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General Information

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Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.
How did you learn about the YODA Project?: Colleague

Conflict of Interest


Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training
1. NCT00638690 - COU-AA-301 - A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Abiraterone Acetate (CB7630) Plus Prednisone in Patients With Metastatic Castration-Resistant Prostate Cancer Who Have Failed Docetaxel-Based Chemotherapy
2. NCT00887198 - COU-AA-302 - 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
3. NCT01695135 - ABI-PRO-3001 - A Phase 3, Randomized, Double-blind, Placebo-Controlled Study of Abiraterone Acetate (INJ-212082) Plus Prednisone in Patients With Metastatic Castration-Resistant Prostate Cancer Who Have Failed Docetaxel-Based Chemotherapy
4. NCT02236637 - 212082PCR4001 - A Prospective Registry of Patients With a Confirmed Diagnosis of Adenocarcinoma of the Prostate Presenting With Metastatic Castrate-Resistant Prostate Cancer
5. NCT00485303 - COU-AA-004 - A Phase II Open Label Study of CB7630 (Abiraterone Acetate) and Prednisone in Patients With Advanced Prostate Cancer Who Have Failed Androgen Deprivation and Docetaxel-Based Chemotherapy
6. NCT01685983 - 212082PCR2007 - A Phase 2 Open Label Study of Abiraterone Acetate (INJ-212082) and Prednisolone in Patients With Advanced Prostate Cancer Who Have Failed Androgen Deprivation and Docetaxel-Based Chemotherapy
7. NCT00474383 - COU-AA-003 - A Phase II Open Label Study of CB7630 (Abiraterone Acetate) in Patients With Advanced Prostate Cancer Who Have Failed Androgen Deprivation and Docetaxel-Based Chemotherapy
8. NCT01795703 - INJ-212082-JPN-202 - A Phase II Study of INJ-212082 (Abiraterone Acetate) in Metastatic Castration-Resistant Prostate Cancer Patients Who Have Received Docetaxel-Based Chemotherapy
9. NCT00544440 - COU-AA-BMA - An Observational Study of Continuous Oral Dosing of an Irreversible CYP17 Inhibitor, Abiraterone Acetate (CB7630), in Castration-Resistant Prostate Cancer Patients Evaluating Androgens and Steroid Metabolites in Bone Marrow Plasma
10. NCT01715285 - 212082PCR3011 - A Randomized, Double-blind, Comparative Study of Abiraterone Acetate Plus Low-Dose Prednisone Plus Androgen Deprivation Therapy (ADT) Versus ADT Alone in Newly Diagnosed Subjects With High-Risk, Metastatic Hormone-naive Prostate Cancer (mHNPC)
11. NCT01591122 - ABI-PRO-3002 - A Phase 3, Randomized, Double-blind, Placebo-Controlled Study of Abiraterone Acetate (INJ-212082) Plus Prednisone in Asymptomatic or Mildly Symptomatic Patients With Metastatic Castration-Resistant Prostate Cancer
12. NCT02257736 - 56021927PCR3001 - A Phase 3 Randomized, Placebo-controlled Double-blind Study of INJ-56021927 in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone in Subjects With Chemotherapy-naive Metastatic Castration-resistant Prostate Cancer (mCRPC)

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Understanding the Symptom Experience of Abiraterone and the Effect on Quality of Life for Men with metastatic Prostate Cancer.

Narrative Summary:

Patients with advanced prostate cancer may experience symptoms due to the disease or treatments that they receive. Control of disease, relief of physical symptoms, and maintaining physical function should all be considerations in treatment. The experience of these symptoms can have a negative
impact on quality of life, functional status, and may be an indicator of progression of disease. Because abiraterone acetate + prednisone is approved in both the hormone sensitive prostate cancer (HSPC) and castrate resistant prostate cancer (CRPC) setting, understanding the HRQoL and potential prognostic impact of patient reported outcomes (PROs) can aid clinicians in treatment sequencing decisions.

Scientific Abstract:

Background

Patients with advanced prostate cancer may experience symptoms due to the disease or the treatments that they receive. Fatigue and pain have been identified as the most dominant reported symptoms. The experience of these symptoms can have a negative impact on quality of life, functional status, and may be an indicator of progression of disease. Abiraterone acetate was the first of the second-generation androgen receptor blockers to be approved in metastatic castrate resistant prostate cancer (mCRPC) and now has indications in the metastatic hormone sensitive prostate cancer (mHSPC) setting. Understanding the health related quality of life (HRQoL) and potential prognostic impact of patient reported outcomes (PROs) can aid clinicians in treatment sequencing decisions.

Objective

Using PRO data (as documented by the Functional Assessment of Cancer Therapy ? Prostate (FACT-P), European Quality of Life-5 Dimensions, 5 Levels Questionnaire (EQ-5D-(5L), Brief Fatigue Inventory ? Short Form (BFI-SF), and Brief Pain Inventory ? Short Form (BPI-SF)) from existing clinical trials, we propose to determine the impact of abiraterone + prednisone on HRQoL, fatigue and pain in individuals with advanced prostate cancer in both the hormone sensitive (HSPC) and castrate-resistant (CRPC) setting.

Study Design

Retrospective cohort study.

Primary and Secondary Outcome Measure

We will examine the pattern of symptom change over time in FACT-P, BFI-SF, BPI-SF scores in abiraterone + prednisone. The patterns will be analyzed and described in both the mHSPC and mCRPC disease state. Additional sub analysis will look for predictive symptom patterns in patients who experienced progression of disease vs disease control. Additional outcome is to identify demographic risk factors that may constitute risk for treatment failure due to symptom intolerability.

Statistical Analysis

The association with PRO scores will be evaluated using repeated measures linear and logistic regression models adjusted for baseline characteristics. Kaplan-Meier time to event analysis will be used on PRO data covering the overall study period to identify the time to the first PRO item showing clinically meaningful change of symptoms to radiographic progression. Cox proportional-hazards models will be used to test association of baseline PRO scores and changes associated with survival, progression free survival, and covariates. Demographic data will be collected, and descriptive statistics will be used. By using PRO data across multiple studies, we intend to increase the racial/ethnic diversity of the analysis.

Brief Project Background and Statement of Project Significance:

Patients with advanced prostate cancer may experience symptoms due to the disease or the treatments that they receive. Because of the non-curative nature of advanced prostate cancer, control of disease, relief of physical symptoms, and maintain physical function should all be considerations in treatment(Yount et al., 2003). Fatigue and pain have been identified as the most dominant reported symptoms, with fatigue listed as the most common experienced adverse event in patient with advanced prostate cancer(Rodrguez Antoln et al., 2019). The experience of these symptoms can have an negative impact on quality of life, functional status, and may be an indicator of prognosis as symptom profiles change with progression of disease (Fan et al., 2007). Because abiraterone acetate + prednisone is approved in both the hormone sensitive prostate cancer (HSPC) and castrate resistant prostate cancer (CRPC) setting, understanding the HRQoL and potential prognostic impact of patient reported outcomes (PROs) can aid clinicians in treatment.
sequencing decisions. Men with advanced prostate cancer have changes in their functional capacity related to the side effects of treatment, resulting in a negative impact on quality of life (Saini et al., 2013) While these men report that maintenance of function and quality of life are their priority, the ability to achieve this is influenced by the experience of fatigue and pain symptoms associated with the disease and standard of care treatments (Feng et al., 2017). The timing and severity of symptoms are important when assessing progression and treatment tolerability.

Incorporating patient experience has been identified as a high-priority area of research in prostate cancer care, with protocols that utilize changes in health related quality of life (HRQoL) as a primary endpoint (Kvorning Ternov et al., 2019; Ternov et al., 2022). Both patients and clinicians report that this data is an important aspect in treatment decisions (Thiery-Vuillemin et al., 2020). Understanding the symptom characteristics through the lifespan of the disease can aid in clinical decision-making and areas of future research.

Using PRO data (as documented by the Functional Assessment of Cancer Therapy ? Prostate (FACT-P), European Quality of Life-5 Dimensions, 5 Levels Questionnaire (EQ-5D-(5L), Brief Fatigue Inventory ? Short Form (BFI-SF), and Brief Pain Inventory ? Short Form (BPI-SF)) from existing clinical trials, we propose to determine the impact of abiraterone + prednisone on HRQoL, fatigue and pain in individuals with advanced prostate cancer in both the hormone sensitive (HSPC) and castrate-resistant (CRPC) setting. We will examine the pattern of symptom change over time in FACT-P, BFI-SF, BPI-SF scores in abiraterone + prednisone. The patterns will be analyzed and described in both the mHSPC and mCRPC disease state. Additional sub analysis will look for predictive symptom patterns in patients who experienced progression of disease vs disease control.

**Specific Aims of the Project:**

**AIM 1:** To describe the PRO symptom experience and quality of life ratings of patients receiving abiraterone acetate plus prednisone in the mHSPC and mCRPC setting. Do patients receiving abiraterone acetate plus prednisone demonstrate a pattern of change from baseline in reported PROs, and is this change clinically meaningful?

**Hypothesis 1:** There will be higher symptom burden and decrease in time deterioration of symptoms in patients receiving abiraterone + prednisone in the CRPC setting because of the later stage of the disease.

