



Clinical trial results:

Treating neovascular age-related Macular Degeneration with Aflibercept: A multi-centre randomized controlled trial comparing Standard Care with an individualised Treat and Extend regimen.

Summary

EudraCT number	2015-002302-36
Trial protocol	GB
Global end of trial date	26 February 2021

Results information

Result version number	v1 (current)
This version publication date	01 March 2022
First version publication date	01 March 2022

Trial information

Trial identification

Sponsor protocol code	MATE2015
-----------------------	----------

Additional study identifiers

ISRCTN number	ISRCTN58955026
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	York and Scarborough Teaching Hospital NHS Foundation Trust
Sponsor organisation address	Wigginton Road, York, United Kingdom, YO31 8HE
Public contact	Deborah Phillips, York and Scarborough Teaching Hospital NHS Foundation Trust, 44 01904725123, deborah.phillips@york.nhs.uk
Scientific contact	Deborah Phillips, York and Scarborough Teaching Hospital NHS Foundation Trust, 44 01904725123, deborah.phillips@york.nhs.uk

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	26 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 February 2021
Global end of trial reached?	Yes
Global end of trial date	26 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Outcome 1. The main objective of the study is to determine if a multicentered phase 3 randomised control trial comparing two treatment regimens of Aflibercept for neovascular age related macular degeneration be safely and effectively conducted and delivered.

Outcome 2. Long term (4 years) changes in visual acuity and the central thickness of the retina. Also focusing on the number of injections and visits in each group

Protection of trial subjects:

No trial specific measures were required for trial subject protection beyond those of standard NHS care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 40
Worldwide total number of subjects	40
EEA total number of subjects	0

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	29
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

Recruitment took place across 6 NHS Trusts in England. between December 2015 and January 2017.

Pre-assignment

Screening details:

93 participants were approached to take part

49 excluded: 10 didn't meet inclusion criteria, 29 declined to participate, 10 excluded for other reasons.

44 randomised evenly but 4 withdrawn by Sponsor as eligibility couldn't be confirmed so weren't included in analysis.

40 participants included in final analysis.

Period 1

Period 1 title	MATE study
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor ^[1]

Blinding implementation details:

Optometrists assessing visual acuity were blinded to the study arm

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard Care

Arm description:

Receive standard care treatment with Aflibercept for neovascular AMD as recommended by NICE in the NHS Ophthalmology clinics

Arm type	Active comparator
Investigational medicinal product name	Eylea 40 mg/ml solution for injection in a vial.
Investigational medicinal product code	
Other name	Aflibercept
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2mg (0.05mL) of aflibercept administered by intravitreal injection at specified intervals during the trial. Should not be administered more frequently than every 28 days.

Arm title	Treat and Extend
------------------	------------------

Arm description:

Individualised treat and extend regimen

Arm type	Experimental
Investigational medicinal product name	Eylea 40 mg/ml solution for injection in a vial.
Investigational medicinal product code	
Other name	Aflibercept
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2mg (0.05mL) of aflibercept administered by intravitreal injection at specified intervals during the trial. Should not be administered more frequently than every 28 days.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The optometrists assessing the participants visual acuity were blinded to the study arm to avoid unintentional bias when performing assessments.

Number of subjects in period 1	Standard Care	Treat and Extend
Started	20	20
12 Months	19	20
Completed	16	18
Not completed	4	2
Consent withdrawn by subject	3	1
Lost to follow-up due to death	1	1

Period 2

Period 2 title	MATE 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Blinding implementation details: Optometrist blinded to treatment allocation.	

Arms

Arm title	Extension
Arm description: All participants who consented to the extension study to evaluate the long term outcomes and burden on patients and services	
Arm type	Single Arm
Investigational medicinal product name	Eylea 40 mg/ml solution for injection in a vial.
Investigational medicinal product code	
Other name	Aflibercept
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2mg (0.05mL) of aflibercept administered by intravitreal injection at specified intervals during the trial. Should not be administered more frequently than every 28 days.

Number of subjects in period 2^[2]	Extension
Started	26
36 Month	24
Completed	21
Not completed	5
Consent withdrawn by subject	1
Physician decision	2
Lost to follow-up due to death	2

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants in the preceding period were asked to consent to continue into the extension study for a further 2 years.

Only those who consented to continue were included in period 2.

