Patient-reported Outcomes for Sarecycline Effectiveness and Safety (PROSES)

Statistical Analysis Plan

Version 3.6

13 June 2022

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LIST OF ABBREVIATIONS

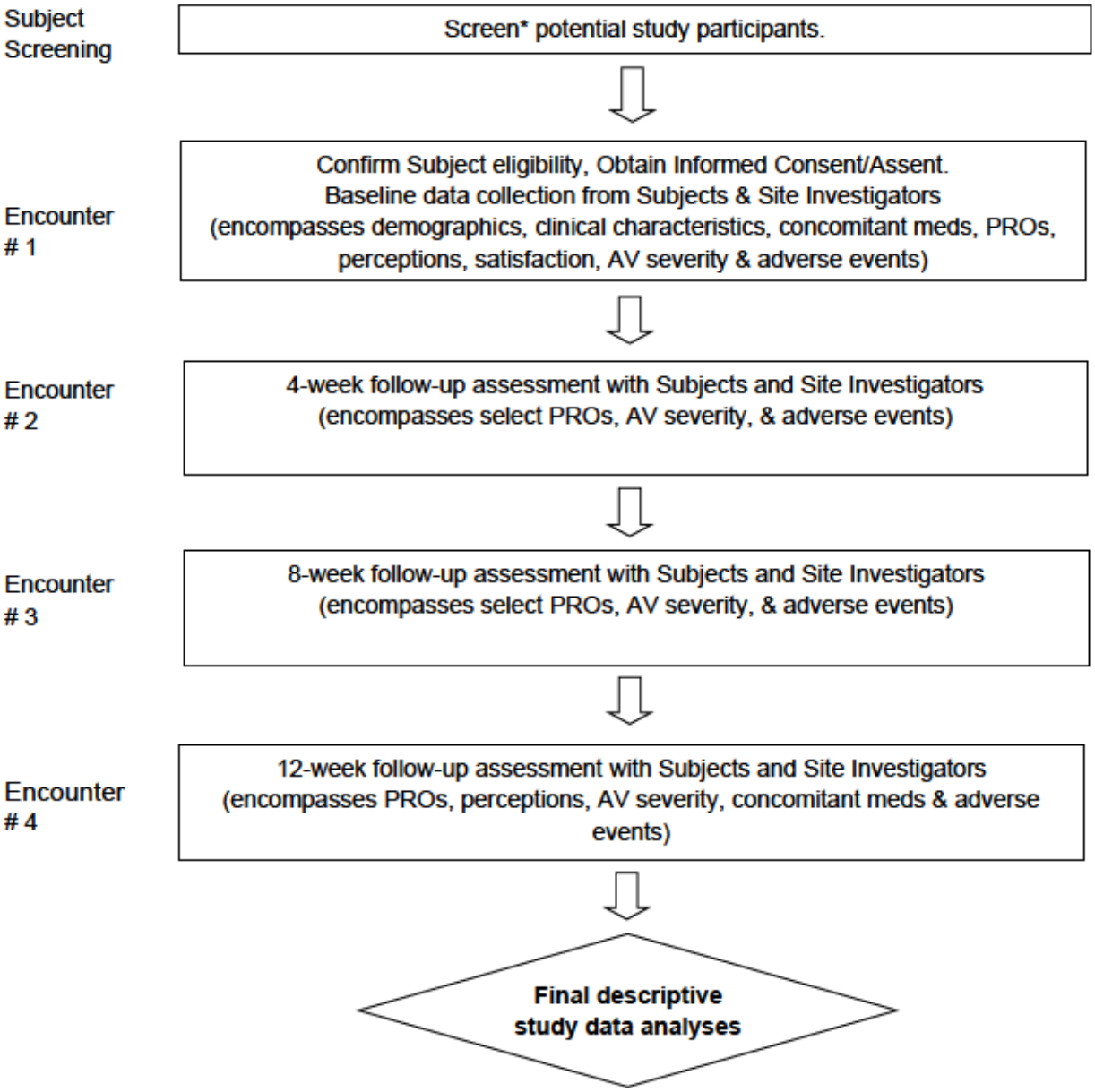
ADR	Adverse Drug Reaction
AE	Adverse Event/Adverse Experience
App	Application / Mobile Application
Approx.	Approximately
ASIS	Acne Symptom and Impact Scale
AV	Acne Vulgaris
CASRO	Council of American Survey Research Organizations
CFB	Change From Baseline
CIRQ	The CASRO Institute for Research Quality
ClinRO	Clinician Reported Outcome
CRO	Clinical Research Organization
DCF	Data Collection Form
EC	Ethics Committee
EDC	Electronic Data Collection
EU	European Union
eDCF	Electronic Data Collection Form
FAS	Full Analysis Set
FDA	The U.S Food and Drug Administration
GEP	Good Epidemiology Practices
HCP	Healthcare Provider
HRQoL	Health Related Quality of Life
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IGA	Investigator's Global Assessment
IRB	Institutional/Independent Review Board
Med	Medication
N	Number (typically refers to participants)
PI	Principal Investigator
PRO	Patient Reported Outcome
PROMS	Patient Reported Outcome Measures
PtGA	Patient Global Assessment
QoL	Quality of Life
Qr	Questionnaire

RCT	Randomized Controlled Trial
RWE	Real World Evidence
SAE	Serious Adverse Event
SAP	Statistical analysis plan
SD	Standard Deviation
SEM	Standard Error of Mean
SOP	Standard Operating Procedure
TBD	To Be Decided
US	United States

PROTOCOL SUMMARY

Title:	Patient-reported Outcomes for Sarecycline Effectiveness and Safety (PROSES).
Précis:	A prospective cohort study of patients with acne vulgaris (AV) treated with sarecycline and followed for 12 weeks post treatment-initiation. Patient Reported Outcomes (PROs) and clinical profile of patients will be gathered for descriptive analyses of patient outcomes over the 12 week study observation period.
Objectives:	Evaluate PROs and clinician reported outcomes among patients with moderate to severe non-nodular AV who are prescribed sarecycline in clinical practice settings in the U.S. Primary: Evaluate PROs related to Acne symptoms and impact. Secondary: Evaluate sarecycline treatment effectiveness, in terms of IGA of AV severity on the face. Additional: Evaluate clinician satisfaction with sarecycline treatment, sarecycline safety/tolerability, and concordance in perception of facial AV severity among clinicians and patients.
Population:	Three hundred (300) patients of age ≥9 years at the time of initiation of treatment with sarecycline from clinical practices across the U.S. For pediatric patients, their parents/primary caregivers will also be recruited.
Number of Sites:	Maximum of fifty sites will be recruited.
Duration of Treatment	12 weeks.
Study Drug & Mode of Administration	Seysara® tablets; 60 mg, 100 mg, 150 mg, providing a dose of approx. 1.5mg/kg/day; oral. Commercial supply of medication may be supplied to clinical sites/Subjects for the duration of the study.
Study Duration:	Approximately eighteen months of study duration, including study set-up, 12 weeks of subject observation period and study close out followed by study data analyses.

Schematic of Study Design



**Subject screening could be done via phone, prior to Subject's visit to the clinic; or it could be combined with Encounter # 1 (baseline data collection).*

*Clinicians shall prescribe sarecycline (*Seysara®*) to eligible Subjects per own clinical judgement and manage them as they normally would, in clinical practice.*

1 PROSES STUDY RATIONALE

General understanding of acne impact on different aspects of patient HRQoL is still evolving. A real-world study leveraging validated HRQoL instruments such as ASIS questionnaire and the complimentary novel Expert Panel Questionnaire (EPQ; developed using modified delphi method) could help portray a broader picture of impact of acne on pediatric and adult patient HRQoL. Further, assessing the impact of sarecycline treatment on acne patient outcomes, including patient HRQoL, in real-world community practice settings could highlight the humanistic and clinical benefits associated this narrow-spectrum antibiotic treatment option.

2 PROSES STUDY OBJECTIVES

2.1 Study Objectives

The primary objective of the study is to evaluate PROs in terms of health related quality of life (HRQoL) among patients with moderate to severe non-nodular AV who are administered sarecycline in real-world community practice settings in the U.S. The secondary objective is to evaluate effectiveness of sarecycline treatment, measured by Investigator Global Assessment (IGA) of AV severity on the face.

The additional study objectives include the following evaluations among study Subjects and Site Investigators*:

- Investigator satisfaction with their sarecycline treatment outcomes.
- Safety and tolerability of sarecycline.
- Comparison of Investigator and Subject perceptions of AV severity.

Note: Dermatologists are expected to predominantly constitute the Site Investigator category, while a few physician assistants and nurse practitioners may be included in the study, reflecting the routine care management of acne in community practice settings.

2.2 Study End Points

The primary endpoint of the study will be the PROs, in terms of self-perceived acne symptoms and impact of acne on emotional functioning, social functioning and activities of daily living, at Week 12.

The secondary endpoint will be the proportion of Subjects with Facial IGA success at Week 12, defined as a 2-point decrease in IGA score from baseline and a score of 0 (clear) or 1 (almost clear).

Additional endpoints of the study will include:

- Proportion of Subjects for whom Site Investigator reported 'very satisfied' or 'satisfied' in the question on global satisfaction with sarecycline treatment, at Week 12.
- Description of changes in PROs from baseline, at Week 12.
- Frequency of documented adverse events (AEs) and severe adverse events (SAEs) during the 12-week study observation period.
- Comparison of Subject perception and Site Investigator perception of AV severity, at Week 12.

3 STUDY DESIGN

This is a single-arm, prospective cohort study which will enroll patients with moderate to severe acne vulgaris (AV) who are prescribed sarecycline in real-world community practices in the U.S. Caregivers also enrolled in the study, in case of pediatric patients. Study Subjects were followed for up to 12 weeks post-index date (with the 'index-date' defined as the date of initiation of sarecycline). Study Site Investigators and Subjects completed online surveys at baseline (at time of study enrollment) and at weeks 4, 8 and 12, post-index date.

This study entailed provision of sarecycline treatment to study participants. Site Investigators decided on who to prescribe sarecycline as part of usual care, based on their best clinical judgment, prior to subject recruitment. The study is sponsored by Almirall, hereinafter referred to as the

Sponsor. The study is managed by Avant Health, hereinafter referred to as the Contract Research Organization (CRO).

3.1 Subject Inclusion Criteria

Patient Inclusion Criteria: In order to be eligible to participate in this study, an individual must meet all of the following criteria:

- Male or female, aged 9 years and above at the time of study recruitment.
- Has facial non-nodular AV with IGA score of moderate (3) or severe (4).
- Considered as a potential candidate for sarecycline treatment to manage their AV, per clinician's judgment.
- Able to read and write English.
- Provide consent (in case of adult patients) or assent (in case of pediatric patients) to participate in the study.
- Willing to comply with all study procedures and be available for the duration of the study.

Caregiver Inclusion Criteria: In order to be eligible to participate in this study, an individual must meet all of the following criteria:

- Male or female, aged 18 years and above.
- Able to read and write English.
- Primary caregiver of the study-eligible patient.
- Provide consent to participate in the study.
- Willing to comply with all study procedures and be available for the duration of the study.

3.2 Subject Exclusion Criteria

An individual who meets any of the following criteria were excluded from participation in this study:

- Patients with any dermatological or physical condition of the face that could interfere with the AV clinical evaluations.
- Patients with any history of allergy to tetracycline-class antibiotics, pseudomembranous colitis or antibiotic-associated colitis.
- Patients with any known resistance to other tetracyclines.
- Patients currently treated with any of the following: penicillin, oral retinoids (incl. Isotretinoin and acitretin).
- Among female Subjects: Currently pregnant, lactating, or is planning a pregnancy during the study period.
- Patients or their caregivers are unable to comply with the requirements of the study or patients who in the opinion of the Site Investigator should not participate in the study.
- Patients for whom medical chart is inaccessible to Site Investigators to complete baseline data collection.

4 STUDY SCHEDULE & PROCEDURES

Study eligible patients who were considered as candidates for sarecycline treatment as part of usual care Acne management were screened, consented and recruited into the study, followed for up to 12 weeks post-index date, encompassing four distinct data collection encounters, namely, baseline, week-4, week-8 and week-12, post-index date. Index date is the date of initiation of sarecycline treatment (at baseline), when the subject was prescribed sarecycline.

Different data elements were collected from Site Investigators and from study Subjects at these data collection encounters, as outlined below. For patients of age 12yrs and older, acne patients themselves completed relevant PRO elements pertinent to study endpoints, at all encounters; for patients of age 9-11yrs, parents/caregivers of pediatric patients completed the PRO elements at all encounters, serving as a proxy, upon consulting with their child on question responses.

The schedule of events is summarized in Appendix A.

5 STUDY ASSESSMENTS

PROs were assessed with study Subjects. Sarecycline treatment effectiveness was assessed by treating Site Investigator using IGA scores. Safety associated with sarecycline was evaluated in terms of adverse events and ADRs during the treatment period.

5.1 PRO Assessments

A combination of a validated questionnaire and an ad hoc questionnaire prepared via modified delphi panel consensus method involving dermatologists, were used for PRO assessments.

ASIS Questionnaire:

The ASIS is a 17-item questionnaire that asks patients about the signs and impact of AV (Appendix B); responses are reported as two scales: Signs (9 items), and Impact (8 items). Impact domain has two subscales, pertinent to Emotional (6 items) and Social impact (2 items). The following questions (items) correspond to each scale:

Scale	Items
Signs	1-9
Impact	10-17

All items are scored on a five-point adjectival response scale, with a potential score of 0 to 4, even though the individual item responses are different for certain question clusters. A domain score is determined by the average of scores in each scale within the domain. A total score is the average of all 17 items. Higher scores on the ASIS Sign domain, comprised of all items that assess symptoms (items 1-9), indicate the presence of more severe symptoms, whereas higher scores on the ASIS Impact domain, comprised of all of the items that assess impacts (items 10-17), indicate a greater negative impact of acne on HRQoL and appearance. The questionnaire was administered in entirety, at baseline and at Week 12 post-index date.

At Weeks 4 & 8 post-index date, Subjects were asked to complete ASIS Item # 9 (how is your acne on your face right now) and ASIS Item # 10 (rate how your face looked because of your acne).

Expert Panel Questionnaire (EPQ):

Ten (10) ad hoc questions related to patient perception of impact of Acne on their social functioning, emotional functioning and activities of daily living were formulated based on an expert consensus involving a panel of dermatologists using modified delphi method. The items relate to how Acne impact patient's mood (anger), social interactions, general thoughts/worries about Acne and one's future goals, and impact on daily activities, including sleep (Appendix B).

All items are scored on a five-point adjectival response scale, with a potential score of 0 to 4, even though the individual item responses are different for certain question clusters. The questions were administered in entirety, at baseline and at Week 12 post-index date.

5.2 Treatment Satisfaction Assessments

Investigator's global satisfaction with sarecycline treatment was assessed at Week 12 using a single question: "how satisfied are you with sarecycline treatment outcomes", with response options ranging from 'Very Satisfied' to 'Very Dissatisfied'.

5.3 Treatment Effectiveness Assessments

The effectiveness of sarecycline treatment was assessed from the perspective of Site Investigators as well the Subjects.

5.3.1 Investigator Assessments

An IGA scale of 0 (Clear) to 4 (Severe) was used by the Site Investigators to assess the severity of a subject's facial acne at the time of study encounters. The IGA is representative of the investigator's overall general assessment of the subject's Acne and takes into account the quality, as well as the quantity, of lesions. These assessments were done at baseline encounter to document AV severity before initiation of sarecycline treatment; the assessments were repeated by the Site Investigators at study subject follow-up encounters at Weeks 4, 8 & 12, post-index

date. The comparison of follow-up assessments to the baseline assessment will help determine treatment effectiveness. All Investigator assessments were conducted via in-person visits/encounters at baseline and week-12. The same evaluator performed all evaluations for a subject during the study.

5.3.2 *Study Subject Assessments - Quantitative*

The study Subjects undertook multiple assessments to report their self-perceived severity of AV in general. These assessments were done at baseline encounter to document the perception of AV severity corresponding to the time of initiation of sarecycline. They were then repeated by the Subjects at ensuing encounters at Weeks 4, 8 & 12, post-index date.

Patient Global Assessment (PtGA)

This is based on the global acne severity question within ASIS (Item # 9), where the question asks the Subjects to assess the severity of acne, with a response ranging from 'Clear' to 'Severe', scored on a scale of 0 to 4. See Section 8.1 for general details on questionnaire scoring and administration.

Patient Rating of Appearance

ASIS Item # 10 asks the Subjects to rate how their face looked because of their Acne, with a response ranging from 'Excellent' to 'Bad', scored on a scale of 0 to 4. See Section 8.1 for general details on questionnaire scoring and administration.

Parent/Caregiver Rating of AV Severity

Parents/caregivers of children of age 12-17yrs reported their own perceived severity of children's AV, in addition to the children providing their perceptions. This was accomplished via a single item "Overall, how is your child's acne on his/her face right now?", with the 5-point likert response scales mimicking the Item # 9 in ASIS. This was scored in the same way as the corresponding ASIS item.

5.3.3 *Study Subject Photographic Assessments*

Site Investigator from one study site took photographs of facial acne of all of their recruited patients at baseline encounter and at Week 12, during the in-person visits. This photographic data is used to document and depict the changes in acne severity that may be associated with sarecycline treatment in the study.

5.3.4 *Study Subject Assessments - Qualitative*

Subjects from the study sites that undertook photography tasks were also asked to record a 1-3 minute audio (using the Mobile App) narrating their perceptions of treatment benefits associated with the sarecycline, at the end of their study participation or at Week 12, whichever occurred earlier. This qualitative data is used to ascertain attributes that study Subjects associate with sarecycline treatment in an un-prompted manner.

5.4 Additional Subject Assessments

Concern about Antibiotics and Antibiotic Resistance

Parents/caregivers and adult patients were asked about their concerns about (themselves or their child) using antibiotics, or concerns about antibiotic resistance, with a 5-point likert response scale of 'not at all' to 'extremely'. These questions were assessed at baseline.

Parent/Caregiver Worries about Acne

The parents/caregivers of pediatric patients with AV were asked - how worried they are about their child's acne, with a response option of 'not at all' to 'extremely', and how concerned they are about their child's ability to accomplish future goals and reach full potential due to acne, with a 5-point likert response scale of 'not at all' to 'extremely'. These questions were asked at baseline and Week 12.

Understanding of Acne-related Concerns

Pediatric patients (of age 12-17) were asked whether their parents understand their acne-related concerns, and correspondingly, the parents/caregivers were asked whether they understand their

child's acne-related concerns. This pair of questions have a response item on a 5-point likert scale of 'not at all' to 'very much'. These questions were asked at baseline and Week 12.

5.5 Compliance to Treatment

Compliance with the assigned treatment regimen was assessed by comparing the number of tablets expected to be used, based on the total number of treatment days, with the actual number used (expressed as a percentage of used/expected) at each encounter. The actual consumption/use of study tablets was evaluated by assessing the left-over pills/tablets in the medication bottles returned to sites/investigators by the Subjects.

5.6 Safety Assessments

5.6.1 Definition of Adverse Events & Adverse Drug Reactions

An AE is any untoward medical occurrence in a patient administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to the medicinal product.

The Site Investigators used the following terms to assess the severity of each AE:

- Mild: Awareness of symptoms or signs, but easily tolerated (acceptable).
- Moderate: Enough discomfort to interfere with usual activity (disturbing).
- Severe: Interferes significantly with ability to do work or usual activity (unacceptable).

A Serious Adverse Event (SAE) is any experience that suggests a significant hazard, contraindication, side effect or precaution. With respect to human clinical experience, this includes any event which:

- results in death,
- is life-threatening,

- requires inpatient hospitalization* or prolongation of hospitalization, unless hospitalization is for:
    - routine treatment or monitoring of the studied indication, not associated with any deterioration in condition.
    - elective or pre-planned treatment for a pre-existing condition that is unrelated to the indication under study and has not worsened since the start of study drug.
    - treatment on an emergency outpatient basis for an event not fulfilling any of the definitions of a SAE given above and not resulting in hospital admission.
    - social reasons and respite care in the absence of any deterioration in the subject's general condition.
- results in persistent of significant disability / incapacity, or
- is a congenital anomaly / birth defect,
- is a significant or important medical event that, based on appropriate medical judgment, may jeopardize the subject or may require intervention to prevent one of the other outcomes listed above.

* Hospitalization is defined as an overnight (in-patient) stay at the hospital or emergency room.

For all AEs (either related or not related to study medication), information about the outcome (resolved or ongoing) and the action taken with the study treatment (drug withdrawn, dose reduced, dose increased, dose not changed, not applicable) were documented.

Each AE, either serious or non-serious for which a causal relationship to sarecycline cannot be excluded, was considered as an ADR. An ADR is an injury caused by taking medication. ADRs may occur following a single dose or prolonged administration of a medicinal product or result from the combination of two or more medicinal products.

The determination of whether an AE is related to study treatment (sarecycline) was based on information regarding the degree to which the study treatment had caused or contributed to the event and will be categorized per the following criteria:

- Related: There were good reasons and sufficient information (e.g. plausible time sequence, dose-response relationship, pharmacology, positive de-challenge and/or re-

challenge) to assume a causal relationship with the study medication in the sense that it is plausible, conceivable or likely.

- Not Related: There were good reasons and sufficient information (e.g. implausible time sequence and/or attributable to concurrent disease or other drugs) to rule out a causal relationship with the study medication.

6 STATISTICAL CONSIDERATIONS

6.1 Sample Size Considerations

No formal sample size and power calculations were undertaken. Considering the descriptive nature of the study and the feasibility of recruiting the study population, approximately 300 study Subjects from across a maximum of 40 clinical sites for the entire study has been identified as a sample to guide the planned analysis addressing the study objectives. It is expected that there will be Subject attrition during the course of the study.

6.2 Analysis Populations and Datasets

Statistical analysis and data tabulation will be performed using the following analysis populations unless specified otherwise:

- Safety Population: All patients who received at least one dose of sarecycline during the study observation period, as part of usual care. This in essence constitute all 300 Subjects recruited into the study.
- Full Analysis Set (FAS): All patients within the Safety Population that had at least one question answered pertaining to study primary research objective. This in essence will constitute all Subjects who completed their Week-12 survey. By definition, this would exclude all Subjects who were terminated (for any reason) at any timepoint (prior to Week-12) in the study.

In the event that the safety population and FAS differ, all safety evaluations (part of additional objectives) will be conducted among the safety population, while FAS will be used to conduct

analyses addressing rest of the study objectives, including the description of population demographics, primary and secondary objectives, and select additional (non-safety related) objectives.

6.3 General Statistical Procedures

6.3.1 Overview

Data from Site Investigators and study Subjects will be treated separately, and combined into one dataset, based on the study assessments of interest. Validated instruments will be scored according to developer guidelines, reporting domain scores and overall summary scores, as appropriate. Home-grown questions/items will be analyzed and reported individually, based on the respective response scales. Change from Baseline (CFB) in scores (for continuous variables) or proportions (for discrete variables) will be computed as Week-12 minus Baseline measure for respective question responses.

Discrete measures will be assessed using summary statistics encompassing percentage of Subjects reporting particular outcome measures. The statistical differences in discrete variables to compare different patient groups (for subgroup analysis) for a given measure at a particular timepoint (such as Baseline or Week-12), or CFB in proportion of patients reporting a particular response to an outcome measure at a particular timepoint (such as Week-12) will be assessed using a $\chi 2$ test. In case of likert scales, to compute P-values for CFB in proportions, the top-two response categories (of a likert scale) for a given question at Baseline will be grouped together into a single group proportion (versus the rest of the population/responders all together) and compared to the same group proportion at Week-12; the procedure will be repeated for the bottom-two response categories (of a likert scale) for a given question, by grouping them together into a single group proportion and compare it to the same group proportion at Week-12. For example, for ASIS item # 1 (how oily is your face right now), proportion of patients reporting "Not at all/A little" at Baseline will be grouped together (vs. rest of the population/responders) and compared to proportion of patients reporting "Not at all/A little" at Week-12; similarly, proportion of patients reporting "Quite a bit/Very" at Baseline will be grouped together and compared to proportion of

patients reporting "Quite a bit/Very" at Week-12, to compute respective P values. Continuous measures will be assessed using summary statistics; paired sample t-tests will be used to assess statistical differences for CFB evaluations, while independent sample t-tests will be used to assess statistical differences between different patient groups (for subgroup analysis) for a given measure at a particular timepoint (such as Baseline or Week-12).

Computation of statistical differences will be performed only as an exploratory step (and not for hypothesis testing), considering the descriptive nature of the study; for such exploratory evaluation, P value ≤ 0.05 will be considered significant. All statistical analyses will be based on all available data assuming that all missing data are uninformative and will be conducted using appropriate statistical software, such as SAS.

An interim analysis will be conducted using FAS, upon completion of 12 weeks of data collection (from both patients and clinicians) for ~200 study Subjects, using the statistical methods identical to the analyses planned for FAS-based final data analyses; the focus of the interim analyses will be the primary objective, secondary objective and select additional objectives, as outlined below; no subgroup analyses will be considered.

- FAS cohort demographics
- PROs: Antibiotic attitudes at baseline
- PROs: CFB in EPQ measures
- PROs: CFB in ASIS measures
- PROs: CFB in Patient Acne Severity and How Face Looks (with and without LOCF imputation)
- PROs: CFB in Parent/caregiver concerns about the child with Acne:
    - Understanding child's concerns
    - Concerned about child's acne
    - Concerned about child's ability to accomplish future goals
- Facial IGA and Facial IGA success (with and without LOCF imputation)
- Select comparison of patient and clinician reported measures: Acne Severity (with LOCF imputation)

- Select comparison of pediatric patient and caregiver reported measures:
  - Understanding child's concerns
  - Concerned about child's acne
  - Concerned about child's ability to accomplish future goals
- Clinician satisfaction with sarecycline
- Sarecycline treatment characteristics

The description of the individual study measures are outlined in the forthcoming sections.

The final study analyses encompassing all study outcome measures will be conducted after the completion of 12 weeks of data collection for all study Subjects, data QC is completed, and upon final database lock.

6.3.1 Summary Statistics

The descriptive statistics for all the continuous variables will include the mean, median, standard deviation (SD), minimum, maximum, and number of Subjects. Descriptive summaries will be provided for raw, and CFB values for relevant endpoints, where applicable. Frequency distributions for all the categorical variables will be presented as counts and percentages. Summaries will be provided by encounters (Baseline, Week-12, and Weeks 4/8 where appropriate). Results from the descriptive analyses will be presented as summary tables and figures.

6.3.2 Subgroup Analysis

Primary and select additional outcome measures (as individually identified in the following sections) will be summarized and repeated for the following subgroups, using FAS:

- Gender: male and female
- Age groups: 9 to 17 years and ≥ 18 years
- Race: white, african-american/black, other

- Body mass index: < 25 kg/m^2 and ≥ 25 kg/m^2
- Baseline facial IGA score: moderate and severe
- Concomitant use of contraceptives in females: yes and no

6.4 Primary Endpoint Analysis

The primary endpoint of PROs at Week 12 will be assessed descriptively, using the FAS dataset.

For ASIS questionnaire, the individual item and domain/subscale scores will be created per instrument developer instructions, analyzed descriptively for the baseline and Week 12 encounters, treating the responses as categorical variables and/or continuous variable, as appropriate. For the overall questionnaire data evaluation, no missing data imputation will be applied to compute domain/subscale scores.

The Patient Global Assessment (PtGA) of acne severity based on the single ASIS item (# 9) will be analyzed separately using descriptive statistics and reported for Week 12. Specifically, proportion of Subjects who reported clear (0) and almost clear (1) on the item scale at Week 12 will be assessed. Last Observation Carried Forward (LOCF) data imputation method will be used to impute responses to ASIS item # 9 at Week 12 for the Subjects with missing data at Week 12.

Patient self-rating of their appearance based on the single ASIS Item (# 10) will be analyzed separately using descriptive statistics and reported for Week 12. Specifically, proportion of Subjects reporting "very good" or "excellent" at Week 12 will be assessed. LOCF data imputation method will be used to impute responses to ASIS item # 10 at Week 12 for the Subjects with missing data at Week 12.

For EPQ, the items will be analyzed individually using descriptive statistics and reported for Week 12.

For all PRO elements, descriptive statistics will be computed. ASIS summary domain scores, ASIS item # 9, ASIS item # 10, and individual EPQ items will be stratified by age and other subgroups outlined in Section 6.3.2, to explore the relationship between these HRQoL items and subject characteristics.

6.5 Secondary Endpoint Analysis

The secondary endpoint of the study is the proportion of Subjects with Facial IGA success at Week 12, defined as ≥ 2-point decrease in IGA score from baseline and a score of 0 (clear) or 1 (almost clear) at Week 12. The analyses of IGA success will be conducted for the overall cohort (using the FAS dataset). LOCF data imputation method will be used to impute responses at Week 12 for the Subjects with missing data at Week 12. Relationship between this endpoint (with LOCF imputation) and subject characteristics will be explored using descriptive analyses, by leveraging subgroup analysis outlined in Section 6.3.2.

6.6 Additional Analysis

6.6.1 Treatment Satisfaction Analyses

Investigator's global satisfaction with sarecycline treatment will be analyzed using data at Week 12 from a single question: "how satisfied are you with sarecycline treatment outcomes", with response options ranging from 'Very Satisfied' to 'Very Dissatisfied'. Frequency of responses will be tallied for all Subjects. Proportion of Subjects for whom Investigators indicated 'Very Satisfied' or 'Satisfied' will be reported.

The analyses will be done for the overall cohort, using FAS, and stratified by age and other relevant subgroups outlined in Section 6.3.2. Relationship between Investigator satisfaction and subject characteristics will be explored using descriptive analyses.

6.6.2 Treatment Compliance

Compliance will be assessed by comparing the expected number of tablets taken, based on the total number of treatment days between the encounters/surveys, with the number of used tablets identified/returned at each encounter/visit.

- The number of tablets expected to be taken/used for a specific treatment period between study encounters is calculated based on the number of treatment days in that period; if the

number of days is greater than 30, it will be set to 30, corresponding to the # of tablets in a single Seysara® bottle supplied to subjects during each study encounter/visit.

- The number of pills used for a specific treatment period between study encounters is calculated as a difference between 30 (maximum # of tablets in a Seysara® bottle dispensed for each study encounter) and # of unused/returned pills (by subject) at the following study encounter.

Compliance (%) for a given treatment/encounter period =
[# of pills expected to be used - # of pills unused] * 100 / [# of pills expected to be used]

Treatment compliance will be calculated for each subject/visit and over all study encounters/visits for the Safety population, as indicated above. For the overall compliance for each subject, average (mean) of % compliance at individual subject encounters/visits will be calculated.

Compliance values that are less than 0% will be set to 0%, and compliance values that are greater than 100% will be set to 100%. For Subjects with missing data, no missing data imputation will be performed, and the compliance statistics will be computed using non-missing values for the study cohort at relevant study timepoints.

6.6.3 Comparison of Investigator and Subject Assessment of AV Severity

The IGA and Subject perception of AV severity at Week 12 will be compared and reported using descriptive statistics, to portray the level of concordance/discordance in stakeholder perceptions. This analysis will be conducted for the entire cohort and for select subgroups outlined in Section 6.3.2. Correspondingly, the Investigator and Subject responses to the questions related to AV severity at baseline will also be compared and reported using descriptive statistics.

6.6.4 CFB in PROs

CFB in ASIS domain scores and subscale scores at Week 12 will be assessed (estimated as Week 12 score minus Baseline score). CFB will be first analyzed descriptively for the entire FAS cohort. For this analysis of domain scores, measures will be considered as continuous variables. No missing data imputation will be used. CFB in proportion of individuals reporting specific response for individual items of ASIS will be conducted by treating these variables as discrete variables, and grouping into top-2 or bottom-2 response scales (within the likert scale), as outlined in Section 6.3.1. Scoring, scaling, and the handling of missing data will be handled in accordance with the recommendations accompanying the ASIS documentation.

CFB in proportion of individuals reporting specific response for select individual items of ASIS, most specifically, items # 9 & 10, will be conducted by treating these variables as discrete variables, and grouping into top-2 or bottom-2 response scales (within the likert scale), as outlined in Section 6.3.1. CFB at Weeks 4 & 8 will be assessed in addition to Week 12. LOCF data imputation method will be used to impute responses to ASIS items # 9 & 10 for respective encounters for the Subjects with missing data at those encounters, prior to analyses. CFB for these two measures (with and without LOCF imputation) will be first analyzed descriptively for the entire cohort, and then analyzed for select subgroups (as outlined in Section 6.3.2) with measures that use LOCF imputation.

Items from EPQ will be analyzed individually and CFB in individual questions/items will be reported descriptively for relevant categories of responses (depending on the response scales). No missing data imputation will be undertaken for these items.

6.6.5 Comparison of Parent/Caregiver and Patient Perceptions of AV Severity and Impact

Parent/caregiver and pediatric patient responses to the questions related to AV severity at Baseline and Week 12 will be compared and reported using descriptive statistics, to portray the

level of concordance/discordance in stakeholder perceptions, within the Subject age group of 12-17 yrs. This analysis will be conducted using FAS.

Responses to select EPQ items at Baseline and Week 12 related to worries about Acne and impact of acne on child's ability to reach future goals will be compared to corresponding questions to parents/caregivers to portray the level of concordance/discordance in stakeholder perceptions, within the Subject age group of 12-17 yrs. This analysis will be conducted using FAS.

Parent/caregiver and pediatric patient responses to the questions at Week 12 related to the parents' understanding of child's concerns will be compared and reported using descriptive statistics, to portray the level of concordance/discordance in stakeholder perceptions, within the Subject age group of 12-17 yrs. This analysis will be conducted for the entire relevant cohort using FAS.

No missing data imputation will be undertaken for these items.

6.7 Prior and Concomitant Medications

Medication usage is coded using the latest (2022) WHO Drug Dictionary. Medications are presented by WHO Drug Anatomical/Therapeutic/Chemical (ATC) category and WHO Drug preferred name. Summaries are presented for prior (prior to the first dose of study treatment, gathered as aggregate indicators as well as at individual item level) medication use and concomitant (after first dose of study treatment had been given, gathered at individual item level) medication use. Medications with an end date occurring before the first study treatment (sarecycline) dose date in the treatment period are identified as prior medications. Medications with a start date occurring on or after the first study treatment (sarecycline) dose date in the treatment period or medications with a start date prior to the first (sarecycline) dose that were ongoing or with end dates that were on or after the first treatment (sarecycline) start date are identified as concomitant medications.

Concomitant Acne and non-Acne medications are captured at Baseline and at the study end (Week-12) to characterize the use of concomitant medications among the study cohort. Accordingly, the Acne and non-Acne concomitant medication use will respectively be summarized in aggregate for the 3-month study observation period, and not separated by study visits.

Contraceptive medications (part of non-Acne concomitant medications) will be grouped into single class/group of medications, irrespective of the route of administration or active ingredients, as reported from patient medical charts.

All summaries present the number (%) of subjects for each medication. The denominators for calculating the percentages are based on the number of subjects in the FAS population.

6.8 Safety Assessments

The safety data will be analyzed descriptively using Safety Population dataset, to report the frequency of occurrences of AEs/ADRs and SAEs. MedDRA database version 2021AB will be used for coding the AEs and ADRs. These will be reported at individual item level as well in aggregate at specific category level (e.g., GI effects, vestibular effects) for each of the subject encounter timepoints (4, 8 & 12 weeks post-index date). The number of patients discontinuing treatment for any reason and the number of patients discontinuing the study because of AEs/ADRs will be assessed within the entire study observation window (of 12 weeks), as documented in patient medical charts and reported in study EDC portal.

6.9 Missing Data Handling

The missing data pertinent to the validated instrument ASIS will be handled per instrument owner instructions / scoring manual. For effectiveness measures obtained from Site Investigators and Subjects, namely, IGA, PtGA (from ASIS item # 9) and Patient appearance rating scale (from ASIS item # 10), LOCF data imputation method will be used to impute

responses for Week 12 for the Subjects with missing data at Week 12. LOCF will also be used to impute responses for Weeks 4 & 8 for the Subjects with missing data at those encounters for these select measures, as appropriate. For all other study variables and endpoints, no missing data imputation is planned.

6.10 Significant Protocol Deviations

A protocol deviation is defined as any intentional or unintentional failure to follow the requirements and procedures described in the study protocol. Deviations may have occurred at the subject level or at the site level, and could have been recorded by the site, or uncovered data review. Considering the real-world study design of PROSES, reflecting the routine clinical practices in the U.S and associated patient encounters and routine/standard of care data documentation, patients are expected to miss clinic visits or reschedule planned visits as life situations change. These will not be considered as protocol deviations.

Significant protocol deviations will be flagged, and these are defined as study-related issues that were likely to result in: significant impairment of the rights, welfare or safety of subjects; misconduct and/or fraud; and significant impairment of the integrity/validity of study results. Significant protocol deviations also include issues that were likely to impair monitoring and oversight of the study.

6.11 Sensitivity Analyses

Sensitivity analyses will explore the impact of critical missing data or variation in study procedures on the robustness of the results. Specifically:

- Primary and secondary endpoints at Week-12 will be analyzed as is (with missing data, if any) and by using missing data imputation methods (using LOCF; in case of missing data observed), and results portrayed separately for comparison.
- If some Subject visits are conducted via remote visits instead of in-person visits, the nature of visit (remote vs. in-person) may be used to stratify the analysis of secondary endpoint

(involving IGA) and results portrayed separately for comparison with the overall (aggregate) results.

7 DATA TABLES

All patients who received at least one dose of sarecycline during the study observation period and had at least some data pertaining to ASIS and EPQ items (related to primary research objective) at Week 12 will be included in **Full Analysis Set (FAS)** to facilitate the planned descriptive analysis. Correspondingly, patients who completed the study survey at Week 12 will be included in FAS, since patients answering Week 12 survey will have completed all relevant PRO related questions.

Safety data analyses will be conducted among the Safety Population, that correspond to the entire study cohort that took at least one does of sarecycline. Correspondingly, all patients completing the baseline survey and took at least one dose of sarecycline, amounting to N=300 will be included in this analysis.

List of Tables & Figures

7.1 Patient Demographics, Perceptions & PROs (FAS Population)

Patient data analysis including demographics, perceptions, and PRO data is analyzed using the FAS dataset. All results depicted in this section pertain to FAS Population.

Table 7.1.1. FAS Population

S1: Population	N=x
Adult Patient	n (%)
Pediatric Patient & Caregiver	n (%)
Total Population	n (%)

Note: Data from Patient DCF

Table 7.1.2. Adult Patient & Caregiver Demographic characteristics

Adult Demographic Data	Caregiver N=x	Adult Patient N=x	Total N=x
S2: Age	mean (SD) Median Min, Max	mean (SD) Median Min, Max	mean (SD) Median Min, Max
S8: Gender			
Male	n (%)	n (%)	n (%)
Female	n (%)	n (%)	n (%)
S9: Marital Status			
Not Married	n (%)	n (%)	n (%)
Not Marries, living with Partner	n (%)	n (%)	n (%)
Married or Civil Union	n (%)	n (%)	n (%)
Divorced or Separated	n (%)	n (%)	n (%)
Widow/Widower	n (%)	n (%)	n (%)
Prefer not to answer	n (%)	n (%)	n (%)
S10: Highest level of Education			
Less than high school	n (%)	n (%)	n (%)
diploma/degree		n (%)	n (%)
High school degree or equivalent	n (%)		
(e.g., GED)		n (%)	n (%)
Some college but not degree	n (%)		
Associated degree	n (%)	n (%)	n (%)
Bachelor's degree	n (%)	n (%)	n (%)
Graduate degree	n (%)	n (%)	n (%)
Prefer not to answer	n (%)	n (%)	n (%)
S11: Employment status			
Employed/Working full-time (paid)	n (%)	n (%)	n (%)
Employed/Working part-time (paid)	n (%)	n (%)	n (%)
Homemaker	n (%)	n (%)	n (%)
Student	n (%)	n (%)	n (%)
Retired	n (%)	n (%)	n (%)
Unemployed	n (%)	n (%)	n (%)
S12: Annual household income			
$20,000 or less	n (%)	n (%)	n (%)
$20,001-$50,000	n (%)	n (%)	n (%)
$50,001-100,000	n (%)	n (%)	n (%)
$100,001 or more	n (%)	n (%)	n (%)
Prefer not to answer	n (%)	n (%)	n (%)
S13: Regions/States			
Northeast	n (%)	n (%)	n (%)
Midwest	n (%)	n (%)	n (%)

West	n (%)	n (%)	n (%)
South	n (%)	n (%)	n (%)
S14: Number of children (aged 0 to 17)			
No children	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)
More than 4	n (%)	n (%)	n (%)
S16: Primary Health Insurance			
Private health insurance	n (%)	n (%)	n (%)
Medicaid	n (%)	n (%)	n (%)
Medicare	n (%)	n (%)	n (%)
Uninsured	n (%)	n (%)	n (%)
S17: Race/Ethnicity*			
S17r1: White	n (%)	n (%)	n (%)
S17r2: Black or African American	n (%)	n (%)	n (%)
S17r3: American Indian or Alaska Native	n (%)	n (%)	n (%)
S17r4: Asian	n (%)	n (%)	n (%)
S17r5: Native Hawaiian or other Pacific Islander	n (%)	n (%)	n (%)
S17r6: Other	n (%)	n (%)	n (%)
S17r7: Prefer not to answer	n (%)	n (%)	n (%)
S18: Hispanic, Latino, or of Spanish Origin			
Yes	n (%)	n (%)	n (%)
No	n (%)	n (%)	n (%)

*Not mutually exclusive. Note: Data from Patient DCF.

Table 7.1.3. Pediatric Patient Demographic Characteristics

Pediatric Demographic Data	N=x
S3: Age	mean, SD, Median Min, Max
S21: Gender	
Male	n (%)
Female	n (%)
S22: Race/Ethnicity*	
S22r1: White	n (%)
S22r2: Black or African American	n (%)
S22r3: American Indian or Alaska Native	n (%)
S22r4: Asian	n (%)
S22r5: Native Hawaiian or other Pacific Islander	n (%)
S22r6: Other	n (%)
S22r7: Prefer not to answer	n (%)
S23: Hispanic, Latino, or of Spanish Origin	
Yes	n (%)
No	n (%)
S24: Child's Academic Accomplishments	
Current/Last grade completed:	
Pre-K - 5th grade	n (%)
6th grade – 8th grade	n (%)
9th grade – 12th grade	n (%)
High School Diploma/Degree	n (%)
Vocational School	n (%)
Not currently enrolled in school	n (%)
S24oe: Other	n (%)

*Not mutually exclusive
Note: Data from Patient DCF

Table 7.1.4. Select Patient Demographics from Clinician Data

Demographic Data	N=x
M1B: Gender	
Male	n (%)
Female	n (%)
M2: Primary Health Insurance	
Private health insurance	n (%)
Medicaid	n (%)
Medicare	n (%)
Uninsured	n (%)

Note: Data from Clinician DCF

Table 7.1.5 Antibiotic Attitudes

Antibiotic Attitudes	Adult Patient N=x	Caregiver N=x
Q5: How concerned are you about [your child] using antibiotics for acne?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Not at all (0)	n (%)	n (%)
Slightly (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Moderately (3)	n (%)	n (%)
Extremely (4)	n (%)	n (%)
S20c: How concerned are you about antibiotic resistance?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Not at all (0)	n (%)	n (%)
Slightly (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Moderately (3)	n (%)	n (%)
Extremely (4)	n (%)	n (%)

Note: Data from Patient DCF; X patients had missing data; The denominator for the percentage is the number of patients with available data (N=XX)

Table 7.1.6.1 Expert Panel Questions (EPQs)

	Baseline (N=x)	Week 12 (N=x)
Emotional Functioning EPQ1 (AH1): Over the past 7 days, how often has your acne made you feel angry (mad/sad)?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Emotional Functioning EPQ2 (AH2): How worried are you about how long your acne will last and how bad it will get?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Not at all (0)	n (%)	n (%)
Slightly (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Moderately (3)	n (%)	n (%)
Extremely (4)	n (%)	n (%)
Emotional Functioning EPQ3 (AH3): How often do you think about your acne?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Emotional Functioning EPQ4 (AH4): Over the past 7 days, how worried have you been about your acne?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Not at all (0)	n (%)	n (%)
Slightly (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Moderately (3)	n (%)	n (%)

Extremely (4)	n (%)	n (%)
Social Functioning **EPQ5 (AH5):** How often do you change, edit, or filter your social media photo or selfie because of your acne?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Social Functioning **EPQ6 (AH6):** How often does acne impact your "in real-life" plans (IRL) (like dating or social engagements, playing sports, swimming or hanging out)?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Social Functioning **EPQ7 (AH7):** How often are you doing something to hide your acne (like mess with, squeeze/pop, or use makeup, concealer, hairstyle, clothes to cover up)?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Activities of Daily Living **EPQ8 (AH8):** How often do you feel picked on or judged because of your acne?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)

Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Activities of Daily Living		
EPQ9 (AH9): How concerned are you that your acne will affect your ability to reach your future goals (in school or work) and be the best you can be?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Not at all (0)	n (%)	n (%)
Slightly (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Moderately (3)	n (%)	n (%)
Extremely (4)	n (%)	n (%)
Activities of Daily Living	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
EPQ10 (AH10): Do you feel that your parents understand your acne-related concerns?		
Not at all (0)	n (%)	n (%)
A little (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
Very Much (4)	n (%)	n (%)
Activities of Daily Living		
EPQ11 (AH11): Over the past 7 days, how often has worrying about or discomfort (itching/hurting) from acne affected your sleep?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)

Note: Data from Patient DCF; X patients had missing data; The denominator for the percentage is the number of patients with available data (N=XX)
Note: For All EPQ items, the responses are re-coded to 0-4, from 1-5 in the study database.

Table 7.1.6.2 EPQs: Change from Baseline at Week-12

Domain	Baseline (N=x)	Week 12 (N=x)	CFB in Proportion at Week-12 (N=x)	*p*-value
Emotional Functioning				
EPQ1 (AH1): Over the past 7 days, how often has your acne made you feel angry (mad/sad)?	n (%)	n (%)	%	*P*
Never / Rarely	n (%)	n (%)	%	*P*
Most of the time / All of the time	n (%)	n (%)	%	
Some of the time				
EPQ2 (AH2): How worried are you about how long your acne will last and how bad it will get?				
Not at all / Slightly	n (%)	n (%)	%	*P*
Moderately / Extremely	n (%)	n (%)	%	*P*
Somewhat	n (%)	n (%)	%	
EPQ3 (AH3): How often do you think about your acne?				
Never / Rarely	n (%)	n (%)	%	*P*
Most of the time / All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
EPQ4 (AH4): Over the past 7 days, how worried have you been about your acne?				
Not at all / Slightly	n (%)	n (%)	%	*P*
Moderately / Extremely	n (%)	n (%)	%	*P*
Somewhat	n (%)	n (%)	%	
Social Functioning				
EPQ5 (AH5): How often do you change, edit, or filter your social media photo or selfie because of your acne?				
Never / Rarely	n (%)	n (%)	%	*P*

Most of the time / All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
EPQ6 (AH6): How often does acne impact your "in real-life" plans (IRL) (like dating or social engagements, playing sports, swimming, or hanging out)?				
Never / rarely	n (%)	n (%)	%	*P*
Most of the time / all of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
EPQ7 (AH7): How often are you doing something to hide your acne (like mess with, squeeze/pop, or use makeup, concealer, hairstyle, clothes to cover up)?				
Never / rarely	n (%)	n (%)	%	*P*
Most of the time / all of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
Activities of Daily Living				
EPQ8 (AH8): How often do you feel picked on or judged because of your acne?				
Never / rarely	n (%)	n (%)	%	*P*
Most of the time / all of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
EPQ9 (AH9): How concerned are you that your acne will affect your ability to reach your future goals (in school or work) and be the best you can be?				
Not at all / Slightly	n (%)	n (%)	%	*P*
Moderately / Extremely	n (%)	n (%)	%	*P*
Somewhat	n (%)	n (%)	%	

EPQ10 (AH10): Do you feel that your parents understand your acne-related concerns?				
Not at all / A little	n (%)	n (%)	%	*P*
Quite a bit / Very much	n (%)	n (%)	%	*P*
Somewhat	n (%)	n (%)	%	
EPQ11 (AH11): Over the past 7 days, how often has worrying about or discomfort (itching/hurting) from acne affected your sleep?				
Never / rarely	n (%)	n (%)	%	*P*
Most of the time / all of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	

Note: X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

Table 7.1.7.1. Sub-group analysis of EPQ 1

AH1: Over the past 7 days, how often has your acne made you feel angry (mad/sad)? Subjects who selected *Never/Rarely*.

	Baseline (N=x)	Week 12 (N=x)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Never/Rarely (N=X for Baseline and N=X for Week-12).
*The denominator for the percentage is the number of 'female' subjects with available data who selected Never/Rarely (N=X for Baseline and N=X for Week-12).

Table 7.1.7.2. Sub-group analysis of EPQ 2

AH2: How worried are you about how long your acne will last and how bad it will get? Subjects who selected *Not at all/Slightly.*

	Baseline (N=x)	Week 12 (N=x)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Not at all / Slightly (N=X for baseline and N=X for week 12)
*The denominator for the percentage is the number of 'female' subjects with available data who selected Not at all / Slightly (N=X for Baseline and N=X for Week-12).

Table 7.1.7.3. Sub-group analysis of EPQ 3

AH3: How often do you think about your acne? Subjects who selected *Never/Rarely*.

	Baseline (N=x)	Week 12 (N=x)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12).
*The denominator for the percentage is the number of 'female' subjects with available data who selected Never/Rarely (N=X for Baseline and N=X for Week-12).

Table 7.1.7.4. Sub-group analysis of EPQ 4

AH4: Over the past 7 days, how worried have you been about your acne?
Subjects who selected *Not at all / Slightly*.

	Baseline (N=x)	Week 12 (N=x)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Not at all / Slightly (N=X for baseline and N=X for week 12).
*The denominator for the percentage is the number of 'female' subjects with available data who selected Not at all / Slightly (N=X for baseline and N=X for week 12).

Table 7.1.7.5. Sub-group analysis of EPQ 5

AH5: How often do you change, edit, or filter your social media photo or selfie because of your acne? Subjects who selected *Never / Rarely*

	Baseline (N=x)	Week 12 (N=x)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12).
*The denominator for the percentage is the number of 'female' subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12).

Table 7.1.7.6. Sub-group analysis of EPQ 6

AH6: How often does acne impact your "in real-life" plans (IRL) (like dating or social engagements, playing sports, swimming, or hanging out)? Subjects who selected *Never / Rarely.*

	Baseline (N=xx)	Week 12 (N=xx)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12)
*The denominator for the percentage is the number of 'female' subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12)

Table 7.1.7.7. Sub-group analysis of EPQ 7

AH7: How often are you doing something to hide your acne (like mess with, squeeze/pop, or use makeup, concealer, hairstyle, clothes to cover up)? Subjects who selected *Never / Rarely*.

	Baseline (N=xx)	Week 12 (N=xx)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12).
*The denominator for the percentage is the number of 'female' subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12).

Table 7.1.7.8. Sub-group analysis of EPQ 8

AH8: How often do you feel picked on or judged because of your acne?
Subjects who selected *Never / Rarely*.

	Baseline (N=xx)	Week 12 (N=xx)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12).
*The denominator for the percentage is the number of 'female' subjects with available data who selected Never/Rarely (N=X for baseline and N=X for week 12).

Table 7.1.7.9. Sub-group analysis of EPQ 9

AH9: How concerned are you that your acne will affect your ability to reach your future goals (in school or work) and be the best you can be? Subjects who selected *Not at all / Slightly*.

	Baseline (N=xx)	Week 12 (N=xx)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Not at all / Slightly (N=X for baseline and N=X for week 12).
*The denominator for the percentage is the number of' 'female' subjects with available data who selected Not at all / Slightly (N=X for baseline and N=X for week 12).

Table 7.1.7.10. Sub-group analysis of EPQ 10

AH10: Do you feel that your parents understand your acne-related concerns? Subjects who selected *Not at all / A little*.

	Baseline (N=xx)	Week 12 (N=xx)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Not at all / A little (N=X for baseline and N=X for week 12).
*The denominator for the percentage is the number of 'female' subjects with available data who selected Not at all / A little (N=X for baseline and N=X for week 12).

Table 7.1.7.11. Sub-group analysis of EPQ 11

AH11: Over the past 7 days, how often has worrying about or discomfort (itching/hurting) from acne affected your sleep? Subjects who selected *Never / Rarely*.

	Baseline (N=xx)	Week 12 (N=xx)
Sex		
Male	n (%)	n (%)
Female	n (%)	n (%)
p-value	*p*	*p*
Age Group		
≥ 9 and < 12 years	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)
≥ 12 years	n (%)	n (%)
p-value	*p*	*p*
Race		
White	n (%)	n (%)
African America/Black	n (%)	n (%)
Other	n (%)	n (%)
p-value	*p*	*p*
Body mass index		
< 25 kg/m^2	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)
p-value	*p*	*p*
Baseline facial IGA		
Moderate	n (%)	n (%)
Severe	n (%)	n (%)
p-value	*p*	*p*
Female who used oral contraceptive*		
Used	n (%)	n (%)
Did not use	n (%)	n (%)
p-value	*p*	*p*

Note: The denominator for the percentage is the number of subjects with available data who selected Never / Rarely (N=X for baseline and N=X for week 12).
*The denominator for the percentage is the number of 'female' subjects with available data who selected Never / Rarely (N=X for baseline and N=X for week 12).

Table 7.1.8. ASIS Panel Questions: Symptom and Impact Domains

	Baseline (N=x)	Week 12 (N=x)
Symptom		
A1: How oily is your face right now?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Not at all (0)	n (%)	n (%)
A Little (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
Very (4)	n (%)	n (%)
Symptom	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
A2: How many pimples do you have on your face right now?		
None (0)	n (%)	n (%)
A few (1)	n (%)	n (%)
Some (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
A lot (4)	n (%)	n (%)
Symptom	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
A3: How many acne scars (holes or indents) do you have on your face right now?		
None (0)	n (%)	n (%)
A few (1)	n (%)	n (%)
Some (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
A lot (4)	n (%)	n (%)
Symptom	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
A4: How many scabs from acne do you have on your face right now?		
None (0)	n (%)	n (%)
A few (1)	n (%)	n (%)
Some (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)

A lot (4)	n (%)	n (%)
Symptom **A5:** How many dark marks from acne do you have on your face right now?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
None (0)	n (%)	n (%)
A few (1)	n (%)	n (%)
Some (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
A lot (4)	n (%)	n (%)
Symptom **A6:** How many blackheads do you have on your face right now?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
None (0)	n (%)	n (%)
A few (1)	n (%)	n (%)
Some (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
A lot (4)	n (%)	n (%)
Symptom **A7:** How many whiteheads do you have on your face right now?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
None (0)	n (%)	n (%)
A few (1)	n (%)	n (%)
Some (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
A lot (4)	n (%)	n (%)
Symptom **A8:** How much redness do you have on your face right now?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
None (0)	n (%)	n (%)
A few (1)	n (%)	n (%)
Some (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
A lot (4)	n (%)	n (%)

Symptom		
A9: Overall, how is the acne on your face right now?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Clear (0)	n (%)	n (%)
Almost Clear (1)	n (%)	n (%)
Mild (2)	n (%)	n (%)
Moderate (3)	n (%)	n (%)
Severe (4)	n (%)	n (%)
Impact/ Emotional		
A10: Over the past 7 days, rate how your face looked because of your acne?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Excellent (0)	n (%)	n (%)
Very good (1)	n (%)	n (%)
Good (2)	n (%)	n (%)
Fair (3)	n (%)	n (%)
Bad (4)	n (%)	n (%)
Impact/ Emotional		
A11: Over the past 7 days, how often did you feel sad because of the acne on your face?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Impact/ Emotional		
A12: Over the past 7 days, how often did you feel embarrassed because of the acne on your face?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)

Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Impact/ Emotional		
A13: Over the past 7 days, how often did you feel self-conscious because of the acne on your face?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Impact/ Emotional		
A14: Over the past 7 days, how often did you feel annoyed because of the acne on your face?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Impact/ Emotional		
A15: Over the past 7 days, how often did you feel not confident because of the acne on your face?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Impact/Social		

A16: Over the past 7 days, how often did you choose not to be around other people?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)
Impact/Social		
A17: Over the past 7 days, how often did someone make bad comments about the acne on your face?	**Mean (SD), Median, Min,Max**	**Mean (SD), Median, Min,Max**
Never (0)	n (%)	n (%)
Rarely (1)	n (%)	n (%)
Some of the time (2)	n (%)	n (%)
Most of the time (3)	n (%)	n (%)
All of the time (4)	n (%)	n (%)

Note: Data from Patient DCF; X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

Note: For All ASIS items, the responses are re-coded to 0-4, from 1-5 in the study database.

Table 7.1.9. ASIS: CFB at Week-12 for Individual Items

Domain	Baseline N=x	Week 12 N=x	CFB in Proportion at Week 12 N=x	*p*-value
Symptom **A1:** How oily is your face right now?				
Not at all/ A little	n (%)	n (%)	%	*P*
Quite a bit/ Very	n (%)	n (%)	%	*P*
Somewhat	n (%)	n (%)	%	
Symptom **A2:** How many pimples do you have on your face right now?				
None/ A few	n (%)	n (%)	%	*P*
Quite a bit/ A lot	n (%)	n (%)	%	*P*
Some	n (%)	n (%)	%	
Symptom **A3:** How many acne scars (holes or indents) do you have on your face right now?				
None/ A few	n (%)	n (%)	%	*P*
Quite a bit/ A lot	n (%)	n (%)	%	*P*
Some	n (%)	n (%)	%	
Symptom **A4:** How many scabs from acne do you have on your face right now?				
None/ A few	n (%)	n (%)	%	*P*
Quite a bit/ A lot	n (%)	n (%)	%	*P*
Some	n (%)	n (%)	%	
Symptom **A5:** How many dark marks from acne do you have on your face right now?				
None/ A few	n (%)	n (%)	%	*P*
Quite a bit/ A lot	n (%)	n (%)	%	*P*

Some	n (%)	n (%)	%	
Symptom **A6:** How many blackheads do you have on your face right now?				
None/ A few	n (%)	n (%)	%	*P*
Quite a bit/ A lot	n (%)	n (%)	%	*P*
Some	n (%)	n (%)	%	
Symptom **A7:** How many whiteheads do you have on your face right now?				
None/ A few	n (%)	n (%)	%	*P*
Quite a bit/ A lot	n (%)	n (%)	%	*P*
Some	n (%)	n (%)	%	
Symptom **A8:** How much redness do you have on your face right now?				
None/ A few	n (%)	n (%)	%	*P*
Quite a bit/ A lot	n (%)	n (%)	%	*P*
Some	n (%)	n (%)	%	
Symptom **A9:** Overall, how is the acne on your face right now?				
Clear/ Almost Clear	n (%)	n (%)	%	*P*
Moderate/ Severe	n (%)	n (%)	%	*P*
Mild	n (%)	n (%)	%	
Impact/ Emotional **A10:** Over the past 7 days, rate how your face looked because of your acne?				
Excellent/ Very Good	n (%)	n (%)	%	*P*
Fair/ Bad	n (%)	n (%)	%	*P*
Good	n (%)	n (%)	%	
Impact/ Emotional **A11:** Over the past 7 days, how often did you feel sad because of the acne on your face?				
Never/ Rarely	n (%)	n (%)	%	*P*
Most of time/ All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	

Impact/ Emotional **A12:** Over the past 7 days, how often did you feel embarrassed because of the acne on your face?				
Never/ Rarely	n (%)	n (%)	%	*P*
Most of time/ All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
Impact/ Emotional **A13:** Over the past 7 days, how often did you feel self-conscious because of the acne on your face?				
Never/ Rarely	n (%)	n (%)	%	*P*
Most of time/ All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
Impact/ Emotional **A14:** Over the past 7 days, how often did you annoyed because of the acne on your face?				
Never/ Rarely	n (%)	n (%)	%	*P*
Most of time/ All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
Impact/ Emotional **A15:** Over the past 7 days, how often did you feel not confident because of the acne on your face?				
Never/ Rarely	n (%)	n (%)	%	*P*
Most of time/ All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
Impact/Social **A16:** Over the past 7 days, how often did you choose not to be around other people?				
Never/ Rarely	n (%)	n (%)	%	*P*
Most of time/ All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	
Impact/Social				

A17: Over the past 7 days, how often did someone make bad comments about the acne on your face?				
Never/ Rarely	n (%)	n (%)	%	*P*
Most of time/ All of the time	n (%)	n (%)	%	*P*
Some of the time	n (%)	n (%)	%	

Note: Data from Patient DCF; X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

Table 7.1.10. ASIS score at Individual Visits and CFB at Week 12

Domain	Baseline (N=x)	Week 12 (N=x)	CFB in Domain Score at Week 12 (N=x)	p-value
Symptom (1)	N, Mean (SD) Median Min,Max	N, Mean (SD) Median Min,Max	N, Mean (SD) Median Min,Max	*p*
Impact (2)	N, Mean (SD) Median Min,Max	N, Mean (SD) Median Min,Max	N, Mean (SD) Median Min,Max	*p*
Emotional Impact (3)	N, Mean (SD) Median Min,Max	N, Mean (SD) Median Min,Max	N, Mean (SD) Median Min,Max	*p*
Social Impact (4)	N, Mean (SD) Median Min,Max	N, Mean (SD) Median Min,Max	N, Mean (SD) Median Min,Max	*p*

(1) ASIS items A1, A2, A3, A4, A5, A6, A7, A8, A9
(2) ASIS items A10*, A11, A12, A13, A14, A15, A16, A17
(3) ASIS items A10*, A11, A12, A13, A14, A15
(4) ASIS items A16, A17
Note: P-values refer to the statistical difference between the means (Week 12 vs. Baseline).

Note: ASIS scoring algorithm (separately provided by tool owner) is used to compute domain scores.

Table 7.1.11. Sub-group Analysis of ASIS Domain Scores

	Baseline				Week 12			
	Symptom	Impact	Emotional Impact	Social Impact	Symptom	Impact	Emotional Impact	Social Impact
Sex:								
Male	n, Mean	n, Mean	n, Mean	n, Mean	n, Mean	n, Mean	n, Mean	n, Mean
Female	n, Mean	n, Mean	n, Mean	n, Mean	n, Mean	n, Mean	n, Mean	n, Mean
p-value	*p*	*p*	*p*	*p*	*p*	*p*	*p*	*p*
Age Group:								
≥ 9 and < 12 years								
≥ 12 and < 18 years								
≥ 12 years								
p-value								
Race:								
White								
African American/Black								
Other								
p-value								
Body mass index:								
< 25 kg/m^2								
≥ 25 kg/m^2								
p-value								
Baseline facial IGA:								
Moderate								
Severe								
p-value								
Female who used oral contraceptive*:								
Used								

Did not use *p*-value

* The denominator for the percentage is the number of 'female' subjects with available data (N=X for baseline and N=X for week 12).
Note: P-values refer to the statistical difference between the means of subgroups for a given variable, at a given timepoint.

Table 7.1.12. Patient Acne Severity and How Face Looks (without imputation)

Domain	Baseline	Week 4	Week 8	Week 12
Acne Severity (ASIS 9)-Patient **A9:** (Overall, how is the acne on your face right now?) (Week 4 & 8)	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max
Clear (0)	n (%)	n (%)	n (%)	n (%)
Almost clear (1)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)
Clear/almost clear	n (%)	n (%)	n (%)	n (%)
Moderate / Severe	n (%)	n (%)	n (%)	n (%)
Mild	n (%)	n (%)	n (%)	n (%)
Acne Severity (ASIS 9) - Caregiver **Q1:** Overall, how is your child's acne on his/her face right now? (Week 4 & 8)	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max
Clear (0)	n (%)	n (%)	n (%)	n (%)
Almost clear (1)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)
Clear/almost clear	n (%)	n (%)	n (%)	n (%)
Moderate / Severe	n (%)	n (%)	n (%)	n (%)
Mild	n (%)	n (%)	n (%)	n (%)
Face Look (ASIS 10)	N Mean (SD)	N Mean (SD) Median	N Mean (SD) Median	N Mean (SD) Median

A10: (Over the past 7 days, rate how your face looked because of your acne.)	Median Min,Max	Min,Max	Min,Max	Min,Max
Excellent (0)	n (%)	n (%)	n (%)	n (%)
Very good (1)	n (%)	n (%)	n (%)	n (%)
Good (2)	n (%)	n (%)	n (%)	n (%)
Fair (3)	n (%)	n (%)	n (%)	n (%)
Bad (4)	n (%)	n (%)	n (%)	n (%)
Excellent / very good	n (%)	n (%)	n (%)	n (%)
Fair / Bad	n (%)	n (%)	n (%)	n (%)
Good	n (%)	n (%)	n (%)	n (%)

Note: Data from Patient DCF; X patients had missing data; The denominator for the percentage is the number of patients with available data for respective outcome measures at Weeks 4, 8 & 12 respectively.

Table 7.1.13. CFB in Patient Acne Severity and How Face Looks (without imputation)

Domain	CFB in Proportion at Week 4 N=xx	*p*-value	CFB in Proportion at Week 8 N=xx	*p*-value	CFB in Proportion at Week 12 N=xx	*p*-value
Acne Severity (ASIS 9) - Patient (**A9:** Overall, how is the acne on your face right now?)						
Clear / Almost clear	%	*p*	%	*p*	%	*p*
Moderate / Severe	%	*p*	%	*p*	%	*p*
Mild	%		%		%	
Acne Severity (ASIS 9) - Caregiver (**Q1:** Overall, how is the acne on your child's face right now?						
Clear / Almost clear	%	*p*	%	*p*	%	*p*
Moderate / Severe	%	*p*	%	*p*	%	*p*
Mild	%		%		%	
How Face Looks (ASIS 10) (**A10:** Over the past 7 days, rate how your face looked because of your acne.)						
Excellent/Very good	%	*p*	%	*p*	%	*p*
Fair / Bad	%	*p*	%	*p*	%	*p*
Good	%		%		%	

Note: Data from Patient DCF; X patients had missing data;

Table 7.1.14. Patient Acne Severity and How Face Looks (with LOCF imputation)

Domain	Baseline (N=xx)	Week 4 (N=xx)	Week 8 (N=xx)	Week 12 (N=xx)
Acne Severity (ASIS 9)-Patient **A9:** (Overall, how is the acne on your face right now?)	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max
Clear (0)	n (%)	n (%)	n (%)	n (%)
Almost clear (1)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)
Clear/almost clear	n (%)	n (%)	n (%)	n (%)
Moderate / Severe	n (%)	n (%)	n (%)	n (%)
Mild	n (%)	n (%)	n (%)	n (%)
Acne Severity (ASIS 9) - Caregiver **Q1:** Overall, how is your child's acne on his/her face right now? (Week 4 & 8)	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max	N Mean (SD) Median Min,Max
Clear (0)	n (%)	n (%)	n (%)	n (%)
Almost clear (1)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)
Clear/almost clear	n (%)	n (%)	n (%)	n (%)
Moderate / Severe	n (%)	n (%)	n (%)	n (%)
Mild	n (%)	n (%)	n (%)	n (%)
Face Look (ASIS 10)	N Mean (SD) Median	N Mean (SD) Median	N Mean (SD) Median	N Mean (SD) Median

A10: (Over the past 7 days, rate how your face looked because of your acne.)	Min,Max	Min,Max	Min,Max	Min,Max
Excellent (0)	n (%)	n (%)	n (%)	n (%)
Very good (1)	n (%)	n (%)	n (%)	n (%)
Good (2)	n (%)	n (%)	n (%)	n (%)
Fair (3)	n (%)	n (%)	n (%)	n (%)
Bad (4)	n (%)	n (%)	n (%)	n (%)
Excellent / very good	n (%)	n (%)	n (%)	n (%)
Fair / Bad	n (%)	n (%)	n (%)	n (%)
Good	n (%)	n (%)	n (%)	n (%)

Note: Data from Patient DCF. The denominator for the percentage is the number of patients with available data (N=X).

Table 7.1.15. CFB in Patient Acne Severity and How Face Looks (with LOCF imputation)

Domain	CFB in Proportion at Week 4 N=xx	*p*-value	CFB in Proportion at Week 8 N=xx	*p*-value	CFB in Proportion at Week 12 N=xx	*p*-value
Acne Severity (ASIS 9) - Patient (**A9:** Overall, how is the acne on your face right now?)						
Clear / Almost clear	%	*p*	%	*p*	%	*p*
Moderate / Severe	%	*p*	%	*p*	%	*p*
Mild	%		%		%	
Acne Severity (ASIS 9) – Caregiver (**Q1:** Overall, how is the acne on your child's face right now?						
Clear / Almost clear	%	*p*	%	*p*	%	*p*
Moderate / Severe	%	*p*	%	*p*	%	*p*
Mild	%		%		%	
How Face Looks (ASIS 10) (**A10:** Over the past 7 days, rate how your face looked because of your acne.)						
Excellent/Very good	%	*p*	%	*p*	%	*p*
Fair / Bad	%	*p*	%	*p*	%	*p*
Good	%		%		%	

Note: Data from Patient DCF.

Table 7.1.16.1 Sub-group Analysis of Patient Acne Severity (ASIS 9) (with LOCF)

% Clear / Almost clear	Weeks			
	Baseline	Week 4	Week 8	Week 12
Sex				
Male	n (%)	n (%)	n (%)	n (%)
Female	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Age Group				
≥ 9 and < 12 years	n (%)	n (%)	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)	n (%)	n (%)
≥ 12 years	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Race				
White	n (%)	n (%)	n (%)	n (%)
African America/Black	n (%)	n (%)	n (%)	n (%)
Other	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Body mass index				
< 25 kg/m^2	n (%), Mean	n (%), Mean	n (%), Mean	n (%), Mean
≥ 25 kg/m^2	n (%), Mean	n (%), Mean	n (%), Mean	n (%), Mean
p-value	*p*	*p*	*p*	*p*
Baseline facial IGA				
Moderate	n (%)	n (%)	n (%)	n (%)
Severe	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Female who used oral contraceptive*				
Used	n (%)	n (%)	n (%)	n (%)
Did not use	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*

*The denominator for the percentage is the number of 'female' patients with available data (N=X).

Table 7.1.16.2 Sub-group Analysis of How Face Looks (ASIS 10) (with LOCF)

% Excellent/Very good	Weeks			
	Baseline	Week 4	Week 8	Week 12
Sex				
Male	n (%)	n (%)	n (%)	n (%)
Female	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Age Group				
≥ 9 and < 12 years	n (%)	n (%)	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)	n (%)	n (%)
≥ 12 years	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Race				
White	n (%)	n (%)	n (%)	n (%)
African America/Black	n (%)	n (%)	n (%)	n (%)
Other	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Body mass index				
< 25 kg/m^2	n (%), Mean	n (%), Mean	n (%), Mean	n (%), Mean
≥ 25 kg/m^2	n (%), Mean	n (%), Mean	n (%), Mean	n (%), Mean
p-value	*p*	*p*	*p*	*p*
Baseline facial IGA				
Moderate	n (%)	n (%)	n (%)	n (%)
Severe	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Female who used oral contraceptive				
Used	n (%)	n (%)	n (%)	n (%)
Did not use	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*

Note: X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X).

*The denominator for the percentage is the number of 'female' patients with available data (N=X).

Table 7.1.17. Impact on Parents/Caregiver

Domain	Baseline	Week 12
Q2: Do you feel that you understand your child's acne-related concerns?	**N Mean (SD), Median, Min, Max**	**N Mean (SD), Median, Min, Max**
Not at all (0)	n (%)	n (%)
A little (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Quite a bit (3)	n (%)	n (%)
Very much (4)	n (%)	n (%)
Q3: Over the past 7 days, how concerned have you been about your child's acne?	**N Mean (SD), Median, Min, Max**	**N Mean (SD), Median, Min, Max**
Not at all (0)	n (%)	n (%)
Slightly (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Moderately (3)	n (%)	n (%)
Extremely (4)	n (%)	n (%)
Q4: How concerned are you about your child's ability to accomplish future goals and reach full potential due to acne?	**N Mean (SD), Median, Min, Max**	**N Mean (SD), Median, Min, Max**
Not at all (0)	n (%)	n (%)
Slightly (1)	n (%)	n (%)
Somewhat (2)	n (%)	n (%)
Moderately (3)	n (%)	n (%)
Extremely (4)	n (%)	n (%)

Note: X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

Table 7.1.18. Change in Impact on Parents/Caregiver

Domain	Baseline (N=xx)	Week 12 (N=xx)	CFB in proportion at Week 12 (N=xx)	*p*-value
Q2: Do you feel that you understand your child's acne-related concerns?				
Not at all / A little	n (%)	n (%)	%	*p*
Quite a bit / Very much	n (%)	n (%)	%	*p*
Somewhat	n (%)	n (%)	%	
Q3: Over the past 7 days, how concerned have you been about your child's acne?				
Not at all / Slightly	n (%)	n (%)	%	*p*
Moderately / Extremely	n (%)	n (%)	%	*p*
Somewhat	n (%)	n (%)	%	
Q4: How concerned are you about your child's ability to accomplish future goals and reach full potential due to acne?				
Not at all / Slightly	n (%)	n (%)	%	*p*
Moderately / Extremely	n (%)	n (%)	%	*p*
Somewhat	n (%)	n (%)	%	

Note: X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

7.2 Tables from clinician's DCF (FAS Population)

Clinician data is analyzed using the FAS dataset. In relevant instances (such as IGA and physician satisfaction evaluations), only FAS dataset with corresponding week 12 clinician data is used. All data tables in this section correspond to FAS population.

Table 7.2.1. Site Characteristics

Domain	(N=xx)
S1: Current workplace	
Private, office-based practice	n (%)
Hospital-based practice	n (%)
S2: Total number of board-certified dermatologists in the practice (including yourself, if applicable)	**N, Mean (SD), Median, Min, Max**
S3: At present, how many patients with acne vulgaris (AV) do you personally manage in a given month?	**N, Mean (SD), Median, Min, Max**
S4: How long have you been practicing dermatology, post-residency?	**N, Mean (SD), Median, Min, Max**
S5: How often do you prescribe broad-spectrum antibiotics (such as doxycycline and minocycline)?	**N, Mean (SD), Median, Min, Max**
Never (0)	n (%)
Rarely (1)	n (%)
Some of the time (2)	n (%)
Most of the time (3)	n (%)
All of the time (4)	n (%)
S6: How concerned are you about antibiotic resistance with long-term antibiotic use?	**N, Mean (SD), Median, Min, Max**
Not at all (0)	n (%)
Slightly (1)	n (%)
Somewhat (2)	n (%)
Moderately (3)	n (%)
Extremely (4)	n (%)
S7: How concerned are you about disruption of the microbiome with long-term antibiotic use?	**N, Mean (SD), Median, Min, Max**
Not at all (0)	n (%)
Slightly (1)	n (%)
Somewhat (2)	n (%)
Moderately (3)	n (%)

Extremely (4)	n (%)
S8: How important is the role of narrow-spectrum antibiotics (such as sarecycline/Seysara®) in supporting antibiotic stewardship?	**N, Mean (SD), Median, Min, Max**
Not at all (0)	n (%)
Slightly (1)	n (%)
Somewhat (2)	n (%)
Moderately (3)	n (%)
Extremely (4)	n (%)

Note: Data from Clinician DCF. The denominator for the percentage is N which refers to total number of unique sites in PROSES study.

Table 7.2.2. Study Subject Selection Criteria

Domain (N=X)	Yes	No
Diagnosed with non-nodular moderate to severe acne vulgaris on the face	n (%)	n (%)
S9Br1. Considered a candidate for sarecycline/Seysara® treatment AND you plan to administer sarecycline/Seysara® treatment	n (%)	n (%)
S9Br2. AT LEAST 9 years of age at the time of initiation of sarecycline/Seysara® treatment	n (%)	n (%)
S9Br3. Able to read and write English	n (%)	n (%)
S9Br4. Able to provide consent (in case of adult patients) or assent (in case of pediatric patients) to participate AND is willing to comply with study procedures	n (%)	n (%)
S9Br5. Currently being treated with any of the following: penicillin, oral retinoids (including isotretinoin and acitretin)	n (%)	n (%)
S9Br6. Among the female subjects: Currently pregnant, lactating or is planning a pregnancy during the study period	n (%)	n (%)
S10r1. Have known resistance to other tetracyclines?	n (%)	n (%)
S10r2. Have another dermatological or physical condition of the face that could interfere with the acne vulgaris clinical evaluations?	n (%)	n (%)
S10r3. Have an history of allergy to tetracycline-class antibiotics, pseudomembranous colitis or antibiotic-associated colitis?	n (%)	n (%)
S10r4. Have a medical chart accessible to complete baseline data collection?	n (%)	n (%)
S11. Is the patient under 18 years of age (9 to 17 years), requiring a legal caretaker for the purposes of this study?	n (%)	n (%)
S12r1. Older than 18 years of age?	n (%)	n (%)
S12r2. Able to read and write English?	n (%)	n (%)
S12r3. The primary caregiver of the study-eligible patient?	n (%)	n (%)

S12r4. Legally able to provide consent to participate in the study and willing to comply with study procedures?	n (%)	n (%)

Note: Data from Clinician DCF. The denominator for the percentage is the number of patients with available data (N=X). There are no missing data.

Table 7.2.3. Patient Clinical Characteristics from Medical Chart

Character	Baseline (N=x)
M1B: Gender	
Male	n (%)
Female	n (%)
M2: Primary Health Insurance	
Private health insurance	n (%)
Medicaid	n (%)
Medicare	n (%)
Uninsured	n (%)
Other	n (%)
Not available	n (%)
M3r1. Height (in inches)	**N, Mean (SD), Median, Min, Max**
M3r2. Weight (in lbs/pound)	**N, Mean (SD), Median, Min, Max**
M5: Waist circumference (in inches)	**N, Mean (SD), Median, Min, Max**
Body Mass Index (BMI - calculated)	**N, Mean (SD), Median, Min, Max**
M6: Blood pressure (in mm HG)	
M6r2. Systolic	**N, Mean (SD), Median, Min, Max**
M6r3. Diastolic	**N, Mean (SD), Median, Min, Max**
M7: Concomitant (comorbid) conditions	
M7r1. Anxiety	n (%)
M7r2. Anemia or other blood disease	n (%)
M7r3. Asthma	n (%)
M7r4. Atopic dermatitis	n (%)
M7r5. Cancer (of any type)	n (%)
M7r6. Crohn's disease / IBD	n (%)
M7r7. Diabetes	n (%)
M7r8. Depression	n (%)
M7r9. Dyslipidemia/Hyperlipidemia	n (%)
M7r10. Gastroesophageal reflux disease	n (%)
M7r11. Heart disease	n (%)

M7r12. Hypertension	n (%)
M7r13. Kidney disease	n (%)
M7r14. Liver damage or disease	n (%)
M7r15. Lung disease	n (%)
M7r16. Osteoarthritis, degenerative arthritis	n (%)
M7r17. Other gastrointestinal disease	n (%)
M7r18. Other	n (%)
M7r18oe A, B, C	n (%)

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

Table 7.2.4.1 Clinician Acne Evaluation (IGA) (without imputation)

Character	Baseline (N=x)	Week 4 (N=x)	Week 8 (N=x)	Week 12 (N=x)
Overall, how is the patient's facial acne right now? (**IGA**)	S9A	P2	P2	P2
	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max
Clear (0)	n (%)	n (%)	n (%)	n (%)
Almost clear (1)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)
Clear/almost clear	n (%)	n (%)	n (%)	n (%)
Moderate / Severe	n (%)	n (%)	n (%)	n (%)
Mild	n (%)	n (%)	n (%)	n (%)
M1A.1: Who did the evaluation of the patient's acne severity?				
Dermatologist	n (%)	n (%)	n (%)	n (%)
Nurse Practitioner	n (%)	n (%)	n (%)	n (%)
Physician's assistant	n (%)	n (%)	n (%)	n (%)
M1A.2: How was the evaluation of acne severity done?				
During in-person patient visit (face-to-face)	n (%)	n (%)	n (%)	n (%)
Via telehealth visit (video)	n (%)	n (%)	n (%)	n (%)

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X)

Table 7.2.4.2. CFB in IGA (without imputation)

Domain	CFB in Proportion at Week 4 N=xx	*p*-value	CFB in Proportion at Week 8 N=xx	*p*-value	CFB in Proportion at Week 12 N=xx	*p*-value
IGA (Overall, how is the patient's facial acne right now?)						
Clear / Almost clear	%	*p*	%	*p*	%	*p*
Moderate / Severe	%	*p*	%	*p*	%	*p*
Mild	%		%		%	

Note: Data from Clinician DCF; X patients had missing data;

Table 7.2.4.3. Facial IGA Success (without imputation)

Character	Week 12
IGA Success	**N=x**
No	n (%)
Yes	n (%)

Note: Facial IGA success at Week 12, defined as a 2-point decrease in IGA score from baseline and a score of 0 (clear) or 1 (almost clear) at Week-12. The denominator for the percentages is the number of patients with available data (N=X)

Table 7.2.4.4. Clinician Acne Evaluation (IGA) (with LOCF imputation)

Character	Baseline (N=xx)	Week 4 (N=xx)	Week 8 (N=xx)	Week 12 (N=xx)
Overall, how is the patient's facial acne right now? (**IGA**)	S9A	P2	P2	P2
	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max
Clear (0)	n (%)	n (%)	n (%)	n (%)
Almost clear (1)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)
Clear/almost clear	n (%)	n (%)	n (%)	n (%)
Moderate / Severe	n (%)	n (%)	n (%)	n (%)
Mild	n (%)	n (%)	n (%)	n (%)

Table 7.2.4.5 Sub-group Analysis of IGA (with LOCF imputation)

% Clear/Almost Clear	Weeks			
	Baseline (N=x)	Week 4 (N=x)	Week 8 (N=x)	Week 12 (N=x)
Sex				
Male	n (%)	n (%)	n (%)	n (%)
Female	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Age Group				
≥ 9 and < 12 years	n (%)	n (%)	n (%)	n (%)
≥ 12 and < 18 years	n (%)	n (%)	n (%)	n (%)
≥ 12 years	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Race				
White	n (%)	n (%)	n (%)	n (%)
African	n (%)	n (%)	n (%)	n (%)
American/Black	n (%)	n (%)	n (%)	n (%)
Other	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Body mass index				
< 25 kg/m^2	n (%)	n (%)	n (%)	n (%)
≥ 25 kg/m^2	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Baseline facial IGA				
Moderate	n (%)	n (%)	n (%)	n (%)
Severe	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*
Female who used oral contraceptive*				
Used	n (%)	n (%)	n (%)	n (%)
Did not use	n (%)	n (%)	n (%)	n (%)
p-value	*p*	*p*	*p*	*p*

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X)

* The denominator for the percentages is the number of 'female' patients with available data (N=X)

Table 7.2.4.6. CFB in IGA (with LOCF imputation)

Domain	CFB in Proportion at Week 4 N=xx	*p*-value	CFB in Proportion at Week 8 N=xx	*p*-value	CFB in Proportion at Week 12 N=xx	*p*-value
IGA (Overall, how is the patient's facial acne right now?)						
Clear / Almost clear	%	*p*	%	*p*	%	*p*
Moderate / Severe	%	*p*	%	*p*	%	*p*
Mild	%		%		%	

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X)

Table 7.2.4.7. Facial IGA Success (with LOCF imputation)

Character	Week 12
IGA Success	**N=x**
No	n (%)
Yes	n (%)

Note: Facial IGA success at Week 12, defined as a 2-point decrease in IGA score from baseline and a score of 0 (clear) or 1 (almost clear) at Week-12. The denominator for the percentages is the number of patients with available data (N=X)

Table 7.2.4.8. Sub-group Analysis of Facial IGA Success (with LOCF imputation)

% IGA Success	
	Week 12 (N=x)
Sex	
Male	n (%)
Female	n (%)
p-value	*p*
Age Group	
≥ 9 and < 12 years	n (%)
≥ 12 and < 18 years	n (%)
≥ 12 years	n (%)
p-value	*p*
Race	
White	n (%)
African America/Black	n (%)
Other	n (%)
p-value	*p*
Body mass index	
< 25 kg/m^2	n (%)
≥ 25 kg/m^2	n (%)
p-value	*p*
Baseline facial IGA	
Moderate	n (%)
Severe	n (%)
p-value	*p*
Female who used oral contraceptive*	
Used	
Did not use	n (%)
p-value	n (%)
	p

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X).
* The denominator for the percentages is the number of 'female' patients with available data (N=X)

Table 7.2.5. Seysara Treatment Characteristics

Character	Baseline (N=x)	Week 4 (N=x)	Week 8 (N=x)	Week 12 (N=x)
Prescription dose	(M12.1)	(P13A1)	(P13A1)	(P13A1)
60 mg	n (%)	n (%)	n (%)	n (%)
100 mg	n (%)	n (%)	n (%)	n (%)
150 mg	n (%)	n (%)	n (%)	n (%)
Prescription frequency	(M12.2)	(P14A1)	(P14A1)	(P14A1)
Once daily	n (%)	n (%)	n (%)	n (%)
Other 1	n (%)	n (%)	n (%)	n (%)
Other 2	n (%)	n (%)	n (%)	n (%)

Table 7.2.6.1 Prior Acne Treatment (ever tried) Including Within the Past 6 Months

Character	Baseline (N=x)
Has not use any acne medication	n (%)
Topical medication	
Topical retinoids	n (%)
Salicylic acid	n (%)
Benzoyl peroxide	n (%)
Topical antibiotics	n (%)
Topical Dapsone	n (%)
Azelaic acid	n (%)
Topical Clascoterone	n (%)
Other (total)	n (%)
A	n (%)
B	n (%)
C	n (%)
Oral medication	
Oral antibiotics (tetracycline or macrolide)	n (%)
Anti-androgen agents	n (%)
Oral antibiotics (non-tetracycline class)	n (%)
Isotretinoin	n (%)
Other	
A	n (%)
B	
C	
Oral contraceptives (any type)	n (%)
Other therapies	
Light therapy	n (%)
Drainage and extraction	n (%)
Chemical peel	n (%)
Steroid injection	n (%)
Other	n (%)

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X)
(Programmer's note: this is a combination of internal Avant tables 7.2.6.x1 & 7.2.6.x2)

Table 7.2.6.2 Acne Concomitant Medication Use

Character	N=x
Has not use any acne medication	n (%)
Topical medication	
Topical retinoids	n (%)
Salicylic acid	n (%)
Benzoyl peroxide	n (%)
Topical antibiotics	n (%)
Topical Dapsone	n (%)
Azelaic acid	n (%)
Topical Clascoterone	n (%)
Other (total)	n (%)
A	n (%)
B	n (%)
C	n (%)
Oral medication	
Oral antibiotics (tetracycline or macrolide)	n (%)
Anti-androgen agents	n (%)
Oral antibiotics (non-tetracycline class)	n (%)
Isotretinoin	n (%)
Other	
A	n (%)
B	
C	
Oral contraceptives (any type)	n (%)
Other therapies	
Light therapy	n (%)
Drainage and extraction	n (%)
Chemical peel	n (%)
Steroid injection	n (%)
Other	n (%)

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X)

Table 7.2.7. Non-Acne Concomitant Medication Use

Non-Acne concomitant medication use during any time of the study	
M15: Is the patient currently taking any concomitant medications to manage conditions other than acne?	
M15Ar1	
<<categories from WHO ATC classifications>>	
A	n (%)
B	n (%)
C	n (%)
D	n (%)
E	n (%)

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X). This concomitant non-Acne medication use correspond to use of medications at any time during the study observation period, overlapping with Seysara medication use.

Table 7.2.8. Physician Satisfaction with Seysara

	Week 12 (N=x)
FP2: How satisfied are you with sarecycline/Seysara® treatment outcomes?	N, Mean (SD), Median, Min, Max
Very Satisfied (5)	n (%)
Satisfied (4)	n (%)
Neutral (3)	n (%)
Dissatisfied (2)	n (%)
Very Dissatisfied (1)	n (%)
Very Satisfied/Satisfied	n (%)
Dissatisfied/Very Dissatisfied	n (%)
Neutral	n (%)

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X).

Table 7.2.9. Subgroup analysis: Physician Satisfaction with Seysara

% Very Satisfied/Satisfied	
	Week 12 (N=x)
Sex	
Male	n (%)
Female	n (%)
p-value	*p*
Age Group	
≥ 9 and < 12 years	n (%)
≥ 12 and < 18 years	n (%)
≥ 12 years	n (%)
p-value	*p*
Race	
White	n (%)
African America/Black	n (%)
Other	n (%)
p-value	n (%)
	p
Body mass index	
< 25 kg/m^2	n (%)
≥ 25 kg/m^2	n (%)
p-value	*p*
Baseline facial IGA	
Moderate	n (%)
Severe	n (%)
p-value	*p*
Female who used oral contraceptive*	
Used	
Did not use	n (%)
p-value	n (%)
	p

Note: Data from Clinician DCF; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X).
*The denominator for the percentages is the number of 'female' patients with available data (N=X).

7.3 Tables for comparison of patient and clinician data

For tables comparing patient and clinician data, the FAS dataset is used for analysis only in the instances patient data has corresponding clinician week 12 data. All data tables in this section pertain to FAS population.

Table 7.3.1. Acne Severity Evaluation for All Patients

Question	Baseline (N=x)		Week 4 (N=x)		Week 8 (N=x)		Week 12 (N=x)	
	A9 Patient	S9A Clinician	A9 Patient	P2 Clinician	A9 Patient	P2 Clinician	A9 Patient	P2 Clinician
Overall, how is the patient's facial acne right now?	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max
Clear (0)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Almost Clear (1)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Clear/Almost Clear	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

NOTE: All patient data corresponds to data from adult patients, pediatric patients aged 12-17, and caregivers of patients aged 9-11.
Data from Clinician and Patient DCF used; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X).

Table 7.3.2. Acne Severity Evaluation for Adult Patients

Question	Baseline (N=xx)		Week 4 (N=xx)		Week 8 (N=xx)		Week 12 (N=xx)	
	A9 Patient	S9A Clinician	A9 Patient	P2 Clinician	A9 Patient	P2 Clinician	A9 Patient	P2 Clinician
Overall, how is the patient's facial acne right now?	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max
Clear (0)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Almost Clear (1)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Clear/Almost Clear	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Note: All patient data corresponds to data from adult patients,
Data from Clinician and Patient DCF used; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X).

Table 7.3.3. Acne Severity Evaluation for Caregivers of Patients aged 9-11 yrs

Question	Baseline (N=xx)		Week 4 (N=xx)		Week 8 (N=xx)		Week 12 (N=xx)	
	A9 Patient	S9A Clinician	A9 Patient	P2 Clinician	A9 Patient	P2 Clinician	A9 Patient	P2 Clinician
Overall, how is the patient's facial acne right now?	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max
Clear (0)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Almost Clear (1)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Clear/Almost Clear	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

NOTE: All patient data corresponds to data from caregivers of patients aged 9-11
Data from Clinician and Patient DCF used; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X).

Table 7.3.4. Acne Severity Evaluation for Pediatric Patients Age 12-17

Question	Baseline (N=xx)			Week 4 (N=xx)			Week 8 (N=xx)			Week 12 (N=xx)		
	A9 Patient	Q1 Caregiver	S9A Clinician	A9 Patient	Q1 Caregiver	P2 Clinician	A9 Patient	Q1 Caregiver	P2 Clinician	A9 Patient	Q1 Caregiver	P2 Clinician
Overall, how is the patient's facial acne right now?	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max	N, Mean (SD), Median, Min, Max
Clear (0)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Almost Clear (1)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Mild (2)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Moderate (3)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Severe (4)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Clear/Almost Clear	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

NOTE: All patient data corresponds to data from pediatric patients aged 12-17
Data from Clinician and Patient DCF used; X patients had missing data; The denominator for the percentages is the number of patients with available data (N=X).

