AZR-MD-001 Improved tear film stability and ocular symptoms in patients with meibomian gland dysfunction: 6-month results

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PURPOSE

- Meibomian gland dysfunction (MGD) causes tear film abnormalities and ocular surface–associated symptoms due to hyperkeratinization.[1-3]
- AZR-MD-001, a selenium sulfide ophthalmic ointment, is a potent keratolytic and keratostatic agent that also induces meibomian gland lipogenesis.[4]
- This phase 2 clinical trial explored tear film stability and its impact on ocular symptoms through 6 months in response to topical applications of AZR-MD-001 (0.5% or 1.0%) in adults with MGD (NCT03652051).

DEMOGRAPHICS

- A total of 245 patients were included in the safety and in the intent-to-treat populations (0.5%, N=82; 1.0%, N=83; vehicle, N=80) (**Table 1**).

TABLE 1. DEMOGRAPHICS AND BASELINE CHARACTERISTICS (SAFETY POPULATION)

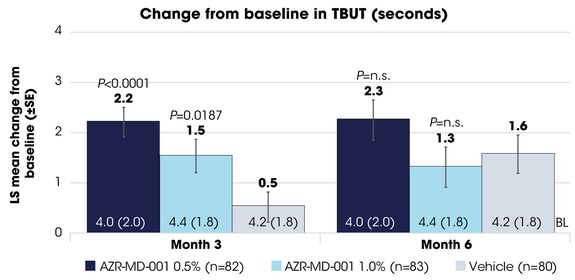
		AZR-MD-001 0.5% (N=82)	AZR-MD-001 1.0% (N=83)	VEHICLE (N=80)
Age (years)	Mean (SD)	52.1 (16.9)	55.6 (17.9)	51.9 (18.5)
	Range	18–80	20–93	20–97
Sex, n (%)	Male	31 (37.8)	27 (32.5)	24 (30.0)
	Female	51 (62.2)	56 (67.5)	56 (70.0)
Race, n (%)	White	57 (69.5)	64 (77.1)	56 (70.0)
	Asian	16 (19.5)	10 (12.0)	21 (26.3)
	Black	3 (3.7)	3 (3.6)	1 (1.3)
	Other	6 (7.3)	6 (7.2)	2 (2.5)
Duration of MGD, n (%)	<5 years	29 (35.4)	30 (36.1)	28 (35.0)
	≥5 years	53 (64.6)	53 (63.9)	52 (65.0)
Number of MGYLS	Mean (SD)	1.7 (1.4)	1.9 (1.4)	1.8 (1.3)
MGS score	Mean (SD)	5.7 (2.8)	6.0 (3.0)	6.0 (2.8)
OSDI total score	Mean (SD)	25.2 (7.5)	24.2 (6.0)	25.0 (6.7)
TBUT score	Mean (SD)	4.0 (2.0)	4.4 (1.8)	4.2 (1.8)
SPEED score	Mean (SD)	12.9 (3.3)	13.0 (4.2)	13.2 (4.1)
Eye Dryness VAS subscore	Mean (SD)	58.4 (22.3)	49.6 (24.5)	52.4 (25.8)
Eye Discomfort VAS subscore	Mean (SD)	46.5 (24.7)	38.1 (23.9)	45.5 (25.2)
Ocular Itch VAS subscore	Mean (SD)	38.9 (25.6)	29.5 (24.3)	34.7 (25.1)

The safety population included all randomized patients administered ≥1 dose of study drug.
MGD, meibomian gland dysfunction; MGS, Meibomian Gland Secretion; MGYLS, Meibomian Glands Yielding Liquid Secretion; OSDI, Ocular Surface Disease Index; SD, standard deviation; SPEED, Standard Patient Evaluation of Eye Dryness; TBUT, tear break-up time; VAS, visual analog scale.

RESULTS

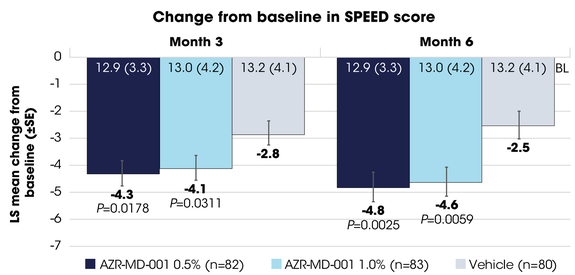
- AZR-MD-001 0.5% met the co-primary endpoints, significantly improving the signs (number of MGYLS) and symptoms (OSDI total score) of MGD versus vehicle at Month 3, with both doses demonstrating good safety and tolerability.[4] (Please see our poster 6578 - B0265 for primary efficacy and safety results over 6 months.)
- At Month 6 compared to vehicle, there was not a statistical difference with AZR-MD-001 0.5% in TBUT improvements (**Figure 1**), but the 0.5% dose did show significantly larger improvements in dry eye symptoms (**Figure 2**), eye dryness (**Figure 3**), eye discomfort (**Figure 4**), and ocular itch (**Figure 5**).

FIGURE 1. INCREASES IN TEAR FILM STABILITY WITH AZR-MD-001 WERE SUSTAINED FROM MONTH 3 TO MONTH 6 (ITT)



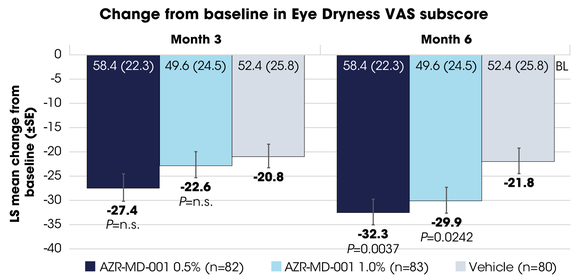
*P*values versus vehicle.
BL, baseline mean (standard deviation) score; ITT, intent-to-treat (all patients randomized to study drug); LS, least squares; n.s., not significant (vs vehicle); SE, standard error; TBUT, tear break-up time (higher scores are better).

FIGURE 2. AZR-MD-001 SIGNIFICANTLY REDUCED SPEED-MEASURED SYMPTOMS OF DRY EYE VS VEHICLE THROUGH MONTH 6 (ITT)



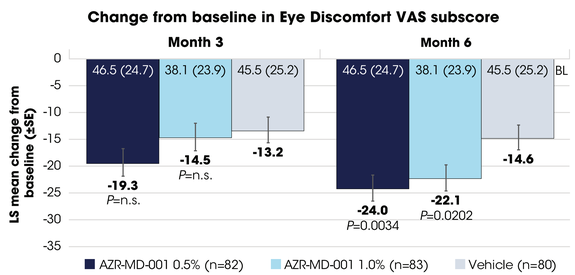
*P*values versus vehicle.
BL, baseline mean (standard deviation) score; ITT, intent-to-treat (all patients randomized to study drug); LS, least squares; n.s., not significant (vs vehicle); SE, standard error; SPEED, Standard Patient Evaluation of Eye Dryness (lower scores are better).

FIGURE 3. AZR-MD-001 SIGNIFICANTLY REDUCED EYE DRYNESS VAS SUBSCORE VS VEHICLE AT MONTH 6 (ITT)



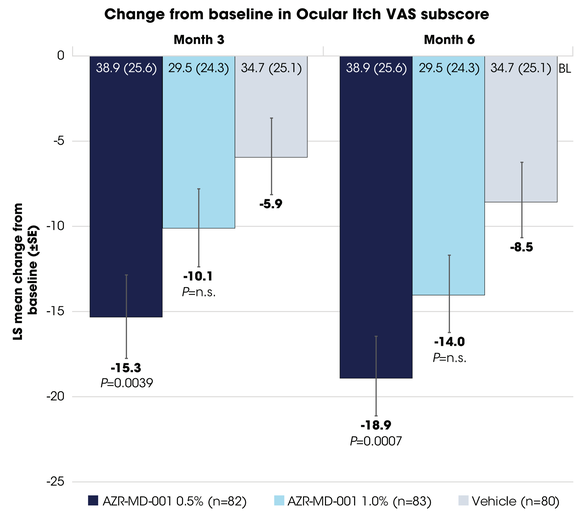
*P*values versus vehicle.
BL, baseline mean (standard deviation) score; ITT, intent-to-treat (all patients randomized to study drug); LS, least squares; n.s., not significant (vs vehicle); SE, standard error; VAS, visual analog scale (lower scores are better).

FIGURE 4. AZR-MD-001 SIGNIFICANTLY REDUCED EYE DISCOMFORT VAS SUBSCORE VS VEHICLE AT MONTH 6 (ITT)



*P*values versus vehicle.
BL, baseline mean (standard deviation) score; ITT, intent-to-treat (all patients randomized to study drug); LS, least squares; n.s., not significant (vs vehicle); SE, standard error; VAS, visual analog scale (lower scores are better).

FIGURE 5. AZR-MD-001 0.5% SIGNIFICANTLY DECREASED OCULAR ITCH VAS SUBSCORE VS VEHICLE THROUGH MONTH 6 (ITT)



*P*values versus vehicle.
BL, baseline mean (standard deviation) score; ITT, intent-to-treat (all patients randomized to study drug); LS, least squares; n.s., not significant (vs vehicle); SE, standard error; VAS, visual analog scale (lower scores are better).

CONCLUSIONS

- Biweekly treatment with AZR-MD-001 0.5% (selenium sulfide ophthalmic ointment) significantly improved tear film quality compared to vehicle, which resulted in clinically significant improvements in ocular symptoms through 6 months of treatment.
- AZR-MD-001 0.5% is the first pharmaceutical therapy to demonstrate significant improvement in clinical signs of MGD and ocular symptoms, which was sustained through 6 months.

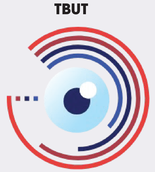
METHODS

- **Purpose:** Phase 2 prospective, multicenter, parallel-group, randomized, double-masked, vehicle-controlled trial evaluating the safety and efficacy of AZR-MD-001 (0.5% or 1.0%) for the treatment of MGD (NCT03652051)
- **Eligible patients:** Male or female; aged ≥18 years; with mild to moderate MGD (Meibomian Gland Secretion [MGS] score ≤12 for 15 glands of the lower lid) and associated ocular symptoms (Ocular Surface Disease Index [OSDI] score 13–33); self-reported dry eye signs and symptoms within 3 months of study entry; and had a Standard Patient Evaluation of Eye Dryness (SPEED) score ≥6, a tear break-up time (TBUT; assessed by sodium fluorescein) <10 seconds in both eyes, and gland dropout <75%
- **Treatment:** Patients randomized (1:1:1) to AZR-MD-001 0.5%, 1.0%, or vehicle applied to the lower eyelid twice-weekly at bedtime
  - No conventional treatments allowed during the study
- **Co-primary endpoints:** Change from baseline versus vehicle in number of Meibomian Glands Yielding Liquid Secretion (MGYLS) and in OSDI total score at Month 3
- **Secondary and exploratory endpoints:** Change from baseline versus vehicle in TBUT, SPEED, and visual analog scales (VAS) at Months 3 and 6

STATISTICAL ANALYSIS

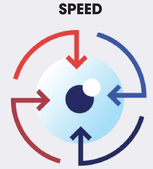
- **Change from baseline endpoints:** Evaluated using analysis of covariance model with continuous baseline score as a covariate and treatment, duration of disease category (<5 or ≥5 years), and baseline MGS score category (<6 or ≥6 and ≤12) as factors; missing data imputed via multiple imputation using a Markov Chain Monte Carlo approach
- **P-values:** All versus vehicle, not adjusted for multiplicity

TBUT



Time taken for the first dry spot to appear on the cornea after a complete blink, evaluated in triplicate using a micropipette (5 µL of 2% non-preserved sodium fluorescein), with a time of ≥10 seconds considered normal[5]

SPEED



Measures the occurrence, frequency, and severity of 4 dry eye symptoms, with total score ranging from 0–28 and higher scores indicating increasing symptom severity[6]

VAS

Subjective rating of ocular symptoms (e.g., dryness, discomfort, and itching) for both eyes on which a vertical mark is placed on a horizontal line ranging from 0% for "no discomfort" and 100% for "maximal discomfort"

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