Trial Management Group Meeting # 28

17th September 2008, [redacted]

Draft Minutes

1. Welcome

[redacted]

2. Apologies

[redacted]

3. Previous minutes of TMG # 27

Accepted at this meeting with one exception: the Royal Free are able to provide all three individual treatments outside of the trial.

Independent review of adverse events

[redacted] will supply input on the names that have been put forward as independent assessors for all trial adverse events and will agree this in collaboration with [redacted].

ACTION 1: [redacted] to contact [redacted] to ensure that [redacted] agrees with the process for appointing independent assessors for adverse events as approved by [redacted].

Definition of drop out versus treatment deviation

ACTION 2: The analysis strategy document needs to be modified to include additional treatments of SSMC patients who have another trial treatment. These people to be removed from the drop out list unless they have withdrawn consent to remain in the trial.

GET guide

This will not be used with PACE participants as it is thought too late in the trial to implement it. A final copy is about to be produced and this will be distributed across centres for use in CFS services for non-PACE patients. The booklets may be put online on centre websites as well

ACTION 3: [redacted] will inform [redacted] when the GET guide becomes widely available so that this can be recorded for analysis.

Doctor's monitoring

ACTION 4: [redacted] or [redacted] to complete doctor's monitoring of King's.

Assessment of therapy recordings

ACTION 5: [redacted] to create a project plan for the assessment of treatment recordings and [redacted] will contact the FINE nurses in order to update them on what is happening.

Writing committee

ACTION 6: [redacted] to circulate a document on how we may constitute writing groups for comment for TMG #29 at King's in December 2008.

4. Ancillary studies

a) Proposal from [redacted]

The circulated proposal was discussed by the members present.

It was noted that the specialism of the doctor and any particular specialist interest they have should be recorded.

It was noted that ethics approval may need to be sought to use the data collected for PACE in this way and ask advice as to whether any separate consents would need to be taken or whether this could be considered audit of clinic notes. The SCID is not a routine clinical test so audit may not be possible. The point may be raised with the ethics committee that there is no benefit to the patient to re-consent them for this research.

ACTION 7: [redacted] will discuss whether the project proposal from [redacted] is audit or research and whether it needs a substantial amendment with LRES and NRES.

b) 2.5 year follow up study

A database has been written for this study and this is currently being tested by some members of the data management team.

At present there is slightly less than 50% return. The TMG discussed what attempts for follow up are currently being made.

[redacted] expressed agreement that this was important data to collect. The point was made that non-response from some participants might reflect either improvement or non-improvement and participants feeling that they no longer want to acknowledge this diagnosis.

ACTION 8: Guidance needs to be drafted and sent to all research staff as to how many attempts for follow up should be made and what methods.

The TMG agreed that they wanted to continue this study and that more work should go into increasing return rates.

ACTION 9: [redacted] to send out the following instructions to RN/As and DMs:

1. GP should be contacted in the first instance to confirm that the participant is still alive and living at the address held in the research notes.
2. If the participant is no longer registered with the GP, please contact the local health authority to obtain details of where the GP notes (which practice) are now held. If the notes are with the health authority then the participant is either not registered with any GP or has left the country.
3. Researchers should assume that unless the participant explicitly states that they do not want further contact or withdrew consent to the whole trial when they were in the main study then continued efforts should be made.
4. Participants should be written to three times over a period of three months (once with the booklet and two reminder letters inviting the participant to post the booklet back or telephone in to give their answers, or offering to visit the participant at home), and at least three follow up phone calls if there is still no response.
5. Researchers should collect email addresses for all participants currently in follow up and these should be recorded in the research file.
6. A tracking sheet should be kept on an Excel spreadsheet. This should detail the PIN and the date the two and a half year follow up is due. Please also record the date sent, the date returned, and annotate other attempts made to contact the participant. You may use this sheet to black out the PINs of anyone who has stated they do not want any further contact with the trial team.
7. Participants who are lost to follow up but never officially withdrew may still be contacted for long term follow up.

The following should be considered by the TMG:

1. Seeking explicit funding for one person to run the whole study.

2. Altering the follow up booklet to a form that could be emailed to participants or having an online internet form that participants can access to complete information.
3. The new trial manager should send out a monthly email of long term follow up turnover by centre.

ACTION 10: [redacted] will ask [redacted] whether an internet form could be created for the long term follow up study.

Continuing contracts for research staff

ACTION 11: All centre leaders and PIs to check that staff contracts should go to the end of January 2010 at the latest.

Use of excess funds

The TMG agreed that any excess funds not spent by a centre should be used, with the agreement of the MRC, for funding the 2.5 year follow up study.

ACTION 12: All centre leaders to agree that any excess monies to be returned to the collective pot to pay for the 2.5 year long term follow up support.

ACTION 13: [redacted] to ask the MRC if any excess funds could be used to support the long tem follow up study.

It was noted that there is discrepancy on some long term follow up booklets between what further treatment the participant reported they had versus what local centre staff know was given after 52 weeks. The TMG thought this was issue was important and needed to be addressed.

ACTION 14: All RN/As to cross reference medical notes and 2.5 year CRF and record any discrepancies.

ACTION 15: The PIs to include reviewing notes for further therapy information as part of the costing for full funding to run the follow up study.

c) SNP study

Funding will be sought to run this from next year.

Advice received cast some doubt on whether saliva sampling would reliably provide sufficient DNA compared to double buccal smears. [redacted] was due to discuss this further with colleagues in Bristol the day after the TMG.

[redacted]

The aim would be to start sample collection in December 2008.

ACTION 16: [redacted] to submit this study for ethics approval as soon as possible so that DNA collection can commence in advance of participants exiting the trial and staff contracts ending.

A case control study is in development. A total of 2000 DNA samples for CFS patients would be required as a minimum data set.

Ethnicity would be criteria for exclusion because of the impact this has on SNPs. White Northern European participants only could be included in this study.

d) [redacted]'s supervision study - Publication status

[redacted] was not available at this meeting to report. [Later information from [redacted] indicated that the paper is in review.]

e) King's study

The study is complete and publication is on hold until the main trial is complete.

5. Recruitment

Bart's has increased clinics for new patients to increase the turnover of potential eligible patients before trial end.

King's have increased screening for new patients.

Bristol will consider increasing research time to process the backlog of participants.

ACTION 17: All centres should sift through the red and black book to see if any potentially eligible patients have been missed.

ACTION 18: All centres should make it clear to potential participants that the decision to enter the study must be made by 19 November 2008 in order to complete randomisations by 5pm on 28th November 2008.

6. Update on the analysis strategy meeting

The morning meeting focused on safety data and health economics analysis. There will be a baseline health economics and costs of CFS/ME paper.

A final version of the analysis strategy document will hopefully be approved at the TSC meeting in April 2009.

7. Baseline data

a) Data lock

The aim will be to lock the baseline data at the end of March 2009, which would allow the 12 week visit to be completed, which can add to or revise baseline data retrospectively, but allowably (e.g. adding medication that was being taken at baseline, but which had not been mentioned at the time).

b) Papers

ACTION 19: Trial manager to add the item of papers, writing committees and authors to the next TMG agenda.

Draft baseline papers may include:

Barriers to recruitment,

Trial management design,

Trial design as a lead to the analysis strategy,

Reasoning behind the design of the trial,

Heterogeneity,

Health economics and societal costs baseline data,

Cognitive responses to belief,

Baseline actigraphy, step and walking test data.

Modelling disability,

Reliability of the WSAS against the SF36 and the physical tests,

Biopsychosocial models

ACTION 20: All to speak to local staff and raise items for potential papers for the next TMG.

It was noted that no potentially controversial papers should be published before the main trial outcome paper is published.

8. Data checking status

[redacted] and others have been checking data. A review suggests that about 40% of data required to be checked has been checked.

Bart's hope to recruit a new data manager on the 19th September.

Bristol have offered the data manager for extra data checking capacity.

The MH&N CTU have suggested a potential data manager.

ACTION 21; All centre leaders to ask their data managers whether they are able to help out in checking another centre's data.

ACTION 22: [redacted] to write to [redacted] with key items for [redacted] and [redacted] to check: adding file notes to the database and participant comments, sweeping through notes to add screening co morbidities, medical history and medications, ensuring medications and co morbidities match and to explain any missing fields.

9. Actigraphy data

This is an ongoing issue and there have been meetings to support the development of an analysis strategy for this data.

10. Long term follow up data

The database has been written and [redacted] has been testing it. [redacted] has also offered [redacted] time to help with testing.

The only current outstanding issue is how registration data gets entered on to the long term follow up database.

ACTION 23: [redacted] will ask [redacted] to put registration data for all participants randomised so far on to the long term follow up database and to send an update with the last randomisations added in next Spring.

11. Therapist data

At present each centre has different methods for recording the visit schedule data.

ACTION 24: [redacted] to email data managers at all centres to check how visit schedule data is being collected and stored. After this, a system to be established to collect this data in a central role.

ACTION 25: The new trial manager to submit a substantial amendment to ethics to consent therapists to use personal data for research and to use tapes for research review of therapeutic alliance and integrity.

12. Homework compliance

ACTION 26: [redacted] to contact [redacted] for a copy of the homework compliance database that [redacted] created. This, or a similar system, to then be distributed for use trial wide.

13. Therapy manual publication

The TMG agreed that no manuals will be published before the main outcome paper.

ACTION 27: All treatment leaders to begin a plan for the publication of the manuals and advise the TMG. These should be available around the time of the main outcome result.

14. Independent review of treatment recordings

This item is ongoing. [redacted] has contacted the FINE nurses with the relevant information.

15. Close down

a) Post trial therapy availability

ACTION 28: All centres to consider how they will keep to the consent contract of offering post-trial PACE therapy.

b) Archive

ACTION 29: New Trial manager to prepare an archive SOP. Items to consider:

- MRC advice
- Local centre costs
- Which essential documents need to be kept and which can be destroyed
- Any local R&D regulations
- Removal of identifiable data from research notes

16. Final PACE day 2009

Wednesday 17th June 2009 in [redacted] from 10:30am.

ACTION 30: The TMG agreed that all staff should be encouraged to attend and that travel and accommodation expenses would be available for this important last trial wide staff meeting.

17. Draft participant newsletter

The TMG approved the draft and thanked the contributors and editor for their work on this.

ACTION 31: Once approved by [redacted] (TSC) this will be sent to MREC for approval for distribution to participants and adding to the website.

18. Centre specific issues

King's – [redacted] and [redacted] has offered cover.

Bristol – [redacted] in December. A person has been identified to cover follow up visits for the last year. The CBT therapist is

on reduced hours [redacted]. [redacted] has prioritised PACE to ensure that cover continues.

Bart's – A data manager will hopefully be recruited on Friday 19th September 2009.

[redacted] is leaving and so there is no GET cover at this centre:

[redacted] may be able to provide half a day a week to begin with, although this will depend on her next rotation at GKT.

[redacted] has been approached but there has been no response as yet. [it later transpired that [redacted] is unable to help.] [redacted] will help if [redacted] has capacity.

[redacted] will be approached to see if [redacted] has any capacity to give a half day of cover.

[redacted] may potentially be able to give a shortened day a week.

Oxford – No issues to report. [redacted] is still covering CBT but is not sure if [redacted] will continue cover after his contract expires in January. There is potential that [redacted] may be able to return to the trial team to cover until trial end but this is unconfirmed.

Royal Free – No representation at this meeting. Treatment leaders don't have any issues to report.

19. Therapy/treatment arm issues

[redacted] (Bart's) is now competent to give CBT.

No other issues to report.

20. Trial end issues

[redacted] advises a date for main trial publication be set early as there is likely to be a lot of interest, including potential questions from Parliament, for the outcome results.

21. Trial management vacancy

Interviews for this post will be held on 2nd October 2008.

22. Proposed dates and venues for TMG meetings in 2008 / 2009:

Thursday 4th December 2008, [redacted]

Wednesday 11 March 2009

Tuesday 23 June 2009

Wednesday 04 November 2009

Summary of Action Points

ALL

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New trial manager

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