

IRIS® Registry Analysis of Anti-VEGF Treatment in Patients With Coexisting Neovascular Age-Related Macular Degeneration and Geographic Atrophy

Theodore Leng,¹ Eric W Schneider,² Ehsan Rahimy,^{1,3} Durga Borkar,⁴ Jennifer Harris,⁵ Kristin Arkin-Leydig,⁵ Roy Schwartz,⁶ Daniel Jones,⁷ Rushi Shah,⁷ Brandon Coughlin,⁷ Caroline R Bauma⁷

¹Byers Eye Institute at Stanford, Stanford University School of Medicine, Palo Alto, California, USA; ²Tennessee Retina, Nashville, Tennessee, USA; ³Palo Alto Medical Foundation, Palo Alto, California, USA; ⁴Duke Eye Center, Duke University School of Medicine, Durham, North Carolina, USA; ⁵Verana Health, San Francisco, California, USA; ⁶Apellis UK Limited, London, UK; ⁷Apellis Pharmaceuticals, Waltham, Massachusetts, USA

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Introduction

- AMD is a progressive degenerative macular disease that can result in nAMD and/or GA in its advanced stage^{1,2}
- GA and nAMD can occur simultaneously in the same eye³
- Anti-VEGF agents are the standard of care for nAMD, with gains in visual acuity seen in clinical trials, but may not be as effective in eyes with both GA and nAMD^{3,4}

AMD, age-related macular degeneration; **GA**, geographic atrophy; **nAMD**, neovascular age-related macular degeneration; **VEGF**, vascular endothelial growth factor.

1. Saade C, et al. *Br J Ophthalmol*. 2014;98(12):1729-1732. 2. Gheorghe A, et al. *Rom J Ophthalmol*. 2015;59(2):74-77. 3. Kaszubski P, et al. *Ophthalmic Res*. 2016;55(4):185-193.

4. Tan CS, et al. *Clin Ophthalmol*. 2022;16:917-933.

Objectives

- In a population of patients with coexisting GA and nAMD who have been treated with anti-VEGF agents, our aim was to characterize:
 - Demographic and clinical characteristics
 - Anti-VEGF treatment patterns
 - Visual acuity outcomes
 - Key adverse events associated with anti-VEGF treatment

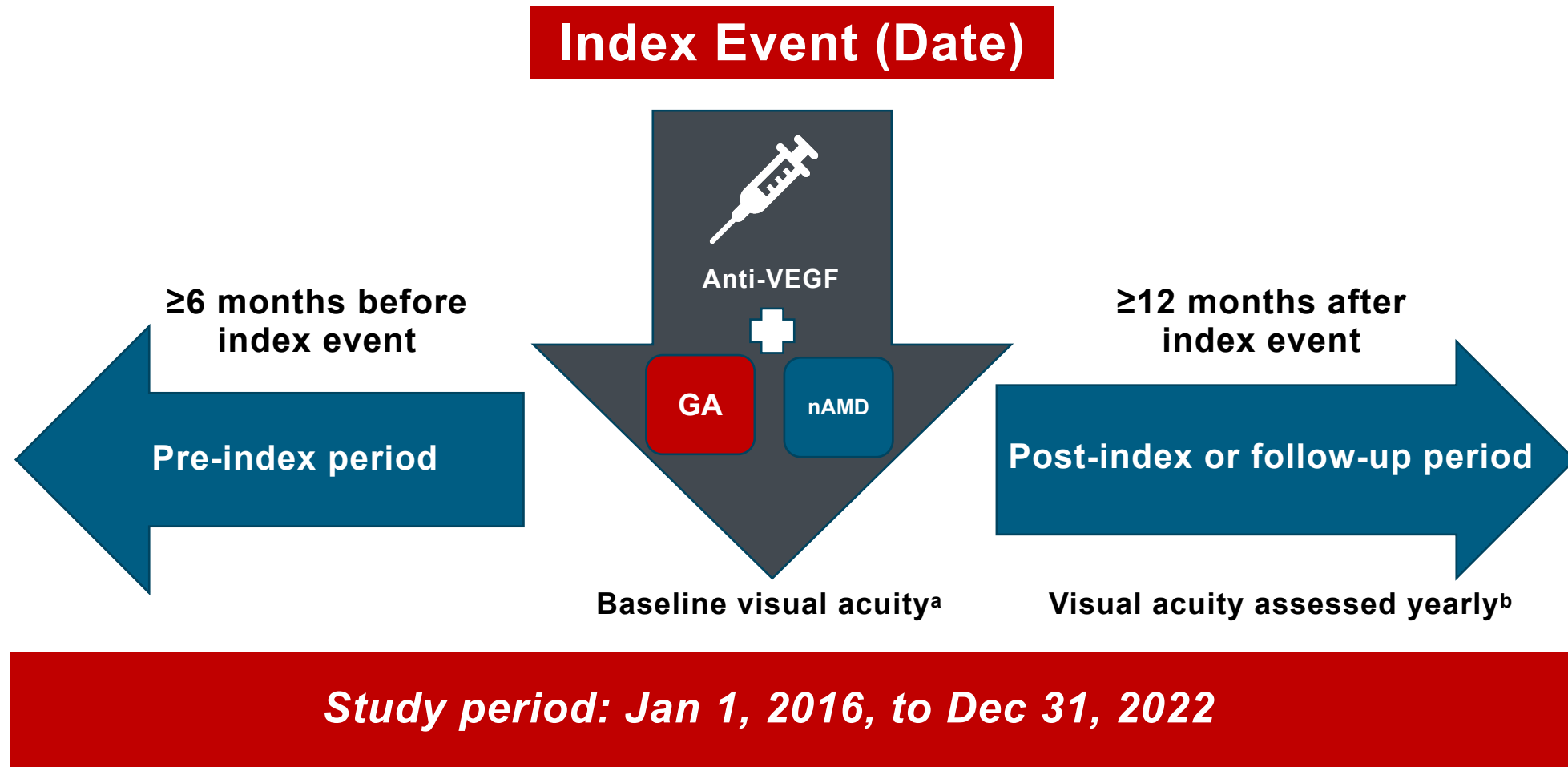
Study Design

IRIS[®] Registry

- The American Academy of Ophthalmology IRIS[®] Registry (Intelligent Research in Sight) is the world's largest specialty clinical data registry, with >80 million unique patients and ~15,000 participating ophthalmic clinicians as of January 2024¹

This retrospective cohort study analyzed IRIS Registry data in patients diagnosed with coexisting GA and nAMD

Study Design



^aBaseline visual acuity assessment nearest the index date and within 6 months prior to index date.

^bAssessment nearest the end of the treatment year; treatment year defined as 52 ± 8 weeks.

GA, geographic atrophy; **nAMD**, neovascular age-related macular degeneration; **VEGF**, vascular endothelial growth factor.

Study Population

First ICD-10 code for GA between July 1, 2016, and Dec 31, 2021 (N=430,948 eyes)



Any nAMD ICD-10 code in same eye as GA diagnosis between July 1, 2016, and Dec 31, 2021 (n=93,786 eyes)



Anti-VEGF injection (index event) in eye with GA and nAMD diagnosis within 36 months after first GA diagnosis (n=41,353 eyes)



Patients ≥ 60 years of age at first GA diagnosis and had >1 VA measurement within 6 months before index event (n=38,372 eyes)

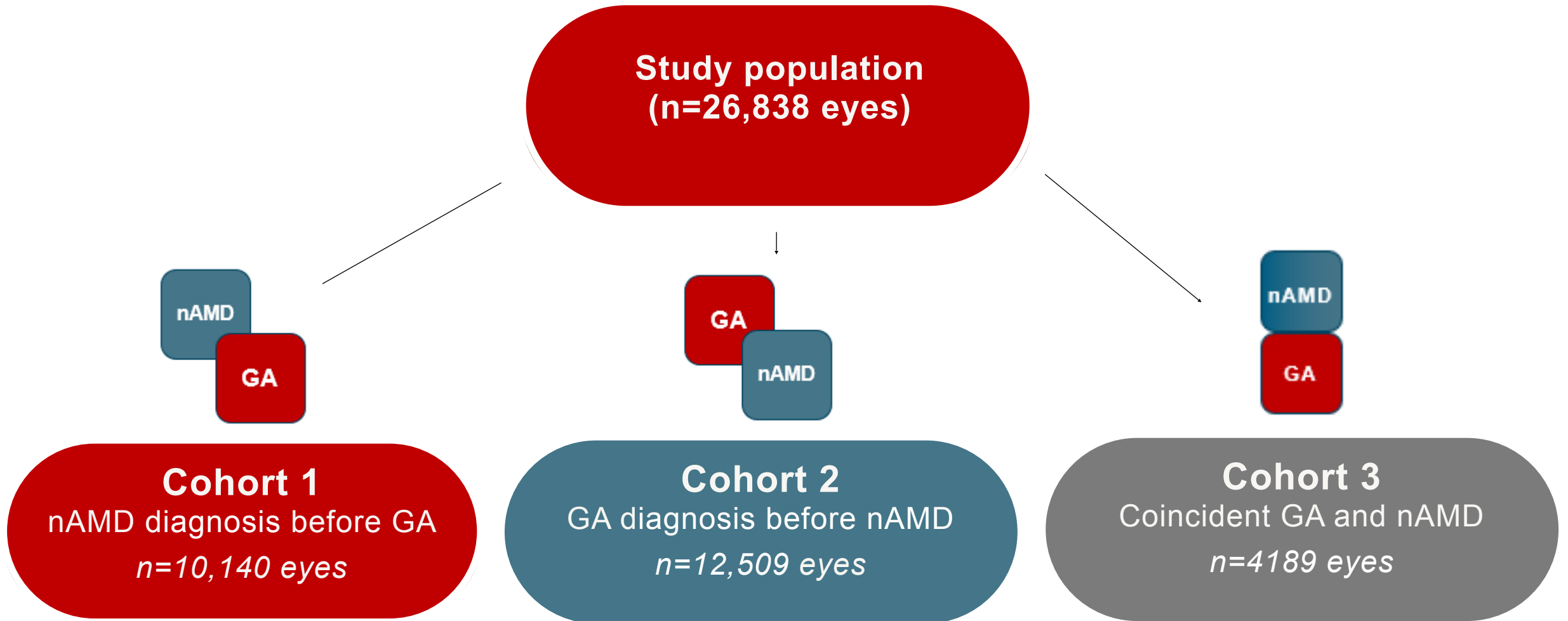


Exclusions (ordered): Missing age or sex (0 eyes); <12 months of data post index (7202 eyes); <6 months of data pre-index (4312 eyes); ≥ 1 exclusionary glaucoma procedures pre-index (20 eyes)



Study population: n=26,838 eyes


Patient Population



Across all cohorts, mean follow-up time was 2.4 years

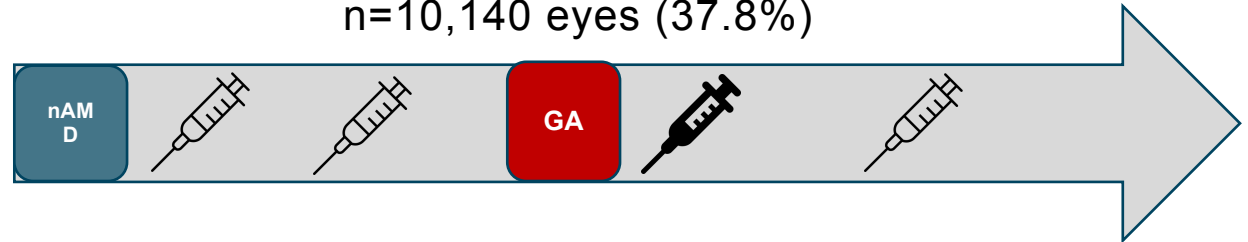
Timing of Index and Non-index Anti-VEGF Injections by Cohort

