RESEARCH INFORMATION AND CONSENT FORM

Project title:	The combination of 0.09% Cyclosporine and Intense Pulsed Light (IPL) Therapy for the Treatment of Dry Eye Disease in Symptomatic Contact Lens Wearers: a Sham-Controlled Randomized Clinical Trial
NCT number :	not yet assigned
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FOR INFORMATION

From Monday to Friday between 8 a.m. and 4 p.m., you can contact:

Dr Éric Lortie-Milner,
Optometrist
Research Student

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We are seeking your participation in a research project to determine whether treatment with a combination of Cequa cyclosporine eyedrops and intense puled light (IPL) is effective in improving in improving the comfort of contact lens wearers. However, before agreeing to participate in this project, please take the time to read, understand and carefully consider the following information. If you agree to participate in this research project, you will be asekd to sign the consent form at the end of this document, and we will provide you with a copy for your records.

This information and consent form explains the purpose of this research project, the procedures, the risks and inconveniences as well as the benefits, and who to contact if necessary. It may contain words you do not understand. We invite you to ask any questions you may have to the researcher in charge of the project or other people involved in the research project, and to ask them to explain any words or information that are not clear.

NATURE AND OBJECTIVES OF THE RESEARCH PROJECT

A large number of contact lens wearers experience some discomfort when wearing their lenses, which in most cases is due to dry eye. Several different mechanisms of dry eye exist, and different treatments can act on dry eye causes, and make each other more effective. One treatment that is widely used is cyclosporine, a medicated eye drop for dry eye. It comes in several forms, and a new formulation was recently approved by Health Canada. This drop is called Cequa and acts on the water layer of the tears. Another mechanism of dry eyes concerns the oil layer of the tears, and occurs when the glands inside the eyelids have altered function. One treatment that has proved effective against this condition is to use IPL to transmit energy to the glands and make them work better. However, these treatments (Cequa and IPL) have never been tried in combination, and only a few studies tried IPL for contact lens wearers. In this study, participants will be randomly assigned to one 2 groups, either one receiving both treatments (Cequa and IPL) or the one receiving only the Cequa treatment with a placebo IPL treatment. Comfort when wearing contact lenses and other signs of dry eye will be assessed at 3 points in the study to determine whether one group has improved more than the other.

We will recruit 44 contact lens wearers who are symptomatic of discomfort while wearing their lenses and who attend one of the Opto-Réseau clinics in the Sherbrooke area to address the following three objectives: 1) Evaluate the improvement in discomfort symptoms caused by the combination of Cequa and IPL in a population of symptomatic contact lens wearers 2) Document the effects of the combination of treatments (Cequa and IPL) on other signs of dryness in contact lens wearers and 3) Confirm the absence of undesirable side effects of the combination of treatments in contact lens wearers.

COURSE OF THE RESEARCH PROJECT

If you agree to take part in the project, your presence will be required for 3 sessions of 45 to 60 minutes each and 2 sessions of 15 to 30 minutes over a 16-week period. These sessions will take place at the Opto-Réseau Sherbrooke Est clinic (29, 10th Avenue N, Sherbrooke, Qc J1E 2T1), in the Place de l'Est complex (corner of King E / 10th Avenue), depending on your availability. You will be asked to answer a questionnaire about your

symptoms. You will also have to undergo a few other tests, which are detailed below along with the description of each session.

Selection process (10-minute telephone interview) :

The first step in participating in this study is the telephone meeting we had and the reading of this consent form. Please keep any questions you may have while reading this form in mind , as they can be asked and answered at the first in-person visit.

Initial visit (Visit #1)

You should arrive at the first session with your contact lenses on your eyes for at least 2 hours. It is advisable to bring you glasses (which you use to read without contact lenses) to this visit. This first session will take approximately 45 minutes. It will begin with questions that you could have on the consent form or the study. Your visual acuity will then be measured. This is a measurement taken during each consultation with an optometrist, where you will be asked to identify letters of different sizes. Various elements will then be checked to ensure that you are eligible for the study. These verifications will be caried out using a slit lamp, an instrument used for all eye examinations. Once your eligibility and desire to participate have been confirmed, you will be asked to sign the consent form.

Following this signature, the capacity of your tears to remain intact on your eye will be measured with your contact lenses in place, using an instrument that projects a light pattern without causing significant glare. This device will also measure the volume of tears in your eye, again without making contact with the eye surface. You will be required to hold your eye open and stare at a target until the investigator gives you the signal to blink. Then, the osmolarity (salt concentration) of your tears will be measured. To collect this data, a small sensor will be hled in place for a few second by the investigator on the red part of the inside of your lower eyelids. This sensor is never in contact with the eyeball itself. You will then be asked to remove your contact lenses. If you don’t have a case to store them in, a case with solution will be provided. A 15-minute pause will be observed to allow your tears to stabilize. During these 15 minutes, you will be asked to answer the f-CLDEQ-8, a quick questionnaire about your symptoms during contact lens wear. A meibomian gland scan will also be taken for each of your eyelids during this break. The scan of the upper eyelid glands requires the eversion of the eyelid, a procedure routinely performed in clinical eye examinations and which can result in a cold sensation on the eyelid when the maneuver is performed. The device used prior to lens removal (lines103-105) will also be repeated without the lenses. When 15 minutes have elapsed since the contact lenses were removed, a small amount of sodium fluorescein, a painless dye that usually disappears from the eye within 15 minutes, will be placed in your eye. The capacity of your tears to remain intact on your eye will be assessed by a second method involving an observation of the front of your eye with the slit lamp with a blue filter. Once again, your role will be to keep your eye open positioned at the slit lamp until the investigator gives you the signal to blink. This procedure is repeated 3 times. A second dye, lissamine green, which disappears from the eye as quickly as fluorescein, will also be placed in you eye in small quantities. Some photos will also be taken of the surface of you eye (in magnification) to enable assessment of any dryness damage to your cornea and conjunctiva. It should be noted that all photos (and videos if needed) will be taken in

this way, where only your eye can be seen in close-up, which does not allow identification by these images.

Your eye pressure will also be measured. Pressure inside the eye is a measurement that is routinely made in almost all eye examinations and is considered important for assessing eye health. This measurement is taken with a non-contact tonometer (air puff tonometer).

Finally, you will be given a supply of Cequa drops for the first 8 weeks of the study, with instructions to apply them twice a day at home. You will also be asked to apply gentle pressure to the inner corner of the eye for 5 minutes to limit absorption of cyclosporine into the rest of the body (a demonstration will be provided).

Starting at this first session, a system will be set up to collect data on your symptoms more frequently during the study. Every Tuesday and Saturday for the duration of the study, you will receive an e-mail containing 4 quick questions that you will be asked to answer in order to obtain more data on the daily comfort you experience with your contact lenses. The questions will also enquire about the use of artificial tears and whether it was possible for you to apply the Cequa drops at the requested frequency. Emails will be sent until your last study session and, of course, at any time you decide to withdraw from the study. A courtesy call will be made by the research team 3 weeks after this meeting to keep you involved in the study and make sure everything is going well.

Treatment visit (Visit #2) :

The second visit will take place 8 weeks after visit #1 and, for this visit too, you will be asked to arrive with your contact lenses in place for at least 2 hours. It is advisable to bring your glasses (which you use for reading without contact lenses) to this visit. This second session will take approximately 60 minutes (the longest of the study). First, visual acuity will be measured, as in visit#1. Thereafter, the description of this visit is identical to that of visit #1 (lines 103 to 131), except for the eyelid glands scan, which will not be performed. You will also be given a short questionnaire on the side effects of the drops. Following these measurements (your contact lenses will have been removed for some time), the first treatment (IPL or IPL-placebo) will be performed. If you are in the experimental group, you will receive IPL therapy. This is a treatment in which gel (similar to ultrasound gel) is applied from temple to temple, passing just below your lower eyelids and over the bridge of your nose. Opaque eye shields will also be applied to your closed eyelids to protect your eyes and maximize your comfort. Next, 15 flashes will be pulsed by applying the IPL prism, disinfected beforehand, to the gel. This series of 15 flashes will be repeated a second time, for a total of 30 flashes. Afterwards, the gel will be removed and you will be given a towel to clean your face, and the protectors will be removed. If you are in the control group (IPL-placebo), the procedure will consist of a placebo procedure that will give you the same sensation. After you have been given safety instructions (to call back the clinic if a significant side effect occurs, and to avoid direct and prolonged exposure to the sun), the session will be completed. Intraocular pressure will then be measured using the air puff tonometer described above. The next session will be scheduled 3 weeks later.

