- Radiotherapy, chemotherapy or immunotherapy within 4 weeks, or single fraction of palliative radiotherapy within 14 days of administration of Cycle 1, Day 1.
- Current enrollment in an investigational drug or device study or participation in such a study within 30 days of Cycle 1, Day 1.
- Any acute toxicities due to prior chemotherapy and/or radiotherapy that have not resolved to a NCI Common Toxicity Criteria for Adverse Effects (CTCAE) version 4 grade of ≤ 1. Chemotherapy induced alopecia and grade 2 peripheral neuropathy are allowed.
- Condition or situation which, in the investigator's opinion, may put the participant at significant risk, may confound the study results, or may interfere significantly with participant's participation in the study.
- Individuals not willing to comply with the procedural requirements of this protocol.
- HIV-positive individuals on combination antiretroviral therapy are ineligible because of the potential for pharmacokinetic interactions with AA.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02025010

Locations

United States, Massachusetts

Brigham and Women's Hospital
Boston, Massachusetts, United States, 02115

Dana-Farber Cancer Institute
Boston, Massachusetts, United States, 02115

United States, New York

Memorial Sloan Kettering Cancer Center Basking Ridge
Basking Ridge, New York, United States, 07920

Memorial Sloan Kettering Cancer Center Commack
Commack, New York, United States, 11725

Memorial Sloan-Kettering Cancer Center
New York, New York, United States, 10065

Memorial Sloan Kettering Cancer Center Rockville Centre

Rockville Centre, New York, United States, 11510

Memorial Sloan Kettering Cancer Center Sleepy Hollow
Sleepy Hollow, New York, United States, 10591

Memorial Sloan Kettering Cancer Center West Harrison
West Harrison, New York, United States, 10604

Sponsors and Collaborators

Dana-Farber Cancer Institute

Janssen Research & Development, LLC

Investigators

Principal Investigator: Mary-Ellen Taplin, MD Dana-Farber Cancer Institute

More Information

Responsible Party:	Mary-Ellen Taplin, MD, Principal Investigators, Dana-Farber Cancer Institute
ClinicalTrials.gov Identifier:	NCT02025010 History of Changes
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Health Authority:	United States: Institutional Review Board

Keywords provided by Dana-Farber Cancer Institute:
castration-resistant prostate cancer

Additional relevant MeSH terms:

Prednisone	Mineralocorticoids
Abiraterone Acetate	Hormones, Hormone Substitutes, and Hormone Antagonists
Prostatic Neoplasms	Physiological Effects of Drugs
Genital Neoplasms, Male	Anti-Inflammatory Agents
Urogenital Neoplasms	Antineoplastic Agents, Hormonal
Neoplasms by Site	Antineoplastic Agents
Neoplasms	Steroid Synthesis Inhibitors
Genital Diseases, Male	Enzyme Inhibitors
Prostatic Diseases	Molecular Mechanisms of Pharmacological Action
Hormones	Hormone Antagonists
Glucocorticoids	Cytochrome P-450 Enzyme Inhibitors

ClinicalTrials.gov processed this record on September 27, 2016