Official Title: Effect of Cequa™ in Subjects with Dry Eye Disease That Is Currently Inadequately Controlled While on Cyclosporine 0.05% Ophthalmic Emulsion

Document: Clinical Study Protocol

NCT number: NCT04357795

Date: 11-Dec-2019

Effect of Cequa TM in Subjects With Dry Eye Disease That Is Currently Inadequately Controlled While on Cyclosporine 0.05% Ophthalmic Emulsion

Protocol Number: OTX101-2019-001
Sponsor: Sun Pharma Global FZE
Version Number: 1.0
11 December 2019

Statement of Compliance:

The trial will be conducted in accordance with International Conference on Harmonisation (ICH) Good
Clinical Practice (GCP), and applicable United States (US) Code of Federal Regulations (CFR). The Principal Investigator will assure that no deviation from, or changes to, the protocol will take place without prior agreement from the Sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have GCP training. The study is conducted also under the Declaration of Helsinki. The protocol, informed consent form(s) [ICF(s)], recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent using a previously approved consent form.

Protocol Summary:

SYNOPSIS

Title: Effect of Cequa TM in Subjects With Dry Eye Disease That Is Currently Inadequately Controlled While on Cyclosporine 0.05% Ophthalmic Emulsion

Study Description:

Objectives:

This is a phase 4, multicenter, open-label, single-arm, 12-week study of subjects with dry eye disease (DED) that is inadequately controlled by cyclosporine (CsA) 0.05% ophthalmic emulsion. Treatment will be one drop of CsA 0.09% ophthalmic solution (Cequa) in each eye twice daily (BID) for 12 weeks. The study hypothesis is that CsA 0.09% ophthalmic solution will show improved clinical benefit in subjects whose dry eye signs and/or symptoms are inadequately controlled while on CsA 0.05% ophthalmic emulsion.

Primary: to evaluate improvement in the signs and/or symptoms of DED following use of CsA 0.09% ophthalmic solution in subjects whose DED is inadequately controlled by CsA 0.05% ophthalmic emulsion.
Secondary: to evaluate changes in additional signs and symptoms over the 12-week course of Cequa therapy.

Statistical Analyses:

Neither masking nor randomization will be employed for operation of this study; this is an open-label study

- Primary efficacy endpoints will be analyzed using descriptive statistics and restricted maximum likelihood repeated measures mixed model (REMLMMRM) models.
- Multiplicity adjustments of observed significance levels for primary efficacy endpoints will be presented.

Study Population:

Subjects will have DED that is not adequately controlled (ie, still symptomatic and/or still exhibiting signs of disease) by current treatment with CsA 0.05% ophthalmic emulsion. Eligible subjects must have been taking CsA 0.05% ophthalmic emulsion treatment for at least 3 months prior to the Screening/Baseline visit. However, subjects who have failed prior treatment with CsA 0.05% ophthalmic emulsion will be excluded from the study.

Inclusion/Exclusion Criteria:

Inclusion Criteria:

1. Male or female subjects with a history of bilateral dry eye disease for a period of at least 3 months.
2. Aged of at least 18 years.
3. Subjects with total corneal fluorescein staining ≥6 or corneal fluorescein staining in an individual zone ≥2 as per National Eye Institute Grading Scale.
4. Subjects with modified symptom assessment in dry eye global symptom score, ≥40 using visual analogue scale.
5. Subjects with best-corrected visual acuity 20/200 or better in both eyes at the Screening/Baseline visit

Exclusion Criteria:

1. Subjects who have used cyclosporine 0.05% ophthalmic emulsion in both eyes for less than 3 months prior to the Screening/Baseline visit.
2. Subjects with history of treatment failure with cyclosporine 0.05% ophthalmic emulsion.
3. Subjects who have active seasonal and/or perennial allergic conjunctivitis in either eye.
4. Subjects who had already Use initiated any systemic or topical ocular medication.

Justification of Dose:

Cyclosporine 0.09% ophthalmic solution (Cequa) is approved by the FDA to increase tear production in patients with KCS (Cequa prescribing information, 2018). It is to be dosed as 1 drop BID (approximately 12 hours apart) into each eye. Therefore, the dosing in the current phase 4 study will match the approved dosing regimen.

Overall Design:

This is a phase 4, multicenter, open-label, single-arm, 12-week study of subjects with DED that is inadequately controlled by CsA 0.05% ophthalmic emulsion. Study subjects will be male or female, at least 18 years of age, with a history and clinical diagnosis of bilateral DED for a period of at least 3 months, corrected BCVA of 20/200 or better in both eyes at the Screening/Baseline visit, and a willingness to discontinue use of all dry eye therapy, aside from continuing any existing ATP use. In addition, subjects must have total CFS ~6 (or CFS ~2 in an individual zone) and/or a modified SAnDE score ~40.

At the Screening/Baseline visit, sites will obtain signed informed consent, medical/ocular/concomitant medication histories, and demographics, perform a urine pregnancy test (for women of childbearing potential only), conduct screening ophthalmic examinations, and review inclusion/exclusion criteria. Site staff will dispense study medication, provide appropriate instructions for use, and supervise administration of first dose. All enrolled subjects will self-administer 1 drop of CsA 0.09% ophthalmic solution in each eye BID for 12 weeks. Subjects will return at Weeks 4, 8, and 12. In addition, at the Week 12 visit, sites will perform a urine pregnancy test (for women of childbearing potential only), and subjects will answer a treatment preference question. At each visit, concomitant medications will be updated, adverse events (AEs) will be collected, the subject's daily diary on the frequency of ATP and CsA 0.09% ophthalmic solution use will be examined, subjects will answer a compliance question, and actual daily use entered into electronic data capture (EDC).

Study Record Retention:

Investigators should retain study-related records at the site for a minimum of 5 years after study closeout.