Statistical Analysis Plan

Evaluation of the LipiFlow System with a New Activator (Model LFD-2100)

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STATISTICAL ANALYSIS PLAN

Evaluation of the LipiFlow System with a New Activator (Model LFD-2100)

PROTOCOL NUMBER: DRYE-105-ACTS

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SAP CHANGE HISTORY

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
1.0	N/A	N/A	Original	N/A

1 INTRODUCTION

This document summarizes the statistical methods to be implemented during the analysis of data for the evaluation of the clinical use of the LipiFlow system with Activator LFD-2100. This is a prospective, open-label clinical study. The study will be conducted at up to 4 sites with minimum 50 eyes and up to 100 eyes to be treated. Each subject will undergo 1-2 visits which include informed consent, screening for study participation, and receiving the LipiFlow treatment.

The primary endpoint is successful completion of LipiFlow treatment with Activator LFD-2100 in at least 95% cases. Additional endpoints include rating of each step in the LipiFlow treatment procedure with Activator LFD-2100, rate of complications and adverse events.

Table listings are included in Appendix I.

2 ANALYSIS POPULATIONS

2.1 ANALYSIS POPULATIONS

All subjects treated who have available data will be included in the analysis population. All the questionnaire responses and the treatment reports generated by LipiFlow system after completion of treatment will be collected and analyzed to confirm successful completion of the procedure. Questionnaire responses for each item and data from the treatment reports will be summarized for Activator LFD-2100. No imputations for missing values will be used.

2.2 DATA CONVENTIONS

Descriptive statistics will typically include sample size (N), mean, standard deviation (SD), median, minimum (Min.), and maximum (Max.) as appropriate for continuous variables. For categorical data, the frequency and proportion will be computed.

3 ACCOUNTABILITY/DEMOGRAPHICS

3.1 ACCOUNTABILITY

The number of enrolled subjects will be tabulated by site. Subjects signed the informed consent but failed the screening procedures will be listed.

3.2 DEMOGRAPHICS

Subject demographic data including age, sex, race and ethnicity will be presented. Age will be summarized with descriptive statistics with mean, standard deviation, median,

minimum and maximum. The frequency distributions of sex, race and ethnicity will be tabulated.

4 STUDY ENDPOINTS

4.1 PRIMARY ENDPOINTS

SUCCESSFUL COMPLETION OF LIPIFLOW TREATMENT WITH ACTIVATOR LFD-2100 IN 95% OR MORE CASES

The treatment reports automatically generated by LipiFlow Console after completion of each treatment will show if the treatment completion is successful. The response of 'Yes' to the question of 'Were the Activators LFD-2100 able to complete a successful treatment' indicates the successful completion. The expected proportion of successful completion of LipiFlow treatment will be greater than or equal to 95%. List of eyes with unsuccessful completion of LipiFlow treatment and the corresponding comment will be provided.

4.2 OTHER ENDPOINTS

4.2.1 QUESTIONNAIRE RESPONSES OF EACH STEP IN THE LIPIFLOW TREATMENT PROCEDURE WITH ACTIVATOR LFD-2100

For questions with a 'Yes' or 'No' responses, the frequency and proportion of each question with response 'Yes' will be reported. For questions with five levels of rating score responses, the frequency and proportion of each level of rating score responses will be tabulated. The mean and median of rating score of each question will also be reported. List of eyes with a rating score of 1 or 2 on a question and the corresponding comment will be provided.

4.2.2 OCULAR SURFACE STAINING

Corneal staining will be evaluated in five corneal regions on a scale of 0 (none), 1 (mild), 2 (moderate) and 3 (severe). The total corneal staining grade will be calculated as the sum of the grades for each of the five corneal regions on a scale from 0 to 15. A lower grade indicates less corneal surface desiccation. Conjunctival staining will be evaluated in six conjunctival regions on a scale of 0 (none), 1 (mild), 2 (moderate) and 3 (severe). The total conjunctival staining grade will be calculated as the sum of the grades for each of the six conjunctival regions on a scale from 0 to 18. A lower grade indicates less conjunctival surface desiccation. Mean ocular surface stain grade score will be reported at pre-treatment visit and treatment visit. Change in ocular surface stain grade score (treatment minus pre-treatment) will be summarized.

4.2.3 MEIBOMIAN GLANDS ASSESSMENT

Summary statistics of total meibomian glands secretion score will be reported at pre-treatment visit if data is available. The proportion of utilization of meibomian gland evaluator will be provided.

4.2.4 RATE OF COMPLICATIONS AND ADVERSE EVENTS

The frequency and proportion of eyes with complications and adverse events will be reported throughout the study.

5 SAMPLE SIZE CALCULATIONS

The study sample size is using a confidence interval approach to estimate precision around the true proportion of successful completion of LipiFlow treatment with Activator LFD-2100. Assuming the proportion of successful completion of LipiFlow treatment is 95%, with n=50 eyes, a two-sided 95% confidence interval will be (89%, 100%), i.e., a precision of 6.0%.

APPENDIX I: TABLE LISTING

Variable	Subjects/Eyes
ENROLLMENT/PRE-TREATMENT	
Accountability/Enrollment	
Subjects by investigational site (n)	**subjects**
Demographics	
Demographic – Age in years (N, Mean, SD, Median, Min, Max), sex, race and ethnicity (n and %)	**subjects**
PRIMARY STUDY ENDPOINT	
Successful completion of LipiFlow treatment – (n, %) List of eyes with unsuccessful cases will be provided	**eyes**
OTHER ENDPOINTS	
Questionnaire responses of each step of LipiFlow treatment (n, %) for Yes/No or rating responses and mean and median for each rating score List of eyes with rating score of 1 or 2	**eyes**
Ocular surface staining at pre-treatment and treatment and the difference (N, Mean, SD, Median, Min, Max)	**eyes**
Meibomian glands assessment Meibomian glands secretion score at pre-treatment (if available) –(N, Mean, SD, Median, Min, Max) Proportion of utilization of meibomian gland evaluator (n,%)	**eyes**
Medical findings from slit lamp exam (n, %)	**eyes**
Ocular symptoms (n, %)	**eyes**
Rate of complications and adverse events (n, %)	**eyes**