Clinical trial results:
Safety, tolerability and pharmacodynamics of single rising intravitreal and multiple rising intravitreal doses of BI 836880 in patients with wAMD (open label, non-randomized, uncontrolled)

Summary

EudraCT number	2017-001221-40
Trial protocol	DE
Global end of trial date	01 November 2023

Results information

Result version number	v1 (current)
This version publication date	14 November 2024
First version publication date	14 November 2024

Trial information

Trial identification

Sponsor protocol code	1336-0007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03861234
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.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	18 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2023
Global end of trial reached?	Yes
Global end of trial date	01 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to investigate the safety, tolerability, and pharmacodynamics of single and multiple intravitreal doses of BI 836880.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all subjects as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 2019
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	Germany: 24
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	United Kingdom: 22
Worldwide total number of subjects	71
EEA total number of subjects	24

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)	4
From 65 to 84 years	61

85 years and over	6

Subject disposition

Recruitment

Recruitment details:

A study consisting of a single rising dose (SRD) part followed by a multiple rising dose (MRD) part. The SRD part and MRD cohort 1 included patients with treatment-resistant wet age-related macular degeneration (wAMD). Patients with treatment-naïve wAMD were included in MRD cohort 2 and patients within 3 years of initial wAMD in MRD cohort 3.

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

Period 1 title	Enrollment Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	0.06 mg BI 836880 - SRD part

Arm description:

0.06 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.06 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	0.18 mg BI 836880 - SRD part

Arm description:

0.18 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.18 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	0.5 mg BI 836880 - SRD part

Arm description:

0.5 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.5 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	1 mg BI 836880 - SRD part

Arm description:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	2 mg BI 836880 - SRD part

Arm description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	1 mg BI 836880 - cohort 1 MRD part

Arm description:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental

Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	2 mg BI 836680 - cohort 2 MRD part

Arm description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-naïve wAMD.

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-naïve wAMD.

Arm title	2 mg BI 836680 - cohort 3 MRD part

Arm description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients within 3 years of initial wAMD.

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients within 3 years of initial wAMD.

Number of subjects in period 1	0.06 mg BI 836880 - SRD part	0.18 mg BI 836880 - SRD part	0.5 mg BI 836880 - SRD part
Started	3	3	3
Completed	3	3	3
Not completed	0	0	0
Not treated	-	-	-

Number of subjects in period 1	1 mg BI 836880 - SRD part	2 mg BI 836880 - SRD part	1 mg BI 836880 - cohort 1 MRD part
Started	3	3	11

Completed	3	3	10
Not completed	0	0	1
Not treated	-	-	1

Number of subjects in period 1	2 mg BI 836680 - cohort 2 MRD part	2 mg BI 836680 - cohort 3 MRD part
Started	4	13
Completed	4	13
Not completed	0	0
Not treated	-	-

Period 2

Period 2 title	Treatment period
Is this the baseline period?	Yes[1]
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	0.06 mg BI 836880 - SRD part

Arm description:

0.06 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.06 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	0.18 mg BI 836880 - SRD part

Arm description:

0.18 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.18 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for

solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	0.5 mg BI 836880 - SRD part

Arm description:

0.5 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

0.5 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	1 mg BI 836880 - SRD part

Arm description:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	2 mg BI 836880 - SRD part

Arm description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836880
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	1 mg BI 836880 - cohort 1 MRD part

Arm description:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29

and Day 57, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm type	Experimental
Investigational medicinal product name	BI 836680
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Arm title	2 mg BI 836680 - cohort 2 MRD part

Arm description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-naïve wAMD.

Arm type	Experimental
Investigational medicinal product name	BI 836680
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-naïve wAMD.

Arm title	2 mg BI 836680 - cohort 3 MRD part

Arm description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients within 3 years of initial wAMD.

Arm type	Experimental
Investigational medicinal product name	BI 836680
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients within 3 years of initial wAMD.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Treatment period is used as baseline period

Number of subjects in period 2[2]	0.06 mg BI 836880 - SRD part	0.18 mg BI 836880 - SRD part	0.5 mg BI 836880 - SRD part
Started	3	3	3
Completed	3	3	3
Not completed	0	0	0
IMP on hold as per sponsor instructions	-	-	-
Adverse event, non-fatal	-	-	-

Medication discontinued due to safety notification	-	-	-
As per sponsor decision	-	-	-

Number of subjects in period 2[2]	1 mg BI 836880 - SRD part	2 mg BI 836880 - SRD part	1 mg BI 836880 - cohort 1 MRD part
Started	3	3	10
Completed	3	3	8
Not completed	0	0	2
IMP on hold as per sponsor instructions	-	-	-
Adverse event, non-fatal	-	-	1
Medication discontinued due to safety notification	-	-	1
As per sponsor decision	-	-	-

Number of subjects in period 2[2]	2 mg BI 836680 - cohort 2 MRD part	2 mg BI 836680 - cohort 3 MRD part
Started	4	13
Completed	1	13
Not completed	3	0
IMP on hold as per sponsor instructions	2	-
Adverse event, non-fatal	-	-
Medication discontinued due to safety notification	-	-
As per sponsor decision	1	-

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Worldwide 71 subjects were enrolled, whereof 43 subjects actually entered the trial.

Baseline characteristics

Reporting groups	
Reporting group title	0.06 mg BI 836880 - SRD part
Reporting group description:	
0.06 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	0.18 mg BI 836880 - SRD part
Reporting group description:	
0.18 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	0.5 mg BI 836880 - SRD part
Reporting group description:	
0.5 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	1 mg BI 836880 - SRD part
Reporting group description:	
1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	2 mg BI 836880 - SRD part
Reporting group description:	
2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	1 mg BI 836880 - cohort 1 MRD part
Reporting group description:	
1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	2 mg BI 836680 - cohort 2 MRD part
Reporting group description:	
2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-naïve wAMD.	
Reporting group title	2 mg BI 836680 - cohort 3 MRD part
Reporting group description:	
2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients within 3 years of initial wAMD.	

Reporting group values	0.06 mg BI 836880 - SRD part	0.18 mg BI 836880 - SRD part	0.5 mg BI 836880 - SRD part
Number of subjects	3	3	3
Age categorical			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
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)	0	0	0
From 65-84 years	2	3	3
85 years and over	1	0	0
Age Continuous			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: years			
arithmetic mean	81.7	76.7	75.3
standard deviation	± 5.7	± 4.2	± 1.5
Sex: Female, Male			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Participants			
Female	2	2	0
Male	1	1	3
Race (NIH/OMB)			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	3	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	3	3
Unknown or Not Reported	0	0	0

Reporting group values	1 mg BI 836880 - SRD part	2 mg BI 836880 - SRD part	1 mg BI 836880 - cohort 1 MRD part
Number of subjects	3	3	10
Age categorical			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
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)	0	0	0
From 65-84 years	3	3	9
85 years and over	0	0	1

Age Continuous			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: years			
arithmetic mean	75.7	70.7	77.0
standard deviation	± 1.5	± 1.2	± 4.8
Sex: Female, Male			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Participants			
Female	0	1	4
Male	3	2	6
Race (NIH/OMB)			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	3	10
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	3	10
Unknown or Not Reported	0	0	0

Reporting group values	2 mg BI 836680 - cohort 2 MRD part	2 mg BI 836680 - cohort 3 MRD part	Total
Number of subjects	4	13	42
Age categorical			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
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)	2	0	2
From 65-84 years	2	11	36
85 years and over	0	2	4
Age Continuous			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: years			
arithmetic mean	69.3	77.0	
standard deviation	± 13.0	± 6.3	-
Sex: Female, Male			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Participants			

Female	2	6	17
Male	2	7	25

Race (NIH/OMB)			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	4	13	42
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Treated Set (TS): All patients who were treated with at least one dose of BI 836880.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	4	13	42
Unknown or Not Reported	0	0	0

End points reporting groups

Reporting group title	0.06 mg BI 836880 - SRD part
Reporting group description:	
0.06 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	0.18 mg BI 836880 - SRD part
Reporting group description:	
0.18 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	0.5 mg BI 836880 - SRD part
Reporting group description:	
0.5 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	1 mg BI 836880 - SRD part
Reporting group description:	
1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	2 mg BI 836880 - SRD part
Reporting group description:	
2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	1 mg BI 836880 - cohort 1 MRD part
Reporting group description:	
1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	2 mg BI 836680 - cohort 2 MRD part
Reporting group description:	
2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-naïve wAMD.	
Reporting group title	2 mg BI 836680 - cohort 3 MRD part
Reporting group description:	
2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients within 3 years of initial wAMD.	
Reporting group title	0.06 mg BI 836880 - SRD part
Reporting group description:	
0.06 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	0.18 mg BI 836880 - SRD part
Reporting group description:	
0.18 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).	
Reporting group title	0.5 mg BI 836880 - SRD part
Reporting group description:	
0.5 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients	

with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	1 mg BI 836880 - SRD part

Reporting group description:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	2 mg BI 836880 - SRD part

Reporting group description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	1 mg BI 836880 - cohort 1 MRD part

Reporting group description:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	2 mg BI 836680 - cohort 2 MRD part

Reporting group description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-naïve wAMD.

Reporting group title	2 mg BI 836680 - cohort 3 MRD part

Reporting group description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients within 3 years of initial wAMD.

Primary: SRD-part: Number of participants with ocular dose limiting events (DLEs)

End point title	SRD-part: Number of participants with ocular dose limiting events (DLEs)[1][2]

End point description:

Single rising dose (SRD)-part: Number of participants with ocular dose limiting events (DLEs).
Treated Set: All patients who were treated with at least on dose of BI 836880. SRD-part.

End point type	Primary

End point timeframe:

From drug administration until the end of trial (EOT) visit in the SRD part, up to 6 weeks.

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: The endpoint has been analyzed descriptively.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed in the SRD part of the trial.

End point values	0.06 mg BI 836880 - SRD part	0.18 mg BI 836880 - SRD part	0.5 mg BI 836880 - SRD part	1 mg BI 836880 - SRD part
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	2 mg BI			

	836880 - SRD part			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: MRD-part: Number of participants with drug related adverse events (AEs)

End point title	MRD-part: Number of participants with drug related adverse events (AEs)[3][4]

End point description:

Multiple rising dose (MRD)-part: Number of participants with drug related adverse events (AEs).
Treated Set: All patients who were treated with at least on dose of BI 836880. MRD-part.

End point type	Primary

End point timeframe:

From first drug administration until the end of trial (EOT) visit in the MRD part, up to 24 weeks.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint was analyzed descriptively.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed in the MRD part of the trial.

End point values	1 mg BI 836880 - cohort 1 MRD part	2 mg BI 836680 - cohort 2 MRD part	2 mg BI 836680 - cohort 3 MRD part	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	4	13	
Units: Participants	2	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: SRD-part: Number of participants with drug related adverse events (AEs)

End point title	SRD-part: Number of participants with drug related adverse events (AEs)[5]

End point description:

Single rising dose (SRD)-part: Number of participants with drug related adverse events (AEs).
Treated Set (TS): All patients who were treated with at least one dose of BI 836680. SRD-part.

End point type	Secondary

End point timeframe:

From drug administration until the end of trial (EOT) visit in the SRD part, up to 6 weeks.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed in the SRD part of the trial.

End point values	0.06 mg BI 836880 - SRD part	0.18 mg BI 836880 - SRD part	0.5 mg BI 836880 - SRD part	1 mg BI 836880 - SRD part
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	0	0	0	0

End point values	2 mg BI 836880 - SRD part			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: SRD-part: Number of participants with any ocular adverse events in the study eye

End point title	SRD-part: Number of participants with any ocular adverse events in the study eye[6]

End point description:

Single rising dose (SRD)-part: Number of participants with any ocular adverse events in the study eye.

End point type	Secondary

End point timeframe:

From drug administration until the end of trial (EOT) visit in the SRD part, up to 6 weeks.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed in the SRD part of the trial.

End point values	0.06 mg BI 836880 - SRD part	0.18 mg BI 836880 - SRD part	0.5 mg BI 836880 - SRD part	1 mg BI 836880 - SRD part
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: Participants	1	0	1	1

End point values	2 mg BI 836880 - SRD part			

Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Participants	2			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD-part: Time to recurrence in the study eye from last administration at each visit

End point title	MRD-part: Time to recurrence in the study eye from last administration at each visit[7]

End point description:

Time to recurrence was assessed from last trial drug administration to occurrence of any of the following in the study eye, leading to the use of wet age-related macular degeneration (wAMD) rescue medication as decided by the investigator:
- Increase in Central Subfield Thickness (CFST) ≥75 µm with a decrease in Best Corrected Visual Acuity (BCVA) of ≥ 5 letters compared to Visit 5,
OR
- Decrease in BCVA of >5 letters compared to baseline (Visit 2), due to worsening wAMD activity,
OR
-Decrease in BCVA of ≥10 letters compared to the best prior BCVA, due to worsening wAMD activity.
From above criteria, if Visit 5 BCVA/CSFT assessment data is missing, BCVA/CSFT values available earlier than Visit 5 will be used. The last trial drug administration is strictly referring to the third injection, if a patient doesn't complete 3 injections, the patient will not be evaluated for time to recurrence endpoint and will be censored.
Treated Set.
99999 = Not calculable (NC).

End point type	Secondary

End point timeframe:

From last drug administration at Week 8 until End of Trial, up to 16 weeks.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed in the MRD part of the trial.

End point values	1 mg BI 836880 - cohort 1 MRD part	2 mg BI 836680 - cohort 2 MRD part	2 mg BI 836680 - cohort 3 MRD part	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	4[8]	13[9]	
Units: Weeks				
median (confidence interval 95%)	8.0 (4.6 to 16.1)	99999 (99999 to 99999)	99999 (8.1 to 99999)	

Notes:

[8] - Not calculable (nc), as there was no event ("recurrence").

[9] - NC., as patients either censored or had events before the probability of recurrence reached to 50%.

Statistical analyses

No statistical analyses for this end point

Secondary: MRD-part: Percentage change from baseline in Central Subfield Thickness (CSFT) in the study eye at Week 12

End point title	MRD-part: Percentage change from baseline in Central Subfield Thickness (CSFT) in the study eye at Week 12[10]

End point description:

Multiple rising dose (MRD)-part: Central subfield thickness was measured using Spectral domain-optical coherence tomography (SD-OCT) with the assessment performed by a qualified person and only specified OCT equipment was used. Optical coherence tomography angiography (OCT-A), a non-invasive imaging technique providing high-resolution volumetric blood flow information without the use of dye was also performed by a qualified person, and only specified device(s) were used. OCT images were sent to an independent CRC for evaluation. A detailed manual for OCT image acquisition and data transmission was provided. CSFT was investigated after 3 doses of BI 836880 in the MRD part of the trial at Week 12.

Full Analysis Set (FAS): All patients who were treated with at least one dose of BI 836880 and have baseline and on-treatment CSFT measurements for the study eye in the time interval from drug administration to Week 12. MRD part.

End point type	Secondary

End point timeframe:

At baseline and at week 12.

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed in the MRD part of the trial.

