# Impact of Initial Monthly Doses of Aflibercept on Visual Outcomes in Eyes With Diabetic Macular Edema in Routine Clinical Practice in the US

**Ferhina S Ali, MD, MPH,[1] Nitish Mehta, MD,[2] Rishi P Singh, MD,[3] Nick Boucher, BSc,[4] Fabiana Q Silva, MD,[5] Rutvi Desai, OD,[5] Steven Sherman, MPH[5]**

*[1]Department of Ophthalmology, New York Medical College, Valhalla, New York; [2]Department of Ophthalmology, NYU Langone Health, New York, New York; [3]Center for Ophthalmic Bioinformatics, Cole Eye Institute, Cleveland, Ohio; [4]Vestrum Health, Naperville, Illinois; [5]Regeneron Pharmaceuticals, Inc., Tarrytown, New York*

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# Disclosures

- Ferhina S Ali is a consultant for Allergan/AbbVie, EyePoint, and Genentech. Nitish Mehta has no disclosures to report. Rishi P Singh has received research funding from Apellis and NGM Biopharma and is a consultant for Alcon, Bausch & Lomb, Genentech/Roche, Novartis, Regeneron Pharmaceuticals, Inc., and Zeiss. Nick Boucher is an employee of Vestrum Health. Fabiana Q Silva, Rutvi Desai, and Steven Sherman are employees and stockholders of Regeneron Pharmaceuticals, Inc.

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# Background and Objectives

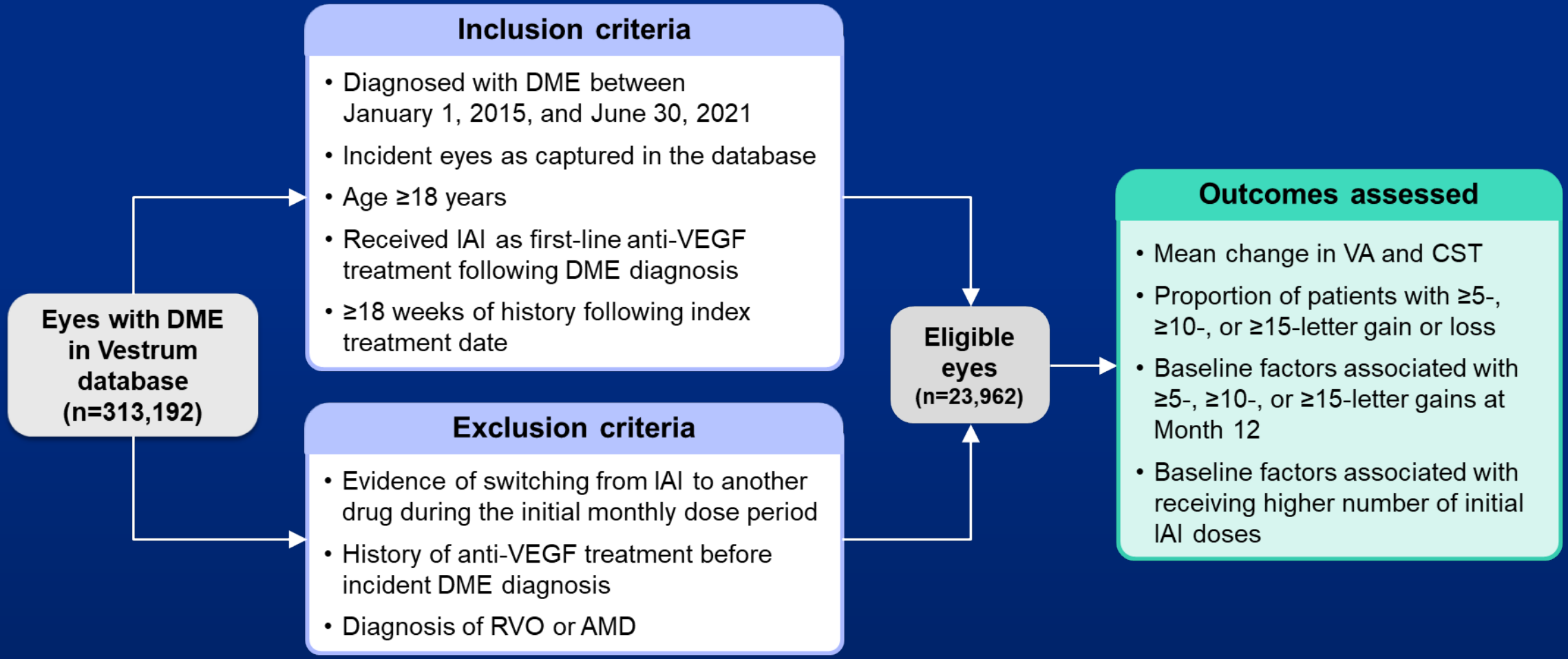
- In routine clinical practice, patients with DME receiving anti–VEGF therapy may not receive the recommended prescribed initial monthly dosing[1,2]
  - In the AQUILA and APOLLON studies, 88% and 62% of patients, respectively, did not receive 5 initial monthly injections of IAI[1,2]
- Real-world studies have demonstrated an association between the number of initial monthly anti-VEGF doses and magnitude of VA improvement[1,3,4]
  - In AQUILA, patients with DME receiving ≥5 initial monthly doses of IAI exhibited greater visual gains than those receiving <5 initial monthly injections (mean change in BCVA: +10.1 versus +7.1 letters)[1]

**This study aimed to evaluate the factors associated with initial monthly dosing of IAI and their impact on visual and anatomic outcomes at 12 months in patients with DME**

DME, diabetic macular edema; BCVA, best-corrected visual acuity; IAI, intravitreal aflibercept injection; VA, visual acuity; VEGF, vascular endothelial growth factor.

1. Rodríguez FJ et al. *Int J Retina Vitreous*. 2022;8:52. 2. Korobelnick J et al. *Sci Rep*. 2022;12(1):18242. 3. Hayashi Y et al. *J Diabetes Res*. 2021;2021:1374891.
4. Mitchell P et al. *PLoS One*. 2020;15(6):e0233595.