<u>Visits #3 and 4</u> :

For visits 3 and 4 (which are similar and take between 20 and 30 minutes), you do not need to arrive with your contact lenses in place. It is advisable to bring you glasses (which you use for reading without contact lenses) to these visits. Your visual acuity will first be measured. If you arrived at the clinic with your contact lenses in place, you will first be asked to remove them and store them in a case. You will then be asked tocomplete a questionnaire on side effects since your last visit, as well as the f-CLDEQ-8 questionnaire. Then, the second treatment (IPL or IPL-placebo) will be performed (in the same way as described for visit 2, respecting your allocation to one of the groups). Intraocular pressure will then be measured using an air-puff tonometer. If this is visit #3, the next session will be scheduled 3 weeks later. If this is visit #4, the next (and last) visit will be scheduled 2 weeks later.

Follow-up visit (Visit #5) :

The fifth session will serve as a final evaluation to assess the effect of the treatments received. This last session will take approximately 45 minutes. You will be asked to arrive with your contact lenses in place for at least 2 hours. It is advisable to bring your glasses (which you use for reading without contact lenses) to this visit. Your visual acuity will be measred. Thereafter, tests will be performed in the same order and in the same way as during visit #1 (procedure described on lines 103 to 135). The only addition to this sequence is that the questionnaire on side effects of the treatments will be administered immediately after the f-CLDEQ-8. Once these tests have been completed, the system sending you electronic communications to answer the weekly questions will be deactivated. You will then be informed of the group to which you had been assigned. Your participation in the study will then be terminated.

Whan the research team publishes the results of the study, if you agree, an e-mail will be sent to you with the findings in lay terms, thanking you again for your participation.

Lorsque l'équipe de recherche publiera les résultats de l'étude, si vous y consentez, un courriel vous sera envoyé pour vous faire part des conclusions vulgarisées et vous remercier à nouveau pour votre participation.

Please refer to the calendar at the end of this document for an overview of the examinations and procedures carried out during the research project

PARTICIPANT COOPERATION

- Not receiving any other clinical treatment (Lipiflow, iLux) during the study period.
- As far as possible, follow the Cequa application protocol (2 drops/day) at home.
- Answer questions about wearing contact lenses as accurately as possible.
- Document side effects.
- Wear contact lenses for a minimum of 2 hours before the visits 1,2, and 5

RISKS THAT MAY ARISE FROM YOUR PARTICIPATION IN THE RESEARCH PROJECT

The risks associated with this study are low. Firstly, the biomicroscopic evaluation of your eye and the taking of the meibography will involve a certain amount of digital manipulations of the eyelids, including eversion of the upper eyelid. This may cause slight discomfort, which disappears as soon as the procedure is over. This is part of a routine

optometric examination. When fluoresceine or lissamine green is placed on the eye, it may, in rare cases, cause slight transient irritation when applied to the lower eyelid. As mentionned earlier, the eye will be more yellow or green in color for a few minutes after observation. During tear stability measurements, keeping the eye open for several seconds (the maximum would be 45 seconds, if breakage, i.e. the moment when tears are no longer intact on the eye, does not occur before then) may cause mild discomfort to the eyes, which usually disappears within a few blinks. If this discomfort persists, you will be offered an eye lubricant for relief.

Treatment with Cequa drops has been shown to be safe in large-scale studies. No serious side effects relate to this drop have been documented in the literature. The side effect of discomfort when the drops are applied to the eye is, however, common (expected in around 20% or participants). No cases have been reported where Cequa drops led to a change in intraocular pressure or a reduction in visual acuity.

There are no data to show that the Cequa drop is safe for use by pregnant or breast-feeding women. Therefore, the use of this drop in pregnant or breast-feeding women is contraindicated. If your pregnancy statuss changes, or if there are plans to change your pregnancy status during your participation in the study, you should discontinue use of Cequa and contact the research team.

As mentionned above, IPL therapy is reputed to be safe, since no serious adverse side effects have been reported to date using the appropriate safety measures (gel and eye protectors). IPL therapy has been evaluated in numerous clinical studies, and no serious adverse side effects have been reported to date. Possible side effects include feeling of discomfort/slight pain on the skin around the eye socket during or after the procedure, loss of eyelashes (only 1 documented case), change in skin tone (very low risk in individuals with pale to moderately pigmented skin (types I to IV on the Fitzpatrick scale) and high risk in individuals with dark or black skin (types V and VI on the Fitzpatrick scale)), slightly blurred vision in the hours following the procedure and redness of the eye or skin around the eye socket. If you experience pain, please inform the investigator so that he/she can try to reduce it during the treatment or interrupt it.

POSSIBLE INCONVENIENCES OF PARTICIPATING IN THE RESEARCH PROJECT

You will need to ensure your own transportation to the Opto-Réseau Sherbrooke Est clinic for the visits, making sure you have had the contact lenses in your eyes for at least 2 hours. The first visit is scheduled to last about 45 minutes, while the second visit is scheduled to last about 60 minutes. The next 2 visits are quicker, lasting between 20 and 30 minutes each. The final visit is scheduled to last 45 minutes. The study will therefore require 190 to 210 minutes of your time. You will also have to answer a few quick questions electronically, 2 times per week.

POSSIBLE BENEFITS OF PARTICIPATING IN THE RESEARCH PROJECT

You may benefit from your participation in this research project, but we cannot guarantee it. Your participation may improve your comfort when wearing your contact lenses. In

addition, it will contribute to the advancement of knowledge about the treatment of dry eye and its impact on contact lens wear.

ALTERNATIVES TO THE PARTICIPATION IN THE RESEARCH PROJECT

You do not have to take part in this research project to be treated for your meibomian gland dysfunction and/or to improve your contact lens comfort. Other treatments include artificial tears, thermopulsation treatments, warm compresses and omega-3 supplements.

VOLUNTARY PARTICIPATION AND POSSIBILITY OF WITHDRAWAL

Your participation in this research project is voluntary. You are therefore free to refuse to take part. You may also withdraw from this project at any time, without giving any reason, by informing the research team.

Your decision not to participate or to withdraw from this research project will not affect the quality of care and services to which you are entitled or your relationship with the research team.

Unless you notify us otherwise, if you withdraw or are withdrawn from the project, the information and materials already collected as part of this project will still be retained, analyzed or used to ensure the scientific integrity of the project.

Any new knowledge acquired during the course of the project that could have an impact on your decision to continue participating in this project will be communicated to you promptly.

PRIVACY

Collection – Purposes for which personal information is requested

During your participation in this research project, the researcher in charge of ths project and his staff will collect, in a research file, the information concerning you and necessary to meet the scientific objectives of this research project.

Collection – What personal information is requested

The information collected may include data contained in your optometric medical file (i.e. only the information contained in your Opto-Réseau clinic file) concerning your past and present state of health, your lifestyle habits, and the results of all tests, examinations and procedures that will be performed. Your file may also include other information such as your name, gender, date of birth and occupation.

Retention of information/data - Protection

All information collected will remain confidential to the extent permitted by the law. You will be identified only by a code number. The code key linking your name to your research file will be kept by the researcher responsible for this research project.

Duration of data storage

This research data will be kept for at least 7 years by the researcher responsible for the research project.

Dissemination of results

Research results may be published in scientific journals or discussed in scientific circles, but it will not be possible to identify you.

Right of access for control and security purposes

For surveillance, control, protection, and security purposes, your research file and your optometric file may be consulted by representatives of the establishment or the research ethics committee. These individuals adhere to a confidentiality policy.

You have the right to consult your research file to verify the information collected, and to have it corrected if necessary. In addition, access to certain information before the of the study may require that you be withdrawn from the project in order to preserve its integrity.

The results of the research project belong to the researchers who conducted the study and to the Université de Sherbrooke. The organizations and companies that contributed funding for this study have no rights to the data or results.

RESEARCH PROJECT FUNDING

Expenses are covered by 3 sources: self-financing, a 1,500$ grant from the Canadian Education Optometric Education Trust Fund (COETF), and a MITACS insternship (15,000$), made possible by the participation of Sun Pharma, the company that manufactures the Cequa drug used in the study. The company is also providing the doses of Cequa used in the study free of charge.

COMPENSATION

You will receive a financial compensation of 40$ for each one of visits 1,2 and 5 and 20$ for visits 3 and 4, which are shorter. So, in total, you will receive 160$ if you complete the study. If you stop participating before the end of the study, you will receive compensation for the visits you have completed (pro rata to your participation). In addition, throughout the study, the treatment(s) will be dispensed free of charge.

IN CASE OF HARM

Should you suffer any harm whatsoever as a result of your participation in the research project, you will receive all the care and services required by your state of health.

By agreeing to participate in this research project, you do not waive any of your rights and you do not release the researcher responsible for this research project and the establishment from their civil and professional responsabilities.

CONTACTS

If you have any questions or problems related to the research project, or if you wish to withdraw from it, you can contact the researcher in charge or a member of the research team. Please refer to the box on page 1.

If you have any questions about your rights as a participant in this research project, or if you have any complaints, you can contact the *Bureau des plaints et de la qualité des services* of CIUSSS de l'Estrie – CHUS at plaints.ciussse-chus@ssss.gouv.qc.ca or 1-866-917-7903.

MONITORING OF ETHICAL ASPECTS

The CIUSSS de l'Estrie – CHUS Research Ethics Committee has approved the project and will monitor its progress.

If you would like to join one of the members of this committee, please contact the CIUSSS de l'Estrie – CHUS Research Project Authorization Office at ethique.recherche.ciussse-chus@ssss.gouv.qc.ca or 819-346-1110 est. 12856.

CONSENT

I have read the information and consent form. The research project and this information and consent form have been explained to me. My questions have been answered and I have been given sufficient time to make a decision. After careful consideration, I consent to participate in this research project under the conditions stated herein.
I authorize the research team to have access to my Opto-Réseau clinic file.
I agree that my recordings and my photographs may be used for training purposes and/or scientific presentations and that they may be kept with my research data. None of these photos or videos will allow me to be identified (as they are very close-up shots of the surface of the eye).

☐ **YES** ☐ **NO**

I agree to be contacted for follow-up or further information about the study.

☐ **YES** ☐ **NO**

Name of participant *(block letters)*	Participant's signature	Date

I have explained the research project and this information and consent form to the participant and answered any questions he/she asked.

Name of the person who obtains consent *(block letters)*	Signature	Date

SCHEDULE OF VISITS AND INTERVENTIONS

	Visit 1		Visit 2		Visit 3		Visit 4		Visit 5	
Group	**Exp**	**Ctrl**	**Exp**	**Ctrl**	**Exp**	**Ctrl**	**Exp**	**Ctrl**	**Exp**	**Ctrl**
Duration (minutes)	**45-60**	**45-60**	**45-60**	**45-60**	**15-30**	**15-30**	**15-30**	**15-30**	**45-60**	**45-60**
Arrival with CL (2 hours)	**X**	**X**	**X**	**X**					**X**	**X**
Visual acuity	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Eligibility checks	**X**	**X**								
Consent signing	**X**	**X**								
Tear stability NIBUT	**X**	**X**	**X**	**X**					**X**	**X**
Tear volume (TMH)	**X**	**X**	**X**	**X**					**X**	**X**
Osmolarity	**X**	**X**	**X**	**X**					**X**	**X**
f-CLDEQ-8 questionnaire	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
adverse effects			**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Meibography	**X**	**X**							**X**	**X**
Tear stability (TBUT)	**X**	**X**	**X**	**X**					**X**	**X**
Corneal staining	**X**	**X**	**X**	**X**					**X**	**X**
Conjunctival staining	**X**	**X**	**X**	**X**					**X**	**X**
IPL procedure			**X**		**X**		**X**			
Placebo IPL procedure				**X**		**X**		**X**		