Early Administration of the Dexamethasone Implant After Anti-VEGF Therapy for the Treatment of Diabetic Macular Edema

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Disclosures

• Consultant or Speaker’s Bureau
  – Allergan
  – EyePoint Pharmaceuticals
  – Alimera Sciences
  – Novartis
  – Spark
  – Biogen
  – Graybug
  – Regeneron
Summary

• Post-hoc analyses find a significant number of patients with DME who receive anti-VEGF monotherapy show a suboptimal response within the first 12 weeks of therapy.

• This retrospective, real-world analysis evaluated treatment-naïve patients with DME who were treated with 1-3 anti-VEGF injections.

• Switching patients who have received few anti-VEGF injections (≤ 3) earlier to the 0.7mg Dexamethasone Implant improved BCVA from 61 after anti-VEGF treatment to 75 letters and reduced central retinal thickness from 377 microns after anti-VEGF treatment to 289 microns.
Background

• The two most common current treatments for DME are anti-VEGFs and intravitreal corticosteroids

• Anti-VEGF use in DME stems from their proven record in improving visual acuity and decreasing macular fluid
  – BUT... not all patients respond equally or consistently

• Pivotal studies found similar results:
  – RIDE/RISE found 66% were not 3-line gainers
  – VIVID/VISTA found 58%-69% were not 3-line gainers

Background

- Post-hoc analysis of anti-VEGF *suboptimal responders* reported that longer duration and greater magnitude of edema resulted in fewer letters gained\(^1\)\(^-\)\(^5\)

- The Protocol I EARLY analysis also showed best-corrected visual acuity (BCVA) response after 3 months was a telltale harbinger of longer term vision gains\(^4\),\(^5\)
  - Three magnitudes of patient responses to anti-VEGF therapy were observed
    - Maximum, moderate and suboptimal responders
    - 40% were <5-letter gainers at 12 weeks\(^5\)

- The outcomes from Protocol T were the same
  - Vision gains at 12 weeks were similar to vision at 3 years, regardless of treatment.\(^3\)

Protocol I (EARLY) and Protocol T Post Hoc Analysis: Percentages of suboptimal responders

Protocol I (EARLY) Post-Hoc Analysis*

* Ranibizumab only

Protocol T Post-Hoc Analysis**

** Afibercept on the left; ranibizumab on the right

Purpose

- Real-world outcomes rarely match clinical study findings\(^1-4\)
- Worse outcomes in real-world settings — suggests that an unmet need exists to address a large number of suboptimal responders

Can switching from anti-VEGF therapy to the Dexamethasone 0.7mg Implant produce better visual and anatomic outcomes if patients are switched early?
Methods

• Retrospective, real-world analysis of 38 treatment-naïve DME patients confirmed with optical coherence tomography (OCT) from 4 clinics

• Clinicians treated patients with intravitreal bevacizumab or aflibercept (no patient was treated with ranibizumab):
  – 11% received 1 injection
  – 8% received 2 injections
  – 81% received 3 injections

• Patients were deemed poor responders based on minimal VA gain or poor anatomic response

• Patients were switched to a single intravitreal Dexamethasone 0.7mg Implant

• Main outcome measures included changes in BCVA and central retinal thickness (CRT)
Methods

- There were 38 unique patients included
  - One patient received two bevacizumab and one aflibercept before switch

<table>
<thead>
<tr>
<th>Anti-VEGF medication</th>
<th>Number of times used</th>
<th>Number of patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab</td>
<td>1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>21</td>
<td>63</td>
</tr>
<tr>
<td>Aflibercept</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10</td>
<td>30</td>
</tr>
</tbody>
</table>

VEGF=vascular endothelial growth factor
## Visual Acuity Results

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean BCVA, in letters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (N=38)</td>
<td>72.25 (±13.36)</td>
</tr>
<tr>
<td>After anti-VEGF*</td>
<td>61 (±11.74)</td>
</tr>
<tr>
<td>P-value</td>
<td>$P=0.50^*$</td>
</tr>
<tr>
<td>3 months s/p dexamethasone 0.7mg</td>
<td>75 (±12.53)</td>
</tr>
<tr>
<td>P-value</td>
<td>$P=0.007^*$</td>
</tr>
</tbody>
</table>

* 2-tailed, unpaired t-test

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**BCVA Results, After anti-VEGF and After Dexamethasone**

<table>
<thead>
<tr>
<th>BCVA, in ETDRS letters</th>
<th>Baseline</th>
<th>Dexamethasone administration</th>
<th>3 months s/p dexamethasone administration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>72.25</td>
<td>60.5</td>
<td>75*</td>
</tr>
</tbody>
</table>

* $P=0.007$
## OCT Results

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (N=38)</td>
<td>439 microns (±152.35)</td>
</tr>
<tr>
<td>After anti-VEGF*</td>
<td>377 microns (±121.6)</td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td><strong>P=0.09</strong></td>
</tr>
<tr>
<td>3 months s/p dexamethasone 0.7mg</td>
<td>289 microns (±47.38)</td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td><strong>P=0.00007</strong></td>
</tr>
</tbody>
</table>

Central Retinal Thickness (in microns)

* P=0.00007
Suboptimal Responder After 3 Anti-VEGF Injections

<table>
<thead>
<tr>
<th>Visit Date</th>
<th>OD</th>
<th>OS</th>
<th>IOP</th>
<th>Central Subfield Thickness</th>
<th>Cube Volume</th>
<th>Cube Average Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Visit Aflibercept Injection</td>
<td>20/60</td>
<td>20/50</td>
<td>OD:19</td>
<td>383</td>
<td>12.1</td>
<td>240</td>
</tr>
<tr>
<td>2nd Visit Aflibercept Injection</td>
<td>20/50</td>
<td>20/80</td>
<td>OD:19</td>
<td>378</td>
<td>9.2</td>
<td>190</td>
</tr>
<tr>
<td>3rd Visit Aflibercept Injection</td>
<td>20/70</td>
<td>20/80</td>
<td>OD:19</td>
<td>383</td>
<td>10.8</td>
<td>200</td>
</tr>
<tr>
<td>Date of Dexamethasone Injection</td>
<td>20/40</td>
<td>20/50</td>
<td>OD:14</td>
<td>207</td>
<td>7.9</td>
<td>229</td>
</tr>
<tr>
<td>Follow up Visit</td>
<td>20/30</td>
<td>20/30</td>
<td>OD:14</td>
<td>243</td>
<td>6.5</td>
<td>250</td>
</tr>
</tbody>
</table>

Images courtesy of M. Singer, MD
Conclusions

• Post-hoc analyses find a significant number of DME patients receiving anti-VEGF monotherapy show a suboptimal response within the first 12 weeks of therapy
  – Addressing the multifactorial mechanism(s) of DME may yield superior outcomes

• An opportunity may exist to improve outcomes in these patients with early introduction of the 0.7mg Dexamethasone Implant

• A larger, prospective study may be warranted to validate this treatment paradigm based on the results of this real-world study
THANK YOU