End point values	1 mg BI 836880 - cohort 1 MRD part	2 mg BI 836680 - cohort 2 MRD part	2 mg BI 836680 - cohort 3 MRD part	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	4	12	
Units: Percentage change				
arithmetic mean (standard deviation)	-7.7554 (± 18.9936)	-26.5552 (± 12.1400)	-0.1372 (± 20.1706)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRD-part: Change from baseline in best corrected visual acuity (BCVA) in the study eye at Week 12

End point title	MRD-part: Change from baseline in best corrected visual acuity (BCVA) in the study eye at Week 12[11]

End point description:

Multiple rising dose (MRD)-part): Visual acuity (VA) measured by ‘early treatment diabetic retinopathy study’ letter charts.
BCVA was measured using the early treatment diabetic retinopathy study (ETDRS) VA chart starting at a test distance of 4 m. The BCVA score was the number of letters read correctly by the patient. The assessment was performed by a trained person under specified conditions regarding examination room and equipment.

Full Analysis Set (FAS): All patients who were treated with at least one dose of BI 836880 and have baseline and on-treatment CSFT measurements for the study eye in the time interval from drug administration to Week 12. MRD part.

End point type	Secondary

End point timeframe:

At baseline and at Week 12.

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed in the MRD part of the trial.

End point values	1 mg BI 836880 - cohort 1 MRD part	2 mg BI 836680 - cohort 2 MRD part	2 mg BI 836680 - cohort 3 MRD part	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	4	13	
Units: Letters				
arithmetic mean (standard deviation)	-1.2 (± 6.4)	1.8 (± 2.5)	-4.7 (± 22.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: MRD-part: Number of participants with any ocular adverse events in the study eye

End point title	MRD-part: Number of participants with any ocular adverse events in the study eye[12]

End point description:

Multiple rising dose (MRD)-part: Number of participants with any ocular adverse events in the study eye.

Treated Set (TS): All patients who were treated with at least one dose of BI 836880. MRD-part.

End point type	Secondary

End point timeframe:

From first drug administration until the end of trial (EOT) visit in the MRD part, up to 24 weeks.

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was only analyzed in the MRD part of the trial.

End point values	1 mg BI 836880 - cohort 1 MRD part	2 mg BI 836680 - cohort 2 MRD part	2 mg BI 836680 - cohort 3 MRD part	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	4	13	
Units: Participants	5	1	9	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SRD-part: From drug administration until the end of trial (EOT) visit, up to 6 weeks. MRD-part: From first drug administration until the end of trial (EOT) visit, up to 24 weeks. All-cause deaths: Up to 6 weeks for SRD-part, up to 24 weeks for MRD-part.

Adverse event reporting additional description:

Treated Set (TS): All patients who were treated with at least one dose of BI 836880.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	0.06 mg BI 836880 - SRD part

Reporting group description:

0.06 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	0.18 mg BI 836880 - SRD part

Reporting group description:

0.18 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	0.5 mg BI 836880 - SRD part

Reporting group description:

0.5 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	2 mg BI 836680 - cohort 3 MRD part

Reporting group description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients within 3 years of initial wAMD.

Reporting group title	2 mg BI 836880 - SRD part

Reporting group description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	1 mg BI 836880 - cohort 1 MRD part

Reporting group description:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Reporting group title	2 mg BI 836680 - cohort 2 MRD part

Reporting group description:

2 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as three IVT injections on Day 1, Day 29 and Day 57, in patients with treatment-naïve wAMD.

Reporting group title	1 mg BI 836880 - SRD part

Reporting group description:

1 mg BI 836880 solution for intravitreal (IVT) injection with diluent for BI 836880 concentrate for solution for injection 80mg/mL, 10 mL vial was administered as single IVT injection on Day 1, in patients with treatment-resistant wet age-related macular degeneration (wAMD).

