STATISTICAL ANALYSIS PLAN (SAP)

NCT05439941

A LONG-TERM EXTENSION TRIAL IN PARTICIPANTS WITH ATOPIC DERMATITIS WHO PARTICIPATED IN PREVIOUS PHASE 2 AND 3 EDP1815 TRIALS

SAP EDP1815-208

VERSION 2.0 / 07 JUNE 2023

STATISTICAL ANALYSIS PLAN

Protocol: EDP1815-208

Protocol Version: V4.0 16MAY2022

A Long-Term Extension Trial in Participants with Atopic Dermatitis who Participated in Previous Phase 2 and Phase 3 EDP1815 Trials

SAP/Amendment Number	Date
Final SAP v1.0	16 Jan 2023
Final SAP v2.0	07 Jun 2023

Prepared for: Evelo Biosciences Inc.

Prepared by: [redacted]

Approved by	Signature	Date
[redacted] Clinical Lead, Evelo Biosciences Inc.	[redacted]	
[redacted] Director of Statistics, Evelo Biosciences Inc.	[redacted]	
[redacted] Lead Statistician, [redacted]	[redacted]	

[redacted]

1 Table of Contents

Table of Tables

Table of Figures

2 Abbreviations and Definitions

AD	Atopic Dermatitis
ADaM	Analysis Dataset Model
ADCT	Atopic Dermatitis Control Tool
AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BL	Baseline
BP	Blood Pressure
BSA	Body Surface Area
CRF	Case Report form
CRO	Contract Research Organization
CTCAE	Common Terminology Criteria for Adverse Events
DLQI	Dermatology Life Quality Index
dp	Decimal Place
DPS	Data Point Set
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EASI	Eczema Area and Severity Index
EudraCT	European Union Drug Regulating Authorities Clinical Trials
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IgE	Immunoglobulin E
IMP	Investigational Medicinal Product
IRT	Interactive Response Technology
JAK	Janus Kinase
LS	Least Squares Mean Estimate
mL	Millilitre
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed Model for Repeated Measures
OLE	Open-Label Extension
PCI	Potentially clinically important
PDE	Phosphodiesterase
POEM	Patient Oriented Eczema Measure
PP-NRS	Peak Pruritus Numerical Rating Scale
PRO	Patient Reported Outcome
PT	Preferred Term
RNA	Ribonucleic Acid
SAE	Serious Adverse Event

SAP	Statistical Analysis Plan
SCORAD	Severity Scoring of Atopic Dermatitis (SCORing Atopic Dermatitis)
SD-NRS	Sleep Disturbance Numerical Rating Scale
SDTM	Standard Data Tabulation Model
SOC	System Organ Class
TCI	Topical Calcineurin Inhibitors
TCS	Topical Corticosteroids
ULN	Upper Limit of Normal
vIGA	Validated Investigator Global Assessment
WHODD	World Health Organization Drug Dictionary

3 Introduction

The purpose of this SAP is to provide all information that is necessary to perform the required statistical analyses of study EDP1815-208. It also defines the summary TFLs to be included in the final clinical study report according to the protocol. The SAP is based upon, and assumes familiarity, with the study protocol, version 4.0, dated 16-MAY-2022. This SAP only covers EDP1815-207 study as the possible parent study.

Changes from the analyses described in the protocol are summarised in Section 14.

If a future protocol amendment necessitates a substantial change to the statistical analysis of the study data, this SAP will be amended accordingly. The content of this SAP is compatible with the ICH E9 Guidance document.

4 Study Objectives and Endpoints

4.1 Study Objectives

The primary objective of the study is:

- To evaluate the long-term safety and tolerability of EDP1815 in the treatment of atopic dermatitis

The secondary objective of the study is:

- To evaluate the efficacy of long-term treatment with EDP1815 in the treatment of atopic dermatitis

The exploratory objectives of the study are:

- To evaluate the time to onset of clinical response to EDP1815
- To evaluate other aspects of the efficacy of EDP1815 as a treatment for atopic dermatitis
- To evaluate the relationship of EDP1815 treatment with biomarkers such as immune protein markers and immune cell RNA profile in blood

4.2 Endpoints

The primary endpoints for the study are:

- The incidence and rate per 100 patient-years of treatment-emergent adverse events during the 36-week treatment and 4-week follow-up period
- The incidence and rate per 100 patient-years of treatment-emergent adverse events during the treatment period of this study and the relevant parent study

The secondary efficacy endpoints for the study will be evaluated at all scheduled visits (unless otherwise specified), with measures involving changes from baseline using the baseline assessment from the relevant EDP1815 parent study. The secondary endpoints are as follows:

- Percentage of participants achieving Eczema Area and Severity Index (EASI)-50
- Percentage of participants achieving EASI-75

- Percentage of participants achieving EASI-90
- Mean absolute change and percentage change from baseline in EASI Score
- Percentage of participants achieving Validated Investigator's Global Assessment (vIGA) of 0 or 1 with a ≥2-point improvement from baseline
- Percentage of participants achieving vIGA of 0 or 1
- Percentage of participants achieving vIGA of 0
- Mean absolute change and percentage change from baseline in vIGA*BSA (BSA=body surface area)
- Mean absolute change and percentage change from baseline in BSA
- Percentage of participants achieving BSA-50
- Percentage of participants achieving BSA-75
- Percentage of participants achieving BSA reduction to 3% BSA or less
- Mean absolute change and percentage change from baseline in SCORing Atopic Dermatitis (SCORAD) score
- Percentage of participants achieving SCORAD-35
- Percentage of participants achieving SCORAD-50
- Percentage of participants achieving SCORAD-75
- Mean absolute change and percentage change from baseline in Dermatology Life Quality Index (DLQI) score
- Percentage of Participants achieving a reduction of ≥4 in the DLQI score, of those with a score of ≥4 at baseline
- Mean absolute change from baseline in Peak Pruritus Numerical Rating Scale (PP-NRS) score
- Percentage of participants achieving a reduction of ≥2 in the PP-NRS, of those with a score of ≥2 at baseline
- Percentage of participants achieving a reduction of ≥4 in the PP-NRS, of those with a score of ≥4 at baseline
- Mean absolute change from baseline in Sleep Disturbance Rating Scale (SD-NRS) score
- Percentage of participants achieving a reduction of ≥2 in SD-NRS score, of those with a score of ≥2 at baseline
- Mean absolute change and percentage change from baseline in Patient Oriented Eczema Measure (POEM) score
- Percentage of participants achieving a reduction of ≥4 in the POEM score, of those with a score of ≥4 at baseline
- Number of courses per patient-year of any rescue medication (not including antibacterial therapy)
- Number of courses per patient-year of topical corticosteroids of any potency
- Number of courses per patient-year of topical tacrolimus (0.1%), topical pimecrolimus (1%) or grade VII topical corticosteroid
- Number of courses per patient-year of moderate potency (grade IV and V) topical steroids

The secondary safety endpoints for the study are:

- Adverse events and serious adverse events

- Change from baseline in vital signs
- Change from baseline in ECG parameters
- Change from baseline in clinical laboratory parameters
- Change from baseline in physical examination findings
- Worst-case change from baseline with respect to potentially clinical important criteria for vital signs, QTcF and clinical laboratory parameters
- Worst-case change from baseline with respect to values outside the normal ranges for clinical laboratory parameters

Exploratory endpoints to evaluate the time to onset of clinical response are:

- Time to first achievement of EASI-50
- Time to first achievement of sustained EASI-50

Other exploratory endpoints will used to evaluate other aspects of the efficacy of EDP1815 as a treatment for atopic dermatitis and are:

- Changes from baseline in Atopic Dermatitis Control Tool (ADCT) scores
- Mean absolute and percentage change in the four body region scores of the EASI
- Percentage of participants achieving at least a 50% reduction in each of the four body region scores of those with a non-zero score for the relevant region at baseline
- Percentage of participants who change response states from Day -1 to Weeks 8, 16, 24 and 36. Response states will be defined using the EASI score percentage change from baseline with categories for >= 25% increase, no change (<25% increase to <25% decrease), 25% to <50% decrease, 50% to <75% decrease, 75% decrease to <90% decrease, >= 90% decrease
- Daily mean absolute change from baseline in PP-NRS and SD-NRS scores

The following endpoints will be used to evaluate the relationship of EDP1815 treatment with biomarkers such as immune protein markers and immune cell RNA profile in blood. Note that analyses of these biomarkers exploratory endpoints will be addressed in a separate analysis plan and will not be further discussed in this document:

- Changes from baseline in serum immune protein markers including Immunoglobulin E (IgE)
- Changes from baseline in immune cell RNA profile

5 Study Methods

5.1 General Study Design and Plan

This is an Open-Label Extension (OLE), multicentre study to evaluate the long-term safety, tolerability and efficacy of EDP1815 in participants with mild, moderate and severe atopic dermatitis. Participants who have completed the 16-week treatment period in the EDP1815-207 parent study may be eligible to enrol in this study.

The doses administered in this study are the same as those administered in the EDP1815-207 parent study and are as follows:

- Group 1: $1.6x10^{11}$ total cells of EDP1815 administered as 2 capsules once daily
- Group 2: $6.4x10^{11}$ total cells of EDP1815 administered as 2 capsules once daily
- Group 3: $8.0x10^{10}$ total cells of EDP1815 administered as 1 capsule once daily

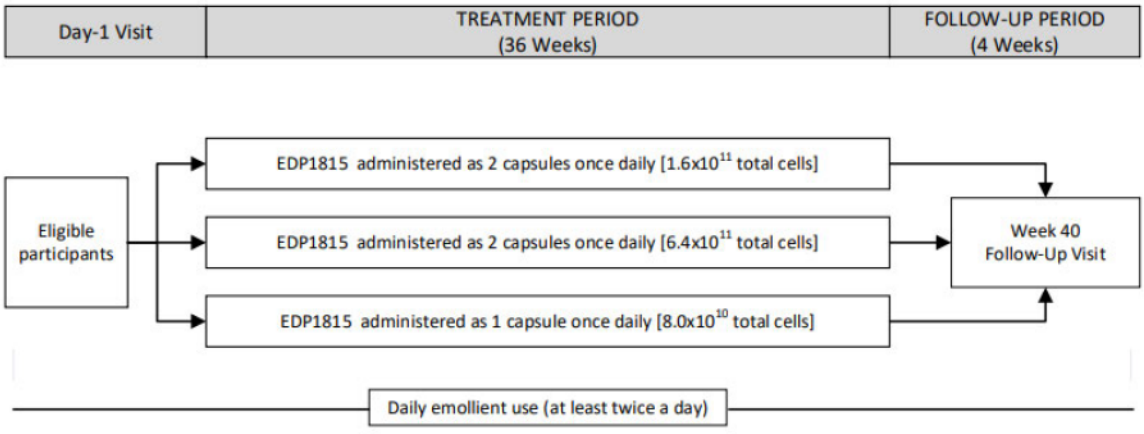
No placebo will be administered in this study. The following will apply for all EDP1815-207 participants who transition into this study:

- EDP1815-207 Cohort 1 participants will receive $1.6x10^{11}$ total cells of EDP1815 in EDP1815-208 (Group 1)
- EDP1815-207 Cohort 2 participants will receive $6.4x10^{11}$ total cells of EDP1815 in EDP1815-208 (Group 2)
- EDP1815-207 Cohort 3 participants will be randomized 1:1 to receive either $1.6x10^{11}$ total cells of EDP1815 (Group 1), or $6.4x10^{11}$ total cells of EDP1815 (Group 2) in EDP1815-208
- EDP1815-207 Cohort 4 participants will receive $8.0x10^{10}$ total cells of EDP1815 in EDP1815-208 (Group 3)

The total number of participants will be dependent on the number of participants who elect and are eligible to participate in the OLE study following participation in the EDP1815-207 parent study.

The total duration of participation in this study is up to a maximum of 40 weeks from Day -1 to follow-up. As shown in Figure 1, participants will undergo a Day -1 visit, a 36-week treatment period consisting of 6 study visits and a 4-week post-treatment follow-up visit.

Figure 1: Study Schema



5.2 Randomisation and Blinding

This is an OLE study with all participants taking EDP1815 capsules and as such no blinding is required for the study medication in this study. Participants in Cohort 3 in the EDP1815-207 parent study that are eligible for this study will be randomized 1:1 to receive either $1.6x10^{11}$ total cells of EDP1815, or $6.4x10^{11}$ total cells of EDP1815.

Investigators and participants will continue to be blinded to the participant's treatment assignment in the EDP1815-207 parent study to minimize bias.

5.3 Derived variables

5.3.1 General

5.3.1.1 Relative Day

The relative day of an assessment since the start of 208 study will be calculated as:

- For measurement performed on or after the date of first dose in this study:
  Date of assessment – date of start of treatment + 1

- For measurements performed before the date of first dose in this study:
  Date of assessment – date of start of treatment

The relative day of an assessment since the first dose of active IMP (in this or parent study) will be calculated as:

- For measurement performed on or after the first dose of active IMP:
  Date of assessment – date of the first dose of active IMP + 1

- For measurements performed before the first dose of active IMP:
  Date of assessment – date of the first dose of active IMP

5.3.1.2 Baseline

The last non-missing value collected before first study dose in the parent study will be taken as the baseline measurement for all parameters. If data is collected on Day 1 of the parent study it will be assumed to be pre-dose regardless of an associated time.

5.3.1.3 Change and Percentage Change from Baseline

Change from baseline will be calculated as:

Change from baseline = value at timepoint – baseline value

Change from baseline will be presented to the same level of precision as the original value in the listings.

Percentage change from baseline will be calculated as:

Percentage change from baseline = 100*(change from baseline / baseline value)

Percentage change from baseline will be presented to 1 decimal place (dp) in the listings.

5.3.2 Demographic and Background Data

Height may be recorded in cm or inches. Height in inches will be converted to height in cm as follows:

Height (cm) = Height (inches)*0.3937

Height (cm) will be presented to 1 dp in the listings.

Weight may be recorded in kg or pounds. Weight in pounds will be converted to weight in kg as follows:

Weight (kg) = Weight (pounds) * 0.4536

Weight (kg) will be presented to 1 dp in the listings.

Body mass index (BMI) will be calculated as:

BMI (kg/m^2) = Weight (kg) / [height (cm)/100]^2

BMI (kg/m^2) will be presented to 1 dp in the listings.

5.3.2.1 Study Drug Compliance

Participants in groups 1 and 2 will be expected to dose once daily with 2 capsules per dose (2 capsules per day); in group 3 – once daily with 1 capsule.

Compliance will be calculated across the whole treatment period in this study.

Expected capsules for the treatment period for groups 1 and 2 will be calculated as:

Expected capsules = 2*(End date of treatment period – Start date of treatment period + 1).

Expected capsules for the treatment period for group 3 will be calculated as:

Expected capsules = End date of treatment period – Start date of treatment period + 1.

End date of treatment period = Date of the last dose of study drug.
Start date of treatment period = Day 1.

Actual capsules taken will be calculated from the dosing log using entries between the start and end days inclusively.

Study drug compliance will be calculated as:

Study drug compliance (%) = 100*Actual capsules taken/Expected capsules taken.

Study drug compliance will also be categorized as:

- <80%
- ≥80%

5.3.2.2 Emollient Compliance

All participants must use an emollient twice daily until the Week 40 Follow-up Visit.

Compliance will be calculated across the whole treatment period and follow-up period in this study.

Expected number of applications for the treatment + follow-up period will be calculated as:

Expected number of applications = 2*(End date of period – Start date of period +1).

End date of period = End of study day. Start date of period = Day 1.

Actual number of applications will be calculated from the emollient usage diary using entries between the start and end days inclusively. In case of more than two applications per day participant will be considered compliant for that day and only two applications will be considered for compliance calculation.

Emollient compliance will be calculated as:

Emollient compliance (%) = 100*Actual number of applications/Expected number of applications

Emollient compliance will also be categorized as:

- <75%
- ≥75%

5.3.2.3 Prohibited Concomitant Medications

Use of any of the following concomitant medications during the study require the IMP to be immediately discontinued where possible. If a participant requires treatment for atopic dermatitis with a prohibited concomitant medication during the study, they will be classified as a treatment failure:

- Topical Corticosteroids (TCS) or Topical Calcineurin Inhibitors (TCI) (unless considered a rescue therapy)
- Topical Phosphodiesterase (PDE) - 4 Inhibitors
- Topical Janus Kinase (JAK) Inhibitors
- Bleach baths
- Phototherapy treatment
- Tanning beds
- Systemic treatments that may lead to clinical improvements in atopic dermatitis, e.g., oral or injectable corticosteroids, methotrexate, azathioprine, cyclosporine, mycophenolate mofetil, JAK-inhibitors, biologic therapy, and other systemic immunosuppressive therapy (note single dose intra-articular or intra-lesional corticosteroid therapy is permitted)
- Leukotriene Receptor Antagonists
- Allergen Immunotherapy
- Live (attenuated) vaccinations

If a prohibited medication is found to have been used, this will be captured into the protocol deviations log.

Prohibited medications will be identified by the sponsor in a separate spreadsheet. In the EDP1815-207 study, prohibited concomitant medications were categorized into two types. Type 1 prohibited medications did not require study withdrawal and as intercurrent events are equivalent to TCS/TCI rescue therapies; Type 2 prohibited medications are equivalent to the prohibited medications in this study.

5.3.3 Efficacy

5.3.3.1 Eczema Area and Severity Index (EASI)

The Eczema Area and Severity Index (EASI) will be calculated within the [redacted] system and taken directly from the supplied data. EASI score ranges from 0 to 72 and combines the individual scores from the four individual body regions of head and neck, upper limbs, trunk, lower limbs. Head and neck body region score ranges from 0 to 7.2, upper limbs – from 0 to 14.4, trunk – from 0 to 21.6, lower limbs – from 0 to 28.8. Further information on the scoring of the EASI is provided in Section 17.

EASI-50, EASI-75 and EASI-90 responses are defined respectively by at least a 50%, 75% and 90% decrease from Baseline in the EASI score.

Sustained EASI-50 response is defined as one which is present at consecutive visits spanning at least 8 weeks in the absence of rescue medication. The sustained response is considered to have been first achieved at the first of the consecutive visits.

5.3.3.2 The Percent of Body Surface Area Involvement (BSA)

The Body Surface Area (BSA) will be calculated as part of EASI score in the [redacted] system and taken directly from the supplied data. The percent of BSA involvement will be estimated for each participant, where 1% is approximately the area of the participant's handprint.

BSA-50 and BSA-75 responses are defined respectively by at least a 50% and 75% reduction from Baseline in the BSA.

5.3.3.3 Validated Investigator's Global Assessment (vIGA)

The Validated Investigator Global Assessment scale for Atopic Dermatitis (vIGA) will be calculated within the [redacted] system and taken directly from the supplied data. There is a standardized grading system based on an overall assessment of the degree of erythema, papulation/induration, lichenification, and oozing/crusting. In indeterminate cases, extent will be used to differentiate between scores - but otherwise extent is not used in the scoring system. The vIGA score ranges from 0 (Clear skin) to 4 (Severe disease).

5.3.3.4 SCORing Atopic Dermatitis (SCORAD)

The SCORing Atopic Dermatitis (SCORAD) will be calculated within the [redacted] system and taken directly from the supplied data. There is an investigator-rated area score which uses the rule of nines to assess disease extent, and a disease intensity score comprising erythema, swelling, oozing/crusting, excoriation, lichenification, and dryness. Additionally, there is a subjective symptoms component which considers itch and sleeplessness scored using a visual analogue scale. These scores combine to give a SCORAD score between 0 and 103.

SCORAD-35, SCORAD-50 and SCORAD-75 responses are defined respectively by at least a 35%, 50% and 75% reduction from Baseline in the SCORAD score.

5.3.3.5 Patient Oriented Eczema Measure (POEM)

The Patient Oriented Eczema Measure (POEM) will be calculated within the [redacted] and taken directly from the supplied data. It includes a series of 7 questions, measuring itch, sleep, bleeding, weeping/oozing, cracking, flaking, and dryness/roughness over the last week, and is scored by the participant. Each of the 7 questions is scored from 0 (no days) to 4 (every day), giving a POEM score range from 0 to 28, with higher scores representing higher disease severity.

POEM response is defined as a reduction of ≥4 in the POEM score if a participant has a score of ≥4 at baseline.

5.3.3.6 Dermatology Life Quality Index (DLQI)

The DLQI is a 10-item questionnaire with each item scored from 0 to 3.

The DLQI score is the sum of the 10 individual items and ranges from 0 to 30, with higher scores indicating greater impairment of quality of life. Further information on the scoring of the DLQI is provided in Section 21.

DLQI response is defined as a reduction of ≥4 in the DLQI score if a participant has a score of ≥4 at baseline (a 4-point change from baseline is considered the minimal clinically important difference threshold).

5.3.3.7 Peak Pruritus Numerical Rating Scale (PP-NRS)

The Peak Pruritus Numerical Rating Scale (PP-NRS) is a scale from 0 to 10 for participants to rate their worst itch that they have experienced over the previous 24 hours. The PP-NRS will be completed daily via a daily questionnaire from the Day-1 visit to the week 40 visit.

PP-NRS score at each visit is calculated as the mean itch daily score for the 7 days prior to and including the visit date. At least 4 daily scores must be available for the score at the relevant visit to be considered evaluable.

PP-NRS responses are defined as a reduction of ≥2 and ≥4 in the PP-NRS score if a participant has a score of ≥2 and ≥4, respectively, at baseline (a ≥2-4-point change from baseline is considered the minimal clinically important difference threshold).

5.3.3.8 Sleep Disturbance Numerical Rating Scale (SD-NRS)

The Sleep Disturbance Numerical Rating Scale (SD-NRS) is a scale from 0 to 10 for participants to rate their worst sleep that they have experienced over the previous 24 hours. The SD-NRS will be completed daily via a daily questionnaire from the Day-1 visit to the week 40 visit.

SD-NRS score at each visit is calculated as the mean sleep daily score for the 7 days prior to and including the visit date. At least 4 daily scores must be available for the score at the relevant visit to be considered evaluable.

SD-NRS response is defined as a reduction of ≥2 in the SD-NRS score if a participant has a score of ≥2 at baseline (a 2-point change from baseline is considered the minimal clinically important difference threshold).

5.3.3.9 Atopic Dermatitis Control Tool (ADCT)

The Atopic Dermatitis Control Tool (ADCT) is a 6-question PRO instrument used to detect change of disease activity in a person over time. There are six main areas that assess the multi-dimensional aspects of disease control over the course of a week, scored between 0-4. ADCT scores range from a minimum score of 0 and a maximum score of 24. A higher score indicates lower AD control.

5.3.3.10 Rescue Therapy

Rescue therapy use is allowed throughout the entire study: selected topical corticosteroids and calcineurin inhibitors, systemic antimicrobials and topical antibacterial may be prescribed. An unscheduled visit will be performed to collect the assessments prior to administering any rescue therapy, if needed.

Rescue therapy use will be documented as concomitant medication once prescribed and in a daily symptom diary during the whole course. Each rescue therapy course will be recorded in concomitant medication CRF separately, resulting in a one record in a concomitant medication dataset for each course.

Any medications taken during the study and classified as TSC/TCI rescue therapy medications in the sponsor provided spreadsheet will be considered as rescue therapy with exception for medications which stopped at least 14 days before Day 1.

The number of courses of TCS/TCI rescue therapy will be evaluated for two periods: the period beginning with the first dose of active IMP in this study and the period beginning with the first dose of active IMP across this study and the parent study up to the end of treatment. Rescue therapy course will only be counted at the start day of course. If the rescue therapy course starts in one period and continues to the next period it will be counted only in the first period where the start of the course belongs.

5.3.4 Safety

5.3.4.1 Duration of Exposure

The duration of exposure in this study will be calculated as

Duration of exposure (days) = Treatment stop date in 208 – Treatment start date in 208 + 1

The duration of active exposure in this and parent study will be calculated as

Duration of exposure (days) = Treatment stop date in 208 – Active treatment start date* + 1

*If patient received active treatment in parent study, then consider the start date of active treatment from parent study, otherwise, start of treatment in 208.

5.3.4.2 Treatment-Emergent Adverse Events

An adverse event (AE) will be classified as 'treatment-emergent' if the onset date/time was after the start date/time of study treatment and on or before 30 days after last dose of study treatment. Where dates or times are missing or partially missing, AEs will be assumed to be treatment-emergent, unless there is clear evidence (through comparison of partial dates/times, see Section 7.3.1) to suggest that the AE started prior to dosing.

AEs will be classified into the following study phases based on the onset date/time of the AE after any imputations:

- Pre-Treatment Phase: All AEs with onset date/time prior to the first dose of study treatment
- Treatment Phase: All AEs with onset date/time at the time of or after the first dose of study treatment (Day 1) up to and including the date of the last dose of treatment received
- Follow-up Phase: All AEs with onset date after the date of the last dose of treatment received

For participants who complete 36 weeks of dosing per protocol, the Treatment Phase will be from Day 1 to the Week 36 visit, and the Follow-up Phase will start after the Treatment Phase and last until their last day in the study. In all cases the day will be assumed to start at 00:00 hours and end at 23:59 hours. Adverse events occurring in both the Treatment Phase and Follow-up Phase are classified as treatment emergent.

For participants who were administered active treatment in the parent study, the Parent Treatment Phase will be defined from the first dose of IMP in the parent study up to the Day 1 in this study.

The onset phase of all AEs will be included in the relevant data listings.

6 Sample Size

The sample size of the study will be determined by the number of participants who enrol from qualifying atopic dermatitis parent studies with EDP1815.

7 General Considerations

7.1 Analysis Populations

7.1.1 Participant Analysis Populations

7.1.1.1 Enrolled Population

The enrolled set will consist of all participants who sign the ICF.

7.1.1.2 Full Analysis Population

The full analysis population will consist of all participants who receive any IMP.

7.1.1.3 Other Populations

Other parent study specific analysis sets may also be used in interim analyses which will be defined by the subset of participants from the FAS who were previously enrolled from the specific parent studies or study cohorts. Such populations will be named xxxxxx Full Analysis Set, where xxxxxx stands for the study specific subset identifier.

7.1.2 Defined Data Point Sets

7.1.2.1 Data Point Set 1 (DPS1)

DPS1 consists of all observed data collected following the first dose of IMP in this study until 30 days after the last dose of IMP.
Note, baseline data will be taken from the parent study.

7.1.2.2 Data Point Set 2 (DPS2)

DPS2 consists of all observed data collected following the first dose of active IMP, either in the parent study or in this study until 30 days after the last dose of IMP in this study.

7.1.2.3 Data Point Set 3 (DPS3)

DPS3 consists of all observed data collected at a scheduled visit in this study.
Note, changes from baseline will be derived using baseline data from the parent study.

7.1.2.4 Data Point Set 4 (DPS4)

DPS4 consists of all observed data collected at a scheduled visits in this study or the parent study for participants who enter this study.

7.1.2.5 Data Point Set 4a (DPS4a)

DPS4a is a subset of DPS4, excluding any data collected within 4 weeks after the use of permitted rescue medications for atopic dermatitis or at any time after the use of prohibited medications for atopic dermatitis.

7.1.2.6 Data Point Set 4b (DPS4b)

DPS4b is a subset of DPS4 for responder endpoints only, where data collected within 4 weeks after the use of permitted rescue medications for atopic dermatitis, at any time after the use of prohibited medications for atopic dermatitis, or at scheduled endpoints after withdrawal from treatment due to treatment-failure related reasons (related AEs, lack of efficacy, requirement for alternate psoriasis therapy) will be replaced by ‘non-responder’.

7.1.2.7 Data Point Set 5 (DPS5)

DPS5 consists of all observed data collected following the first dose of IMP in this study.

7.2 Covariates and Subgroups

No inferential statistical testing will be performed so no covariates will be defined.

7.3 Missing Data

Unless otherwise specified as part of the intercurrent event strategy, missing data will not be imputed. Imputation of missing efficacy data due to intercurrent events will be performed in DPS4a and DPS4b as described in Section 7.1.2.

7.3.1 Partial Dates/Times

Partial dates and times for AEs, medical conditions and concomitant medications will be imputed for the purpose of assigning study phases and calculating duration. Listings will always include the reported date/time information rather than any imputations.

Partial AE onset and concomitant medication start dates will be imputed as follows:

- If only the month and year are specified, and the month and year of the start of treatment in 208 are not the same as the month and year of the start date, then use the 1st of the month.
- If only the month and year are specified, and the month and year of the start of treatment in 208 are the same as the month and year of the start date, then use the date of start of treatment. If this results in a start date after a known or partial end date, then use the 1st of the month.
- If only the year is specified, and the year of the start of treatment in 208 is not the same as the year of the start date, then use January 1 of the year of the start date.
- If only the year is specified, and the year of the start of treatment in 208 is the same as the year of the start date, then use the date of the start of treatment. If this results in a start date after a known or partial end date, then use January 1 of the year of the start date.
- If the start date is completely unknown, then use the date of the start of treatment in 208. If this results in a start date after a known or partial end date, do not impute the start date.

Partial AE onset start times will be imputed as follows:

- If the actual or imputed start date is the same as the 208 treatment start date, and the start time is completely missing, then use the time of start of treatment.
- If the actual or imputed start date is not the same as the 208 treatment start date, and the start time is completely missing, then use 00:00.
- If the actual or imputed start date is the same as the 208 treatment start date, and the start time is partially missing (hh:XX) then use the following:
    - If the hour is the same as the hour of the start of treatment time then use the complete time of the start of treatment (i.e., both hours and minutes)
    - If the hour is not the same as the hour of the start time than use hh:00.
- If the actual or imputed start date is not the same as the 208 treatment start date, and the start time is partially missing (hh:XX) then use hh:00.

Partial medical conditions start dates will be imputed as follows:

- If only the month and year are specified, then use the 1st day of the month.
- If only the year is specified, then use January 1st of that year.
- If the start date is completely unknown, do not impute the start date.

Partial AE resolution, medical condition stop dates and concomitant medication stop dates and date last smoked will be imputed as follows:

- If the event, condition or medication is flagged as ongoing, do not impute the stop date.
- If only the month and year are specified, then use the last day of the month.
- If only the year is specified, then use December 31 of that year.
- If the stop date is completely unknown, do not impute the stop date.

Partial AE resolution and concomitant medication stop times will be imputed as follows:

- If the actual or imputed stop date is non-missing, and the stop time is completely missing, then use 23:59 on that date.
- If the actual or imputed stop date is non-missing, and the stop time is partially missing, then hh:59 for missing minutes.
- If the actual or imputed stop date is missing, do not impute the stop time.

7.3.2 Adverse Event Information

AEs with missing relationship will be considered 'Related' for summary purposes but recorded as missing in the listings.

7.4 Study Deliveries

7.4.1 Early Stopping

In the event that some or all of the cohorts stop the study early, it may be decided to make a single delivery for all study cohorts with reduced number of TFLs.

7.4.2 Purpose of Study Deliveries

Interim safety and efficacy analyses may be performed throughout the life cycle of the study as required for ongoing evaluation of the risk benefit profile of EDP1815. These may include either all participants enrolled in the study or use a subset of participants who transitioned to this study from a specific parent study or a specific parent study cohort. Analyses performed once participants from a specific parent study or a specific parent study cohort complete 208 study will be considered as final deliveries.

All analyses will also incorporate data collected on the parent atopic dermatitis EDP1815 studies which feed into this study.

7.4.3 Planned Schedule of Deliveries

The interim and final analyses will be performed throughout the life cycle of the study as required.

At a minimum, there will be EDP1815-207 parent-study specific analysis performed after all participants from

- 207 cohorts 1-3 (Delivery 1)
- 207 cohort 4 (Delivery 2)

have completed this study.

Analysis will be restricted to participants from the corresponding cohorts in the parent study who transitioned to this study.

7.4.4 Endpoints to be Included in the Study Deliveries

All endpoints will be included into the parent-study specific analyses.

7.4.5 Adjustment of Confidence Intervals and p-values

No inferential comparisons of efficacy will be performed so no adjustments for alpha-spending are required.

7.4.6 Practical Measures to Minimise Bias

This is an OLE study with all participants taking EDP1815 capsules so no blinding is required for the study medication in this study. However, investigators and participants will continue to be blinded to the participant's treatment assignment in the parent study in order to minimize bias.

Unblinded results will not be shared with any study site staff or participants.

7.4.7 Documentation of Study Deliveries

The study is open label but the [redacted] team will be unblinded to the treatment assignment only from the time of parent study DBL.
As the patients' assignments data will be only available for [redacted] after the parent study DBL, there is no risk of unblinding and there will be no separate unblinded team. Any interim analysis data will be held in the non-restricted file structure available to the whole [redacted] team working on 208 study.

7.5 Multi-centre Studies

Results will be presented for all centres combined.

7.6 Multiple Testing

The focus of this study is on safety, specifically the incidence and rate of TEAEs per 100-patient years, and as such no adjustments will be made for multiple testing in this study.

7.7 Visit Windows

All data will be reported according to nominal visits. For example, if a Week 4 visit occurred on Day 30 instead of the nominally expected Day 28 it will be reported and included in the summary statistics/statistical analyses for Week 4.

Scheduled visits which occur outside the protocol-specified visit window (e.g., if the Week 4 visit occurred on Day 32, outside of the Day 25-31 window), this will be noted as a protocol deviation but data collected will still be included in all summary and analysis tables.

Unscheduled visits and Early Termination visit will not be included in summary or analysis tables, unless they are baseline measurements or provide data towards a safety endpoint which looks at worst-case post-baseline.

All listings will include all collected data even if they are from an unscheduled visit.

8 Summary of Study Data

All continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, SD, median, maximum, and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures.

In general, all data will be listed, sorted by group (1, 2, and 3), country, site number and participant number. Relevant listings will include whether the assessment was performed and the date, study day/visit and time of the assessment as applicable.

Any study population or safety tables, listings or figures that display treatment will always present the actual treatment received rather than the planned treatment as the primary objective is to evaluate the safety of EDP1815. For efficacy summaries planned treatment will be used.

Unless otherwise specified below, all summary tables will be structured with a column for each group (groups 1 and 2 will be presented in 207 cohorts 1-3 delivery and group 3 will be presented in 207 cohort 4 delivery) and an additional 'Total' column which contains all patients included in the relevant interim or final analysis.

The labels presented for each group will be as follows:

- Group 1 = $1.6x10^{11}$ TCPD
- Group 2 = $6.4x10^{11}$ TCPD
- Group 3 = $8.0x10^{10}$ TCPD

For summaries of safety endpoints that look at the period defined since first dose of active IMP either in this study or the relevant parent study, the data will be ordered and labelled as follows:

- $1.6x10^{11}$ TCPD (For 207 cohorts 1-3 delivery only)
- $6.4x10^{11}$ TCPD (For 207 cohorts 1-3 delivery only)

- $6.4x10^{11}$ TCPD to $1.6x10^{11}$ TCPD (For 207 cohorts 1-3 delivery only)
- $8.0x10^{10}$ TCPD (For 207 cohort 4 delivery only)
- Total

For efficacy outputs, columns will be ordered and labelled as follows:

- For 207 cohorts 1-3 delivery:
  - $1.6x10^{11}$ TCPD in this study, Placebo in the parent study
  - $1.6x10^{11}$ TCPD in this study, $1.6x10^{11}$ TCPD in the parent study
  - $1.6x10^{11}$ TCPD in this study, $6.4x10^{11}$ TCPD in the parent study
  - $6.4x10^{11}$ TCPD in this study, Placebo in parent study
  - $6.4x10^{11}$ TCPD in this study, $6.4x10^{11}$ TCPD in the parent study
  - Total
- For 207 cohort 4 delivery:
  - $8.0x10^{10}$ TCPD in this study, Placebo in the parent study
  - $8.0x10^{10}$ TCPD in this study, $8.0x10^{10}$ TCPD in the parent study
  - Total

For the analysis:

- For study disposition summaries where it is appropriate to report information on participants that have failed screening, the enrolled population will be used.
- For the primary estimands around adverse events, together with estimands based on efficacy count endpoints looking into the use of rescue medications, the FAS will be used along with DPS1 and DPS2.
- For the responder efficacy endpoints the FAS along with DPS4b will be used
- For supplementary estimands for the key efficacy responder endpoints the FAS along with DPS4 and DPS4a will be used.
- For continuous endpoints the FAS along with DPS4a will be used.
- For safety endpoints where data is collected at specific timepoints the FAS along with DPS3 and DPS4 will be used.

8.1 Early Stopping

In the event that the study is stopped early and only a reduced amount of outputs are needed, the following will presented:

- Completion/withdrawal from the study/treatment will be summarised and listed (per Section 8.2)
- The number and percentage of participants enrolled within each region, country and site will be summarized (per Section 8.2)
- Demography data of age, sex, race, and ethnicity will be summarized and listed (per Section 8.4)

Data will be presented as collected, no imputations or data exclusion will be made.

The list of outputs produced in the case the study is stopped early are provided in 16Appendix 1: List of Tables, Figures and Listings.

8.2 Study Disposition

Completion/withdrawal from the study and completion/discontinuation from treatment, together with reasons for withdrawal from the study or discontinuation from treatment will be listed and the following will also be tabulated:

- Number and percentage of participants who completed the study
- Number and percentage of participants withdrawn from the study and the reported reason for withdrawal
- Number and percentage of participants who completed the 36-week treatment period
- Number and percentage of participants who discontinued treatment early and reason for discontinuation

For participants who fail to meet the eligibility criteria the reasons for failure, including the inclusion/exclusion criteria that were not met will be summarized and listed.

The number and percentage of participants enrolled within each region, country and site will be summarized.

For the enrolled population, the number and percentage of participants in each analysis population will be presented. Inclusion/exclusion in each study population will also be listed, together with reasons for exclusion.

The number and percentage of participants with data available for each scheduled visit (including the early termination visit) will be summarized.

Missed visits due to COVID-19 will also be summarized and listed.

8.3 Protocol Deviations

The number and percentage of participants in the full analysis population with at least one significant protocol deviation will be summarized by deviation category.

All protocol deviations will also be listed.

8.4 Demographic and Baseline Variables

Demography data of age, sex, race, and ethnicity will be summarized and listed together with height, weight, and BMI at the parent study baseline.

8.5 Medical History

Medical history and concurrent illnesses will be captured and coded using the Medical Dictionary for Regulatory Activities (MedDRA®). The dictionary will be updated through the life of the study with version 24.0 used initially.

Parent study medical history will be used in the summaries together with 208 data to present all past and concurrent medical history. Parent study medical history won't be recoded if the MedDRA will be updated through the life of 208 study, the dictionary from the time of the parent study data base lock will be used.

Concurrent illnesses and medical conditions will be classified as 'current' if the end date is on or after the date of first dose of study drug, or the condition has been marked as ongoing. Otherwise, they will be classified as 'past'.

Past and current medical history will be summarized separately by System Organ Class (SOC) and Preferred Term (PT). Summary tables will contain the number and percentage of patients. A patient who has multiple conditions in the same SOC or with the same PT will be counted only once in the patient counts. Medical history summaries will be sorted by the internationally agreed SOC order (Table 10) and decreasing frequency of PT within SOC in the Total column.

All medical history data will be listed.

8.6 Prior and Concomitant Medications

Medications collected during the 208 study will be coded according to the World Health Organization Drug Dictionary (WHODD). The dictionary will be updated through the life of the study with the version dated 01Mar2021 used initially. Medical procedures will not be coded.

Parent study medications data will be used in the summaries together with 208 data to present all prior and concomitant medications from the whole period before and during 208 study. Parent study medications won't be recoded if the dictionary will be updated through the life of 208 study, the dictionary from the time of the parent study data base lock will be used.

Concomitant medications are defined as any medications taken during the 208 treatment period or follow-up period after treatment. This includes any medications started before the 208 first dose and ongoing after the first dose. Prior medications are defined as any medication taken before or during the parent study which were stopped before the first dose of 208 study medication.

Missing and partial start and stop dates will be imputed using the rules specified in Section 7.3.1 before classifying therapies as prior or concomitant. If the classification is still ambiguous after missing and partial dates have been imputed, then the medication will be considered concomitant.

Medications will be summarized by WHODD Anatomical Main Group (Level 1), Therapeutic Subgroup (Level 2) and preferred term. The summaries will report incidence within each relevant level so that

a participant taking multiple medications coded to the same relevant Level 1, Level 2 or preferred term would only be counted once within the incidence count for that level or term.

Separate summaries will be produced for each of the following:

- All concomitant medications
- Concomitant medications started before or during the parent study
- Concomitant medications started during the 208 treatment period
- Concomitant medications started during the 208 follow-up period

All prior and concomitant medications will be listed.

