Real-World Outcomes of Pegcetacoplan and Avacincaptad Pegol for Geographic Atrophy: A Systematic Review and Meta-Analysis

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INTRODUCTION

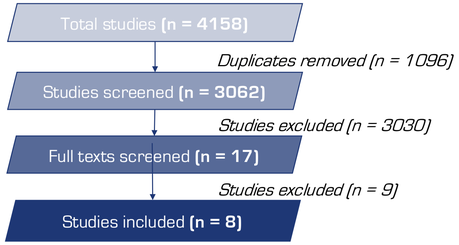
- GA is the advanced stage of dry AMD and a leading cause of severe visual impairment, driven by dysregulation of the complement cascade
- Pegcetacoplan and avacincaptad pegol were FDA-approved in 2023 as the first disease-modifying complement inhibitors shown to reduce GA lesion growth
- RCT populations excluded high-risk patients common in clinical practice, necessitating real-world evidence to inform patient counseling and treatment decisions

OBJECTIVE

To evaluate the real-world baseline patient characteristics, 12-month efficacy, and safety profile of intravitreal pegcetacoplan and avacincaptad pegol for GA secondary to AMD

METHODS

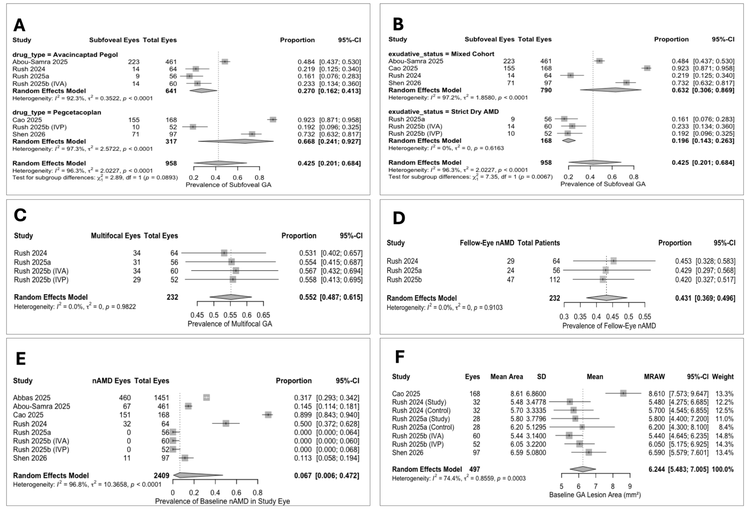
MEDLINE, EMBASE, Cochrane Library from inception to Jan 14, 2026



- **Inclusion**: Observational cohorts, chart reviews, registries, consecutive case series (≥10 treated eyes)
- **Exclusion:** Phase 2/3 RCTs, open-label extensions, non-English
- **Baseline Characteristics:** Subfoveal involvement, lesion morphology (unifocal vs. multifocal), fellow-eye nAMD status, GA lesion area
- **Efficacy (12 mo, treatment-naïve dry AMD cohorts only)**: Absolute GA lesion growth, VA change (logMAR)
- **Safety Profile:** Annualized nAMD conversion (at-risk eyes only), IOI incidence, all-cause and adverse event-related treatment discontinuation
- **Risk of Bias & Evidence Quality:** ROBINS-I and GRADE framework

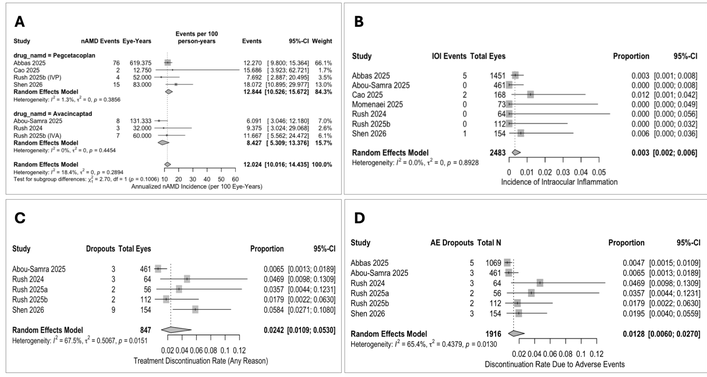
RESULTS

Figures 1A–F. Forest Plots of Pooled Baseline Demographics and GA Lesion Characteristics



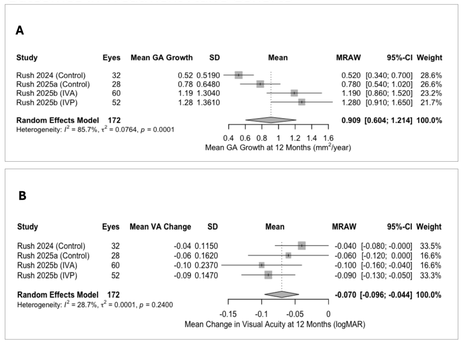
A = Subfoveal GA prevalence, stratified by complement inhibitor (pegcetacoplan vs. avacincaptad pegol); B = Subfoveal GA prevalence, stratified by cohort exudative status (mixed vs. strict dry AMD); C = Multifocal GA lesion morphology prevalence; D = Concurrent fellow-eye nAMD prevalence at baseline; E = Concurrent nAMD or prior anti-VEGF exposure in the treated study eye; F = Pooled mean baseline GA lesion area (mm²)

Figures 2A–D. Forest Plots of Pooled Safety Outcomes



A = Annualized incidence of conversion to neovascular AMD per 100 eyeyears, stratified by complement inhibitor (pegcetacoplan vs. avacincaptad pegol); B = Intraocular inflammation incidence proportion; C = All-cause treatment discontinuation rate; D = Adverse event-related treatment discontinuation rate

Figures 3A–B. Forest Plots of Pooled 12-Month Efficacy Outcomes in Treatment-Naïve Cohorts



A = Mean GA lesion area growth (mm²); B = Mean VA change (logMAR)

Summary of Results and Subgroup Analysis

1. **8 observational studies** included (**1,879 patients; 2,488 treated eyes**); pooled mean baseline GA lesion area **6.24 mm²**
2. Real-world patients carried a substantially higher baseline disease burden than pivotal RCT populations, with **42.5% subfoveal** involvement, **55.2% multifocal** morphology, and **43.1% concurrent fellow-eye nAMD**
3. At 12 months, pooled absolute **GA lesion growth was 0.91 mm²** and **VA declined by 0.07 logMAR** (approximately 3.5 ETDRS letters)
4. Annualized nAMD conversion rate (**12.02 per 100 eye-years**); pegcetacoplan trended higher than avacincaptad pegol (12.84 vs. 8.43 per 100 eye-years, *P*=0.101)
5. IOI was reported in **0.32% of treated eyes** (approximately 1 in 310 eyes); all-cause discontinuation 2.42%, adverse event-related discontinuation 1.28%

DISCUSSION

1. Real-world patients represent **higher-risk population** than those in RCTs: prior studies show that **multifocal morphology** is associated with 46.3% faster effective radius growth, while **fellow-eye nAMD more than doubles** risk of exudative conversion within 36 months
2. **GA continues to progress anatomically**: pooled lesion growth of 0.91 mm² falls **below natural history estimates** (1.28–2.6 mm²/year), suggesting a treatment effect, though direct comparison is limited by absent concurrent sham arms
3. Observed nAMD conversion rate (approximately 11.3% cumulative at 1 year) exceeds RCT sham rates (2–4%), confirming that **neovascularization persists in routine clinical practice**
4. High baseline subfoveal involvement likely limits measurable visual benefit despite anatomical slowing, explaining the **dissociation between lesion growth and VA outcomes**
5. Rare IOI (0.32%) and discontinuation (2.42%) support real-world **tolerability** of both agents