SUMMITANALYTICAL	**STATISTICAL ANALYSIS PLAN** **CONFIDENTIAL**

aTyr Pharma, Inc.

STATISTICAL ANALYSIS PLAN

Protocol Title:	A Randomized, Double-Blind, Placebo-Controlled Multiple Ascending Dose Study of Intravenous ATYR1923 in Patients with Pulmonary Sarcoidosis
Protocol Number:	ATYR1923-C-002
Phase:	Phase 1b/2a
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Approval of Statistical Analysis Plan for Study ATYR1923-C-002

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2. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Only abbreviations and terms relevant to the SAP are repeated herein. The reader is referred to the protocol for the complete and comprehensive list of abbreviations and definitions of terms for the study.

Abbreviation/Term	Definition
^{18}F-FDG-PET/CT	^{18}F-fluorodeoxyglucose positron-emission tomography combined with computed tomography.
Ab	Antibody
ADA	Anti-drug antibody
ADaM	Analysis data Model
AE	Adverse Event
AESI	Adverse Events of Special Interest
AUC_{0-t}	Area under the curve from time zero to time t
BDI	Baseline Dyspnea Indices
BSA	Body surface area
C_{max}	Maximum concentration
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL	Clearence
CSR	Clinical Study Report
DL_{CO}	Diffusion capacity of the lungs for carbon dioxide
DSMB	Data Safety Review Board
eCRF	Electronic Care Report Form
ECG	Electrocardiogram
EOI	End of infusion
FEV_1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
FVC%	Percent predicted forced vital capacity
IV	Intravenous
KSQ	King's Sarcoidosis Questionnaire
LCQ	Leicester Cough Questionnaire
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat
OCS	Oral Corticosteroid

Abbreviation/Term	Definition
PBMC	Peripheral blood mononuclear cells
PD	Pharmacodynamics
PK	Pharmacokinetics
PT	Prothrombin time
PTT	Partial thromboplastin time
RCRM	Random Coefficient Regression Model
SAC BDI-TDI	Self-administered computerized Baseline/Transitional Dyspnea Indices
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SASI	Sarcoidosis Activity and Severity Index
SAT	Sarcoidosis Assessment Tool
SD or sd	Standard Deviation
SDTM	Study Data Tabulation Model
SE or se	Standard Error
sIL-2R	Soluble IL-2 receptor
SPGA	Skin Physician Global Assessment
SUV	Standardized uptake value
SUV_{max}	Maximum standardized uptake value
$t_{1/2}$	Half-life
T_{max}	Maximum concentration
TEAE	Treatment Emergent Adverse Event
TDI	Transition Dyspneas Indices
V_{ss}	Volume of distribution at steady state
V_z	Volume of distribution
VEGFC	Vascular endothelial growth factor C
WHO-DD	World Health Organization Drug Dictionary

3. INTRODUCTION

3.1. Preface

This document presents a statistical analysis plan (SAP) for aTyr Pharma, Inc. Protocol ATYR1923-C-002 (*A Randomized, Double-Blind, Placebo-Controlled Multiple Ascending Dose Study of Intravenous ATYR1923 in Patients with Pulmonary Sarcoidosis).*

Reference materials for this statistical plan include the Protocol Version 3.0 dated 25Sep2020 and Case Report Forms (Version 15.0, 9APR2021).

The SAP described hereafter is an *a priori* plan. The SAP will be finalized and approved prior to unblinding of any study data. Statistical programming may occur as study data accumulate in order to have analysis programs ready at the time the study finishes. In such an event, arbitrary treatment group assignments must be randomly linked to patients, effectively rendering any output of programs meaningless.

For the reasons stated here the conduct of the study in the field is considered to be independent of any study outcome that might materialize upon enactment of the currently proposed statistical plan.

3.2. Purpose of Analyses

The purposes of the planned analyses described in this SAP are to evaluate the safety and tolerability of multiple ascending intravenous (IV) doses of ATYR1923 in patients with pulmonary sarcoidosis. Results from the analyses completed will be included in the final clinical study report for ATYR1923, and may also be utilized for regulatory submissions, manuscripts, or other clinical development activities.

Post-hoc exploratory analyses not identified in this SAP may be performed to further examine the study data. These analyses will be clearly identified, where appropriate, in the final clinical study report. Additional analyses not prospectively identified in this SAP may also be completed for publications, or regulatory or funding inquiries. These analyses, if performed, may not be reported in the clinical study report, but will be fully documented in the document containing the additional analyses.

