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General Information

Key Personnel (in addition to PI):
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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?: Scientific Publication

Conflict of Interest

https://yoda.yale.edu/system/files/coizy.pdf

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 (JNJ-212082) Plus Prednisone in Patients With Metastatic Castration-Resistant Prostate Cancer Who Have Failed Docetaxel-Based Chemotherapy
4. NCT01591122 - ABI-PRO-3002 - A Phase 3, Randomized, Double-blind, Placebo-Controlled Study of Abiraterone Acetate (JNJ-212082) Plus Prednisone in Asymptomatic or Mildly Symptomatic Patients With

Metastatic Castration-Resistant Prostate Cancer

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

Research Proposal

Project Title

Overall Survival and Radiographic Progression Free Survival difference among Asian, White and Black mCRPC patients treated with Abiraterone

Narrative Summary:

In patients with metastatic castration-resistant prostate cancer (mCRPC), there may be differences in the sensitivity of different races to various treatments. This difference will be reflected in the overall survival (OS) and radiographic progress free survival (rPFS). We hope to determine the differences in OS and rPFS among patients of different races under the same treatment conditions by analyzing these four clinical trials, and further analyze the deep-seated reasons for the differences. So as to provide a factual basis for the study of the genetic basis of treatment sensitivity in different races and the necessity of including different races in future clinical trials.

Scientific Abstract:

Background?
Prostate cancer (PCa) is the second most commonly diagnosed cancer and the fifth leading cause of cancer-related deaths among men worldwide, with an estimated 1,414,259 new cancer cases and 375,304 deaths in 2020[1]. Although Asian has a relatively lower incidence and mortality rate than White[2], data on racial disparities in men with advanced prostate cancer are limited[3-4]. Furthermore, In multi-center clinical trials for prostate cancer, Asian as well as Black are always under-represented[5]. As Abiraterone has become a standardized treatment for patients with metastatic castration-resistant prostate cancer (mCRPC), we hypothesized that Asian, Black and White patients may have difference in overall survival (OS) and radiographic progress free survival (rPFS) after treated with Abiraterone.

Objective?
Using individual patient data from NCT00638690, NCT01695135, NCT00887198, NCT01591122 these four clinical trials which including mCRPC patients treated with Abiraterone to perform race-stratified analysis for OS and PFS survival.

Study Design?
A post-hoc analysis of NCT00638690, NCT01695135, NCT00887198, NCT01591122 will be performed to estimate the distribution of outcomes according to patients' geographic locations. Compare the sensitivity difference to Abiraterone among Asian, Black and White.

Participants?
Patients enrolled in NCT00638690, NCT01695135, NCT00887198, NCT01591122 trials treated with Abiraterone. Patients treated with placebo will be used as a reference.

Primary and Secondary Outcome Measure(s)?
Overall survival & Radiographic progression free survival

Statistical Analysis?
R Statistical software will be used for all assessments. Baseline data of patients (Asian, Black and White) will be first balanced by Propensity Score Matching (PSM) and then estimated by Kaplan-Meier analysis, with hazard ratios calculated using a multivariate Cox proportional-hazard model.

Brief Project Background and Statement of Project Significance:

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Prostate cancer (PCa) is the second most commonly diagnosed cancer and the fifth leading cause of cancer-related deaths among men worldwide, with an estimated 1,414,259 new cancer cases and 375,304 deaths in 2020[1]. Although Asian has a relatively lower incidence and mortality rate than White[2], data on racial disparities in men with advanced prostate cancer are limited[3-4]. Furthermore, In multi-center clinical trials for prostate cancer, Black and Asian are always under-represented[5]. As Abiraterone has become a standardized treatment for patients with metastatic castration-resistant prostate cancer (mCRPC), we hypothesized that Asian, Black and White patients may have difference in overall survival (OS) and radiographic progress free survival (rPFS) after treated with Abiraterone.
All the four clinical trails in this application include “Abiraterone-prednisone” group and “placebo- prednisone” group. Among them, NCT00638690 mainly included white patients with mCRPC who have failed Docetaxel-Based Chemotherapy, NCT01695135 mainly included Asian patients with mCRPC who have failed Docetaxel-Based Chemotherapy, NCT00887198 mainly included white patients with mCRPC and no prior chemotherapy, NCT01591122 mainly included Asian patients with mCRPC and no prior chemotherapy. Therefore, to test our hypothesis, we will combine NCT00638690 trial with NCT01695135 trail and combine NCT00887198 with NCT01591122 to ensure the Asian, Black and white patients enrolled have received the same treatment.
Our study, although hypothesis generating, may advance our understanding the disparity of mCRPC between the East and West. Besides, our study will provide a factual basis for the further exploration of the genetic basis of Abiraterone sensitivity in different races and the necessity of including different races in future clinical trials.

Specific Aims of the Project:

Objective: Using individual patient data from NCT00638690, NCT01695135, NCT00887198, NCT01591122 these four clinical trials which including mCRPC patients treated with Abiraterone to perform race-stratified (Asian, Black and White) analysis for OS and PFS survival.
Hypothesis: Asian, Black and White mCRPC patients may have difference in overall survival (OS) and progress free survival (PFS) after treated with Abiraterone.

What is the purpose of the analysis being proposed? Please select all that apply.
New research question to examine treatment effectiveness on secondary endpoints and/or within subgroup populations
Participant-level data meta-analysis
Meta-analysis using data from the YODA Project and other data sources
Research on comparison group

Research Methods

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

We have identified 4 clinical trials that tested the treatment effect of Abiraterone in men with mCRPC. Among these 4 trials, NCT01695135 mainly included East Asian patients with mCRPC who have failed Docetaxel-Based Chemotherapy, NCT00887198 mainly included white and some Black patients with mCRPC and no prior chemotherapy, NCT01591122 mainly included East Asian patients with mCRPC and no prior chemotherapy. Patients in all these trials had histologically or cytologically confirmed prostate cancer and were considered to have disease progression. All the Asian, Black and White patients from these 4 trails will be included. Meanwhile, patients whose baseline information or outcomes were incomplete will be excluded.
Other data source include SEER database will be used to confirm the outcome after analyzing above 4 clinical trials. Participant-level data from SEER will be processed on our own computer.

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

Primary end points include overall survival and radiographic progression-free survival in Asian, Black and White with metastatic castration-resistant prostate cancer after treated with Abiraterone.
Secondary end points include PSA response and safety.

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

Race (Asian, Black and White), Clinicopathological variables as age, body mass index, Gleason score, tumor

stage, performance of status, site of metastases, PSA, medication, comorbidity, et al.

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

Race (White, African American, Asian, other)

Statistical Analysis Plan:

Participants who had the same treatment will be divided by race (Asian, Black and White). Propensity score methods (PSM) will be used to balance the baseline differences among different races. PSM will be performed by MatchIt package in Rstudio. Base on the data after PSM, Kaplan-Meier analysis and established multivariate Cox proportional-hazard model will be performed by survival and survminer package.
Software Used:
RStudio
Project Timeline:

We anticipated start the project In September this year, finish the analysis before 1 Sep 2023, and draft the manuscript for submission before 1 Mar 2024.

Dissemination Plan:

We plan to submit the project to well-known meetings (GU-ASCO, ESMO) and journals (European Urology, Annals of Oncology)

Bibliography:

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5.Owens-Walton J, Williams C, Rompré-Brodeur A, Pinto PA, Ball MW. Minority Enrollment in Phase II and III Clinical Trials in Urologic Oncology. J Clin Oncol. 2022 May 10;40(14):1583-1589.