CONFIDENTIAL

STATISTICAL ANALYSIS PLAN

A multicenter, open label, single-arm pilot study to evaluate the efficacy and safety of oral apremilast in patients with moderate to severe palmoplantar pustulosis (PPP) (APLANTUS)

Sponsor Study Code: AP-CL-PSOR-PI-006639

TFS Project Code: DHM1002

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TABLE OF CONTENTS

1 INTRODUCTION 5
2 STUDY OBJECTIVES 5
2.1 Primary Objective 5
2.2 Secondary Objective(s) 5
3 EFFICACY AND EXPLORATORY ENDPOINTS 6
3.1 Primary Efficacy Endpoint 6
3.2 Secondary Efficacy Endpoints 6
3.3 Exploratory Endpoints 6
4 OVERALL STUDY DESIGN 7
4.1 Overview of Study Design 7
4.2 Determination of Sample Size 9
5 DATA SETS TO BE ANALYSED 9
6 STATISTICAL AND ANALYTICAL PLANS 9
6.1 Changes in the Planned Analyses 9
6.2 Data Review 10
6.3 Hypotheses and Statistical Methods 10
6.3.1 Definitions 10
6.3.2 Summary Statistics 14
6.3.3 Patient Data Listings 14
6.3.4 Demographic and Other Baseline Characteristics 14
6.3.5 Primary Efficacy analysis 15
6.3.6 Secondary Efficacy Analyses 16
6.3.7 Exploratory Analyses 16
6.3.8 Exposure to Treatment 16
6.3.9 Prior and Concomitant Medications 16
6.3.10 Adverse Events (AEs) 17
6.3.11 Other Safety Assessments 18
6.4 Level of Significance, Multiple Comparisons and Multiplicity 18
6.5 Adjustment for Covariates 18
6.6 Handling of Dropouts and Missing Data 18
6.7 Examination of Subgroups 18
6.8 Interim Analysis 18
6.9 Data Monitoring 19
7 APPENDIX 1 19
7.1 Tables to be Produced for the Clinical Study Report (Section 14 according to ICH E3) 19
7.2 Listings of Individual Patient Data and Other Information to be Produced for the Clinical Study Report (Sections 16.1 and 16.2 in ICH E3) 22

ABBREVIATIONS

AE	Adverse Event
ATC	Anatomic-Therapeutically-Chemical
BMI	Body Mass Index
CRF	Case Report Form
CSP	Clinical Study Protocol
CSR	Clinical Study Report
DLQI	Dermatology Life Quality Index
FAS	Full Analysis Set
H&F PGA	Hand and Feet Physician Global Assessment
LOCF	Last-Observation-Carried-Forward
LP	Left Palm
LS	Left Sole
Max	Maximum
MedDRA	Medical Dictionary for Regulatory Activities
Min	Minimum
PASI	Psoriasis Area and Severity Index
PGA	Physician Global Assessment
PPP	Palmoplantar Pustulosis
PPPASI	Palmoplantar Pustulosis Psoriasis Area and Severity Index
PPPASI 50 / 75	50% / 75% decrease in PPPASI
PPS	Per Protocol Set
PRTC	Psoriasis Research and Treatment Center
PT	Preferred Term
Q1	First Quartile
Q3	Third Quartile
RP	Right Palm
RS	Right Sole
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
VAS	Visual Analogue Scale
WHO	World Health Organization

1 INTRODUCTION

This Statistical Analysis Plan (SAP) is based on Clinical Study Protocol (CSP) Version Final 3.0, dated June 07th, 2018.

2 STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this study is:

- To demonstrate a significant improvement of Palmoplantar Pustulosis Psoriasis Area and Severity Index (PPPASI) at week 20 compared with baseline in moderate to severe chronic palmoplantar pustulosis under apremilast therapy

2.2 Secondary Objective(s)

The secondary objectives of the study are:

- To evaluate an improvement of PPPASI at all assessment times compared with baseline in moderate to severe chronic palmoplantar pustulosis under apremilast therapy
- To evaluate differences in life quality assessment measures during treatment with apremilast: Dermatology Life Quality Index (DLQI) at all assessment times compared with baseline
- To evaluate safety of apremilast in patients with moderate to severe palmoplantar pustulosis

Exploratory objectives are:

- Time course of Hand and Feet Physician Global Assessment (H&F PGA) at all assessment times
- Pustules count 50 response and Pustules count 75 response, defined as a 50% and 75% decrease in pustules count from baseline, during the 20 weeks treatment period
- To evaluate differences of Visual Analogue Scale (VAS) pruritus / itch, VAS discomfort / pain in the mean change from baseline at all assessment times relatively to day 0 (baseline)
- To evaluate changes in Psoriasis Area Severity Index (PASI), Physician Global Assessment (PGA) and dynamic H&F PGA if plaque psoriasis is present between baseline and all assessment times
- To explore the effect of apremilast on immunological markers in serum / plasma

- To explore the effect of apremilast on immunological markers in skin biopsies (sub-study*)

* Skin biopsy samples will be collected in an optional (voluntary) exploratory sub-study to explore the effect of apremilast on levels of immunological markers in skin and/or PPP-specific alterations (separate Informed Consent Form will be required). Details on this sub-study, which will be performed separately from the main study by Dr. Sabat (Psoriasis Research and Treatment Center (PRTC)) and colleagues, will be outlined in a separate document and will not be included in the Clinical Study Report (CSR).

3 EFFICACY AND EXPLORATORY ENDPOINTS

3.1 Primary Efficacy Endpoint

- Percentage change from baseline in PPPASI after 20 weeks of treatment with apremilast

3.2 Secondary Efficacy Endpoints

- Absolute and percent change from baseline in PPPASI during the 20 weeks treatment period with apremilast
- PPPASI 50 response and PPPASI 75 response, defined as a 50% and 75% decrease in PPPASI from baseline, during the 20 weeks treatment period with apremilast
- DLQI bands (0-1 no effect, 2-5 small effect, 6-10 moderate effect, 11-20 very large effect, 21-30 extremely large effect) during the 20 weeks treatment period
- Absolute and percent change from baseline in DLQI during the 20 weeks treatment period
- Safety as assessed by Treatment-Emergent Adverse Events (TEAEs), vital signs and physical examination

3.3 Exploratory Endpoints

- Absolute and percentage change from baseline in level of immunological markers in plasma / serum during the 20 weeks treatment period with apremilast
- Percentage change from baseline in level of immunological markers in skin biopsy samples after 20 weeks of treatment with apremilast (sub-study)

4 OVERALL STUDY DESIGN

4.1 Overview of Study Design

This is a multicenter, open-label, single-arm, phase II, pilot study to evaluate the efficacy and safety of apremilast involving approximately 20 patients with PPP. The screening period is up to 4 weeks and treatment takes place over 20 weeks per patient. No follow up period takes place. No extension is planned.

Recruitment period is 4 months; hence, study duration from FPI to LPO is approx. 9 months. 4 patients per site are expected to be recruited, assuming enrolment of both genders with distribution according to prevalence of condition. If recruitment is not running as anticipated after 2 months, recruitment will be opened to become competitive.

Patient recruitment will take place at approximately 5 sites in Germany. The investigators should have relevant expertise in diagnosing and treating PPP or be specialized in dermatology. Patients will be enrolled until 20 patients are included into the study. Drop-outs will not be replaced.

Five visits per patients are planned including:
Visit 1 at week -4 - -1 (screening)
Visit 2 at week 0 (baseline)
Visit 3 at week 4
Visit 4 at week 12
Visit 5 at week 20 (end of study)

Please refer to the Study Flow Chart below for the time schedule of the assessments.

Study Flow Chart

Phase	**Screening**	**Treatment Phase**				
Visits	V1	V2 Baseline	V3	V4	V5 End of Study	Early Termi-nation
Week	-4 - -1	0	4	12	20	
Day	-28 - -1	0	28 ± 4	84 ± 4	140 ± 7	
In- / exclusion criteria	X	x	-	-	-	-
Pregnancy test[1]	X	x	x	x	x	x
Informed consent	X	-	-	-	-	-

