Clinical trial results:
A phase IIa study of GR3027 in patients with idiopathic hypersomnia (IH) involving an open-label part to assess safety, tolerability and pharmacokinetics (PK) of a single oral GR3027 dose in female patients and a randomized, double-blind, placebo-controlled crossover study to assess safety, tolerability, exposure and exploratory efficacy of multiple oral doses of GR3027 in male and female IH patients.

Summary

EudraCT number	2017-002127-16
Trial protocol	FI DK SE
Global end of trial date	19 October 2018

Results information

Result version number	v1 (current)
This version publication date	03 November 2019
First version publication date	03 November 2019

Trial information

Trial identification

Sponsor protocol code	UCAB-CT-03

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Umecrine Cognition AB
Sponsor organisation address	Fogdevreten 2, Solna, Sweden, 171 65
Public contact	Chief Executive Officer, Umecrine Cognition AB, 46 852484484, magnus.doverskog@umecrine.com
Scientific contact	Chief Executive Officer, Umecrine Cognition AB, 46 852484484, magnus.doverskog@umecrine.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	12 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part A: The primary objective is to assess the safety and tolerability of GR3027 after a single oral dose of GR3027 in female patients with IH.

Part B: The primary objective is to assess the safety and tolerability of GR3027 after multiple dose administration in patients with IH.

Protection of trial subjects:

The protocol and the statement of informed consent were approved in the respective countries by an Independent Ethics Committee (IEC) prior to each centre's initiation. The trial was conducted in accordance with the Declaration of Helsinki and its revisions as well as with the valid local and national law(s), with the International Conference on Harmonisation (ICH) Harmonised Tripartite Guideline for Good Clinical Practice (GCP) (E6) issued in July 1996, and with the Commission Directives 2001/20/EC, 2005/28/EC and 2001/83/EC. Written Informed Consent was received from all subjects prior to enrolment into the trial, as dictated by the Declaration of Helsinki.

Background therapy:

None

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 September 2017
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	Sweden: 2
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Finland: 5
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	10
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was initiated in Sept 2017 and was done simultaneously in FI, DK and SE

Pre-assignment

Screening details:

Female patients 18 to 55 years with a diagnosis of IH and with no current treatment for hypersomnolence disorder were enrolled in the study. There was a wash-out period of 14 days before randomization to study treatment.

Period 1

Period 1 title	Overall study (overall period part B)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

The investigators, staff at the trial sites, trial monitors, and data analysis/management personnel were blinded to the subject assignment in order to ensure that information that could potentially bias handling of data was not disclosed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence: GR3027-Placebo

Arm description:

Randomized subjects received GR3027 in the first study period (Day 1-14) and placebo in the second study period (Day 1-14). There was a 7 days wash-out period between study treatments.

Arm type	Experimental
Investigational medicinal product name	GR3027
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

8 capsules received twice daily for 14 days

Investigational medicinal product name	GR3027 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

8 capsules twice daily for 14 days

Arm title	Sequence: Placebo-GR3027

Arm description:

Randomized subjects received Placebo in the first study period (Day 1-14) and GR3027 in the second study period (Day 1-14). There was a 7 days wash-out period between study treatments.

Arm type	Experimental

Investigational medicinal product name	GR3027
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

8 capsules of 80 mg twice daily for 14 days

Investigational medicinal product name	GR3027 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

8 capsules twice daily for 14 days

Number of subjects in period 1	Sequence: GR3027-Placebo	Sequence: Placebo-GR3027
Started	4	6
Completed	4	6

Baseline characteristics

Reporting groups	
Reporting group title	Sequence: GR3027-Placebo
Reporting group description:	
Randomized subjects received GR3027 in the first study period (Day 1-14) and placebo in the second study period (Day 1-14). There was a 7 days wash-out period between study treatments.	
Reporting group title	Sequence: Placebo-GR3027
Reporting group description:	
Randomized subjects received Placebo in the first study period (Day 1-14) and GR3027 in the second study period (Day 1-14). There was a 7 days wash-out period between study treatments.	

Reporting group values	Sequence: GR3027-Placebo	Sequence: Placebo-GR3027	Total
Number of subjects	4	6	10
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Patients aged 18-55 were enrolled in the study			
Units: years			
arithmetic mean	28.5	32.2	
standard deviation	± 5.4	± 7.0	-
Gender categorical			
Males and females aged 18-55 were enrolled in the study			
Units: Subjects			
Female	1	4	5
Male	3	2	5

End points

End points reporting groups

Reporting group title	Sequence: GR3027-Placebo
Reporting group description:	
Randomized subjects received GR3027 in the first study period (Day 1-14) and placebo in the second study period (Day 1-14). There was a 7 days wash-out period between study treatments.	
Reporting group title	Sequence: Placebo-GR3027
Reporting group description:	
Randomized subjects received Placebo in the first study period (Day 1-14) and GR3027 in the second study period (Day 1-14). There was a 7 days wash-out period between study treatments.	
Subject analysis set title	GR3027 (Full Analysis Set)
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set included all subjects who were randomized and received study treatment.	
Subject analysis set title	Placebo (Full Analysis Set)
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set included all subjects imho were randomized and received study treatment.	

Primary: ESS

End point title	ESS
End point description:	
End point type	Primary
End point timeframe:	
From baseline to end of study treatment period (14 days)	

End point values	GR3027 (Full Analysis Set)	Placebo (Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: Minutes				
least squares mean (confidence interval 95%)	-0.71 (-2.21 to 0.79)	-0.75 (-2.27 to 0.77)		

Statistical analyses

Statistical analysis title	Mixed model analysis
Statistical analysis description:	
The mixed model analysis for ESS included baseline as a fixed effect. No other baseline covariates were adjusted for in the model. The significance level was not adjusted for multiple inferential tests, and type I error was therefore not be controlled, which is considered acceptable for exploratory efficacy evaluations. P-values below 0.05 were considered nominally statistically significant.	
Comparison groups	GR3027 (Full Analysis Set) v Placebo (Full Analysis Set)

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	≤ 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.27
upper limit	2.36

Notes:

[1] - P-values below 0.05 were considered nominally statistically significant.

Primary: MWT

End point title	MWT

End point description:

End point type	Primary

End point timeframe:

From baseline to end of study treatment (14 days)

End point values	GR3027 (Full Analysis Set)	Placebo (Full Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: Minutes				
least squares mean (confidence interval 95%)	0.28 (-3.18 to 3.74)	-3.35 (-6.82 to 0.11)		

Statistical analyses

Statistical analysis title	Mixed model analysis

Statistical analysis description:

The mixed model analyses for MWT included baseline as a fixed effect. No other baseline covariates were adjusted for in the model.The significance level was not adjusted for multiple inferential tests, and type I error was therefore not be controlled, which is considered acceptable for exploratory efficacy evaluations. P-values below 0.05 were considered nominally statistically significant.

Comparison groups	GR3027 (Full Analysis Set) v Placebo (Full Analysis Set)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	≤ 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.63

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.76
upper limit	8.03

Notes:

[2] - P-values below 0.05 were considered nominally statistically significant.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study treatment at Day 1, up to 14 days after end of study treatment in period 2

Adverse event reporting additional description:

An adverse event (AE) was any untoward medical occurrence in a subject administered the study treatment (GR3027 or placebo) which did not necessarily have a causal relationship with the study treatments

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	GR3027

Reporting group description:

Randomized subjects for the sequence GR3027 - Placebo received GR3027 in the first study period (Day 1-14) and placebo in the second study period Day 1-14. There was a 7 days wash-out period between treatments.
Randomized subjects for the sequence Placebo - GR3027 received placebo in the first study period (Day 1-14) and GR3027 in the second study period Day 1-14. There was a 7 days wash-out period between treatments.

Reporting group title	Placebo

Reporting group description:

Randomized subjects for the sequence GR3027 - Placebo received GR3027 in the first study period (Day 1-14) and placebo in the second study period Day 1-14. There was a 7 days wash-out period between treatments.
Randomized subjects for the sequence Placebo - GR3027 received placebo in the first study period (Day 1-14) and GR3027 in the second study period Day 1-14. There was a 7 days wash-out period between treatments.

Serious adverse events	GR3027	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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: 0 %

Non-serious adverse events	GR3027	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)	9 / 10 (90.00%)	
Investigations			

Heart rate increased			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Body temperature increased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Poor quality sleep			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Gastrointestinal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2018	Clarification and change of inclusion criteria
14 March 2018	Update of exclusion criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported