Twelve-month Natural History Study of CEP290-associated Retinal Degeneration

Bright S. Ashimatey1, Thiran Jayasundera2, Eric A. Pierce3, Carel Hoyng4, Byron L. Lam5, Marc Dellacanonica1, Keunpyo Kim1, Alia Rashid1, Rene Myers1, Mark E. Pennesi6

1Edits Medicine Inc., Cambridge, MA, USA; 2University of Michigan Kellogg Eye Center, Ann Arbor, MI, USA; 3Ocular Genomics Institute, Massachusetts Eye and Ear, Boston, MA, USA; 4Radboud University, Nijmegen, The Netherlands; 5Bascom Palmer Eye Institute, Miami, FL, USA; 6Casey Eye Institute, Oregon Health & Science University, Portland, OR, USA

To define the clinical characteristics of CEP290-associated IRD caused by the c.2991+1655A>G IVS26 mutation and to determine which assessments may provide reliable endpoints in future interventional trials.

METHODS

• Patients with CEP290-associated IRD and best-corrected visual acuity (BCVA) from light perception to 0.4 logMAR were recruited in eight cohorts that spanned four age ranges (3–5, 6–11, 12–17, ≥ 18 years) and two BCVA ranges (light perception to > 1.0 logMAR, 1.0 logMAR to 0.4 logMAR).

• Functional outcomes included BCVA, full-field stimulus threshold (FST) sensitivity, and Visual Navigation Challenge (Ora-VNC®) composite score.

• Optical coherence tomography–outer nuclear layer (OCT–ONL) thickness was included as an anatomical outcome.

• BCVA, FST sensitivity, VNC composite score, and OCT–ONL thickness were assessed at screening, baseline test, baseline retest, and months 3, 6 and 12 (Figure 1).

RESULTS

Baseline Characteristics of Participants

• Nineteen of 26 enrolled participants were female.

• At screening, 13/16 adult and 9/10 pediatric participants had BCVA > 1.0 logMAR. At baseline, median (range) BCVA was 2.0 (0.5–3.9) logMAR.

• BCVA was not correlated with age or zygosity.

• BCVA mean (SD) between-eye difference was 0.13 (0.27) logMAR, with ~73% of participants having a between-eye difference ≤ 0.1 logMAR (Figure 2).

• There were no between-eye differences in FST, VNC score, or OCT–ONL thickness.

Test-retest Variability and Stability at 12 Months

• Table 1 presents assessment test-retest variability and stability. A greater than expected test-retest variability was observed for OCT–ONL average thickness.

• Table 1. Assessment Variability and Stability at 12 Months

<table>
<thead>
<tr>
<th>Assessment (Worse eye)</th>
<th>N</th>
<th>Mean (95% CI) change from baseline to test-retest</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCVA (logMAR)</td>
<td>25</td>
<td>-0.04 (-0.09, 0.01)</td>
</tr>
<tr>
<td>VNC composite score</td>
<td>18</td>
<td>0.6 (0.1, 1.3)</td>
</tr>
<tr>
<td>Red FST (log cd/m²)</td>
<td>14</td>
<td>0.01 (-0.07, 0.27)</td>
</tr>
<tr>
<td>OCT–ONL avg thickness</td>
<td>14</td>
<td>0.1 (0.0, 0.2)</td>
</tr>
<tr>
<td>OCT–ONL central thickness</td>
<td>14</td>
<td>-0.13 (-0.23, 0.0)</td>
</tr>
</tbody>
</table>

• Baseline BCVA, two standard deviations below the mean in one or both eyes, was observed for all participants.

• A large BCVA decline from baseline to 12 months was noticed for two participants, one of whom was observed to have had intra-retinal cysts across the study visits.

BCVA is Stable over 12 Months

• Across age groups, mean (95% CI) change in BCVA from baseline to 12 months was 0.06 (-0.17, 0.29) logMAR, indicating good stability (Figure 3).

• Figure 3. Change in BCVA from Baseline to 12 Months

CONCLUSION

• BCVA, FST, and VNC composite score demonstrated good test-retest variability and stability over 12 months.

• BCVA, FST, and VNC composite score are viable endpoints for future clinical studies in patients with CEP290-associated IRD.

• Repeatability of OCT measures poses potential challenges for quantifying anatomical changes in this population as nystagmus impact ability to repeat measures at the same retinal location.

• The mostly stable nature of retinal degeneration and the similarity in disease trajectory between eyes opens the possibility of using the contralateral eye as a within-subject control in future interventional trials in patients with CEP290-associated IRD.

REFERENCES


DISCLOSURES

At the time of abstract submission, BSA, MD, KK, AR, and RM were employees of Edits Medicine. MP is a paid consultant for Editas Medicine.

ACKNOWLEDGEMENTS

This work was funded by Edits Medicine. The authors would like to thank all Edits colleagues for helping to plan, perform, analyze, and present this work. Editorial assistance was provided by Shervone Poitoe, PhD of Porthouse Medical, and was funded by Edits Medicine in accordance with Good Publication Practice (GPP) guidelines.

© 2023 Edits Medicine