Data Monitoring Committee Charter for DCP-Sponsored Trials

Version 1: October 1, 2021

I. Purpose

To describe the procedures to be used by the NRG Oncology (NRG) Data Monitoring Committee (DMC) Panel C overseeing NRG cancer care delivery, cancer prevention, and low-risk cancer control/symptom management trials that are sponsored by the Division of Cancer Prevention and Control at the National Cancer Institute (NCI).

II. Scope

This Charter applies to the NRG Oncology DMC Panel C.

III. Procedures

A. Study inclusion

1. All NRG cancer care delivery, cancer prevention, and low-risk cancer control/symptom management trials are under the purview of the NRG DMC Panel C. Cancer control trials will be deemed low-risk by mutual agreement from the NRG Oncology Group Statistician, NRG Oncology NCI Oncology Research Program (NCORP) Chairs, the study Principal Investigator, and the NRG Cancer Prevention and Control co-chair(s).

B. Responsibilities

1. The primary responsibilities of a DMC are to monitor the safety and welfare of trial participants, review safety analyses, review interim analyses of outcome data, and to recommend whether the study needs to be changed or terminated based on findings of safety, interim analyses or other pertinent observations. Committee members should familiarize themselves with the NRG Oncology research protocols under their purview and proposed plans for monitoring contained therein. The committee also determines whether and to whom safety or outcome results can be released prior to the protocol-specified time for reporting trial findings.

2. The DMC reviews trial status reports, reports of related studies and considers other information and recommendations supplied by members of the protocol team (Protocol Statistician, Protocol Chair, and an NRG Oncology Group Chair) to determine if any of the trials being monitored need to be modified or terminated.

3. The DMC reviews and approves major modifications to trial protocols proposed by the protocol team prior to the implementation of the modification (e.g., study termination, dropping of a treatment arm, increasing sample size, etc.).

C.. Membership

1. DMC members are nominated and appointed by the NRG Oncology NCI Community Oncology Research Program (NCORP) Chairs or their designees. Prior to their appointment, all nominees are reviewed and approved by the NCI NCORP Director Each member is appointed for a fixed term. The term lengths of individual DMC members should be established so the term of no more than three voting members will expire within any given year. Members with expiring terms can be reappointed.

2. The committee may include physicians, statisticians, consumer representatives and other professionals from within and outside the NRG Oncology with expertise in clinical trials, including

prevention, symptom management, patient-reported outcome, and/or cancer care delivery research. Members are selected based on their experience, reputation for objectivity and knowledge of good clinical trial methodology.

3. The number of the DMC members can vary depending on the nature of the trials being monitored and potential safety issues that may be involved. However, the total membership of the DMC Panel C should not exceed ten individuals.

4. The DMC will include one NCI physician from DCP, one NCI statistician and the NRG Oncology Group Statistician who will all serve as non-voting members. One or two additional individuals from within the NRG Oncology membership, who will have voting rights, can be appointed by agreement of the NRG NCORP Chairs. This individual should not be a member of any of the study teams being monitored or from the leadership of the disease or program committee for the studies being monitored. The DMC should also include at least four other individuals as voting members who are external to the NCI and NRG Oncology. At least one of these external individuals must be a statistician and one must be a consumer representative.

5. The DMC Chair is appointed by the NRG NCORP Chairs from among the members of the DMC who have been appointed to the committee and who are external to the NCI and NRG Oncology.

D.. Meetings

1. Regular DMC meetings are held at least twice a year on an approximate six-month cycle. If the need arises, additional special meetings can be held at the discretion of the DMC Chair, and may be recommended by the one of the NRG Oncology members. All trials being monitored by the DMC are reviewed at each regular meeting. Meetings are held by video conference. Face-to-face meetings will be held every third meeting.
2. Major modifications not motivated by confidential outcome data or patient safety (e.g., increase or decrease in sample size must be discussed with DCP before it is presented to the DSMC for consideration.

3. The meeting will consist of three parts. The first part is an open session at which, in addition to the voting and non-voting DMC members, the Protocol Statisticians and others involved in the implementation of the trials being monitored may be in attendance. In this session, the focus is on review and discussion of accrual, toxicity data, and data reporting completeness. Discussion is also held on any issues that may be raised by the committee members, the Protocol Statisticians or others involved in the implementation of the trials being monitored. No outcome results (tumor response, recurrence of any type, second primary cancer, survival, or quality of life information) or, if the trial involves blinded treatments study, no treatment arm-specific toxicity data may be presented in the open session (Note: For blinded studies, the only toxicity data shown in the open session is that which has been pooled across all treatment groups.). Following the open session, there will be a closed session. Attendance at the closed session is restricted by NCI guidelines to the Protocol Statisticians for the trials being monitored and all voting and non-voting members of the DMC. Information reviewed in the closed session includes: treatment arm-specific data from trials which involve blinded treatment assignment including toxicity and compliance; in addition, if the protocol-specified time for such analyses has been reached, the results of trial-specific interim analyses of safety or efficacy outcome. Following the closed session, there will be an executive session. Attendance at the executive session is restricted by NCI guidelines to only the voting and non-voting members of the DMC. During this session, the attending members of the DMC discuss the information they have reviewed and make a final decision regarding their recommendation for each trial being monitored. A quorum of the DMC is considered met at 50% of the voting members being present to vote and render the decision.

4. At least two weeks before each scheduled DMC meeting, all DMC members will be provided with

open- and closed-session reports for each trial being monitored describing the current status of information for each trial. The open session reports will be prepared by the Protocol Statisticians in collaboration with the Protocol Chairs. The closed session report is prepared by the Protocol Statisticians. The specific contents of these reports are defined in NRG Oncology SOP: STAT-02.

