Long-term treatment of dry eye disease and severe keratitis with ciclosporin A 0.1% cationic emulsion in a real-world setting: PERSPECTIVE study - UK results

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INTRODUCTION

- Dry eye disease (DED) is a multifactorial and complex condition, requiring long-term treatment, which may be challenging to diagnose and treat in clinical practice[1–4]
- Initiation of anti-inflammatory treatment should be considered when first-line artificial tears (ATs) no longer suffice[4]
  - Ciclosporin A 0.1% cationic emulsion (CsA 0.1% CE) is a topical anti-inflammatory therapy that has demonstrated efficacy and safety outcomes in the treatment of DED, with significant improvement observed concerning ocular signs and symptoms[4–9]
- Real-world outcomes from the European PERSPECTIVE study showed that in routine clinical practice CsA 0.1% CE was effective and well-tolerated in controlling the signs and symptoms of severe keratitis in adults with DED who had not improved despite treatment with tear substitutes[10]

PURPOSE

- The current analysis examined country-level efficacy, tolerability and safety data from ophthalmology clinics in the United Kingdom (UK) that participated in the PERSPECTIVE study, to provide population-specific recommendations for the use of CsA 0.1% CE

METHODS

- PERSPECTIVE was a 12-month, European, non-interventional, multicentre, prospective study
  - The current analysis examined PERSPECTIVE study data collected from 16 ophthalmology clinics in the UK
- Adults (aged ≥18 years) with dry eye and severe keratitis currently treated with ATs were included
- Study exclusion criteria included treatment with CsA 0.1% CE (within 6 months), immunosuppressant therapy (within 6 months), previous/planned eye surgery, pregnancy or nursing
- CsA 0.1% CE was instilled (one drop daily) into both eyes at bedtime for 12 months. Concomitant use of ATs and steroid treatments was allowed
- Data were collected from routine appointments at participating ophthalmology clinics at baseline and then following CsA 0.1% CE initiation
- Attendance at baseline and Month 12 was mandatory for inclusion in the study, and data were reported for patients choosing to attend interim study visits (Weeks 4, 12 and 24)
- Baseline measures were recorded under AT treatment and the eye with the highest baseline corneal fluorescein staining (CFS; Oxford Grade Scale; grade 0–V) grade was chosen as the study eye
- The primary endpoint was mean change from baseline in CFS grade at Month 12 following CsA 0.1% CE initiation
- Secondary endpoints included change in CFS grade at each study visit (Weeks 4, 12 and 24), change in severity of eyelid and conjunctival erythema, change from baseline in visual acuity (VA), Schirmer's test and tear break up time (TBUT), and change in severity of ocular symptoms
- Safety endpoints included adverse event (AE) and treatment-related AE reporting

RESULTS

Study population

- The study included 160 patients from the UK; 79.4% were female. Mean (SD) age was 63.9 (15.6) years (range: 20.8–95.4 years)
- Mean (SD) baseline CFS grade was 2.97 (1.18; n=159) (**Table 1**)
  - CFS grade at baseline was typically grade II (26.4%), grade III (27.0%) or grade IV (25.8%)
- The main reasons for initiating CsA 0.1% CE treatment were insufficient control of keratitis/DED with prior medication (83.1%) and progression of keratitis/DED (18.8%). Clinicians were allowed to give more than one reason for starting CsA 0.1% treatment

Efficacy outcomes

Change in CFS grade from baseline at all study visits

- Mean (SD) CFS grade at Month 12 was 1.54 (1.24), representing a statistically significant reduction from baseline of 1.24 (1.23) (p<0.0001; **Table 2**)
- Significant reductions in CFS grade were achieved from Week 4 and maintained through Month 12 (p<0.0001)

Change in CFS grade from baseline at Month 12

- From baseline, most patients (72.7%) demonstrated an improvement in CFS grade at Month 12 following initiation of CsA 0.1% CE (**Figure 1**)

Change in severity of ocular signs and symptoms

- Severity of eyelid erythema and conjunctival erythema was significantly reduced, compared with baseline, at Month 12 (p<0.001; **Figure 2**)
- Subjective symptoms were also significantly reduced in severity from baseline at Month 12 following initiation of CsA 0.1% CE (**Figure 3**): foreign body sensation (p<0.001); photophobia (p<0.001); itching (p=0.002); blurred vision (p<0.001); eye pain (p<0.001); sticky feeling (p<0.001); burning/stinging (p=0.011)
- Mean TBUT was significantly increased compared with baseline from Week 4 (p=0.005) through Month 12 (p=0.003). At Month 12, mean (SD) TBUT was increased by 1.32 (3.76) seconds
- Mean VA was significantly increased compared with baseline from Week 12 (p<0.001) through Month 12 (p=0.015). At Month 12, mean (SD) VA was increased by 0.07 (0.29)
- Changes in Schirmer's test were not statistically significant at Month 12 (p=0.469)

Table 1. Patient characteristics at baseline

Patient characteristics	n (%)	Patient characteristics	n (%)
Study eye (worst CFS grade at baseline)†		**AT use**	
Left	33 (20.6)	6 times per day	33 (10.5)
Right	127 (79.4)	5 times per day	3 (1.0)
CFS grade		4 times per day	39 (12.4)
0	1 (0.6)	3 times per day	14 (4.5)
I	16 (10.1)	Twice per day	9 (2.9)
II	42 (26.4)	Daily/Once	67 (21.3)
III	43 (27.0)	Other	10 (3.2)
IV	41 (25.8)	Unknown	61 (19.4)
V	16 (10.1)	As needed	71 (22.6)
Missing	1 (0.6)	None	7 (2.2)
Mean (SD) CFS grade (n=159)	2.97 (1.18)		

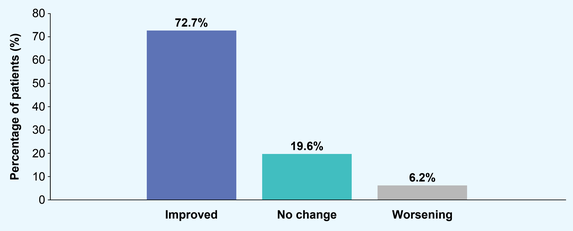
†If both eyes presented with the same CFS grade at baseline, the right eye was chosen as the study eye. AT, artificial tears; CFS, corneal fluorescein staining; SD, standard deviation

Table 2. CFS grade at each study visit

	n‡	Mean (SD)	n‡	Change from baseline, Mean (SD)	p-value*
Baseline	159	2.97 (1.18)	-	-	-
Week 4	100	1.86 (1.29)	99	–1.10 (1.04)	<0.0001
Week 12	91	1.51 (1.26)	90	–1.28 (1.17)	<0.0001
Week 24	80	1.46 (1.27)	79	–1.48 (1.25)	<0.0001
Month 12	98	1.54 (1.24)	97	–1.24 (1.23)	<0.0001

‡Number of patients with a CFS measurement at each study visit. ‡Number of patients with a CFS measurement at baseline and at each subsequent study visit, used to calculate the change. *Significant testing using two-sided test. CFS: corneal fluorescein staining; SD, standard deviation

Figure 1. Change from baseline in CFS grade at Month 12 following initiation of CsA 0.1% CE

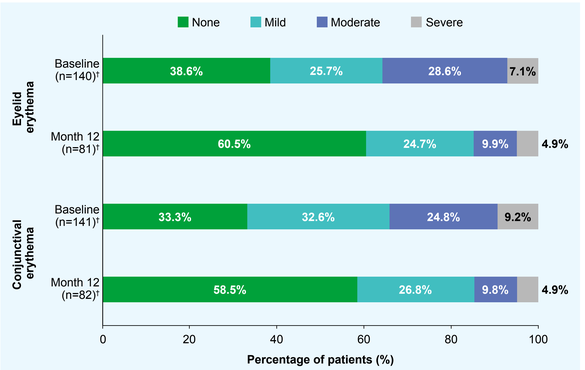


CFS, corneal fluorescein staining; CsA 0.1% CE, ciclosporin A 0.1% cationic emulsion

Physician and patient assessments

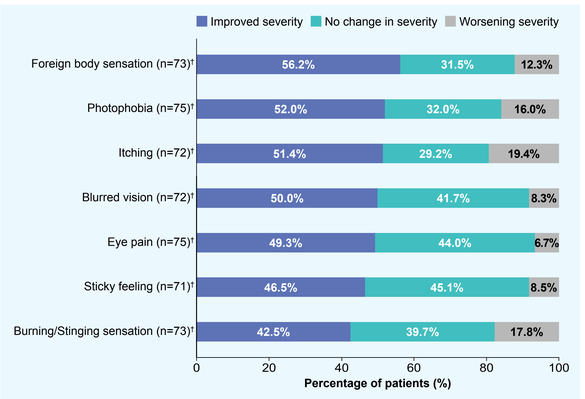
- Clinical effectiveness of CsA 0.1% CE was rated by 67.6% of physicians as better when compared to prior treatment at Month 12. The remaining physicians rated clinical effectiveness of CsA 0.1% CE the same (23.9%) or worse (8.5%) when compared with prior treatment at Month 12 (**Figure 4**)
- Most physicians (62.0%) considered clinical signs to be improved with CsA 0.1% CE treatment. The remaining physicians considered clinical signs to be the same (29.6%) or worse (8.5%) with CsA 0.1% CE treatment (**Figure 4**)

Figure 2. Severity of eyelid erythema and conjunctival erythema at baseline and at Month 12 following initiation of CsA 0.1% CE



†Number of patients with conjunctival erythema or eyelid erythema data available/reported at study visit. CsA 0.1% CE, ciclosporin A 0.1% cationic emulsion

Figure 3. Change from baseline in severity of subjective symptoms at Month 12 following initiation of CsA 0.1% CE

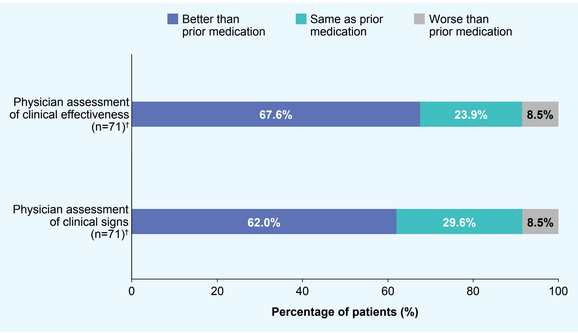


†Number of patients with subjective symptom data available/reported at Month 12. CsA 0.1% CE, ciclosporin A 0.1% cationic emulsion

Tolerability and safety outcomes

- Tolerability was rated as satisfactory/good/very good by 88.3% of physicians (n=77) and 88.0% of patients (n=75) at Month 12
- Overall, 46 treatment-related AEs were reported, 37 of which were considered ocular. No treatment-related AEs were serious
- Most treatment-related AEs (80.4%) were resolved/resolving at the end of the study

Figure 4. Physician assessment of clinical effectiveness and clinical signs with CsA 0.1% CE treatment compared with prior therapy at Month 12



†Number of physicians with assessment data available/reported at Month 12. CsA 0.1% CE, ciclosporin A 0.1% cationic emulsion

DISCUSSION

- In a real-world clinical practice setting, patients in the UK who were diagnosed with DED and severe keratitis showed benefit from CsA 0.1% CE treatment
- Statistically significant reductions in mean CFS grade were observed from Week 4 and maintained throughout the 12-month study period (p<0.0001)
- Improvements in the severity of clinical signs and ocular symptoms were statistically significant from Week 4 with CsA 0.1% CE treatment and were sustained through Month 12
- Physicians rated treatment effectiveness and clinical signs to be better with CsA 0.1% CE compared with prior therapies and a majority of both physicians and patients regarded tolerability with CsA 0.1% CE treatment to be very good, good or satisfactory
- Safety data were consistent with the known safety profile of CsA 0.1% CE

CONCLUSIONS

- Analysis of PERSPECTIVE study data from ophthalmology clinics in the UK is consistent with the outcomes reported for the full European dataset and is indicative of the treatment results that ophthalmologists may expect to see with CsA 0.1% CE treatment in real-life clinical practice
- CsA 0.1% CE provided statistically significant reductions in the severity of dry eye and keratitis signs and symptoms. Significant improvements were demonstrated from Week 4 and maintained through Month 12. CsA 0.1% CE treatment was generally well-tolerated

References: 1. Craig JP, et al. Ocul Surf. 2017;15(3):276–283. **2.** Baudouin C, et al. Br J Ophthalmol. 2016;100(3):300–306. **3.** Gayton JL. Clin Ophthalmol. 2009;3:405–412. **4.** Pleyer U, et al. Klin Monbl Augenheilkd. 2020;237(5):655–668. **5.** Leonardi A, et al. Br J Ophthalmol. 2019;103(1):125–131. **6.** Leonardi A, et al. Eur J Ophthalmol. 2016;26(4):287–296. **7.** Baudouin C, et al. Eur J Ophthalmol. 2017;27(6):678–685. **8.** Baudouin C, et al. Eur J Ophthalmol. 2017;27(5):520–530. **9.** Labetoulle M, et al. Clin Ther. 2018;40(11):1894–1906 **10.** Geerling G, et al. Ophthalmol Ther. 2022;11(3):1101–1117.

Abbreviations: AE: adverse events; AT: artificial tears; CFS: corneal fluorescein staining; CsA 0.1% CE: ciclosporin A 0.1% cationic emulsion; DED: dry eye disease; SD: standard deviation; TBUT: tear break up time; UK: United Kingdom; VA: visual acuity

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