Clinical trial results:
SAFETY AND EFFICACY OF THN102 ON SLEEPINESS IN NARCOLEPTIC PATIENTS

Summary

EudraCT number	2015-005035-41
Trial protocol	BE
Global end of trial date	28 December 2018

Results information

Result version number	v1 (current)
This version publication date	09 October 2021
First version publication date	09 October 2021
Summary attachment (see zip file)	THN102-201 clinical study report synopsis (THN102-201_CSR Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	THN102-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02821715
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Theranexus
Sponsor organisation address	86 route de Paris, Orsay, France, 91400
Public contact	Werner Rein, Theranexus SA, +33 680 02 67 79 , werner.rein@theranexus.fr
Scientific contact	Werner Rein, Theranexus SA, +33 680 02 67 79 , werner.rein@theranexus.fr

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	28 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 December 2018
Global end of trial reached?	Yes
Global end of trial date	28 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the superiority of THN102 (combination modafinil and flecainide acetate) vs modafinil for improving the residual daytime sleepiness assessed by Epworth Sleepiness Scale (ESS) in patients with narcolepsy treated by modafinil

Protection of trial subjects:

The study was conducted in accordance with applicable laws and regulations, GCP, and the ethical principles that have their origin in the Declaration of Helsinki. All informed consent forms were compliant with the ICH of Technical Requirements for Pharmaceuticals for Human Use guideline on GCP.

Background therapy:

The double-blind 3-period, 3-treatment cross-over was preceded by a baseline period during which the patients were stabilized to 300 mg modafinil administered as open label. This period aimed to stabilize the patient to the same low dose of modafinil investigated during the double-blind periods while still providing potential improvement in sleep parameters when associated with flecainide. There was no wash-out between any of the study period of the cross-over. After the last period of the cross-over, subjects continued to be dosed with modafinil 300 mg only, as open label for an additional week.

Evidence for comparator:

This study design was selected to demonstrate the superiority of each THN102 treatment, as the combination of 300 mg modafinil associated with two different dose levels of flecainide (3 and 27 mg), as compared to modafinil alone (300 mg, control) and to determine which of the two THN102 treatments had best efficacy as based primarily on ESS parameters. The control condition was modafinil alone i.e. associated with placebo of flecainide to ascertain double-blind conditions.

Actual start date of recruitment	20 October 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	Belgium: 4
Country: Number of subjects enrolled	France: 47
Worldwide total number of subjects	51
EEA total number of subjects	51

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	51
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

54 patients were screened, 51 patients were randomized and 48 started the double-blind treatment period

Pre-assignment

Screening details:

Study starts with open-label run in period with modafinil 300 mg/d. 51 patients met study inclusion/exclusion criteria and entered the run-in period, 48 subjects still fulfilled inclusion criteria after run-in and entered the double-blind period.

Pre-assignment period milestones

Number of subjects started	51
Number of subjects completed	48

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 3

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, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Capsules of flecainide or Placebo (in vials) could not be differentiated by either the Investigators or the patients. Modafinil was administered as open label (commercial presentation, capsules in blister) throughout the complete study with no corresponding placebo.

Arms

Are arms mutually exclusive?	No
Arm title	THN102: 300mg/0mg

Arm description:

Participants received either:
A Modafinil 300mg/d/Flecainide placebo,
B Modafinil 300mg/d/Flecainide 3mg/d
C Modafinil 300mg/d/Flecainide 27mg/d

Arm type	Active comparator
Investigational medicinal product name	THN102: 300mg/0mg (Reference)
Investigational medicinal product code	THN102: 300mg/0mg
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

300 mg modafinil, total daily dose and placebo of flecainide

Arm title	THN102: 300mg/3mg

Arm description:

THN102: 300mg/3mg, 300 mg modafinil and 3 mg of flecainide acetate, total daily dose

Arm type	Experimental

Investigational medicinal product name	THN102: 300mg/3mg
Investigational medicinal product code	THN102: 300mg/3mg
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

THN102: 300mg/3mg, 300 mg modafinil and 3 mg of flecainide acetate, total daily dose

Arm title	THN102: 300mg/27mg

Arm description:

THN102: 300mg/27mg

Arm type	Active comparator
Investigational medicinal product name	THN102: 300mg/27mg
Investigational medicinal product code	THN102: 300mg/27mg
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

THN102: 300mg/27mg 300 mg modafinil and 27 mg of flecainide acetate, total daily dose

Number of subjects in period 1	THN102: 300mg/0mg	THN102: 300mg/3mg	THN102: 300mg/27mg
Started	48	48	48
Completed	48	48	48

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	51	51	
Age categorical			
The age range of the randomized subjects (n=51) was from 19 to 60 years old at screening (mean of 35.7 years and median of 35.0 years) with 24 men (47%) and 27 women (53%). The BMI range was from 18.00 to 35.80 (mean of 26.753 and median of 26.600). Most of the subjects had diagnostic of narcolepsy Type 1 (n=48, 88%) and 6 subjects (12%) with Type 2 narcolepsy at inclusion; no change of diagnosis (from Type 1 to Type 2) was observed during the study			
Units: Subjects			
Adults (18-64 years)	51	51	
Age continuous			
Units: years			
arithmetic mean	35.7		
standard deviation	± 9.96	-	
Gender categorical			
Units: Subjects			
Female	27	27	
Male	24	24	

End points

End points reporting groups	
Reporting group title	THN102: 300mg/0mg
Reporting group description: Participants received either: A Modafinil 300mg/d/Flecainide placebo, B Modafinil 300mg/d/Flecainide 3mg/d C Modafinil 300mg/d/Flecainide 27mg/d	
Reporting group title	THN102: 300mg/3mg
Reporting group description: THN102: 300mg/3mg, 300 mg modafinil and 3 mg of flecainide acetate, total daily dose	
Reporting group title	THN102: 300mg/27mg
Reporting group description: THN102: 300mg/27mg	

Primary: Epworth Sleeping Scale (ESS)	
End point title	Epworth Sleeping Scale (ESS)
End point description: Range of the scale : 0 to 24. A low score indicates a good outcome. Results shown are corresponding to a change from baseline of the ESS score	
End point type	Primary
End point timeframe: 14 days after the beginning of treatment period	

End point values	THN102: 300mg/0mg	THN102: 300mg/3mg	THN102: 300mg/27mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	48	48	
Units: ESS Score				
least squares mean (standard error)	14.68 (± 0.689)	15.34 (± 0.695)	15.34 (± 0.694)	

Statistical analyses

Statistical analysis title	THN102 300mg/0mg vs THN102 300mg/3mg
Comparison groups	THN102: 300mg/0mg v THN102: 300mg/3mg v THN102: 300mg/27mg
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.319
Method	mixed linear regression modeL
Parameter estimate	Mean difference (final values)
Point estimate	-0.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.97
upper limit	0.65
Variability estimate	Standard error of the mean
Dispersion value	0.658

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected for each 2 week treatment period during the 3 crossover periods.

Adverse event reporting additional description:

Adverse events were collected by investigator - open question to patient. No scale or questionnaire based collection of events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	THN102:300mg/0mg
Reporting group description: -	
Reporting group title	THN102:300mg/3mg
Reporting group description: -	
Reporting group title	THN102:300mg/27mg

Reporting group description: -

Serious adverse events	THN102:300mg/0mg	THN102:300mg/3mg	THN102:300mg/27mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	0 / 48 (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: 0 %

Non-serious adverse events	THN102:300mg/0mg	THN102:300mg/3mg	THN102:300mg/27mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 48 (18.75%)	15 / 48 (31.25%)	13 / 48 (27.08%)
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Hunger			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1

Sluggishness			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Nightmare			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
violence related symptom			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			

Palpitation			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	2 / 48 (4.17%)
occurrences (all)	1	0	2
Dysgeusia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	2 / 48 (4.17%)	2 / 48 (4.17%)	1 / 48 (2.08%)
occurrences (all)	2	2	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Chalazion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
abdominal upper pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	1 / 48 (2.08%)
occurrences (all)	0	1	1
Dry mouth			
subjects affected / exposed	0 / 48 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0

Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 48 (2.08%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 48 (0.00%)	2 / 48 (4.17%)	0 / 48 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	0 / 48 (0.00%)	2 / 48 (4.17%)	0 / 48 (0.00%)
occurrences (all)	0	2	0
Laryngitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 48 (0.00%)	2 / 48 (4.17%)	2 / 48 (4.17%)
occurrences (all)	0	2	2
Tracheitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 48 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Pain in extremity			
subjects affected / exposed	0 / 48 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences (all)	0	1	0

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