

Title: The Role of Topical Antibiotic Prophylaxis in Oculofacial Plastic Surgery: A Randomized Controlled Pilot Study.

NCT number: NCT03199911

Document date: 4/1/2020

Statistical Analysis Plan (SAP)

The Role of Topical Antibiotic Prophylaxis in Oculofacial Plastic Surgery: A Randomized Controlled Pilot Study.

Principal Investigator

Robert Kersten, MD

Professor of Ophthalmology

Department of Ophthalmology

University of California, San Francisco

San Francisco, CA 94143

Protocol identification number

IRB 17-22309

ClinicalTrials.gov identifier

NCT03199911

Author

Davin Ashraf MD

Clinical Instructor and Fellow

Department of Ophthalmology

University of California, San Francisco

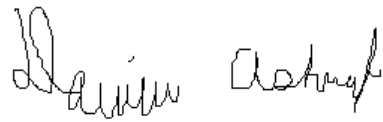
San Francisco, CA 94143

SIGNATURE PAGE

A handwritten signature in black ink, consisting of several overlapping loops and a long horizontal stroke extending to the right.

Principal Investigator

Robert Kersten, MD (4/1/2020)

A handwritten signature in black ink, appearing to read 'Davin Ashraf' in a cursive style.

Author

Davin Ashraf (4/1/2020)

Table of contents

| | |
|---|---|
| 1. Introduction..... | 5 |
| 2. Study design | 5 |
| 2.1 Sample size calculation..... | 5 |
| 3. Aims and objectives..... | 5 |
| 4. Outcomes | 6 |
| 4.1 Primary outcome | 6 |
| 4.2 Secondary outcomes | 6 |
| 4.3 Safety outcomes | 6 |
| 5. Populations and subgroups to be analyzed | 6 |
| 5.1 Populations..... | 6 |
| 5.2 Subgroups..... | 6 |
| 6. Analyses..... | 6 |
| 6.1 Primary outcome | 6 |
| 6.2 Secondary outcomes | 6 |
| 7. Missing data | 6 |
| 8. References..... | 7 |

1. Introduction

There is no consensus on the need for topical antibiotic prophylaxis after routine periocular surgery. This study is intended to act as a pilot to determine whether non-antibiotic ointment has a higher risk of infection than antibiotic ointment.

This statistical analysis plan (SAP) will give more detailed descriptions of the endpoints in the study and the corresponding analyses.

2. Study design

This is a randomized, unmasked clinical trial. Participants are recruited from the Oculofacial Plastic Surgery clinic at UCSF after deciding to proceed with periocular surgery. Inclusion and exclusion criteria are as detailed in the study protocol. The recruitment target is 400 individuals, approximately 200 per arm, based on the expected institutional surgical volume of eligible patients over a 2 year period.

The study is a parallel-group RCT with two arms spanning approximately 24 months. Participants were randomized to receive either topical antibiotic ointment or topical non-antibiotic ointment for a 7 day course after routine periocular surgery.

Outcomes were assessed at the first post-operative visit, approximately 1-2 weeks after surgery.

2.1 Sample size calculation

The primary outcome measure for the power calculation is the difference in surgical site infection frequency between the antibiotic and non-antibiotic arms.

| Sample Size per Arm | | Infection Rate (No Antibiotics) | | |
|-----------------------------------|------|---------------------------------|-------|-------|
| | | 0.7% | 2% | 4% |
| Infection Rate (With Antibiotics) | 0% | 1,388 | 483 | 239 |
| | 0.1% | 2,056 | 551 | 255 |
| | 0.2% | 3,200 | 633 | 273 |
| | 1% | 15,358 | 2,515 | 489 |
| | 2% | 1,386 | N/A | 1,239 |
| | | | | |

Based on these calculations, a non-inferiority study was deemed to be infeasible based on institutional surgical volume. Therefore, the decision was made to select a sample size approximating the surgical volume of eligible patients over a 2 year period in order to serve as a pilot study to detect whether a clinically relevant difference in infections occurred. For clean wounds, an infection rate greater than 5% is considered unacceptable(1-3); therefore, this sample size allowed 87% power at a 95% confidence level to detect a difference between an expected infection rate of 0.2% with antibiotics versus a maximum acceptable rate of 5% without antibiotics.

3. Aims and objectives

To study whether topical antibiotic prophylaxis significantly reduces the rate of infection after oculofacial plastic surgery.

4. Outcomes

This section will present the outcomes investigated to answer the study aims and objectives. The analyses are described in section 6 Analyses.

4.1 Primary outcome

Frequency of surgical site infection (superficial and deep incisional)

4.2 Secondary outcomes

Frequency of wound complications

Allergic contact dermatitis

Wound dehiscence

Frequency of surgical site infection (superficial and deep incisional) among subgroups (low- versus high-risk patients for infection)

4.3 Safety outcomes

Adverse events

Adverse events are reported at each clinic visit.

Concomitant medications

Usage of medications during study period will be recorded.

5. Populations and subgroups to be analyzed

5.1 Populations

Intention-to-treat (ITT)

All randomized study subjects. This will be seen as the primary population for the analysis.

5.2 Subgroups

Low- versus high-risk for infection patients (listed as secondary outcome)

6. Analyses

Continuous outcomes will be presented with descriptive statistics; normally distributed data by the mean and standard deviation (SD). Binary and categorical variables will be presented using counts and percentages. R version 4.0.0 will be used for all statistical analysis.

The subsections below will describe analyses in addition to the descriptive statistics.

6.1 Primary outcome

The primary analysis will compare intervention groups using Fisher's exact test due to the expected small sample size of the outcome. A risk ratio will be computed and 95% confidence intervals will be presented.

6.2 Secondary outcomes

The secondary analysis will compare intervention groups using Fisher's exact test due to the expected small sample size of the outcomes. A risk ratio will be computed and 95% confidence intervals will be presented.

7. Missing data

Missing data will not be imputed. Participants with missing data for baseline demographic and clinical characteristics will be reported as "Unknown." Participants missing the primary outcome will not be included in the primary analysis, and the reason for the missing outcome data will be included in the

patient flow diagram. Participants missing data for a secondary outcome will not be included in the analysis for that particular outcome.

8. References

1. Cruse PJ, Foord R. The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. *Surg Clin North Am* 1980;60:27–40.
2. Culver DH, Horan TC, Gaynes RP, et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index. National Nosocomial Infections Surveillance System. *Am J Med* 1991;91:152S-157S.
3. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;27:97–132; quiz 133–134; discussion 96.