DSMB Charter

The UC Cancer Institute Data Safety and Monitoring Board (UCCI DSMB) provides expert medical, scientific and statistical oversight for the conduct of cancer-related therapeutic clinical trials that require a data safety monitoring board as part of their data safety monitoring plan. This dynamic process facilitates the highest standards of scientific research at the UC Cancer Institute. This document defines the responsibilities for the study principal investigator and DSMB members and sets guidelines for the conduct of DSMB meetings.

The DSMB Charter has been approved by the UCCI Director.

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DATA SAFETY AND MONITORING BOARD CHARTER

OBJECTIVES:

All cancer related therapeutic clinical trials required to be monitored by a safety committee as part of their Data Safety and Monitoring Plan at the University of Cincinnati Cancer Institute (UCCI), will be monitored by the Data Safety Monitoring Board (DSMB). The DSMB’s will determine monitoring parameters. Which may vary and are flexible to support each study? The DSMB will focus on the analytic plan to include: Hypothesis, Primary Objective, and Endpoints. The DSMB will monitor for conduct (includes accrual, protocol required tests, IND etc.), toxicities and efficacy. The DSMB will use case report forms, data points and the data safety monitoring plan to complete their safety assessment and make recommendation for a continued monitoring plan.

A. **The Committee**

The Chair of the DSMB Committee shall be appointed by the Director of UCCI. Membership of the DSMB will be determined and reviewed on an annual basis by the DSMB Chair, DSMB administrator and DSMB Coordinator. Members are selected based on their experience in designing or conducting research studies or special clinical expertise.

B. **Responsibilities of DSMB Chair**

The DSMB Chair will preside over the committee meetings to ensure consistent and fair proceedings and deliberations, and he/she will communicate with investigators regarding any outstanding issues from the monitoring session so that the anonymity of the review is protected.

In the event that the Chair is unable to attend a meeting, he/she shall designate the Vice Chair or another full voting member to act on his/her behalf.

C. **Responsibilities of Committee**

1. The Primary mission of the DSMB is to assure patient safety in the conduct of clinical trials.
2. Follow the preferred process review order of PRMC, DSMB and IRB. Understanding that the process is not static but dynamic and the DSMB process can go parallel to the IRB process but it is preferred to go in consecutive order of PRMC, DSMB and IRB.
3. The DSMB will determine the monitoring parameters that are flexible and fit each specific clinical trial. This monitoring session will be initiated approximately 6 months from the studies first accrual date.
4. Periodically monitor and evaluate the accumulated study data for participant safety, study conduct (includes accrual, protocol required tests, IND etc.) and progress, and when appropriate efficacy.
5. Make recommendations as appropriate to the study investigators and regulatory agencies (IRB, IBC, FDA, etc.) concerning the continuation, modification, or termination of the trial.

6. Define opportunities to improve studies and determine system changes that most optimally allocate resources and protect research participants to foster a successful cancer Clinical Trial Program.

D. **Membership**

The DSMB is an independent group of experts who will advise the study investigators. The members of the DSMB serve in an individual capacity and provide their expertise and recommendations. Membership consists of persons independent of the investigators and any conflict of interest with the trial. The DSMB includes experts in or representatives of the fields of relevant clinical expertise, and biostatistics.

1. **Length of Term**

   - For all board members as well as the Chair, a term shall consist of two to four years. There is no limitation to the number of terms one may serve.

3. **Recruitment**

   - The DSMB Committee Members will provide feedback and give suggestions to the DSMB Chair regarding membership recruitment. DSMB members will vote and the chair will have final decision on membership assignment. New appointments, reappointments and revisions to the processes will be overseen by the DSMB Chair.

E. **Documentation**

   - To ensure coordinated documentation and monitoring of UCCI research studies activities, the DSMB Coordinator will act as the single recording secretary for the Data Safety Monitoring Board (DSMB). The recording secretary will be responsible for coordinating the meetings, recording the meeting minutes and facilitate communication between the committee members and investigators.
F. **DSMB Meetings:**

1. **Meeting conduct**

   - The DSMB will meet monthly, as needed, and quorum will require at least 4 members in attendance. If the quorum cannot be reached due to multiple members with conflicts, the Chair can appoint ad hoc members for that particular study or reschedule the meeting.

   - The meeting will consist of three sessions, Open, Closed and Closed Executive for each study.

     - **Open Session:** The study investigators and biostatistician are invited to attend this session, present results and respond to questions. This study is open to all study investigators, data coordinators, and representatives from the FDA, Industry sponsors and IRB.

     - **Closed Session:** The Safety data and, if appropriate, efficacy data will be presented in this session. Participants of this session will be determined by the DSMB.

     - **Closed Executive Session:** This final session involves only members of the DSMB to ensure complete objectivity as they discuss outcome results, make decisions, and formulate recommendations regarding the study. Decisions will be made by the DSMB member majority with statistical input.

   - Members of the DSMB will meet a minimum of two times per year over the duration of the study. The meetings will be scheduled on a regularly scheduled monthly DSMB meeting. Date and time will be communicated by the DSMB coordinator.
G. Meeting Coordination

The DSMB Data Coordinator will prepare the appropriate data points provided in Oncore. The DSMB Coordinator will schedule and communicate the meeting date, time, location and study to be reviewed to the Principal Investigator and DSMB members. This communication will provide the scheduled timeline and distribution dates of review materials. The data distribution will occur over a four week period in the following order:

1. **DSMB PI Data Distribution**

   - The data source for studies requiring a data safety and monitoring board will be tracked in the regulatory database, Oncore. The UCCI Clinical Trials Office has oversight of the input of data into Oncore. The data will be used to generate data points that will be provided to the PI in the form of a data packet. The data packet will consist of the following:

   - DSMB Report (Oncore), detailing the data points listed below.
     - Protocol Details (information, Treatment, Eligibility)
     - Protocol Reviews (PRMC History)
     - Protocol Accrual
     - Protocol Accrual History
     - Protocol Disposition
     - Protocol Demographics
     - Protocol Toxicities
     - Protocol Worst Grade Toxicities
     - Protocol SAEs
     - Protocol AE Toxicities
     - Protocol Deviations
     - Protocol Status History

   The initial review will also include the following.

   - Study Calendar
   - Membership List
   - Case Report Forms

   - The data packet will be provided to the PI for review and completion of a PI Summary four weeks prior to the scheduled meeting. The summary will be returned to the UCCI Clinical Trials Office DSMB Coordinator one week from the date of receipt of the data packet. The PI's summary should focus on the following components that define the analytic plan.

   - Hypothesis
   - Primary Objectives
   - End Points
2. **CTO distribution to the DSMB**

- The UCCI CTO Data Coordinator has one week to review and enter additional data into Oncore. The DSMB Report, Study Calendar and Case Report Forms will be updated as needed and new reports generated based on the PI's feedback. The DSMB Coordinator will create a Review packet consisting of the following documents to be distributed to the DSMB two weeks prior to the scheduled meeting in preparation of the Boards review.
  
  - PI Summary
  - DSMB Report
  - Study Calendar (initial review only)
  - Case Report Forms (initial review only)
  - Current Protocol
  - Template Form (PI Summary)

3. **Distribution of Recommendations and Outcomes**

- The DSMB review process is dynamic and can consist of multiple reviews until the DSMB has resolved all of its concerns for the study in process. Each Board Members review of the data is presented verbally and recorded by the DSMB Coordinator. The DSMB Coordinator will prepare a notification letter and comprehensive meeting minutes consisting of both open/closed sessions with Action/Outcomes and follow-Up responsibilities. These reports will be distributed as follows:
  
  - Comprehensive meeting minutes that capture both Open and Closed meeting sessions with Action lists are distributed as follows:
    
    - The DSMB Coordinator will distribute to Data Coordinator for review and comments.
    
    - The DSMB Coordinator will distribute to the DSMB Board for Review and comments. Final comments are added, the minutes are sent to the DSMB Chair for final approval. Final Comprehensive minutes are distributed to the DSMB.

- Open Session Meeting minutes with Action list.
  
  - The DSMB Coordinator will distribute Open Session meeting minutes to the Principal Investigator (PI). Closed Session and Closed Executive Session meeting minutes are not distributed to the PI.
• Notification Letter

  - The DSMB Coordinator will create and distribute for review by the DSMB Administrator.
  
  - Upon approval by the DSMB Administrator, the DSMB Coordinator will distribute for approval and signature by the DSMB Chair.
  
  - The DSMB Coordinator will distribute the signed notification letter to the Principal Investigator with the Open Session meeting minutes.

H. **DSMB Monitoring Conduct and Outcomes:**

1. **Monitoring Process**

   - The DSMB monitoring process is dynamic and allows for a study to be custom fitted with a safety board that will facilitate good clinical practice and adhere to the highest standards of research. Each study will have its own monitoring parameters based on the scientific risk involved. In the initial monitoring session the DSMB will determine the review cycle and will follow with recommendations based on the monitoring results. The DSMB will continue monitoring the progress of the study based on the monitoring parameters set by the DSMB.

• **Recommendations**

  - The DSMB can make recommendations for a study base on monitoring results and professional/expert concerns. The DSMB’s primary focus is safety. Monitoring parameters can be changed based on findings resulting in a change of scientific risk or a study can be stopped if patient safety is a concern. If there are no findings of safety concerns or other major issues, the DSMB will likely recommend the continuation of the current monitoring parameters. The DSMB Coordinator will generate a notification letter providing an outline of the board’s recommendations.

  - If the DSMB finds that a major change is required in the study design or the PI wants to significantly amend the study design, the PRMCs initial approval is void. The study will need to be submitted to the PRMC for approval before the PI can respond to the DSMBs concerns.

  - The PRMC Coordinator will schedule the review based on the Boards recommendations.
I. **Serious Adverse Events:**

All serious, unexpected and related adverse events will be reported immediately to the DSMB Chair and other members of the DSMB by the study sponsor or designee. The DSMB Chair can be contacted through the UCCI CTO by contacting the DSMB Administrator or DSMB Coordinator. The DSMB Coordinator will orchestrate the review process as determined by the board members. The decision to meet by teleconference or on site to discuss the adverse event will be left to the discretion of the members of the DSMB. If the DSMB determines that the study procedures present a greater risk than expected, the board may recommend to the PI and the IRB that the study enrollment be suspended pending further evaluation.

The DSMB Chair or DSMB Administrator will notify the Study Sponsor (or sponsor designee) directly of any findings of a serious and immediate nature or recommendations to discontinue all or part of the trial within 24 hours of knowledge of the event. An Immediate Action report will be created and submitted to the UCCI CTO Regulatory Coordinator for appropriate dissemination to regulatory authorities.

J. **Appendices**

- **Appendix 1:** *DSMB (Current Year) Calendar*
- **Appendix 2:** *PI Summary Template*
- **Appendix 3:** *DSMB Member List*
- **Appendix 4:** *IIT DSMB Statement*