DSMB Charter
Data Safety Monitoring Board

University of Cincinnati Cancer Institute
06/18/2015
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.

William Barrett, MD
Director, UCCI
# DSMB Charter

## TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objectives</td>
<td>3</td>
</tr>
<tr>
<td>A. The Committee</td>
<td>4</td>
</tr>
<tr>
<td>B. Responsibilities of DSMB Chair</td>
<td>4</td>
</tr>
<tr>
<td>C. Responsibilities of the Committee</td>
<td>4</td>
</tr>
<tr>
<td>1. Preferred process</td>
<td>4</td>
</tr>
<tr>
<td>2. Initial Review</td>
<td>4</td>
</tr>
<tr>
<td>3. Periodic Review</td>
<td>4</td>
</tr>
<tr>
<td>4. Recommendations</td>
<td>5</td>
</tr>
<tr>
<td>5. Participation</td>
<td>5</td>
</tr>
<tr>
<td>6. Opportunities</td>
<td>5</td>
</tr>
<tr>
<td>D. Membership</td>
<td>5</td>
</tr>
<tr>
<td>1. Comprehensive Membership List</td>
<td>5</td>
</tr>
<tr>
<td>2. Length of Term</td>
<td>5</td>
</tr>
<tr>
<td>3. Committee Rotation</td>
<td>5</td>
</tr>
<tr>
<td>4. Documentation</td>
<td>6</td>
</tr>
<tr>
<td>E. DSMB Meetings</td>
<td>6</td>
</tr>
<tr>
<td>1. Meeting Conduct</td>
<td>6</td>
</tr>
<tr>
<td>F. Meeting Coordination</td>
<td>7</td>
</tr>
<tr>
<td>1. DSMB PI Data Distribution</td>
<td>7</td>
</tr>
<tr>
<td>2. CTO Distribution to the DSMB</td>
<td>8</td>
</tr>
<tr>
<td>3. Distribution of Review Outcomes</td>
<td>8</td>
</tr>
<tr>
<td>H. DSMB Review Outcomes</td>
<td>9</td>
</tr>
<tr>
<td>1. Types of Review Outcomes</td>
<td>9</td>
</tr>
<tr>
<td>I. Serious Adverse Events</td>
<td>11</td>
</tr>
<tr>
<td>J. Appendices</td>
<td>11</td>
</tr>
</tbody>
</table>
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 initial meeting will be to determine the monitoring parameters. The parameters 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 review.

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. 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 protocol review 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. 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.

2. Initial review cancer related therapeutic clinical trials required to be monitored by a safety committee and determine the monitoring parameters that are flexible and fit each specific clinical trial. This review will be initiated approximately 6 months from the studies first accrual date.

3. Periodically review and evaluate the accumulated study data for participant safety, study conduct (includes accrual, protocol required tests, IND etc.) and progress, and when appropriate efficacy.
4. Make recommendations to the study investigators and regulatory agencies (IRB, IBC, FDA, etc.) concerning the continuation, modification, or termination of the trial.

5. Participate in collaborative discussion that promotes a partnership that aids in discovering scientific possibilities specific to each clinical trial being monitored.

6. Define and re-define areas of opportunity upon each study review building relationships that form a foundation to build a successful cancer institute.

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. Comprehensive Membership List

