Clinical Research Study, Management & Compliance

Data and Safety Monitoring Committee (DSMC)

September 25, 2025

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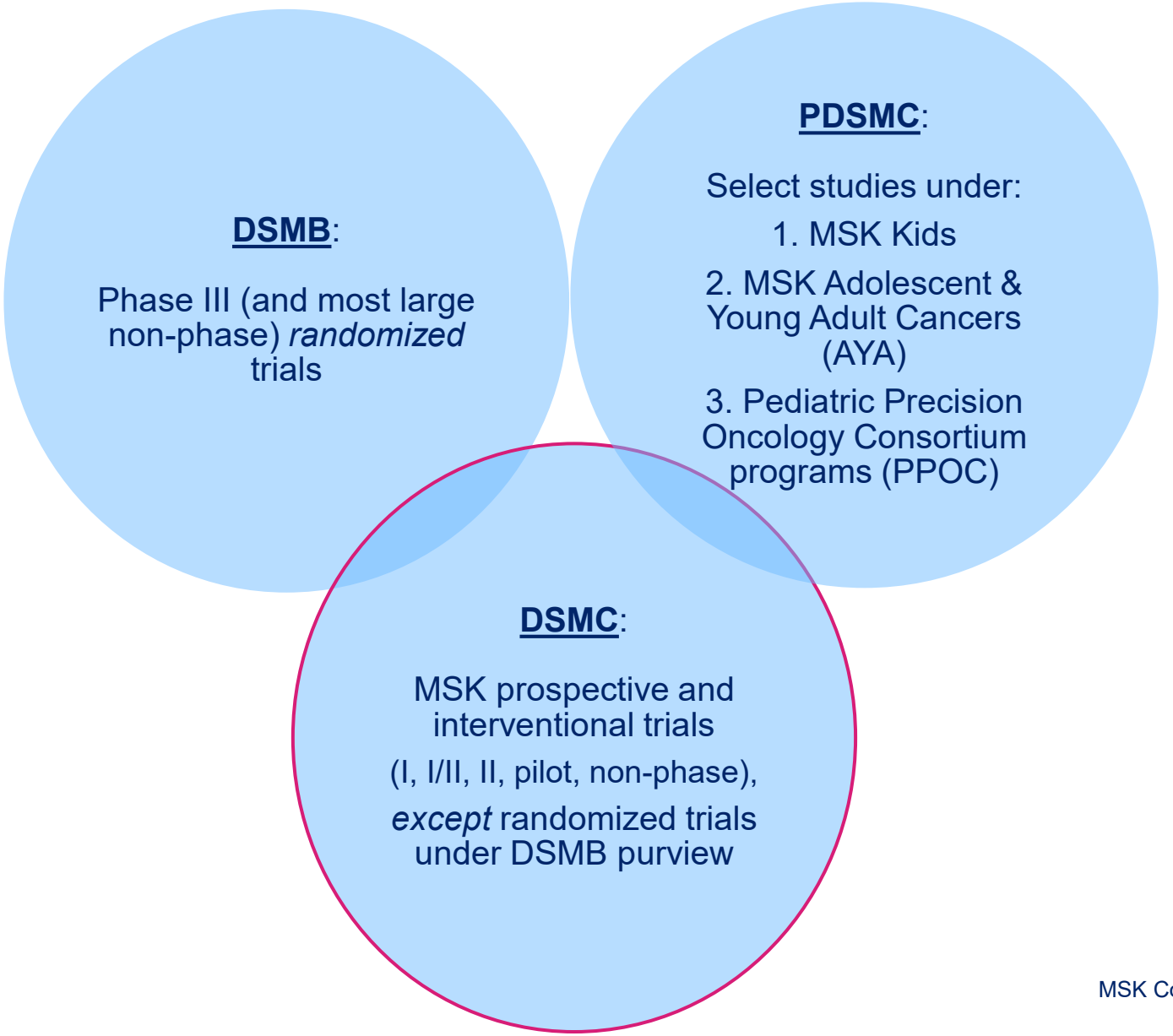
Memorial Sloan Kettering Cancer Center

