The YODA Project
Research Proposal Review

The following page contains the final YODA Project review approving this proposal.

The Yale University Open Data Access (YODA) Project
Yale University Center for Outcomes Research and Evaluation (CORE)
1 Church Street, Suite 200, New Haven, CT 06510

The YODA Project
Research Proposal Review - Final
(Protocol #: 2015-0565)

Reviewers:

- ☒ Nihar Desai
- ☒ Cary Gross
- ☒ Harlan Krumholz
- ☒ Richard Lehman
- ☒ Joseph Ross

Review Questions:	**Decision:**
1. Is the scientific purpose of the research proposal clearly described?	Yes
2. Will request create or materially enhance generalizable scientific and/or medical knowledge to inform science and public health?	Yes
3. Can the proposed research be reasonably addressed using the requested data?	Yes, or it's highly likely
4. Recommendation for this data request:	Approve

Comments:

Use of this feedback is at your discretion: Aim 2 may not be feasible, depending on the number of the "screen failures" that had the reason for failure documented.

The YODA Project
Research Proposal Review

Revisions were requested during review of this proposal.
The following pages contain the original YODA Project review and the original submitted proposal.

The Yale University Open Data Access (YODA) Project
Yale University Center for Outcomes Research and Evaluation (CORE)
1 Church Street, Suite 200, New Haven, CT 06510

The YODA Project
Research Proposal Review - Revisions Requested
(Protocol #: 2015-0565)

Reviewers:

- ☒ Nihar Desai
- ☒ Cary Gross
- ☒ Harlan Krumholz
- ☒ Richard Lehman
- ☒ Joseph Ross

Review Questions:	**Decision:**
1. Is the scientific purpose of the research proposal clearly described?	No
2. Will request create or materially enhance generalizable scientific and/or medical knowledge to inform science and public health?	Yes
3. Can the proposed research be reasonably addressed using the requested data?	Yes, or it's highly likely
4. Recommendation for this data request:	Not Approve

Comments:

Please specify the variables you intend to include as candidate covariates in your multivariable model.

The project timeline may not be feasible as written. The YODA Project aims to complete the review of your revised proposal within 30 days of submission. If approved, you and your institution will then be required to sign the relevant Data Use Agreement. After the DUA has been signed, the YODA Project aims to provide access to the data within 30 days of receipt of the DUA. More details can be found here. As such, you may wish to revise the project timeline.

Principal Investigator

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Country: Canada

2015-0565

General Information

Key Personnel (in addition to PI): **First Name:** Sarah
Last name: Wong
Primary Affiliation: Princess Margaret Cancer Center

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

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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

Understanding reasons for screen failures in late phase trials in advanced GU cancers

Narrative Summary:
In clinical trials, screen failures are defined as subjects who consented to participate in research but who were disqualified during screening procedures. Screen failures can occur for patient or study specific reasons and can significantly increase the resource requirements and costs of doing clinical trials. The goal of this project is to better understand why screen failures occur in late phase clinical trials in advanced genitourinary cancers (prostate, kidney and bladder cancer). Understanding screen failures could lead to better trial design in GU oncology that aims to limit the potential for screen failures.

Scientific Abstract:
Background: Screen failures in clinical trials represent a significant cost and resource expenditure. Understanding the reasons behind screen failures and developing strategies to minimize them, could significantly improve efficiency and reduce the costs of doing clinical trials.

Objective: To review published phase III trials in advanced prostate cancer and collect data on number and timing of screen failures as well as document reasons for screen failures.

Study Design: Retrospective cohort study

Participants: All patients enrolled on the COU 301 study, with a specific focus on those patients who were deemed to be screen failures.

Main Outcome Measures:
1. The number (percent) of screen failures.
2. The specific reasons for screen failures - identifying if they are are study or patient related.
3. The main predictors of screen failures using univariate and multivariate binary logistic regression analysis.

Statistical Analysis: We will evaluate predictors of screen failures using uni-variate and if possible multivariate binary logistic regression analysis.

Brief Project Background and Statement of Project Significance:
Screen failures in late phase clinical trials in GU oncology are not uncommon with rates of about 25%, similar to what has been previously reported for Phase 1 trials by Mckane et al (Investigational New Drugs 2013). Both patient specific and study specific factors may contribute to screen failures. Understanding the reasons behind screen failures and developing strategies to minimize them, may significantly improve efficiency and reduce the cost of doing clinical trials not only in advanced prostate cancer, but widely across the field of oncology.

Specific Aims of the Project:
1. Document the number (percent) of screen failures.
2. Document the specific reasons for screen failures - identifying if they are are study or patient related.
3. Evaluate the predictors of screen failures using univariate and multivariate binary logistic regression analysis.

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:
Retrospective analyses of the COU 301 clinical trial will be conducted to assess for screen failures, and reasons for screen failures.
Patient level data will be required to clearly delineate reasons for screen failures.

Main Outcome Measure and how it will be categorized/defined for your study:
1. Document the number (percent) of screen failures.
2. Document the specific reasons for screen failures - identifying if they are are study or patient related.
3. Evaluate the predictors of screen failures using univariate and multivariate binary logistic regression analysis.

Main Predictor/Independent Variable and how it will be categorized/defined for your study:
Evaluate the predictors of screen failures using univariate and multivariate binary logistic regression analysis.

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:
We will also be interested in determining the timing of screen failures.

Statistical Analysis Plan:
Results will be analyzed using descriptive analyses.
The predictors of screen failures will be analyzed using univariate and multivariate binary logistic regression analysis.

Project Timeline:
Completion of Contract - 07/2015
Obtain Deidentified Dataset - 08/2015
Analysis and report submitted to YODA 09/2015
Circulation of abstract targeting GU ASCO to YODA 09/2015
Circulation of paper to YODA targeting JCO, Lancet Oncology, or Journal of Urology

Dissemination Plan:
Circulation of abstract targeting GU ASCO to YODA 09/2015
Circulation of paper to YODA targeting JCO, Lancet Oncology, or Journal of Urology

Bibliography:
1) McKane et al., Determinants of patient screen failures in Phase 1 clinical trials.
Invest New Drugs. 2013 Jun;31(3):774-9. doi: 10.1007/s10637-012-9894-7. Epub 2012 Nov
de Bono J et al
2) Abiraterone and increased survival in metastatic prostate cancer
N Engl J Med. 2011 May 26;364(21):1995-2005
3) Ryan CJ et al
Abiraterone in metastatic prostate cancer without previous chemotherapy.
N Engl J Med. 2013 Jan 10;368(2):138-48.