Lotilaner Ophthalmic Solution, 0.25% for Meibomian Gland Disease in Patients with *Demodex* Blepharitis

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INTRODUCTION

- Meibomian gland disease (MGD) is a chronic, diffuse abnormality of the meibomian glands.[1] *Demodex* mites can pathologically colonize the meibomian glands and contribute to the progression of MGD.[2] *Demodex* can also negatively affect meibum quality by causing meibomian gland atrophy.[3]
- Lotilaner ophthalmic solution, 0.25% (Tarsus Pharmaceuticals, Irvine, CA) is an ectoparasiticide that was approved by the Food & Drug Administration for treating *Demodex* blepharitis in humans.[4]
- **Purpose:** To evaluate the safety and efficacy of lotilaner ophthalmic solution, 0.25% (ERSA) compared with vehicle (RHEA) in *Demodex* blepharitis (DB) patients with MGD.

METHODS

- ERSA is a randomized, double-masked study in DB patients with MGD (N=39) who were randomly assigned to receive a twice daily (BID) or three times daily (TID) 12-week course of lotilaner ophthalmic solution, 0.25%, whereas RHEA is a randomized vehicle study in DB patients with MGD (N=40) evaluating the vehicle group (**Figure 1**).
- Patients were included in the studies if they met all of the following criteria (in at least one eye): >10 upper lid lashes with collarettes (Grade 2+), ≥1.0 mites/lash on upper/lower lids combined, meibomian gland secretion score (MGSS) 12-32 (out of 45), ≥Grade 1 erythema of lower lid, tear breakup time (TBUT) <10 seconds, and ≥33% total gland area of lower lid with intact partial to full meibomian glands (per meibography).
- Meibomian gland function was evaluated by assessing 15 central glands of the lower eyelid.
- Meibum quality was scored on a scale of 0 – 3: 3=clear, 2=cloudy, 1=inspissated/toothpaste, 0=no secretion **(Table 3).** Meibum scores of the 15 glands were summed up to create the total meibomian gland secretion score (MGSS, range: 0 – 45).[5]
- Patient-reported outcomes [visual analog scale (VAS) ranging from 0 (no discomfort) to 100 (maximal discomfort)], collarette grade and safety assessments were also measured.
- The two studies were pooled for analysis after establishing between-group baseline equivalence. No statistical differences between ERSA and RHEA were observed at baseline, except for collarette grade. Patients in the ERSA study started off with a worse (higher) collarette grade (p=0.0068).

RESULTS

- Baseline demographic is shown in **Table 1**.
- All baseline parameters and follow-up measures analyzed in the BID and TID arms of the ERSA study and in the BID, TID and crossover arms of the RHEA study were not statistically different from each other and therefore, combined.
- For the lotilaner 0.25% treatment group, statistically significant improvements from baseline were observed at day 43 and day 85 in mean MGSS, mean number of glands secreting any liquid, and percentage of patients achieving ≥3 glands with improvement to clear meibum (score 3) (p<0.001) and when compared with vehicle group (p<0.01) **(Figures 2-4)**. There were no statistically significant improvements from baseline in the vehicle group.
- For patient-reported outcomes, statistically significant improvements from baseline were observed in the lotilaner 0.25% group at day 43 (p<0.01) and day 85 (p<0.0001) and when compared with vehicle group (p<0.05) **(Figure 5).**
- Proportion of patients with collarette reduction to grade 0 (0-2 collarettes/lid) was 42% vs. 0% in the lotilaner 0.25% group and vehicle group, respectively, at day 43 and 66% vs. 0% at day 85 (both p<0.0001). Collarette reduction to grade 0-1 (0-10 collarettes/lid) was 82% vs. 6% in the lotilaner 0.25% group and vehicle group, respectively, at day 43 and 100% vs. 8% at day 85 (both p<0.0001).
- Two patients (5.1%) in the ERSA study and 6 patients (15%) in the RHEA study reported treatment-related ocular adverse events (AEs) **(Table 2)**. No serious treatment-related AEs were reported in either study.

Figure 1. Study Design

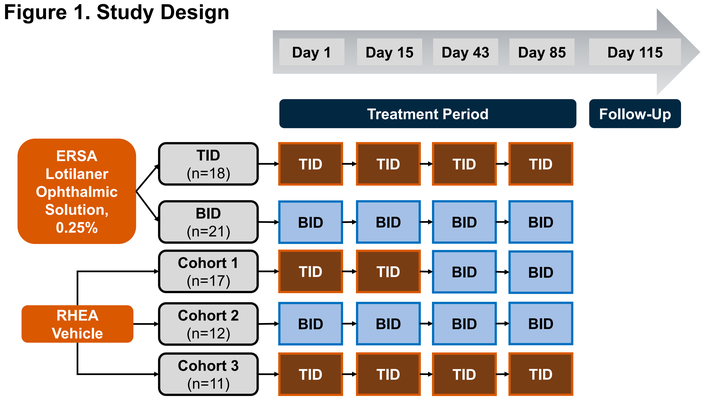


Table 1. Demographic Characteristics

	ERSA	RHEA	p-value
	Lotilaner ophthalmic solution, 0.25% (N=39)	Vehicle (N=40)	
Age, years	63.7	63.4	>0.1
Sex, n (%)			
Female	23 (59)	23 (58)	>0.1
Male	16 (41)	17 (43)	
Race, n (%)			
White	33 (84.6)	34 (85.0)	>0.1
African American/Black	3 (7.7)	3 (7.5)	
Asian	3 (7.7)	3. (7.5)	
Collarette Grade ± SD	2.9 ± 0.8	2.7 ± 0.8	0.0068
MGSS, mean ± SD	21.9 ± 5.1	22.1 ± 5.0	>0.1
Number of Expressible Glands, mean ± SD	7.1 ± 4.0	7.3 ± 3.2	0.05
Number of Glands Yielding Clear Liquid Secretion (Score 3), mean ± SD	0.8 ± 1.1	0.7 ± 1.2	>0.1

MGSS = meibomian gland secretion score; SD = standard deviation; Data are presented as mean ± standard deviation or no. (%).

Table 2. Summary of Treatment-Related Ocular Adverse Events

	ERSA	RHEA
	Lotilaner ophthalmic solution, 0.25% (N=39)	Vehicle (N=40)
Patients with ≥1 AEs*, n (%)	**2 (5.1)**	**6 (15)**
Conjunctival hemorrhage	0	2 (5.0)
Conjunctival irritation	0	1 (2.5)
Conjunctivitis	1 (2.6)	0
Eye Irritation	0	1 (2.5)
Ocular discomfort	1 (2.6)	0
Ocular hyperemia	0	1 (2.5)
Punctate keratitis	0	3 (7.5)
Visual impairment	0	1 (2.5)

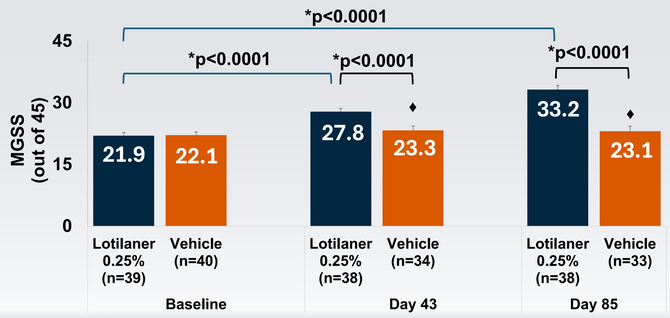
*Patients may have reported >1 AE

Most AEs were mild; there were no serious treatment-related AEs or drug-related withdrawals.

Table 3. Meibum Quality Score Scale

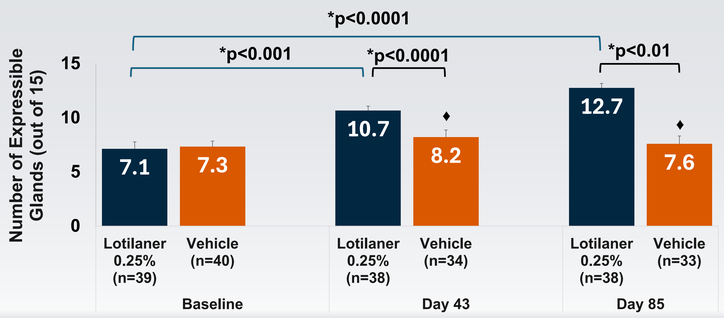
Meibum Quality Score Scale	
Grade 3	Clear liquid secretion
Grade 2	Cloudy liquid secretion
Grade 1	Granularly opaque liquid secretion to inspissated/toothpaste consistency
Grade 0	No secretion

Figure 2. Meibomian Gland Secretion Score (MGSS)



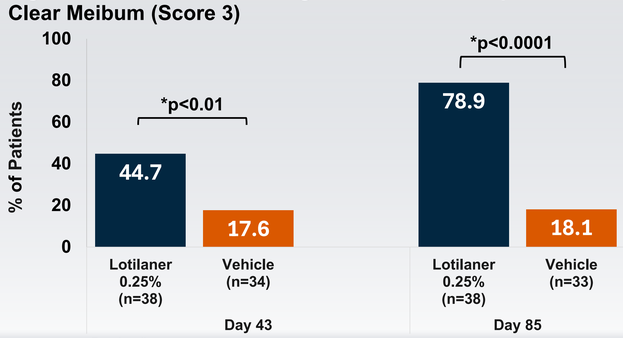
♦p>0.1 compared to baseline

Figure 3. Number of Glands Yielding any Liquid (Score 2-3)



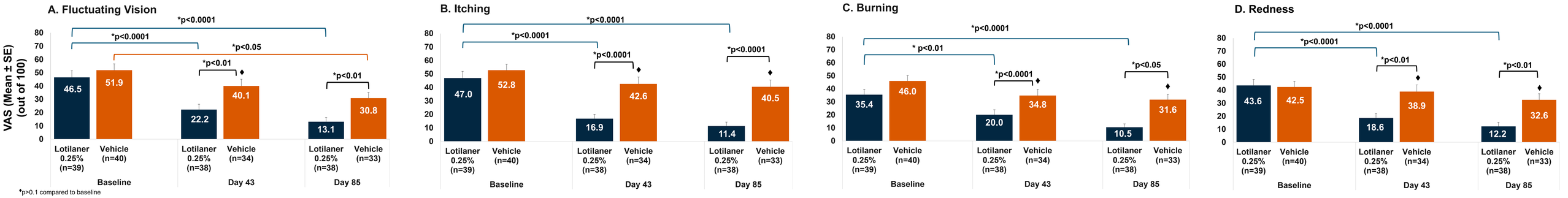
♦p>0.1 compared to baseline

Figure 4. % Patients Achieving ≥ 3 Glands with Improvement† to Clear Meibum (Score 3)



†From baseline

Figure 5. Patient-Reported Outcomes based on Visual Analog Scale (VAS, 0-100)



♦p>0.1 compared to baseline

CONCLUSION

- Lotilaner ophthalmic solution, 0.25% demonstrated statistically significant improvements in measures of meibum quality, meibomian gland function, and patient-reported outcomes at 6 weeks and 12 weeks compared to baseline and vehicle. Lotilaner ophthalmic solution, 0.25% was well tolerated with a similar safety profile as the vehicle group.

Acknowledgement
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