Outcomes of Intravitreal Anti-VEGF Therapy for Diabetic Macular Edema in Routine Clinical Practice

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Disclosures

– Regeneron - Investigator, consultant
– Genentech - investigator, speaker
– Allergan - consultant
Dosing Approaches in Clinical Trials are Varied

Quarterly
- PIER\textsuperscript{8}
- SAILOR\textsuperscript{9}
- EXCITE\textsuperscript{10}

PRN\textsuperscript{11,12}
- HARBOR\textsuperscript{3}
- CATT\textsuperscript{4}
- RESOLVE\textsuperscript{13}
- RESTORE\textsuperscript{14}
- Protocol I\textsuperscript{15}
- Protocol T\textsuperscript{16}

Treat-and-Extend\textsuperscript{11,12}
- LUCAS\textsuperscript{17}
- TREX\textsuperscript{18}

Monthly
- ANCHOR\textsuperscript{1}
- MARINA\textsuperscript{2}
- HARBOR\textsuperscript{3}
- CATT\textsuperscript{4}
- RISE/RIDE\textsuperscript{5}
- VIEW 1/2\textsuperscript{6}
- VISTA/VIVID\textsuperscript{7}

Bimonthly
- VIEW 1/2\textsuperscript{6}
- VISTA/VIVID\textsuperscript{7}

Frequent Monitoring and Consistent Treatment Resulted in Optimal Outcomes in Clinical Trials for DME
Limited Vision Improvement when Initial Treatment Approach was not Optimized in Patients with DME

- Final vision was limited in patients who were treated with intravitreal aflibercept following vision loss with initial laser treatment

Analysis of Outcomes in Routine Clinical Practice
Study Design

• **Objective**
  – To evaluate visual acuity outcomes following treatment of DME with intravitreal anti-VEGF agents in routine clinical practice through 2 years

• **Methods**
  – Electronic medical record data* collected from 251 Retina Specialists for patients with –
    • *Diabetic macular edema*
  – Anti-VEGF treatment naïve eyes
    • 1\textsuperscript{st} anti-VEGF injection between January 1\textsuperscript{st}, 2012 and April 30\textsuperscript{th}, 2015
  – Two subgroups evaluated –
    • *Group 1: \leq 6 injections/year*
    • *Group 2: \geq 7 injections/year*

*Source: Vestrum Database*
Patient Selection
Year 1

Assessed for eligibility
\( n = 155,240 \)

1st anti-VEGF between 01/01/12 – 04/30/15
\( n = 16,207 \)

VA reading on index date
\( n = 13,016 \)

No treatment break for >11 months through year 1
\( n = 11,148 \)

VA reading at month 12
\( n = 3,674 \)

VA reading in all 4 quarters
\( n = 3,032 \)

Gender identified
\( n = 3,028 \)
### Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total  ( n=3028 )</th>
<th>≤6 injections  ( n=1303 )</th>
<th>≥7 injections  ( n=1725 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>62</td>
<td>61</td>
<td>63</td>
</tr>
<tr>
<td>Female, %</td>
<td>46%</td>
<td>47%</td>
<td>44%</td>
</tr>
<tr>
<td>Mean VA, letters</td>
<td>71</td>
<td>71</td>
<td>70</td>
</tr>
<tr>
<td>Median VA, letters</td>
<td>76</td>
<td>77</td>
<td>76</td>
</tr>
<tr>
<td>VA subgroups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥20/40</td>
<td>27%</td>
<td>29%</td>
<td>25%</td>
</tr>
<tr>
<td>&lt;20/40 – 20/100</td>
<td>51%</td>
<td>50%</td>
<td>51%</td>
</tr>
<tr>
<td>&lt;20/100 – 20/200</td>
<td>11%</td>
<td>11%</td>
<td>12%</td>
</tr>
<tr>
<td>&lt;20/200</td>
<td>11%</td>
<td>10%</td>
<td>12%</td>
</tr>
</tbody>
</table>

*Patients included in Year 1 analysis*
Mean Visual Acuity Change By Injection Subgroups (Year 1)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Mean BSL VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤6 injs</td>
<td>(n=1303) 71</td>
</tr>
<tr>
<td>≥7 injs</td>
<td>(n=1725) 70</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Mean Number of Injections</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤6 injs</td>
<td>(n=1303) 4.0</td>
</tr>
<tr>
<td>≥7 injs</td>
<td>(n=1725) 9.1</td>
</tr>
</tbody>
</table>

Visual acuity is reported in visual acuity score (VAS)

*P < 0.001 compared with ≤6 injs
Mean Visual Acuity by Injection Subgroups (Year 1)

<table>
<thead>
<tr>
<th>Mean # of Injections</th>
<th>3.0</th>
<th>2.2</th>
<th>2.0</th>
<th>2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range of Injections</td>
<td>1.5</td>
<td>0.4</td>
<td>0.4</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Mean # of Injections

Range of Injections

≥7 injs  
(n=1725)

≤6 injs  
(n=1303)
Patient Selection

Year 2

Assessed for eligibility
n = 155,240

1st anti-VEGF between 01/01/12 – 04/30/15
n = 16,207

VA reading on index date
n = 13,016

Year 1

No treatment break for >11 months through year 1
n = 11,148

VA reading at month 12
n = 3,674

VA reading in all 4 quarters
n = 3,032

Gender identified
n = 3,028

Year 2

No treatment break for >11 months through year 2
n = 3,575

VA reading at month 12
n = 2,241

VA reading in all 8 quarters
n = 1,292

Gender identified
n = 1,292

45% qualified

28% had no visits in Year 2
Mean Visual Acuity by Injection Subgroups (Year 2)

Patients Receiving ≤6 injections in Year 1

Mean number of injections

<table>
<thead>
<tr>
<th>Year</th>
<th>≤6 injs / ≤6 injs</th>
<th>≤6 injs / ≥7 injs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>4.6</td>
<td>4.9</td>
</tr>
<tr>
<td>Year 2</td>
<td>4.3</td>
<td>8.2</td>
</tr>
</tbody>
</table>
Mean Visual Acuity by Injection Subgroups (Year 2)

Patients Receiving ≥7 injections in Year 1

Mean number of injections

<table>
<thead>
<tr>
<th>Year</th>
<th>Mean (n=364)</th>
<th>Mean (n=574)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>8.8</td>
<td>9.7</td>
</tr>
<tr>
<td>Year 2</td>
<td>4.7</td>
<td>9.0</td>
</tr>
</tbody>
</table>

Start of Y2

End of Y2
Change Over Time in Injection Frequency During Year 1 of Treatment

### Annual Mean Number of Injections

- **2012**: 6.73
- **2013**: 6.78
- **2014**: 7.02
- **2015**: 6.81

### Annual Proportion of Patients

- **2012** (n = 143):
  - <= 6 injections: 43%
  - >= 7 injections: 57%
- **2013** (n = 594):
  - <= 6 injections: 48%
  - >= 7 injections: 52%
- **2014** (n = 1585):
  - <= 6 injections: 41%
  - >= 7 injections: 59%
- **2015** (n = 706):
  - <= 6 injections: 43%
  - >= 7 injections: 57%
Summary

- Consistent with results of clinical trials, in routine clinical practice, maintenance of visual gains was associated with more frequent anti-VEGF injections in patients with DME.
- Patients with DME were more likely to receive more frequent injections (≥7) rather than fewer injections (≤6) during the first year of treatment.
  - A substantial proportion (43%) of DME patients received ≤6 injections during their first year of treatment.
Thank You
Back-Up
# Overview of Trials

## Diabetic Macular Edema

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment Groups</th>
<th>Mean Change in BCVA at Year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>RISE</td>
<td>RBZ 0.3mg monthly</td>
<td>+14.3</td>
</tr>
<tr>
<td></td>
<td>sham</td>
<td>+5.1</td>
</tr>
<tr>
<td>RIDE</td>
<td>RBZ 0.3mg monthly</td>
<td>+13.1</td>
</tr>
<tr>
<td></td>
<td>sham</td>
<td>+4.5</td>
</tr>
<tr>
<td>VISTA</td>
<td>IAI 2mg monthly</td>
<td>+12.5</td>
</tr>
<tr>
<td></td>
<td>IAI 2mg bi-monthly*</td>
<td>+10.7</td>
</tr>
<tr>
<td></td>
<td>laser</td>
<td>+0.2</td>
</tr>
<tr>
<td>VIVID</td>
<td>IAI 2mg monthly</td>
<td>+10.5</td>
</tr>
<tr>
<td></td>
<td>IAI 2mg bi-monthly*</td>
<td>+10.7</td>
</tr>
<tr>
<td></td>
<td>laser</td>
<td>+1.2</td>
</tr>
<tr>
<td>Protocol T</td>
<td>IAI 2mg PRN</td>
<td>+13</td>
</tr>
<tr>
<td></td>
<td>RBZ 0.3mg PRN</td>
<td>+11</td>
</tr>
<tr>
<td></td>
<td>BVZ 1.25mg PRN</td>
<td>+10</td>
</tr>
</tbody>
</table>

RBZ=ranibizumab, IAI=intravitreal aflibercept injection, BVZ=bevacizumab

*following 5 initial monthly doses