DSMB CHARTER

Principal Investigators: Vincent Mor, PhD, Brown University
Susan L Mitchell, MD, MPH, Hebrew SeniorLife

Grant #: U54 AG063546-01

Title: National Institute on Aging (NIA) Imbedded Pragmatic AD/ADRD Clinical Trial Collaboratory

The Data and Safety Monitoring Board (DSMB) will act in an advisory capacity to the National Institute of Aging (NIA) Director to monitor participant safety, data quality and progress of the NIA IMPACT Collaboratory, grant # U54 AG063546-01 by MPIs, Vincent Mor, PhD, Brown University and Susan L. Mitchell MD, MPH, Hebrew SeniorLife.

DSMB Responsibilities

The DSMB responsibilities are to:

Initial meeting

- Review all the IRB-approved multiple study protocols, with regard to participant safety, recruitment, randomization, intervention, data management, quality control and analysis and the informed consent documents with regard to applicability and readability.

- Recommend changes to each pilot study protocol and the informed consent form, when applicable.

- Identify the relevant data parameters and the format of the information to be regularly reported.

- Recommend participant recruitment be initiated after receipt of a satisfactory protocol for each pilot study. If the need for modifications to each pilot study protocol, MOP (if applicable), consent form, DSMP or any other study document is indicated by the DSMB and/or the NIA Program Officer (PO), the DSMB will postpone its recommendation for the initiation of participant recruitment until after the receipt of a satisfactory revised pilot study protocol or other study documents.

- If an interim analysis is planned, the DSMB will review investigators’ plan and advise NIA on its appropriateness.

During the study meetings

- Review masked and unmasked data, as applicable. These data can be related to safety, recruitment, randomization, retention, protocol adherence, trial operations, data completeness, form completion, intervention effects, gender and minority inclusion.

- Identify needs for additional data relevant to safety issues and request these data from the study investigators.
- Propose additional analyses and periodically review developing data on safety and endpoints.
- Assist the NIA by commenting on any problems with study conduct, enrollment, sample size, and/or data collection
- Consider factors external to the study, when relevant information becomes available, which may have an impact on the safety of the participants or the ethics of the trial.
- Review study performance, make recommendations, and assist in the resolution of problems reported by the Principal Investigator.
- Protect the safety of the study participants and ensure the confidentiality of the study data and the results of monitoring.
- At each meeting, consider the rationale for continuation of the study, with respect to progress of randomization, retention, protocol adherence, data management, safety issues, and outcome data (if relevant) and make a recommendation for or against the trial's continuation.
- Review and make recommendations on proposed protocol changes, and/or new protocols proposed during the trial. When the DSMBs are unblinded, the Boards may recommend to NIA to appoint a blinded working group of the DSMB to review the proposed protocol changes and make recommendations to NIA on whether to approve the requests.
- Provide advice on issues regarding data discrepancies found by the data auditing system or other sources.
- Review manuscripts of trial results if requested by the Board or the NIA PO who may seek DSMB review of manuscripts reporting major outcomes prior to their submission for publication.

The DSMB will discharge itself from its duties when the study is complete.

Membership
Membership consists of persons completely independent of the investigators who have no financial, scientific or other conflict of interest with the trial. Collaborators or associates of the pilot study PIs are not eligible to serve on the DSMB. Written documentation attesting to absence of conflict of interest is required and will be collected by NIA. The Director of NIA will approve the number and names of DSMB members.

The DSMB includes experts in, or representatives of, the fields of:

- Biostatistics
- Dementia
- Health services research
- Clinical trials
A chairperson will be selected by NIA and will be responsible for facilitating the meetings, reviewing the first draft of the meeting notes with the NIA Program Official and any decision making in the case of a tie vote. The Chair and NIA Program Officer are the contact people for the DSMB. The Brown University will provide the logistical management and support for the DSMB.

A safety officer may also be recommended by the DSMB, if necessary, with the NIA Program Officer’s concurrence. Approval of the SO will be the responsibility of the NIA Program Officer.

Any serious adverse events (SAEs) that might be related to the intervention will be reported the NIA-Appointed Safety Officer and the NIA Program Official within 48 hours of learning of the event. The NIA-Appointed Safety Officer will make recommendations to the DSMB regarding these related SAEs, and the DSMB will make recommendation to the NIA regarding study continuation or termination.

Meeting Format

The Principal Investigators will prepare and present the following study materials, as applicable, for review and approval: MOP, DSMP, modifications to the study protocol or new protocols, informed consent document(s), reporting of adverse events, and statistical analysis plan for the first meeting. This will be in consultation with the DSMB Chairperson and NIA Program Official.

