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Wet AMD Symposium 3

Exudative Age-Related Macular Degeneration Events from the OAKS and DERBY Clinical Trials of Pegcetacoplan in Geographic Atrophy

- Roger Goldberg, MD, MBA
- Min Tsuboi
- Mark Burch
- Ramiro Ribeiro, PhD

Objective: To characterize exudative age-related macular degeneration (eAMD) events that occurred in two Phase 3 clinical trials of pegcetacoplan in patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD).
Purpose: OAKS and DERBY, two 24-month, Phase 3, randomized, double-masked, sham-controlled clinical trials, compared the efficacy and safety of intravitreal pegcetacoplan monthly (PM) or every-other-month (PEOM) with sham treatment in patients with GA secondary to AMD. We provide information on events of investigator-determined new-onset eAMD in OAKS and DERBY.
Methods: Enrolled patients (OAKS: N=637; DERBY: N=621) were ≥60 years old, had best-corrected visual acuity ≥24 Early Treatment Diabetic Retinopathy Study letters, with baseline GA lesion area between 2.5 and 17.5 mm^2 or at least one focal lesion ≥1.25 mm^2, if multifocal. Studies were combined for this safety analysis (PM n=419; PEOM n=420; sham n=417). Patients with eAMD received on-label anti-vascular endothelial growth factor (VEGF) therapy at the investigator's discretion.
Results: Nearly 12,000 pegcetacoplan injections were administered over 2 years. At 24 months, pegcetacoplan was generally well tolerated, with a safety profile consistent with that reported at 12 and 18 months. Rates of investigator-determined new-onset eAMD were 12.2% PM, 6.7% PEOM and 3.1% sham, 75% of which were confirmed by the reading center during the study. The presence/absence of double-layer sign at baseline did not meaningfully affect eAMD rates, although rates were lower in patients who did not have fellow eye choroidal neovascularization at baseline (11.0% PM, 5.6% PEOM, 1.5% sham) (Table 1). Time to development of eAMD averaged 372, 282, and 223 days for PM, PEOM and sham, respectively. One patient (sham arm) discontinued the study owing to eAMD. No serious adverse events (SAEs) of eAMD were reported. The majority (85.7%) of eAMD cases were classified as occult lesions. Most patients who developed eAMD (98.0% PM [n=50], 96.4% PEOM [n=27], 84.6% sham [n=11]) were treated with anti-VEGF injections, and received a mean of 0.53, 0.52, and 0.45 injections per month following eAMD diagnosis.
Conclusion: Pegcetacoplan was generally well tolerated over 24 months. While the rates of eAMD were higher in the pegcetacoplan arms versus sham, there were no SAEs nor study discontinuations due to eAMD among those treated with pegcetacoplan, and patients were able to safely continue both anti-VEGF and pegcetacoplan.

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OAKS and DERBY combined

	PM	PEOM[b]	Sham Pooled
New-onset eAMD, 0–12 months[a], n/N (%)	25/419 (6.0%)	17/419 (4.1%)	10/417 (2.4%)
Without fellow eye CNV at baseline, n/N (%)	19/335 (5.7%)	13/338 (3.8%)	3/330 (0.9%)
New-onset eAMD, 0–24 months[a], n/N (%)	51/419 (12.2%)	28/419 (6.7%)	13/417 (3.1%)
Without fellow eye CNV at baseline, n/N (%)	37/335 (11.0%)	19/338 (5.6%)	5/330 (1.5%)

[a]Events include preferred terms of CNV and neovascular AMD. [b]Number of patients at risk for new-onset eAMD in PEOM arms from OAKS and DERBY combined was 419.
AMD=age-related macular degeneration; CNV=choroidal neovascularization; eAMD=exudative AMD; N=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan every month.

Incidence of new-onset eAMD at Months 12 and 24 in OAKS and DERBY

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Additional Visual and Anatomic Outcomes of Intravitreal Aflibercept Injection, 8 mg vs 2 mg: Post Hoc Analysis of the Phase 2 CANDELA Study

Priya Vakharia, MD

Objective: To examine the effect of intravitreal aflibercept 8 mg on visual and anatomic outcomes in patients with neovascular age-related macular degeneration (nAMD).
Purpose: This analysis aimed to understand additional visual and anatomic benefits with aflibercept 8 mg as compared with aflibercept 2 mg.
Methods: In CANDELA, treatment-naive patients with nAMD were randomized to receive 3 monthly doses of either aflibercept 2 mg (n=53) or aflibercept 8 mg (n=53) followed by doses at Weeks 20 and 32. This post hoc analysis was conducted to assess the proportion of eyes without intraretinal fluid (IRF), subretinal fluid (SRF), or sub–retinal pigment epithelium (RPE) fluid in the central subfield at Weeks 16 and 44; proportion of eyes that achieved >239 µm reduction in central subfield thickness (CST), ≥15-letter gain, best-corrected visual acuity (BCVA) ≥20/40, and BCVA ≥20/20 at Week 44; and proportion of eyes with baseline BCVA <20/40 that achieved ≥10- and ≥15-letter gains at Week 44.
Results: For eyes receiving aflibercept 8 mg versus those receiving aflibercept 2 mg, the proportion of eyes without IRF, SRF, or sub-RPE fluid in the central subfield was 38% versus 19% at Week 16, respectively (nominal *P*=0.031), and 25% versus 11% at Week 44 (nominal *P*=0.076). At Week 44, a greater proportion of eyes had >239 µm reduction in CST with aflibercept 8 mg versus aflibercept 2 mg (27% vs 20%). Additionally, at Week 44, a greater proportion of eyes in the aflibercept 8 mg versus aflibercept 2 mg group gained ≥15 letters (33% vs 14%), achieved BCVA ≥20/40 (61% vs 49%), and achieved BCVA ≥20/20 (10% vs 2%). Conversely, a smaller proportion of eyes had vision loss or no BCVA change at Week 44: 20% versus 27% in the aflibercept 8 mg and aflibercept 2 mg groups, respectively. Among eyes with baseline BCVA <20/40, a greater proportion in the aflibercept 8 mg versus aflibercept 2 mg group gained ≥10 letters (65% vs 47%) and ≥15 letters (43% vs 18%) at Week 44.
Conclusion: Eyes treated with aflibercept 8 mg achieved improved visual and anatomic outcomes, suggesting potential therapeutic benefit compared with aflibercept 2 mg in patients with nAMD.

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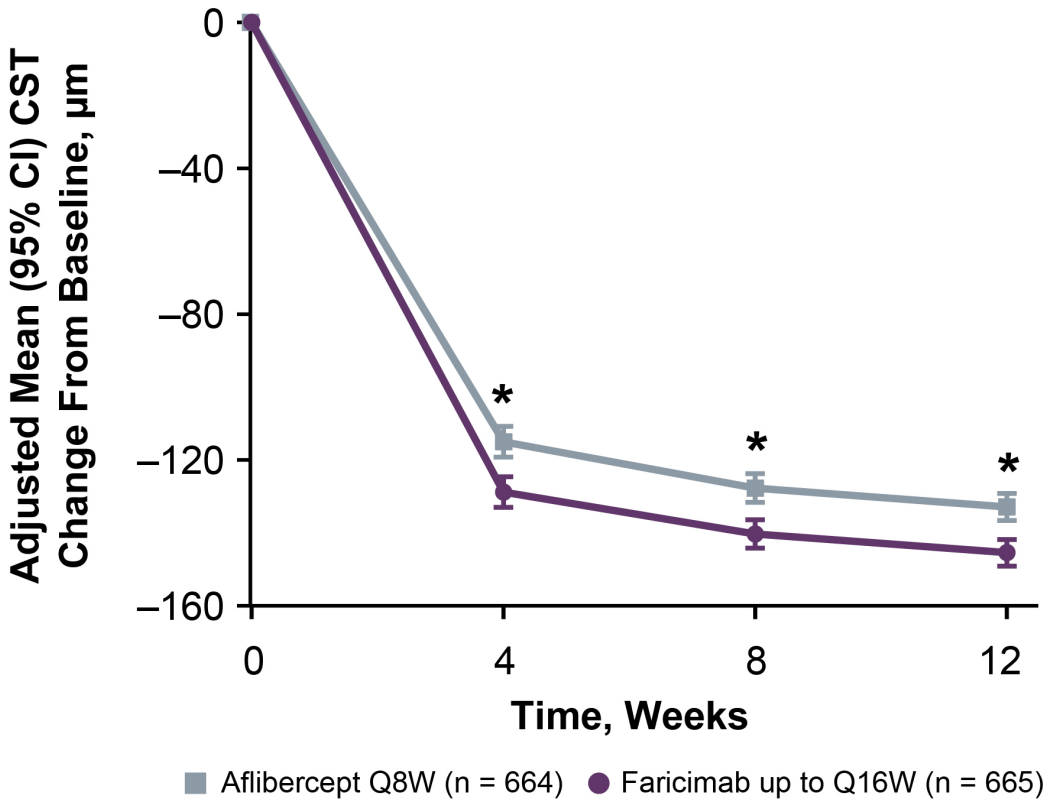
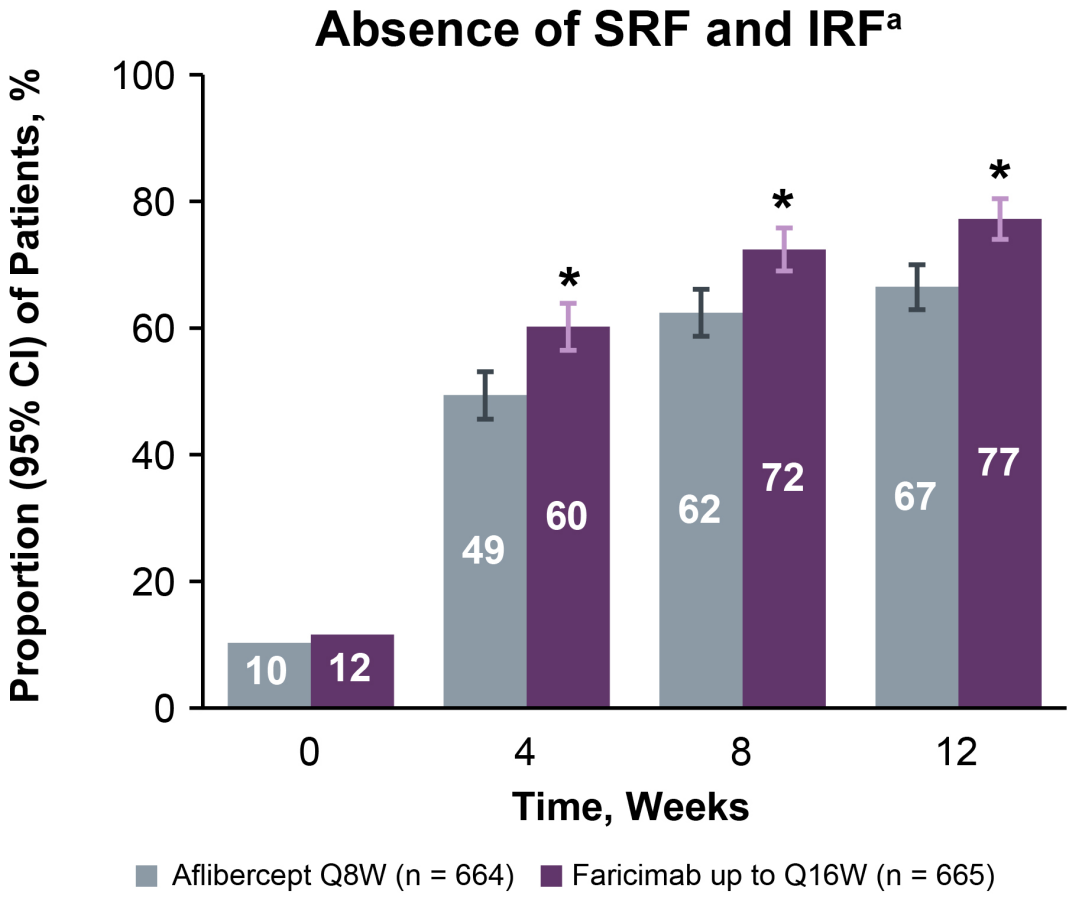
Faricimab Rapidly Improves Fluid Parameters in Patients With nAMD

- Nikolas London, MD, FACS, FASRS
- Giuseppe Querques
- Aachal Kotecha, PhD
- Jeffrey Willis, MD/PhD
- Audrey Souverain, PharmD, MSc
- Yevgeniy Shildkrot, MD
- Philippe Margaron

Objective: To evaluate anatomical outcomes, including fluid resolution, in patients with nAMD during the initial matched-dosing period of the TENAYA/LUCERNE trials.
Purpose: Year 2 data from the phase 3 TENAYA/LUCERNE (NCT03823287/NCT03823300) trials demonstrated that faricimab, a dual angiopoietin-2 (Ang-2)/vascular endothelial growth factor-A (VEGF-A) inhibitor, maintained vision with extended treatment durability and fewer injections versus aflibercept. The purpose of this analysis was to evaluate fluid outcomes, including the time to first absence of fluid in patients with neovascular age-related macular degeneration (nAMD).
Methods: TENAYA/LUCERNE were double-masked, active comparator–controlled, 112-week trials. Treatment-naïve patients (pooled N = 1329) were randomized 1:1 to faricimab 6.0 mg up to every 16 weeks (Q16W; n = 665) based on protocol-defined disease activity criteria, with fixed up to Q16W dosing in the first year and a treat-and-extend regimen (personalized treatment interval per protocol) in the second or aflibercept 2.0 mg Q8W (n = 664). In this post hoc analysis, change in central subfield thickness (CST), absence of subretinal and intraretinal fluid (SRF and IRF), and time to absence of SRF and IRF were assessed in the faricimab versus aflibercept arms during the initial matched-dosing period through week 12.
Results: At the end of the matched-dosing period, the reduction in CST from baseline was significantly greater in eyes treated with faricimab versus aflibercept (week 12: –145 vs –133 μm; $P \leq 0.0001$; Fig 1). Likewise, a significantly larger proportion of patients achieved absence of SRF and IRF with faricimab versus aflibercept (week 12: 77% vs 67%; $P \leq 0.0001$; Fig 1). In patients with SRF and IRF at baseline, absence of IRF and SRF was achieved faster and with fewer injections with faricimab versus aflibercept. Specifically, the 75th percentile of first absence of IRF and SRF was reached at week 8 for patients treated with faricimab versus week 12 with aflibercept (corresponding median number of injections: 2 vs 3).
Conclusion: Dual inhibition of Ang-2 and VEGF-A with faricimab resulted in more rapid improvement in anatomical outcomes, including absence of fluid, in patients with nAMD during the matched-dosing period in TENAYA/LUCERNE.

IRB APPROVAL Yes





*$P \leq 0.0001$ for faricimab vs aflibercept. [a]IRF and SRF are as measured in the central subfield (center 1 mm). CST, central subfield thickness; IRF, intraretinal fluid; Q8W, every 8 weeks; Q16W, every 16 weeks; SRF, subretinal fluid.

Change from baseline in CST/proportion of patients with SRF and IRF

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Early Treatment Patterns and Outcomes in Patients With Neovascular Age-Related Macular Degeneration Initiating Faricimab: The FARETINA-AMD Study

- Theodore Leng, MD, MS, FASRS
- David Tabano, PhD
- Vincent Garmo, MHS
- Durga Borkar, MD
- Jacqueline Shaia
- Blanche Kuo, BS
- Rachel Myers
- Andrew LaPrise
- Rishi Singh, MD

Objective: To describe real world treatment patterns and early clinical response of nAMD patients initiating faricimab.
Purpose: Anti-Vascular Endothelial Growth Factor (VEGF) intravitreal agents are the standard of care for neovascular age-related macular degeneration (nAMD), and require frequent injections. Faricimab is the only bispecific antibody for intraocular use that binds angiopoietin-2 and VEGF-A. Limited real-world data exists on treatment patterns and outcomes of faricimab. FARETINA-AMD describes the largest real-world evaluation of injection frequency and early clinical response of nAMD patients initiating faricimab.
Methods: FARETINA-AMD is a retrospective real world study using electronic health record (EHR) data from the IRIS registry. Data was analyzed February-September 2022 to identify faricimab starts among patients diagnosed with nAMD. Rules-based text search using regular expression keywords was used to identify faricimab use. Patients with ≥ 12 months of EHR data prior to initiation and known laterality were included. Patients with ≥6 months of EHR data following faricimab initiation (through December 2022) were included in the analyses of injection intervals. Injection intervals were categorized as “extended” if any interval was >6 weeks apart.
Results: 15,533 eyes (13,436 patients) were treated with faricimab for nAMD, with a mean (SD) of 3.4 (1.7) injections over a mean (SD) of 127.9 (64.8) days of follow-up. 2,351 (15.1%) of eyes were anti-VEGF treatment naïve; 13,182 (84.9%) were previously treated. Most (54.7%) previously treated eyes had been treated with aflibercept. Nearly half of eyes (45.2% treatment naïve; 47.3% previously treated) had 20/40 or better BDVA at initiation of faricimab.

520 (22.1%) treatment naïve and 3,192 (24.2%) previously treated eyes had ≥6 months follow-up. Mean (SD) faricimab injections were 4.8 (2.1) and 4.6 (2.3) for previously treated and treatment naïve eyes, respectively. 397 (76.3%) of treatment naïve eyes (2,624 (82.2%) of previously treated eyes) “extended” in 1-3 injections.
Conclusion: Over 15,000 eyes were initiated faricimab for nAMD in the US through September 2022. Among eyes with ≥ 6 months of follow-up, a majority of eyes began extending treatment intervals within 1-3 initial doses. Early treatment extensions may indicate positive anatomical response to faricimab for nAMD patients.

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Real-World Efficacy and Safety of Faricimab in Neovascular Age-Related Macular Degeneration: The TRUCKEE Study

- Emmanuel Chang, MD PhD FACS FASRS
- Aamir Aziz, BS
- Hannah Khan, MPH
- Ohidul Mojumder
- Nicole Somani, MD, MPH
- Ashkan Abbey, MD, FASRS, FAAO
- David Almeida, MD, MBA, PhD, DABO, FRCSC, FASRS
- Robert Avery, MD
- Himanshu Banda, MD
- Mark Barakat, MD
- Ramanath Bhandari, MD
- Sara Haug, MD, PhD
- Nikolas London, MD, FACS, FASRS
- Jared Nielsen, MD, MBA
- Veeral Sheth, MD, MBA, FASRS, FACS
- Jeremy Wolfe, MD, MS
- Michael Singer, MD
- Carl Danzig, MD
- Arshad Khanani, MD, MA, FASRS

Objective: This multi-center, prospective study evaluates the safety and efficacy of faricimab in real-world patients diagnosed with neovascular age-related macular degeneration (nAMD).
Purpose: Faricimab was FDA-approved for nAMD in Jan 2022. Current agents provide benefit to patients but demonstrate declines in visual acuity as treatments continue. Faricimab is the first bispecific agent inhibiting dual pathways to provide comparable efficacy and safety to current agents while demonstrating increased durability, and is investigated in this real-world prospective study.
Methods: This multi-center prospective study investigates faricimab treatment for nAMD in both treatment-naïve patients and patients switched to faricimab from other anti-VEGF agents. Data collected includes demographics, treatment history, best-corrected visual acuity (BCVA), central subfield thickness (CST), and presence of subretinal or intraretinal fluid (SRF or IRF). Snellen visual acuity was converted to the Early Treatment Diabetic Retinopathy Study (ETDRS) scoring. Improvements in visual acuity and CST are evaluated as averages. Improvements in retinal fluid are evaluated as a proportion of patients. Observed and calculated data is reported. Safety is summarized.
Results: A total of 670 eyes across 584 patients were recorded. Of the 475 eyes with at least one follow-up, 60.4% had switched from aflibercept (AFL). All eyes post one faricimab injection (n=475) had a BCVA increase of +0.98 letters (p=0.025), a CST decrease of -30.99mm (p<0.00001), and SRF/IRF resolution rates of 33.6% and 15.1%. Eyes switched from AFL post one faricimab injection (n=287) had a BCVA increase of +0.36 letters (p=0.75), a CST decrease of -25.73mm (p<0.00001), and SRF/IRF resolution rates of 32.0% and 9.4%. All eyes post three faricimab injections (n=213) had a BCVA increase of +3.17 letters (p=0.001), a CST decrease of -45.04mm (p<0.00001), and SRF/IRF resolution rates of 38.1% and 31.1%. Eyes switched from AFL post three faricimab injections (n=140) had a BCVA increase of +2.89 letters (p=0.008), a CST decrease of -40.74mm (p=0.00007), and SRF/IRF resolution rates of 37.3% and 15.7%. No cases of faricimab related vasculitis or retinal artery occlusion have been reported.
Conclusion: Faricimab has demonstrated efficacy via anatomic and visual parameters, in both treatment-naïve and previously treated patients, a demographic not studied in the trials leading to FDA-approval. Safety is comparable to current agents, with multiple cases attributable to non-drug related processes. Future results will continue to investigate the safety and efficacy of faricimab in real-world patients suffering from nAMD. Latest data will be available at time of presentation.

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