Study/Trial Full Title: Physiotherapy Rehabilitation for Osteoporotic VErtebral fracture trial

Protocol short title: PROVE.

REC No: 12/SC/0411

ISRCTN Number: : ISRCTN 49117867

Chief Investigator: Dr Karen Barker

Sponsor: University of Oxford

Introduction

The role of the Trial Steering Committee (TSC) is to provide overall supervision for the PROVE trial on behalf of the Trial Sponsor and the Trial Funder and to ensure that the trial is conducted according to the guidelines for Good Clinical Practice (GCP), Research Governance Framework for Health and Social Care and all relevant regulations and local policies.

The background to this trial, its objectives, assessments, interventions, etc, are described in the study/trial protocol.

The purpose of this document is to define the roles and responsibilities of the TSC and to guide its activities, its relationship with other trial committees, its membership, and the format, purpose and timings of its meetings. The charter also describes the procedures for ensuring confidentiality and proper communication to and from the TSC and an outline of the content of the reports to be provided to the TSC.

Terms of reference

- To provide advice, through its Chair, to the Trial Management Group (TMG), the Sponsor and the Trial Funder on all aspects of the trial.
- To monitor and supervise the progress of the trial towards its overall objectives, review accrual and results of the trial, adherence to the protocol, patient safety and the consideration of new information of relevance to the trial and the research question.
- To ensure that the rights, safety and wellbeing of the trial participants are the most important considerations and should prevail over the interests of science and society.
- To ensure that all relevant approvals are obtained before a project begins
- To agree proposals for substantial protocol amendments and provide advice to the TMG regarding approvals of such amendments.

- To consider the recommendations of Ethics committees, the trial/study DMEC (if applicable) and/or other trial/study committees.
- The TSC/SSC should inform the TMC if:
    - There are concerns about the safety of participants
    - Accrual is too low to provide meaningful results
    - It is evident that if the study continues it would fail to provide a clear benefit
- To recommend whether to continue or terminate the study or further adapt it based on safety and efficacy considerations.

Membership and Primary responsibilities of the TSC/SSC

The PROVE TSC is a multidisciplinary group comprising of the following members who jointly have responsibility for the design, conduct and evaluation of the clinical research project.

- An independent Chair
- Chief Investigator
- Members of the TMG (trial manager, study statistician)
- Independent clinician(s) or Scientist(s) with relevant experience
- Representatives from collaborating organisations co-applicants one per site
- Independent Statistician with relevant experience
- Patient Group Representative
- Clinician representative

The responsibility for calling and organising TSC/SSC meetings lies with the Chief Investigator in association with the Chair.

The Chair assisted by the Chief Investigator is responsible for facilitating the meetings and summarise discussions.

The make up of the TSC must meet the specifications set by the HTA – namely independent chair, 75% of TSC to be independent.

For decisions to be made, at least 2 independent members of the TSC should be present (including the chair), the CI and a representative from the TMG.

The TSC/SSC membership is for the duration of the trial/study. If any members leave the TSC/SSC, the TMG should provide replacements promptly for appointment by the Chair subject to approval by the HTA.

Agreements

TSC/SSC members should formally register their agreement to be a member of the committee as well as their agreement with the contents of the charter, trial confidentiality and should declare any potential conflicts of interest.

Independent members should complete and return a signed agreement and competing interests form provided at the end of this charter.

Responsibilities
The TSC/SSC on behalf of the Sponsor and Funder will have overall responsibility for the design and conduct of the trial and for safeguarding the rights, safety and well being of participants. Responsibilities of the TSC include:

- Reviewing selection/recruitment/retention of participants and their management
- Finalising and reviewing study protocol and other study documentation.
- Determine if amendments to the protocol or changes to study conduct are required and deciding on changes to these and to study conduct in general. Any changes to trial documentation or conduct must be notified to the TSC/SSC.
- Reviewing adherence to the protocol by Investigators and participants
- Assessing integrity and completeness of data collected
- Monitoring the overall conduct of the trial, ensuring that it follows the standards set out in the guidelines of GCP, assessing the safety and efficacy of the interventions, recruitment figures and completion of trial assessments.
- Reviewing, commenting and making decisions on extension requests.
- Reviewing the recommendations of the DMEC and suggesting appropriate action to the TMG
- Monitoring the progress of study/trial and deciding on appropriate action in order to maximise the chances of completing it within the agreed timelines.
- Considering new information relevant to the study e.g. results from other studies that may have a bearing to the conduct of the study and deciding on appropriate action.
- Endorsing the progress reports to the funder

The TSC may recommend early termination of the trial or modification of the study design in the event of a clear outcome derived from accumulating data or on the basis of information available from other sources or on safety grounds.