Meetings of the DSMB will be held regularly (e.g., every six to nine months) at the call of NIA or the DSMB Chair. The NIA Program Officer or designee (NIA staff) will be present at every meeting. An emergency meeting of the DSMB may be called at any time by the Chair or the NIA, should participant safety questions or other unanticipated problems arise.

DSMB meetings will consist of open, closed and optional executive sessions, all closed to the public because discussions may address confidential participant data. The study PIs and key staff members, DSMB members and NIA Program Officer and/or authorized NIA staff attend the open sessions. Discussions at these sessions focus on the review of the aggregate data, conduct and progress of the study, including participant accrual, protocol compliance, and problems encountered. Data by treatment group are not presented in the open session.

The closed session will be attended by unblinded study staff, the DSMB members and the NIA PO or designee(s). The NIA PO attends the closed and open sessions as an observer, not as a DSMB member, to answer any policy or administrative questions the DSMB members may have. The primary objective of the closed sessions is to review data by study group. To ensure participants safety and well-being, DSMBs for NIA-funded trials are required to review safety data by the actual treatment group. In many instances, safety data could also be the outcome data. Therefore, the unblinded Boards no longer review and provide recommendations to NIA on any, but safety-related protocol changes. All other protocol modifications are subject to review by the blinded working groups of the DSMBs. DSMBs' working groups are appointed by NIA and provide their recommendations to NIA Director who makes decisions about whether to approve or decline proposed modifications.

If necessary, an executive session may be requested by the DSMB and will be attended only by voting DSMB members. The NIA Program Officer or designee is not permitted to attend the executive sessions.
The IMPACT Administrative Core and KAI in coordination with the NIA PO, DSMB Chair, or Principal Investigator will prepare the meeting agenda (to be approved by the NIA PO) that usually includes the following:

1. Welcome and introduction – study team, DSMB members, NIA and KAI staff
2. Open session (review study protocol and its amendments, consent form, open study report, etc.) - study team, DSMB members, NIA and KAI staff
3. Closed session (review closed session report, including unblinded data, etc.) – unblinded study statistician, DSMB members, NIA and KAI staff
4. Executive session (optional, upon DSMB request) – DSMB members only
5. Debriefing (optional, upon DSMB request, time permitting) - study team, DSMB members, NIA and KAI staff

The DSMB may modify its processes and procedures at any time with the approval of the NIA PO.

Meeting Materials

DSMB interim report templates developed by the study staff or study-specific versions of NIA report templates for both the open and closed sessions and plans for interim analyses will be reviewed and either approved at the initial DSMB meeting or changes requested. Upon DSMB request and approval by NIA, reports could be modified at any time during the study. All meeting materials should be submitted to KAI 7 to 10 calendar days prior to the meeting. KAI will distribute the reports to the DSMB and other meeting attendees.

Part 1 - Open Session Reports (Template): Open Session reports will include administrative reports that describe participants screened, enrolled, completed, and discontinued, as well as baseline characteristics of the study population. Other general information on study status may also be presented. Listings of adverse events and serious adverse events as well as any other information requested by the DSMB may also be in the Open Session report, but none of the data will be presented in an unblinded manner.

Part 2 – Closed Session Report (Template): Closed Session reports will present the same information as presented in the Open Session but by unblinded treatment group. The Closed Session reports should be destroyed at the conclusion of the meeting. If the meetings are held by telephone, printed copies of the closed reports should be destroyed immediately following the meeting.

Reports from the DSMB

A report containing the recommendations for continuation or modification of the study will be prepared by the DSMB, NIA PO or NIA contractors. The draft report will be sent to the DSMB members for review and approval not later than three weeks after the meeting. Once approved by the DSMB members, KAI or the NIA PO (or designee) will forward the DSMB recommendations to the Principal Investigator(s) indicating NIA’s concurrence with the report or its parts. It is the responsibility of the Principal Investigator to distribute the DSMB recommendation to all co-investigators and to ensure that copies are submitted to the IRB that reviewed and approved the study documents.

As stated above, each meeting must include a recommendation to continue or terminate the study made by a formal DSMB majority or unanimous vote. Every effort will be made to obtain a consensus. If consensus cannot be obtained, a majority vote is required to carry any
recommendation and a minority report should be appended. The DSMB Chair will participate in discussions and will vote only when his/her vote would actually affect the outcome (such as to break the tie in a 50-50 split vote). Should the DSMB decide to issue a termination recommendation, the full vote of the DSMB is required.

A recommendation to terminate the study may be made by the DSMB at any time by majority vote. If this recommendation was made during the DSMB’s Executive Session, the Chair should notify the NIA immediately by telephone and email. After the NIA Director makes a decision about whether to accept or decline the DSMB recommendation to terminate the study, the NIA PO informs the PI about the decision.

Confidentiality

All materials, discussions and proceedings of the DSMB are completely confidential. Members and other participants in DSMB meetings are expected to maintain confidentiality.