Categorization of all concomitant medications prescribed during the study will be done by Evelo clinician in order to identify TCS/TCI rescue therapy, antimicrobial rescue therapy and prohibited medications.

8.7 Treatment Compliance

Treatment compliance will be summarized for the whole 36-week treatment period.

Summary statistics (n, mean, SD, median and range) will be produced together with the number and percentage of participants within each of the categories defined in Section 5.3.2.1. Percentages will use the number of participants who started the treatment period as the denominator.

Data from the dosing log and the calculated treatment compliance will also be listed.

8.8 Emollient Compliance

Emollient compliance will be summarized for the whole treatment and follow-up periods.

Summary statistics (n, mean, SD, median and range) will be produced together with the number and percentage of participants within each of the categories defined in Section 5.3.2.2. Percentages will use the number of participants who started the period as the denominator.

Data from the daily diary and the calculated emollient compliance will also be listed.

9 Primary Safety Analysis

9.1 Early Stopping

In the event that the study is stopped early and only a reduced amount of outputs are needed, safety data will only be reported for the period beginning with the first dose of active IMP in this study. Only incidence and number of events will be presented for the following categories:

- TEAEs
- Serious TEAEs

Data will be presented as collected, no imputations or data exclusion will be made.

The list of outputs produced in the case the study is stopped early are provided in 16Appendix 1: List of Tables, Figures and Listings.

9.2 Primary Estimand of the Primary Objective

Safety data will be reported for two periods:

- The period beginning with the first dose of active IMP in this study
- The period beginning with the first dose of active IMP across this study and the parent study

The primary safety endpoints will be the incidence and rate per 100 patient-years for:

- TEAEs
- TEAEs of Grade 2 or above
- TEAEs of Grade 3 or above
- Serious TEAEs
- Fatal TEAEs
- TEAEs causing discontinuation of study drug
- Study drug related TEAEs (defined by an investigator assessment of possible, probable, or definite relationship to IMP)
- Study drug related TEAEs of Grade 2 or above
- Study drug related TEAEs of Grade 3 or above
- Study drug related serious TEAEs
- Study drug related fatal TEAEs
- Study drug related TEAEs causing discontinuation of study drug

9.2.1 Estimands

The primary safety estimands will use the FAS or the parent study specific FAS for the study/cohort specific analysis.

Treatment condition: actual treatment received will be considered.

Population summary measure of interest:

- For the endpoints looking at the period defined by this study only - the incidence and rate per 100 patient-years of each category of TEAEs (DPS1)
- For the endpoints looking at the period defined since first dose of the active IMP in this study and the relevant parent study - the rate per 100 patient-years of each category of TEAEs by treatment group (DPS2)

Intercurrent events will be accounted for in the following manner:

Table 1: Intercurrent Event Strategies of the Primary Estimand

Discontinuation of treatment	The use of prohibited medications or TCS/TCI rescue therapy, non-compliance with study drug, and any deviations from protocol
Composite strategy Only events which start within 30 days after discontinuation of treatment (TEAEs) will be included in the assessments of incidences and rates	Treatment policy strategy: Data will be used as collected

9.2.2 Analytical Approach

The endpoints described for the primary safety analysis will be summarised in the overall summary of adverse events table with a row for each endpoint. The number and percentage of patients with each TEAE, the total number of events and the rate per 100 patient-years will be presented for each treatment group.

Other adverse events summaries considered as secondary safety endpoints are further described in Section 11.2.

10 Efficacy Analyses

All efficacy estimands will use the FAS or the parent study specific FAS for the study/cohort specific analysis.

Treatment condition: planned treatment will be considered.
Descriptive statistics will be provided to summarize all efficacy endpoints using the grouping specified in Section 8 which considers treatment groups in this study and the parent study.

All efficacy data will be listed, including both individual item scores and calculated questionnaire summary scores.

10.1 Early Stopping

In the event that the study is stopped early due to efficacy concerns based on results of the parent study, no inferential efficacy analysis will be carried out. No outputs for the efficacy endpoints will be presented.

The list of outputs produced in the case the study is stopped early are provided in 16Appendix 1: List of Tables, Figures and Listings.

10.2 Secondary Efficacy Analysis

10.2.1 Responder Analysis

10.2.1.1 Estimands

The key secondary response endpoints will be evaluated at all scheduled visits and are as follows:

- EASI-50, EASI-75, EASI-90
- IGA of 0 or 1 with a ≥2-point improvement from baseline
- IGA of 0 or 1
- BSA-50, BSA-75
- SCORAD-35, SCORAD-50, SCORAD-75
- Improvement of ≥4 points in POEM score from baseline*

The other secondary endpoints are:

- IGA of 0
- BSA ≤3%
- Improvement of ≥4 points in DLQI from baseline*
- Improvement of ≥2 points in PP-NRS score from baseline*
- Improvement of ≥4 points in PP-NRS score from baseline*
- Improvement of ≥2 points in SD-NRS score from baseline*

* Of those with a relevant score of ≥2/4 at baseline

The population summary measure of interest for all response estimands will be the percentage of participants with the relevant response at each visit.

Intercurrent events for response endpoints will be accounted for in the following manner:

Table 2: Intercurrent Event Strategies of the Secondary Response Endpoints

Estimand	DPS	Use of TCS/TCI rescue medications within 4 weeks or type 1 prohibited meds from 207, use at any time of other prohibited medications for atopic dermatitis, discontinuation of treatment for treatment failure related reasons*	Discontinuation of treatment for reasons not related to treatment-failure**, non-compliance with study drug, any other deviations from the protocol
Response Estimand 1	DPS4b	Composite strategy Replace with 'non-response' all data collected 1) within 4 weeks after the use of TCS/TCI rescue medications or type 1 prohibited meds from 207 2) at any time after the use of other prohibited medications for atopic dermatitis 3) at scheduled visits after treatment discontinuation for treatment-related reasons*	Treatment policy strategy All data is used regardless of the intercurrent event
Supplementary Response Estimand 1	DPS4	Treatment policy strategy Include all data collected regardless of use of TCS/TCI rescue medications or other prohibited medications for atopic dermatitis or treatment discontinuation	Treatment policy strategy (as per response estimand 1)
Supplementary Response Estimand 2	DPS4a	If rescue or prohibited medications used: While on treatment strategy Exclude all data collected within 4 weeks after the use of TCS/TCI rescue medication or at any time after the use of other prohibited medications for atopic dermatitis If treatment discontinuation: Treatment policy strategy All data is used regardless of the treatment discontinuation	Treatment policy strategy (as per response estimand 1)

* related AEs, lack of efficacy, requirement for alternate psoriasis therapy

** participants will be withdrawn from the study following discontinuation of treatment and as such it is expected that data collected at the scheduled visits will only include participants who are on treatment (or very recently discontinued) with the exception of those visits specifically scheduled to occur 4 and 12 weeks after last dose.

All response secondary endpoints will be analysed with a response estimand 1 (DPS4b). Key secondary endpoints will be also analysed with supplementary response estimands 1 and 2 (DPS4 and DPS4a).

10.2.1.2 Analytical Approach

Summary tabulations of frequency and percentage of participants within each category will be presented at each scheduled visit that the variable is recorded. The following visits should be presented unless otherwise stated: Baseline, 207 Week 4, 8, 12, 16 (labelled as "207 / Week X") and 208 week 4, 8, 12, 16, 24, 36, 40 (labelled as "208 / Week X").

Figures for the proportion of participants achieving response over time for each of the criteria will be created for the same scheduled visits as summaries.

10.2.2 Continuous Variables Analysis

10.2.2.1 Estimands

The secondary continuous endpoints are as follows:

- Change and percentage change from baseline in EASI score
- Change and percentage change from baseline in IGA*BSA
- Change and percentage change from baseline in BSA
- Change and percentage change from baseline in SCORAD score
- Change and percentage change from baseline in DLQI score
- Change and percentage change from baseline in POEM score
- Change from baseline in PP-NRS*
- Change from baseline in SD-NRS*

* The score at each visit is calculated as the mean daily score for the 7 days prior to and including the visit date. At least 4 daily scores must be available for the score at the relevant visit to be considered evaluable.

The population summary measure of interest will be the mean at each scheduled visit.

Intercurrent events for continuous estimand 1 will be accounted for in the following manner:

Table 3: Intercurrent Event Strategies of Continuous Estimand 1

Use of TCS/TCI rescue medications within 4 weeks or type 1 prohibited meds from 207, use at any time of other prohibited medications for atopic dermatitis	Discontinuation of treatment for any reason*, non-compliance with study drug, any other deviations from protocol
While on treatment strategy Exclude all data collected 1) within 4 weeks after the use of TCS/TCI rescue medications or type 1 prohibited meds from 207 2) at any time after the use of other prohibited medications for atopic dermatitis	Treatment policy strategy All data is used regardless of the intercurrent even

* participants will be withdrawn from the study following discontinuation of treatment and as such it is expected that data collected at the scheduled visits will only include participants who are on treatment (or very recently discontinued) with the exception of those visits specifically scheduled to occur 4 and 12 weeks after last dose.

Note, for PP-NRS and SD-NRS intercurrent event strategy should be applied for daily scores before the weekly scores are calculated.

All continuous secondary endpoints will be analysed with continuous estimand 1 (DPS4a).

10.2.2.2 Analytical Approach

The number of participants, mean, median, standard deviation (SD), minimum, and maximum values will be presented at each scheduled visit that the variable is recorded. The following visits should be presented unless otherwise stated: Baseline, 207 week 4, 8, 12, 16 (labelled as "207 / Week X") and 208 week 4, 8, 12, 16, 24, 36 and 40 (labelled as "208 / Week X").

Figures for the mean percentage change and change from baseline in each of the continuous endpoints will be displayed over time. Waterfall plots for the percentage change and change from baseline will also be produced for the same scheduled visits as presented in tables.

10.2.3 Rate Variables Analysis

10.2.3.1 Estimands

The secondary rate endpoints are:

- Number of courses per patient-year of any TCS/TCI rescue medication (excluding antibacterial rescue)
- Number of courses per patient-year of topical corticosteroids of any potency
- Number of courses per patient-year of topical tacrolimus (0.1%), topical pimecrolimus (1%) or grade VII topical corticosteroid
- Number of courses per patient year of moderate potency (grade IV and V) topical steroids

The population summary measure of interest will be the number of events per patient-year.

Intercurrent events for rate endpoints looking at rescue medication will be accounted for in the following manner:

Table 4: Intercurrent Event Strategies for Rate Estimand 1

Discontinuation of treatment	The use of prohibited medications or TCS/TCI rescue therapy, non-compliance with study drug, any deviations from protocol
While on treatment strategy Exclude all data collected more than 30 days after the last dose of IMP	Treatment policy strategy: Data will be used as collected

Data point sets DPS1 and DPS2 will be used for all secondary rate endpoints.

10.2.3.2 Analytical Approach

The rate of each endpoint per patient year will be presented for each treatment group.
In addition the number of patients with 0, 1, 2, 3 or more courses and with at least one course will be displayed.

Histograms for the number of rescue therapy periods, topical corticosteroid periods, topical tacrolimus, pimecrolimus or grade VII corticosteroid periods and moderate potency topical steroids periods will be produced.

The proportion of participants using rescue therapy, topical corticosteroids, topical tacrolimus, pimecrolimus or grade VII corticosteroid and moderate potency topical steroids periods will be also be plotted.

10.3 Exploratory Efficacy Analysis

10.3.1 Time to Event Analysis

10.3.1.1 Estimands

The exploratory time to event endpoints are:

- Time to first achievement of EASI-50
- Time to first achievement of sustained EASI-50 (See section 5.3.3.1)

The population summary measure of interest will be the cumulative percentage of participants achieving response at each scheduled visit.

Intercurrent events for the exploratory time to event endpoints will be accounted for in the following manner:

Table 5: Intercurrent Event Strategies for Time to Event Estimand 1

Use of TCS/TCI rescue medications within 4 weeks or type 1 prohibited meds from 207, use at any time of other prohibited medications for atopic dermatitis	Treatment discontinuation, non-compliance with treatment, other deviations from the protocol
Composite strategy Participants will be considered as 'non-responders' 1) within 4 weeks after the use of TCS/TCI rescue medications or type 1 prohibited meds from 207 2) at any time after the use of other prohibited medications for atopic dermatitis	Treatment policy strategy: Data will be used as collected

For all exploratory time to event endpoints data point set DPS4b will be used.

10.3.1.2 Analytical Approach

The number of participants meeting the criteria for the endpoint and the number of participants 'at risk' of meeting the criteria at each visit will be presented together with the cumulative incidence. Cumulative incidence is calculated as the total number of events on or before the visit divided by the total number of participants at risk of the event. Unless otherwise stated, the results will be summarised at the following visits: Baseline, 207 week 4, 8, 12, 16 (labelled as "207 / Week X") and 208 week 4, 8, 12, 16, 24, 36 and 40 (labelled as "208 / Week X").

Plots for the cumulative incidence of participants achieving EASI-50 and sustained EASI-50 over time will be produced for each treatment group.

10.3.2 Continuous Variables Analysis

10.3.2.1 Estimands

The exploratory continuous endpoints in set 1 are:

- Change and percentage change from baseline in each of the four body-region scores of the EASI
- Daily absolute change from baseline in PP-NRS and SD-NRS scores

The population summary measure of interest will be the mean change from baseline at each scheduled visit for the body-region scores endpoint and daily for PP-NRS and SD-NRS endpoints.

The exploratory continuous endpoints in set 1 will be analysed with continuous estimand 1 (DPS4a). Intercurrent events for the exploratory continuous endpoints in set 1 will be accounted for as described in Table 3 for continuous estimand 1.

The exploratory continuous endpoints in set 2 are:

- Change from baseline in ADCT score

The population summary measure of interest will be the mean change from baseline at each scheduled visit.

Intercurrent events for the exploratory continuous endpoints in set 2 will be accounted for in the following manner:

Table 6: Intercurrent Event Strategies for Continuous Estimand 3

For all possible intercurrent events
Treatment policy strategy: Data will be used as collected at scheduled visits

The exploratory continuous endpoints in set 2 will use data point set DPS4.

10.3.2.2 Analytical Approach

The number of participants, mean, median, standard deviation (SD), minimum, and maximum values will be presented at each scheduled visit that the variable is recorded. The following visits should be presented unless otherwise stated: Baseline, 207 week 4, 8, 12, 16 (labelled as "207 / Week X") and 208 week 4, 8, 12, 16, 24, 36 and 40 (labelled as "208 / Week X").

As ADCT scores were not collected at week 8 during the 207 parent study they will not be summarised at these visits.

Figures for the mean percentage change and change from baseline for ADCT score will be displayed over time. Waterfall plots for the percentage change and change from baseline will also be produced for the same visits as presented in tables.

For the daily PP-NRS and SD-NRS endpoints, only graphical summaries will be presented.

10.3.3 Responder Analysis

10.3.3.1 Estimands

The exploratory response endpoints are:

- Achievement of 50% reduction in each of the four region scores of the EASI
- Change in response states from Day -1 to weeks 8, 16, 24 and 36. Response states will be defined using the EASI score percentage change from baseline with categories for: ≥25% increase, no change (<25% increase to <25% decrease), 25% to <50% decrease, 50% to <75% decrease, 75% to <90% decrease, ≥90% decrease

Achievement of 50% reduction in each of the four region scores of the EASI

The population summary measure of interest will be the percentage of participants achieving response at each visit.

Change in response states from Day -1 to weeks 8, 16, 24 and 36

The population summary measure of interest will be the percentage of participants with each change in response state.

Intercurrent events will be accounted for in the following manner:

Table 7: Intercurrent Event Strategies of the 50% reduction of EASI in body regions

Use of TCS/TCI rescue medications within 4 weeks or type 1 prohibited meds from 207, use at any time of other prohibited medications for atopic dermatitis	**Treatment discontinuation, non-compliance with treatment, other deviations from the protocol**
Composite strategy Participants will be considered as 'non-responders' 1) within 4 weeks after the use of TCS/TCI rescue medications or type 1 prohibited meds from 207 2) at any time after the use of other prohibited medications for atopic dermatitis	Treatment policy strategy: Data will be used as collected

Data point set DPS4b will be used for exploratory response endpoints.

10.3.3.2 Analytical Approach

Summary tabulations of frequency and percentage of participants within each category will be presented at each scheduled visit that the variable is recorded. The following visits should be presented unless otherwise stated: Baseline, 207 Week 4, 8, 12, 16 (labelled as "207 / Week X") and 208 week 4, 8, 12, 16, 24, 36, 40 (labelled as "208 / Week X").

Plots for the mean percentage change and change from baseline in EASI score over time by region will be produced along with waterfall plots for the percentage change and change from baseline in EASI score. The proportion of participants achieving 50% reduction in EASI score over time by region will also be displayed.

11 Safety Analyses

The FAS or the parent study specific FAS for the study/cohort specific analysis will be used for all Safety estimands and summaries. A **treatment policy** approach will be used for all safety estimands, including all data collected regardless of treatment discontinuation, treatment compliance and use of other medications. All safety endpoints will be listed.

11.1 Early Stopping

In the event that the study is stopped early and only a reduced amount of outputs are needed, safety data will only be reported for the period beginning with the first dose of active IMP in this study.

Additionally to the primary safety endpoints, only the non-serious TEAEs will be summarized by SOC and PT, however, PTs will be presented only in case of TEAEs reported by at least 5% of participants in any treatment group.

Data will be presented as collected, no imputations or data exclusion will be made.

The list of outputs produced in the case the study is stopped early are provided in 16Appendix 1: List of Tables, Figures and Listings.

11.2 Extent of Exposure

The duration of exposure (days) and number of doses taken will be summarized using summary statistics for continuous data. Two summary tables will be produced, one for the duration of exposure from first dose in this study and one from the first dose of active treatment across this study and the parent study.

For the 208 specific summary the number and percentage of participants with at least 4, 8, 12, 16, 24 and 36 weeks (28, 56, 84, 112, 168, 252 days respectively) of exposure will also be presented.

For the 208 and parent study summary the number and percentage of participants with at least 16, 20, 24, 28, 32, 40 and 52 weeks (112, 140, 168, 196, 224, 280, 364 days respectively) of exposure will also be presented.

The total exposure per 100 patient-years will also be summarised for each treatment group for both summaries.

Treatment start and stop dates, exposure duration (days), number of doses administered, number of capsules taken and reasons for dose adjustments and dose interruptions will be listed by participant.

11.3 Adverse Events

In this study adverse events will be reported from the date of signed informed consent and through the Week 36 visit up to 30 days after the last dose of IMP. Adverse events occurring after 30 days post-treatment would only be reported if the investigator considers it to be related to the study treatment.

AEs reported during the parent study that are ongoing at the end of treatment visits will continue to be followed up in this study until resolution or the participant completes the study, whichever is first.

Two summaries will be produced for each classification of adverse events. One will use DPS1 and report only those adverse events that started during this study until 30 days after the last dose of IMP and one that will use DPS2 and report those adverse events that occur following the first dose of active IMP, either in the parent study or in this study until 30 days after the last dose of IMP in this study.

Only treatment emergent AEs (TEAEs) will be included in the summaries, pre-treatment AEs will be included in the listings of all AEs.

All AEs will be coded using MedDRA. The dictionary will be updated through the life of the study with version 24.0 used initially. Severity of event will be coded using the Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

In addition to the primary AE summary specified in Section 9, TEAEs will be summarized by system organ class (SOC) and preferred term (PT) for each of the reporting periods. For the period defined by this study only, the number and percentage of participants reporting events, and the number and rate per 100 patient-years of events will be presented. For the summary looking at the period defined since first dose of active IMP by either in this study and the relevant parent study, the number and percentage of participants reporting events, and the number and rate per 100 patient-years of events will be presented.

For the incidence statistics, a participant who has multiple events in the same SOC or the same preferred term will be counted only once. All events will be counted in the number and rate per 100 years statistics. Adverse event summaries will be sorted by the internationally agreed SOC order (Table 10) and decreasing incidence of preferred term within SOC in the total column.

Related TEAEs, TEAEs of Grade 3 or above, serious TEAEs and TEAEs leading to discontinuation of study drug will also be summarised by SOC and PT in the manner described above.

Non-serious TEAEs will be also summarized by SOC and PT, however, PTs will be presented only in case of TEAEs reported by at least 5% of participants in any treatment group.

11.4 Deaths, Serious Adverse Events and other Significant Adverse Events

Serious AEs, fatal AEs and AEs leading to discontinuation of study drug will each be listed separately by participant.

No specific adverse events are considered to be of special interest for EDP1815.

11.5 Pregnancies

Pregnancy test data will be listed only.

11.6 Clinical Laboratory Evaluations

Central laboratory data will be used for all safety laboratory evaluations. Table 11 shows the parameters which will be collected and the units in which they will be supplied. Lab data will be transformed as appropriate to the International System of Units (SI units) as part of the SDTM programming and SI units will be used for all summaries.

Haematology and chemistry parameters will be summarized by visit, including change from baseline for all post-baseline visits, using DPS3.

The number and percentage of participants showing shifts from baseline to worst-case post-baseline with respect to the normal ranges will also be summarized for each haematology and chemistry parameter, using DPS1. Categories will be:

- Low
- Normal
- High

Haematology and chemistry values will also be flagged for potentially clinically important (PCI) values if they meet any of the criteria for Grade 2 or higher events according to CTCAE V5.0. The PCI criteria are listed in Table 11. The number and percentage of participants showing shifts from baseline to worst-case baseline with respect to PCI criteria will be summarized for all parameters where PCI criteria have been defined, using DPS1. Categories will be:

- Low
- Within range
- High

For both the normal range and PCI summaries, the determination of worst-case post-baseline will consider both scheduled and unscheduled assessments which occur after the first dose of study treatment. Percentages will use the number of participants with at least one post-baseline assessment available as the denominator. If the baseline value is missing it will be assumed to be normal/within range. Worst-case can be either High or Low and if a participant has post-baseline values both above and below the normal range/PCI criteria then they will be counted in both relevant categories.

Haematology and chemistry data will be listed, including changes from baseline, normal ranges, flags for measurements outside the normal range, and flags for meeting PCI criteria. In addition, for participants who meet at least one PCI criteria, all values within the laboratory type (haematology or chemistry) will be listed separately.

Urinalysis data will be listed only.

11.7 Other Safety Measures

11.7.1 ECG

Ventricular rate, PR interval, RR interval, QRS duration, QT interval and QTcF interval will be summarized by visit, including change from baseline, using DPS3.

In addition, the QTcF interval will be flagged for PCI if it meets the CTCAE (v5.0) criteria for a Grade 3 or above event (>500 ms or a >60 ms increase from baseline).
The number and percentage of participants showing a shift from baseline to worst-case post-baseline with respect to the QTcF PCI criteria will be summarized and will use DPS1. Categories will be:

- Within range
- High

The determination of worst-case post-baseline will consider all scheduled and unscheduled assessments which occur after the first dose of study treatment. Percentages will use the number of participants with at least one post-baseline assessment available. If the baseline value is missing it will be assumed to be normal for this summary.

All ECG data will be listed, including flags for values which meet the PCI criteria for QTcF. In addition, a separate listing of all ECG assessments for any participant who has at least one value meeting the QTcF PCI criteria will be produced.

11.7.2 Vital Signs

Systolic blood pressure (BP), diastolic BP, pulse rate, respiratory rate and temperature will be summarized by visit, including change from baseline, using DPS3.

In addition, vital signs data will be flagged as potentially clinically important (PCI) if they meet the CTCAE (v5.0) criteria for a Grade 3 or above event as shown in Table 8.

Table 8: PCI Criteria for Vital Signs

Parameter	Units	PCI Criteria
Systolic Blood Pressure	mmHg	≥ 160
Diastolic Blood Pressure	mmHg	≥ 100

The number and percentage of participants showing shifts from baseline to worst-case post-baseline with respect to the PCI criteria will also be summarized for each parameter and will use DPS1. Categories will be:

- Within range
- High

The determination of worst-case post-baseline will consider all scheduled and unscheduled assessments which occur after the first dose of study treatment. Percentages will use the number of

participants with at least one post-baseline assessment available. If the baseline value is missing it will be assumed to be within range for this summary.

All vital signs data will be listed, including flags for values which meet the PCI criteria. In addition, a separate listing of all vital signs assessments for any participant who meet has at least one value meeting the PCI criteria will be produced.

11.7.3 Physical Examination

All clinically significant abnormalities identified through physical examination should be recorded as adverse events and listed with adverse events. No separate listings of physical examinations will be produced.

12 Reporting Conventions

When reporting relative frequencies or other percentage values, the following rules apply:

- For values where all subjects fulfil certain criteria, the percentage value will be displayed as 100
- For values where the absolute frequency is 0, there will be no percentage presented at all
- All other percentage displays will use 1 decimal place

When reporting descriptive statistics, the following rules will apply in general:

- n will be an integer
- Mean and median will use 1 decimal place more than the original data
- Standard deviation will use 2 decimal places more than then original data
- Minimum and maximum will be reported using the same number of decimal places as the original value
- If no subjects have data at a given timepoint, for example, then only n=0 will be presented. However, if n<3, present the n, min and maximum only. If n=3, n, mean, median, minimum and maximum will be presented only. The other descriptive statistics will be left blank

13 Technical Details

Statistical evaluation will be performed by [redacted]

The datasets for the interim and final analyses will follow analysis dataset model (ADaM) data specifications and will used standard data tabulation model (SDTM) data sets provided by [redacted] data management as the source data.

All analyses will be performed using SAS version 9.4 or higher (SAS Institute, Cary, NC, USA).

14 Summary of Changes from the Protocol

The SAP is based on the latest Protocol v4.0.

Table 9: Summary of Changes from the Protocol

Protocol Version	Summary of Change	Justification for change
V4.0	DSP5 Added which consists of all data collected following the first dose of IMP in this study	Added the DPS5 for use in the listings
V4.0	DPS1 and DPS2 will consider 30-days period instead of 28-days The same applies to the TEAE definition where 30-days period after the last dose of treatment is considered.	Serious AEs are reported if they occur within 30 days of last dose so only summarising TEAEs up to 28 days doesn't seem adequate.
V4.0	DPS3, 3a, 3b are removed	The results for DPS3, DPS3a and DPS3b will be a subset of the results for DPS4, DPS4a and DPS4b, so these summaries are not needed
V4.0	While on treatment strategy for the use of rescue medications within 4 weeks, use at any time of other prohibited medications for atopic dermatitis added in SAP for continuous endpoints	While on treatment strategy not included in the protocol section 11.3.2 for the mentioned intercurrent events.
V4.0	While on treatment strategy is to be used instead of composite for the intercurrent event of discontinuation of treatment for rate variables analysis	Renaming the intercurrent event strategy as these endpoints don't have discontinuation of treatment in the definition.
V4.0	Daily mean absolute change from baseline in PP-NRS and SD-NRS scores will be analysed by DPS4b and not DPS1 and DPS2	DPS1 and DPS2 incorrectly listed in the protocol. The same estimand should be used as for the change from baseline scores that are averaged for the 7 days prior to and including the visit date
V4.0	Change in response states will be analysed with DPS4b only and not DPS3b	DPS3b has been removed and all the information needed is available in DPS4b
V4.0	Intercurrent events strategy for exploratory continuous endpoints in set 1 will be as for continuous estimand 1 defined for the secondary continuous analysis. DPS4a will be used instead of DPS4b	Continuous endpoints analysis should be consistent between exploratory and secondary endpoints
V4.0	The response states estimand composite strategy updated to consider patients after the intercurrent event as 'non-responders'	The response states estimand should use the same composite strategy as all other response estimands
V4.0	Intercurrent events relating to rescue therapy updated to only relate to TCS/TCI rescue therapy	TCS/TCI rescue therapy is of interest
V4.0	Secondary rate endpoint for number of courses per patient-year of any rescue medication (excluding antibacterial	TCS/TCI rescue therapy is of interest

Protocol Version	Summary of Change	Justification for change
	rescue) updated to only include any TCS/TCI rescue medication	
V4.0	Added SCORAD-35 Endpoint	Evelo decided to add SCORAD-35 at the time of 207 study Dry Run
V4.0	Removed endpoints for worst-case change from baseline with respect to values outside the normal ranges for vital signs and ECG parameters	Worst-case change from baseline with respect to values outside the normal ranges for vital signs, ECG parameters and clinical laboratory parameters for given as secondary safety endpoint but only changes with respect to normal ranges were summarized for the lab parameters. For ECG and vital signs, it was felt that only changes from PCI criteria were of specific interest.
V4.0	Efficacy outputs will not be produced as planned	The study was early terminated after the parent study primary endpoint was not met.
V4.0	Only reduced amount of disposition, demography and safety data will be summarised and listed	The study was early terminated after the parent study primary endpoint was not met.

15 Bibliography

16 Appendix 1: List of Tables, Figures and Listings

All outputs detailed in the following sections will be produced for the final analysis. In addition, those which will be produced for the interim analysis are flagged in the 'Interim' column.

If the study is stopped early, outputs will be produced as specified in the Early Stop column.

16.1 Study Population

If the study is stopped early, study population outputs will be produced as planned originally.

16.1.1 Tables

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.1.1.1	Summary of Disposition	FAS		Yes	No treatment related evaluation
14.1.1.2	Summary of Screening Status	Enrolled		No	
14.1.1.3	Summary of Participants by Region, Country, and Site	FAS		Yes	New number 14.1.1.2
14.1.1.4	Summary of Attendance at Each Visit	FAS		No	
14.1.1.5	Summary of Missed Visits Due to COVID-19	FAS		No	
14.1.1.6	Summary of Significant Protocol Deviations	FAS		No	
14.1.1.7	Summary of Populations	Enrolled		No	
14.1.2.1	Summary of Demography	FAS		Yes	New number 14.1.2

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
					Excluding weight, height and BMI
14.1.2.2	Summary of Baseline Disease Characteristics	FAS		No	
14.1.3.1	Summary of Past Medical History	FAS		No	
14.1.3.2	Summary of Current Medical History	FAS		No	
14.1.4.1	Summary of Prior Medications	FAS		No	
14.1.4.2	Summary of All Concomitant Medications	FAS		No	
14.1.4.3	Summary of Concomitant Medications Started Pre-treatment	FAS		No	
14.1.4.4	Summary of Concomitant Medications Started During the Treatment Period	FAS		No	
14.1.4.5	Summary of Concomitant Medications Started During the Follow-up Period	FAS		No	
14.1.5	Summary of Treatment Compliance	FAS		No	
14.1.6	Summary of Emollient Compliance	FAS		No	
14.1.7	Summary of Treatment Exposure	FAS		Yes	New number 14.1.3 Excluding total number of doses analysis

16.2 Efficacy

If the study is stopped early, efficacy tables and figures will be excluded from the final package.

16.2.1 Tables

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.1.1.1	Summary of EASI-50 Response	FAS	DPS4b	No	
14.2.1.1.2	Summary of EASI-50 Response	FAS	DPS4a	No	
14.2.1.1.3	Summary of EASI-50 Response	FAS	DPS4	No	
14.2.1.2.1	Summary of EASI-75 Response	FAS	DPS4b	No	
14.2.1.2.2	Summary of EASI-75 Response	FAS	DPS4a	No	
14.2.1.2.3	Summary of EASI-75 Response	FAS	DPS4	No	
14.2.1.3.1	Summary of EASI-90 Response	FAS	DPS4b	No	
14.2.1.3.2	Summary of EASI-90 Response	FAS	DPS4a	No	
14.2.1.3.3	Summary of EASI-90 Response	FAS	DPS4	No	
14.2.1.4.1	Summary of the percentage change from baseline in EASI score	FAS	DPS4a	No	
14.2.1.4.2	Summary of the absolute change from baseline in EASI score	FAS	DPS4a	No	
14.2.1.5.1	Summary of the time to first achievement of EASI-50	FAS	DPS4b	No	
14.2.1.6.1	Summary of the time to first achievement of sustained EASI-50	FAS	DPS4b	No	
14.2.1.7.1	Summary of the absolute and percentage change from baseline in each of the four body-region scores of the EASI	FAS	DPS4a	No	
14.2.1.8.1	Summary of the achievement of 50% reduction in each of the four region scores of the EASI	FAS	DPS4b	No	
14.2.1.9.1	Summary of the change in response states using percentage change from baseline EASI score	FAS	DPS4b	No	
14.2.2.1.1	Summary of vIGA Score	FAS	DPS4a	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.2.2.1	Summary of vIGA of 0 or 1 With a >=2 Point Improvement from Baseline	FAS	DPS4b	No	
14.2.2.2.2	Summary of vIGA of 0 or 1 With a >=2 Point Improvement from Baseline	FAS	DPS4a	No	
14.2.2.2.3	Summary of vIGA of 0 or 1 With a >=2 Point Improvement from Baseline	FAS	DPS4	No	
14.2.2.3.1	Summary of vIGA of 0 or 1	FAS	DPS4b	No	
14.2.2.3.2	Summary of vIGA of 0 or 1	FAS	DPS4a	No	
14.2.2.3.3	Summary of vIGA of 0 or 1	FAS	DPS4	No	
14.2.2.4.1	Summary of vIGA of 0	FAS	DPS4b	No	
14.2.3.1.1	Summary of Percentage Change from Baseline in vIGA*BSA	FAS	DPS4a	No	
14.2.3.2.1	Summary of Absolute Change from Baseline in vIGA*BSA	FAS	DPS4a	No	
14.2.4.1.1	Summary of BSA-50 Response	FAS	DPS4b	No	
14.2.4.1.2	Summary of BSA-50 Response	FAS	DPS4a	No	
14.2.4.1.3	Summary of BSA-50 Response	FAS	DPS4	No	
14.2.4.2.1	Summary of BSA-75 Response	FAS	DPS4b	No	
14.2.4.2.2	Summary of BSA-75 Response	FAS	DPS4a	No	
14.2.4.2.3	Summary of BSA-75 Response	FAS	DPS4	No	
14.2.4.3.1	Summary of BSA ≤ 3%	FAS	DPS4b	No	
14.2.4.1.1	Summary of Percentage Change from Baseline in BSA	FAS	DPS4a	No	
14.2.4.2.1	Summary of Absolute Change from Baseline in BSA	FAS	DPS4a	No	
14.2.5.1.1	Summary of SCORAD-35 Response	FAS	DPS4b	No	
14.2.5.1.2	Summary of SCORAD-35 Response	FAS	DPS4a	No	
14.2.5.1.3	Summary of SCORAD-35 Response	FAS	DPS4	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.5.2.1	Summary of SCORAD-50 Response	FAS	DPS4b	No	
14.2.5.2.2	Summary of SCORAD-50 Response	FAS	DPS4a	No	
14.2.5.2.3	Summary of SCORAD-50 Response	FAS	DPS4	No	
14.2.5.3.1	Summary of SCORAD-75 Response	FAS	DPS4b	No	
14.2.5.3.2	Summary of SCORAD-75 Response	FAS	DPS4a	No	
14.2.5.3.3	Summary of SCORAD-75 Response	FAS	DPS4	No	
14.2.5.4.1	Summary of Percentage Change from Baseline in SCORAD Score	FAS	DPS4a	No	
14.2.5.5.1	Summary of Absolute Change from Baseline in SCORAD Score	FAS	DPS4a	No	
14.2.6.1.1	Summary of Improvement of ≥4 Points in DLQI from Baseline for Participants with a Score of ≥4 at Baseline	FAS	DPS4b	No	
14.2.6.2.1	Summary of Percentage Change from Baseline in DLQI Score	FAS	DPS4a	No	
14.2.6.3.1	Summary of Absolute Change from Baseline in DLQI Score	FAS	DPS4a	No	
14.2.7.1.1	Summary of ≥2 Point Improvement in PP-NRS Score from Baseline for Participants with a Score of ≥2 at Baseline	FAS	DPS4b	No	
14.2.7.2.1	Summary of ≥4 Point Improvement in PP-NRS Score from Baseline for Participants with a Score of ≥4 at Baseline	FAS	DPS4b	No	
14.2.7.3.1	Summary of Absolute Change from Baseline in PP-NRS Score	FAS	DPS4a	No	
14.2.8.1.1	Summary of >=2 Point Improvement in SD-NRS Score from Baseline for Participants with a Score of >=2 at Baseline	FAS	DPS4b	No	
14.2.8.2.1	Summary of Absolute Change from Baseline in SD-NRS Score	FAS	DPS4a	No	
14.2.9.1.1	Summary of >=4 Point Improvement in POEM Score from Baseline for Participants with a Score of >=4 at Baseline	FAS	DPS4b	No	
14.2.9.1.2	Summary of >=4 Point Improvement in POEM Score from Baseline for Participants with a Score of >=4 at Baseline	FAS	DPS4a	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.9.1.3	Summary of >=4 Point Improvement in POEM Score from Baseline for Participants with a Score of >=4 at Baseline	FAS	DPS4	No	
14.2.9.2.1	Summary of Percentage Change from Baseline in POEM Score	FAS	DPS4a	No	
14.2.9.3.1	Summary of Absolute Change from Baseline in POEM Score	FAS	DPS4a	No	
14.2.10.1.1	Summary of Absolute Change from Baseline in ADCT Score	FAS	DPS4	No	
14.2.11.1.1	Summary of the Number of Courses Per-Patient Year of any Rescue Medication	FAS	DPS1	No	
14.2.11.1.2	Summary of the Number of Courses per Patient-Year of any Rescue Medication	FAS	DPS2	No	

16.2.2 Figures

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.1.1.1	Proportion of Participants Achieving EASI-50 Response Over Time	FAS	DPS4	No	
14.2.1.1.2	Proportion of Participants Achieving EASI-50 Response Over Time	FAS	DPS4a	No	
14.2.1.1.3	Proportion of Participants Achieving EASI-50 Response Over Time	FAS	DPS4b	No	
14.2.1.2.1	Proportion of Participants Achieving EASI-75 Response Over Time	FAS	DPS4	No	
14.2.1.2.2	Proportion of Participants Achieving EASI-75 Response Over Time	FAS	DPS4a	No	
14.2.1.2.3	Proportion of Participants Achieving EASI-75 Response Over Time	FAS	DPS4b	No	
14.2.1.3.1	Proportion of Participants Achieving EASI-90 Response Over Time	FAS	DPS4	No	
14.2.1.3.2	Proportion of Participants Achieving EASI-90 Response Over Time	FAS	DPS4a	No	
14.2.1.3.3	Proportion of Participants Achieving EASI-90 Response Over Time	FAS	DPS4b	No	
14.2.1.4.1	Waterfall Plot of Percentage Change from Baseline in EASI Score	FAS	DPS4	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.1.5.1	Mean (+/-SD) Percentage Change from Baseline in EASI Score Over Time	FAS	DPS4	No	
14.2.1.6.1	Waterfall Plot of Change from Baseline in EASI Score	FAS	DPS4	No	
14.2.1.7.1	Mean (+/-SD) Change from Baseline in EASI Score Over Time	FAS	DPS4	No	
14.2.2.1.1	Proportion of Participants Achieving vIGA of 0 or 1 With a >=2 Point Improvement from Baseline	FAS	DPS4	No	
14.2.2.1.2	Proportion of Participants Achieving vIGA of 0 or 1 With a >=2 Point Improvement from Baseline	FAS	DPS4a	No	
14.2.2.1.3	Proportion of Participants Achieving vIGA of 0 or 1 With a >=2 Point Improvement from Baseline	FAS	DPS4b	No	
14.2.2.2.1	Proportion of Participants Achieving vIGA of 0 or 1 Response	FAS	DPS4	No	
14.2.2.2.2	Proportion of Participants Achieving vIGA of 0 or 1 Response	FAS	DPS4a	No	
14.2.2.2.3	Proportion of Participants Achieving vIGA of 0 or 1 Response	FAS	DPS4b	No	
14.2.2.3.1	Proportion of Participants Achieving vIGA of 0	FAS	DPS4	No	
14.2.2.4.1	Waterfall Plot of Percentage Change from Baseline in IGA*BSA	FAS	DPS4	No	
14.2.2.5.1	Mean (+/-SD) Percentage Change from Baseline in IGA*BSA Over Time	FAS	DPS4	No	
14.2.2.6.1	Waterfall Plot of Change from Baseline in IGA*BSA	FAS	DPS4	No	
14.2.2.7.1	Mean (+/-SD) Change from Baseline in IGA*BSA Over Time	FAS	DPS4	No	
14.2.3.1.1	Proportion of Participants Achieving BSA-50 Response Over Time	FAS	DPS4	No	
14.2.3.1.2	Proportion of Participants Achieving BSA-50 Response Over Time	FAS	DPS4a	No	
14.2.3.1.3	Proportion of Participants Achieving BSA-50 Response Over Time	FAS	DPS4b	No	
14.2.3.2.1	Proportion of Participants Achieving BSA-75 Response Over Time	FAS	DPS4	No	
14.2.3.2.2	Proportion of Participants Achieving BSA-75 Response Over Time	FAS	DPS4a	No	
14.2.3.2.3	Proportion of Participants Achieving BSA-75 Response Over Time	FAS	DPS4b	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.3.3.1	Proportion of Participants Achieving BSA ≤ 3%	FAS	DPS4	No	
14.2.3.4.1	Waterfall Plot of Percentage Change from Baseline in BSA	FAS	DPS4	No	
14.2.3.5.1	Mean (+/-SD) Percentage Change from Baseline in BSA Over Time	FAS	DPS4	No	
14.2.3.6.1	Waterfall Plot of Change from Baseline in BSA	FAS	DPS4	No	
14.2.3.7.1	Mean (+/-SD) Change from Baseline in BSA Over Time	FAS	DPS4	No	
14.2.4.1.1	Proportion of Participants Achieving SCORAD-35 Response Over Time	FAS	DPS4	No	
14.2.4.1.2	Proportion of Participants Achieving SCORAD-35 Response Over Time	FAS	DPS4a	No	
14.2.4.1.3	Proportion of Participants Achieving SCORAD-35 Response Over Time	FAS	DPS4b	No	
14.2.4.2.1	Proportion of Participants Achieving SCORAD-50 Response Over Time	FAS	DPS4	No	
14.2.4.2.2	Proportion of Participants Achieving SCORAD-50 Response Over Time	FAS	DPS4a	No	
14.2.4.2.3	Proportion of Participants Achieving SCORAD-50 Response Over Time	FAS	DPS4b	No	
14.2.4.3.2	Proportion of Participants Achieving SCORAD-75 Response Over Time	FAS	DPS4	No	
14.2.4.3.3	Proportion of Participants Achieving SCORAD-75 Response Over Time	FAS	DPS4a	No	
14.2.4.3.6	Proportion of Participants Achieving SCORAD-75 Response Over Time	FAS	DPS4b	No	
14.2.4.4.1	Waterfall Plot of Percentage Change from Baseline in SCORAD Score	FAS	DPS4	No	
14.2.4.5.1	Mean (+/-SD) Percentage Change from Baseline in SCORAD Score Over Time	FAS	DPS4	No	
14.2.4.6.1	Waterfall Plot of Change from Baseline in SCORAD Score	FAS	DPS4	No	
14.2.4.7.1	Mean (+/-SD) Change from Baseline in SCORAD Score Over Time	FAS	DPS4	No	
14.2.5.1.1	Proportion of Participants Achieving DLQI With a >=4 Point Improvement from Baseline for Participants with a Score of >=4 at Baseline Over Time	FAS	DPS4	No	
14.2.5.2.1	Waterfall Plot of Percentage Change from Baseline in DLQI Score	FAS	DPS4	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.5.3.1	Mean (+/-SD) Percentage Change from Baseline in DLQI Score Over Time	FAS	DPS4	No	
14.2.5.4.1	Waterfall Plot of Change from Baseline in DLQI Score	FAS	DPS4	No	
14.2.5.5.1	Mean (+/-SD) Change from Baseline in DLQI Score Over Time	FAS	DPS4	No	
14.2.6.1.1	Proportion of Participants Achieving POEM With a >=4 Point Improvement from Baseline for Participants with a Score of >=4 at Baseline Over Time	FAS	DPS4	No	
14.2.6.2.1	Waterfall Plot of Percentage Change from Baseline in POEM Score	FAS	DPS4	No	
14.2.6.3.1	Mean (+/-SD) Percentage Change from Baseline in POEM Score Over Time	FAS	DPS4	No	
14.2.6.4.1	Waterfall Plot of Change from Baseline in POEM Score	FAS	DPS4	No	
14.2.6.5.1	Mean (+/-SD) Change from Baseline in POEM Score Over Time	FAS	DPS4	No	
14.2.7.1.1	Proportion of Participants Achieving PP-NRS With a >=2 Point Improvement from Baseline for Participants with a Score of >=2 at Baseline Over Time	FAS	DPS4	No	
14.2.7.2.1	Proportion of Participants Achieving PP-NRS With a >=4 Point Improvement from Baseline for Participants with a Score of >=4 at Baseline Over Time	FAS	DPS4	No	
14.2.7.3.1	Waterfall Plot of Change from Baseline in PP-NRS Score	FAS	DPS4	No	
14.2.7.4.1	Mean (+/-SD) Change from Baseline in PP-NRS Score Over Time	FAS	DPS4	No	
14.2.7.5.1	Proportion of Participants Achieving PP-NRS Score with a >=4 Point Improvement from Baseline for Participants with a Score of >=4 at Baseline – Daily	FAS	DPS4	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.8.1.1	Proportion of Participants Achieving SD-NRS With a >=4 Point Improvement from Baseline for Participants with a Score of >=4 at Baseline Over Time	FAS	DPS4	No	
14.2.8.2.1	Waterfall Plot of Change from Baseline in SD-NRS Score	FAS	DPS4	No	
14.2.8.3.1	Mean (+/-SD) Change from Baseline in SD-NRS Score Over Time	FAS	DPS4	No	
14.2.8.4.1	Proportion of Participants Achieving SD-NRS Score with a >=4 Point Improvement from Baseline for Participants with a Score of >=4 at Baseline – Daily	FAS	DPS4	No	
14.2.9.1.1	Histogram of Number of Rescue Therapy Periods	FAS	DPS4	No	
14.2.9.2.1	Proportion of Participants Achieving Requirement for Rescue Therapy Over Time	FAS	DPS4	No	
14.2.9.3.1	Histogram of Number of Topical Corticosteroids Periods	FAS	DPS4	No	
14.2.9.4.1	Proportion of Participants Achieving Requirement for Topical Corticosteroids Over Time	FAS	DPS4	No	
14.2.9.5.1	Histogram of Number of Topical Tacrolimus, Pimecrolimus or Grade VII Corticosteroid Periods	FAS	DPS4	No	
14.2.9.6.1	Proportion of Participants Achieving Requirement for Topical Tacrolimus, Pimecrolimus or Grade VII Corticosteroid Over Time	FAS	DPS4	No	
14.2.9.7.1	Histogram of Number of Moderate Potency Topical Steroids Periods	FAS	DPS4	No	
14.2.9.8.1	Proportion of Participants Achieving Requirement for Moderate Potency Topical Steroids Over Time	FAS	DPS4	No	
14.2.10.1.1	Cumulative Incidence (+/- 95% CI) of Participants Achieving EASI-50	FAS	DPS4b	No	
14.2.10.2.1	Cumulative Incidence (+/- 95% CI) of Participants Achieving Sustained EASI-50	FAS	DPS4b	No	
14.2.11.1.1	Waterfall Plot of Change from Baseline in ADCT Score	FAS	DPS4	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.2.11.2.1	Mean (+/-SD) Change from Baseline in ADCT Score Over Time	FAS	DPS4	No	
14.2.12.1.1	Waterfall Plot of Percentage Change from Baseline in EASI Score by Region	FAS	DPS4	No	
14.2.12.2.1	Mean (+/-SD) Percentage Change from Baseline in EASI Score Over Time by Region	FAS	DPS4	No	
14.2.12.3.1	Waterfall Plot of Change from Baseline in EASI Score by Region	FAS	DPS4	No	
14.2.12.4.1	Mean (+/-SD) Change from Baseline in EASI Score Over Time by Region	FAS	DPS4	No	
14.2.12.5.1	Proportion of Participants Achieving 50% Reduction in EASI Score Over Time by Region	FAS	DPS4b	No	
14.2.13.5.1	Change in Response States	FAS	DPS4b	No	

16.3 Safety

If the study is stopped early, safety outputs will be produced as planned originally.

16.3.1 Tables

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.3.1.1.1	Overview of TEAEs reported in 208	FAS	DPS1	Yes	New number 14.3.1.1
14.3.1.1.2	Overview of TEAEs reported since first active dose in 207 or 208	FAS	DPS2	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.3.1.2.1	Summary of the Incidence and Rate per 100 Patient-Years of TEAEs by System Organ Class and Preferred Term	FAS	DPS1	Yes	New number 14.3.1.2 Only present E (number of events); exclude rate
14.3.1.2.2	Summary of the Incidence and Rate per 100 Patient-Years of TEAEs by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.3.1	Summary of the Incidence and Rate per 100 Patient-Years of TEAEs of Grade 2 or Above by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.3.2	Summary of the Incidence and Rate per 100 Patient-Years of TEAEs of Grade 2 or Above by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.4.1	Summary of the Incidence and Rate per 100 Patient-Years of TEAEs of Grade 3 or Above by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.4.2	Summary of the Incidence and Rate per 100 Patient-Years of TEAEs of Grade 3 or Above by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.5.1	Summary of the Incidence and Rate per 100 Patient-Years of Serious TEAEs by System Organ Class and Preferred Term	FAS	DPS1	Yes	New number 14.3.1.4 Only present E (number of events); exclude rate
14.3.1.5.2	Summary of the Incidence and Rate per 100 Patient-Years of Serious TEAEs by System Organ Class and Preferred Term	FAS	DPS2	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.3.1.6.1	Summary of the Incidence and Rate per 100 Patient-Years of Fatal TEAEs by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.6.2	Summary of the Incidence and Rate per 100 Patient-Years of Fatal TEAEs by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.7.1	Summary of the Incidence and Rate per 100 Patient-Years of TEAEs Causing Discontinuation of Study Drug by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.7.2	Summary of the Incidence and Rate per 100 Patient-Years of TEAEs Causing Discontinuation of Study Drug by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.8.1	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related TEAEs by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.8.2	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related TEAEs by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.9.1	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related TEAEs of Grade 2 or Above by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.9.2	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related TEAEs of Grade 2 or Above by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.10.1	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related TEAEs of Grade 3 or Above by System Organ Class and Preferred Term	FAS	DPS1	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.3.1.10.2	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related TEAEs of Grade 3 or Above by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.11.1	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related Serious TEAEs by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.11.2	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related Serious TEAEs by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.12.1	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related Fatal TEAEs by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.12.2	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related Fatal TEAEs by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.13.1	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related TEAEs Causing Discontinuation of Study Drug by System Organ Class and Preferred Term	FAS	DPS1	No	
14.3.1.13.2	Summary of the Incidence and Rate per 100 Patient-Years of Study Drug Related TEAEs Causing Discontinuation of Study Drug by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.1.14.1	Summary of Non-serious TEAEs Reported by at Least 5% of Participants in Any Treatment Group by System Organ Class and Preferred Term	FAS	DPS1	Yes	New number 14.3.1.3 Only present E (number of events); exclude rate

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
14.3.1.14.2	Summary of Non-serious TEAEs Reported by at Least 5% of Participants in Any Treatment Group by System Organ Class and Preferred Term	FAS	DPS2	No	
14.3.4.1.1	Summary of Haematology Parameters	FAS	DPS3	No	
14.3.4.1.2	Shifts from Baseline to Worst-case Post-Baseline with Respect to the Normal Range for Haematology Parameters	FAS	DPS1	No	
14.3.4.1.3	Shifts from Baseline to Worst-case Post-Baseline with Respect to the PCI Criteria for Haematology Parameters	FAS	DPS1	No	
14.3.4.2.1	Summary of Chemistry Parameters	FAS	DPS3	No	
14.3.4.2.2	Shifts from Baseline to Worst-case Post-Baseline with Respect to the Normal Range for Chemistry Parameters	FAS	DPS1	No	
14.3.4.2.3	Shifts from Baseline to Worst-case Post-Baseline with Respect to the PCI Criteria for Chemistry Parameters	FAS	DPS1	No	
14.3.5.1	Summary of ECG Parameters	FAS	DPS3	No	
14.3.5.2	Shifts from Baseline to Worst-case Post-Baseline with Respect to the PCI Criterion for QTcF	FAS	DPS1	No	
14.3.6.1	Summary of Vital Signs	FAS	DPS3	No	
14.3.6.2	Shifts from Baseline to Worst-case Post-Baseline with Respect to the PCI Criterion for Vital Signs	FAS	DPS1	No	

16.4 Data Listings

If the study is stopped early, listings will be produced as specified in the Early Stop column.

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
16.2.1.1	Reasons for Screen Failure	Enrolled	DPS5	No	
16.2.1.2	End of Treatment Disposition	FAS	DPS5	Yes	New number 16.2.1 Reduced, combined with study disposition
16.2.1.3	End of Study Disposition	FAS	DPS5	No	
16.2.1.4	Participants for Whom the Blind for the Parent Study was Broken	FAS	DPS5	No	
16.2.1.5	Actual Treatments	FAS	DPS5	No	
16.2.1.6	Visits Missed Due to COVID-19	FAS	DPS5	No	
16.2.2	Protocol Deviations	FAS	DPS5	No	
16.2.3	Participants Excluded from Any Population	Enrolled	DPS5	No	
16.2.4.1	Demographics	FAS	DPS5	Yes	New number 16.2.2 Excluding height, weight and BMI
16.2.4.2	Smoking Status	FAS	DPS5	No	
16.2.4.3	Baseline Disease Characteristics	FAS	DPS5	No	
16.2.4.4.1	Past Atopic Dermatitis Treatment	FAS	DPS5	No	
16.2.4.4.2	Current Atopic Dermatitis Treatment	FAS	DPS5	No	
16.2.4.5	Medical History	FAS	DPS5	No	
16.2.4.6	Prior Medications	FAS	DPS5	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
16.2.4.7	Concomitant Medications	FAS	DPS5	No	
16.2.5.1	Participant Dosing Diary	FAS	DPS5	No	
16.2.5.2	Study Drug Compliance	FAS	DPS5	Yes	New number 16.2.3 Modify to present duration of exposure only
16.2.5.3	Exposure to Emollient	FAS	DPS5	No	
16.2.5.4	Emollient Compliance	FAS	DPS5	No	
16.2.6.1	Individual Components of the EASI Questionnaire	FAS	DPS5	No	
16.2.6.2	EASI Endpoints	FAS	DPS5	No	
16.2.6.3	BSA Individual Region Components and Total BSA	FAS	DPS5	No	
16.2.6.4.1	vGIA and vIGA*BSA	FAS	DPS5	No	
16.2.6.4.2	vGIA and BSA Response Endpoints	FAS	DPS5	No	
16.2.6.5	Individual Components of the SCORAD Questionnaire	FAS	DPS5	No	
16.2.6.6	SCORAD Endpoints	FAS	DPS5	No	
16.2.6.7	DLQI Items and Score	FAS	DPS5	No	
16.2.6.8.1	Daily PP-NRS and SD-NRS Scores	FAS	DPS5	No	
16.2.6.8.2	PP-NRS and SD-NRS Scores at Scheduled Visits	FAS	DPS5	No	
16.2.6.9	POEM Items and Score	FAS	DPS5	No	
16.2.6.10	Rescue Therapy Use	FAS	DPS5	No	
16.2.6.11	Rescue Therapy Endpoints	FAS	DPS5	No	
16.2.6.12	Skin infections requiring topical or systemic antibiotic treatment	FAS	DPS5	No	

Number	Title	Population	Data Point Set	Early Stop	Programming notes for Early Stop
16.2.6.13	Time to Event Endpoints	FAS	DPS5	No	
16.2.6.14	ADCT Individual Components and Scores	FAS	DPS5	No	
16.2.7.1.1	Adverse Events	FAS	DPS5	Yes	New number 16.2.4
16.2.7.1.2	Serious Adverse Events	FAS	DPS5	No	
16.2.7.1.3	Fatal Adverse Events	FAS	DPS5	No	
16.2.7.1.4	Adverse Events Leading to Treatment Discontinuation or Early Termination of the Study	FAS	DPS5	No	
16.2.7.2.1	Haematology Parameters	FAS	DPS5	No	
16.2.7.2.2	Haematology Parameters for Participants with at Least one PCI Value	FAS	DPS5	No	
16.2.7.2.3	Chemistry Parameters	FAS	DPS5	No	
16.2.7.2.4	Chemistry Parameters for Participants with at Least one PCI Value	FAS	DPS5	No	
16.2.7.2.5	Urinalysis Parameters	FAS	DPS5	No	
16.2.7.3.1	ECG Parameters	FAS	DPS5	No	
16.2.7.3.2	ECG Parameters for Participants with at Least one PCI Value	FAS	DPS5	No	
16.2.7.4.1	Vital Signs	FAS	DPS5	No	
16.2.7.4.2	Vital Signs for Participants with at Least one PCI Value	FAS	DPS5	No	
16.2.7.5	Female Fertility Status and Pregnancy Test Results	FAS	DPS5	No	

17 Appendix 2: Eczema Area and Severity Index

Intensity

A representative area of psoriasis is selected for each body region (head and neck, upper limbs, trunk, lower limbs).

The average severity of each of four signs (erythema/redness, edema/papulation, excoriation, lichenification) in each body region is scored as:

- 0 = None
- 1 = Mild
- 2 = Moderate
- 3 = Severe

Half points (1.5 and 2.5) may be used. 0.5 is not permitted – if a sign is present it should be at least mild.

A severity score is calculated for each body region as the sum of the four scores for erythema/redness, edema/papulation, excoriation and lichenification.

- A1 = A severity score for head and neck
- A2 = A severity score for upper extremities
- A3 = A severity score for trunk
- A4 = A severity score for lower extremities

Each subtotal is multiplied by the body surface area represented by that region as follows:

- B1 = 0.1 x A1
- B2 = 0.2 x A2
- B3 = 0.3 x A3
- B4 = 0.4 x A4

Percentage area affected

The percentage area affected by psoriasis is evaluated in each of the four body regions. In each body region the area is expressed as:

- 0 = not affected at all
- 1 = 1 – 9%
- 2 = 10-29%
- 3 = 30-49%
- 4 = 50%-69%
- 5 = 70-89%
- 6 = 90-100%

EASI score calculation

Each of the body area scores is multiplied by the severity score for the relevant body region (B1-B4) to give four area intensity scores (C1-C4).

The EASI score is the sum of the four area intensity scores:

EASI score = C1 + C2 + C3 + C4.

EASI score ranges from 0 to 72.

18 Appendix 3: Validated Investigator Global Assessment

The vIGA score is selected using the descriptors below that best describe the overall appearance of the lesions at a given time point. It is not necessary that all characteristics under Morphological Description be present.

- **0 = Clear**
  No inflammatory signs of atopic dermatitis (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Post-inflammatory hyperpigmentation and/or hypopigmentation may be present.
- **1 = Almost clear**
  Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting.
- **2 =Mild**
  Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting.
- **3 = Moderate**
  Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present.
- **4 = Severe**
  Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.

The vIGA score ranges from 0 to 4.

19 Appendix 4: Severity Scoring of Atopic Dermatitis

Investigator-rated area score

Extent

The rule of 9 is used to calculate the affected area (A) as a percentage of the whole body.

In each affected area the area involved is assessed:

	Front	Back
Head and Neck	0 to 4.5	0 to 4.5
Upper limbs (left)	0 to 4.5	0 to 4.5
Upper limbs (right)	0 to 4.5	0 to 4.5
Palms	0, 1, 2	
Trunk	0 to 18	0 to 18
Genitals	0, 0.5, 1	
Lower limbs (left)	0 to 9	0 to 9
Lower limbs (right)	0 to 9	0 to 9

The scores for each area are added together to give 'A'. It should be noted that this gives a theoretical maximum of 102% BSA.

Intensity

An intensity of each of six signs (erythema/redness, edema/papulation, oozing/crust, excoriation, lichenification, dryness) in each body region is scored as:

- 0 = Absence
- 1 = Mild
- 2 = Moderate
- 3 = Severe

The intensity scores are added together to give 'B' (maximum 18).

Subjective symptoms component

- Pruritus is measured on visual analogue scale and ranges from 0 to 10.
- Sleep loss is measured on visual analogue scale and ranges from 0 to 10.

The subjective symptoms scores are added together to give 'C' (maximum 20).

SCORAD calculation

The SCORAD score is defined as:

SCORAD score = A/5 + 7B/2 + C.

SCORAD score ranges from 0 to 103.

20 Appendix 5: Patient Oriented Eczema Measure

The POEM consists of 7 questions:

1. Over the last week, on how many days has your skin been itchy because of the eczema?
2. Over the last week, on how many nights has your sleep been disturbed because of the eczema?
3. Over the last week, on how many days has your skin been bleeding because of the eczema?
4. Over the last week, on how many days has your skin been weeping or oozing clear fluid because of the eczema?
5. Over the last week, on how many days has your skin been cracked because of the eczema?
6. Over the last week, on how many days has your skin been flaking off because of the eczema?
7. Over the last week, on how many days has your skin felt dry or rough because of the eczema?

Each question is scored as:

- 0 = No days
- 1 = 1-2 days
- 2 = 3-4 days
- 3 = 5-6 days
- 4 = Every day

If one question is left unanswered this is scored 0 and the scores are summed and expressed as usual out of a maximum of 28.
If two or more questions are left unanswered the questionnaire is not scored.

The POEM score is the sum of the 7 item scores and ranges from 0 to 28.

21 Appendix 6: Dermatology Quality of Life Index

The DLQI consists of 10 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 influences 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 for 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 taking up time?

Questions 1 and 2 is scored on a four-point Likert scale:

- 3 = Very much
- 2 = A lot
- 1 = A little
- 0 = Not at all

Questions 3-6 and 8-10 also have an option of not relevant and are scored as:

- 3 = Very much
- 2 = A lot
- 1 = A little
- 0 = Not at all
- 0 = Not relevant

Question 7 is a 2-part question and is scored as:

- 3 = Yes
- 2 = No; A lot
- 1 = No; A little
- 0 = No; Not at all
- 0 = Not relevant

Any unanswered question is scored as 0.

The DLQI score is the sum of the 10 item scores.

22 Appendix 9: Atopic Dermatitis Control Tool

The ADCT consists of 6 questions:

1. Over the last week, how would you rate your eczema-related symptoms (for example, itching, dry skin, skin rash)?
2. Over the last week, how many days did you have intense episodes of itching because of your eczema?
3. Over the last week, how bothered have you been by your eczema?
4. Over the last week, how many nights did you have trouble falling or staying asleep because of your eczema?
5. Over the last week, how much did your eczema affect your daily activities?
6. Over the last week, how much did your eczema affect your mood or emotions?

Questions 1 is scored as:

- 0 = None
- 1 = Mild
- 2 = Moderate
- 3 = Severe
- 4 = Very severe

Question 2 is scored as:

- 3 = Not at all
- 2 = 1-2 days
- 1 = 3-4 days
- 0 = 5-6 days
- 0 = Every day

Question 3 is scored as:

- 0 = Not at all
- 1 = A little
- 2 = Moderately
- 3 = Very
- 4 = Extremely

Question 4 are scored as:

- 3 = No nights
- 2 = 1-2 nights
- 1 = 3-4 nights
- 0 = 5-6 nights

- 0 = Every night

Questions 5 and 6 are scored as:

- 0 = Not at all
- 1 = A little
- 2 = Moderately
- 3 = A lot
- 4 = Extremely

The ADCT total score is the sum of the 6 ADCT questions and ranges from 0 to 24.

23 Appendix 10: MedDRA Internationally Agreed Order for System Organ Class

The internationally agreed SOC order to be used for medical history and AE summary tables is provided in Table 10.

Table 10: MedDRA Internationally Agreed SOC Order

Order Number	System Organ Class
1	Infections and infestations
2	Neoplasms benign, malignant and unspecified (incl. cysts and polyps)
3	Blood and lymphatic system disorders
4	Immune system disorders
5	Endocrine disorders
6	Metabolism and nutrition disorders
7	Psychiatric disorders
8	Nervous system disorders
9	Eye disorders
10	Ear and labyrinth disorders
11	Cardiac disorders
12	Vascular disorders
13	Respiratory, thoracic and mediastinal disorders
14	Gastrointestinal disorders
15	Hepatobiliary disorders
16	Skin and subcutaneous tissue disorders
17	Musculoskeletal and connective tissue disorders
18	Renal and urinary disorders
19	Pregnancy, puerperium and perinatal conditions
20	Reproductive system and breast disorders
21	Congenital, familial and genetic disorders
22	General disorders and administration site conditions
23	Investigations
24	Injury, poisoning and procedural complications
25	Surgical and medical procedures
26	Social circumstances
27	Product issues

24 Appendix 11: Safety Laboratory Evaluations

Table 11: Safety Laboratory Parameters and Units

Category	Parameter	Conventional Unit	SI Units	PCI Criteria (SI units)	
				Low	High
Haematology	Hemoglobin	g/dL	g/L	<100 ≥20 decrease from BL	>20 increase from BL
	Hematocrit	%	L/L		
	Red blood cell count	10^6/uL	10^12/L		
	White blood cell count	10^3/uL	10^9/L	<3	
	Platelet count	10^3/uL	10^9/L	<75	
	Mean corpuscular volume	fL	fL		
	Mean corpuscular hemoglobin	pg	pg		
	Mean corpuscular hemoglobin concentration	g/dL	g/L		
	Absolute neutrophils	10^3/uL	10^9/L	<1.5	
	Absolute lymphocytes	10^3/uL	10^9/L	<0.8	>4
	Absolute monocytes	10^3/uL	10^9/L		
	Absolute eosinophils	10^3/uL	10^9/L		
	Relative neutrophils	%	%		
	Relative lymphocytes	%	%		
	Relative monocytes	%	%		
	Relative eosinophils	%	%		
	Relative reticulocytes	%	%		

Category	Parameter	Conventional Unit	SI Units	PCI Criteria (SI units)	
				Low	High
Chemistry	Aspartate aminotransferase (AST)	U/L	U/L		>3xULN if BL did not exceed ULN, >3xBL if BL was above ULN
	Alanine aminotransferase (ALT)	U/L	U/L		>3xULN if BL did not exceed ULN, >3xBL if BL was above ULN
	Creatinine	mg/dL	mcmol/L		>1.5xULN if did not exceed ULN, >1.5xBL if BL was above ULN
	Potassium	mEq/L	mmol/L		>5.5
	Sodium	mEq/L	mmol/L	<125	>150
	Blood urea nitrogen	mg/dL	mmol/L		
	Total bilirubin	mg/dL	mcmol/L		>1.5xULN if BL did not exceed ULN, >1.5xBL if BL was above ULN
	C-Reactive Protein (CRP)	mg/L	nmol/L		
	Gamma-glutamyl transpeptidase	U/L	U/L		

Category	Parameter	Conventional Unit	SI Units	PCI Criteria (SI units)	
				Low	High
Urinalysis	Protein	mg/dL	mg/dL		
	Blood				
	Glucose	mg/dL	mg/dL		
	Ketones	mg/dL	mg/dL		
	Bilirubin				
	pH	pH	pH		
	Nitrites				
	Specific gravity				

BL=Baseline, PCI = potentially clinically important, ULN = Upper limit of normal range.