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| Independent Data Monitoring Committee (IDMC) CHARTER | | | |
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| Study Title | | ***Insert*** | |
| **Chief Investigator** | | ***Insert*** | |
| **Principal Investigator** | | ***Insert*** | |
| **Protocol Registration Number** | | ***Insert*** | |
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| **Scope of IDMC Charter** | | | |
| The purpose of this document is to describe the roles and responsibilities of the independent IDMC for the above trial. | | | |
| **IDMC Responsibilities and Terms of Reference** | | | |
| The IDMC will provide oversight of the trial, including safeguarding the interests of trial participants, assessing the safety and efficacy of the Investigational Medicinal Product (IMP) and monitoring the overall conduct of the trial. The IDMC will make recommendations to the Trial Steering Committee (TSC).  Terms of Reference: The IDMC will receive and review the progress and accruing data of the trial and provide advice on the conduct of the trial to the TSC. The IDMC should inform the Chair of the TSC, if, in their view, there is a requirement to stop or modify the trial because:   1. There are safety concerns regarding the treatment. 2. The treatment has achieved a target statistical outcome (i.e. hit a stopping boundary). 3. The trial is not expected to reach a conclusion (i.e. accrual rates so low that it is unlikely sufficient patients will be recruited to provide meaningful results). | | | |
| Specific Roles | | | |
| The IDMC members will:   1. Review the research protocol, statistical assessment, data monitoring and safety reporting documents. 2. Review data from the Safety Cohort (i.e. first 4 patients, each having received a minimum of 3 doses) and advise on opening recruitment to all eligible patients. If appropriate, an expansion of the safety cohort may be advised. 3. Review data on the first 15 patients enrolled and treated and advise whether eligibility may be extended to patients 5 years or older or to some other intermediate age between 5 to 18 years. 4. Evaluate the progress of the trial, including periodic assessments of data quality, completeness and timeliness, participant recruitment, accrual and retention, participant risk versus benefit, performance of the trial site, compliance with the protocol and other factors that can affect study outcome. 5. Monitor planned sample size assumptions and recommend amendment if appropriate. 6. Monitor and evaluate trial outcome using primary end-point data. 7. Monitor safety evidence (e.g. SAR/SUSAR data, signs and symptoms tables and any reported deaths). 8. Decide whether to recommend that the trial continues to recruit participants or whether recruitment should be terminated or suspended for everyone or for some participant subgroups. 9. Report on the safety and progress of the trial and make recommendations to the TSC. 10. Advise on any major protocol modifications suggested by investigators or sponsors. 11. Assess the impact and relevance of external evidence. 12. Suggest any additional data analyses required where this is relevant to the trial continuing or stopping. 13. Monitor the continuing appropriateness of patient information. 14. Consider the ethical and regulatory implications of any recommendations made by the IDMC. | | | |
| Membership | | | |
| The members of the IDMC for RAPIDE-TKM are:   1. ***Insert*** 2. ***Insert*** 3. ***Insert***   Membership consists of persons completely independent of the investigators who have no financial, scientific, or other conflict of interest with the trial. | | | |
| IDMC Meetings | | | |
| Meeting/review frequency: The first meeting will take place via teleconference to discuss the protocol, statistical assessment plan and to review the documents to monitor the study. Thereafter, it is anticipated that ***specify i.e. weekly/monthly*** review of study progress, data and safety will, for the most part and when there are no major issues, be undertaken through email correspondence. The Chair will decide when it is necessary for the IDMC to meet via teleconference. This teleconference may replace the specify ***i.e. weekly/monthly*** email review or be called at any time if a review of safety data is required (e.g. safety cohort data are available, a time point for review of safety with a view to inclusion of children is reached or another question of patient safety arises) or a stopping boundary is reached.  Attendance: All IDMC members should endeavour to attend meetings and teleconferences. If, at short notice, any IDMC members cannot attend or respond then the IDMC may still meet/review if at least two members are present/corresponding. The subsequent report, including any recommended major actions, should be reviewed and approved by all members. The trial statistician and other trial staff, including the CI, will attend the IDMC meetings as required and appropriate.  Minutes: The IDMC members will decide on how findings and /or recommended action of the meetings and email correspondence will be kept. When minutes are to be made of IDMC teleconference meetings, the teleconference may be recorded to assist with this. Minutes will be circulated to IDMC members as soon as possible following the meeting. Teleconferences may include both open and closed sessions (closed sessions, held for confidentiality reasons, will be minuted and the minutes kept in confidence by the IDMC until the end of the trial, at which time they should be copied to the sponsor).  Confidentiality: All materials, discussions and proceedings of the IDMC are completely confidential. Members and other participants in IDMC meetings are expected to maintain confidentiality. | | | |
| Reports for review by IDMC | | | |
| The ***insert trial name*** Data Monitor, or another member of the Trials Operations Group, will send the following information for review by members prior to the IDMC meetings.   1. ***Insert*** 2. ***Insert*** 3. ***Insert***   For the weekly IDMC review, when possible, the above information will be sent on Tuesdays in time for a mid-week IDMC meeting. For meetings called at other times, it will be sent as early as possible ahead of the meeting.  In addition, the Data Manager or Trials Manager will also inform the IDMC Chair when:   1. ***Insert*** 2. ***Insert*** 3. ***Insert***   IDMC members should store the papers/emails safely. After the trial is reported, the IDMC members should destroy all interim reports. | | | |
| **IDMC review and decision making** | | | |
| When IDMC review is conducted via email, IDMC members will be asked to review the reports submitted (as outlined above) and comment on the following:-   * Findings * Recruitment * Safety * Trial outcome * Recommended action   The Chair will review email responses and decide upon any action to be taken (e.g. recommendation to TSC, arrange IDMC teleconference).  When a teleconference call or meeting is held, the Chair will decide how the meeting and review are to be conducted. Every effort should be made for the IDMC to reach a unanimous decision. If the IDMC cannot achieve this, a vote may be taken. | | | |
| Reporting IDMC recommendations | | | |
| The IDMC chair will be responsible for determining the outcome of any email review or teleconference meeting and reporting the recommended action to the TSC.  Within two days (when possible) following the meeting, an email from the IDMC Chair (or designated IDMC Member) containing the IDMC’s recommendation and rationale for continuing, modifying, suspending or stopping the study will be forwarded to the CI and Chair of the TSC and cc to the Trial Manager.  If there is a disagreement between the IDMC and the TSC, a meeting of these groups should be held. The information to be presented would depend on the recommended action and the IDMC’s concerns. The meeting may be chaired by an external professional with relevant expertise who is not directly involved in the trial. | | | |
| After the trial | | | |
| At the end of the trial there the IDMC may request to examine the final data, and comment on data interpretation.  IDMC members will be named and their affiliations listed in the main report, unless they explicitly request otherwise. | | | |
| IDMC members’ contact details | | | |
| **Name** | **Email Address** | | **Contact Number** |
| ***Insert*** | ***Insert*** | | ***Insert*** |
| ***Insert*** | ***Insert*** | | ***Insert*** |
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