The TSC should be available to provide independent advice as required not just when meetings are scheduled.

The TSC should maintain confidentiality of all information it receives.
Members should not discuss confidential issues from their involvement in the study until the primary results have been published.

Role of the TSC Chair

- Arrange the first meeting of the TSC with the assistance of the CI to agree contents of charter and set up schedule of meetings

- Establish clear reporting lines – to the Funder, Sponsor etc
- Become familiar with the role of the DMEC
- Provide an independent, experienced opinion if conflicts arise between the needs of the research team, the Funder, the Sponsor and/or any other agencies
- Leading the TSC to provide regular, impartial oversight of the trial, especially to identify and pre-empt problems
- Ensuring that changes to the protocol are debated and endorsed by other members of the TSC

TSC meetings

- The responsibility for calling and organising a TSC meeting lies with the CI in association with the TSC Chair.
- At least 50% of meetings (and one per year) will be face to face
- All TSC members will be provided with study documents (e.g. protocol, proposed statistical analysis plan (SAP), PIS, CRF etc) and the TSC report prior to the meeting.
- The first TSC meeting should ideally be held face-to-face to discuss, revise and finalise the terms of reference, agree the content of the TSC charter and sign any declaration, and agree the frequency of the meetings.
- Meetings can also be held at any time at the request of the CI or TSC chair
- The final TSC meeting will be arranged when target recruitment is completed, all data collected and cleaned and the database is locked. This final meeting will be held to discuss final/completed data and interpretation, and publication timeless. If the study is terminated prematurely, no final study meeting is required.

Attendance

Every effort will be made to ensure that all TSC members can attend the meetings. The study coordinator or delegate should try and find a date that enables this. The CI must try to attend all meetings, especially if major actions are expected.

If the TSC is considering major actions the TSC Chair should communicate with absent members, including the CI, as soon after the meeting as possible to determine whether they all agree. If there is disagreement amongst absent members a further meeting should be arranged with the full TSC.

Reporting

Prior to a TSC/SSC meeting a report will be prepared by the TMG with input from study coordinator/manager, data manager, statistician etc and circulated to TSC members at least a week before the meeting.

On consideration of the information presented at these meetings, the TSC should provide recommendations of appropriate action in writing to the TMG who will be responsible for implementing any actions. The TSC may also provide feedback to the IDMEC and where appropriate to the Sponsor/Funder.

Minutes of the meeting including key points and actions will be prepared by study coordinator/manager . These minutes will describe the proceedings and include the recommendations of the TSC. All members of the TSC must agree the minutes and these will be signed off by the TSC Chair on behalf of all members. Minutes will be circulated to all TSC members, the TMG, the Sponsor and, if appropriate, the Trial Funder. Approved Minutes will be filed in the Trial Master File.

Decisions and recommendations by the TSC should be unanimous if not a vote may be taken. The role of the Chair is to summarise discussions and encourage consensus. Therefore it is best for the chair to give their own opinion last. It is important that the implications (ethical, statistical, practical and financial) for the trial be considered before any decision is made.

Conflicts of interest

TSC members should not have any apparent financial, scientific or intellectual conflict of interest that could prevent them from objectively reviewing the study protocol, interim and final data and giving advice to the TMG. TSC members should disclose to the Chair any other conflicts they consider relevant. Any members who develop significant conflicts of interest during the course of the trial should resign from the TSC.

Publication

Manuscripts that arise from the trial will be shared with the TSC and members will be able to comment. The TSC/SSC members and their affiliations will be acknowledged in reports of the trial.