Demography, educational status	X	-	-	-	-	-
Medical and psoriasis history, prior medication	X	-	-	-	-	-
PsA, comorbidity	X	x	-	x	x	x
Concomitant medications	X	x	x	x	x	x
Nicotine anamnesis	X	-	-	-	x	-
Physical examination incl. weight and height[2] (BMI)	X	x	-	-	x	x
Vital signs[3]	X	x	x	x	x	x
Results of routine blood test / urinalysis available[4]	X	-	-	-	-	-
Investigator assessments						
PASI	-	x	x	x	x	x
PPPASI	x[5]	x	x	x	x	x
PGA	-	x	x	x	x	x
H&F PGA	-	x	x	x	x	x
Dynamic H&F PGA	-		x	x	x	x
Pustules count	-	x	x	x	x	x
Patient reported outcomes						
VAS (pruritus / itch and discomfort / pain) on hands and feet	-	x	x	x	x	x
DLQI	-	x	-	x	x	-
Photographs[6] (optional)	-	x	-	-	x	-
Serum and plasma	-	x	x	x	x	x
Biopsies[7] (optional sub-study)	-	x	-	-	x	x
Documentation for drug accountability and treatment compliance	-	x	x	x	x	x
Medication dispensing[8]	-	x	x	x	-	-
Return of study medication	-	-	x	x	x	x
AEs / SAEs	X	x	x	x	x	x
Reason for discontinuation						x

1. Urine pregnancy test for female patients of childbearing potential
2. Only at V1: height
3. Sitting blood pressure and pulse rate
4. Within the ranges given in the exclusion criteria **not older than 8 weeks** prior to screening
5. For inclusion PPPASI must be ≥ 12

6. From both hands and feet (optional)
7. Two lesional biopsies from feet or hands (optional)
8. Including instructions for medication intake

AE / SAE	Adverse Event / Serious Adverse Event
BMI	Body Mass Index
DLQI	Dermatology Life Quality Index
H&F PGA	Hand and Feet Physician Global Assessment
PASI	Psoriasis Area and Severity Index
PGA	Physician's Global Assessment
PPPASI	Palmoplantar Pustulosis Psoriasis Area and Severity Index
PsA	Psoriasis Arthritis
V	Visit
VAS	Visual Analogue Scale

After completion of participation in the study, patients are advised to follow medical management of their treating physician.

4.2 Determination of Sample Size

This is a pilot study intended to gain first data on the effects of apremilast on PPP; therefore the sample size is not based on statistical considerations.

5 DATA SETS TO BE ANALYSED

The following analysis sets will be used for the statistical analysis and presentation of data:

- **The full analysis set (FAS)** will consist of all patients who received at least one dose of study drug.
- **The per protocol set (PPS)** will consist of all patients who received at least one dose of study drug who completed the study with no major protocol violations.

The definition of the PPS set will be finalized in the data review meeting prior to database closure.

The FAS and PPS will be used for analyses of efficacy endpoints. Since the FAS consists of all patients who received at least one dose of study drug, the FAS will additionally serve as safety analysis set and will be used for analysis of safety endpoints.

6 STATISTICAL AND ANALYTICAL PLANS

The planned tables and listings are presented in APPENDIX 1.

6.1 Changes in the Planned Analyses

Any changes in the statistical analyses (if needed) once the SAP has been finalised and the database has been locked should be documented in a file note and in the CSR.

6.2 Data Review

Before database lock, a data review meeting will take place. During this meeting, study data will be reviewed and final decisions regarding protocol violations and analysis populations will be taken. The content of this meeting will be described in a separate document outside of this SAP.

6.3 Hypotheses and Statistical Methods

6.3.1 Definitions

- Baseline

The assessments performed at Visit 2 (Day 0) will be considered the baseline values. For variables that are measured at Visit 1 and not at Visit 2, e.g. demography and educational status, baseline is defined as Visit 1 (Day -28 - -1).

- First intake of study drug

Date of Visit 2 +1 will be considered as the date of the first intake of study drug.

- Body mass index (BMI)

BMI will be calculated as:

$$\text{BMI (kg/m}^2\text{)} = \text{weight (kg)} / (\text{height (m)})^2$$

- Percentage change from baseline

Percentage change from Baseline at Visit x is defined as:

$$(\text{Visit x} - \text{Baseline}) / \text{Baseline}$$

- Absolute change from baseline

Absolute change from Baseline at Visit x is defined as:

$$\text{Visit x} - \text{Baseline}$$

- PPPASI

To be assessed by the investigator:

The severity of the disease is calculated by scoring the signs of the disease (erythema, pustules and scaling) for each of the following 4 body-regions: Right Palm (RP), Left Palm (LP), Right Sole (RS) and Left Sole (LS). The scoring system for the signs of the disease is: 0 = none, 1 = slight, 2 = moderate, 3 = severe, 4 = very severe.

The scale for estimating the area of involvement for psoriatic lesions is outlined below.

0 = No involvement

1 = 1% to 9% involvement

2 = 10% to 29% involvement

3 = 30% to 49% involvement

4 = 50% to 69% involvement

5 = 70% to 89% involvement

6 = 90% to 100% involvement

Body region	**Erythema (E)**	**Pustules / (P) vesicles**	**Scaling (D) (desquamation)**	**Area score (A) (based on true Area %) ***
Right palm (RP)	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = no Involvement 1 = >0 - < 10% 2 = 10 - <30% 3 = 30 - <50% 4 = 50 - <70% 5 = 70 - <90% 6 = 90 - 100%
Left palm (LP)	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = no Involvement 1 = >0 - < 10% 2 = 10 - <30% 3 = 30 - <50% 4 = 50 - <70% 5 = 70 - <90% 6 = 90 - 100%
Right sole (RS)	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = no Involvement 1 = >0 - < 10% 2 = 10 - <30% 3 = 30 - <50% 4 = 50 - <70% 5 = 70 - <90% 6 = 90 - 100%
Left sole (LS)	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = none 1 = slight 2 = moderate 3 = severe 4 = very severe	0 = no Involvement 1 = >0 - < 10% 2 = 10 - <30% 3 = 30 - <50% 4 = 50 - <70% 5 = 70 - <90% 6 = 90 - 100%

The PPPASI score is calculated using the formula:

PPPASI = 0.2 (ERP + PRP + DRP) ARP + 0.2 (ELP + PLP + DLP) ALP + 0.3 (ERS + PRS + DRS) ARS + 0.3 (ELS + PLS + DLS) ALS

- PPPASI 50

PPPASI 50 is defined as:

Yes: if Visit x ≤ Baseline / 2

No: if Visit x > Baseline / 2

- PPPASI 75

PPPASI 75 is defined as:

Yes: if Visit x ≤ Baseline / 4

No: if Visit x > Baseline / 4

- DLQI

To be filled out by the patient:

The Dermatology Life Quality Index or DLQI, developed in 1994, was the first dermatology-specific Quality of Life instrument. It is a simple 10-question validated questionnaire which has been used in 33 different skin conditions in 33 countries and is available in 85 languages. Its use has been described in over 800 publications including many multinational studies. It is a validated questionnaire. At present the DLQI is the most frequently used instrument in studies of randomized controlled studies in dermatology. (http://www.dermatology.org.uk/quality/dlqi/quality-dlqi.html, accessed 17-JUN-2011). The DLQI is validated for use in patients with PPP (https://www.ncbi.nlm.nih.gov/pubmed/28541870).

The DLQI questionnaire is designed for use in adults, i.e. patients over the age of 16. It is self-explanatory and is handed to the patient who is asked to fill it in without the need for detailed explanation. It addresses the disease-related quality of life over the last 7 days.

The questionnaire contains the following questions:

1. Over the last week, how itchy, sore, painful or stinging has your skin been?
2. Over the last week, how embarrassed or self-conscious have you been because of your skin?

3. Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?
4. Over the last week, how much has your skin influenced the clothes you wear?
5. Over the last week, how much has your skin affected any social or leisure activities?
6. Over the last week, how much has your skin made it difficult for you to do any sport?
7. Over the last week, has your skin prevented you from working or studying?
   If 'No', over the last week how much has your skin been a problem at work or studying?
8. Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives?
9. Over the last week, how much has your skin caused any sexual difficulties?
10. Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?

Scoring

The scoring of each question is as follows:

Very much	scored 3
A lot	scored 2
A little	scored 1
Not at all	scored 0
Not relevant	scored 0
Question unanswered	scored 0
Question 7: 'prevented work or studying'	scored 3

The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.

Meaning of DLQI Scores

0 to 1	=	no effect at all on patient's life
2 to 5	=	small effect on patient's life
6 to 10	=	moderate effect on patient's life
11 to 20	=	very large effect on patient's life
21 to 30	=	extremely large effect on patient's life

Interpretation of incorrectly completed questionnaires

There is a very high success rate of accurate completion of the DLQI. However, sometimes patients do make mistakes.

- If one question is left unanswered this will be scored 0 and the scores will be summed and expressed as usual out of a maximum of 30.
- If two or more questions are left unanswered the questionnaire will not be scored.
- If question 7 is answered 'yes' this will be scored 3. If question 7 is answered 'no' or 'not relevant' but then either 'a lot' or 'a little' is ticked this will then be scored 2 or 1.
- If two or more response options are ticked, the response option with the highest score will be recorded.
- If there is a response between two tick boxes, the lower of the two score options will be recorded.

6.3.2 Summary Statistics

Data will be summarised by means of summary statistics. For continuous data the following summary statistics will be presented: number of observations, number of missings, mean, standard deviation (SD), minimum (Min), first quartile (Q1), median, third quartile (Q3) and maximum (Max). Categorical data will be summarized by the number and percentage of patients in each category. The percentages will be calculated based on the number of patients in the corresponding analysis set.

6.3.3 Patient Data Listings

Data collected in the Case Report Form (CRF) will generally be listed in Appendix 16.2 (see section 7.2). CRF check questions [e.g. Lab samples taken (Yes/No)] and reminders will not be listed.

Listings will be sorted by study centre and patient number.

6.3.4 Demographic and Other Baseline Characteristics

The analyses of patient demographic data will be presented for the FAS and PPS. Other baseline characteristics including medical history will be based on the FAS.

Patient disposition, demographic data and other baseline data will be presented using summary statistics.

<u>Patient disposition</u>

Number and percentage of patients enrolled, patients treated, patients on follow-up at each study visit, patients completed, patients who discontinued the study and the reasons for discontinuation together with date of first screening visit and date of last contact/study termination will be summarized for all screened patients, and study populations and inclusion and exclusion criteria will be summarised for all enrolled patients.

Demographic data

The following demographic data will be summarized: age (years), sex and its nested variable, ethnicity, highest educational and smoking status.

Psoriasis history

Descriptive statistics for the following psoriasis data will be provided: age at initial diagnosis of psoriasis (years), age of initial diagnosis of PPP (years), current involvement of scalp, current involvement of nails and its nested variables, psoriatic arthritis and its nested variables, and parallel occurrence of other psoriasis forms at the same time?

Prior psoriasis medication

Prior psoriasis medication will be coded according to World Health Organization (WHO) Anatomic-Therapeutically-Chemical (ATC) classification. The data will be summarized by ATC class 2 (therapeutic main group) and ATC class 3 (pharmacological sub-group) and by kind of therapy, ATC class 2 and ATC class 3, together with the number of patients with at least one prior psoriasis medication.

Medical history

Medical history will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA). The data will be summarized by System Organ Class (SOC) and by Preferred Term (PT).

Comorbidity

Any changes of the coexisting forms of psoriasis and its nested variables will be analysed with descriptive statistics by visit.

6.3.5 Primary Efficacy analysis

The primary endpoint, percentage change from baseline in PPPASI after 20 weeks of treatment with apremilast, will be summarized descriptively as continuous variable together

with 95%-confidence limits. Statistical comparison between post- versus pre-treatment values will be done based on the Wilcoxon signed-rank test with two-sided p-value <0.05 indicating significance. Missing values will be replaced using Last-Observation-Carried-Forward (LOCF) method for the analysis of the primary endpoint based on the FAS.

The analysis of the primary endpoint will be repeated for the PP set, this analysis will be considered as supportive.

6.3.6 Secondary Efficacy Analyses

Analyses of secondary efficacy endpoints will be based on the FAS and PPS.
Summary statistics will be provided for the secondary efficacy endpoints which are defined as follows:

- Absolute PPPASI at each study visit (baseline, 4 weeks, 12 weeks and 20 weeks), together with absolute change and percent change (with 95%-confidence limits) from baseline at 4 weeks, 12 weeks and 20 weeks
- PPPASI 50 response and PPPASI 75 response, defined as a 50% and 75% decrease in PPPASI from baseline, during the 20 weeks treatment period
- DLQI bands (0-1 no effect, 2-5 small effect, 6-10 moderate effect, 11-20 very large effect, 21-30 extremely large effect on the disease related quality of life) during the 20 weeks treatment period
- Absolute DLQI at each study visit (baseline, 4 weeks, 12 weeks and 20 weeks), together with absolute change and percent change (with 95%-confidence limits) from baseline at 4 weeks, 12 weeks and 20 weeks

6.3.7 Exploratory Analyses

Exploratory analyses will not be part of statistical analyses and will be analyzed outside of the study setting by Robert Sabat Charite, Berlin.

6.3.8 Exposure to Treatment

The variables of modules: return of medication, dispense of medication, dosing and treatment compliance assessment, will be summarized descriptively by visit.

6.3.9 Prior and Concomitant Medications

Prior and concomitant medications will be coded according to WHO ATC classification.

Frequency tables for prior and concomitant medications will present the number and percentage of patients per ATC class 2 (therapeutic main group) and ATC class 3 (pharmacological sub-group).

Prior medications are defined as medications taken prior to first intake of study drug. Any medication given at least once after the first intake of study drug will be considered as concomitant medication. This means, a medication might be assigned to both, prior and concomitant medications. If no unambiguous assignment to prior and concomitant medication is possible due to incomplete or missing dates, the medication will be assigned to both, prior and concomitant medications.

6.3.10 Adverse Events (AEs)

All safety evaluations will be performed on the FAS.

AEs will be coded according to the MedDRA system.

TEAEs are defined as AEs which started after first intake of study drug. If no unambiguous assignment to treatment emergent is possible due to incomplete or missing dates, the AE will be considered as treatment emergent.

A summary table will be presented with No. of patients with TEAEs, No. of patients with serious TEAEs, No. of patients with related TEAEs, No. of patients with at least one TEAE leading to discontinuation, No. of patients with serious related TEAEs and also the number of TEAEs, serious TEAEs, related TEAEs, TEAEs leading to discontinuation and serious related TEAEs.

The total number of patients with at least one TEAE and the number of TEAEs will be derived and summarised by SOC and PT. A similar table will be created for serious TEAEs and TEAEs leading to discontinuation.

TEAEs will also be tabulated versus intensity and causality to study drug. If a patient has more than one event classified with the same preferred term, then the worst intensity and the worst relationship will be used. Similar tables will be created for serious TEAEs.

All AEs for each patient, including multiple occurrences of the same event, will be listed including additionally SOC and PT. Serious AEs and AEs leading to death or withdrawal will be listed separately in addition to the listing including all AEs. A separate listing for TEAEs leading to discontinuation will be provided.

6.3.11 Other Safety Assessments

All safety evaluations will be performed on the FAS.

Vital Signs

For all vital signs parameters (systolic and diastolic blood pressure and pulse rate), summary statistics will be provided by visit.

Physical Examination

Height, weight, BMI and numbers of values that are normal or abnormal will be tabulated by visit.

6.4 Level of Significance, Multiple Comparisons and Multiplicity

The level of significance will be 5%. No adjustment for multiple comparisons will be applied.

6.5 Adjustment for Covariates

Not applicable.

6.6 Handling of Dropouts and Missing Data

Missing values will be replaced using LOCF method for the analysis of the primary endpoint based on the FAS.

For all other analyses, missing values will not be replaced.

6.7 Examination of Subgroups

Not applicable.

6.8 Interim Analysis

There is no interim analysis planned.

6.9 Data Monitoring

No Data Monitoring Committee is planned.

7 APPENDIX 1

7.1 Tables to be Produced for the Clinical Study Report (Section 14 according to ICH E3)

(Table numbers refer to section numbers in ICH E3)

14.1 DEMOGRAPHIC DATA

14.1.1	Patient Disposition. All screened patients.
14.1.2	Study populations. All enrolled patients.
14.1.3	Inclusion and exclusion criteria. All enrolled patients.
14.1.4	Demographic data. FAS and PPS population.
14.1.5	Psoriasis history. FAS population.
14.1.6.1	Prior psoriasis medication. FAS population.
14.1.6.2	Prior psoriasis medication by kind of therapy. FAS population.
14.1.7	Medical history. FAS population.
14.1.8	Comorbidities by visit. FAS population.

14.2 EFFICACY DATA

Primary efficacy analysis

14.2.1.1	Percentage change from baseline in PPPASI after 20 weeks of treatment with apremilast. Descriptive statistics and Wilcoxon signed-rank test.

FAS population.

14.2.1.2 Percentage change from baseline in PPPASI after 20 weeks of treatment with apremilast.

Descriptive statistics and Wilcoxon signed-rank test.

FAS (LOCF) population.

14.2.1.3 Percentage change from baseline in PPPASI after 20 weeks of treatment with apremilast.

Descriptive statistics and Wilcoxon signed-rank test.

PPS population.

Secondary efficacy analysis

14.2.2 Absolute PPPASI at each study visit. Absolute and percent change from baseline in PPPASI by visit.

Descriptive statistics and 95% CI

FAS and PPS population.

14.2.3 PPPASI 50 response by visit.

Descriptive statistics.

FAS and PPS population.

14.2.4 PPPASI 75 response by visit.

Descriptive statistics.

FAS and PPS population.

14.2.5 DLQI bands (0-1 no effect, 2-5 small effect, 6-10 moderate effect, 11-20 very large effect, 21-30 extremely large effect on the disease related quality of life) by vist.

Descriptive statistics.

FAS and PPS population.

14.2.6 Absolute DLQI at each study visit. Absolute and percent change from baseline in DLQI by visit.

Descriptive statistics and 95% CI.

FAS and PPS population.

14.3 SAFETY DATA

14.3.1.1 Summary of TEAEs.

FAS population.

14.3.1.2 TEAEs by SOC and PT.
FAS population.

14.3.1.3 Serious TEAEs by SOC and PT.
FAS population.

14.3.1.4 TEAEs leading to discontinuation by SOC and PT.
FAS population.

14.3.1.5 TEAEs by SOC and PT stratified by intensity.
FAS population.

14.3.1.6 TEAEs by SOC and PT stratified by causality.
FAS population.

14.3.1.7 Serious TEAEs by SOC and PT stratified by intensity.
FAS population.

14.3.1.8 Serious TEAEs by SOC and PT stratified by causality.
FAS population.

14.3.2.1 Listings of Deaths, Other Serious and Significant Treatment Emergent Adverse Events.
FAS population.

14.3.2.2 Listing of Treatment Emergent Adverse Events leading to discontinuation.
FAS population.

14.3.5.1 Return of medication by visit.
FAS population.

14.3.5.2 Dispense of medication by visit.
FAS population.

14.3.5.3 Dosing by visit.
FAS population.

14.3.5.4 Treatment compliance assessment by visit.
FAS population.

14.3.6 Vital signs by visit.
FAS population.

14.3.7 Physical examination by visit.
FAS population.

14.3.8.1 Prior medications.
FAS population.

14.3.8.2 Concomitant medications.
FAS population.

7.2 Listings of Individual Patient Data and Other Information to be Produced for the Clinical Study Report (Sections 16.1 and 16.2 in ICH E3)

(Listing numbers refer to the relevant appendix number in ICH E3. CRF check questions/reminders will not be listed.)

16.2.1.1 Discontinued patients, reason for discontinuation

16.2.1.2 Visit dates and other important dates (informed consent, first intake of study drug, last day on study and last dose of Apremilast)

16.2.2 Protocol deviations

16.2.3 Patients excluded from the analysis populations with reasons for exclusion

16.2.4.1 Demographic data

16.2.4.2 Nicotine anamnesis

16.2.4.3 Psoriasis history

16.2.4.4 Prior psoriasis medication

16.2.4.5 Medical history

16.2.4.6 Inclusion criteria not met and exclusion criteria met

16.2.4.7 Urine pregnancy test

16.2.5.1 Return of medication and dispense of medication and dosing

16.2.5.2 Treatment compliance assessment

16.2.6.1 PPPASI

16.2.6.2 DLQI

16.2.7 Adverse events

16.2.9 Vital signs

16.2.10 Physical examination

16.2.12 Prior and concomitant medication