AZR-MD-001 efficacy in resolving the signs and associated symptoms of meibomian gland dysfunction (MGD) in a phase 2 trial: responder status analysis

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INTRODUCTION

- Meibomian gland dysfunction (MGD) is MGD is characterized by hyperkeratinization of the ductal epithelium and aberrant keratin aggregation within the meibum.[1]
- 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.[2]
- AZR-MD-001 (selenium sulfide ophthalmic ointment) is a potent keratolytic and keratostatic agent that induces meibomian gland lipogenesis and is under investigation for the treatment of MGD.
- A phase 2 clinical trial was conducted that identified the percentage of patients with MGD who demonstrated clinically meaningful improvement in signs and symptoms in response to treatment with AZR-MD-001 (selenium sulfide ophthalmic ointment) versus vehicle over 3 months.

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)

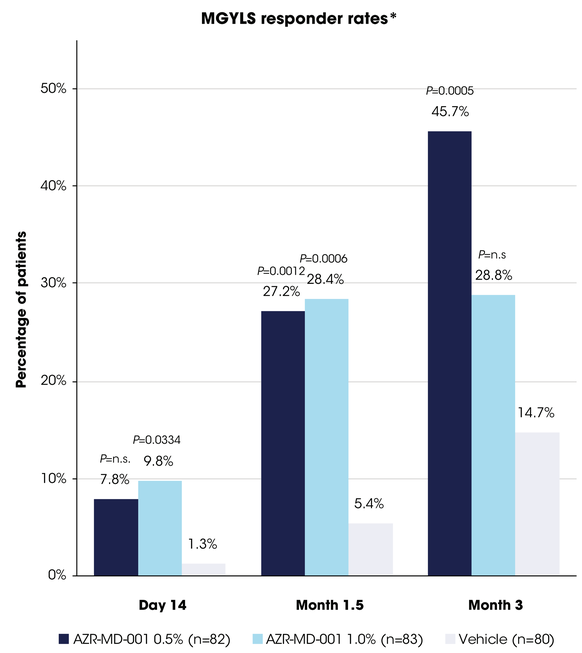
		AZR-MD-001 0.5% (N=82)	AZR-MD-001 1.0% (N=83)	VEHICLE (N=80)
Age (years)	Mean (SD)	52.1 (16.9)	55.6 (17.9)	51.9 (18.5)
	Range	18–80	20–93	20–97
Sex, n (%)	Male	31 (37.8)	27 (32.5)	24 (30.0)
	Female	51 (62.2)	56 (67.5)	56 (70.0)
Race, n (%)	White	57 (69.5)	64 (77.1)	56 (70.0)
	Asian	16 (19.5)	10 (12.0)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

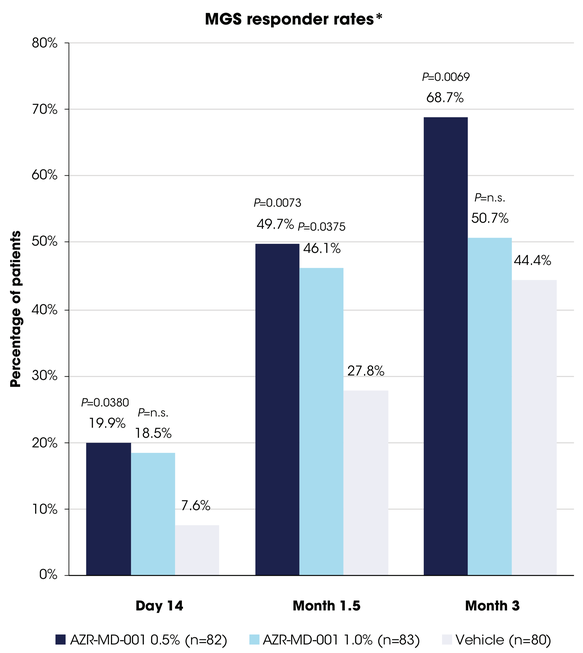
- AZR-MD-001 0.5% met the co-primary endpoints, significantly improving the signs (number of MGLYS) and symptoms (OSDI total score) of MGD vs vehicle at Month 3 (For complete results, see ARVO 2023 abstract 5175 - B0072).
- Compared to vehicle, AZR-MD-001 0.5% resulted in a significantly increased number of functional glands (**Figure 1**), higher meibum quality (**Figure 2**), and greater percentage of patients considered asymptomatic (**Figure 3**) at Month 3; AZR-MD-001 0.5% resulted in numerically higher rates relative to placebo.
- A significantly higher rate of clinically meaningfully improvement in the signs (MGLYS, MGS) of MGD was observed as early as Day 14.
- AZR-MD-001 demonstrated good safety and tolerability during the 3 months of treatment (For complete results see ARVO 2023 abstract 5175 - B0072).

FIGURE 1. SIGNIFICANTLY MORE PATIENTS TREATED WITH AZR-MD-001 THAN VEHICLE SHOWED CLINICALLY MEANINGFUL IMPROVEMENT IN THE NUMBER OF FUNCTIONAL GLANDS



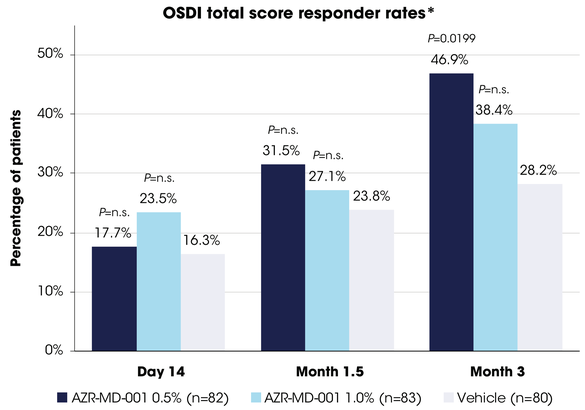
*MGYLS responder: Patients with an ≥5-gland increase from baseline in the study eye typically become asymptomatic.[3]
ITT, intent-to-treat (all patients randomized to study drug); n.s., not significant (*P*>0.05) relative to vehicle; MGLYS, Meibomian Glands Yielding Liquid Secretion (higher scores are better).

FIGURE 2. SIGNIFICANTLY MORE PATIENTS TREATED WITH AZR-MD-001 THAN VEHICLE SHOWED RESOLUTION OF MGD BASED ON MEIBUM QUALITY



*MGS responder: Patients with an MGS score >12 are considered not having MGD anymore.[4]
ITT, intent-to-treat (all patients randomized to study drug); MGS, Meibomian Gland Secretion (higher scores are better); n.s., not significant (*P*>0.05) relative to vehicle.

FIGURE 3. SIGNIFICANTLY MORE PATIENTS TREATED WITH AZR-MD-001 THAN VEHICLE BECAME ASYMPTOMATIC FOR DISEASE



*OSDI responder: Patients with an OSDI score >12 are considered asymptomatic for disease.[3,5] ITT, intent-to-treat (all patients randomized to study drug); n.s., not significant (*P*>0.05) relative to vehicle; OSDI, Ocular Surface Disease Index (lower scores are better).

SUMMARY

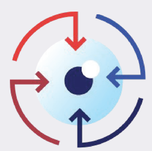
- This phase 2 efficacy study demonstrated that a significantly higher percentage of patients treated with AZR-MD-001 experienced resolution of MGD signs and symptoms compared to vehicle.
- AZR-MD-001 is the first pharmacotherapy to demonstrate significant rates of resolution of both clinical signs and symptoms of MGD.
- Future work should explore the impact of the changes in glandular function with AZR-MD-001 therapy on longer-term ocular surface health.

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
- Co-primary endpoints: change from baseline vs vehicle in number of Meibomian Glands Yielding Liquid Secretion (MGYLS) and in OSDI total score at Month 3
- Response thresholds: all prespecified and based on literature cutoffs
- Responder rates were analyzed using a 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

MGYLS measures number of glands of 15 yielding liquid secretion following diagnostic expressability (open vs not open), with the total score ranging 0–15 and a change from baseline of ≥5 indicating significant response.[4]

MGS measures the meibum quality of 15 glands on the lower eyelid on a scale from 0 (no secretion) to 3 (clear liquid secretion), with the total score ranging 0–45 and scores >12 indicating good meibum quality.[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 scores <13 considered normal or asymptomatic.[3,5]

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QR Code

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