E.. Recommendations

1. DMC recommendations should be based upon results for the protocols being monitored as well as upon data available from other relevant studies and other general relevant information that may become available. The DMC provides recommendations to the NRG Oncology NCORP Chair member of the Committee who then provides the recommendations to the NRG Oncology Group Chairs. The committee's recommendations are documented in minutes of the meeting that include a brief summary of the general activities that occurred in the open and closed sessions, as well as the specific recommendation that the DMC has for each protocol being monitored. At a minimum, the DMC should make a recommendation for each protocol regarding one of three possible scenarios: 1) to continue a trial as planned; 2) to modify the implementation of the study; 3) to stop the trial earlier than planned; or 4) report results earlier than planned. If a DMC recommendation includes modifying a trial due to safety concerns or if the recommendations include stopping of a trial earlier than planned, the DMC Chair should contact the NRG Oncology NCORP Chair member of the committee immediately following the conclusion of the executive session of the DMC meeting and inform him/her of such recommendations directly. NRG Oncology NCORP Chair member will inform and discuss unplanned modifications, including early study closure or early reporting of results, with the NCI NCORP Director prior to disclosing the information to any NRG Oncology investigator.

2. In the event that a recommendation made by the DMC is one other than to continue the study as planned, the NRG Oncology NCORP Chairs will act on the recommendation as expeditiously as possible. In the process of doing so, the NRG Oncology NCORP Chairs may seek the advice, in a confidential manner, of the Protocol Chair, NRG Oncology Disease Committee Chair, NRG Oncology Group Chairs, and/or the NRG Oncology Group Statistician.

5. In the unlikely situation that the NRG Oncology NCORP Chairs do not concur with the DMC recommendation, the NRG Oncology Group Chairs and NCI NCORP Director must be informed of the recommendation of the DMC and of the NRG Oncology NCORP Chairs' reason(s) for disagreeing with the recommendation. The NCI NCORP Director and the NRG Oncology NCORP Chair DMC member, in consultation with the DMC Chair, will be responsible for reaching a mutually acceptable decision about the study. Confidentiality will be maintained during these discussions, but relevant confidential trial data may be shared by the DMC Chair with the NRG Oncology NCORP Chair, the Group Chair, and NCI NCORP Director to the extent needed to convey justification for the DMC's recommendation.

6. If the DMC recommends a change in a study for reasons other than patient safety (e.g., to extend accrual because of an event rate lower than expected) or study closure due to slow accrual, the DMC will provide to the NRG Oncology NCORP Chair an adequate rationale. In the absence of disagreement, the NRG Oncology NCORP Chair will be responsible for having an amendment prepared and submitted to DCP reflecting the recommendations of the DMC and providing the rationale for the changes.

F.. Confidentiality

1. A statement of confidentiality, as provided in Appendix A of this document, must be signed by all DMC members.

2. No communication of the deliberations or recommendations of the DMC, either written or oral, are to be made outside of the committee except as specified in this document. Outcome (efficacy) results and toxicity data from masked trials are confidential and must not be divulged to any non-member of the DMC (except to the NRG and NCI officials as described in Section D.3) until such time when the trial has been concluded and the trial results are made public.

3. There may be circumstances where it may be appropriate to release some aspect of confidential information from a trial before the time when a trial is concluded. The conditions for such release are described in Section F of this document.

G.. Early Release of Trial Findings

Any planned release of outcome data external to the DMC [to NRG or NCI personnel not members of the committee, DMC's of other organizations or to the public (e.g., presentation at meetings, journal publication, media interview, etc.)] prior to the completion of a trial must be approved by the DMC. In general, outcome data would not be routinely made available to individuals outside of the DMC until accrual has ceased and all patients have concluded their randomized treatment. After this point, the DMC may approve the release of outcome data on a confidential basis to the study chairs for planning the preparation of manuscripts, and/or to a small group of individuals for purposes of planning future trials. The DMC will also consider, on a case-by-case basis, special requests for release of information prior to the time point when accrual and treatment of all patients has been completed. Examples of such circumstances would be requests for toxicity findings from the Chair of a DMC of another trial external to the NRG, or situations where it is important for the health community to be informed of the possible presence or non-presence of a possible toxicity.

H.. Conflict of Interest

All individuals invited to serve on the DMC (voting and non-voting) will disclose to NRG Oncology any potential, real, or perceived conflicts of interest. These will include professional interest, proprietary interest, and miscellaneous interest considerations as described in the attached conflict of interest policy. A conflict of interest statement, as provided in Appendix B of this document, must be signed by all DMC members prior to their appointment as a DMC member. After appointment, DMC members should disclose to NRG Oncology any potential conflicts which may develop during the course of serving on the DMC. The NRG Oncology Conflicts of Interest Officer will review possible conflicts and determine whether there is sufficient basis to exclude the individual from serving on the DMC or sufficient to retire a DMC member who is already serving.

I.. Intergroup Trials

These guidelines apply also to intergroup trials for which NRG is the coordinating group.

J.. NCI Oversight

In order to satisfy its objectives of protecting patients, ensuring study integrity, and assuring public confidence in the conduct of clinical trials, it is essential that a DMC function in a manner that demonstrates competences, experience, and independence of NRG, career or financial interests. If the NCI determines that the DMC for the NRG is not functioning in this manner, it will discuss with the NRG Oncology NCORP Chair what changes are needed to the composition or structure of the DMC.

IV. Reference

The data monitoring committee policy of the National Cancer Institute

V. Appendices

NRG Oncology Data Monitoring Committee Statement on Confidentiality
NRG Oncology Data Monitoring Committee Conflict of Interest Statement

VI. Regulations and Guidelines

NIH Policy for Data and Safety Monitoring
Further NIH Guidance on Data Safety Monitoring for Phase 1 and Phase 2 Trials