Evaluation of Intraoperative use of Dexycu on the Signs and Symptoms of Dry Eye

Sponsor:	**SR Cornea Consultants** **16 Kimberley Circle, Oak Brook, IL 60523** **847 668 5498** **Name and title of person(s) authorized to sign the protocol for the sponsor: Sanjay Rao, MD**
Monitor:	**Sanjay Rao, MD**
Medical Expert:	**Sanjay Rao, MD**
Investigators:	**Sanjay Rao, MD**
Clinical Laboratory(ies):	**NA**
Study Product:	**DEXYCU (dexamethasone intraocular suspension) 9%**
Protocol Number:	**NCT04184999** **April 10, 2019**

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STUDY SUMMARY

Title	*Evaluation of intraoperative use of Dexycu on the Signs and Symptoms of Dry Eye*
Protocol Number	*10*
Phase	*Phase IV*
Methodology	*Prospective Randomized Controlled Trial*
Study Duration	*3 weeks*
Study Center(s)	*Single-Center*
Objectives	*To evaluate the impact of intraoperative Dexycu during cataract surgery on the signs and symptoms of dry eye*
Number of subjects	*40*
Main Inclusion and Exclusion Criteria	*Inclusion: Patients undergoing bilateral cataract surgery* *Exclusion: Patients with severe ocular surface disease as defined by central corneal staining with fluorescein and/or a tear film osmolarity of greater than 340 in either eye*
Study product, Dose, Route, Regimen	*DEXYCU (dexamethasone intraocular suspension) 9%, administered as a single dose, intraocularly in the posterior chamber at the end of surgery. The dose is .005 mL of dexamethasone 9% (equivalent to 517 micrograms)*
Duration of subjects participation	*Patients scheduled to undergo bilateral cataract surgery will be screened and have dry eye testing. If enrolled in the study, patients will have dry eye testing at 1 week and 3 weeks after surgery.*
Reference product	*The control group will utilize a standard post-cataract surgery regimen of topical gatifloxacin and topical prednisolone acetate.*

1 Introduction

Evaluation of intraoperative use of Dexycu on the Signs and Symptoms of Dry Eye is a clinical research protocol and the study will be conducted in accordance with the protocol, Good Clinical Practice Standards, and applicable regulatory requirements.

1.1 Background

Multiple studies have established the relationship between dry eye and cataract surgery. First, a majority of patients undergoing cataract surgery have dry eye signs including decreased tear break up time (63%) and positive corneal staining (77%). Second, patients experience an increase in dry eye symptoms after cataract surgery compared to baseline. Third, Snellen visual acuity and contrast sensitivity are impacted by dry eye after cataract surgery.

The objective of this clinical research is to evaluate whether the signs and symptoms of dry eye after cataract surgery improve with the addition of a DEXYCU intraocular injection.

1.2 Investigational/Study Product

DEXYCU contains dexamethasone 9% as a sterile suspension for intraocular ophthalmic administration. DEXYCU is provided as a kit for administration of a single dose of 0.005 mL of 9% dexamethasone.

1.3 Preclinical Data

Not applicable.

1.4 Clinical Data to Date

Clinical efficacy was evaluated in a randomized, double masked, placebo controlled trial (NCT2006888) in which subjects received either DEXYCU or placebo (vehicle). A dose of 5 microliters of DEXYCU or vehicle was administered by the physician at the end of the surgical procedure. The primary efficacy endpoint for the study was the proportion of patients with anterior chamber cell clearing on postoperative day 8. The percentage of patients with anterior chamber clearing at Day 8 was 2-% in the placebo group, and 57%, and 60% in the 342 and 517 microgram treatment groups.

1.5 Dose Rationale

See section 1.4

1.6 Risk/Benefits

The following adverse events rates are derived from three clinical trials in which 339 patients received the 517 microgram dose of DEXYCU. The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema, and iritis. Other ocular adverse reactions occurring in 1-5% of subjects included, corneal endothelial cell loss, blepharitis, eye pain, cystoid macular edema, dry eye, ocular inflammation, posterior capsular opacification, blurred vision, reduced visual acuity, vitreous floaters, foreign body sensation, photophobia, and vitreous detachment.

2 Study Objectives

The objective of this clinical research is to evaluate whether the signs and symptoms of dry eye after cataract surgery improve with the addition of a DEXYCU intraocular injection. Multiple studies have established that dry eye worsens after cataract surgery. There is also

a strong body of evidence that shows that dry eye is inflammatory. The objective of this study is to evaluate whether the intraocular use of steroid impacts dry eye.

3 Study Design

3.1 General Design

- The type/design of the study:
  - Prospective randomized controlled trial
- A description of the measures taken to minimize/avoid bias:
  - Patients undergoing bilateral cataract surgery will be randomized to the DEXYCU group (standard postoperative cataract regimen + intraoperative DEXYCU) in one eye or the STANDARD group (standard postoperative cataract regimen). Randomization will be done after screening visit, prior to surgery on the first eye and will be done by coin flip. Standard cataract regimen to be used: topical prednisolone acetate 1% qid and topical gatifloxacin qid for 1 week, then tid for 1 week, then bid for 1 week.
- Expected duration of subject participation
  - 3 weeks after cataract surgery
  - Patients undergoing cataract surgery will have dry eye testing prior to surgery, 1 week after surgery, and 3 weeks after surgery
- A summary description of the sequence and duration of all trial periods including follow-up, if any
  - Patients undergoing cataract surgery will have dry eye testing prior to surgery, 1 week after surgery, and 3 weeks after surgery

3.2 Primary/Secondary Endpoints

Primary endpoints:

1) Tear film Osmolarity as measured on Tear Lab system
2) Corneal Staining (Oxford grading scale 0-15)

Secondary endpoint:

3) Satisfaction questionnaire – How satisfied are you with your surgery? (Graded 0-4)

4 Subject Selection and Withdrawal

4.1 Inclusion Criteria

1) Patients diagnosed with bilateral cataracts and scheduled to undergo bilateral cataract surgery
2) Must be able to understand and sign an informed consent from that has been approved by an Institutional Review Board
3) Patient is over the age of 18
4) Patient must agree to comply with visit schedule and other requirements of the study
5) Females who are not pregnant and are not lactating. Females who are post-menopausal or surgically sterilized.

If the answer to any of the inclusion criteria are NO, the subject is ineligible to continue study participation

4.2 Exclusion Criteria

1) Patients with several ocular surface disease as defined by central corneal staining with fluorescein and/or a tear film osmolarity of greater than 340 in either eye

4.3 Subject Recruitment and Screening

Subjects will be recruited for the study from principal investigator's clinical practice. As part of the informed consent process, patients will be offered a DEXYCU injection and given a brochure/handout discussing DEXYCU. As part of the standard cataract evaluation process, both tear film osmolarity and corneal staining will be performed.

4.4 Early Withdrawal of Subjects

Subjects will be carefully monitored after surgery, including visual acuity measurements, intraocular pressure measurements, anterior and posterior segment evaluation, as well as dry eye testing. If patients have an intraocular pressure elevation over 35mm that requires additional medication, they will be withdrawn from the study. Also, if patients require a deviation from the standard cataract postoperative regimen, they will be withdrawn from the study.

5 Investigational Product

5.1 Description

Each kit of DEXYCU contains a single dose for a single patient. The 2 mL glass vial is filled with 0.5 mL of 9% dexamethasone.

5.2 Treatment/Dosing Regimen

DEXYCU (dexamethasone intraocular suspension) 9%, administered as a single dose, intraocularly in the posterior chamber at the end of surgery. The dose is .005 mL of dexamethasone 9% (equivalent to 517 micrograms)

5.3 Method for Assigning Subjects to Treatment/Dosing Groups

Patients undergoing bilateral cataract surgery will be randomized to the DEXYCU group (standard postoperative cataract regimen + intraoperative DEXYCU) in one eye or the STANDARD group (standard postoperative cataract regimen). Randomization will be done after screening visit, prior to surgery on the first eye and will be done by coin flip. Patients who are randomly assigned to the DEXYCU group will receive a sequentially numbered drug kit.

5.4 Subject Compliance Monitoring

The study team will assess and track compliance on each study visit (1 day, 1 week, 3 weeks). At all postoperative visits, the study team will monitor adherence to the eyedrop regimen. If there is a significant deviation from the eyedrop regimen, the principal investigator will determine continuation in the study.

A case report binder will be created for each subject in the study. Binder tabs will include:
Screening Visit
Day 1 Visit
Day 7 Visit
Day 21 Visit
Exit Form
Early Exit Visit
Nonserious Adverse Event Forms
Serious Adverse Event Forms

5.5 Prior and Concomitant Therapy

All medications that subjects are taking prior to cataract surgery will be permitted. Subjects are also permitted to utilize artificial tears in addition to the therapeutic regimens. The use of artificial tears will be tracked by the study team.

5.6 Packaging, Receiving, Storage, Dispensing and Return

Dexycu will be stored in a locked cabinet. Usage of the medication will be logged.

6 Study Procedures

Screening Visit
Day 1 Postoperative Visit
Day 7 Postoperative Visit
Day 21 Postoperative Visit

At all visits, visual acuity, eye pressure measurements, tear film osmolarity, and corneal staining will be measured and recorded. At days 7 and 21, patient satisfaction scores will be measured.

7 Statistical Procedures

7.1 Sample Size Determination

The determination of sample size was based on a review of similar cataract and dry eye studies. As this is a single center, pilot study, it was determined that a sample size of 40 patients would be feasible.

7.2 Statistical Methods

An ANOVA analysis will be performed to compare the dry eye testing data between the DEXYCU group and the standard regimen group.

7.3 Subject Population(s) for Analysis

All patient who met inclusion criteria and complete the study will be included in the selection of subjects to be included in the analyses.

8 Safety and Adverse Events

8.1 Definitions

An adverse event is any untoward medical occurrence in a patient who is administered a test article (DEXYCU). The adverse event does not necessarily have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of the test article, whether or not related to the test article.

A nonserious adverse event is defined as a change in a patient's ophthalmic and or medical health that is not life-threatening, does not require hospitalization, does not prolong a current hospitalization and is not disabling. Nonserious adverse events must be reported by use of a Nonserious Adverse Event Form and may also be reported by a telephone call. All nonserious advese events must be reported on a Nonserious Adverse Event Form whether they are considered related or unrelated to the test article.

A serious adverse event is defined as any adverse experience occurring at any dose that results in any of the following outcomes: death; a life threatening adverse event, inpatient hospitalization, prolongation of existing hospitalization, or a persistent or significant disability/incapacity.

8.2 Recording and Reporting of Adverse Events

An Adverse Event Form must be completed for all serious adverse events within 24 hours of the investigator's knowledge of the event and to the Institutional Review Board according to their requirements.

8.4 Randomization Codes

Patients undergoing bilateral cataract surgery will be randomized to the DEXYCU group (standard postoperative cataract regimen + intraoperative DEXYCU) in one eye or the STANDARD group (standard postoperative cataract regimen). Randomization will be done after screening visit, prior to surgery on the first eye and will be done by coin flip. Patients who are randomly assigned to the DEXYCU group will receive a sequentially numbered drug kit.

8.5 Stopping Rules

Upon completion of the study, an "Exit Form" will be completed and signed by the Principal Investigator. Patients who withdraw early from the study will complete an "Early Exit Visit" form detailing the last visit and reasons for early withdrawal.

8.6 Medical Monitoring

The medical monitoring plan will be dictated by the protocol and recorded in the patient case report binder.

9 Data Handling and Record Keeping

9.1 Confidentiality

A confidential study binder will be maintained and secured in a locked cabinet by the principal investigator.

All identifiable, sensitive information will be protected on a password protected, encrypted device.

What information is being collected?

- Visit Date
- Date of Surgery
- Eye
- Concomitant Medication
- Ocular Symptoms (Graded 0-3)
  - Foreign Body Sensation
  - Tearing
  - Photophobia
- Visual Acuity
- Intraocular Pressure
- Tear Film Osmolarity
- Corneal Staining
- Patient satisfaction score

Will identifiers be removed? When?

Identifiers will be removed 3 months after study completion

How will the information be used?

The information will be used to determine if Dexycu treatment impacts dry eye parameters after cataract surgery

Will the information be sold to third parties?

No

Will the information be used for future research?

No

Who has access?

Only Principal Investigator

When will the information be destroyed?

12 months after study completion

9.2 Source Documents

A case report binder will be created for each subject in the study. Binder tabs will include:

A. Screening Visit
B. Day 1 Postoperative Visit
C. Day 7 Posteoperative Visit
D. Day 21 Postoperative Visit
E. Exit Form
F. Early Exit Visit
G. Nonserious Adverse Event Forms
H. Serious Adverse Event Forms

A copy of the Source Documents are included.

9.4 Records Retention

Study records will be retained in a locked cabinet for 2 years.

10 Study Monitoring, Auditing, and Inspecting

The study and patients will be monitored on a weekly basis by the Principal Investigator. Patient will be followed as part of the study and will receive further follow-up per a standard cataract surgery protocol 3 months and 1 year after the study, as well as on as clinically needed basis.

11 Ethical Considerations

There are no significant ethical considerations as the study is evaluating an FDA approved therapy.