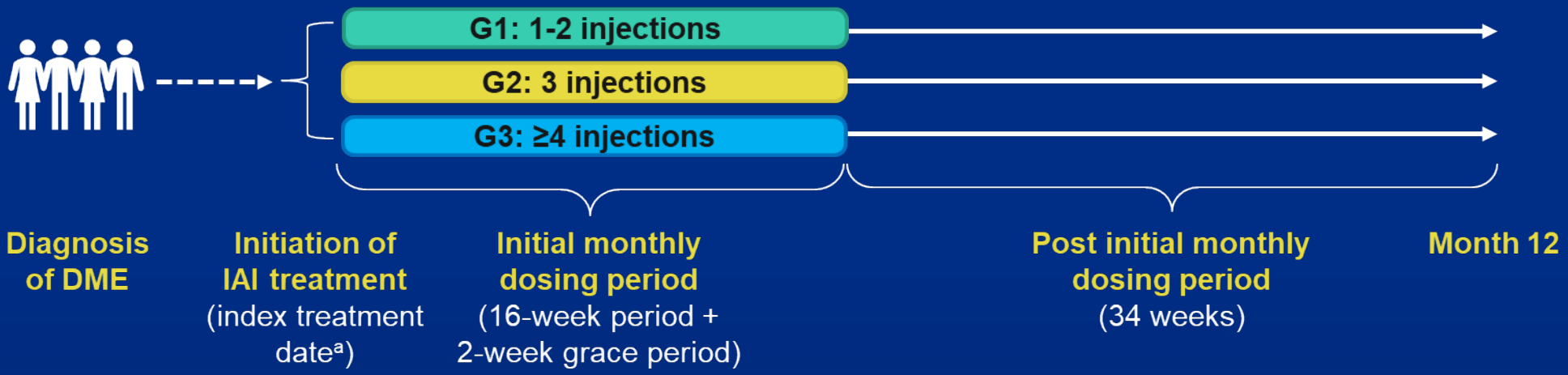
# Study Design




AMD, age-related macular degeneration; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; RVO, retinal vein occlusion.

# Methods

Treatment timeline




- Eligible eyes were analyzed in subgroups (G) based on the number of IAI doses administered during the initial monthly dosing period (G1: 1-2 injections; G2: 3 injections; G3: ≥4 injections)
- The relationships between baseline characteristics and the likelihood of receiving ≥4 initial monthly injections and of gaining ≥5, ≥10, or ≥15 ETDRS letters at 12 months were examined with logistic regression

[a]Index treatment defined as date of first IAI treatment. A 30-day grace period prior to index treatment date was used to identify VA and CST records.

# Baseline Characteristics by Subgroups of IAI Initial Monthly Doses

| | G1 (1-2 injections) (n=7781) | G2 (3 injections) (n=6922) | G3 (≥4 injections) (n=9259) |
|---|---|---|---|
| **Age, mean, years** | 60.0 | 61.1 | 62.0 |
| **Male, n (%)** | 4293 (55) | 3778 (55) | 5248 (57) |
| **Comorbid conditions, n (%)** | | | |
| Type 2 diabetes | 5319 (68) | 4862 (70) | 6837 (74) |
| Type 1 diabetes | 2051 (26) | 1723 (25) | 2002 (22) |
| Hypertension | 4428 (57) | 4004 (58) | 5129 (55) |
| **DR severity, n (%)** | | | |
| PDR | **3363 (43)** | **2490 (36)** | **3083 (33)** |
| Severe NPDR | **1156 (15)** | **1317 (19)** | **2042 (22)** |
| Moderate NPDR | **2117 (27)** | **2110 (30)** | **2884 (31)** |
| Mild NPDR | 753 (10) | 665 (10) | 879 (9) |
| Unknown | 392 (5) | 340 (5) | 371 (4) |

**At baseline, there was a decreasing proportion of patients with PDR, and an increasing proportion with severe and moderate NPDR across eyes in G1, G2, and G3**

DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

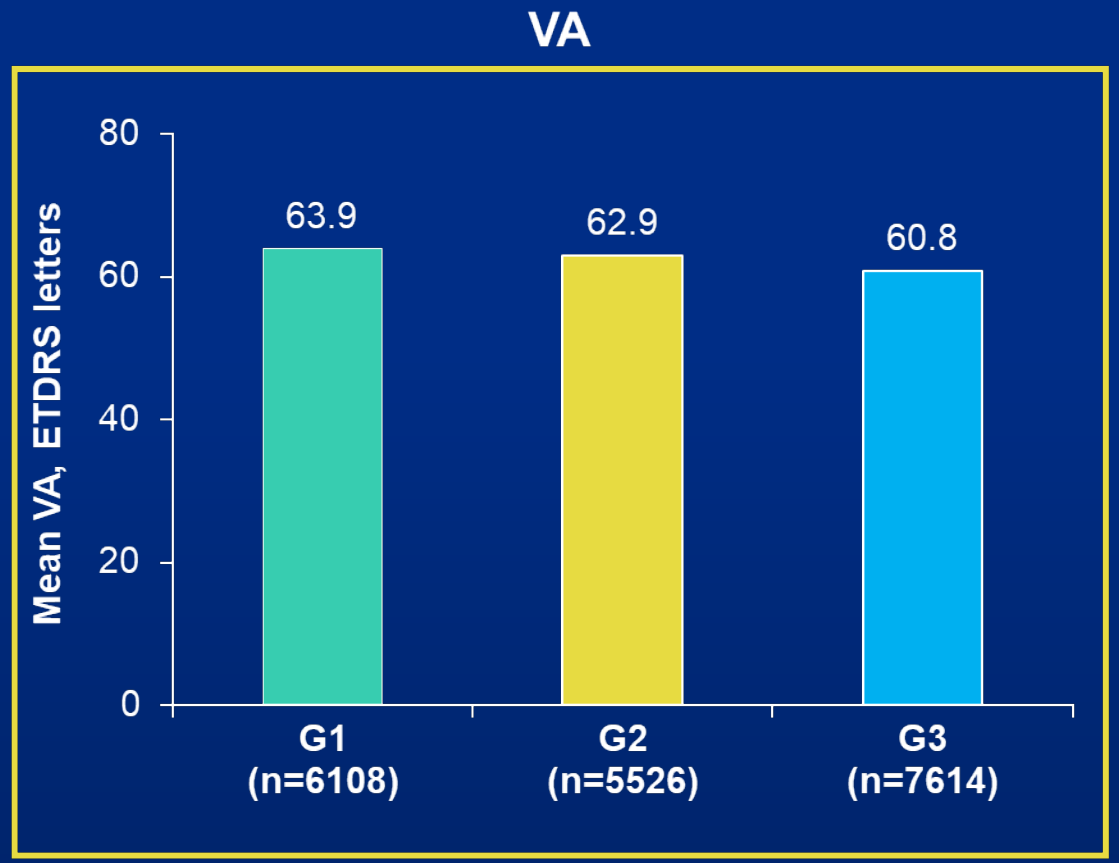
# Visits and Treatment Frequency Through 12 Months by Subgroups of IAI Initial Monthly Doses

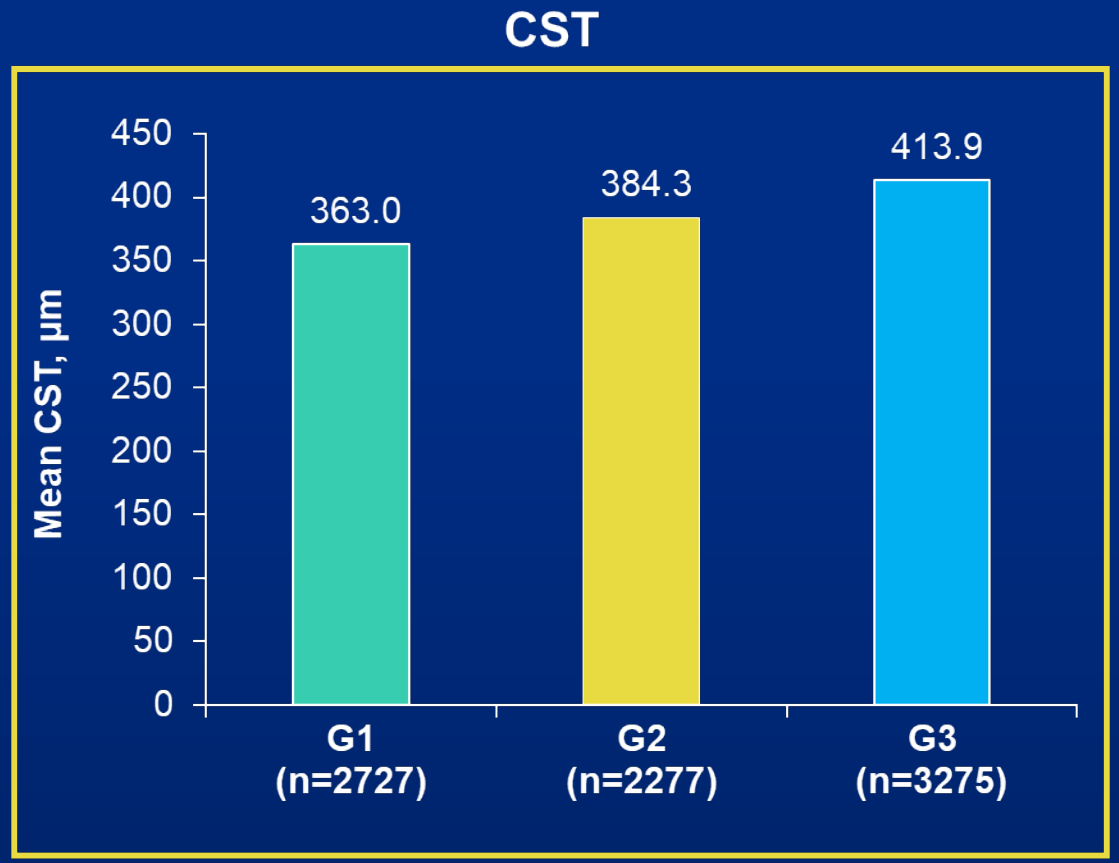
| | G1 (1-2 injections) (n=7781) | G2 (3 injections) (n=6922) | G3 (≥4 injections) (n=9259) |
|---|---|---|---|
| **Time from diagnosis to first anti-VEGF treatment, mean, days** | **137.6** | **103.9** | **88.8** |
| **Visit frequency through 12 months** | | | |
| Visits through 12 months, mean | 6.9 | 8.5 | 10.5 |
| Visits during initial monthly dosing period, mean | 3.9 | 4.3 | 5.3 |
| Visits after initial monthly dosing period, mean | 3.5 | 4.4 | 5.3 |
| **Treatment frequency through 12 months** | | | |
| Eyes receiving treatment after initial monthly dosing period, n (%) | 4111 (53) | 5288 (76) | 8456 (91) |
| Injections after initial monthly dosing period, mean | 2.4 | 2.9 | 3.7 |
| Time between treatments, mean, days | 98.7 | 54.3 | 41.7 |
| Time between last injection and 12 months, mean, days | 87.2 | 88.2 | 78.1 |
| **Eyes with treatment break through 12 months, n (%)[a]** | 5437 (70) | 2698 (39) | 1807 (20) |
| **Eyes lost to follow-up through 12 months, n (%)[b]** | 1207 (16) | 315 (5) | 102 (1) |

**Patients in G1 had a longer time from diagnosis to treatment, fewer visits, more breaks in treatment, and more losses to follow-up compared with G2 and G3**

[a]Treatment break: gap of >6 months between 2 treatments. [b]Lost to follow-up: gap of >8 months between 2 visits.

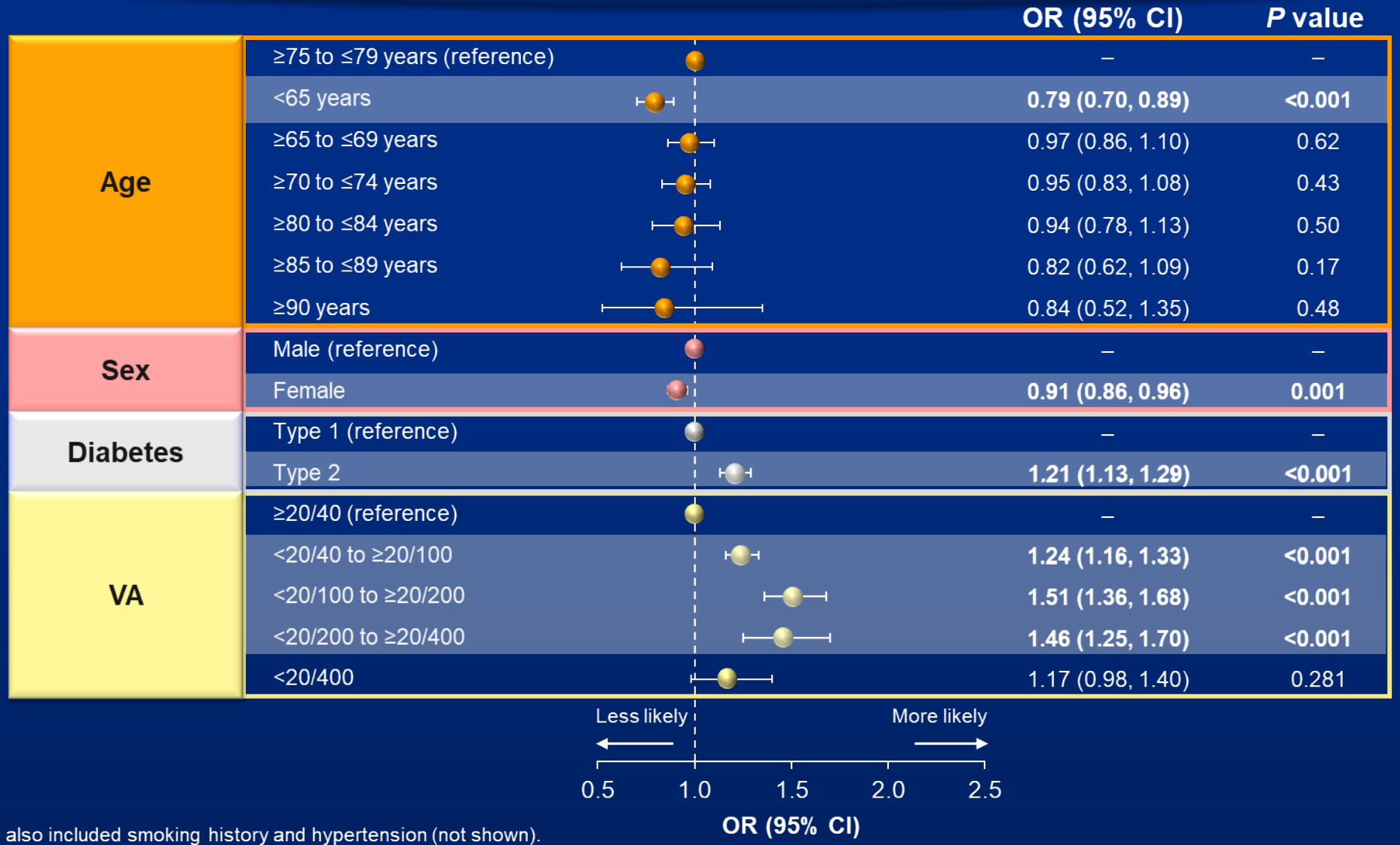
# Mean Baseline VA and CST by Subgroups of IAI Initial Monthly Doses



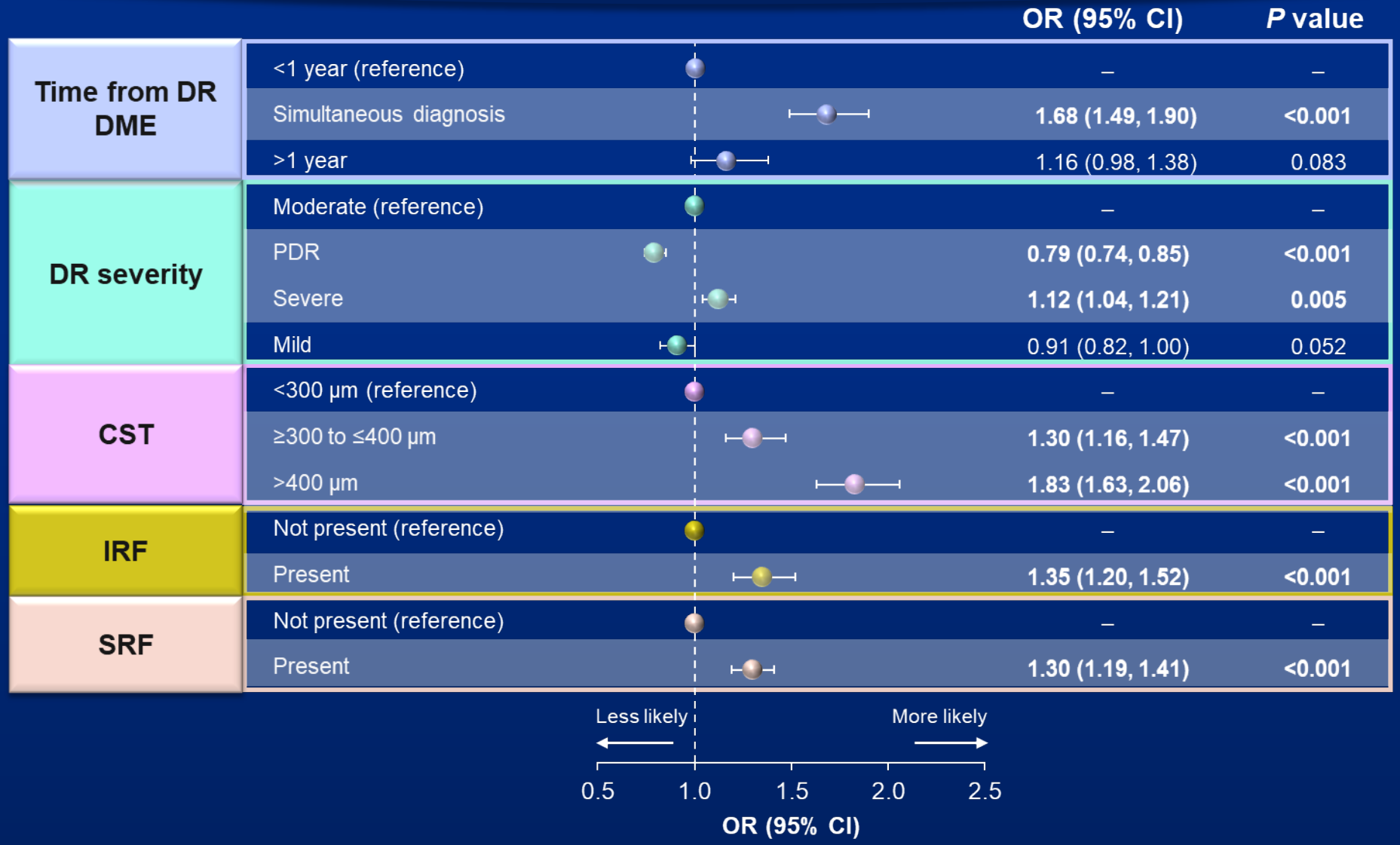

VA was reported as logMAR and converted to ETDRS letters. VA was identified at the date of first anti-VEGF treatment. A 30-day grace period prior to index treatment date was used to identify VA record.
G1: 1-2 injections; G2: 3 injections; G3: ≥4 injections.
logMAR, logarithm of the minimum angle of resolution.

# Baseline Factors Associated With Receiving ≥4 Initial Monthly IAI Doses




Logistic regression model also included smoking history and hypertension (not shown).
CI, confidence interval; OR, odds ratio.

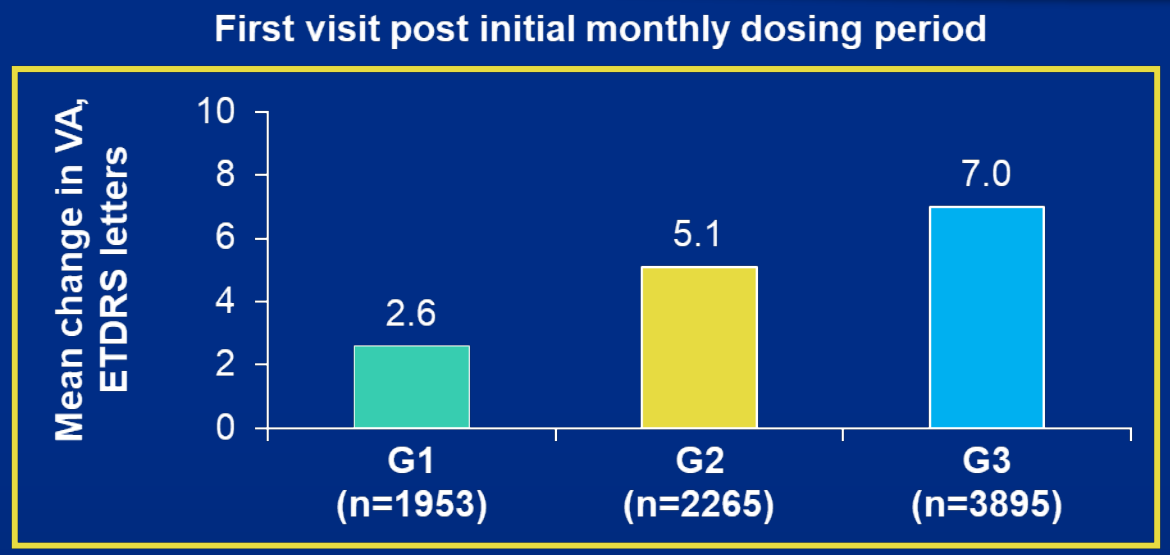
# Baseline Factors Associated With Receiving ≥4 Initial Monthly IAI Doses

