

**Merz North America**  
**Protocol Number ULT-302 / M960001052**

*Statistical Analysis Plan*

NCT03351335, redacted  
version v1.0, 25Jul2019

**IMPROVEMENT IN OVERALL LIFTING AND TIGHTENING OF  
SUBMENTAL (UNDER THE CHIN) AND NECK TISSUE AS DETERMINED  
BY A MASKED, QUALITATIVE ASSESSMENT OF PHOTOGRAPHS  
TAKEN BY VECTRA M3 SYSTEM**

Final Version 1.0  
23 August 2018

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## **1. INTRODUCTION**

This Statistical Analysis Plan (SAP) is based on the study Protocol Amendment 1 Final v4.0 dated January 26, 2018.

This document provides additional details concerning the statistical analyses outlined in the protocol and reflects any changes to the protocol from any amendments. This plan will not repeat all the definitions given in the protocol but will provide further details of the summaries and analyses planned therein.

The analysis described in this document is only a part of the efficacy analysis outlined in the study protocol to assess the improvement in overall lifting and tightening of skin as determined by a masked, qualitative assessment of photographs at 90 days post-treatment compared to baseline. The analyses for all the other endpoints will be included in a separate statistical analysis plan.

## **2. OBJECTIVE**

The objective is to assess improvement in overall lifting and tightening of skin as determined by a masked, qualitative assessment of photographs at 90 days post-treatment compared to baseline using photographs taken with Mirror Photofile software and a Vectra 3D digital imaging system in each of the treatment groups in Chinese subjects.

## **3. STUDY DESIGN**

This study is an open-label, non-randomized clinical study to be conducted at up to seven clinical sites. Approximately 60 subjects (20 subjects per treatment group) who meet the eligibility criteria will be enrolled and treated with the Ulthera® System. Enrollment eligibility will be determined by the physician and trained assessors' review and approval of screening images, and by the physician's review of inclusion and exclusion criteria.

Eligible subjects enrolled in the study will be treated using the Ulthera® System by the study investigator and/or trained clinician. Standardized images will be taken at screening, baseline (prior to treatment) and following treatment (30 to 60 minutes post-treatment) and at the 90-day post treatment visit using Mirror Photofile software and a Vectra 3D digital imaging system.

Qualitative masked assessment will be conducted following the procedure outlined below:

Ulthera will provide each blinded assessor with identical sets of photos to be assessed: pre-treatment and Day 90 post-treatment photos. The pre/post treatment photos should be consistent in lighting, subject positioning and focus. Each photo's visit interval, i.e., pre and post treatment, will not be marked and randomly assigned to the left and right photo. Each blinded assessor will compare the left and right photo for improvement in the face and rate independently with no inputs from other assessors.

If the assessor sees a change, the assessor marks “Improvement” and chooses which photo shows the improvement (i.e., Left photo or Right photo). If the assessor sees no change, the assessor marks “No change” and does not choose which photo shows improvement.

#### **4. TREATMENT ASSIGNMENT**

Subjects are not randomized in this study. All subjects will receive an Ultherapy™ treatment at dual depth using the 4-4.5mm and 7-3.0mm transducers. Treatments will be provided to the lower face, submental (under the chin) and neck area. Enrolled subjects will be assigned to one of 3 treatment groups:

Group EL2: Subjects will receive an Ultherapy™ treatment at energy level 2 (EL2).

Group EL3: Subjects will receive an Ultherapy™ treatment at energy level 3 (EL3).

Group EL4: Subjects will receive an Ultherapy™ treatment at energy level 4 (EL4).

#### **5. HARDWARE AND SOFTWARE**

Statistical analysis will be performed following [REDACTED] standard operating procedures and on the [REDACTED] computer network. All statistical analysis will be performed using SAS Version 9.3 or higher with program code prepared specifically for the project by qualified [REDACTED] statisticians and SAS programmers.

#### **6. ANALYSIS POPULATION**

The analysis specified in this document will be based on all subjects enrolled in the study and have both baseline and Day 90 photos available.

#### **7. HANDLING OF MISSING DATA**

No imputation will be performed for missing data.

#### **8. STATISTICAL EVALUATION**

The proportion of responders will be summarized using frequency counts and percentages by treatment groups and overall.

In the qualitative assessment, if the assessor marks “Improvement” and the marked photo is not the Post treatment photo, this will be considered as non-response as well as if the assessor rated “No Change”. If the assessor marks “Improvement” and correctly chooses the Post treatment photo, this will be considered as a response. A responder subject is defined as at least 2 out of 3 assessors

select the correct response (i.e., Day 90 photo is deemed as to show improvement) based on the subject's pre/post-treatment photos.

The above endpoint will be summarized for left and right face region separately and combined. A response on both left and right face region will be considered as a response on the whole face region (combing left and right). In addition, a by-subject by-treatment listing will be provided with all results displayed.

## **9. CHANGES FROM THE PROTOCOL AND PLANNED ANALYSES**

No changes from protocol.

## 10. OUTLINE OF PROPOSED TABLES AND LISTINGS

Table No.	Table Title
1.1	Proportion of responders by treatment group by face region
1.2	Proportion of responders by treatment group

Listing No.	Listing Title
1	Qualitative assessment results

Table 1.1: Proportion of Responders by Treatment and Face Region

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	<b>EL2</b> (N=XXX)	<b>EL3</b> (N=XXX)	<b>EL4</b> (N=XXX)	<b>Overall</b> (N=XXX)
<b>Proportion of Responders, n (%)</b>				
Left Face/Neck	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Right Face/Neck	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

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Note: N = number of subjects with both baseline and Day 90 photos available.

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Table 1.2: Proportion of Responders by Treatment

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	<b>EL2</b> (N=XXX)	<b>EL3</b> (N=XXX)	<b>EL4</b> (N=XXX)	<b>Overall</b> (N=XXX)
<b>Proportion of Responders, n (%)</b>				
Whole Face/Neck	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

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Note: N = number of subjects with both baseline and Day 90 photos available.

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Data Listing 1: Qualitative Assessment Results  
 Treatment: [EL2] [EL3] [EL4]

Site/Subject	Subject Initials	Face/Neck Region	Assessor 1		Assessor 2		Assessor 3		Responder?
			Response	Selected Visit	Response	Selected Visit	Response	Selected Visit	
093/003	XXX	Left	No Change	-	Left	Day 90	Left	Day 90	Y
		Right	Left	Baseline	Left	Baseline	Right	Day 90	N
XXX/XXX	XXX	XXX	XXX	X	XX	X	XX	XX	X

Note: The response column shows which photo was selected by assessors to show improvement. Selected visit is the visit of the selected photo.

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