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ORIGINAL RESEARCH

A Prospective Study of Cyclosporine A 0.1% Combined with Loteprednol 0.2% vs Cyclosporine A 0.05% Alone in the Treatment of Dry Eye

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Purpose: To examine the efficacy and tolerability of a combination of cyclosporine 0.1% and loteprednol 0.2% (CsA–LE; Klarity CL) in comparison to commercially available cyclosporine 0.05% (CsA; Restasis) in improving signs and symptoms of dry eye.

Methods: This multicenter, prospective, randomized, controlled, open-label study evaluated 60 patients randomized to a single treatment for 4 weeks and evaluated at day 0, day 14, and day 28. Comparison was made of corneal higher-order aberrations (HOAs), dry-eye symptoms (SPEED score), tear-breakup time (TBUT), corneal staining, and ocular hyperemia, as well as tolerability of each medication with the validated COMTOL instrument.

Results: A total of 56 patients completed enrollment. Corneal HOAs improved significantly with CsA–LE, but not CsA alone. Both groups showed significant improvement (with no significant differences between groups) in SPEED scores, corneal staining, TBUT, and conjunctival hyperemia. Tolerability was similar between the drugs, and no significant safety issues were identified.

Conclusion: The combination of CsA 0.1%–LE 0.2% provided significant improvement in corneal HOAs, while CsA 0.05% did not. For all other measures of ocular surface improvement, both medications showed similar benefits. Tolerability was comparable between the formulations. When rapid rehabilitation of the ocular surface is needed to reduce aberrations, CsA–LE is an appropriate choice.

Keywords: dry eye, higher-order aberrations, loteprednol, cyclosporine

Plain Language Summary

This study compared treatment of dry eyes with two regimens: one with cyclosporine 0.05% alone and one with a combination of cyclosporine 0.1% and loteprednol 0.2%. Both regimens improved ocular surface health, but the combination regimen also improved irregularities of the cornea more effectively than cyclosporine alone.

Introduction

Thirty million people in the US are thought to suffer from dry eye.[1] Patients with this condition manifest with ocular surface disruption, such as corneal fluorescein staining and reduced tear-breakup time (TBUT).[2] Successful treatment is a high priority for both patients and physicians, reducing symptoms and improving visual acuity and corneal higher-order aberrations (HOAs), which have been closely linked with visual benefits and treatment satisfaction when refractive or cataract surgery is performed.[3,4] A number of studies have shown the benefit of both cyclosporine and steroids in managing dry eye.[5] However, existing formulations of these products are challenged by limited tolerability, high out-of-pocket cost, or both. Combination therapy with these agents in an advanced formulation has the potential to improve both tolerability and cost. However, the available formulation of preservative-free Klarity CL (cyclosporine 0.1% and loteprednol 0.2% in a chondroitin sulfate vehicle) has not been studied rigorously. The purpose of this study was to examine the efficacy and tolerability of a combination of cyclosporine 0.1% and loteprednol 0.2% (Klarity CL) in comparison to commercially available cyclosporine 0.05% (Restasis) in improving signs and symptoms of dry eye.

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Methods

This was a multicenter, prospective, randomized, controlled, open-label study of two commercially available products used to treat dry eye: cyclosporine A 0.1% combined with loteprednol etabonate 0.2% in a chondroitin sulfate emulsion containing dextran, glycerol, and hydroxypropylmethylcellulose (Klarity CL, ImprimisRx, Carlsbad, California), and cyclosporine A 0.05% in a castor oil emulsion (Restasis, AbbVie, Irvine, California).

The study was registered on ClinicalTrials.gov as NCT05322148 and conducted under US FDA IND number 161424. The study was conducted under the approval of WCG IRB as protocol 2010 CLEAN Klarity CL Dry Eye Success. None of the authors has any affiliation with WCG IRB. The study adhered to principles of both the Declaration of Helsinki and good clinical practices as defined by the US Food and Drug Administration. All patients provided informed consent prior to enrollment using an informed consent document that was approved by the IRB.

To calculate sample size, we relied on data from an earlier study we published on refractive accuracy after treating dry eye with lifitegrast.[2] In that study, we measured the change in HOAs after 1 month of lifitegrast treatment and found a mean difference from pre- to posttreatment measurements of 0.11±0.26 µm at 1 month. If we assume the same mean ± standard deviation for 1-month results with this study and a rate of type 1 error of 0.05 and type 2 error rate of 0.2, we would require a sample size of 56 patients (using a paired *t*-test calculator at sample-size.net).

Sixty sequential patients who presented to the clinic, met the inclusion/exclusion criteria, and gave informed consent were to be enrolled. Inclusion criteria included age >18 years and the presence at baseline of central or inferior corneal fluorescein staining defined by the Oxford scale,[6] reduced TBUT ≤10 seconds, the ability to comprehend and sign a statement of informed consent, willingness to take an electronic survey about their tolerability of either study medication, and willingness to complete all required study visits.

Exclusion criteria are listed in Box 1 and were designed to exclude eyes with conditions that would confound the study's outcome measures, such as recent (within the last 3 months) surgery, trauma, infection, inflammation, or other abnormality, or systemic treatment that might alter the course of dry-eye management.

Enrolled patients were randomized in a 2:1 proportion, with 40 in the cyclosporine A–loteprednol etabonate (CsA–LE) group and 20 in the cyclosporine A 0.05% (CsA) group. Randomization was accomplished by assigning each patient a number sequentially according to the order of enrollment in the study. A randomization key document assigned each patient number to a study drug. All patients in both groups were dosed with medication BID of one drop per dose, and all patients were treated in both eyes. At each assessment visit, patients were queried about dryness symptoms according to the Standardized Patient Evaluation of Eye Dryness (SPEED) questionnaire.[7] Following this assessment, conjunctival redness

Box 1 Exclusion criteria

- Ocular surgery (eg, intraocular, oculoplastic, corneal, or refractive surgical procedure) performed within the last 3 months or at any time that in the investigator's clinical judgment if it would interfere with the outcome measures of this study.
- Clinically significant ocular trauma.
- Active ocular herpes simplex or herpes zoster infection
- Ocular inflammation (uveitis, iritis, scleritis, episcleritis, keratitis, conjunctivitis) at the discretion of the investigator.
- Ocular infection (eg, viral, bacterial, mycobacterial, protozoan, or fungal infection or the cornea, conjunctiva, lacrimal gland, lacrimal sac, or eyelids, including hordeolum/stye).
- Active, systemic, or local disease condition that causes clinically significant ocular surface irritation such that it could interfere with the study findings.
- Moderate to severe (grade 2–4) allergic, vernal or giant papillary conjunctivitis.
- Severe (grade 3 or 4) inflammation of the eyelid (eg, blepharochalasis, staphylococcal blepharitis, or seborrheic blepharitis)
- Eyelid abnormalities that significantly affect the lid function (eg, entropion, ectropion, tumor, edema, blepharospasm, lagophthalmos, severe trichiasis, severe ptosis).
- Ocular surface abnormality that may compromise corneal integrity (eg, prior chemical burn, recurrent corneal erosion, corneal epithelial defect, grade 3 corneal fluorescein staining, map-dot-fingerprint dystrophy, or the effect of any other ophthalmic medication that might in the opinion of the investigator compromise the ocular surface integrity).
- Participation in this trial in the same patient's fellow eye.
- Patients aged <18 years, pregnant or breastfeeding, or who may become pregnant during participation in the study.

was evaluated with the Schulze scale.[8] Corneal staining was next assessed using the Oxford scale[6] (0–5). Finally, TBUT was assessed as described by Lee and Kee.[9]

If both eyes met the study inclusion and not exclusion criteria, the eye with the more severe corneal staining at the baseline assessment was chosen as the study eye. If both eyes met the enrollment criteria and had the same severity of staining, the right eye was chosen as the study eye. Three sites enrolled patients, and the duration of treatment was 4 weeks. Subjects were examined and evaluated at baseline (day 0), 2 weeks (day 10–18), and 4 weeks (day 21–35). Patients who were already using anti-inflammatory medications for dry eye, such as cyclosporine, steroids, or nonsteroidals, were not enrolled in the study. Patients taking lubricant drops or using other treatment measures for dry eye, such as eyelid hygiene, were permitted to continue these regimens with no changes so as not to confound the study outcome measures.

The data collected at each visit included manifest refraction and best-corrected visual acuity (BCVA), corneal topography with the Zeiss Atlas topographer used to calculate total HOAs in the central 6 mm of the cornea, slit-lamp examination for corneal staining (Oxford scale), intraocular pressure (IOP), TBUT, and conjunctival hyperemia using the Schulze scale.[10] Patients also completed the validated SPEED questionnaire[7] and at week 2 and 4 visits a modified version of the validated Comparison of Ophthalmic Medications for Tolerability (COMTOL) to assess tolerability symptoms at 4 weeks.

The primary outcome measures of the study were the change in corneal HOAs from baseline to 2 and 4 weeks of treatment. Secondary outcome measures included the change in SPEED score at baseline vs 2 and 4 weeks as well as the change in TBUT, corneal staining, and ocular hyperemia. An exploratory outcome measure was the tolerability scores for individual symptoms on the validated COMTOL scale at 4 weeks. Side effects queried included burning, redness, blurred vision, bitter taste, unusual taste, itchy eyes, discharge, swelling of eyelids, browache, dimming of vision, difficulty focusing, and dry eyes.

Results

Sixty eyes of sixty patients were enrolled in the study. Of these, 56 (93%) completed all visits. These were evenly distributed between the three study sites, and each site had a 2:1 distribution of patients in the CsA–LE and CsA groups, respectively. The distribution of age and sex favored women over men at all sites and in both treatment cohorts (Table 1 and Table 2). Of the four patients who were not included in the analysis because they did not complete all study visits, two (3.3%) withdrew after the enrollment visit without reportedly taking any drops, one (1.6%) reported medication intolerance with the combination drop (stinging), and one (1.6%) had incomplete data that could not be recovered.

Primary Outcome Measure — Higher-Order Aberrations

Statistically significant improvement was seen in total corneal HOAs in the central 6 mm of the cornea between baseline and each of week 2 and week 4 for the CsA–LE group ($P<0.014$ and $P<0.012$ vs baseline, respectively, paired t-test). No significant improvement was seen among patients treated with CsA alone (Table 3, $P<0.18$ and $P<0.48$ vs baseline, respectively, paired t-test). From baseline to week 2, HOAs moved in a positive direction in 23 (62%) of eyes taking CsA–LE vs 8 (42%) with CsA. HOAs remained unchanged in six (16%) vs five (26%), and were worse in eight (22%) vs

Table 1 Enrollment by site

	Harvard Eye Associates (Hovanesian)	Cleveland Eye Clinic (Chester)	Inland Eye Specialists (Sorensen)	Combined
n	19	19	18	56
Age, years	69±5.7, range 61–85	56±17.0, range 24–79	67±9.7, range 50–82	64.0±12.9, range 24–85
Women	15 (79%)	16 (84%)	12 (67%)	43 (77%)
Right eye enrolled	12 (63%)	13 (68%)	8 (44%)	33 (61%)

Table 2 Enrollment by Treatment Group

	Cyclosporine–loteprednol	Cyclosporine	Combined	*P*
n	37	19	56	
Age (years)	64.4±14.6, range 24–85	63.3±9.2, range 32–73	64±12.9, range 24 to 85	<0.77, (Student's *t*-test)
Women	29 (78%)	14 (74%)	43 (77%)	<0.61 (χ^2 test)
Right eye enrolled	32 (86%)	11 (57%)	43 (77%)	<0.28 (χ^2 test)
Currently using lubricant drops	24 (65%)	15 (79%)	39 (70%)	<0.29 (χ^2 test)

Table 3 Significant improvements in total corneal higher order aberrations in the central 6 mm of the cornea were seen between baseline and each of week 2 and week 4 for the combination drop, while no significant improvement was seen for patients treated with cyclosporine alone

	Cyclosporine–loteprednol (n=37)		Cyclosporine (n=19)	
Baseline	0.78±0.46 µm		0.78±0.82 µm	
Week 2	0.64±0.36 µm	*P*<0.014 vs baseline, paired *t*-test	0.60±0.34 µm	*P*<0.18 vs baseline, paired *t*-test
Week 4	0.63±0.48 µm	*P*<0.012 vs baseline, paired *t*-test	0.78±0.74 µm	*P*<0.48 vs baseline, paired *t*-test

six (32%) in each group, respectively. From baseline to week 4, HOA improvement was seen in 20 (54%) with CsA–LE vs seven (37%) with CsA, the same in five (14%) vs 5 (26%), and worse in 12 (32%) vs seven (37%), respectively. These differences were not statistically significant. Figure 1 shows the change in HOAs among patients in each cohort at the three study visits.

Among the special population of cataract patients with dry eye who are being considered for multifocal IOL candidacy, an HOA threshold of 0.5 µm is considered a soft criterion to safely allow multifocal use. The proportion of eyes in this study that met this criterion is shown in Figure 2 for each cohort and each study visit. Although this study was not powered to demonstrate statistical significance for this outcome measure, a clear trend favoring CsA–LE over CsA alone is shown in Figure 2, with an increase in "candidacy" from 35% to 60% for CsA–LE vs 47% to 43% at baseline vs 4 weeks (Figure 2).

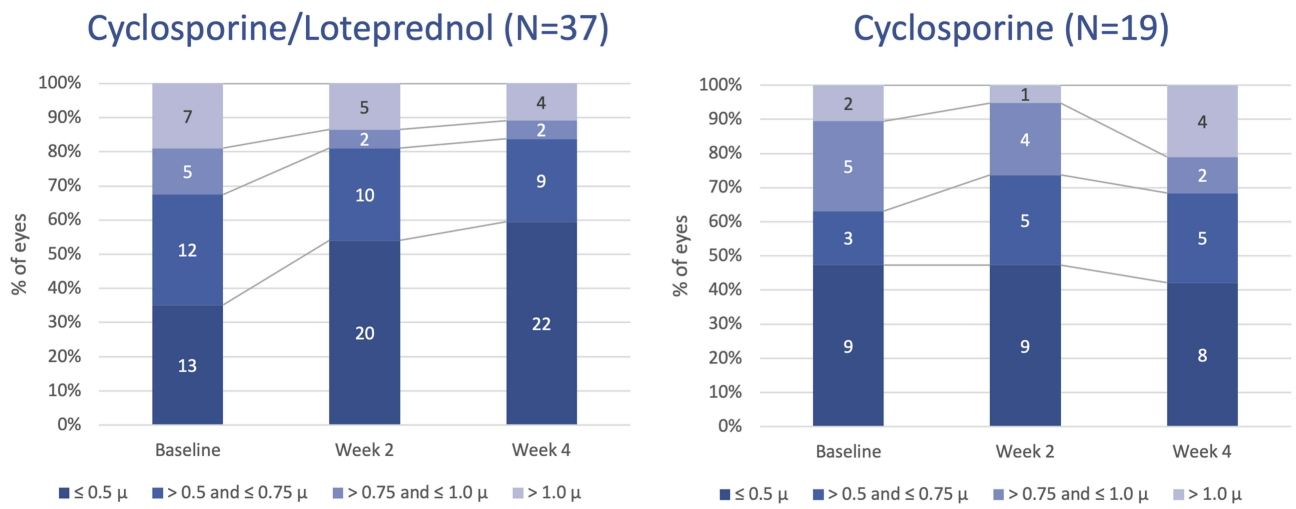

Figure 1 Significant improvements in HOAs were seen from baseline to week 2 and week 4 in eyes treated with the combination drop, whereas no significant change in HOAs was seen with cyclosporine.

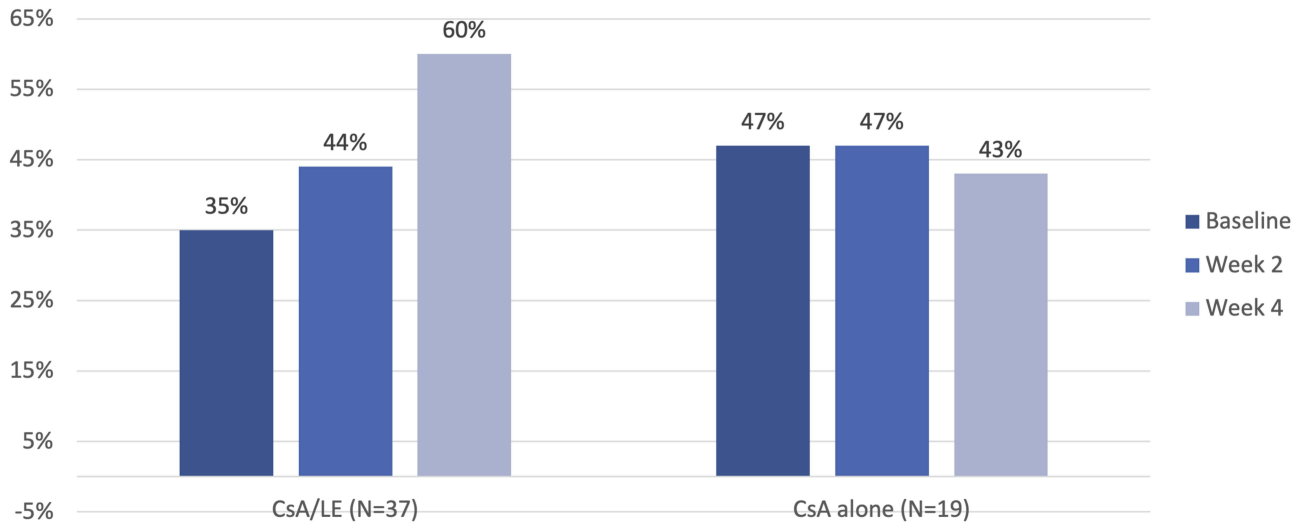

Figure 2 Multifocal candidacy almost doubled among eyes receiving CsA–LE vs those taking CsA alone.

Other Symptoms and Signs of Dry Eye

SPEED scores (Figure 3) significantly improved after treatment with both CsA–LE and CsA, with mean SPEED scores of 11.8±5.7 and 13.1±6.1 at baseline, 7.6±6.1 and 8.6±5.8 at 2 weeks, and 6.4±5.9 and 6.8±5.8 and at 4 weeks, respectively ($P<0.0001$ and $P<0.0005$ for baseline vs 2 weeks and $P<0.0001$ for both drugs for baseline vs 4 weeks, paired *t*-test). Among the patients treated with CsA–LE and CsA, SPEED scores of 5 or less were observed significantly more commonly at 2 and 4 weeks than at baseline. These scores occurred in five (14%) and one (5%) patients before treatment, 15 (41%) and eight (42%) after 2 weeks, and 17 (46%) and nine (47%) after 4 weeks, respectively ($P<0.01$ and $P<0.008$ for baseline vs 2 weeks and $P<0.003$ and $P<0.0004$ for baseline vs 4 weeks, respectively, McNemar's χ^2 test). No significant difference in SPEED score improvement was noted comparing the two drugs.

Corneal staining (Figure 4), measured by the Oxford scale, significantly improved among patients treated with CsA–LE from a mean grade of 1.86±0.59 to 0.73±0.84 and 0.59±0.76 at baseline, week 2 and week 4, respectively ($P<0.0001$ for baseline vs both 2 and 4 weeks, paired *t*-test). Among patients treated with CsA alone, similar improvement was seen

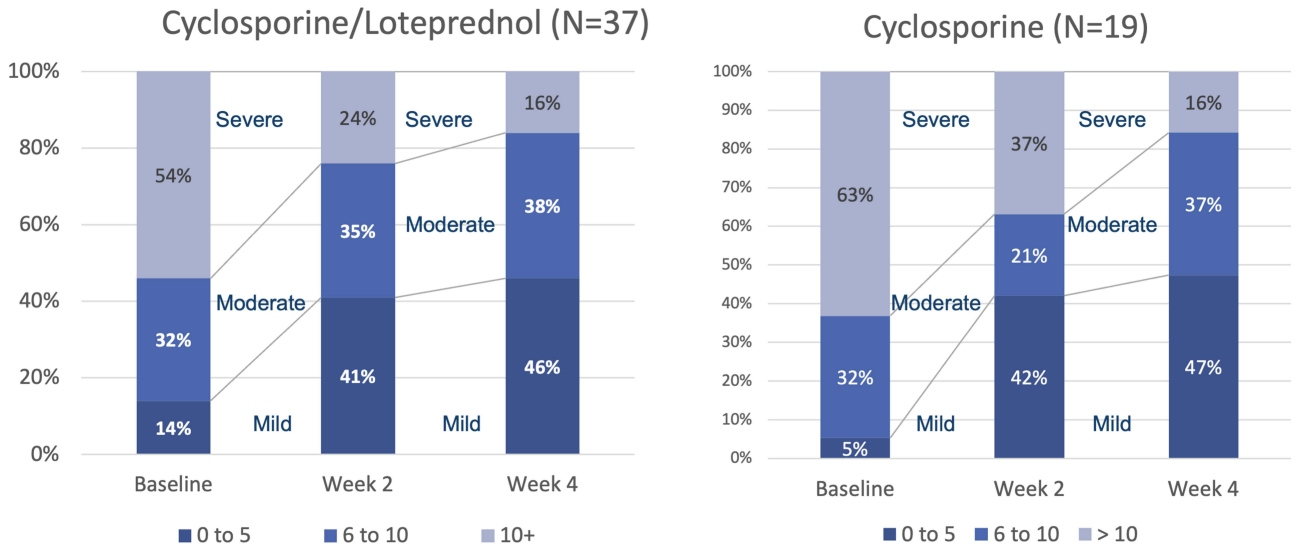

Figure 3 Both cyclosporine/–loteprednol and cyclosporine alone significantly reduced corneal staining ($P<0.0001$ for both drops for baseline vs 2 and 4 weeks, paired *t*-test).

