A Prospective, Single-Blind, Randomized Study to Evaluate Intravitreal Aflibercept Injection versus Sham as PROphylaxis against CONversion to Neovascular Age-Related Macular Degeneration in High-Risk Eyes

The PRO-CON Study

Month 24 Results

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Financial Disclosures

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• Nadia Waheed
  • Director, Boston Imaging Reading Center
• Sabin Dang, Sumit Shah
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Summary

• Aflibercept quarterly prophylaxis did not affect conversion through Month 24

• Exudative disease in fellow eye ≤ 2 years had a higher conversion rate

• Presence of non-exudative CNV confirmed on OCTA was more likely to convert in either group

• Development or progression of geographic atrophy was not affected by quarterly aflibercept treatment
Rates of CNV Conversion in Fellow Eyes at 24 Months

- **MARINA/ANCHOR**: 24-38%
- **CATT**: 17-21%
- **HARBOR (M 12)**: 12% (FA)
- **VIEW**: 50% (SD-OCT)
- **VIEW**: 26-32%
Study Objective

To evaluate if intravitreal anti-VEGF therapy in eyes with high-risk dry AMD would provide a prophylactic effect against the conversion to nAMD
Study Design

- **128* eyes with high risk dry AMD randomized 1:1 to quarterly treatments** with:
  - Intravitreal aflibercept injection (IAI)
  - Sham Injection

- **Study Duration: 24 months**
  - Planned Interim Analysis: 12 months

- **Primary Endpoint:**
  - **Proportion of patients converting to nAMD at 24 months** characterized by CNV development as assessed by:
    - CNV leakage on FA, and
    - Evidence of any fluid on SD-OCT

  *Conversion confirmed by masked, central reading center*

*sample size based on 35% conversion rate at 2 years and 8% dropout/deaths annually*
### Study Schedule

<table>
<thead>
<tr>
<th>IAI</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSL</td>
<td>M3</td>
</tr>
<tr>
<td>M6</td>
<td>M9</td>
</tr>
<tr>
<td>M12</td>
<td>M15</td>
</tr>
<tr>
<td>M18</td>
<td>M21</td>
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</tbody>
</table>

**M24** Final Visit

Assessments at all study visits *(including Unscheduled Suspected Conversion Visits)* -

- Best-Corrected Visual Acuity
- Spectral Domain-Optical Coherence Tomography
- Fluorescein Angiography
- Fundus Photos
- OCT-Angiography
Imaging at Every Visit

- Enrollment & Conversion decisions based upon FA and OCT
Mandatory Reading Center Confirmation
Boston Imaging Reading Center

Screening: FA & OCT
OCT-A (exploratory)

- 1 hour read (FA & OCT)

Follow-up visit with suspected conversion

- 1 hour read (FA & OCT)

Treatment (post RC confirmation)
Key Entry Criteria

- **High risk** defined as having
  - **Intermediate AMD** in one eye (study eye) defined as the presence of
    - > 10 intermediate sized drusen (≥ 63 and < 125 µm)
    - ≥ 1 large druse (≥ 125 µm)
    - and/or retinal pigmentary changes

  *and*

  - **Neovascular AMD** in the fellow eye

- Absence of exudative disease confirmed by independent, masked reading center before enrollment
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>IAI n = 63*</th>
<th>Sham n = 64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>78.4</td>
<td>79.2</td>
</tr>
<tr>
<td>Female</td>
<td>27 / 63 (42.8%)</td>
<td>32 / 64 (50%)</td>
</tr>
<tr>
<td>Duration of fellow eye nvAMD ≤ 2y (%)</td>
<td>48%</td>
<td>48%</td>
</tr>
<tr>
<td>Non-Exudative Macular NV (OCTA)</td>
<td>6.3%</td>
<td>9.2%</td>
</tr>
<tr>
<td>Mean BCVA</td>
<td>78.7</td>
<td>77.3</td>
</tr>
</tbody>
</table>

* 1 patient had exudative disease in the study eye at baseline
** As determined by OCT-A
<table>
<thead>
<tr>
<th></th>
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<th>Sham</th>
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<tbody>
<tr>
<td></td>
<td>n = 64</td>
<td>n = 64</td>
</tr>
<tr>
<td>Month 24, n (%)</td>
<td>60 (94%)</td>
<td>53 (83%)</td>
</tr>
<tr>
<td>Withdrew</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>
Rate of CNV Conversion

Overall Population

Proportion of Eyes

<table>
<thead>
<tr>
<th></th>
<th>Proportion</th>
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<tbody>
<tr>
<td>IAI</td>
<td>6.35%</td>
</tr>
<tr>
<td></td>
<td>4/63</td>
</tr>
<tr>
<td>Sham</td>
<td>9.38%</td>
</tr>
<tr>
<td></td>
<td>6/64</td>
</tr>
</tbody>
</table>

\( p = 0.76 \)
Rate of CNV Conversion
Overall Population

<table>
<thead>
<tr>
<th></th>
<th>Proportion of Eyes</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAI</td>
<td>9.52%</td>
<td>0.98</td>
</tr>
<tr>
<td>Sham</td>
<td>10.90%</td>
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</tbody>
</table>

6/63 7/64
Time to Conversion
Overall Population

p=0.50
Rate of CNV Conversion
By Duration of Exudative Disease in the Fellow Eye

Month 24

Proportion of Eyes

< 2 years

IAI  Sham  Total

13%  16%  14%
31  32  63

> 2 years

6%  6%  6%
32  32  64

p = 0.135
Presence of Non-Exudative Choroidal Neovascularization*

- Few patients developed NE-CNV during the 24-month period

* As measured by OCT-A at any time during the trial before conversion
Rate of CNV Conversion
In Eyes with Non-Exudative Choroidal Neovascularization*

Patients with non exudative CNV had a higher conversion rate

* As measured by OCT-A at any time during the trial before conversion
Non-exudative CNV at Baseline with Conversion

Baseline

Conversion – Month 6

Month 24
Non-exudative CNV at Baseline without Conversion

Baseline

Month 12

Month 24
Safety

- One related, significant ocular adverse event reported by M24
  - Endophthalmitis in fellow eye related to injection procedure
- Safety data were consistent with previous studies involving intravitreal injections.
Conclusions

• Aflibercept quarterly prophylaxis did not affect conversion through Month 24

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• Development or progression of geographic atrophy was not affected by quarterly aflibercept treatment
Thank you to study sites, BIRC, consultants, patients

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