Clinical trial results:
Double-blind, 36 month, placebo-controlled trial of mifepristone on cognition in alcoholics

Summary

EudraCT number	2009-015837-55
Trial protocol	GB
Global end of trial date	24 June 2016

Results information

Result version number	v1 (current)
This version publication date	28 October 2018
First version publication date	28 October 2018
Summary attachment (see zip file)	FINAL STUDY REPORT (Final report 06-02-2018.pdf)

Trial information

Trial identification

Sponsor protocol code	RAA09-004

Additional study identifiers

ISRCTN number	ISRCTN54001953
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	King's College London
Sponsor organisation address	The Strand, London, United Kingdom, WC2R 2LS
Public contact	Professor Colin Drummond, Institute of Psychiatry, King's College London, 0044 2078480817, colin.drummond@kcl.ac.uk
Scientific contact	Professor Colin Drummond, Institute of Psychiatry, King's College London, 0044 2078480817, colin.drummond@kcl.ac.uk
Sponsor organisation name	South London & Maudsley NHS Foundation Trust
Sponsor organisation address	Bethlem Royal Hospital, Monks Orchard Road, Beckenham, United Kingdom, BR3 3BX
Public contact	Professor Colin Drummond,, South London & Maudsley NHS Foundation Trust, 0044 2078480817, colin.drummond@kcl.ac.uk
Scientific contact	Professor Colin Drummond,, South London & Maudsley NHS Foundation Trust, 0044 2078480817, colin.drummond@kcl.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2016
Global end of trial reached?	Yes
Global end of trial date	24 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Does the action of the drug, mifepristone, in preventing the effects of the naturally released glucocorticoid hormone cortisol on the Type II glucocorticoid receptor reduce the cognitive deficits and/or the depression experienced by alcoholics?

Protection of trial subjects:

The procedures involved in this research are unlikely to cause significant discomfort or distress to participants.
All questionnaire measures and research procedures have been widely validated and used in previous research without causing any problems to participants. Mifepristone has a good safety record and has been used clinically for over 15 years for other applications. However should any distress or discomfort occur with any of the procedures trained medical and nursing staff will be available on a 24 h basis to provide help and support.

Background therapy:

None

Evidence for comparator: -

Actual start date of recruitment	02 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 27
Worldwide total number of subjects	27
EEA total number of subjects	27

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	27
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 57 people were screened to take part in the trial and 27 (47%) were randomised

Pre-assignment

Screening details:

Inclusion criteria:
(i) diagnosis of alcohol dependence by DSM-IV for 5 years or more
(ii) male
(iii) aged between 18 and 60 years (inclusive)
(iv) willingness to provide informed consent.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The placebo tablets will be identical in appearance to the mifepristone tablets (light yellow, cylindrical biconvex tablets) but will contain no active ingredient.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A -Mifepristone

Arm description:

Participants were randomised to receive 600mg of mifepristone or placebo (one 200mg tablet three times a day) for 7 days starting on the first day of detoxification and 400mg for the following 7 days (one 200mg tablet twice a day)

Arm type	Experimental
Investigational medicinal product name	Mifepristone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomised to receive 600mg of mifepristone (one 200mg tablet three times a day) for 7 days starting on the first day of detoxification and 400mg for the following 7 days (one 200mg tablet twice a day)

Arm title	Group B - Placebo

Arm description:

Participants were randomised to receive 600mg of mifepristone or placebo (one 200mg tablet three times a day) for 7 days starting on the first day of detoxification and 400mg for the following 7 days (one 200mg tablet twice a day)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomised to receive 600mg of mifepristone or placebo (one 200mg tablet three times a day) for 7 days starting on the first day of detoxification and 400mg for the following 7 days

(one 200mg tablet twice a day)

Number of subjects in period 1	Group A - Mifepristone	Group B - Placebo
Started	14	13
Completed	2	8
Not completed	12	5
Physician decision	1	-
Consent withdrawn by subject	2	3
Lost to follow-up	9	2

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	27	27	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	27	27	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	0	
Male	27	27	

End points

End points reporting groups

Reporting group title	Group A -Mifepristone

Reporting group description:

Participants were randomised to receive 600mg of mifepristone or placebo (one 200mg tablet three times a day) for 7 days starting on the first day of detoxification and 400mg for the following 7 days (one 200mg tablet twice a day)

Reporting group title	Group B - Placebo

Reporting group description:

Participants were randomised to receive 600mg of mifepristone or placebo (one 200mg tablet three times a day) for 7 days starting on the first day of detoxification and 400mg for the following 7 days (one 200mg tablet twice a day)

Primary: Primary Outcome

End point title	Primary Outcome[1]

End point description:

Cognitive function measured using the CANTAB and depressive symptomatology measured by the Beck depression scale (BDI-II).

End point type	Primary

End point timeframe:

Duration of trial

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Please see attached document for details of results.

End point values	Group A - Mifepristone	Group B - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	8		
Units: whole	2	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Outcome Measure

End point title	Secondary Outcome Measure

End point description:

Severity of the acute phase of alcohol withdrawal, alcohol craving, and symptoms of protracted withdrawal including sleep disturbances

End point type	Secondary

End point timeframe:

Duration of trial

End point values	Group A - Mifepristone	Group B - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	8		
Units: whole	2	8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events are reported from initial dose until 14 days after the last dose of IMP or placebo.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Mifeprestone - Active Group
Reporting group description: -	
Reporting group title	Placebo group
Reporting group description: -	

Serious adverse events	Mifeprestone - Active Group	Placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Mifeprestone - Active Group	Placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 14 (64.29%)	6 / 13 (46.15%)	
Injury, poisoning and procedural complications			
Bitten tongue			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			

High blood pressure			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 14 (28.57%)	6 / 13 (46.15%)	
occurrences (all)	4	6	
Nose Bleed			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Poor balance			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Swollen Glands			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Night chills			
subjects affected / exposed	2 / 14 (14.29%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Shooting pain in temples			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergic reaction to penicillin			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
allergic reaction hands & torso			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Toothache			
subjects affected / exposed	0 / 14 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Stomach cramps and pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Heartburn			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Nausea & Vomitting			
subjects affected / exposed	1 / 14 (7.14%)	3 / 13 (23.08%)	
occurrences (all)	1	3	
Indigestion			
subjects affected / exposed	0 / 14 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
headache & flu like symptoms			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Chest Infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Itchy skin			
subjects affected / exposed	2 / 14 (14.29%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Rash on arms			

subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Self harmed			
subjects affected / exposed	0 / 14 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Panic attack			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Low mood			
subjects affected / exposed	1 / 14 (7.14%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Exacerbation of sciatica			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infections and infestations			
Dry Eyes			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 January 2011	Change in Labaratory providing analysis services and changes to sampling (blood and urine) within the protocol.
14 April 2011	Administrative changes in the protocol and change from in-patient services to out patient services
27 September 2011	Removal of 'independent clinician' to determine the patients' capacity to give consent. This will be determined by the delegated physician. Addition of AUQ in the trial summary. Correction to timing of CIWA-Ar administration during Weeks 2-4. Removal of illicit drug urine test during initial screening Removal of Appendix to reduce potential confusion from having two lists of contraindicated drugs Removal of Appendix A to reduce potential confusion Removal of illicit drug urine test during initial screening. Re-numbering of items Specification of follow-up measures (3, 6, 12 months) Removal of 'independent clinician' to determine the patients' capacity to give consent. This will be determined by the delegated physician. Patients with psychoses will be excluded from the trial.
16 April 2012	Addition of Barnsley Path lab contact details Removal of University of Bern because arrangements changed for proteomic analysis. Addition of Epsom (formerly West Park) Path lab contact details SHAPS questionnaire added to list of abbreviations Return to wording of Protocol 5.1 for an 'independent clinician' to determine the patients' capacity to give consent. Change to the normal admission period, owing to the recent changes in the NHS alcohol services Addition of AUQ in the trial summary. Clarification to wording as patients may be outpatient during week 3 and/or week 4. Change to number of saliva samples Inclusion of the SHAPS instrument to assess anhedonia. Correction to wording Change to number of saliva samples Removal of path lab names. Where possible, Path tests will be performed at the local path lab for each site. Path lab details are listed on pg. 2 Removal of path lab names as these are listed on pg. 2 Change to number and timing of saliva samples Correction to wording Where possible pathology tests will be performed at the local (CPA certified) pathology lab at each site. Removal of reference to the University of Bern Return to wording of Protocol 5.1 for an 'independent clinician' to determine the patients' capacity to give consent. Correction to Exclusion criteria. Renal dysfunction cannot be diagnosed from a urine sample.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26912003