Table 7.3.5. Patient-Caregiver Comparison: Parent Understanding of Child's Acne-Related Concerns

	Statistics	Baseline (N=x)		Week 12 (N=x)	
		Parent	Child	Parent	Child
Question:		**Q2:** Do you feel that you understand your child's acne-related concerns right now?	**AH10:** Do you feel that your parents understand your acne-related concerns?	**Q2:** Do you feel that you understand your child's acne-related concerns right now?	**AH10:** Do you feel that your parents understand your acne-related concerns?
Answers:					
	N, Mean (SD), Median, Min, Max				
Not at all (0)	n (%)				
A little (1)	n (%)				
Somewhat (2)	n (%)				
Quite a bit (3)	n (%)				
Very Much (4)	n (%)				
Not at all/A little	n (%)				
Quite a bit/Very Much	n (%)				
Somewhat	n (%)				

Note: X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

Table 7.3.6. Patient-Caregiver Comparison: Parental Concerns of Child's Acne Vs. Child's Concerns

	Statistics	Baseline (N=x)		Week 12 (N=x)	
		Parent	**Child**	**Parent**	**Child**
Question:		**Q3:** Over the past 7 days, how concerned have you been about your child's acne?	**AH4:** Over the past 7 days, how worried have you been about your acne?	**Q3:** Over the past 7 days, how concerned have you been about your child's acne?	**AH4:** Over the past 7 days, how worried have you been about your acne?
Answers:					
	N, Mean (SD) Median, Min, Max				
Not at all (0)	n (%)				
Slightly (1)	n (%)				
Somewhat (2)	n (%)				
Moderately (3)	n (%)				
Extremely (4)	n (%)				
Not at all/Slightly	n (%)				
Moderately/Extremely	n (%)				
Somewhat	n (%)				

Note: X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

Table 7.3.7. Patient-Caregiver Comparison: Child's Ability to Reach Future Goals

	Statistics	Baseline (N=x)		Week 12 (N=x)	
		Parent	Child	Parent	Child
Question:		**Q4:** How concerned are you about your child's ability to accomplish future goals and reach full potential due to acne?	**AH9:** How concerned are you that your acne will affect your ability to reach your future goals (in school or work) and be the best you can be?	**Q4:** How concerned are you about your child's ability to accomplish future goals and reach full potential due to acne?	**AH9:** How concerned are you that your acne will affect your ability to reach your future goals (in school or work) and be the best you can be?
Answers:					
	N, Mean ± SD, Median, Range				
Not at all (0)	n (%)				
Slightly (1)	n (%)				
Somewhat (2)	n (%)				
Moderately (3)	n (%)				
Extremely (4)	n (%)				
Not at all/Slightly	n (%)				
Moderately/Extremely	n (%)				
Somewhat	n (%)				

Note: X patients had missing data; The denominator for the percentage is the number of patients with available data (N=X)

7.4 Tables from Clinician DCF: Safety Data Analysis

These analyses will use Safety Population dataset.

All patients who started the study and received at least one dose of the sareycline during the study observation period, as part of usual care. This corresponds to the entire cohort of 300 eligible patients who started the study.

Table 7.4.1. Safety Analysis Population

S1: Population	Total
Adult Patient	n (%)
Pediatric Patient & Caregiver	n (%)
Total Population	n (%)

Note: Data from Patient DCF

Table 7.4.2. PROSES Study Duration & Seysara Treatment Duration

	Total
Cumulative study duration, n (%)[a]	
Day 1 (all)	300 (100%)
≥ 4 Weeks[1]	N (%)
≥ 8 Weeks[2]	N (%)
= 12 Weeks[3]	N (%)
Cumulative treatment duration, n (%)[a]	
Day 1 (all)	300 (100%)
≥ 4 Weeks[1]	N (%)
≥ 8 Weeks[2]	N (%)
= 12 Weeks[3]	N (%)
Treatment duration (days)[b]	N Mean (SD) Median Min, Max

N = number of subjects in the safety population; n = number of subjects within a specific Category.
[a]Distribution categories were cumulative; subjects were included in each category for which they qualified.
[b]Treatment duration is the total number of pills used across each treatment period between study encounters. Number of pills used for each encounter is calculated as a difference between 30 (maximum # of tablets in a Seysara® bottle dispensed for each study encounter) and # of unused/returned pills (by subject) at the following study encounter.
[1]XX patients discontinued before week-4 encounter.
[2]XX patients discontinued between week-4 and week-8 encounter.
[3]XX patients discontinued between week-8 and week-12 encounter.

Table 7.4.3. Seysara Treatment Compliance

Average Compliance	
At Week 4 encounter	N, Mean % (SD) Median Min, Max
At Week 8 encounter	N, Mean % (SD) Median Min, Max
At Week 12 encounter	N, Mean % (SD) Median Min, Max

Compliance (%) for Week-4 encounter period =
[# of pills expected to be used - # of pills unused] * 100 / [# of pills expected to be used]

Compliance (%) for Week-4 encounter period =
[(AB2 - AB201) – (AA2 - AA201)] *100 / [(AB2 – AB201)]

Compliance (%) for Week-8 encounter period =
[# of pills expected to be used - # of pills unused] * 100 / [# of pills expected to be used]

Compliance (%) for Week-8 encounter period =
[(R2 - R201) – (Q2 - Q201)] *100 / [(R2 – R201)]

Compliance (%) for Week-12 encounter period =
[# of pills expected to be used - # of pills unused] * 100 / [# of pills expected to be used]

Compliance (%) for Week-12 encounter period =

[(H2 - H201) – (G2 - G201)] *100 / [(H2 – H201)]

Note: Variables for "# of expected pills to be used" for each encounter needs to be calculated, and final Compliance % needs to be transformed, as outlined in Section 6.6.2.

Table 7.4.4.1. Overall Summary of Adverse Events – Any Type (Subject Level)

	N=300
[P4 or P5] Subjects with at least 1 adverse event (any type)*	n (%)
[P4_i_4 or P5_i_4]: Intensity of adverse event, among Subjects with at least 1 adverse event (any type)*	
R1: Mild	n (%)
R2: Moderate	n (%)
R3: Severe	n (%)
[P4_i_3 or [P5_i_3]: Action taken with Seysara, among Subjects with at least 1 adverse event (any type)*	
[P4_i_3r1 or P5_i_3r1]: Drug withdrawal / study discontinuation	n (%)
Other Actions	n (%)
[P4_i_5 or [P5_i_5]: Subjects with at least 1 SAE or Serious ADR	n (%)
Subjects with at least 1 SAE or Serious ADR resulting in death	n (%)

*includes not related AEs and ADRs (related-AEs); excludes special safety events.
Note: Percentages were based on the total number of subjects in the study.
Deaths, AEs/ADRs, SAEs, and Serious ADRs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.

Table 7.4.4.2. Overall Summary of 'Not-Related' AEs (Subject Level)

	N=300
[P4] Subjects with at least 1 'not-related' AE	n (%)
[P4_i_4]: Intensity of adverse event, among Subjects with at least 1 'not-related' AE	n (%)
R1: Mild	n (%)
R2: Moderate	n (%)
R3: Severe	
[P4_i_3]: Action taken with Seysara, among Subjects with at least 1 'not-related' AE	
[P4_i_3r1]: Drug withdrawal / study discontinuation	n (%)
Other Actions	n (%)
[P4_i_5]: Subjects with at least 1 SAE*	n (%)
Subjects with at least 1 SAE resulting in death	n (%)

*for not related AEs.

Note: Percentages were based on the total number of subjects in the study
Deaths, AEs and SAEs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.

Table 7.4.4.3. AEs (Not-Related) – by Organ Class & Preferred Term (Subject level)

System Organ Class: Preferred Term	N=300	Intensity	Action Taken*
Gastrointestinal disorders	n (%)		
GI Upset	n (%)	A	A
Y	n (%)	B	B
Infections and infestations	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Injury, poisoning and procedural complication	n (%)	A	
X	n (%)	B	A
Y	n (%)		B
Investigations	n (%)	A	
X	n (%)	B	A
Y	n (%)		B
Nervous system disorders	n (%)	A	
Headache	n (%)	B	A
Y	n (%)		B
Skin and subcutaneous tissue disorders	n (%)	A	
X	n (%)	B	A
Y	n (%)		B
Respiratory, thoracic and mediastinal disordersX	n (%)	A	
X	n (%)	B	A
Y	n (%)		B
General disorders and administration site conditions	n (%)	A	
X	n (%)	B	A
Y	n (%)		B

*Action taken as a result of the AE.

Note: Percentages were based on the total number of patients in Safety Population, i.e., 300.
If a same AE occurred more than once for a given patient, the AE was counted only once at Subject-level.
For any of the safety events, a single patient may have reported more than one event.
Deaths, AEs and SAEs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.
Adverse events were coded using MedDRA version 2021AB.

This table will be replicated to characterize SAEs, if any observed.

Table 7.4.4.4. Overall Summary of ADRs (Subject level)

	N=300
[P5] Subjects with at least 1 ADR*	n (%)
[P5_i_4]: Intensity of adverse event, among Subjects with at least 1 ADR	n (%)
R1: Mild	n (%)
R2: Moderate	n (%)
R3: Severe	
[P5_i_3]: Action taken with Seysara, among Subjects with at least 1 ADR	
[P5_i_3r1]: Drug withdrawal / study discontinuation	n (%)
Other Actions	n (%)
[P5a_i_5]: Subjects with at least 1 Serious ADR	n (%)
Subjects with at least 1 Serious ADR, resulting in death	n (%)

*excludes special safety events.
Note: Percentages were based on the total number of subjects in the study
Deaths, ADRs and Serious ADRs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.

Table 7.4.4.5. ADRs – by Organ Class & Preferred Term (Subject level)

System Organ Class: Preferred Term	N=300	Intensity	Action Taken*
Gastrointestinal disorders	n (%)		
GI Upset	n (%)	A	A
Y	n (%)	B	B
Infections and infestations	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Injury, poisoning and procedural complication	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Investigations	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Nervous system disorders	n (%)		
Headache	n (%)	A	A
Y	n (%)	B	B
Skin and subcutaneous tissue disorders	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Respiratory, thoracic and mediastinal disorders	n (%)	A	A
X	n (%)	B	B
Y	n (%)		
General disorders and administration site conditions	n (%)		
X	n (%)	A	A
Y	n (%)	B	B

*Action taken as a result of the AE.

Note: Percentages were based on the total number of patients in Safety Population, i.e., 300.
If a same ADR occurred more than once for a given patient, the ADR was counted only once at Subject-level. For any of the safety events, a single patient may have reported more than one event.
Deaths, ADRs and Serious ADRs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.
Adverse events were coded using MedDRA version 2021AB.

This table will be replicated to characterize Serios ADRs, if any observed.

Table 7.4.4.6. Overall Summary of Adverse Events – Any Type (Event Level)

[P4 or P5] Total number of adverse events (any type)*	N
[P4_i_4 or P5_i_4]: Intensity of adverse events, among documented adverse events (any type)*	
R1: Mild	n (%)
R2: Moderate	n (%)
R3: Severe	n (%)
[P4_i_3 or [P5_i_3]: Action taken with Seysara, for documented adverse events (any type)*	
[P4_i_3r1 or P5_i_3r1]: Drug withdrawal / study discontinuation	n (%)
Other Actions	n (%)
[P4_i_5 or [P5_i_5]: Number of SAEs or Serious ADRs	n (%)
Number of SAEs or Serious ADRs resulting in death	n (%)

*includes not-related AEs and ADRs (related-AEs); excludes special safety events.
Note: Percentages were based on the total number of adverse events (any type) observed in the study, i.e., N=x.
The same AE or ADR was counted as many times as it occurred, for a given patient. For any of the safety events, a single patient may have reported more than one event.
Deaths, AEs/ADRs, SAEs, and Serious ADRs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.

Table 7.4.4.7. Overall Summary of 'Not-Related' AEs (Event Level)

[P4] Total number of 'not-related' AE	N
[P4_i_4]: Intensity of adverse event, among documented 'not-related' AEs	n (%)
R1: Mild	n (%)
R2: Moderate	n (%)
R3: Severe	
[P4_i_3]: Action taken with Seysara, for documented 'not-related' AEs	
[P4_i_3r1]: Drug withdrawal / study discontinuation	n (%)
Other Actions	n (%)
[P4_i_5]: Number of SAEs*	n (%)
Number of SAEs resulting in death	n (%)

*refers to 'not-related AEs'.
Note: Percentages were based on the total number of 'not-related' AEs observed in the study, i.e., N=x.
The same AE was counted as many times as it occurred, for a given patient. For any of the safety events, a single patient may have reported more than one event.
Deaths, AEs and SAEs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.

Table 7.4.4.8. AEs (Not-Related) – by Organ Class & Preferred Term (Event level)

System Organ Class: Preferred Term	N=x	Intensity	Action Taken*
Gastrointestinal disorders	n (%)		
GI Upset	n (%)	A	A
Y	n (%)	B	B
Infections and infestations	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Injury, poisoning and procedural complication	n (%)	A	
X	n (%)	B	A
Y	n (%)		B
Investigations	n (%)	A	
X	n (%)	B	A
Y	n (%)		B
Nervous system disorders	n (%)	A	
Headache	n (%)	B	A
Y	n (%)		B
Skin and subcutaneous tissue disorders	n (%)	A	
X	n (%)	B	A
Y	n (%)		B
Respiratory, thoracic and mediastinal disordersX	n (%)	A	
X	n (%)	B	A
Y	n (%)		B
General disorders and administration site conditions	n (%)	A	
X	n (%)	B	A
Y	n (%)		B

*Action taken as a result of the AE.

Note: Percentages were based on the total number of 'not-related' AEs observed in the study, i.e., N=x.
The same AE was counted as many times as it occurred, for a given patient. For any of the safety events, a single patient may have reported more than one event.
Deaths, AEs and SAEs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.
Adverse events were coded using MedDRA version 2021AB.

This table will be replicated to characterize SAEs, if any observed.

Table 7.4.4.9. AEs (Not-Related) – by Patient-ID (Event level)

<<all events will be reported at Patient-ID level AND ORDERED BY 'System Organ Class and then Preferred Term' >>

Patient-ID # 1	Study/Survey Timepoint	[P4_i] Reported Term for the Adverse Event	AE Preferred Term	Primary System Organ Class

[P4_i_1] Date of Onset	[P4_i_2] Date of Resolution	[P4_i_3] Action taken with Seysara*	[P4_i_4] Intensity of Adverse Event	[P4_i_5] Is this a SAE?

Patient-ID # 2	Study/Survey Timepoint	[P4_i] Reported Term for the Adverse Event	AE Preferred Term	Primary System Organ Class

[P4_i_1] Date of Onset	[P4_i_2] Date of Resolution	[P4_i_3] Action taken with Seysara*	[P4_i_4] Intensity of Adverse Event	[P4_i_5] Is this a SAE?

*Action taken as a result of the AE.
Deaths, AEs and SAEs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.
Adverse events were coded using MedDRA version 2021AB.

Table 7.4.4.10. Overall Summary of ADRs (Event level)

[P5] Total number of ADRs*	N
[P5_i_4]: Intensity of adverse events, among documented ADRs	
R1: Mild	n (%)
R2: Moderate	n (%)
R3: Severe	n (%)
[P5_i_3]: Action taken with Seysara, for documented ADRs	
[P5_i_3r1]: Drug withdrawal / study discontinuation	n (%)
Other Actions	n (%)
[P5a_i_5]: Number of Serious ADR	n (%)
Number of Serious ADR, resulting in death	n (%)

*excludes special safety events.
Note: Percentages were based on the total number of ADRs observed in the study, i.e., N=x.
The same ADR was counted as many times as it occurred, for a given patient. For any of the safety events, a single patient may have reported more than one event.
Deaths, ADRs and Serious ADRs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.

Table 7.4.4.11. ADRs – by Organ Class & Preferred Term (Event level)

System Organ Class: Preferred Term	N=x	Intensity	Action Taken*
Gastrointestinal disorders	n (%)		
GI Upset	n (%)	A	A
Y	n (%)	B	B
Infections and infestations	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Injury, poisoning and procedural complication	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Investigations	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Nervous system disorders	n (%)		
Headache	n (%)	A	A
Y	n (%)	B	B
Skin and subcutaneous tissue disorders	n (%)		
X	n (%)	A	A
Y	n (%)	B	B
Respiratory, thoracic and mediastinal disorders	n (%)	A	A
X	n (%)	B	B
Y	n (%)		
General disorders and administration site conditions	n (%)		
X	n (%)	A	A
Y	n (%)	B	B

*Action taken as a result of the AE.
Note: Percentages were based on the total number of ADRs observed in the study, i.e., N=x.
The same ADR was counted as many times as it occurred, for a given patient. For any of the safety events, a single patient may have reported more than one event.
Deaths, ADRs and Serious ADRs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.
Adverse events were coded using MedDRA version 2021AB.

This table will be replicated to characterize Serios ADRs, if any observed.

Table 7.4.4.12. ADRs – by Patient-ID (Event level)

<<all events will be reported at Patient-ID level AND ORDERED BY 'System Organ Class and then Preferred Term' >>

Patient-ID # 1	Study/Survey Timepoint	[P5_i] Reported Term for the Adverse Event	Preferred Term	Primary System Organ Class

[P5_i_1] Date of Onset	[P5_i_2] Date of Resolution	[P5_i_3] Action taken with Seysara*	[P5_i_4] Intensity of Adverse Event	[P5_i_5] Is this a SAE?

Patient-ID # 2	Study/Survey Timepoint	[P5_i] Reported Term for the Adverse Event	Preferred Term	Primary System Organ Class

[P5_i_1] Date of Onset	[P5_i_2] Date of Resolution	[P5_i_3] Action taken with Seysara*	[P5_i_4] Intensity of Adverse Event	[P5_i_5] Is this a SAE?

*Action taken as a result of the ADR.
Deaths, ADRs and Serious ADRs were those that started on or after the date of the first dose of the study treatment and no more than 30 days after the date of the last dose of the study treatment.
Adverse events were coded using MedDRA version 2021AB.

Table 7.4.4.13. Summary of Other Safety Events (Subject Level)

Safety events	N=300
[P6]: Lack of effectiveness	n (%)
[P7]: Drug overdose	n (%)
[P8]: Off-label use	n (%)
[P9]: Misuse	n (%)
[P10]: Abuse	n (%)
[P11]: Medication errors	n (%)
[P12]: Occupational exposure	n (%)

Note: Table portrays number of unique subjects with at least one event in respective categories. Denominator for percentages is the total number of patients (N=300).

Table 7.4.4.14. Summary of Other Safety Events (Event Level)

Safety events	N=X
[P6]: Lack of effectiveness	n (%)
[P7]: Drug overdose	n (%)
[P8]: Off-label use	n (%)
[P9]: Misuse	n (%)
[P10]: Abuse	n (%)
[P11]: Medication errors	n (%)
[P12]: Occupational exposure	n (%)

Note: Table portrays number of unique safety events, allowing for multiple events per patients. Denominator for percentages is the total number of events during the treatment period (N=x).

Table 7.4.5. Adult Patient & Caregiver Demographic Characteristics

Adult Demographic Data	Caregiver (N=x)	Adult Patient (N=x)	Total (N=300)
S2: Age	mean (SD) Median Min, Max	mean (SD) Median Min, Max	mean (SD) Median Min, Max
S8: Gender			
Male	n (%)	n (%)	n (%)
Female	n (%)	n (%)	n (%)
S9: Marital Status			
Not Married	n (%)	n (%)	n (%)
Not Marries, living with Partner	n (%)	n (%)	n (%)
Married or Civil Union	n (%)	n (%)	n (%)
Divorced or Separated	n (%)	n (%)	n (%)
Widow/Widower	n (%)	n (%)	n (%)
Prefer not to answer	n (%)	n (%)	n (%)
S10: Highest level of Education			
Less than high school diploma/degree	n (%)	n (%)	n (%)
High school degree or equivalent (e.g., GED)	n (%)	n (%)	n (%)
Some college but not degree	n (%)	n (%)	n (%)
Associated degree	n (%)	n (%)	n (%)
Bachelor's degree	n (%)	n (%)	n (%)
Graduate degree	n (%)	n (%)	n (%)
Prefer not to answer	n (%)	n (%)	n (%)
S11: Employment status			
Employed/Working full-time (paid)	n (%)	n (%)	n (%)
Employed/Working part-time (paid)	n (%)	n (%)	n (%)
Homemaker	n (%)	n (%)	n (%)
Student	n (%)	n (%)	n (%)
Retired	n (%)	n (%)	n (%)
Unemployed	n (%)	n (%)	n (%)
S12: Annual household income			
$20,000 or less	n (%)	n (%)	n (%)
$20,001-$50,000	n (%)	n (%)	n (%)
$50,001-100,000	n (%)	n (%)	n (%)
$100,001 or more	n (%)	n (%)	n (%)
Prefer not to answer	n (%)	n (%)	n (%)
S13: Regions/States			
Northeast	n (%)	n (%)	n (%)
Midwest	n (%)	n (%)	n (%)

West	n (%)	n (%)	n (%)
South	n (%)	n (%)	n (%)
S14: Number of children (aged 0 to 17)			
No children	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)
More than 4	n (%)	n (%)	n (%)
S16: Primary Health Insurance			
Private health insurance	n (%)	n (%)	n (%)
Medicaid	n (%)	n (%)	n (%)
Medicare	n (%)	n (%)	n (%)
Uninsured	n (%)	n (%)	n (%)
S17: Race/Ethnicity*			
S17r1: White	n (%)	n (%)	n (%)
S17r2: Black or African American	n (%)	n (%)	n (%)
S17r3: American Indian or Alaska Native	n (%)	n (%)	n (%)
S17r4: Asian	n (%)	n (%)	n (%)
S17r5: Native Hawaiian or other Pacific Islander	n (%)	n (%)	n (%)
S17r6: Other	n (%)	n (%)	n (%)
S17r7: Prefer not to answer	n (%)	n (%)	n (%)
S18: Hispanic, Latino, or of Spanish Origin			
Yes	n (%)	n (%)	n (%)
No	n (%)	n (%)	n (%)

*Not mutually exclusive. Note: Data from Patient DCF
Note: Data from Clinician DCF. Percentages are based on the total sample within respective groups.

Table 7.4.6. Pediatric Patient Demographic Characteristics

Pediatric Demographic Data (N=x)	
S3: Age	mean, SD, Median Min, Max
S21: Gender	
Male	n (%)
Female	n (%)
S22: Race/Ethnicity*	
S22r1: White	n (%)
S22r2: Black or African American	n (%)
S22r3: American Indian or Alaska Native	n (%)
S22r4: Asian	n (%)
S22r5: Native Hawaiian or other Pacific Islander	n (%)
S22r6: Other	n (%)
S22r7: Prefer not to answer	n (%)
S23: Hispanic, Latino, or of Spanish Origin	
Yes	n (%)
No	n (%)
S24: Child's Academic Accomplishments	
Current/Last grade completed:	
Pre-K - 5th grade	n (%)
6th grade – 8th grade	n (%)
9th grade – 12th grade	n (%)
High School Diploma/Degree	n (%)
Vocational School	n (%)
Not currently enrolled in school	n (%)
S24oe: Other	n (%)

*Not mutually exclusive

Note: Data from Clinician DCF. Percentages are based on the total pediatric sample of N=x.

Table 7.4.7. Patient Disposition Throughout the Study

This will be summarized, accounting for N=300 for each study visit.

Table 7.4.8. Significant Protocol Deviations

This will be summarized, if any observed.

7.5 Sensitivity Analyses

Analyses of ASIS Items 9 & 10 that utilized LOCF imputation:

- Tables 7.1.12, 7.1.13: Depict stats without imputation
- 7.1.14 and 7.1.15: Depict stats without imputation

Analyses of clinician IGA related endpoints that utilized LOCF imputation:

- Tables 7.2.4.1, 7.2.4.2, 7.2.4.3: Depict stats without imputation
- Tables 7.2.4.4, 7.2.4.6, 7.2.4.7: Depict stats with imputation

Analysis of clinician IGA related endpoints (with imputation), stratified by type of subject visit are depicted below.

Table 7.5.1 Sub-group Analysis of IGA (with LOCF imputation)

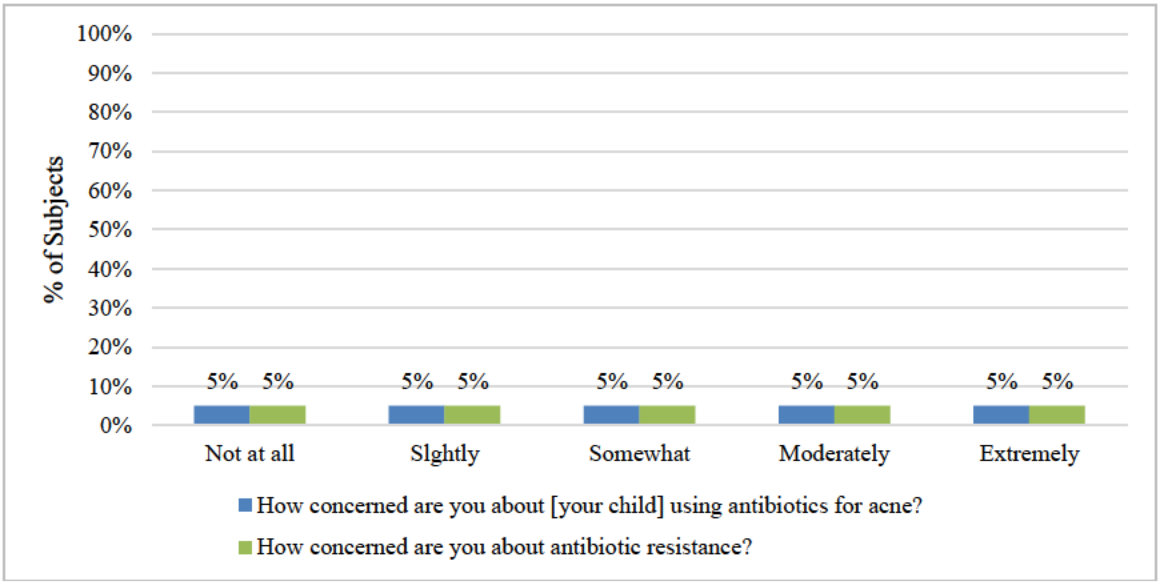
IGA Success / % Clear/Almost Clear	Weeks			
	Baseline	Week 4	Week 8	Week 12
Subject visit type				
In-person visit	n (%)	n (%)	n (%)	n (%)
Remote/ Tele-health visit	n (%)	n (%)	n (%)	n (%)

Note: Facial IGA success at Week 12 (and at Wks 4 & 8), defined as a 2-point decrease in IGA score from baseline and a score of 0 (clear) or 1 (almost clear) at Week 12.

8 FIGURES FROM PATIENT AND CLINICIAN REPORTED MEASURES

Figure 8.1: Patient and Caregiver Concerns About Antibiotics and Antibiotic Resistance

Figure 8.1 corresponds to table 7.1.5 Antibiotic Attitudes



Section 8.2: Patient and Caregiver EPQs: Change from Baseline & Week-12

Figures in section 8.2 corresponds to table 7.1.7. EPQs: Change from Baseline at Week-12
Display percentage for bottom two categories only (Never/Rarely, Not at all/Slightly, Not at all/A little)
Figures 8.2.2 – 8.2.11 will mimic figure 8.2.1

Figure 8.2.1: Over the past 7 days, how often has your acne made you feel angry (mad/sad): Change from Baseline & Week 12

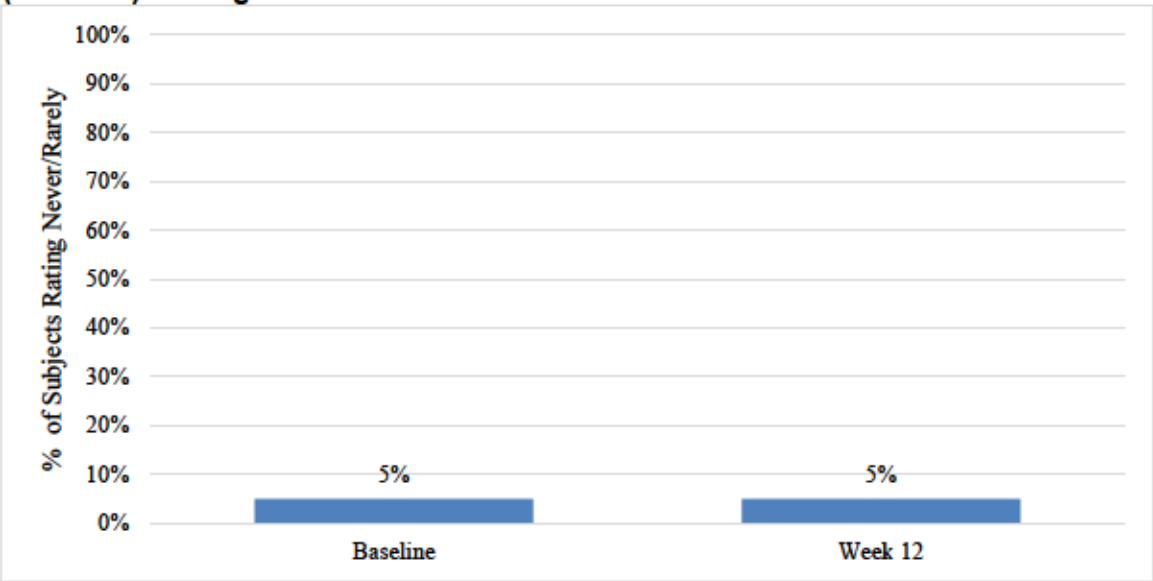


Figure 8.2.2: How worried are you about how long your acne will last and how bad it will get: Change from Baseline & Week-12

Figure 8.2.3: How often do you think about your acne: Change from Baseline & Week-12

Figure 8.2.4: Over the past 7 days, how worried have you been about your acne: Change from Baseline & Week-12

Figure 8.2.5: How often do you change, edit, or filter your social media photo or selfie because of your acne: Change from Baseline & Week-12

Figure 8.2.6: How often does acne impact your "in real-life" plans (IRL) (like dating or social engagements, playing sports, swimming, or hanging out): Change from Baseline & Week-12

Figure 8.2.7: How often are you doing something to hide your acne (like mess with, squeeze/pop, or use makeup, concealer, hairstyle, clothes to cover up): Change from Baseline & Week-12

Figure 8.2.8: How often do you feel picked on or judged because of your acne: Change from Baseline & Week-12

Figure 8.2.9: How concerned are you that your acne will affect your ability to reach your future goals (in school or work) and be the best you can be: Change from Baseline & Week-12

Figure 8.2.10: Do you feel that your parents understand your acne-related concerns: Change from Baseline & Week-12

Figure 8.2.11: Over the past 7 days, how often has worrying about or discomfort (itching/hurting) from acne affected your sleep: Change from Baseline & Week-12

Figure 8.3: Patient Acne Severity: Overall, how is the acne on your face right now (with LOCF imputation)

Figure 8.3 corresponds to A9 from table 7.1.14 Patient Acne Severity and How Face Looks (with LOCF imputation)

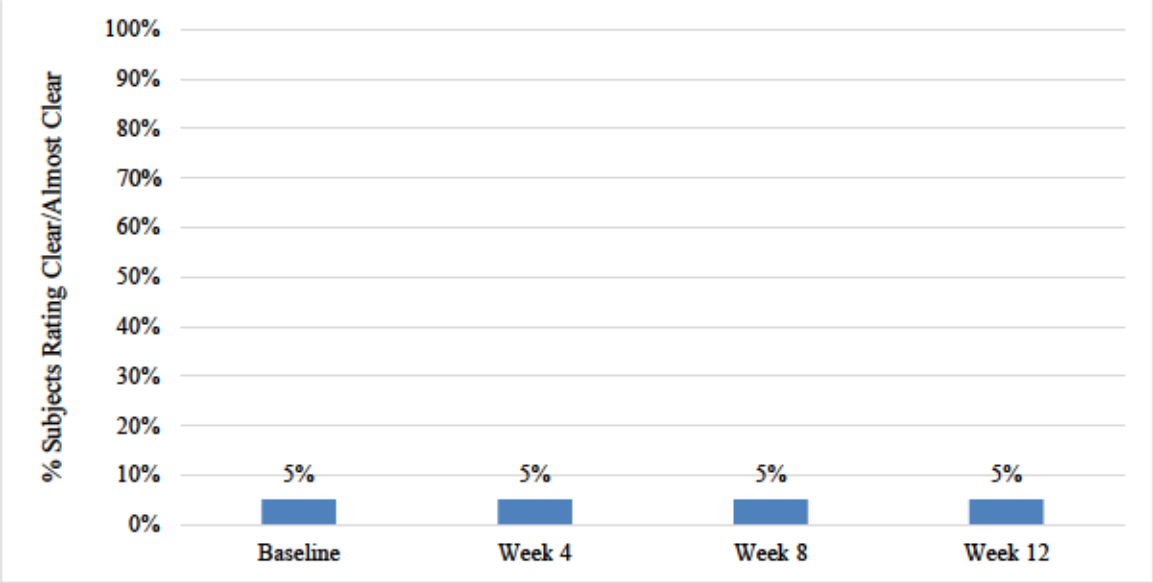
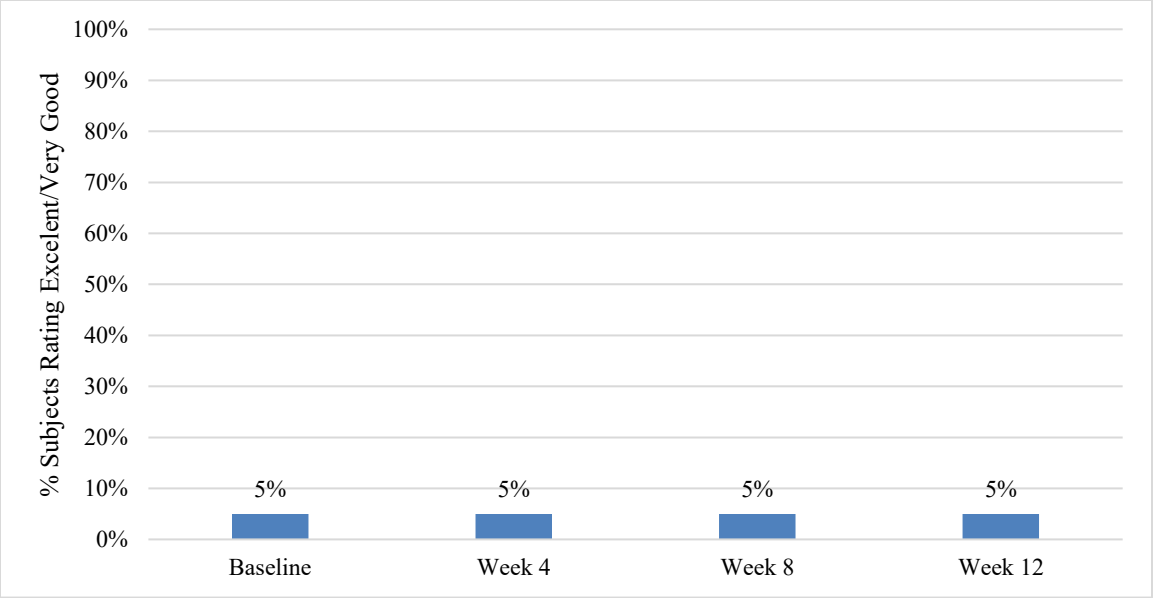


Figure 8.4: Patient Face Look: Over the past 7 days, rate how your face looked because of your acne (with LOCF imputation)

Figure 8.4 corresponds to A10 from table 7.1.14 Patient Acne Severity and How Face Looks (with LOCF imputation)



Section 8.5 Impact on Parents/Caregivers

Figures in section 8.5 corresponds to table 7.1.17. Impact on Parents/Caregiver

Figure 8.5.1: Impact on Parents/Caregivers: Do you feel that you understand your child's acne-related concerns?

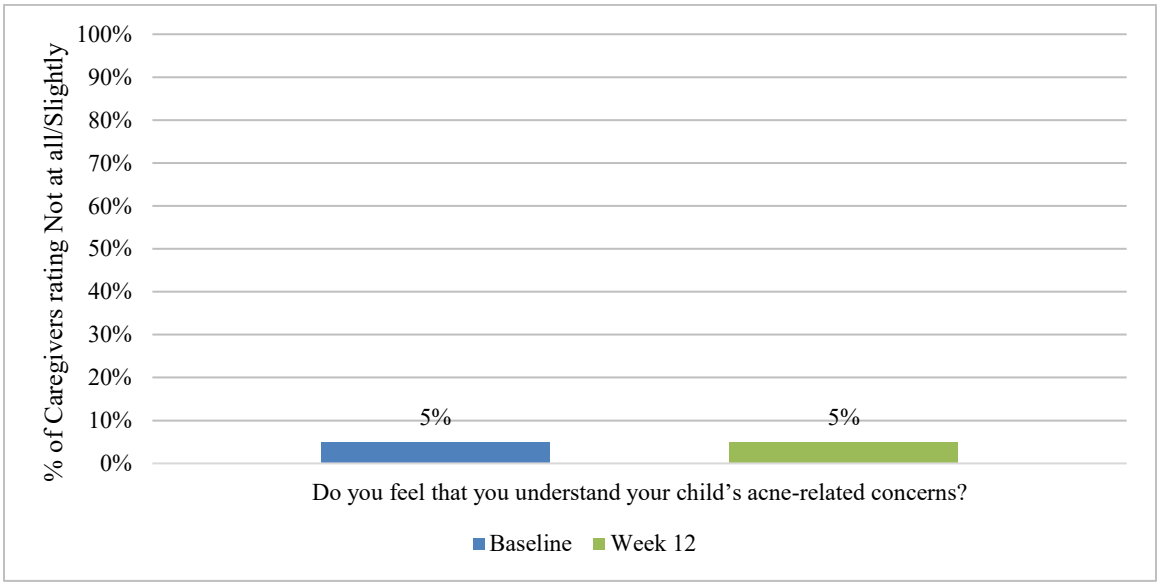


Figure 8.5.2: Impact on Parents/Caregivers: Over the past 7 days, how concerned have you been about your child's acne?

