Safety and Efficacy of Different Doses and Regimens of Faricimab vs Ranibizumab in Neovascular Age-Related Macular Degeneration: The AVENUE Phase 2 Randomized Clinical Trial

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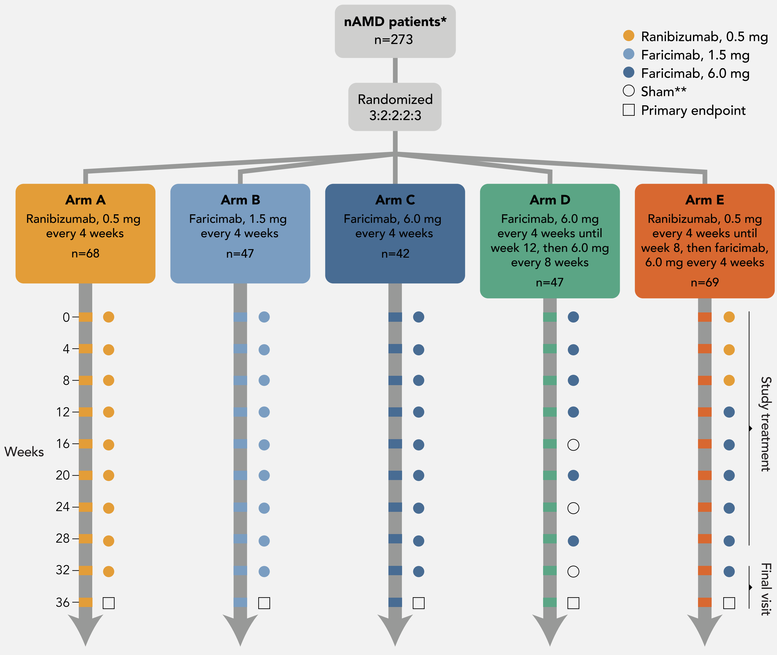
Although anti-vascular endothelial growth factor (anti-VEGF) monotherapy has become the standard-of-care treatment for patients with neovascular age-related macular degeneration (nAMD), selective VEGF-A neutralization may not completely inhibit choroidal neovascularization and nAMD development. As many patients are unable to achieve and maintain the visual outcomes observed in clinical trials, alternative, multitarget therapies with improved efficacy and extended durability are needed for patients with nAMD.

Faricimab is the first bispecific antibody designed for intraocular use. It simultaneously and independently binds and neutralizes angiopoietin 2 in addition to vascular endothelial growth factor A (VEGF-A). Previous randomized clinical trials (RCTs) of faricimab have resulted in favorable structural outcomes as well as significant improvement in best-corrected visual acuity (BCVA) compared with ranibizumab (BOULEVARD phase 2 RCT). The present AVENUE trial assessed the safety and efficacy of different doses and regimens of faricimab, compared with ranibizumab, in patients with nAMD.

AVENUE was a 36-week, multiple-dose-regimen, active comparator-controlled, double-masked, phase 2 randomized clinical study performed at 58 sites in the United States.



Primary Outcomes

- Mean change in BCVA from baseline to week 36.
- Proportion of participants gaining at least 15 letters.
- BCVA of 20/40 or better or 20/200 or worse.
- Ocular coherence tomographic outcomes in anti-VEGF treatment-naive participants (arms A, B, C, D) and from weeks 12 to 36 in those with incomplete response (participants in arms A and E with week 12 BCVA ETDRS letter score of ≤68 [Snellen equivalent, 20/50 or worse]).

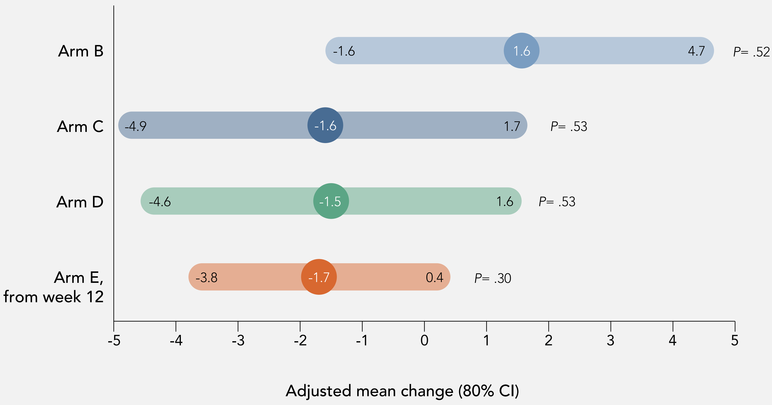
BCVA = best-corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study.

*Eligible participants were anti-VEGF treatment naive with choroidal neovascularization secondary to nAMD and BCVA ETDRS letter score of 73 (Snellen equivalent, 20/40) to 24 (Snellen equivalent, 20/320).

**Sham injections were administered to maintain double masking in arm D throughout the fixed every-8-weeks regimen period at weeks 16, 24, and 32.

There were no statistically significant differences in BCVA between any of the faricimab treatment arms and the monthly ranibizumab control arm at week 12 or week 36.

Adjusted mean change in BCVA vs ranibizumab from baseline at week 36



- Ocular and systemic safety findings for faricimab observed in AVENUE were comparable with the safety profile of intravitreal anti-VEGF monotherapy with ranibizumab.

CI = confidence interval.

Conclusions

Participants treated with faricimab every 4 or 8 weeks had a mean change in visual acuity that was neither superior nor inferior to that of participants receiving monthly ranibizumab. Thus, AVENUE did not meet its primary end point of superiority of faricimab over ranibizumab in BCVA at week 36. However, overall visual and anatomical gains noted with faricimab support pursuing phase 3 trials for a potential alternative to monthly anti-VEGF therapy.