STATISTICAL ANALYSIS PLAN

Protocol Title:	Observational study to assess the effectiveness, safety profile and real-life prescribing and utilization patterns of tildrakizumab (Ilumetri®) in patients with moderate to severe plaque psoriasis in routine clinical practice.
Sponsor's Protocol Number:	NIS Study M/14745/43
QPS Study Number:	AT10112
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2 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

ADR	Adverse Drug Reaction
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BP	Blood Pressure
BSA	Body Surface Area
CRF	Case Report Form
CSR	Clinical Study Report
DLQI	Dermatology Life Quality Index
DLQI-R	Dermatology Life Quality Index adjusted for not relevant responses
eCRF	electronic CRF
EC	Ethics Committee
EOS	End-of-study
FAS	Full Analysis Set
FG	Fasting Glucose
HbA1c	Hemoglobin A1c
max	Maximum
MedDRA	Medical Dictionary for Regulatory Activity
mFAS	Modified Full Analysis Set
mg	milligram
MI	Multiple Imputation
MH	Medical history
min	Minimum
N, n	Population size (N for sample size, n for available data)
NIS	Non-Interventional Study
OC	Observed Cases
PASI	Psoriasis Area and Severity Index
PGA	Physician Global Assessment
PR	Pulse Rate
RR	Respiration rate
PD	Protocol deviation
PT	Preferred term
SAE	Serious AE
SAP	Statistical Analysis Plan
SmPC	Summary of Product Characteristics
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SOC	System Organ Classification
SOE	Schedule of Events
TG	Triglyceride
TSQM	Treatment Satisfaction Questionnaire for Medication
WHO	World Health Organization
WHO-DD	Drug Dictionary of the World Health Organization

3 INTRODUCTION

3.1 Preface

This statistical analysis plan (SAP) is based on protocol NIS Study M/14745/43, dated 01-Jul-2019, Amendment I, dated 14-Oct-2019, and Amendment II, dated 13-Oct-2020. The SAP provides details of data handling procedures and statistical analysis methods for effectiveness and safety evaluations. It also outlines statistical programming specifications for tables and listings, and other details on the analyses not provided in the study protocol.

4 DOCUMENTS USED

Study Protocol
Observational study to assess the effectiveness, safety profile and real-life prescribing and utilization patterns of tildrakizumab (Ilumetri®) in patients with moderate to severe plaque psoriasis in routine clinical practice, NIS Study M/14745/43, Version 1.0, and Date of Release:01-Jul-2019
Amendment I, Date of Release: 14-Oct-2019
Amendment II, Date of Release: 13-Oct-2020

Source/CRF
CRF, Version 1.3, Date of Release: 20-Sep-2019
CRF, Version 1.4, Date of Release: 14-May-2020

4.1 Study Objectives

Primary Objective

- To assess the effectiveness and maintenance of response of tildrakizumab (Ilumetri®) treatment in routine clinical practice

Secondary Objectives

- To describe the profile of the patients who start treatment with tildrakizumab (Ilumetri®)
- Correlation between absolute PASI scores and Dermatology Life Quality Index (DLQI)-R
- To evaluate changes in body weight, waist and hip circumference, BMI and arterial blood pressure
- To evaluate changes in food intake, physical activity and lipid blood parameters
- To evaluate tolerability of tildrakizumab (Ilumetri®) in patients with moderate to severe plaque psoriasis
- To evaluate prescribing and utilization patterns of 2 doses of tildrakizumab (100 mg and 200 mg, if appropriate), understanding factors that influence the study physician decision making regarding the tildrakizumab dose
- To assess treatment satisfaction from the study physician's and patient's perspective and to describe reasons for therapy discontinuation
- To assess long term safety profile of tildrakizumab in real life clinical setting

4.2 Data Sources

All analyses will be carried out using data from the eCRF (Rave). Dataset will be extracted from Rave and converted to Study Data Tabulation Model (SDTM) dataset.

5 OVERALL STUDY DESIGN AND PLAN

5.1 Study Design

This is an observational, non-interventional, multicenter study according to Directive 2001/20/EC in the frame of the long-term therapy with tildrakizumab (Ilumetri®) of patients with moderate to severe plaque-psoriasis in routine practice.

The treatment, including diagnosis and monitoring of patients, exclusively follows routine medical practice. The study physicians will choose the treatment independently from this NIS. In order to be able to assess the study objectives formulated above on a sufficiently large number of patients, a multicenter, non-interventional study is best suited, since only this study type allows evaluation of the therapy under practice conditions. In particular, it should be noted that the selection of patients to be included in the NIS is made by the study physician only after his assessment of the medical utility and necessity.

All patients will be informed about the purpose and the content of the NIS. Written informed consent will be obtained from all participating patients before any data collection.

The study plan together with the written patient information and informed consent form will be submitted to the responsible Ethics Committee before study start.

Up to 430 patients will be included in this study. These patients will be assigned to one of the following cohorts:

- Cohort 1: patients who completed tildrakizumab clinical trials
- Cohort 2: newly tildrakizumab prescribed patients

Patients meeting all of inclusion and none of exclusion criteria may be included in the study in every participating site.

The study will be performed at approximately 76 study sites across seven European countries:

- Austria
- Belgium
- Germany
- Italy
- The Netherlands
- France
- UK

Each patient will be followed for approximately 2 years. Tildrakizumab will become commercially available at different time-points in the participating countries. This will lead to variation of the actual time-points of the study start from country to country. Therefore, the total study duration from the inclusion of the first patient first visit to the last patient last visit will be approximately 4 years.

Patients will not be compensated for participating in this NIS.

5.2 Study Medication

Each newly prescribed patient should receive tildrakizumab (Ilumetri®) by subcutaneous injections at Weeks 0, 4 and every 12 weeks thereafter, according to the SmPC. For patients who completed (extension) studies with tildrakizumab, no induction period is needed.

5.3 Sample Size

The maximum total number of patients to be included in this study will be 430. Patients meeting all of inclusion and none of exclusion criteria may be included in the study in every participating site.

Due to the exploratory nature of this study, this maximum number of patients has been considered enough to meet the objectives of the study.

5.4 Study Flow Chart/Schedule of Events (SOE)

In this study, the visit structure is not defined by the study protocol, but is driven by routine clinical practice in accordance to the SmPC. The Visit and Assessment Schedule is presented in Table 5-1.

The Study Medication Administration Schedule based on the SmPC of tildrakizumab (Ilumetri®) and is outlined in Table 5-2.

Table 5-1 Visit and Assessment Schedule based on SmPC

Visit(s) [a]		1 (Baseline)		2 -8	9 (EOS)	Early Termination Visit (ET)	Follow-up Evaluation
approximate week of study [b]	patients who completed tildrakizumab clinical trials	0 (Day 0)	N.A.	12, 24, 36, 48, 60, 72, 84	96	N.A.	12 Weeks after last Injection [f]
	newly tildrakizumab prescribed patients		4 (Induction Visit)	16, 28, 40, 52, 64, 76, 88	100		
Data of documentation							
Visit date (day/month/year)		X	X	X	X	X	
Inclusion/Exclusion criteria		X					
Informed consent		X					
Demographic data (age, gender)		X					
Height		X					
Routine physical examination parameters including vital signs (temperature, BP, RR, PR) and weight measurements (weight, BMI, waist and hip circumference (optional), waist/hip ratio (optional))		X	X	X	X	X	
Anamnesis/medical history incl. psoriasis history, comorbidities (including information from preceding tildrakizumab clinical trials if relevant)		X					
Prior and concomitant medications/psoriasis therapy (systemic, topicals, etc) including info from preceding tildrakizumab clinical trials, if relevant		X					
Concomitant therapies (Psoriasis and Non-Psoriasis)			X	X	X	X	
Register blood (total cholesterol, HDL-c, LDL-c, VLDL-c, TG, lipoprotein (a), MetS – HbA1c and FG) and urine analyses results (if available) [c]		X	X	X	X	X	
Study Physician's Assessments							
Reasons for prescribing tildrakizumab (Ilumentri®), reason for choosing a dose 100 mg or200 mg, if applicable		X					
Reasons for changing tildrakizumab dose, if applicable			X	X	X		
PASI, BSA, PGA, Scalp/Nail PGA		X	X	X	X	X	
Study physician´s satisfaction with tildrakizumab therapy			X	X	X	X	
Patient's Questionnaires							
DLQI, DLQI-R, VAS Itch, VAS Pain		X	X	X	X	X	
Patient satisfaction with tildrakizumab therapy (TSQM [g])			X	X	X	X	
Patient questionnaire regarding physical activity [d] and food intake [e]		X	X	X	X	X	
Alcohol consumption		X		X	X	X	
Cigarette consumption		X		X	X	X	
Tolerability and Safety							
(S)AEs, (S)ADRs		X	X	X	X	X	X
Assessment for severe infections		X	X	X	X	X	X
Date and reason for the tildrakizumab (Ilumetri®) therapy stop and new therapy						X	
Check for completeness and consistency of patient questionnaires		X	X	X	X	X	

a) Information available at the respective visits will be captured in the observational form; diagnostic and therapeutic measures are solely at the discretion of the physician.
b) Visit windows are following clinical practice and will allow a systemic assessment of observed data. The timing of the study visits is in accordance with and based on the SmPC for Ilumetri® and routine clinical practice.
c) Fasting serum total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL-c) levels, Lipoprotein (a). Low-density lipoprotein cholesterol (LDL-c) value calculated according to Friedwald's equation: LDL-c =TC − (HDL-c + [Tg/5]) .
d) The extent of physical activity is captured in terms of stable or more or less physical activity (minutes / day) during the observational study. Type of physical activity (tick box).
e) Food consumption: restrictions to an upper calory limit intake per day: yes no / other diet yes: specify type of diet/ etc..
f) A follow-up evaluation will be performed 12 weeks after last injection by phone call or during patient´s visit at the physician´s office/clinic to evaluate (S)AEs, (S)ADRs and severe infections.
g) Atkinson MJ, Sinha A, Hass SL, et al. Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire for Medication (TSQM), using a national panel study of chronic disease. Health Qual Life Outcomes. 2004;2:12. Those seeking information regarding or permission to use the TSQM are directed to IQVIA at www.iqvia.com/TSQM or TSQM@iqvia.com

Table 5-2 Study Medication Administration Schedule based on SmPC

	Administration of tildrakizumab (Ilumetri®)									
patients who completed tildrakizumab clinical trials	Week 0/Day 0 (1st injection)		Week 12	Week 24	Week 36	Week 48	Week 60	Week 72	Week 84	Week 96
Patients newly prescribed tildrakizumab	Week 0/Day 0 (1st injection)	Week 4	Week 16	Week 28	Week 40	Week 52	Week 64	Week 76	Week 88	Week 100
	Visit 1	**Induction Visit**	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visit 8**	**Visit 9**

6 DESCRIPTION OF INCLUDED SUBJECTS

6.1 Analysis Populations

6.1.1 Safety population

The safety population is defined as all patients for whom it is known that they had at least one tildrakizumab dose during the study duration.

6.1.2 Full Analysis Set (FAS)

The full analysis set is defined as all those patients in safety population that had at least some effectiveness data.

6.1.3 Modified Full Analysis Set (mFAS)

The modified full analysis set is defined as all those patients in FAS population that had not changed their tildrakizumab dose.

To clarify the relationship between dose adjustments and the effectiveness endpoint results, additional analyses will be performed in mFAS (on the specified effectiveness endpoints). See the section 8 for the details of additional analysis.

6.2 Subjects Disposition

Subjects disposition will be presented using a status dataset that will be created and used throughout the tables and listings. This status dataset will contain information on the screened (if available in the database) and completed subjects. In addition, it contains the information for subjects in the safety and the FAS population. The status dataset will contain treatment group and visit as additional variables. The treatment dose group will be divided into six groups according to the actual treatment situation of the subjects:
(1) 100 mg
(2) 200 mg
(3) 100 to 200 mg (increased mix)
(4) 200 to 100 mg (decreased mix)
(5) 100 to 200 to 100 mg
(6) 200 to 100 to 200 mg

This applies to subjects of Cohort 1 and to subjects of Cohort 2.

6.3 Protocol Deviations

A protocol deviation is any change, divergence, or departure from the study design or procedures of a research protocol. All identified protocol deviations related to study inclusion or exclusion criteria, conduct of the trial, subject management or subject assessment will be collected during the conduct of the study and listed (by study site, if more than one study center). The predetermined categories for relevant protocol deviations are:

- Those who entered the study even though they did not satisfy the entry criteria
- Those who developed withdrawal criteria during the study but were not withdrawn
- Those who were withdrawn prematurely, not completing all planned evaluations
- Those who received the wrong treatment or incorrect dose
- Those who received an excluded concomitant treatment
- Those who received disallowed concomitant medication

The Protocol Deviation list is a list that presents the deviations by subject, description of actual deviation, and by type/category. The Protocol Deviation list is created by the Data Manager, but may involve collaboration with the Biostatistician and/or the SAS programmer, and is preferably based upon a predefined set of protocol deviations that is as inclusive as possible.

7 REPORT SPECIFICATIONS AND STATISTICAL ANALYSES

7.1 General Considerations

According to the non-interventional character of the study, the statistical analysis is descriptive and explorative. No statistical hypotheses are formulated.

Descriptive summary statistics (mean, median, standard deviation, min, max, number of available observations) will be provided for all effectiveness endpoints over time based on observed data (without imputation for missing data). Multiple Imputation (MI) analysis will be conducted as a sensitivity analysis in primary and secondary effectiveness endpoints, if applicable. These analyses will be based on FAS population.

For safety, number and percentage of patients with any Adverse Event will be provided. These analyses will be based on Safety Population.

Appropriate rounding will be performed for the summary statistics of baseline and effectiveness endpoints: arithmetic mean, median and SD will be presented with one more decimal than the original data; minimum and maximum values will be presented with the same precision as the original data. Percentages will be presented with 2 decimals.

Extra measurements (such as unscheduled or repeat assessments) will not be included in the descriptive statistics, but will be included in subject listings only.

For the calculation of baseline corrected values, Baseline is defined as the last value measured on Day 0 (Week 0) prior to the first tildrakizumab (Ilumetri®) administration (also if patients participated in tildrakizumab (Ilumetri®) clinical trials). If no baseline or previous to baseline evaluations exist, then the baseline value will be treated as missing.

For baseline and safety presentations, data for all study subjects combined (“overall”) will also be presented, when appropriate.

Note: some minor modifications may be necessary to the planned design of tables, figures, and listings to accommodate data collected during the actual study conduct. This is not considered a deviation from the preplanned statistical analysis.

7.2 Incomplete and Missing Data

No imputation will be performed on missing data unless otherwise specified. Since this study is observational, some patients may not have followed the assessment schedule due to personal factors or medical instructions, resulting in a large gap between the assessment and Tildrakizumab administration, so the effectiveness of administration cannot be estimated.

Therefore, the valid data will be defined according to the following instructions. The results of the analysis will be based on valid data, and the listing will be presented in two separate sets, one for data as it was collected, and the other for valid data. A total of 9 efficacy-related questionnaires (PASI, BSA, PGA, DLQI and DLQI-R, VAS, TSQM, Physician's Satisfaction with Tildrakizumab Therapy, Food Intake and Physical Activity) and 3 assessments (weight, blood pressure and blood analyses) need to process data according to instructions.

Instructions for Valid Data:

1. If for a given visit, the date of assessments is **AFTER** the date of Tildrakizumab administration for this visit, the assessments (PASI, BSA, PGA, DLQI, DLQI-R, VAS, TSQM, Physician's Satisfaction with Tildrakizumab Therapy, Food Intake, Physical Activity, weight, blood pressure and blood analyses) will be considered valid if no more than 14 days have elapsed and as long as the data of Tildrakizumab administration for this visit is in the 56 to 112 day window (i.e., 84 days [12 weeks] +/- 28 days) subsequent to the date of Tildrakizumab administration of the previous visit. For Visit 1 (W4), the day window between the date of Tildrakizumab administration and the date of Tildrakizumab administration of the previous visit is in the 14 to 42 days (i.e., 28 days [4 weeks] +/- 14 days).

   If more than 14 days have elapsed, the assessments of the visit will only be considered valid if they can be moved to the next visit in the event that the next visit has not been conducted and as long as the assessments that were made after the date of Tildrakizumab administration were performed in the 14 to 42 day window (i.e. 28 days [4 weeks] +/- 14 days) for Visit 1 (W4) and 56 to 112 day window (i.e., 84 days [12 weeks] +/- 28 days) for other visits subsequent to the date of Tildrakizumab administration from that same visit that is going to be moved.
   For the baseline visit (Visit 1 [W0]), the assessments will NOT be considered valid if they were made after the Tildrakizumab administration on Day 1.

   For example (see below table), the data of Visit 2 (W12) will be considered invalid and will be deleted if the assessment date is later than the administration date and differs by more than 14 days. For exception, if more than 14 days have elapsed (Visit 4 [W36]) and the next visit has not been conducted, the assessment date of Visit 4 (W36) can be moved to Visit 5 (W48). Also, the assessment date (2021/12/9) is after the administration date of Visit 4 (W36) (2021/9/20) and the difference is within the 56 to 112 day window (2021/12/9 – 2021/9/20 = 80).

SUBJID	VISIT	Assessment Date [1]	Administration Date [2]	Duration ([1]-[2])	Days elapsed between Dosing Date and Previous Dosing Date	Valid Data
0001	Visit 1 (W0)	2021/2/25	2021/2/25	0	-	Yes
0001	Visit 1 (W4)	2021/4/6	2021/3/25	12	28	Yes
0001	Visit 2 (W12)	2021/6/15	2021/5/15	31	51	No

SUBJID	VISIT	Assessment Date [1]	Administration Date [2]	Duration ([1]-[2])	Days elapsed between Dosing Date and Previous Dosing Date	Valid Data
0001	Visit 3 (W24)	2021/9/5	2021/8/25	11	102	Yes
0001	Visit 4 (W36)	2021/12/9	2021/9/20	80	26	No
0001	Visit 5 (W48)	**(2021/12/9)**	2022/3/17			Yes

2. If for a given visit, the date of the assessments is **PRIOR** to the date of Tildrakizumab administration for this visit, the assessments will be considered valid if they are made in the 56 to 112 day window (i.e., 84 days [12 weeks] +/- 28 days) subsequent to the date of Tildrakizumab administration from the previous visit. For Visit 1 (W4), the assessments will be considered valid if they are made in the 14 to 42 day window ((i.e., 28 days [4 weeks] +/- 14 days) subsequent to the date of Tildrakizumab administration from the previous visit.

   For the baseline visit (Visit 1 [W0]), the assessments will be considered valid if they were NOT made more than 14 days before the Tildrakizumab administration on Day 1.

   For example, the data of Visit 1 (W0) will be considered invalid and will be deleted if the assessment date was more than 14 days before the Tildrakizumab administration on Day 1. Another example, the data of Visit 3 (W24) will be considered invalid and will be deleted if the assessment date is prior than the administration date and out of day window (56 to 112) between the date of the assessments and the date of Tildrakizumab administration from the previous visit.

SUBJID	VISIT	Assessment Date [1]	Administration Date [2]	Duration ([1]-[2])	Days elapsed between Assessment Date and Previous Dosing Date	Valid Data
0001	Visit 1 (W0)	2021/2/10	2021/2/25	-15	-	No
0001	Visit 1 (W4)	2021/3/25	2021/4/1	-7	35	Yes
0001	Visit 2 (W12)	2021/5/15	2021/6/15	-31	70	Yes
0001	Visit 3 (W24)	2021/8/25	2021/12/9	-106	177	No

3. If for a given visit, the date of the assessments is **THE SAME** as the date of the Tildrakizumab administration for this visit, the assessments will be considered valid if they are made in the 56 to 112 day window (i.e., 84 days [12 weeks] +/- 28 days) subsequent to the date of Tildrakizumab administration from the previous visit. For Visit 1 (W4), the assessments will be considered valid if they are made in the 14 to 42 day window (i.e., 28 days [4 weeks] +/- 14 days) subsequent to the date of Tildrakizumab administration from the previous visit.

   For example, the data of Visit 1 (W4) will be considered invalid and will be deleted if the assessment date is the same as the administration date and out of day window (14 to 42) between the date of assessment and the date of Tildrakizumab administration from the previous visit. Also, the date of Visit 3 (W24) will be deleted because of out of day window (56 to 112).

SUBJID	VISIT	Assessment Date [1]	Administration Date [2]	Duration ([1]-[2])	Days elapsed between Assessment Date and Previous Dosing Date	Valid Data
0001	Visit 1 (W0)	2021/2/25	2021/2/25	0	-	Yes
0001	Visit 1 (W4)	2021/4/10	2021/4/10	0	44	No

SUBJID	VISIT	Assessment Date [1]	Administration Date [2]	Duration ([1]-[2])	Days elapsed between Assessment Date and Previous Dosing Date	Valid Data
0001	Visit 2 (W12)	2021/6/15	2021/6/15	0	66	Yes
0001	Visit 3 (W24)	2021/11/9	2021/11/9	0	147	No

4. (1) For the patients who received Tildrakizumab every 24 weeks (as per investigator's decision due to the very good patient's response to the drug) instead of every 12 weeks, the mentioned 24-week dosing interval will be respected and accepted, and the same instructions as the ones above will be applied, but considering a **window of 140 to 196 days** (i.e., 168 days [24 weeks] +/- 28 days).

   The day window for the following patients will be adjusted based on investigator's decision:

Site	Patient	Visit
BE07	BE07-01-011	V7
BE07	BE07-01-012	V6
BE07	BE07-02-009	V6

4. (2) For the patients who received Tildrakizumab every 4 months (as per investigator's decision) instead of every 12 weeks, the mentioned 4-month dosing interval will be respected and accepted, and the same instructions 1, 2 and 3 will be applied, but considering a **window of 94 to 150 days** (i.e., 122 days [4 months] +/- 28 days)."

   The day window for the following patients will be adjusted based on investigator's decision:

Site	Patient	Visit
NL01	NL01-01-001	V6
NL01	NL01-01-001	V7
NL01	NL01-01-001	V8
NL01	NL01-01-001	V9
NL01	NL01-01-002	V6
NL01	NL01-01-002	V7
NL01	NL01-01-002	V8
NL01	NL01-01-002	V9
NL01	NL01-01-004	V6
NL01	NL01-01-004	V7
NL01	NL01-01-004	V8
NL01	NL01-01-004	V9

5. If there are extra visits, they should be ordered chronologically.

6. Data of Early Termination Visits will to be considered valid and included in the analysis. Early Termination Visits will be treated as a separate visit to present the results and its changes from the baseline visit.

In summary tables, the number of subjects without missing data will be presented unless otherwise specified. In calculations of percentages, subjects with missing data will not be considered in numerator of denominator unless otherwise specified.

For effectiveness endpoints, MI analysis will be conducted as a sensitivity analysis, if applicable. Different covariates such as baseline characteristics, demographics (Age, Gender), prescribed dose at Visit 1 (W0), etc. will be included in the MI model. In this study, SAS Procedure MI will be used for MI analysis. Monotone Logistic Regression method will be used with the seed number 190827.

For the safety evaluation, subjects with missing data are included until their last assessment in both listings and tables.

In listings, dates will be presented as exported from the database, also in case of partial dates. A unit will be added to clarify the day-, month- and year-part of the dates, if necessary.

7.3 Demographic and Baseline Characteristics

Descriptive tabulations of the screening data for demographics will be made. Appropriate descriptive statistics for age and gender will be given. Additionally, demographic data will be listed, along with patient ID, date of informed consent form signed, screen number, cohort number, treatment group and study site number.

Age will not be calculated in SAS, but taken from the eCRF/database.

Other baseline data, such as eligibility will only be listed.

Medical history (MH) data will in addition be coded with the latest version of the MedDRA coding system used during the clinical conduct of the study. The SAS programmer or Data Manager of the study will add the coding (using the MedDRA system and SAS) to the medical history descriptions extracted from the database. From the SAS dataset, an Excel sheet will be created for approval, containing the term as well as the coding information. The sponsor/investigator/medical director will approve the MH coding before database lock. Preferably, these Excel lists are created based on a clean database.

Based on the status dataset (see Section 6.2), a summary of all enrolled, treated, and completed subjects by treatment group, as well as overall, will be given (“subject disposition”).

7.3.1 Concomitant Medication

Previous medications are defined as any medication discontinued prior to the first dose of study drug. Concomitant medications are defined as any medication taken during the course of the study.
Previous and concomitant medication (COMED) will be coded by Data Management using the WHO-DD Codes (see Data Management Plan). An excel sheet will be created by Data Management for approval, containing the term as well as the coding information. The sponsor will approve the COMED coding before database lock. Preferably, these excel lists are created based on a clean database.

7.4 Study Subjects and Conduct

The subject disposition will be given in a summary table by treatment group, as well as overall:

- the number of subjects screened
- the number of subjects completed study
- the number of subjects in the FAS population
- the number of subjects in the Safety population

In addition, these data will be listed in a Subject Disposition listing. Reasons for discontinuation will be listed in the Study Termination listing, together with the relevant dates.

7.5 Interim Analysis

During study, interim analyses including dry run, interim, preliminary and topline analysis will be performed. All tables and listings that listed in section 10.2 and 10.3 will be provided to sponsor for the review. For data review meeting, an excel file for raw data/data listing will be provided to sponsor for the review.

Timeline for interim analyses is scheduled based on Biostatistics Management Plan (BSMP) as follows:

Task	Timeline
Biostatistics Management Plan	BSMP shall be provided to sponsor after related personnel are assigned and protocol is finalized.
Statistical Analysis Plan	The 1st SAP shall be provided to sponsor in 15 working days while protocol, CRF/eCRF and BSMP are finalized. SAP shall be finalized before database lock (DBL).
1st Interim SDTM package	Datasets and annotated CRF only. The 1st Interim SDTM package shall be provided to sponsor when 25% eligible subjects enrolled.
Dry-Run of TLF	Dry-Run of TLF shall be provided to sponsor when 25% eligible subjects enrolled.
1st raw data/data listing excel file for data review meeting	Raw data/data listing excel file for data review meeting shall be provided to sponsor when 12 months after each site's first subject first visit.
2nd raw data/data listing excel file for data review meeting	Raw data/data listing excel file for data review meeting shall be provided to sponsor when 24 months after each site's first subject first visit.
2nd Interim SDTM package	Datasets and annotated CRF only. The 2nd Interim SDTM package shall be provided to sponsor in 5 working days when database is freeze after 150 patients completed Visit 5.
Interim TLF	Interim TLF shall be provided to sponsor in 10 working days when database is freeze after 150 patients completed Visit 5.
Interim SAR	Interim SAR shall be provided to sponsor in 10 working days when interim TLF is approved by sponsor.
3rd Interim SDTM package	Datasets only. The 3rd Interim SDTM package shall be provided to sponsor when 50% eligible subjects enrolled.
3rd raw data/data listing excel file for data review meeting	Raw data/data listing excel file for data review meeting shall be provided to sponsor when 36 months after each site's first subject first visit.
4th raw data/data listing excel file for data review meeting	Raw data/data listing excel file for data review meeting shall be provided to sponsor after each site's last subject last visit and before DBL.
Preliminary TLF	Preliminary TLF shall be provided to sponsor in 10 working days before DBL.
4th Interim SDTM package	Datasets only. The 4th Interim SDTM package shall be provided to sponsor in 10 working days before DBL.
Topline TLF	Topline TLF shall be provided to sponsor in 10 working days after DBL.

Task	Timeline
Final TLF	The 1st draft TLF shall be provided to sponsor in 15 working days after DBL. The final TLF shall be provided to sponsor in 25 working days after DBL.
Final SDTM package	Final SDTM package shall be provided to sponsor in 15 working days after DBL.

7.6 Safety and Tolerability Evaluations

7.6.1 General Considerations

Safety evaluations will be conducted at screening, periodically throughout study conduct, end-of-study evaluation and at the follow-up evaluation. See Table 5-1 for the details of evaluation time points. All safety assessments, including but not limited to AEs will be listed and where appropriate summarized with descriptive statistics.

7.6.2 Safety and Tolerability Variables

The safety variables to be presented are:

- Adverse Event (AE)
- Adverse Drug Reaction (ADR)
- Serious Adverse Event (SAE)

The safety population will be used.

7.6.3 Analysis of Safety and Tolerability Endpoints

7.6.3.1 Adverse Events

The standard definition of an adverse drug reaction (ADR) is: "Adverse drug reactions to medicinal products intended for human use are harmful and unintended reactions to the medicinal product." Moreover, an ADR is a special type of adverse event (AE) in which a causative relationship to the medicinal product can be shown. Therefore, it is defined as an adverse event RELATED to the medicinal product. Any AE with the causality Certain, Probable or Possible will be classified as an ADR.

Adverse event data will in addition be coded with the latest version of the MedDRA coding system used during the clinical conduct of the study. The SAS programmer or Data Manager of the study will add the coding (using the MedDRA system and SAS) to the AE descriptions extracted from the database. From the SAS dataset, an excel sheet will be created for approval, containing the term as well as the coding information. The sponsor will approve the MH coding before database lock. Preferably, these excel lists are created based on a clean database.
The ADRs and AEs are tabulated by system organ class (SOC), and individual preferred terms within each SOC by treatment group (100 mg or 200 mg tildrakizumab). The number and percentage of patients who experienced AEs coded with the same preferred term and SOC will be summarized by treatment group (in descending order according to the incidence in the investigational study drug group). ADRs and AEs will also be tabulated by severity and by relationship to study drug. Summary tables will be accompanied by individual patient listings broken down by treatment group, including pre-dose events.

SAEs will be listed and summarized similarly to AEs.

All AEs and SAEs are coded using the MedDRA version 25.1 or higher.

Reasons for death will only be listed.

AE duration and onset to AE (Study Day) will be added in the AE listings as “XXD” and “Day XX”. The following calculations and derivations will be used, making the most conservative judgment.

For duration of AE:

- AE Duration = AE resolution date of the event minus AE onset date of the event, and +1 is added.
- If “Date” of AE onset date or resolution date is unknown, the date would be replaced to 01, ex: "2020-07" would be replaced to "2020-07-01" to calculate AE duration. If AE onset date or resolution date is unknown or partial year or month, AE duration will be missing.

For time to onset of AE:

- Time to onset (Study Day) = AE onset date of the event minus date of prior of administration, and +1 is added.
- If “Date” of AE onset date is unknown, the date would be replaced to 01, ex: "2020-07" would be replaced to "2020-07-01" to calculate the study day. If AE onset date is unknown or partial year or month, the time to onset (Study Day) will be missing.

7.7 Effectiveness Evaluations

7.7.1 General Considerations

Effectiveness evaluations will be conducted at screening, periodically throughout study conduct, and at the end-of-study evaluation. See Table 5-1 for the details of evaluation time points. All effectiveness assessments, including but not limited to laboratory assessments, routine physical examination including vital signs, study physician's assessments and patient's questionnaires will be listed and where appropriate summarized with descriptive statistics.

Baseline is defined as the last value measured on Day 0 (Week 0) prior to the first tildrakizumab (Ilumetri®) administration (also if patients participated in tildrakizumab (Ilumetri®) clinical trials).

7.7.2 Effectiveness Variables

<u>The following primary effectiveness parameters have been defined, observed cases (OC) and MI will be used in analysis:</u>

<u>Cohort 1 (Subgroup of patients continuing treatment with tildrakizumab):</u>

- Absolute PASI scores and change from baselines (reSURFACE and SAIL) value at Visit 5 and Visit 9 (EOS)
- Correlation between absolute PASI scores and DLQI-R at Visit 5 and Visit 9 (EOS)
- Percentage of patients maintaining PASI 75, 90, 100 responses at Visit 5 and Visit 9 (EOS) (re-SURFACE studies (if available) and Week 0/Day 0 of SAIL study)
- Absolute BSA and change of BSA from baselines (reSURFACE and SAIL) at Visit 5 and Visit 9 (EOS)
- Absolute PGA (general, nail, scalp) and change from baseline values (reSURFACE and SAIL) at Visit 5 and Visit 9 (EOS)

Cohort 2 (Newly prescribed patients):

- Absolute PASI scores and change from baseline value at Visit 5 and Visit 9 (EOS)
- Correlation between absolute PASI scores and DLQI-R at Visit 5 and Visit 9 (EOS)
- Percentage of patients achieving PASI 75, 90, 100 at Visit 5 and Visit 9 (EOS)
- Absolute BSA and change from baseline value at Visit 5 and Visit 9 (EOS)
- Absolute PGA (general, nail, scalp) and change from baseline value at Visit 5 and Visit 9 (EOS)

The following secondary effectiveness parameters have been defined:

- Absolute DLQI and DLQI-R score and change from baseline value at Visit 5 and Visit 9 (EOS) (both baselines for continuing patients if data available), OC and MI will be used in analysis
- Absolute VAS (pain and itch) scores and change from baseline (both baselines for continuing patients if data available), OC and MI will be used in analysis
- Absolute TSQM (patient's satisfaction with treatment) scores, OC and MI will be used in analysis
    - Effectiveness: ([(Item 1 + Item 2 + Item 3) – 3] divided by 18) * 100
        - If one item is missing: ([Sum(the two completed items)) – 2] divided by 12) * 100
    - Side effects:
        - If Question 4 is answered 'No' then score = 100
        - Else:
            - ([Sum(Item 5 to Item 8) – 4] divided by 16) * 100
            - If one item is missing: ([(Sum(the three completed items)) – 3] divided by 12) * 100
    - Convenience: ([Sum(Item 9 to Item 11) – 3] divided by 18) * 100
        - If one item is missing: ([(Sum(the two completed items)) – 2] divided by 12) * 100
    - Global Satisfaction: ([(Sum(Item 12 to Item 14)) – 3] divided by 14) * 100
        - If Item 12 or 13 is missing: ([(Sum(the two completed items)) – 2] divided by 10) * 100
        - If Item 14 is missing: ([(Sum(Item 12 and Item 13)) – 2] divided by 8) * 100
- Absolute physician's satisfaction with treatment scores, OC and MI will be used in analysis
- Proportion of patients adding concomitant medications from baseline at Visit 5 and Visit 9 (EOS), only OC will be used in analysis
- Changes in weight measurements (body weight, BMI, waist and hip circumference (optional), waist/hip ratio (optional)) and blood pressure from baseline at Visit 9 (EOS) or Early Termination, only OC will be used in analysis
- Changes in food intake: quantitative and qualitative from baseline up to Visit 9 (EOS) or Early Termination, only OC will be used in analysis
- Changes in physical activity: quantitative and qualitative from baseline up to Visit 9 (EOS), only OC will be used in analysis
- Changes in lipid blood parameters in patients from baseline up to Visit 9 (EOS), if routinely available, only OC will be used in analysis
- Number and proportion of patients withdrawing from the study, only OC will be used in analysis
- Number of patients changing the dose (if any) and factors that influence the study physician's decision regarding the prescription of a dose of tildrakizumab (100 mg or 200 mg, if appropriate) (option based scale), only OC will be used in analysis
- Drug survival up to Visit 9 (EOS), only OC will be used in analysis
- Patient adherence up to Visit 9 (EOS), only OC will be used in analysis

The FAS population will be used.

7.7.3 Analysis of Effectiveness Endpoints

Change from baseline

- The analysis of change from baseline includes: absolute PASI scores, absolute BSA, absolute PGA (general, nail, scalp), absolute DLQI and absolute DLQI-R score, absolute VAS (pain and itch) scores, patient (TSQM) and physician's satisfaction with therapy scores, weight measurements (body weight, BMI, waist and hip circumference (optional), waist/hip ratio (optional), blood pressure and lipid blood parameters.
- The change from baseline is defined as: result at post-baseline visit – result at baseline visit.
- For Cohort 1, absolute PASI scores, absolute BSA, PGA, DLQI and DLQI-R: The change from baseline of reSURFACE study is defined as: result at post-baseline visit – result at baseline visit (W0) of reSURFACE study.
- The percentage change from baseline is defined as: 100% x [(Result at post-baseline visit) - (Result at baseline visit)]/ (Result at baseline visit).
- For Cohort 1, absolute PASI scores, absolute BSA, PGA, DLQI and DLQI-R: The percentage change from baseline of reSURFACE study is defined as: 100% x [(Result at post-baseline visit) - (Result at baseline visit [W0] of reSURFACE study)]/ (Result at baseline visit [W0] of reSURFACE study).

Descriptive summary statistics (mean, median, standard deviation, min, max, number of available observations) will be provided for change from baseline.

Correlation between absolute PASI scores and DLQI-R

- SAS Procedure, CORR with PEARSON method will be used for correlation analysis. PASI scores and DLQI-R will be set to VAR and WITH statement.

Percentage of patients maintaining /achieving PASI 75, 90, 100

- The definition of patients maintaining PASI 75, 90 and 100 are as below:
  - At baseline visit: the status of 'maintaining' means that a patient maintained the PASI responder status at baseline of the SAIL study versus the PASI responder status achieved at the end of the reSURFACE study.
  - At post-baseline visits: the status of 'maintaining' means that a patient maintained the PASI responder status at the post-baseline visit of the SAIL study and also maintained it at baseline of the SAIL study.

- The definitions of patients achieving PASI 75, 90 and 100 are as below:
  - The PASI 75 is defined as the percentage of patients who have achieved ≥75% reduction in their PASI score from baseline.
  - The PASI 90 is defined as the percentage of patients who have achieved ≥90% reduction in their PASI score from baseline.
  - The PASI 100 is defined as the percentage of patients who have achieved a complete resolution of all disease.
- Percentage of patients will be presented by time point, per treatment and cohort.

Proportion of patients adding concomitant medications

- Patients received concomitant medications or not from baseline to Visit 9 (EOS) will be classified as 'Yes' or 'No' for analysis. The concomitant medications are tabulated by

Anatomical Therapeutic Chemical (ATC) level, and individual preferred term (active ingredient) for each subcategory by treatment group (100 mg or 200 mg tildrakizumab). The number and percentage of patients who took concomitant medications coded with the same ATC level and preferred term (active ingredient) will be summarized by treatment group (in descending order according to the incidence in the investigational study drug group).

Food intake

- Number and percentage of questionnaire about food intake will be presented by treatment and cohort. The quantitative analysis and 'Change' in qualitative analysis are not feasible since quantitative data of questionnaire is not available.

Physical activity

- Number and proportion of patients perform which kind of physical activity will be presented by treatment and cohort. Furthermore, descriptive summary statistics (mean, median, standard deviation, min, max, number of available observations) will be provided for the exercise time for each physical activity by visits and change from baseline.
- For any un-ticked physical activity (Workout, Weight training and Stretch exercise) in CRF page 'PATIENT'S QUESTIONNAIRES PHYSICAL ACTIVITY', it's 'Exercise time in minutes' will be set to '0 per day' in analysis. If patients tick 'No physical activity' at a scheduled visit, the 'Exercise time in minutes' of Workout, Weight training and Stretch exercise will be set to '0 per day' in analysis.
- For any physical activity (Workout, Weight training and Stretch exercise) in CRF page 'PATIENT'S QUESTIONNAIRES PHYSICAL ACTIVITY' is ticked 'Unknown', it's 'Exercise time in minutes' will be set to null value in analysis.
- In summary table, the 'Exercise time in minutes' will be summarized by using the frequency 'per day'. For the frequency that ticked 'per week' and 'per month', the 'Exercise time in minutes' will be divided by 7 and 30.5 to make it consistent with 'per day' in analysis.

Number and proportion of patients withdrawing from the study

- Number and proportion of patients withdrawing from the study will be presented by the reasons for withdrawal. For calculating the proportion, the algorithm is defined as below.

  Percentage of the Reason for Non-Completion:
  100%*[The number of subject(s) in the category / The number of subject(s) who did not complete study]

Number of patients changing the dose

- Number and percentage of subject regarding the change in dose will be presented by reasons (Intolerance, Lack of effectiveness and Other), time point, per treatment and cohort.

Drug survival

- Time to discontinuation of the study drug (months) will be presented by treatment and cohort. Time to discontinuation of the study drug is defined as: (first dosing date to the last dosing date)/30.5. Descriptive summary statistics (mean, median, standard deviation, min, max, number of available observations) will be provided.

Patient adherence

- Time to study discontinuation (months) will be presented by treatment and cohort. Time to study discontinuation is defined as: (first dosing date to the study completion date or decided to discontinue date)/30.5. Descriptive summary statistics (mean, median, standard deviation, min, max, number of available observations) will be provided.

Cigarette consumption and alcohol intake

- Number and percentage of questionnaire about cigarette consumption and alcohol intake will be presented by treatment and cohort.

8 CHANGES FROM PROTOCOL AND OTHER REMARKS

In this study, the dose can be adjusted according to the patient's situation. In order to avoid dose adjustment affecting the effectiveness endpoint results, this study will use the mFAS population for additional analysis of the effectiveness endpoints.

Additional analysis includes the following:

- Table 14.1.2: Summary of Subject Demographics (mFAS Population)
- Table 14.2.1: Summary of Absolute PASI Scores (mFAS Population, Primary Endpoint, OC and MI)
- Table 14.2.2: Correlation Between Absolute PASI Scores and DLQI-R Between Visit 5 and 9 (mFAS Population, Primary Endpoint, OC and MI)
- Table 14.2.3: Percentage of Patients Maintaining PASI 75, 90, 100 Responses (mFAS Population, Primary Endpoint, OC)
- Table 14.2.4: Percentage of Patients Achieving PASI 75, 90, 100 Responses (mFAS Population, Primary Endpoint, OC and MI)
- Table 14.2.5: Summary of Absolute Body Surface Area (BSA) (mFAS Population, Primary Endpoint, OC and MI)
- Table 14.2.6: Summary of Absolute Physician's Global Assessment (PGA) (mFAS Population, Primary Endpoint, OC and MI)
- Table 14.2.7: Summary of Dermatology Life Quality Index (DLQI) and Adjusted for Not Relevant Responses (DLQI-R) (mFAS Population, Secondary Endpoint, OC and MI)
- Table 14.2.8: Summary of Absolute VAS Scores (mFAS Population, Secondary Endpoint, OC and MI)
- Table 14.2.9: Summary of Absolute TSQM Scores (mFAS Population, Secondary Endpoint, OC and MI)
- Table 14.2.10: Summary of Absolute Scores of Physician's Satisfaction with Tildrakizumab Therapy (mFAS Population, Secondary Endpoint, OC and MI)
- Table 14.2.12: Summary of Weight Measurements and Blood Pressure (mFAS Population, Secondary Endpoint, OC)
- Table 14.2.13: Summary of Food Intake (mFAS Population, Secondary Endpoint, OC)
- Table 14.2.14: Summary of Physical Activity (mFAS Population, Secondary Endpoint, OC)
- Table 14.2.15: Summary of Blood Analyses (mFAS Population, Secondary Endpoint, OC)

9 SOFTWARE

9.1 Coding Systems

Adverse events, Medical History, Prior and Concomitant Medication and Anti-Psoriatic Non Medication Therapies will be coded as described in the Data Management documentation.

9.2 Statistical Software

The statistical analysis and reporting will be done using SAS for Windows™ version 9.4 or higher.

9.3 Reporting

All safety output will be generated as SAS tables and listings. All tables and listings will be created such that they fit landscape pages. All tables and listings will be created using SAS with an RTF output, and font Times New Roman size 9 will be used.

A list of tables, graphs and listings is presented (per report section) in Section 10.

The QPS template tables and listings will be used, and a separate templates document will be supplied together with the SAP. Adaptations to template layout are possible depending on the design of the study, the length of variables and the number of variables. It should be noted that all data as collected will be presented in listings and/or tabulations. The examples in the templates document may not cover all possible collected data, or examples may be present of data not collected for this specific study.

All tables and listings created will need to adhere to the following margins to fit the appendix layout if the CSR:

Landscape: Top – 1.25 inch
Bottom – 1.0 inch
Left – 0.5 inch
Right – 0.5 inch

10 TABLES, LISTINGS AND FIGURES

10.1 List of Tables– core text

All tables mentioned here will be presented in the report, and will be supplied to the Medical Writer as separate .RTF or .DOCX files.

- Summary table of demographic data, including age and gender at screening. Mean and SD for quantitative variables. Frequency and percentage for qualitative variables.

- Adverse event summary containing the number and percentage of subjects experiencing any ADR or SAE. Table will contain information concerning the severity and relationship,

concomitant medication given and discontinuation due to an AE. Table will be presented by treatment group.

- Adverse event summary containing the number and percentage of subjects experiencing treatment-emergent AEs. AEs are tabulated by MedDRA SOC and preferred term, and summarized by treatment group. AEs will be summarized in descending order according to incidence of SOC and preferred term.

- If applicable, the same tabulations will be presented for SAEs.

- If applicable: summary listing of serious adverse events containing description of event, MedDRA preferred term, subject number, relationship, action taken and outcome.

10.2 List of Tables – end of text

All tables mentioned here will be presented according to ICH guidelines in appendix 14 of the report. A complete document (batch load) will be created in Word for the Medical Writer, in the order and with section number and title as stated.

14.1 Demographic Data Summary figures and tables
14.2 Efficacy Data Summary figures and Tables
14.3 Safety Data Summary figures and tables
- 14.3.1 Displays of Adverse Events
- 14.3.2 Listings of Deaths, Other Serious and Significant Adverse Events
- 14.3.3 Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events
- 14.3.4 Abnormal Laboratory Value Listing (each subject)

Section	Title	Notes
14.1.1	Summary of Subject Disposition (All Enrolled Subjects)	Summary of all enrolled and completed subjects and the number of subjects in the safety and FAS population. (Excluded subjects will be mentioned in a footnote.)
14.1.2	Summary of Subject Demographics (FAS Population)	Descriptive statistics for demographic data.
14.1.3.1	Summary of Prior Therapies - Anti-Psoriatic Medications (Safety Population)	Summary containing the number and percentage of subjects taking prior anti-psoriatic medications.
14.1.3.2	Summary of Prior Therapies - Non-Psoriatic Medications (Safety Population)	Summary containing the number and percentage of subjects taking prior non-psoriatic medications.
14.1.3.3	Summary of Prior Therapies - Anti-Psoriatic Non Medication Therapies (Safety Population)	Summary containing the number and percentage of subjects taking prior anti-psoriatic non medication therapies.
14.1.4.1	Summary of Prior but Continued Medications during the Study -	Summary containing the number and percentage of subjects taking any concomitant medications prior to the study

Section	Title	Notes
	Anti-Psoriatic Medications (Safety Population)	onset but continued during study (anti-psoriatic medications medications).
14.1.4.2	Summary of Prior but Continued Medications during the Study - Non-Psoriatic Medications (Safety Population)	Summary containing the number and percentage of subjects taking any concomitant medications prior to the study onset but continued during study (non-psoriatic medications).
14.1.5	Medical/Surgery History - MedDRA (Safety Population)	Summary containing the number and percentage of subjects experiencing medical/surgery histories. Medical/surgery histories are tabulated by SOC and PT, and summarized by treatment. The summary will be presented in descending according to SOC and preferred term.
14.2.1	Summary of Absolute PASI Scores (FAS Population, Primary Endpoint, OC and MI)	Descriptive statistics for absolute values and change from baseline by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.
14.2.2	Correlation Between Absolute PASI Scores and DLQI-R Between Visit 5 and 9 (FAS Population, Primary Endpoint, OC and MI)	Correlation by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.
14.2.3	Percentage of Patients Maintaining PASI 75, 90, 100 Responses (FAS Population, Primary Endpoint, OC)	Percentage of patients by time point, per treatment and cohort.
14.2.4	Percentage of Patients Achieving PASI 75, 90, 100 Responses (FAS Population, Primary Endpoint, OC and MI)	Percentage of patients by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.
14.2.5	Summary of Absolute Body Surface Area (BSA) (FAS Population, Primary Endpoint, OC and MI)	Descriptive statistics for absolute values and change from baseline by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.
14.2.6	Summary of Absolute Physician's Global Assessment (PGA) (FAS Population, Primary Endpoint, OC and MI)	Descriptive statistics for absolute values and change from baseline by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.
14.2.7	Summary of Dermatology Life Quality Index (DLQI) and Adjusted for Not Relevant Responses (DLQI-R) (FAS	Descriptive statistics for absolute values and change from baseline by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.

Section	Title	Notes
	Population, Secondary Endpoint, OC and MI)	
14.2.8	Summary of Absolute VAS Scores (FAS Population, Secondary Endpoint, OC and MI)	Descriptive statistics for absolute values and change from baseline by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.
14.2.9	Summary of Absolute TSQM Scores (FAS Population, Secondary Endpoint, OC and MI)	Descriptive statistics for absolute values by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.
14.2.10	Summary of Absolute Scores of Physician's Satisfaction with Tildrakizumab Therapy (FAS Population, Secondary Endpoint, OC and MI)	Descriptive statistics for absolute values by time point, per treatment and cohort. Multiple Imputation analysis will be conducted as a sensitivity analysis.
14.2.11	Proportion of Patients with Newly Added Concomitant Medications during the Study (Safety Population, Secondary Endpoint, OC)	Proportion of patients taking any newly concomitant medication during the study by time point, per treatment and cohort.
14.2.12	Summary of Weight Measurements and Blood Pressure (FAS Population, Secondary Endpoint, OC)	Descriptive statistics for absolute values and change from baseline by time point, per treatment and cohort.
14.2.13	Summary of Food Intake (FAS Population, Secondary Endpoint, OC)	Summary containing the number and percentage of subject questionnaire regarding the food intake by time point, per treatment and cohort.
14.2.14	Summary of Physical Activity (FAS Population, Secondary Endpoint, OC)	Summary containing the number and percentage of subject questionnaire regarding the physical activity, and descriptive statistics for absolute values and change from baseline by time point, per treatment and cohort.
14.2.15	Summary of Blood Analyses (FAS Population, Secondary Endpoint, OC)	Descriptive statistics for absolute values and change from baseline by time point, per treatment and cohort.
14.2.16	Summary of Patients Changing the Dose (Safety Population, Secondary Endpoint, OC)	Summary containing the number and percentage of subject regarding the change in dose by time point, per treatment and cohort.
14.2.17	Summary of Drug Survival (Safety Population, Secondary Endpoint, OC)	Descriptive statistics for time to discontinuation of the study drug per treatment and cohort.

Section	Title	Notes
14.2.18	Summary of Patient Adherence (Safety Population, Secondary Endpoint, OC)	Descriptive statistics for time to study discontinuation per treatment and cohort.
14.3.1.1	Adverse Events (Safety Population)	Adverse event summary containing the number and percentage of subjects experiencing any AE. Table will contain information on the intensity, SAE, action taken with study medication, relationship to study medication, treatment required and outcome. Table will be presented per treatment.
14.3.1.2	Adverse Events - MedDRA (Safety Population)	Summary containing the number and percentage of subjects experiencing AEs. AEs are tabulated by SOC and PT, and summarized by treatment. The summary will be presented in descending according to SOC and preferred term.
14.3.1.3	Adverse Events - MedDRA (Preferred Term at least (>=) 2%) (Safety Population)	Summary containing the number and percentage of subjects experiencing AEs. AEs are tabulated by PT, and summarized by treatment. The summary will be presented in descending according to the preferred term.
14.3.1.4	Adverse Events By Intensity - MedDRA (Safety Population)	The same tabulation as 14.3.1.2 will be created for AEs by intensity.
14.3.1.5	Adverse Events By Relationship To Study Medication - MedDRA (Safety Population)	The same tabulation as 14.3.1.2 will be created for AEs by relationship to study medication.
14.3.1.6	Serious Adverse Events - MedDRA (Safety Population)	Summary containing the number and percentage of subjects experiencing SAEs. SAEs are tabulated by SOC and PT, and summarized by treatment. The summary will be presented in descending according to SOC and preferred term.
14.3.1.7	Serious Adverse Events By Intensity - MedDRA (Safety Population)	The same tabulation as 14.3.1.6 will be created for SAEs by intensity.
14.3.1.8	Serious Adverse Events By Relationship To Study Medication - MedDRA (Safety Population)	The same tabulation as 14.3.1.6 will be created for SAEs by relationship to study medication.
14.3.1.9	Adverse Drug Reactions - MedDRA (Safety Population)	Summary containing the number and percentage of subjects experiencing ADRs. ADRs are tabulated by SOC and PT, and summarized by treatment. The summary will be presented in descending according to SOC and preferred term.

Section	Title	Notes
14.3.1.10	Adverse Drug Reactions By Intensity - MedDRA (Safety Population)	The same tabulation as 14.3.1.9 will be created for ADRs by intensity.
14.3.2.1	Listing of Subjects with AEs Leading to Death (Safety Population)_1/3	Listing all AEs leading to death.
14.3.2.2	Listing of Subjects with AEs Leading to Death (Safety Population)_2/3	Listing all AEs leading to death.
14.3.2.3	Listing of Subjects with AEs Leading to Death (Safety Population)_3/3	Listing all AEs leading to death.
14.3.2.4	Listing of Subjects with Serious AEs (Safety Population)_1/3	Listing all the subjects with Serious AEs.
14.3.2.5	Listing of Subjects with Serious AEs (Safety Population)_2/3	Listing all the subjects with Serious AEs.
14.3.2.6	Listing of Subjects with Serious AEs (Safety Population)_3/3	Listing all the subjects with Serious AEs.
14.3.2.7	Listing of Subjects with AEs Leading to Premature Discontinuation of the Study Medication (Safety Population)_1/3	Listing the subjects who withdraw due to AEs.
14.3.2.8	Listing of Subjects with AEs Leading to Premature Discontinuation of the Study Medication (Safety Population)_2/3	Listing the subjects who withdraw due to AEs.
14.3.2.9	Listing of Subjects with AEs Leading to Premature Discontinuation of the Study Medication (Safety Population)_3/3	Listing the subjects who withdraw due to AEs.
14.3.4	Abnormal Laboratory Values (Safety Population)	Listing all the clinical significant abnormalities results for Blood Analyses and Urinalysis.
14.3.5.1	Summary of Cigarette Consumption (Safety Population)	Summary containing the number and percentage of subject questionnaire regarding the cigarette consumption by time point, per treatment and cohort.
14.3.5.2	Summary of Alcohol Intake (Safety Population)	Summary containing the number and percentage of subject questionnaire regarding the alcohol intake by time point, per treatment and cohort.

10.3 List of Subject Data Listings

All listings mentioned here will be presented according to ICH guidelines in Appendix 16.2 of the report. A complete document ("batch load") will be created in Word for the Medical Writer, in the order and with section number and title as stated.

16.2 Subject data listings
16.2.1 Discontinued subjects
16.2.2 Protocol deviations
16.2.3 Subjects excluded from the efficacy analysis
16.2.4 Demographic data
16.2.5 Compliance and/or drug concentration data
16.2.6 Individual efficacy response data
16.2.7 Adverse event listings
16.2.8 Listing of individual laboratory measurements by subject
16.4 Individual Subject Data Listing

Individual listings will be prepared of all the data collected in the database. No combining of data other than mentioned in this paragraph will be performed. Listings will be presented per treatment/sequence. The key variables in all listings will be subject number and treatment/sequence. If applicable, period/visit number, day and time point will be listed additionally. For AE data, duration and time to onset will be added.

Section	Title	Notes
16.2.1.1	Subject Disposition (Date of Visit) (All Enrolled Subjects)	
16.2.1.2	Subject Disposition (Study Completion/ Study Discontinuation) (All Enrolled Subjects)_1/2	
16.2.1.3	Subject Disposition (Study Completion/ Study Discontinuation) (All Enrolled Subjects)_2/2	
16.2.1.4	Subject Disposition (Follow Up - Evaluation) (All Enrolled Subjects)	
16.2.1.5	Eligibility (All Enrolled Subjects)	
16.2.2	Protocol Deviation (All Enrolled Subjects)	
16.2.3	Subjects Excluded from Analysis (All Enrolled Subjects)	Reason for excluded from full analyses set and safety population.
16.2.4.1	Individual Subject Demographics (All Enrolled Subjects)	
16.2.4.2	Medical/Surgery History (All Enrolled Subjects)	Including MedDRA coding
16.2.4.3	Psoriasis History (All Enrolled Subjects)	
16.2.5.1	Study Drug Administration (All Enrolled Subjects)	

Section	Title	Notes
16.2.5.2	Anti-Psoriatic Medications (All Enrolled Subjects)	Including WHO-DD coding
16.2.5.3	Non Psoriatic Medications (All Enrolled Subjects)	Including WHO-DD coding
16.2.5.4	Anti-Psoriatic Non-Medication Therapies (All Enrolled Subjects)	Including MedDRA and WHO-DD coding
16.2.5.5	Non Psoriatic Non-Medication Therapies (All Enrolled Subjects)	
16.2.6.1	Physician's Assessments - Psoriasis Area and Severity Index (PASI) (All Enrolled Subjects)	
16.2.6.2	Physician's Assessments - Body Surface Area (BSA) (All Enrolled Subjects)	
16.2.6.3	Physician's Assessments - Physician's Global Assessment (PGA) (All Enrolled Subjects)	
16.2.6.4	Physician's Assessments - Satisfaction with Tildrakizumab Therapy (All Enrolled Subjects)	
16.2.6.5	Patient's Questionnaires - Dermatology Life Quality Index (DLQI) (All Enrolled Subjects)	
16.2.6.6	Patient's Questionnaires - VAS (All Enrolled Subjects)	
16.2.6.7	Treatment Satisfaction Questionnaire for Medication (All Enrolled Subjects)	
16.2.6.8	Patient's Questionnaires - Physical Activity (All Enrolled Subjects)	
16.2.6.9	Patient's Questionnaires - Food Intake (All Enrolled Subjects)_1/2	
16.2.6.10	Patient's Questionnaires - Food Intake (All Enrolled Subjects)_2/2	
16.2.6.11	Individual Subject Physical Examination (All Enrolled Subjects)	
16.2.6.12	Individual Subject Blood Analyses (All Enrolled Subjects)	
16.2.7.1	Individual Subject Adverse Events (All Enrolled Subjects)_1/3	Including MedDRA coding
16.2.7.2	Individual Subject Adverse Events (All Enrolled Subjects)_2/3	Including MedDRA coding
16.2.7.3	Individual Subject Adverse Events (All Enrolled Subjects)_3/3	Including MedDRA coding
16.2.7.4	Individual Subject Adverse Drug Reactions (All Enrolled Subjects)_1/3	Including MedDRA coding

Section	Title	Notes
16.2.7.5	Individual Subject Adverse Drug Reactions (All Enrolled Subjects)_2/3	Including MedDRA coding
16.2.7.6	Individual Subject Adverse Drug Reactions (All Enrolled Subjects)_3/3	Including MedDRA coding
16.2.8	Clinical Laboratory Tests - Urinalysis (All Enrolled Subjects)	
16.4.1.1	Patient's Questionnaires - Cigarette Consumption, Alcohol Intake (All Enrolled Subjects)_1/2	
16.4.1.2	Patient's Questionnaires - Cigarette Consumption, Alcohol Intake (All Enrolled Subjects)_2/2	