AZR-MD-001 restores gland function and improves signs and ocular symptoms of meibomian gland dysfunction (MGD)

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INTRODUCTION

- Meibomian gland dysfunction (MGD) is a chronic and progressive condition associated with blockage of meibomian glands and alteration in meibum quality,[1] with prevalence estimates up to 70% in population-based studies.[2]
- With currently no approved pharmacotherapies for MGD, suboptimally treated MGD can lead to gland blockage/dilation, decreased meibum quality/quantity, irreversible glandular atrophy/loss, altered tear film composition, ocular surface damage, and evaporative dry eye.[3]
- A phase 2 clinical trial was conducted to investigate the safety and efficacy of AZR-MD-001 (selenium sulfide ophthalmic ointment)—a potent keratolytic and keratostatic agent that induces meibomian gland lipogenesis—versus vehicle for the treatment of MGD.

DEMOGRAPHICS

- A total of 245 patients were included in the safety and 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)

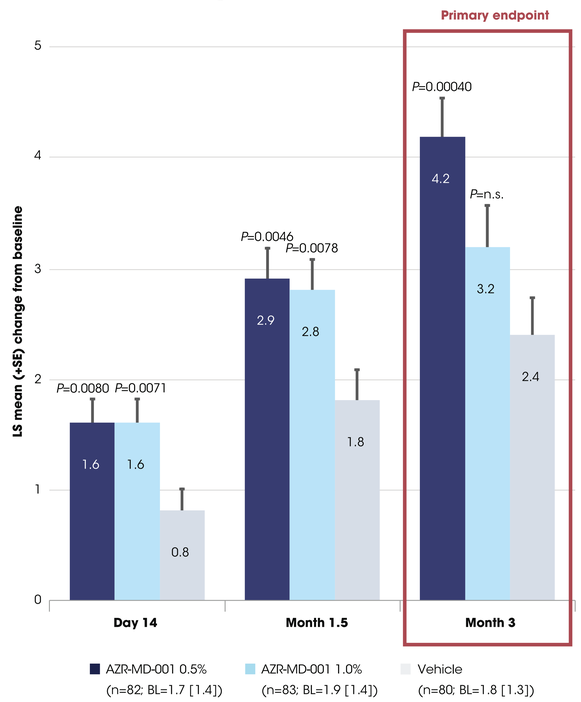
		AZR-MD-001 0.5% (N=82)	AZR-MD-001 1.0% (N=83)	VEHICLE (N=80)
Age (years)	Mean (SD)	52.1 (16.9)	55.6 (17.9)	51.9 (18.5)
	Range	18–80	20–93	20–97
Sex, n (%)	Male	31 (37.8)	27 (32.5)	24 (30.0)
	Female	51 (62.2)	56 (67.5)	56 (70.0)
Race, n (%)	White	57 (69.5)	64 (77.1)	56 (70.0)
	Asian	16 (19.5)	10 (12.0)	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, 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)

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.

RESULTS

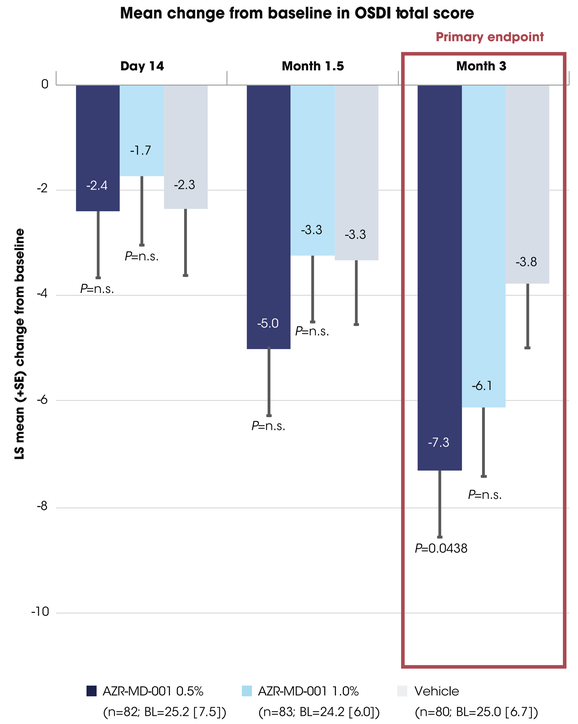
- AZR-MD-001 0.5% met the co-primary endpoints, significantly improving the signs (number of MGYLS; **Figure 1**) and associated ocular symptoms (OSDI total score; **Figure 2**) of MGD versus vehicle at Month 3.
- Significant clinical changes were seen as early as Day 14, after a total of 4 applications of the drug (**Figure 1**).

FIGURE 1. AZR-MD-001 0.5% STATISTICALLY SIGNIFICANT IMPROVEMENT IN MORE OPEN MEIBOMIAN GLANDS THAN VEHICLE AT MONTH 3 (ITT)



P-value versus vehicle (n.s., not significant); *P*-values at Month 3 adjusted for multiplicity.
BL, baseline mean (standard deviation) score; ITT, intent-to-treat (all patients randomized to study drug); MGYLS, Meibomian Glands Yielding Liquid Secretion (higher scores are better).

FIGURE 2. AZR-MD-001 0.5% STATISTICALLY SIGNIFICANT IMPROVEMENT IN MGD DRY EYE SYMPTOMS VS VEHICLE AT MONTH 3 (ITT)



P-value versus vehicle (n.s., not significant); *P*-values at Month 3 adjusted for multiplicity.
BL, baseline mean (standard deviation) score; ITT, intent-to-treat (all patients randomized to study drug); MGD, meibomian gland dysfunction; OSDI, Ocular Surface Disease Index (lower scores are better).

STUDY DESIGN

- 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 score ≥6, a Tear Break-Up Time <10 seconds in both eyes, and gland dropout <75%
- 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
- Study timepoints: baseline, Day 14, Month 1.5, and Month 3
- Co-primary endpoints: change from baseline in number of Meibomian Glands Yielding Liquid Secretion (MGYLS) and in OSDI total score at Month 3, analyzed using a hierarchical approach
- Changes from baseline evaluated using an 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

Co-primary efficacy endpoints

MGYLS measures the number of glands yielding liquid secretion through observing 15 glands on the lower lid, following diagnostic expressability, to determine whether they secrete any liquid (binary outcome); with a score range of 0–15, higher scores are better.[4]

OSDI measures 12 items centered on ocular symptoms, environmental triggers, and vision-related functioning, with each item rated from 0 (none of the time) to 4 (all of the time), the total score ranging 0–100, and lower scores better.[4]

Safety and tolerability

Safety and tolerability were assessed by the nature, incidence, and severity of treatment-emergent adverse events (TEAEs).

SAFETY AND TOLERABILITY

- AZR-MD-001 demonstrated good safety and tolerability during the 3 months of treatment (**Table 2**).
- Only 3 patients were discontinued from the study due to an adverse event (2 in the AZR-MD-001 0.5% group and 1 in the AZR-MD-001 1.0% group).

TABLE 2. SUMMARY OF TEAES (SAFETY POPULATION)

	AZR-MD-001 0.5% (N=82)	AZR-MD-001 1.0% (N=83)	VEHICLE (N=80)
Any TEAEs, n (%)	54 (65.9)	61 (73.5)	22 (27.5)
Any ophthalmic TEAEs (in either eye), n (%)	47 (57.3)	57 (68.7)	14 (17.5)
TEAEs reported in ≥5% of patients, n (%)			
Application-site pain	14 (17.1)	13 (15.7)	0
Lacrimation increased	9 (11.0)	1 (1.2)	0
Superficial punctate keratitis*	5 (6.1)	6 (7.2)	1 (1.3)
Eye pain	5 (6.1)	6 (7.2)	1 (1.3)
Corneal staining*†	4 (4.9)	7 (8.4)	1 (1.3)
Eye irritation	4 (4.9)	5 (6.0)	2 (2.5)
Eye inflammation	3 (3.7)	8 (9.6)	1 (1.3)
Application-site irritation	2 (2.4)	5 (6.0)	0
Any serious TEAEs, n (%)‡	1 (1.2)	1 (1.2)	2 (2.5)

*Defined as associated with an increase in corneal staining of ≥2 grades.
†62% baseline incidence of corneal staining (Oxford Score 1 or 2 units) signifying early moderate inflammation.
‡No serious TEAEs were considered related to study drug.
TEAE, treatment-emergent adverse event.

SUMMARY

- This phase 2 study demonstrated that AZR-MD-001 0.5% significantly improved signs and reduced associated symptoms of MGD at Month 3.
- Improvements in signs of MGD were seen as early as Day 14 (after only 4 applications) of AZR-MD-001 0.5%.
- AZR-MD-001 was safe and well tolerated in this study.

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