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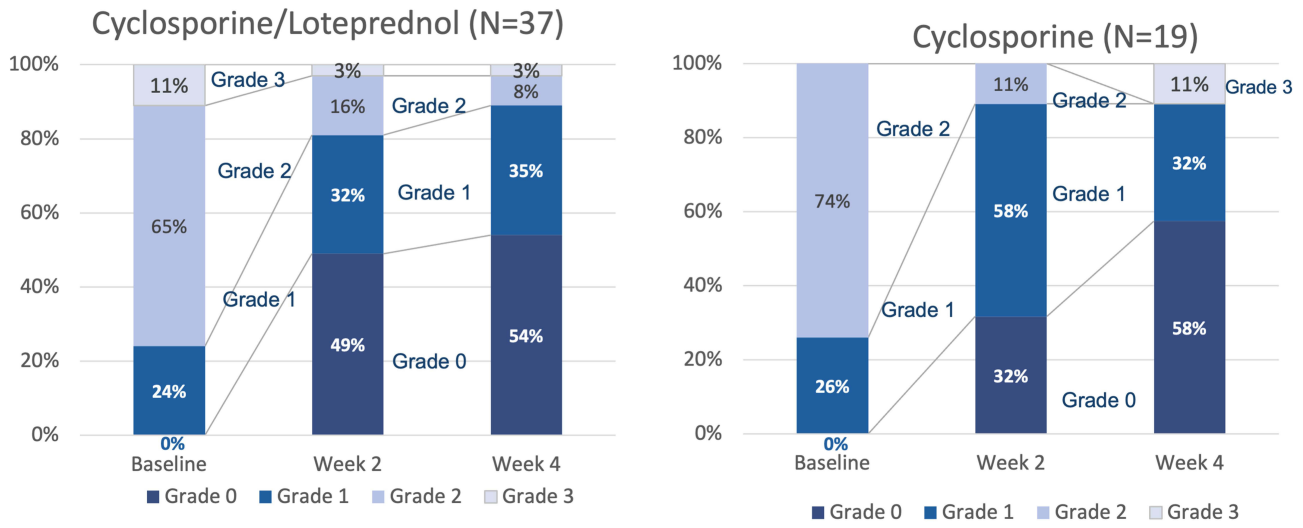

Figure 4 Corneal staining improved significantly in both groups from baseline to both week 2 and 4 ($P<0.00001$, paired *t*-test for all comparisons).

from 1.73±0.45 at baseline to 0.78±0.63 after 2 weeks and 0.63±0.96 after 4 weeks ($P<0.0001$ for baseline vs both 2 and 4 weeks, paired *t*-test).

All eyes had at least grade 1 staining before treatment, which was an inclusion criterion for the study. Of these, improvement to grade 0 was seen in 18 (49%) with CsA–LE and six (32%) with CsA alone at 2 weeks, and 20 (54%) with CsA–LE and 11 (58%) with CsA at 4 weeks. This improvement was statistically significant for each drug ($P<0.0001$, McNemar's test for baseline vs both 2 and 4 weeks for both drugs), and the difference in improvement between CsA–LE and CsA was not statistically significant.

Mean TBUT improved significantly for patients treated with both drug regimens. These changes were statistically significant compared to baseline at each follow-up visit (McNemar's χ^2 test, Table 4). The proportion of patients with an abnormally low TBUT (<5 seconds) decreased in all groups. This change was statistically significant for CsA–LE at both 2 and 4 weeks ($P<0.003$ and $P<0.0001$, respectively, McNemar's χ^2 test) and for CsA alone at 4 weeks ($P<0.01$, Figure 5).

Both cohorts had significantly reduced conjunctival redness (Figure 6), with significant improvement in CsA–LE and CsA groups from baseline to week 2 ($P<0.0002$ and $P<0.01$, respectively, McNemar's χ^2 test) and from baseline to week 4 ($P<0.0005$ and $P<0.02$). BCVA is reported in Table 5. There were no statistically significant differences in logMAR BCVA between treatment groups at any visit. Mean BCVA did improve significantly in the CsA–LE group between baseline and week 2, but the improvement from baseline to week 4 was not statistically significant.

Tolerability

The validated COMTOL questionnaire includes questions about burning/stinging, redness, blurred vision, bitter taste, unusual taste, itchy eyes, discharge, swelling of eyelids, brow ache, dimming of vision, difficulty in focusing from near to far, dry eyes, trouble reading, trouble seeing at night, and tearing. Of these symptoms, only burning/stinging was reported at any level in a number of patients to allow a meaningful comparison between the CsA–LE and CsA groups, which each included 37 and 19 patients, respectively. Burning/stinging was reported by 26 (70%) of patients with CsA–LE and nine (47%) patients with CsA

Table 4 Mean tear-breakup time (TBUT) compared to baseline had improved significantly at each follow-up visit

	Baseline mean TBUT	Week 2 mean TBUT	Week 4 mean TBUT
Cyclosporine–loteprednol (n=37)	4.11±1.98	6.48±2.30 ($P<0.0001$)	6.37±5.86 ($P<0.0001$)
Cyclosporine (n=19)	4.05±2.07	8.58±5.78 ($P<0.0005$)	6.84±5.81 ($P<0.0001$)

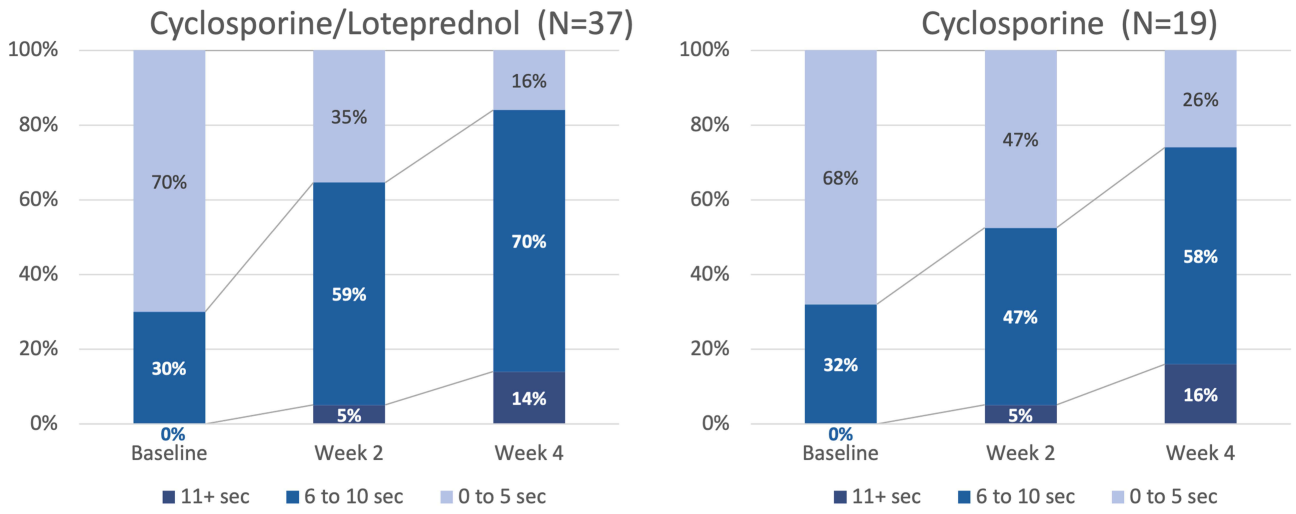

Figure 5 The proportion of patients with an abnormally low TBUT (<5 seconds) decreased in all groups. This change was statistically significant for cyclosporine/–loteprednol at both 2 and 4 weeks ($P<0.003$ and <0.0001, respectively, McNemar's χ^2 test) and for cyclosporine at 4 weeks ($P<0.01$).

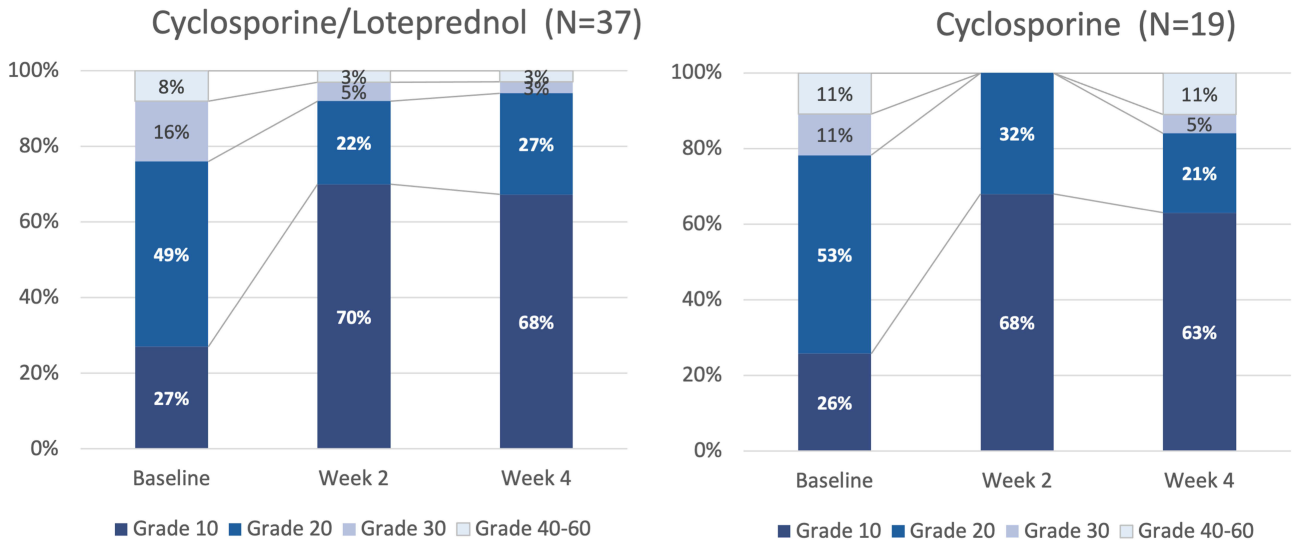

Figure 6 Conjunctival redness (Schulze scale) improved significantly in both groups.

alone. The distribution of frequency of burning/stinging symptoms is shown in Figure 7. The overall frequency of side effects is shown in Figure 8.

Safety

IOP did not rise significantly in either group. Abnormal pressure readings (>21 mmHg) were limited to a single patient (3%) in the CsA–LE group with an IOP of 30 mmHg at visit 3 (Table 6).

Table 5 Best-corrected visual acuity improved significantly between baseline and week 2 in patients taking CsA–LE, but not CsA alone, while no other differences were statistically significant

	Baseline	Week 2	Week 4
CsA–LE	0.17±0.15	0.13±0.15 ($P<0.02$ vs baseline, paired *t*-test)	0.13±0.19
CsA	0.13±0.16	0.08±0.15	0.15±0.21

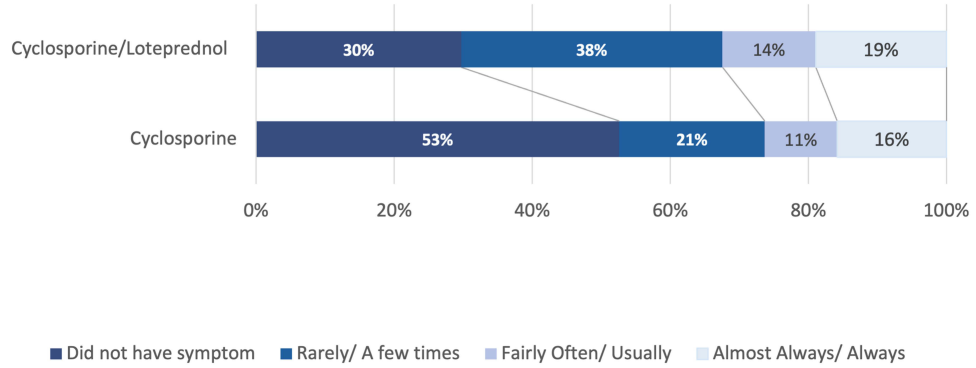

Figure 7 Frequency distribution of side effects of each medication.

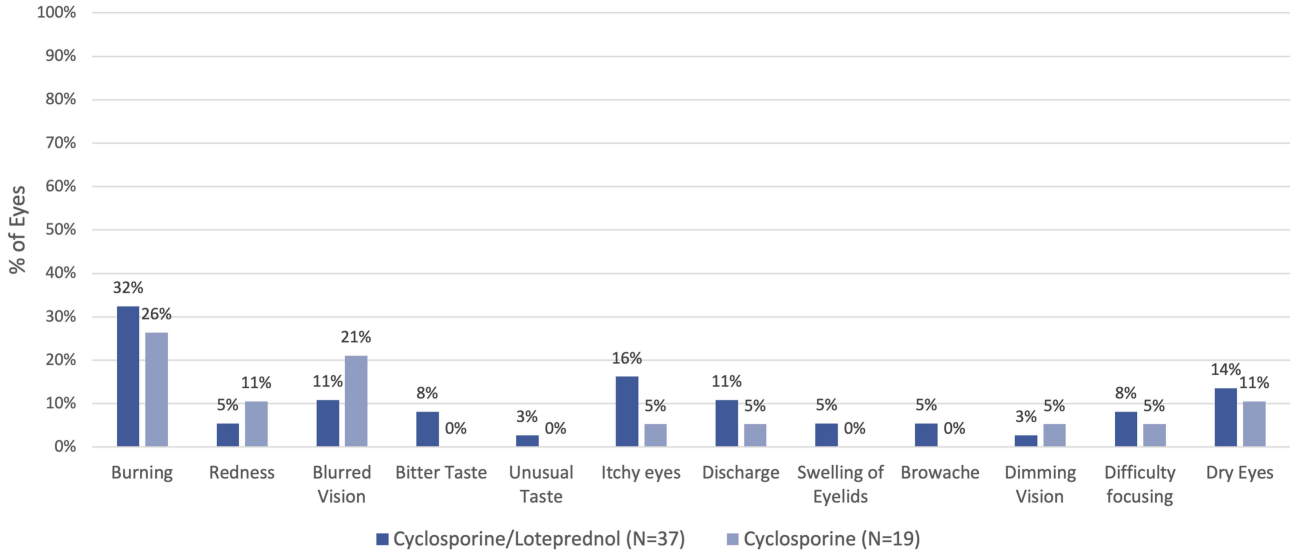

Figure 8 Frequency of all side effects queried in the validated COMTOL questionnaire.

Discussion

To our knowledge, this randomized, controlled, multicenter study is the first comparison of a commercially available novel formulation of cyclosporine 0.1%–loteprednol 0.2% (Klarity CL) to cyclosporine 0.05% (Restasis) for treatment of dry eye. This study showed that the CsA–LE combination drop significantly reduced HOAs at both 2 and 4 weeks in a dry-eye population. Improvement in HOAs in patients taking the comparator drug, CsA alone, did not show significant

Table 6 IOP did not rise significantly in either group: abnormal pressure readings (>21 mmHg) were limited to a single patient (3%) in the combination drop group with an IOP of 30 MmHg at visit 3

	Baseline	Week 2	Week 4
Cyclosporine–loteprednol (n=37)	14.6±2.3, range 10–19	14.6±2.4, range 10–19 (*P*<0.47 vs baseline, paired *t*-test)	15.2±3.5, range 9–30 (*P*<0.11 vs baseline, paired *t*-test)
Cyclosporine (n=19)	14.03±2.5, range 11–21	14±3, range 10–19 (*P*<0.29 vs baseline, paired *t*-test)	13.2±2.6, range 9–19 (*P*<0.12 vs baseline, paired *t*-test)

improvement in HOAs. Both drugs led to significant improvements in SPEED scores, corneal staining (Oxford scale), TBUT, and conjunctival redness (Schulze scale). Both drugs were well tolerated with no significant differences between them in their tolerability profile (validatedCOMTOL instrument). No significant safety concerns were raised by the study in either drug group.

Improvement in HOAs positively influences visual quality in all patients, but has particular relevance for patients preparing for cataract surgery because it can lead to a more accurate prediction of what lens-implant power will achieve the desired refractive result.[2] Patients with lower degrees of HOAs are also more likely to have a satisfactory result with today's popular multifocal implants.[3] A treatment like CsA–LE being shown to rapidly and significantly reduce HOAs, therefore, is particularly valuable in preparing patients for surgery, just as it is important for all patients with dry eye.

Cyclosporine is a well-proven treatment for dry eye, but its therapeutic benefit is thought to begin only after 4 weeks of treatment.[11] We have unpublished data from other work suggesting this therapeutic effect may occur more quickly, and in this study, outcome measures such as corneal staining, TBUT, SPEED scores, and conjunctival redness all improved significantly as early as 14 days. Cyclosporine's vehicle might have contributed to this treatment success, and this study's design did not examine vehicles alone. However, our previous experience suggests that the cyclosporine component of Restasis was at least somewhat to credit for ocular surface improvement. Further study on the speed of onset of cyclosporine is merited.

The differences between groups are most likely attributable to the addition of loteprednol in Klarity CL, but there are other differences between these drug regimens: Klarity CL's cyclosporine at 0.1% is double the concentration of that in Restasis (0.05%). For cyclosporine, a drug with historically poor tolerability, a significantly higher concentration would be expected to significantly decrease its tolerability compared to Restasis.[12] The observed lack of significant difference may be attributable to the presence of loteprednol 0.2%, the difference in vehicle, or both. Klarity has a vehicle of chondroitin sulfate emulsion containing dextran, glycerol, and hydroxypropylmethylcellulose, while Restasis uses a caster-oil emulsion as vehicle. With this study design, which did not include separate vehicle-only groups, it is impossible to distinguish the effect of each of these differences. Nevertheless, this was designed to be a "real world" study comparing the commercially available formulation of each drug, rather than just the drug components themselves. Whatever the difference in outcomes is attributable to is of more academic than practical interest.

Four patients (6.7%) withdrew from the study. Of these, one (1.7%) withdrew because the combination drops were not tolerable, with reported stinging. The remaining three dropped out because of reasons not related to the medication. This low rate of medication intolerance is consistent with previous studies of CsA 0.05%.[13–15]

This study is not without its limitations. First, the sample size of 56 patients randomized to two treatment groups limits detection of more subtle trends that might appear in the data. One example relates to HOAs, which showed significant improvement from before to after treatment in the CsA–LE group, but not the CsA group. On a cursory view, this might be attributed to the smaller group of patients taking CsA alone, especially since the mean HOA measures were similar in both drug groups at baseline and week 2 (Table 3). However, further analysis showed that if the CsA group had been similar in size to the CsA–LE group, the results still would not be statistically significant at the 95% confidence interval.

Though the mean HOA scores were similar between groups, the percentage of patients who improved vs stayed the same or worsened were different between the groups. Since the significance of "improvement" depends on the aggregate change in each patient, rather than mean change in the group as a whole, the analysis showed CsA–LE to be significantly more effective in improving HOAs.

LogMAR BCVA improved in the CsA–LE group from baseline to week 2, but not vs week 4, and no other significant differences were noted in BCVA. This contrasts with the significant improvements in other measures of dry eye, but is not surprising. Though Snellen acuity has been a time-honored metric of visual performance, it is not highly sensitive to the small but visually important changes that occur in dry eye. Snellen acuity was included in this study because of its historical significance and its potential role in evaluating safety concerns, but it was not chosen as the primary outcome measure for this reason.

Another potential criticism of this study is its open-label design. While observer bias is a possibility in any study, this study's primary outcome measure was HOAs, an objective measure that is derived from corneal topography. Also, to fully mask this study would have required dispensing each product in a similar bottle. This would not be possible with commercially available Restasis (the CsA group), which is provided in single-use tear-off dispensers, whereas Klarity CL

(the CsA–LE group) is provided in a multidose bottle. Since the purpose of this study was to compare these two products as sold, some degree of masking was unavoidable by virtue of the design of the dispensers.

This study has shown that the combination of CsA–LE in a chondroitin sulfate vehicle is more effective in improving HOAs than the most widely used commercially available formulation of CsA alone. As expected, it also demonstrated consistent efficacy in improving corneal staining, TBUT, conjunctival redness, and patient symptoms (SPEED score). Perhaps more importantly, it achieved these goals in a time frame that suggests its use might be appropriate for patients with DED preparing to undergo ocular surgery.

Data Sharing

Reasonable requests for deidentified patient data relating to the study findings, including any outcome measures, will be available through the corresponding author for 5 years following the publication date.

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Disclosure

Dr John Hovanesian reports grants and personal fees from ImprimisRx and personal fees from Allergan during the conduct of the study. Dr Thomas Chester reports personal fees from Allergan, personal fees from Dompe, personal fees from Glaukos, personal fees from Novartis, personal fees from Oyster Point, grants and personal fees from Sight Sciences, personal fees from Sun Ophthalmics, personal fees from Tarsus, and personal fees from Versea outside the submitted work. The authors report no other conflicts of interest in this work.

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