



Trial Management Group Meeting #32

[Redacted]

[Redacted]

Wednesday 4th November 2009

Draft Minutes

1. Welcome

Welcome to all present, and introduction of [Redacted] who replaces [Redacted].

Condolences were expressed following [Redacted]. [Redacted] hard work and support for the trial were acknowledged. [Redacted] has agreed to write [Redacted] of the trial management group.

2. Those present

[Redacted]

[Redacted]

Observers

[Redacted]

3. Apologies

[Redacted]

4. Agreement of agenda

The agenda was agreed by all. The only amendment was to discuss the XMRV retrovirus under section 14. The amended date of the next TMG was agreed by all.

5. Previous minutes of TMG #31

All accepted at this meeting.

6. Ongoing actions from TMG #31

TMG #31 ACTION 4: ■■■ to ask treatment leads to resend therapist data so this can progress.

It was decided that a summary of the overall training, judgment of competency and ongoing supervision was all that was required for the main paper

ACTION 1: ■■■ to ask TLs for summary therapist information, this data will be kept centrally.

TMG #31 ACTION 10: CL to inform RN/As to try and organise patient visits as soon as possible within the patients' visit schedule.

It was highlighted that CGI forms may be completed by telephone in order to ensure that collection of the follow up data is completed on schedule.

ACTION 2: CLs to ensure that SSMC visits are arranged early in the visit schedule (protocol permits one week early) so that the final data may be collected before Christmas. CLs to feedback any potential problems to ■■■.

TMG #31 ACTION 19: ■■■ to review all clinician's monitoring reports and arrange for further monitoring visits at sites as required.

ACTION 3: ■■■ to conduct final review of all clinician's monitoring reports

7. Update from recent meetings

a) TSC/ASG

■■■ fed back that the analysis strategy was close to completion. There had been a number of final issues to resolve. It was highlighted that an important change has been made to the reporting of the primary outcome measures. Previously it had been decided that the results would be presented categorically using thresholds derived from the binary scoring of the Chalder questionnaire and the continuous SF36 scale. It has since been decided that the original question posed by the study would be better answered by comparing the continuous scores on both the Chalder and SF36 scales. The originally planned categorical scores will also be reported in the main paper, as a secondary analysis, reflecting clinically important differences.

A few concerns were raised that making a change at this stage may invite criticism. It was highlighted that the change will increase the sensitivity of the study and that the changes have been made before the reviewing of any data, and that the change will be reported in the paper. It was agreed by the TMG that these changes should go ahead.

Multiplicity and therapist clustering effects were also discussed with no objections made.

A proposal was made regarding setting up an analysis implementation sub-group (AISG), which would be a sub-group of the ASG, and later WAPOC, once the ASG had completed its work. The AISG would meet regularly and frequently (every three weeks and more often if necessary) in order to oversee the analysis strategy for the main paper. This analysis would be done by ■■■, supported by means of the AISG. Members of the AISG would include all three statisticians, ■■■■■■■■■■, and ■■■, as well as the trial manager, ■■■ and one or more PIs. ■■■ agreed to take particular responsibility for this on behalf of the PIs, but ■■■ and ■■■ would attend as and when they could. This arrangement was agreed by the TMG.

8. Analysis Strategy sign off by TMG

This is not possible yet and the TMG will sign off this off at the next meeting in February.

ACTION 4: All to send final comments on the analysis strategy to ■■■ who will distribute to the ASG group

9. 2.5 year follow up study

a) Return rates

■■■ fed back that the return rate was 72% when including those who hadn't been through the full follow up process. This figure went up to 93% when only those who had completed the follow up arrangements had been completed. ■■■ added that most of these questionnaires had been returned within 2 months of first request.

b) Decision to continue

It was agreed by all that as this was above the 70% rate previously decided to be the threshold that collection should continue.

c) Resource implications

■■■■■■■■■■ has made a database for this study; this needs to be checked before entry can begin.

