Clinical trial results:
An open-label, multi-center, 6-month extension study comparing the long-term efficacy and safety of Lucentis (Ranibizumab) intravitreal injections versus Ozurdex (Dexamethasone) intravitreal implant in patients with visual impairment due to macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) who have completed the respective core study (CRFB002EDE17 or CRFB002EDE18)

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Summary

EudraCT number	2011-005045-13
Trial protocol	DE
Global end of trial date	07 October 2014
Results information	
Result version number	v1 (current)
This version publication date	07 July 2018
First version publication date	07 July 2018

Trial information

Trial identification	
Sponsor protocol code	CRFB002EDE20
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01580020
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111x, trialandresults.registries@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111x, trialandresults.registries@novartis.com

Notes:

Paediatric regulatory details	
Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	07 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the ocular and non-ocular adverse events during the 6-months study period in patients treated with Lucentis (0.5 mg) vs. treated with Ozurdex®

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 175
Worldwide total number of subjects	175
EEA total number of subjects	175

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	83
From 65 to 84 years	90
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 140 patients with (BRVO) completed the core study CRFB002EDE17, and 127 patients with (CRVO) completed the core study CRFB002EDE18. 92 patients with BRVO and 83 patients with CRVO were enrolled into the extension study. A total of 175 patients (113 in the ranibizumab group and 62 in the dexamethasone group) were enrolled

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ranibizumab (BRVO)

Arm description:

Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitreally

Arm type	Experimental
Investigational medicinal product name	Ranibizumab
Investigational medicinal product code	RFB002
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.5 mg/0.05 ml solution injected intraviterally

Arm title	Dexamethasone (BRVO)

Arm description:

A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required.

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intravitreal implant in applicator
Routes of administration	Intravitreal use

Dosage and administration details:

intravitreal implant 700ug LAR, over 6 months

Arm title	Ranibizumab (CRVO)

Arm description:

Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitrally

Arm type	Experimental

Investigational medicinal product name	Ranibizumab
Investigational medicinal product code	RFB002
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.5 mg/0.05 ml solution injected intraviterally

Arm title	Dexamethasone (CRVO)

Arm description:

A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required.

Arm type	Active comparator
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Intravitreal implant in applicator
Routes of administration	Intravitreal use

Dosage and administration details:

intravitreal implant 700ug LAR, over 6 months

Number of subjects in period 1	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)
Started	52	40	61
Completed	51	33	57
Not completed	1	7	4
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	1	1	1
Administrative Problems	-	-	1
Lost to follow-up	-	-	1
Lack of efficacy	-	5	-

Number of subjects in period 1	Dexamethasone (CRVO)
Started	22
Completed	20
Not completed	2
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Administrative Problems	-
Lost to follow-up	-
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Ranibizumab (BRVO)
Reporting group description:	
Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitreally	
Reporting group title	Dexamethasone (BRVO)
Reporting group description:	
A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required.	
Reporting group title	Ranibizumab (CRVO)
Reporting group description:	
Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitrally	
Reporting group title	Dexamethasone (CRVO)
Reporting group description:	
A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required.	

Reporting group values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)
Number of subjects	52	40	61
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	24	21	26
From 65-84 years	28	19	33
85 years and over	0	0	2
Age Continuous Units: Years			
arithmetic mean	64.5	64.6	66.6
standard deviation	± 9.7	± 9.9	± 10.1
Gender, Male/Female Units: Participants			
Male	18	22	31
Female	34	18	30

Reporting group values	Dexamethasone (CRVO)	Total	
Number of subjects	22	175	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	12	83	
From 65-84 years	10	90	
85 years and over	0	2	
Age Continuous Units: Years			
arithmetic mean	61.1		
standard deviation	± 11	-	
Gender, Male/Female Units: Participants			
Male	14	85	
Female	8	90	

Subject analysis sets

Subject analysis set title	Ranibizumab
Subject analysis set type	Full analysis

Subject analysis set description:

Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitreally

Subject analysis set title	Dexamethasone
Subject analysis set type	Full analysis

Subject analysis set description:

A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required.

Reporting group values	Ranibizumab	Dexamethasone	
Number of subjects	113	62	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	50	33	
From 65-84 years	61	29	
85 years and over	2	0	

Age Continuous Units: Years			
arithmetic mean	65.6	63.3	
standard deviation	± 9.9	± 10.3	
Gender, Male/Female Units: Participants			
Male	49	36	
Female	64	26	

End points

End points reporting groups

Reporting group title	Ranibizumab (BRVO)
Reporting group description:	
Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitreally	
Reporting group title	Dexamethasone (BRVO)
Reporting group description:	
A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required.	
Reporting group title	Ranibizumab (CRVO)
Reporting group description:	
Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitrally	
Reporting group title	Dexamethasone (CRVO)
Reporting group description:	
A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required.	
Subject analysis set title	Ranibizumab
Subject analysis set type	Full analysis
Subject analysis set description:	
Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitreally	
Subject analysis set title	Dexamethasone
Subject analysis set type	Full analysis
Subject analysis set description:	
A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required.	

Primary: Number of participants with adverse events as a measure of safety and tolerability

End point title	Number of participants with adverse events as a measure of safety and tolerability[1]
End point description:	
The number of participants who experienced Adverse events, serious AE and death	
End point type	Primary
End point timeframe:	
6 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this primary outcome measure is safety, only descriptive analysis performed for this outcome measure.

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	40	61	22
Units: Participants				
Adverse event	35	28	45	16
Serious adverse event	2	3	6	1
Death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Raw mean Best Corrected Visual Acuity (BCVA) by treatment group

End point title	Raw mean Best Corrected Visual Acuity (BCVA) by treatment group

End point description:

Best-Corrected Visual Acuity (BCVA) letters was measured using Early Treatment Diabetic Retinopathy Study (EDTRS)-like chart while participants were in a sitting position at a testing distance of 4 meters. An ETDRS visual acuity score of 85 is approximately 20/20. The range of BCVA (EDTRS) is 0 to 100 letters. A positive change from baseline of BCVA indicates improvement

End point type	Secondary

End point timeframe:

Baseline, 6 months and 12 months

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	40	60	22
Units: Letters read correctly				
arithmetic mean (standard deviation)				
Baseline	56.8 (± 10)	58.3 (± 10.8)	53.8 (± 15.7)	53.2 (± 16.1)
Month 6	77.9 (± 10.6)	69.2 (± 11.9)	72.6 (± 13.5)	64.1 (± 24)
Month 12	79 (± 10.1)	70.6 (± 13.9)	72.6 (± 15.8)	66.6 (± 22.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients gaining / losing ≥ 15 / 10 / 5 letters at month 12 compared to baseline

End point title	Percentage of patients gaining / losing ≥ 15 / 10 / 5 letters at month 12 compared to baseline

End point description:

BCVA score was based on the number of letters read correctly on the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart assessed at a starting distance of 4 meters. An ETDRS visual acuity score of 85 is approximately 20/20. An increased score indicates improvement in acuity.

This outcome assessed the percentage of participants who were gaining/losing ≥15, 10 or 5 more letters of visual acuity at month 12 as compared with baseline

End point type	Secondary

End point timeframe:

12 month

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	40	60	22
Units: Percentage of participants				
number (not applicable)				
Gain≥15 letters	80.8	50	58.3	45.5
Gain ≥10 letters	88.5	65	75	68.2
Gain ≥5 letters	100	80	86.7	77.3
Loss of ≥15 letters	0	7.5	0	4.5
Loss of ≥10 letters	0	10	0	4.5
Loss of ≥5 letters	0	10	3.3	4.5

Statistical analyses

No statistical analyses for this end point

Secondary: Change in central subfield thickness (CSRT) from baseline to month 12

End point title	Change in central subfield thickness (CSRT) from baseline to month 12

End point description:

High Resolution OCT was performed at every study visit by Spectral Domain OCT (if not available Time Domain OCT was acceptable) and the images were transferred to a digital video disc. These assessments were performed by trained and adequately qualified experts at the sites and prior to any study drug administration. CSFT is the average retinal thickness of the circular area with 1 mm diameter around the foveal center.

End point type	Secondary

End point timeframe:

Baseline , Month 12

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	40	59	22
Units: um				
arithmetic mean (standard deviation)	-288.1 (± 180.6)	-211.5 (± 199.3)	-374.6 (± 239.8)	-360.3 (± 260.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Foveal Center Point thickness (FCPT) from baseline to month 12

End point title	Change of Foveal Center Point thickness (FCPT) from baseline to month 12

End point description:

FCPT (foveal center point thickness) was assessed by central reading center to ensure error- corrected measurements of retinal thickness and volumes,

End point type	Secondary

End point timeframe:

Baseline, Month 12

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	39	58	21
Units: um				
arithmetic mean (standard deviation)	-341.8 (± 226.2)	-252.6 (± 197.9)	-439.4 (± 279.8)	-432.3 (± 245.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in mean Visual Function Questionnaire (VFQ-25)

End point title	Change in mean Visual Function Questionnaire (VFQ-25)

End point description:

The VFQ-25 composite and subscale scores range from 0 to 100, a higher score indicating better functioning. The 12 subscales in the VFQ-25 are general health, general vision, ocular pain, near activities, distance activities, social function, mental health, role difficulties, dependency, driving, color vision, and peripheral vision. The scores on the subscales were added together for a total score, which ranged from 0 to 100. A higher score indicated improvement in quality of life due to vision function.

End point type	Secondary

End point timeframe:

Baseline, 12 months

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	40	60	22
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Overall Composite	8.1 (± 10.6)	5.5 (± 11.3)	9.1 (± 15.5)	10 (± 15.9)
General Health	-1.4 (± 15.2)	6.3 (± 18.6)	1.7 (± 18.9)	5.7 (± 20.3)

General Vision	15 (± 16.7)	9.5 (± 16.3)	20 (± 17.7)	13.6 (± 23.4)
Ocular Pain	5.3 (± 15.7)	5.3 (± 13.8)	4.2 (± 20.8)	3.4 (± 15)
Near Activities	13.3 (± 18.9)	10.8 (± 20.6)	12.3 (± 20.5)	12.3 (± 23.2)
Distance Activities	8.9 (± 17.5)	5.6 (± 15.3)	7.8 (± 18.3)	8.3 (± 23.4)
Social Functioning	3.4 (± 16.8)	2.2 (± 12)	3.3 (± 16.7)	2.8 (± 21.1)
Mental Health	10.2 (± 14.9)	2.9 (± 20.4)	10.7 (± 21.7)	15.1 (± 18.3)
Role Difficulties	4.8 (± 26.8)	10.6 (± 20.5)	14.6 (± 29.9)	24.4 (± 27.8)
Dependency	3.2 (± 9.2)	0.4 (± 16.6)	5.1 (± 16.7)	4.4 (± 12.8)
Driving (BRVO n=44,31) (CRVO n=42,16)	11.7 (± 23.9)	4.8 (± 21.3)	14.2 (± 24.6)	17.7 (± 25.1)
Color Vision(BRVO n=52,39)	0.5 (± 10.5)	1.9 (± 10.6)	0.4 (± 17.5)	-1.1 (± 14.4)
Peripheral Vision(BRVO n=51,40)	10.3 (± 24.1)	6.9 (± 23.3)	11.7 (± 25)	14.8 (± 22.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in SF-36 summary scores

End point title	Change in SF-36 summary scores

End point description:

The SF-36 measures the impact of disease on overall quality of life and consists of eight subscales (physical function, pain, general and mental health, vitality, social function, physical and emotional health) which can be aggregated to derive a physical-component summary score and a mental-component summary score. Scores for each subscale range from 0 to 10, and the composite scores range from 0 to 100, with higher scores indicating better health. A positive change from Baseline score indicates improvement in quality of life.

End point type	Secondary

End point timeframe:

Baseline, month 12

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	40	60	22
Units: Score on a scale				
arithmetic mean (standard deviation)				
Physical Component(BRVO n=50,39) (CRVO n=58,20)	1.6 (± 5)	0.2 (± 7)	-1.1 (± 8.2)	1.3 (± 7.2)
Mental Component (BRVO n=50,39) (CRVO n=58,20)	3.3 (± 9.7)	2.1 (± 13.2)	2.1 (± 9.3)	2.4 (± 12.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Euro Quality of Life Questionnaire (EQ-5D) VAS summary scores

End point title	Change in Euro Quality of Life Questionnaire (EQ-5D) VAS summary scores

End point description:

The Euro Quality of Life Questionnaire (EQ-5D) standardized instrument was utilized to measure health outcomes related to mobility, self care, usual activities, pain/discomfort, and anxiety/depression. Participants self-rate their health on a visual, vertical analogue scale from 0 to 100 where the endpoints are labeled "Best imaginable health state" (100) and "worst imaginable health state" (0).

End point type	Secondary

End point timeframe:

Baseline, month 12

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	40	58	21
Units: Score on a scale				
arithmetic mean (standard deviation)	3.3 (± 15.2)	2.6 (± 16.9)	1.5 (± 16.4)	0.2 (± 20.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to the first retreatment of both treatment arms

End point title	Time to the first retreatment of both treatment arms

End point description:

Time to the first retreatment

End point type	Secondary

End point timeframe:

6 months

End point values	Ranibizumab (BRVO)	Dexamethasone (BRVO)	Ranibizumab (CRVO)	Dexamethasone (CRVO)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	40	61	22
Units: Days				
median (confidence interval 95%)	37 (3 to 56)	9999.9 (328 to 99999.99)	62 (5 to 67)	9999.9 (309 to 99999.99)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	BRVO- Ranibizumab

Reporting group description:

Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitreally

Reporting group title	BRVO- Dexamethasone

Reporting group description:

A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required

Reporting group title	CRVO- Ranibizumab

Reporting group description:

Injections consisted of 0.5 mg/0.05 ml solution to be injected intravitreally

Reporting group title	CRVO- Dexamethasone

Reporting group description:

A PRN re-treatment scheme will be applied for the Dexamethasone arm during this extension study, i.e. patients may receive an implant at V1E or later as needed. Intravitreal implant as per commercial label (700 µg Dexamethasone; long acting release (LAR) Minimum period of 5 months in between implantations was required

Serious adverse events	BRVO- Ranibizumab	BRVO- Dexamethasone	CRVO- Ranibizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 52 (3.85%)	3 / 40 (7.50%)	6 / 61 (9.84%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

LUMBAR RADICULOPATHY			
subjects affected / exposed	0 / 52 (0.00%)	1 / 40 (2.50%)	0 / 61 (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
Eye disorders			
GLAUCOMA (Fellow eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLAUCOMA (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRIS NEOVASCULARISATION (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MACULAR OEDEMA (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OCULAR ISCHAEMIC SYNDROME (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINAL DETACHMENT (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (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
VISUAL ACUITY REDUCED (Study eye)			

subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITREOUS HAEMORRHAGE (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 52 (1.92%)	0 / 40 (0.00%)	0 / 61 (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
Skin and subcutaneous tissue disorders			
PSORIASIS			
subjects affected / exposed	0 / 52 (0.00%)	1 / 40 (2.50%)	0 / 61 (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
Psychiatric disorders			
SUBSTANCE ABUSE			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 52 (1.92%)	1 / 40 (2.50%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 52 (0.00%)	1 / 40 (2.50%)	0 / 61 (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

Serious adverse events	CRVO-Dexamethasone		

Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
LUMBAR RADICULOPATHY			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
GLAUCOMA (Fellow eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GLAUCOMA (Study eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
IRIS NEOVASCULARISATION (Study eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MACULAR OEDEMA (Study eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OCULAR ISCHAEMIC SYNDROME (Study eye)			

subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RETINAL DETACHMENT (Study eye)				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VISUAL ACUITY REDUCED (Study eye)				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VITREOUS HAEMORRHAGE (Study eye)				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
PULMONARY EMBOLISM				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
PSORIASIS				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
SUBSTANCE ABUSE				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
INTERVERTEBRAL DISC PROTRUSION				

subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ROTATOR CUFF SYNDROME			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	BRVO- Ranibizumab	BRVO- Dexamethasone	CRVO- Ranibizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 52 (67.31%)	28 / 40 (70.00%)	45 / 61 (73.77%)
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
INTRAOCULAR PRESSURE DECREASED (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
INTRAOCULAR PRESSURE INCREASED (Study eye)			
subjects affected / exposed	3 / 52 (5.77%)	10 / 40 (25.00%)	3 / 61 (4.92%)
occurrences (all)	4	12	8
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	1 / 52 (1.92%)	2 / 40 (5.00%)	0 / 61 (0.00%)
occurrences (all)	2	2	0
MUSCLE STRAIN			
subjects affected / exposed	1 / 52 (1.92%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0

