Clinical trial results:
Randomised, double-blind, placebo-controlled, complete 3-way cross-over phase IIa trial to investigate safety and efficacy of two THN102 doses in subjects with excessive daytime sleepiness associated with Parkinson's disease

Summary

EudraCT number	2017-004475-31
Trial protocol	HU CZ
Global end of trial date	20 December 2019

Results information

Result version number	v1 (current)
This version publication date	07 July 2021
First version publication date	07 July 2021
Summary attachment (see zip file)	THN102-202 clinical study report synopsis (THN102-202_CTR Synopsis_final 1.0_20200723.pdf)

Trial information

Trial identification

Sponsor protocol code	THN102-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03624920
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Theranexus
Sponsor organisation address	86 route de Paris, Orsay, France, 91400
Public contact	Damien Bouvier, Theranexus S.A., 0033 146548524, damien.bouvier@theranexus.com
Scientific contact	Damien Bouvier, Theranexus S.A., 0033 146548524, damien.bouvier@theranexus.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	18 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2019
Global end of trial reached?	Yes
Global end of trial date	20 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety profile of THN102 (modafinil/flecainide combination) at two doses (200 mg/18 mg and 200 mg/2 mg) versus placebo in subjects with excessive daytime sleepiness associated with Parkinson's disease (PD).

Protection of trial subjects:

All subjects were closely monitored during the trial. Subjects who discontinued trial participation prematurely were asked to come to the site for an early discontinuation and follow-up visits to exclude the possibility of an adverse event (AE) being the cause and otherwise to assess if the AE had any potential relationship to the trial medication. Serious adverse events (SAEs) were to be followed-up until resolution or until no further improvement could be expected, and follow-up information was to be recorded by the investigators. SAEs detected after the last subject's visit, were to be collected if in the investigator's opinion, they were related either to the investigational medicinal product (IMP) or to the trial procedure.
Subjects with electrocardiogram (ECG) signs of left ventricular hypertrophy had to be withdrawn from further participation in the trial and were to be referred to a cardiologist for further examination.
Subjects who answered "yes" to point 4 and/or 5 of the Columbia-Suicide Severity Rating Scale (C-SSRS), were to be withdrawn from the trial and sent for psychiatric consultation. Subjects with alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥ 5 times the upper limit of normal (ULN), or ALT and AST ≥ 3 times the ULN together with bilirubin ≥ 2 times the ULN were to be withdrawn from the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 July 2018
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	Czechia: 25
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	77
EEA total number of subjects	72

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)	36
From 65 to 84 years	41
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

105 patients were screened and 77 were randomized and 75 were exposed to study medication

Pre-assignment

Screening details:

Randomised, double-blind, placebo-controlled, complete 3-way cross-over trial in subjects aged 18 to 80 years with excessive daytime sleepiness associated with Parkinson's disease. The study consisted of a screening period, followed by three 2-week treatment periods separated by washout periods of 1 to 2 weeks each, and 1-week follow-up.

Pre-assignment period milestones

Number of subjects started	77
Number of subjects completed	75[1]

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	Protocol deviation: 1

Notes:

[1] - The number of subjects reported to be in the pre-assignment period is not consistent with the number starting period 1. It is expected that the number completing the pre-assignment period are also present in the arms in period 1.
Justification: Crossover design

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:

Modafinil 100 mg capsules and modafinil placebo capsules as well as flecainide 1 mg or 9 mg capsules and matching placebo capsules were identical in size and appearance, as well as colour of modafinil and respective placebo (orange), and flecainide and respective placebo (white). The packaging and labelling did not allow for any distinction between them.

Arms

Are arms mutually exclusive?	No
Arm title	THN102 Placebo

Arm description:

Dosage A

Arm type	Placebo
Investigational medicinal product name	THN102 placebo
Investigational medicinal product code	dose A
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

In this trial, all subjects received the same doses of IMP (modafinil/flecainide 200 mg/2 mg, 200 mg/18 mg and matching placebo). IMP (2 capsules modafinil or placebo plus 2 capsules flecainide or placebo; 4 capsules in total) were to be administered in the morning. The IMP was to be swallowed before meal with 150 mL tap water at 8:00 h (± 1 h). The interval of 24 h between the 2 intakes should be followed. Subjects aged above 65 years were asked to take half a dose of IMP (2 capsules) during the first 3 days

of each treatment period, followed by the full IMP dose since the fourth treatment day.

Arm title	THN102 200/2
Arm description: Dosage B	
Arm type	Experimental
Investigational medicinal product name	THN102 200/2
Investigational medicinal product code	Dosage B
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

In this trial, all subjects received the same doses of IMP (modafinil/flecainide 200 mg/2 mg, 200 mg/18 mg and matching placebo). IMP (2 capsules modafinil or placebo plus 2 capsules flecainide or placebo; 4 capsules in total) were to be administered in the morning. The IMP was to be swallowed before meal with 150 mL tap water at 8:00 h (± 1 h). The interval of 24 h between the 2 intakes should be followed. Subjects aged above 65 years were asked to take half a dose of IMP (2 capsules) during the first 3 days of each treatment period, followed by the full IMP dose since the fourth treatment day.

Arm title	THN102 200/18
Arm description: Dosage C	
Arm type	Experimental
Investigational medicinal product name	THN102 200/18
Investigational medicinal product code	dosage C
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

In this trial, all subjects received the same doses of IMP (modafinil/flecainide 200 mg/2 mg, 200 mg/18 mg and matching placebo). IMP (2 capsules modafinil or placebo plus 2 capsules flecainide or placebo; 4 capsules in total) were to be administered in the morning. The IMP was to be swallowed before meal with 150 mL tap water at 8:00 h (± 1 h). The interval of 24 h between the 2 intakes should be followed. Subjects aged above 65 years were asked to take half a dose of IMP (2 capsules) during the first 3 days of each treatment period, followed by the full IMP dose since the fourth treatment day.

Number of subjects in period 1	THN102 Placebo	THN102 200/2	THN102 200/18
Started	68	72	73
Completed	68	68	68
Not completed	0	4	5
Adverse event, non-fatal	-	3	3
Protocol deviation	-	1	2

Baseline characteristics

Reporting groups[1]	
Reporting group title	overall trial
Reporting group description: -	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: among the 77 patients randomized 2 left the study before any IMP intake. These 2 patients have been exluded from the safety set.

Reporting group values	overall trial	Total	
Number of subjects	75	75	
Age categorical Units: Subjects			
Adults (18-64 years)	35	35	
From 65-84 years	40	40	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	63.5		
standard deviation	± 9.35	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	50	50	

Subject analysis sets	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set (FAS) includes all randomised subjects with an evaluable ESS score at the end of at least one treatment period. Evaluability of treatment periods is described in Section 5.6. The efficacy analyses will be conducted on the FAS.

Subject analysis set title	SAFETY SET
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set (SS) includes all subjects with at least one IMP administration.

Reporting group values	Full analysis set	SAFETY SET	
Number of subjects	72	75	
Age categorical Units: Subjects			
Adults (18-64 years)	34	35	
From 65-84 years	38	40	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	63.3	63.5	
standard deviation	± 9.43	± 9.35	

Gender categorical Units: Subjects			
Female	24	25	
Male	48	50	

End points

End points reporting groups

Reporting group title	THN102 Placebo
Reporting group description:	
Dosage A	
Reporting group title	THN102 200/2
Reporting group description:	
Dosage B	
Reporting group title	THN102 200/18
Reporting group description:	
Dosage C	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set (FAS) includes all randomised subjects with an evaluable ESS score at the end of at least one treatment period. Evaluability of treatment periods is described in Section 5.6. The efficacy analyses will be conducted on the FAS.	
Subject analysis set title	SAFETY SET
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Set (SS) includes all subjects with at least one IMP administration.	

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:	
2 weeks	

End point values	THN102 Placebo	THN102 200/2	THN102 200/18	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	69	71	
Units: ESS score				
least squares mean (standard error)	-2.4 (± 3.65)	-3.9 (± 4.87)	-3.1 (± 4.12)	

Statistical analyses

Statistical analysis title	THN102 200/2 vs THN102 placebo A ESS Score

Statistical analysis description:

Continuous efficacy endpoints – the change from baseline at each key visit (end of treatment period I, II, and III) in ESS, PVT and MoCA - were analysed using a mixed linear regression model, which included the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/2 v THN102 Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.012 [2]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.3994
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4861
upper limit	-0.3128
Variability estimate	Standard error of the mean
Dispersion value	0.5492

Notes:

[1] - Analysis of Epworth Sleepiness Scale Score

[2] - Estimates are based on the mixed linear regression model with the fixed effects of treatment, period, treatment by period interaction, sequence, baseline score, and the random effect of subjects within sequences.

Statistical analysis title	THN102 200/18 vs THN102 placebo A ESS score

Statistical analysis description:

Continuous efficacy endpoints – the change from baseline at each key visit (end of treatment period I, II, and III) in ESS, PVT and MoCA - were analysed using a mixed linear regression model, which included the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/18 v THN102 Placebo
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.1769 [4]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.7427
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8249
upper limit	0.3394
Variability estimate	Standard error of the mean
Dispersion value	0.547

Notes:

[3] - Analysis of Epworth Sleepiness Scale Score

[4] - Estimates are based on the mixed linear regression model with the fixed effects of treatment, period, treatment by period interaction, sequence, baseline score, and the random effect of subjects within sequences.

Statistical analysis title	THN102 200/18 vs THN102 200/2 A ESS score

Statistical analysis description:

Continuous efficacy endpoints – the change from baseline at each key visit (end of treatment period I, II, and III) in ESS, PVT and MoCA - were analysed using a mixed linear regression model, which included the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/18 v THN102 Placebo

Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.2303 [6]
Method	mixed linear regression model
Parameter estimate	Mean difference (final values)
Point estimate	0.6567
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4212
upper limit	1.7346
Variability estimate	Standard error of the mean
Dispersion value	0.5449

Notes:

[5] - Analysis of Epworth Sleepiness Scale Score

[6] - Estimates are based on the mixed linear regression model with the fixed effects of treatment, period, treatment by period interaction, sequence, baseline score, and the random effect of subjects within sequences.

Secondary: Psychomotor Vigilance Test (PVT) : Reaction Time (Miliseconds) Change From Baseline

End point title	Psychomotor Vigilance Test (PVT) : Reaction Time (Miliseconds) Change From Baseline

End point description:

PVT measures reaction time in milliseconds. The results below are corresponding to the reaction time change from baseline

Continuous efficacy endpoints – the change from baseline at each key visit (end of treatment period I, II, and III) in ESS, PVT and MoCA - were analysed using a mixed linear regression model, which included the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

End point type	Secondary

End point timeframe:

2 weeks

End point values	THN102 Placebo	THN102 200/2	THN102 200/18	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	64	67	67	
Units: miliseconds				
least squares mean (standard error)	-16.69 (± 84.983)	-24.92 (± 81.279)	-18.89 (± 78.450)	

Statistical analyses

No statistical analyses for this end point

Secondary: ESS Responder rate

End point title	ESS Responder rate

End point description:

ESS score responder rate, defined as the proportion of subjects with at least 25% ESS improvement from baseline, at the end of each treatment period

End point type	Secondary

End point timeframe:

2 weeks

End point values	THN102 Placebo	THN102 200/2	THN102 200/18	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	70	72	
Units: count of participant				
number (not applicable)	68	69	71	

Statistical analyses

Statistical analysis title	ESS Responder rate THN102 200/2 vs placebo

Statistical analysis description:

Categorical efficacy endpoints – absence of residual somnolence and ESS responder status at each key visit – were analysed using a generalised linear mixed regression model (GLMM), with the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 Placebo v THN102 200/2
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1209
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.9766
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8342
upper limit	4.6835

Statistical analysis title	ESS Responder rate THN102 200/18 vs placebo

Statistical analysis description:

Categorical efficacy endpoints – absence of residual somnolence and ESS responder status at each key visit – were analysed using a generalised linear mixed regression model (GLMM), with the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/18 v THN102 Placebo

Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3534
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.4985
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6357
upper limit	3.5323

Statistical analysis title	THN102 200/18 vs 200/2

Statistical analysis description:

Categorical efficacy endpoints – absence of residual somnolence and ESS responder status at each key visit – were analysed using a generalised linear mixed regression model (GLMM), with the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/18 v THN102 200/2
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4971
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.7581
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3397
upper limit	1.6919

Secondary: ESS Patients in remission

End point title	ESS Patients in remission

End point description:

Number of patients in remission (=without residual sleepiness), i.e. ESS < 11 at the end of each treatment period

End point type	Secondary

End point timeframe:

2 weeks

End point values	THN102 Placebo	THN102 200/2	THN102 200/18	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	70	72	
Units: count of participant				
number (not applicable)	68	69	71	

Statistical analyses

Statistical analysis title	ESS remission THN102 200/2 vs Placebo

Statistical analysis description:

Categorical efficacy endpoints – Number of patients in remission (=without residual sleepiness), i.e. ESS < 11 at the end of each treatment period– were analysed using a generalised linear mixed regression model (GLMM), with the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/2 v THN102 Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05332
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.0831
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9842
upper limit	9.6577

Statistical analysis title	ESS remission THN102 200/18 vs Placebo

Statistical analysis description:

Categorical efficacy endpoints – Number of patients in remission (=without residual sleepiness), i.e. ESS < 11 at the end of each treatment period– were analysed using a generalised linear mixed regression model (GLMM), with the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/18 v THN102 Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.102
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.619
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8246
upper limit	8.3182

Statistical analysis title	ESS remission THN102 200/18 vs 200/2

Statistical analysis description:

Categorical efficacy endpoints – Number of patients in remission (=without residual sleepiness), i.e. ESS < 11 at the end of each treatment period– were analysed using a generalised linear mixed regression model (GLMM), with the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/18 v THN102 200/2
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7177
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.8495
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3493
upper limit	2.0657

Secondary: MoCA score analysis

End point title	MoCA score analysis

End point description:

MoCA score reflects the cognitive capacities of a person. Range of the total score of 10 test items: 0 to 30 points. A high score indicates good cognitive functioning. A score of 26 and above is considered normal.

End point type	Secondary

End point timeframe:

2 weeks

End point values	THN102 Placebo	THN102 200/2	THN102 200/18	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	70	72	
Units: score on a scale				
number (not applicable)	68	69	70	

Statistical analyses

Statistical analysis title	MoCA THN102 200/2 vs Placebo

Statistical analysis description:

Continuous efficacy endpoints – the change from baseline at each key visit (end of treatment period I, II, and III) in ESS, PVT and MoCA - were analysed using a mixed linear regression model, which included the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/2 v THN102 Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3815
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.1913
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6223
upper limit	0.2397
Variability estimate	Standard error of the mean
Dispersion value	0.2178

Statistical analysis title	MoCA THN102 200/18 vs Placebo

Statistical analysis description:

Continuous efficacy endpoints – the change from baseline at each key visit (end of treatment period I, II, and III) in ESS, PVT and MoCA - were analysed using a mixed linear regression model, which included the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/18 v THN102 Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3566
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.2012
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.229
upper limit	0.6313
Variability estimate	Standard error of the mean
Dispersion value	0.2174

Statistical analysis title	MoCA THN102 200/18 vs 200/2

Statistical analysis description:

Continuous efficacy endpoints – the change from baseline at each key visit (end of treatment period I, II, and III) in ESS, PVT and MoCA - were analysed using a mixed linear regression model, which included the treatment, period, treatment by period interaction, sequence, and baseline scores as fixed effects, and the subject nested within sequence as a random effect.

Comparison groups	THN102 200/18 v THN102 200/2
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0722
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.3924
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0359
upper limit	0.8208
Variability estimate	Standard error of the mean
Dispersion value	0.2165

Secondary: MoCA score

End point title	MoCA score

End point description:

MoCA score reflects the cognitive capacities of a person. Range of the total score of 10 test items: 0 to 30 points. A high score indicates good cognitive functioning. A score of 26 and above is considered normal.

End point type	Secondary

End point timeframe:

2 weeks

End point values	THN102 Placebo	THN102 200/2	THN102 200/18	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	68	70	72	
Units: score on a scale				
arithmetic mean (standard deviation)	28 (± 2.02)	27.8 (± 2.47)	28.2 (± 1.78)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AE collection through study duration, starts with screening until follow up visit (last phone call), a total of 13 weeks.	
Adverse event reporting additional description:	
Number of participants with spontaneously reported treatment-related adverse events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	THN102 placebo
Reporting group description:	
Dosage A	
Reporting group title	THN102 200/2
Reporting group description:	
Dosage B	
Reporting group title	THN102 200/9
Reporting group description:	
dosage C	

Serious adverse events	THN102 placebo	THN102 200/2	THN102 200/9
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 68 (0.00%)	0 / 72 (0.00%)	1 / 73 (1.37%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 68 (0.00%)	0 / 72 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	THN102 placebo	THN102 200/2	THN102 200/9
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 68 (4.41%)	10 / 72 (13.89%)	22 / 73 (30.14%)
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 68 (0.00%)	2 / 72 (2.78%)	4 / 73 (5.48%)
occurrences (all)	0	2	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 68 (2.94%)	0 / 72 (0.00%)	2 / 73 (2.74%)
occurrences (all)	2	0	2
Chest pain			
subjects affected / exposed	1 / 68 (1.47%)	2 / 72 (2.78%)	1 / 73 (1.37%)
occurrences (all)	1	2	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 68 (0.00%)	2 / 72 (2.78%)	3 / 73 (4.11%)
occurrences (all)	0	2	3
Dry mouth			
subjects affected / exposed	0 / 68 (0.00%)	0 / 72 (0.00%)	3 / 73 (4.11%)
occurrences (all)	0	0	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 68 (0.00%)	1 / 72 (1.39%)	2 / 73 (2.74%)
occurrences (all)	0	1	2
Confusional state			
subjects affected / exposed	0 / 68 (0.00%)	0 / 72 (0.00%)	2 / 73 (2.74%)
occurrences (all)	0	0	2
Nightmare			
subjects affected / exposed	0 / 68 (0.00%)	0 / 72 (0.00%)	2 / 73 (2.74%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 68 (0.00%)	2 / 72 (2.78%)	0 / 73 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 72 (1.39%)	3 / 73 (4.11%)
occurrences (all)	0	1	3

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