Serious adverse events	0.06 mg BI 836880 - SRD part	0.18 mg BI 836880 - SRD part	0.5 mg BI 836880 - SRD part
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Injury, poisoning and procedural complications			
Depressed fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Eye disorders			
Neovascular age-related macular degeneration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Retinal occlusive vasculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Serious adverse events	2 mg BI 836680 - cohort 3 MRD part	2 mg BI 836880 - SRD part	1 mg BI 836880 - cohort 1 MRD part
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 13 (30.77%)	0 / 3 (0.00%)	2 / 10 (20.00%)
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 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Depressed fracture			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (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
Eye disorders			
Neovascular age-related macular degeneration			
subjects affected / exposed	2 / 13 (15.38%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal occlusive vasculitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	2 mg BI 836680 - cohort 2 MRD part	1 mg BI 836880 - SRD part	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Depressed fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal occlusive vasculitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	0.06 mg BI 836880 - SRD part	0.18 mg BI 836880 - SRD part	0.5 mg BI 836880 - SRD part
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood folate decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave inversion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Heart rate irregular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tear break up time decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Foreign body in eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Corneal abrasion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cataract operation complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Labile hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Anterior chamber cell			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lenticular opacities			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Meibomian gland dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Punctate keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cataract subcapsular			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Subretinal fluid			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitreal cells			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitreous haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitreous opacities			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitreous detachment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pigmentation disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chorioretinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	2 mg BI 836680 - cohort 3 MRD part	2 mg BI 836880 - SRD part	1 mg BI 836880 - cohort 1 MRD part
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 13 (84.62%)	2 / 3 (66.67%)	8 / 10 (80.00%)
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood folate decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Blood creatine phosphokinase			

increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase MB increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood potassium increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram T wave inversion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Heart rate irregular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tear break up time decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oxygen saturation abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Foreign body in eye			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Corneal abrasion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cataract operation complication			

subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Labile hypertension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eye disorders			
Anterior chamber cell			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye inflammation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lenticular opacities			

subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Meibomian gland dysfunction			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ocular discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Punctate keratitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Conjunctival haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cataract subcapsular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Retinal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Retinal oedema			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Subretinal fluid			
subjects affected / exposed	2 / 13 (15.38%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Visual acuity reduced			
subjects affected / exposed	2 / 13 (15.38%)	0 / 3 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	2
Visual impairment			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Vitreal cells			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vitreous floaters			

subjects affected / exposed	1 / 13 (7.69%)	2 / 3 (66.67%)	1 / 10 (10.00%)
occurrences (all)	1	2	1
Vitreous haemorrhage			
subjects affected / exposed	2 / 13 (15.38%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Vitreous opacities			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vitreous detachment			
subjects affected / exposed	2 / 13 (15.38%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pigmentation disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
Chorioretinitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 3 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Product issues			
Device dislocation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 3 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2

Non-serious adverse events	2 mg BI 836680 - cohort 2 MRD part	1 mg BI 836880 - SRD part	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood folate decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Blood potassium increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Heart rate irregular			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Tear break up time decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Oxygen saturation abnormal			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Foreign body in eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Corneal abrasion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Cataract operation complication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Peripheral venous disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Labile hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Eye disorders			

Anterior chamber cell			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Eye inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Foreign body sensation in eyes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Lenticular opacities			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Meibomian gland dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ocular discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Punctate keratitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Conjunctival haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Cataract subcapsular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Retinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Retinal oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Subretinal fluid			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Visual acuity reduced			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Visual impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vitreal cells			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vitreous floaters			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Vitreous haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vitreous opacities			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vitreous detachment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Pigmentation disorder subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0	
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 3 (0.00%) 0	
Chorioretinitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	
Product issues Device dislocation subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 3 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2019	Amendment 1 became effective without approval by the Independent ethics committee (IEC)/ Institutional review board (IRB)/Competent authority (CA). The amendment introduced minor changes to the Clinical Trial Protocol (CTP) as follows: - Minor corrections to the flow charts regarding the timing of Anit-drug antibody (ADA) sampling to align with the rest of the CTP - Clarified endpoint definitions to specify that that they should be measured in the study eye - Correction of the calculated relative dose increases - Removed electrocardiogram (ECG) interval measurement analytical methods and deleted stipulations for blinding of the central ECG lab with regards to interval measurements as no interval measurements were to be collected and ECGs were only to be checked for baseline conditions and adverse events (AEs) - Clarification of vascular occlusion dose-limiting events (DLE) definition - Updated the methods of SAE submittal to Boehringer Ingelheim (BI) - Clarified that no hypothesis testing was to be accomplished due to the exploratory nature of the trial - Minor typing error corrections
11 November 2019	Amendment 2 became effective without approval by the IEC/IRB/CA. The amendment introduced minor changes to the CTP as follows: - Clarification of inclusion criteria 1, 2, and 7 with regards to the methods to be used for Wet age-related macular degeneration (wAMD) diagnosis, applicability to sinlge rising dose (SRD) vs multiple rising dose (MRD), and degree of fibrosis, respectively.
06 October 2020	Amendment 3 became effective after approval by the IEC/IRB/CA. The amendment introduced substantial changes to the CTP as follows: - Minor corrections to wording to more accurately describe endpoints and criteria - Removal of biobanking for SRD part and clarification of height and weight measurement timing - Addition of pharmacokinetic (PK) and biomarker sampling at Visits 6, 7, and 8 and ADA sampling at Visit 8 for MRD cohort 1 - Update of drug profile with data from 10 treated SRD patients - Added an assessment of the impact of the COVID-19 pandemic on the trial and the overall impact on the benefit-risk assessment along with changes to trial conduct with regard to COVID-19 testing and individual participation in the trial - Several adaptations were introduced to more accurately describe respective endpoints - Clarified the safety monitoring committee (SMC) role in selection of doses to be used in the MRD part - Clarification with regard to the timing of prior vascular endothelial growth factor (VEGF) treatments prior to screening/randomisation

06 October 2020	Amendment 3 (continued): - Clarification of the definition of child bearing potential and contraceptive requirements - 'Qualified personnel' were added as an alternative to the site pharmacist - Clarification that standard of care was allowed from Visit 5 (Follow up period) - Corrected the timeframe for dose limiting events - Clarification of criteria to accurately determine recurrence leading to the use of rescue medication by adding specific central subfield retinal thickness (CSFT) and best corrected visual acuity (BCVA) changes - Added PK and plasma derived biomarker assessments for 56, 84, and 112 days after the 3rd treatment for the MRD part - Clarification of timelines and requirements for ocular tonometry and the exchange of optional fluorescein angiography for optical coherence tomography-angiography (OCT-A) acquisitions during follow up - Increased Follow up period from 14 to 28 days - Added text allowing an informal preliminary analysis of efficacy data after the completion of Visit 5
26 March 2021	Amenment 4 became effective after approval by the IEC/IRB/CA. The amendment introduced substantial changes to the CTP as follows: - Increased the time from the last injection of VEGF therapy prior to screening from 12 to 16 weeks and removed the requirement for patients to have had the first anti-VEGF treatment in the study eye within 18 months (inclusion criterion 2) in order to increase eligibility and recruitment to the trial - Clarified exclusion criteria regarding previous incidences of increased IOP, allowed yttrium aluminium garnet laser capsulotomy within 1 month prior to enrolment, and allowed previous participation in other trials for the treatment of wAMD if washout requirements were met in order to increase eligibility and recruitment to the trial
28 July 2021	Amendment 5 became effective after approval by the IEC/IRB/CA. The amendment introduced major changes to the CTP through the addition of MRD cohort 2 (treatment naïve patients) as follows: - Integration of cohort 2 via the additions of Flow Chart III and eligibility criteria (including specific inclusion and exclusion criteria), integration of associated increase in the number of entered/treated patients and sample size calculation, adaptation of the tested doses (2 mg BI 836880 for cohort 2), and an update of the trial rationale. - Update of drug profile and dose escalation scheme with data from the completed SRD part, including the highest safe dose (2 mg BI 836880). - Update of benefit risk assessment considering published faricimab data. Integration of risks and a corresponding update to the informed consent form (ICF) with regard to the silicon oil coated needle caution statement by Becton Dickson. - Description of new drug formulation (40 mg/mL BI 836880 solution for injection) - Addition of optional safety visits within 1 week of treatment visits (Visits 2, 3, and 4) and description of remote monitoring calls. - Increase in pre-dose sampling PK blood sampling windows
25 October 2021	Amendment 6 became effective after approval by the IEC/IRB/CA. The amendment introduced substantial changes to the CTP as follows: Clarification of sample size and the overlap of cohorts 1 and 2 - Reduction of required CSFT >330 µm to CSFT >300 µm inclusion criteria to increase eligibility and recruitment - Broadening of early treatment diabetic retinopathy study (ETDRS) inclusion criteria from 'ETDRS visual acuity (VA) in the study eye between 70 and 24 letters inclusive' to 'between 75 and 24 letters inclusive (approximately 20/32 or 6/9.5)'for MRD cohort 1 in line with the positive safety data collected to date. - Added description of diluent and its use for both 40 mg/mL and 80 mg/mL formulations.