Time between diagnoses for patient eyes

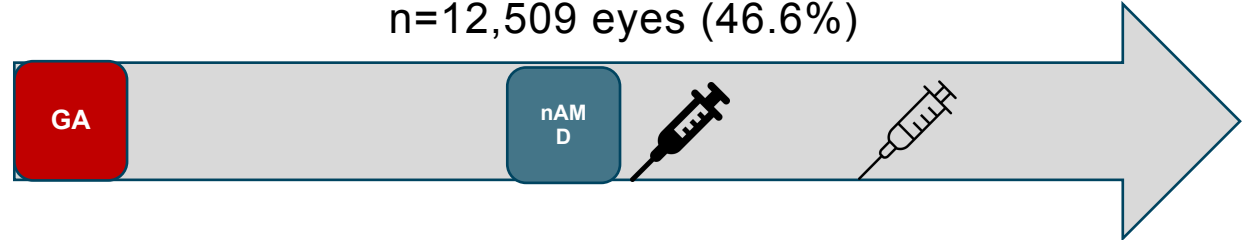


	nAMD GA	GA nAMD	nAMD GA
	n (% of cohort)	n (% of cohort)	n (% of cohort)
Within 14 days	—	—	4189 (100%)
15–180 days	2162 (21.3%)	2379 (19.0%)	—
181–365 days	1847 (18.2%)	3495 (27.9%)	—
366–730 days	2527 (24.9%)	4248 (34.0%)	—
≥731 days	3604 (35.5%)	2387 (19.1%)	—

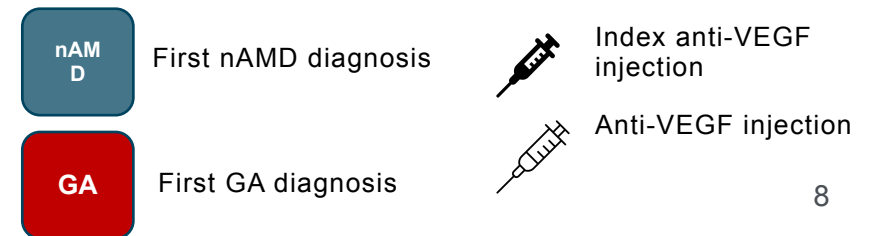
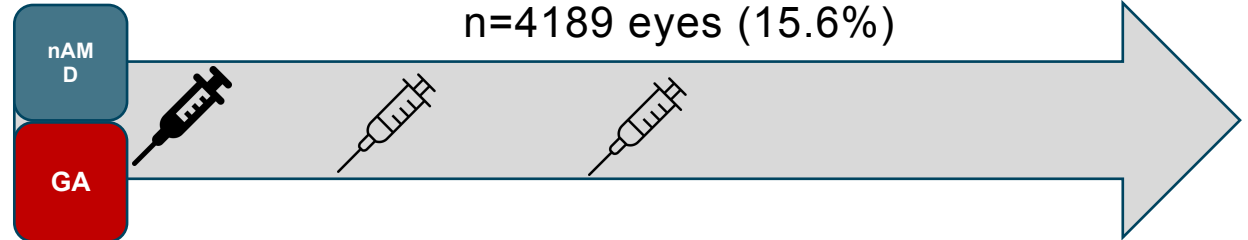
Cohort 1: First observed GA diagnosis after nAMD diagnosis
n=10,140 eyes (37.8%)



Cohort 2: First observed GA diagnosis before nAMD diagnosis
n=12,509 eyes (46.6%)



Cohort 3: First observed GA diagnosis coincident with nAMD diagnosis
n=4189 eyes (15.6%)

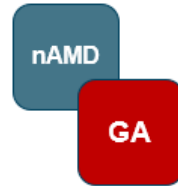


Patient Demographic Characteristics



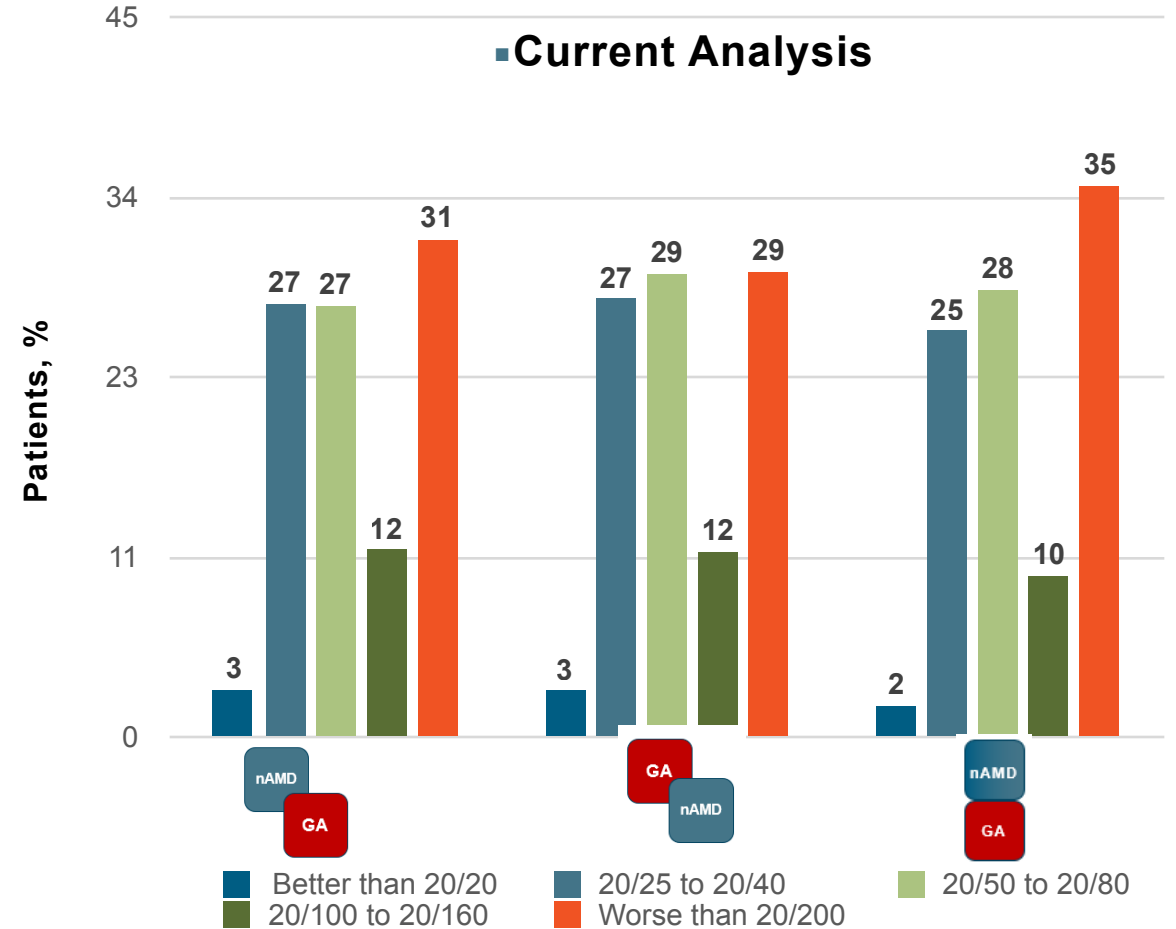
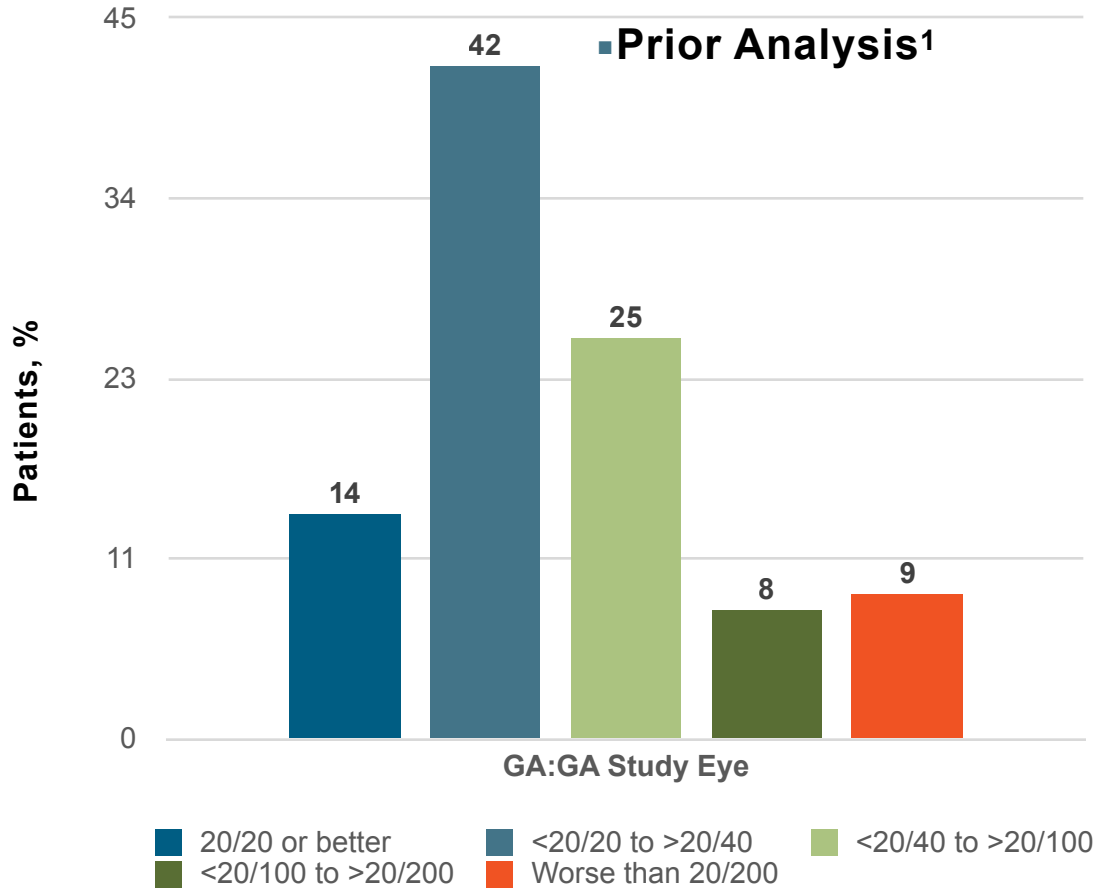
Total patients (% total)	8324 (36.4%)	11,778 (51.5%)	3570 (15.6%)
Age, mean (SD), years	82.0 (5.3)	81.1 (5.6)	81.1 (5.0)
Female, n (% cohort)	5657 (68.0%)	7977 (67.7%)	2438 (68.3%)
Race, n (% cohort)			
White	6733 (80.9%)	9347 (79.4%)	2946 (82.5%)
Other/unknown	1591 (19.1%)	2431 (20.6%)	624 (17.5%)
Not Hispanic or Latino, n (% cohort)	6737 (80.9%)	8766 (74.4%)	2853 (79.9%)
Payer type, n (% cohort)			
Medicare	5838 (70.1%)	8246 (70.0%)	2309 (64.7%)
Medicare Advantage	1039 (12.5%)	1660 (14.1%)	432 (12.1%)
Commercial insurance	1004 (12.1%)	1176 (10.0%)	583 (16.3%)

Patient Eye Clinical Characteristics



	10,140 (37.8%)	12,509 (46.6%)	4189 (15.6%)
Total patient eyes (% total)			
Top baseline comorbidities, n (% cohort)			
Cataracts	2754 (27.2%)	3350 (26.8%)	1149 (27.4%)
Glaucoma	1703 (16.8%)	1453 (11.6%)	557 (13.3%)
Ocular hypertension	290 (2.9%)	204 (1.6%)	89 (2.1%)
Intraocular inflammation	350 (3.5%)	404 (3.2%)	123 (2.9%)
Provider subspecialty, n (% cohort)			
Retina/vitreous specialist	9383 (92.5%)	11,446 (91.5%)	3793 (90.5%)

