Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. IRIS Registry and Komodo Healthcare Map Inclusion and Exclusion Criteria

Criteria	IRIS Registry	Komodo Healthcare Map
Inclusion Criteria		
≥1 HCPCS code (J code) or EHR note for treatment with brolucizumab during the index period (date of earliest code or EHR note=index date)	√	
≥1 HCPCS code (J code or unlisted J code before January 1, 2020) or NDC for treatment with brolucizumab during the index period (date of earliest code=index date)		√
≥18 years old on the index date	√	√
≥1 CPT code for intravitreal administration on the index date	√	
≥1 CPT code for intravitreal administration on the index date or ≤7 days afterwards*		√
≥1 ICD-CM-9/10 code for neovascular AMD in the 36 months prior to or on the index date	√	√
≥1 post-index ophthalmology visit†	√	
≥1 VA eye assessment on the index date or within 365 days prior to the index date‡	√	
Exclusion Criteria		
Use of brolucizumab prior to October 8, 2019 (e.g., clinical trials)	√	√
Unknown laterality of the index eye on the index date (to allow for evaluation of outcomes at the patient-eye level)	√	√
Patients with no data throughout the 12 months immediately prior to the index date		√

AMD, age-related macular degeneration; CM, Clinical Modification; CPT, Current Procedural Terminology; EHR, electronic health records; HCPCS, Healthcare Common Procedure Coding System; ICD, International Classification of Diseases; NDC, National Drug Code; VA, visual acuity.
*Off-label use of brolucizumab is not expected given payer access restrictions in the US
†Similarly, the definition of a new injection of the same VEGF agent for a given patient eye is if there is no history of that same VEGF agent within 7 days prior to the claim observed. Otherwise, the observation is considered a duplicate.
‡For future analyses of larger sample sizes with longer follow-up time.

eTable 2. Adverse Events Definitions

Any form of IOI (including RV) and/or RO	ICD-10 Code
Intraocular Inflammation (IOI)	
Acute and Subacute Iridocyclitis	H20.0X (excluding H20.03X and H20.04X)
Chronic Iridocyclitis	H20.1X
Other Iridocyclitis	H20.9
Posterior Synechiae	H21.54X
Focal Chorioretinal Inflammation, Juxtapapillary	H30.0X
Disseminated Chorioretinal Inflammation, Peripheral	H30.1X
Posterior Cyclitis (Pars Planitis)	H30.2X
Other Chorioretinal inflammations	H30.8
Unspecified Chorioretinal Inflammation	H30.9X
Changes in Retinal Vascular Appearance (Vascular Sheathing)	H35.01X
Exudative Retinopathy	H35.02X
Vitritis/Other disorders of Vitreous Body	H43.89
Unspecified Papilledema	H47.10
Papilledema associated with decreased ocular pressure	H47.12
Papilledema associated with retinal disorder	H47.13
Optic neuritis (optic papillitis, retrobulbar neuritis, toxic optic neuropathy, other optic neuritis, unspecified optic neuritis)	H46X (excluding H46.2 for nutritional optic neuropathy)
Panuveitis	H44.11X
Retinal Vasculitis (RV)	
Retinal Vasculitis	H35.06X
Retinal Vascular Occlusion (RO)	
Retinal Artery Occlusion (RAO)	H34.0X (Transient retinal artery occlusion); H34.1X (Central retinal artery occlusion); H34.21X (Partial retinal artery occlusion); H34.23X (Retinal artery branch occlusion)
Retinal Vein Occlusion (RVO)	H34.81X (Central retinal vein occlusion [CRVO]); H34.83X (Branch retinal vein occlusion [BRVO])
Unspecified RO	H34.9 (Unspecified retinal vascular occlusion)
Ischemic Optic Neuropathy	H47.01X (Ischemic optic neuropathy)
Endophthalmitis	
Other Endophthalmitis	H44.19
Purulent Endophthalmitis	H44.0X
Hypopyon	H20.05X

IOI, Intraocular Inflammation; RO, Retinal Vascular occlusion inclusive of retinal vein occlusion and retinal artery occlusion; RV, Retinal vasculitis.
*Same definition was applied for the variable – 'prior inflammation and/or occlusion; inflammation/occlusion only includes immune mediated events and excluded infectious events.
ICD, International Classification of Diseases.

eTable 3. Baseline patient/eye characteristics (overall cohort) at Index.*

Eye level		
Characteristic	**IRIS Registry** (N=10,654)	**Komodo Healthcare Map** (N=11,161)
Eye level		
Age (years), mean ± SD	80.86 ± 8.39	80.26 ± 7.40
Female, n (%)	6,105 (57.30)	6,452 (57.81)
Laterality of treatment with brolucizumab at index date, Unilateral, n (%)	8,258 (77.51)	7,361 (65.95)
Time since diagnosis of neovascular AMD,[a] days/years, mean ± SD	760 ± 360/ 2.08 ± 0.99	964 ± 492/ 2.64 ± 1.35
VA (approximate ETDRS) letter score,[b] mean ± SD	62.00 ± 19	NA
Prior treatment status, Switcher, n (%)	9,686 (90.91)	10,487 (93.96)
Median time on prior anti-VEGF agent, days/years	526/1.44	663/1.82
≥2 prior anti-VEGF agents,[c] n (%)	3,667 (37.86)	5,087 (45.51)
Immediately prior anti-VEGF,[d] n (%)		
Aflibercept[c]	7,160 (73.92)	7,156 (68.24)
Bevacizumab[c]	1,000 (10.32)	1,706 (16.27)
Ranibizumab[c]	1,478 (15.26)	1,623 (15.48)
Number of brolucizumab injections[e], n (%)		
1	5,458 (51.23%)	4,699 (42.10%)
2	3,289 (30.87%)	3,086 (27.65%)
3+	1,907 (17.90%)	3,376 (30.25%)

AMD, age-related macular degeneration; ETDRS, Early Treatment Diabetic Retinopathy Study; NA, Not available; VA, visual acuity; VEGFs, vascular endothelial growth factor. Index date is the date of first brolucizumab injection. *Measured in the 36-month period prior to the index date (inclusive of the index date) unless otherwise stated. For variables assessed on the index date, the 36-month period prior to the index date (inclusive of the index date) was assessed if information was not available on the index date.

[a]Time from first neovascular AMD diagnosis to index date. [b]Approximate Snellen equivalent 20/63 in IRIS; Komodo Healthcare Map does not capture visual outcomes. [c]Sample size of switch patients used as denominator. [d]The last prior anti-VEGF treatment before initiation of brolucizumab, among patient eyes previously treated with an anti-VEGF agent, and 48 eyes in IRIS and 2 eyes in Komodo had 'pegaptanib' as the immediate prior anti-VEGF. [e]All patients included in this analysis were new to brolucizumab treatment; number of brolucizumab injections refers to the follow-up period.

eTable 4. Baseline patient/eye characteristics by cohorts

	IRIS Registry			Komodo Healthcare Map		
	Cohort 1	Cohort 2	Cohort 3	Cohort 1	Cohort 2	Cohort 3
	Control: No IOI and/or RO	All forms of IOI and/or RO	RV and/or RO	Control: No IOI and/or RO	All forms of IOI and/or RO	RV and/or RO
Characteristic	N=10,399 eyes	N=255 eyes	N=59 eyes	N=10,893 eyes	N=268 eyes	N=63 eyes
Age (years), mean ± SD	80.92 ± 8.38	78.78 ± 8.32	80.12 ± 7.66	80.27 ± 7.40	79.96 ± 7.33	80.79 ± 6.23
Female, n (%)	5915 (56.88)	190 (74.51)	47 (79.66)	6253 (57.40)	199 (74.25)	50 (79.37)
Duration of follow-up (days), mean ± SD	92.74 ± 33.55	102.69 ± 28.10	112.20 ± 25.68	92.75 ± 44.60	110.29 ± 36.98	113.10 ± 35.05
Prior treatment status, Switcher, n (%)	9450 (90.87)	236 (92.55)	49 (83.05)	10234 (93.95)	253 (94.40)	61 (96.83)
Any Prior IOI and/or RO*						
Past 36 months	547 (5.26)	42 (16.47)	19 (32.20)	599 (5.50)	58 (21.64)	20 (31.75)
Past 12 months	376 (3.62)	37 (14.51)	18 (30.51)	331 (3.04)	45 (16.79)	17 (26.98)
Past 6 months	309 (2.97)	37 (14.51)	18 (30.51)	235 (2.16)	34 (12.69)	12 (19.05)

IOI, Intraocular Inflammation; RO, Retinal Vascular occlusion inclusive of retinal vein occlusion and retinal artery occlusion; RV, Retinal vasculitis.
*1 patient eye each with RV and panuveitis had a history of IOI and/or RO in the past 12 months in IRIS Registry and Komodo Healthcare Map