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# STATISTICAL ANALYSIS PLAN

## CLINICAL TRIAL NUMBER: 43CH1507

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APPENDIX A: Planned Tables and Figures

# 1 Study Information

## 1.1 Background

### 1.1.1 Study design

This is a randomized, evaluator-blinded, no-treatment controlled study in subjects with Midface Volume Deficit and/or Midface Contour Deficiency. The first 2 eligible subjects for each Treating Investigator will receive treatment as Group A. Before start of enrolment into Group B, the injection technique will be evaluated by the Sponsor. This evaluation will be performed after the first treatment of the subjects in Group A for each Treating Investigator. Subjects in group B will be randomized either to the Treatment group or the Control group in a 3:1 ratio.

Summaries of the results for Group A and B will be done separately in the study report.

Each subject assigned to Group A or to the Treatment group in Group B will receive an initial treatment on Day 1. A touch-up treatment may be performed 4 weeks after the initial treatment if optimal midface augmentation has not been obtained.

Subjects assigned to the Control group in Group B will not receive treatment at baseline but will be offered a treatment at Month 6, and an optional touch-up treatment 4 weeks later.

### 1.1.2 Number of subjects and randomization

Approximately 148 subjects will be randomized in a 3:1 ratio to treatment with Restylane Perlane Lidocaine (Perlane-Lido) or to no treatment. The randomization will be stratified by site.

## 1.2 Study Objectives

### 1.2.1 Primary Objective

The primary objective is to demonstrate superiority of Perlane-Lido relative to no-treatment in the treatment of Midface volume Deficit and/or Midface Contour Deficiency by comparing the percent responders, defined by at least 1 point improvement from baseline on the MMVS on both sides of the face, as measured by blinded evaluator at 6 months.

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### 1.2.3 Safety objectives and endpoints

The safety objectives and endpoints are:

- To evaluate the safety of Perlane-Lido during the whole study by collecting Adverse Events (AEs).

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## 1.3 Efficacy assessment

For all assessments, baseline will be defined as the observation that is closest to but prior to study treatment on Day 1. Likewise, change from baseline will be calculated as the value at a given time point minus the baseline value.

### 1.3.1 Medicis Midface Volume Scale (MMVS)

MMVS is a 4-grade scale assesses the fullness of the midface from Fairly Full (1) to Substantial Loss of Fullness (4) as described below.

The blinded evaluator will rate the subject's right and left midface for severity of volume deficiency using the MMVS at screening, baseline, CCI 6, CCI months after last treatment in Group A and Treatment group; and at screening, baseline, CCI 6 months after randomization, CCI in the Control group.

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**Table 1-1. The Medicis Midface Volume Scale.**

| MMVS | |
|---|---|
| 1 | Fairly full midface |
| 2 | Mild loss of fullness in midface area |
| 3 | Moderate loss of fullness with slight hollowing below malar prominence |
| 4 | Substantial loss of fullness in the midface area, clearly apparent hollowing below malar prominence |

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## 1.4 Efficacy endpoints

### 1.4.1 Primary efficacy endpoint

Responder rate based on the MMVS as assessed by the blinded evaluator at 6 months after last treatment for the Treatment group, and at 6 months after randomization for the Control group.

A responder is defined as a subject who achieves a score of at least 1 grade improvement from baseline to 6 months on both sides of the face.

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## 1.5 Safety assessments

The methods for collecting safety data are described in Section 8 of the Clinical Study Protocol

(CSP) and include assessments of CCI [redacted] Adverse Events (AE), Serious Adverse Events (SAE), and Device Deficiency.

A two-point scale ("Yes" or "No" response) will be used for the causality assessments. The Treating Investigator should be asked to indicate a response to each of the following questions in the eCRF:

- "Do you consider that there is a reasonable possibility that the event may have been caused by the study product?"
- "Do you consider that there is a reasonable possibility that the event may have been caused by the injection procedure?"

If any of these questions is answered with a 'Yes', the AE will be considered related. These assessments will also be reviewed by the Sponsor. In the case of a disagreement, the AE will be classified as "Related".

Time to onset of an AE will be derived as the start date minus Day 1. If the start date is missing, it will be assumed that the AE started on Day 1.

Duration of an AE will be derived as the stop date minus the start date + 1. If the start date is missing, it will be assumed that the AE started on Day 1. Missing stop date will not be imputed and therefore no duration will be calculated in these cases. Instead, the number of AEs that were ongoing at the end of the study will be given.



## 1.6 Safety endpoints

Safety endpoints include:

*(vii) Incidence of AEs*

All AEs collected at all visits following screening.

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## 2 Analysis Populations

The following populations will be defined:

- **Safety** — Includes all subjects in Group B who were treated with Perlane-Lido or randomized to no-treatment group. Subjects are analyzed based on the as treated principle.
- **Full Analysis Set (FAS)** — Includes all subjects in Group B who were treated with Perlane-Lido or randomized to no-treatment group. Subjects are analyzed according to the randomisation assignment.
- **Per Protocol (PP)** — Includes all subjects in FAS that comply to the protocol procedures with no deviations that can affect the evaluation of the primary variable.

The FAS population is the primary population for all efficacy analyses. All safety analyses will be based on the Safety population.

## 3 Statistical Methods

### 3.1 General methods

All summaries for Group A and B will be done separately. The same presentations will be made for both groups, but for Group A, only descriptive statistics will be used and the presentations will not be done by treatment group since all subjects in group A received treatment at baseline.

All statistical analyses, including summary tables and data listings, will be performed using the SAS® system (version 9).

All efficacy, safety and baseline characteristics variables will be presented using descriptive statistics and in subject data listings. Continuous data will be summarized by descriptive statistics n (number of observations), mean, standard deviation, median, minimum and maximum value, while categorical data will be presented by number and percentage. Graphs might be used as appropriate.

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Further details of efficacy analyses can be found in Section 3.3 and definition of endpoints in Section 1.4.

Any change made to the finalized statistical analysis plan (SAP) will be documented in the Clinical Study Report (CSR).

## 3.2 Study subjects

### 3.2.1 Subject disposition

The number of subjects in each study population (i.e. FAS, PP and Safety) will be summarized by site and in total.

The disposition of subjects (including reasons for screening failures and withdrawals) will be presented by treatment group and in total. This presentation will also be done by site.

The number of completed and withdrawn subjects will also be presented by visit.

### 3.2.2 Protocol deviations

All withdrawn subjects will be listed individually, including at least subject number, date and reason for withdrawal, and last visit performed. Subjects with CSP deviations disqualifying them from PP will be listed individually, including subject number and observed deviation.

For this study, the protocol deviations that will exclude subjects from PP are identified (but not limited to) in Table 3-1 below.



**Table 3-1. Protocol deviations.**

| | | Deviation |
|---|---|---|
| **GENERAL** | | |
| | | **Visit out-of-window** |
| | * | Follow-up at 6 months after last treatment performed earlier than 1 week before the scheduled visit or later than 2 weeks after the visit in Treatment Group |
| | * | Follow-up at 6 months after randomization performed earlier than 1 week before the scheduled visit or later than 2 weeks after the visit in Control Group |
| **EFFICACY** | | |
| | | **MMVS assessed by blinded evaluator** |
| | * | Not done for both sides of the face at 6 months after last treatment in Treatment Group, or at 6 months after randomization in Control Group |
| | * | Pre-treatment MMVS not available for both sides of the face |
| | * | More than 1 grade difference in baseline MMVS score between the two sides of the face |
| **OTHER** | | |
| | | **Inclusion/exclusion criteria** |
| | * | Any key inclusion criteria not met |
| | * | Any key exclusion criteria met |



Deviations from the SAP will be documented in the CSR.

### 3.2.3 Demographic characteristics

Subject demographic and baseline characteristics data will be summarized for the FAS population by treatment group and in total.

### 3.2.4 Medical history and concomitant medication/procedures

All summaries will be done by treatment group based on the FAS population. Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary. Medical History will be coded according to MedDRA.

The number and percentage of subjects reporting medical history, and the number of conditions will be summarized by system organ class (SOC), in total and for ongoing conditions. Previous facial procedures, fillers or implants as collected in the medical history, will be summarized by procedure and treatment group.

The number and percentage of subjects reporting concomitant medications will be summarized. In addition, the number and percentage of subjects reporting concomitant medication, and the number of drugs (total number and the number of drugs ongoing at study end), will be summarized by reason. The same summaries will be done for concomitant procedures/treatments. Also, for concomitant medication, the number and percentage of subjects and the number of drugs, will be summarized by ATC code. Concomitant medications that started due to an AE will be summarized separately.

### 3.2.5 Post-treatment examinations

BMI will be summarized for the FAS population, by visit and group, using descriptive statistics.
A summary of urine pregnancy test results by visit and group will also be provided.

## 3.3 Efficacy analysis

### 3.3.1 Datasets analyzed

All efficacy variables will be analyzed using the FAS population. The primary analysis will be repeated using the PP population. If it is deemed necessary, other analyses will be repeated using the PP population.

### 3.3.2 Handling of missing data

Number of missing values will be summarized and reported as appropriate. The baseline observation carried forward (BOCF) method will be used as the primary imputation method to handle missing data on MMVS up to the Month 6 visit in the FAS analysis set. This strategy is a conservative approach as it treats subjects with missing data as non-responders. Impact of missing data on the primary analysis for Month 6 endpoint will be evaluated by performing sensitivity

analysis based on the PP population. In addition, missing data for the primary analysis will also be handled using the multiple imputation (MI) method.

All other endpoints will be analyzed on available data, i.e. no imputations will be done.

If the baseline value is missing, the screening value will be used instead.

Use of MI

The imputation using MI will assume a Missing Completely at Random (MAR) mechanism. The MI procedure of the SAS® system will be used to generate five sets of data with missing values imputed from observed data. It is expected that the pattern of missing data will be monotonic, with slight deviations being corrected by the Markov Chain Monte Carlo (MCMC) method of the MI procedure. Linear regression will be employed to model the missing MMVS score, with the following covariates included in the imputation model: treatment and non-missing data from earlier time points (baseline CCI [redacted]). The imputed datasets will be analyzed using the methodology described for the primary analysis of responder rates at Month 6. The results from the analysis of the multiple imputed datasets will be presented as appropriate. The seed number to be used will be 431507 (the clinical trial number of this study, with the letters removed).

### 3.3.3 Primary analysis

The responder rate will be calculated for each group at Month 6 based on the blinded evaluator's assessment. CCI [redacted]

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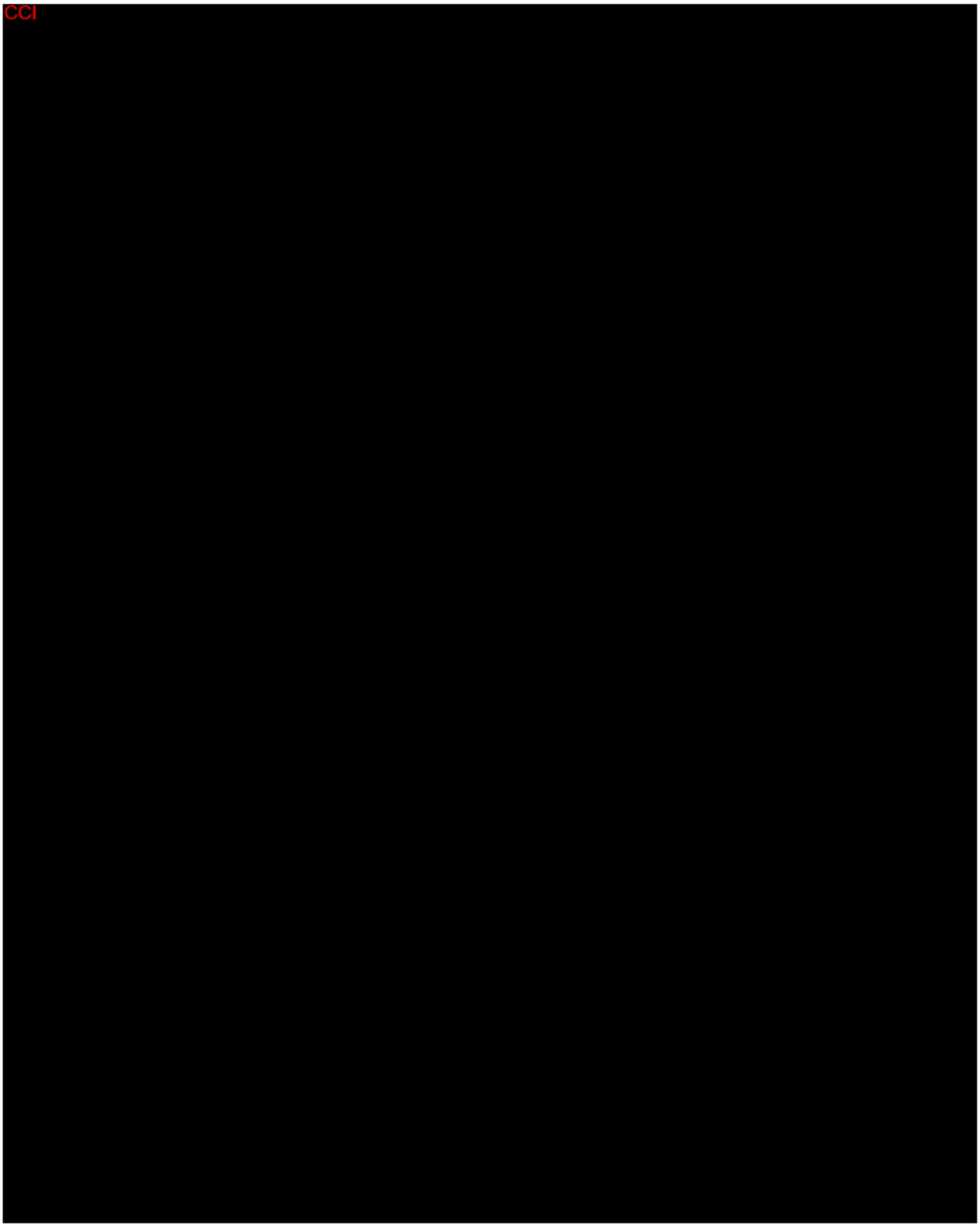
In addition, to evaluate the impact of missing data, the primary analysis will be re-run using the PP analysis set.

Site effects will be explored by using descriptive statistics of the treatment effects by site (estimates and confidence intervals of the response rates within site).




### 3.4 Safety analysis

All safety variables will be summarized descriptively based on the safety population.

### 3.4.1 Extent of exposure

Data on extent of exposure and treatment procedure will be summarized by group, for initial treatment and touch-up separately. Injection volume will also be summarized for initial treatment and touch-up totally.

### 3.4.2 Adverse events

All AEs will be coded according to MedDRA. All AE summaries defined below will be presented by treatment (no treatment at baseline vs. all treated subjects (at baseline and Month 6)).

The number of subjects with AEs related to study product or injection procedure as well as the number of events will be summarized by SOC and preferred term (PT). In addition, AEs related to study product or injection procedure will be summarized by SOC, PT and intensity. The number of days to onset and the duration of related AEs will be summarized by SOC and PT using mean, SD, min, max and median.

Serious AEs and device deficiencies will be listed, if applicable.

Non related AEs will be summarized by SOC, PT, and intensity.




## 3.5 Interim Analysis

Not applicable.

# 4 Determination of Sample Size

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## 5 Changes in the Analysis Planned in the Protocol

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Cohorts used for analysis of adverse events will be defined differently, as follows.

Text in CSP:

*"Since the no-treatment control group will receive treatment at the month 6 visit, only AEs occurring up until that time point will be included in this presentation, for both groups.*
*Furthermore, all AEs will also be summarised by SOC and PT using the Perlane-L group for the whole study period, and also using the no-treatment group for the study period following their treatment at Month 6."*

Revised text in SAP:

*"All AE summaries defined below will be presented by treatment (no treatment at baseline vs. all treated subjects)."*

## 6 Reference List

## Appendix A: Planned Tables and Figures

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**Table A 1. Subject disposition (all subjects)**

| Number of subjects | | Perlane-Lido | Control | Total |
|---|---|---|---|---|
| Screened | | - | - | xx |
| Screening failures | | | | xx (%) |
| Randomized | | xx | xx | xx |
| Completed primary endpoint | | xx (%) | xx (%) | xx (%) |
| Completed | | xx (%) | xx (%) | xx (%) |
| Withdrawn | | xx (%) | xx (%) | xx (%) |
| Reason for withdrawal | Withdrawn consent | xx (%) | xx (%) | xx (%) |
| | Lost to follow-up | xx (%) | xx (%) | xx (%) |
| | Medical reason | xx (%) | xx (%) | xx (%) |
| | Other | xx (%) | xx (%) | xx (%) |

% screening failures is based on total number of screened subjects.
% I/E criteria not met and withdrawn consent is based on the number of screening failures.
In all other cases: % is based on the number of randomized subjects.

**Table A 2. Analysis populations (all randomized subjects)**

| Site | Subject Number | Safety | | FAS | | PP | |
|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % |
| Site 1 | 101-1xx | xx | xx.x | xx | xx.x | xx | xx.x |
| Site 2 | 201-2xx | xx | xx.x | xx | xx.x | xx | xx.x |
| Site x | x01-xxx | xx | xx.x | xx | xx.x | xx | xx.x |
| Total (N) | - | xx | 100.0 | xx | 100.0 | xx | 100.0 |

% = n/N*100

**Table A 3. Subject accountability (all subjects in Perlane-Lido group)**

| Number of subjects | Observed | Missed | Withdrawals | Continuing on study |
|---|---|---|---|---|
| Baseline/initial treatment | xx | xx | xx | xx |
| 4W follow-up/optional touch-up | xx | xx | xx | xx |
| 4W follow-up | xx | xx | xx | xx |
| 3M after last treatment | xx | xx | xx | xx |
| 6M after last treatment | xx | xx | xx | xx |
| 9M after last treatment | xx | xx | xx | xx |
| 12M after last treatment | xx | xx | xx | xx |

**Table A 4. Subject accountability (all subjects in Control group)**

| Number of subjects | Observed | Missed | Withdrawals | Continuing on study |
|---|---|---|---|---|
| Baseline | xx | xx | xx | xx |
| 4W follow-up | xx | xx | xx | xx |
| 3M after baseline | | | | |
| 6M after baseline/treatment | | | | |
| 4W follow-up/optional touch-up | | | | |
| 4W follow-up | | | | |
| 3M after last treatment | | | | |
| 6M after last treatment | | | | |

**Table A 5. Withdrawn subjects**

| Site | Subject number | Group | Date of treatment | | Last visit performed | Date of withdrawal | Reason for withdrawal |
|---|---|---|---|---|---|---|---|
| | | | Treatment | Optional touch-up | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

Any extra comments here …

**Table A 6. Protocol deviations affecting PP population**

| Protocol deviation (category) | Number of subjects/Subject number | Number of deviations |
|---|---|---|
| | | |
| | | |
| | | |

(if only a few number of subjects, list subject numbers in second column)

**Table A 7. Protocol deviation not affecting PP population**

| Protocol deviation category | Number of subjects | Number of deviations |
|---|---|---|
| | | |
| | | |
| | | |

**Table A 8. Demographic and baseline characteristics (FAS)**

| Variable | Parameter | Perlane-Lido N=XX | Control N=XX | Total N=XX |
|---|---|---|---|---|
| Age (years) | N | xx | | |
| | Mean | xx.x | | |
| | SD | xx.x | | |
| | Median | xx.x | | |
| | Minimum | xx.x | | |
| | Maximum | xx.x | | |
| Gender n (%) | Female | xx (xx.x) | | |
| | Male | xx (xx.x) | | |
| Baseline BMI | N | xx | | |
| | Mean | xx.x | | |
| | SD | xx.x | | |
| | Median | xx.x | | |
| | Minimum | xx.x | | |
| | Maximum | xx.x | | |

% = n/N*100

Additional variables in this table:

- Ethnicity
- Baseline MMVS Blinded Evaluator, right and left side respectively
- CCI [redacted]

**Table A 9. Subjects reporting medical history/concurrent disease and number of conditions by MedDRA System Organ Class (FAS)**

| | Perlane-Lido N=xx | | | | | | Control N=xx | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Primary SOC | All | | | Ongoing at study start | | | All | | | Ongoing at study start | | |
| | Events | Subjects | | Events | Subjects | | Events | Subjects | | Events | Subjects | |
| | *n* | *n* | % | *n* | *n* | % | *n* | *n* | % | *n* | *n* | % |
| | Xx | Xx | xx.x | Xx | Xx | xx.x | Xx | Xx | xx.x | Xx | xx | xx.x |
| | Xx | Xx | xx.x | Xx | Xx | xx.x | Xx | Xx | xx.x | Xx | Xx | xx.x |
| Total1) | xx | xx | xx.x | Xx | xx | xx.x | xx | xx | xx.x | xx | Xx | xx.x |

% = *n* / N * 100

1) A single subject may have reported medical history (relevant or major illness) by more than one primary SOC category.

**Table A 10. Prior use of facial dermatological procedures (FAS)**

| Procedure | Perlane-Lido N=xx | | | Control N=xx | | |
|---|---|---|---|---|---|---|
| | Events | Subjects | | Events | Subjects | |
| | n | n | % | n | n | % |
| Xxx | xx | xx | xx.x | xx | xx | xx.x |
| Xxx | xx | xx | xx.x | xx | xx | xx.x |
| Xx | xx | xx | xx.x | xx | xx | xx.x |
| | xx | xx | xx.x | xx | xx | xx.x |
| | xx | xx | xx.x | xx | xx | xx.x |
| | xx | xx | xx.x | xx | xx | xx.x |
| Total | xx | xx | xx.x | xx | xx | xx.x |

% = n/N*100

**Table A 11. Subjects reporting concomitant medication (FAS)**

| Concomitant medication | Any concomitant medication? | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Pelane-Lido N=xx | | | | Control N=xx | | | |
| | No | | Yes | | No | | Yes | |
| | n | % | n | % | n | % | n | % |
| Ongoing at study start | | | | | | | | |
| Initiated during study | | | | | | | | |
| Total | | | | | | | | |

% = n/N*100

**Table A 12. Subjects reporting concomitant medication and number of medications by reason (FAS)**

| | Pelane-Lido N=xx | | Control N=xx | |
|---|---|---|---|---|
| Reason for concomitant medication | No. of subjects | No. of drugs | No. of subjects | No. of drugs |
| Medical History | xx (xx.x) | xx | xx (xx.x) | xx |
| Adverse Event | xx (xx.x) | xx | xx (xx.x) | xx |
| Other | xx (xx.x) | xx | xx (xx.x) | xx |

% = n/N*100

**Table A 13. Subjects reporting concomitant medication and number of medications by ATC code (FAS)**

| | | Perlane-Lido N=xx | | | Control N=xx | | |
|---|---|---|---|---|---|---|---|
| ATC code | ATC text | Subjects | | Medications | Subjects | | Medications |
| | | n | % | n | n | % | n |
| | | Xx | xx.x | Xx | xx | xx.x | Xx |
| | | Xx | xx.x | Xx | Xx | xx.x | Xx |
| | | xx | xx.x | xx | Xx | xx.x | Xx |

% = n/N*100

**Table A 14. Concomitant medication taken due to an AE by ATC code (FAS)**

| Concomitant medication | | | Adverse Event | |
|---|---|---|---|---|
| ATC text (ATC code) | No of subjects | No. of drugs | MedDRA Preferred term | Related |
| ATC 1 | Xx | Xx | PT 1 | Yes/No |
| | | | PT 2 | Yes/No |
| | | | . | Yes/No |
| | | | . | Yes/No |
| | | | . | Yes/No |
| | | | . | Yes/No |
| ATC 2 | Xx | Xx | PT | Yes/No |
| ATC 3 | Xx | Xx | PT | Yes/No |
| . | Xx | Xx | . | Yes/No |
| Total | xx | xx | - | - |

**Table A 15. Subjects reporting concomitant procedure/treatment by reason (FAS)**

| | Pelane-Lido N=xx | | Control N=xx | |
|---|---|---|---|---|
| Reason for concomitant procedure/treatment | No. of subjects | No. of Procedures/ treatments | No. of subjects | No. of Procedures/ treatments |
| Medical History | xx (xx.x) | xx | xx (xx.x) | xx |
| Adverse Event | xx (xx.x) | xx | xx (xx.x) | xx |
| Other | xx (xx.x) | xx | xx (xx.x) | xx |
| Total | xx (xx.x) | xx | xx (xx.x) | xx |

% = n/N*100

**Table A 16. MMVS responder rate by treatment and side of the face at Month 6, Blinded Evaluator (FAS)**

| Assessment/Time Point | Treatment Group | # of Subjects in FAS | # of Responders | Proportion of Responders | 95% Confidence Interval | P-Value |
|---|---|---|---|---|---|---|
| Right and Left Midface Combined at Month 6 | Perlane-Lido | Xx | Xx | x.xx | x.xx, x.xx | |
| | Control | Xx | Xx | x.xx | x.xx, x.xx | |
| | Difference | - | - | x.xx | x.xx, x.xx | x.xx |
| Right Midface at Month 6 | Perlane-Lido | Xx | Xx | x.xx | x.xx, x.xx | |
| | Control | Xx | Xx | x.xx | x.xx, x.xx | |
| | Difference | - | - | x.xx | x.xx, x.xx | x.xx |
| Left Midface at Month 6 | Perlane-Lido | Xx | Xx | x.xx | x.xx, x.xx | |
| | Control | Xx | Xx | x.xx | x.xx, x.xx | |
| | Difference | - | - | x.xx | x.xx, x.xx | x.xx |

Note: Subjects with a missing MMVS have their values imputed using BOCF up to Month 6.
Note: Responder is defined as a subject with an improvement of at least one grade on the MMVS from baseline.
Note: Responder rate is calculated as the number of Responders at the visit of interest divided by the number of subjects in the FAS population for the specific treatment group.
Note: P-values for the difference in proportions are based on the Fisher's Exact test.
Note: 95% Confidence Intervals are two-sided confidence intervals calculated using the exact interval.

**Table A 17. MMVS responder rate by treatment and side of the face at Month 6, Blinded Evaluator (PP)**

As Table A 16 (only Left and Right Side Combined)
Note: No imputation is used for PP analysis. Only subjects with complete data are included.
Note: Responder is defined as a subject with an improvement of at least one grade on the MMVS from baseline.
Note: Responder rate is calculated as the number of Responders at the visit of interest divided by the number of subjects in the PP population for the specific treatment group.

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**Table A 18. Sensitivity analysis for the MMVS responder rate by treatment and side of the face at Month 6, Blinded Evaluator (FAS )**

As Table A 16 (only Left and Right Side Combined)
Note: Missing MMVS values are handled using multiple imputation methods.
Note: Responder is defined as a subject with an improvement of at least one grade on the MMVS from baseline.
Note: Responder rate is calculated as the number of Responders at the visit of interest divided by the number of subjects in the FAS population for the specific treatment group.

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**Table A 19. MMVS responder rate corrected for baseline MMVS by treatment and side of the face at Month 6, Blinded Evaluator (FAS)**

As Table A 16 (only Left and Right Side Combined)
Note: Subjects with a missing MMVS have their values imputed using BOCF up to Month 6.
Note: Responder is defined as a subject with an improvement of at least one grade on the MMVS from baseline.
Note: Responder rate is calculated as the number of Responders at the visit of interest divided by the number of subjects in the FAS population for the specific treatment group.

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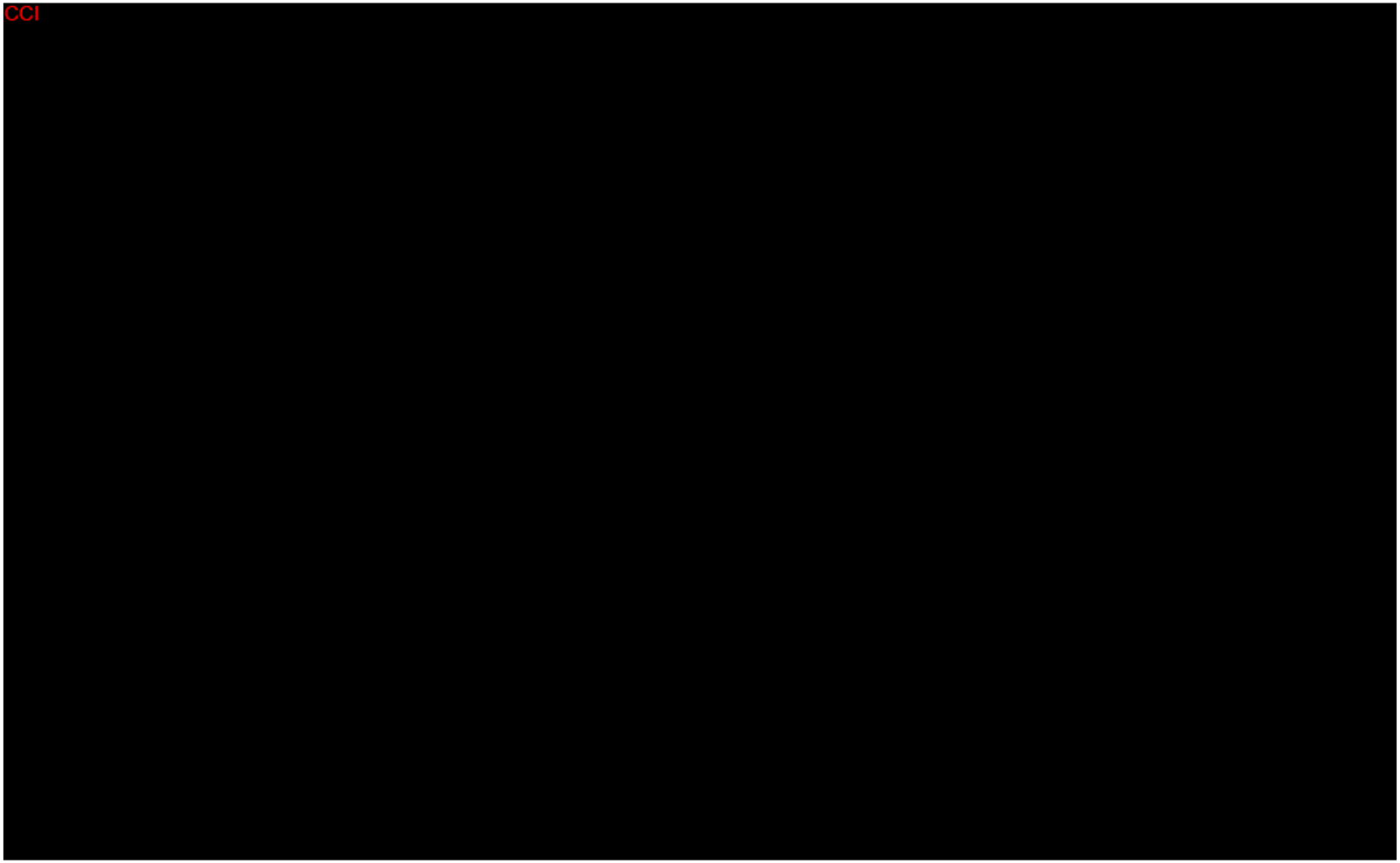
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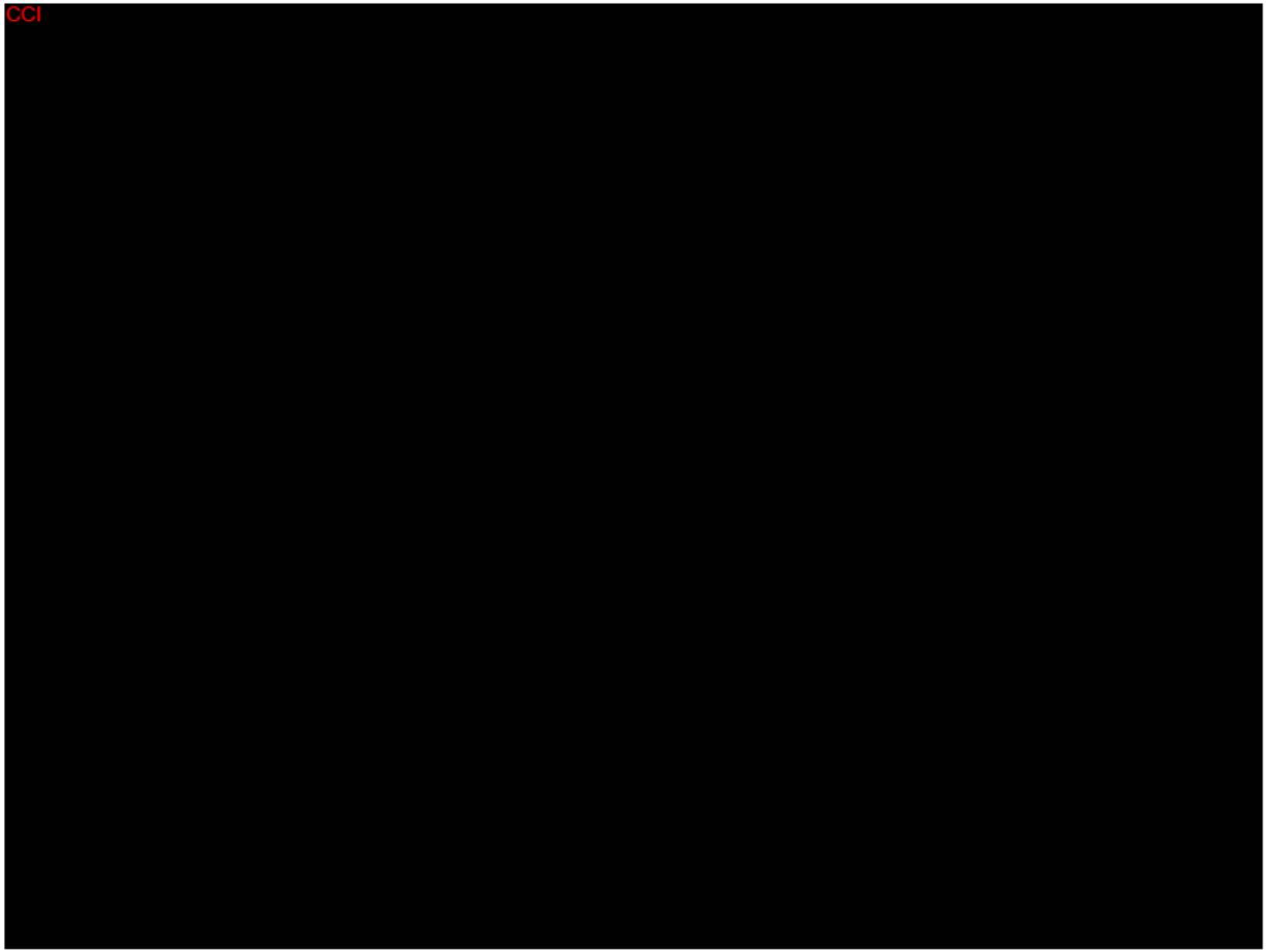

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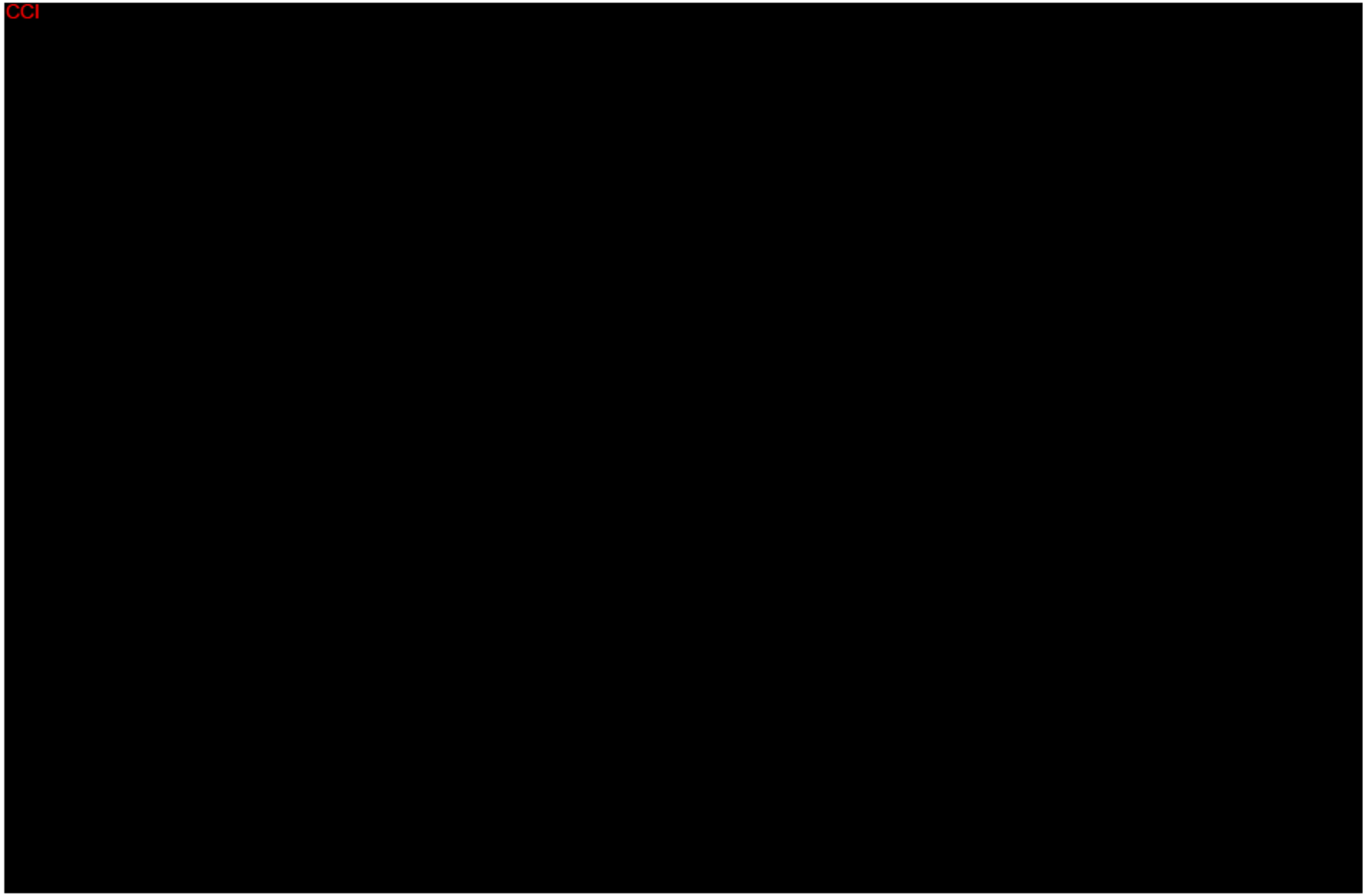

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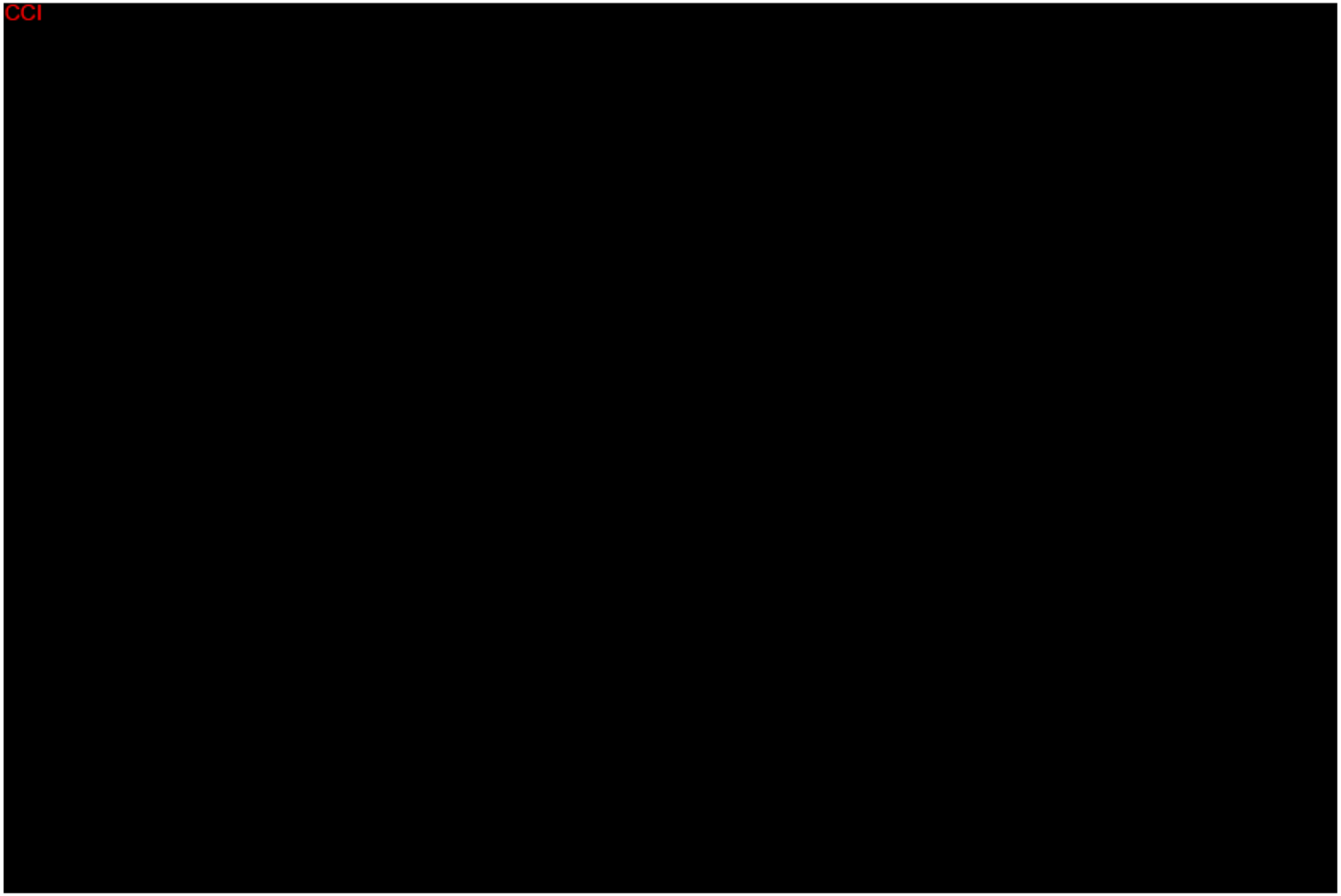

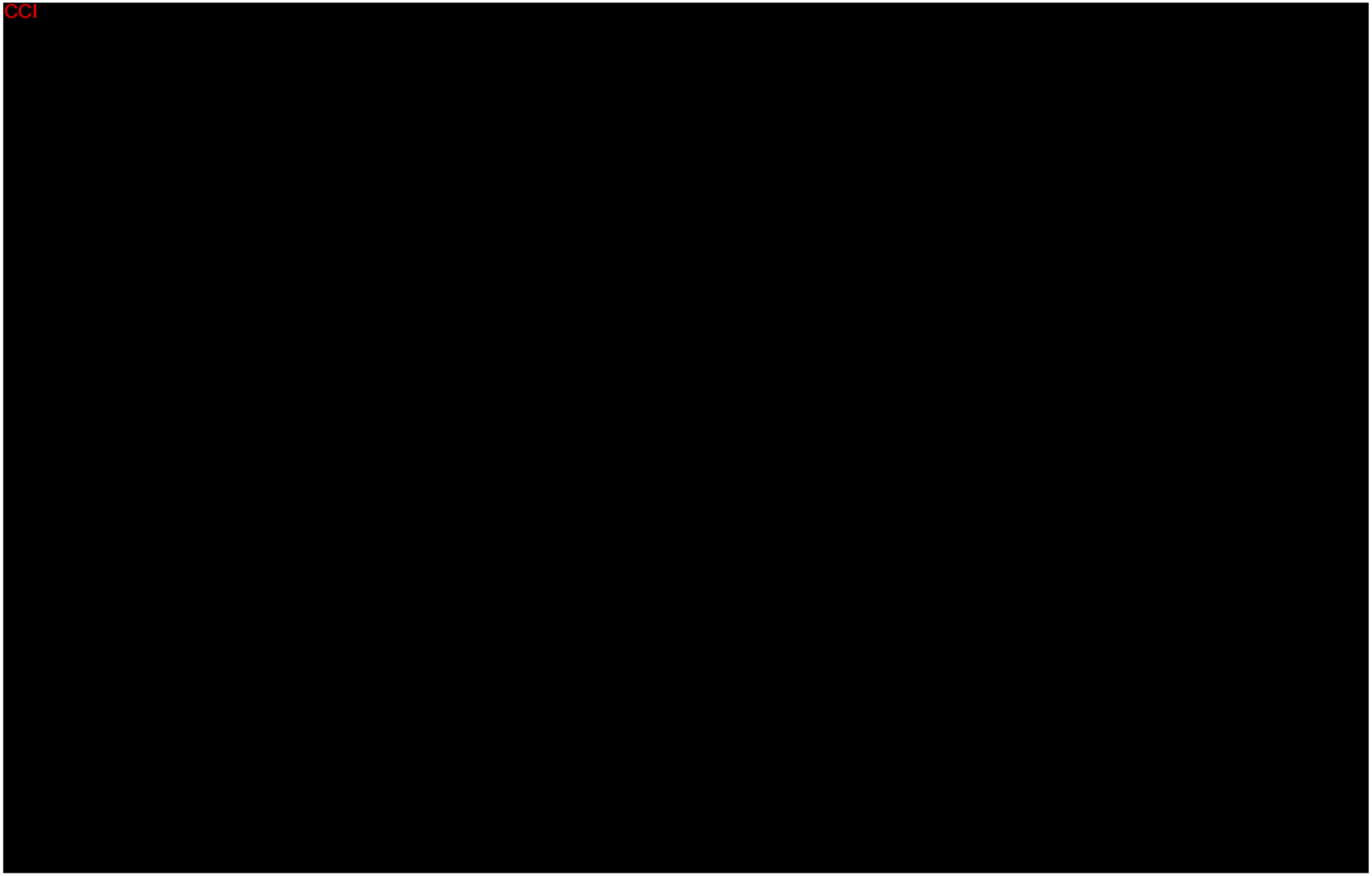
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**Table A 32. Exposure to study treatment (Safety)**

| Assessment (Right and Left Midface Combined) | | Perlane-Lido N=xx | Control (Optional Treatment) N=xx |
|---|---|---|---|
| Volume of injection (mL) for treatment | N | Xx | Xx |
| | Mean (SD) | x.xxx (x.xxx) | x.xxx (x.xxx) |
| | Median | x.xxx | x.xxx |
| | Min, Max | x.xx, x.xx | x.xx, x.xx |
| Volume of injection (mL) for touch-up | N | Xx | Xx |
| | Mean (SD) | x.xxx (x.xxx) | x.xxx (x.xxx) |
| | Median | x.xxx | x.xxx |
| | Min, Max | x.xx, x.xx | x.xx, x.xx |
| Total volume of injection (mL) for treatment+touch-up | N | Xx | Xx |
| | Mean (SD) | x.xxx (x.xxx) | x.xxx (x.xxx) |
| | Median | x.xxx | x.xxx |
| | Min, Max | x.xx, x.xx | x.xx, x.xx |
| Depth of injection for treatment | Subcutaneous | Xx (xx.x%) | Xx (xx.x%) |
| | Supraperiosteal | Xx (xx.x%) | Xx (xx.x%) |
| | Other | Xx (xx.x%) | Xx (xx.x%) |
| Depth of injection for touch-up | Subcutaneous | Xx (xx.x%) | Xx (xx.x%) |
| | Supraperiosteal | Xx (xx.x%) | Xx (xx.x%) |
| | Other | Xx (xx.x%) | Xx (xx.x%) |
| Method of injection for treatment | . | . | . |
| | . | . | . |
| | . | . | . |
| Method of injection for touch-up | . | . | . |
| | . | . | . |

% = 100*n/N

**Table A 33. Treatment procedure (Safety)**

| Time Point | Assessment | Category | Perlane-Lido N=xx | Control (Optional Treatment) N=xx |
|---|---|---|---|---|
| Treatment | Local anaesthesia used? | Yes | Xx (xx.x%) | Xx (xx.x%) |
| | | No | Xx (xx.x%) | Xx (xx.x%) |
| | Whereof topical cream | | Xx (xx.x%) | Xx (xx.x%) |
| | Whereof local infiltration | | Xx (xx.x%) | Xx (xx.x%) |
| Touch-up | Local anaesthesia used? | Yes | Xx (xx.x%) | Xx (xx.x%) |
| | | No | Xx (xx.x%) | Xx (xx.x%) |
| | Whereof topical cream | | Xx (xx.x%) | Xx (xx.x%) |
| | Whereof local infiltration | | Xx (xx.x%) | Xx (xx.x%) |
| Treatment | Post-treatment care | None | Xx (xx.x%) | Xx (xx.x%) |
| | | Massage | Xx (xx.x%) | Xx (xx.x%) |
| | | Ice pack | Xx (xx.x%) | Xx (xx.x%) |
| | | Other | Xx (xx.x%) | Xx (xx.x%) |
| Touch-up | Post-treatment care | None | Xx (xx.x%) | Xx (xx.x%) |
| | | Massage | Xx (xx.x%) | Xx (xx.x%) |
| | | Ice pack | Xx (xx.x%) | Xx (xx.x%) |
| | | Other | Xx (xx.x%) | Xx (xx.x%) |

% = 100*n/N

- Any device deficiencies will be listed in text or in a separate table, as appropriate.

**Table A 34. Brief summary of all AEs (Safety)**

| | No treatment at baseline N=xx | | | Treatment with Perlane-Lido N=xx | | |
|---|---|---|---|---|---|---|
| | Subjects | | Event | Subjects | | Event |
| | n | % | n | n | % | n |
| Any AEs reported, total | xx | xx.x | xx | xx | xx.x | xx |
| Any TEAEs reported, total | xx | xx.x | xx | xx | xx.x | xx |
| Of which were serious | xx | xx.x | xx | xx | xx.x | xx |
| TEAEs related to product and/or injection procedure | xx | xx.x | xx | xx | xx.x | xx |
| Of which were serious | xx | xx.x | xx | xx | xx.x | xx |
| TEAEs unrelated to product and/or injection procedure | xx | xx.x | xx | xx | xx.x | xx |
| of which were serious | xx | xx.x | xx | xx | xx.x | xx |
| Subjects with no AE reported | xx | xx.x | - | xx | xx.x | - |

Note: Treatment with Perlane-Lido columns include data from subjects in the Perlane-Lido group after their initial treatment at baseline, as well as data from subjects in the Control group after their initial treatment at Month 6.
% = 100*n/N

**Table A 35. Related TEAEs by MedDRA System Organ Class, Preferred Term, and intensity (Safety)**

| | | No treatment at baseline N=xx | | Treatment with Perlane-Lido N=xx | |
|---|---|---|---|---|---|
| Primary System Organ Class Preferred Term | Intensity | Events | Subjects | Events | Subjects |
| Any related AE | Total | Xx | Xx (xx.x) | Xx | Xx (xx.x) |
| | Mild | Xx | Xx (xx.x) | Xx | Xx (xx.x) |
| | Moderate | Xx | Xx (xx.x) | Xx | Xx (xx.x) |
| | Severe | xx | Xx (xx.x) | xx | Xx (xx.x) |
| SOC1 | Total | Xx | Xx (xx.x) | Xx | Xx (xx.x) |
| | Mild | Xx | Xx (xx.x) | Xx | Xx (xx.x) |
| | Moderate | | | | |
| | Severe | | | | |
| PT11 | Total | | | | |
| | Mild | | | | |
| | Moderate | | | | |
| | Severe | | | | |
| PT12 | Total | | | | |
| | Mild | | | | |
| | Moderate | | | | |
| | Severe | | | | |
| SOC2 | Total | | | | |
| | Mild | | | | |
| | Moderate | | | | |
| | Severe | | | | |
| PT21 | Total | | | | |

Note: Treatment with Perlane-Lido columns include data from subjects in the Perlane-Lido group after their initial treatment at baseline, as well as data from subjects in the Control group after their initial treatment at Month 6.
% = 100*n/N

**Table A 36. Duration (days) of related TEAEs by MedDRA System Organ Class and Preferred Term (Safety)**

| | No treatment at baseline N=xx | | | | | | | Treatment with Perlane-Lido N=xx | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Ongoing | n | Mean | SD | Min | Median | Max | Ongoing | n | Mean | SD | Min | Median | Max |
| General disorders and administration site conditions | | | | | | | | | | | | | | |
| Injection site xxx | | | | | | | | | | | | | | |
| Injection site xxx | | | | | | | | | | | | | | |
| ALL | | | | | | | | | | | | | | |

Note: Treatment with Perlane-Lido columns include data from subjects in the Perlane-Lido group after their initial treatment at baseline, as well as data from subjects in the Control group after their initial treatment at Month 6.
% = 100*n/N

**Table A 37. Time to onset (days) of related TEAEs, by MedDRA System Organ Class and Preferred Term (Safety)**

| | No treatment at baseline N=xx | | | | | | Treatment with Perlane-Lido N=xx | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Mean | SD | Min | Median | Max | n | Mean | SD | Min | Median | Max |
| General disorders and administration site conditions | | | | | | | | | | | | |
| Injection site xxx | | | | | | | | | | | | |
| Injection site xxx | | | | | | | | | | | | |
| ALL | | | | | | | | | | | | |

Note: Treatment with Perlane-Lido columns include data from subjects in the Perlane-Lido group after their initial treatment at baseline, as well as data from subjects in the Control group after their initial treatment at Month 6.
% = 100*n/N

**Table A 38. Action taken due to related TEAEs by MedDRA System Organ Class and Preferred Term (Safety)**

| System Organ Class<br>*Preferred Term* | Action Taken | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | No treatment at baseline N=xx | | | | Treatment with Perlane-Lido N=xx | | | |
| | None | Medication treatment | Non-pharmacological treatment or other procedures/tests | Subject withdrawn | None | Medication treatment | Non-pharmacological treatment or other procedures/tests | Subject withdrawn |
| General disorders and administration site conditions | | | | | | | | |
| Injection site xxx | | | | | | | | |
| Injection site xxx | | | | | | | | |
| SOC 2 | | | | | | | | |
| PT 1 | | | | | | | | |
| PT 2 | | | | | | | | |
| ... | | | | | | | | |
| **All** | | | | | | | | |

**Table A 39. Unrelated TEAEs by MedDRA System Organ Class, Preferred Term and intensity (Safety)**

As Table A 35

CCI

CCI


**Figure A 11. Proportion of subjects affected by a specific event (to any intensity level) after touch-up (Safety)**

As Figure A 10

| GALDERMA | Title<br>Statistical Analysis Plan 43CH1507 | Doc id<br>MA-32268 |
|---|---|---|



# SIGNATURES PAGE

| Date | Signed by |
|---|---|
| 2017-04-20 15:12 | PPD |
| **Justification** | Approved by Owner |

| | |
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| 2017-04-21 06:29 | PPD |
| **Justification** | Approved by Technical Expert |

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| 2017-04-21 07:58 | PPD |
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| 2017-04-21 08:38 | PPD |
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| 2017-04-21 09:20 | PPD |
| **Justification** | Approved by Technical Expert |