Clinical trial results:
A Phase 2, single-masked, multicentre study to evaluate the safety and efficacy of 2 dose levels of THR-317 for the treatment of diabetic macular oedema (DME)

Summary

EudraCT number	2016-002100-25
Trial protocol	HU CZ SK
Global end of trial date	11 April 2018

Results information

Result version number	v1 (current)
This version publication date	31 March 2019
First version publication date	31 March 2019

Trial information

Trial identification

Sponsor protocol code	THR-317-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03071068
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ThromboGenics NV
Sponsor organisation address	Gaston Geenslaan 1, Leuven, Belgium, 3001
Public contact	Global Clinical Development, ThromboGenics NV, 32 16751310, info@oxurion.com
Scientific contact	Global Clinical Development, ThromboGenics NV, 32 16751310, info@oxurion.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	01 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 April 2018
Global end of trial reached?	Yes
Global end of trial date	11 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of 3 intravitreal injections of 2 dose levels of THR-317 (4mg or 8mg) and to assess its efficacy in improving best-corrected visual acuity (BCVA) and reducing central subfield thickness (CST), in subjects with centre-involved DME

Protection of trial subjects:

All study procedures, including the intravitreal injections, were performed by qualified and trained personnel. Only eligible subjects were enrolled in the study and only subjects who did not meet any withdrawal criteria received repeat injections. All subjects were supervised in the immediate post-injection period with appropriate medical treatment readily available. Subjects were followed up for 3 months after the last intravitreal injection. Adverse events were recorded throughout the study period. At each study visit, a full ophthalmic examination and BCVA assessment was performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 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	Hungary: 11
Country: Number of subjects enrolled	Slovakia: 18
Country: Number of subjects enrolled	Czech Republic: 20
Worldwide total number of subjects	49
EEA total number of subjects	49

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	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Before enrolment in the study, a Screening Visit took place during which in- and exclusion criteria were checked.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	THR-317 4mg

Arm description:

3 intravitreal injections of THR-317 4mg approximately 1 month apart

Arm type	Experimental
Investigational medicinal product name	THR-317 4mg
Investigational medicinal product code	THR-317
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

3 intravitreal injections of THR-317 4mg approximately 1 month apart

Arm title	THR-317 8mg

Arm description:

3 intravitreal injections of THR-317 8mg approximately 1 month apart

Arm type	Experimental
Investigational medicinal product name	THR-317 8mg
Investigational medicinal product code	THR-317
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

3 intravitreal injections of THR-317 8mg approximately 1 month apart

Number of subjects in period 1	THR-317 4mg	THR-317 8mg
Started	24	25
Completed	23	25
Not completed	1	0
Consent withdrawn by subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	THR-317 4mg
Reporting group description:	
3 intravitreal injections of THR-317 4mg approximately 1 month apart	
Reporting group title	THR-317 8mg
Reporting group description:	
3 intravitreal injections of THR-317 8mg approximately 1 month apart	

Reporting group values	THR-317 4mg	THR-317 8mg	Total
Number of subjects	24	25	49
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 Units: years			
arithmetic mean	62.8	65.8	
standard deviation	± 8.40	± 8.61	-
Gender categorical Units: Subjects			
Female	12	14	26
Male	12	11	23

End points

End points reporting groups

Reporting group title	THR-317 4mg
Reporting group description:	
3 intravitreal injections of THR-317 4mg approximately 1 month apart	
Reporting group title	THR-317 8mg
Reporting group description:	
3 intravitreal injections of THR-317 8mg approximately 1 month apart	

Primary: Incidence of acute (up to the 7 day follow-up visit) ocular (serious) adverse events ([S]AEs) in the study eye, after each injection and across injections per subject

End point title	Incidence of acute (up to the 7 day follow-up visit) ocular (serious) adverse events ([S]AEs) in the study eye, after each injection and across injections per subject[1]
End point description:	
End point type	Primary
End point timeframe:	
up to 7-day follow-up visit after each injection	

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: The scope of the primary endpoint was descriptive, no statistical hypothesis test was performed.

