Real-world frequency and management of ocular adverse events in eyes with neovascular age-related macular degeneration treated with brolucizumab

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Table S1: Visual acuity in all 8 cases of moderate and severe vision loss reported in patient eyes with IOI-related AEs.

			Visual acuity (ETDRS letters)			
Vision loss at time of AE	**AE type**	**IOI/RV/RO**	**Latest pre-AE**	**At time of AE**	**3 months after AE**	**6 months after AE**
Severe	Endophthalmitis	IOI	69.9	-30.1	65.1	65.1
Severe	Endophthalmitis	IOI	61.1	-15	-30.1	65.1
Severe	Posterior uveitis*	IOI	57.8	-30.1	19.9	19.9
Moderate	Panuveitis	IOI	69.9	54.9	61.1	65.1
Moderate	Panuveitis	IOI	61.1	35	57.8	54.9
Moderate	Vitritis	IOI	54.9	35	69.9	NA
Moderate	Vasculitis and anterior uveitis	IOI+RV	61.1	35	57.8	54.9
Moderate	Vascular occlusion and vasculitis and panuveitis*	IOI+RV+RO	54.9	35	54.9	57.8

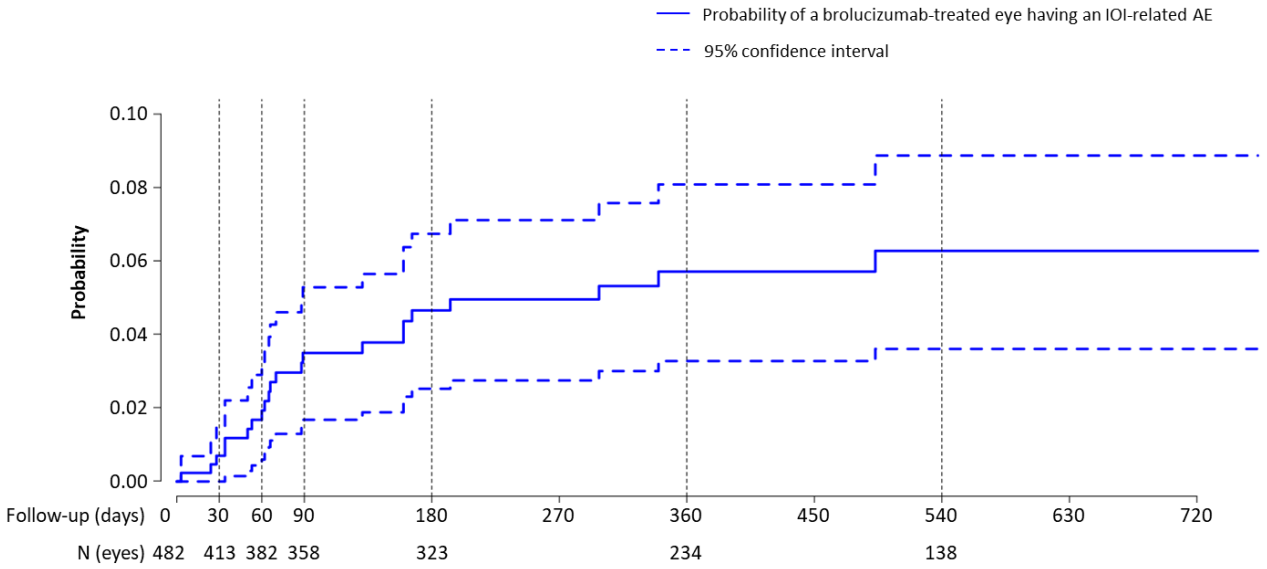
*Details of these cases can be found in the clinical cases section.
AE, adverse event; ETDRS, Early Treatment Diabetic Retinopathy Study; IOI, intraocular inflammation; RO, retinal vascular occlusion; RV, retinal vasculitis.

Table S2: Management of IOI-related AEs in the 22 affected eyes.

Treatment for IOI-related AE	**Eyes, n (%)***
Topical antibiotic	2 (9)
Topical steroid	15 (68)
Oral steroid	2 (9)
Intravitreal steroid	1 (5)
Intravitreal antibiotic	1 (5)
Surgery	2 (9)
No treatment/observation	2 (9)

***Some of the 22 eyes received more than one of the treatments listed. AE, adverse event; IOI, intraocular inflammation.

Figure S1: Kaplan-Meier modelling of the probability of eyes experiencing an intraocular inflammation (IOI)-related adverse event (AE) after initiation of brolucizumab treatment.



A Kaplan-Meier survival model was generated using the study cohort of 482 patient eyes. The time value for the eyes with IOI-related AEs was the time from the first brolucizumab injection to the IOI-related AE, and the total follow-up time (from the first brolucizumab injection to the last injection of any anti-VEGF) was used for eyes that did not experience IOI-related AEs as their censoring time (i.e., end of follow-up). Each time an IOI-related AE occurred, the probability of survival (i.e., not having an IOI-related AE) decreased, and the probability of an IOI-related AE increased. The Kaplan-Meier estimator for survival probability at the eye level at time t is thus given by

$$\hat{S}(t) = \prod_{t_i \leq t} \left(1 - \frac{d_i}{n_i}\right),$$

where d_i is the number of IOI-related AEs occuring at time t_i and n_i is the number of eyes that have not experienced an adverse event and have also not been censored before time t_i. The inverse of the survival probability at each time point gives the probability of experiencing an IOI-related AE at each time (counted from the first brolucizumab injection) as shown in the graph. [1]

1. Borgan Ø. Kaplan–Meier Estimator. http://www.medicine.mcgill.ca/epidemiology/hanley/c609/material/KaplanMeierEstimator.pdf. Accessed 16 March 2023.

Figure S2: Time from the last brolucizumab injection until an IOI-related AE. Percentages presented above bars, and absolute number of eyes presented at bar base. AE, adverse event; IOI, intraocular inflammation. *Maximum time for follow-up was 102 days.

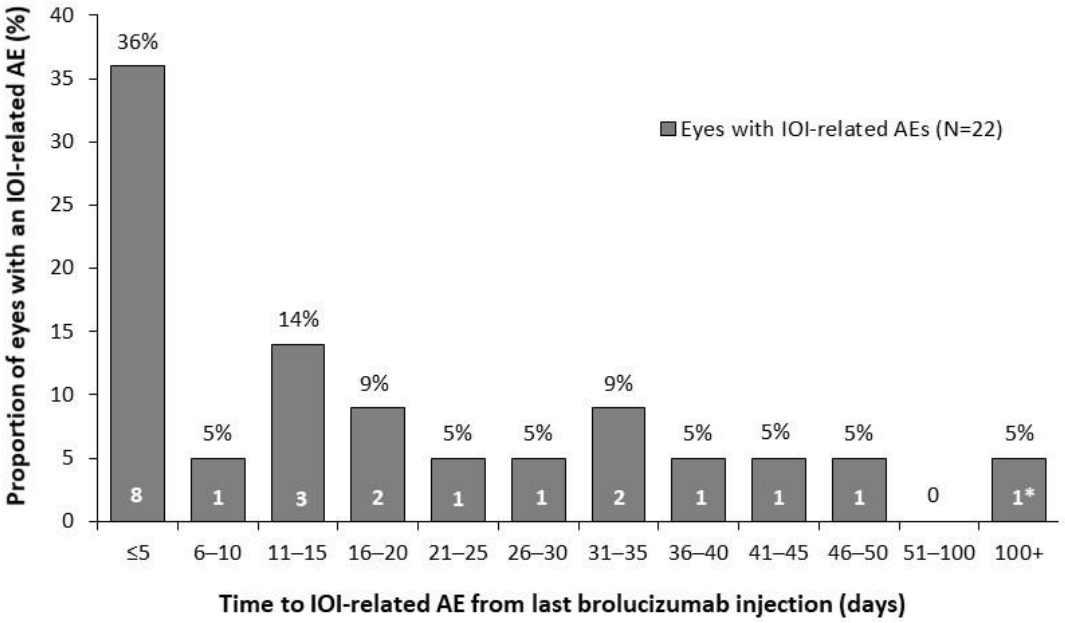


Figure S3: OCT images from Case 2, a 66-year old male with AE occurring 28 days after initiating brolucizumab taken **A)** 6 weeks prior to switching and **B)** at the time of the switch to brolucizumab; **C)** and **D)** at the time of AE; **E)** and **F)** 4 weeks after AE. AE, adverse event; OCT, optical coherence tomography.

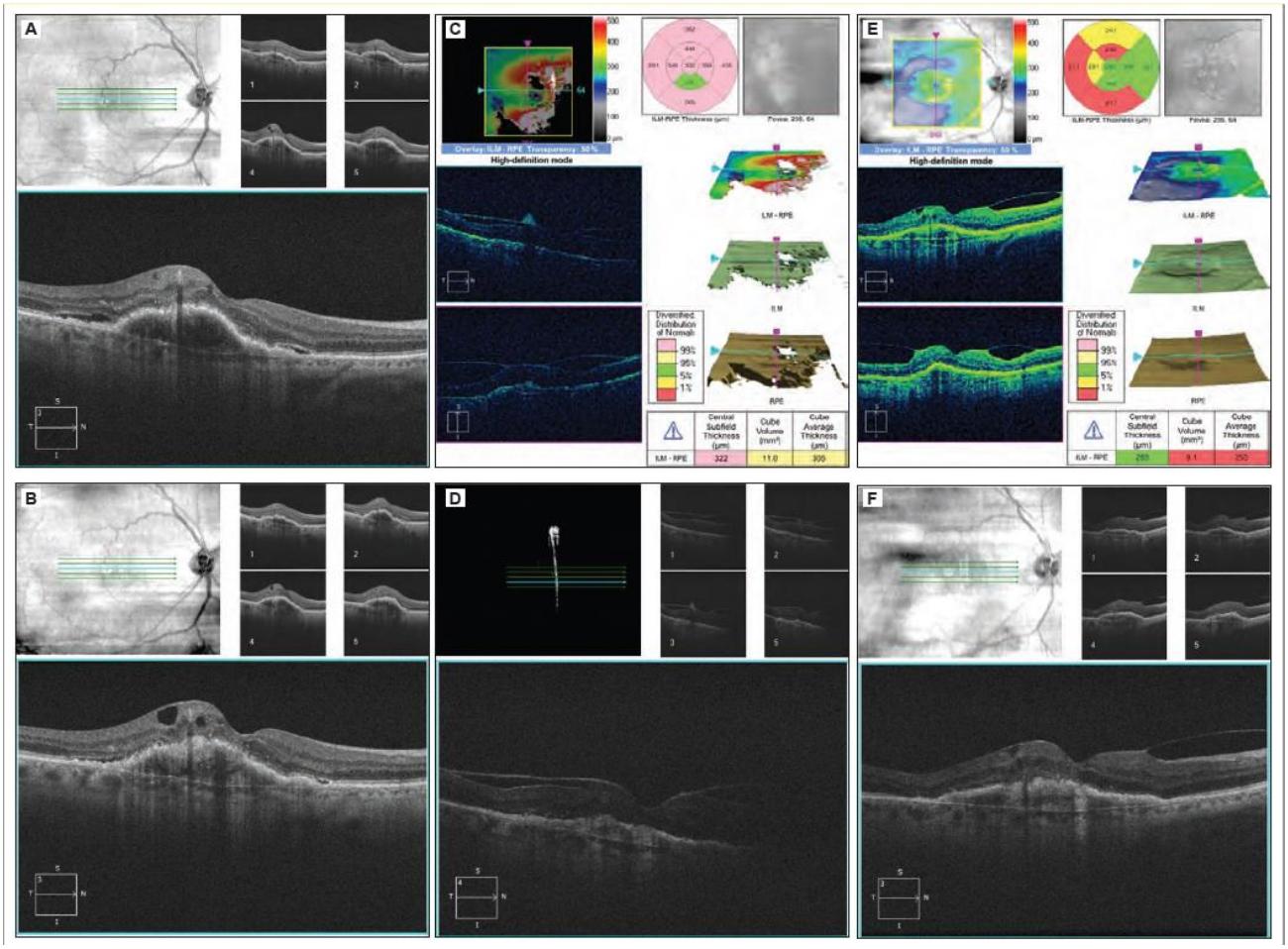


Figure S4: OCT images from Case 3, a 78-year old female with AE occurring 66 days after initiating brolucizumab taken **A)** before the initiation of brolucizumab treatment; **B)** prior to the second brolucizumab injection; **C)** at AE onset; and **D)** 3 months and **E)** 6 months after AE onset. AE, adverse event; OCT, optical coherence tomography.