Viral Conjunctivitis Treatment Study

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1) **Protocol Title**

Treatment of Viral Conjunctivitis with Avenova ® (0.01% hypochlorous acid)

2) **Objectives**

The objective of this study is to determine the efficacy Avenova® (0.01% hypochlorous acid) in the treatment of viral conjunctivitis. We hypothesize that patients treated with Avenova® will have a quicker resolution of their ocular signs and symptoms of Viral Conjunctivitis.

3) **Background**

Avenova® is a proprietary pure hypochlorous acid under a family of skin cleansing products by NovaBay that has been approved by the FDA as a 510(k) medical device. Many in vitro studies have evaluated the efficacy of hypochlorous acid against bacterial and viral agents. In ophthalmology, it is commonly used as a lid cleanser in the treatment of blepharitis and meibomian gland dysfunction. It is applied directly to the lid margin and has an excellent skin and ocular safety profile, which includes a lack of ocular irritation on application. (See included supplemental "Material safety data sheet")

We propose a study to evaluate the role of Avenova® (0.1% hypochlorous acid) in the treatment of common ocular viral infections.

4) **Inclusion and Exclusion Criteria***

Inclusion:

Patients who present to Bascom Palmer Eye Institute with a clinical diagnosis of viral conjunctivitis will be allowed to participate in the study. Patients with viral conjunctivitis will be diagnosed clinically with symptoms of either unilateral or bilateral conjunctivitis of less than 1 week duration. These diagnoses will then be confirmed with a viral PCR. These patients will also need to have one of the following: 1. follicular conjunctivitis of the inferior tarsal conjunctiva, 2. mucoid discharge, 3. preauricular lymphadenopathy, or 4. associated upper respiratory symptoms.

Exclusion:

Patients with a history of allergic conjunctivitis, history of herpetic eye disease, concurrent diagnosis of bacterial conjunctivitis, purulent discharge, intraocular inflammation, or current contact lens use will be excluded from the study. Immunocompromised/Immunosupressed patients, patients with HIV, pregnant women, prisoners, or adults who are unable to provide consent will be excluded. Age less than 18 years old will be excluded viral conjunctivitis treatment arm of the study.

5) **Number of Subjects***

Total number of subjects to be enrolled is 125

6) **Study-Wide Recruitment Methods***

N/A.

7) **Study Timelines***

Patients will participate for 3 weeks in total. Enrollment will be complete by 2 years and the primary analyses will be completed in 2.5 years duration.

8) **Study Endpoints***

The primary endpoint of the study is the resolution of follicular conjunctivitis and symptomatic improvement in the viral conjunctivitis arm.

9) **Procedures Involved***

Patients will be diagnosed by clinical exam in the Bascom Palmer Emergency Department. Those meeting inclusion criteria will be randomized to Avenova® spray vs artificial tears (placebo), to be used in the affected eye four times a day for two weeks duration in total. Samples of the tears from the ocular surface and conjunctiva will be obtained through cotton swabs from the patient's initial visit and daily to every-other-day through 1 week, and finally at week 2 (e.g. Day 0, 1, 2, 3, 4, 5, 6, 7, and 14 +/- 1 day). These samples will be obtained in both groups (Avenova® spray and artificial tears). Collected samples will be sent to the Bascom Palmer Microbiology laboratory for PCR evaluation and microbiology evaluation and then promptly disposed of. Patients will return once every week for 3 weeks duration in order to assess for resolution of follicular conjunctivitis and symptomatic relief based off the subjective scoring guidelines (see supplemental material) as well as physical exam findings (lymphadenopathy, follicular conjunctivitis, injection, discharge, subepithelial infiltrates, conjunctival pseudomembranes) *See Objective Questionnaire*. Patients will be questioned about adverse effect to treatment each visit and be assessed for surrounding periorbital dermatitis. However, Avenova® has a wide range of indications for use and is approved by the FDA as a medical device for use on the skin.

10) **Data Management***

Viral conjunctivitis

POWER ANALYSIS:

%spontaneous resolution in 7 days: 20%

%Resolution with treatment: 50%

N=39 for each treatment group for power of 80%

Data will include medical record number, diagnosis, type of therapy, commentary on improvement/worsening of signs and symptoms. It will also include adverse events.

Research data can only be accessed by clinicians (whose names have been added to the IRB) in direct care of the patient or those listed on the IRB. All identifiable data will be stored on a locked and encrypted USB drive and will be de-identified of personal identifying information at the conclusion of the study once all data is analyzed, which will again be stored on a locked and encrypted USB drive. The investigatory team will assign subject identifiers and study records will be locked in the office of Dr. Lee on the 4th floor Suite 450M of the Bascom Palmer Eye Institute located at 900 NW 17th Street, Miami, FL 33136.

11) **Provisions to Monitor the Data to Ensure the Safety of Subjects***

Subjects will return for follow up appointments at weekly intervals for three weeks total. It is safe to monitor these patients at these intervals as these viral infections are self-limiting and often resolve with time. As there is currently no treatment for these infections, observation and symptomatic management is standard of practice.

Co-investigators on the study will assess patients at each of the follow-up visits for any side effects (listed in the informed consent) to the assigned medical treatment and document this in the electronic medical health record. Patients will be given the telephone number of a principle investigator if they believe they are having a significant side effect or may also present at the 24 hour emergency department at the Bascom Palmer Eye Institute. If there are noted adverse reactions to the device, participation in the study will be terminated for that individual patient. Data will be analyzed by members of the IRB team at weekly intervals, and if during the study, greater than 20% of patients are observed to have an adverse reaction to the spray, the study will be terminated prematurely.

12) **Withdrawal of Subjects***

Patients will be withdrawn from the study if the physician deems their symptoms to be clinically related to administration of the device. Patients may withdraw voluntarily from the study at any time, but will be continued to be followed for the duration of the study. Non-compliant patients (those who do not take the study device) will be allowed to continue in their respective groups (Avenova® versus artificial tears) for the duration of the study.

13) **Risks to Subjects***

Avenova® (0.1% hypochlorous acid) has been extensively studied and has been approved by the FDA as a 510(k) medical device wound cleanser for any skin and undergone extensive in-vitro toxicity testing. In ophthalmology, it is commonly used as a lid cleanser in the treatment of

blepharitis and meibomian gland dysfunction. It is applied directly to the lid margin and has an excellent safety profile. There has been no noted ocular side effects, which includes a lack of ocular irritation. (see included "Material safety data sheet")

We see no foreseeable risk to the artificial tear group.

There is no foreseeable risk of obtaining the cotton swabs from the conjunctiva. These tests will be performed without adding additional costs to the patient.

Exclusion criteria include pregnancy and thus this group would not be included in the study. Those who may become pregnant during the study may choose to leave the study—however the topical spray is safe to be used in pregnancy.

14) **Potential Benefits to Subjects***

Benefits to patients would include earlier resolution of lesions and discomfort from conjunctivitis compared to control. These treatments could shorten duration of viral conjunctivitis, a common and extremely contagious viral infection that stops patients from carrying out their normal activities. If our study shows a shortened duration of infection from this therapy, it could result in symptomatic relief from the effects of viral conjunctivitis for which there have been no beneficial treatments at present.

15) **Vulnerable Populations***

Not applicable

16) **Setting**

Bascom Palmer Eye Institute is an ophthalmic hospital with a 24 hour emergency department specializing in ophthalmic disease. Research will be collected as the patient is followed in the emergency department as well as by physicians staffing clinic.

17) **Resources Available**

Bascom Palmer Eye Institute is an ophthalmic hospital with a 24 hour emergency department specializing in ophthalmic disease. The institute receives a wide referral base including all of Florida and the surrounding sites, as well as numerous international referrals due to its prominence in the field of ophthalmology. This institute is staffed with residents, fellows and attending's, all specialized only in the field of ophthalmology. Each week, the emergency department diagnoses at least 10 cases of viral conjunctivitis. If half of these cases agree to participate in the study, there will be adequate number of patients to power the study.

Before the start of the study, all participating members will be informed of the study, as well as possible risks, benefits and their role within the study.

We plan to devote 24 months to collecting patients as well as the statistical analysis for the study.

18) **Recruitment Methods**

Patients will be recruited from the Bascom Palmer Eye institute emergency department as a referral. Potential subjects are those identified as being infected with viral conjunctivitis by the ophthalmologist. There will be no advertisements for this study and no payment will be offered to participants of the study. If the patient consents to the study, he/she will be randomly assigned to Avenova® vs artificial tears through a randomization computer program.

19) **Confidentiality**

Identifiable data will be stored on a locked and encrypted USB drive to be locked in the office of Dr. Lee on the 4th floor Suite 450M of the Bascom Palmer Eye Institute located at 900 NW 17th Street, Miami, FL 33136. This data will be de-identified of personal identifying information at the conclusion of the study. The investigatory team will assign subject identifiers and study records will only be accessed by the study coordinators.

20) **Provisions to Protect the Privacy Interests of Subjects**

To limit intrusiveness to patients, data will only be collected during clinic follow-up (once every week for three weeks). Patients will receive a subjective questionnaire (see supplemental material) each visit to ensure consistency between patients and between visits. The research team will then review the data collected through these questionnaires for analysis.

21) **Compensation for Research-Related Injury**

Patients will not be compensated for research related injuries. This will be written in the consent and described to the patient before participation in the study.

22) **Economic Burden to Subjects**

The device will be provided free of cost to patients as provided by Novabay. Also, there is no cost to participants for the collection of tears via the use of cotton swab.

23) **Consent Process**

Consent will be obtained during an Emergency Room visit by the physician and will follow the SOP: Informed Consent Process for Research (HRP-090). The informed consent will occur that same visit to the ER; if the patient decides that he/she does not want to participate, he/she will be unable to participate at a later visit. Each visit, the patient will be asked and have the option to leave the study.

Non-English Speaking Subjects

- Spanish will be used to obtain consent in those who prefer the Spanish language—translation will be offered if needed with consent offered in the Spanish language.

24) **Process to Document Consent in Writing**

Eligible subjects will be informed of the nature, risks, and benefits of the study and informed that they are not required to participate. If interested in participating, they will be given the consent form to read, asked if they have any questions or need further explanations, and will have the option of taking the consent form home to have more time to decide about participating.

The consent process will be obtained by one of the research team members whose name and signature will be mentioned in the consent form. The details of the study will be explained to the prospective subjects.

25) **Drugs or Devices**

The device will be stored, handled and dispensed by the Bascom Palmer Pharmacy and the designated IRB study team members. The device will be administered by the patient. Avenova® has received FDA approval as a 510(k) medical device with a wide range of indications including for use on the skin surface. Note: although Novabay has been described as a funding source, only Avenova® will be provided, no direct funding will be provided.

References

1. Kim HJ, Lee JG, Kang JW, Cho HJ, Kim HS, Byeon HK, Yoon Effects of a low concentration hypochlorous acid nasal irrigation solution on bacteria, fungi, and virus. *H.Laryngoscope*. 2008 Oct;118(10):1862-7

2. Debabov D, Noorbakhsh C, Wang L, et al. Avenova™ with Neutrox™ (pure 0.01% HOCl) compared with OTC product (0.02% HOCl). NovaBay Pharmaceuticals, Inc., Emeryville, California, USA.