

Results of Phase 2 program for the treatment of Meibomian Gland Dysfunction with AZR-MD-001



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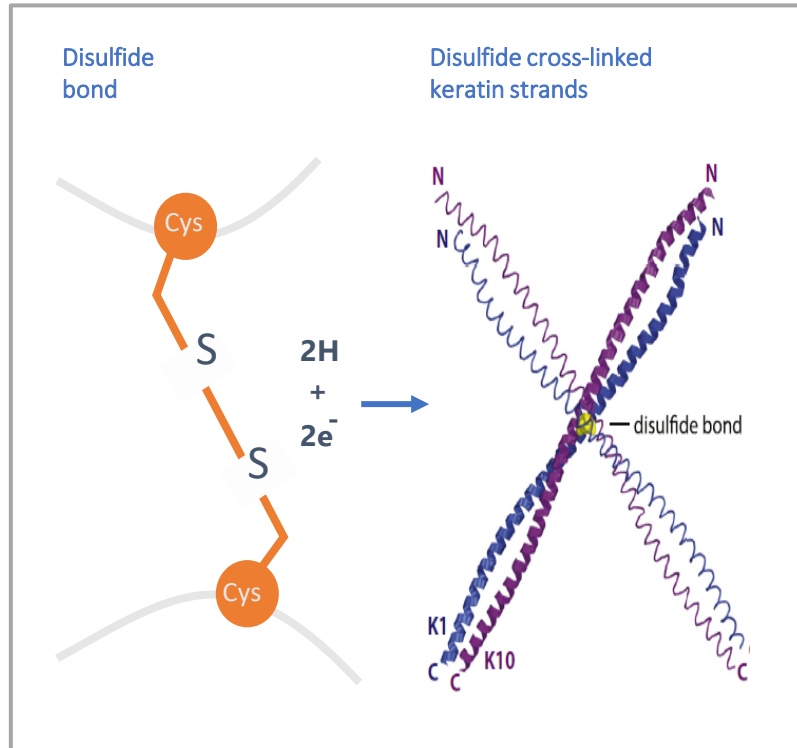
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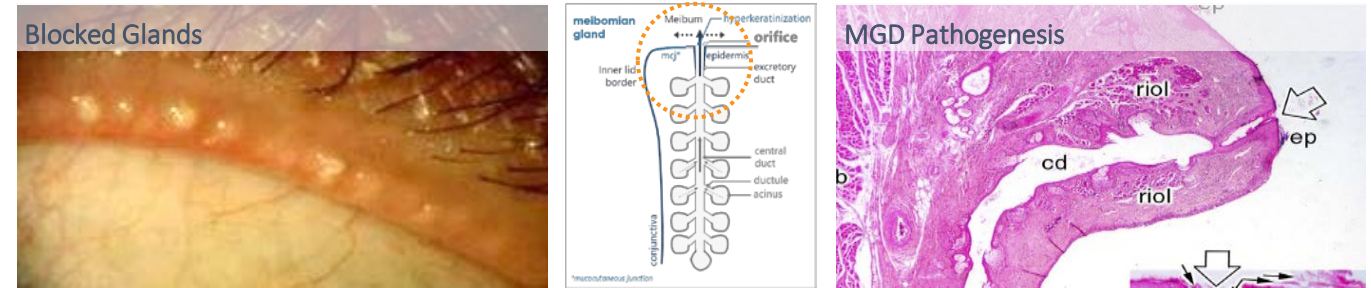


ABERRANT DISULFIDE BOND FORMATION RESULTS IN HYPERTINIZATION AT THE ORIFICE AND MEIBUM ALTERATION

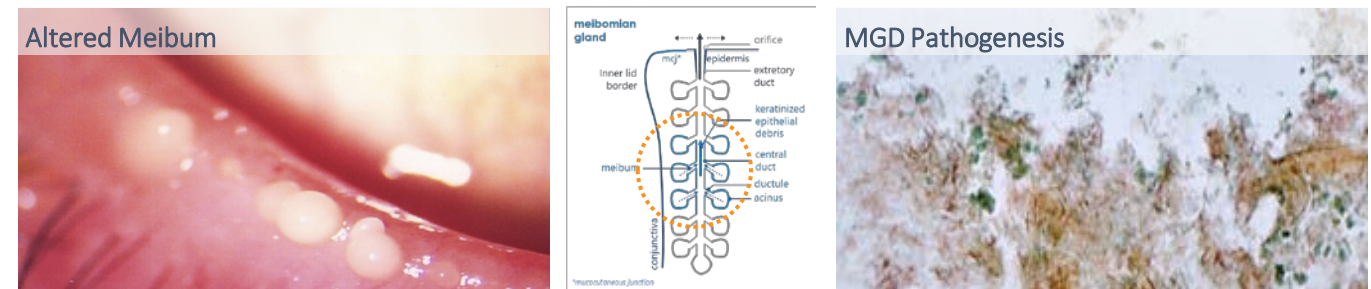
Hyperkeratosis and Oxidative stress
Result in excess formation of disulfide bonds¹



Gland obstruction^{2,3}



Thick lipid/protein aggregation^{2,3}



¹ Ibrahim OM, Dogru M, Matsumoto Y, et al. Oxidative stress induced age dependent meibomian gland dysfunction in Cu, Zn-superoxide dismutase-1 (Sod1) knockout mice. PLoS One. 2014;9(7):e99328.

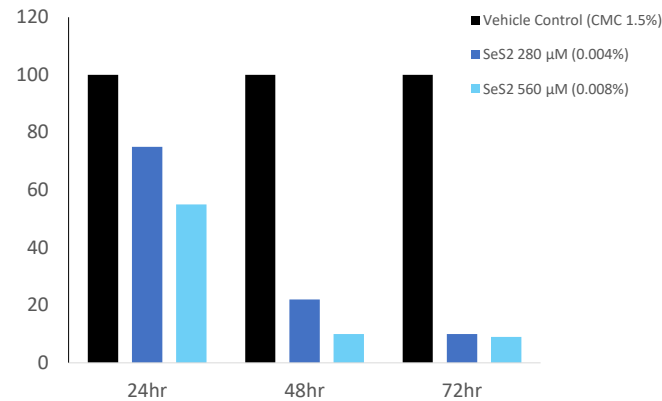
² Knop E et al, Ophthalmologie 2009;106:872-833

³ Knop E et al, Invest Ophthalmol Vis Sci. 2011;52(4):1938-78.8 .

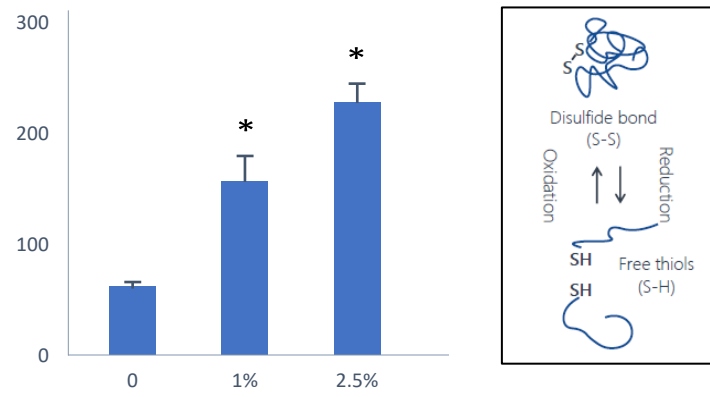
AZR-MD-001- ophthalmic selenium sulfide ointment

- first therapy to target hyperkeratinization in MGD using keratolytics
- multimodal mechanisms of action to target excess keratin formation and build up

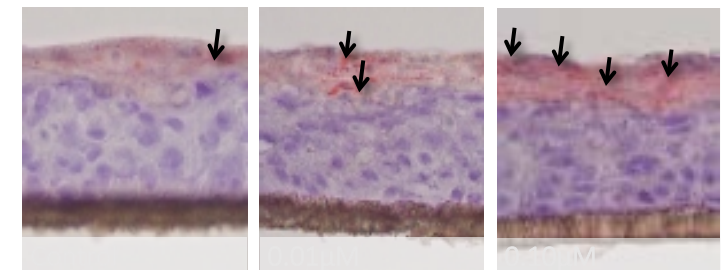
Slows down both the rate of keratinocyte proliferation and keratin production¹



Softens keratin plug by breaking down disulfide (s-s) bonds, alleviating hyperkeratinization¹



Stimulates lipogenesis to increase the quantity of lipids produced by the meibomian glands²

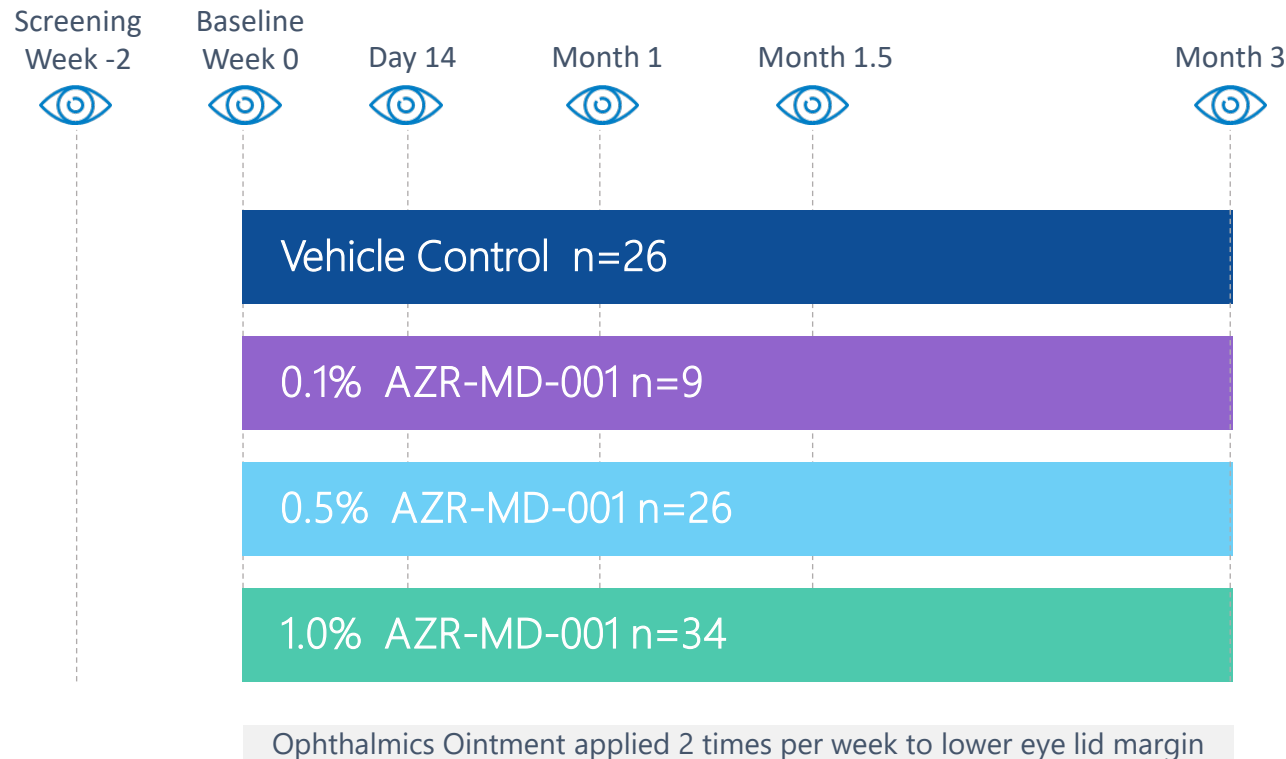


* Arrows point to lipid staining

¹Knop E, Knop N, Millar T, Obata H, Sullivan DA. IOVS, Special Issue 2011. 1938-1978 | ²Korb DR, Henriquez AS. J Am Optom Assoc. 1980;51:243-251
³Tomlinson et al. Invest Ophthalmol Vis Sci. 2011 | ⁴Ong et al. Curr Eye Res. 1991 | ⁵Obata et al. 2002;:ARVO E-Abstract 60

AZR-MD-001 PHASE 2 PROGRAM

- MULTICENTER, RANDOMIZED, DOUBLE MASKED VEHICLE CONTROLLED CLINICAL TRIAL
- TO EVALUATE SAFETY AND EFFICACY NEW TX FOR MEIBOMIAN GLAND DYSFUNCTION



Primary Sign Endpoints:

- Change from baseline of MGS at 3 months
- Change from baseline of MGYLS at 3 months
- Either can serve for approval

Primary Symptom Endpoints:

- Change from baseline to month 3 in total OSDI
- Change from baseline to month 3 in Eye Dryness VAS

MGS = Meibomian Gland Score

MGYLS = Meibomian Gland Yielding Liquid Secretion

APPROVAL FOR MGD TREATMENT

REQUIRES BOTH A SIGN & A SYMPTOM ENDPOINT FOR FDA APPROVAL

EFFICACY SIGN ENDPOINTS

MGYLS (Meibomian Glands Yielding Liquid Secretion)

- Number of open glands

Number of open glands out of 15 glands on the lower lid

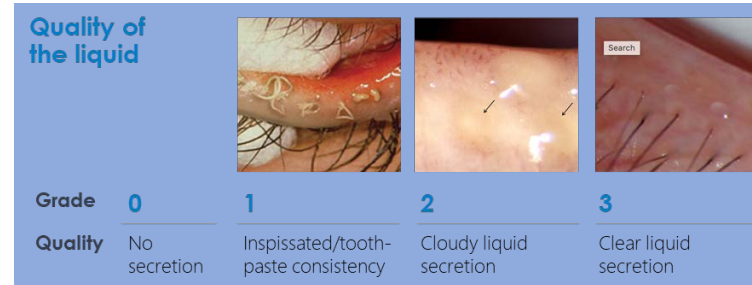
Liquid – Yes/No



MGS (Meibomian Gland Score)

- Quality of the liquid from the glands

Liquid grading (0-3) of the 15 glands



EFFICACY SYMPTOM ENDPOINT

Validated in Target MGD Population

Ocular Surface Disease Index (OSDI)

Multivariant validated questionnaire

HAVE YOU EXPERIENCED ANY OF THE FOLLOWING DURING THE LAST WEEK:						
	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
1. Eyes that are sensitive to light?	4	3	2	1	0	
2. Eyes that feel gritty?	4	3	2	1	0	
3. Painful or sore eyes?	4	3	2	1	0	
4. Blurred vision?	4	3	2	1	0	
5. Poor vision?	4	3	2	1	0	
HAVE PROBLEMS WITH YOUR EYES EXCLUDED YOU IN PERFORMING ANY OF THE FOLLOWING DURING THE LAST WEEK:						
	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or a bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A
HAVE YOUR EYES FELT UNCOMFORTABLE IN ANY OF THE FOLLOWING SITUATIONS DURING THE LAST WEEK:						
	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A

✓ FDA has confirmed both MGYLS and MGS can be used for approval

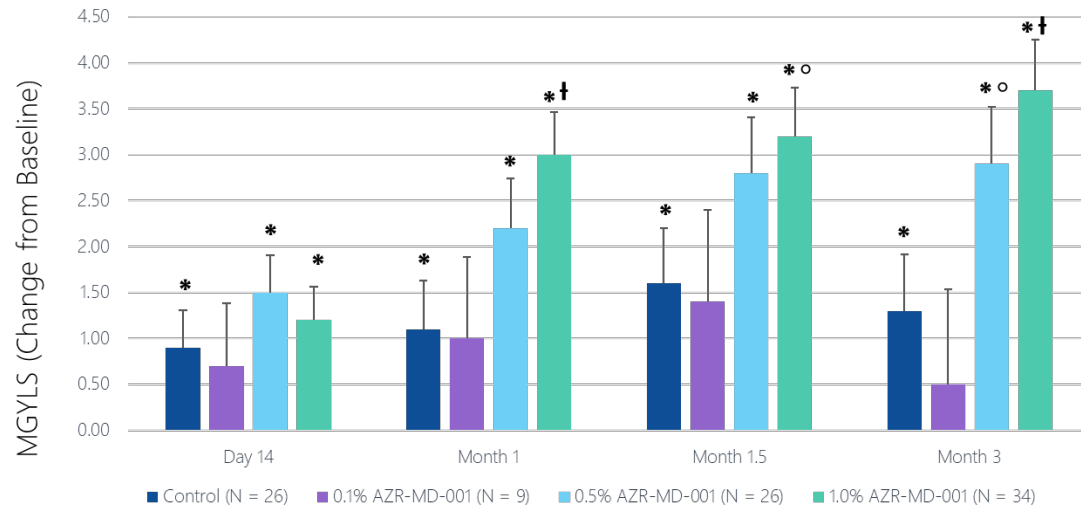
RESULTS

STATISTICALLY SIGNIFICANT IMPROVEMENT IN SIGNS

- MEIBOMIAN GLAND YIELDING LIQUID SECRETION (MGYLS) AND MEIBOMIAN GLAND SCORE (MGS) – CHANGE FROM BASELINE

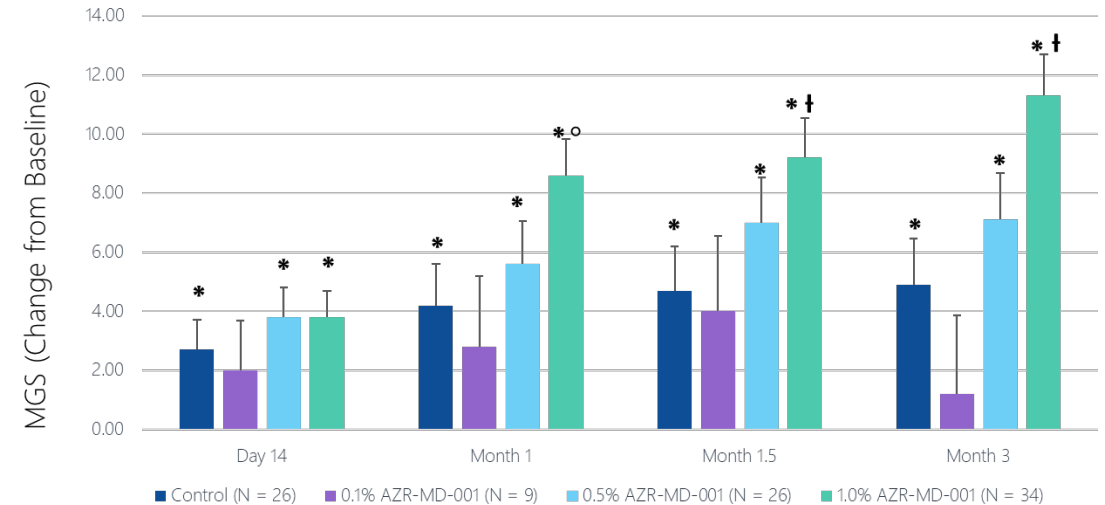
Number of Open Glands

*Statistically Significant Difference from Baseline
($P < 0.05$)



Quality of Meibum

*Statistically Significant Difference from Baseline
($p < 0.05$)



Integrated mITT Population

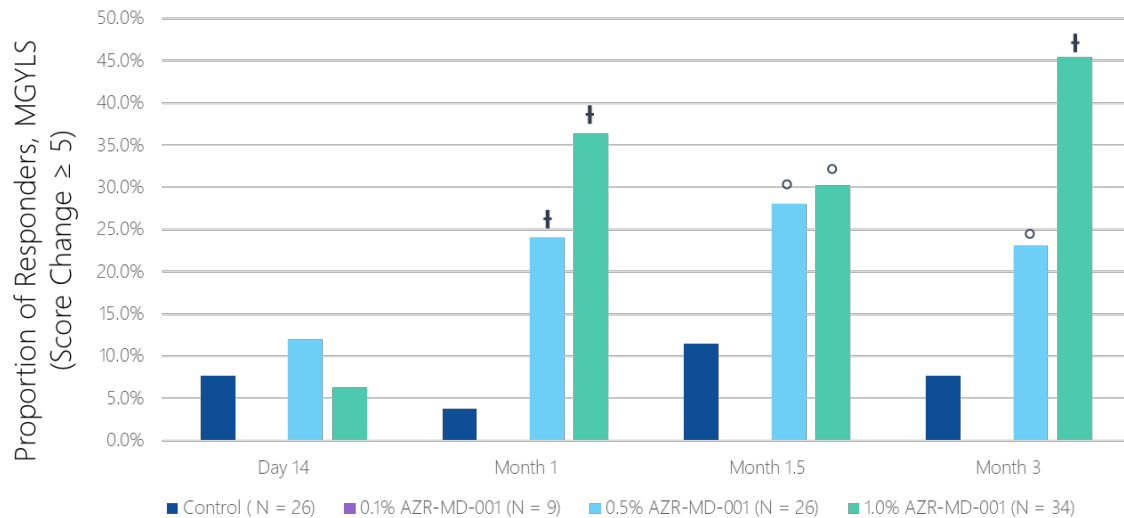
† significantly different from control ($p < 0.05$) | ° significantly different from control ($p < 0.10$) | * significantly different from baseline ($p < 0.05$)

RESULTS

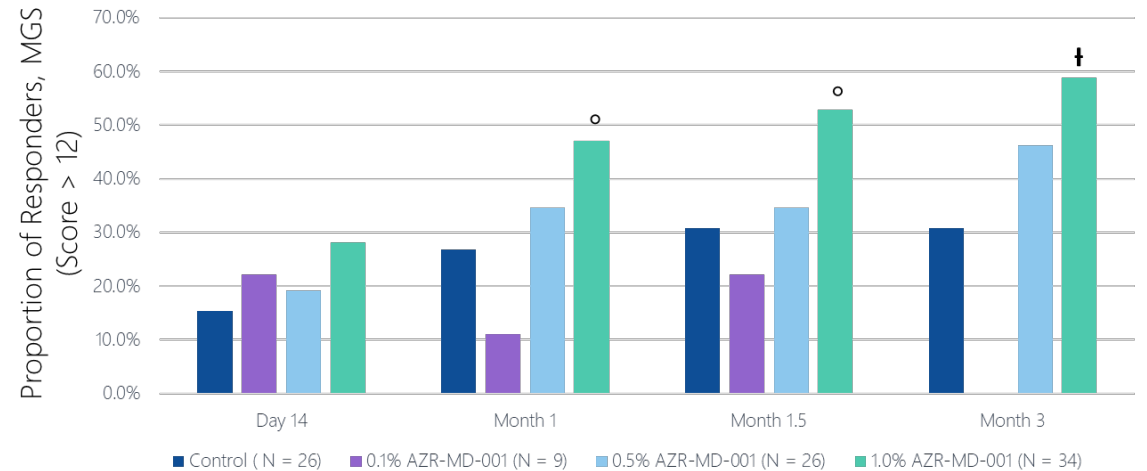
CLINICALLY MEANINGFUL IMPROVEMENT IN SIGNS

- AT 3 MONTHS, 46% OF PATIENTS ON (1.0%) ACHIEVED NORMAL MGYSL COMPARED 8% ON VEHICLE

% of Patients with Normal Open Glands (MGYLS ≥ 5)
Clinically Significant Difference from Control ($p < 0.05$)



% of Patients with Normal Meibum (MGS > 12)
Clinically Significant Difference from Control ($p < 0.05$)



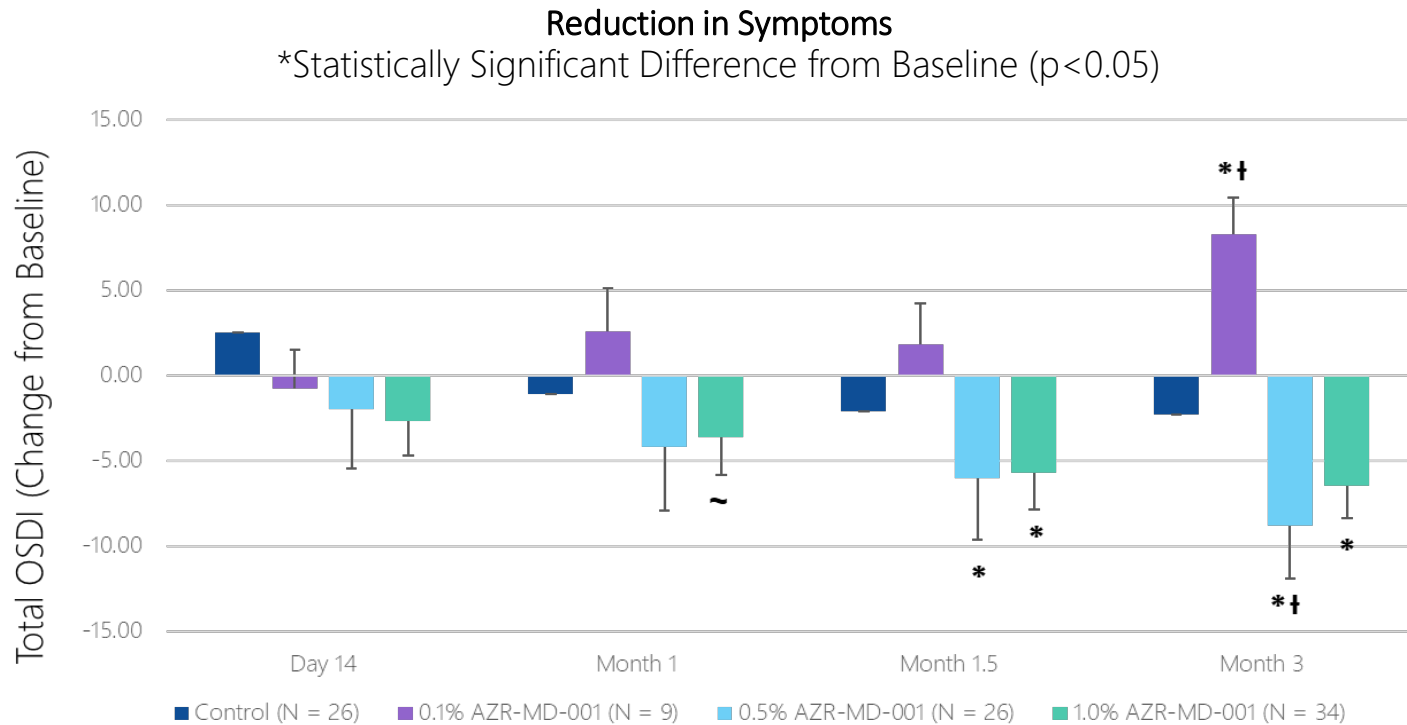
Integrated mITT Population

† significantly different from control ($p < 0.05$) | * significantly different from baseline ($p < 0.05$)

RESULTS

SIGNIFICANT IMPROVEMENT IN SYMPTOMS

TOTAL OCULAR SURFACE DISEASE INDEX (OSDI) – CHANGE FROM BASELINE



No one subscale is driving the change in total OSDI

Symptom improvement consistent across all subscale

MICD for OSDI: 4.5 – 7.3 for Mild to Moderate Disease, 7.3 – 13.4 for Moderate to Severe Disease¹

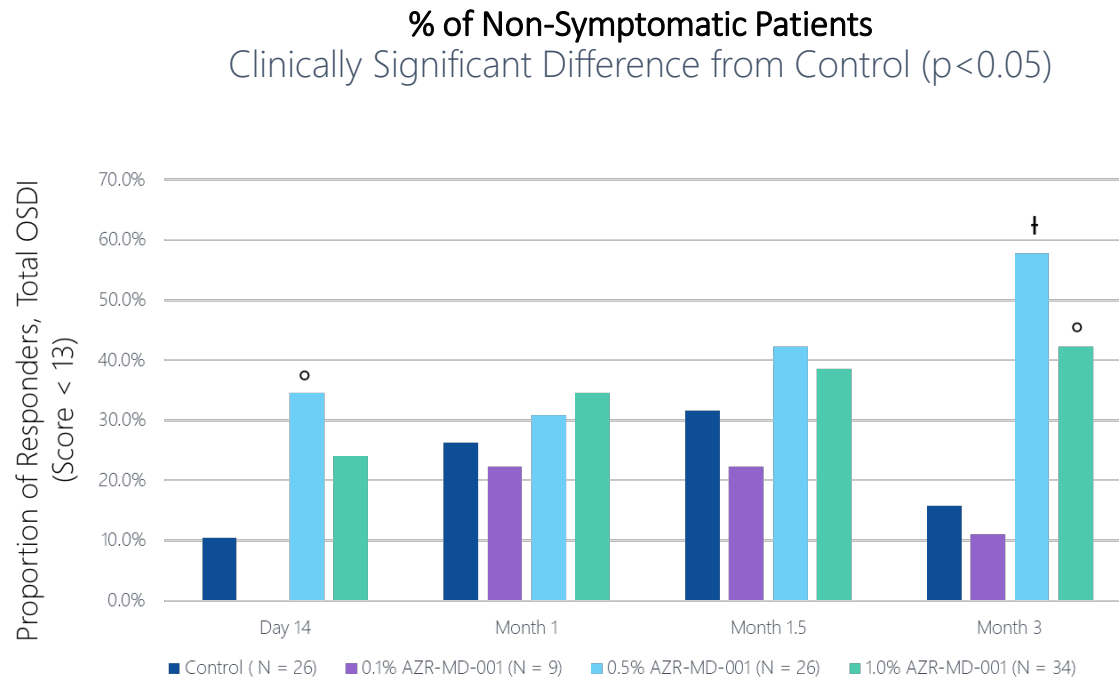
Integrated mITT Population † significantly different from control ($p < 0.05$) | ° significantly different from control ($p < 0.10$) | *significantly different from baseline ($p < 0.05$)

¹Miller KL et al. Minimal Clinically Important Difference for the Ocular Surface Disease Index. Arch Ophthalmol. 2010;128(1):94-101

RESULTS

- SIGNIFICANTLY IMPROVED SYMPTOMS

- AT 3 MONTHS, 42% OF PATIENTS ON (1.0%) ACHIEVED SYMPTOM FREE COMPARED TO 15% ON VEHICLE



- At month 3, for both 0.5% and 1%, statistically significant and clinically meaningful reductions were observed in Total OSDI compared to baseline and control
- with up to 58% of patients becoming non-symptomatic (OSDI <13) compared to 16% in control (p<0.05)

MICD for OSDI: 4.5 – 7.3 for Mild to Moderate Disease, 7.3 – 13.4 for Moderate to Severe Disease¹

Integrated mITT Population

† significantly different from control (p < 0.05) | ° significantly different from control (p < 0.10) | *significantly different from baseline (p < 0.05)

¹Miller KL et al. Minimal Clinically Important Difference for the Ocular Surface Disease Index. Arch Ophthalmol. 2010;128(1):94-101

RESULTS

- SAFETY AND TOLERABILITY PROFILE FOR SELECTED DOSING REGIMEN
- OCULAR ADVERSE EVENTS OCCURRING IN ≥10% OF PATIENTS BY TREATMENT GROUP

	AZR-MD-001 0.1% (N=9)*	AZR-MD-001 0.5% (N=15)	AZR-MD-001 1.0% (N=28)	Control (N=31)
Eye Pain	0	3 (20%)	9 (32%)	2 (6%)
Eye Irritation	1 (11%)	2 (13%)	5 (18%)	2 (6%)
Lacrimation increased	0	0	5 (18%)	0
Vision Blurred	0	2 (13%)	1 (4%)	0
Application site pain	1 (11%)	0	0	0
Application site reaction	1 (11%)	0	0	0

NO SERIOUS OCULAR TEAES
OCCURRED DURING THE STUDY

MOST TEAE'S (96%) WERE MILD TO
MODERATE IN SEVERITY

DOSING IS TWICE WEEKLY AT BEDTIME

*Dosed in the daytime at study visits

CONCLUSION:

AZR-MD-001 HAS THE POTENTIAL TO BE THE FIRST PHARMACOTHERAPY TO BE EFFECTIVE FOR TREATING THE SIGNS AND SYMPTOMS OF MGD

Met primary signs efficacy endpoints - Meibomian Glands Yielding Liquid Secretion and MGS Meibomian Gland Score Change from Baseline

Met primary symptom efficacy endpoints (Symptoms)—Total OSDI (Ocular Surface Disease Index) and EDS VAS Change from Baseline

Acceptable safety and tolerability profile

Both doses (0.5% and 1.0%) achieved meaningful improvements in both signs and symptoms required for FDA approval and is advancing to Phase 3 development