POST PROCEDURAL SWELLING (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
FACTOR V LEIDEN MUTATION			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 52 (0.00%)	2 / 40 (5.00%)	1 / 61 (1.64%)
occurrences (all)	0	2	1
SCIATICA			
subjects affected / exposed	1 / 52 (1.92%)	0 / 40 (0.00%)	2 / 61 (3.28%)
occurrences (all)	1	0	2
TRIGEMINAL NEURALGIA			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
CHEST DISCOMFORT			
subjects affected / exposed	1 / 52 (1.92%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
PYREXIA			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CATARACT (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	3 / 40 (7.50%)	2 / 61 (3.28%)
occurrences (all)	0	3	2
CONJUNCTIVAL HAEMORRHAGE (Study eye)			
subjects affected / exposed	2 / 52 (3.85%)	7 / 40 (17.50%)	3 / 61 (4.92%)
occurrences (all)	2	9	3
CONJUNCTIVAL HYPERAEMIA (Study			

eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
CONJUNCTIVAL IRRITATION (Study eye)			
subjects affected / exposed	1 / 52 (1.92%)	2 / 40 (5.00%)	0 / 61 (0.00%)
occurrences (all)	2	3	0
CONJUNCTIVITIS ALLERGIC (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	1 / 40 (2.50%)	0 / 61 (0.00%)
occurrences (all)	0	1	0
DRY EYE (Fellow eye)			
subjects affected / exposed	2 / 52 (3.85%)	1 / 40 (2.50%)	0 / 61 (0.00%)
occurrences (all)	2	1	0
DRY EYE (Study eye)			
subjects affected / exposed	3 / 52 (5.77%)	1 / 40 (2.50%)	0 / 61 (0.00%)
occurrences (all)	3	1	0
EYE PAIN (Study eye)			
subjects affected / exposed	4 / 52 (7.69%)	0 / 40 (0.00%)	7 / 61 (11.48%)
occurrences (all)	5	0	11
FOREIGN BODY SENSATION IN EYES (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	1 / 40 (2.50%)	4 / 61 (6.56%)
occurrences (all)	0	1	5
GLAUCOMA (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	1 / 40 (2.50%)	1 / 61 (1.64%)
occurrences (all)	0	2	1
LACRIMATION INCREASED (Study eye)			
subjects affected / exposed	6 / 52 (11.54%)	2 / 40 (5.00%)	2 / 61 (3.28%)
occurrences (all)	6	3	2
MACULAR FIBROSIS (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
MACULAR OEDEMA (Study eye)			
subjects affected / exposed	9 / 52 (17.31%)	3 / 40 (7.50%)	14 / 61 (22.95%)
occurrences (all)	13	3	15
OCULAR DISCOMFORT (Study eye)			

subjects affected / exposed	2 / 52 (3.85%)	4 / 40 (10.00%)	1 / 61 (1.64%)
occurrences (all)	2	4	1
OCULAR HYPERAEMIA (Study eye)			
subjects affected / exposed	7 / 52 (13.46%)	3 / 40 (7.50%)	4 / 61 (6.56%)
occurrences (all)	8	4	6
PHOTOPSIA (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
RETINAL EXUDATES (Study eye)			
subjects affected / exposed	2 / 52 (3.85%)	1 / 40 (2.50%)	0 / 61 (0.00%)
occurrences (all)	2	1	0
RETINAL ISCHAEMIA (Study eye)			
subjects affected / exposed	5 / 52 (9.62%)	4 / 40 (10.00%)	2 / 61 (3.28%)
occurrences (all)	5	4	2
RETINAL OEDEMA (Study eye)			
subjects affected / exposed	2 / 52 (3.85%)	1 / 40 (2.50%)	0 / 61 (0.00%)
occurrences (all)	2	1	0
VISION BLURRED (Study eye)			
subjects affected / exposed	1 / 52 (1.92%)	0 / 40 (0.00%)	4 / 61 (6.56%)
occurrences (all)	1	0	4
VISUAL ACUITY REDUCED (Study eye)			
subjects affected / exposed	4 / 52 (7.69%)	4 / 40 (10.00%)	8 / 61 (13.11%)
occurrences (all)	5	4	9
VISUAL IMPAIRMENT (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences (all)	0	0	1
VITREOUS DETACHMENT (Fellow eye)			
subjects affected / exposed	0 / 52 (0.00%)	2 / 40 (5.00%)	1 / 61 (1.64%)
occurrences (all)	0	2	1
VITREOUS DETACHMENT (Study eye)			
subjects affected / exposed	2 / 52 (3.85%)	2 / 40 (5.00%)	1 / 61 (1.64%)
occurrences (all)	2	2	1
Gastrointestinal disorders			

ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 52 (1.92%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences (all)	1	0	1
GASTRITIS			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	3 / 52 (5.77%)	1 / 40 (2.50%)	1 / 61 (1.64%)
occurrences (all)	3	1	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 52 (3.85%)	1 / 40 (2.50%)	1 / 61 (1.64%)
occurrences (all)	4	1	1
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	3 / 52 (5.77%)	2 / 40 (5.00%)	6 / 61 (9.84%)
occurrences (all)	3	2	6
OSTEOARTHRITIS			
subjects affected / exposed	2 / 52 (3.85%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	2	0	0
SJOGREN'S SYNDROME			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	1 / 52 (1.92%)	2 / 40 (5.00%)	2 / 61 (3.28%)
occurrences (all)	1	2	2
CONJUNCTIVITIS (Study eye)			
subjects affected / exposed	0 / 52 (0.00%)	1 / 40 (2.50%)	2 / 61 (3.28%)
occurrences (all)	0	1	2
CYSTITIS			
subjects affected / exposed	2 / 52 (3.85%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	4	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0

GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	2 / 61 (3.28%)
occurrences (all)	0	0	2
HERPES ZOSTER			
subjects affected / exposed	1 / 52 (1.92%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	1	0	0
INFLUENZA			
subjects affected / exposed	1 / 52 (1.92%)	1 / 40 (2.50%)	0 / 61 (0.00%)
occurrences (all)	1	1	0
NASOPHARYNGITIS			
subjects affected / exposed	9 / 52 (17.31%)	3 / 40 (7.50%)	12 / 61 (19.67%)
occurrences (all)	12	3	15
PERIODONTITIS			
subjects affected / exposed	1 / 52 (1.92%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences (all)	1	0	1
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	2 / 52 (3.85%)	0 / 40 (0.00%)	1 / 61 (1.64%)
occurrences (all)	2	0	1
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 52 (3.85%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 52 (0.00%)	0 / 40 (0.00%)	0 / 61 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	CRVO-Dexamethasone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 22 (72.73%)		
Investigations			

ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
INTRAOCULAR PRESSURE DECREASED (Study eye)			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
INTRAOCULAR PRESSURE INCREASED (Study eye)			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
MUSCLE STRAIN			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
POST PROCEDURAL SWELLING (Study eye)			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
FACTOR V LEIDEN MUTATION			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		

SCIATICA			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
TRIGEMINAL NEURALGIA			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
General disorders and administration site conditions			
CHEST DISCOMFORT			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
PYREXIA			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Eye disorders			
CATARACT (Study eye)			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
CONJUNCTIVAL HAEMORRHAGE (Study eye)			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
CONJUNCTIVAL HYPERAEMIA (Study eye)			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
CONJUNCTIVAL IRRITATION (Study eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
CONJUNCTIVITIS ALLERGIC (Study eye)			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
DRY EYE (Fellow eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
DRY EYE (Study eye)			

subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
EYE PAIN (Study eye)				
subjects affected / exposed	4 / 22 (18.18%)			
occurrences (all)	4			
FOREIGN BODY SENSATION IN EYES (Study eye)				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
GLAUCOMA (Study eye)				
subjects affected / exposed	1 / 22 (4.55%)			
occurrences (all)	1			
LACRIMATION INCREASED (Study eye)				
subjects affected / exposed	2 / 22 (9.09%)			
occurrences (all)	2			
MACULAR FIBROSIS (Study eye)				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
MACULAR OEDEMA (Study eye)				
subjects affected / exposed	3 / 22 (13.64%)			
occurrences (all)	3			
OCULAR DISCOMFORT (Study eye)				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
OCULAR HYPERAEMIA (Study eye)				
subjects affected / exposed	3 / 22 (13.64%)			
occurrences (all)	4			
PHOTOPSIA (Study eye)				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
RETINAL EXUDATES (Study eye)				
subjects affected / exposed	0 / 22 (0.00%)			
occurrences (all)	0			
RETINAL ISCHAEMIA (Study eye)				

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
RETINAL OEDEMA (Study eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
VISION BLURRED (Study eye)			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
VISUAL ACUITY REDUCED (Study eye)			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
VISUAL IMPAIRMENT (Study eye)			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
VITREOUS DETACHMENT (Fellow eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
VITREOUS DETACHMENT (Study eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
GASTRITIS			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		

Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
OSTEOARTHRITIS			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
SJOGREN'S SYNDROME			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
CONJUNCTIVITIS (Study eye)			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
CYSTITIS			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
GASTROENTERITIS			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
HERPES ZOSTER			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
INFLUENZA			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
NASOPHARYNGITIS			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	4		
PERIODONTITIS			

subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
RHINITIS			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
SINUSITIS			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
VITAMIN D DEFICIENCY			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

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

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Notes: