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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Lisa M. Nijm[1,2]; Jennifer P. Craig[3]; Mark Hinds[4]; Yair Alster[5]; Charles Bosworth[5]; The CELESTIAL STUDY Group

[1]Warrenville EyeCare & LASIK, Warrenville, IL, USA; [2]University of Illinois Eye and Ear Infirmary, Department of Ophthalmology, Chicago, IL, USA; [2]Department of Ophthalmology, New Zealand National Eye Centre, The University of Auckland, Auckland, New Zealand; [3]Ophthalmic Trials Australia, Brisbane-Queensland, Australia; [4]Azura Ophthalmics Ltd, Tel Aviv, Israel

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INTRODUCTION

- Meibomian gland dysfunction (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 to identify 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 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)

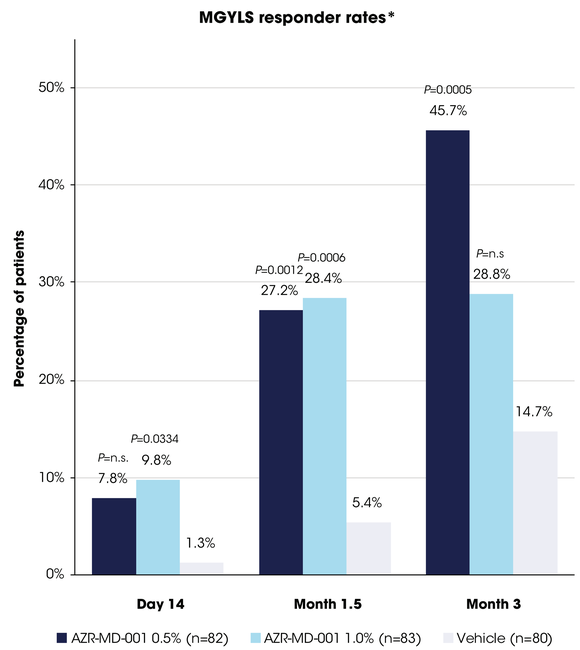
		AZR-MD-001 0.5% (N=82)	AZR-MD-001 1.0% (N=83)	VEHICLE (N=80)
Age (years)	Mean (SD)	52.1 (16.9)	55.6 (17.9)	51.9 (18.5)
	Range	18–80	20–93	20–97
Sex, n (%)	Male	31 (37.8)	27 (32.5)	24 (30.0)
	Female	51 (62.2)	56 (67.5)	56 (70.0)
Race, n (%)	White	57 (69.5)	64 (77.1)	56 (70.0)
	Asian	16 (19.5)	10 (12.0)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

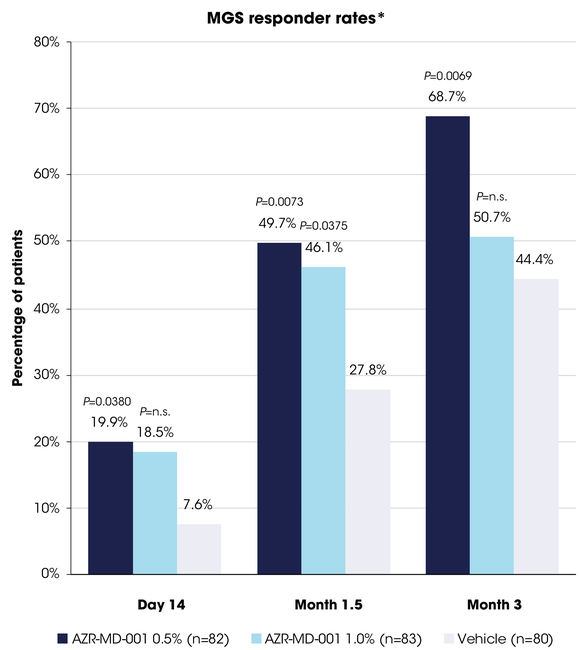
- AZR-MD-001 0.5% met the co-primary endpoints, significantly improving the signs (number of MGYLS) and symptoms (OSDI total score) of MGD versus vehicle at Month 3, and demonstrated good safety and tolerability. (For complete results, see ARVO 2023 abstract 5175 - B0072.)
- Compared to vehicle, AZR-MD-001 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 numerical higher rates relative to vehicle.
- A significantly higher rate of clinically meaningful improvement in the signs (MGYLS, MGS) of MGD was observed as early as Day 14.

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



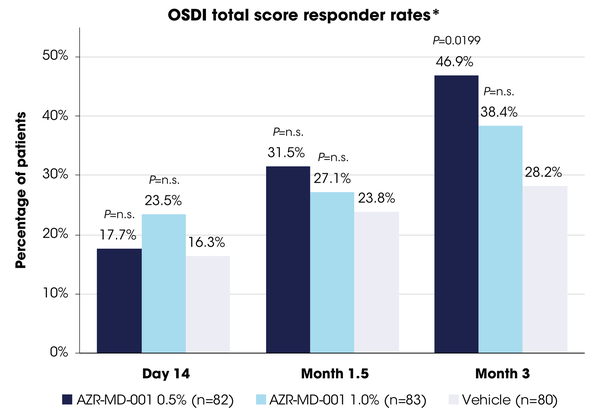
*MGYLS responder: Patients with an ≥5-gland increase from baseline in the study eye typically become asymptomatic.[3]
ITT, intent-to-treat (all patients randomized to study drug); n.s., not significant (*P*>0.05) relative to vehicle; MGLYS, Meibomian Glands Yielding Liquid Secretion (higher scores are 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 <13 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

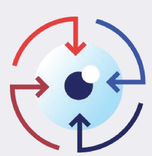
- This phase 2 efficacy study demonstrated that a significantly higher percentage of patients treated with AZR-MD-001 experienced resolution of MGD signs and symptoms compared to vehicle.
- AZR-MD-001 is the first pharmacotherapy to demonstrate significant rates of resolution of both clinical signs and 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

- **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 score ≥6, a Tear Break-Up Time <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
- **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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Contact

Lisa M. Nijm, MD, JD
Warrenville EyeCare & LASIK, Warrenville, IL, USA
University of Illinois Eye and Ear Infirmary, Department of Ophthalmology, Chicago, IL, USA
nijm77@aol.com

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