Clinical trial results:
Interventional, randomized, double-blind, cross-over, placebo-controlled study to investigate the effects of nalmefene after single dose on the blood oxygen level dependent (BOLD) fMRI signal in the ventral striatum to reward responding in the monetary incentive delay task (MIDT), in non-treatment seeking subjects with alcohol dependence following alcohol challenge

Summary

EudraCT number	2013-001154-98
Trial protocol	GB
Global end of trial date	30 October 2014

Results information

Result version number	v1 (current)
This version publication date	25 June 2016
First version publication date	25 June 2016

Trial information

Trial identification

Sponsor protocol code	15660A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01969617
WHO universal trial number (UTN)	-
Other trial identifiers	HMR code: 13-506

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark,
Public contact	Lundbeck Clinical Trials, H Lundbeck A/S, LundbeckClinicalTrials@lundbeck.com
Scientific contact	Lundbeck Clinical Trials, H Lundbeck A/S, LundbeckClinicalTrials@lundbeck.com

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	30 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 October 2014
Global end of trial reached?	Yes
Global end of trial date	30 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effects of nalmefene after single dose on the blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) signal in the ventral striatum to reward responding using the monetary incentive delay task (MIDT) task following alcohol clamp challenge.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2008) and ICH Good Clinical Practice (1996)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	22
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at one site in UK (single centre study)

Pre-assignment

Screening details:

Subjects who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Selincro/Placebo

Arm description:

Subjects were randomised to receive 18 mg Selincro (nalmefene) on Day 1 and matching placebo on Day 8. There was a washout period of at least 1 week between dosing/scanning days.

Arm type	Experimental
Investigational medicinal product name	Selincro
Investigational medicinal product code	
Other name	Nalmefene
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of Selincro 18 mg, orally

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

Dosage and administration details:

Single dose, tablet, orally

Arm title	Placebo/Selincro

Arm description:

Subjects were randomised to receive placebo on Day 1 and 18 mg Selincro (nalmefene)on Day 8. There was a washout period of at least 1 week between dosing/scanning days.

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:

Single dose, tablet, orally

Investigational medicinal product name	Selincro
Investigational medicinal product code	
Other name	Nalmefene
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Single dose of Selincro 18 mg, orally

Number of subjects in period 1	Selincro/Placebo	Placebo/Selincro
Started	11	11
Completed	11	10
Not completed	0	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	22	22	
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)	22	22	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	0	
Male	22	22	
Race Units: Subjects			
Asian	1	1	
Black or African American	2	2	
White	18	18	
Other	1	1	

End points

End points reporting groups

Reporting group title	Selincro/Placebo
Reporting group description:	
Subjects were randomised to receive 18 mg Selincro (nalmefene) on Day 1 and matching placebo on Day 8. There was a washout period of at least 1 week between dosing/scanning days.	
Reporting group title	Placebo/Selincro
Reporting group description:	
Subjects were randomised to receive placebo on Day 1 and 18 mg Selincro (nalmefene)on Day 8. There was a washout period of at least 1 week between dosing/scanning days.	
Subject analysis set title	Selincro
Subject analysis set type	Full analysis
Subject analysis set description:	
18 mg Nalmefene	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo	

Primary: Blood oxygen level dependent (BOLD) fMRI signal in the ventral striatum to reward responding using the monetary incentive delay task (MIDT) task

End point title	Blood oxygen level dependent (BOLD) fMRI signal in the ventral striatum to reward responding using the monetary incentive delay task (MIDT) task
End point description:	
End point type	Primary
End point timeframe:	
4-6 hours after dosing	

End point values	Selincro	Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	18		
Units: Percent change	16	25		

Statistical analyses

Statistical analysis title	Reward respond signal (activity)
Statistical analysis description:	
The analysis was a paired t-test (a linear mixed-effects model, with subject as the random effect and drug condition as the fixed effect). Data were excluded in the MIDT for three sessions (head movement), so 18 subjects were included in the analysis	
Comparison groups	Selincro v Placebo

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.013
Method	Mixed models analysis

Notes:

[1] - Mixed effect Model Repeat Measurement

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From dosing to end of study	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1
Reporting groups	
Reporting group title	Selincro
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Selincro	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Selincro	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 21 (47.62%)	4 / 22 (18.18%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 21 (28.57%)	0 / 22 (0.00%)	
occurrences (all)	6	0	
Sinus Headache			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Somnolence			

subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Vessel Puncture Site Haematoma			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Catheter Site Pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 21 (19.05%)	0 / 22 (0.00%)	
occurrences (all)	4	0	
Vomiting			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Dyspepsia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dermatitis Allergic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported