Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Brolucizumab

Trial Indication(s)

Age-related macular degeneration (AMD)

Protocol Number

CRTH258AUS21

Protocol Title

Real-world evaluation of brolucizumab for the treatment of neovascular (wet) age-related macular degeneration (AMD) (Komodo Health)

Clinical Trial Phase

NA

Phase of Drug Development

NA

Study Start/End Dates

Study Start Date: 17 June 2020

Study End Date: 18 December 2020

Reason for Termination

NA

Study Design/Methodology

This study was a retrospective cohort study of patients with wet AMD who received brolucizumab. Evidence was generated to describe their patient characteristics and clinical outcomes. The study was conducted using the Komodo Healthcare Map.

Setting and study population

Komodo Healthcare Map claims data from 08-Oct-2016 to the date of most recent data from patients with wet AMD who initiated brolucizumab were analyzed in this study.

· Identification period of the index date (index period): The patients fulfilling the selection criteria were identified during the period from 08-Oct-2019 to 30-Apr-2020.

· Index date: Defined as the date of the earliest brolucizumab injection during the index period.

· Study Period: The period from 08-Oct-2016 to the most recent data extraction date (05-Jun - 2020).

  · Note since 05-Jun-2020 was the date data was pulled, claims data from recent months (e.g. May) may be incomplete (relative to the final DB state) as well.

· Pre-index period: The period 36 months prior to the index date

  · Note: Data within 36 months prior to the index date will be used to assess baseline characteristics.

· Post-index period: The period of 180 days after the index date

· Follow-up: The longest duration of follow-up was 6 months. Patient eyes included in the studies have varying lengths of follow-up depending on when they initiated brolucizumab treatment and when the last visit was recorded in the respective databases.

The last follow-up date was defined as the date of the last follow-up recorded.

Centers

Novartis Investigative Site

Objectives:

Primary objective(s)

To assess Intraocular Inflammation (IOI) events observed after starting treatment with brolucizumab

Secondary objective(s)

Secondary objectives of this study were to assess baseline demographic and clinical characteristics, and the incidence of specific ocular AEs among patients treated with brolucizumab

Test Product (s), Dose(s), and Mode(s) of Administration

≥1 Brolucizumab Intravitreal injection

Statistical Methods

All analyses were performed by Komodo Health.

Descriptive statistics were tabulated for the baseline demographic and clinical characteristics and outcome variables. Analyses were performed at the patient level or patient eye level. Python was used to run all planned analyses.

Continuous and categorical variables

Continuous variables were summarized by providing the number of observations, means, medians, standard deviations, and minimum and maximum values. Categorical variables were summarized by providing counts and proportions, with missing data considered a separate category

Multivariable analyses

Generalized estimating equations were used to assess the association between the specific AEs (any form of IOI [including RV] and/or RO, RV and/or RV) and baseline patient demographics and clinical characteristics. Independent variables were selected based on clinical and statistical significance. GEE models were fit and output estimated marginal means based on the models to derive probabilities.

Key Inclusion/Exclusion Criteria

Inclusion criteria:

1. ≥1 Healthcare Common Procedure Coding System (HCPCS) code (J code) or National Drug Code (NDC) for treatment with brolucizumab during the index period (date of earliest code = index date)
2. ≥18 years old on the index date
3. ≥1 International Classification of Diseases, Clinical Modification-9/10 (ICD-9/10) code for wet AMD in the 36 months prior to or on the index date
    - Note: Off-label use of brolucizumab is not expected given payer access restrictions in the US
4. ≥24 months of continuous enrollment prior to the index date
5. ≥1 follow-up visit related to their wet AMD after the index date

Exclusion criteria

1. Use of brolucizumab prior to 08-Oct-2019 (e.g. clinical trials)
2. Unknown laterality of the index eye on the index date
3. Patients with no data throughout the 12 months immediately prior to the index date

Participant Flow Table

Patients with a diagnosis of wet AMD who were treated with brolucizumab from 08-Oct-2016 to 30-Apr-2020 in the Komodo Healthcare Map were included. The dataset included 11,434 eyes and 9,498 patients who received ≥1 brolucizumab injection between 08-Oct-2019 and 30-Apr-2020. After applying further inclusion and exclusion criteria, there were 11,161 eyes (11,801 patients) and 9,261 patients remaining. The following criteria were applied to derive the study population

Criteria	Number of Patients	% of Patient Remaining	Number of Eyes	% of Eyes Remaining
≥1 brolucizumab injection between 08-Oct-2019 and 30-Apr-2020	9,498	100.0%	11,434	100.0%
Patient ≥18 years old at index date	9,498	100.0%	11,434	100.0%
Known laterality on index date	9,480	99.8%	11,413	99.8%
≥24 months of continuous enrollment prior to the index date	9,368	98.6%	11,279	98.6%
ICD-9/10 code for wet AMD in the 36 months prior to or on the index date	9,289	97.8%	11,194	97.9%
Patients with no data throughout the 12 months immediately prior to the index date	9,261	97.5%	11,161	97.6%

AMD, age-related macular degeneration; CPT, Current Procedural Terminology; HCPCS, Healthcare Common Procedure Coding System; ICD, International Classfication of Diseases; IVI, intravitreal injection; VA, visual acuity.

Baseline Characteristics

Refer to Secondary Outcomes section for baseline characteristics.

Primary Outcome Result(s)

The overall incidence of any form of IOI (including RV) and/or RO after initiation of brolucizumab (180 days) was 2.40%. Incidence of RV and/or RO after initiation of brolucizumab (180 days) was 0.56%

Overall incidence rates of any form of IOI (including RV) and/or RO[a] up to 6 months after the first brolucizumab injection

Primary Safety Outcome: Incidence of Ocular AEs among Patients Treated with Brolucizumab in the 180 days after Treatment

	Number of Patient Eyes	Incidence Rate (n eyes / total eyes)	Incidence per 10,000 Injections
TOTAL	11,161	100.00%	
No IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 1]	10,893	97.60%	
IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 2]	268	2.40%	120.11
RV or RO [Cohort 3]	63	0.56%	28.24
RV [Cohort 4]	18	0.16%	8.07
RV Only (RV no RO)	14	0.13%	6.27
RO (incl. RAO and RVO)	49	0.44%	21.96
RAO [Cohort 5]	29	0.26%	13.00
BRAO (Branch)	10	0.09%	4.48
CRAO (Central)	12	0.11%	5.38
Other RAO	8	0.07%	3.59
RVO	19	0.17%	8.52
BRVO (Branch)	10	0.09%	4.48
CRVO (Central)	5	0.04%	2.24
Other RVO	4	0.04%	1.79
Unspecified RO	4	0.04%	1.79
Intraocular inflammation (IOI) incl Panuveitis	174	1.56%	77.98
Endophthalmitis relevant to safety evaluation	49	0.44%	21.96
Panuveitis [Cohort 6]	13	0.12%	5.83

IOI, intraocular inflammation; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis; RVO, retinal vein occlusion; SD, standard deviation.

Secondary Outcome Result(s)

Patient-level demographics and clinical characteristics for all brolucizumab-treated patients are presented below. A total of 9,261 patients, representing 11,161 patient eyes, were found to be treated with brolucizumab and meeting the study criteria for the Komodo Healthcare Map. The median follow-up time was 95.0 days. In the Komodo Health database, 100% and 99.4% of all patient eyes in the analyses had 2 and 3 years of pre-index data, respectively. The mean (SD) ages of the patient eyes were 80.26 (7.40) years. Most patient eyes (57.40%) were female and most eyes were treated unilaterally with brolucizumab (65.95%).

Baseline Patient Demographics

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
Totals							
Patient Level, n (%)	9261 (100)	9043 (100)	238 (100)	58 (100)	17 (100)	25 (100)	13 (100)
Patient Eye Level, n (%)	11161 (100)	10893 (100)	268 (100)	63 (100)	18 (100)	29 (100)	13 (100)
Age, Patient Level, n (%)							
18-49 years	14 (0.15)	14 (0.15)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
50-64 years	238 (2.57)	234 (2.59)	5 (2.10)	0 (0)	0 (0)	0 (0)	0 (0)
65-74 years	1876 (20.26)	1826 (20.19)	54 (22.69)	13 (22.41)	8 (47.06)	3 (12.00)	2 (15.38)
75-84 years	3942 (42.57)	3842 (42.49)	104 (43.70)	28 (48.28)	6 (35.29)	15 (60.00)	8 (61.54)
85+ years	3206 (34.62)	3140 (34.72)	76 (31.93)	18 (31.03)	4 (23.53)	7 (28.00)	3 (23.08)
Mean	80.14	80.15	79.95	80.76	78.65	81.20	79.54
SD	7.46	7.47	7.26	6.39	6.51	5.87	5.68
Median	81	81	81	82.5	78	82	77
Age, Patient Eye Level, n (%)							
18-49 years	17 (0.15)	17 (0.16)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
50-64 years	271 (2.43)	264 (2.42)	7 (2.61)	0 (0)	0 (0)	0 (0)	0 (0)
65-74 years	2201 (19.72)	2143 (19.67)	58 (21.64)	13 (20.63)	8 (44.44)	3 (10.34)	2 (15.38)
75-84 years	4769 (42.73)	4652 (42.71)	117 (43.66)	31 (49.21)	6 (33.33)	18 (62.07)	8 (61.54)
85+ years	3903 (34.97)	3817 (35.04)	86 (32.09)	19 (30.16)	4 (22.22)	8 (27.59)	3 (23.08)
Mean	80.26	80.27	79.96	80.79	78.39	81.45	79.54
SD	7.40	7.40	7.33	6.23	6.41	5.51	5.68
Median	81	81	81	82	76.5	82	77
Gender, Patient Level, n (%)							

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
Male	3945 (42.60)	3889 (43.01)	61 (25.63)	13 (22.41)	2 (11.76)	9 (36.00)	4 (30.77)
Female	5316 (57.40)	5154 (56.99)	177 (74.37)	45 (77.59)	15 (88.24)	16 (64.00)	9 (69.23)
Gender, Patient Eye Level, n (%)							
Male	4709 (42.19)	4640 (42.60)	69 (25.75)	13 (20.63)	2 (11.11)	9 (31.03)	4 (30.77)
Female	6452 (57.81)	6253 (57.40)	199 (74.25)	50 (79.37)	16 (88.89)	20 (68.97)	9 (69.23)
Region, Patient Level, n (%)							
West	1200 (12.96)	1168 (12.92)	43 (18.07)	6 (10.34)	2 (11.76)	1 (4.00)	4 (30.77)
Northeast	1616 (17.45)	1585 (17.53)	34 (14.29)	8 (13.79)	2 (11.76)	3 (12.00)	2 (15.38)
Midwest	2903 (31.35)	2833 (31.33)	73 (30.67)	16 (27.59)	8 (47.06)	9 (36.00)	2 (15.38)
South	3336 (36.02)	3257 (36.02)	82 (34.45)	27 (46.55)	5 (29.41)	12 (48.00)	3 (23.08)
Unknown	2 (0.02)	2 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Region, Patient Eye Level, n (%)							
West	1467 (13.14)	1419 (13.03)	48 (17.91)	6 (9.52)	2 (11.11)	1 (3.45)	4 (30.77)
Northeast	1890 (16.93)	1852 (17.00)	38 (14.18)	8 (12.70)	2 (11.11)	3 (10.34)	2 (15.38)
Midwest	3479 (31.17)	3397 (31.19)	82 (30.60)	19 (30.16)	8 (44.44)	12 (41.38)	2 (15.38)
South	4069 (36.46)	3976 (36.50)	93 (34.7)	29 (46.03)	6 (33.33)	13 (44.83)	3 (23.08)
Unknown	2 (0.02)	2 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Insurance, Patient Level, n (%)							
Private	1913 (20.66)	1885 (20.84)	35 (14.71)	6 (10.34)	3 (17.65)	2 (8.00)	4 (30.77)
Medicare	6555 (70.78)	6381 (70.56)	186 (78.15)	45 (77.59)	12 (70.59)	19 (76.00)	9 (69.23)
Medicare Advantage	656 (7.08)	642 (7.10)	15 (6.30)	7 (12.07)	2 (11.76)	4 (16.00)	0 (0)
Medicaid	135 (1.46)	133 (1.47)	2 (0.84)	0 (0)	0 (0)	0 (0)	0 (0)
Other / Unknown	16 (0.17)	16 (0.18)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Insurance, Patient Eye Level, n (%)							
Private	2259 (20.24)	2218 (20.36)	41 (15.30)	6 (9.52)	3 (16.67)	2 (6.90)	4 (30.77)
Medicare	7934 (71.09)	7728 (70.94)	206 (76.87)	48 (76.19)	13 (72.22)	21 (72.41)	9 (69.23)
Medicare Advantage	790 (7.08)	771 (7.08)	19 (7.09)	9 (14.29)	2 (11.11)	6 (20.69)	0 (0)
Medicaid	159 (1.42)	157 (1.44)	2 (0.75)	0 (0)	0 (0)	0 (0)	0 (0)
Other / Unknown	19 (0.17)	19 (0.17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

AE, Adverse event; IOI, intraocular inflammation; IOP, intraocular pressure; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis; RVO, retinal vein occlusion; SD, standard deviation.

Baseline Patient Clinical Characteristics

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
Totals							
Patient Level, n (%)	9261 (100)	9043 (100)	238 (100)	58 (100)	17 (100)	25 (100)	13 (100)
Patient Eye Level, n (%)	11161 (100)	10893 (100)	268 (100)	63 (100)	18 (100)	29 (100)	13 (100)
Concurrent eye disease, 180d pre-index							
Cataracts	2059 (18.45)	2018 (18.53)	41 (15.30)	12 (19.05)	4 (22.22)	6 (20.69)	1 (7.69)
Posterior vitreous detachment	2670 (23.92)	2592 (23.80)	78 (29.10)	18 (28.57)	4 (22.22)	12 (41.38)	3 (23.08)
Macular pucker (Epiretinal membrane)	699 (6.26)	678 (6.22)	21 (7.84)	4 (6.35)	1 (5.56)	1 (3.45)	3 (23.08)
Amblyopia	13 (0.12)	13 (0.12)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Macular hole	55 (0.49)	54 (0.50)	1 (0.37)	1 (1.59)	0 (0)	0 (0)	0 (0)
Vitreomacular traction	50 (0.45)	46 (0.42)	4 (1.49)	2 (3.17)	1 (5.56)	1 (3.45)	0 (0)
Glaucoma	1503 (13.47)	1455 (13.36)	48 (17.91)	8 (12.70)	2 (11.11)	6 (20.69)	1 (7.69)
Intraocular inflammation (see endpoint 16)	116 (1.04)	99 (0.91)	17 (6.34)	1 (1.59)	0 (0)	0 (0)	1 (7.69)
Papillitis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ischemic optic atrophy	7 (0.06)	5 (0.05)	2 (0.75)	2 (3.17)	0 (0)	0 (0)	0 (0)
Diabetic retinopathy	205 (1.84)	202 (1.85)	3 (1.12)	2 (3.17)	1 (5.56)	1 (3.45)	0 (0)
Diabetic macular edema	85 (0.76)	85 (0.78)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hypertensive retinopathy	259 (2.32)	253 (2.32)	6 (2.24)	1 (1.59)	0 (0)	0 (0)	0 (0)
Pathologic myopia	35 (0.31)	35 (0.32)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retinal vascular occlusion (RO)	115 (1.03)	101 (0.93)	14 (5.22)	11 (17.46)	0 (0)	3 (10.34)	0 (0)
Retinal artery occlusion (RAO)	21 (0.19)	18 (0.17)	3 (1.12)	2 (3.17)	0 (0)	2 (6.90)	0 (0)
Retinal vein occlusion (RVO)	88 (0.79)	78 (0.72)	10 (3.73)	8 (12.70)	0 (0)	2 (6.90)	0 (0)
Retinal vasculitis	2 (0.02)	0 (0)	2 (0.75)	1 (1.59)	1 (5.56)	0 (0)	0 (0)
Vitritis	14 (0.13)	12 (0.11)	2 (0.75)	0 (0)	0 (0)	0 (0)	0 (0)
Endophthalmitis (safety)	49 (0.44)	47 (0.43)	2 (0.75)	0 (0)	0 (0)	0 (0)	0 (0)
Panuveitis	12 (0.11)	8 (0.07)	4 (1.49)	0 (0)	0 (0)	0 (0)	1 (7.69)
Uveitis	12 (0.11)	8 (0.07)	4 (1.49)	0 (0)	0 (0)	0 (0)	1 (7.69)
Choroidal neovascularization	236 (2.11)	229 (2.10)	7 (2.61)	3 (4.76)	1 (5.56)	2 (6.90)	0 (0)
Ocular Procedures, 180d pre-index							
Laser photocoagulation (or laser therapy)	68 (0.61)	65 (0.60)	3 (1.12)	1 (1.59)	0 (0)	0 (0)	0 (0)
Photodynamic therapy (PDT)	85 (0.76)	84 (0.77)	1 (0.37)	1 (1.59)	1 (5.56)	0 (0)	0 (0)
Glaucoma surgery (trabeculectomy, MIGS)	34 (0.30)	34 (0.31)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cataract surgery	298 (2.67)	289 (2.65)	9 (3.36)	1 (1.59)	0 (0)	1 (3.45)	0 (0)
Iridotomy	8 (0.07)	8 (0.07)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ocular radiation	3 (0.03)	3 (0.03)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Panretinal photocoagulation	2 (0.02)	2 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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Submacular surgery, other surgical intervention or laser treatment for AMD	161 (1.44)	156 (1.43)	5 (1.87)	2 (3.17)	1 (5.56)	0 (0)	0 (0)
Vitrectomy	34 (0.30)	33 (0.30)	1 (0.37)	0 (0)	0 (0)	0 (0)	0 (0)
Scleral buckle	13 (0.12)	13 (0.12)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pneumatic retinopexy	6 (0.05)	6 (0.06)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cryopexy	16 (0.14)	16 (0.15)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Systemic comorbidities, 36m pre-index							
Obesity	1649 (14.77)	1622 (14.89)	27 (10.07)	2 (3.17)	1 (5.56)	0 (0)	2 (15.38)
Cerebrovascular disease	1946 (17.44)	1908 (17.52)	38 (14.18)	11 (17.46)	3 (16.67)	6 (20.69)	0 (0)
Peripheral vascular disease	1375 (12.32)	1344 (12.34)	31 (11.57)	6 (9.52)	2 (11.11)	3 (10.34)	1 (7.69)
Diabetes	2841 (25.45)	2781 (25.53)	60 (22.39)	12 (19.05)	1 (5.56)	7 (24.14)	3 (23.08)
Renal disease	1960 (17.56)	1930 (17.72)	30 (11.19)	4 (6.35)	0 (0)	0 (0)	1 (7.69)
Chronic pulmonary disease	2932 (26.27)	2867 (26.32)	65 (24.25)	13 (20.63)	5 (27.78)	7 (24.14)	1 (7.69)
Congestive heart failure	1352 (12.11)	1334 (12.25)	18 (6.72)	5 (7.94)	1 (5.56)	3 (10.34)	0 (0)
Any malignancy, including lymphoma and leukemia	1951 (17.48)	1919 (17.62)	32 (11.94)	9 (14.29)	3 (16.67)	4 (13.79)	2 (15.38)
Myocardial infarction	670 (6.00)	661 (6.07)	9 (3.36)	1 (1.59)	0 (0)	1 (3.45)	1 (7.69)
Dementia	435 (3.90)	429 (3.94)	6 (2.24)	4 (6.35)	1 (5.56)	2 (6.90)	0 (0)
Arteriothrombotic event	154 (1.38)	153 (1.40)	1 (0.37)	0 (0)	0 (0)	0 (0)	0 (0)
Thromboembolytic event	470 (4.21)	466 (4.28)	4 (1.49)	2 (3.17)	0 (0)	2 (6.90)	0 (0)
Atherosclerosis	3287 (29.45)	3229 (29.64)	58 (21.64)	10 (15.87)	3 (16.67)	3 (10.34)	2 (15.38)
Arterial hypertension	7584 (67.95)	7396 (67.90)	188 (70.15)	44 (69.84)	12 (66.67)	21 (72.41)	6 (46.15)
Ischemic heart disease	2808 (25.16)	2764 (25.37)	44 (16.42)	5 (7.94)	1 (5.56)	3 (10.34)	2 (15.38)
Atrial fibrillation	2027 (18.16)	1990 (18.27)	37 (13.81)	14 (22.22)	2 (11.11)	7 (24.14)	0 (0)
Lipid disorders	6974 (62.49)	6812 (62.54)	162 (60.45)	34 (53.97)	11 (61.11)	14 (48.28)	6 (46.15)
Cardiac septal defect	53 (0.47)	49 (0.45)	4 (1.49)	2 (3.17)	0 (0)	2 (6.90)	0 (0)
Valvular cardiac defect	1966 (17.61)	1931 (17.73)	35 (13.06)	6 (9.52)	0 (0)	2 (6.90)	0 (0)
Hyperlipidemia	5271 (47.23)	5149 (47.27)	122 (45.52)	23 (36.51)	7 (38.89)	10 (34.48)	5 (38.46)
Hypercholesterolemia	2401 (21.51)	2345 (21.53)	56 (20.90)	13 (20.63)	5 (27.78)	5 (17.24)	0 (0)
Atherosclerotic disease	3287 (29.45)	3229 (29.64)	58 (21.64)	10 (15.87)	3 (16.67)	3 (10.34)	2 (15.38)
Thrombosis	58 (0.52)	58 (0.53)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Carotid artery disease	1038 (9.30)	1016 (9.33)	22 (8.21)	5 (7.94)	2 (11.11)	2 (6.90)	0 (0)
Eye-involving autoimmune disorders, 36m pre-index							
Systemic vasculitis	24 (0.22)	23 (0.21)	1 (0.37)	1 (1.59)	0 (0)	1 (3.45)	0 (0)
Rheumatoid arthritis	388 (3.48)	378 (3.47)	10 (3.73)	5 (7.94)	3 (16.67)	2 (6.90)	0 (0)
Multiple sclerosis	26 (0.23)	24 (0.22)	2 (0.75)	0 (0)	0 (0)	0 (0)	0 (0)
Behcet's Disease	2 (0.02)	2 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
Sarcoidosis	24 (0.22)	23 (0.21)	1 (0.37)	0 (0)	0 (0)	0 (0)	0 (0)
Vogt-Koyonagi-Harada Disease	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
HLA-B27 Syndromes	66 (0.59)	61 (0.56)	5 (1.87)	0 (0)	0 (0)	0 (0)	0 (0)
Drug hypersensitivity	83 (0.74)	79 (0.73)	4 (1.49)	1 (1.59)	0 (0)	0 (0)	0 (0)
Systemic Lupus Erythematosus (SLE)	32 (0.3)	28 (0.3)	4 (1.5)	0 (0)	0 (0)	0 (0)	0 (0)
Giant cell arteritis	54 (0.48)	52 (0.48)	2 (0.75)	1 (1.59)	0 (0)	1 (3.45)	0 (0)
Ankylosing Spondylitis	27 (0.24)	26 (0.24)	1 (0.37)	0 (0)	0 (0)	0 (0)	0 (0)
Crohn Disease	91 (0.82)	88 (0.81)	3 (1.12)	0 (0)	0 (0)	0 (0)	0 (0)
Concomitant systemic medications, 36m pre-index							
Corticosteroids	606 (5.43)	586 (5.38)	20 (7.46)	5 (7.94)	3 (16.67)	2 (6.90)	2 (15.38)
Systemic anti-VEGFs	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Lipid lowering agents	61 (0.55)	60 (0.55)	1 (0.37)	1 (1.59)	0 (0)	0 (0)	0 (0)
Antihypertensives	365 (3.27)	359 (3.30)	6 (2.24)	3 (4.76)	0 (0)	0 (0)	0 (0)
Biologic/Monoclonal Antibody	34 (0.30)	33 (0.30)	1 (0.37)	1 (1.59)	1 (5.56)	0 (0)	0 (0)
Antimetabolites/cancer therapy	118 (1.06)	117 (1.07)	1 (0.37)	1 (1.59)	1 (5.56)	0 (0)	0 (0)
Anticoagulants	671 (6.01)	657 (6.03)	14 (5.22)	4 (6.35)	1 (5.56)	1 (3.45)	0 (0)
Antiplatelets	143 (1.28)	139 (1.28)	4 (1.49)	1 (1.59)	0 (0)	0 (0)	0 (0)
Concomitant ocular medications, 36m pre-index							
Corticosteroids	25 (0.22)	21 (0.19)	4 (1.49)	0 (0)	0 (0)	0 (0)	0 (0)
Biologics [adalimumab]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cyclosporine	1 (0.01)	1 (0.01)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Azathioprine	1 (0.01)	1 (0.01)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Methotrexate	5 (0.04)	5 (0.05)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ganciclovir	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Acyclovir	5 (0.04)	5 (0.05)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Valacyclovir	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Foscarnet/Foscavir	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Trifluridine	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Mycophenolate	4 (0.4)	4 (0.04)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Rituximab	15 (0.13)	14 (0.13)	1 (0.37)	1 (1.59)	1 (5.56)	0 (0)	0 (0)
Vancomycin	211 (1.89)	207 (1.90)	4 (1.49)	0 (0)	0 (0)	0 (0)	0 (0)
Prostaglandins	8 (0.07)	8 (0.07)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cataract status (binary), 36m pre-index	4927 (44.14)	4810 (44.16)	117 (43.66)	25 (39.68)	9 (50.00)	13 (44.83)	5 (38.46)
Intraocular inflammation history, 180d pre-index							
No history of IOI or endophthalmitis (safety) or RO or RV or Panuveitis	10892 (97.59)	10658 (97.84)	234 (87.31)	51 (80.95)	17 (94.44)	26 (89.66)	12 (92.31)

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
History of IOI or endophthalmitis (safety) or RO or RV or Panuveitis	269 (2.41)	235 (2.16)	34 (12.69)	12 (19.05)	1 (5.56)	3 (10.34)	1 (7.69)
History of Panuveitis	12 (0.11)	8 (0.07)	4 (1.49)	0 (0)	0 (0)	0 (0)	1 (7.69)
History of IOI or endophthalmitis (safety) or panuveitis	160 (1.43)	141 (1.29)	19 (7.09)	1 (1.59)	0 (0)	0 (0)	1 (7.69)
History of endophthalmitis related to safety evaluation	49 (0.44)	47 (0.43)	2 (0.75)	0 (0)	0 (0)	0 (0)	0 (0)
History of IOI or panuveitis and not endophthalmitis	111 (0.99)	94 (0.86)	17 (6.34)	1 (1.59)	0 (0)	0 (0)	1 (7.69)
History of anterior inflammation	57 (0.51)	49 (0.45)	8 (2.99)	0 (0)	0 (0)	0 (0)	0 (0)
History of posterior inflammation	63 (0.56)	53 (0.49)	10 (3.73)	1 (1.59)	0 (0)	0 (0)	1 (7.69)
History of infectious ioi / endophthalmitis	6 (0.05)	6 (0.06)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Intraocular inflammation history, 12m pre-index							
No history of IOI or endophthalmitis (safety) or RO or RV or Panuveitis	10785 (96.63)	10562 (96.96)	223 (83.21)	46 (73.02)	17 (94.44)	23 (79.31)	12 (92.31)
History of IOI or endophthalmitis (safety) or RO or RV or Panuveitis	376 (3.37)	331 (3.04)	45 (16.79)	17 (26.98)	1 (5.56)	6 (20.69)	1 (7.69)
History of Panuveitis	13 (0.12)	9 (0.08)	4 (1.49)	0 (0)	0 (0)	0 (0)	1 (7.69)
History of IOI or endophthalmitis (safety) or panuveitis	227 (2.03)	202 (1.85)	25 (9.33)	1 (1.59)	0 (0)	0 (0)	1 (7.69)
History of endophthalmitis related to safety evaluation	79 (0.71)	76 (0.70)	3 (1.12)	0 (0)	0 (0)	0 (0)	0 (0)
History of IOI or panuveitis and not endophthalmitis	148 (1.33)	126 (1.16)	22 (8.21)	1 (1.59)	0 (0)	0 (0)	1 (7.69)
History of anterior inflammation	81 (0.73)	71 (0.65)	10 (3.73)	0 (0)	0 (0)	0 (0)	0 (0)
History of posterior inflammation	83 (0.74)	70 (0.64)	13 (4.85)	1 (1.59)	0 (0)	0 (0)	1 (7.69)
History of infectious ioi / endophthalmitis	10 (0.09)	10 (0.09)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Intraocular inflammation history, 36m pre-index							
No history of IOI or endophthalmitis (safety) or RO or RV or Panuveitis	10504 (94.11)	10294 (94.50)	210 (78.36)	43 (68.25)	17 (94.44)	20 (68.97)	11 (84.62)
History of IOI or endophthalmitis (safety) or RO or RV or Panuveitis	657 (5.89)	599 (5.50)	58 (21.64)	20 (31.75)	1 (5.56)	9 (31.03)	2 (15.38)
History of Panuveitis	21 (0.19)	17 (0.16)	4 (1.49)	0 (0)	0 (0)	0 (0)	1 (7.69)
History of IOI or endophthalmitis (safety) or panuveitis	444 (3.98)	408 (3.75)	36 (13.43)	2 (3.17)	0 (0)	1 (3.45)	2 (15.38)
History of endophthalmitis related to safety evaluation	142 (1.27)	132 (1.21)	10 (3.73)	0 (0)	0 (0)	0 (0)	1 (7.69)

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
History of IOI or panuveitis and not endophthalmitis	302 (2.71)	276 (2.53)	26 (9.70)	2 (3.17)	0 (0)	1 (3.45)	1 (7.69)
History of anterior inflammation	168 (1.51)	154 (1.41)	14 (5.22)	1 (1.59)	0 (0)	1 (3.45)	0 (0)
History of posterior inflammation	177 (1.59)	163 (1.50)	14 (5.22)	1 (1.59)	0 (0)	0 (0)	1 (7.69)
History of infectious IOI / endophthalmitis	23 (0.21)	21 (0.19)	2 (0.75)	0 (0)	0 (0)	0 (0)	0 (0)

Note all analysis performed at patient eye level unless otherwise stated. IOI, intraocular inflammation; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis; RVO, retinal vein occlusion; PDT, photodynamic therapy; SLE, Systemic Lupus Erythematosus

More than 90% of patient eyes had switched from another anti-VEGF agent, with aflibercept being the most common immediate prior anti-VEGF agent (68.24%, of prior aVEGF treated eyes). Approximately, over one-third of the patient eyes (48.51%) that had switched from another anti-VEGF agent had received ≥ 2 prior anti-VEGF agents. The median duration of treatment on the prior anti-VEGF agent, among patient eyes that were not anti-VEGF treatment-naive at the time of brolucizumab initiation, was 663.

Baseline Patient AMD & aVEGF Treatment Information

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
Totals							
Patient Level, n (%)	9261 (100)	9043 (100)	238 (100)	58 (100)	17 (100)	25 (100)	13 (100)
Patient Eye Level, n (%)	11161 (100)	10893 (100)	268 (100)	63 (100)	18 (100)	29 (100)	13 (100)
Duration of follow-up (days, eye-level), mean (SD)	93.17 (44.51)	92.75 (44.60)	110.29 (36.98)	113.10 (35.05)	113.89 (31.29)	123.76 (39.06)	102.38 (44.19)
Provider specialty on date of first brolucizumab injection (index date)							
Ophthalmology	10521 (94.27)	10261 (94.20)	260 (97.01)	61 (96.83)	18 (100)	27 (93.10)	13 (100)
Internal Medicine	40 (0.36)	39 (0.36)	1 (0.37)	1 (1.59)	0 (0)	1 (3.45)	0 (0)
General Practice	11 (0.10)	10 (0.09)	1 (0.37)	0 (0)	0 (0)	0 (0)	0 (0)
Hospitalist	8 (0.07)	8 (0.07)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Optometrist	4 (0.04)	4 (0.04)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Other	577 (5.17)	571 (5.24)	6 (2.24)	1 (1.59)	0 (0)	1 (3.45)	0 (0)
Type of exam performed before first injection							

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
CP	216 (1.94)	209 (1.92)	7 (2.61)	2 (3.17)	0 (0)	0 (0)	0 (0)
CP & FA	130 (1.16)	126 (1.16)	4 (1.49)	2 (3.17)	0 (0)	2 (6.90)	0 (0)
FA & OCT	164 (1.47)	162 (1.49)	2 (0.75)	0 (0)	0 (0)	0 (0)	0 (0)
FA	5 (0.04)	5 (0.05)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
CP & OCT	318 (2.85)	313 (2.87)	5 (1.87)	2 (3.17)	1 (5.56)	1 (3.45)	0 (0)
CP, FA, & OCT	165 (1.48)	160 (1.47)	5 (1.87)	1 (1.59)	0 (0)	0 (0)	0 (0)
OCT	9634 (86.32)	9402 (86.31)	232 (86.57)	54 (85.71)	16 (88.89)	25 (86.21)	12 (92.31)
Eye Treated with brolucizumab							
OD [eye, right]	5656 (50.68)	5504 (50.53)	152 (56.72)	36 (57.14)	9 (50.00)	17 (58.62)	6 (46.15)
OS [eye, left]	5505 (49.32)	5389 (49.47)	116 (43.28)	27 (42.86)	9 (50.00)	12 (41.38)	7 (53.85)
Bilateral	3800 (34.05)	3720 (34.15)	80 (29.85)	19 (30.16)	3 (16.67)	10 (34.48)	0 (0)
Unilateral	7361 (65.95)	7173 (65.85)	188 (70.15)	44 (69.84)	15 (83.33)	19 (65.52)	13 (100)
aVEGF Treatment Status (60m pre-index)							
Treatment Naïve	674 (6.04)	659 (6.05)	15 (5.60)	2 (3.17)	0 (0)	0 (0)	1 (7.69)
Prior Treatment	10487 (93.96)	10234 (93.95)	253 (94.40)	61 (96.83)	18 (100)	29 (100)	12 (92.31)
ranibizumab	1623 (15.48)	1600 (15.63)	23 (9.09)	2 (3.28)	0 (0)	1 (3.45)	1 (8.33)
aflibercept	7156 (68.24)	6963 (68.04)	193 (76.28)	48 (78.69)	15 (83.33)	20 (68.97)	10 (83.33)
pegaptanib	2 (0.02)	2 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
off-label bevacizumab	1706 (16.27)	1669 (16.31)	37 (14.62)	11 (18.03)	3 (16.67)	8 (27.59)	1 (8.33)
Prior aVEGF Agents (60m pre-index)							
0 Agents (Naïve)	674 (6.04)	659 (6.05)	15 (5.60)	2 (3.17)	0 (0)	0 (0)	1 (7.69)
1 Agent	5400 (48.38)	5275 (48.43)	125 (46.64)	28 (44.44)	9 (50.00)	11 (37.93)	5 (38.46)
2 Agents	4089 (36.64)	3974 (36.48)	115 (42.91)	30 (47.62)	8 (44.44)	16 (55.17)	6 (46.15)
3 Agents	996 (8.92)	983 (9.02)	13 (4.85)	3 (4.76)	1 (5.56)	2 (6.90)	1 (7.69)
4 Agents	2 (0.02)	2 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Prior aVEGF Injections (all, not limited to prior avegf)							
<6	1648 (14.77)	1613 (14.81)	35 (13.06)	11 (17.46)	2 (11.11)	5 (17.24)	2 (15.38)
6 to <12	2091 (18.73)	2046 (18.78)	45 (16.79)	8 (12.70)	1 (5.56)	5 (17.24)	3 (23.08)
12 to <24	3633 (32.55)	3530 (32.41)	103 (38.43)	23 (36.51)	8 (44.44)	9 (31.03)	4 (30.77)
≥24	3115 (27.91)	3045 (27.95)	70 (26.12)	19 (30.16)	7 (38.89)	10 (34.48)	3 (23.08)
Mean	18.37	18.35	19.12	19.41	22.28	19.45	17.83
SD	12.71	12.71	12.91	13.65	12.70	13.86	11.56
Median	16	16	17	17	20.5	17	17.5
Laterality of wAMD, Patient Level, n (%)							
Bilateral	1990 (21.49)	1952 (21.59)	51 (21.43)	14 (24.14)	3 (17.65)	5 (20.00)	1 (7.69)
Unilateral	7318 (79.02)	7134 (78.89)	188 (78.99)	43 (74.14)	14 (82.35)	20 (80.00)	12 (92.31)
Unspecified	209 (2.26)	206 (2.28)	4 (1.68)	1 (1.68)	0 (0)	0 (0)	0 (0)

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
Time since first wet AMD diagnosis for patient to index (all)							
<6 months	1006 (9.01)	978 (8.98)	28 (10.45)	7 (11.11)	1 (5.56)	2 (6.90)	2 (15.38)
6 to <12 months	841 (7.54)	825 (7.57)	16 (5.97)	5 (7.94)	0 (0)	4 (13.79)	1 (7.69)
12 to <24 months	1589 (14.24)	1550 (14.23)	39 (14.55)	8 (12.70)	4 (22.22)	0 (0)	2 (15.38)
≥24 months	7725 (69.21)	7540 (69.22)	185 (69.03)	43 (68.25)	13 (72.22)	23 (79.31)	8 (61.54)
Mean (days)	963.82	963.79	965.10	937.43	987.28	1061.31	772.00
SD	492.29	492.33	491.56	499.74	396.94	510.98	460.56
Median	1011	1012	1007	1011	998.50	1301	961
Laterality of any AMD, Patient Level, n (%)							
Bilateral	2061 (22.26)	2023 (22.37)	51 (21.43)	14 (24.14)	3 (17.65)	5 (20.00)	1 (7.69)
Unilateral	7258 (78.37)	7074 (78.23)	188 (78.99)	43 (74.14)	14 (82.35)	20 (80.00)	12 (92.31)
Unspecified	191 (2.06)	188 (2.08)	4 (1.68)	1 (1.72)	0 (0)	0 (0)	0 (0)
Time since first any AMD diagnosis for patient to index (all)							
<6	630 (5.64)	616 (5.66)	14 (5.22)	4 (6.35)	0 (0)	0 (0)	1 (7.69)
6 to <12	570 (5.11)	559 (5.13)	11 (4.10)	4 (6.35)	0 (0)	3 (10.34)	1 (7.69)
12 to <24	1244 (11.15)	1205 (11.06)	39 (14.55)	9 (14.29)	4 (22.22)	1 (3.45)	1 (7.69)
≥24	8717 (78.10)	8513 (78.15)	204 (76.12)	46 (73.02)	14 (77.78)	25 (86.21)	10 (76.92)
Time since any aVEGF treatment to Index date (all)							
<6 months	9817 (87.96)	9585 (87.99)	232 (86.57)	54 (85.71)	17 (94.44)	25 (86.21)	12 (92.31)
6 to <12 months	296 (2.65)	287 (2.63)	9 (3.36)	3 (4.76)	0 (0)	3 (10.34)	0 (0)
12 to <24 months	235 (2.11)	227 (2.08)	8 (2.99)	2 (3.17)	1 (5.56)	0 (0)	0 (0)
≥24 months	139 (1.25)	135 (1.24)	4 (1.49)	2 (3.17)	0 (0)	1 (3.45)	0 (0)
Prior # aVEGF Injections (last aVEGF only)							
<6	2705 (25.79)	2658 (25.97)	47 (18.58)	14 (22.95)	3 (16.67)	7 (24.14)	3 (25.00)
6 to <12	2480 (23.65)	2420 (23.65)	60 (23.72)	12 (19.67)	2 (11.11)	6 (20.69)	3 (25.00)
12 to <24	3205 (30.56)	3109 (30.38)	96 (37.94)	19 (31.15)	7 (38.89)	9 (31.03)	4 (33.33)
≥24	2097 (20.00)	2047 (20.00)	50 (19.76)	16 (26.23)	6 (33.33)	7 (24.14)	2 (16.67)
Mean	14.56	14.53	15.8	16.43	18.67	16	14.08
SD	11.46	11.46	11.56	13.37	12.31	13.45	10.57
Median	12	12	14	14	16	14	11.5
Last injection interval of prior agent in weeks (if applicable, excl. patients with only 1 injection of prior agent)							
<4 weeks	270 (2.57)	264 (2.58)	6 (2.37)	1 (1.64)	1 (5.56)	0 (0)	1 (8.33)
4 to <6 weeks	4286 (40.87)	4159 (40.64)	127 (50.20)	30 (49.18)	10 (55.56)	16 (55.17)	4 (33.33)
6 to <8 weeks	2549 (24.31)	2503 (24.46)	46 (18.18)	12 (19.67)	5 (27.78)	4 (13.79)	1 (8.33)

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
8 to <12 weeks	1898 (18.10)	1858 (18.16)	40 (15.81)	9 (14.75)	2 (11.11)	6 (20.69)	3 (25.00)
≥12 weeks	1003 (9.56)	977 (9.55)	26 (10.28)	7 (11.48)	0 (0)	2 (6.90)	2 (16.67)
Mean	60.46	60.33	65.85	67.93	38.17	81.57	69.18
SD	94.38	93.07	136.72	141.80	12.27	201.60	87.54
Median	42	42	38	41	37.5	39	43
Duration of last anti-VEGF treatment (if applicable, excl. patients with only 1 injection of prior agent)							
<6	1748 (16.67)	1716 (16.77)	32 (12.65)	9 (14.75)	2 (11.11)	5 (17.24)	1 (8.33)
6 to <12	1426 (13.60)	1392 (13.60)	34 (13.45)	8 (13.11)	3 (16.67)	2 (6.90)	0 (0)
12 to <24	2112 (20.14)	2052 (20.05)	60 (23.72)	11 (18.03)	4 (22.22)	4 (13.79)	4 (33.33)
≥24	4720 (45.01)	4601 (44.96)	119 (47.04)	31 (50.82)	9 (50.00)	17 (58.62)	6 (50.00)
Mean	732.71	731.82	768.16	814.71	796.83	903.36	741.82
SD	521.92	522.15	512.64	556.85	562.76	594.52	357.82
Median	663	662	707	821	747	875	720

Note all analysis performed at patient eye level unless otherwise stated. IOI, intraocular inflammation; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis; RVO, retinal vein occlusion; OD, right eye; OS, left eye; SD, standard deviation; AMD, age-related macular degeneration; FA, fluorescein angiography; CP, color photo; OCT, optical coherence tomography

The median duration of treatment on brolucizumab, among eligible patient eyes was 63 days. The median number of brolucizumab injections in 180 days post-index was 2.

Brolucizumab Treatment Characteristics

	Master Cohort (All Brolucizumab-treated Patients)	Cohort 1X (Control: No IOI or Endophthal-mitis or Panuveitis or RV or RO)	Cohort 2X (IOI or Endophthal-mitis (Related to Safety) or Panuveitis or RV or RO)	Cohort 3X (Patients with RV and/or RO [RAO and/or RO])	Cohort 4X (Patients with RV)	Cohort 5X (Patients with RAO)	Cohort 6X (Patients with Panuveitis)
TOTALS							
Patient Level, n (%)	9261 (100)	9043 (100)	238 (100)	58 (100)	17 (100)	25 (100)	13 (100)
Patient Eye Level, n (%)	11161 (100)	10893 (100)	268 (100)	63 (100)	18 (100)	29 (100)	13 (100)
# Injections of brolucizumab (180d post-index)							
1	4699 (42.10)	4582 (42.06)	117 (43.66)	34 (53.97)	10 (55.56)	11 (37.93)	5 (38.46)
2	3086 (27.65)	2985 (27.40)	101 (37.69)	19 (30.16)	7 (38.89)	9 (31.03)	4 (30.77)
3	2334 (20.91)	2297 (21.09)	37 (13.81)	6 (9.52)	0 (0)	5 (17.24)	4 (30.77)
4+	1042 (9.34)	1029 (9.45)	13 (4.85)	4 (6.35)	1 (5.56)	4 (13.79)	0 (0)
Mean	2.00	2.00	1.80	1.68	1.56	2.07	1.92

SD	1.07	1.07	0.87	0.89	0.78	1.07	0.86
Median	2	2	2	1	1	2	2
Duration of Therapy on brolucizumab (excludes patient eyes that had 1 injection)							
1 month (0 - 29 d)	702 (6.29)	676 (6.21)	26 (9.70)	4 (6.35)	1 (5.56)	2 (6.90)	2 (15.38)
2 months (30 - 59 d)	2082 (18.65)	2013 (18.48)	69 (25.75)	12 (19.05)	5 (27.78)	6 (20.69)	4 (30.77)
3 months (60 - 89 d)	1784 (15.98)	1753 (16.09)	31 (11.57)	6 (9.52)	1 (5.56)	5 (17.24)	1 (7.69)
4 months (90 - 119 d)	994 (8.91)	978 (8.98)	16 (5.97)	5 (7.94)	0 (0)	3 (10.34)	1 (7.69)
5 months (121 - 149 d)	633 (5.67)	625 (5.74)	8 (2.99)	2 (3.17)	1 (5.56)	2 (6.90)	0 (0)
6 months (150 d+)	267 (2.39)	266 (2.44)	1 (0.37)	0 (0)	0 (0)	0 (0)	0 (0)
Mean	72.54	72.91	57.18	60.62	53.13	67.06	55.13
SD	37.64	37.71	31.22	34.13	38.73	35.60	28.86
Median	63	63	48	42	36.5	66.5	52

Note all analysis performed at patient eye level unless otherwise stated. IOI, intraocular inflammation; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis; RVO, retinal vein occlusion; SD, standard deviation.

Secondary Outcome: Time from Last aVEGF Treatment to Index Date by Event

	Number of Patient Eyes	Mean (SD), days	Median, days	Minimum, days	Maximum, days	<30d, n (%)	30-59d, n (%)	60+ d, n (%)
Total	11161	82.12 (141.42)	46	1	1813	1612 (14.44)	5266 (47.18)	3609 (32.34)
No IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 1]	10893	82.02 (140.78)	46	1	1813	1564 (14.36)	5127 (47.07)	3543 (32.53)
IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 2]	268	86.01 (165.59)	42	3	1575	48 (17.91)	139 (51.87)	66 (24.63)
RV or RO [Cohort 3]	63	108.77 (194.54)	49	21	1041	7 (11.11)	37 (58.73)	17 (26.98)
RV [Cohort 4]	18	76.06 (142.20)	46.5	21	644	2 (11.11)	15 (83.33)	1 (5.56)
RV Only (RV no RO)	14	87.14 (160.66)	49.5	28	644	1 (7.14)	12 (85.71)	1 (7.14)
RO (incl. RAO and RVO)	49	115.21 (204.65)	48	21	1041	6 (12.24)	25 (51.02)	16 (32.65)
RAO [Cohort 5]	29	104.07 (194.35)	46	26	1041	5 (17.24)	16 (55.17)	8 (27.59)
BRAO (Branch)	10	69 (54.15)	48.5	35	217	0 (0)	7 (70.00)	3 (30.00)
CRAO (Central)	12	154.75 (292.40)	47.5	26	1041	2 (16.67)	7 (58.33)	3 (25.00)
Other RAO	8	64.63 (74.23)	40	28	246	3 (37.50)	3 (37.50)	2 (25.00)
RVO	19	148.44 (229.18)	53.5	28	896	0 (0)	10 (52.63)	8 (42.11)
BRVO (Branch)	10	195.7 (291.84)	59.5	31	896	0 (0)	5 (50.00)	5 (50.00)
CRVO (Central)	5	55.8 (21.76)	43	40	91	0 (0)	3 (60.00)	2 (40.00)
Other RVO	4	145.33 (172.05)	46	46	344	0 (0)	2 (50.00)	1 (25.00)
Unspecified RO	4	53.67 (39.80)	42	21	98	1 (25.00)	1 (25.00)	1 (25.00)
Intraocular inflammation (IOI) incl Panuveitis	174	80.64 (162.41)	42	3	1575	33 (18.97)	85 (48.85)	44 (25.29)
Endophthalmitis relevant to safety evaluation	49	63.08 (88.40)	38.5	26	473	10 (20.41)	29 (59.18)	9 (18.37)
Panuveitis [Cohort 6]	13	50.17 (32.82)	35.5	28	146	2 (15.38)	7 (53.85)	3 (23.08)

IOI, intraocular inflammation; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis; RVO, retinal vein occlusion.

In relation to time-to-event, the median number of days from the start of brolucizumab treatment (first brolucizumab injection) to an event of any form of IOI (including RV) and/or RO was 56 days. To an event of RV and/or RO, the median time to event was 66 days

Secondary Outcome: Time from Index Date to Event

	Number of Patient Eyes	Mean (SD), days	Median, days	Minimum, days	Maximum, days	<30d, n (%)	30-59d, n (%)	60+ d, n (%)
Total	11161	N/A	N/A			N/A	N/A	N/A
No IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 1]	10893	N/A	N/A			N/A	N/A	N/A
IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 2]	268	59.69 (36.95)	56	2	168	58 (21.64)	93 (34.70)	117 (43.66)
RV or RO [Cohort 3]	63	71 (36.29)	66	6	168	8 (12.70)	20 (31.75)	35 (55.56)
RV [Cohort 4]	18	65.56 (27.96)	56	25	153	1 (5.56)	9 (50.00)	8 (44.44)
RV Only (RV no RO)	14	61.36 (19.07)	56	25	97	1 (7.14)	7 (50.00)	6 (42.86)
RO (incl. RAO and RVO)	49	74.37 (40.51)	70	6	174	7 (14.29)	12 (24.49)	30 (61.22)
RAO [Cohort 5]	29	78.79 (46.15)	70	6	174	4 (13.79)	7 (24.14)	18 (62.07)
BRAO (Branch)	10	74.6 (45.87)	64.5	20	174	1 (10.00)	3 (30.00)	6 (60.00)
CRAO (Central)	12	90.25 (49.60)	79.5	6	168	1 (8.33)	2 (16.67)	9 (75.00)
Other RAO	8	62.75 (39.49)	46	14	121	2 (25.00)	3 (37.50)	3 (37.50)
RVO	19	59.95 (29.82)	56	6	99	3 (15.79)	7 (36.84)	9 (47.37)
BRVO (Branch)	10	70.1 (23.11)	74	42	99	0 (0)	4 (40.00)	6 (60.00)
CRVO (Central)	5	60.4 (40.10)	84	7	96	2 (40.00)	0 (0)	3 (60.00)
Other RVO	4	34 (18.69)	43	6	44	1 (25.00)	3 (75.00)	0 (0)
Unspecified RO	4	79 (40.46)	88	28	112	1 (25.00)	0 (0)	3 (75.00)
Intraocular inflammation (IOI) incl Panuveitis	174	58.01 (36.51)	55.5	2	168	38 (21.84)	64 (36.78)	72 (41.38)
Endophthalmitis relevant to safety evaluation	49	50.35 (41.17)	41	2	148	18 (36.73)	14 (28.57)	17 (34.69)
Panuveitis [Cohort 6]	13	57.31 (38.33)	56	4	141	3 (23.08)	4 (30.77)	6 (46.15)

47.01%, 40.30%, and 12.69% of patient eyes had 1, 2, and ≥ 3 injections prior to the first event of any form of IOI (including RV) and/or RO. 55.56%, 33.33%, and 11.11% of patient eyes had 1, 2, and ≥ 3 injections prior to the first event of RV and/or RO

Secondary Outcome: Briolucizumab Injections to Event

	Number of Patient Eyes	Mean (SD), Inj	Median, inj	Minimum, inj	Maximum, inj	1 Inj, n (%)	2 Inj, n (%)	3+ Inj, n (%)
TOTAL	11161	N/A	N/A			N/A	N/A	N/A
No IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 1]	10893	N/A	N/A			N/A	N/A	N/A
IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 2]	268	1.68 (0.75)	2	1	4	126 (47.01)	108 (40.30)	34 (12.69)
RV or RO [Cohort 3]	63	1.00 (4.00)	0	1	4	35 (55.56)	21 (33.33)	7 (11.11)
RV [Cohort 4]	18	1.00 (4.00)	0	1	4	10 (55.56)	7 (38.89)	1 (5.56)
RV Only (RV no RO)	14	1.00 (2.00)	0	1	2	8 (57.14)	6 (42.86)	0 (0)
RO (incl. RAO and RVO)	49	1.00 (4.00)	0	1	4	27 (55.10)	15 (30.61)	7 (14.29)
RAO [Cohort 5]	29	2.00 (4.00)	0	1	4	12 (41.38)	10 (34.48)	7 (24.14)
BRAO (Branch)	10	2.00 (4.00)	0	1	4	3 (30.00)	4 (40.00)	3 (30.00)
CRAO (Central)	12	1.00 (4.00)	0	1	4	7 (58.33)	2 (16.67)	3 (25.00)

