AZR-MD-001 efficacy in improving tear film stability and its impact on associated symptoms of meibomian gland dysfunction in a phase 2 trial

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INTRODUCTION

- 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 induces meibomian gland lipogenesis.
- A phase 2 clinical trial was conducted to explore tear film function and its impact on ocular symptoms in response to topical AZR-MD-001 (0.5% or 1.0%) in adults with MGD (NCT03652051).

DEMOGRAPHICS

- 245 patients were included in the safety and in the intent-to-treat (ITT) populations (**Table 1**).

TABLE 1. DEMOGRAPHICS AND BASELINE CHARACTERISTICS (SAFETY POPULATION)

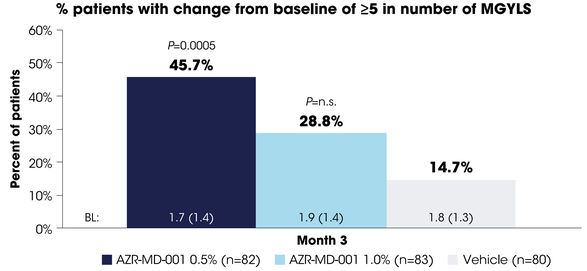
		AZR-MD-001 0.5% (N=82)	AZR-MD-001 1.0% (N=83)	VEHICLE (N=80)
Age (years)	Mean (SD)	52.1 (16.9)	55.6 (17.9)	51.9 (18.5)
	Range	18–80	20–93	20–97
Sex, n (%)	Male	31 (37.8)	27 (32.5)	24 (30.0)
	Female	51 (62.2)	56 (67.5)	56 (70.0)
Race, n (%)	White	57 (69.5)	64 (77.1)	56 (70.0)
	Asian	16 (19.5)	10 (12.0)	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, n (%)	<6	38 (46.3)	33 (39.8)	34 (42.5)
	≥6 and ≤12	44 (53.7)	50 (60.2)	46 (57.5)
OSDI total score	Mean (SD)	25.2 (7.5)	24.2 (6.0)	25.0 (6.7)

MGD, meibomian gland dysfunction; MGS, Meibomian Gland Secretion; MGYLS, Meibomian Glands Yielding Liquid Secretion; OSDI, Ocular Surface Disease Index; SD, standard deviation.

RESULTS

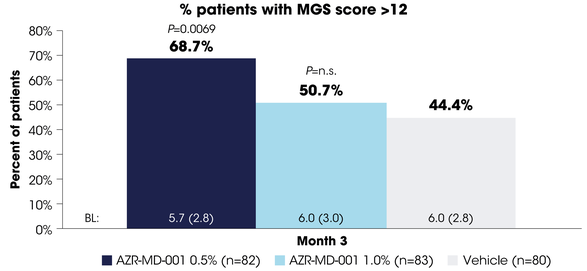
- AZR-MD-001 0.5% met the co-primary endpoints, significantly improving the signs (number of MGYLS) and symptoms (OSDI total score) of MGD vs vehicle at Month 3, with both doses demonstrating good safety and tolerability. (For complete results, see ARVO 2023 abstract 5175 - B0072.)
- At Month 3 compared to vehicle, AZR-MD-001 0.5% resulted in an increased number of functional open glands (**Figure 1**), higher meibum quality (**Figure 2**), greater percentage of patients considered asymptomatic (**Figure 3**), larger improvement in dry eye symptoms (**Figure 4**), and higher rates of normal TBUT (**Figure 5**)

FIGURE 1. AZR-MD-001 0.5% SIGNIFICANTLY INCREASED THE NUMBER OF FUNCTIONAL GLANDS VS VEHICLE AT MONTH 3 (ITT)



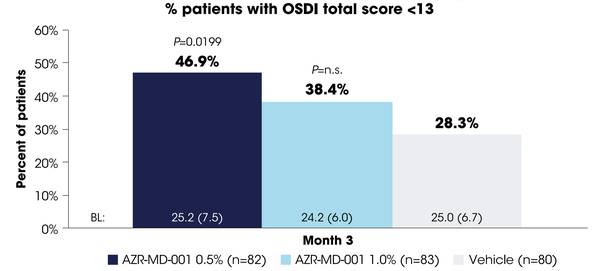
BL, baseline mean (standard deviation) score; ITT, intent-to-treat; MGYLS, Meibomian Glands Yielding Liquid Secretion (higher scores are better); n.s., not significant (vs vehicle).

FIGURE 2. SIGNIFICANTLY MORE PATIENTS TREATED WITH AZR-MD-001 0.5% THAN VEHICLE HAD GOOD MEIBUM QUALITY AT MONTH 3 (ITT)



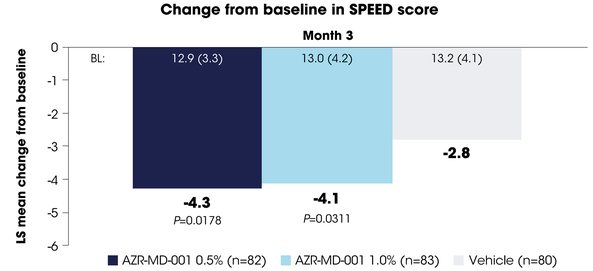
BL, baseline mean (standard deviation) score; ITT, intent-to-treat; MGS, Meibomian Gland Secretion (higher scores are better); n.s., not significant (vs vehicle).

FIGURE 3. SIGNIFICANTLY MORE PATIENTS TREATED WITH AZR-MD-001 0.5% THAN VEHICLE WERE CONSIDERED ASYMPTOMATIC FOR DISEASE (ITT)



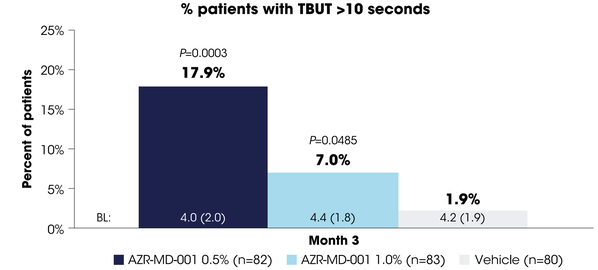
BL, baseline mean (standard deviation) score; ITT, intent-to-treat; n.s., not significant (vs vehicle); OSDI, Ocular Surface Disease Index (lower scores are better).

FIGURE 4. AZR-MD-001 0.5% SIGNIFICANTLY IMPROVED SYMPTOMS OF DRY EYE AT MONTH 3 RELATIVE TO VEHICLE (ITT)



BL, baseline mean (standard deviation); ITT, intent-to-treat; LS, least squares; n.s., not significant (vs vehicle); SPEED, Standard Patient Evaluation of Eye Dryness (lower scores are better).

FIGURE 5. AT MONTH 3, AZR-MD-001 SIGNIFICANTLY INCREASED TEAR FILM STABILITY COMPARED WITH VEHICLE (ITT)



BL, baseline mean (standard deviation) score; ITT, intent-to-treat; TBUT, Tear Break-Up Time (higher scores are better).

SUMMARY

- A statistically significant, higher percentage of patients treated with AZR-MD-001 experienced resolution of MGD signs and symptoms compared to vehicle.
- AZR-MD-001 0.5% is the first therapy showing significant resolution of MGD clinical signs and ocular symptoms, such that ~50% of mild to moderate cases were symptom-free by 3 months.

STUDY DESIGN

- **Purpose:** Phase 2 prospective, 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) <10 seconds in both eyes, and gland dropout <75%
  - For patients with 2 qualifying eyes, the study eye had lower numerical MGS score; if the eyes had the same MGS score, then the right eye was selected
- **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
- **Co-primary endpoints:** change from baseline in number of Meibomian Glands Yielding Liquid Secretion (MGYLS) and in OSDI total score at Month 3
- **Responder rates:** All response thresholds were prespecified.

STATISTICAL ANALYSIS

- **Populations:**
  - Safety = all randomized patients administered ≥1 dose of study drug
  - Intent-to-treat (ITT) = all randomized patients
- **Responder rates:** Cochran-Mantel-Haenszel test, controlling for duration of disease category (<5 or ≥5 years) and baseline MGS score category (<6 or ≥6 and ≤12), using Wilson-Hilferty transformation
- **Changes from baseline:** 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
- ***P*-values:** All versus vehicle, not adjusted for multiplicity

MGYLS
Number of glands yielding liquid secretion, with the total score ranging 0–15 and a change from baseline of ≥5 indicating significant response[4]

MGS
Meibum quality of 15 glands on the lower eyelid on a scale of 0–3, with the total score ranging 0–45 and scores >12 indicating good meibum quality[5]

OSDI
Ocular symptoms, environmental triggers, and vision-related functioning, with the total score ranging 0–100 and scores <13 considered normal or asymptomatic[4,6]

SPEED
Occurrence, frequency, and severity of 4 dry eye symptoms, with total score ranging 0–28 and higher scores indicating increasing symptom severity[7]

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[8]

Contact

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