



Clinical trial results: Individualizing therapy for neovascular age-related macular degeneration with aflibercept

Summary

EudraCT number	2014-002381-73
Trial protocol	GB
Global end of trial date	26 January 2018

Results information

Result version number	v1 (current)
This version publication date	20 November 2019
First version publication date	20 November 2019

Trial information

Trial identification

Sponsor protocol code	PATP1023
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02441816
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Moorfields Eye Hospital NHS Foundation Trust
Sponsor organisation address	162 City Road, London, United Kingdom, EC1V 2PD
Public contact	Tania West, Moorfields Eye Hospital, +44 02072533411,
Scientific contact	Tania West, Moorfields Eye Hospital, +44 02072533411, moorfields.resadmin@nhs.net

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	17 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 January 2018
Global end of trial reached?	Yes
Global end of trial date	26 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Our primary aim is to estimate the average change in vision function in eyes treated with aflibercept.

Protection of trial subjects:

In line with standard care, topical anaesthetic was used prior to aflibercept injection treatment. Non-study eye was treated in accordance with NHS standards of care and was monitored throughout the study.

Background therapy:

Treatment to the non-study eye could continue throughout the study. Patients had not received prior treatment for wet age-related macular degeneration in the study eye.

Evidence for comparator:

The study drug was not compared to another drug during this trial

Actual start date of recruitment	01 December 2014
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	United Kingdom: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	3
From 65 to 84 years	39

85 years and over	8
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Subject disposition

Recruitment

Recruitment details:

Between 24 November 2014 to 17 March 2016 we recruited 50 patients with wet age-related macular degeneration to the study. The patients were recruited from clinics at Moorfields Eye Hospital.

Pre-assignment

Screening details:

84 patients were potentially suitable for the study. 16 refused to take part, 68 patients were screened for the study.

Period 1

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

Blinding implementation details:
not blinded

Arms

Arm title	aflibercept treatment
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Arm description:

Intravitreal aflibercept for wet (neovascular) age-related macular degeneration

Arm type	Experimental
Investigational medicinal product name	aflibercept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Eylea solution is supplied in a vial (40mg/ml). Each vial contains 100 microlitres, equivalent to 4 mg aflibercept. This provides a usable amount to deliver a single dose of 50 microlitres containing 2 mg aflibercept. The dose used in this trial will be 0.05ml (2mg) per intravitreal injection.

Number of subjects in period 1	aflibercept treatment
Started	50
Completed	43
Not completed	7
Consent withdrawn by subject	7

Baseline characteristics

Reporting groups

Reporting group title	overall trial
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	50	50	
Age categorical			
all patients were over 50 years of age			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	3	
From 65-84 years	39	39	
85 years and over	8	8	
Gender categorical			
Units: Subjects			
Female	35	35	
Male	15	15	

End points

End points reporting groups

Reporting group title	aflibercept treatment
Reporting group description:	
Intravitreal aflibercept for wet (neovascular) age-related macular degeneration	

Primary: Mean change in visual acuity at 24 months from baseline

End point title	Mean change in visual acuity at 24 months from baseline ^[1]
End point description:	
Mean change in visual acuity at 24 months from baseline	
End point type	Primary
End point timeframe:	
24 months	

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: there was no comparator arm so no statistical test was carried out

End point values	aflibercept treatment			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: ETDRS letters				
arithmetic mean (standard deviation)	6.4 (± 11.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

SAE/SUSAR reporting as per the protocol

Assessment type	Systematic
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Dictionary used

Dictionary name	bayer plc
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Dictionary version	2015
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Reporting groups

Reporting group title	aflibercept treated patients
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Reporting group description: -

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 non-serious adverse events have been recorded. All events recorded are serious adverse events

Serious adverse events	aflibercept treated patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 50 (30.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian cancer recurrent			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
cerebrovascular accident	Additional description: occipital lobe infact		
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Hernia			

subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Endometrial hypertrophy			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
broken leg			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
collapse			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia	Additional description: required blood transfusion		
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Fall	Additional description: patient admitted to hospital with fall. Made a full recovery		
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

planned cataract surgery subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	2 / 50 (4.00%) 0 / 2 0 / 0		
Gastrointestinal disorders Colon cancer recurrent subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 50 (2.00%) 0 / 1 0 / 0		
Hepatobiliary disorders Cholecystectomy subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 50 (2.00%) 0 / 1 0 / 0		
Musculoskeletal and connective tissue disorders Hip fracture subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 50 (2.00%) 0 / 1 0 / 0		
Knee arthroplasty subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 50 (2.00%) 0 / 1 0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	aflibercept treated patients		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 50 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 December 2014	Protocol updated as Levofloxacin no longer standard of care
07 December 2015	<p>Update to eligibility criteria for study eyes - clarification of one of the inclusion criteria relating to the size of the wet AMD lesion.</p> <p>Addition of several secondary and exploratory outcomes to the protocol.</p> <p>Clarification of when optometrists may wish to re-refract patients at an un-refracted vision study visit.</p> <p>In line with standard care at our Trust, the option to use nursing staff for delivery of Eylea intravitreal injections has been added to the protocol.</p> <p>Clarification on the reporting requirements for systemic and ocular events in the safety section of the protocol.</p> <p>Change to the trial specific monitoring plan.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported