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

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

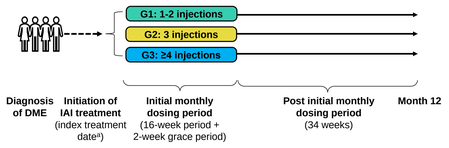
BACKGROUND & PURPOSE

- In routine clinical practice, patients receiving anti–vascular endothelial growth factor (VEGF) therapy may not receive the recommended prescribed initial monthly dosing[1,2]
- Real-world studies have demonstrated an association between the number of initial monthly anti-VEGF doses and magnitude of visual acuity (VA) improvement[1,3,4]
- Patients with diabetic macular edema (DME) receiving the label-recommended initial monthly doses of intravitreal aflibercept injection (IAI) exhibit greater visual gains than those receiving fewer than the recommended number of injections[1]
- This study evaluated the factors associated with initial monthly dosing of IAI and the impact on visual outcomes at 12 months in patients with DME

METHODS

- This retrospective analysis using the Vestrum Health database included patients aged ≥18 years, with newly diagnosed DME from January 2015 to June 2021, treated with IAI as first-line anti-VEGF therapy and with ≥18 weeks of follow-up
- Eyes that were switched to another drug during the initial monthly dosing period (16 weeks + 2-week grace period), had a history of anti-VEGF treatment before DME diagnosis, or had a diagnosis of age-related macular degeneration or retinal vein occlusion were excluded
- Of 313,192 eyes with DME identified in the Vestrum database, 23,962 were eligible for inclusion
- Eligible eyes were analyzed in subgroups based on the number of IAI doses administered during the initial monthly dosing period (Group 1 [G1]: 1-2 injections; G2: 3 injections; G3: ≥4 injections) (**Figure 1**)
- The relationships between baseline characteristics and the likelihood of receiving ≥4 initial monthly injections and of gaining ≥5, ≥10, or ≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters at 12 months were examined with logistic regression

Figure 1. Treatment Timeline



[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 central subfield thickness records.

RESULTS

- At baseline, there was a decreasing proportion of patients with proliferative diabetic retinopathy (PDR), an increasing proportion with severe and moderate non-proliferative diabetic retinopathy (NPDR), and an increasing proportion with baseline central subfield thickness (CST) across eyes in G1, G2, and G3 (**Table 1**)

Table 1. 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 (54)	5248 (57)
Comorbidities, 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)
Mean VA, ETDRS letters	(n=6108) 63.9	(n=5526) 62.9	(n=7614) 60.8
Mean CST, µm	(n=2727) **363.0**	(n=2277) **384.3**	(n=3275) **413.9**

- Compared with eyes treated with 1-2 IAI doses in the initial monthly dosing period, eyes treated with 3 or ≥4 IAI initial doses had greater VA gains and greater CST reduction from baseline at first visit post initial monthly dosing period and at 12 months (**Table 2**)

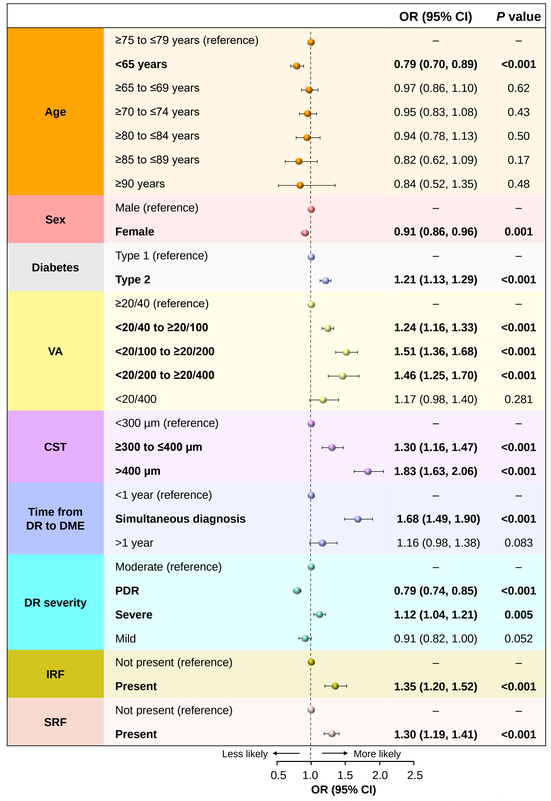
Table 2. Mean Change in VA and CST From Baseline at First Visit Post Initial Dosing and at 12 Months

	G1 (1-2 injections)	G2 (3 injections)	G3 (≥4 injections)
Mean change in VA, ETDRS letters			
First visit post initial monthly dosing period	(n=1953) 2.6	(n=2265) 5.1	(n=3895) 7.0
12 months	(n=2637) 2.4	(n=2615) 4.8	(n=4205) 6.9
Mean change in CST, µm			
First visit post initial monthly dosing period	(n=736) −41.9	(n=813) −80.2	(n=1370) −105.6
12 months	(n=855) −59.3	(n=846) −81.0	(n=1341) −114.4

Analysis included eyes with values at baseline (index treatment date) and Month 12.

- Baseline factors associated with receiving ≥4 doses during the initial monthly dosing period included VA <20/40 to ≥20/400 versus ≥20/40, CST ≥300 µm versus <300 µm, and presence of intraretinal fluid (IRF) or subretinal fluid (SRF) (**Figure 2**)

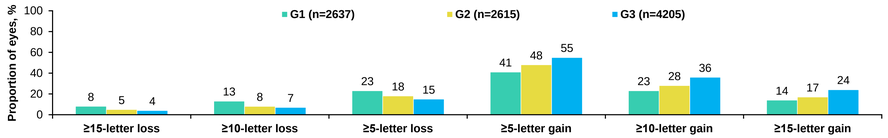
Figure 2. Baseline Factors Associated With Receiving ≥4 Initial Monthly IAI Doses



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

- A decreasing proportion of eyes across the subgroups G1, G2, and G3 lost ≥5, ≥10, and ≥15 letters, and an increasing proportion of eyes across these subgroups gained ≥5, ≥10, and ≥15 letters (**Figure 3**)

Figure 3. Proportion of Eyes With ≥5-, ≥10-, and ≥15-Letter Gain or Loss From Baseline to Month 12



- Baseline factors associated with ≥15-letter gain at 12 months included baseline VA subcategories <20/100 versus 20/40 to 20/100, number of IAI doses in the initial monthly dosing period, and number of IAI doses in the post initial monthly dosing period (**Figure 4**)

Figure 4. Factors Associated With ≥5-, ≥10-, and ≥15-Letter Gain at Month 12

		≥5-letter gain OR (95% CI)	≥10-letter gain OR (95% CI)	≥15-letter gain OR (95% CI)
VA	20/40 to 20/100 (reference)	–	–	–
	≥20/40	**0.23 (0.21, 0.25)‡**	**0.10 (0.09, 0.12)‡**	**0.04 (0.03, 0.06)‡**
	<20/100 to ≥20/200	**1.82 (1.53, 2.16)‡**	**3.11 (2.65, 3.66)‡**	**4.97 (4.24, 5.85)‡**
	<20/200 to ≥20/400	**1.91 (1.49, 2.49)‡**	**3.95 (3.09, 5.08)‡**	**7.36 (5.78, 9.41)‡**
	<20/400	**2.42 (1.80, 3.32)‡**	**5.39 (4.01, 7.34)‡**	**11.98 (8.91, 16.30)‡**
CST	<300 µm (reference)	–	–	–
	300-400 µm	1.19 (0.98, 1.44)	1.11 (0.87, 1.41)	1.00 (0.74, 1.38)
	>400 µm	**1.35 (1.11, 1.64)†**	1.09 (0.87, 1.37)	1.20 (0.90, 1.61)
IAI doses in IMDP	1-2 (reference)	–	–	–
	3	**1.16 (1.03, 1.31)***	**1.16 (1.00, 1.34)***	1.16 (0.97, 1.39)
	≥4	**1.32 (1.17, 1.49)‡**	**1.43 (1.24, 1.64)‡**	**1.49 (1.25, 1.77)‡**
Post IMDP IAI	**IAI count (0-9 injections)**	**1.08 (1.06, 1.11)‡**	**1.08 (1.05, 1.11)‡**	**1.07 (1.04, 1.10)‡**

Less likely ← → More likely
−5.0 0.0 5.0 10.0 15.0 20.0
OR (95% CI)

*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.

CONCLUSIONS

- Patients with baseline VA <20/40 to 20/400 (vs ≥20/40), type 2 diabetes, CST >300 µm, simultaneous diagnosis of DME and DR at baseline (vs <1 year from DR diagnosis), severe NPDR (vs moderate NPDR), IRF, or SRF were more likely to receive ≥4 injections during the initial monthly dosing period
- Patients receiving ≥4 initial monthly doses of IAI experienced substantially improved VA and anatomic benefits
- Among other factors, eyes receiving ≥4 versus 1-2 initial monthly doses were more likely to gain ≥5, ≥10, and ≥15 letters at 12 months, suggesting more frequent IAI treatment during the initial monthly dosing period may be beneficial

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