Other RAO	8	2.00 (3.00)	0	1	3	2 (25.00)	5 (62.50)	1 (12.50)
RVO	19	1.00 (2.00)	0	1	2	13 (68.42)	6 (31.58)	0 (0)
BRVO (Branch)	10	1.00 (2.00)	0	1	2	8 (80.00)	2 (20.00)	0 (0)
CRVO (Central)	5	1.00 (2.00)	0	1	2	4 (80.00)	1 (20.00)	0 (0)
Other RVO	4	2.00 (2.00)	0	1	2	1 (25.00)	3 (75.00)	0 (0)
Unspecified RO	4	1.00 (2.00)	0	1	2	3 (75.00)	1 (25.00)	0 (0)
Intraocular inflammation (IOI) incl Panuveitis	174	2.00 (4.00)	0	1	4	79 (45.40)	74 (42.53)	21 (12.07)
Endophthalmitis relevant to safety evaluation	49	2.00 (4.00)	0	1	4	24 (48.98)	16 (32.65)	9 (18.37)
Panuveitis [Cohort 6]	13	2.00 (3.00)	0	1	3	5 (38.46)	5 (38.46)	3 (23.08)

IOI, intraocular inflammation; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis; RVO, retinal vein occlusion.

In relation to time-to-event, the median number of days from the last brolucizumab injection to an event of any form of IOI (including RV) and/or RO was 28 days

Secondary Outcome: Time from last Brolucizumab Injection to Event

	Number of Patient Eyes	Mean (SD), days	Median, days	Minimum, days	Maximum, days	<30d, n (%)	30-59d, n (%)	60+ d, n (%)
TOTAL	11161	N/A	N/A			N/A	N/A	N/A
No IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 1]	10893	N/A	N/A			N/A	N/A	N/A
IOI or Endophthalmitis or Panuveitis or RV or RO [Cohort 2]	268	33.22 (30.21)	28	0	139	147 (54.85)	70 (26.12)	51 (19.03)
RV or RO [Cohort 3]	63	47.24 (34.24)	47	0	135	20 (31.75)	21 (33.33)	22 (34.92)
RV [Cohort 4]	18	41.94 (23.91)	47.5	0	84	5 (27.78)	9 (50.00)	4 (22.22)
RV Only (RV no RO)	14	41.14 (25.44)	48.5	0	84	4 (28.57)	7 (50.00)	3 (21.43)
RO (incl. RAO and RVO)	49	49.59 (36.18)	44	0	135	15 (30.61)	15 (30.61)	19 (38.78)
RAO [Cohort 5]	29	44.41 (35.56)	42	0	135	10 (34.48)	9 (31.03)	10 (34.48)
BRAO (Branch)	10	31.4 (25.50)	29	0	70	5 (50.00)	3 (30.00)	2 (20.00)
CRAO (Central)	12	62.5 (41.21)	62	2	135	2 (16.67)	3 (25.00)	7 (58.33)
Other RAO	8	28.88 (25.95)	24.5	0	73	4 (50.00)	3 (37.50)	1 (12.50)
RVO	19	44.89 (36.35)	42	0	97	7 (36.84)	5 (26.32)	7 (36.84)
BRVO (Branch)	10	55.6 (28.16)	49	8	97	1 (10.00)	5 (50.00)	4 (40.00)
CRVO (Central)	5	54.8 (47.10)	84	0	96	2 (40.00)	0 (0)	3 (60.00)
Other RVO	4	5.75 (0.96)	5.5	5	7	4 (100)	0 (0)	0 (0)
Unspecified RO	4	76.75 (41.72)	83.5	28	112	1 (25.00)	1 (25.00)	2 (50.00)
Intraocular inflammation (IOI) incl Panuveitis	174	31.91 (26.85)	28	0	131	98 (56.32)	47 (27.01)	29 (16.67)
Endophthalmitis relevant to safety evaluation	49	21.9 (29.73)	7	0	139	37 (75.51)	6 (12.24)	6 (12.24)
Panuveitis [Cohort 6]	13	29.69 (22.35)	28	3	71	8 (61.54)	3 (23.08)	2 (15.38)

IOI, intraocular inflammation; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis; RVO, retinal vein occlusion.

The overall incidence of any form of IOI (including RV) and/or RO after initiation of brolucizumab (180d) excluding 6 months, 12 months, and 36 months prior IOI was 2.15%, 2.07%, and 2.00%, respectively. Incidence of RV and/or RO after initiation of brolucizumab (180d) excluding 6 months, 12 months, and 36 months prior IOI was 0.47%, 0.43%, and 0.41%, respectively

Safety Results

Refer to primary and secondary outcome results (Overall incidence rates of any form of IOI (including RV) and/or RO[a] up to 6 months after the first brolucizumab injection)

Other Relevant Findings

None

Limitations

There are certain limitations with these types of retrospective analyses using data collected from routine clinical practice. Although these analyses were pre-specified, they were non-interventional and retrospective as opposed to a clinical trial in which data are collected prospectively. Limitations of these analyses include lack of access to patient charts or imaging, the use of ICD codes to identify observed events, and a median follow-up of only 3 months. Codes can only constitute a proxy for the event of interest and the severity remains unknown, thus, in the absence of charts or imaging a causality link of events with brolucizumab treatment cannot be confirmed. Other risk factors and confounders are not available in the dataset. The combination of the low number of events and the absence of robust discriminatory risk factors that can clearly distinguish patients with the risk factor from those without means that the risk factors identified in these analyses cannot be used as a predictor for the occurrence of IOI and/or RO in routine clinical practice. It is unknown whether not initiating brolucizumab treatment in patients with prior IOI (including RV) and/or RO in the past 12 months would reduce the incidence of AEs of interest observed following exposure to brolucizumab.

It was noted that there may have been a truncation bias introduced in these analyses due to the potential for the end of the index period and the end of the study period to coincide for some patients. This coincidence could reduce the follow-up window for observation of AEs if brolucizumab treatment was initiated later in the index period. Moreover, early 2020 coincided with the first wave of COVID-19 cases in the US, which led to decreased clinic attendance of AMD patients for follow-up anti-VEGF injections.22-24 AE estimates could be subject to bias as a result of patient failure to attend follow-up appointments before the end of the study period. In defining the boundary conditions of the analysis, we attempted to balance providing enough time for patient follow-up and obtaining early insights into the prevalence of AEs following brolucizumab injection.

Conclusion:

In conclusion, data from the Komodo Health provided insights into the safety of patients with wet AMD who initiated brolucizumab.

Patients with intraocular inflammation and/or retinal vascular occlusion in the 12 months prior to the first brolucizumab injection had the highest estimated incidence rate for an event of any form of IOI (including RV) and/or RO among patient eyes in the 6 months post first brolucizumab treatment. Similar findings were observed for the sub-group of patient eyes with RV and/or RO.

Additional studies are needed with longer follow-up intervals to assess the long-term safety of brolucizumab treatment and further analyses of the Komodo Health data may be warranted. These results represent key early real-world findings that explore potential risk factors for inflammation-related AEs that may occur following treatment with brolucizumab.

Date of Clinical Study Report

04 February 2021