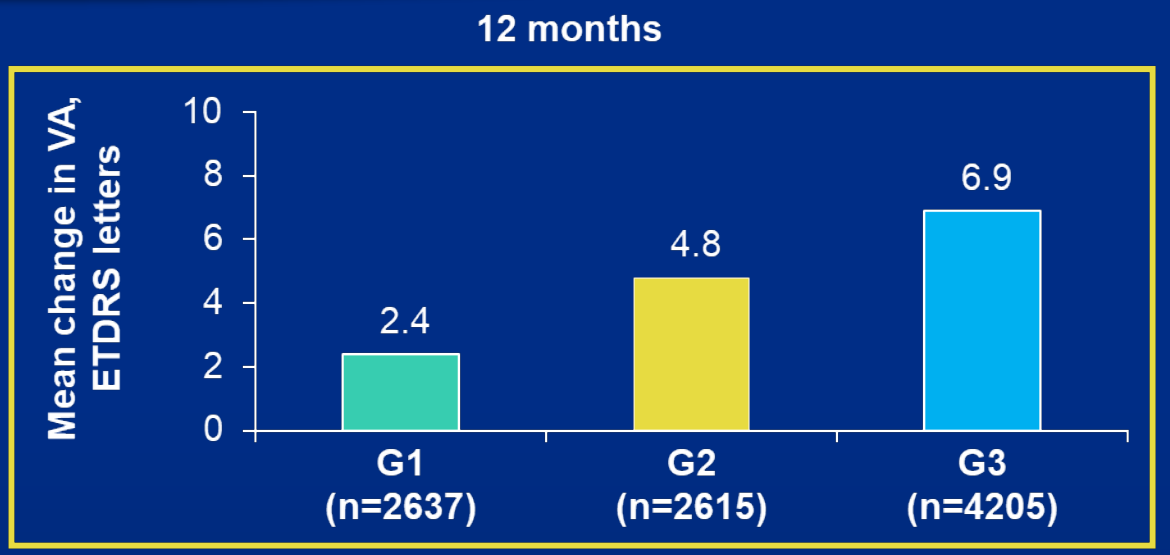


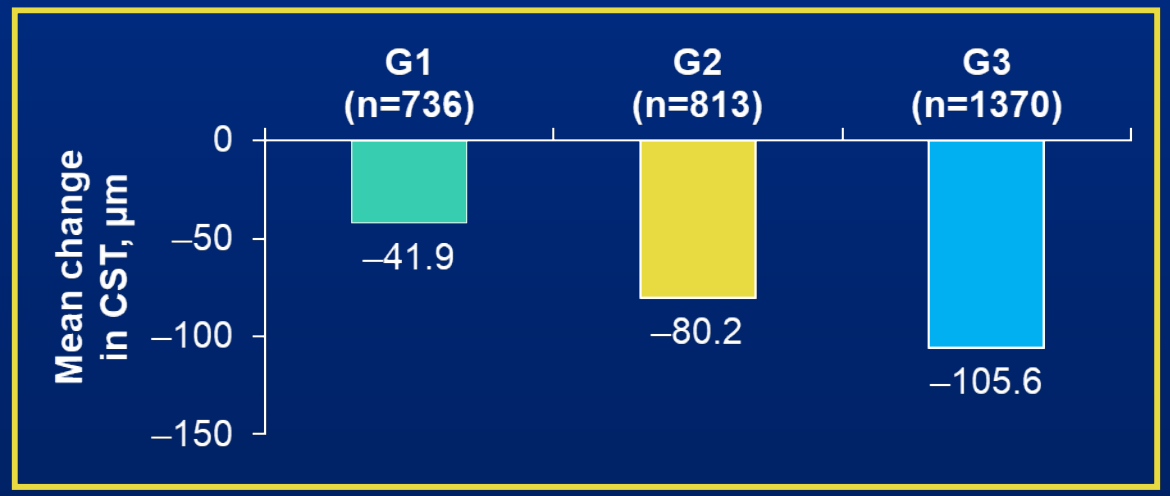

IRF, intraretinal fluid; SRF, subretinal fluid.

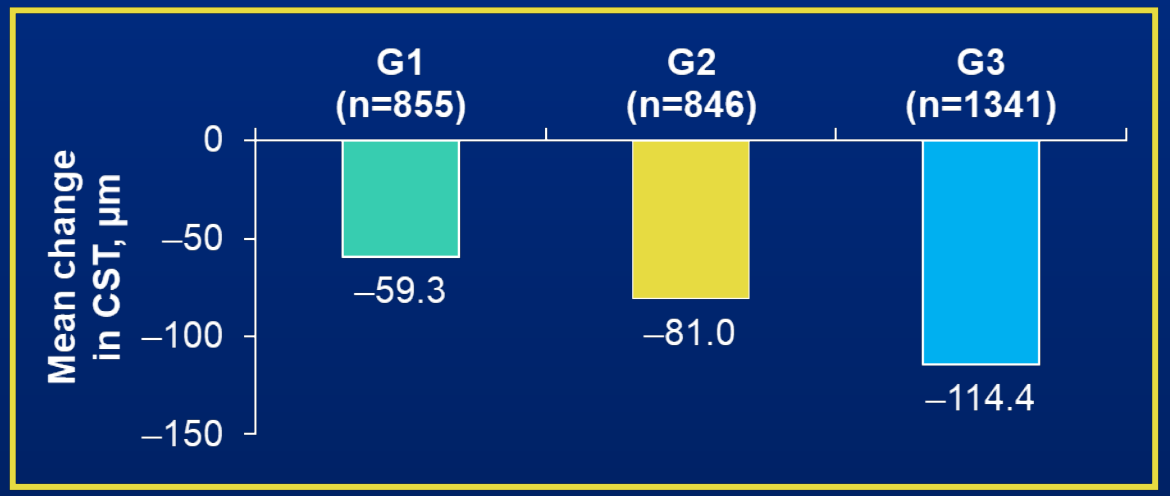
# Visual and Anatomic Outcomes at Month 12 by Subgroups of IAI Initial Monthly Doses

# Mean Changes in VA and CST From Baseline at First Visit Post Initial Dosing and at 12 Months



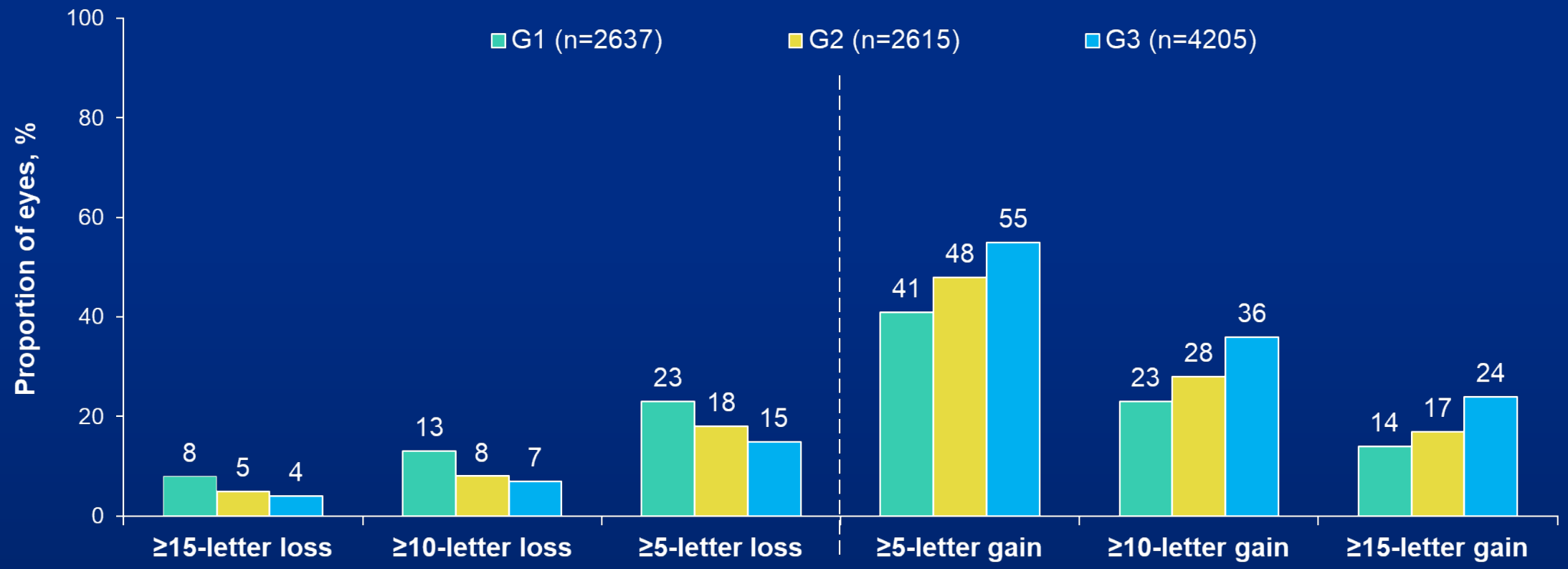



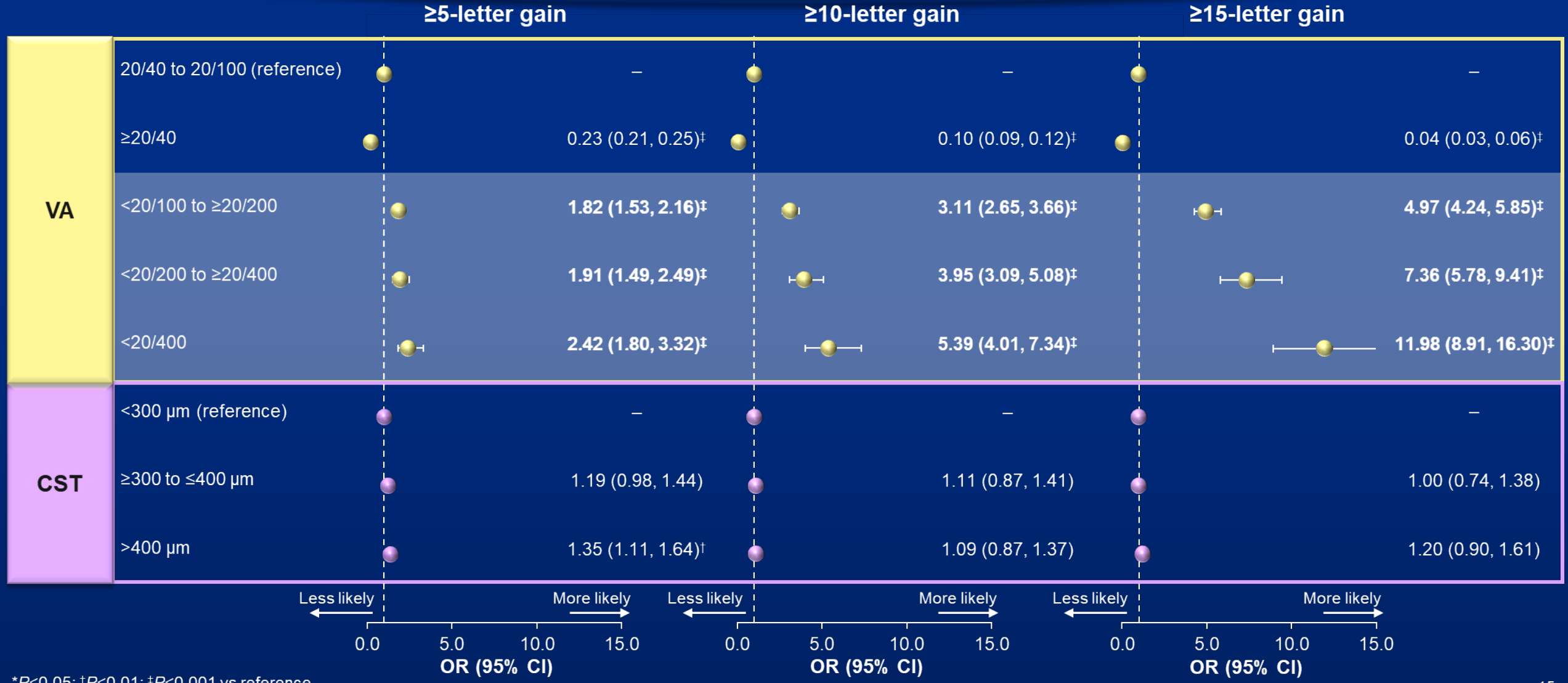

Analysis included eyes with values at baseline (index treatment date) and Month 12.
G1: 1-2 injections; G2: 3 injections; G3: ≥4 injections.

# Proportion of Eyes With ≥5-, ≥10-, and ≥15-Letter Gain or Loss From Baseline to Month 12



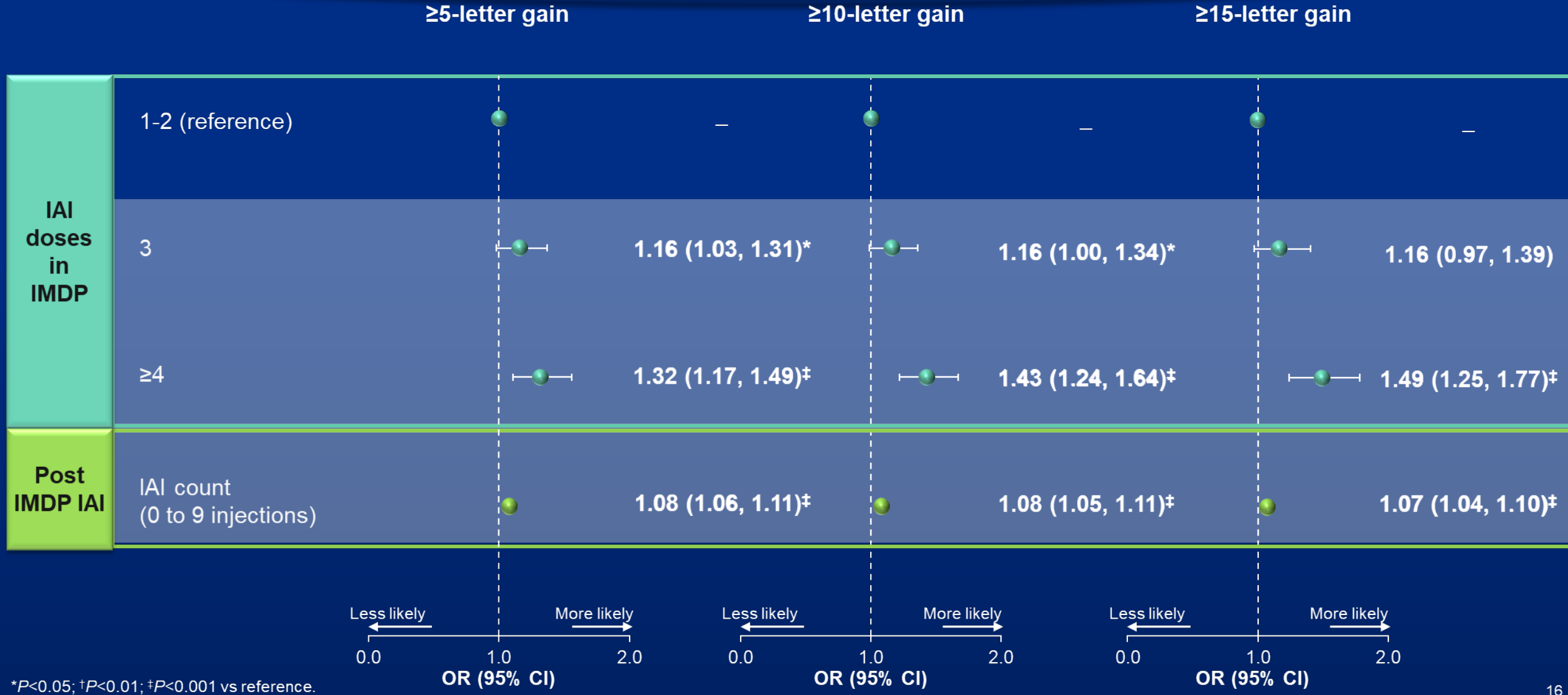

Analysis included eyes with values at baseline (index treatment date), post initial monthly dosing period, and Month 12.
Baseline VA was identified at or 30 days before the date of first IAI treatment. VA at first visit post initial dosing was identified within 90 days of initial dosing end date.
VA at Month 12 was defined within ±30 days of the latest date.
G1: 1-2 injections; G2: 3 injections; G3: ≥4 injections.

# Baseline Factors Associated With ≥5-, ≥10-, and ≥15-Letter Gain at Month 12




*$P$<0.05; †$P$<0.01; ‡$P$<0.001 vs reference.
Logistic regression model also included age, sex, time from DR to DME diagnosis, and DR severity (not shown). IMDP, initial monthly dosing period.

# Baseline Factors Associated With ≥5-, ≥10-, and ≥15-Letter Gain at Month 12

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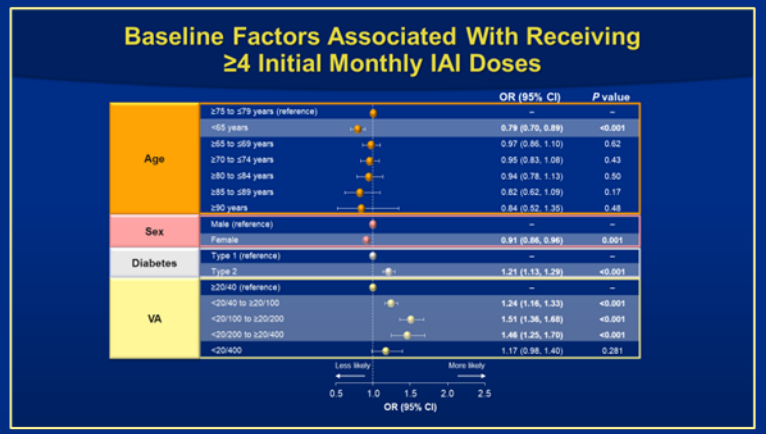
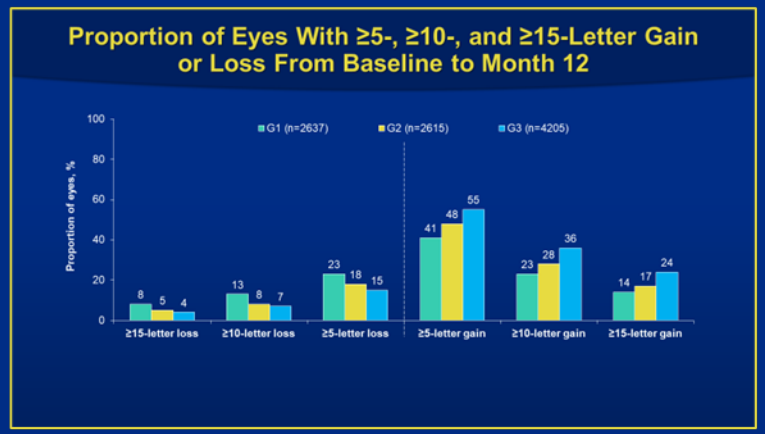
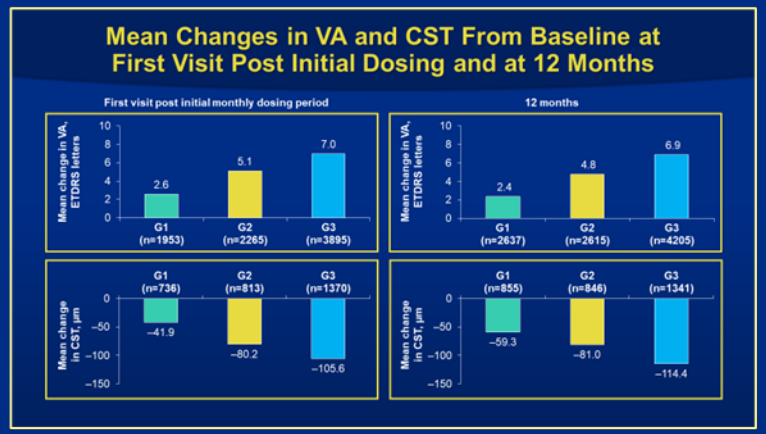
Logistic regression model also included age, sex, time from DR to DME diagnosis, and DR severity (not shown). IMDP, initial monthly dosing period.

# Conclusions




- Key baseline factors associated with receiving ≥4 injections during the initial monthly dosing period included baseline VA <20/40 to >20/400 (vs ≥20/40), CST >300 µm, and presence of IRF and/or SRF
- Trends of improved visual and anatomic outcomes were observed with increasing number of IAI doses during the initial monthly dosing period and at month 12 following initiation of IAI treatment
- Thus, this study suggests that the number of initial monthly treatments may play an important role in achieving optimal visual and anatomic outcomes