Randomized Controlled Trial Evaluating Novel Keratolytic for MGD Treatment

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Abstract # 3543051

BACKGROUND

Meibomian gland dysfunction (MGD) is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and changes in the glandular secretion. Terminal duct obstruction is linked to hyperkeratinization of the ductal epithelium.[1] Meibomian excreta is a mixture of lipid secretions and keratinized epithelial debris. Keratin levels increase in meibum by up to 10% in MGD patients and keratin can alter meibum consistency due to disulfide bond crosslinking of proteins (e.g., Keratin 7 and 13) produced from the acinar cells.[2,3] Recent studies have also observed that keratin mixes into meibomian lipid films destabilizing them *in vitro*.[4] These changes have the potential to induce evaporative dry eye disease (DED) and symptoms of eye irritation . Indeed, the principal clinical consequence of obstructive MGD is evaporative DED and as many as 86% of patients with dry eye symptoms exhibit clinical signs of MGD.[5]

No approved pharmacological treatments for MGD currently exist. As part of a series of related studies (see also ARVO abstract #3544345 and #3542787), Clinical Study AZ202001 (STARLET) investigated a novel keratolytic, keratostatic and lipogenic compound, AZR-MD-001 ointment/semi-solid drug containing selenium sulfide (SeS_2; Azura Ophthalmics® VIC, Australia), as a potential treatment for MGD.

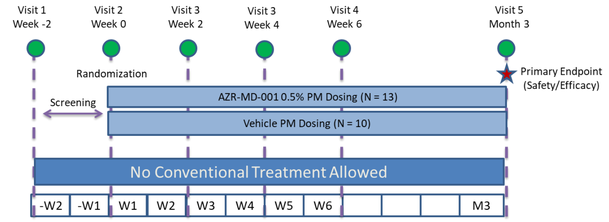
OBJECTIVES

To evaluate safety, tolerability, and efficacy of AZR-MD-001 ointment (AZR) relative to vehicle, when applied twice weekly to the lower lid margin for up to 3 months, in patients with MGD.

METHODS

MGD patients (n=23) fulfilling all study inclusion criteria were randomized to a multicenter, investigator-masked, vehicle-controlled, parallel group study conducted from Jul to Oct 2020.

Study design:



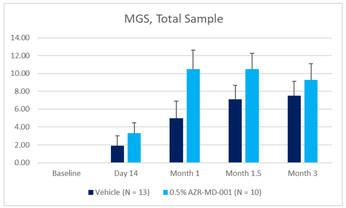
- Key inclusion criteria: Meibomian Gland Score (MGS) ≤ 12 for 15 lower lid glands and Total Ocular Surface Disease Index (OSDI) score ≥ 13
- Outcome measures: MGS, Meibomian Glands Yielding Liquid Secretion (MGYLS), Total OSDI score and Eye Dryness Visual Analogue Scale (ED-VAS) score
- Analyzed two populations: ***Total Sample***: mild-to-severe MGD (OSDI range: 13 to 100) and ***Mild to Moderate***: mild-to-moderate MGD (OSDI range: 13 to 33)

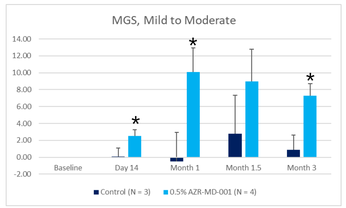
RESULTS

Subject Demographics

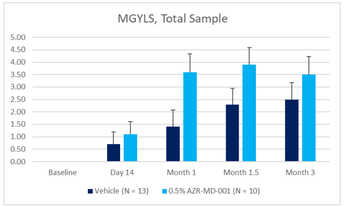
	AZR-MD-001 0.5%	Vehicle	p
Age (Years ± SD)	52.0 ± 21.8	57.8 ± 14.41	0.453
Sex (M, F in %)	60.0%, 40.0%	46.2%, 53.8%	0.510
Duration of MGD (< 5 years, ≥ 5 years in %)	50.0%, 50.0%	23.1%, 76.9%	0.179

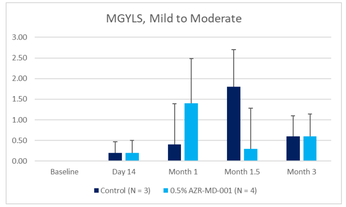
Meibomian Gland Score (MGS)





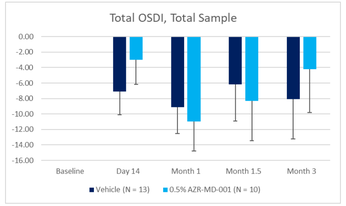
Meibomian Glands Yielding Liquid Secretion (MGYLS)

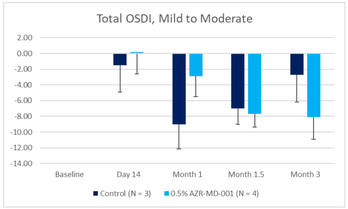




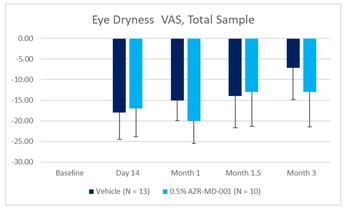
* P < 0.05 (Vehicle Vs. AZR)

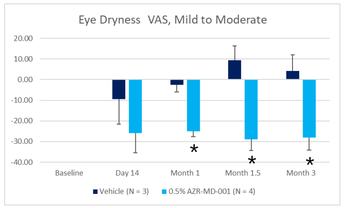
Total OSDI





Eye Dryness VAS





* P < 0.05 (Vehicle Vs. AZR)

Safety and Tolerability

AZR-MD-001 0.5% was safe and well tolerated. No Serious Adverse Events (SAEs) were reported, nor treatment related AEs leading to discontinuation of treatment. Only 2 subjects (01-001, eye pain; 03-008, ocular discomfort) reported events likely or very likely related to therapy.

CONCLUSIONS

Study outcomes suggest that AZR-MD-001 0.5% can significantly restore gland function (as measured by MGS) in patients with MGD and improve symptoms (as measured by Eye Dryness VAS). The benefits of AZR-MD-001 were consistently observed across all patients at Month 3, but reached statistical significance in a small subset of patients with mild-to-moderate MGD. More severe ocular surface disease is recognised to cause increased variance on patient outcome measures and may also be associated with mixed disease that is more challenging to treat with monotherapy.[6] Larger studies are warranted, but AZR-MD-001 shows promise as the first drug demonstrating improvements on both the signs and symptoms of MGD.

REFERENCES

1. Nichols KK, Foulks GN, Bron AJ, et al. The International Workshop on Meibomian Gland Dysfunction: Executive Summary. Invest Ophthalmol Vis Sci. 2011;52:1922-1929.
2. Tomlinson A, Bron AJ, Korb DR, et al. The International Workshop on Meibomian Gland Dysfunction: Report of the Diagnosis Subcommittee. Invest Ophthalmol Vis Sci. 2011;52:2006-2049.
3. Ong BL Hodson SA, Wigham T, et al. Evidence for Keratin proteins in normal and abnormal human meibomian fluids. Curr Eye Res. 1991; 10, 1113-1119.
4. Jeyalatha MV, Qu Y, Liu Z, et al. Function of meibomian gland: Contribution of proteins. 2017; Exp Eye Res. 163:29-36.
5. Lemp MA, Crews LA, Bron AJ, et al. Distribution of aqueous-deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study. Cornea. 2012; 31; 472-478.
6. Sullivan BD, Whitmer D, Nichols KK, et al. An Objective Approach to Dry Eye Disease Severity. Invest Ophthalmol Vis Sci. 2010;51:6125-6130.

DISCLOSURES

Jennifer P. Craig: Azura Ophthalmics: F
Fiona Stapleton: Azura Ophthalmics: F
Jacqueline Tan: Azura Ophthalmics: F
Susan Thackwray: Azura Ophthalmics: F
Jagrut Lallu: Azura Ophthalmics: F
Scott Read: Azura Ophthalmics: F
Karien Nel: Azura Ophthalmics: F
Charles Bosworth: Azura Ophthalmics: I