Clinical trial results:
A 12-month, Prospective, Open-label, Phase 4 Study to Evaluate the Efficacy and Safety of OZURDEX® (Dexamethasone Intravitreal Implant) in Treatment Naïve Patients (According to Standard Clinical Practice) with Diabetic Macular Edema

Summary

EudraCT number	2018-004785-33
Trial protocol	ES
Global end of trial date	04 July 2022

Results information

Result version number	v1
This version publication date	14 July 2023
First version publication date	14 July 2023

Trial information

Trial identification

Sponsor protocol code	CMO-MA-EYE-0603

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03953807
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	AbbVie, Global Medical Services, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	AbbVie, Global Medical Services, 001 8006339110, abbvieclinicaltrials@abbvie.com

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 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were to evaluate the efficacy and safety of OZURDEX in subjects with diabetic macular edema (DME) when used in a real world setting in Spain.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 September 2019
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	Spain: 75
Worldwide total number of subjects	75
EEA total number of subjects	75

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)	27
From 65 to 84 years	45
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 75 subjects were with DME were enrolled to receive the study treatment on Day 1 and were followed up for safety up to 14 months.

Period 1

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

Arms

Arm title	OZURDEX® 700 µg

Arm description:

Participants enrolled in Spain received OZURDEX® 700 µg intravitreal implant as needed per investigator assessment on Day 1.

Arm type	Experimental
Investigational medicinal product name	OZURDEX®
Investigational medicinal product code	
Other name	Dexamethasone Intravitreal Implant
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use

Dosage and administration details:

Intravitreal implant administered.

Number of subjects in period 1	OZURDEX® 700 µg
Started	75
Completed	55
Not completed	20
Physician decision	1
Adverse event, non-fatal	1
Death	3
Screen failure	1
Lost to follow-up	4
Reason not specified	3
Protocol deviation	6
Withdrawal by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	OZURDEX® 700 µg
Reporting group description:	
Participants enrolled in Spain received OZURDEX® 700 µg intravitreal implant as needed per investigator assessment on Day 1.	

Reporting group values	OZURDEX® 700 µg	Total	
Number of subjects	75	75	
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			
arithmetic mean	67.5		
standard deviation	± 10.04	-	
Gender categorical			
Units: Subjects			
Female	25	25	
Male	50	50	

End points

End points reporting groups

Reporting group title	OZURDEX® 700 µg

Reporting group description:

Participants enrolled in Spain received OZURDEX® 700 µg intravitreal implant as needed per investigator assessment on Day 1.

Primary: Mean Change From Baseline in Best Corrected Visual Acuity (BCVA) at 2 Months After the Last Injection

End point title	Mean Change From Baseline in Best Corrected Visual Acuity (BCVA) at 2 Months After the Last Injection[1]

End point description:

BCVA was measured using an eye chart and is reported as the number of letters read correctly using the early treatment diabetic retinopathy study (ETDRS) Scale (ranging from 0 to 100 letters) in the study eye. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). An increase in the number of letters read correctly means that vision has improved. A positive number indicates improvement. 'n' indicates number of subjects with data available for analysis for the below categories. Full Analysis Set included all enrolled subjects who received >=1 administration of study medication. Study eye = treated eye (with Ozurdex), fellow eye=untreated.

End point type	Primary

End point timeframe:

Baseline, at Month 10 through Month 12

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a single arm study and due to system limitation we were unable to add the statistical analysis.

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: letters				
arithmetic mean (standard deviation)				
Baseline (n=75)	59.4 (± 14.33)			
Change From Baseline (n=29)	-0.7 (± 10.84)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Central Retinal Thickness (CRT) 2 months (± 2 weeks) After the Last Injection Received

End point title	Mean Change in Central Retinal Thickness (CRT) 2 months (± 2 weeks) After the Last Injection Received[2]

End point description:

CRT is defined as the central 1000 microns from the center of the fovea and was measured using spectral domain (SD)-OCT. OCT is a laser-based, non-invasive, diagnostic system providing high-resolution imaging optical sections of the retina. A negative number indicates improvement. 'n' indicates number of subjects with data available for analysis for the below categories. Full Analysis Set included

all enrolled subjects who received >=1 administration of study medication.

