Category: Finance/CCSG/PRMS – Completed Project

Creation of a Consort Diagram to Visualize Participant Enrollment and Allocation at the Memorial Sloan Kettering Data and Safety Monitoring Committee

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1. Background

Memorial Sloan Kettering's (MSK) data and safety monitoring committee (DSMC) requires the submission of a database summary report along with a completed monitoring form with each DSMC submission. Both documents require that enrollment and analysis information be included; however, the numbers generated from different sources are often discordant for a series of different reasons. Thus, an improved process for reconciliation was required.

2. Goals

Our goal was to create a visualization tool that provides study teams and DSMC reviewers with an accurate status regarding overall study flow, including enrollment breakdowns, assignments to arms/cohorts, on-and-off study statuses, number evaluable for key endpoints, and interim analyses results. This document required manual entry and provided an opportunity to clarify enrollment and analysis data.

3. Solutions and Methods

In response to this need, and in collaboration with committee leadership and the department of biostatistics, the protocol review core (PRC) created and piloted two consort diagram templates, one for phase and one for non-phase studies. For the pilot, PRC included protocols for which DSMC, and protocol review and monitoring system (PRMS) committee members were principal investigators (PI). Feedback was provided by investigators, study staff, and DSMC reviewers. The pilot was successful based on demonstrated feasibility, positive feedback, and improved submission quality.

4. Outcomes

Following the pilot, consort diagrams were included as a mandatory submission requirement for studies opened to accrual in 2018 or later. This requirement impacts 67 percent of the current DSMC portfolio (203/305). Of this subset of protocols, 74 percent are therapeutic trials and 60 percent are from the Department of Medicine.

Implementation has positively impacted:

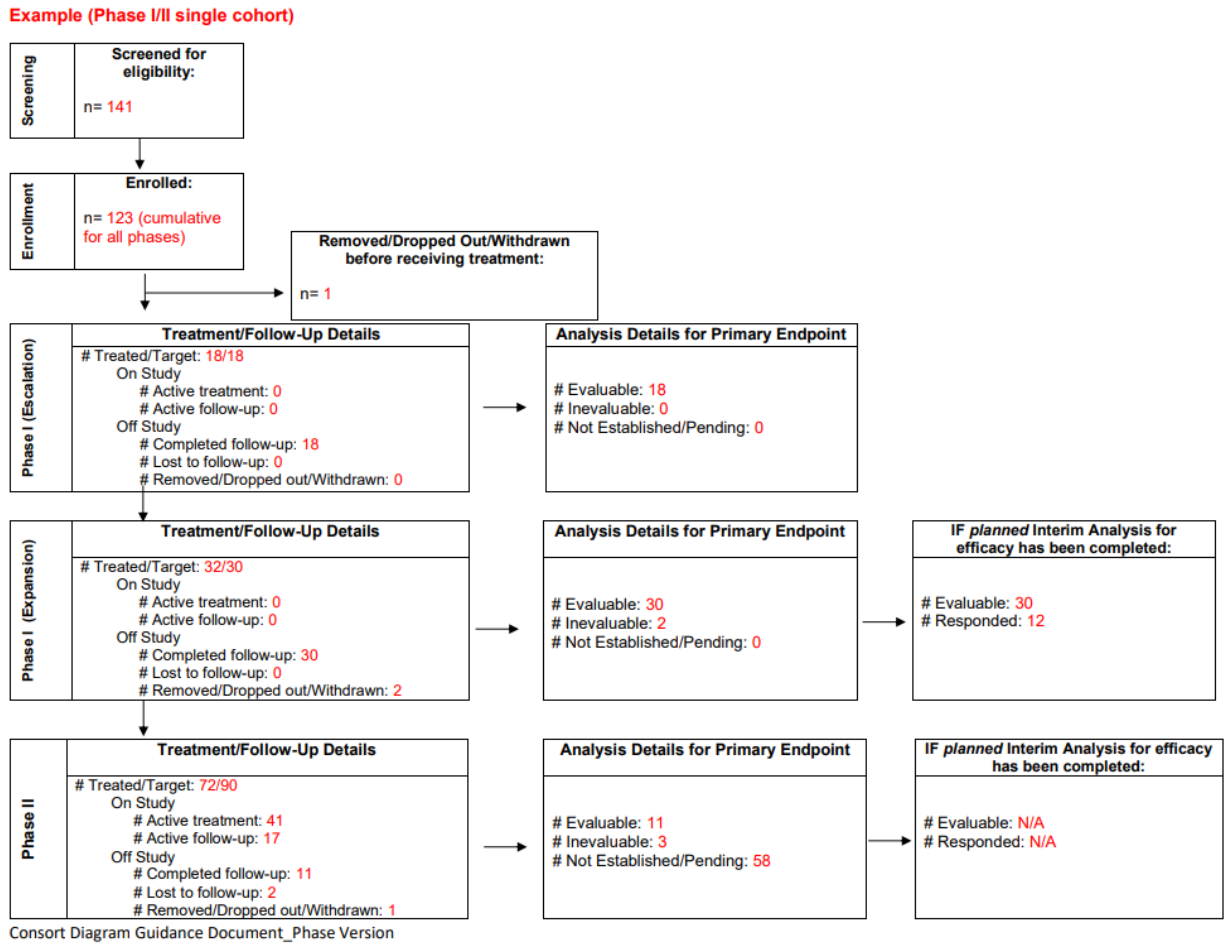
- PRC:
    - Identification of protocols that could be removed from DSMC monitoring (e.g., no active participants)
- PI, study team, statistician:
    - To prospectively track participants and engage biostatistical input throughout the lifecycle of the study, facilitating data analysis and subsequent publication
- DSMC members:
    - Improved monitoring of trials as the schematic depiction indicates withdrawal and dropout rates, missing data and errors in database reports, and enhanced protocol compliance by confirming data matches the trial design (i.e., dose escalation, or treatment arm assignment is proceeding as per protocol specification)

- All:
    - Improved understanding of participant flow within a the trial, and overall study status
    - Clearer understanding of study analyses (i.e., evaluable participants for a specific endpoint and interim analysis details)
    - Validated data integrity by following the numbers (e.g., accrual breakdowns are easy, reproducible, and logistically beneficial)

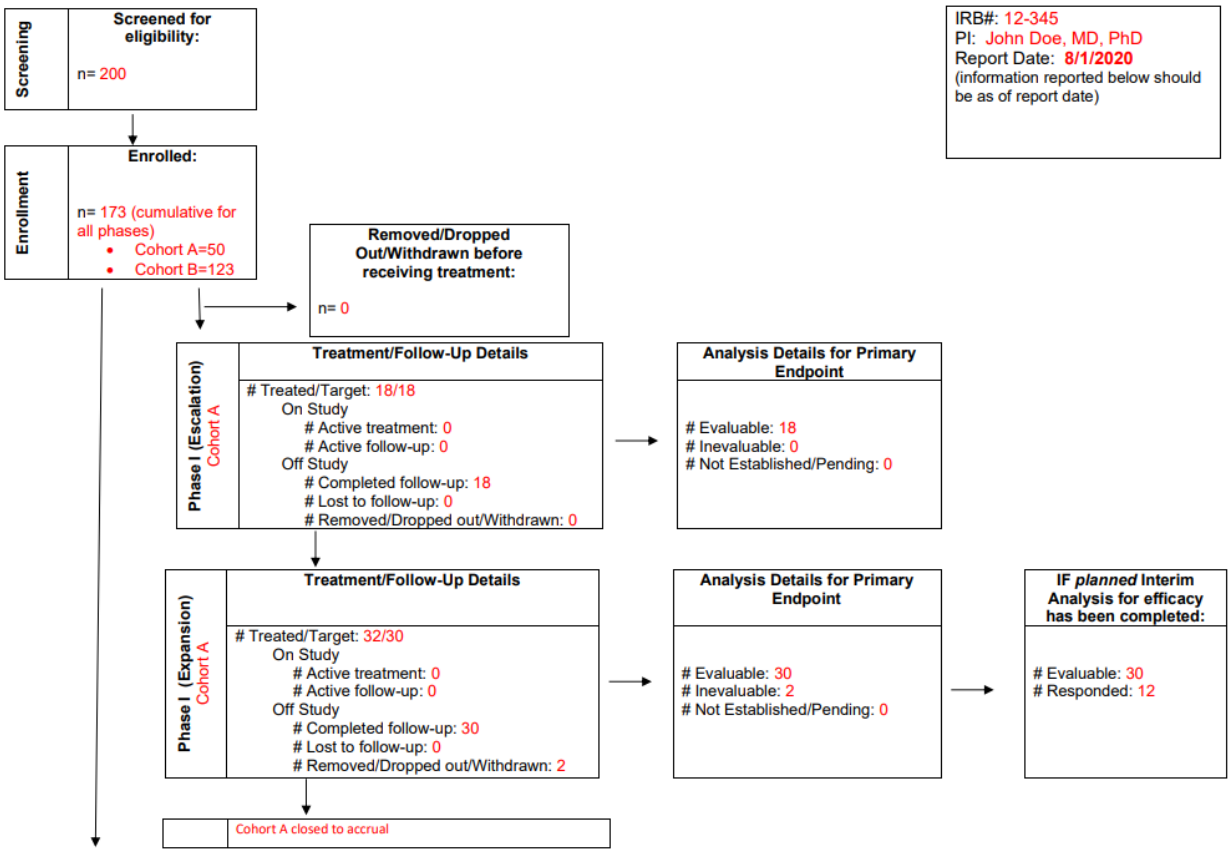
5. Lessons Learned and Future Directions

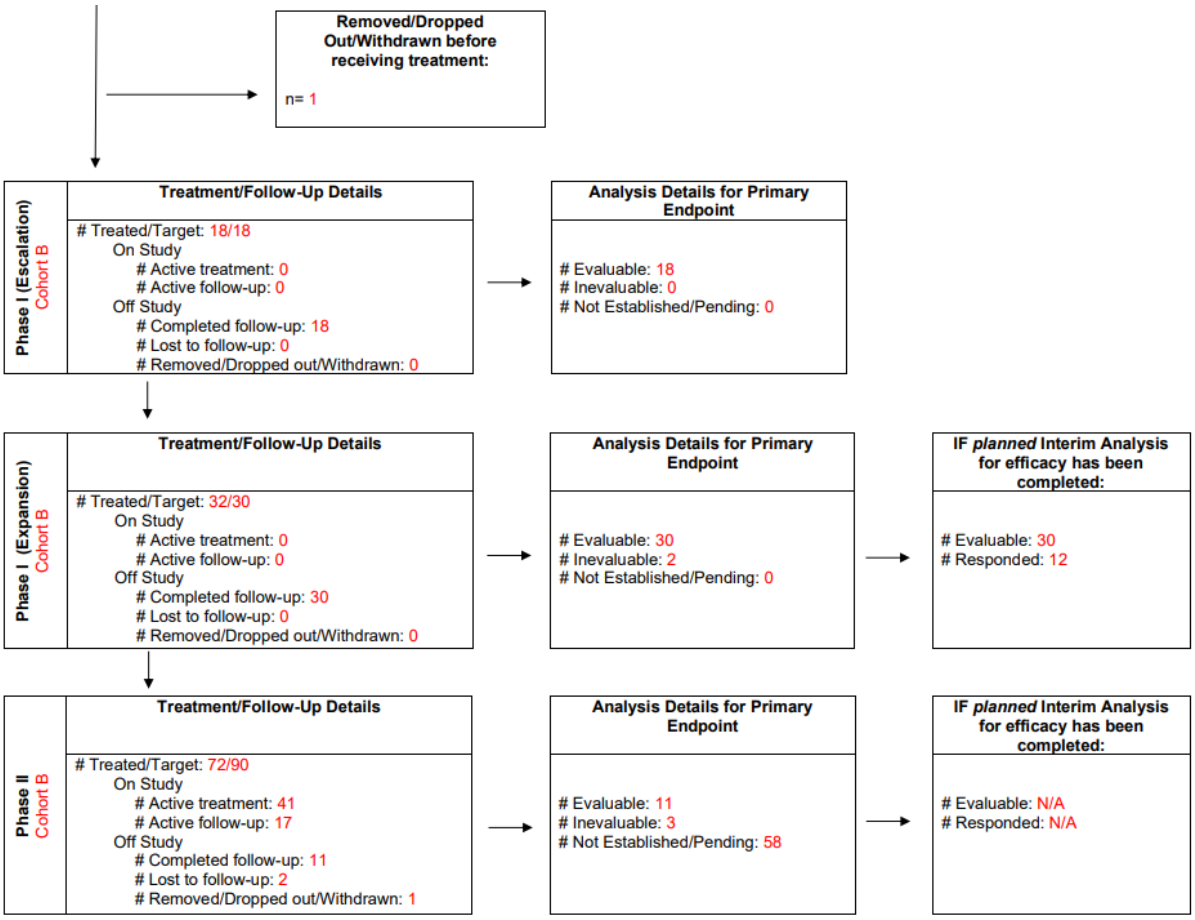
Given the success of implementation of these consort diagrams, MSK is exploring transition to a smart form that can account for varied study designs along with integration of the data in our electronic protocol information management system (PIMS) or external consort software. With many different trial designs at the institution, we had to create a general diagram that allows for flexibility among the studies. Creation of a smart form using electronic software could also allow for visual depiction of data from non-traditional study designs. Other future applications of the consort diagrams beyond the DSMC include as part of the annual IRB continuing review, at publication, and summary data for federal reporting requirements.

Figure:



Example (Phase I/II multi cohort)




Removed/Dropped Out/Withdrawn before receiving treatment:
n= 1
Phase I (Escalation) Cohort B
Treatment/Follow-Up Details
Treated/Target: 18/18
On Study
Active treatment: 0
Active follow-up: 0
Off Study
Completed follow-up: 18
Lost to follow-up: 0
Removed/Dropped out/Withdrawn: 0
Analysis Details for Primary Endpoint
Evaluable: 18
Inevaluable: 0
Not Established/Pending: 0
Phase I (Expansion) Cohort B
Treatment/Follow-Up Details
Treated/Target: 32/30
On Study
Active treatment: 0
Active follow-up: 0
Off Study
Completed follow-up: 30
Lost to follow-up: 0
Removed/Dropped out/Withdrawn: 0
Analysis Details for Primary Endpoint
Evaluable: 30
Inevaluable: 2
Not Established/Pending: 0
IF planned Interim Analysis for efficacy has been completed:
Evaluable: 30
Responded: 12
Phase II Cohort B
Treatment/Follow-Up Details
Treated/Target: 72/90
On Study
Active treatment: 41
Active follow-up: 17
Off Study
Completed follow-up: 11
Lost to follow-up: 2
Removed/Dropped out/Withdrawn: 1
Analysis Details for Primary Endpoint
Evaluable: 11
Inevaluable: 3
Not Established/Pending: 58
IF planned Interim Analysis for efficacy has been completed:
Evaluable: N/A
Responded: N/A