ACTION 5: ■■■ to arrange for validation checks to be made on the follow up study database.

■■■ estimated the time required for someone to collect and enter the remaining follow up data would be 0.5 days per week per centre from 1st April 2010 until 1st July 2011. It was noted that if this collection was to occur locally, and preferably by someone previously known to the patient, this may have a positive effect on response rates by participants. It was noted that central co-ordination of this was possible if necessary. The funding from the MRC finishes on 13.09.10 and an application would need to be made to use the underspend beyond this point.

ACTION 6: ■■■ to approach all centre leaders and enquire whether they wish to do this within their centres (preferably) after 1st April 2010, using their forecast underspend, or whether they would prefer this collection to be done centrally.

ACTION 7: ■■■■ to apply to the MRC for a time extension to use PACE unspent funds for the 2.5 year follow up study until July 2011 to ensure all collection can be completed.

ACTION 8: The analysis strategy for the 2.5 year follow up study will be discussed at the next ASG meeting and should be decided before the main results are available.

It was noted that this analysis was not factored into the CTU funding.

10. Financial Projections

These were circulated and discussed. It was highlighted that future projections were based on previous spending and weren't exact figures.

The figures for Edinburgh were likely to have been based on a non-representative month as the local figures suggest an underspend of 14k.

ACTION 9: All CLs to check that the figures for their centre are representative.

The future plans for use of the under spend were discussed in detail (for this discussion the Chair was taken by ■■■ and ■■■ left the room).

The possibility of ■■■■ employing a locum to fulfill his clinical responsibilities for six months so that ■■■ could use ■■■ time to support the analysis and the writing of PACE papers was suggested. After a lengthy discussion this proposal was agreed on the understanding that the Bart's underspend were used to support it. It was also agreed that there needed to be adequate trial funds remaining in the total projected underspend for other purposes essential to maximizing PACE outputs such as collecting follow up data and statistical and data support. It was agreed that extra statistical and data management support is definitely needed and must be budgeted for. It was considered that there were sufficient funds in the underspend to achieve all these tasks.

The mobility of funds was a substantial issue for some centres but not others. It was proposed that expenditure could remain associated with the centre to which the budget has been allocated rather than the money necessarily being reallocated to PACE tasks at other centres, subject to agreement by the TMG, MRC and the existing financial contracts between QM and centres. It was suggested that if there was still underspend other centres could submit proposals for use of the underspend locally, mainly for additional supportive analyses. It was strongly proposed that if money was to be allocated to 'sub projects' this allocation be made transparently and agreed by the TMG. ■■■ proposed use of underspend to undertake a more detailed analysis of therapist recordings for therapeutic alliance.

On ■■■'s return it was clarified that centres may only bill for actual costs 'up to' the amount set out in the financial agreement with QMUL and are not guaranteed the full sum. Any underspend may need to be vired across budget lines and centres to cover national PACE expenses, with the agreement of all PIs and the MRC. After 13th September 2010, MRC permission will be required to use the remaining underspend.

ACTION 10: ■■■ will compile a document of planned expenditure of any underspend and circulate to the TMG along with a call for proposals for additional supportive analyses. Proposals will be discussed by WAPOC and if necessary a peer group.

ACTION 11: ■■■ to request no-cost extension from MRC (once planned uses of underspend agreed by TMG).

11. Independent assessment of adverse events

It was agreed that all new co-morbid conditions should be recorded as AEs. All AEs/comorbid conditions will be reviewed by a trial psychiatrist and a physician prior to the independent review. As part of this review, all pre-existing co-morbid conditions will be 'greyed out' and the remaining AEs are to be assessed for their relationship to the trial and distinguished as CFS/non CFS related. ■■■ may be able to assist ■■■ with this. The list of new co-morbid conditions and AEs would then be reviewed by the independent assessors and summarised in the final paper.

ACTION 12: ■■■ to collaborate to produce an excel file of all the AE and co-morbid data which could then be cleaned by ■■■.

ACTION 13: TMG physician to volunteer to review all co-morbid condition and AEs along with ■■■

12. Measurement of therapeutic differentiation and quality

█ fed back on therapy differentiation, having circulated a proposal for achieving this. Independent therapists will review the recordings from therapy session 10 (or the nearest one to this) for 20% of participants. Raters will be blind to the actual treatment and will assess:

- a) What the therapy was
- b) To what extent certain therapeutic elements are present, using the same measure used to judge therapy competence

These ratings will be used to generate a composite score.

ACTION 14: █ to draw up a practical plan and guidance on rating of tapes, with a view to implementing this, once agreed.

POST MEETING COMMENT: Section 10.6 of the protocol states: 'The strength of the therapeutic alliance will be measured by the therapy integrity rating scale (Appendix 7) by an independent and blinded observer.' This will be discussed further at January's ASG/WAPOC meeting and subsequently February's TMG meeting.

█ and █ have sampled the SSMC recordings and it has been decided unless SSMC emerges as the best overall treatment it is not worth investing time in a formal QC review. Variation in SSMC delivery can be generalized to the community so this is not of concern.

13. Timelines for final data collection

This was discussed under TMG #31 ACTION 10

14. Ancillary studies

a) Genetics study: █ reported that an application for this genome wide study is in progress with assessment of funding by the MRC on February 3rd. This study will involve 8000 CFS pts. This study would involve the collection of saliva by post. Data could be collected from PACE participants as they are a well characterised group that will allow analysis of sub-phenotypes, using existing research nurses. This idea was fully supported by all.

ACTION 15: █ to submit a substantial amendment to obtain ethical permission to approach PACE participants for a sample and any reminders.

Following the recent interest in XMRV it was also agreed that if this can be included in the study this would be supported. This idea is to be discussed further with ID Consultants. The high postal return rates for the 2.5 year follow up study should be cited as part of the feasibility for this study.

b) Qualitative study of therapy content:

This was discussed under item number 10

15. Archiving arrangements

■ fed back that archiving was needed for at least 20 years. It was suggested that this time may be longer in light of new legislation.

ACTION 16: ■ to check the length of time data is to be archived for.

QMUL have facilities available to them. Oxford to use an out sourced company. King's appear to have office space available, and Bristol and Edinburgh have limited space with outsourcing being a possibility. These arrangements need to be finalised.

ACTION 17: CLs to confirm to ■ archiving arrangements including costs before Christmas.

Supervision documents held by Therapy Leads were discussed and it was decided these should be archived centrally as part of the TMF and that confidentiality of these documents must be maintained.

ACTION 18: ■/Therapy Leads to collate therapy supervision documentation for archiving purposes

16. Risk assessment and staff turnover.

Due to time constraints these were not discussed.

17. Centre specific issues

Due to time constraints these were not discussed

18. Therapy/treatment arm issues.

Due to time constraints these were not discussed

19. Any other business

■ queried how ■ may claim back maternity pay from the PACE budget

ACTION 19: ■ to clarify with QMUL finance team whether maternity pay is covered by the MRC grant

20. Proposed dates and venues for next TMG meetings:

Wednesday 10th February 2010, ■■■■■

ACTION POINT SUMMARY LIST

All

ACTION 4: All to send final comments on the analysis strategy to [REDACTED] who will distribute to the ASG group

ASG

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TMG

ACTION 13: TMG physician to volunteer to review all co-morbid condition and AEs along with [REDACTED]

PIs/CLs

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ACTION 9: All CLs to check that the figures for their centre are representative.

ACTION 17: CLs to confirm to [REDACTED] archiving arrangements including costs before Christmas.

[REDACTED]
ACTION 3: [REDACTED] to conduct final review of all clinician's monitoring reports

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