MifeMiso

Mifepristone and misoprostol versus misoprostol alone in the medical management of missed miscarriage: the MifeMiso randomised controlled trial

Appendix V: Blinded Endpoint Review Committee Charter

MifeMiso trial
Blinded Endpoint Review Committee Charter

Outline of scope of the charter

The purpose of this document is to describe the membership, roles, responsibilities, authority and decision-making of the Blinded Endpoint Review Committee (BERC) for the MifeMiso trial, including the methods of providing information to and from the BERC, frequency and format of meetings.

Study details	
Study acronym:	MifeMiso
Full title of study:	A randomised placebo-controlled trial of mifepristone and misoprostol versus misoprostol alone in the medical management of missed miscarriage
Chief Investigator:	Professor Arri Coomarasamy
Funder:	NIHR HTA
Sponsor:	University of Birmingham
Funder Reference No.	15/160/02
Sponsor Reference No.	RG_16-076
REC Reference No.	17/WM/0017
ISRCTN No.	17405024
EudraCT No.	2016-005097-35
Coordinating Centre:	Birmingham Clinical Trials Unit (BCTU), University of Birmingham
Primary outcome:	Failure to spontaneously pass the gestational sac within 7 days after randomisation. This will be assessed by pelvic ultrasonography where possible.
Objectives of the study:	Primary objective: To test the hypothesis that treatment with mifepristone plus misoprostol is superior to misoprostol alone for the resolution of miscarriage within 7 days in women diagnosed with missed miscarriage by pelvic ultrasound scan in the first 13+6 weeks of pregnancy.
	Key secondary objective: To test the hypothesis that the addition of mifepristone reduces the need for surgical intervention to resolve the miscarriage.

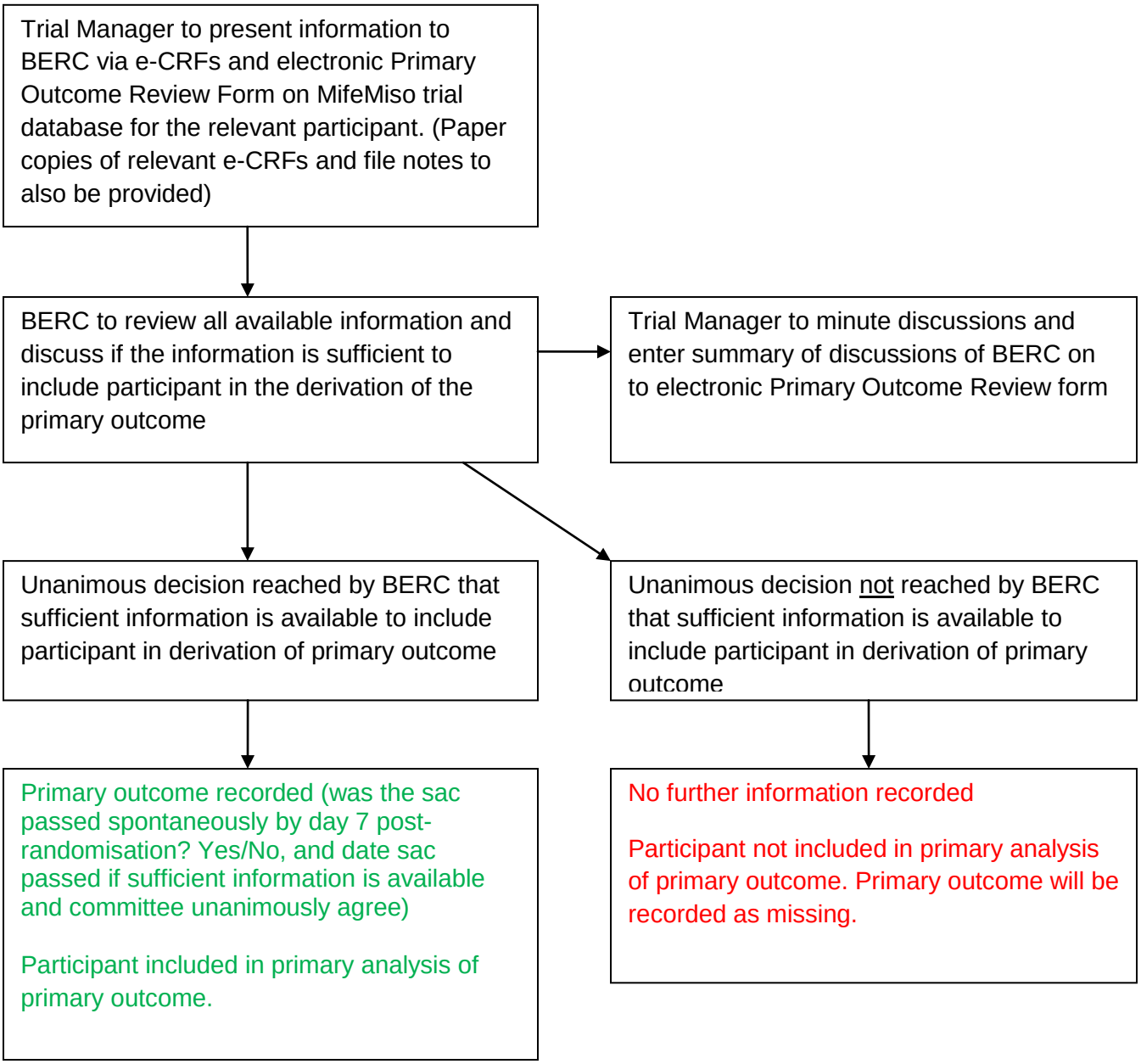
	Other secondary objectives: 1. To evaluate if the addition of mifepristone reduces the need for further doses of misoprostol. 2. To evaluate if the addition of mifepristone improves other clinical outcomes including surgical intervention before and after 7 days post-randomisation, duration of bleeding, infection, negative pregnancy test at 21 days post-randomisation, time from randomisation to discharge from EPU care, side effects and complications. 3. To evaluate if the addition of mifepristone improves patient satisfaction. 4. To assess the cost-effectiveness of the combination of mifepristone and misoprostol in the medical management of missed miscarriage.

Blinded Endpoint Review Committee members
1. Professor Arri Coomarasamy, Professor of Gynaecology/Director of the National Centre for Miscarriage Research. MifeMiso Chief Investigator, MifeMiso Non-Independent TSC member and MifeMiso TMG Chair, Birmingham Women's Hospital (BERC CHAIR) 2. Dr Justin Chu, Sub-Specialist Trainee in Reproductive Medicine. MifeMiso National Clinical Coordinator and MifeMiso TMG member, Birmingham Women's Hospital 3. Ms Oonagh Pickering, Tommy's Research Midwife recruiting to MifeMiso, Birmingham Women's Hospital 4. Mr Kim Hinshaw, Consultant Obstetrician and Gynaecologist and MifeMiso TMG member, Sunderland Royal Hospital 5. Dr Meenakshi Choudhary, Consultant Gynaecologist, Sub Specialist in Reproductive Medicine and MifeMiso TMG member, Royal Victoria Infirmary, Newcastle

Blinded Endpoint Review Committee roles and responsibilities	
Aims of the BERC:	Assess participant data relevant to the primary outcome for women who have not received an ultrasound scan within 7 days post-randomisation (or have received a scan but scan results regarding passage of the gestational sac have not been recorded) and to reach a unanimous decision as to whether sufficient additional information is available for the participant data to be included in the derivation of the primary outcome.
Objectives of the BERC:	The Blinded Endpoint Review Committee will meet at a face-to-face meeting following the end of recruitment to MifeMiso in order to review participant data for women who have not received an ultrasound scan within 7 days post-randomisation (or have received a scan but scan results regarding passage of the gestational sac have not been recorded) and determine if there is sufficient additional information available in order to derive the primary outcome. The review will be undertaken blinded to treatment allocation. Only cases where the Committee unanimously decide that there is sufficient additional information available to derive the primary outcome will be included in the primary analysis of the primary outcome.
Information to be used by the BERC:	Data recorded by the site research team in the e-CRFs (electronic case report forms) including dates participant started and stopped bleeding, dates of any scans confirming if sac passed or not, date the woman self-reported passage of sac, date of urine pregnancy test and the result and whether surgical intervention was required (if available/applicable including the date of surgery).

	Information obtained by the National Clinical Coordinator (Dr Justin Chu) from contacting the woman directly by telephone or email. This information will be made available to Committee members on the day of their meeting via an electronic Primary Outcome Review Form held on the trial database, along with the relevant e-CRF data. Paper copies of relevant e-CRFs and file notes detailing self-report information from women will also be provided.
Membership of the BERC:	Members of the Committee should formally register their assent to join the Committee by signing the signature page at the end of this Charter. By signing they confirm that they agree to join the Blinded Endpoint Review Committee, agree to treat all sensitive trial data and discussions confidentially, agree with the contents of this Charter, and agree to follow the instructions as set out in this Charter. Charter signature pages are required to be wet ink signed and either returned to the Trial Manager in person at the meeting, a scanned copy returned by email to mifemiso@trials.bham.ac.uk or a copy posted to MifeMiso Trial Office, BCTU, Institute of Applied Health Research, Public Health Building, University of Birmingham, Edgbaston, Birmingham, B15 2TT
Responsibilities of the BERC Chair:	The nominated Chair has experience of chairing meetings, and will facilitate and summarise discussions. The Chair has been nominated by the Trial Management Group.
Responsibilities of the Trial Manager:	The Trial Manager will attend the meeting of the Committee. The Trial Manager will minute Committee discussions and enter a summary of the discussions along with the decision as to whether a participant case can be included in the derivation of the primary outcome data on to the electronic version of the Primary Outcome Review form on the trial database.

Blinded Endpoint Review Committee meeting flowchart



Blinded Endpoint Review Committee Agreement Form

	Initial to agree
I have read, understood and agree with the MifeMiso Blinded Endpoint Review Committee Charter version 1.0, dated 30th May 2019	☐
I agree to join the Blinded Endpoint Review Committee for this trial	☐
I agree to treat all trial documentation, data and discussions confidentially	☐

The avoidance of any perception that members of a Blinded Endpoint Review Committee may be biased in some undisclosed fashion is important for the credibility of the decisions made by the Blinded Endpoint Review Committee and for the integrity of the trial.

Possible competing interests should be disclosed via the Birmingham Clinical Trials Unit. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) Blinded Endpoint Review Committee member should remove the conflict or stop participating in the Blinded Endpoint Review Committee. **Table 1** lists potential competing interests.

☐ **No,** I have no competing interests to declare other than involvement in the trial
☐ **Yes,** I have competing interests to declare (please detail below)

Please provide details of any competing interests:

_____

_____

_____

Print name: _____

Signed: _____ **Date:** DD / MM / YYYY

Table 1: Potential competing interests

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Consulting arrangements with the Sponsor/Funder
- Ongoing advisory role to a company providing drugs to the trial
- Frequent speaking engagements on behalf of the intervention
- Intellectual conflict e.g. strong prior belief in the trial's experimental arm
- Involvement in regulatory issues relevant to the trial procedures
- Investment (financial or intellectual) in competing products