<table>
<thead>
<tr>
<th>BOARD MEMBERS</th>
<th>Role</th>
<th>Affective Date</th>
<th>Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boaz, Billie Assistant</td>
<td>Assistant</td>
<td>03/29/2010</td>
<td>N/A</td>
</tr>
<tr>
<td>Kastl, Alison BS CCRC</td>
<td>DSMB Administrator</td>
<td>01/28/2010</td>
<td>N/A</td>
</tr>
<tr>
<td>Keller, Jessica CCRC</td>
<td>Data Coordinator</td>
<td>04/01/2015</td>
<td>N/A</td>
</tr>
<tr>
<td>Herzog, Tom MD</td>
<td>Chair</td>
<td>08/01/2014</td>
<td>2-3 yrs</td>
</tr>
<tr>
<td>Hashemi, Nooshin MD</td>
<td>Member</td>
<td>04/08/2014</td>
<td>2-3 yrs</td>
</tr>
<tr>
<td>Pater, Luke MD</td>
<td>Member</td>
<td>07/01/2014</td>
<td>2-3 yrs</td>
</tr>
<tr>
<td>Starnes, Sandra MD</td>
<td>Member</td>
<td>11/30/2011</td>
<td>2-3 yrs</td>
</tr>
<tr>
<td>Ying, Jun</td>
<td>Member</td>
<td>05/13/2014</td>
<td>2-3 yrs</td>
</tr>
<tr>
<td>TBD</td>
<td>Member</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TBD</td>
<td>Member</td>
<td></td>
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2. Length of Term

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

3. Committee Rotation

- The DSMB Rotation Sub-Committee will meet once a year to review membership status and DSMB processes. The DSMB Rotation Sub-Committee will be selected by the DSMB Chair. New appointments,
reappointments and revisions to the processes will be overseen by the sub-committee and executed by the DSMB Chair.

4. Documentation

- To ensure coordinated documentation and monitoring of UCCI research studies activities, the PRMC Coordinator will act as the single recording secretary for PRMC and 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.

E. DSMB Meetings:

1. Meeting conduct

- The DSMB will meet monthly, as needed, on the second Tuesday of the month. The committee will meet quorum when more than half the members are present. If the quorum cannot be reached due to multiple members with conflicts, the Chair will appoint ad hoc members for that particular study.

  • The length of the DSMB meeting is 2 hours. The meeting will consist of three sessions, Open, Closed and Closed Executive.

    - **Open Session**: The study investigators and biostatistician will 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.

  • New protocols will be placed on the agenda upon approval of the Protocol Review and Monitoring Committee (PRMC). The DSMB review will be scheduled for the next regularly scheduled available DSMB meeting. Only one study will be discussed at the monthly meetings.
• Study monitoring parameters will be determined by the DSMB upon the initial review and will meet the specific needs of each protocol. The initial review date will scheduled 6 months from the first patient accrual date. 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.

F. 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
  • 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

3. **Distribution of Review 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 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 Review Outcomes:**

1. **Types of Review Outcomes**

   - The DSMB review 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 review parameters based on the scientific risk involved. The DSMB will determine the review cycle and will follow the following review outcomes till the board unanimously approves the study.

• Tabled:

  - The DSMB can vote to table a study base on review outcomes and professional/expert concerns. The DSMB Coordinator will generate a notification letter providing an outline of the boards concerns. The letter and a copy of the open session minutes will be distributed to the PI.

  - If the DSMB finds that a change is required in the study design or the PI wants to add to the study in a way that changes 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 PI must respond with a written response 6 months from the date of the DSMB notification letter or the study will be administratively closed.

- The DSMB Coordinator will schedule the review for the next available regularly scheduled review date. The review process will continue until the study is approved.

- **Approved with Contingencies:**

  - The DSMB can vote to approve the study with contingencies based on review outcomes and professional/expert concerns. The DSMB Coordinator will generate a notification letter providing an outline of the board's concerns. The letter and a copy of the open session minutes will be distributed to the PI.

  - The PI must respond with a written response 6 months from the date of the DSMB notification letter or the study will be administratively closed.

  - The DSMB Coordinator will schedule the review for the next available regularly scheduled review date. The review process will continue until the study is approved.

- **Approved:**

  - The DSMB can vote to approve the study based on review outcomes and professional/expert opinions. The DSMB Coordinator will generate a notification letter. The letter and a copy of the open session minutes will be distributed to the Principal Investigator.

  - The DSMB Coordinator will schedule the continuing review for the next available regularly scheduled review date based on the study parameters determined by the DSMB. This review process will continue for the life of the study.
I. **Serious Adverse Events:**

All serious 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 PRMC 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 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. 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 2016 Calendar*
*Appendix 2: DSMB Membership List*