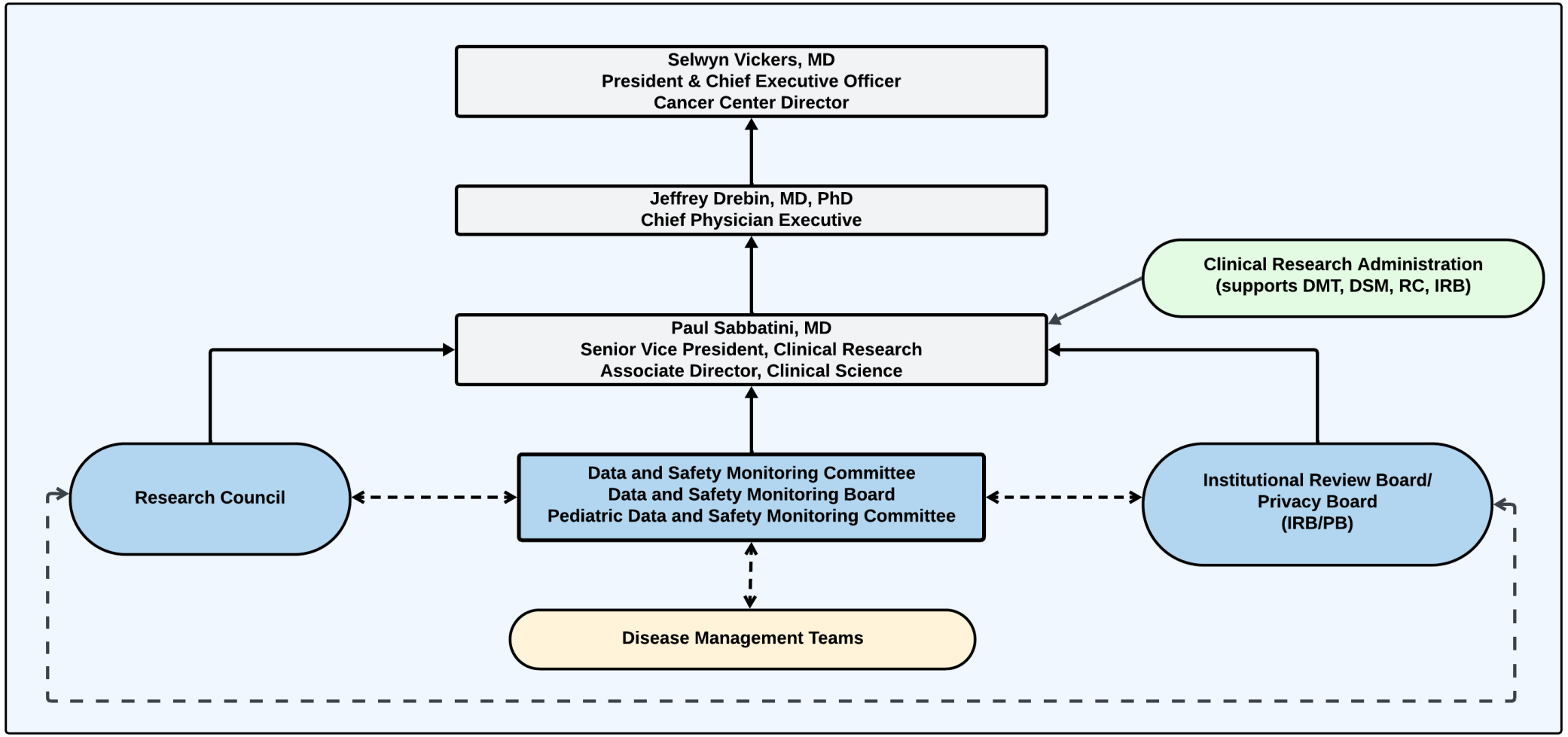
Agenda

- MSK’s DSM Strategy
- Purpose & structure of DSMC
- Criteria & timing of DSMC reviews
- Submission requirements & preparing for DSMC review
- DSMC review process & outcomes

MSK's Data and Safety Monitoring Strategy



MSK's Data and Safety Monitoring Structure



Purpose & Structure of DSMC

DSMC Overview

Independently convened committee

- DSMC can intervene if concerns arise and request information, changes, or escalate as needed

Provides monitoring oversight for MSK's clinical research portfolio

- Scope: MSK-sponsored or externally sponsored trials with MSK as data coordinating center
- Criteria: Includes Phase I, I/II, II, pilot, and non-phase prospective and interventional clinical trials

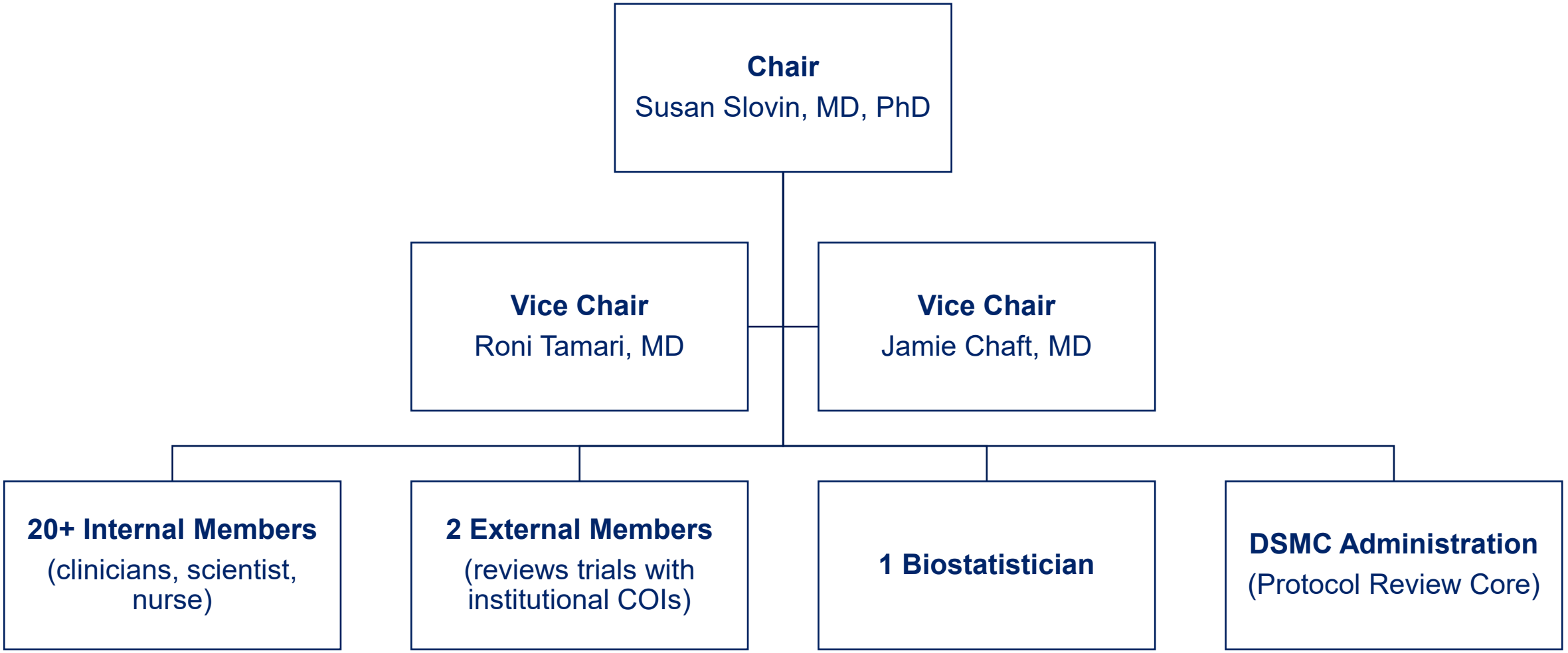
Responsibilities determined by:

- P30 Cancer Center Support Grant (CCSG) and Federal Requirements
- DSMC Standard Operating Procedures (SOPs) and Data and Safety Monitoring Plan (DSMP)

DSMC Purpose

Safety	Monitor toxicity trends (expectedness, severity)
	Monitor dosing
Data Integrity & Completeness	Confirm correct database is used
	Confirm sufficient data entry and external site data reporting
Study Conduct & Compliance	Ensure compliance to design/statistics (stopping rules, DLTs)
	Ensure data collection/management plan is followed
Study Progress	Monitor study progress (accrual)
	Confirm that trials/sites are proceeding as expected

DSMC Membership



YOUR TURN, IN THE CHAT:

MSK'S DSMC IS PRIMARILY RESPONSIBLE FOR MONITORING:

A. Participant rights
B. Scientific merit
C. Data integrity, safety, study conduct and progress
D. All of the above

C

DSMC's scope is safety, data integrity, study conduct, and progress

DSMC Review Frequency & Volume

DSMC Monitoring Frequency

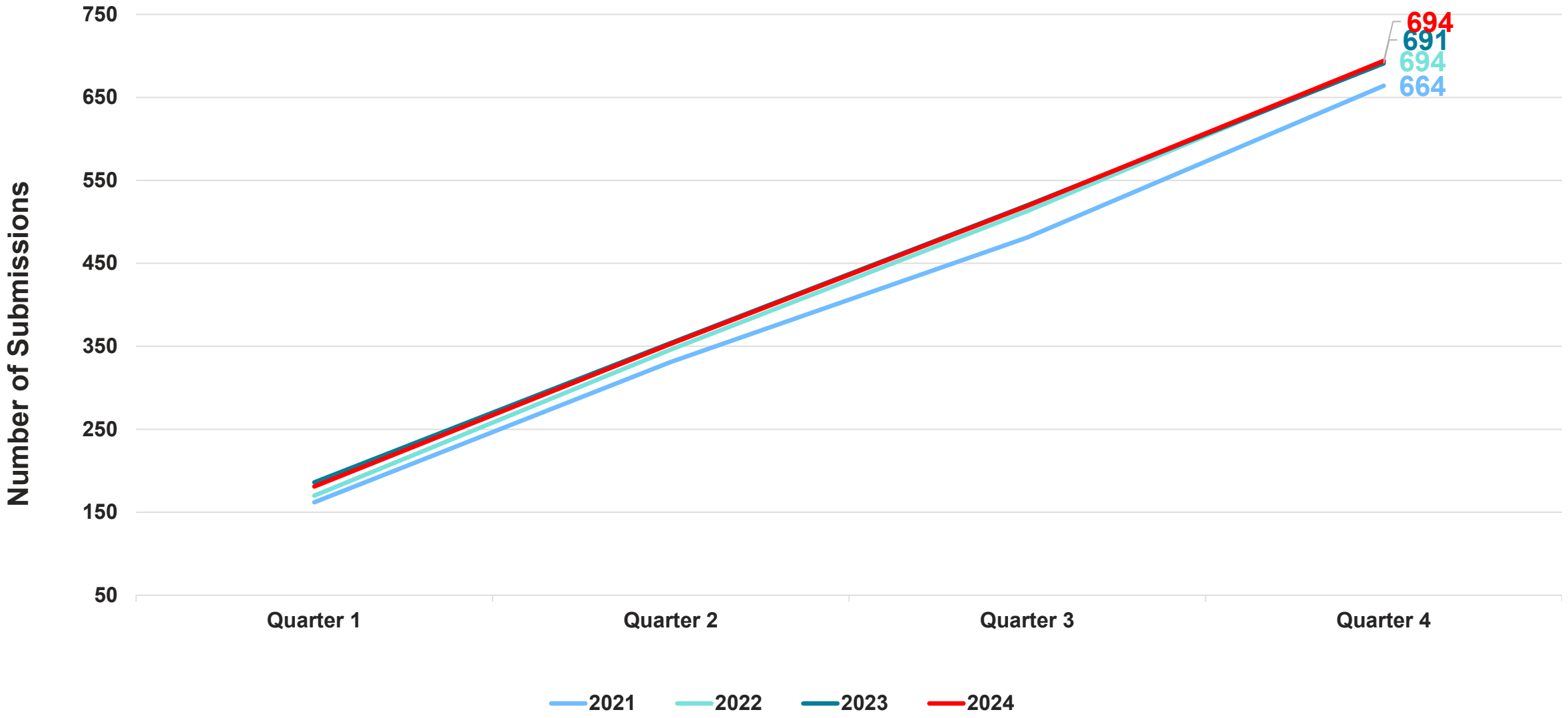
Risk-based monitoring

Quarterly (high risk)
Semi-Annually (moderate risk)
Annually (low risk)

Monitoring begins after 1st accrual or by the end of year 1 if no accruals

Monitoring ends once there are no active participants & protocol is closed to accrual

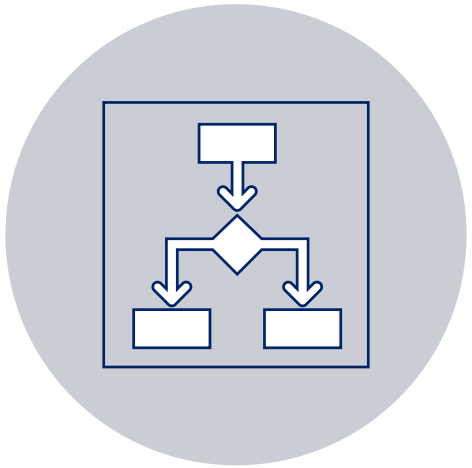
DSMC Review Volume (2020 – 2024)



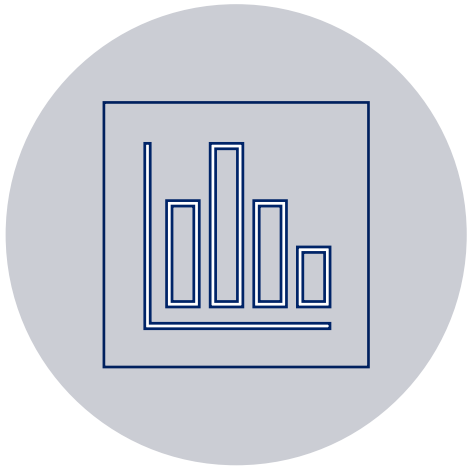
Submission Requirements & Preparing for DSMC Review

DSMC Submission Requirements

DSMC MONITORING FORM



CONSORT DIAGRAM



DATABASE REPORT

USE OF PROTOCOL OVERVIEW DASHBOARD

DSMC Monitoring Form

Study Overview

- Phase, accrual goals, participating centers, objectives, etc.

Study Updates (since last DSMC review)

- Accruals, dose escalation breakdown, amendments, audits, monitoring visits, etc.

Study Safety and Status

- SAEs, deaths, unanticipated problems.

Data Integrity

- Data storage, data entry percentage and plan if data backlog.

Study Analyses

- Stopping rules, planned/unplanned interim or other analyses, abstract submissions, presentations, publications, etc.

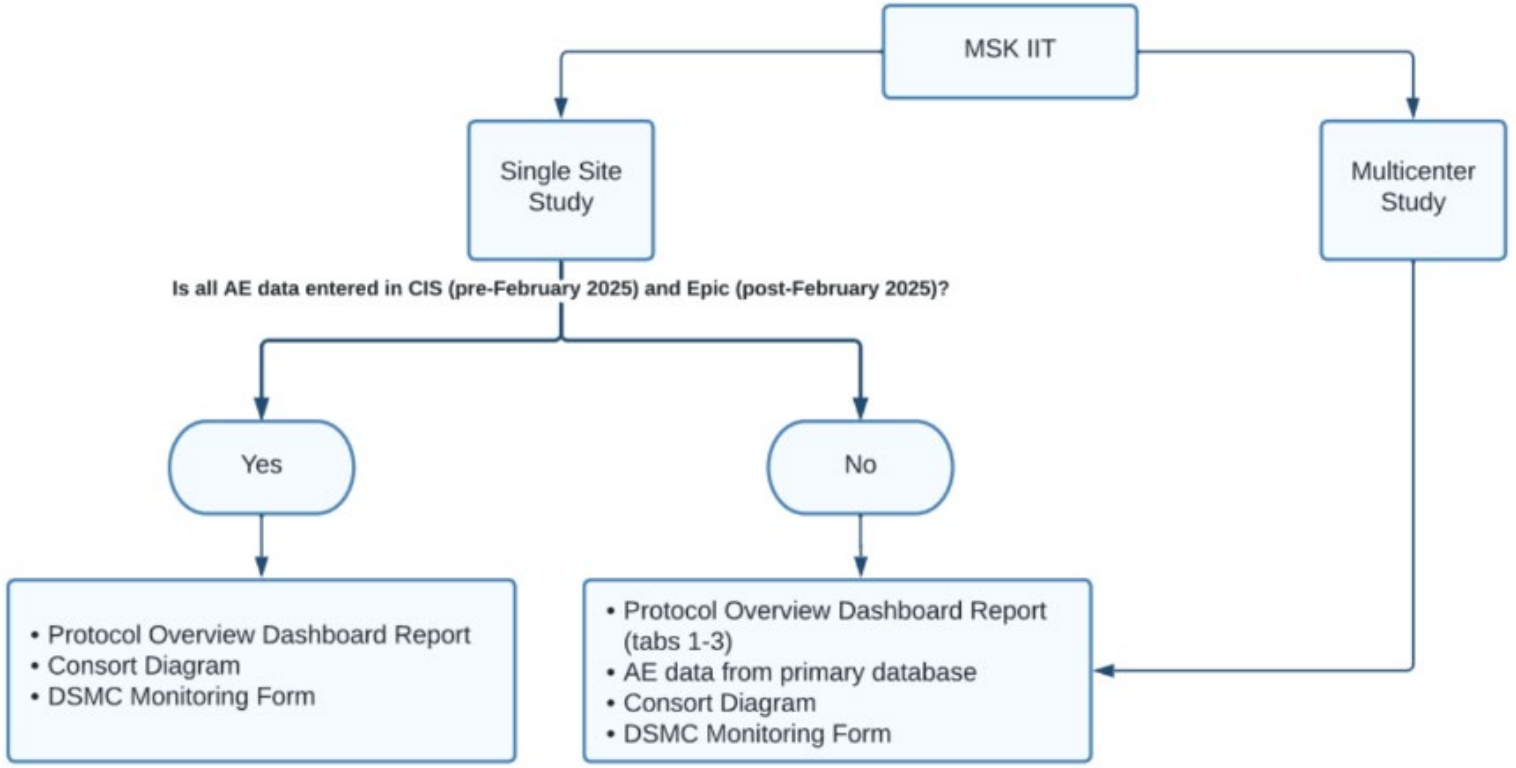
Additional Comments & Signatures (PI/Study Team)

- Address prior comments and space to provide additional information (re: safety, data, study conduct, progress, funding, future plans)

Database Report

- **Reviewers view participant and toxicity data to identify safety trends and confirm study is progressing as planned**

