Clinical trial results:
Treatment of retinal angiomatous proliferation lesions due to age-related macular degeneration with ranibizumab (Lucentis®) and photodynamic therapy with verteporfin (Visudyne®)

Summary

EudraCT number	2006-004367-57
Trial protocol	AT
Global end of trial date	31 July 2009

Results information

Result version number	v1 (current)
This version publication date	13 July 2024
First version publication date	13 July 2024
Summary attachment (see zip file)	Publication (Acta Ophthalmologica - 2013 - Seidel - Combination treatment of photodynamic therapy with verteporfin and intravitreal.pdf)

Trial information

Trial identification

Sponsor protocol code	n/a

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University Graz Deparment of ophthalmology
Sponsor organisation address	Auenbruggerplatz 4, Graz, Austria,
Public contact	Anton Haas, Medical University Graz Deparment of ophthalmology, anton.haas@medunigraz.at
Scientific contact	Anton Haas, Medical University Graz Deparment of ophthalmology, anton.haas@medunigraz.at

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 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2009
Global end of trial reached?	Yes
Global end of trial date	31 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This case-series is designed to evaluate the safety and efficacy of intravitreal ranibizumab (Lucentis®) used in combination with verteporfin photodynamic therapy (Visudyne®) in the treatment of sub- and juxtafoveal retinal angiomatous proliferations (RAP) secondary to AMD.

Protection of trial subjects:

The study was approved by the local ethics committee and was conducted in accordance with the Declaration of Helsinki. All patients provided written consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2008
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	Austria: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	0
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The present prospective study comprised 15 patients with RAP, who were included between July 2008 and July 2009 at the Department of Ophthalmology of the Medical University of Graz /Austria.

Pre-assignment

Screening details:

Inclusion criteria for the study were the presence of treatment-naıve RAP at any stage and a best-corrected visual acuity (BCVA) in
the affected eye between 24 and 73 letters. RAP lesions only less or equal to 5400 lm in greatest linear dimension and and lying within 200 µm of the geometric centre of the foveal avascular zone were included.

Pre-assignment period milestones

Number of subjects started	15
Number of subjects completed	15

Period 1

Period 1 title	Baseline Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Patients wit retinal angiomatous proliferation

Arm description:

All patients who met the study criteria and consented to participate in the study were scheduled for baseline
examination. Within 7 days after examination, every patient received verteporfin photodynamic therapy according to the standard protocol as
described by the TAP study group (1999). This was followed by an intravitreal injection of 0.5-mg ranibizumab the next day. The regimen included additional injections of
0.5-mg ranibizumab both 1 and 2 months after the first treatment. After that, patients received intravitreal ranibizumab injections according to
a PRN regime.

Arm type	Experimental
Investigational medicinal product name	Verteporfin photodynamic therapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Verteporfin photodynamic therapy according to the standard protocol as described by the TAP study group (1999)

Investigational medicinal product name	Ranibizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Intravitreal use

Dosage and administration details:

3 intravitreal injection of 0.5-mg ranibizumab at baseline, month 1 and month 2, after that PRN regime till month 12

Number of subjects in period 1	Patients wit retinal angiomatous proliferation
Started	15
Completed	14
Not completed	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Baseline Period
Reporting group description: n/a	

Reporting group values	Baseline Period	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
From 65-84 years	15	15	
Gender categorical Units: Subjects			
Female	10	10	
Male	5	5	
RAP classification Units: Subjects			
Stage I	7	7	
Stage IIa	4	4	
Stage IIb	4	4	
Stage III	0	0	
BCVA - EDTRS letters			
Best Corrected Visual Acuity with Early Treatment Diabetic Retinopathy Study visual acuity chart testing			
Units: letters			
arithmetic mean	58.1		
standard deviation	± 13.2	-	
Foveal thickness			
Foveal thickness measurement with optical cohernece tomography			
Units: µm			
arithmetic mean	355.9		
standard deviation	± 83	-	

End points

End points reporting groups

Reporting group title	Patients wit retinal angiomatous proliferation

Reporting group description:

All patients who met the study criteria and consented to participate in the study were scheduled for baseline
examination. Within 7 days after examination, every patient received verteporfin photodynamic therapy according to the standard protocol as
described by the TAP study group (1999). This was followed by an intravitreal injection of 0.5-mg ranibizumab the next day. The regimen included additional injections of
0.5-mg ranibizumab both 1 and 2 months after the first treatment. After that, patients received intravitreal ranibizumab injections according to
a PRN regime.

Primary: Change in BCVA between baseline and month 12

End point title	Change in BCVA between baseline and month 12[1]

End point description:

The primary end-point was the change in BCVA between baseline and month 12.

End point type	Primary

End point timeframe:

Baseline, Month 12

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: Single arm study, not possible to enter statistical analysis in the system.

See summary attachment for statistical analysis

End point values	Patients wit retinal angiomatous proliferation			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: BCVA letters				
arithmetic mean (standard deviation)	8.7 (± 11.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in BCVA between baseline and month 6

End point title	Change in BCVA between baseline and month 6

End point description:

Secondary end-points included the mean change in BCVA between baseline and month 6

End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	Patients wit retinal angiomatous proliferation			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: BCVA Letters				
arithmetic mean (standard deviation)	9.2 (± 8.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with a gain of >5 letters, >10 letters and >15 letters at month 6

End point title	Proportion of patients with a gain of >5 letters, >10 letters and >15 letters at month 6

End point description:

Proportion of patients with a gain of 5, 10 or 15 letters

End point type	Secondary

End point timeframe:

6 month

End point values	Patients wit retinal angiomatous proliferation			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: No. of patients				
>5 letters	12			
>10 letters	9			
>15 letters	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with a gain of >5 letters, >10 letters and >15 letters at month 12

End point title	Proportion of patients with a gain of >5 letters, >10 letters and >15 letters at month 12

End point description: Proportion of patients with a gain of 5, 10 or 15 letters at month 12	
End point type	Secondary
End point timeframe: Month 12	

End point values	Patients wit retinal angiomatous proliferation			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: No. of patients				
>5 letters	9			
>10 letters	7			
>15 letters	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean injections month 6 and month 12

End point title	Mean injections month 6 and month 12
End point description: Total number of treatments, mean injections in No. (min/max)	
End point type	Secondary
End point timeframe: Month 6, Month 12	

End point values	Patients wit retinal angiomatous proliferation			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: Mean injections				
arithmetic mean (full range (min-max))				
Month 6	3.3 (3 to 4)			
Month 12	4.8 (3 to 8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with a loss of 15 letters at month 6 and month 12

End point title	Proportion of patients with a loss of 15 letters at month 6 and month 12

End point description:

Proportion of patients with a loss of 15 letters at month 6 and month 12

End point type	Secondary

End point timeframe:

Month 6 and Month 12

End point values	Patients wit retinal angiomatous proliferation			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: letters				
Month 6	0			
Month 12	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Time to first retreatment following the initial loading dose

End point title	Mean Time to first retreatment following the initial loading dose

End point description:

Mean Time to first retreatment following the initial loading dose

End point type	Secondary

End point timeframe:

monthly

End point values	Patients wit retinal angiomatous proliferation			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: month				
arithmetic mean (full range (min-max))	3.7 (3 to 7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change in foveal thickness on OCT at month 6 and month 12

End point title	Mean change in foveal thickness on OCT at month 6 and month 12

End point description:

Mean change in foveal thickness on OCT

End point type	Secondary

End point timeframe:

monthly

End point values	Patients wit retinal angiomatous proliferation			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: µm				
arithmetic mean (standard deviation)				
Month 6	201.6 (± 53)			
Month 12	211.3 (± 82.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 12 months	
Adverse event reporting additional description: n/a	
Assessment type	Systematic

Dictionary used	
Dictionary name	n/a
Dictionary version	n/a

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

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: no AE or SAE occurred

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