Poster Number 5

Reproxalap Exhibits No Safety Concerns and Statistically Significantly Improves Vision in a Pivotal Dry Eye Disease Safety Trial

Desiree Owen,[1] Blake Simmons,[2] John Sheppard,[3] Bill Cavanagh,[4] Todd C. Brady[4]

[1]Allergan, an AbbVie company, Irvine, CA, USA; [2]Vision Institute, Colorado Springs, CO, USA; [3]Virginia Eye Consultants, Norfolk, VA, USA; [4]Aldeyra Therapeutics, Inc, Lexington, MA, USA

OBJECTIVE

To evaluate the long-term safety of reproxalap 0.25% ophthalmic solution compared with vehicle in patients with dry eye disease (DED)

CONCLUSIONS

The study results support the safety of long-term topical reproxalap therapy in patients with DED

To our knowledge, this was the first demonstration of improved distance BCVA in patients treated with a topically administered DED therapy for up to 1 year

Reproxalap therapy has the potential to improve visual acuity in patients with DED

AbbVie and the authors thank the participants, study sites, and investigators who participated in this clinical trial. Aldeyra Therapeutics funded this trial and participated in the trial design, research, data collection, analysis, interpretation of data, and review and approval of the publication. AbbVie participated in the interpretation of data and the review and approval of the publication. All authors had access to relevant data and participated in the drafting, review, and approval of this publication. Medical writing support was provided by Evidence Scientific Solutions, Inc (Raleigh, NC).

Financial arrangements of the authors with companies whose products may be related to the present report are listed as declared by the authors: D. Owen is an employee of AbbVie and may own stock/stock options. B. Simmons was an investigator in other studies of reproxalap. J. Sheppard is a consultant for Bausch + Lomb, GmbH, Harrow, and Novaliq. B. Cavanagh and T.C. Brady are employees of Aldeyra Therapeutics.

For additional information or to obtain a PDF of this poster

For additional information or to obtain a PDF of this poster
Scan QR code or use the following link to download an electronic version of this presentation and other AbbVie AAOpt 2025 scientific presentations:
https://abbvie1.outsystemsenterprise.com/CongressPublications/CongressHome?CongressId=cbed45d4-9463-4750-b6c3-94070c784034

QR code expiration: September 8, 2026

To submit a medical question, please visit www.abbviemedinfo.com

References

1. Tsubota K, et al. *Int J Mol Sci*. 2020;21:9271.
2. Clark D, et al. *J Ocul Pharmacol Ther*. 2021;37:193–199.
3. Choi W, et al. *Curr Eye Res*. 2016;41:1143–1149.
4. Clark D, et al. *Am J Ophthalmol*. 2021;226:22–31.

INTRODUCTION

- Dry eye disease (DED) is a common ocular disorder characterized by tear film instability, inflammation, and symptoms including ocular discomfort and visual disturbance[1]
- Reactive aldehyde species (RASP) are proinflammatory molecules that have been implicated in ocular inflammatory diseases including DED[2]
  - Levels of malondialdehyde (MDA), a well-characterized RASP, are elevated in the tears of patients with DED, and the increase in MDA levels is associated with disease severity[3]
- Reproxalap is a small molecule RASP inhibitor that rapidly and covalently binds RASP[2]
- Studies have demonstrated effectiveness of topical reproxalap treatment in alleviating the signs and symptoms of DED[2,4]
- Reproxalap 0.25% ophthalmic solution is currently under review by the US Food and Drug Administration for treatment of DED
- It is important to demonstrate safety and effectiveness of new treatments for DED over the long term, as DED is generally a chronic condition requiring long-term management

METHODS

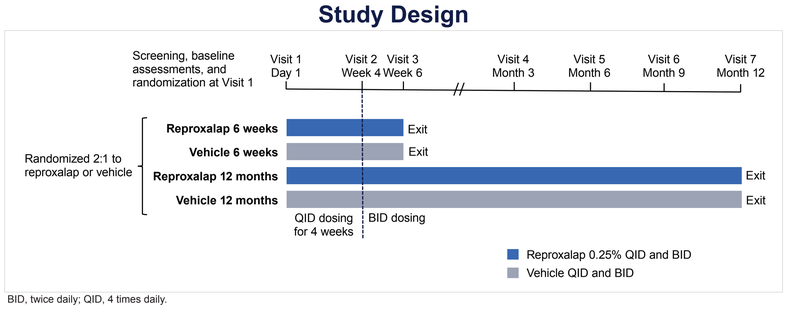
- Phase 3, multicenter, double-masked, randomized, vehicle-controlled, parallel-group safety study in patients with DED (ClinicalTrials.gov: NCT04735393)

Key Eligibility Criteria Evaluated at Screening

Inclusion Criteria
✓ Age ≥18 years with history of dry eye for ≥6 months
✓ History of use or desire for use of eyedrops for dry eye symptoms within previous 6 months
✓ Score ≥2 on the Ora Calibra® Ocular Discomfort & 4-Symptom Questionnaire in ≥1 symptom
✓ Schirmer test score ≤10 mm and ≥1 mm
Exclusion Criteria
✓ Clinically significant slit-lamp findings (eg, active blepharitis, meibomian gland dysfunction, ocular allergies) that require treatment or may interfere with study parameters
✓ Ongoing ocular infection or active ocular inflammation
✓ Use of contact lenses within the previous 7 days (or anticipated use during the study) or any eyedrops within the previous 2 hours
✓ Laser-assisted in situ keratomileusis (LASIK) surgery within the previous 12 months
✓ Use of topical cyclosporine or lifitegrast within the previous 90 days
✓ Planned temporary punctal plug use during the study that has not been stable during the previous 30 days
✓ Unwillingness to discontinue all topical ophthalmic prescriptions and over-the-counter solutions, gels, and scrubs during the study
✓ Best-corrected visual acuity (BCVA) ≥0.7 logMAR (20/100 or worse Snellen equivalent) in both eyes

- Eligible patients were randomized to bilateral treatment with reproxalap 0.25% ophthalmic solution or vehicle for 6 weeks or 12 months, with the study treatment administered 4 times daily (QID) for the first 4 weeks then twice daily (BID) for the remainder of the study

Study Design



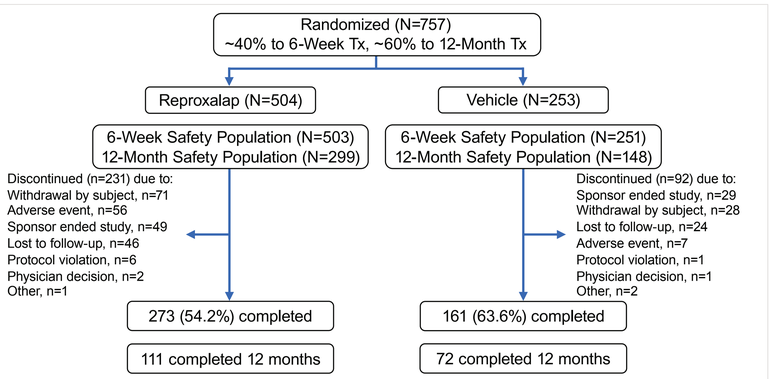
BID, twice daily; QID, 4 times daily.

- Safety assessments included adverse events (AEs), BCVA at 4 meters, slit-lamp biomicroscopy, dilated fundoscopy, and intraocular pressure (IOP) at each study visit; central corneal endothelial cell density (CECD) at baseline and months 6 and 12; and laboratory assessments (clinical chemistry and hematology) at baseline and month 12
- The primary endpoints were the occurrence of specified serious treatment-emergent adverse events (TEAEs) (ie, visual acuity decrease serious TEAE, IOP increase serious TEAE, corneal serious TEAE detected on slit-lamp biomicroscopy, and retinal serious TEAE detected on fundoscopy) categorized as probably or definitely related to treatment
- Analysis populations for the primary endpoints:
  - 6-week safety population: all patients randomized to either treatment who received ≥1 dose of study drug and had ≥1 subsequent safety assessment; patients were analyzed as treated over 6 weeks
  - 12-month safety population: all patients who were randomized to a 12-month study arm, received ≥1 dose of study drug, and had ≥1 subsequent safety assessment; patients were analyzed as treated over 12 months
- Post hoc analysis of overall change in BCVA from baseline across eyes and visits in the 12-month safety population used the BCVA in the left and right eye of each patient and a mixed-model for repeated measures (MMRM) model with baseline BCVA as a covariate and visit, treatment, and treatment-by-visit interaction as factors
- IOP and CECD change from baseline were evaluated using similar MMRM models with the baseline value as a covariate
- A sample size of approximately 175 patients completing 12 months of treatment (116 reproxalap and 58 vehicle) was planned to provide ≥80% power to demonstrate a significant difference between reproxalap and vehicle in the proportion of patients with a specific AE

RESULTS

- A total of 757 patients with DED were enrolled and randomized to treatment with reproxalap or vehicle
- The percentage of patients who discontinued from the study because of AEs was 11.1% with reproxalap and 2.8% with vehicle
  - The AE most commonly resulting in patient discontinuation was instillation site irritation (8.0% and 9.0% of patients in the reproxalap 6-week and 12-month safety populations, respectively)

Patient Disposition



Baseline Patient Characteristics

Parameter	Safety Population: 6-Week Reproxalap (N=503)	6-Week Vehicle (N=251)	12-Month Reproxalap (N=299)	12-Month Vehicle (N=148)
Age, mean (SD) age, y	55.7 (15.8)	56.9 (15.8)	55.8 (16.1)	55.4 (16.2)
Range	19–96	19–96	19–96	19–96
Female, n (%)	356 (70.8)	176 (70.1)	221 (73.9)	102 (68.9)
Symptom score, mean (SD)[a]				
Ocular discomfort	3.0 (1.2)	3.0 (1.2)	3.0 (1.2)	2.9 (1.2)
Burning	2.1 (1.6)	2.1 (1.6)	2.2 (1.6)	2.0 (1.6)
Dryness	3.5 (1.1)	3.6 (1.1)	3.5 (1.2)	3.5 (1.1)
Grittiness	2.4 (1.5)	2.4 (1.5)	2.6 (1.5)	2.3 (1.5)
Stinging	2.0 (1.5)	2.0 (1.5)	2.1 (1.6)	1.8 (1.5)
BCVA OD, mean (SD), logMAR	0.13 (0.16)	0.15 (0.16)	0.14 (0.16)	0.15 (0.17)
BCVA OS, mean (SD), logMAR	0.12 (0.15)	0.14 (0.15)	0.13 (0.16)	0.14 (0.15)
Schirmer test OD, mean (SD), mm	6.4 (4.6)	6.4 (5.1)	6.4 (4.5)	6.6 (4.6)
Schirmer test OS, mean (SD), mm	6.0 (4.3)	5.4 (3.8)	6.1 (4.4)	5.8 (4.0)

[a]Scores on the Ora Calibra® Ocular Discomfort and 4-Symptom Questionnaire; scores on the questionnaire range from 1–5 with 5 = worst.
[b]Unanesthetized Schirmer tests.
BCVA, best-corrected visual acuity; logMAR, logarithm of the minimal angle of resolution; OD, right eye; OS, left eye.

Primary Endpoint

- There were no treatment-related serious TEAEs in any study arm

Ocular TEAEs

- The most common TEAE in reproxalap-treated patients was transient, mild, instillation site irritation, most commonly lasting <1 minute
- With the exception of instillation site irritation, ocular TEAEs were similar with reproxalap and vehicle

Visual Acuity

- In the 12-month safety population, BCVA improved from baseline in both treatment groups, with reproxalap statistically superior to vehicle in the improvement in BCVA
- The least-squares (LS) mean difference in change from baseline BCVA over 12 months (reproxalap minus vehicle) was −0.014 logMAR (95% confidence interval [CI]: −0.025 to −0.002; *P*=.0185)

Ocular TEAEs Reported in ≥1% of Patients

Ocular TEAE, n (%)	Safety Population: 6-Week Reproxalap (N=503)	6-Week Vehicle (N=251)	12-Month Reproxalap (N=299)	12-Month Vehicle (N=148)
Overall (any ocular TEAE)	221 (43.9)	32 (12.7)	143 (47.8)	31 (20.9)
Instillation site irritation	205 (40.8)	8 (3.2)	127 (42.5)	3 (2.0)
Dry eye	6 (1.2)	2 (0.8)	6 (2.0)	1 (0.7)
Foreign body sensation in eye	5 (1.0)	3 (1.2)	4 (1.3)	3 (2.0)
Vision blurred	5 (1.0)	3 (1.2)	3 (1.0)	1 (0.7)
Visual impairment	5 (1.0)	1 (0.4)	3 (1.0)	1 (0.7)
Blepharitis	2 (0.4)	2 (0.8)	2 (0.7)	2 (1.4)
Ocular hyperemia	2 (0.4)	2 (0.8)	2 (0.7)	4 (2.7)
Vitreous detachment	2 (0.4)	2 (0.8)	5 (1.7)	3 (2.0)
Eye pain	1 (0.2)	3 (1.2)	2 (0.7)	3 (2.0)
Borderline glaucoma	0	0	3 (1.0)	0
Chalazion	0	2 (0.8)	0	3 (2.0)

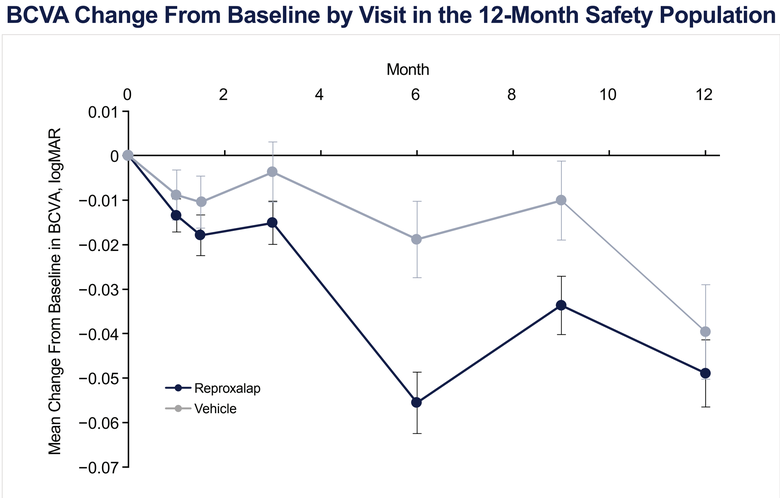
TEAE, treatment-emergent adverse event.

MMRM Analysis of BCVA Change From Baseline

Statistic	12-Month Reproxalap (N=296)	12-Month Vehicle (N=145)
LS mean (SE) overall change in BCVA from baseline, logMAR	−0.030 (0.0035)	−0.016 (0.0046)
95% CI	−0.037 to −0.023	−0.025 to −0.007
LS mean (SE) difference (reproxalap – vehicle), logMAR	−0.014 (0.0058)	
95% CI	−0.025 to −0.002	
P value	.0185	

BCVA, best-corrected visual acuity; CI, confidence interval; logMAR, logarithm of the minimal angle of resolution; LS, least-squares; MMRM, mixed model for repeated measures.

BCVA Change From Baseline by Visit in the 12-Month Safety Population



The analysis used the average value from both eyes of the subject. Error bars show the standard error of the mean.
BCVA, best-corrected visual acuity; logMAR, logarithm of the minimal angle of resolution.

Other Safety Findings

- No safety concerns were identified in other safety assessments
- No reproxalap-treated patient had a shift in fundoscopy findings from normal or abnormal (not clinically significant) to abnormal (clinically significant) associated with an AE considered at least possibly related to treatment
- No clinically significant changes in laboratory assessments were reported as AEs considered at least possibly related to treatment
- Clinically significant changes from baseline on slit-lamp biomicroscopy were reported as AEs at least possibly related to treatment in 2 patients in the reproxalap 6-week safety population
  - One patient had abnormal conjunctival and lid findings on day 3 and AE reports of contact dermatitis on the lids, chemosis, and conjunctival injection deemed possibly related to study drug that resulted in patient withdrawal from the study
  - The second patient had abnormal conjunctival findings at the week 6 visit, and an AE of conjunctivitis deemed possibly related to study drug was recorded and resolved the same day; the patient completed the study
- There was no significant difference between reproxalap and vehicle in overall IOP change from baseline (LS mean difference = 0.2 mm Hg [95% CI: −0.2 to 0.5], *P*=.330)
- There was no significant difference between reproxalap and vehicle in overall CECD change from baseline (LS mean difference = −10.2 cells/mm^2 [95% CI: −51.4 to 31.1], *P*=.627)

Presented at the American Academy of Optometry (AAOpt) 2025 Annual Meeting, October 8–11, 2025, Boston, MA, USA, Ref DV-016934