Long-term Treatment Patterns and Vision With Intravitreal Anti-VEGF in Patients With nAMD Analysis of the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight)

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Disclosures

Financial Disclosures


- VG, EN: Employee, Salary: Genentech, Inc.
- HBF, AL: Employee, Salary: Verana Health
- TL: Consultant: Astellas, Boehringer Ingelheim, Genentech, Inc., Kanaph, Nanoscope, Regeneron, Verana Health; Grants: Kodiak, Targeted Therapy Technologies

Study Disclosures

- This study includes research conducted on human subjects
- Study exempt from Institutional Review Board approval due to deidentified data
- Funding was provided by Genentech, Inc., a member of the Roche Group, for the study and third-party writing assistance, which was provided by Nibedita Gupta, PhD, of Envision Pharma Group
Patient eyes were required to have a minimum of 2 years of contribution to the IRIS Registry after their index date (defined as the date of the first documented anti-VEGF injection). However, visual acuity measurements were only required at baseline, so some patient eyes may not have visual acuity measurements during follow-up.

To show demographic characteristics at the patient level, 1 eye was selected among patients with 2 eyes enrolled in this study. If eyes were enrolled on the same day, the worse eye was selected. If eyes were enrolled on different days, the first eye enrolled was selected.

Purpose, Methods, and Demographic Characteristics

**Purpose**
- To date, real-world treatment patterns and outcomes in patients with nAMD have relatively limited follow-up and are not generalizable to the population in the United States.
- The purpose of this study was to evaluate 6-year outcomes among patients with nAMD receiving intravitreal anti-VEGF therapy using the IRIS® Registry database, the largest specialty clinical data registry.

**Methods**
- This was a retrospective, noncomparative, nonrandomized cohort study.
- Patients aged ≥ 50 years with nAMD treated with intravitreal anti-VEGF injections between July 1, 2013 and June 30, 2018 were included. In addition, patients were required to have:
  - ≥ 2-year follow-up (up to 6 years) in the IRIS Registry
  - 3 doses of anti-VEGF injection within 180 days of beginning treatment
  - Available baseline visual acuity data

**Demographic Characteristic**

<table>
<thead>
<tr>
<th>Demographic Characteristic</th>
<th>Patientsb (N = 147,888)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>79.55 (8.74)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>92,407 (62.48%)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>132,505 (89.60%)</td>
</tr>
<tr>
<td>Black</td>
<td>1667 (1.13%)</td>
</tr>
<tr>
<td>Other</td>
<td>13,716 (9.27%)</td>
</tr>
<tr>
<td>Insurance payer, n (%)</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>67,267 (45.49%)</td>
</tr>
<tr>
<td>Medicare Advantage</td>
<td>46,423 (31.39%)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1620 (1.10%)</td>
</tr>
<tr>
<td>Commercial</td>
<td>23,749 (16.06%)</td>
</tr>
<tr>
<td>Other</td>
<td>8829 (5.97%)</td>
</tr>
<tr>
<td>Provider specialty, n (%)</td>
<td></td>
</tr>
<tr>
<td>Retina specialist</td>
<td>121,205 (81.96%)</td>
</tr>
<tr>
<td>Other</td>
<td>26,683 (18.05%)</td>
</tr>
</tbody>
</table>

The mean (SD) length of follow-up was 3.68 (1.28) years

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a Patient eyes were required to have a minimum of 2 years of contribution to the IRIS Registry after their index date (defined as the date of the first documented anti-VEGF injection). However, visual acuity measurements were only required at baseline, so some patient eyes may not have visual acuity measurements during follow-up.

b To show demographic characteristics at the patient level, 1 eye was selected among patients with 2 eyes enrolled in this study. If eyes were enrolled on the same day, the worse eye was selected. If eyes were enrolled on different days, the first eye enrolled was selected.

IRIS, Intelligent Research in Sight; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.
Although Vision Declined After 1 Year, Longer Total Follow-up Time Positively Correlated With Better Baseline and Follow-up Visual Acuity

Visual Acuity at BL and Over the Follow-up Years

Change in Visual Acuity From BL and Year 1

* The number of patients eyes included in each follow-up year were not mutually exclusive; i.e., patient eyes with 6 years of follow-up were included in all previous follow-up years.

Patient eyes must have had consecutive visual acuity measurements.

BL, baseline; ETDRS, Early Treatment Diabetic Retinopathy Study.
Mean Injection Frequency Decreased Over Time and Then Reached a Plateau Around Year 3

**Number of Anti-VEGF Injections**

- Year 1: 7.2
- Year 2: 5.6
- Year 3: 4.6
- Year 4: 4.5
- Year 5: 4.6
- Year 6: 4.2

**Weeks Between Anti-VEGF Injections**

- Year 1: 7.1
- Year 2: 11.5
- Year 3: 13.1
- Year 4: 14.3
- Year 5: 15.0
- Year 6: 14.6

VEGF, vascular endothelial growth factor.
In Years 3–6, the Most Common Injection Frequency in Patient Eyes Was 1–3 Injections Per Year

Percentage of Patient Eyes by Anti-VEGF Injection Frequency Category

<table>
<thead>
<tr>
<th>Follow-up Years</th>
<th>1–3 injections</th>
<th>4–6 injections</th>
<th>7–9 injections</th>
<th>10–13 injections</th>
<th>&gt; 13 injections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>30.1</td>
<td>8.1</td>
<td>43.2</td>
<td>18.6</td>
<td>0.1</td>
</tr>
<tr>
<td>Year 2</td>
<td>22.7</td>
<td>24.9</td>
<td>43.4</td>
<td>9.0</td>
<td>0.04</td>
</tr>
<tr>
<td>Year 3</td>
<td>39.1</td>
<td>17.4</td>
<td>37.6</td>
<td>5.9</td>
<td>0.04</td>
</tr>
<tr>
<td>Year 4</td>
<td>40.9</td>
<td>16.5</td>
<td>36.8</td>
<td>5.8</td>
<td>0.04</td>
</tr>
<tr>
<td>Year 5</td>
<td>39.6</td>
<td>16.9</td>
<td>37.3</td>
<td>6.1</td>
<td>0.05</td>
</tr>
<tr>
<td>Year 6</td>
<td>46.3</td>
<td>14.4</td>
<td>34.7</td>
<td>4.6</td>
<td>0.06</td>
</tr>
</tbody>
</table>

VEGF, vascular endothelial growth factor.
Nearly 40% of Patient Eyes Discontinued Treatment, With Mean Time to Discontinuation of 89 Weeks

Of 160,423 eyes, treatment discontinuation was observed in 38.8% (n = 62,188) of eyes. Treatment discontinuation occurred 89 weeks (1.7 years) after starting treatment.

- Treatment gap was defined as a time period of 18 weeks to 1 year without an anti-VEGF injection.
- Treatment discontinuation was defined as > 1 year of contribution to the IRIS Registry without an anti-VEGF injection.
Most Patients Were at Risk of Severe Vision Loss of \( \geq 10 \) Letters

### Kaplan-Meier Curve

**Patients Without an Event**

<table>
<thead>
<tr>
<th>Follow-up Years</th>
<th>BL</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
<th>Year 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number at Risk, n (%)</td>
<td>Better than or equal to 20/20</td>
<td>6054 (100)</td>
<td>3680 (61)</td>
<td>2836 (47)</td>
<td>1348 (22)</td>
<td>616 (10)</td>
<td>289 (5)</td>
</tr>
<tr>
<td></td>
<td>Worse than 20/20–20/40</td>
<td>51,854 (100)</td>
<td>31,833 (61)</td>
<td>24,109 (46)</td>
<td>11,759 (23)</td>
<td>5494 (11)</td>
<td>2437 (5)</td>
</tr>
<tr>
<td></td>
<td>Worse than 20/40–20/80</td>
<td>53,516 (100)</td>
<td>36,666 (69)</td>
<td>29,568 (55)</td>
<td>15,084 (28)</td>
<td>7508 (14)</td>
<td>3438 (6)</td>
</tr>
<tr>
<td></td>
<td>Worse than 20/80–20/160</td>
<td>15,975 (100)</td>
<td>9349 (59)</td>
<td>7524 (47)</td>
<td>3855 (24)</td>
<td>1912 (12)</td>
<td>893 (6)</td>
</tr>
<tr>
<td></td>
<td>Worse than 20/160–20/200</td>
<td>13,237 (100)</td>
<td>8016 (61)</td>
<td>6581 (50)</td>
<td>3469 (26)</td>
<td>1764 (13)</td>
<td>826 (6)</td>
</tr>
<tr>
<td></td>
<td>Worse than or equal to 20/200</td>
<td>19,782 (100)</td>
<td>16,674 (84)</td>
<td>15,753 (80)</td>
<td>9019 (46)</td>
<td>4847 (25)</td>
<td>2409 (12)</td>
</tr>
</tbody>
</table>

An event was defined as the time to loss of \( \geq 10 \) letters stratified by BL visual acuity categories.

BL, baseline.
Association of Change in Visual Acuity From Baseline to Year 1 With Baseline Clinical and Demographic Characteristics

For every additional anti-VEGF injection, a 0.68-letter improvement was observed when adjusted for other BL characteristics.

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**Generalized linear model.** Continuous variables.
BL, baseline; ETDRS, Early Treatment Diabetic Retinopathy Study; ref, reference; VEGF, vascular endothelial growth factor.

* P < 0.05 was considered significant.
Conclusions

- This is the largest and longest follow-up study known to date, where outcomes extending up to 6 years were evaluated in patients with nAMD in the IRIS Registry.

- Patients experienced high rates of treatment discontinuation and received relatively few anti-VEGF injections in years 3–6, with the most common injection frequency in patient eyes being 1–3 injections per year.

- Significant vision loss was high among patients with nAMD who were followed up for 6 years.

- For every additional anti-VEGF injection, a 0.68-letter improvement was observed in year 1.

- Given the size and inclusivity of the IRIS Registry, these findings are generalizable to the population in the United States.

- IRIS Registry data are limited by the accuracy of physician documentation.
References


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