The YODA Project
Research Proposal Review - Final
(Protocol #: 2019-2946)

Reviewers:
- Nihar Desai
- Cary Gross
- Harlan Krumholz
- Richard Lehman
- Joseph Ross

Review Questions:

1. Is the scientific purpose of the research proposal clearly described?
   - Decision: Yes

2. Will request create or materially enhance generalizable scientific and/or medical knowledge to inform science and public health?
   - Decision: Yes

3. Can the proposed research be reasonably addressed using the requested data?
   - Decision: Yes, or it's highly likely

4. Recommendation for this data request:
   - Decision: Approve

Comments:

This is an interesting exploratory study examining the incidence of (and reasons behind) re-challenging patients with trabectedin after experiencing drug related CK elevation. My only concern with the proposal is with whether the investigators know what the 4 RCT protocols required investigators to do in the event of a CK elevation during the trial. Did the investigators have any leeway to decide whether or not to re-challenge patient with trabectedin? Or were investigators told to discontinue treatment for the remainder of the trial? This study will only be able to characterize incidence in the trials, not in the real world, and the trials may have had explicit protocols instructing investigators what to do in the event of a CK elevation.

The investigators are encouraged to consider incorporating a comparison group of patients who experienced CK-elevation but were not restarted on trabectedin. This would allow the Aim 3 analysis (identify outcomes of those experiencing CK elevation who were then re-challenged with trabectedin) to provide more clinically relevant information.