Visual Functional Loss in Geographic Atrophy (GA): Learnings From Lampalizumab Trial Data

Usha Chakravarthy, FRCOphth, PhD, CBE

Neha Anegondi, MTech; Verena Steffen, MSc; and Daniela Ferrara, MD, PhD, FASRS

1 Royal Victoria Hospital (The Belfast Trust) and Queens University of Belfast, Belfast, Northern Ireland
2 Genentech, Inc., South San Francisco, CA

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Disclosures

Financial Disclosures

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  - Unrelated: Consultant: AbbVie, Alimera, Boehringer Ingelheim, DeepEye, Janssen, Kyowa Kirin, RetinaAI, Unity
- Data Safety Monitoring Board: Adverum, Oxurion

Study and Product Disclosures

- This presentation includes analyses of data from historical studies conducted in patients
- Institutional Review Board approval was obtained prior to study initiation
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Geographic Atrophy Is Pleomorphic

- GA lesions can vary in size, location, and appearance

Intervenitional trials have shown reductions in GA growth (measured by FAF) with no corresponding reduction in BCVA, a commonly used measure of retinal function.
Established GA Growth Rate Modifiers

A. Effective Radius Growth Rate in Center Point Involved GA is Lower than Center Point Spared GA

B. Effective Radius Growth Rate in Foveal Zone Involved GA is Lower than Foveal Zone Spared GA

However, data on changes in function by growth rate and by GA features at baseline are limited and come from small samples


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Published in Shen LL et al. Ophthalmol Retina. 2020.2

Lampalizumab Clinical Trial Data Used to Explore the Impact of GA Lesion Growth Rate on Retinal Function

Lampalizumab Program

The large, long-term lampalizumab clinical trials provide a rich and unique source of data to explore the impact of GA lesion growth rate on retinal function

Key Inclusion Criteria

- Age ≥ 50 years

**Study Eye**
- BCVA ≥ 49 letters (ETDRS)
- Well-demarcated area(s) of GA secondary to AMD with no active or prior CNV
- GA lesion size ≥ 2.54 mm² (1 DA) and ≥ 17.78 mm² (7 DAs)
- Banded or diffused hypoautofluorescence adjacent to GA area
- Sufficiently clear ocular media

**Fellow Eye**
- GA secondary to AMD with no active or prior CNV

Number of Eyes Per Study: Chroma (n = 858; NCT02247479), Spectri (n = 935; NCT02247531) and Proxima A (n = 269; NCT02479386)
• In a previous analysis of data from the Chroma and Spectri trials, Heier et al1 showed that the magnitude of the fall in BCVA was similar in subfoveal and extrafoveal lesions but more pronounced in unifocal vs multifocal lesions.


BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; GA, geographic atrophy; RPD, reticular pseudodrusen.
The present analysis explored the effect of lesion characteristics and GA growth rate quartiles on BCVA loss using a time-to-event approach.
KM Plots of Time to 5-, 10-, and 15-Letter Loss

Cox regression model adjusted for baseline characteristics, including BCVA, GA area, foveal involvement, and focality

**METHODS**
- 5-letter loss occurred in 50% of study eyes by 12 months and 75% by 24 months
- 10-letter loss occurred in 50% by 24 months
- 15-letter loss occurred in 25% by 24 months

**RESULTS**

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<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>15</th>
<th>18</th>
<th>21</th>
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<tr>
<td>5-letter loss</td>
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<td>2044</td>
<td>1535</td>
<td>1228</td>
<td>948</td>
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<td>582</td>
<td>559</td>
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<td>10-letter loss</td>
<td>2044</td>
<td>2044</td>
<td>1799</td>
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<td>1434</td>
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</tbody>
</table>

BCVA, best-corrected visual acuity; GA, geographic atrophy; KM, Kaplan–Meier.
KM Plots by Baseline Characteristics

The probability of loss of 5, 10, and 15 letters was generated by KM analysis for baseline BCVA, GA size, foveal involvement and focality.

**METHODS**
- Baseline BCVA, GA area, and foveal involvement did not influence the rate of BCVA loss.
- Time-to-BCVA loss of 5 letters was faster in unifocal compared with multifocal lesions.

**RESULTS**

Time-to-BCVA loss for 5 letters is shown in the above figures. BCVA, best-corrected visual acuity; GA, geographic atrophy; KM, Kaplan–Meier; Q, quarter.
KM Plots of Time To 5-, 10-, and 15-Letter Loss by GA Growth Rate Quartiles

METHODS

- GA growth rate was calculated for each eye and took into account all area measurements during the 2-year follow-up
- Growth rate quartiles were generated KM curves and plotted for 5-, 10-, and 15-letter loss

RESULTS

- Study eyes classified in higher GA growth rate quartiles experienced shorter times to 5-, 10-, and 15-letter losses.
Take-Home Messages

- 2 years after enrollment into studies of GA, some three-quarters of eyes will have lost 5 letters of BCVA and one-quarter will have lost 15 letters.
- Most baseline features did not influence rapidity of BCVA loss except for focality, with unifocal lesions losing BCVA at a faster rate.
- Fast-growing lesions in higher quartiles of GA growth experienced more rapid losses of BCVA compared with slow-growing lesions.
- Time-to-event analyses based on pragmatic measures of vision have the potential to discriminate between eyes with slower versus more rapid GA lesion growth.

BCVA, best-corrected visual acuity; GA, geographic atrophy.
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