GA Visual Acuity^a: Comparison With Previous Work



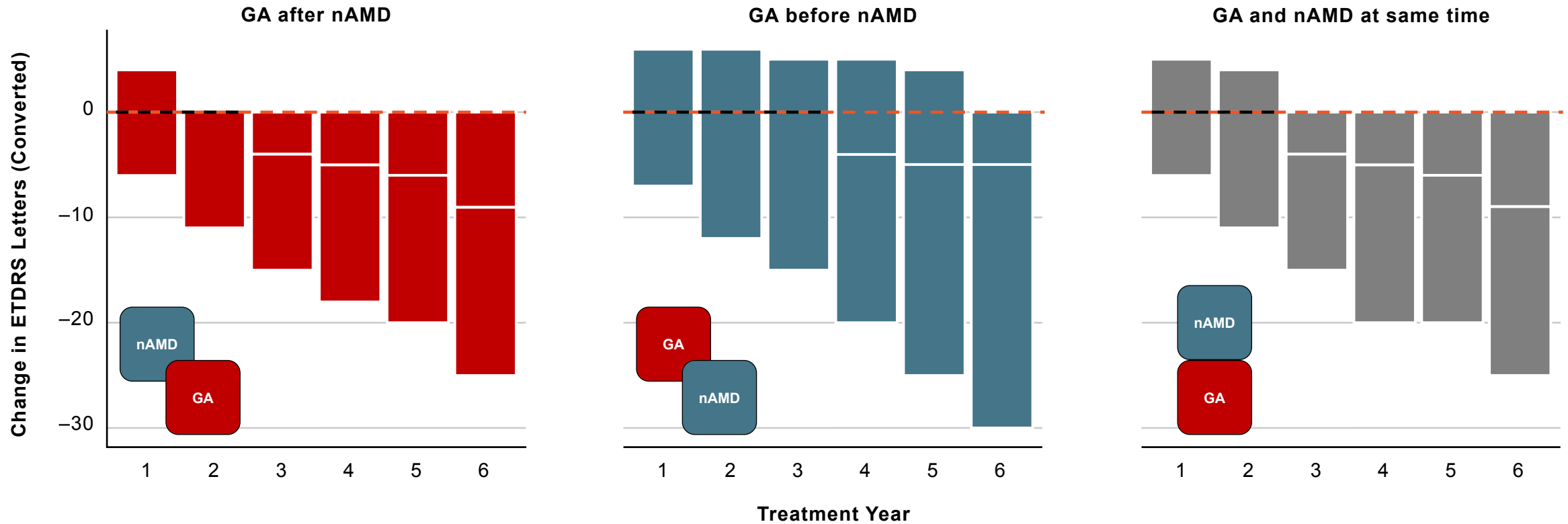
A higher proportion of patients with visual acuity <20/200 with combined pathologies

^aPatients may be represented across >1 visual acuity category if they had different eyes with different visual acuities; therefore, patient sums may be greater than cohort total.

GA, geographic atrophy; nAMD, neovascular age-related macular degeneration.

1. Rahimy E, et al. *Ophthalmol Sci.* 2023;3(4):100318.

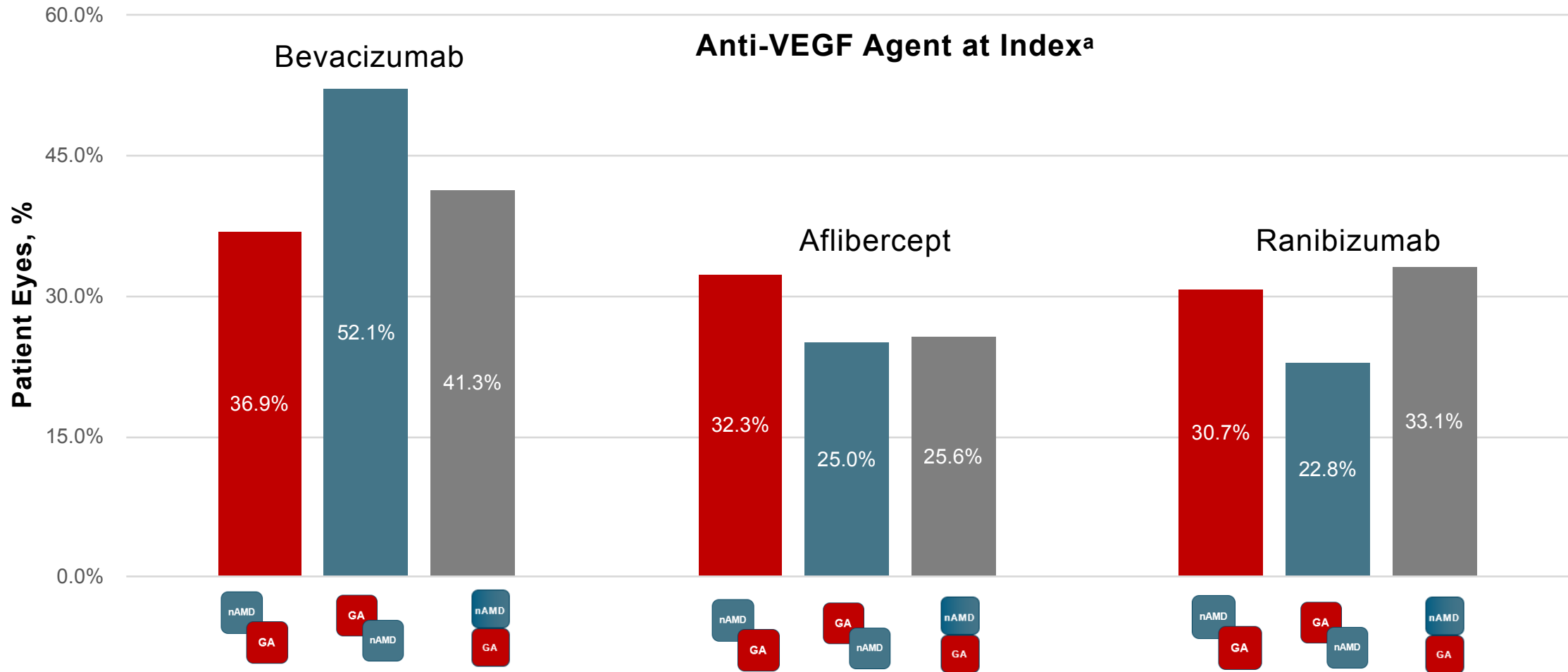
Change in Visual Acuity After 6 Years of Follow-up^a



Less median vision loss in patients with GA before nAMD over time

^aChange in visual acuity from baseline is reported for each year of treatment when available. Percent of baseline cohort available in Year 1 includes 92% in Cohort 1, 91% in Cohort 2, and 91% in Cohort 3. A treatment year is defined as 52 ± 8 weeks (eg, Year 1, Year 2). The visual acuity reading nearest the end of the treatment year was selected. If visual acuity readings were taken equidistant from the end of the treatment year, the later measurement was selected. When >1 visual acuity reading was taken on the same day, the best measurement was used. ETDRS, Early Treatment Diabetic Retinopathy Study; GA, geographic atrophy; nAMD, neovascular age-related macular degeneration.


Index Anti-VEGF Agent by Cohort



^aRanibizumab port delivery system and brolucizumab are not shown here due to low numbers and were excluded from further analysis (US Food and Drug Administration approvals in 2021 and 2019, respectively).

GA, geographic atrophy; **nAMD**, neovascular age-related macular degeneration; **VEGF**, vascular endothelial growth factor.

Time Between Index and Last Anti-VEGF Injection by Cohort



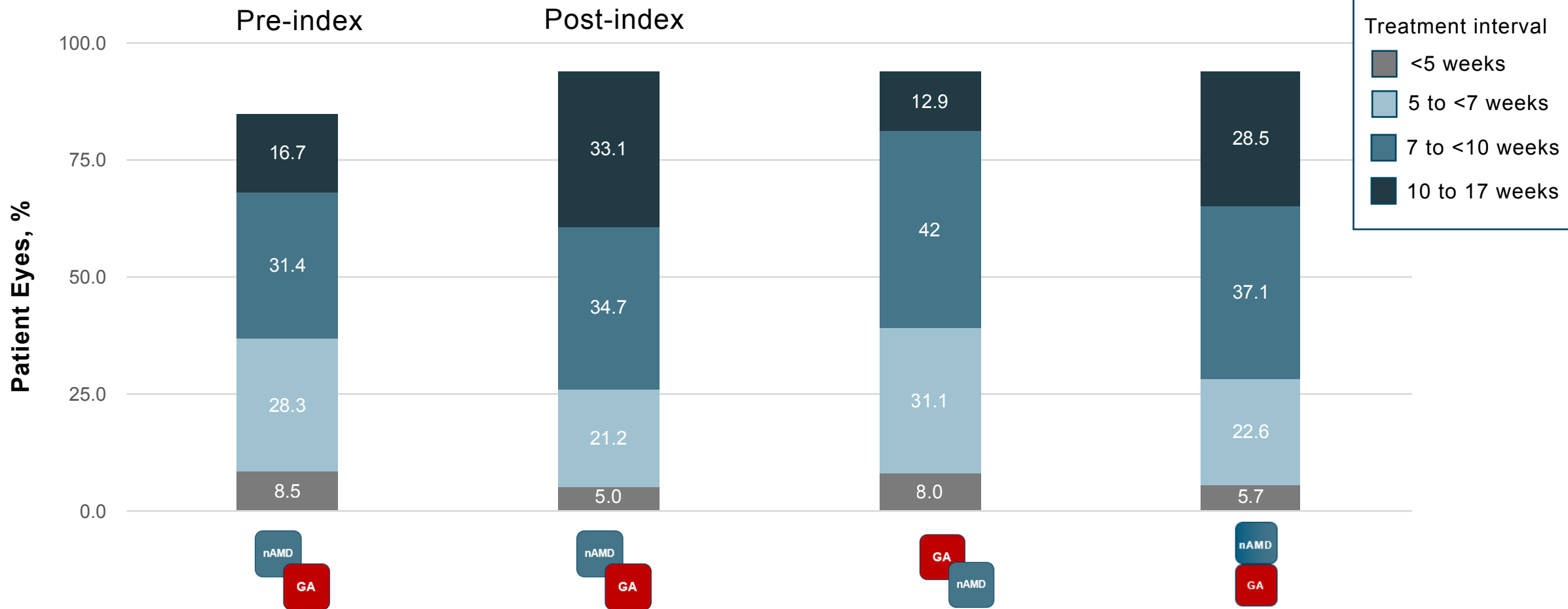
	nAMD GA	GA nAMD	nAMD GA
Total patient eyes,^a n (% total)	10,140 (37.8%)	12,509 (46.6%)	4189 (15.6%)
Time between index anti-VEGF injection and last anti-VEGF injection, n (% cohort)			
15–180 days	554 (5.5%)	1206 (9.6%)	317 (7.6%)
181–365 days	583 (5.7%)	911 (7.3%)	260 (6.2%)
366–730 days	3372 (33.3%)	3667 (29.3%)	1012 (24.2%)
≥731 days	5208 (51.4%)	6146 (49.1%)	2405 (57.4%)

A higher proportion of patients with GA before nAMD discontinued anti-VEGF treatment in <1 year

^aLimited to patient eyes with more than one injection in the study period. Twelve months of follow-up were required for study inclusion, indicating patients with <6 months of anti-VEGF treatment discontinued treatment without restarting within ≥6 months of discontinuation.

GA, geographic atrophy; **nAMD**, neovascular age-related macular degeneration; **VEGF**, vascular endothelial growth factor.

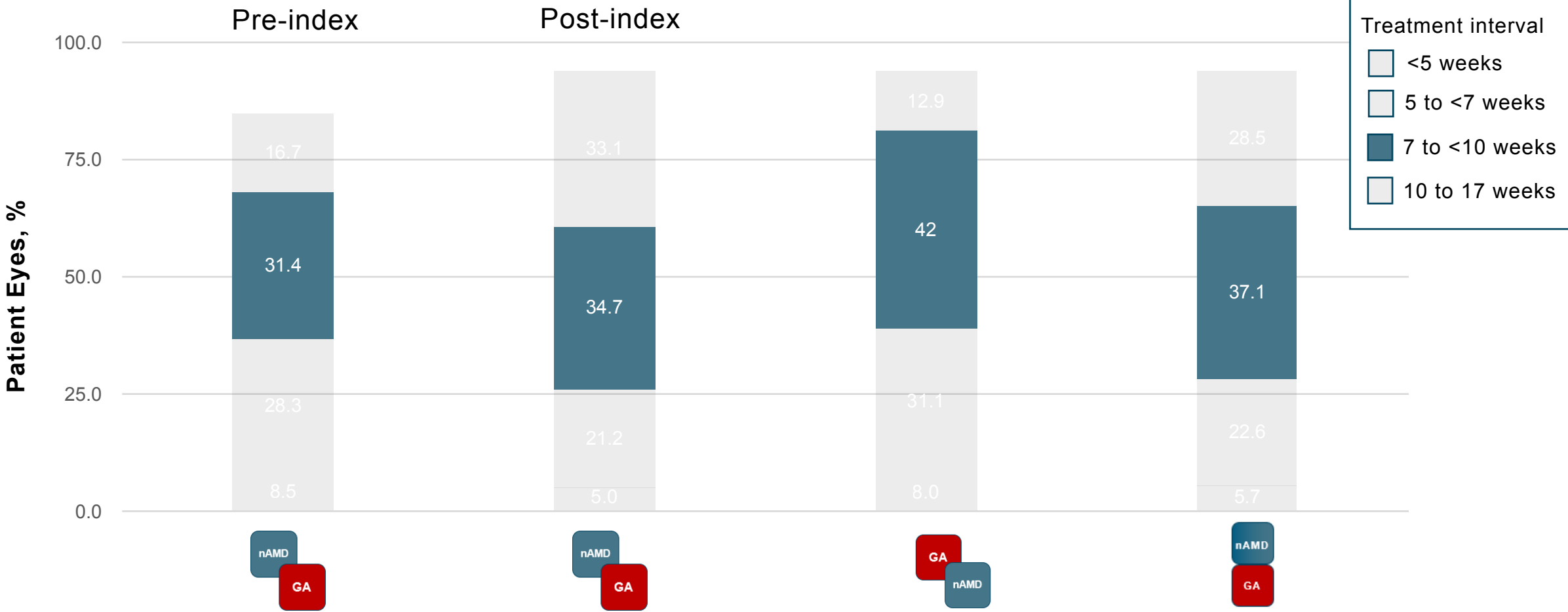
Average Interval of Anti-VEGF Injection After Index Date^a



^aLimited to patient eyes with ≥ 2 injections that had not discontinued.

GA, geographic atrophy; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

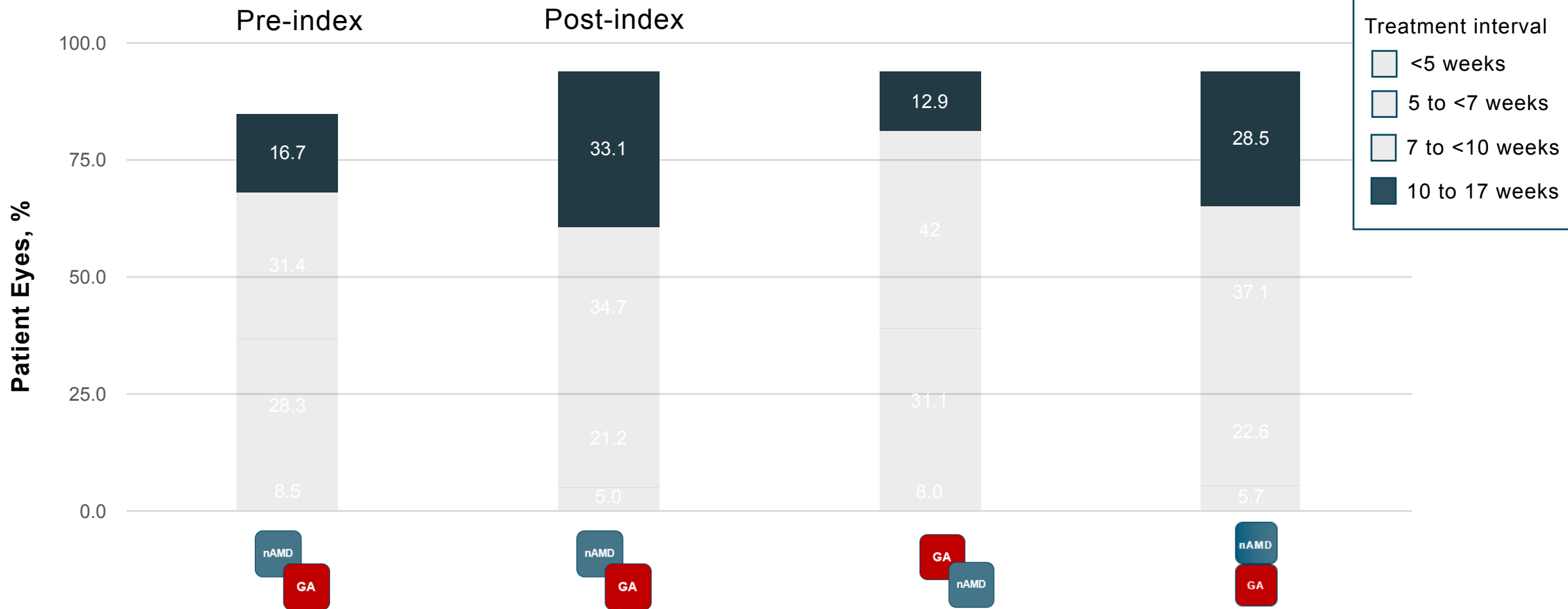
Average Interval of Anti-VEGF Injection After Index Date^a



7- to <10-week intervals were most common across all cohorts

^aLimited to patient eyes with ≥2 injections that had not discontinued.
GA, geographic atrophy; **nAMD**, neovascular age-related macular degeneration; **VEGF**, vascular endothelial growth factor.

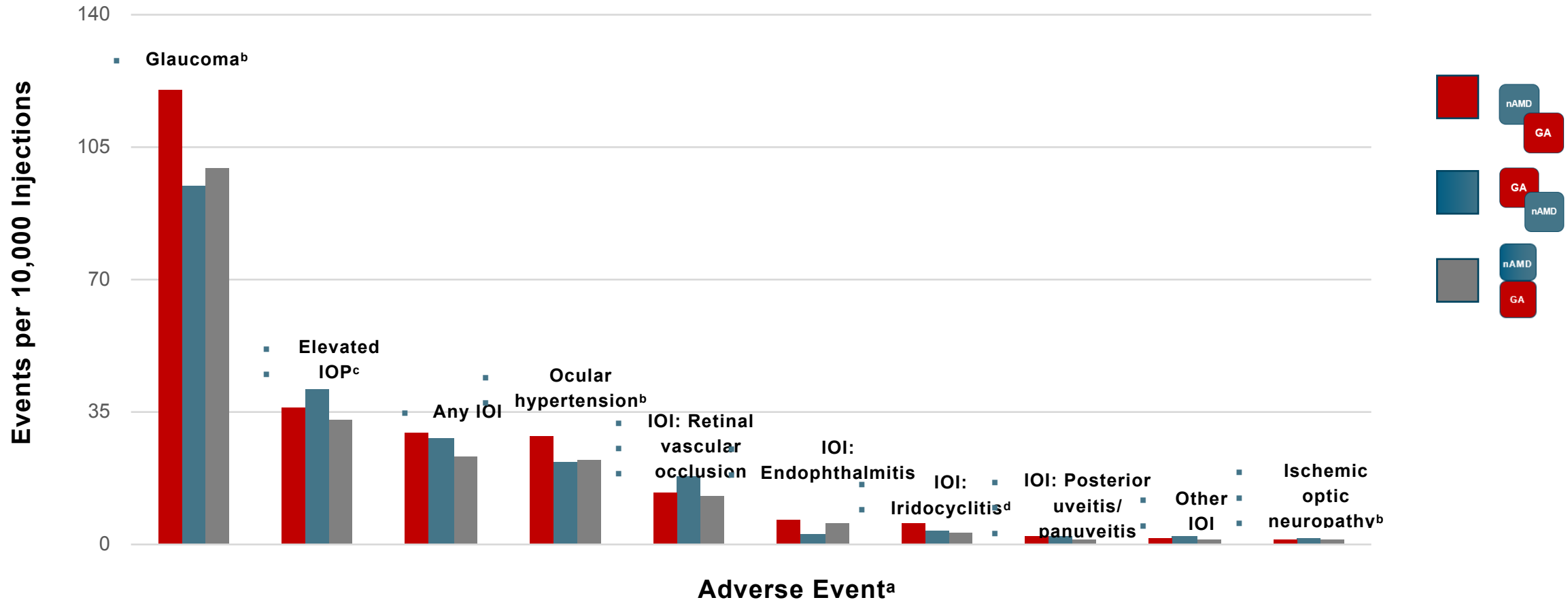
Average Interval of Anti-VEGF Injection After Index Date^a



For patients with nAMD, the interval between anti-VEGF injections increased in the year after GA diagnosis

^aLimited to patient eyes with ≥2 injections that had not discontinued.
 GA, geographic atrophy; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.




Incidence of Adverse Events^a During Study Period



^aAdverse events were defined as events occurring within 120 days of an injection event in the treated eye without prior history. ^bMeasured by diagnosis codes (ICD-10 CM) assigned during routine clinical practice within 120 days of an injection event. ^cIOP elevation defined as an increase >6 mmHg from baseline with concurrent reading ≥25 mmHg within 120 days of an injection event. ^dUnspecified diagnosis codes, such as iridocyclitis, are sporadically documented in electronic health records resulting in artificially low volumes. Unspecified codes may be included in patient records after issue has resolved.

GA, geographic atrophy; ICD-10 CM, International Classification of Diseases, Tenth Revision, Clinical Modification; IOI, intraocular inflammation; IOP, intraocular pressure; nAMD, neovascular age-related macular degeneration.

Incidence Rates of Intraocular Inflammation Adverse Events^a

			
Any IOI (incidence rate per 10,000 injections)	29.5	28.0	23.3
Posterior uveitis/panuveitis	2.1	1.9	1.3
Endophthalmitis	6.6	2.4	5.3
Retinal vasculitis	0.1	0.2	0.1
Retinal vascular occlusion	13.4	18.0	12.5
Iridocyclitis ^b	5.4	3.3	3.1
Vitritis	0.3	0.1	0.0
Other IOI	1.6	2.0	0.9

^aAdverse event incidence rates (per 10,000 injections) using diagnosis codes (ICD-10 CM). ^bUnspecified diagnosis codes, such as iridocyclitis, are sporadically documented in electronic health records resulting in artificially low volumes. Unspecified codes may be included in patient records after issue has resolved.

GA, geographic atrophy; **ICD-10**, International Classification of Diseases, Tenth Revision, Clinical Modification; **IOI**, intraocular inflammation; **nAMD**, neovascular age-related macular degeneration.

Limitations

- Does not reflect clinical treatment patterns after approvals of anti-complement therapies for GA
- Differences in treatment patterns may be underestimated when including the first year of treatment with subsequent years of treatment
- May not generalize to patients outside of the IRIS Registry
 - IRIS Registry is representative of approximately 70% of US ophthalmology practices
- To preserve study population size, patients with bilateral disease were included
 - Patients may differ from those with GA and nAMD in only 1 eye

Conclusions

- Coincident diagnosis of GA and nAMD was associated with the worst baseline vision
- Following initiation of anti-VEGF therapy, patients with GA before nAMD had less median vision loss than the other cohorts
- A higher proportion of patients with GA before nAMD discontinued anti-VEGF treatment in <1 year
- On average, patients diagnosed with GA before nAMD have shorter anti-VEGF intervals compared with other cohorts
- Adverse events observed include glaucoma, elevated IOP, retinal vascular occlusion, and endophthalmitis

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Contact information: tedleng@gmail.com

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