Clinical trial results:
Periocular and Intravitreal Corticosteroids for Uveitic Macular Edema (POINT) Trial

Summary

EudraCT number	2016-000304-29
Trial protocol	GB
Global end of trial date	04 January 2018

Results information

Result version number	v1 (current)
This version publication date	12 November 2021
First version publication date	12 November 2021

Trial information

Trial identification

Sponsor protocol code	140840

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02374060
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MUST Coordinating Centre Johns Hopkins Bloomberg School of Public Health
Sponsor organisation address	415 N. Washington St, 2nd Floor, Baltimore, MD, United States, 21231
Public contact	Sue Lightman, University College London, 44 02075662266, s.lightman@ucl.ac.uk
Scientific contact	Sue Lightman, University College London, 44 02075662266, s.lightman@ucl.ac.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	04 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 January 2018
Global end of trial reached?	Yes
Global end of trial date	04 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To find out which therapy for uveitic macular oedema (swelling of the macula at the back of the eye due to inflammation in the eye) offers the best balance of effectiveness and tolerability, specifically by comparing the relative efficacy and safety of three commonly used treatments for macular oedema: periocular steroid (triamcinolone acetonide); intravitreal steroid (triamcinolone acetonide); and intravitreal slow release steroid implant (dexamethasone implant - Ozurdex®) for the treatment of uveitic macular edema.
The primary outcome measure will be change in macular thickness (i.e. decreased swelling of the macula) at the 8 week visit.

Protection of trial subjects:

The injection procedures, dosage of medication and treatment algorithm within the study were consistent with standard clinical treatment. To minimize risks associated with increased ocular pressure post-injection, patients with uncontrolled ocular hypertension or glaucomatous changes were excluded from the trial. Patients in the trial were not exposed to risk beyond what they would be exposed to with standard clinical care for their condition.

Background therapy: -

Evidence for comparator:

Active Comparator: Periocular triamcinolone 40 mg injection (by posterior sub-Tenon's or orbital approach):
A Johns Hopkins Medical Institution study of 126 patients (156 eyes) with uveitic ME who received a single periocular injection of corticosteroid reported clinical resolution of ME among 53% and 57% of eyes at 1 month and 3 months respectively. 46 Of the 83 eyes that had resolution of ME at 1 month, 50 (60%) had no recurrence of the ME at 3 months after the first periocular corticosteroid injection. Forty eyes were treated with more than one periocular injection due to persistence of ME one month following the first injection. Of the 21 eyes treated with a second periocular injection, 81% and 43% had no ME at one and 3 months, respectively, after the second injection. Overall, a 3-line improvement in visual acuity was observed in 52% at one month and in 57% at 3-months.
Active Comparator: Intravitreal triamcinolone 4 mg injection
A study of intravitreal triamcinolone acetonide in patients with uveitic ME was performed at Moorfields Eye Hospital. This retrospective case series of 65 eyes in 54 patients found an improvement in ME and visual acuity in 83% of eyes and a mean 12-letter gain (2.4 lines) in BCVA with intravitreal triamcinolone acetonide with a mean follow-up of 8 months
Active Comparator: Intravitreal triamcinolone 4 mg injection

Active Comparator: Dexamethasone intravitreal (0.7 mg)

The HURON study (a sham controlled clinical trial among 229 participants) compared the safety and efficacy of a single intravitreal injection of two dexamethasone implant doses (0.7mg and 0.35mg). While both implant doses were shown to be effective in controlling vitreous inflammation and in improving visual acuity, the higher dose implant proved to have a longer duration of action. At 8 weeks, 43% of treated eyes versus 7% in the sham group had at least a 15 letter improvement from baseline BCVA. The central macular thickness was significantly lowe

Actual start date of recruitment	01 June 2015
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: 42
Country: Number of subjects enrolled	United States: 133
Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Canada: 6
Worldwide total number of subjects	192
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)	144
From 65 to 84 years	45
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

391 screened, 192 randomized
Excluded 199
Major reasons for exclusion were
No macular edema (central subfield macular thickness within the normal range for the OCT machine (>300 µm for Zeiss Cirrus/Topcon 3DOCT or >320 µm for Heidelberg Spectralis) - 19%
Visual acuity >20/40 or <5/200 (13%)
Patient preference -16%

Period 1

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

Blinding implementation details:

Reading center graders assessing primary outcome and visual acuity examiners masked to treatment

Arms

Are arms mutually exclusive?	Yes
Arm title	Periocular triamcinolone 40mg

Arm description:

Periocular triamcinolone acetonide (Kenalog® , Bristol-Myers Squibb Company, Princeton, NJ),), 40 mg
Initial injection at
Week 0
Periocular triamcinolone acetonide, 40 mg injection may be given either by posterior sub-Tenon's approach or by the orbital floor approach, as both appear to have similar efficacy; the approach to the periocular injection will be recorded for analysis if needed

Arm type	Active comparator
Investigational medicinal product name	Periocular triamcinolone 40mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Injection

Dosage and administration details:

Periocular triamcinolone 40 mg: Periocular triamcinolone acetonide, 40 mg injection may be given either by
posterior sub-Tenon’s approach or by the orbital floor approach, as both appear to have similar efficac

Arm title	Intravitreal triamcinolone 4mg

Arm description:

Intravitreal triamcinolone (Triesence™, Alcon Pharmaceuticals, Fort Worth, TX)(preservative-free preparation,
Triescence at U.S. clinics; Triesence preferred at non-U.S. clinics but Kenalog allowed) (4 mg)
Initial injection at Week 0
Second injection permitted at Week 8 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;

Intravitreal triamcinolone acetonide, 4 mg injection procedures should be carried out under controlled aseptic conditions which include the use

of sterile gloves and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum microbicide such as betadine, applied to the periocular skin, eyelid and ocular surface are required prior to an intravitreal injection.

Arm type	Active comparator
Investigational medicinal product name	Intravitreal triamcinolone (Triesence™, Alcon Pharmaceuticals, Fort Worth, TX)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection
Routes of administration	Injection

Dosage and administration details:

Intravitreal triamcinolone 4 mg: Intravitreal triamcinolone acetonide, 4 mg injection procedures should be
carried out under controlled aseptic conditions which include the use of sterile gloves and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum microbicide such as betadine, applied to
the periocular skin, eyelid and ocular surface are required prior to an intravitreal injection

Arm title	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg)

Arm description:

Dexamethasone intravitreal implant (Ozurdex) (0.7 mg) implant (Ozurdex®, Allergan, Irvine CA)
Initial injection at
Week 0
Second injection permitted at Week 12 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;
• IOP of ≤21 or mm Hg and treatment with ≤3 IOP-lowering agents;

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg) implant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant in pre-filled syringe
Routes of administration	Implantation

Dosage and administration details:

Standard preparation
Initial injection at Week 0
Second injection permitted at Week 12 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;
• IOP of ≤21 or mm Hg and treatment with ≤3 IOP-lowering agents

Number of subjects in period 1	Periocular triamcinolone 40mg	Intravitreal triamcinolone 4mg	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg)
Started	65	63	64
week 8	65	63	64
Completed	65	63	64

Baseline characteristics

Reporting groups

Reporting group title	Periocular triamcinolone 40mg

Reporting group description:

Periocular triamcinolone acetonide (Kenalog® , Bristol-Myers Squibb Company, Princeton, NJ),), 40 mg
Initial injection at
Week 0
Periocular triamcinolone acetonide, 40 mg injection may be given either by posterior sub-Tenon's approach or by the orbital floor approach, as both appear to have similar efficacy; the approach to the periocular injection will be recorded for analysis if needed

Reporting group title	Intravitreal triamcinolone 4mg

Reporting group description:

Intravitreal triamcinolone (Triesence™, Alcon Pharmaceuticals, Fort Worth, TX)(preservative-free preparation,
Triescence at U.S. clinics; Triesence preferred at non-U.S. clinics but Kenalog allowed) (4 mg)
Initial injection at Week 0
Second injection permitted at Week 8 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;

Intravitreal triamcinolone acetonide, 4 mg injection procedures should be carried out under controlled aseptic conditions which include the use of sterile gloves and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum microbicide such as betadine, applied to the periocular skin, eyelid and ocular surface are required prior to an intravitreal injection.

