Rates of Intraocular Inflammation Following Intravitreal Aflibercept Prefilled Syringe and Vial Injections in US Clinical Practice, 2014–2022

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Disclosures: AM, JA, SG, HM, and RES are employees and shareholders of Regeneron Pharmaceuticals, Inc. RES is also a shareholder of Pfizer, Inc. DB serves as a scientific advisor for Regeneron/Bayer and Genentech/Roche and as a member of the Regeneron Combination Products Steering Committee. KSW is an employee and shareholder of Bayer AG. NB and NA are employees of Vestrum Health.

BACKGROUND

- Intraocular inflammation (IOI) is an infrequent complication of intravitreal anti-vascular endothelial growth factor (VEGF) injections that may be associated with substantial visual impairment[1,2]
- Prefilled syringes (PFS) provide ease of injection and require fewer preparation steps than vials,[3,4] and several studies and analyses of spontaneous reports suggest that incidences of IOI and endophthalmitis following intravitreal anti-VEGF injection may be lower with PFS compared with vials[5-9]

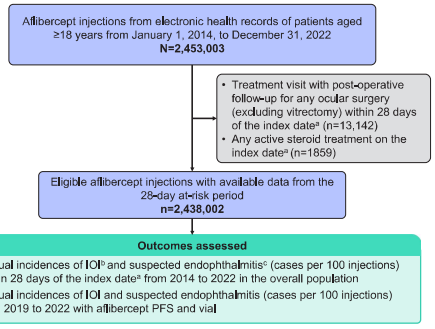
OBJECTIVE

- To evaluate incidences of IOI and suspected endophthalmitis following intravitreal aflibercept 2 mg injections administered from PFS and vials in US clinical practice

METHODS

- This observational cohort study was conducted using electronic health record data from the Vestrum Health Retina Treatment and Outcomes database, which contains data from patients in retina practices across the United States[10]
- Data from patients aged ≥18 years who received ≥1 aflibercept injection between January 1, 2014, and December 31, 2022, were analyzed (**Figure 1**)
- IOI cases in the same eye as the aflibercept injection within 28 days of the index date (date of aflibercept injection) were assessed
  - Patients had multiple treatment episodes if they received multiple injections in one or both eyes, including bilateral injections
- Annual incidences of IOI events, including a subset of suspected endophthalmitis events, were calculated as cases per 100 injections administered overall and by dispensing device
  - Corresponding 95% CIs were estimated using generalized estimating equations

Figure 1. Study Design



[a]Date of aflibercept injection.
[b]IOI events were identified using ICD-9 or ICD-10 diagnosis codes that included but were not limited to ophthalmia nodosa, iridocyclitis, cyclitis, panuveitis, pars planitis, sympathetic uveitis, vitreous abscess, vitreous disorders, and endophthalmitis.
[c]Suspected endophthalmitis cases included infectious and non-infectious endophthalmitis and were identified using ICD-9 or ICD-10 diagnosis codes that were based on published literature and ophthalmologist review.
ICD, International Classification of Diseases.

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RESULTS

- Overall, 2,438,002 aflibercept injections were administered to 168,572 unique patients from 2014 to 2022 (**Table 1**)
  - More than 75% of patients received aflibercept injections for the treatment of neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME), and 60.4% of patients had ≥12 months of follow-up
  - Each patient received a mean of 13.8 aflibercept injections during the study period, and the mean duration of treatment was 20.3 months

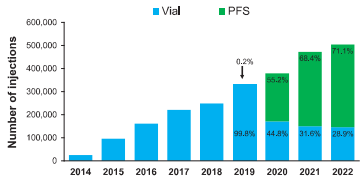
Table 1. Characteristics of Patients Receiving Aflibercept Injections From 2014–2022

	Patients[a] (N=168,572)
Female, n (%)	91,136 (54.1)
Age, mean (SD), years	71.6 (13.3)
Indications, n (%)	
nAMD	79,845 (47.4)
DME	48,505 (28.8)
RVO	26,480 (15.7)
Other	8881 (5.3)
DR	4861 (2.9)
Follow-up time, n (%)	
<12 months	66,697 (39.6)
12+ months	101,875 (60.4)
24+ months	70,987 (42.1)
36+ months	49,413 (29.3)
48+ months	32,528 (19.3)
60+ months	21,211 (12.6)
Aflibercept injections per patient, mean (SD)	13.8 (16.3)
Duration of treatment[b], mean (SD), months	20.3 (22.0)

[a]Patients identified from the Vestrum database received a total of 2,438,002 aflibercept injections.
[b]Time between first and last aflibercept injection irrespective of any ophthalmic treatments that occurred between both treatments.
DR, diabetic retinopathy; RVO, retinal vein occlusion; SD, standard deviation.

- The number of administered aflibercept injections increased over time, from approximately 25,000 injections in 2014 to approximately 500,000 injections in 2022 (**Figure 2**)
  - PFS use steadily increased since December 2019, with the majority of aflibercept injections administered from PFS compared with vials between 2020 and 2022

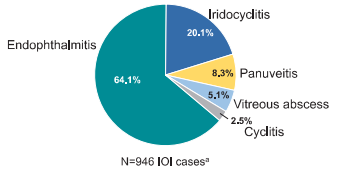
Figure 2. Number of Administered Aflibercept Injections From Aflibercept PFS[a] and Vial, 2014–2022



[a]Aflibercept PFS were introduced in December 2019.

- Of the 946 IOI cases that were identified during the study period, 64.1% were coded as endophthalmitis (**Figure 3**)

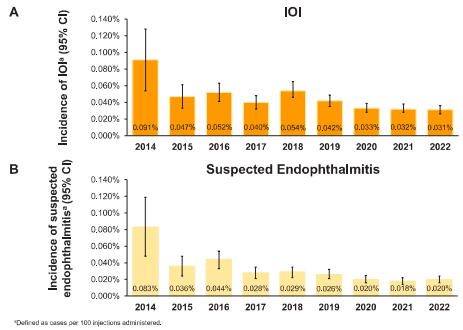
Figure 3. IOI Cases From 2014–2022



[a]Patients identified from the Vestrum database received a total of 2,438,002 aflibercept injections.

- The overall incidence of IOI and suspected endophthalmitis following aflibercept injection decreased from 2014 to 2022 (**Figure 4**)

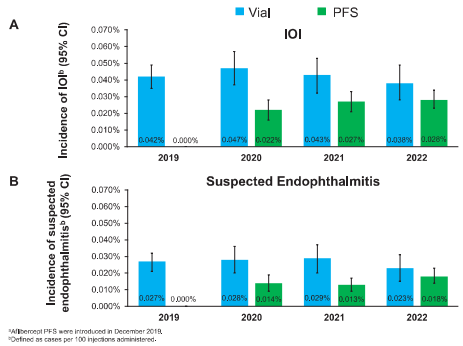
Figure 4. Annual Incidence of (A) IOI and (B) Suspected Endophthalmitis Following Aflibercept Injection From 2014–2022



[a]Defined as cases per 100 injections administered.

- The annual incidence of IOI and suspected endophthalmitis following aflibercept injection was lower with PFS compared with vials (**Figure 5**)
  - PFS was associated with a lower incidence of IOI and suspected endophthalmitis than vials in 2020 and 2021
  - However, there was no conclusive difference in the incidence of IOI and suspected endophthalmitis with PFS and vials in 2022

Figure 5. Annual Incidence of (A) IOI and (B) Suspected Endophthalmitis With Aflibercept PFS[a] and Vial From 2019–2022



[a]Aflibercept PFS were introduced in December 2019.
[b]Defined as cases per 100 injections administered.

LIMITATIONS

- Distinguishing between culture-positive and sterile endophthalmitis was not possible based on available data
- Factors such as physician behaviors and injection techniques, which may explain underlying differences in the incidences of IOI and suspected endophthalmitis between aflibercept PFS and vials, could not be assessed in this study

CONCLUSIONS

- Overall incidences of IOI and suspected endophthalmitis following intravitreal aflibercept injection decreased from 2014 to 2022
- Incidences of IOI and suspected endophthalmitis were lower with PFS than with vials in 2020 and 2021, with no conclusive difference in 2022
- Further studies are warranted to identify factors that may be associated with observed trends in the incidences of IOI with aflibercept PFS and vials

Poster presented by Angelika Manthripragada, PhD, MPH, email: angelika.manthri@regeneron.com, at the ICPE 2023 Meeting, August 23-27, 2023