Inflammation in Patients Receiving Aflibercept, Bevacizumab, or Ranibizumab: Analysis of 936,926 Intravitreal Injections

Szilárd Kiss,[1] Pravin U. Dugel,[2] Eunice Chang,[3] Michael S. Broder,[3] Adam Turpcu[4]

[1]Department of Ophthalmology, Weill Cornell Medical College, New York, NY; [2]Retinal Consultants of Arizona, Phoenix, Arizona and Department of Ophthalmology and Keck School of Medicine. University of Southern California, Los Angeles, California; [3]Partnership for Health Analytic Research, LLC, Beverly Hills, CA; [4]Genentech Inc., South San Francisco, CA

Disclosures: **SK:** Consultant: Allergan, Alimera, Alcon, Genentech, Regeneron, and Optos; Research funding: Allergan, Alimera, Genentech, Regeneron, and Optos; **PUD:** Consultant: Genentech, Novartis and Regeneron; **EC, MSB:** Employees of Partnership for Health Analytic Research, LLC, and consultants for Genentech. **AT:** Employee of Genentech.

Support for third-party writing assistance was furnished by Rebecca Jarvis, PhD, CMPP, and Grace H. Lee, PharmD, of Envision Scientific Solutions, and provided by Genentech, Inc.

Objective and Methods

- Objective:
  - To examine inflammation in clinical practice following intravitreal injection of aflibercept, bevacizumab, or ranibizumab in patients with neovascular age-related macular degeneration (nAMD) or central retinal vein occlusion (RVO)

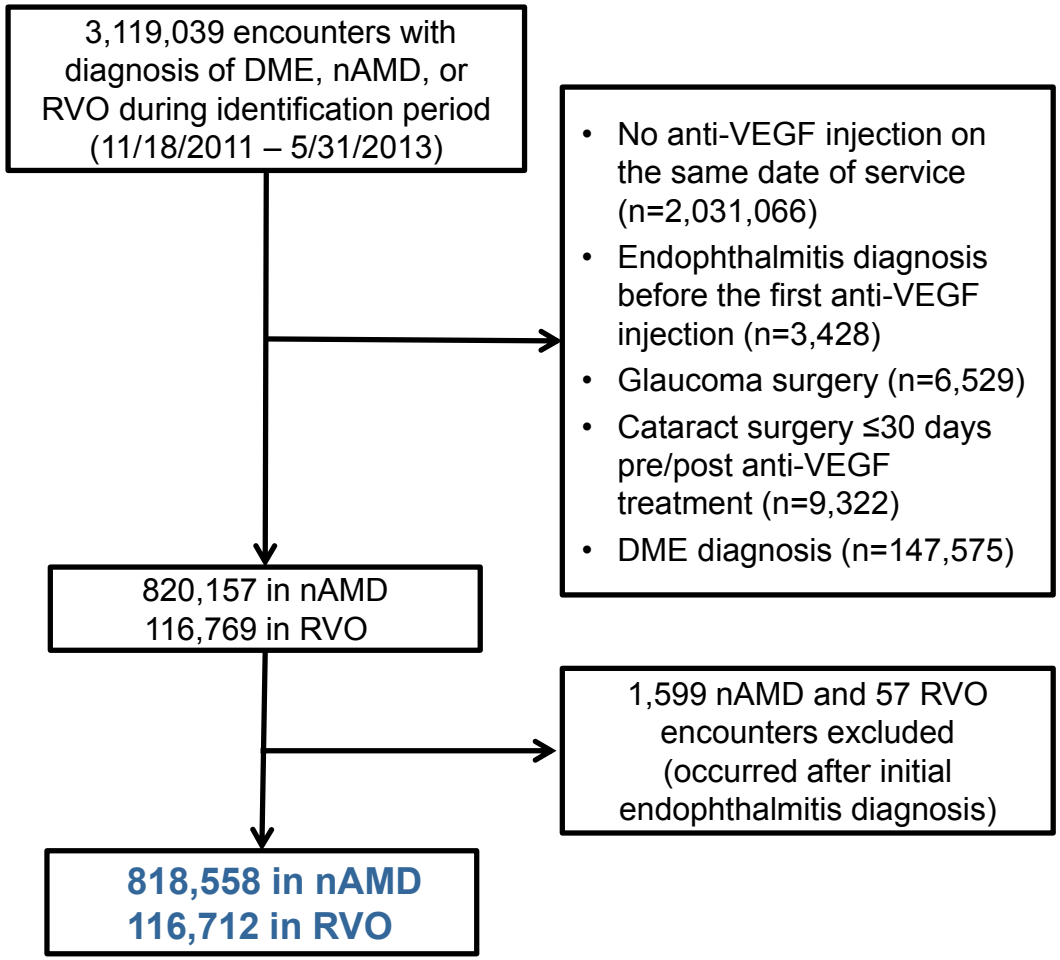
- Comparisons are made between:
  - Ranibizumab injection (Lucentis®)
  - Aflibercept injection (Eylea®)
  - Bevacizumab injection (Avastin®)
- Outcomes:
  - Risk of endophthalmitis stratified by anti-VEGF use for nAMD or RVO

- Study period:
  - November 18, 2011–June 30, 2013
- Database:
  - Wolters Kluwer Health's Source® Lx database (HIPAA-compliant administrative claims database)

HIPAA = Health Insurance Portability and Accountability Act.

Inclusion Criteria and Patient Identification

- This claim analysis included encounters with a
  - Diagnosis of nAMD[a] or RVO[b] during the identification period (11/18/11–5/31/2013)
    AND
  - A claim[c] for intravitreal anti-VEGF injection[d] on the same date of the selected diagnosis
- Date of encounter = date of anti-VEGF injection
- Each encounter was followed for 30 days[e] for claims for endophthalmitis[f] (surrogate marker for inflammation)

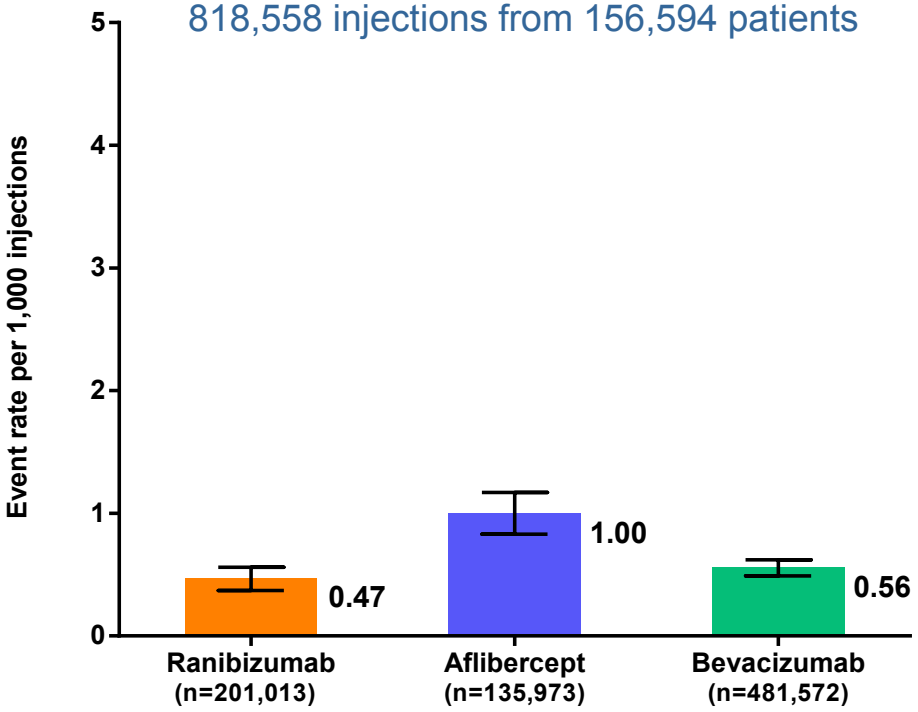


[a]ICD-9-CM 362.52; [b]ICD-9-CM 362.35; [c]Current Procedural Terminology code 67028; [d]HCPCS codes: Ranibizumab: 11/18/2011–Present, J2778. Bevacizumab: 1) 11/18/2011–Present, J3490 or J3590; payment: $1–500. 2) 11/18/2011–Present, J9035. 3) 11/18/2011–Present, C9257. Aflibercept: 1) 11/18/2011–Present, J3490 or J3590; payment: $1,500+ 2) 04/01/2012– 06/30/2012, C9291. 3) 07/01/2012–12/31/2012, Q2046. 4) 01/01/2013–Present, J0178; [e]Fintak DR, et al. *Retina*. 2008 Nov-Dec;28(10):1395-9. [f]ICD-9-CM codes 360.0x and 360.19

Risk of Endophthalmitis Stratified by Anti-VEGF Therapy and Indication

nAMD

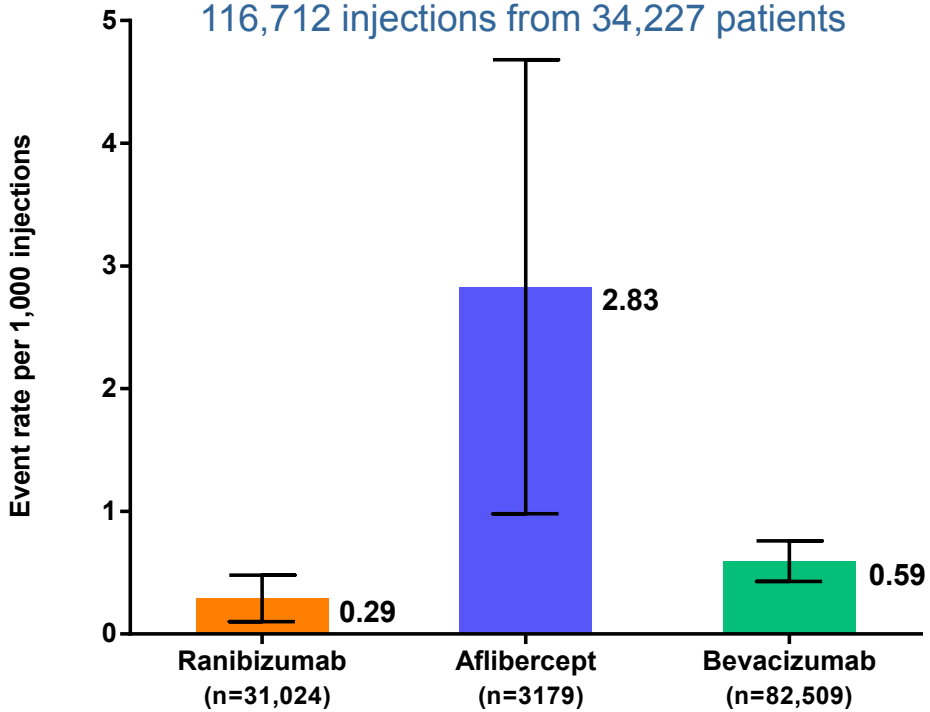
818,558 injections from 156,594 patients



Repeated Measures Analysis for Risk of Endophthalmitis	Adjusted Odds Ratio (95% CI)	*P* value
Aflibercept vs. Ranibizumab	2.19 (1.68-2.85)	*P* < 0.0001
Bevacizumab vs. Ranibizumab	1.17 (0.93-1.49)	*P* = 0.18

RVO

116,712 injections from 34,227 patients



Repeated Measures Analysis for Risk of Endophthalmitis	Adjusted Odds Ratio (95% CI)	*P* value
Aflibercept vs. Ranibizumab	9.59 (3.82-24.02)	*P* < 0.0001
Bevacizumab vs. Ranibizumab	2.13 (1.04-4.37)	*P* = 0.04

Repeated measures analysis was adjusted for age, gender, region, number of chronic conditions, Charlson comorbidity index, diabetes mellitus, cataract, glaucoma, and first injection (vs. subsequent injection). Bars above and within each column represent the upper and lower limits of the 95% confidence intervals.

Conclusions

- This claims database analysis was conducted to evaluate real-world experiences of inflammation following intravitreal anti-VEGF injections in patients with nAMD or RVO
- In nAMD and RVO patients, rates of inflammation were higher following intravitreal injection with aflibercept compared with both ranibizumab and bevacizumab
  - In nAMD patients, the difference between ranibizumab and bevacizumab was not statistically significant
  - In RVO patients, rates of inflammation were higher for bevacizumab compared with ranibizumab ($P = 0.04$)