Reporting group title	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg)

Reporting group description:

Dexamethasone intravitreal implant (Ozurdex) (0.7 mg) implant (Ozurdex®, Allergan, Irvine CA)
Initial injection at
Week 0
Second injection permitted at Week 12 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;
• IOP of ≤21 or mm Hg and treatment with ≤3 IOP-lowering agents;

Reporting group values	Periocular triamcinolone 40mg	Intravitreal triamcinolone 4mg	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg)
Number of subjects	65	63	64
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			
Units: years			
median	55	56	55
full range (min-max)	22 to 87	18 to 86	19 to 85
Gender categorical			
Units: Subjects			
Female	39	40	40
Male	26	23	24
Retinal thickness at the center subfield			
Retinal thickness at the center subfield measured by OCT			
Units: um			
median			
full range (min-max)			
Visual acuity			
easure Description: Participants' visual acuity was measured by certified examiners with best refractive correction in place.Participants were challenged with reading letters on lines of the standard ETDRS eye chart (5 letters per line). Lines became smaller as participants progressed from the top to the bottom of the chart. Participants read down the chart until no more meaningful readings could be made and were scored by how many letters could be correctly identified. More letters read is associated with higher visual acuity.			
Units: standard letters			
median			
full range (min-max)			
Intraocular pressure (IOP)			
Units: mm Hg			
median			
full range (min-max)			

Reporting group values	Total		
Number of subjects	192		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
median			
full range (min-max)	-		

Gender categorical Units: Subjects			
Female	119		
Male	73		
Retinal thickness at the center subfield			
Retinal thickness at the center subfield measured by OCT			
Units: um median full range (min-max)	--		
Visual acuity			
easure Description: Participants' visual acuity was measured by certified examiners with best refractive correction in place.Participants were challenged with reading letters on lines of the standard ETDRS eye chart (5 letters per line). Lines became smaller as participants progressed from the top to the bottom of the chart. Participants read down the chart until no more meaningful readings could be made and were scored by how many letters could be correctly identified. More letters read is associated with higher visual acuity.			
Units: standard letters median full range (min-max)	--		
Intraocular pressure (IOP) Units: mm Hg median full range (min-max)	--		

Subject analysis sets

Subject analysis set title	Macular edema eyes from Arm 1 (Periocular triamcinolone)
Subject analysis set type	Per protocol

Subject analysis set description:

Eyes with macular edema from Arm 1 (Periocular triamcinolone acetonide (Kenalog® , Bristol-Myers Squibb Company, Princeton, NJ),), 40 mg)Initial injection

Subject analysis set title	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Subject analysis set type	Per protocol

Subject analysis set description:

Macular edema eyes from Arm 2 (Intravitreal triamcinolone (Triesence™, Alcon Pharmaceuticals, Fort Worth, TX)(preservative-free preparation, Triescence at U.S. clinics; Triesence preferred at non-U.S. clinics but Kenalog allowed) (4 mg)

Subject analysis set title	Macular edema eyes from Arm 3 (Dexamethasone implant)
Subject analysis set type	Per protocol

Subject analysis set description:

Macular edema eyes from Arm 3 (Dexamethasone intravitreal implant (Ozurdex) (0.7 mg) implant (Ozurdex®, Allergan, Irvine CA))

Reporting group values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects	74	82	79
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 Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female Male			
Retinal thickness at the center subfield			
Retinal thickness at the center subfield measured by OCT			
Units: um median full range (min-max)	 438 278 to 922	 485 236 to 824	 449 243 to 1300
Visual acuity			
easure Description: Participants' visual acuity was measured by certified examiners with best refractive correction in place.Participants were challenged with reading letters on lines of the standard ETDRS eye chart (5 letters per line). Lines became smaller as participants progressed from the top to the bottom of the chart. Participants read down the chart until no more meaningful readings could be made and were scored by how many letters could be correctly identified. More letters read is associated with higher visual acuity.			
Units: standard letters median full range (min-max)	 68 25 to 91	 63 13 to 88	 64 23 to 86
Intraocular pressure (IOP) Units: mm Hg median full range (min-max)	 14 6 to 20	 14 7 to 21	 13 6 to 20

End points

End points reporting groups

Reporting group title	Periocular triamcinolone 40mg

Reporting group description:

Periocular triamcinolone acetonide (Kenalog® , Bristol-Myers Squibb Company, Princeton, NJ),), 40 mg Initial injection at
Week 0
Periocular triamcinolone acetonide, 40 mg injection may be given either by posterior sub-Tenon's approach or by the orbital floor approach, as both appear to have similar efficacy; the approach to the periocular injection will be recorded for analysis if needed

Reporting group title	Intravitreal triamcinolone 4mg

Reporting group description:

Intravitreal triamcinolone (Triesence™, Alcon Pharmaceuticals, Fort Worth, TX)(preservative-free preparation,
Triescence at U.S. clinics; Triesence preferred at non-U.S. clinics but Kenalog allowed) (4 mg)
Initial injection at Week 0
Second injection permitted at Week 8 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;

Intravitreal triamcinolone acetonide, 4 mg injection procedures should be carried out under controlled aseptic conditions which include the use of sterile gloves and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum microbicide such as betadine, applied to the periocular skin, eyelid and ocular surface are required prior to an intravitreal injection.

Reporting group title	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg)

Reporting group description:

Dexamethasone intravitreal implant (Ozurdex) (0.7 mg) implant (Ozurdex®, Allergan, Irvine CA)
Initial injection at
Week 0
Second injection permitted at Week 12 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;
• IOP of ≤21 or mm Hg and treatment with ≤3 IOP-lowering agents;

Subject analysis set title	Macular edema eyes from Arm 1 (Periocular triamcinolone)
Subject analysis set type	Per protocol

Subject analysis set description:

Eyes with macular edema from Arm 1 (Periocular triamcinolone acetonide (Kenalog® , Bristol-Myers Squibb Company, Princeton, NJ),), 40 mg)Initial injection

Subject analysis set title	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Subject analysis set type	Per protocol

Subject analysis set description:

Macular edema eyes from Arm 2 (Intravitreal triamcinolone (Triesence™, Alcon Pharmaceuticals, Fort Worth, TX)(preservative-free preparation, Triescence at U.S. clinics; Triesence preferred at non-U.S. clinics but Kenalog allowed) (4 mg)

Subject analysis set title	Macular edema eyes from Arm 3 (Dexamethasone implant)
Subject analysis set type	Per protocol

Subject analysis set description:

Macular edema eyes from Arm 3 (Dexamethasone intravitreal implant (Ozurdex) (0.7 mg) implant (Ozurdex®, Allergan, Irvine CA))

Primary: Change in central subfield thickness at 8 weeks measured as the proportion of the baseline central subfield thickness

End point title	Change in central subfield thickness at 8 weeks measured as the proportion of the baseline central subfield thickness

End point description:

The primary outcome is the change in central subfield thickness assessed with OCT by masked readers from baseline to 8 weeks measured on a relative scale as the the proportion of the baseline central subfield thickness. Values less than 1 indicate a decrease in retinal thickness with lower values indicating greater decreases. Smaller values are better.

End point type	Primary

End point timeframe:

The time point of 8 weeks from randomization was chosen for assessment of the primary outcome because it encompasses the window for maximum benefit for all three treatment strategies. Retinal thickness was evaluated using masked assessments of OCT images

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: Proportion of Baseline Central Subfield				
arithmetic mean (confidence interval 95%)	.77 (.67 to .89)	.61 (.53 to .70)	.54 (.46 to .63)	

Statistical analyses

Statistical analysis title	Intravitreal over Periocular

Statistical analysis description:

Proportion of Baseline Central Subfield Thickness Observed at 8 Weeks.
Compare Intravitreal Triamcinolone 4mg
to periocular Triamcinolone 40mg,

Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Mixed effects model
Parameter estimate	Ratio of the proportion of BL
Point estimate	0.79
Confidence interval	
level	Other: 99.87 %
sides	2-sided
lower limit	0.65
upper limit	0.96

Notes:

[1] - Two sided type I error threshold was 0.00132 since recruitment was halted after the single pre-planned interim analysis

Statistical analysis title	Dexamethasone implant over Periocular Triamcinolon
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Ratio of the proportion of BL
Point estimate	0.69
Confidence interval	
level	Other: 99.87 %
sides	2-sided
lower limit	0.56
upper limit	0.86

Statistical analysis title	Dexamethasone implant over intravitreal
Comparison groups	Macular edema eyes from Arm 3 (Dexamethasone implant) v Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Ratio of the proportion of BL
Point estimate	0.88
Confidence interval	
level	Other: 99.87 %
sides	2-sided
lower limit	0.71
upper limit	1.08

Secondary: Change in central subfield thickness at 24 weeks measured as the proportion of the baseline central subfield thickness

End point title	Change in central subfield thickness at 24 weeks measured as the proportion of the baseline central subfield thickness

End point description:

The primary outcome is the change in central subfield thickness from baseline to 24 weeks measured on a relative scale as the the proportion of the baseline central subfield thickness. Values less than 1 indicate a decrease in retinal thickness with lower values indicating greater decreases. Smaller values are better. The time point of 24 weeks was chosen to evaluate the duration of response and the need for additional injections. Retinal thickness was evaluated using masked assessments of OCT images

End point type	Secondary

End point timeframe:

At baseline and the 24 week visit

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: proportion of the baseline central subfi				
arithmetic mean (confidence interval 99.87%)	0.68 (0.59 to 0.79)	0.64 (0.56 to 0.74)	0.61 (0.52 to 0.71)	

Statistical analyses

Statistical analysis title	Ratio of intravitreal over periocular
Statistical analysis description:	
Two sided type I error threshold was 0.00132 since recruitment was halted after the single preplanned interim analysis	
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	Mixed models analysis
Parameter estimate	Ratio of the proportion of BL
Point estimate	0.95
Confidence interval	
level	Other: 99.87 %
sides	2-sided
lower limit	0.77
upper limit	1.16

Statistical analysis title	Ratio of dexamethasone over periocular
Statistical analysis description:	
he 2 sided type 1 error threshold was 0.000132 since recruitment was halted after the single preplanned interim analysis	
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)

Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	Ratio of the proportion of BL
Point estimate	0.89
Confidence interval	
level	Other: 99.87 %
sides	2-sided
lower limit	0.72
upper limit	1.1

Statistical analysis title	Ratio of dexamethasone over intravitreal
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	Mixed models analysis
Parameter estimate	Ratio of the proportion of BL
Point estimate	0.94
Confidence interval	
level	Other: 99.87 %
sides	2-sided
lower limit	0.77
upper limit	1.16

Notes:

[2] - The noninferiority margin for the comparison between dexamethasone and intravitreal treatment was 1.16, that is, dexamethasone is considered noninferior if the upper boundary of the 99.87% CI is less than 1.16.

Secondary: Proportion of Eyes With >= 20% Reduction in Macular Thickness (or Normalization Even if <20% Reduction) at 8 Weeks

End point title	Proportion of Eyes With >= 20% Reduction in Macular Thickness (or Normalization Even if <20% Reduction) at 8 Weeks

End point description:

Proportion of eyes with >=20% reduction in macular thickness (or normalization of macular thickness even if there is <20% reduction) at 8 weeks.

End point type	Secondary

End point timeframe:

Over 8 weeks of follow-up

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: proportion of eyes				
arithmetic mean (confidence interval 95%)	0.41 (0.29 to 0.52)	0.79 (0.7 to 0.88)	0.84 (0.74 to 0.94)	

Statistical analyses

Statistical analysis title	Intravitreal over Periocular
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	0.53

Statistical analysis title	Dexamethasone implant over Periocular Triamcinolon
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.59

Statistical analysis title	Dexamethasone implant over Intravitre Triamcinolon

Statistical analysis description:	
Dexamethasone - intravitreal	
Comparison groups	Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.19

Secondary: Proportion of Eyes With >= 20% Reduction in Macular Thickness (or Normalization Even if <20% Reduction) at 24 Weeks

End point title	Proportion of Eyes With >= 20% Reduction in Macular Thickness (or Normalization Even if <20% Reduction) at 24 Weeks
End point description:	
Proportion of eyes with >=20% reduction in macular thickness (or normalization of macular thickness even if there is <20% reduction) at 24 week	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: Proportion of eyes				
arithmetic mean (confidence interval 95%)	0.61 (0.50 to 0.72)	0.73 (0.63 to 0.83)	0.74 (0.61 to 0.85)	

Statistical analyses

Statistical analysis title	Intravitreal over Periocular
Statistical analysis description:	
Intravitreal - Periocular	
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)

Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.27

Statistical analysis title	Dexamethasone implant over Periocular Triamcinolon
Statistical analysis description:	
Dexamethasone implant - Periocular Triamcinolone	
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.28

Statistical analysis title	Dexamethasone implant over Intravit Triamcinolon
Statistical analysis description:	
Dexamethasone implant - Intravitreal Triamcinolone	
Comparison groups	Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.002

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.16

Secondary: Proportion of Eyes With Resolution of Macular Edema at 8 Weeks

End point title	Proportion of Eyes With Resolution of Macular Edema at 8 Weeks

End point description:

Proportion of eyes with resolution of macular edema defined as normalization of the macular thickness (i.e., < 260
um on the standardized scale) at 8 weeks. The greater the proportion the more eyes achieved resolution of macular
edema.

End point type	Secondary

End point timeframe:

Over 8 weeks of follow-up

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: Proportion of eyes				
arithmetic mean (confidence interval 95%)	.20 (.12 to .30)	.47 (.34 to .60)	.61 (.48 to .73)	

Statistical analyses

Statistical analysis title	Intravitreal over Periocular

Statistical analysis description:

Intravitreal - Periocular

Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.43

Statistical analysis title	Dexamethasone implant over Periocular Triamcinolon
Statistical analysis description:	
Dexamethasone implant - Periocular Triamcinolone	
Comparison groups	Macular edema eyes from Arm 3 (Dexamethasone implant) v Macular edema eyes from Arm 1 (Periocular triamcinolone)
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.56

Statistical analysis title	Dexamethasone implant over Intravit Triamcinolon
Statistical analysis description:	
Dexamethasone implant - Intravitreal Triamcinolone	
Comparison groups	Macular edema eyes from Arm 3 (Dexamethasone implant) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.3

Secondary: Proportion of Eyes With Resolution of Macular Edema at 24 Weeks

End point title	Proportion of Eyes With Resolution of Macular Edema at 24 Weeks

End point description:

End point type	Secondary

End point timeframe:

Over 24 weeks of follow up

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: Proportion of eyes				
arithmetic mean (confidence interval 95%)	0.35 (0.24 to 0.47)	0.36 (0.24 to 0.48)	0.41 (0.28 to 0.54)	

Statistical analyses

Statistical analysis title	Intravitreal over Periocular

Statistical analysis description:

Intravitreal - Periocular

Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.96
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.004
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.17

Statistical analysis title	Dexamethasone implant over Periocular Triamcinolon

Statistical analysis description:

Dexamethasone implant - Periocular Triamcinolone

Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)

Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.23

Statistical analysis title	Dexamethasone implant over Intravit Triamcinolon
Statistical analysis description: Dexamethasone implant over IntravitrealTriamcinolone	
Comparison groups	Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.54
Method	Mixed models analysis
Parameter estimate	Difference in proportion
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.22

Secondary: Change in Best-corrected Visual Acuity at 8 Week	
End point title	Change in Best-corrected Visual Acuity at 8 Week
End point description:	

End point type	Secondary
End point timeframe: Over 8 weeks of follow-up	

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: Stamdard letters				
arithmetic mean (confidence interval 95%)	4.37 (1.86 to 6.89)	9.70 (7.26 to 12.13)	9.53 (7.01 to 12.05)	

Statistical analyses

Statistical analysis title	Intravitreal over Periocular
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	Difference in mean change from baseline
Point estimate	5.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.82
upper limit	8.82

Statistical analysis title	Dexamethasone implant over Periocular Triamcinolon
Statistical analysis description: Dexamethasone implant -Periocular Triamcinolone	
Comparison groups	Macular edema eyes from Arm 3 (Dexamethasone implant) v Macular edema eyes from Arm 1 (Periocular triamcinolone)
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	Difference in mean change from baseline
Point estimate	5.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	8.72

Statistical analysis title	Dexamethasone implant over Intravit Triamcinolon
Statistical analysis description: Dexamethasone implant - Intravitreal Triamcinolone	
Comparison groups	Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.93
Method	Mixed models analysis
Parameter estimate	Difference in mean change from baseline
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.67
upper limit	3.34

Secondary: Change in Best-corrected Visual Acuity at 24 Weeks

End point title	Change in Best-corrected Visual Acuity at 24 Weeks
End point description: Mean change in best-corrected visual acuity from baseline to 24 weeks. Participants' visual acuity was measured by certified examiners with best refractive correction in place. Participants were challenged with reading letters on lines of the standard ETDRS eye chart (5 letters per line). Lines became smaller as participants progressed from the top to the bottom of the chart. Participants read down the chart until no more meaningful readings could be made and were scored by how many letters could be correctly identified. More letters read is associated with higher visual acuity	
End point type	Secondary
End point timeframe: Over 24 weeks of follow-up	

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: standard letters				
arithmetic mean (confidence interval 95%)	4.07 (0.64 to 7.51)	9.60 (6.87 to 12.34)	9.21 (6.62 to 11.80)	

Statistical analyses

Statistical analysis title	Intravitreal over Periocular
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Mixed models analysis
Parameter estimate	Difference in mean change from baseline
Point estimate	5.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	9.92

Statistical analysis title	Dexamethasone implant over Periocular Triamcinolon
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	Mixed models analysis
Parameter estimate	Difference in mean change from baseline
Point estimate	5.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	9.44

Statistical analysis title	Dexamethasone implant over Intravitre Triamcinolon
Statistical analysis description:	
Dexamethasone implant Intravitreal Triamcinolone	
Comparison groups	Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.84
Method	Mixed models analysis
Parameter estimate	Difference in mean change from baseline
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.16
upper limit	3.37

Secondary: Cumulative Proportion of Eyes With an IOP Elevation >=30 mm Hg

End point title	Cumulative Proportion of Eyes With an IOP Elevation >=30 mm Hg
End point description:	
End point type	Secondary
End point timeframe:	
During 24 weeks of follow-up	

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	82	79	
Units: Cumulative proportion of eyes				
number (confidence interval 95%)	0.06 (0.00 to 0.12)	0.06 (0.01 to 0.12)	0.04 (0.00 to 0.08)	

Statistical analyses

Statistical analysis title	Intravitreal over Periocular
Comparison groups	Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 1 (Periocular triamcinolone)
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.92
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	4.01

Statistical analysis title	Dexamethasone implant over Periocular Triamcinolon
Comparison groups	Macular edema eyes from Arm 1 (Periocular triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.65
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	3.11

Statistical analysis title	Dexamethasone implant over Intravit Triamcinolon
Comparison groups	Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 3 (Dexamethasone implant)
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.53
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	2.59

Secondary: Cumulative Proportion of Eyes With Severe Vision Loss	
End point title	Cumulative Proportion of Eyes With Severe Vision Loss
End point description:	
Cumulative proportion of eyes with uveitic macular edema who experience severe vision loss (>= 15 standard letters) during the 24 weeks of follow-up.	
End point type	Secondary
End point timeframe:	
During 24 weeks of follow up	

End point values	Macular edema eyes from Arm 1 (Periocular triamcinolone)	Macular edema eyes from Arm 2 (Intravitreal triamcinolone)	Macular edema eyes from Arm 3 (Dexamethasone implant)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	74	81	78	
Units: cumulative proportion of eyes at 24 week				
number (confidence interval 95%)	0.11 (0.04 to 0.18)	0.10 (0.0 to 0.22)	0.05 (0.05 to 0.10)	

Statistical analyses

Statistical analysis title	Intravitreal triamc over Periocular triamcinolone
Statistical analysis description:	
Intravitreal triamcinolone over Periocular triamcinolone - cumulative proportion of eyes with severe vison loss	
Comparison groups	Macular edema eyes from Arm 2 (Intravitreal triamcinolone) v Macular edema eyes from Arm 1 (Periocular triamcinolone)
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	1.24

Statistical analysis title	Dexamethasone over periocular triamcinolone
Statistical analysis description:	
Dexamethasone over periocular triamcinolone. Cumulative Proportion of Eyes With Severe Vision Loss	
Comparison groups	Macular edema eyes from Arm 3 (Dexamethasone implant) v Macular edema eyes from Arm 1 (Periocular triamcinolone)
Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	0.46

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	1.5

Statistical analysis title	Dexamethasone over intravitreal triamcinolone
Statistical analysis description:	
Dexamethasone over intravitreal triamcinolone - Cumulative Proportion of Eyes With Severe Vision Loss	
Comparison groups	Macular edema eyes from Arm 3 (Dexamethasone implant) v Macular edema eyes from Arm 2 (Intravitreal triamcinolone)
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.62
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	6.26

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were reported to coordinating center within 72 hours and immediately referred to safety officer. Non-serious adverse events were reported monthly on the case report form as responses to questions about specific ocular events

Adverse event reporting additional description:

Serious adverse event defined as an event that results in any of the following outcomes: Death, Life-threatening adverse event, Hospitalization , inpatient, Disability or permanent damage, Congenital anomaly/birth defect, other significant medical events. Also reported were ocular events that could be related to study treatment or procedures.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Periocular triamcinolone 40mg

Reporting group description:

Periocular triamcinolone acetonide (Kenalog® , Bristol-Myers Squibb Company, Princeton, NJ),), 40 mg
Initial injection at
Week 0
Periocular triamcinolone acetonide, 40 mg injection may be given either by posterior sub-Tenon's approach or by the orbital floor approach, as both appear to have similar efficacy; the approach to the periocular injection will be recorded for analysis if needed

Reporting group title	Intravitreal triamcinolone 4mg

Reporting group description:

Intravitreal triamcinolone (Triesence™, Alcon Pharmaceuticals, Fort Worth, TX)(preservative-free preparation,
Triescence at U.S. clinics; Triesence preferred at non-U.S. clinics but Kenalog allowed) (4 mg)
Initial injection at Week 0
Second injection permitted at Week 8 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;

Intravitreal triamcinolone acetonide, 4 mg injection procedures should be carried out under controlled aseptic conditions which include the use of sterile gloves and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum microbicide such as betadine, applied to the periocular skin, eyelid and ocular surface are required prior to an intravitreal injection.

Reporting group title	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg)

Reporting group description:

Dexamethasone intravitreal implant (Ozurdex) (0.7 mg) implant (Ozurdex®, Allergan, Irvine CA)
Initial injection at
Week 0
Second injection permitted at Week 12 IF:
• Eye does not meet the improvement definition (a 20% decrease in central subfield thickness of the macula) OR eye has a normal central subfield thickness but has cystoid spaces in the 1 mm central subfield OR ME is worse after initial improvement;
• IOP of ≤21 or mm Hg and treatment with ≤3 IOP-lowering agents;

Serious adverse events	Periocular triamcinolone 40mg	Intravitreal triamcinolone 4mg	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 65 (9.23%)	5 / 63 (7.94%)	6 / 64 (9.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 65 (0.00%)	2 / 63 (3.17%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinoscopy			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shoulder arthroplasty			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Injection site injury			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
choroidal effusion			
subjects affected / exposed	0 / 65 (0.00%)	0 / 63 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular hypertension			

subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	0 / 65 (0.00%)	0 / 63 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 63 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric polyps			
subjects affected / exposed	0 / 65 (0.00%)	0 / 63 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 65 (0.00%)	1 / 63 (1.59%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bursitis			

subjects affected / exposed	1 / 65 (1.54%)	0 / 63 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 65 (0.00%)	0 / 63 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Periocular triamcinolone 40mg	Intravitreal triamcinolone 4mg	Dexamethasone intravitreal implant (Ozurdex) (0.7 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 65 (1.54%)	10 / 63 (15.87%)	0 / 64 (0.00%)
General disorders and administration site conditions			
Injection site reaction	Additional description: Increase in interocular pressure to > 30 mmHg immediately following injection. (Temporary reaction to ocular injection of fluid)		
alternative assessment type: Systematic			
subjects affected / exposed	1 / 65 (1.54%)	10 / 63 (15.87%)	0 / 64 (0.00%)
occurrences (all)	1	13	0

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30269924