End point type	Primary

End point timeframe:

Baseline, at Month 10 through 12

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This is a single arm study and due to system limitation we were unable to add the statistical analysis.

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: micrometer				
arithmetic mean (standard deviation)				
Baseline (n=74) Change from Baseline (n=27)	458.6 (± 114.43) -156.8 (± 103.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Second Injection

End point title	Percentage of Subjects With Second Injection

End point description:

Full Analysis Set included all enrolled subjects who received >=1 administration of study medication.

End point type	Secondary

End point timeframe:

Up to Month 14

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: percentage of subjects				
number (not applicable)	78.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Third Injection

End point title	Percentage of Subjects With Third Injection

End point description:

Full Analysis Set included all enrolled subjects who received >=1 administration of study medication.

End point type	Secondary

End point timeframe:

Up to Month 14

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: percentage of subjects				
number (not applicable)	58.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Retreatment Interval in Study Eye

End point title	Mean Retreatment Interval in Study Eye

End point description:

First retreatment interval is defined as the number of days between the initial treatment and the first retreatment. Second retreatment interval is defined as the number of days between the first retreatment and the second retreatment. 'n' indicates number of subjects with data available for analysis for the below categories. Full Analysis Set includes all enrolled subjects who received >=1 administration of study medication. Study eye = treated eye (with Ozurdex), fellow eye=untreated.

End point type	Secondary

End point timeframe:

From initial treatment to the first and second re-treatment to (Up to Month 14)

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: days				
arithmetic mean (standard deviation)				
First Retreatment Interval (n=59)	140.2 (± 42.41)			
Second Retreatment Interval (n=44)	127.1 (± 43.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Number of Injections Administered

End point title	Number of Subjects With Number of Injections Administered

End point description:

Full Analysis Set included all enrolled subjects who received >=1 administration of study medication. Study eye = treated eye (with Ozurdex), fellow eye=untreated.

End point type	Secondary

End point timeframe:

Up to Month 14

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: subjects				
Study Eye: 1 Injection	16			
Study Eye: 2 Injections	15			
Study Eye: 3 Injections	25			
Study Eye: 4 Injections	18			
Study Eye: 5 Injections	0			
Study Eye: 6 Injections	1			
Fellow Eye: 1 Injection	9			
Fellow Eye: 2 Injections	3			
Fellow Eye: 3 Injections	6			
Fellow Eye: 4 Injections	1			
Fellow Eye: 5 Injections	0			
Fellow Eye: 6 Injections	0			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for BCVA

End point title	AUC for BCVA

End point description:

BCVA was measured using an eye chart and is reported as the number of letters read correctly using the early treatment diabetic retinopathy study (ETDRS) Scale (ranging from 0 to 100 letters) in the study eye. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). 'n' indicates number of subjects with data available for analysis for the below categories. Full Analysis Set includes all enrolled subjects who received >=1 administration of study medication. Study eye = treated eye (with Ozurdex), fellow eye=untreated.

End point type	Secondary

End point timeframe:

Baseline up to Month 14

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: ng.h/ml				
arithmetic mean (standard deviation)				
0 to Month 2 (n=62)	124.1 (± 23.95)			
0 to Month 4 (n=74)	228.5 (± 66.62)			
0 to Month 6 (n=74)	350.5 (± 84.52)			
0 to Month 8 (n=74)	472.3 (± 105.96)			
0 to Month 10 (n=74)	594.8 (± 129.05)			
0 to Month 12 (n=74)	716.9 (± 153.79)			
0 to Month 14 (n=74)	838.3 (± 180.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change in the National Eye Institute Visual Functioning Questionnaire-25 (NEI VFQ-25)

End point title	Mean Change in the National Eye Institute Visual Functioning Questionnaire-25 (NEI VFQ-25)

End point description:

NEI VFQ-25 includes 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items were scored so that a high score represents better functioning. Original numeric values from the survey were recorded with the worst and best possible scores set at 0 and 100 points. In this format, scores represent the achieved percentage of the total possible score, e.g. a score of 50 represents 50% of the highest possible score. 'n' indicates number of subjects with data available for analysis for the below categories. Full Analysis Set includes all enrolled subjects who received >=1 administration of study medication.

End point type	Secondary

End point timeframe:

Baseline, at Month 14

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=69)	79.0 (± 16.77)			
Change from Baseline (n=45)	3.1 (± 15.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve (AUC) for CRT

End point title	Area Under the Curve (AUC) for CRT

End point description:

CRT is defined as the central 1000 microns from the center of the fovea and was measured using spectral domain (SD)-OCT. OCT is a laser-based, non-invasive, diagnostic system providing high-resolution imaging optical sections of the retina. 'n' indicates number of subjects with data available for analysis for the below categories. Full Analysis Set includes all enrolled subjects who received >=1 administration of study medication.

End point type	Secondary

End point timeframe:

Baseline up to Month 14

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: nanogram.hour/millilitre (ng.h/ml)				
arithmetic mean (standard deviation)				
0 to Month 2 (n=61)	764.8 (± 134.31)			
0 to Month 4 (n=73)	1339.9 (± 329.03)			
0 to Month 6 (n=73)	2063.5 (± 461.09)			
0 to Month 8 (n=73)	2771.3 (± 615.52)			
0 to Month 10 (n=73)	3482.3 (± 768.70)			
0 to Month 12 (n=73)	4172.3 (± 936.43)			
0 to Month 14 (n=73)	4852.1 (± 1135.54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Second Injection

End point title	Time to Second Injection

End point description:

Full Analysis Set included all enrolled subjects who received >=1 administration of study medication. Number of subjects analyzed indicates the number of subjects available for analysis.

End point type	Secondary

End point timeframe:

Up to Month 14

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: days				
median (full range (min-max))	126.0 (56 to 287)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Third Injection

End point title	Time to Third Injection

End point description:

Full Analysis Set included all enrolled subjects who received >=1 administration of study medication. Number of subjects analyzed indicates the number of subjects available for analysis.

End point type	Secondary

End point timeframe:

Up to Month 14

End point values	OZURDEX® 700 µg			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: days				
median (full range (min-max))	245.0 (168 to 507)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline to final visit (up to 14 months)	
Adverse event reporting additional description:	
Safety Set consisted of all enrolled patients who received ≥1 administration of study medication/procedure.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	OZURDEX® 700 µg
Reporting group description:	
Participants enrolled in Spain received OZURDEX® 700 µg intravitreal implant as needed per investigator assessment on Day 1.	

Serious adverse events	OZURDEX® 700 µg		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 75 (13.33%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
LEUKAEMIA			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
LARYNGEAL SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RENAL NEOPLASM			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Investigations			
BLOOD PRESSURE DECREASED			

subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HIP FRACTURE			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SPINAL FRACTURE			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
SHOCK HAEMORRHAGIC			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			

subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 PNEUMONIA			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ENDOPHTHALMITIS			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SEPTIC SHOCK			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
UROSEPSIS			
subjects affected / exposed	1 / 75 (1.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	OZURDEX® 700 µg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 75 (21.33%)		
Investigations			
INTRAOCULAR PRESSURE INCREASED			
subjects affected / exposed	9 / 75 (12.00%)		
occurrences (all)	12		

Eye disorders CATARACT subjects affected / exposed occurrences (all)	 5 / 75 (6.67%) 6		
Metabolism and nutrition disorders VITAMIN D DEFICIENCY subjects affected / exposed occurrences (all)	 4 / 75 (5.33%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 May 2019	Amendment 03: - Changes in Efficacy Endpoints. - Changes on Exclusion Criteria (on regards contraception and WOCBP). - Change on repeat doses. - Change on Permitted Medications (Panretinal photocoagulation) This modification does not affects reference safety information or urgent safety measure, but the scientific value of the trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported