APL-2 in Geographic Atrophy
12-Month Results

Retina Subspecialty Day
November 10, 2017
Central inhibition of complement

Lectin Pathway

Classical Pathway

Alternative Pathway

APL-2

C3

STOP

C3a

STOP

C3b

STOP

C5

STOP

C5a

STOP

C5b

MAC

Cell removal, Antigen uptake by APCs

Cell death, secretion, lysis, or proliferation

Inflammation

Inflammation
Endpoints

Primary Efficacy

• Mean change in square root GA area from baseline to month 12\(^{1,2}\)

Primary Safety

• Incidence and severity of ocular and systemic AEs

Key Secondary Endpoints

• Change in best corrected visual acuity

• Incidence of new onset exudative AMD

1. Based on fundus autofluorescence photographs (FAF)
Study Design

Eligible Patients with Geographic Atrophy*
246 subjects in 42 sites†

Randomized 2:2:1:1

APL-2 Monthly
N=86

APL-2 Every Other Month
N=79

Sham Monthly
N=41

Sham Every Other Month
N=40

GA due to AMD confirmed by the central reading center using FAF images:
- Total GA area 2.5 to 17.5 mm² (1 to 7 DA) at Screening
- BCVA (ETDRS): 24 letters or better (20/320 Snellen equivalent)
- No exclusion for fellow-eye disease (including exudative AMD)

*Confirmed by the central reading center using FAF images, †Not counting the 3 satellite sites.
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>APL-2 Monthly N=86</th>
<th>APL-2 Every Other Month N=79</th>
<th>Sham Pooled N=81</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral GA, n (%)</td>
<td>71 (85.5%)</td>
<td>64 (82.1%)</td>
<td>72 (90.0%)</td>
</tr>
<tr>
<td>History of CNV in Fellow Eye, n (%)</td>
<td>36 (41.9%)</td>
<td>28 (35.4%)</td>
<td>29 (35.8%)</td>
</tr>
<tr>
<td>GA lesion size, mean, mm(^2) (SD)</td>
<td>8.0 (3.8)</td>
<td>8.9 (4.5)</td>
<td>8.2 (4.1)</td>
</tr>
<tr>
<td>BCVA score, mean letters (SD)</td>
<td>59.8 (15.7)</td>
<td>58.4 (16.0)</td>
<td>59.8 (17.2)</td>
</tr>
<tr>
<td>BCVA score (Snellen equivalent)</td>
<td>20/63</td>
<td>20/80</td>
<td>20/63</td>
</tr>
<tr>
<td>LL-BCVA score, mean letters (SD)</td>
<td>36.3 (16.6)</td>
<td>31.4 (17.1)</td>
<td>33.6 (17.8)</td>
</tr>
</tbody>
</table>

• Groups were well balanced as to age, gender and race
Primary Endpoint: GA Lesion Growth

Modified Intent to Treat population (mITT). Observed, Mixed-Effect Model
A mixed effect model with main effects of treatment, visit and GA lesion at baseline, and interactions of treatment $\times$ visit, visit $\times$ baseline.
mITT = All subjects receiving at least one injection and having at least one FAF image after day 1
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Treatment effect independent of genetic biomarkers, including CFI

* p=0.067 vs Sham
† p=0.008 vs Sham
No differences were observed in visual outcomes between groups
New Onset Wet AMD

- 1% (n=1) in Sham Pooled
- 8% (n=6) in APL-2 Every Other Month
- 18% (n=15) in APL-2 Monthly

Subjects with new onset exudation in study eye:
- All subjects
New Onset Wet AMD

Subjects with new onset exudation in study eye

History/Presence of CNV Fellow Eye

No History/Presence of CNV Fellow Eye

- 0% (n=0)
- 14% (n=4)
- 29% (n=10)
- 2% (n=1)
- 4% (n=2)
- 10% (n=5)

Sham Pooled
APL-2 Every Other Month
APL-2 Monthly
## Adverse Event Profile

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>APL-2 Monthly N=86</th>
<th>APL-2 Every Other Month N=79</th>
<th>Sham Pooled N=81</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular SAEs in study eye*</td>
<td>4 (4.7%)</td>
<td>2 (2.5%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Systemic (non-ocular) SAEs</td>
<td>11 (12.8%)</td>
<td>23 (29.1%)</td>
<td>16 (19.8%)</td>
</tr>
<tr>
<td>Treatment related ocular AEs in the study eye</td>
<td>21 (24.4%)</td>
<td>11 (13.9%)</td>
<td>0</td>
</tr>
<tr>
<td>Treatment related systemic (non-ocular) AEs</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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<tr>
<th>Ocular SAEs</th>
<th>APL-2 Monthly N=86</th>
<th>APL-2 EOM N=79</th>
<th>Sham Pooled N=81</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endophthalmitis*</td>
<td>2 (2.3%)</td>
<td>1 (1.3%)</td>
<td>0</td>
</tr>
<tr>
<td>IOP increased</td>
<td>1 (1.2%)†</td>
<td>1 (1.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>1 (1.2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>0</td>
<td>0</td>
<td>1 (1.2%)</td>
</tr>
</tbody>
</table>

*2 culture positive for coagulase-negative Staphylococcus. 1 culture negative in the monthly group.
†2 events in a subject
Conclusions

- APL-2 slowed growth of GA, independent of genetics
- APL-2 appeared to increase risk of new onset wet AMD
  - No adverse impact on visual outcomes
- No safety issues preclude further development
Thank you to patients, investigators and staff!