



Trial Management Group Meeting # 24

20th September 2007

Draft Minutes

1. Those present

[Redacted]

2. Observer

[Redacted]

[Redacted]

3. Apologies

[Redacted]

4. Previous minutes of TMG # 23

TMG #23 - ACTION 1: [Redacted] to send the GET self help guide to MREC once completed.

TMG #23 - ACTION 2: [Redacted] to ask permission from REC for the list of approved self help guides to be added to the PACE trial website.

The website updates are still ongoing and this is to include the extension to the trial recruitment period.

ACTION 1: [Redacted] to contact REC for advice as to whether therapists competence assessments and CVs may be used as part of the analysis.

5. TSC and DMEC feedback

ACTION 2: [Redacted] to submit to the REC the extension for trial recruitment period.

Volunteers are needed for vignettes for the participant newsletter.

ACTION 3: All TMG members to ask staff and participants for contributions to the newsletters.

a) CGI for doctors session timings

TSC asked that all centres try hard to collect this as completely as possible. The most important part of this data is number of sessions even if session lengths are not always known.

The TMG would like to give [REDACTED] a prize for the exceptional rate of recruitment.

ACTION 4: Pls to send [REDACTED] a prize for [REDACTED] remarkable rate of recruitment, for catching up to target and for doing this with no other doctor support.

ACTION 5: [REDACTED] will start a staff sweepstake for the 450th randomisation.

6. Recruitment (item #2)

At this meeting it was announced that the September target had been reached already and that three centres have exceeded target at this time (Edinburgh, Oxford and the Royal Free).

The TSC and TMG congratulate all centres on this fantastic achievement.

7. Budget and contract extensions

Contracts will shortly be sent out to all centres for the revised funding which will allow research staff contracts to be extended. Research contracts are recommended to be extended to September 2009 allowing a couple of months flexibility to allow for a struggling centre to be closed earlier or a successful centre to be allowed a little more time for data cleaning, archiving and close down.

ACTION 6: All Pls/CLs to go back to centre financiers and discuss a likely contract extension for research staff until at least September 2009 with potential further flexibility and extension.

Therapists' salary issues present another problem. In addition, therapy needs to be available at centre for beyond 52 week follow ups. This extra paper doesn't have to be provided by PACE therapists.

Centres that over recruit will be financially sound as they will have been able to claim more than the expected amount of subvention money.

National Pay Framework, four month delay to trial staff and extension of recruitment by 12 months will affect how far the subvention funding will stretch.

ACTION 7: All PIs/CLs to complete risk assessments on when staff contracts are due to expire and when funding will run out.

8. Update from Analysis strategy group (MS)

The main issues from the morning Analysis Strategy meeting were presented. The team aims to have the Analysis Strategy Document completed for the May TMG.

Discussion will follow with all centres shortly about data entry of visit scheduling and homework compliance modelled on that which is already completed by ██████████ at Edinburgh.

ACTION 8: ██████████ and ██████████ to lead by asking all centres to begin this data entry.

There are concerns that participants who choose not to attend SSMC because they prefer therapy will not be included in the per protocol analysis as not having trial treatment as defined by the protocol, although it was noted that they will still be included in the intention to treat analysis.

The APT team of therapists raised that 10 sessions of therapy was too high a threshold and that 8 was more realistic to achieve an adequate dose. The TMG agreed to stay at 10 sessions of therapy plus 3 SSMC as a minimum as this was previously discussed and agreed at TSC.

9. Randomisation errors – strategies for resolution

There have been a small number of randomisation errors which are due to transcription errors or confusion about how to stratify. Most of these errors have occurred within the first few participants of a new research worker.

None of the participants randomised were ineligible.

All centres have been asked to be mindful of stratification details at randomisation, particularly when this is done by telephone, and to very carefully check the email from CTU for correct details.

ACTION 9: ██████████ to email ██████████ to ask for two full days of ██████████ time so that we may run another RN/A and Data Manager training day in either November or December.

10. GET self help guide

The GET team, with input from other professionals such as exercise physiologists, have created a self-help guide over the last six months and this has been piloted with six patients and has been written to be in-line with NICE guidelines. The near final draft of the guide was tabled at the TMG. Once completed this will be sent for REC approval to be added to the self-help reading list. It is intended for use with SSMC alone participants that request guidance on GET.

The TMG suggested that the PACE logo was removed and agreed that this should not go on to the PACE website as this would disrupt equipoise. A copyright statement should be added to the authors and the Bart's contact details be removed.

ACTION 10: [REDACTED] to lead on the suggested changes of removing the PACE logo and Bart's contact details and add a copyright.

ACTION 11: [REDACTED] and [REDACTED] to seek advice on how and where to copyright the guide book.

ACTION 12: [REDACTED] to send the completed GET self-help guide to the REC for approval.

11. Screening data collection [REDACTED]

The main reason for ineligibility is not meeting Oxford criteria (coded as 02). This may mean that the participants either do not have CFS/ME or that fatigue is not the primary complaint (e.g. pain or depression may be the main symptom).

The TSC was asked whether it was thought important to review the patients who do not meet Oxford criteria. The TSC suggested that a random sample of notes could be reviewed or that collection of future data could be altered and that the TMG should review whether this could be operationalised. The TSC did not think this would be necessary for the whole trial data.

[REDACTED] has reviewed the Edinburgh system which seems to be the clearest system of data collection. [REDACTED] is currently canvassing opinions from all centres as to what elements of screening data are hard to collect and what the preferred method by centres would be for collecting this data. So far the Oxford team have been the only centre to respond.

Two key issues were discussed, one is that this system tracks the patient pathway and aids research staff with tracking patients from clinic to consideration for trial. The second issue is that with robust information as to whether patients referred to the clinics have CFS at all we could remove a large number who are not CFS patients and should not be included in the CONSORT diagram.

ACTION 13: All PIs/CLs to encourage research staff to respond to [REDACTED] email about collecting screening data and to discuss with screening colleagues adding detail as to why patients do not meet Oxford, put in parentheses beside the code number 02. [REDACTED] to send an email to all PIs/CLs to prompt this action.

ACTION 14: [REDACTED] to add collection of screening data to the next RN/A & DM training day's agenda.

12. Concomitant medication collection

The concomitant medications need to be formally categorised. The suggestion from the Analysis Strategy group was that drugs are stratified by BNF sub-groups rather by indication.

Discussion took place as to whether drugs should be linked to indication for database cleaning. The decision was made that this did not need to be done but that the research teams need to continue the cross-check adverse events and indications with medications as before.

ACTION 15: [REDACTED] to reiterate to all centre staff the importance of cross-checking medications with adverse events and concomitant medication forms.

The purposes of collecting concomitant medication data are for economic reasons, to see if there is a change in medication from baseline to 52 weeks.

The decision has been made that repeated medications do not need to be re-entered at every visit but the RN/A merely needs to state that conditions are ongoing and that there is no change to dose, frequency or indication. Only new drugs, changes to drugs or close out of drugs will be entered at follow-up visits.

13. Coding of adverse events

There is an ongoing process to code adverse events according to a numerical system.

PIs and CLs will shortly start to receive monthly reports of local adverse events for sign off and review to ensure that no SAEs are being missed.

ACTION 16: [REDACTED] will add the issue of coding adverse events to the RN/A & DM training day.

14. Missed activity data

If a patient refuses to do one of the physical tests (step or walking test) or does a test by phone, this data is not classed as missing as long as there is a completed CRF with an explanation. If a test is started but the participant refuses to continue, that is not missing.

15. Ancillary studies

a) 2-year follow-up

██████████ propose that a person is employed for one day a week to collect the two-year outcome data for the first wave of participants who have passed the two-year follow-up point, as a pilot study. The CFQ, SF-36, WSAQ, CSRI and questions of beliefs and treatment received post-52 weeks.

ACTION 17: ██████████ and ██████████ to meet and discuss the best presentation of the CSRI for the two-year follow-up study.

ACTION 18: ██████████ to complete the protocol for the two-year follow-up study.

ACTION 19: ██████████ to submit this sub-study to the REC for approval.

b) ██████████ supervision study

Fourteen of nineteen therapists responded and the data is being analysed. ██████████ will now begin writing the paper for presentation at the next TMG.

c) King's study

This has now been completed and is being written up. It should be ready for presentation at the next TMG.

d) Edinburgh study

No update this time.

e) SNP study

██████████ is awaiting information from centres on what would be needed at centres to facilitate this study.

16. Feedback from the PACE team day

The next team day activity is recommended to be something that facilitates more discussion between team members. This will be hosted on 20 June 2008 at King's.

17. Specific centre issues

Bart's

The centre is down on recruitment at present and have not seen many new cases in clinic in the last two months. Patients from wider regions are

being approached and a new doctor has been recruited to the centre, starting in October. It was mentioned that the NICE guidelines have led to CNCC's being obliged to provide more treatments.

ACTION 20: Pls to discuss PACE with CFS professionals at the Milton Keynes conference in October.

Kings

The new research assistant is trained up and in post and recruitment has increased recently.

Royal Free

██████████ has agreed to cover CBT at the Royal Free. ██████████
██████████ is currently covering APT at the Royal Free.

18. Therapy/treatment arm issues

██████████ is identifying blind assessors to rate CD's for an interim analysis of therapy differentiation.

CBT

Every third week full-day supervision takes place and now that all therapists are competent the supervision process is changing. There is differential in terms of the amount of support needed. The team is working well.

APT

Peer support supervision has changed group supervision as all therapists have reached competence. The level of support needed by therapists is related to their own confidence.

GET

The GET team have asked for a list of commonly used medications and their indications to help support their discussions with participants.

SSMC

██████████ has most recently reviewed ██████████ tapes and reports that the standard is extremely high.

19. Any other business

CGI session lengths for therapy

Ten minutes over the allowed session length constitutes a protocol violation and the therapist needs to complete a file note. This facilitates data cleaning.

Coeliac screen

False negatives can be given if the IgA level is low. The question was asked to whether IgA should be added to the basic number of screening blood tests.

At Oxford the labs check for this automatically and flag with the doctors if there is an issue.

ACTION 20: All PIs/CLs to check with local labs to check that coeliacs don't give false negatives. 5% results are false negatives.

ACTION 21: If any centre has to add IgA as an additional blood test, [REDACTED] must be informed as this will affect the CSRI data checking process.

20. Proposed dates and venues for TMG meetings in 2007:

- a) Tuesday 11th December 2007, [REDACTED]
- b) Wednesday 13th February 2008, [REDACTED]
- c) Thursday 8th May 2008, [REDACTED]
- d) Wednesday 17th September 2008, [REDACTED]
- e) Thursday 4th December 2008, [REDACTED]