Real-world Use of Aflibercept 8 mg in Eyes With Diabetic Macular Edema: Analysis of the IRIS® Registry

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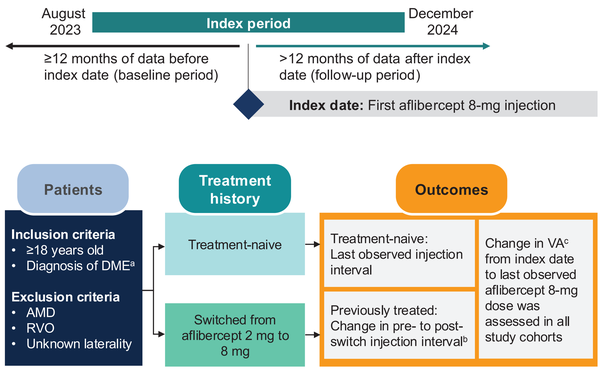
BACKGROUND & PURPOSE

- Diabetic macular edema (DME) is a leading cause of vision impairment, and can have profound effects on patients' quality of life[1]
- Although anti–vascular endothelial growth factor (VEGF) therapies can allow for effective management of DME, patients may require frequent intravitreal injections and close monitoring, which can pose a substantive burden[2]
- The pivotal PHOTON trial showed that visual and anatomic improvements following aflibercept 8 mg were comparable to those observed with aflibercept 2 mg, with fewer injections over 96 weeks[3,4]
- However, compliance with prescribed treatment including initial monthly dosing in a real-world setting may not mirror those observed in controlled studies and may affect clinical outcomes
- This analysis of the American Academy of Ophthalmology IRIS® (Intelligent Research in Sight) Registry[5] evaluated treatment patterns and visual acuity (VA) outcomes in patients with DME initiating aflibercept 8 mg, in separate cohorts of treatment-naive patients and in patients previously treated with aflibercept 2 mg

METHODS

- The study population included patients aged ≥18 years old with a diagnosis of DME receiving >1 aflibercept 8-mg injection between August 2023 and December 2024 (defined as the index period)
- Eligible eyes received aflibercept 8 mg for ≥12 months with the last aflibercept 8-mg injection >364 days post index
- This analysis included treatment-naive eyes (ie, no prior anti–VEGF treatment, or intravitreal steroid, photodynamic or laser therapy during the baseline period) and eyes previously treated with aflibercept 2 mg in the 16 weeks prior to the index date, with a last pre-switch injection interval >6 weeks
- Treatment intervals and VA outcomes were reported in the overall study population and a subset of eyes that completed the initial monthly dosing schedule (3 doses with 28 ± 7 days intervals)[6]
- All statistical analyses were descriptive. Outcome distributions were displayed using box-and-whisker plots

Figure 1. Study Design



[a]If both eyes met the eligibility criteria, one eye was randomly selected for analysis.
[b]Also stratified by last pre-switch injection interval of 6 to ≤8 weeks, >8 to ≤10 weeks, >10 to ≤12 weeks, and >12 to ≤16 weeks.
[c]Also stratified by baseline VA category of ≤65 versus >65 ETDRS letters.
AMD, age-related macular degeneration; ETDRS, Early Treatment Diabetic Retinopathy Study; RVO, retinal vein occlusion.

RESULTS

Baseline Demographics, Clinical Characteristics, and Follow-up

- Baseline characteristics and follow-up were generally similar in the overall cohort of eyes and eyes receiving initial monthly dosing (**Table 1**)

Table 1. Demographic and Clinical Characteristics at the Index Date and Follow-up Information

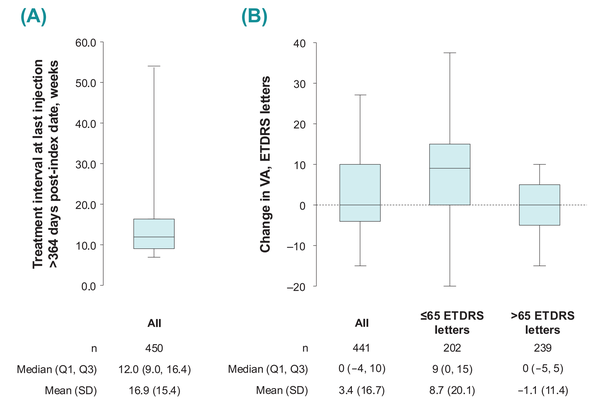
	Overall cohort		Cohort receiving initial monthly dosing	
	Treatment-naive (n=450)	Previously treated with aflibercept 2 mg (n=2744)	Treatment-naive (n=103)	Previously treated with aflibercept 2 mg (n=74)
Age, years, mean (SD)	68.3 (9.9)	66.8 (10.7)	68.2 (9.9)	67.1 (9.7)
Age category, years, n (%)				
18-34	2 (0.4)	29 (1.1)	1 (1.0)	1 (1.4)
35-44	7 (1.6)	69 (2.5)	2 (1.9)	1 (1.4)
45-54	38 (8.4)	247 (9.0)	8 (7.8)	4 (5.4)
55-64	73 (16.2)	642 (23.4)	17 (16.5)	18 (24.3)
>65	330 (73.3)	1757 (64.0)	75 (72.8)	50 (67.6)
Male, n (%)	257 (57.1)	1482 (54.0)	63 (61.2)	43 (58.1)
Race/Ethnicity, n (%)[a]				
White	250 (66.1)	1662 (68.6)	59 (67.8)	45 (71.4)
Black or African American	45 (11.9)	253 (10.5)	11 (12.6)	11 (17.5)
Other[b]	54 (14.3)	348 (14.4)	12 (13.8)	4 (6.3)
Hispanic or Latino	29 (7.7)	158 (6.5)	5 (5.7)	3 (4.8)
Diabetes, n (%)				
Type 1	29 (6.4)	261 (9.5)	8 (7.8)	7 (9.5)
Type 2	421 (93.6)	2483 (90.5)	95 (92.2)	67 (90.5)
Bilateral DME, n (%)	415 (92.2)	2500 (91.1)	92 (89.3)	68 (91.9)
Functional VA[c] category on index date, n (%)				
≤65 ETDRS letters	207 (46.0)	919 (33.5)	46 (44.7)	42 (56.8)
>65 ETDRS letters	241 (53.6)	1819 (66.3)	57 (55.3)	31 (41.9)
Follow-up				
Post-index follow-up, median (Q1, Q3), days	505 (441, 596)	527 (450, 617)	512 (464, 579)	545 (456, 603)
Number of injections during follow-up,[d] mean (SD)	7.6 (2.7)	7.8 (2.3)	9.3 (1.9)	10.2 (2.2)

[a]Patients with missing values were excluded when calculating percentages.
[b]Other includes Asian, Pacific Islander, or Other.
[c]Assessed as ETDRS letters.
[d]Number of aflibercept 8-mg injections inclusive of index date.
Q, quartile; SD, standard deviation.

Last Observed Injection Interval and VA Outcomes With Aflibercept 8 mg in the Overall Treatment-naive Cohort

- The median duration of the last treatment interval >364 days after the index date was 12.0 weeks in the overall treatment-naive cohort (**Figure 2A**)
- No change in VA from index date to last injection was observed in the overall treatment-naive cohort. However, VA change was numerically greater for eyes with VA ≤65 ETDRS letters at baseline (**Figure 2B**)

Figure 2. (A) Last Injection Interval at >364 Days Post-index Date and (B) Change in VA From Index to Last Injection in the Overall Treatment-naive Cohort

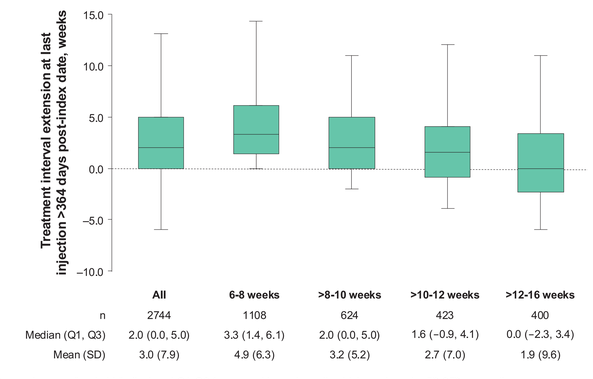


Boxes show median (middle line) and Q1-Q3 (upper and lower bound); whiskers show the 5th-95th percentiles.

Last Observed Injection Interval and VA Outcomes With Aflibercept 8 mg in the Overall Previously Treated Cohort

- The median (Q1, Q3) duration of the last treatment interval in eyes switched from aflibercept 2 mg to 8 mg was 12 (9, 15) weeks, representing an extension of 2.0 weeks versus the last observed pre-switch interval in this cohort (**Figure 3**)
- Treatment intervals varied by last observed pre-switch injection interval category

Figure 3. Injection Interval Extension With Aflibercept 8 mg at >364 Days Post-index Date in the Overall Previously Treated Cohort



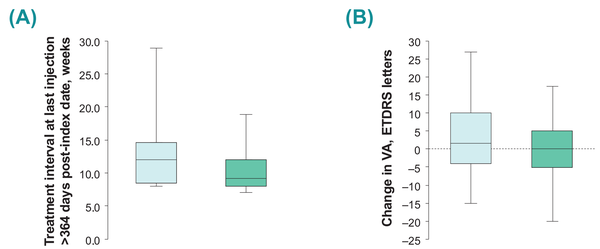
Boxes show median (middle line) and Q1-Q3 (upper and lower bound); whiskers show the 5th-95th percentiles.

- The median (Q1, Q3) change in VA from index date to last injection was 0 (–5, 5) letters in the overall cohort switched from aflibercept 2 mg to 8 mg, and 0 (–4, 9) and 0 (–5, 0) letters in VA subgroups with ≤65 and >65 ETDRS letters, respectively

Last Observed Injection Interval With Aflibercept 8 mg and VA Outcomes in Eyes Who Received Initial Monthly Dosing

- The median durations of the last observed treatment intervals >364 days post-index date were 12 and 9 weeks, respectively, for treatment-naive and previously treated eyes who received initial monthly dosing (**Figure 4A**)
- VA outcomes were stable over the study period, although a trend toward improved VA was observed in eyes with ≤65 ETDRS letters at baseline (**Figure 4B**)

Figure 4. (A) Injection Interval at >364 Days Post-index Date and (B) Change in VA From Index to Last Aflibercept 8-mg Dose in Cohorts Who Received Initial Monthly Dosing



Boxes show median (middle line) and Q1-Q3 (upper and lower bound); whiskers show the 5th-95th percentiles.

Key Limitations

- Electronic medical records may not have captured patients' complete medical history
- Best-corrected VA data were not consistently available

CONCLUSIONS

- The median last observed aflibercept 8-mg injection interval >364 days post index date in the overall cohort of treatment-naive and previously treated eyes was 12.0 weeks, with VA maintained overall
- Treatment-naive eyes with lower baseline VA (≤65 ETDRS letters) showed the greatest visual improvement
- Treatment interval and VA outcomes following initiation of aflibercept 8 mg were generally similar between the overall cohorts and the cohorts who completed the initial monthly dosing schedule

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