

Principal Investigator

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General Information

Key Personnel (in addition to PI): **First Name:** Daniel
Last name: Moreira
Degree: MD, MHS
Primary Affiliation: University of Illinois at Chicago

Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.

 [yoda_project_coi_form_for_data_requestors_2016-signed.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

Associated Trial(s): [NCT00638690 - 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](#)

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

Research Proposal

Project Title

Predictors of survival in metastatic castration-resistant prostate cancer

Narrative Summary:

Metastatic castration-resistant prostate cancer (mCRPC) patients generally have an unfavorable prognosis but not all patients have an identical clinical course. While some patients quickly progress to widespread metastatic disease and die of cancer, others have a much more indolent disease progression. Thus, we seek to identify the predictors of time from initial diagnosis of mCRPC to all-cause death. The results of this research will help patients and physicians better determine the prognosis of patients with mCRPC.

Scientific Abstract:

Background: Metastatic castration-resistant prostate cancer (mCRPC) patients generally have an unfavorable prognosis but not all patients have an identical clinical course. While some patients quickly progress to widespread metastatic disease and die of cancer, others have a much more indolent disease progression (1-4).

Objective: We seek to investigate the predictors of time from mCRPC to all-cause mortality.

Study design: Retrospective cohort study

Participants: Men with mCRPC in the placebo arm of 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.

Main outcome: Overall survival

Secondary outcome: Disease-specific survival, disease progression

Statistical analysis: Survival will be estimated and plotted using the Kaplan-Meier method. The uni- and multivariable survival predictors will be evaluated with Cox proportional hazards model.

Brief Project Background and Statement of Project Significance:

Although metastatic castration-resistant prostate cancer (mCRPC) patients generally have an unfavorable prognosis, not all patients have an identical clinical course (1-4). Indeed, some patients quickly progress to widespread metastatic disease and die of cancer while others have a much more indolent disease progression. Thus, we seek to investigate the predictors of time from mCRPC to all-cause mortality. The results of our study will help physicians and researchers stratify mCRPC patients according to their risk of death.

Specific Aims of the Project:

Objective: To determine the predictors of time from metastatic castration-resistant prostate cancer (mCRPC) to all-cause mortality.

Hypothesis: Based on previous reports, we hypothesize that older age at mCRPC, greater number of bone metastasis, higher PSA levels and shorter PSA doubling time at mCRPC will be significantly associated with shorter overall survival.

What is the purpose of the analysis being proposed? Please select all that apply. Other

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

Data source: 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.

Inclusion criteria: patients in the placebo arm

Exclusion criteria: missing data

Main Outcome Measure and how it will be categorized/defined for your study:

Main outcome: overall survival

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

For this study we will not focus on one single predictors. We seek to determine the variables associated with all-cause mortality. The variables of interest include: included patient's age at metastatic castration-resistant prostate cancer (mCRPC, continuous, in years), year of mCRPC diagnosis (continuous), patient's race (black or non-black), treatment center, biopsy Gleason score (2-6, 3+4, 4+3-10 or unknown/not available), localized treatment for PC (none, radical prostatectomy ± radiation ± ADT, radiation alone ± ADT, other), number of bone metastases (1, 2, 3-9, ? 10 or visceral/lymph node metastasis only), metastases to lymph nodes (yes or no), metastases in visceral tissue (yes or no), PSA at mCRPC (continuous and log-transformed, in log[ng/mL]) PSADT at mCRPC (continuous

and log-transformed, in log[months]), and PSAV at mCRPC (continuous, in ng/mL/year).

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

Please see above.

Statistical Analysis Plan:

Baseline patient and disease characteristics at the time of metastatic castration-resistant prostate cancer (mCRPC) diagnosis will be presented as absolute numbers and percentages, and as median and interquartile range (IQR) for categorical and continuous variables, respectively. Time from mCRPC diagnosis to all-cause death will be evaluated and plotted using the Kaplan-Meier function. The association of patient and disease characteristics with time from mCRPC to all-cause mortality will be evaluated with Cox proportional hazards model in multivariable analysis. Variables considered for the model include patient's age at mCRPC (continuous, in years), year of mCRPC diagnosis (continuous), patient's race (black or non-black), treatment center, biopsy Gleason score (2-6, 3+4, 4+3-10 or unknown/not available), localized treatment for PC (none, radical prostatectomy ± radiation ± ADT, radiation alone ± ADT, other), number of bone metastases (1, 2, 3-9, ? 10 or visceral/lymph node metastasis only), metastases to lymph nodes (yes or no), metastases in visceral tissue (yes or no), PSA at mCRPC (continuous and log-transformed, in log[ng/mL]) PSADT at mCRPC (continuous and log-transformed, in log[months]), and PSAV at mCRPC (continuous, in ng/mL/year). The proportional hazard assumption was addressed by examining Schoenfeld residuals of each variable and tested with Grambsch and Therneau's statistic. All statistical analyses will be performed using Stata 12.1 (StataCorp, College Station, TX) and R 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided $P < 0.05$ will be considered to indicate statistical significance.

Project Timeline:

Day 0: Approval of the project

Day 30: Data transfer

Day 60: Data processing (data re-coding/formatting)

Day 90: Data analysis

Day 120: Manuscript writing

Day 180: Manuscript submission

Dissemination Plan:

We plan to publish the results of this project in the form of a manuscript in oncology and urology medical journal(s).

Bibliography:

1. Halabi S, Lin CY, Kelly WK, et al. Updated prognostic model for predicting overall survival in first-line chemotherapy for patients with metastatic castration-resistant prostate cancer. *J Clin Oncol*. 2014;32:671-677.
2. Armstrong AJ, Tannock IF, de Wit R, George DJ, Eisenberger M, Halabi S. The development of risk groups in men with metastatic castration-resistant prostate cancer based on risk factors for PSA decline and survival. *European journal of cancer*. 2010;46:517-525.
3. Halabi S, Lin CY, Small EJ, et al. Prognostic model predicting metastatic castration-resistant prostate cancer survival in men treated with second-line chemotherapy. *J Natl Cancer Inst*. 2013;105:1729-1737.
4. Armstrong AJ, Garrett-Mayer ES, Yang YC, de Wit R, Tannock IF, Eisenberger M. A contemporary prognostic nomogram for men with hormone-refractory metastatic prostate cancer: a TAX327 study analysis. *Clinical cancer research : an official journal of the American Association for Cancer Research*. 2007;13:6396-6403.