**AIM 2:** To determine if patterns in quality-of-life PROs have a predictive correlational relationship to abiraterone acetate plus prednisone treatment response. Identify if clinically meaningful changes (CMC) in PRO related to response to therapy. The expected outcome is that CMC of PRO symptoms will be a clinical predictor response to treatment.

**Sub-AIM:** If a pattern is identified with PRO and HRQoL in clinical trial data, does it correspond to real world data with abiraterone or other androgen receptor blockers in the real-world setting.

**Hypothesis 2:** CMC with worsening symptoms will correlate with lack of response to abiraterone acetate plus prednisone treatment for both hormone sensitive and castrate resistant advanced prostate cancer.

**Study Design:**

Meta-analysis (analysis of multiple trials together)

**Research Methods**

**Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:**

We have identified 11 phase II/III clinical trials using abiraterone + prednisone and one real world registry of patients with CRPC, some of which were receiving abiraterone acetate + prednisone, with data available for public access. A meta-analysis of each of individual patient data from each these trials that had patients answer questions on symptom burden and impact using the FACT-P, EQ-5D-(5L), BFI-SF and/or BPI-SF questionnaire at baseline and at least every three months after the initiation of treatment.
We will include all patients who participated in these trials, received the relevant treatment, and completed the FACT-P, EQ-5D- (5L), BFI-SF, and/or BPI-SF questionnaire. Participants who did not complete the baseline assessments will be excluded.

**Primary and Secondary Outcome Measure(s) and how they will be categorized/defined for your study:**

FACT-P survey results (continuous) all individual survey data for participants
EQ-5D-(5L) survey results (continuous) all individual survey data for participants
BFI-SF survey results (continuous) all individual survey data for participants
BPI-SF survey results (continuous) all individual survey data for participants
Mean changes from baseline in PRO item scores (continuous variable)

**Main Predictor/Independent Variable and how it will be categorized/defined for your study:**

- Treatment arm: Categorical
- Ethnicity, Race: Categorical
- Region of study: Categorical
- Birthdate, Age, height, weight: Continuous
- Presence of bone, node, and visceral metastases at baseline: yes/no (categorical)
- Site of visceral metastasis: Categorical
- Number of bone metastasis: Ordinal
- Gleason Score: Ordinal
- TNM stage
- Prior surgery or radiation therapy to primary: yes/no
- Duration of prior therapies
- Bone pain (yes/no)
- Opioid use at baseline (yes/no)
- Initiation of Opioid use date of prescription (day of study)
- ECOG PS: Ordinal (0-2)
- Prior exposure to docetaxel
- Receipt of ADT in the neoadjuvant/adjuvant setting: yes/no
- Duration of neoadjuvant/adjuvant ADT if any (continuous)
- Date of randomization (date format) ? to calculate PFS and OS
- Date of metastatic diagnosis (date format)
- Date of diagnosis (date format)
- Time from ADT to trial treatment start in months

**Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:**

PSA: Continuous
- PSA nadir: continuous
- Testosterone: Continuous
- Hemoglobin: Continuous
- Serum albumin: Continuous
- Serum alkaline phosphatase: Continuous
- Serum LDH: Continuous
- Total WBC count with differential counts
- Platelet count
- Post-baseline radiographic evaluation (BS/CT scan): categorical
- Last follow-up (date format)
- Censoring information for PFS and OS
- Time of treatment discontinuation
- Time of radiographic progression (date format) ? to calculate PFS
- Time of clinical progression (date format) ? to calculate PFS
- Time of PSA progression (date format) ? to calculate PFS
- Time of death (date format) to calculate OS
- Cause of death
- Censoring information for PFS and OS
- Life prolonging therapy received after progression? (Yes/no) and its details

Statistical Analysis Plan:

Continuous PRO variables will be analyzed using repeated measures linear and logistic regression models adjusted for baseline characteristics. Kaplan-Meier time to event analysis will be used on PRO data covering the overall study period to identify the time to the first PRO item showing CMC of symptoms to radiographic progression. Demographic data will be collected, and descriptive statistics will be used. Cox proportional-hazards models will be used to test association of baseline PRO scores and changes associated with survival, progression free survival, and covariates.

Project Timeline:

May 2023 Project submission
May 2023 - August 2023 Data cleaning
August 2023 - October 2023 Data analysis
October 2023 - February 2024 Manuscript drafting.
March 2024 Submission for publication

Dissemination Plan:

Dissemination Plan: Results will be submitted for presentation at local, regional, national, and international oncology conferences. The publications will be submitted to high-impact oncology journals.

Bibliography: