Protocol Number: JBT101-DM-001

A Phase-2 Double-Blind Placebo-Controlled Randomized Clinical Trial to Evaluate Safety, Tolerability, and Efficacy of JBT-101 in Subjects with Dermatomyositis

September 6, 2017

Statistical Analysis Plan for Part A
Version 1.0

Prepared by:

[redacted]

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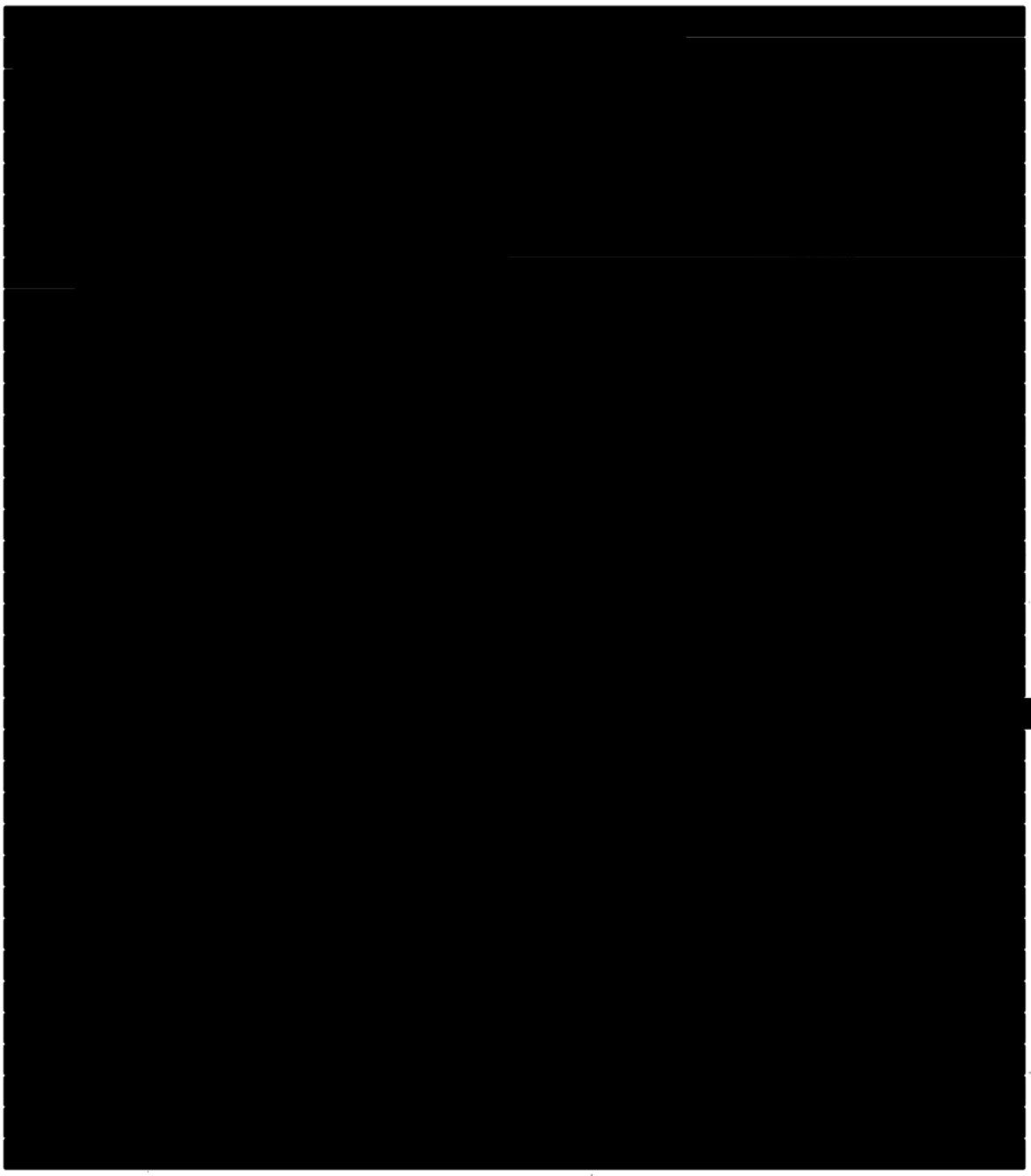

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Statistical Analysis Plan Approval

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List of Abbreviations

AE	Adverse event
ANCOVA	Analysis of Covariance
CDASI	Cutaneous Dermatomyositis Disease Area and Severity Index
CIs	Confidence Intervals
Corbus	Corbus Pharmaceuticals, Inc.
CSR	Clinical start report
CRF	Case report form
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
LOCF	Last observation carried forward
mITT	Modified Intent to Treat
Max	Maximum
Min	Minimum
MMRM	Mixed model repeated measures
PP	Per protocol
QTc	Corrected QT
QTcF	QT Interval Corrected by Fridericia's formula
QTcB	QT Interval Corrected by Bazett's formula
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDC	Statistics and Data Corporation
SOC	System Organ Class
PT	Preferred Term
TEAE	Treatment emergent adverse event
WHO	World Health Organization
WOCBP	Women of child-bearing potential

1. Introduction

This statistical analysis plan (SAP) is being developed in conjunction with the protocol JBT101-DM-001 (Version 2.0, October 19, 2016) sponsored by Corbus Pharmaceuticals Inc. The SAP contains detailed information to aid in the performance of the statistical analysis and reporting study data from Part A of the study in the final clinical study report (CSR). This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonization (ICH) E9 Guideline entitled: Statistical Principles for Clinical Trials and the most recent ICH E3 Guideline, entitled: Structure and Content of Clinical Study Reports.

This SAP describes the data that will be analyzed and the subject characteristics, efficacy, and safety assessments that will be evaluated. This SAP provides details of the specific statistical methods that will be used. If additional analyses are required to supplement the planned analyses described in this SAP, they may be completed and will be identified in the CSR.
A separate SAP and CSR will be prepared for Part B (open-label dosing) of the study.

2. Objectives

2.1. Primary Objectives

The primary objectives of this trial are:

1. Evaluate the safety (vital signs, physical examinations, adverse events (AEs), blood and urine laboratory safety tests, electrocardiograms (ECGs) with QT/QTc intervals, and psychotropic activity) and tolerability of JBT-101 in subjects with skin-predominant dermatomyositis (DM);

2. Evaluate efficacy of JBT-101 in skin-predominant DM, measuring changes from baseline in the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score, a validated measure of skin disease severity.

[redacted]

[redacted]

3. Investigational Plan

3.1. Overall Study Design and Plan

This study is designed as a double-blind placebo-controlled randomized clinical trial to test the safety, tolerability, and efficacy of JBT-101 compared to placebo for the treatment of DM, to determine plasma concentration of JBT and its metabolites, and to test JBT-101's mechanism of action and impact on biomarkers of disease activity, and inflammation in DM patients.

This Study is broken into two parts: Part A and Part B. Only data from Part A of the study are summarized in this SAP.

1. Part A: An interventional, double-blind, randomized, placebo-controlled design will be used. Approximately 33 subjects will be screened to identify 22 eligible males and females $\geq$ 18 and $\leq$ 70 years of age (at the time of signing consent) with moderate-to-severely active skin-predominant DM. Subjects will be randomized in a 1:1 ratio to receive:

    - Cohort 1: JBT-101 20 mg q a.m. on Days 1-28, then JBT-101 20 mg q a.m. and 20 mg q p.m. on Days 29-84; or
    - Cohort 2: Placebo q a.m. on Days 1-28, then placebo q a.m. and placebo q p.m. on Days 29-84.

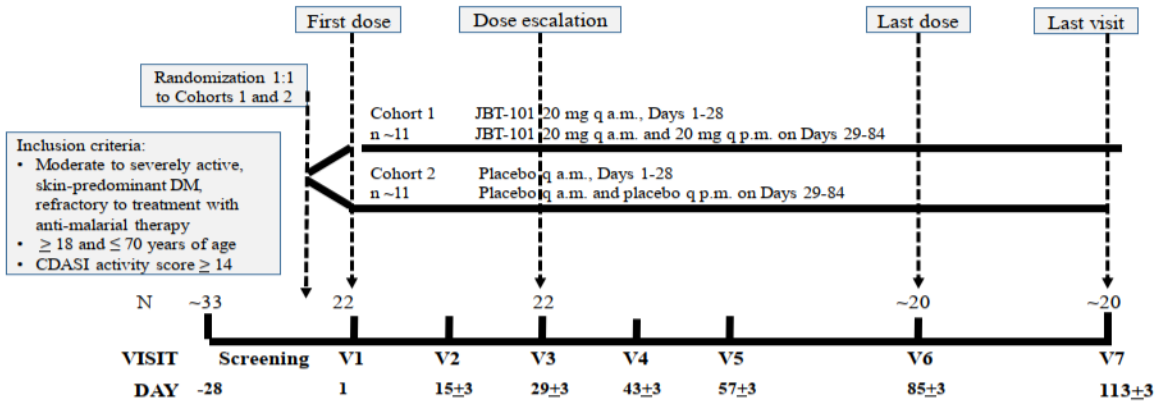
2. Part B: An interventional, open-label design will be used. All subjects who complete dosing in Part A without permanent discontinuation of study drug for safety reasons or intolerance and who pass repeat safety screening will be eligible for enrollment (n = ~20-22). Subjects will receive JBT-101 20 mg twice a day on Days 1-364.

Below are the overall design and plan for Part A:

The target population in this phase 2 study (Part A) is subjects with DM who have failed or are intolerant to treatment with hydroxychloroquine and who are ≥ 18 and ≤ 70 years of age at the time of signing the informed consent form. Subjects must be on stable medication for DM for at least 28 days prior to Visit 1. See Protocol V2.0 (Section 6.3) for a full list of inclusion and exclusion criteria. Figure 1 shows the study schematic for Part A.

A single site at the University of Pennsylvania will be used. Recruitment of about 22 eligible subjects will take place over 12-24 months, for a recruitment rate of about 0.9 to 1.8 subjects per month. Screening will be up to 28 days prior to Visit 1 and there will be seven study visits, Visits 1-7 on Days 1, 15 ± 3, 29 ± 3, 43 ± 3, 57 ± 3, 85 ± 3 and 113 ± 3, respectively. Treatment occurs from Visits 1-6 and Visit 7 is a follow-up visit after treatment ends. The 3-day window on visits is included in case of holidays or unusual circumstances, and it is expected that most if not all visits will be on the scheduled date, as possible. The total duration of an individual subject's participation in the study is about 112 days (84 days treatment and 28 days follow-up), plus Screening. As mentioned, the treatment period is 84 ± 3 days, unless an AE occurs that requires discontinuation of treatment or the subject withdraws. If an AE related to JBT-101 prompts discontinuation of treatment or the subject withdraws, the study subject will be followed in the clinic to document the resolution or stabilization of the event. For therapeutic stability, the subjects will remain on their current treatment regimen for DM, for the duration of this study. The entire study is expected to take between about 21-33 months to complete (about 12-24 months enrollment, up to 1 month Screening, 3 months treatment, 1 month follow-up, and 2-4 months for database lock and generation of data Tables, Listings, Figures, and the Study Report).

The screening period is up to 28 days. Subjects will be screened prior to Visit 1 to assess eligibility for randomization into the study. A master log will be maintained of all consented subjects and will document all screening failures, including the reason for screening failure. The target enrollment is 22 eligible subjects. The number of subjects enrolled in the study may be expanded by up to 4 additional subjects, only if these additional eligible subjects have signed the informed consent form and are actively engaged in the screening process at the time 22 subjects have been randomized into the study.



N	~33	22		22			~20	~20
VISIT	**Screening**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**
DAY	**-28**	**1**	**15±3**	**29±3**	**43±3**	**57±3**	**85±3**	**113±3**
Physical examination	X	X					X	X
Adverse events		X	X	X	X	X	X	X
Lab safety tests	X	X	X	X	X	X	X	X
Tolerability		X	X	X	X	X	X	
CDASI	X	X	X	X	X	X	X	X
C-reactive protein		X	X	X		X	X	X
Metabolipidomic profile		X	X	X		X	X	
JBT-101 concentration		X	X	X		X	X	
CPK, aldolase	X	X		X		X	X	X
MMT8, Physician and Patient Global Assessments, Skindex-29+3, PROMIS-29		X		X		X	X	X
Physical Examination	X	X					X	X
ARCI-M		X		X			X	
IFNα, type I IFN signature, cytokine analyses, PBMC studies		X		X			X	
Skin biomarkers and histology, optional		X		X			X	
Skin photography, optional		X		X			X	

Figure 1. JBT-101-DM trial schematic

After successful screening and before Visit 1, each subject will receive a Subject Identification Number (SID), assigned in serial order on site. That SID will have a corresponding treatment assignment that will have been determined randomly prior to start of the study by a Corbus contractor, who is independent from the study team. Randomization will be done in a 1:1 ratio to JBT-101 or placebo. There are no stratification criteria that could impact the rate of enrollment.

The JBT-101 20 mg capsule and placebo capsule are indistinguishable size 2 capsules. Study product will be administered orally qd on Days 1-28 and bid on Days 29-84, with at least 8 hours between doses. The first dose of study product will be taken in the clinic, and subjects will be observed in the clinic for at least 30 minutes afterwards, or longer until vital signs and clinical symptoms are acceptable for discharge from the clinic, in the opinion of the investigator, if the subject experiences an AE. Study product can be taken without regard to fed state.

Vital signs, AEs, blood laboratory safety tests, and CDASI will be evaluated on Visits 1-7. The type, nature, severity, expectedness and relationship to study product of AEs that occur from after the time informed consent is signed through Visit 7 will be recorded. Urine pregnancy testing will be done in women of child-bearing potential (WOCBP) at Visits 1, 3 and 5-7. Muscle strength will be assessed by physical examination on Visits 1, 3, and 5-7, using Manual Muscle Testing-8 (MMT-8), preferably by Dr. Werth at each visit. Additional physical examinations will be done on Visits 1, 6 and 7. Urinalysis will be evaluated at Visits 1, 3, 5, and 6.

Tolerability will be evaluated from Visits 1-6. Psychoactivity of JBT-101 will be assessed using the ARCI-M survey on Visits 1, 3, and 6. Twelve-lead ECGs and QT/QTc intervals will be assessed on Visits 1, 3, 5, and 6.

Efficacy of JBT-101 will be measured at Visits 1-7 using CDASI to identify subjects who have had an improvement in disease activity. Efficacy also will be evaluated using the Physician Global Assessment, Patient Global Assessment, Skindex-29+3, PROMIS-29 Short Form (all on Visits 1-3, 5-7), and optional skin photography (on Visits 1, 3, and 6). Photography will be incorporated on Visits 1, 3, and 6 for research purposes only if the subject consents to the photos. The photos will have all identifiers removed to protect the identity and privacy of subjects and be referred to by Subject number.

Blood samples will be taken at various visits, depending upon the individual test, for studies of biomarkers of disease activity and inflammation. Optional skin biopsies will be performed for histology and studies of biomarkers of inflammation on Visits 1, 3, and 6. Metabolipidomic profiles and plasma concentrations of JBT-101 will be obtained on Visits 1-3, 5, and 6.

Data will be collected on an electronic data capture (EDC) system. A clinical laboratory at the University of Pennsylvania will be used for routine laboratory testing. Measurement of metabolipidomic profiles and JBT-101 concentrations will be done at a central contract laboratory. The QT/QTc intervals will be determined by a single reader at the University of Pennsylvania.

3.2. Study Endpoints

3.2.1. Safety Endpoints

The main safety assessments include:

- Vital signs;
- Physical examination including Manual Muscle Testing-8;
- Adverse events;
- Blood and urine laboratory safety assessments including:
  - Complete blood count with differential and platelets;

- Metabolic panel that includes electrolytes, renal function and liver function tests;
- Urinalysis;
- Pregnancy tests for women of childbearing potential;

- 12-lead ECGs, including QT/QTc interval measurements;
- National Institute of Drug Abuse Addiction Research Center Inventory-Marijuana scale.

Tolerability will be assessed by incidence of discontinuation of study product due to toxicity results related to study product from Visits 1-6.

3.2.2. Efficacy Endpoints

The primary efficacy endpoint includes as follows:

- CDASI activity score

[redacted]

3.2.3. Pharmacokinetic endpoints

[redacted]

3.3. Assessment of Efficacy Endpoints

3.3.1 Primary Efficacy Variable-CDASI Activity Score

The CDASI is a validated outcome measure that systematically quantifies cutaneous DM disease activity (Klein et al., 2008; Yassaee et al., 2010). In the CDASI, DM skin disease activity is

scored from 0 to 100 based on the physician's evaluation of erythema, scale, and erosion or ulceration at fifteen anatomic locations as well as alopecia, Gottron's sign or papules on the hands, and periungual changes. A five point or greater decrease in the CDASI activity score indicates clinically relevant improvement based on statistical analysis using a receiver operating characteristic curve to maximize sensitivity and specificity (Anyanwu et al., 2015). Data collected at the University of Pennsylvania resulted in a cutoff of 20 points to differentiate mild from moderate and severe disease activity.

Refer to Appendix B for the questionnaires and CDASI activity score calculation.

3.3.2 Secondary Efficacy Variables

[redacted]

[redacted]

3.4. Study Hypotheses

This is a small-scale study designed to examine the safety, tolerability, and efficacy of JBT-101 in subjects with DM. To evaluate mechanism of action of JBT-101 in DM, the effects of JBT-101 on metabolipidomic profiles and biomarkers of disease activity, inflammation, and fibrosis will be assessed.

The study hypotheses are as follows:

- Exposure to JBT-101 for 84 days in doses up to 20 mg bid will be well tolerated and have a safety profile that will support testing in a larger future study of safety and efficacy in adults with DM. The main safety endpoints are vital signs, AEs, blood and urine laboratory safety tests, ECG results including QT/QTc intervals, ARCI-M scores, and MMT-8 scores.

- Exposure to JBT-101 will cause a significant improvement in skin-predominant DM, measured as a reduction in CDASI activity score for the treatment group compared to controls

- Compared to placebo, JBT-101 will improve secondary measures of efficacy, including Physician Global Assessment, Patient Global Assessment, Skindex-29+3, PROMIS-29 Short Form, and biomarkers of disease activity and inflammation.

4. Study Treatment

4.1. Dosage, Preparation and Administration

The doses of study products are:

- JBT-101 20 mg qd or bid;
- Placebo, no dose.

No onsite preparation or masking of clinical supplies is required by site personnel. The study product will be self-administered and taken orally in the following doses in Part A:

- Cohort 1: JBT-101 20 mg q a.m. on Days 1-28, then JBT-101 20 mg q a.m. and 20 mg q p.m. on Days 29-84;
- Cohort 2: Placebo q a.m. on Days 1-28, then placebo q a.m. and placebo q p.m. on Days 29-84.

4.2. Method of Assigning Subjects to Treatment Groups

A randomization scheme for serial SIDs randomized 1:1 to Cohort 1 or Cohort 2 will be generated by a Corbus contractor. Based on this randomization scheme, study product vials containing the appropriate treatment for each SID will be labeled with the SID by the manufacturer.

As each new eligible subject is identified, the principal investigator will assign in consecutive order the next unassigned SID to that subject. The principal investigator or qualified designee will maintain a log of subjects, by name, initials, date of birth, SID assigned, and date SID was assigned. This log will be kept in a secure location. An eligible subject is considered randomized into the study upon assignment of the SID by the principal investigator, because that SID is linked to a treatment assignment. The subject does not need to be present for randomization.

4.3. Masking and Blinding Procedures

This study is double-blinded in Part A. The blinding of the trial must be maintained throughout Part A until all data entry and processing are complete and the Part A database has been locked. Except for emergency unblinding during Part A (see Protocol Section 7.6.2), all Corbus medical and clinical operations staff associated with this study, both internal Corbus staff and contract staff, and including the Medical Monitor, will remain blinded to treatment randomization until the Part A is completed and the Part A database is closed. Study subjects and the study site staff, including the investigator and any co-investigator who will do safety and clinical assessments, qualified designees, study nurses, and study coordinators will be blinded to intervention groups during Part A. The final unblinding of all study participants in Part A will occur only after the data analysis set has been locked. In the event that the treatment allocation for a subject in Part A otherwise becomes known to the clinical site staff, the principal investigator must be notified immediately, and the principal investigator will notify Corbus.

Corbus clinical research pharmacy services personnel will be unmasked to the study product randomization. They are required not to reveal randomization information in Part A to others, unless a formal unmasking of information for a given subject is undertaken for safety reasons. A limited number of contract laboratory personnel who will perform and interpret assays of JBT-101 concentrations and metabolipidomic profiling may be unmasked during Part A. These results will be provided to Corbus using dummy subject identifications until the database is locked. Certain data management, programming, and a biostatistician may be unmasked. These unmasked personnel will not be associated with the clinical conduct of the study and will not reveal to any clinical personnel involved in the study the treatment to which a subject is assigned.

4.4. Emergency Unblinding Procedures

In the event of a safety concern that requires immediate emergency unblinding of treatment assignment for an individual subject in Part A, the investigator will have 24-hour access to break the randomization code for that subject by opening an individual sealed envelope that is kept on file with other subjects' sealed envelopes in the investigator's secure research office. The sealed envelopes will be labeled on the outside with the subject's SID and inside they will contain the treatment assignment that matches the SID of the individual subjects. In all circumstances, other than a medical emergency, unblinding will be done only by the Medical Monitor, and only after discussion with the investigator.

5. Determination of Sample Size

[redacted]

6. General Statistical Considerations

6.1. Missing Data or Dropout Handling

Sensitivity analyses will be performed where missing data will be primarily imputed using last observation carried forward (LOCF). Secondary analyses will include analyses of observed data only.

The analyses will be based on visit designation. Visit dates are required within specified time windows relative to Day 1 Visit. The visits out of the visit window are considered protocol deviations, but the measurements at these visits are included in the analyses.

For subjects withdrawing early, the end of study data (Early Termination visit) will be mapped to the next planned visit for summarization and analysis of efficacy data.

6.2. Definition of Baseline

Baseline values will be defined as the last non-missing value on or before Visit 1 and prior to the first dose of study drug.

6.3. Adjustments for Multiplicity

Adjustments for multiplicity will not be made due to the early phase of the study.

6.4. Reporting Conventions

- Descriptive statistics include: Mean, Median, Standard Deviation (SD), Minimum (Min), Maximum (Max), and sample size (n). Unless specified in the actual table shells, the mean, median, the upper and lower limits of the confidence interval (CI) will be displayed to one more decimal place than the original data (derived analysis data). SD values will be displayed to two more decimal places than the original data. The minimum and maximum will be displayed to the same number of decimal places as the original data.

- The number and percentage of responses will be presented in the form XX (XX.X%), where the percentage is in parentheses. The denominator of all percentages will be number of subjects in the analysis population, unless otherwise stated. When count data are presented, the percent will be suppressed when the count is zero in order to draw attention to the non-zero counts. A row denoted "Missing" will be included in count tabulations where necessary to account for dropouts and missing values. Non-zero percentages will be rounded to one decimal place, except 100%, which will be displayed without any decimal places.

- The day of the first dose of study drug will be defined as Day 1. All study days prior to day 1 will be calculated as assessment date – first dose date of study drug. The study day on or post Day 1 will be calculated as assessment date - first dose date of study drug + 1.

- Change from baseline will be calculated as the value at the post-baseline visit minus the baseline value.

- Differences between treatment groups will be calculated as JBT-101 minus placebo.
- Listings will be presented for all enrolled subjects unless otherwise specified.
- Sensitivity analyses will be performed where missing data will be primarily imputed using last observation carried forward (LOCF). Secondary analyses will include analyses of observed data only.
- All efficacy variables will be summarized by treatment and visit descriptively, unless specified otherwise.
- For efficacy endpoints, changes from baseline will be compared to 0 using one-sample t-tests or paired rank sum tests for continuous and ordinal data within each treatment group.
- The intent-to-treat (mITT) method will be our primary analysis. In addition, the per-protocol analysis as a sensitivity analysis will be conducted for the primary efficacy endpoints and selected secondary endpoints.
- P-values for CDASI activity score will be assessed at a 2-sided alpha = 0.05 level. Other P-values will be assessed at a 1-sided alpha = 0.10 level.
- All analyses will be conducted using SAS Version 9.4.

6.5. Statistical Hypotheses

[redacted]

6.6. Analysis Populations

The modified intent to treat (mITT) population will consist of all randomized subjects who have received at least one dose of study product. Analysis of the mITT population will be used as the primary efficacy analyses and will analyze subjects under the treatment to which they were randomized, regardless of compliance with assigned treatment.

The per protocol (PP) population will consist of subjects who further complete the study without major protocol violations deemed likely to affect the efficacy outcomes of interest. The PP population will be used as secondary efficacy analyses, analyzing subjects under the treatment actually received. If the PP population is the same as the mITT population, the analysis based on the PP population will not be performed.

The safety population will consist of all subjects who received any study product. Analyses performed on the safety population will use the treatment actually received.

Inclusion of subjects in the pharmacokinetic (PK) population for analyses of JBT-101 PK will be based upon the frequency and timing of the samples obtained for JBT-101 plasma concentration.

7. Subject Disposition

7.1. Disposition

The disposition of all subjects in Part A of the trial will be presented for two arms separately and combined. A tabulation of subject disposition data will present the number and percentage of subjects in each analysis population, subjects who randomized, completed, and discontinued from the study. All percentages will be based on the number of subjects randomized. The primary reason for study discontinuation (adverse event, withdrawal of consent, lost to follow-up, and other) will also be summarized in this table.

The number and percentage of subjects with major protocol deviations will be summarized by significance (major and minor), deviation category (e,g. non-compliance with study inclusion or exclusion criteria, and use of disallowed concomitant mediations), and treatment group for the mITT population.

8. Demographics and Baseline Characteristics

8.1. Demographics and Baseline Characteristics

Demographic and baseline information will be summarized for each treatment arm and combined for the PP and mITT populations. Baseline demographic data including age (years), gender, race, ethnicity, height (cm), weight (kg), and body mass index (BMI) (kg/m^2) will be summarized in a table. CDASI activity and damage at baseline and use of immunosuppressive medications will also be included. All these data will also be presented in a table.

8.2. General Medical History

General medication history will be coded using Medical Dictionary for Regulatory Activities (MedDRA)Version 19.1. The number and percentage of subjects with any general medical history will be summarized overall and by coded system organ class (SOC) and preferred term (PT). A summary table will be presented for the two treatment arms separately and combined for the safety population. The data will also be presented in a listing.

8.3. Dermatomyositis Medical History

The DM medical histories will be summarized in the same way as general medical history for safety population in a table and presented in a listing:

8.4. Cardiac Medical History

The cardiac medical histories will be summarized in the same way as general medical history for the safety population in a table and presented in a listing:

9. Treatments and Medications

9.1. Concomitant Medications

Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary (WhoDrug, Enhanced B2, September 2016). Concomitant medications will include all medications given to subjects during the study, which are reported on the Concomitant Medications CRF.

Newly initiated medications are defined as medications taken on/after the first dose date of study drug and not used before the first dose of study drug.

The number and percentage of subjects in the safety population taking concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) Level 4 and preferred term using the safety population. Similarly, newly initiated medications will also be summarized. The data will be summarized overall for two arms separately and combined.

Concomitant medications will be presented in a listing and newly initiated medications will be flagged.

9.2. Study Treatments

9.2.1. Extent of Exposure

Duration of exposure to study drug will be calculated as:

- Treatment period 1: Date of last dose prior to Visit 3 – date of Visit 1 + 1
- Treatment period 2: Date of last dose – date of Visit 3 + 1
- Total duration of exposure is defined as sum of the durations of both periods.

For subjects who discontinue study product or withdraw from the study, treatment periods will be defined as above for periods when the subject is actively taking study product. Last dose date will be imputed using last contact date for the subjects lost to follow up/missing last dose date.

The duration of exposure in each treatment period will be summarized by treatment.

All summaries will be based on the safety population.

9.2.2. Treatment Compliance

Study drug compliance will be calculated for each subject by taking into account whether a subject takes all doses of study drug as instructed. The number of capsules taken will be calculated by subtracting the number of capsules returned from the number of capsules dispensed for a given treatment period.

The study drug compliance (%) for treatment periods 1 and 2 and the total treatment period will be calculated by dividing the total number of capsules taken in a treatment period by the total number of capsules prescribed and then multiplying by 100. For calculations of compliance, the number of capsules prescribed will be adjusted downward if the subject was instructed not to take study capsules on certain days.

Compliance (%) = [(no. of capsules dispensed – no. of capsules returned) / (no. of days in treatment period for which capsules were prescribed x no. of capsules prescribed per day)] x 100

The overall study drug compliance and the study drug compliance for each treatment period will be summarized in the JBT-101 and placebo arms.

A subject will be considered compliant in a given treatment period if the study drug compliance is greater than or equal to 80%. A categorical summary (number of subjects and percentage) of whether subjects were compliant (yes/no) will be presented

The overall study drug compliance and compliance for each treatment period will be presented in a listing.

10. Efficacy Analysis

10.1. Primary Efficacy Endpoint

The primary efficacy endpoint is the CDASI activity score. The following variables will be analyzed:

- Change from baseline to Visit 6 (Day 85) in CDASI activity score
- Change from baseline to other visits and actual value at each visit in CDASI activity score
- Change form Visit 3 in CDASI activity score
- Proportion of subjects with ≥ 5, ≥ 8, and ≥ 10 points improvement (decrease from baseline) in CDASI activity score at each post-baseline visit
- Proportion of subjects in each CDASI activity category [None (CDASI activity score < 14), Mild (CDASI activity score of 14 – 20), Moderate and Severe (CDASI activity score > 20)] at each visit.

Primary analysis is to compare treatment difference (Cohort 1 (JBT-101) vs Cohort 2 (Placebo) in change from baseline to Visit 6 (Day 85) in CDASI activity score using the mixed model with repeated measures. The model will have the change from baseline as a dependent variable,

treatment, visit, treatment*visit as fixed factors, prednisone use (new use or increased dose) as a time-varying factor, and baseline as a covariate, and subject as the repeated random effect using unstructured covariance matrix.

Two-sided p-value and 95% confidence interval associated with the least-square (LS) mean difference between each JBT-101 group and placebo will be presented for each visit.

Change from baseline to other visits and change from Visit 3 in CDASI activity score will be analyzed in the same way as the primary analysis.

[redacted]

10.2. Secondary Efficacy Endpoints

[redacted]

[redacted]

[redacted]

10.3. Other Efficacy Endpoints

[redacted]

[redacted]

11. Safety Analysis

Summaries of the safety data will be done using observed data. No formal statistical testing will be performed to compare safety in different treatment groups. Safety data will be analyzed based on the safety population.

All safety data will be presented in listings.

11.1. Adverse Events

AEs will be coded to system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA®, Version 19.1). Treatment-emergent AEs (TEAEs) will be defined as AEs onset on/after the first dose date of the study drug.

TEAEs onset during each period (Treatment Period 1, Treatment Period 2, and After Treatment) and during Part A will be summarized by SOC and PT for each treatment arms.

In summary, the following tables will be presented:

- All TEAEs
- TEAEs by strongest relationship to study drug (in order of Definite > Probable > Possible > Unlikely > Not Related)
- TEAEs by maximum severity (in order of Life Threatening > Severe > Moderate > Mild)
- Treatment-emergent SAEs
- Treatment-emergent SAEs related to study drug (defined as Definite, Probable, or Possible relationship reported on AE eCRF)

- TEAEs leading to study drug discontinuation
- TEAEs leading to study discontinuation
- Treatment-emergent events of special interest, the event of special interest reported on AE eCRF including:
    - QTc prolongation > 500 msec and > 60 msec from baseline (both)
    - Worsening of muscle disease so that treatment with oral corticosteroids > 10 mg/day or > 20 mg every other day, or equivalent dose, is indicated
    - Aspartate aminotransferase or alanine aminotransferase ≥ 3 x upper limit of normal, with total bilirubin > 1.5 x the upper limit of normal, present on repeat testing

All AEs, SAEs, AEs leading to study discontinuation, AEs leading to study drug discontinuation, Fatal AEs, and events of special interest will be presented in listings separately.

11.2. Clinical Laboratory Evaluations

For the purposes of summarization in both the tables and listings, results of laboratory safety tests, including CBC with cell differential and platelets, metabolic panel, and urinalysis will be converted to standard international (SI) units. The actual values, changes from baseline to each post-baseline visit, and change from Visit 3 to each post-Visit 3 visit in each laboratory test with numeric results will be summarized for each treatment arm.

Laboratory test results will be classified as Low, Normal, and High, or Normal/Abnormal according to the normal ranges. These categorical data will be summarized in shift tables for shift from baseline to each post-baseline visit and shift from Visit 3 to each post-Visit 3 visit for each treatment arm.

11.3. Vital Signs

Vital signs will include systolic blood pressure (mmHg), diastolic blood pressure (mmHg), pulse respiration (beat/min), and body temperature (C) will be assessed at Screening and Visits 1 to 6,

The actual values, changes from baseline to each post-baseline visit, and change from Visit 3 to each post-Visit 3 visit in each vital sign parameter, weight (kg), and BMI (kg/m^2) will be summarized for each treatment arm.

11.4. Physical Examination

Physical examination results will be presented in a listing only. A listing of treatment-emergent medically significant abnormal results will also be provided.

11.5. ECG

ECG will be assessed at Screening and Visits 1, 3, 5 and 6. ECG parameters include heart rate, QT interval, QT interval corrected by Fridericia's formula (QTcF) and Bazett's formula (QTcB) and ECG results will be described as medically significant abnormalities present or absent at Screening and the specified visits.

The actual values, changes from baseline to each post-baseline visit, and change from Visit 3 to each post-Visit 3 visit in each ECG parameter will be summarized for each treatment arm.

Medically significant abnormalities will be tabulated by treatment and visit using number and proportion of subjects.

11.6. ARCI-M

The ARCI-M questionnaire will be completed by subjects at Visits 1, 3, and 6. This is a 12-item yes/no questionnaire developed by the National Institute on Drug Abuse, designed to detect the full range of subjective responses experienced by marijuana users. The ARCI-M questionnaire has been validated by subjects following marijuana smoking. Subjects will be asked to fill out the ARCI-M prior to other interactions with study staff.

Table 1. ARCI-M questionnaire

No	Question	Score
1	Things around me seem more pleasing than usual.	1=True 0=False
2	I feel as if something pleasant had just happened to me.	
3	I have difficulty in remembering.	
4	I feel a very pleasant emptiness.	
5	My mouth seems very dry.	
6	Some parts of my body are tingling.	
7	I have a weird feeling.	
8	My movements seem slower than usual.	
9	I notice that my heart is beating faster.	
10	My thoughts seem to come and go.	
11	I notice my hands are shaking.	
12	I have an increasing awareness of my bodily sensations.	

A score of 1 is given for each question where the answer is "True" and 0 where the answer is "False". The Total Score will be calculated as the sum of the scores of 12 questions varying from 0 to 12 with higher score for higher psychotropic effect of study drug.

The actual values, changes from baseline to each post-baseline visit, and change from Visit 3 to Visit 6 in ARCI-M total score will be summarized for each treatment arm.

The proportion of subjects with an increase score from baseline of ≥ 1 and <3, ≥ 3 and < 5, and ≥ 5 will also be summarized.

11.7. Manual Muscle Testing 8

The MMT-8 is a partially validated tool that assesses muscle strength. A 0 – 10 points scale and an abbreviated group of 8 proximal, distal, and axial muscles will be used. The MMT-8 total score (ranged 0 – 150) is the sum of item scores for right proximal and distal muscles, left proximal and distal muscles, and axial muscle. The MMT-8 will be assessed at Visits 1, 3, 5 and 6. Refer to the CRF for the muscle groups.

The actual values, changes from baseline to each post-baseline visit, and change from Visit 3 to Visits 5 and 6 in MMT-8 total score will be summarized for each treatment arm.

12. Pharmacokinetics

12.1. Pharmacokinetic (PK) Endpoints

JBT-101 plasma concentrations will be measured on Visits 1, 2, 3, 5, and 6. JBT-101 metabolites will be measured at the same visits.

12.2. Analysis of PK Endpoints

All PK analyses will be conducted using the PK analysis population.

JBT-101 concentrations at each visit will be summarized descriptively for each treatment arm. Concentrations that are below the limit of quantitation will be treated as zero in the summary statistics of concentration data.

Additionally, JBT-101 concentrations will be summarized by gender, by age (<60, ≥ 60 years) and by BMI (<25, 25 to < 30, ≥ 30 kg/m^2) separately.

Analysis of JBT-101 metabolites data will not be conducted by SDC and the analysis method will not be included in this SAP.

13. Interim Analysis

No interim analysis of efficacy data for effect size, or sample size adjustment is planned for this study.

14. References

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15. Appendices

Appendix A: Schedule of Study Procedure, Part A

STUDY ACTIVITY	Visit and Study Day							
	Screening	1	2	3	4	5	6	7
	Up to 28 Days Prior to Visit 1	Day 1	Day 15 ± 3	Day 29 ± 3	Day 43 ± 3	Day 57 ± 3	Day 85 ± 3	Day 113 ± 3 or Withdrawal Visit
ELIGIBILITY								
Written informed consent	X							
Verify eligibility criteria	X	X						
Medical history (including LMP for WOCBP[a])	X							
Record concomitant medications	X	X	X	X	X	X	X	X
Contraceptive assessment, for WOCBP	X	X	X	X	X	X	X	X
Physical examination	X	X					X	X
Human immunodeficiency virus, Hepatitis B core antibody, Hepatitis B surface antigen and Hepatitis C antibody	X							
QuantiFERON	X							
Follicle stimulating hormone, if applicable	X							
Serum β human chorionic gonadotropin, for WOCBP	X							
Urine β human chorionic gonadotropin, for WOCBP		X		X		X	X	X
RANDOMIZATION								
Randomization, prior to		X						
STUDY PRODUCT ADMINISTRATION								
Dispense study product for home administration		X		X[b]		X[b]		
Administer study product in clinic		X[c]						
Count capsules of unused study product			X	X	X	X	X	X
SAFETY ASSESSMENTS								
Blood pressure[d], pulse, respiratory rate, temperature	X	X	X	X	X	X	X	X
Weight		X					X	X
Height		X						
Adverse event monitoring		X	X	X	X	X	X	X
Complete blood count with differential and platelets	X	X	X	X	X	X	X	X
Metabolic panel[e]	X	X	X	X	X	X	X	X
Urine dipstick[f]	X	X		X		X	X	
12 lead electrocardiograms with QT/QTc intervals	X	X		X		X	X	

STUDY ACTIVITY	Visit and Study Day							
	Screening	1	2	3	4	5	6	7
	Up to 28 Days Prior to Visit 1	Day 1	Day 15 ± 3	Day 29 ± 3	Day 43 ± 3	Day 57 ± 3	Day 85 ± 3	Day 113 ± 3 or Withdrawal Visit
Addiction Research Center Inventory-Marijuana		X		X			X	
Manual Muscle Testing-8		X		X		X	X	X
PRIMARY EFFICACY ASSESSMENT								
Cutaneous Dermatomyositis Disease Activity and Severity Index	X	X	X	X	X	X	X	X
SECONDARY EFFICACY ASSESSMENTS								
[redacted]								
MECHANISM OF ACTION								
[redacted]								
PHARMACOKINETICS								
JBT-101 plasma concentrations and metabolites		X	X	X		X	X	
BIOMARKERS								
[redacted]								

[a] Abbreviation: WOCBP; women of childbearing potential.
[b] Study product will be dispensed in WOCBP only if urine pregnancy test is negative.
[c] The first dose of study product on Visit 1 will be taken in clinic from the dispensed study product. Afterwards, subjects will be observed in clinic for at least 30 minutes, or until stable, if longer.
[d] Seated or reclining (≥ 5 minutes) blood pressure and pulse.
[e] Metabolic panel includes glucose, urea nitrogen, creatinine, estimated glomerular filtration rate, blood urea nitrogen/creatinine, sodium, potassium, chloride, carbon dioxide, calcium, protein total, albumin, bilirubin total, alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase.
[f] Includes blood, albumin/protein, and glucose.
[g] One 4 mm punch biopsy will be obtained from an area of non-lesional skin on Visit 1 (optional). One 4 mm punch biopsy will be obtained from an area of lesional skin on Visits 1, 3, and 6 (optional).

[redacted]

Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) *ver02*

Select the score in each anatomical location that describes the most severely affected dermatomyositis-associated skin lesion

Extent

	activity			damage		
Anatomical Location	Erythema	Scale	Erosion/ Ulceration	Poikiloderma (Dyspigmentation or Telangiectasia)	Calcinosis	Anatomical Location
	0-absent 1-pink; faint erythema 2-red 3-dark red	0-absent 1-scale 2-crust; lichenification	0-absent 1-present	0-absent 1-present	0-absent 1-present	
Scalp						Scalp
Malar Area						Malar Area
Periorbital						Periorbital
Rest of the face						Rest of the face
V-area neck (frontal)						V-area neck (frontal)
Posterior Neck						Posterior Neck
Upper Back & Shoulders						Upper Back & Shoulders
Rest of Back & Buttocks						Rest of Back & Buttocks
Abdomen						Abdomen
Lateral Upper Thigh						Lateral Upper Thigh
Rest of Leg & Feet						Rest of Leg & Feet
Arm						Arm
Mechanic's Hand						Mechanic's Hand
Dorsum of Hands (not over joints)						Dorsum of Hands (not over joints)
Gottron's – Not on Hands						Gottron's – Not on Hands

Gottron's – Hands

Examine patient's hands and double score if papules are present		Ulceration	Examine patient's hands and score if damage is present	
0-absent 1-pink; faint erythema 2-red erythema 3-dark red			0-absent 1-dyspigmentation 2-scarring	

Periungual

Periungual changes (examine)			
0-absent 1-pink/red erythema/microscopic telangiectasias 2-visible telangiectasias			

Alopecia

Recent Hair loss (within last 30 days as reported by patient)			
0-absent 1-present			

Total Activity Score
(For the activity score, please add up the scores of the left side, i.e. Erythema, Scale, Excoriation, Ulceration, Gottron's, Periungual, Alopecia)

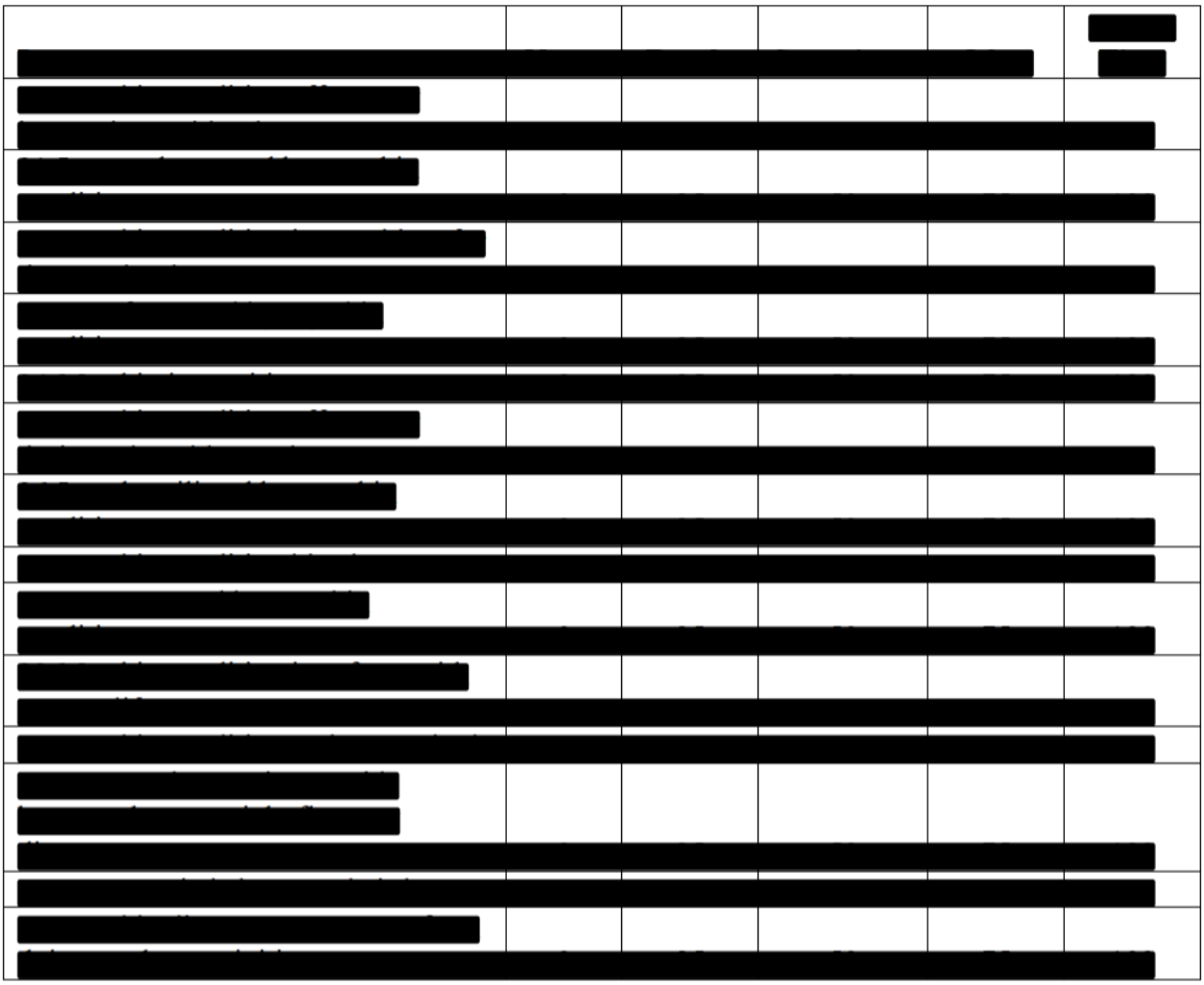
Total Damage Score
(For the damage score, add up the scores of the right side, i.e. Poikiloderma, Calcinosis)

[redacted]

[redacted]

[redacted]

[redacted]

