

Memorial Sloan Kettering Cancer Center

Creation of a Consort Diagram to Visualize Participant Enrollment and Allocation at the Data and Safety Monitoring Committee (DSMC) Christina Kolenut, MPH, Krista Napolitano, MA, Xhenete Lekperic, Kay See Tan, PhD, Sara Hanley, MSW, Eileen M. O'Reilly, MD, Susan Slovin, MD, PhD

Background

- The Data and Safety Monitoring Committee (DSMC) requires a database report and monitoring form with each submission.
- > Both documents require the inclusion of enrollment and analysis information; however, the numbers generated from different data sources are often discordant for multiple reasons (Figures 1 and 2).

Figure 1:

Sample Database Report Breakdown

Figure 2: Sample Monitoring Form Breakdown

Target Accrual	15
#Enrolled	12
#Eligible	12
#Ineligible	0
#Evaluable	5
#Inevaluable	0
#Treated	2

ċ	Participant Breakdown		
	1 Scrooned for eligibility: 14		

- Enrolled (on each arm/phase/cohort): . Phase I Cohort 1 Dose Level 1: 8 patients
- ii. Phase I Cohort 1 Dose Level 2: 6 patients
- 3. Treated (on each arm/phase/cohort) Phase I Cohort 1 Dose Level 1: 7 patients
 - ii. Phase I Cohort 1 Dose Level 2: 5 patients
- Active follow-up: 8 (6 off treatment for survival, 2 on active treatment
- 5. Lost to follow-up: 0
- 6. Evaluable: 10 (8 for protocol, 2 for toxicity only)
- 7. Inevaluable: 4
- 8. Withdrawn: 2 (after start of treatment)

Goals

Improve data reconciliation by creating a visualization tool that:

- Provides an accurate status regarding overall study flow, enrollment breakdowns, assignments to arms/cohorts, onand-off study statuses, number evaluable for key endpoints, and interim analyses results.
- > Allows for customized manual entry and an opportunity to clarify enrollment and analysis data.

Methods & Solutions

- In collaboration with Committee Leadership and the department of biostatistics, the administrative team created and piloted two consort diagram templates, one for phase studies (e.g., phase I, I/II, and II therapeutic protocols) and one for non-phase studies (e.g., psychosocial) studies (Figure 3).
- The pilot included protocols for which DSMC members and Protocol Review and Monitoring System (PRMS) committee members were Principal Investigators.
- Feedback regarding the functionality and clarity of the templates was provided by investigators, study staff, and DSMC reviewers.
- The pilot was deemed successful based on demonstrated feasibility, positive feedback, and improved submission quality.
- Feasibility was initially impacted by unclear instructions which resulted in creating a guidance document containing definitions for each diagram category (Figure 4) and hosting trainings.
- Following the pilot and updates to the templates based on feedback, consort diagrams became a submission requirement for studies opened to accrual in 2018 or later.







Removed/Dropped out/Withdrawn:



Example Completed Consort Diagram for a Phase Study

Example (Phase I/II single cohort)

Figure 4: Excerpt of Consort Diagram Guidance Document for Phase Studies

Treatment/Follow-Up Details	Analysis Details for Primary Endpoint	Author
Target: otal number of participants treated on otocol phase (<i>sub-bullets below should add</i> o to this total) out of the target accrual for otocol phase. multiple arms/cohorts, the actual treated	 Note: Analysis details should be provided based on the definition of the primary endpoint in the protocol. Depending on the protocol's definition of primary endpoint, participants may not need to complete all study-related activities and follow-up to be 	Analysis Details: the analysis totals sho for the primary endpoint only.
 Active treatment: Number of participants currently receiving treatment per protocol. Active follow-up: Number of participants currently in active follow-up per protocol. 	 evaluable. More participants may be evaluable for primary endpoint than who completed whole study. # Evaluable: Indicate the number of participants who can be evaluated for the primary endpoint based on protocol definition(s). The number evaluable might match the 	Analysis Details: the total number of the participants listed in the Treatment be match the combined total of participa Analysis Details box (all treated partic should be accounted for in the analysi
Do not include participants in follow-up for survival only (unless survival is primary endpoint) <u>Study</u> Completed follow-up:	 number of participants who have completed follow-up, depending on the protocol's definition of the primary endpoint. The PI and/or study statistician should determine who is evaluable. 	Author Example of Evaluable: participant mus complete a three-month assessment t evaluated for the primary endpoint pe protocol and participant completed al
 Number of participants who have completed (active) follow-up per protocol. Lost to follow-up: Number of participants who are lost to follow-up per protocol. Removed/Dropped out/Withdrawn: 	 # Inevaluable: Indicate the number of participants who are not able to be evaluated for the primary endpoint based on protocol definition(s). The number inevaluable might match the number of participants who are lost to follow- up or have been removed/dropped 	assessments and procedures, includin three-month assessment, then they a evaluable.
 Anyone removed according to the criteria for removal section of the protocol (MSK IIT template). Anyone who dropped out of study on their own for any reason. Anyone withdrawn from study by investigator or clinician for any reason (e.g., progression of disease, excessive toxicity, death, etc.). 	 automatical and the presentation of the primary endpoint. # Not Established/Pending: This number should match the number of participants still on active treatment and active follow-up. This number may also include anyone who the PI and/or statistician are still determining if evaluable. 	Author Example of Inevaluable: participant m complete a three-month assessment t evaluated for the primary endpoint pe protocol, but participant did not comp three-month assessment, then they ar inevaluable.

Outcomes

> Implementing the consort diagram has had a positive impact on all stakeholders:

DSMC Administration:

Easily identifies protocols eligible to be removed from monitoring

Principal Investigators, Study Staff & Statisticians: Facilitates data analysis and publication by tracking participants and engaging biostatistical input throughout the lifecycle of the study

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DSMC members:

Improves monitoring by highlighting withdrawal and inevaluable rates, data errors, and protocol noncompliance (i.e., following design/analysis plan)

All:

- Fosters data integrity by providing a platform that can be easily followed at each requisite timepoint of monitoring
- Improves understanding of participant flow within a trial, and overall study status
- · Clarifies study analyses details (i.e., evaluable participants for a specific endpoint, interim analysis details)
- \succ The requirement impacts 67% of the DSMC portfolio (Figure 5).
- \geq 74% are therapeutic trials and 71% are phase trials.
- \geq 60% are from the Department of Medicine.

Figure 5: Impact of Consort Diagram Requirement on DSMC Portfolio



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Lessons Learned and Future Directions

- > The consort diagram requires adaptation to fit varied and nontraditional study designs.
- Plan to transition to a 'smart' (electronic) form and potentially pool data from multiple data sources.
- \succ Expand beyond DSMC to other key committees (e.g., IRB, INDC) and as a template for investigators (e.g., accrual monitoring, federal reporting, publication).