Baseline characteristics

Reporting groups

Reporting group title	Standard Care
Reporting group description: Receive standard care treatment with Aflibercept for neovascular AMD as recommended by NICE in the NHS Ophthalmology clinics	
Reporting group title	Treat and Extend
Reporting group description: Individualised treat and extend regimen	

Reporting group values	Standard Care	Treat and Extend	Total
Number of subjects	20	20	40
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			
Baseline demographics			
Units: years			
arithmetic mean	78.98	78.4	
standard deviation	± 7.7	± 6.5	-
Gender categorical			
Units: Subjects			
Female	11	11	22
Male	9	9	18
VA Baseline			
Best corrected visual acuity at baseline			
Units: ETDRS letters			
arithmetic mean	60.8	63.6	
standard deviation	± 12.5	± 10.0	-
CRT Baseline			
Central retinal Thickness			
Units: µm			
arithmetic mean	414.3	406.6	
standard deviation	± 144.5	± 114.6	-
MacDQoL Baseline			
MacDQoL Average weighted impact score at baseline			
Units: AWI			
arithmetic mean	-2.4	-2.5	
standard deviation	± 1.7	± 2.0	-

MacTSQ Baseline			
MacTSQ total score			
Units: MacTSQ single scale score			
arithmetic mean	66.9	64.2	
standard deviation	± 4.5	± 9.2	-

Subject analysis sets

Subject analysis set title	Extension
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who consented to continue into the MATE extension at their 24 month visit.	

Reporting group values	Extension		
Number of subjects	26		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Baseline demographics			
Units: years			
arithmetic mean	77.1		
standard deviation	± 6.6		
Gender categorical			
Units: Subjects			
Female	15		
Male	11		
VA Baseline			
Best corrected visual acuity at baseline			
Units: ETDRS letters			
arithmetic mean	60.7		
standard deviation	± 11.4		
CRT Baseline			
Central retinal Thickness			
Units: µm			
arithmetic mean	423.7		
standard deviation	± 134.2		
MacDQoL Baseline			
MacDQoL Average weighted impact score at baseline			
Units: AWI			
arithmetic mean	-2.1		
standard deviation	± 1.7		

MacTSQ Baseline			
MacTSQ total score			
Units: MacTSQ single scale score			
arithmetic mean	67.2		
standard deviation	± 4.5		

End points

End points reporting groups

Reporting group title	Standard Care
Reporting group description: Receive standard care treatment with Aflibercept for neovascular AMD as recommended by NICE in the NHS Ophthalmology clinics	
Reporting group title	Treat and Extend
Reporting group description: Individualised treat and extend regimen	
Reporting group title	Extension
Reporting group description: All participants who consented to the extension study to evaluate the long term outcomes and burden on patients and services	
Subject analysis set title	Extension
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who consented to continue into the MATE extension at their 24 month visit.	

Primary: Change in ETDRS visual acuity at 36 months

End point title	Change in ETDRS visual acuity at 36 months
End point description: Mean change in ETDRS visual acuity at 36 months	
End point type	Primary
End point timeframe: 36 Month Visit data, defined as either the visit occurring immediately after the 3 year anniversary for the participant, or a visit within 7 days of the 3 year anniversary.	

End point values	Extension	Extension		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	22	22		
Units: ETDRS Letters				
arithmetic mean (standard deviation)	-1.1 (\pm 24.3)	-1.1 (\pm 24.3)		

Statistical analyses

Statistical analysis title	Change in ETDRS letters at 36 months
Statistical analysis description: Change in ETDRS visual acuity from baseline at 36 months.	
Comparison groups	Extension v Extension

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.833
Method	Wilcoxon (Mann-Whitney)

Primary: Change in ETDRS visual acuity at 48 months

End point title	Change in ETDRS visual acuity at 48 months
End point description:	
Mean change in ETDRS visual acuity at 48 months	
End point type	Primary
End point timeframe:	
48 Month Visit data, defined as either the visit occurring immediately after the 4 year anniversary for the participant, or a visit within 7 days of the 4 year anniversary.	

End point values	Extension	Extension		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	20	20		
Units: EDTRS letters				
arithmetic mean (standard deviation)	4.5 (± 21.6)	4.5 (± 21.6)		

Statistical analyses

Statistical analysis title	Change in ETDRS letters at 48 months
Statistical analysis description:	
Change in ETDRS visual acuity from baseline at 48 months	
Comparison groups	Extension v Extension
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.212
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - Single arm study

Primary: Patients gaining or losing more than or equal to 15 ETDRS letters at 36 months

End point title	Patients gaining or losing more than or equal to 15 ETDRS letters at 36 months ^[2]
End point description:	
End point type	Primary
End point timeframe:	
36 Month Visit data, defined as either the visit occurring immediately after the 3 year anniversary for	

the participant, or a visit within 7 days of the 3 year anniversary.

Notes:

[2] - 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: Descriptive statistics only for this analysis

End point values	Extension			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Number of patients				
Loss of 15 or more letters	6			
Change of -14 to 14 letters	11			
Gain of 15 or more letters	5			

Statistical analyses

No statistical analyses for this end point

Primary: Patients gaining or losing more than or equal to 15 ETDRS letters at 48 months

End point title	Patients gaining or losing more than or equal to 15 ETDRS letters at 48 months ^[3]
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

48 Month Visit data, defined as either the visit occurring immediately after the 4 year anniversary for the participant, or a visit within 7 days of the 4 year anniversary.

Notes:

[3] - 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: Descriptive statistics only for this analysis

End point values	Extension			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Number of patients				
Loss of 15 or more letters	4			
Change of -14 to 14 letters	8			
Gain of 15 or more letters	8			

Statistical analyses

No statistical analyses for this end point

Primary: Change in CRT at 36 months

End point title	Change in CRT at 36 months
-----------------	----------------------------

End point description:

End point type	Primary
----------------	---------

End point timeframe:

36 Month Visit data, defined as either the visit occurring immediately after the 3 year anniversary for the participant, or a visit within 7 days of the 3 year anniversary.

End point values	Extension	Extension		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	24	24		
Units: μm				
arithmetic mean (standard deviation)	-183.8 (\pm 138.3)	-183.8 (\pm 138.3)		

Statistical analyses

Statistical analysis title	CRT change from baseline at 36 months
----------------------------	---------------------------------------

Statistical analysis description:

Change in CRT from baseline at 36 months

Comparison groups	Extension v Extension
-------------------	-----------------------

Number of subjects included in analysis	48
---	----

Analysis specification	Pre-specified
------------------------	---------------

Analysis type	other ^[4]
---------------	----------------------

P-value	= 183.8
---------	---------

Method	Wilcoxon (Mann-Whitney)
--------	-------------------------

Notes:

[4] - Single arm

Primary: Change in CRT at 48 months

End point title	Change in CRT at 48 months
-----------------	----------------------------

End point description:

End point type	Primary
----------------	---------

End point timeframe:

48 Month Visit data, defined as either the visit occurring immediately after the 4 year anniversary for the participant, or a visit within 7 days of the 4 year anniversary.

End point values	Extension	Extension		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	21	21		
Units: μm				
arithmetic mean (standard deviation)	-134.1 (\pm 152.7)	-134.1 (\pm 152.7)		

Statistical analyses

Statistical analysis title	Change in CRT at 48 months
Statistical analysis description: Change in Central retinal thickness (CRT) from baseline at 48 months	
Comparison groups	Extension v Extension
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	other ^[5]
P-value	= 0.002
Method	Wilcoxon (Mann-Whitney)

Notes:

[5] - Single Arm

Primary: Number of treatments in the study eye at 36 months

End point title	Number of treatments in the study eye at 36 months ^[6]
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

36 Month Visit data, defined as either the visit occurring immediately after the 3 year anniversary for the participant, or a visit within 7 days of the 3 year anniversary.

Notes:

[6] - 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: Descriptive statistics only for this analysis

End point values	Extension			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Treatments				
arithmetic mean (standard deviation)	23.8 (± 5.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of treatments in the study eye at 48 months

End point title	Number of treatments in the study eye at 48 months ^[7]
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

48 Month Visit data, defined as either the visit occurring immediately after the 4 year anniversary for the participant, or a visit within 7 days of the 4 year anniversary.

Notes:

[7] - 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: Descriptive statistics only for this analysis

End point values	Extension			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Treatments				
arithmetic mean (standard deviation)	27.9 (± 8.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of visits for the study eye at 36 months

End point title | Number of visits for the study eye at 36 months^[8]

End point description:

End point type | Primary

End point timeframe:

36 Month Visit data, defined as either the visit occurring immediately after the 3 year anniversary for the participant, or a visit within 7 days of the 3 year anniversary.

Notes:

[8] - 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: Descriptive statistics only for this analysis

End point values	Extension			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Visits				
arithmetic mean (standard deviation)	24.5 (± 4.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of visits for the study eye at 48 months

End point title | Number of visits for the study eye at 48 months^[9]

End point description:

End point type | Primary

End point timeframe:

48 Month Visit data, defined as either the visit occurring immediately after the 4 year anniversary for the participant, or a visit within 7 days of the 4 year anniversary.

Notes:

[9] - 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: Descriptive statistics only for this analysis

End point values	Extension			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Visits				
arithmetic mean (standard deviation)	30.0 (± 6.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Change in Mac DQoL at 36 months

End point title | Change in Mac DQoL at 36 months

End point description:

Mean change in MacDQoL average weighted impact score (AWI)

End point type | Primary

End point timeframe:

36 Month Visit data, defined as either the visit occurring immediately after the 3 year anniversary for the participant, or a visit within 7 days of the 3 year anniversary.

End point values	Extension	Extension		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	23	23		
Units: Mac DQoL score				
arithmetic mean (standard deviation)	-0.2 (± 1.7)	-0.2 (± 1.7)		

Statistical analyses

Statistical analysis title | Change in MacDQoL AWI at 36 months

Statistical analysis description:

Change in MacDQoL Average Weighted Impact Score (AWI) at 36 month visit.

Comparison groups | Extension v Extension

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.375
Method	Wilcoxon (Mann-Whitney)

Primary: Change in Mac DQoL at 48 months

End point title	Change in Mac DQoL at 48 months
End point description:	Mean change in MacDQoL average weighted impact score (AWI)
End point type	Primary
End point timeframe:	48 Month Visit data, defined as either the visit occurring immediately after the 4 year anniversary for the participant, or a visit within 7 days of the 4 year anniversary.

End point values	Extension	Extension		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	22	22		
Units: AWI score				
arithmetic mean (standard deviation)	-0.3 (± 2.1)	-0.3 (± 2.1)		

Statistical analyses

Statistical analysis title	Change in MacDQoL AWI at 48 Months
Statistical analysis description:	Change in MacDQoL Average Weighted Impact Score (AWI) at 48 month visit.
Comparison groups	Extension v Extension
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other ^[10]
P-value	= 0.375
Method	Wilcoxon (Mann-Whitney)

Notes:

[10] - Single Arm

Primary: Change in MacTSQ at 36 months

End point title	Change in MacTSQ at 36 months
End point description:	Mean change in MacTSQ total score
End point type	Primary
End point timeframe:	36 Month Visit data, defined as either the visit occurring immediately after the 3 year anniversary for the participant, or a visit within 7 days of the 3 year anniversary.

End point values	Extension	Extension		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	18	18		
Units: MacTSQ score				
arithmetic mean (standard deviation)	0.9 (\pm 2.8)	0.9 (\pm 2.8)		

Statistical analyses

Statistical analysis title	Change in MacTSQ score at 36 months			
Statistical analysis description:				
Change from baseline in MacTSQ total score at 36 month visit				
Comparison groups	Extension v Extension			
Number of subjects included in analysis	36			
Analysis specification	Pre-specified			
Analysis type	other ^[11]			
P-value	= 0.462			
Method	Wilcoxon (Mann-Whitney)			

Notes:

[11] - Single Arm

Primary: Change in MacTSQ at 48 months

End point title	Change in MacTSQ at 48 months			
End point description:				
Mean change in MacTSQ Total score				
End point type	Primary			
End point timeframe:				
48 Month Visit data, defined as either the visit occurring immediately after the 4 year anniversary for the participant, or a visit within 7 days of the 4 year anniversary.				

End point values	Extension	Extension		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	16	16		
Units: MacTSQ score				
arithmetic mean (standard deviation)	1.2 (\pm 3.6)	1.2 (\pm 3.6)		

Statistical analyses

Statistical analysis title	Change in MacTSQ score at 48 months			
-----------------------------------	-------------------------------------	--	--	--

Statistical analysis description:

Change in MacTSQ total score from baseline at 48 month visit

Comparison groups	Extension v Extension
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other ^[12]
P-value	= 0.232
Method	Wilcoxon (Mann-Whitney)

Notes:

[12] - Single arm

Secondary: Change in ETDRS visual acuity at 12 months

End point title	Change in ETDRS visual acuity at 12 months
-----------------	--

End point description:

Mean Change in ETDRS visual acuity at 12 months

End point type	Secondary
----------------	-----------

End point timeframe:

12 Month Visit data, defined as either the visit occurring immediately after the 1 year anniversary for the participant, or a visit within 7 days of the 1 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	26	
Units: ETDRS Letters				
arithmetic mean (standard deviation)	0.7 (± 18.6)	5.7 (± 15.6)	3.6 (± 5.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ETDRS visual acuity at 24 months

End point title	Change in ETDRS visual acuity at 24 months
-----------------	--

End point description:

Mean change in ETDRS visual acuity at 24 months

End point type	Secondary
----------------	-----------

End point timeframe:

24 Month Visit data, defined as either the visit occurring immediately after the 2 year anniversary for the participant, or a visit within 7 days of the 2 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	26	
Units: ETDRS Letters				
arithmetic mean (standard deviation)	-2.4 (± 23.6)	2.9 (± 19.2)	1.2 (± 21.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Patients gaining or losing more than or equal to 15 ETDRS letters at 12 months

End point title	Patients gaining or losing more than or equal to 15 ETDRS letters at 12 months
End point description:	Percentage of patients gaining or losing more than or equal to 15 ETDRS letters at 12 months
End point type	Secondary
End point timeframe:	12 Month Visit data, defined as either the visit occurring immediately after the 1 year anniversary for the participant, or a visit within 7 days of the 1 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	26	
Units: Number of patients				
Loss of 15 or more letters	5	6	5	
Change of -14 to 14 letters	9	12	13	
Gain or 15 or more letters	5	2	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Patients gaining or losing more than or equal to 15 ETDRS letters at 24 months

End point title	Patients gaining or losing more than or equal to 15 ETDRS letters at 24 months
End point description:	
End point type	Secondary
End point timeframe:	24 Month Visit data, defined as either the visit occurring immediately after the 2 year anniversary for the participant, or a visit within 7 days of the 2 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	26	
Units: Number of patients				
Loss of 15 or more letters	5	2	7	
Change of -14 to 14 letters	9	12	13	
Gain of 15 or more letters	5	6	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in CRT at 12 months

End point title	Change in CRT at 12 months
-----------------	----------------------------

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

12 Month Visit data, defined as either the visit occurring immediately after the 1 year anniversary for the participant, or a visit within 7 days of the 1 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	26	
Units: μm				
arithmetic mean (standard deviation)	-116.5 (\pm 111.2)	-147.8 (\pm 104.0)	-136.5 (\pm 115.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in CRT at 24 months

End point title	Change in CRT at 24 months
-----------------	----------------------------

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

24 Month Visit data, defined as either the visit occurring immediately after the 2 year anniversary for the participant, or a visit within 7 days of the 2 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	26	
Units: µm				
arithmetic mean (standard deviation)	-148.8 (± 122.5)	-164.8 (± 117.8)	-138.6 (± 115.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatments in the study eye at 12 months

End point title | Number of treatments in the study eye at 12 months

End point description:

End point type | Secondary

End point timeframe:

12 Month Visit data, defined as either the visit occurring immediately after the 1 year anniversary for the participant, or a visit within 7 days of the 1 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	26	
Units: Treatments				
arithmetic mean (standard deviation)	8.3 (± 0.7)	9.5 (± 1.8)	9.3 (± 1.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatments in the study eye at 24 months

End point title | Number of treatments in the study eye at 24 months

End point description:

End point type | Secondary

End point timeframe:

24 Month Visit data, defined as either the visit occurring immediately after the 2 year anniversary for the participant, or a visit within 7 days of the 2 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	26	
Units: Treatments				
arithmetic mean (standard deviation)	17.3 (± 2.0)	16.4 (± 3.8)	17.3 (± 2.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of visits for the study eye at 12 months

End point title | Number of visits for the study eye at 12 months

End point description:

End point type | Secondary

End point timeframe:

12 Month Visit data, defined as either the visit occurring immediately after the 1 year anniversary for the participant, or a visit within 7 days of the 1 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	20	26	
Units: Number of Visits				
arithmetic mean (standard deviation)	8.3 (± 0.7)	9.5 (± 1.8)	9.3 (± 1.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of visits for the study eye at 24 months

End point title | Number of visits for the study eye at 24 months

End point description:

End point type | Secondary

End point timeframe:

24 Month Visit data, defined as either the visit occurring immediately after the 2 year anniversary for the participant, or a visit within 7 days of the 2 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	18	26	
Units: Visits				
arithmetic mean (standard deviation)	17.3 (± 2.0)	16.4 (± 3.8)	17.4 (± 2.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Mac DQoL at 12 months

End point title	Change in Mac DQoL at 12 months
End point description:	Mean change in MacDQoL average weighted impact score (AWI)
End point type	Secondary
End point timeframe:	12 Month Visit data, defined as either the visit occurring immediately after the 1 year anniversary for the participant, or a visit within 7 days of the 1 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	19	26	
Units: Mac DQoL				
arithmetic mean (standard deviation)	0.1 (± 1.9)	-1.1 (± 2.1)	0.4 (± 2.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Mac DQoL at 24 months

End point title	Change in Mac DQoL at 24 months
End point description:	Mean change in MacDQoL average weighted impact score (AWI)
End point type	Secondary

End point timeframe:

24 Month Visit data, defined as either the visit occurring immediately after the 2 year anniversary for the participant, or a visit within 7 days of the 2 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	18	26	
Units: Mac DQoL score				
arithmetic mean (standard deviation)	0.3 (± 1.7)	-0.1 (± 2.1)	-0.4 (± 1.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in MacTSQ at 12 months

End point title	Change in MacTSQ at 12 months
End point description:	
Mean change in MacTSQ Total score	
End point type	Secondary
End point timeframe:	
12 Month Visit data, defined as either the visit occurring immediately after the 1 year anniversary for the participant, or a visit within 7 days of the 1 year anniversary.	

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	15	20	
Units: MacTSQ score				
arithmetic mean (standard deviation)	1.7 (± 4.2)	3.7 (± 14.2)	-0.6 (± 5.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in MacTSQ at 24 months

End point title	Change in MacTSQ at 24 months
End point description:	
Mean change in MacTSQ total score	
End point type	Secondary

End point timeframe:

24 Month Visit data, defined as either the visit occurring immediately after the 2 year anniversary for the participant, or a visit within 7 days of the 2 year anniversary.

End point values	Standard Care	Treat and Extend	Extension	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	12	20	
Units: MacTSQ score				
arithmetic mean (standard deviation)	0.4 (\pm 4.6)	-0.9 (\pm 6.1)	0.7 (\pm 5.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Enrolment through to end of study, either 24 or 48 months later.

Adverse event reporting additional description:

Adverse events were self-reported by participants upon prompts from the research team.

Participants were asked if they'd experienced any perceived change to vision or perceived distortions in the study eye since the previous visit, any reported worsening was reported as an adverse event.

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24.1
--------------------	------

Reporting groups

Reporting group title	Standard Care
-----------------------	---------------

Reporting group description:

Participants receiving treatment according to the standard care within the NHS.

Phase 1: Monthly treatments for 3 consecutive visits

Phase 2: 8 weekly treatment until the end of year one

Phase 3: Treatment intervals may be extended or reduced by 2 weeks at the discretion of the treating physician. Minimum shortened duration of 4 weeks and maximum duration capped at 12 weeks.

Reporting group title	Treat and Extend
-----------------------	------------------

Reporting group description:

Individualised Treat and Extend treatment regimen.

Phase 1: Monthly treatments for 3 consecutive visits

Phase 2: The treatment interval progressively extended by 2 weeks allowing a treatment interval to be found maintaining stability as per the investigators decision. Treatment interval capped at 12 weeks.

Phase 3: If any relapse in activity or reactivation treatment interval progressively reduced by 2 weeks until stability is reached again.

Phase 4: Further extension of the interval may be attempted following a fixed interval at the discretion of the the treating physician, capped to 12 weeks.

Minimum shortened duration between doses of 4 weeks, maximum extension of intervals capped at 12 weeks.

Serious adverse events	Standard Care	Treat and Extend	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 19 (47.37%)	8 / 20 (40.00%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm malignant stage unspecified			
Additional description: Tongue neoplasm malignant stage unspecified & carcinoma in situ of skin.			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Thermal burn			
Additional description: Fall and Thermal burn			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures	Additional description: Partial seizure and pneumonia		
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye haemorrhage	Additional description: Led to vision loss >30 letters between visits defined as an SAE by Protocol		

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 19 (10.53%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia and sepsis			

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (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	Standard Care	Treat and Extend
Total subjects affected by non-serious adverse events		
subjects affected / exposed	16 / 19 (84.21%)	18 / 20 (90.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma		
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	0
Vascular disorders		
Hypertension		
subjects affected / exposed	1 / 19 (5.26%)	2 / 20 (10.00%)
occurrences (all)	1	2
Surgical and medical procedures		
Blepharoplasty		
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	1
Cataract operation		
subjects affected / exposed	2 / 19 (10.53%)	3 / 20 (15.00%)
occurrences (all)	2	3
Office visit		
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)
occurrences (all)	0	2
Skin lesion removal		
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	0
General disorders and administration site conditions		
Cold sweat, altered state of consciousness & vomiting		
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	0
Death	Additional description: Death as a result of progression of pre-existing condition, not considered an SAE for the purposes of the study.	

subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1	
Facial pain subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1	
Fatigue subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1	
Influenza like illness subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 20 (5.00%) 1	
Malaise & Dizziness subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 3	
Reproductive system and breast disorders Breast mass subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 20 (5.00%) 1	
Cough, nasopharyngitis & conjunctivitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1	
Epistaxis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	
Haemoptysis			

<p>subjects affected / exposed occurrences (all)</p> <p>Nasal congestion subjects affected / exposed occurrences (all)</p>	<p>1 / 19 (5.26%) 1</p> <p>1 / 19 (5.26%) 1</p>	<p>0 / 20 (0.00%) 0</p> <p>0 / 20 (0.00%) 0</p>	
<p>Investigations Weight decreased subjects affected / exposed occurrences (all)</p>	<p>0 / 19 (0.00%) 0</p>	<p>1 / 20 (5.00%) 1</p>	
<p>Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)</p> <p>Ligament sprain subjects affected / exposed occurrences (all)</p>	<p>7 / 19 (36.84%) 7</p> <p>1 / 19 (5.26%) 1</p>	<p>4 / 20 (20.00%) 4</p> <p>0 / 20 (0.00%) 0</p>	
<p>Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)</p> <p>Atrial fibrillation subjects affected / exposed occurrences (all)</p>	<p>1 / 19 (5.26%) 1</p> <p>0 / 19 (0.00%) 0</p>	<p>0 / 20 (0.00%) 0</p> <p>1 / 20 (5.00%) 1</p>	
<p>Nervous system disorders Carpal tunnel syndrome subjects affected / exposed occurrences (all)</p> <p>Dizziness subjects affected / exposed occurrences (all)</p> <p>Memory impairment subjects affected / exposed occurrences (all)</p> <p>Migraine subjects affected / exposed occurrences (all)</p>	<p>1 / 19 (5.26%) 1</p> <p>2 / 19 (10.53%) 3</p> <p>1 / 19 (5.26%) 1</p> <p>1 / 19 (5.26%) 1</p>	<p>0 / 20 (0.00%) 0</p> <p>1 / 20 (5.00%) 1</p> <p>0 / 20 (0.00%) 0</p> <p>0 / 20 (0.00%) 0</p>	

Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences (all)	1	2	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Blepharitis			
subjects affected / exposed	4 / 19 (21.05%)	1 / 20 (5.00%)	
occurrences (all)	6	1	
Cataract			
subjects affected / exposed	0 / 19 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	4	
Cataract nuclear			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Charles Bonnet syndrome			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Choroidal neovascularisation			
subjects affected / exposed	3 / 19 (15.79%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Corneal abrasion			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Diplopia			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Dry eye			
subjects affected / exposed	2 / 19 (10.53%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Eye inflammation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Eye pain			

subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)
occurrences (all)	1	1
Eyelid contusion		
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	0
Eyelid disorder		
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	1
Eyelid thickening		
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	0
Intraocular pressure increased		
alternative assessment type: Systematic		
subjects affected / exposed	1 / 19 (5.26%)	2 / 20 (10.00%)
occurrences (all)	3	2
Iris transillumination defect		
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	0
Lens disorder		
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	1
Lenticular opacities		
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)
occurrences (all)	1	0
Metamorphopsia		
subjects affected / exposed	3 / 19 (15.79%)	1 / 20 (5.00%)
occurrences (all)	5	2
Neovascular age-related macular degeneration		
subjects affected / exposed	0 / 19 (0.00%)	4 / 20 (20.00%)
occurrences (all)	0	4
Retinal haemorrhage		
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	1
Retinal oedema		

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Retinal pigment epithelial tear			
subjects affected / exposed	2 / 19 (10.53%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Sensation of foreign body			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Subretinal fibrosis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Visual acuity reduced			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Visual impairment	Additional description: Patient reported perceived worsening of vision between study visits.		
alternative assessment type: Systematic			
subjects affected / exposed	10 / 19 (52.63%)	5 / 20 (25.00%)	
occurrences (all)	18	10	
Visual impairment & metamorphosia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Visual impairment & Nuclear cataract			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Vitreoretinal traction syndrome			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Vitreous detachment			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Vitreous floaters			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2	0 / 20 (0.00%) 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 19 (5.26%)	2 / 20 (10.00%)	
occurrences (all)	1	3	
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Diverticulitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Nausea & back pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

Decubitus ulcer			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Psoriasis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin ulcer			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Foot fracture			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Osteoarthritis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pain in jaw			

subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2	0 / 20 (0.00%) 0	
Trigger finger subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	
Infections and infestations			
Campylobacter gastroenteritis subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1	
Candida infection subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1	
Cellulitis subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	1 / 20 (5.00%) 1	
Cystitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	
Fungal skin infection subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	
Herpes zoster subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	1 / 20 (5.00%) 1	
Hordeolum subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	
Influenza subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	
Lower respiratory tract infection subjects affected / exposed occurrences (all)	5 / 19 (26.32%) 5	4 / 20 (20.00%) 9	
Nasopharyngitis & Influenza subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 20 (0.00%) 0	

Pneumonia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Postoperative wound infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Tooth infection			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2016	<p>SA02</p> <p>This amendment was submitted to allow screening and baseline/treatment to either be on the same day, Day 0, or over two days, within a seven day permitted window. This alteration allowed flexibility for patients as some may wish to stay longer and have their treatment on the same day; other patients may prefer to come back to clinic as the appointments can be quite long.</p> <p>Screening procedures were also clarified to enable Patient Information Sheets to be sent to patients at home. This would be done following initial consultation with the Doctor and only if it was not possible to provide one during their consultation. The PIS would only be sent out following confirmation with the Doctor that this was suitable.</p> <p>Randomisation and labelling procedures were also clarified.</p>
17 March 2016	<p>SA04</p> <p>Addition of two new sites for recruitment</p>
24 July 2016	<p>SA06</p> <p>This amendment was submitted to amend the parameters for the blood pressure exclusion criteria to 170mmHg and/or 110mmHg. This change was proposed as most patients had an element of white coat hypertension when they attended clinics, and the new values would assist in recruiting those with white coat hypertension rather than true hypertension.</p> <p>Furthermore, the QoL questionnaire was to be administered following the first injection, as participants had commented the completion of this at baseline visit was confusing.</p> <p>Also amended within the protocol was a clarification of staff and the removal of the reference to the NEI-VFQ as this was not being measured.</p>
13 January 2017	<p>SA10</p> <p>This amendment was submitted to amend Appendix 7 of the study protocol to state that interviews would be conducted with staff. A new Participant Information Sheet and consent form were included for review, along with a topic guide which detailed what would be asked.</p>
20 October 2017	<p>SA12</p> <p>Update of SmPC containing RSI for the study to version 11 following review</p>
14 February 2018	<p>SA13, SA15 and NSA16. (multiple references for regulatory approvals)</p> <p>This amendment was submitted to address a number of points including:</p> <ul style="list-style-type: none">- An extension for a further two years- The addition of a 'monitor and extend' element in years 3 and 4- Authorisation for Trusts to follow their standard injection practice- Addition of an SAE of special interest: Vision loss of >30 letters between visits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

MATE was designed and run as a pilot study therefore the numbers aren't large enough to draw comparison between the arms.

Covid-19 restrictions impacted on visit attendance between 36 and 48 months.

Notes: