



Clinical trial results:

Proof of concept trial to evaluate the effectiveness of combined treatment with Valerian extract (Euvegal®) and Lavender oil (Lasea®) in patients suffering from inability to fall or stay asleep

Summary

EudraCT number	2015-003265-29
Trial protocol	DE
Global end of trial date	14 August 2018

Results information

Result version number	v1 (current)
This version publication date	05 January 2020
First version publication date	05 January 2020
Summary attachment (see zip file)	750598.01.003_SummaryofResultsEudraCTDatabase_2019_12_20 (750598.01.003 SummaryOfResults_EUDRA_CT_Version 1.0_ 20191220 Final_mit Schwärzung.pdf)

Trial information

Trial identification

Sponsor protocol code	750598.01.003
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dr. Willmar Schwabe GmbH & Co. KG
Sponsor organisation address	Willmar-Schwabe Straße 4, Karlsruhe, Germany, 76227
Public contact	Clinical Research Department, Dr. Willmar Schwabe GmbH & Co. KG, +49 7214005573,
Scientific contact	Clinical Research Department, Dr. Willmar Schwabe GmbH & Co. KG, +49 7214005573,

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	05 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2018
Global end of trial reached?	Yes
Global end of trial date	14 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the trial is to assess the effectiveness of a combined treatment with Valerian extract (Euvegal®) and Lavender oil (Lasea®) in patients with inability to fall or stay asleep.

Protection of trial subjects:

Possibility to withdraw informed consent. Monitoring of adverse events and laboratory parameters.

Background therapy: -

Evidence for comparator:

Active substances contained in Synalan.

Actual start date of recruitment	30 August 2016
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	Germany: 94
Worldwide total number of subjects	94
EEA total number of subjects	94

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)	94
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total 175 patients were screened for eligibility. Two of these patients were re-screened due to scheduling conflicts. 32 subjects were randomized. 1 drop out subject was replaced.

Pre-assignment

Screening details:

32 subjects were randomised to one of six treatment sequences (Silexan - Synalan - Valeriana/Silexan - Valeriana - Synalan/Synalan - Silexan - Valeriana/Synalan - Valeriana - Silexan/Valeriana - Silexan - Synalan/Valeriana - Synalan - Silexan) in a 3-period, 3-way cross-over design.

Pre-assignment period milestones

Number of subjects started	94
Number of subjects completed	94

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Silexan

Arm description:

WS® 1265 1x80mg

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

Dosage and administration details:

WS® 1265 1x80 mg + WS® 1014 Placebo 1x1

Arm title	Synalan
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Arm description:

WS® 1265 1x80 mg + WS® 1014 1x500 mg

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

Dosage and administration details:

WS® 1265 1x80 mg + WS® 1014 1x500mg

Arm title	Valerian
Arm description: WS® 1014 1x500 mg	
Arm type	Experimental
Investigational medicinal product name	Valerian
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use
Dosage and administration details: WS® 1265 Placebo 1x1 + WS® 1014 1x500mg	

Number of subjects in period 1	Silexan	Synalan	Valerian
Started	31	32	31
Completed	31	31	31
Not completed	0	1	0
Adverse event, non-fatal	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Silexan
Reporting group description: WS® 1265 1x80mg	
Reporting group title	Synalan
Reporting group description: WS® 1265 1x80 mg + WS® 1014 1x500 mg	
Reporting group title	Valerian
Reporting group description: WS® 1014 1x500 mg	

Reporting group values	Silexan	Synalan	Valerian
Number of subjects	31	32	31
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	31	32	31
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	34.81	34.63	34.81
standard deviation	± 7.78	± 7.72	± 7.78
Gender categorical Units: Subjects			
Female	18	19	18
Male	13	13	13

Reporting group values	Total		
Number of subjects	94		
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)	94		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	55		
Male	39		

Subject analysis sets

Subject analysis set title	Silexan
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects, which received Silexan in period I or period II or period III.

The full analysis set (FAS) included all patients of the safety analysis who completed at least one treatment period including the Polysomnographic sleep measures (PSG) night.

Subject analysis set title	Synalan
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects, which received Synalan in period I or period II or period III.

The full analysis set (FAS) included all patients of the safety analysis who completed at least one treatment period including the Polysomnographic sleep measures (PSG) night.

Subject analysis set title	Valerian
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects, which received Valerian in period I or period II or period III.

The full analysis set (FAS) included all patients of the safety analysis who completed at least one treatment period including the Polysomnographic sleep measures (PSG) night.

Reporting group values	Silexan	Synalan	Valerian
Number of subjects	31	31	31
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	31	31	31
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	34.81	34.81	34.81
standard deviation	± 7.78	± 7.78	± 7.78

Gender categorical			
Units: Subjects			
Female	18	18	18
Male	13	13	13

End points

End points reporting groups

Reporting group title	Silexan
Reporting group description: WS® 1265 1x80mg	
Reporting group title	Synalan
Reporting group description: WS® 1265 1x80 mg + WS® 1014 1x500 mg	
Reporting group title	Valerian
Reporting group description: WS® 1014 1x500 mg	
Subject analysis set title	Silexan
Subject analysis set type	Full analysis
Subject analysis set description: Subjects, which received Silexan in period I or period II or period III. The full analysis set (FAS) included all patients of the safety analysis who completed at least one treatment period including the Polysomnographic sleep measures (PSG) night.	
Subject analysis set title	Synalan
Subject analysis set type	Full analysis
Subject analysis set description: Subjects, which received Synalan in period I or period II or period III. The full analysis set (FAS) included all patients of the safety analysis who completed at least one treatment period including the Polysomnographic sleep measures (PSG) night.	
Subject analysis set title	Valerian
Subject analysis set type	Full analysis
Subject analysis set description: Subjects, which received Valerian in period I or period II or period III. The full analysis set (FAS) included all patients of the safety analysis who completed at least one treatment period including the Polysomnographic sleep measures (PSG) night.	

Primary: Polysomnographic endpoints

End point title	Polysomnographic endpoints ^[1]
End point description: This document in its section "End points" specifies commercially confidential information of Dr. Willmar Schwabe GmbH & Co. KG, Karlsruhe referred to in Article 81 Section (4) b) Regulation (EU) 536/2014 that is a trade secret and released by the holder for purposes of Regulation (EU) 536/2014 only under the condition of confidence. Trade secrets may not - even in part - be published or released to third parties other than to competent authorities without express permission of the trade secret holder.	
End point type	Primary
End point timeframe: Day 3	

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: See document for a complete description of the statistical methods and results.

There were no primary end points defined for analysis. Because at least one primary end point is required to be entered study results into the database, the parameters presented here have been chosen to this purpose.

End point values	Silexan	Synalan	Valerian	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	31	31	
Units: minutes				
median (inter-quartile range (Q1-Q3))	9999.99 (9999.99 to 9999.99)	9999.99 (9999.99 to 9999.99)	9999.99 (9999.99 to 9999.99)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

3 Days

Adverse event reporting additional description:

5 adverse events occurred in 32 patients treated with Synalan, 1 adverse events occurred in 31 patients treated with valeriana, 1 adverse events occurred in 31 patients treated with Silexan.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19
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Reporting groups

Reporting group title	Synalan
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Reporting group description:

Synalan

Reporting group title	Valeriana
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Reporting group description:

Valerian

Reporting group title	Silexan
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Reporting group description:

Silexan

Serious adverse events	Synalan	Valeriana	Silexan
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Synalan	Valeriana	Silexan
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 31 (0.00%)	0 / 31 (0.00%)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Overall, 6 of the randomized 32 subjects experienced non-serious adverse events during treatment phase. This number was not be entered into the database, because each adverse event occurred with a frequency which did not exceed the frequency threshold of 5% for reporting non-serious adverse events. Therefore, the number of subjects with non-serious adverse events resulted in 0 when considering the 5% frequency threshold.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2016	The determination of the creatinine clearance was replaced by the determination of the glomerular filtration rate. The allowed time for the Digit-symbol substitution test (DSST) has been prolonged from 90 to 120 seconds. The use of a patient diary had not been described in the clinical trial protocol by error. Therefore, its use was added by this amendment.
06 December 2016	The time window of up to 7 days between screening visit and the polysomnography, polysomnographic sleep measures (PSG) screening nights was too short for several patients. Therefore, the period was changed to 14 days. The inclusion criteria Wake-time during sleep, Total sleep time (TST) and Insomnia Severity Index (ISI) were adapted.
17 March 2017	The exclusion criterion regarding concomitant diseases was changed.
30 June 2017	The exclusion criterion regarding concomitant diseases was changed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported