Efficacy and Safety of Pegcetacoplan in Patients With Geographic Atrophy From the Phase 3 OAKS and DERBY Trials

Purpose:

To evaluate the safety and efficacy of pegcetacoplan in patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Methods:

In the 24-month, phase 3 OAKS (N=637; NCT03525600) and DERBY (N=621; NCT03525613) trials, patients aged ≥60 years with GA were randomized (2:2:1:1) to intravitreal pegcetacoplan monthly (PM), pegcetacoplan every other month (PEOM), sham monthly, or sham every other month. The main outcome for this analysis was the change from baseline in GA lesion area by fundus autofluorescence at month 24. A subgroup efficacy analysis based on patient baseline demographics and GA lesion characteristics was also performed. Patients were pooled across studies, and treatment responses of subgroups based on age, sex, GA lesion location, focality and laterality, and best-corrected visual acuity were determined. Using lesion growth values and the density of healthy retinal pigment epithelium (RPE), areas of retinal tissue and numbers of RPE cells saved with pegcetacoplan treatment were estimated. Safety outcomes, including rates of treatment-emergent adverse events (TEAEs) and exudative AMD, were assessed.

Results:

In a prespecified pooled analysis of OAKS and DERBY, PM (n=403) reduced GA lesion growth by 21% ($p<0.0001$; nominal) and PEOM (n=406) reduced GA lesion growth by 17% ($p<0.0001$; nominal) vs pooled sham (n=400) at month 24. Changes from baseline in GA lesion growth at month 24 consistently favored PM and PEOM vs sham across subgroups, including patients with nonsubfoveal lesions (PM=26%, $p<0.0001$; PEOM=22%, $p<0.0001$), subfoveal lesions (PM=19%, $p<0.0001$; PEOM=16%, $p=0.0003$), unifocal lesions (PM=26%, $p<0.0001$; PEOM=21%, $p=0.0007$), and multifocal lesions (PM=20%, $p<0.0001$; PEOM=17%, $p<0.0001$). Reductions in GA lesion growth with pegcetacoplan equated to ~0.8 mm2 and ~0.7 mm2 tissue preserved and between 3500 and 6300 RPE cells saved in PM and PEOM, respectively. Pegcetacoplan was well tolerated; most study eye ocular TEAEs were mild or moderate. TEAE rates across arms in both studies ranged from 82.5%–88.3%; 46.3%–61.6% of patients had ocular TEAEs and 71.9%–80.4% of patients had nonocular TEAEs. The rate of intraocular inflammation per injection was 0.20%, excluding 4 events attributed to drug impurity. The rate of infectious endophthalmitis per injection was 0.034%. Over 24 months, new-onset exudative AMD was reported in 12.2%, 6.7%, and 3.1% of patients in the PM, PEOM, and pooled sham arms, respectively.

Conclusions:

Treatment with pegcetacoplan slowed lesion growth and was well tolerated over 24 months. Efficacy was consistently observed across patient subgroups in the PM and PEOM groups. The reduction in GA lesion growth translated into preservation of retinal tissue and RPE cells over 24 months.

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