- **A decision tree is used to determine the best source for pulling data**



Protocol Overview Dashboard

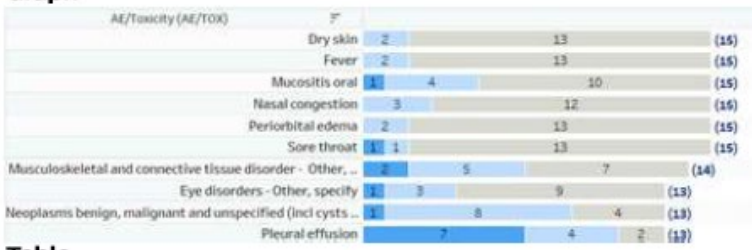
Adverse Events Summary Example

AE/System Organ Class	AE/Toxicity	Cohorts	AE/Intervention
Blood and lymphatic system disorders	Anemia	Arm A1: Gemcitabine 1000 mg/m2 D1 and 8, Cisplatin 70 mg/m2 D1	cisplatin
			gemcitabine
			pegfilgrastim (neulasta)
	Anemia	Arm A1: Gemcitabine 1000 mg/m2 D1 and 8, Cisplatin 70 mg/m2 D1	cisplatin

AE/Relationship	AE Source	Grade=1	Grade=2
Possible	EPIC	1 (0.30%)	
Unlikely	EPIC	1 (0.30%)	
Unrelated	EPIC	1 (0.30%)	
Definite	CIS		
Possible	CIS	5 (1.49%)	5 (1.49%)
Probable	CIS	2 (0.60%)	1 (0.30%)
Unrelated	CIS	1 (0.30%)	

Adverse Events Visualization Example

Graph



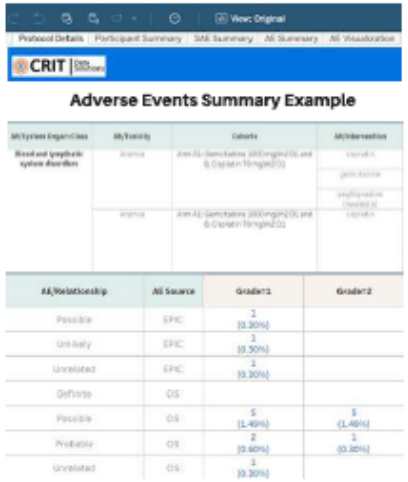
Table

System Organ Class (SOC)	AE/Toxicity (AE/TOX)	Total (n)	Grade 1
Respiratory, thoracic and mediastinal disorders	Dyspnea	35	17
	Epistaxis	6	6
	Hoarseness	12	12
	Hypoxia	3	
	Laryngeal edema	1	
	Nasal congestion	15	12
	Pharyngeal hemorrhage	1	1
	Pleural effusion	13	2
	Pleuritic pain	2	1

Links

- Protocol Overview Dashboard
- Instructions to Download Data
- DSMC Portal Page

Dashboard Landing Page



OVERVIEW

The Protocol Overview Dashboard consolidates trial data from multiple sources (e.g., CRDB, CTMS, PIMS, CIS, Epic) in one place.

PURPOSE

The dashboard can be used for study oversight, monitoring, data visualization, and review committee (e.g., DSMC) submissions.

Filters allow users to narrow down and easily visualize large data sets.

DATA IS DISPLAYED ACROSS FOUR TABS

1 Protocol Details

High level overview of the trial characteristics.

2 Participant Summary

Detailed overview of enrollment by study cohort and/or arm, including demographics, disease and survival data, treatment and analysis details, and site accruals.

3 Serious Adverse Events Summary

Tabulated SAEs, grouped by system organ class, toxicity, cohort, intervention, relationship, and grade; sourced from PIMS and CRDB.

4 Adverse Events Summary

Tabulated AEs, grouped by system organ class, toxicity, cohort, intervention, relationship, and grade; sourced from the ClinRsrch CIS tab and Epic.

5 Adverse Events Visualization NEW

Two ways to view participant counts by highest-grade AE:

- **Bar Graph –** Shows each participant's highest-grade AE by grade. Darker colors = greater severity.
- **Highlight Table –** Shows highest-grade AE by grade and system organ class. Darker shades = more participants.

For DSMC submission inquires, email dsmc@mskcc.org
For access or data issues in tableau, submit a CRIT ticket
For general inquiries about tableau or the blended data model, email the CRIT team

YOUR TURN, IN THE CHAT:

WHAT SHOULD DSMC RECOMMEND BASED ON THE DATA SUMMARY BELOW?

A. Improve accrual rate

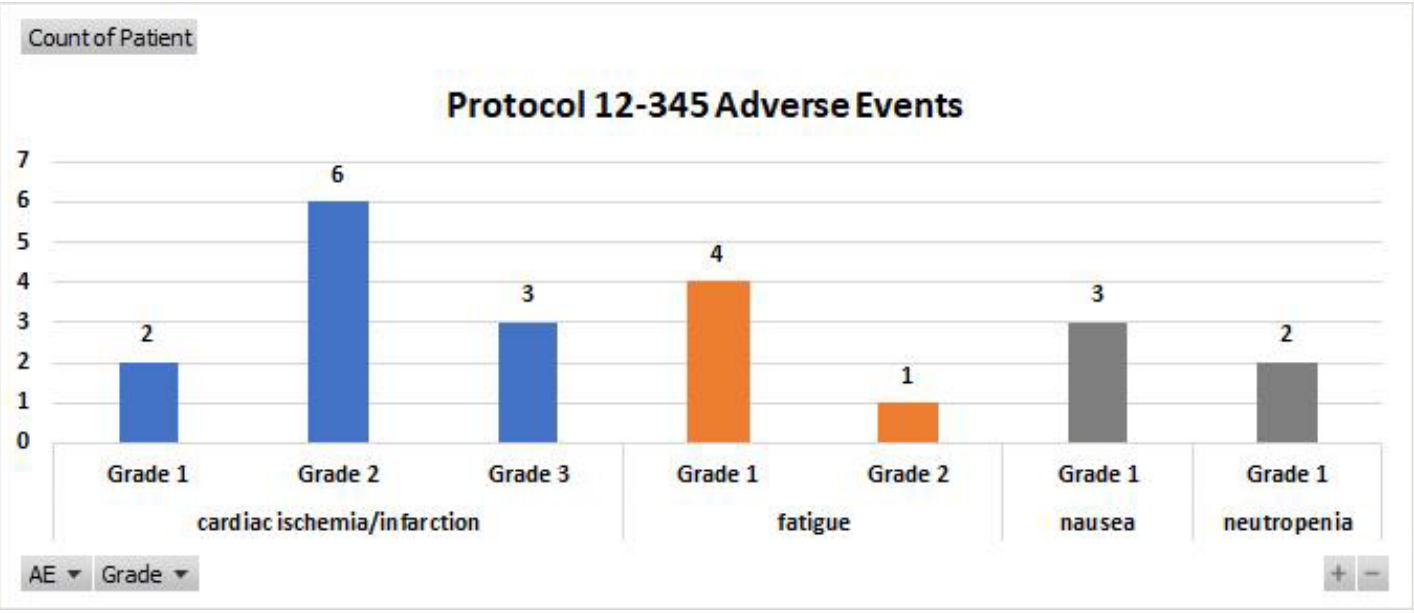
B. Amend eligibility criteria to exclude previous cardiac conditions