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: subjects				
after the first injection	0	1		
after the second injection	3	1		
after the third injection	0	2		
across injections	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of systemic and ocular (S)AEs up to the 30 day follow-up visit, after each injection and across injections per subject

End point title	Incidence of systemic and ocular (S)AEs up to the 30 day follow-up visit, after each injection and across injections per subject
End point description:	
End point type	Secondary

End point timeframe:
up to 30-day follow-up visit after each injection

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: subjects				
after the first injection	3	3		
after the second injection	5	3		
after the third injection	3	4		
across injections	9	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of systemic and ocular (S)AEs from first injection up to Day 90 and up to Day 150

End point title	Incidence of systemic and ocular (S)AEs from first injection up to Day 90 and up to Day 150

End point description:

End point type	Secondary

End point timeframe:
from first injection, up to Day 90 and up to Day 150

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: subjects				
from first injection up to Day 90	9	9		
from first injection up to Day 150	9	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a loss of ≥ 15, ≥ 10 or ≥ 5 ETDRS letters in BCVA from baseline by study visit

End point title	Number of subjects with a loss of ≥ 15, ≥ 10 or ≥ 5 ETDRS letters in BCVA from baseline by study visit

End point description:

End point type	Secondary

End point timeframe:

at Day 150

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: subjects				
loss of ≥ 15 ETDRS letters in BCVA from Baseline	0	1		
loss of ≥ 10 ETDRS letters in BCVA from Baseline	1	1		
loss of ≥ 5 ETDRS letters in BCVA from Baseline	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with an acute loss (up to the 7 day follow-up visit) of ≥ 15, ≥ 10 or ≥ 5 ETDRS letters in BCVA after the first injection

End point title	Number of subjects with an acute loss (up to the 7 day follow-up visit) of ≥ 15, ≥ 10 or ≥ 5 ETDRS letters in BCVA after the first injection

End point description:

End point type	Secondary

End point timeframe:

after the first injection

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: subjects				
acute loss of ≥ 15 ETDRS letters in BCVA	0	0		
acute loss of ≥ 10 ETDRS letters in BCVA	0	0		
acute loss of ≥ 5 ETDRS letters in BCVA	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with an acute loss (up to the 7 day follow-up visit) of ≥ 15, ≥ 10 or ≥ 5 ETDRS letters in BCVA after the second injection

End point title	Number of subjects with an acute loss (up to the 7 day follow-up visit) of ≥ 15, ≥ 10 or ≥ 5 ETDRS letters in BCVA after the second injection

End point description:

End point type	Secondary

End point timeframe:

after the second injection

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: subjects				
acute loss of ≥ 15 ETDRS letters in BCVA	0	0		
acute loss of ≥ 10 ETDRS letters in BCVA	0	0		
acute loss of ≥ 5 ETDRS letters in BCVA	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with an acute loss (up to the 7 day follow-up visit) of ≥ 15, ≥ 10 or ≥ 5 ETDRS letters in BCVA after the third injection

End point title	Number of subjects with an acute loss (up to the 7 day follow-up visit) of ≥ 15, ≥ 10 or ≥ 5 ETDRS letters in BCVA after the third injection

End point description:

End point type	Secondary

End point timeframe:

after the third injection

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: subjects				
acute loss of ≥ 15 ETDRS letters in BCVA	0	0		
acute loss of ≥ 10 ETDRS letters in BCVA	0	0		
acute loss of ≥ 5 ETDRS letters in BCVA	1	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a ≥ 15 ETDRS letters gain in BCVA from baseline or ≥ 83 ETDRS letters, by study visit

End point title	Number of subjects with a ≥ 15 ETDRS letters gain in BCVA from baseline or ≥ 83 ETDRS letters, by study visit

End point description:

End point type	Secondary

End point timeframe:

at Day 90

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: subjects	1	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in BCVA, by study visit

End point title	Mean change from baseline in BCVA, by study visit

End point description:

End point type	Secondary

End point timeframe:

at Day 90

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: ETDRS letters				
arithmetic mean (confidence interval 95%)	3.2 (0.4 to 6.0)	6.8 (2.9 to 10.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in CST, by study visit, based on SD-OCT

End point title	Mean change from baseline in CST, by study visit, based on SD-OCT

End point description:

End point type	Secondary

End point timeframe:

at Day 90

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: µm				
arithmetic mean (confidence interval 95%)	-19.0 (-56.9 to 18.9)	-30.3 (-64.3 to 3.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects withdrawn from repeat injection

End point title	Number of subjects withdrawn from repeat injection

End point description:

End point type	Secondary

End point timeframe:

prior to the second injection and prior to the third injection

End point values	THR-317 4mg	THR-317 8mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: subjects				
prior to the second injection	1	0		
prior to the third injection	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first injection up to Day 150	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1
Reporting groups	
Reporting group title	THR-317 4mg
Reporting group description: 3 intravitreal injections of THR-317 4mg approximately 1 month apart	
Reporting group title	THR-317 8mg
Reporting group description: 3 intravitreal injections of THR-317 8mg approximately 1 month apart	

Serious adverse events	THR-317 4mg	THR-317 8mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 24 (4.17%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	THR-317 4mg	THR-317 8mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 24 (16.67%)	3 / 25 (12.00%)	
Eye disorders			
Visual Impairment			
subjects affected / exposed	2 / 24 (8.33%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	1 / 25 (4.00%) 1	
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	2 / 25 (8.00%) 2	

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