

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

Participant Breakdown				
1 Scrooned for eligibility:	11			

- 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 Withdrawn: 2 (after start of treatment)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
Farget: al number of participants treated on tocol phase ( <i>sub-bullets below should add</i> to <i>this total</i> ) out of the target accrual for tocol phase. ultiple arms/cohorts, the actual treated sus target should be arm/cohort-specific. <u>dy</u> ctive treatment:	<ul> <li>Note:</li> <li>Analysis details should be provided based on the definition of the primary endpoint in the protocol.</li> <li>Depending on the protocol's definition of primary endpoint, participants may not need to complete all study-related activities and follow-up to be evaluable.</li> <li>More participants may be evaluable for primary endpoint than who completed whole study.</li> </ul>	Analysis Details: the analysis totals s for the primary endpoint only. Author Analysis Details: the total number of participants listed in the <b>Treatment</b> match the combined total of particip
<ul> <li>Number of participants currently receiving treatment per protocol.</li> <li>Number of participants currently in active follow-up per protocol.</li> <li>Do not include participants in follow-up for survival only (unless survival is primary endpoint)</li> <li>ady ompleted follow-up:</li> </ul>	<ul> <li># Evaluable:</li> <li>Indicate the number of participants who can be evaluated for the primary endpoint based on protocol definition(s).</li> <li>The number evaluable might match the number of participants who have completed follow-up, depending on the protocol's definition of the primary endpoint.</li> <li>The PI and/or study statistician should determine who is evaluable.</li> </ul>	Analysis Details box (all treated part should be accounted for in the analy Author Example of Evaluable: participant m complete a three-month assessmen evaluated for the primary endpoint protocol and participant completed
<ul> <li>Number of participants who have completed (active) follow-up per protocol.</li> <li>ost to follow-up:</li> <li>Number of participants who are lost to follow-up per protocol.</li> </ul>	<ul> <li># Inevaluable:</li> <li>Indicate the number of participants who are not able to be evaluated for the primary endpoint based on protocol definition(s).</li> <li>The number inevaluable might match the number of participants who are lost to follow-</li> </ul>	assessments and procedures, includ three-month assessment, then they evaluable.
<ul> <li>Anyone removed according to the criteria for removal section of the protocol (MSK IIT template).</li> <li>Anyone who dropped out of study on their own for any reason.</li> <li>Anyone withdrawn from study by investigator or clinician for any reason (e.g., progression of disease, excessive toxicity, death, etc.).</li> </ul>	<ul> <li>up or have been removed/dropped out/withdrawn, depending on the protocol's definition of the primary endpoint.</li> <li># Not Established/Pending:</li> <li>This number should match the number of participants still on active treatment and active follow-up.</li> <li>This number may also include anyone who the PI and/or statistician are still determining if evaluable.</li> </ul>	Author Example of Inevaluable: participant complete a three-month assessment evaluated for the primary endpoint protocol, but participant did not con three-month assessment, then they 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).