C. Amend protocol to include prophylactic anti-nausea medication

D. Put study on hold until drug safety is evaluated

B

Amend eligibility given # of cardiac events



YOUR TURN, IN THE CHAT:

WHAT SHOULD DSMC RECOMMEND BASED ON THE DATA SUMMARY BELOW?

A. Improve accrual rate

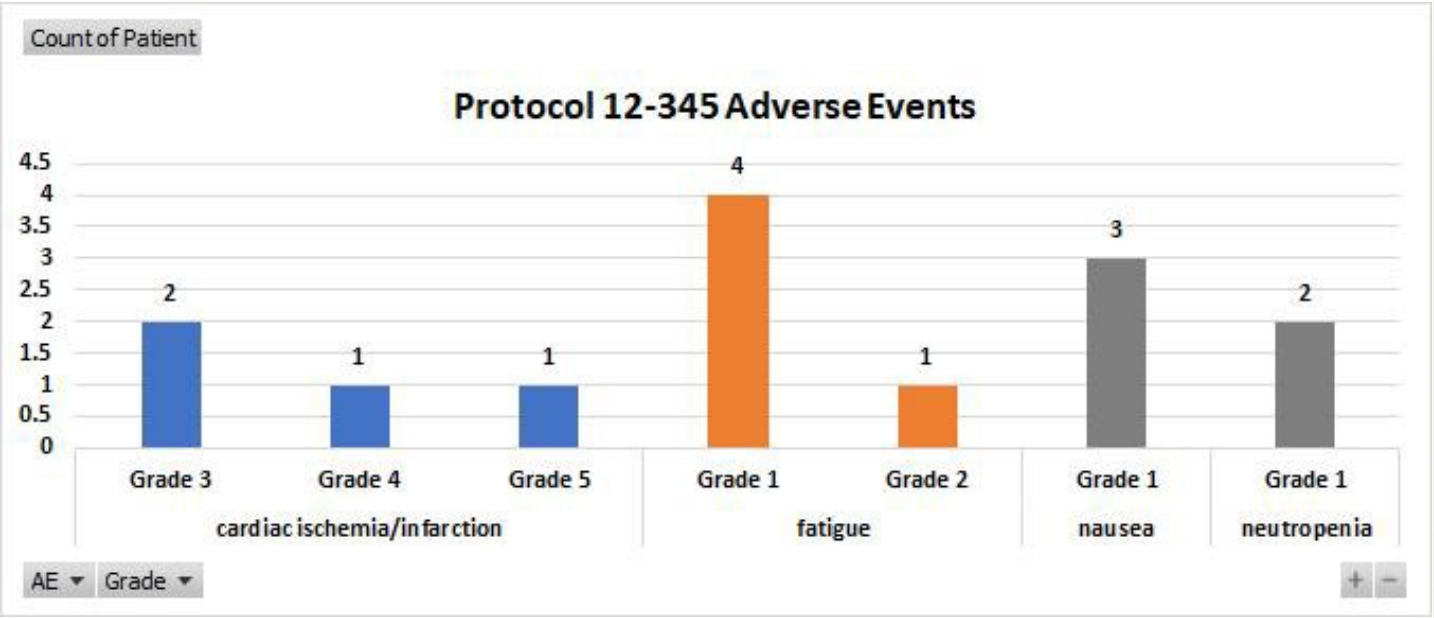
B. Amend eligibility criteria to exclude previous cardiac conditions