Figure 8.5.3: Impact on Parents/Caregivers: How concerned are you about your child's ability to accomplish future goals and reach full potential due to acne?

Figure 8.6 Clinician Acne Evaluation (IGA Success) (with LOCF imputation)

Figure 8.6 corresponds to Table 7.2.4.4. Clinician Acne Evaluation (IGA) (with LOCF imputation) with % of clear/almost clear category

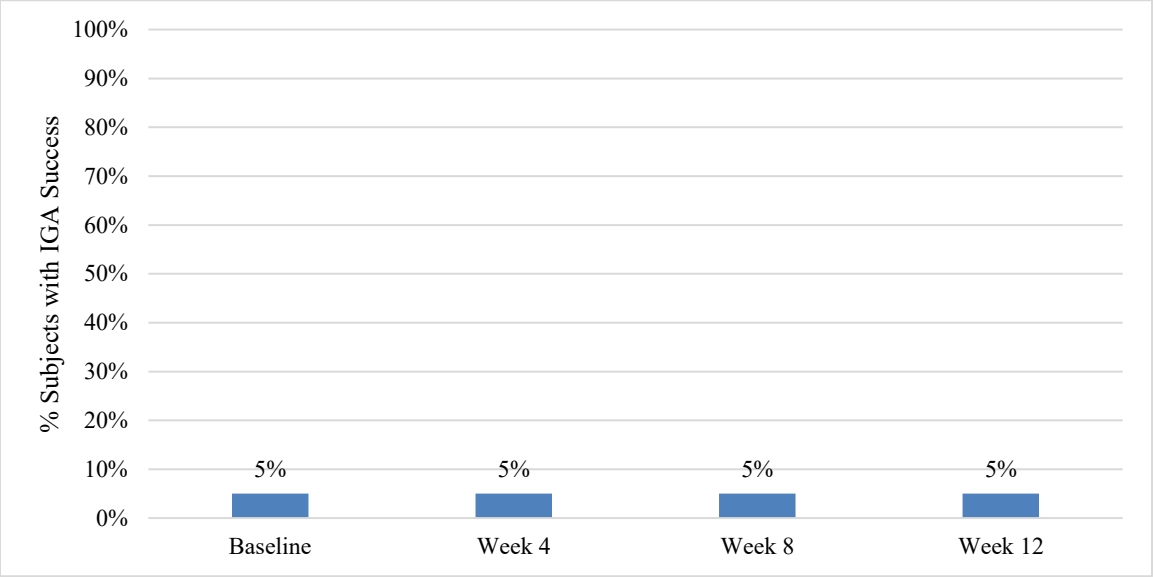
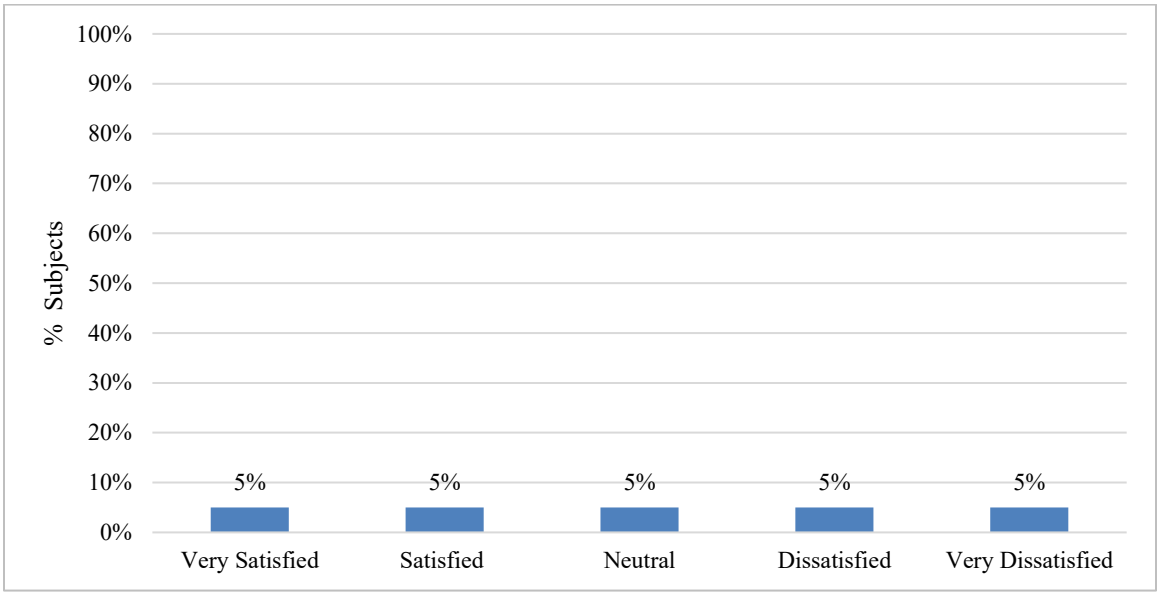


Figure 8.7 Clinician Satisfaction with Seysara Treatment at Week-12

Figure 8.7 corresponds to Table 7.2.8. Seysara Treatment Satisfaction (Physician)



Section 8.9 Comparison of Patient and Clinician data

Figures in section 8.9 corresponds to table 7.3.1 – 7.3.4 Comparison of patient and clinician data

Figure: 8.9.1 Acne Severity Evaluation for All Patients

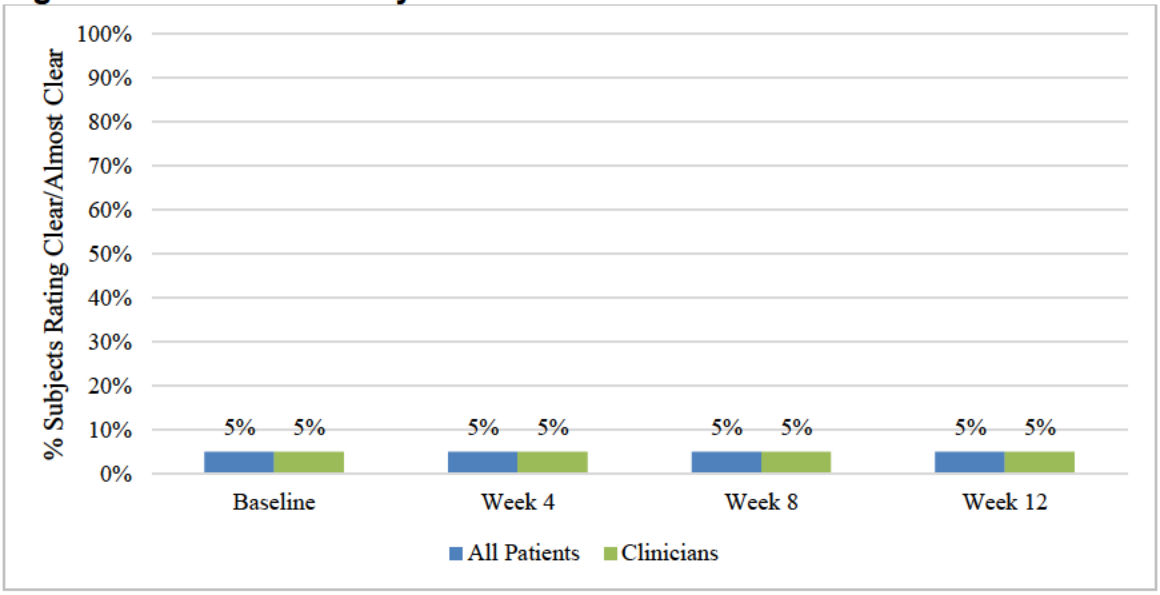


Figure 8.9.2 Acne Severity Evaluation for Adult Patients

Figure 8.9.2 will be the same as 8.9.1 with adult patient data only and corresponding clinician data

Figure 8.9.3 Acne Severity Evaluation for Caregivers of Patients aged 9-11 yrs

Figure 8.9.3 will be the same as 8.9.1 with Patients aged 9-11 yrs data only and corresponding clinician data

Figure 8.9.4 Acne Severity Evaluation for Pediatric Patients Age 12-17

Figure 8.9.4 will be the same as 8.9.1 with Pediatric Patients Age 12-17 data only and corresponding clinician data

Section 8.10 Comparison of Patient and Caregiver Data

Figures in section 8.9 corresponds to table 7.3.5 – 7.3.7

Figure 8.10.1 Patient-Caregiver Comparison: Parent understanding of child's acne-related concerns

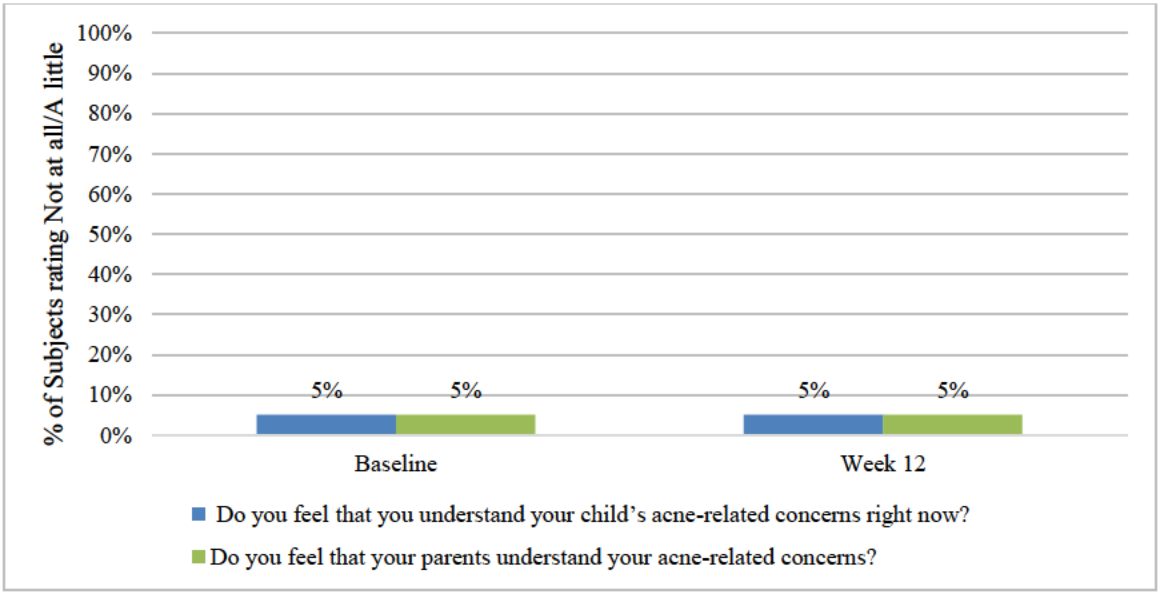


Figure 8.10.2 Patient-Caregiver Comparison: Parental concerns of child's acne vs. child's concerns

Figure 8.10.2 will be the same as 8.10.1 but with data from table 7.3.6

Figure 8.10.3 Patient-Caregiver Comparison: Child's ability to reach future goals

Figure 8.10.3 will be the same as 8.10.1 but with data from table 7.3.7

9 PATIENT QUALITATIVE INPUT FROM SITE S01

Table summarizing verbatims from audio-input from patients at end of study from Site # S01 will be added here.

10 CANFIELD PHOTOS OF ACNE PATIENTS FROM SITE S01

A separate file will be attached, summarizing the canfield photos of Acne patients from Site # S01.

11 LITERATURE REFERENCES

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12 APPENDICES

Appendix A: Study Schedule of Events

Appendix B: Select Study Questionnaires

12.1 Appendix A: Study Schedule of Events

Study Encounter (physical or virtual)	**Baseline E1**	**E2**	**E3**	**End of Study E4**	**Early Termination Visit**
Week†		Wk 4 (± 4 d)	Wk 8 (± 4 d)	Wk 12 (± 4 d)	-
Informed consent	X				
Selection criteria	X				
Demographics & baseline clinical characteristics[1]	X				
Physical examination[2]	X			X	X
AV medical history and relevant comorbidites[3]	X			X	X
Seysara dose[4]	X	X	X	X	X
Dispensing and return of study medication	X	X	X	X	X
Prior acne medication (since diagnosis & past 6 months)	X				
Concomitant general medication	X			X	X
Concomitant anti acne medication	X			X	X
Site Investigator's clinical assessment of acne[5]	X	X	X	X	X
Study subject questionnaires[6]	X	X	X	X	X
AEs/SAEs[7]	X	X	X	X	X
Reasons for premature study withdrawal					X

† Expected in-person or virtual encounter/visit schedule, in relation to the index date (date of first administration of sarecycline).

[1] Clinical characteristics data assessed retrospectively based on what is documented in patient medical charts.

[2] Routine physical examination conducted as part of usual care alone and as documented in patient medical charts; such data may include - blood pressure, waist circumference, height/weight measurements.

[3] May include AV date of diagnosis, baseline severity, relevant comorbidities, per clinician judgment and/or as documented in patient medical charts immediately before the index date; new emerging comorbidities during the study period will be recorded, based on the documentation in patient medical charts.

[4] Expected usage is once daily, every day during the duration of the trial.

[5] Site Investigator assessments of AV severity of Subjects may be conducted during subject visit to clinician offices, or via remote/virtual (telehealth) visits owing to Covid-related travel restrictions.

[6] Subject self-assessments will include PtGA of acne severity; various HRQOL assessments will be conducted at baseline and Week 12.

[7] In the case of premature study discontinuation due to an AE, the Investigator should make every effort to collect the AE duration and outcome. Any SAE that is ongoing at the End of the Study or at the time of premature withdrawal will be followed up until the SAE is resolved or at least up to 4 weeks. AE follow-up information will be reported in the eDCF.

Note: AE, adverse event; eDCF, electronic Data Collection Form; E, encounter; W, week.

12.2 Appendix B: Select Study Questionnaires

ASIS

Please read and answer each of the following questions about **acne signs and symptoms**. Before answering each question, **look in the mirror and think about the acne on your face**. Select one answer for each question that best describes your experience with acne **right now**. There are no right or wrong answers.

1. How oily is your face right now?

Not at all	A little	Somewhat	Quite a bit	Very
☐	☐	☐	☐	☐

2. How many pimples do you have on your face right now?

None	A few	Some	Quite a bit	A lot
☐	☐	☐	☐	☐

3. How many acne scars (holes or indents) do you have on your face right now?

None	A few	Some	Quite a bit	A lot
☐	☐	☐	☐	☐

4. How many scabs from acne do you have on your face right now?

None	A few	Some	Quite a bit	A lot
☐	☐	☐	☐	☐

5. How many dark marks from acne do you have on your face right now?

None	A few	Some	Quite a bit	A lot
☐	☐	☐	☐	☐

6. How many blackheads do you have on your face right now?

None	A few	Some	Quite a bit	A lot
☐	☐	☐	☐	☐

7. How many whiteheads do you have on your face right now?

None	A few	Some	Quite a bit	A lot
☐	☐	☐	☐	☐

8. How much redness do you have on your face right now?

None	A few	Some	Quite a bit	A lot
☐	☐	☐	☐	☐

9. Overall, how is the acne on your face right now?

Clear	Almost clear	Mild	Moderate	Severe
☐	☐	☐	☐	☐

Please read and answer each of the following questions about how **acne impact your quality of life**. Before answering each question, look in the mirror and think about the acne on your face. Select one answer for each question that best describes your experience with acne in the past 7 days. There are no right or wrong answers.

10. Over the past 7 days, rate how your face looked because of your acne.

Excellent	Very good	Good	Fair	Bad
☐	☐	☐	☐	☐

11. Over the past 7 days, how often did you feel sad because of the acne on your face?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

12. Over the past 7 days, how often did you feel embarrassed because of the acne on your face?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

13. Over the past 7 days, how often did you feel self-conscious because of the acne on your face?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

14. Over the past 7 days, how often did you feel annoyed because of the acne on your face?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

15. Over the past 7 days, how often did you feel not confident because of the acne on your face?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

16. Over the past 7 days, how often did you choose not to be around other people because of the acne on your face?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

17. Over the past 7 days, how often did someone make bad comments about the acne on your face?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

Expert Panel Questionnaire (EPQ)

Please read and answer each of the following questions about how **acne affect your emotional wellbeing, social interactions, and other daily activities**. Before answering each question, look in the mirror and think about the acne on your face. Select one answer for each question that best describes your experience with acne over the past 7 days. There are no right or wrong answers.

1. Over the past 7 days, how often has your acne made you feel angry (mad/sad)?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

2. How worried are you about how long your acne will last and how bad it will get?

Not at all	Slightly	Somewhat	Moderately	Extremely
☐	☐	☐	☐	☐

3. How often do you think about your acne?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

4. Over the past 7 days, how worried have you been about your acne?

Not at all	Slightly	Somewhat	Moderately	Extremely
☐	☐	☐	☐	☐

5. How often do you change, edit, or filter your social media photo or selfie because of your acne?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

6. How often does acne impact your “in real-life” plans (IRL) (like dating or social engagements, playing sports, swimming or hanging out)?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

7. How often are you doing something to hide your acne (like mess with, squeeze/pop, or use makeup, concealer, hairstyle, clothes to cover up)?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

8. How often do you feel picked on or judged because of your acne?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

9. How concerned are you that your acne will affect your ability to reach your future goals (in school or work) and be the best you can be?

Not at all	Slightly	Somewhat	Moderately	Extremely
☐	☐	☐	☐	☐

10. Over the past 7 days, how often has worrying about or discomfort (itching/hurting) from acne affected your sleep?

Never	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

12.3 Appendix-C: Signature Page

The signature below constitutes the approval of this SAP, and provides the necessary assurances that this study analysis will be conducted according to all stipulations of the SAP.

Avant Health:

[redacted] [redacted]

Name Signature Date

Almirall Approvals:

[redacted] MD PPD [redacted]

PPD Signature Date

Global Medical Affairs

PPD PPD 21.June.2022

PPD Signature Date

Global Development – R&D