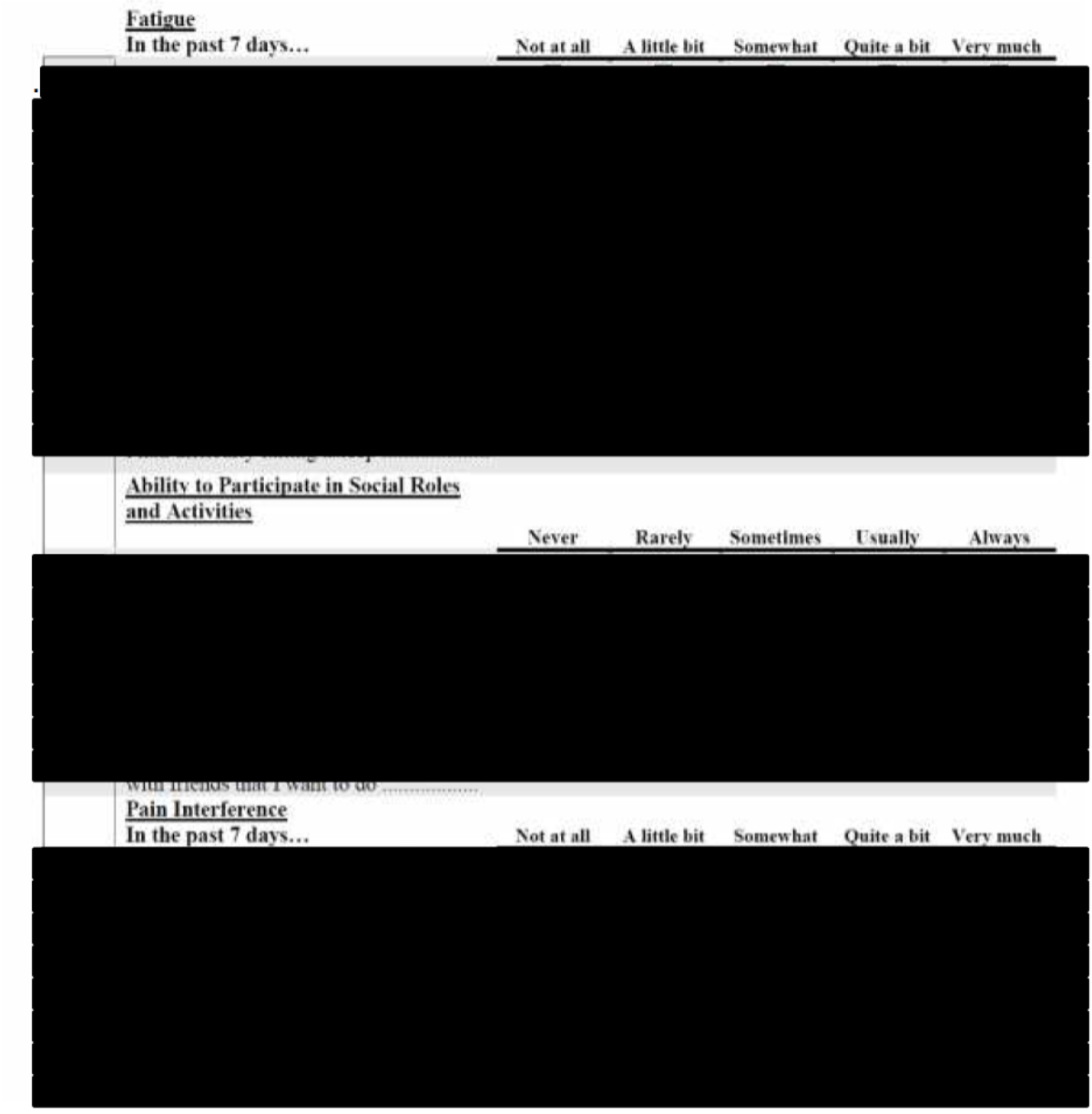


[redacted]

[redacted]

Please respond to each question or statement by marking one box per row.

[redacted]



Fatigue
In the past 7 days… Not at all | A little bit | Somewhat | Quite a bit | Very much

[redacted]

Ability to Participate in Social Roles and Activities
Never | Rarely | Sometimes | Usually | Always

[redacted]

Pain Interference
In the past 7 days… Not at all | A little bit | Somewhat | Quite a bit | Very much

[redacted]

[redacted]

[redacted]

[redacted]

Anxiety 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	40.3	6.1
5	48.0	3.6
6	51.2	3.1
7	53.7	2.8
8	55.8	2.7
9	57.7	2.6
10	59.5	2.6
11	61.4	2.6
12	63.4	2.6
13	65.3	2.7
14	67.3	2.7
15	69.3	2.7
16	71.2	2.7
17	73.3	2.7
18	75.4	2.7
19	77.9	2.9
20	81.6	3.7

*SE = Standard Error

Depression 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	41.0	6.2
5	49.0	3.2
6	51.8	2.7
7	53.9	2.4
8	55.7	2.3
9	57.3	2.3
10	58.9	2.3
11	60.5	2.3
12	62.2	2.3
13	63.9	2.3
14	65.7	2.3
15	67.5	2.3
16	69.4	2.3
17	71.2	2.4
18	73.3	2.4
19	75.7	2.6
20	79.4	3.6

*SE = Standard Error

Fatigue 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	33.7	4.9
5	39.7	3.1
6	43.1	2.7
7	46.0	2.6
8	48.6	2.5
9	51.0	2.5
10	53.1	2.4
11	55.1	2.4
12	57.0	2.3
13	58.8	2.3
14	60.7	2.3
15	62.7	2.4
16	64.6	2.4
17	66.7	2.4
18	69.0	2.5
19	71.6	2.7
20	75.8	3.9

*SE = Standard Error

Pain Interference 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	41.6	6.1
5	49.6	2.5
6	52.0	2.0
7	53.9	1.9
8	55.6	1.9
9	57.1	1.9
10	58.5	1.8
11	59.9	1.8
12	61.2	1.8
13	62.5	1.8
14	63.8	1.8
15	65.2	1.8
16	66.6	1.8
17	68.0	1.8
18	69.7	1.9
19	71.6	2.1
20	75.6	3.7

*SE = Standard Error

Physical Function 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	22.9	3.9
5	26.9	2.7
6	29.1	2.4
7	30.7	2.2
8	32.1	2.2
9	33.3	2.1
10	34.4	2.1
11	35.6	2.1
12	36.7	2.1
13	37.9	2.2
14	39.1	2.2
15	40.4	2.2
16	41.8	2.3
17	43.4	2.4
18	45.3	2.6
19	48.0	3.1
20	56.9	6.7

*SE = Standard Error

Sleep Disturbance 4a
Short Form Conversion Table

Raw Score	T-score	SE*
4	32.0	5.2
5	37.5	4.0
6	41.1	3.7
7	43.8	3.5
8	46.2	3.5
9	48.4	3.4
10	50.5	3.4
11	52.4	3.4
12	54.3	3.4
13	56.1	3.4
14	57.9	3.3
15	59.8	3.3
16	61.7	3.3
17	63.8	3.4
18	66.0	3.4
19	68.8	3.7
20	73.3	4.6

*SE = Standard Error

Ability to Participate in Social Roles and Activities 4a

Short Form Conversion Table

Raw Score	T-score	SE*
4	27.5	4.1
5	31.8	2.5
6	34.0	2.3
7	35.7	2.2
8	37.3	2.1
9	38.8	2.2
10	40.5	2.3
11	42.3	2.3
12	44.2	2.3
13	46.2	2.3
14	48.1	2.2
15	50.0	2.2
16	51.9	2.2
17	53.7	2.3
18	55.8	2.3
19	58.3	2.7
20	64.2	5.1

*SE = Standard Error

[redacted]