Efficacy and Safety of Faricimab Every 16 or 12 Weeks for Neovascular Age-Related Macular Degeneration: STAIRWAY Phase 2 Results

Key Clinical Question

What is the efficacy of faricimab dosed every 16 weeks (Q16W) or every 12 weeks (Q12W) compared with ranibizumab dosed every 4 weeks (Q4W) for the treatment of neovascular age-related macular degeneration (nAMD)?

Introduction

• Angiopoietin-2 (Ang-2) and vascular endothelial growth factor (VEGF) are key drivers of neovascularization, with Ang-2 also driving vessel destabilization and inflammatory signaling; both are upregulated in patients with nAMD and Faricimab, the first bispecific antibody designed for intravitreal use, binds and neutralizes both Ang-2 and VEGF-A.

• The phase 2 AVENUE (NCT02484690) study for nAMD demonstrated that the efficacy and safety of faricimab dosed at Q4W and Q8W intervals (1.5 mg and 6.0 mg doses) were comparable with ranibizumab Q4W

Methods

• STAIRWAY (NCT03388880) assessed the efficacy, durability, and safety of Q16W flex and Q12W faricimab compared with Q4W ranibizumab in patients with nAMD.

• A disease activity assessment was performed at week 24 (Figure 4).

• Patients randomized to the Q16W flex arm who had active disease at week 24 received treatment Q12W until the end of the trial.

Conclusions

• At week 40 and 52 endpoints, Q16W and Q12W faricimab dosing resulted in meaningful and fully sustained vision gains compared with Q4W ranibizumab.

• There were no new or unexpected safety signals, showing a safety profile comparable with ranibizumab.

• Simultaneous neutralization of Ang-2 and VEGF may reduce vascular destabilization and leakage, leading to improved durability in nAMD compared with anti-VEGF treatment alone.

• Two global phase 3 trials evaluating faricimab for nAMD, TENAYA (NCT03823287) and LUCERNE (NCT03823300), are currently recruiting worldwide.

1. Faricimab is the First Bispecific Antibody Designed for Intravitreal Use

- Anti-Ang-2 Fab
- Enhanced vessel stabilization through Ang-2 inhibition
- Anti-VEGF-A Fab
- Proven efficacy through VEGF-A inhibition
- Modified Fc
- Reduced systemic exposure
- Reduced inflammatory potential
- 1 molecule, 2 targets

2. STAIRWAY Was Designed to Evaluate Q16W and Q12W Dosing With Faricimab in nAMD

- 2:2:1 randomized design for 3 treatment arms.
- Data from 1 site is excluded from the analyses owing to protocol violations.

3. Baseline Characteristics Were Relatively Equally Balanced Across Treatment Arms

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Q4W (n = 16)</th>
<th>Q16W Flex (n = 28)</th>
<th>Q12W (n = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (SD)</td>
<td>77.7 (8.3)</td>
<td>80.3 (7.2)</td>
<td>77.3 (10.3)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>10 (62.5)</td>
<td>15 (53.6)</td>
<td>8 (33.3)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>14 (87.5)</td>
<td>25 (89.3)</td>
<td>20 (83.3)</td>
</tr>
<tr>
<td>BCVA, best-corrected visual acuity at baseline</td>
<td>20/20</td>
<td>20/20</td>
<td>20/20</td>
</tr>
<tr>
<td>ETDRS, Early Treatment Diabetic Retinopathy Study,</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>CST, central subfield thickness</td>
<td>400 µm</td>
<td>400 µm</td>
<td>400 µm</td>
</tr>
<tr>
<td>Central subfield thickness, mean (µm)</td>
<td>204.2 (50.8)</td>
<td>211.3 (56.1)</td>
<td>204.6 (50.7)</td>
</tr>
</tbody>
</table>

4. At Week 24, 12 Weeks After the Last Loading Dose, Disease Activity Was Assessed Using 6 Per-Protocol-Defined Criteria

- 50 µm versus average CST over last 2 visits on SD-OCT
- 75 µm versus average CST over last 2 visits on SD-OCT
- ≥20 letters of BCVA versus average BCVA over last 2 visits
- ≥10 letters of CST versus average CST over last 2 visits
- Presence of any new macular hemorrhage
- Any other death

5. Q16W Flex and Q12W Faricimab Resulted in Full Maintenance of Robust Vision Gains Compared With Q4W Ranibizumab

- At week 40 and 52 endpoints, Q16W and Q12W faricimab dosing resulted in meaningful and fully sustained vision gains compared with Q4W ranibizumab.

- No new or unexpected safety signals were observed.

6. Q16W Flex and Q12W Faricimab Were Comparable With Q4W Ranibizumab in the Proportion of Patients Gaining or Maintaining Vision at Week 52

- No new or unexpected safety signals were observed.