28 September 2022	Amendment 7 became effective while the trial was on voluntary medical hold by the sponsor due to 2 incidences inflammatory eye disorders that were judged as related to BI 836880 by investigators. Amendment 7 implemented safety measures to mitigate the risk and ensure early detection of intraocular inflammation. The trial was resumed only after approval by the IEC/IRB/CA. The amendment included the addition of cohort 3 and other updates to the CTP as follows: - Integration of cohort 3 via the additions of Flow Chart IV and eligibility criteria (including specific inclusion and exclusion criteria), dose groups (cohort 3 dosed at 2 mg per treatment), an update of the trial rationale. - Descriptions of increased safety measures included: fluorescein angiography imaging during screening, wide angle colour fundus photos with vitreous haze assessment at every visit, and the requirement to report any intraocular inflammation events as adverse events of special interests (AESIs). Furthermore, certain exclusion criteria were amended to exclude patients with a high potential of developing ocular inflammation from MRD cohort 3. - Revised and clarified the patients entered, cohort sizes, and dose groups in MRD part. All remaining patients were allocated to cohort 3. Reiteration of replacement strategy. - Updated current summary of clinical safety data including descriptions of 2 serious adverse events (SAEs) reported in MRD cohort 1. Described evidence of efficacy detected during exploratory analysis of interim data in patients requiring frequent standard of care which were the target patient population for MRD cohort 3.
28 September 2022	Amendment 7 (continued): Added the following MRD cohort 3 further exploratory endpoints to gather insight of the treatment effect: o Absence (yes/no) of intra-retinal or sub-retinal fluid (IRF, SRF) in the study eye at Week 16 (Visit 6, cohort 3 only) o Resolution (yes/no) of subretinal hyper-reflective material/retinal pigment epithelial detachment (SHRM/PED) in the study eye at Week 16 (Visit 6, cohort 3 only) o A responder analysis that was further modified in the trial statistical analysis plan (TSAP) - Reworded statistical sections to make clear that no statistical testing was planned for descriptive statistics. Updated/clarified analytical details regarding MRD cohort 3 including the addition of the evaluable responders' analytical dataset. - Added new BI 836880 formulation where an initial trial formulation (CMC1) was switched to an intended final formulation (CMC2) for MRD cohort 3. - Amended the restrictions to concomitant treatment to clarify that standard of care (SoC) therapy could be administered if there is a worsening in disease before Visit 6, and as deemed medically appropriate during/after Visit 6 to make clear that investigators could treat patients with SoC during the follow up period even if patients did not meet time to recurrence or AESI criteria. - Clarified DLE criteria and amended AESI criteria for cohorts that received the maximum dose (2 mg BI 836880, MRD cohorts 2 & 3). - Clarified the evaluation of ECGs by site personnel to allow operational flexibility. - Clarified the requirement of written consent of the pregnant partner of a study participant for drug exposure reporting and pregnancy outcome. - Extended PK dose sampling window prior to 1st intravitreal (IVT) dose.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported