Neurofilament Light Chain (NfL) as a Potential Biomarker of Treatment Response in Hereditary Transthyretin-Mediated Amyloidosis: Data from the Patisiran Global OLE Study

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Conclusions

- Patisiran treatment lowered levels of neurofilament light chain (NfL) in patients with hereditary transthyretin-mediated (hATTR) amyloidosis, also known as ATTR amyloidosis, with neuroprogression and led to sustained and dramatic improvement in neuropathy versus parent study baseline1-7
- NfL levels were lower in patients with less severe disease, supporting the potential relationship between NfL and disease activity in hATTR amyloidosis

Results

Table 1. Patient demographics and disease characteristics at Global OLE baseline

<table>
<thead>
<tr>
<th>NfL Study</th>
<th>OLE Baseline</th>
<th>APOLLO Baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NfL C</td>
<td>29.0 (15.0)</td>
<td>44.0 (21.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NfL B</td>
<td>37.5 (16.0)</td>
<td>50.0 (24.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NfL A</td>
<td>51.0 (23.0)</td>
<td>64.0 (21.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Background

- The NfL threshold of 37 pg/mL, which was previously reported to distinguish between healthy controls and patients with hATTR amyloidosis with polyneuropathy7, would include many Phase 2 OLE patients and, therefore, underscores the need for further research into additional NfL level thresholds that may be age or disease severity-dependent

- Although the NfL levels of patients in the APOLLO-placebo group were decreased to a similar value with the APOLLO-patisiran group at 24 months in the Global OLE, their overall clinical burden remained higher, indicating the value of earlier intervention

Methods

- The reduction of NfL levels from baseline in the Global OLE study may indicate that NfL measurement could further improve the precision of clinical endpoints in Phase 3 studies and aid in the interpretation of clinical trials for patients with hATTR amyloidosis

Figure 1. Study design with participants who had NfL levels measured, showing APOLLO and Phase 2-OLE enrollment in the Global OLE, and healthy controls

NfL Sample Collection

- Placebo=74.6 (4.2); APOLLO placebo=74.0 (4.3); Global OLE placebo=74.6 (4.2); Global OLE patient=74.6 (4.2)

Figure 2B. Numerical change in NfL levels in (A) APOLLO and Global OLE and (B) the Phase 2 OLE and Global OLE

Figure 3B. Numerical change in NfL levels in (A) APOLLO and Global OLE and (B) the Phase 2 OLE and Global OLE

Figure 4B. Levels measured in NfL in the APOLLO placebo group and a similar level in the Global OLE placebo group

There are no patients, patient identifiers, research study, and collaborations for this section. See Figure 2B, APOLLO, and the placebo.

Abbreviations: OLE: Open Label Extension; APOLLO: Amyloidosis Polyneuropathy Outcome with Patisiran Long-term Options Observational Long-term study; Global OLE: Norfolk Quality of Life in Amyloidosis Global Open Label Extension; OLE Baseline: Amyloidosis Polyneuropathy Outcome with Patisiran Long-term Options Observational Long-term study (matched to APOLLO patients’ baseline demographics); APOLLO Baseline: Amyloidosis Polyneuropathy Outcome with Patisiran Long-term Options Observational Long-term study; Global OLE Baseline: Norfolk Quality of Life in Amyloidosis Global Open Label Extension (matched to APOLLO patients’ baseline demographics)