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Observation of tear film break-up time in patients with evaporative dry eye symptoms using EvoTears® eye drops compared to eye drops containing lipids

Submission date
14/10/2020

Recruitment status
No longer recruiting

Registration date
02/11/2020

Overall study status
Completed

Last Edited
07/01/2022

Condition category
Eye Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
In order to maintain the optimal functioning of the cornea and conjunctiva of the eye, the surface of this tissue (epithelium) must be kept continuously moist. Only then can the eye be kept healthy and discomfort avoided. Usually this moistening occurs through the tear film. In the case of dry eyes, a lack of tears or insufficient composition of the tear film causes the tear film on the surface of the eye to break up. As a result, dry areas occur where the epithelium comes into direct contact with the ambient air and is damaged in the long term. Dry eyes are therefore caused by various factors. The surface of the eye reacts to insufficient humidification with inflammatory symptoms. Continuous and adequate humidification of the eye ensures the regeneration of the superficial tissues of the eye.
According to the definition of the Dry Eye Workshop (DEWS 2007), a distinction is made between hyposecretory (lack of tears) and hyperevaporative (increased evaporation) dry eye, depending on the cause of the symptoms. The type of dry eye can change in the course of the disease and mixed forms are possible.
In 1995 it was found that the vast majority of patients suffer from a disorder of the lipid phase and thus from hyperevaporative dry eye. Restoration of the lipid film of the tears and thus reduction of evaporation is therefore the goal of an effective treatment. EvoTears® achieves this due to the specific properties of the only ingredient perfluorohexyloctane (F6H8). Perfluorohexyloctane has proven to be particularly suitable due to the excellent stability of the surface wetting. Due to the low viscosity, there is only a low surface tension and it therefore has good imaging properties. The positive influence on tear volume, tear stability and the corneal epithelium has been proven by studies. The aim of this study is to compare the performance of three products in the treatment of hyperevaporative dry eye and meibomian gland dysfunction.

Who can participate?
Patients aged over 18 with evaporative dry eye and mild to moderate meibomian gland dysfunction

What does the study involve?
The study involves only routine eye investigations to diagnose evaporative dry eye and meibomian gland disease. Participants are randomly allocated to be treated with either EvoTears®, Cationorm® MD sine or Systane® Balance eye drops. The need for treatment is determined at day 1 by the treating physician and the treatment is carried out and monitored according to the investigator's instructions. Any deviation from the dosage 4 x 1 drop per day is documented separately.
As part of a follow-up examination (day 7 ± 2) and a final examination (day 28 ± 2), the attending physician assesses whether the use of EvoTears®, Cationorm® MD sine or Systane® Balance eye drops has shown the desired effect and was well tolerated. In total, each patient should use the observed preparation for at least 4 weeks. The attending physician gives a final assessment of whether the administration of the eye drops was well tolerated. The study ends with the last examination of the patient.

What are the possible benefits and risks of participating?
As the three products contain lipids it is assumed that the patients benefit from the treatment regardless of which product they use in this study.
The treatment with EvoTears®, Cationorm® MD sine or Systane® Balance can lead to side effects or symptoms. The side effects and symptoms observed to date for EvoTears® include local irritation of the eye such as a burning sensation or itching of the eye. These symptoms have so far only been observed very rarely (<0.01% = in 1 or less in 10,000 patients). As with any new preparation, new, previously unknown side effects can occur when using EvoTears®. After application of Cationorm® MD sine a slight discomfort to the eye might occur. In addition, the measures taken as part of this clinical trial can lead to discomfort (e.g. irritation of the eye) or even involve risks (e.g. allergy to a preparation required for diagnostics). No specific risks are expected for this study. Participants in this study benefit from the close support of the investigator during the study period.

Where is the study run from?
URSAPHARM Arzneimittel GmbH (Germany)

When is the study starting and how long is it expected to run for?
September 2016 to March 2018

Who is funding the study?
URSAPHARM Arzneimittel GmbH (Germany)

Who is the main contact?
Dorothea Gross
d.gross@ursapharm.de

Contact information

Type(s)
Scientific

Contact name
Mrs Dorothea Gross

Contact details

Industriestrasse 35
Saarbrücken
Germany
66129
+49 (0)6805 9292 132
d.gross@ursapharm.de

Additional identifiers

Study information

Scientific Title
Observation of tear film break-up time using the Dry Eye Monitor (KOWA DR-1 α) using EvoTears® eye drops compared to eye drops containing lipids: a monocentric, prospective, randomized open clinical study

Acronym
EvoKOWA

Study objectives
By definition, dry eye can be caused by an evaporation disorder due to an insufficient lipid layer and meibomian gland dysfunction. The present clinical study aims to evaluate the efficacy and tolerability of EvoTears® (perfluorohexyloctane in direct comparison with eye drops containing lipids. Particular attention is paid to the stability of the tear film.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Confirmed 05/07/2017, this study does not require approval by an ethics committee (§23b German MPG) but the professional advice of the Medical Association of Baden-Württemberg (Jahnstrasse 40, 70597 Stuttgart, Germany; +49 (0) 711-76989-60; ethikkommission@laek-bw.de)

Primary study design
Interventional

Study design
Single-center prospective randomized comparative open clinical trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Evaporative dry eye and meibomian gland dysfunction

Interventions
Screening comprises 30 patients with evaporative dry eye disease and mild to moderate meibomian gland dysfunction. 30 patients are included and treated (10 patients per treatment group). The three groups formed are:

Group 1: EvoTears® eye drops q.i.d. unless prescribed otherwise by the doctor
Group 2: Cationorm® MD sine eye drops q.i.d. unless prescribed otherwise by the doctor
Group 3: Systane® Balance eye drops q.i.d. unless prescribed otherwise by the doctor
The dosage of the eye drops is 4 x 1 drop per day.
Randomization numbers are calculated using block randomization for sequence generation. A randomization list is generated by an independent person. Due to the open trial design, it is evident for the investigator and for the patient, whether EvoTears®, Cationorm® MD sine or Systane® Balance is applied. Thus, there is no need to create emergency envelopes (code breakers).

Test parameters:
1. Change in non-invasive Tear Break Up Time (NIBUT) measured via Dry Eye Monitor (KOWA DR-1 α). Day 1 compared to measurement on day 28 ±2 days.
2. Subjective discomfort feeling according to a questionnaire (VAS/OSDI)
3. Visual acuity (VA)
4. Thickness of lipid layer (LLT) measured with LipiView
5. Slit-lamp examination of eyelids, conjunctiva, and cornea
5.1. Assessment of eyelid margin (redness, secretion, manual expression of meibomian glands)
5.2. Conjunctival hyperemia
5.3. LIPCOF
5.4. Corneal staining with fluorescein
6. Intraocular Pressure (IOP)
7. Subjective assessment of tolerability by the patient
8. Evaluation of efficacy and tolerability by the investigator

The need for therapy with EvoTears®, Cationorm® MD sine or Systane® Balance eye drops is determined at day 1 by the treating physician and the therapy is carried out and monitored according to the investigator's instructions. Any deviation from the dosage 4 x 1 / d must be documented separately.

As part of a follow-up examination (day 7 ± 2) and a final examination (day 28 ± 2), the attending physician assesses whether the use of EvoTears®, Cationorm® MD sine or Systane® Balance eye drops has shown the desired effect and was well tolerated. In total, each patient should use the observed preparation for at least 4 weeks. The attending physician gives a final assessment of whether the administration of the eye drops was well tolerated. The study ends with the last examination of the patient.

Intervention Type
Other

Primary outcome(s)
Non-invasive Tear Break Up Time (NIBUT) measured using Dry Eye Monitor (KOWA DR-1 α) at day 1, day 7 ±2 and day 28 ±2

Key secondary outcome(s)
1. Subjective discomfort feeling measured using a questionnaire (VAS/OSDI) at day 1, day 7 ±2 and day 28 ±2
2. Visual acuity (VA) measured by refraction at day 1, day 7 ±2 and day 28 ±2
3. Thickness of lipid layer (LLT) measured using LipiView at day 1, day 7 ±2 and day 28 ±2
4. Examination of eyelids, conjunctiva, and cornea using slit lamp at day 1, day 7 ±2 and day 28 ±2 as follows:

4.1. Assessment of eyelid margin (redness, secretion, manual expression of meibomian glands)
4.2. Conjunctival hyperemia
4.3. LIPCOF
4.4. Corneal staining with fluorescein
5. Intraocular pressure (IOP) measured using tonometry at day 1, day 7 ±2 and day 28 ±2
6. Subjective assessment of tolerability by the patient using interview at day 28 ±2
7. Evaluation of efficacy and tolerability by the investigator using interview at day 28 ±2

Completion date
06/03/2018

Eligibility

Key inclusion criteria
1. Male and female patients aged > 18 years
2. Patients with evaporative dry eye and mild to moderate meibomian gland dysfunction:
2.1. Hyposecretion and reduced manual expression of meibomian glands
2.2. NIBUT ≤ 10 s
2.3. Staining of the ocular surface: ≥ 4 and ≤ 9 points on the Oxford grading scale (15 points max)
3. Subjective feeling of evaporative dry eye discomfort more than 3 months
3.1. Visual analogue scale (VAS) ≥ 2/10
3.2. OSDI ≥ 15
4. Stable therapy (topical and systemic) ≥ 4 weeks
5. Patient willing and being able to fulfil the requirements of the trial protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
30

Key exclusion criteria
1. Dry eye due to systemic disease, concomitant medication, malign conditions or idiopathic causes
2. History of ocular surgery during the past 3 months
3. Malposition of the lids and/or lagophthalmos
4. Punctum plugs during the past 3 months
5. Contact lens wearers

6. Use of lipid-containing eye drops during the past 3 months
7. Use of other therapeutic ophthalmics during the past 3 months
8. Sensitivity against any of the ingredients
9. Patient pregnant or breastfeeding
10. Women with childbearing potential without regular and correct use of contraception with an error rate < 1% (e.g. sexual abstinence, estrogen and gestagen containing contraceptives, vasectomy, intrauterine pessary with hormones)
11. Concomitant clinical trial participation within the last 4 weeks
12. Earlier participation at this clinical trial or the patient being an investigator or a member of the personnel involved at this clinical trial
13. Inability to understand written patient information

Date of first enrolment
13/11/2017

Date of final enrolment
06/03/2018

Locations

Countries of recruitment
Germany

Study participating centre
Dr. Thomas Kaercher
Dossenheimer Landstraße 48
Heidelberg
Germany
69121

Sponsor information

Organisation
URSAPHARM Arzneimittel GmbH

Funder(s)

Funder type
Industry

Funder Name
URSAPHARM Arzneimittel GmbH

Results and Publications

Individual participant data (IPD) sharing plan

As the study was initiated in 2016, no data sharing statement is available and the study documentation will not be shared for this study.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		28/05/2021	07/01/2022	Yes	No