C. Amend protocol to include prophylactic anti-nausea medication

D. Put study on hold until drug safety is evaluated

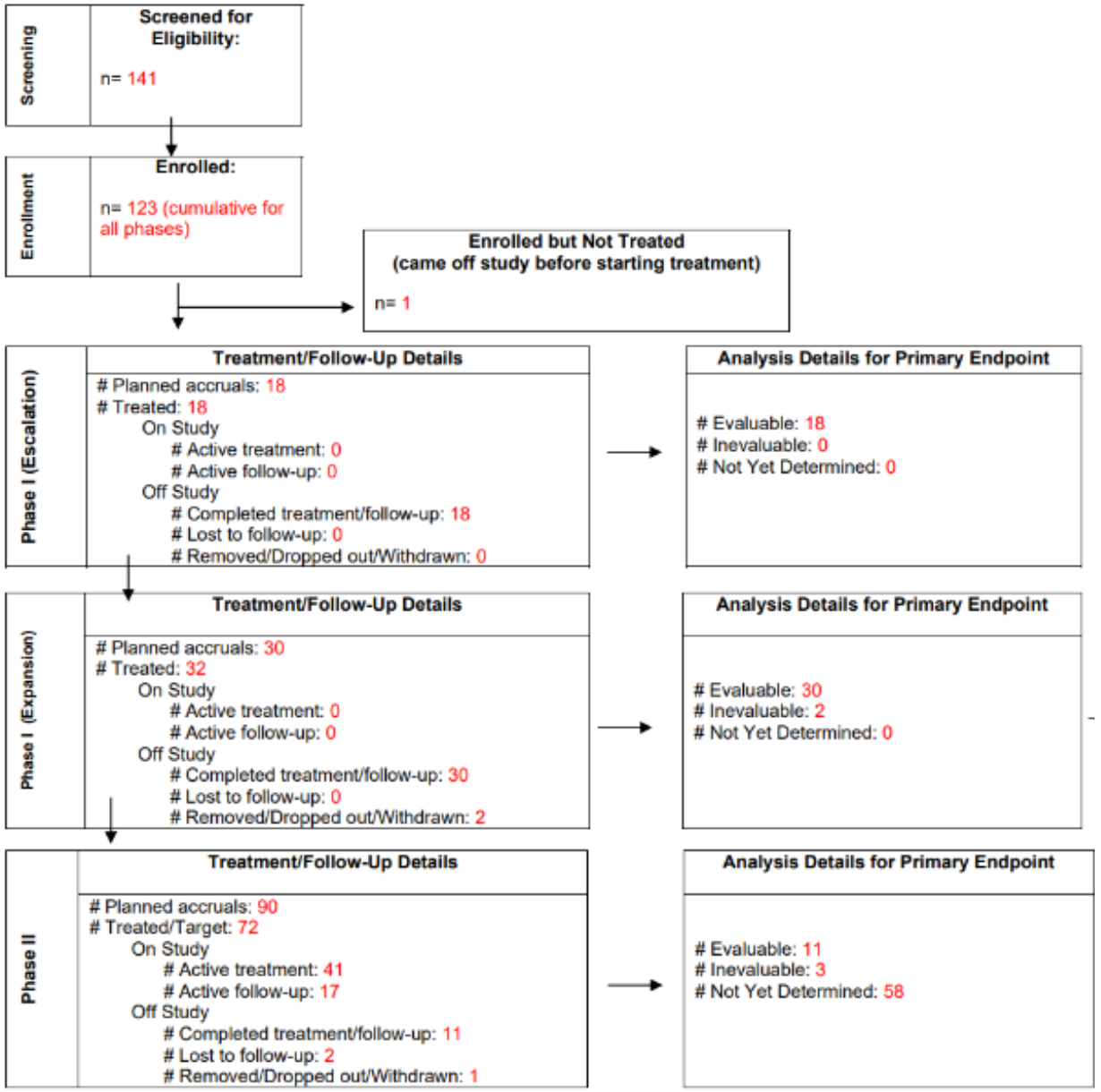
D

Put on hold due to grade 4/5 events



Consort Diagram

- Template version depends on trial type
  - Phase
  - Non-phase
  - Randomized
- Helps study team and reviewer understand accrual/study progress
- **Numbers must add up!**



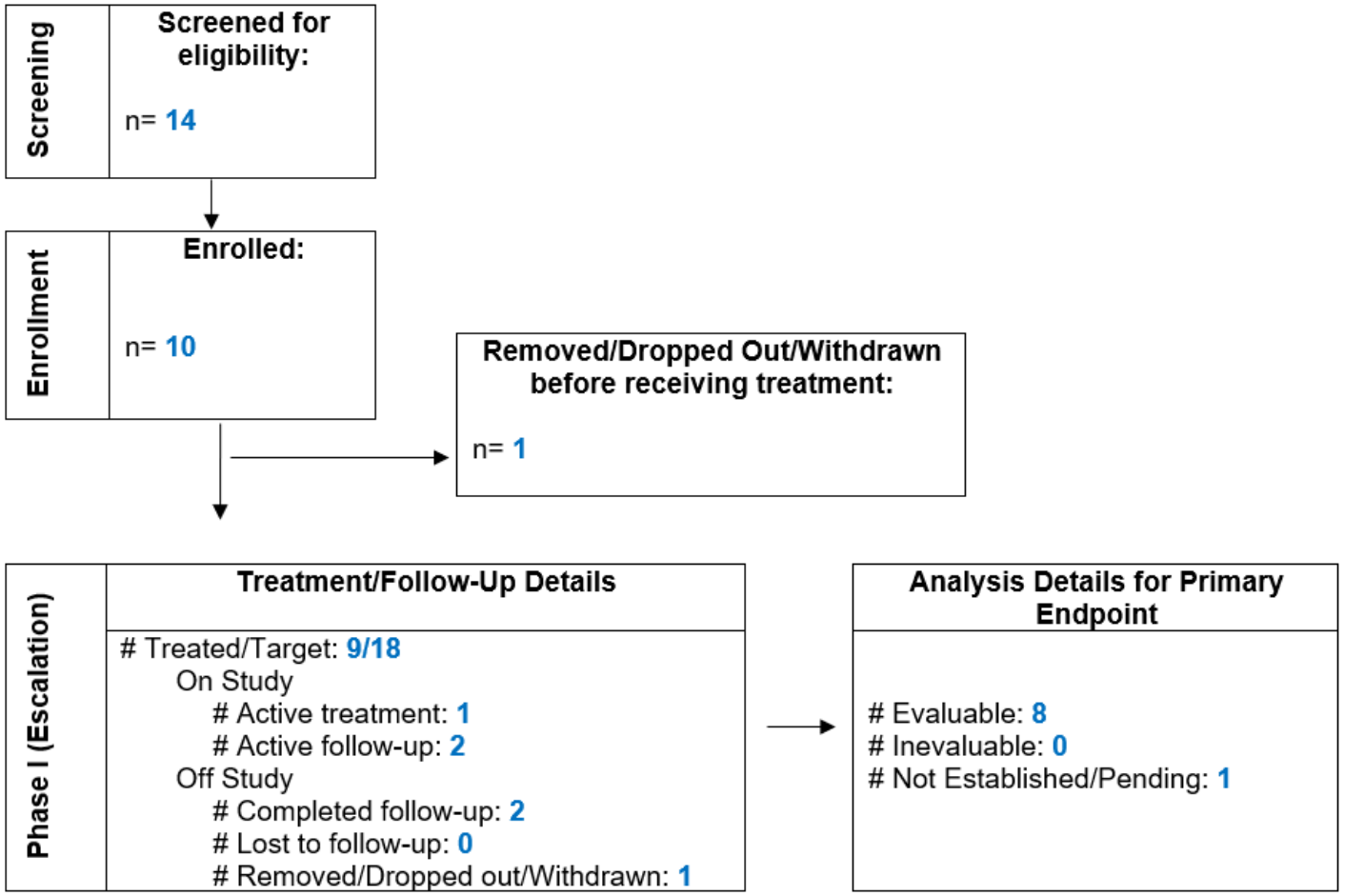
YOUR TURN, IN THE CHAT:

IS THE <u>TREATMENT/FOLLOW-UP DETAILS</u> SECTION IN THE FOLLOWING CONSORT DIAGRAM CORRECT?

A. Yes
B. No

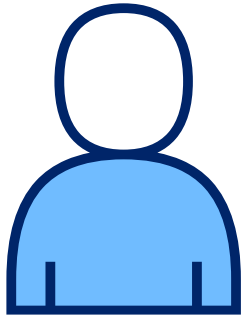
B

No, on/off study breakdown does not add up to #Treated



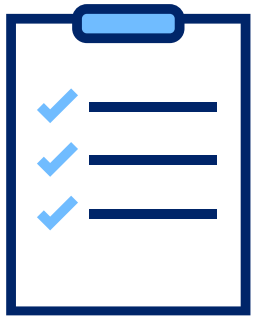
DSMC Review Process & Outcomes

DSMC Review Process



1 reviewer assigned for life cycle of protocol

- Biostatistics reviewer added as needed (e.g., interim analysis data)
- DSMC Administration conducts administrative reviews (e.g., database compliance)



All reviews completed in PIMS

- Structured reviewer checklist

Reviewer Checklist

Reviewers identify any concerns about:

- Safety trends
- Data integrity
- Protocol compliance
- Study progress
- PI's response to previous DSMC comments

Includes free text fields for reviewer comments to PI & personal notes

Reviewers identify protocols requiring discussion at DSMC meeting

1. **Previous Review: Are there comments from the last DSMC review that have not been adequately addressed?**	YES ○	NO ◉	N/A ○
2. **Safety: Are there concerning toxicity trends** (e.g., severity/frequency/expectedness)?	YES ○	NO ◉	N/A ○
3. **Data: Are there issues with data integrity** (e.g., completeness/accuracy/storage)?	YES ○	NO ◉	N/A ○
4. **Compliance: Are there concerns with adherence to the protocol's biostatistical plan?**	YES ○	NO ◉	N/A ○
Example: Lack of adherence to protocol-specific requirements (e.g., DLT/escalation/expansion/stopping rules/analysis timepoints)			
5. **Study Progress: Are there concerns about this protocol not progressing as planned or not meeting its goals?**	YES ◉	NO ○	N/A ○
Example: Lack of progress with primary objective(s), recruitment/enrollment, and/or milestones			
Example: A large number of withdrawn and/or inevaluable participants			
6. **DSMC Oversight: Should this protocol be removed from monitoring?**	YES ○	NO ◉	N/A ○
Criteria for Removal: Closed to accrual with no active participants or participants being followed for survival only. Flag for discussion if other compelling reason to remove from monitoring.			

DSMC Review: Should this protocol be discussed at the DSMC meeting (e.g., major concerns or concerns requiring committee discussion)?	YES ⌄

Approved ○	**Approved With Comments** ○	**Interim Approved** ◉	**Not Approved** ○

Common Errors Identified by DSMC

Safety	• Safety trend(s) identified • Stopping criteria met but enrollment continues
Data	• Database compliance issues (correct and appropriate database is being used) • Inadequate timely data entry (<75%, plan for backlog) • Data entry errors
Statistical Goals	• Unplanned analyses (type 1 error rates) • Escalation plan(s) compliance • Decision rule compliance (e.g., stopping, proceeding to next phase, etc.)
Study Progress	• Low/slow accrual • Compliance issues (escalation/expansion, interim analysis, objective response)
General	• Excessive inevaluable participants • High screen failure rate • Criteria for review

YOUR TURN, IN THE CHAT!

IF THE DSMC REVIEWER NOTICED A PREMATURE ANALYSIS, WHAT WOULD BE THE NEXT STEP(S) FOR DSMC?

A. Review stopping rules/criteria in protocol
B. Request the PI to work with the study statistician to ensure Type I error rate is controlled for
C. Request results from the analysis to see if any signals (i.e., safety/efficacy) have been observed
D. All of the above

D
All of the above

DSMC Meeting Actions

Meeting Action	Definition
Approved as is	• No comments
Approved with comments	• Address comments at next submission
Interim approved	• Address comments within 2 weeks (reviewed outside of DSMC meeting)
Not approved	• Similar process to Interim Approved, but more severe • Involves escalation to Clinical Research leadership (e.g. IRB, RC, PMC) • Changes required (e.g., protocol and/or workflows) • Could include hold or closure recommendation

Helpful Tips for PIs (to ensure approval!)

Reference

DSMC portal page and guidance documents

Previous DSMC submission(s) and/or review letter(s)

Recent institutional submissions and ensure consistency across reporting:
- Continuing Review Report
- Amendment Submission Form
- IND annual report
- Performance monitoring responses

Review

Database report(s), consort diagram, and monitoring form before signing off

Meet

With study team to ensure data is up to date and submissions are on track

With study statistician to review interim analyses, stopping rules, etc.

Resources

- CCSG P30
- DSMC Portal Page
  - DSMC SOPs
  - Submission documents
  - Guidance & How To documents
  - Protocol Overview Dashboard
- MSK's Data and Safety Monitoring Plan

Questions?