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US Department of Health and Human Services
200 Independence Ave SW
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TITLE	:	TrueTear in Sjogren's Disease Patients
PROTOCOL #	:	830076

The following document spells out the study protocol and statistical analysis plan for this trial.

Sincerely,

Jonathan Lilley
Research Coordinator

Protocol

In this trial, the protocol is straightforward. The study consists of two visit days for the patient. The first day is considered the screening day. On the first day, a baseline Schirmer's test is performed after the patient's eyes have been anesthetized. The duration of this test is five minutes. At the end of the five minutes, the tear production is measured using the Schirmer strips. The patient must produce ten millimeters or less in at least one eye to qualify for the study. Next, the TrueTear device is simulated using two cotton swabs. One cotton swab is inserted into each nostril. Using Schirmer strips to measure tear production, the patient swirls the cotton swabs around in their nostrils until they produce four millimeters above their baseline in at least one eye. The patient is then to hold the cotton swabs in their nose for the remainder of the five minutes. In order to qualify for the study, the patient must produce four millimeters or greater in the study eye. In instances where the patient is of child-bearing age, a pregnancy test is performed to ensure that the patient is not pregnant.

After visit one, visit two can be completed the following day or any day during the next forty-five days. During visit two, the effectiveness of the device is tested. The patient is randomized to which application method, internal or external, is used first. During both the first and second applications, Schirmer strips are used to measure tear production over the course of five minutes. For the first three minutes, the device is used. For the remaining two minutes, the device is removed. Between the first and second applications, there must be a waiting period of at least forty-five minutes. This break ensures that the patient's tear glands have enough time to restore. This is necessary for accurate measurement of the effectiveness of the device.

Statistical Analysis Plan

Our plan to analyze the data from this trial will involve a few different comparisons, as well as factoring in a few different variables. First, we will look to compare both the internal and external stimulation results to the baseline results. When making these comparisons, the order in which application method was used first will be factored in. This will help us determine whether or not the order of application methods impacts the final results. Next, we will examine each stimulation method (cotton swabs, internal application with TrueTear device, and external application with TrueTear device) relative to baseline to see if the changes are statistically significant from baseline, and to determine an estimated mean change. We also plan to compare each application method to each other to determine if there is a statistically significant difference. While making the comparison, we also want to separately account for two different factors, patients on Sjogren's medication vs. patients not on Sjogren's medication and patients with a baseline Schirmer of less than 5 mm. vs. patients with a baseline Schirmer of greater than or equal to 5 mm. In a similar fashion, we also want to examine each application method individually to determine the p-value, confidence interval, mean, and standard deviation.