Clinical trial results:
A Phase 2, randomised, single-masked, active-controlled, multicentre study to evaluate the efficacy and safety of intravitreal THR-317 administered in combination with ranibizumab, for the treatment of diabetic macular oedema (DME)

Summary

EudraCT number	2017-003897-15
Trial protocol	FR GB SK ES DE BE
Global end of trial date	18 July 2019

Results information

Result version number	v1 (current)
This version publication date	25 July 2020
First version publication date	25 July 2020

Trial information

Trial identification

Sponsor protocol code	THR-317-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03499223
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Oxurion NV
Sponsor organisation address	Gaston Geenslaan 1, Leuven, Belgium, 3001
Public contact	Global Clinical Development, Oxurion NV, 32 16751310, info@oxurion.com
Scientific contact	Global Clinical Development, Oxurion 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	02 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 July 2019
Global end of trial reached?	Yes
Global end of trial date	18 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of THR-317 administered in combination with ranibizumab, in subjects with central-involved DME (CI-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 study treatment. All subjects were supervised in the immediate post-treatment period with appropriate medical treatment readily available. Subjects were followed for 3 months after the last study treatment. Adverse events were recorded throughout the study period. At each study visit, a full ophthalmic examination and BCVA assessment were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 April 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	Slovakia: 26
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 6
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	34
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a Screening visit during which in- and exclusion criteria were checked

Period 1

Period 1 title	Overall Trial (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	Ranibizumab + THR-317

Arm description:

Subjects received intravitreal ranibizumab in combination with intravitreal THR-317

Arm type	Experimental
Investigational medicinal product name	Ranibizumab 0.5mg
Investigational medicinal product code	Ranibizumab
Other name	Lucentis
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

intravitreal ranibizumab 0.5mg at Day 0, Month 1 and Month 2

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:

intravitreal THR-317 8mg at Day 0, Month 1 and Month 2

Arm title	Sham + ranibizumab

Arm description:

Subjects received a sham injection in combination with intravitreal ranibizumab

Arm type	Active comparator
Investigational medicinal product name	Ranibizumab 0.5mg
Investigational medicinal product code	Ranibizumab
Other name	Lucentis
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

intravitreal ranibizumab 0.5mg at Day 0, Month 1 and Month 2

Number of subjects in period 1	Ranibizumab + THR-317	Sham + ranibizumab
Started	47	23
Completed	44	21
Not completed	3	2
Adverse event, serious fatal	-	1
Consent withdrawn by subject	2	-
Adverse event, non-fatal	-	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Ranibizumab + THR-317
Reporting group description:	
Subjects received intravitreal ranibizumab in combination with intravitreal THR-317	
Reporting group title	Sham + ranibizumab
Reporting group description:	
Subjects received a sham injection in combination with intravitreal ranibizumab	

Reporting group values	Ranibizumab + THR-317	Sham + ranibizumab	Total
Number of subjects	47	23	70
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)	24	10	34
From 65-84 years	23	13	36
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	63.9	64.0	
standard deviation	± 10.64	± 8.94	-
Gender categorical Units: Subjects			
Female	14	8	22
Male	33	15	48

End points

End points reporting groups

Reporting group title	Ranibizumab + THR-317
Reporting group description:	
Subjects received intravitreal ranibizumab in combination with intravitreal THR-317	
Reporting group title	Sham + ranibizumab
Reporting group description:	
Subjects received a sham injection in combination with intravitreal ranibizumab	

Primary: Change from Baseline in best-corrected visual acuity (BCVA)

End point title	Change from Baseline in best-corrected visual acuity (BCVA)[1]
End point description:	
End point type	Primary
End point timeframe:	
Day 84 (Month 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: No inferential statistics to compare treatment arms was performed

End point values	Ranibizumab + THR-317	Sham + ranibizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	22		
Units: ETDRS letters				
arithmetic mean (standard deviation)	8.7 (± 6.83)	8.2 (± 5.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of systemic and ocular (serious) adverse events, from first administration of study treatment up to the end of the study

End point title	Incidence of systemic and ocular (serious) adverse events, from first administration of study treatment up to the end of the study
End point description:	
End point type	Secondary
End point timeframe:	
From first administration of study treatment up to end of study	

End point values	Ranibizumab + THR-317	Sham + ranibizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	23		
Units: subjects	33	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in BCVA, by study visit

End point title	Change from Baseline in BCVA, by study visit

End point description:

End point type	Secondary

End point timeframe:

Month 5

End point values	Ranibizumab + THR-317	Sham + ranibizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	21		
Units: ETDRS letters				
arithmetic mean (standard deviation)	7.1 (± 8.20)	8.0 (± 4.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in central subfield thickness (CST), based on spectral domain optical coherence tomography (SD-OCT), as assessed by the central reading centre (CRC), by study visit

End point title	Change from Baseline in central subfield thickness (CST), based on spectral domain optical coherence tomography (SD-OCT), as assessed by the central reading centre (CRC), by study visit

End point description:

End point type	Secondary

End point timeframe:

Day 84 (Month 3)

End point values	Ranibizumab + THR-317	Sham + ranibizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	22		
Units: µm				
arithmetic mean (standard deviation)	-114.1 (± 112.87)	-105.9 (± 116.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Withdrawal from repeat study treatment and reason for withdrawal

End point title	Withdrawal from repeat study treatment and reason for withdrawal

End point description:

End point type	Secondary

End point timeframe:

Prior to the second study treatment and prior to the third study treatment

End point values	Ranibizumab + THR-317	Sham + ranibizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	23		
Units: subjects				
Prior to the second study treatment	1	1		
Prior to the third study treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first administration of study treatment up to end of study	
Adverse event reporting additional description:	
Reported adverse events include all adverse events (including study eye and non-study eye adverse events)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Ranibizumab + THR-317
Reporting group description:	
Subjects received intravitreal ranibizumab in combination with intravitreal THR-317	
Reporting group title	Sham + ranibizumab
Reporting group description:	
Subjects received a sham injection in combination with intravitreal ranibizumab	

Serious adverse events	Ranibizumab + THR-317	Sham + ranibizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 47 (6.38%)	1 / 23 (4.35%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	1 / 47 (2.13%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
VIth Nerve Paresis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes Mellitus			
subjects affected / exposed	1 / 47 (2.13%)	0 / 23 (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	Ranibizumab + THR-317	Sham + ranibizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 47 (40.43%)	8 / 23 (34.78%)	
Investigations			
Intraocular Pressure Increased			
subjects affected / exposed	7 / 47 (14.89%)	1 / 23 (4.35%)	
occurrences (all)	9	2	
Eye disorders			
Cataract			
subjects affected / exposed	3 / 47 (6.38%)	1 / 23 (4.35%)	
occurrences (all)	4	1	
Conjunctival Haemorrhage			
subjects affected / exposed	3 / 47 (6.38%)	1 / 23 (4.35%)	
occurrences (all)	3	1	
Diabetic Retinopathy			
subjects affected / exposed	4 / 47 (8.51%)	0 / 23 (0.00%)	
occurrences (all)	7	0	
Eye Pain			
subjects affected / exposed	3 / 47 (6.38%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Retinal Haemorrhage			
subjects affected / exposed	1 / 47 (2.13%)	2 / 23 (8.70%)	
occurrences (all)	1	2	
Visual Acuity Reduced			
subjects affected / exposed	5 / 47 (10.64%)	2 / 23 (8.70%)	
occurrences (all)	8	3	
Diabetic Retinal Oedema			
subjects affected / exposed	4 / 47 (8.51%)	3 / 23 (13.04%)	
occurrences (all)	4	3	
Infections and infestations			

Influenza subjects affected / exposed occurrences (all)	2 / 47 (4.26%) 2	2 / 23 (8.70%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2018	Addition of visit at Month 4 for better characterisation of the response to treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported