Real-world Treatment Patterns in Patients With Macular Edema due to Retinal Vein Occlusion

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Disclosures

• Financial Disclosures
  - **VH:** Consultant: Genentech, Inc.; Opthea Ltd.; Kodiak
  - **AA, GCC, C-YC, S-CC, ZH:** Employee: Genentech, Inc.

• Study Disclosures
  - This study includes research conducted on human subjects
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Objective

To compare real-world treatment patterns in patients with macular edema (ME) due to retinal vein occlusion (RVO) in the United States based on data from a medical claims database and a direct survey of retina specialists.

ME, macular edema; RVO, retinal vein occlusion.
Introduction

- RVO occurs as a result of impaired venous return from the retinal circulation and is classified as BRVO or CRVO based on the location of the occlusion.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Features</th>
<th>Associated Complications</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher age</td>
<td>High intravitreal levels of VEGF-A, angiopoietin-2</td>
<td>ME (most common)</td>
<td>~16.4 million (95% CI: 13.9–18.9) adults (^4,a)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>High levels of inflammatory cytokines IL-6 and IL-8</td>
<td>Macular ischemia</td>
<td>ME due to RVO affected ~1.3 million patients in 2019 globally (^5)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
<td>Retinal neovascularization</td>
<td></td>
</tr>
<tr>
<td>Arteriosclerosis</td>
<td></td>
<td>Vitreous haemorrhage</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>Neovascular glaucoma</td>
<td></td>
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</tbody>
</table>

- Intravitreal anti-VEGF therapy is the most common treatment for ME associated with RVO in developed countries.

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\(^a\) Pooled studies from the United States, Europe, Asia, and Australia.

BRVO, branch retinal vein occlusion; CI, confidence interval; CRVO, central retinal vein occlusion; IL, interleukin; ME, macular edema; RVO, retinal vein occlusion; VEGF, vascular endothelial growth factor.
Methods: Medical Claims Database and Retina Specialist Survey

• **RVO medical claims database analysis**
  - **Study Design:** Descriptive analysis of Truven MarketScan claims data in the United States
  - **Time period:** January 2017–June 2018
  - **Target population:** RVO patients with macular edema from across any clinical practice in Truven MarketScan database eligible based on
    - Inclusion: Age ≥ 18 years, diagnosis of ME secondary to BRVO (H34.8310, H34.8320, H34.8330, H34.8390) or CRVO (H34.8110, H34.8120, H34.8130, H34.8190) using ICD-10-CM codes, ≥ 180 days of observation before and ≥ 365 days of follow-up after index (first) diagnosis
    - Exclusion: Neovascular age-related macular degeneration or diabetic macular edema at any time; prior history of any treatment with intravitreal anti-VEGF, laser, or corticosteroid injection or implant

• **RVO retina specialist (RS) experience analysis**
  - **Study design:** Descriptive analysis of the results from a prospectively designed advice seeking survey of 35 retina specialty sites across the United States
  - **Survey period:** June 2019–August 2019
  - **Target (patient) population:** RVO patients with macular edema based on RS assessment from US practices

BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ME, macular edema; RS, retina specialist; US, United States; VEGF, vascular endothelial growth factor.
RVO Medical Claims Database Analysis

• Descriptive statistics for treatments (anti-VEGF, laser, corticosteroid injection or implant, or combination therapy) received by patients within 1 year of diagnosis of RVO with ME
  – Treatments identified using HCPCS or CPT codes

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Code Type</th>
<th>Code(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranibizumab</td>
<td>HCPCS</td>
<td>J2778</td>
</tr>
<tr>
<td>Aflibercept</td>
<td>HCPCS</td>
<td>J0178</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>HCPCS</td>
<td>C9257, J9035, J3490, J3590, J7999, Q9977 (also required CPT code 67028 for intravitreal injection on same day)</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>HCPCS</td>
<td>J3300, J3301</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>HCPCS</td>
<td>J1100, J7312</td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>HCPCS</td>
<td>J7313</td>
</tr>
<tr>
<td>Laser</td>
<td>CPT</td>
<td>67210, 67228</td>
</tr>
</tbody>
</table>

### RVO Medical Claims Database Analysis: Target Population

**Patients with a diagnosis of ME secondary to BRVO**
- **(n = 7173)**

**Patients aged ≥ 18 years**
- **(n = 7173)**

**Patients with ≥ 180 days of enrollment before index diagnosis**
- **(n = 5948)**

**Patients with ≥ 365 days of enrollment after index diagnosis**
- **(n = 1019)**

**Patients with no diagnosis of DME or nAMD at any time**
- **(n = 881)**

**Treatment-naïve patients with ME secondary to BRVO**
- **(n = 246)**

**Excluded n = 1225**
- (< 180 days of enrollment before index diagnosis)

**Excluded n = 4929**
- (< 365 days of enrollment after index diagnosis)

**Excluded patients with DME (n = 88) or nAMD (n = 50)**

**Excluded patients with prior treatment:**
- Anti-VEGF (n = 510); Laser (n = 23); corticosteroids (injection or implant) (n = 102)

**Patients with a diagnosis of ME secondary to CRVO**
- **(n = 4866)**

**Patients aged ≥ 18 years**
- **(n = 4861)**

**Patients with ≥ 180 days of enrollment before index diagnosis**
- **(n = 3981)**

**Patients with ≥ 365 days of enrollment after index diagnosis**
- **(n = 661)**

**Patients with no diagnosis of DME or nAMD at any time**
- **(n = 573)**

**Treatment-naïve patients with ME secondary to CRVO**
- **(n = 135)**

**Excluded n = 5**
- (patients aged < 18 years)

**Excluded n = 880**
- (< 180 days of enrollment before index diagnosis)

**Excluded n = 3320**
- (< 365 days of enrollment after index diagnosis)

**Excluded patients with DME (n = 59) or nAMD (n = 29)**

**Exclude patients with prior treatment:**
- Anti-VEGF (n = 387); Laser (n = 5); corticosteroids (injection or implant) (n = 46)

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*“Stable” and “retinal neovascularization” RVO codes were not included in the case definition.*

BRVO, branch retinal vein occlusion; DME, diabetic macular edema; ME, macular edema; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.
### RVO Medical Claims Database Analysis: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BRVO and ME (n = 246)</th>
<th>CRVO and ME (n = 135)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years, median [IQR]</strong></td>
<td>60 [54, 70]</td>
<td>61 [54, 74]</td>
</tr>
<tr>
<td><strong>Age group, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18–34</td>
<td>3 (1.2)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>35–44</td>
<td>15 (6.1)</td>
<td>10 (7.4)</td>
</tr>
<tr>
<td>45–54</td>
<td>44 (17.9)</td>
<td>23 (17.0)</td>
</tr>
<tr>
<td>55–64</td>
<td>106 (43.1)</td>
<td>50 (37.0)</td>
</tr>
<tr>
<td>≥65</td>
<td>78 (31.7)</td>
<td>50 (37.0)</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>115 (46.7)</td>
<td>56 (41.5)</td>
</tr>
<tr>
<td>Men</td>
<td>131 (53.3)</td>
<td>79 (58.5)</td>
</tr>
<tr>
<td><strong>Insurance type, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comprehensive</td>
<td>37 (15.0)</td>
<td>13 (9.6)</td>
</tr>
<tr>
<td>HMO</td>
<td>39 (15.9)</td>
<td>29 (21.5)</td>
</tr>
<tr>
<td>POS</td>
<td>14 (5.7)</td>
<td>4 (3.0)</td>
</tr>
<tr>
<td>PPO</td>
<td>109 (44.3)</td>
<td>57 (42.2)</td>
</tr>
<tr>
<td>Other</td>
<td>36 (14.6)</td>
<td>25 (18.5)</td>
</tr>
<tr>
<td>Missing</td>
<td>11 (4.5)</td>
<td>7 (5.2)</td>
</tr>
<tr>
<td><strong>Geographic region, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North Central</td>
<td>43 (17.5)</td>
<td>23 (17.0)</td>
</tr>
<tr>
<td>Northeast</td>
<td>49 (19.9)</td>
<td>23 (17.0)</td>
</tr>
<tr>
<td>South</td>
<td>104 (42.3)</td>
<td>59 (43.7)</td>
</tr>
<tr>
<td>West</td>
<td>48 (19.5)</td>
<td>28 (20.7)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (0.8)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td><strong>Follow-up time after index, years, median [IQR]</strong></td>
<td>1.3 [1.1, 1.4]</td>
<td>1.3 [1.2, 1.4]</td>
</tr>
</tbody>
</table>

BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; ME, macular edema; HMO, health maintenance organization; IQR, interquartile range; POS, point of service; PPO, preferred provider organization.
RVO Medical Claims Database Analysis: Treatments Received Within 1 Year of Diagnosis

- Within the first year of diagnosis, ~40% of patients received no treatment for RVO
- The most common treatment was anti-VEGF injection alone (38% BRVO with ME; 45% CRVO with ME)
- ≤ 4% of patients received either laser or corticosteroids monotherapy
- < 15% of patients received combination therapy; nearly all combinations included anti-VEGF therapy

Patients were identified using the newest ICD-10-CM codes for BRVO with macular edema (H34.8310, H34.8320, H34.8330, H34.8390) or CRVO with macular edema (H34.8110, H34.8120, H34.8130, H34.8190). Patients were required have a look-back period of ≥180 days and ≥365 days of follow-up after index (first) diagnosis. Patients were excluded if they were aged <18 years at the index diagnosis, had DME or nAMD at any time, or had prior treatment of any type before the index diagnosis. Different treatments administered within a two-week period were considered a combination treatment.

BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; ME, macular edema; nAMD, neovascular age-related macular degeneration; RVO, retinal vein occlusion; VEGF, vascular endothelial growth factor.
RVO Medical Claims Database Analysis: Anti-VEGF Injections Received Within 1 Year of Diagnosis Among Persons With ≥ 1 Anti-VEGF Injection

- Among patients who were treated with anti-VEGF injections, about half of patients received ≤ 5 anti-VEGF injections and ~10% received ≥ 10 injections within the first year of diagnosis.

Mean (SD) injections at 1 year:
- BRVO with ME: 5.5 (3.0)
- CRVO with ME: 5.6 (3.1)
RVO Retina Specialist Experience Analysis: Anti-VEGF Was Reported as the Most Common Choice of Treatment

BRVO Treatment

- Anti-VEGF, 100%

CRVO Treatment

- Anti-VEGF, 100%

N = 35

BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; IVT, intravitreal; PRP, panretinal photocoagulation; VEGF, vascular endothelial growth factor.
RVO Retina Specialist Experience Analysis: Majority Reported Treatment Initiation Immediately or Within 1–2 Weeks After Diagnosis

- 37% of the specialists treated patients immediately
- ~39% of the specialists chose to delay treatment by 1–2 weeks
- ~20% of the specialists started treatment after 1 month

BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion.
RVO Retina Specialist (RS) Experience Analysis: Treatment Duration in a Typical Patient

- The most commonly reported duration of treatment among retina specialists was > 2 years. 56% and 72% of RSs reported treating patients for > 2 years for BRVO and CRVO respectively, with 19% reporting 1–2 year-treatment duration.
- More than half of the patients with ME due to BRVO/CRVO required long-term management.

BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; ME, macular edema; RS, retina specialist.
The most commonly reported anti-VEGF regimen was monthly injections (69% and 63% respondents for BRVO and CRVO, respectively), with PRN (11% respondents) and T&E (20% and 26% respondents) regimens used less often.
Conclusions

• Based on MarketScan claims data of diagnoses from HCPs of any provider type or specialty during January 2017 through June 2018, ~40% of treatment-naïve patients newly diagnosed with RVO and ME did not receive treatment within the first year of diagnosis.

• In contrast, data from surveyed RSs indicated that ~80% patients with ME due to RVO initiated treatment within 2 weeks from diagnosis.

• Both datasets, from HCPs overall and from RSs, showed that anti-VEGF injections were the most common first therapy.

• While HCPs overall reported that only 10% of patients received ≥10 injections among the anti-VEGF treated subset within the 1st year, the majority of RSs reported treating with anti-VEGF for > 2 years with monthly being the most common regimen, followed by T&E, and less commonly, PRN.

BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; HCP, healthcare provider; ME, macular edema; RS, retina specialists; RVO, retinal vein occlusion; VEGF, vascular endothelial growth factor.
Discussion

• Diagnosis of ME due to RVO from diverse US HCP practices did not lead to treatment in ~40% of patients during the first year of diagnosis

• By contrast, surveyed US RSs reported treating all patients with ME due to RVO, with the majority initiating treatment within 2 weeks and treating patients for > 2 years

• Based on these findings, we hypothesize that RVO patients with ME may not be referred to RSs until advanced vision-threatening stage

Limitations and Outlook

• The MarketScan analyses were limited by lack of VA data in the claims database

• HCP classification was unreliable in MarketScan and it was not possible to differentiate HCPs by provider type/specialty (e.g., RS vs. others) for treatment pattern comparisons

• RSs’ survey relied on the reports based on RS experience, and did not include specific patient data analyses

• Further research is needed to evaluate real-world treatment patterns in patients with ME due to RVO in correlation with VA outcomes