Effect of Dual Angiopoietin-2/VEGF-A Inhibition with Faricimab on Macular Anatomy in the STAIRWAY Phase 2 Study of Neovascular Age-Related Macular Degeneration (nAMD)

Eleonora Lad, MD, PhD
Durham, NC

Hugh Lin, MD, MBA, David Silverman, MSc, MBChB, MRCOphth, FFPM, Karen Basu, PhD, Carlos Quezada Ruiz, MD, Zdenka Haskova, MD, PhD

Purpose:

Faricimab is a bispecific antibody that binds and neutralizes both Angiopoietin-2 (Ang-2) and VEGF-A. In preclinical studies, dual Ang-2/VEGF-A inhibition synergistically reduced inflammation, leakage and neovascularization, indicating vascular stabilization effect through combined Ang-2 and VEGF neutralization. The goal of this work was to examine the anatomical effects of faricimab in the Phase 2 nAMD STAIRWAY study using multimodal imaging in the context of the preclinical data and Ang-2 biology.

Methods:

STAIRWAY (NCT03038880) was a 52-week, multicenter, randomized, active comparator–controlled, parallel-group, phase 2 trial. Treatment-naïve nAMD patients were randomized 2:2:1 to faricimab 6.0 mg every 16 weeks (Q16W) flexible (flex) dosing or Q12W fixed (both with four Q4W initiation injections) or ranibizumab 0.5 mg Q4W. Patients in the Q16W flex arm with protocol-defined disease activity at Week 24 were switched to Q12W dosing. No rescue treatment was allowed. Anatomical changes were evaluated by spectral domain optical coherence tomography (SD-OCT), OCT angiography and fluorescein angiography.

Results:

In STAIRWAY, improvements in best-corrected visual acuity with faricimab Q16W flex and Q12W were comparable with ranibizumab Q4W. No new or unexpected safety signals were identified. Mean (80% CI) change in central subfield thickness from baseline were similar between the ranibizumab Q4W, faricimab Q12W, and faricimab Q16W flex arms. Change from baseline in CNV component area was $-4.8$, $-5.6$, and $-4.3 \text{ mm}^2$, respectively; change from baseline in neovascular leakage area was $-5.3$, $-5.6$, and $-4.6 \text{ mm}^2$.

Conclusions:

Visual and anatomical improvements observed in the phase 2 STAIRWAY trial support preclinical evidence indicating that simultaneous Ang-2/VEGF-A neutralization results in sustained vascular stability, reduced leakage and anti-angiogenic effects, leading to sustained efficacy and durability of treatment effect beyond anti-VEGF monotherapy. Two large, global, phase 3 trials (TENAYA and LUCERNE) are currently underway to further investigate the efficacy and durability of faricimab compared to aflibercept in nAMD.