

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

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# Disclosures

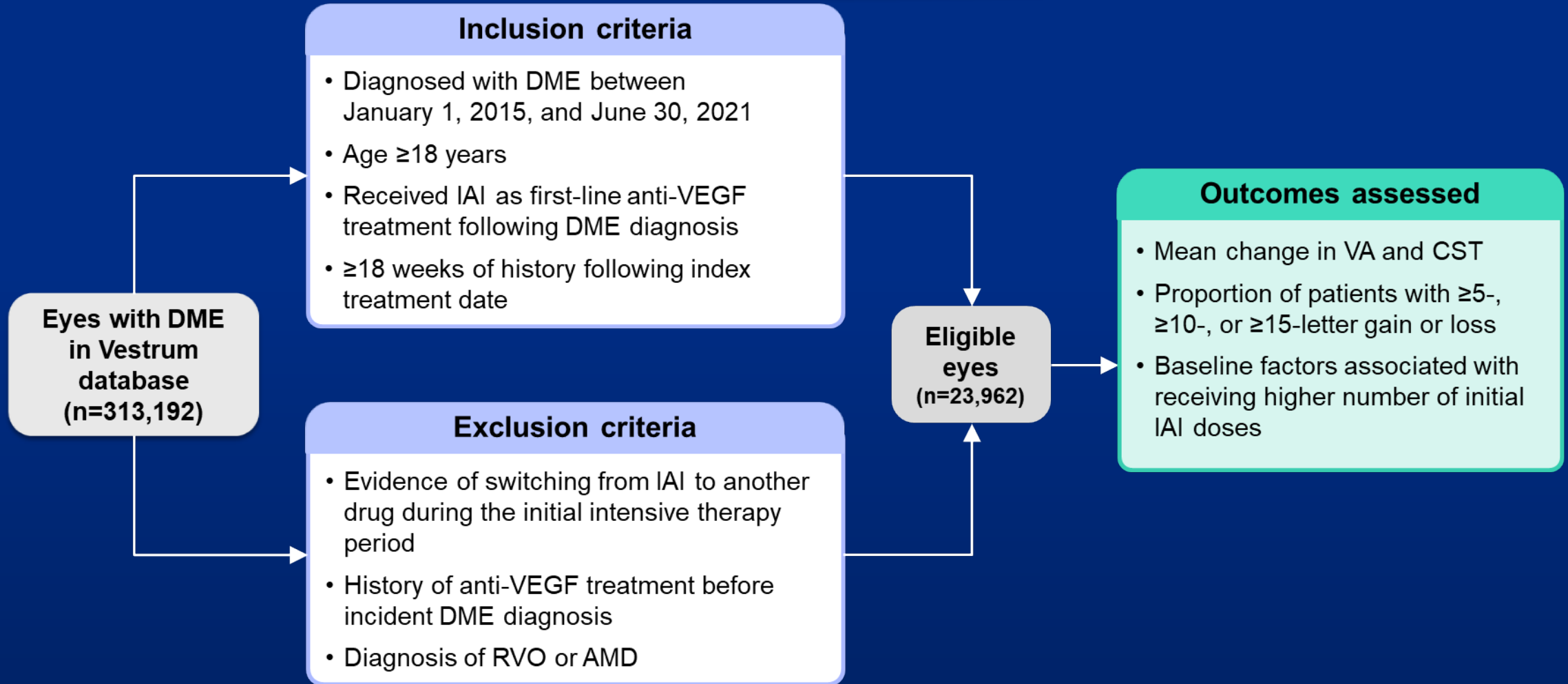
- Yasha S Modi is a consultant for Alimera, Allergan, Genentech, Théa, and Zeiss. Ferhina S Ali is a consultant for Allergan/AbbVie, EyePoint, and Genentech. Nitish Mehta has no disclosures to report. Rishi P Singh has received research funding from Apellis and NGM Biopharma and is a consultant for Alcon, 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

- Real-world studies have demonstrated an association between the number of initial monthly anti-VEGF doses and magnitude of VA improvement<sup>1-3</sup>
  - In AQUILA, patients with DME receiving  $\geq 5$  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)<sup>1</sup>

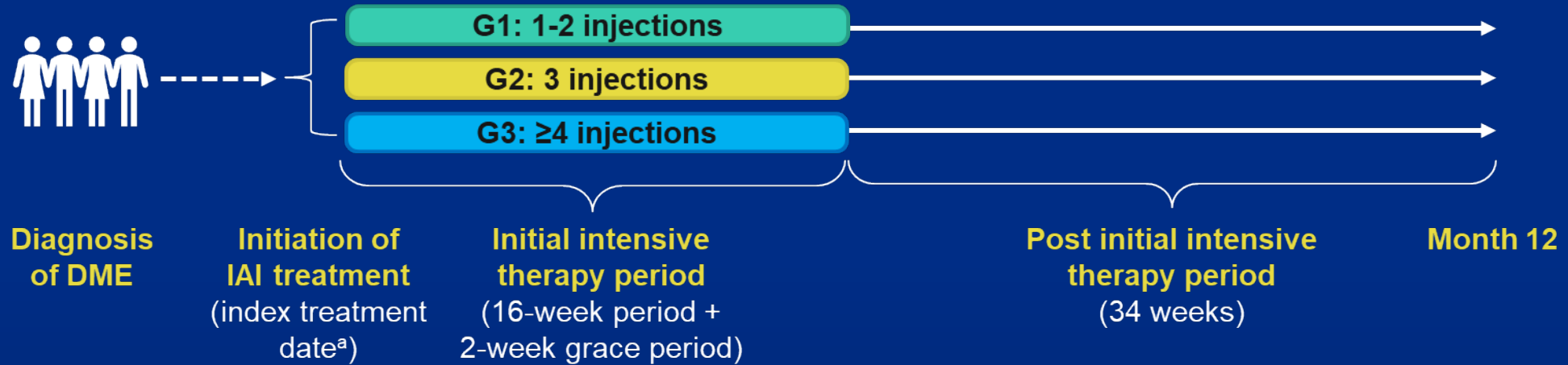
**This study aimed to evaluate the factors associated with initial intensive therapy with IAI and the impact on visual outcomes at 12 months in patients with DME**

# Study Design



# Methods

## Treatment timeline



- A 16-week initial intensive therapy period allowed for 5 monthly IAI doses, or an intensive treat-and-extend regimen
- The relationships between baseline characteristics and the likelihood of receiving  $\geq 4$  initial monthly injections and of gaining  $\geq 5$ ,  $\geq 10$ , or  $\geq 15$  ETDRS letters at 12 months were examined with logistic regression

<sup>a</sup>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)
<b>Age, mean, years</b>	60.0	61.1	62.0
<b>Male, n (%)</b>	4293 (55)	3778 (55)	5248 (57)
<b>Comorbid conditions, n (%)</b>			
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)
<b>DR severity, n (%)</b>			
PDR	<b>3363 (43)</b>	<b>2490 (36)</b>	<b>3083 (33)</b>
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)

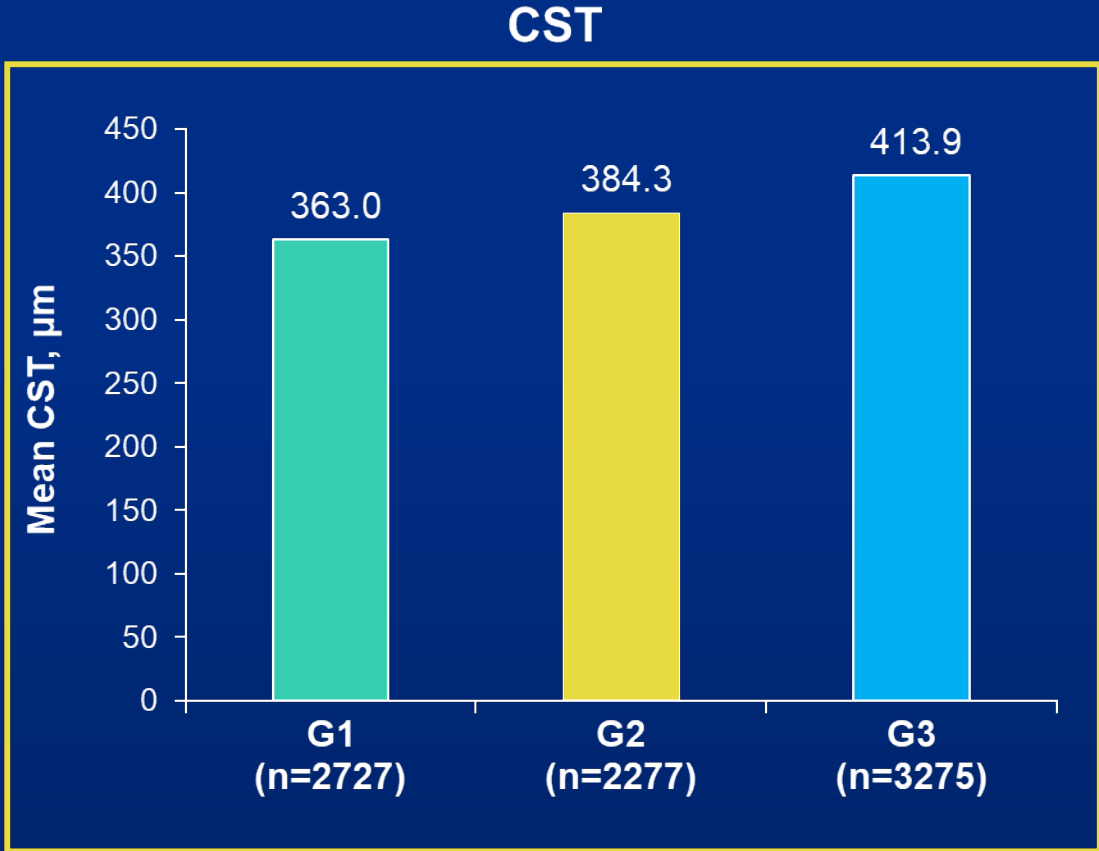
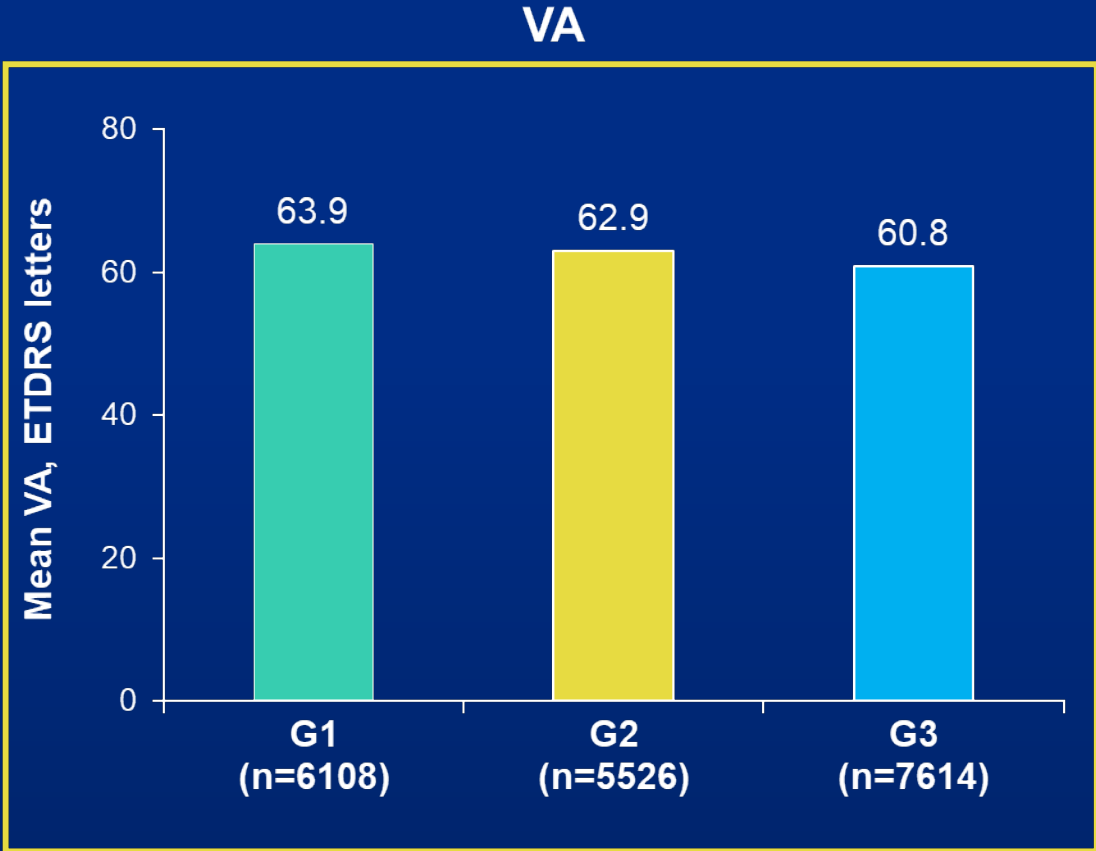
# Visits and Treatment Frequency Through 12 Months by Subgroups of IAI Initial Monthly Doses

	G1 (1-2 injections) (n=7781)	G2 (3 injections) (n=6922)	G3 (≥4 injections) (n=9259)
<b>Visit frequency through 12 months</b>			
Visits through 12 months, mean	6.9	8.5	10.5
<b>Treatment frequency through 12 months</b>			
Eyes receiving treatment after initial intensive therapy period, n (%)	4111 (53)	5288 (76)	8456 (91)
Injections after initial intensive therapy period, mean	2.4	2.9	3.7
<b>Eyes with treatment break through 12 months, n (%)<sup>a</sup></b>	<b>5437 (70)</b>	<b>2698 (39)</b>	<b>1807 (20)</b>
<b>Eyes lost to follow-up through 12 months, n (%)<sup>b</sup></b>	<b>1207 (16)</b>	<b>315 (5)</b>	<b>102 (1)</b>

**Patients with more frequent injections during the initial intensive therapy period had more visits, fewer breaks in treatment, and fewer losses to follow-up through 12 months compared with less frequent injections**

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

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



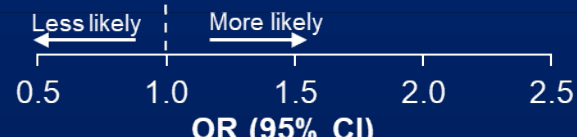
**Patients with more intensive initial therapy had worse VA and greater CST at baseline**

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 $\geq 4$ Initial Monthly IAI Doses

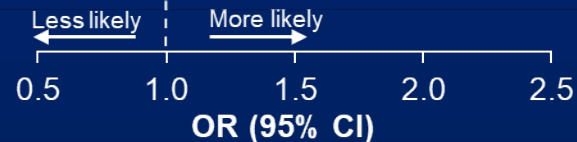
		OR (95% CI)	P value
Age	$\geq 65$ (reference)	—	—
	$\geq 40$ to $\leq 64$ years	0.84 (0.78, 0.90)	<0.001
	$\geq 18$ to $\leq 39$ years	<b>0.58 (0.50, 0.67)</b>	<b>&lt;0.001</b>
Sex	Male (reference)	—	—
	Female	0.91 (0.86, 0.96)	0.001
Diabetes	Type 1 (reference)	—	—
	Type 2	1.21 (1.13, 1.29)	<0.001



Logistic regression model also included smoking history and hypertension, time from DR to DME, intraretinal fluid, and subretinal fluid (not shown). CI, confidence interval; OR, odds ratio.

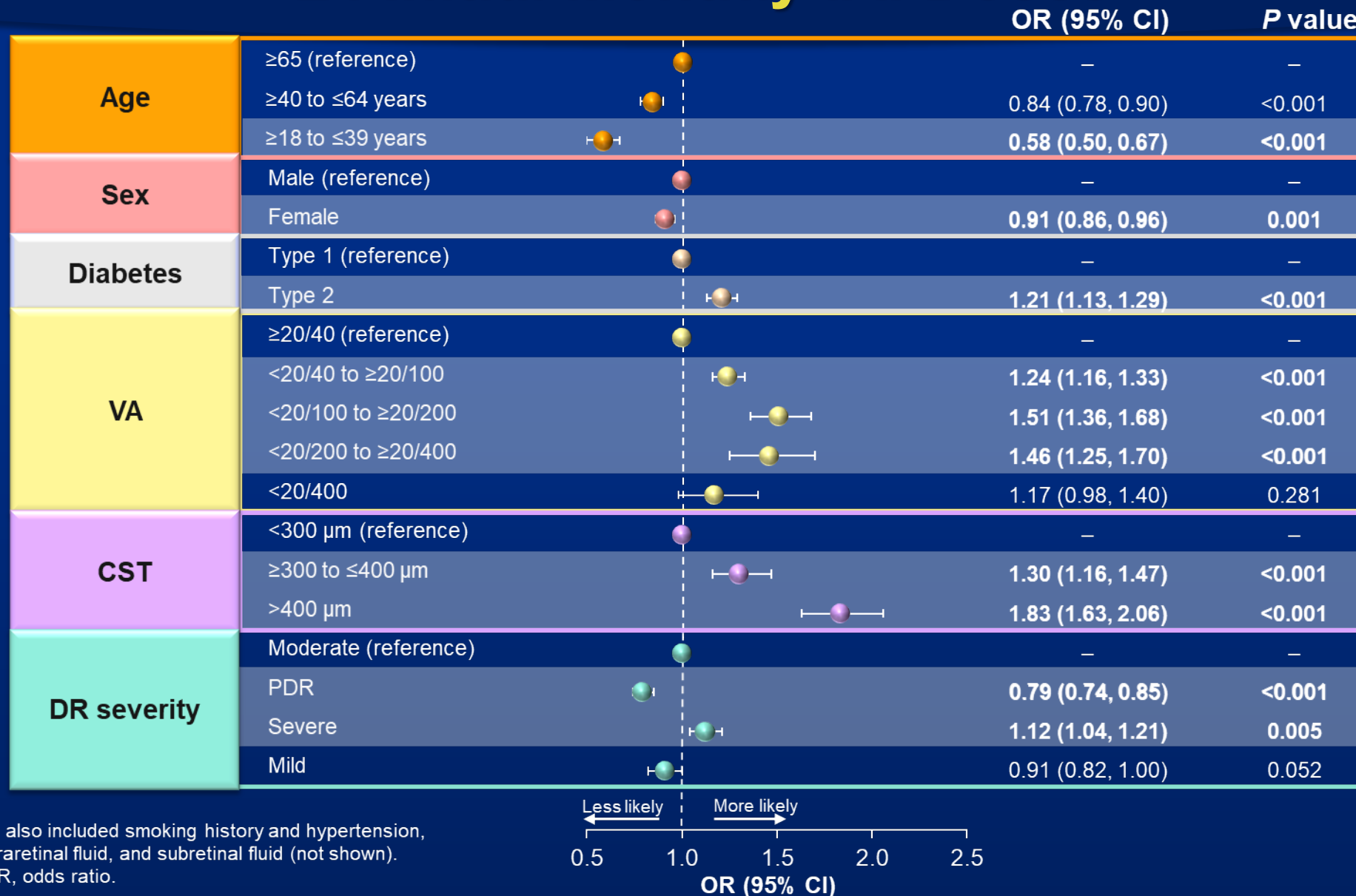
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Sex	Male (reference)	—	—
	Female	0.91 (0.86, 0.96)	0.001
Diabetes	Type 1 (reference)	—	—
	Type 2	1.21 (1.13, 1.29)	<0.001
VA	$\geq 20/40$ (reference)	—	—
	<20/40 to $\geq 20/100$	1.24 (1.16, 1.33)	<0.001
	<20/100 to $\geq 20/200$	1.51 (1.36, 1.68)	<0.001
	<20/200 to $\geq 20/400$	1.46 (1.25, 1.70)	<0.001
	<20/400	1.17 (0.98, 1.40)	0.281
CST	<300 $\mu\text{m}$ (reference)	—	—
	$\geq 300$ to $\leq 400$ $\mu\text{m}$	1.30 (1.16, 1.47)	<0.001
	>400 $\mu\text{m}$	1.83 (1.63, 2.06)	<0.001



Logistic regression model also included smoking history and hypertension, time from DR to DME, intraretinal fluid, and subretinal fluid (not shown). CI, confidence interval; OR, odds ratio.

# Baseline Factors Associated With Receiving $\geq 4$ Initial Monthly IAI Doses



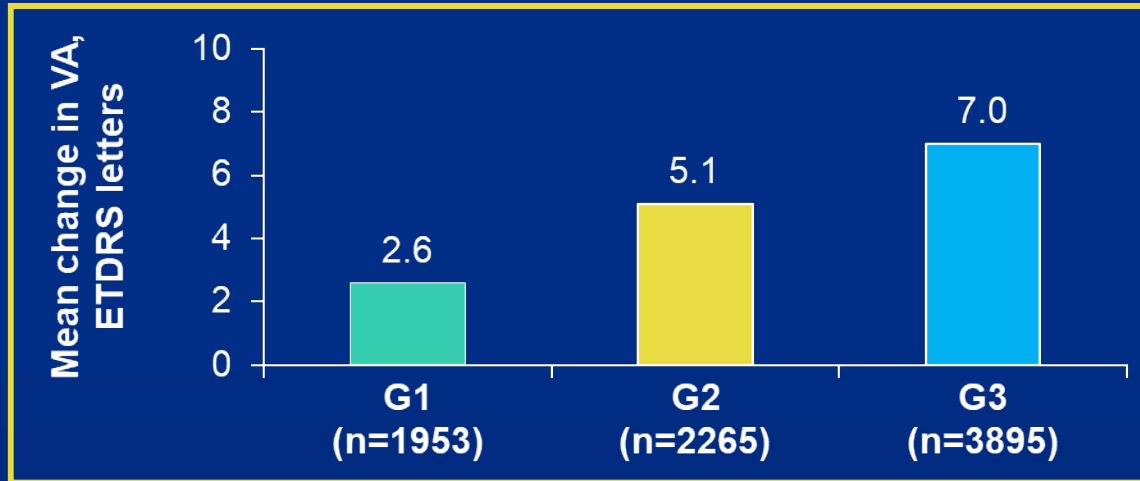
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The background is a solid dark blue color. It features several decorative white curved lines that sweep across the frame, creating a sense of motion and depth. The lines are of varying thickness and curvature, framing the central text.

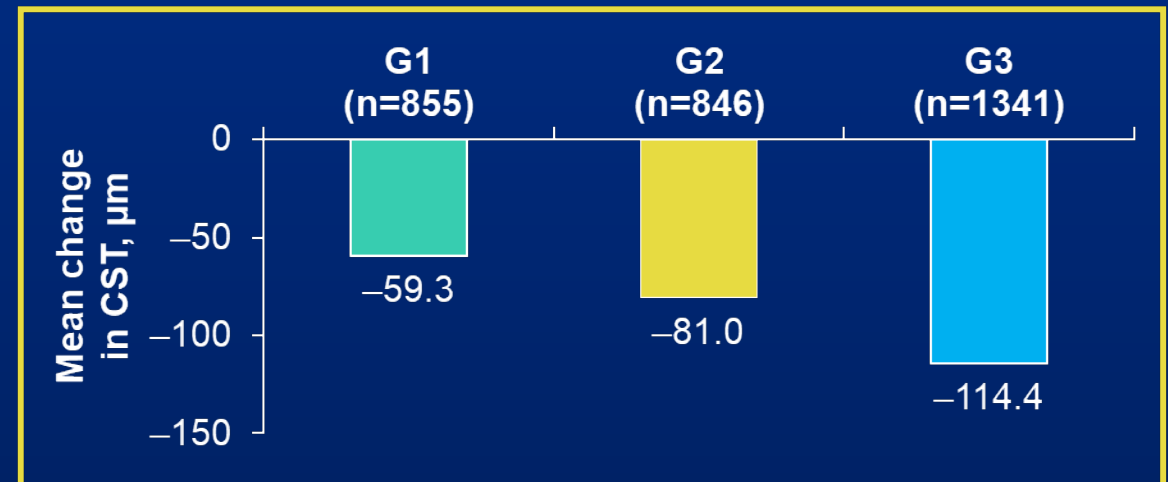
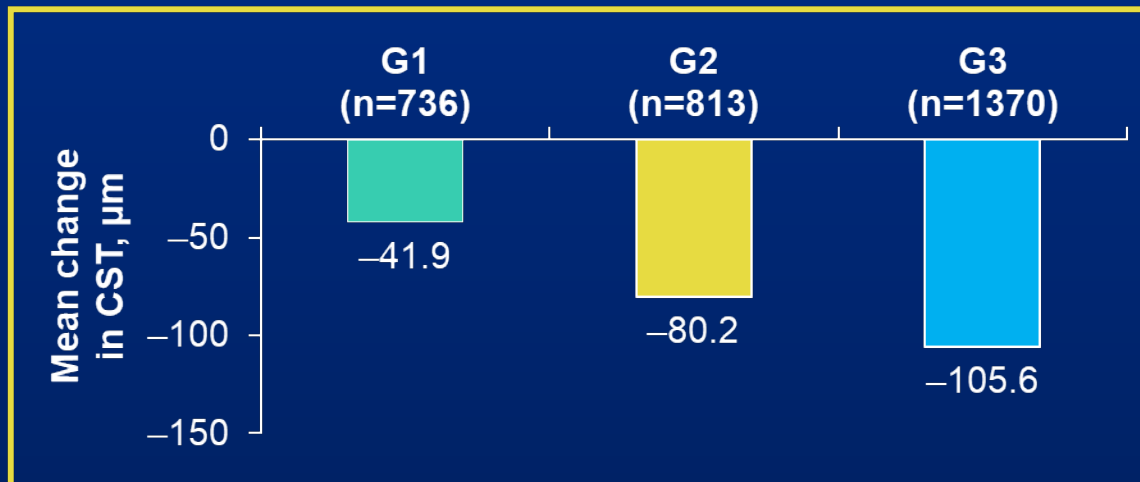
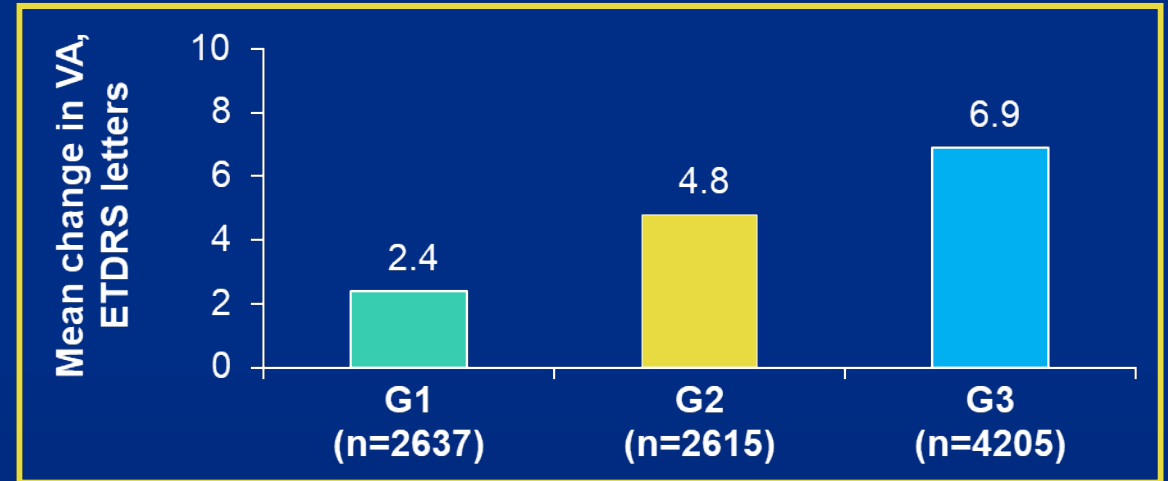
# **Visual and Anatomic Outcomes at Month 12 by Subgroups of IAI Initial Monthly Doses**

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

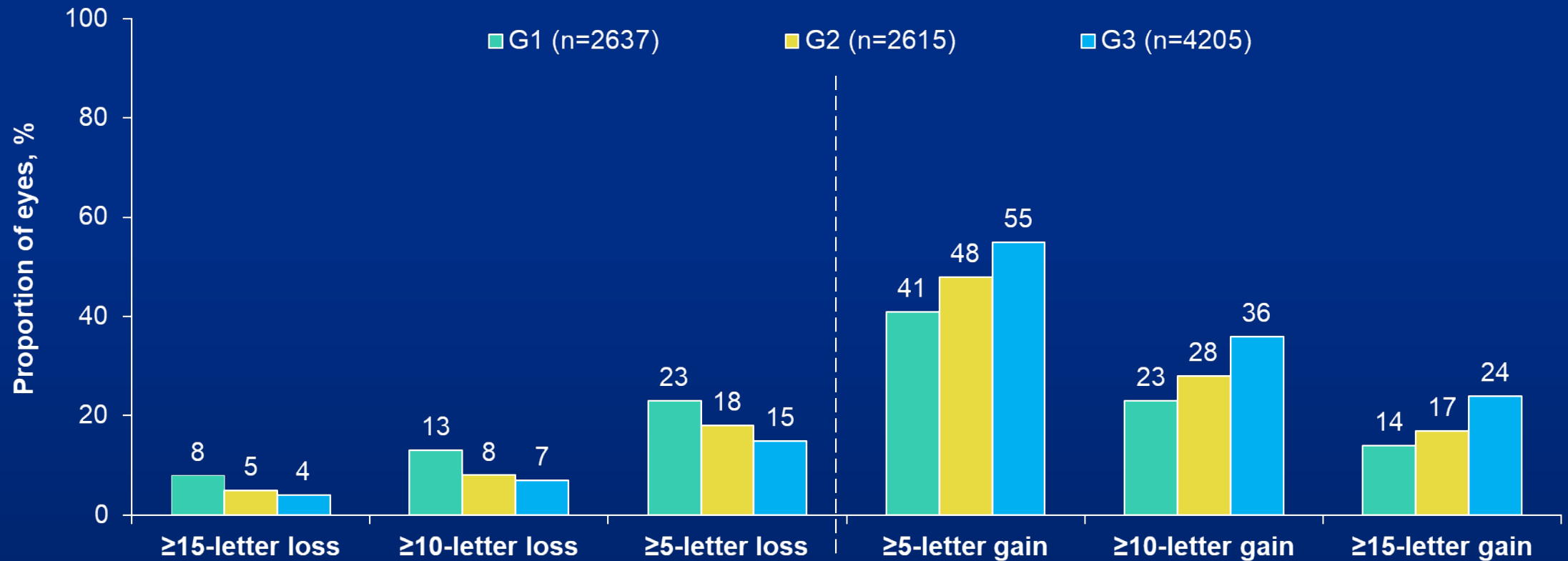
First visit post initial intensive therapy period



12 months



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



**A multivariable regression analysis confirmed that receiving  $\geq 4$  doses (vs 1-2 or 3 doses) in the initial intensive therapy period predicted  $\geq 5$ -,  $\geq 10$ -, and  $\geq 15$ -letter gain**

# Conclusions

- Patients with less initial intensive treatment had higher losses to follow-up at 12 months
- Initial intensive therapy was more commonly administered to patients with lower VA and thicker CST at baseline
- Trends towards improved vision and central subfield thickness were observed with an increasing number of IAI doses administered during the initial intensive treatment period
- Intensive initial therapy led to immediate visual and anatomic improvements, with sustained benefits evident at 1 year