New Insights on Treating Diabetic Retinopathy & Diabetic Macular Edema from the 2018 AAO Meeting
Protocol T: Mean Change in VA Over 2 Years

By Baseline VA Subgroup

20/32 to 20/40

Mean Change in VA Letter Score

Weeks

0 8 16 24 32 40 48 56 64 72 80 88 96 104

0 2 4 6 8 10 12 14 16 18 20

+8.6

+7.8

+6.8

20/50 or Worse

+18.1

+16.1

+13.3

Aflibercept

Bevacizumab

Ranibizumab

Wells et al. Ophthalmo. 2016;123:1351-1359. For educational purposes only.

PROTOCOL T = Comparative Effectiveness Study of Intravitreal Aflibercept, Bevacizumab, and Ranibizumab for Diabetic Macular Edema; VA = visual acuity.
Anti-VEGF Agents in DR

- Meta-analysis of RIDE, RISE, Protocol I and Protocol T
- Implications for DR
- Evaluated ranibizumab

<table>
<thead>
<tr>
<th>Baseline DRSS</th>
<th>≥2 Step DRSS Improvement (%) at Year 2</th>
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<tbody>
<tr>
<td></td>
<td>RBZ</td>
</tr>
<tr>
<td>≤43 (NPDR)</td>
<td>11</td>
</tr>
<tr>
<td>47–53 (NPDR)</td>
<td>73</td>
</tr>
<tr>
<td>≥60 (PDR)</td>
<td>44</td>
</tr>
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Anti-VEGF = antivasculat angiostatic growth factor; DR = diabetic retinopathy; DRSS = diabetic retinopathy severity scale; NPDR = nonproliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy; PROTOCOL 1 = Laser-Ranibizumab-Triamcinolone for Diabetic Macular Edema (LRT for DME); RBZ = ranibizumab; RIDE = A Study of Ranibizumab Injection in Subjects with Clinically Significant Macular Edema with Center Involvement Secondary to Diabetes Mellitus; RISE = Anti-VEGF Treatment for Prevention of PDR/DME.

Protocol U: Ranibizumab plus Dexamethasone Implant

Outlying values were truncated to 3 standard deviations from the mean. One image was nongradable due to low resolution.

Maturi et al. *JAMA Ophthalmol.*, 2018;135:29-38. For educational purposes only. AUC = area under the curve; CST = central subfield thickness.
Pan-American Collaborative Retina Study Group: 5 Year Results

- Gains obtained at 3 years were lost at years 4 and 5

- Undertreatment of patients is prevalent and compromises patient outcomes

BCVA – best corrected visual acuity; logMAR - logarithm of minimum angle of resolution.
Anti-VEGF Frequency in DR

- RISE, RIDE, Protocol T, Protocol I¹
  - 0.3 mg or 0.5 mg RBZ administered q4w → PRN
  - Reduction/reversal of DR with this schedule

- PANORAMA study²
  - Aflibercept administered as 3 to 5 loading doses → q8w or q16w
  - 4.4 average injections over 24 weeks

<table>
<thead>
<tr>
<th></th>
<th>≥2 Step DRSS Improvement (%) at 24 weeks</th>
<th>% Developing Vision Threatening Complications</th>
</tr>
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<tbody>
<tr>
<td>Sham</td>
<td>6.0</td>
<td>25.6</td>
</tr>
<tr>
<td>All IAI</td>
<td>58.4</td>
<td>4.5</td>
</tr>
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</table>

IAI = Intravitreal aflibercept injection; PANORAMA = Study of the Efficacy and Safety of Intravitreal Aflibercept for the Improvement of Moderately Severe to Severe Nonproliferative Diabetic Retinopathy; PRN = as needed.

Onset of Improvements in DME with Anti-VEGF Agents: READ 3 Analysis

- **READ 3 study**
  - 0.5 mg and 2.0 mg RBZ q4w for 6 months → PRN for 24 months
  - Substudy evaluated response at 3 and 6 months

- **Benefits of anti-VEGF in DR evident as early as 3 months**
  - Comparable to 12 month results of VISTA trial
  - Comparable to 24 month results of RIDE/RISE trials

<table>
<thead>
<tr>
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<th>Percent with ETDRS DR Severity Mild or Better</th>
<th>≥2 Step DRSS Improvement (%) at Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5 mg</td>
<td>2.0 mg</td>
</tr>
<tr>
<td>Baseline</td>
<td>12.8</td>
<td>4.2</td>
</tr>
<tr>
<td>Month 3</td>
<td>32.4</td>
<td>36.4</td>
</tr>
<tr>
<td>Month 6</td>
<td>41</td>
<td>50</td>
</tr>
</tbody>
</table>

ETDRS = Early Treatment Diabetic Retinopathy Study; READ 3 = Ranibizumab for Edema of the Macula in Diabetes: Protocol 3 with High Dose - the READ 3 Study; VISTA = Study of Intravitreal Aflibercept Injection in Patients with Diabetic Macular Edema.

Treatment Continuation Is the Key to the Success with Anti-VEGF Therapy

- One-fourth of patients initiating anti-VEGF agents LTFU over 4 years\(^1\)
- Diverse reasons for interruption: illness, noncompliance, financial issues, etc\(^2\)
- Anti-VEGF interruption is associated with deteriorating outcomes and treatment complications compared to eyes receiving PRP\(^2,3\)
  - Vitreous hemorrhage, neovascular glaucoma, traction retinal detachment\(^2\)
  - Worsening VA\(^2,3\)


logMAR = logarithm of minimum angle of resolution; IVI = intravitreal injection; LTFU = lost to follow-up; PRP = panretinal photocoagulation.