Avacincaptad Pegol – GATHER2 Open-Label Extension Study

Summary

- The safety and efficacy of avacincaptad pegol (ACP) in patients with GA secondary to AMD was assessed in two key studies (GATHER1 over 18 months, and GATHER2 over 24 months).[1–4]
- ISEE2009 (NCT05536297) was a Phase 3, OLE study for patients who completed treatment in GATHER2 through the Month 24 visit on study treatment (either ACP or sham) to assess the long term (up to 3.5 years) safety and efficacy of monthly ACP.[5,6]
  - A total of 278 patients were enrolled into the study. The study was completed and 85.3% (n = 237) of patients completed the OLE study.
  - ACP 2 mg showed an increasing benefit in slowing GA lesion growth over 42 months vs. projected sham.
  - The safety profile of ACP 2 mg during the 18-month OLE was consistent with the GATHER2 study. Ocular TEAEs in the study eye occurred in 59.2% (n = 74/125) of patients in the ACP treatment arm, and in 58.3% (n = 88/151) of patients in the sham to ACP treatment arm.

Clinical data

ISEE2009 – GATHER2 open label extension study[5,6]

Study design

ISEE2009 (NCT05536297) was a Phase 3, OLE study for patients who completed treatment in GATHER2 through the Month 24 visit on study treatment (either ACP or sham).[6]

Patients were administered monthly ACP 2 mg from Month 1 through Month 17 (maximum 17 total doses), with a final follow-up visit at Month 18. At the time of OLE study initiation, the GATHER2 study was still ongoing, and the two-year analysis for EM and EOM dosing had not been conducted.[7]

A total of 278 patients were enrolled in the study, of which 126 patients continued receiving ACP treatment (Figure 1).[6]

Figure 1. GATHER2 OLE extension study design[6]

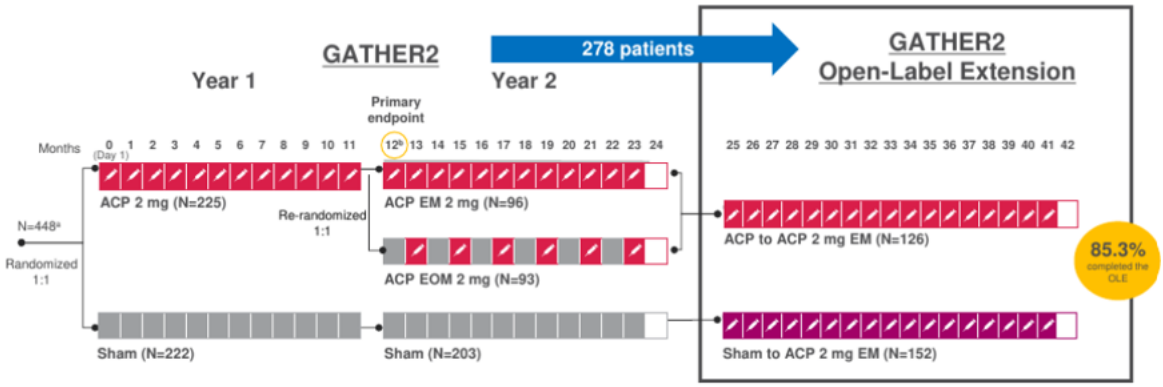

Figure adapted from Khanani et al. presented at AAO 2025.

The study was completed as of 10-APR-2025, and 85.3% (n = 237) of patients completed the OLE study. The baseline patient demographics and characteristics for the OLE were generally balanced across the two treatment groups (Table 1).

Table 1. Baseline patient demographics and characteristics at the start of the OLE[6]

Patient demographic or characteristic	ACP to ACP EM (N = 126)	Sham to ACP EM (N = 152)
Age, years, mean (SD)	77.2 (8.8)	77.9 (8.4)

Patient demographic or characteristic	ACP to ACP EM (N = 126)	Sham to ACP EM (N = 152)
Female, n (%)	84 (66.7)	105 (69.1)
GA lesion area, mm^2, mean (SD)	11.56 (5.13)	13.17 (5.44)
GA lesion focality, multifocal, n (%)	104 (82.5)	122 (80.3)
BCVA, letters, mean (SD)	64.6 (16.8)	66.6 (15.8)
LLVA, letters, mean (SD)	32.2 (21.0)	31.4 (20.4)

Results

The long-term safety and efficacy of ACP 2 mg up to 42 months (3.5 years) of patients enrolled in the GATHER2 OLE study was assessed and presented at the AAO 2025 congress.

Click here to watch the recording of the presentation covering the OLE study at AAO 2025

During the OLE study, treatment with ACP 2 mg showed increased efficacy over time in slowing GA lesion growth in both treatment arms (Figure 2). Treatment with ACP 2 mg showed a reduction in GA lesion growth by 40.5% vs. projected sham from Month 24 to Month 42 (mm^2/year), $p < 0.001$. Treatment with ACP 2 mg showed a reduction in GA lesion growth after switching from sham treatment by 37.1% vs. projected sham from Month 24 to Month 42 (mm^2/year), $p < 0.001$.

Figure 2. LS mean change from Baseline in GA lesion area from Month 24 to Month 42[6]

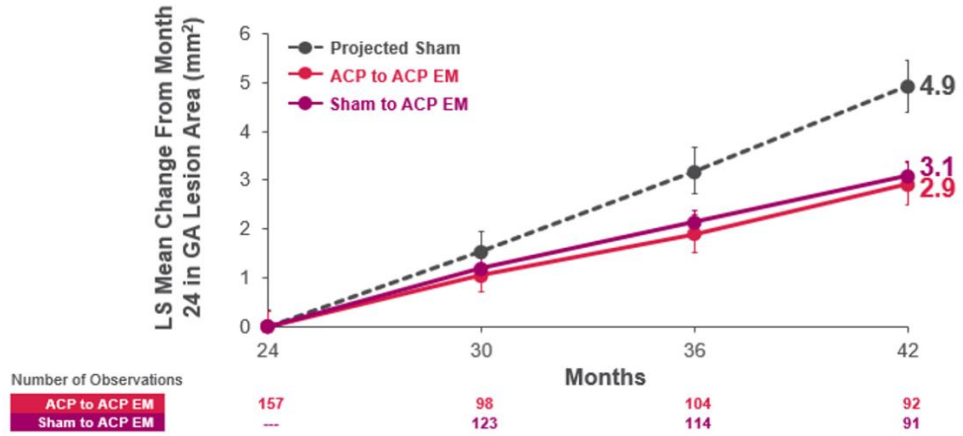

Figure adapted from Khanani et al. presented at AAO 2025.
Note: For each group (ACP or sham) in GATHER2 ITT population, a separate piecewise MMRM model was applied using square root transformed GA area data from Baseline through Month 42, with study ID, GATHER2 randomization stratification factors, time (in days) in each study, and 6-month knots in each study. GA lesion growth rates were then converted from the square root transformed scale to the untransformed scale. A Jackknife method was used to compute the associated standard error. For projected sham, GA lesion growth rate from Month 24 to Month 42 was first calculated as the average of the transformed GA growth rates from the four 6-month intervals spanning from Baseline through Month 24 in GATHER2 sham group and subsequently converted to the untransformed scale.

Additionally, earlier treatment with ACP 2 mg resulted in greater protection of retina tissue (Figure 3).

Figure 3. Area of retina protected by ACP 2 mg vs. sham/projected sham[6]

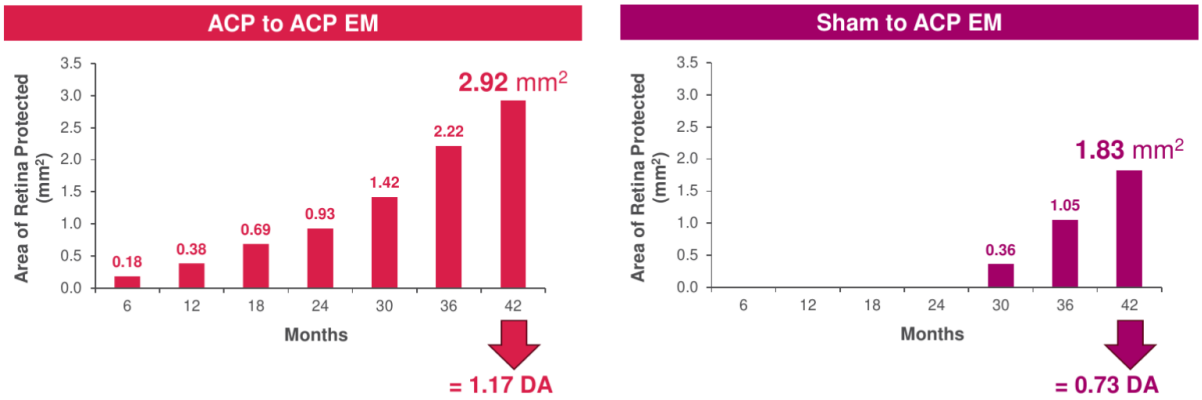

Figure adapted from Khanani et al. presented at AAO 2025.
Note: 1 DA = 2.5 mm^2

The safety profile of ACP 2 mg during the 18-month OLE was consistent with the GATHER2 study, with no new safety signals and no cases of retinal vasculitis or occlusive vasculitis observed. Ocular TEAEs in the study eye occurred in 59.2% (n = 74/125) of patients in the ACP treatment arm, and in 58.3% (n = 88/151) of patients in the sham treatment arm (Table 2).

There were five cases (0.1%) of IOI out of 4203 total injections, all of which were anterior and none were classified as serious or related to ACP treatment. All AEs resolved with no reoccurrence following the continued use of ACP.

Table 2. Ocular TEAEs occurring ≥ 2% during OLE[6]

Ocular TEAEs in study eye, n (%)	ACP to ACP EM (N = 125)	Sham to ACP EM (N = 151)
	74 (59.2)	88 (58.3)
IOP increased	19 (15.2)	20 (13.2)
Cataract	16 (12.8)	11 (7.3)
Conjunctival hemorrhage	13 (10.4)	15 (9.9)
Vitreous detachment	7 (5.6)	1 (0.7)
Visual acuity reduced	7 (5.6)	20 (13.2)
New onset CNV[a]	7 (5.6)	14 (9.3)
Punctate keratitis	4 (3.2)	9 (6.0)
Transient vision loss	4 (3.2)	3 (2.0)
Posterior capsule opacification	3 (2.4)	7 (4.6)

[a]New onset CNV includes CNV incidence during OLE portion, and not CNV that occurred during GATHER2 study.

Abbreviations

AAO: American Association of Ophthalmology; **ACP**: avacincaptad pegol; **AE**: adverse event; **AMD**: age-related macular degeneration; **BCVA**: best corrected visual acuity; **CNV**: choroidal neovascularization; **DA**: disc area; **EM**: every month; **EOM**: every other month; **GA**: geographic atrophy; **IOI**: intraocular inflammation; **IOP**: intraocular pressure; **ITT**: intention to treat population; **LLVA**: low-luminance visual acuity; **LS**: least squares; **MMRM**: Mixed Model for Repeated Measures; **OLE**: open-label extension; **SD**: standard deviation; **TEAE**: treatment emergent AE; **vs**.: versus.

References:

1. Jaffe GJ, Westby K, Csaky KG, et al. C5 Inhibitor Avacincaptad Pegol for Geographic Atrophy Due to Age-Related Macular Degeneration A Randomized Pivotal Phase 2/3 Trial. *Ophthalmology*. 2021;128(4):576-586. Available at: https://doi.org/10.1016/j.ophtha.2020.08.027.

2. Patel SS, Lally DR, Hsu J, et al. Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 18-month findings from the GATHER1 trial. *Eye*. 2023;37(17):3551-3557. Available at: https://doi.org/10.1038/s41433-023-02497-w.

3. Khanani AM, Patel SS, Staurenghi G, et al. Efficacy and safety of avacincaptad pegol in patients with geographic atrophy (GATHER2): 12-month results from a randomised, double-masked, phase 3 trial. *Lancet*. 2023;402(10411):1449-1458. Available at: https://doi.org/10.1016/s0140-6736(23)01583-0.

4. Khanani AM, Danzig CJ, Heier JS, et al. Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 2-year efficacy and safety results from the GATHER2 phase 3 trial. *Ophthalmology*. 2025;epub ahead of print. Available at: https://doi.org/10.1016/j.ophtha.2025.12.011.

5. Electronic Citation. NIH. Clinicaltrials.gov. Avacincaptad Pegol Open-Label Extension for Patients with Geographic Atrophy (NCT05536297). https://clinicaltrials.gov/study/NCT05536297. Available at: https://clinicaltrials.gov/study/NCT05536297/. Accessed November 7, 2025.

6. Khanani AM, Heier JS, Danzig CJ, et al. Avacincaptad Pegol for GA: 3-Year Results From the GATHER2 Open-Label Extension Trial [oral slide presentation]. American Association of Ophthalmology (AAO). Oct 17-20 2025. Orlando, FL, USA. 2025.

7. Data on File.