3.3. Summary of Statistical Analysis Changes to the Protocol

The PK Conecntration Parameter Analysis Set included in the protocol, Section 10.1.1.4, is not included in this SAP. Instead, an Efficacy Evaluable Set has been added. The Intent to Treat (ITT) Analysis Set is included in the Protocol, Section 10.1.1.1. However, due to the possibility of subjects who have been randomized but not dosed, a modified Intent-to-Treat (mITT) population is used in the SAP.

The first secondary endpoint specified in the protocol specifies the following.

- Total cumulative steroid dose administered over the primary study period (Day 1 through Week 24) by treatment cohort

During planning of this analysis, it was brought to attention that subjects may be dosed for different periods of time, and visits may occur at different study days for different subjects due to scheduling conflicts. Therefore, a time adjusted AUC will be used to examine OCS use.

In the protocol secondary endpoints below are specified for Week 24 visit.

- Total cumulative steroid dose administered over the primary study period (Day 1 through Week 24) by treatment cohort
- Number of patients who achieve the targeted tapered dose of prednisone 5 mg/day (or equivalent) and maintain it through Week 24 by treatment cohort

In light of the half-life of the investigational product, it was decided that the endpoints will be examined for the end of dosing period instead. The end of dosing period is defined as 30 days after the last dose.

In addition, due to protocol prescribed taper prior to Day 51, an additional period, Day 51 through end of dosing interval, will also be examined, together with Day 1 through end of dosing interval.

4. STUDY OBJECTIVES AND ENDPOINTS

Study objectives and endpoints defined in the protocol include safety, immunogenicity, pharmacokinetics and efficacy. Objectives and pre-specified endpoints are as follows:

4.1. Study Objectives

4.1.1. Primary Objective

To evaluate the safety and tolerability of multiple ascending intravenous (IV) doses of ATYR1923 in patients with pulmonary sarcoidosis.

4.1.2. Secondary Objectives

To assess the potential steroid-sparing effect of multiple ascending doses of ATYR1923 in patients with pulmonary sarcoidosis.

To assess the potential immunogenicity of multiple ascending IV doses of ATYR1923 in patients with pulmonary sarcoidosis.

To characterize the PK of multiple ascending IV doses of ATYR1923 in patients with pulmonary sarcoidosis. This objective and its corresponding endpoints are analyzed in a separate analysis plan.

4.1.3. Exploratory Objectives

One exploratory objective has been defined for the study as follows:

To explore the preliminary efficacy of multiple ascending IV doses of ATYR1923 in patients with pulmonary sarcoidosis by evaluating changes over time in:

- Disease activity (pulmonary parenchymal inflammation), assessed by ^{18}F-fluorodeoxyglucose positron-emission tomography combined with computed tomography (^{18}F-FDG-PET/CT).
- Lung function, assessed by percent predicted forced vital capacity (FVC%) and diffusing capacity of the lungs for carbon monoxide (DLCO).
- Serum biomarkers, including angiotensin converting enzyme (ACE), soluble IL-2 receptor (sIL-2R), extracellular HARS, NRP2, and vascular endothelial growth factor C (VEGFC).
- State of immune cell anergy in peripheral blood mononuclear cells (PBMCs).
- Health-related quality of life scales, including the Sarcoidosis Assessment Tool (SAT), King's Sarcoidosis Questionnaire (KSQ), Leicester Cough Questionnaire (LCQ), Fatigue Assessment Scale (FAS), and the self-administered computerized Baseline/Transitional Dyspnea Indices (SAC BDI-TDI).

- Skin lesions, for patients with cutaneous disease involvement at baseline, as assessed by Skin Physician Global Assessment (SPGA), body surface area (BSA) assessment, and the Sarcoidosis Activity and Severity Index (SASI; on a target lesion), as well as serial biopsies of non-target lesion(s) (optional at select sites).

4.2. Study Endpoints

4.2.1. Primary Endpoint

Incidence of TEAEs and serious adverse events (SAEs).

4.2.2. Secondary Endpoints

1) Potential to Decrease Background Oral Corticosteroid Dose
   - Time adjusted Area Under the Curve (AUC) of steroid dose administered over the study periods (Day 1 through the end of dosing interval and Day 51 through the end of dosing interval) by treatment cohort
   - Number of patients who achieve the targeted tapered dose of prednisone 5 mg/day (or equivalent) and maintain it through the end of dosing interval by treatment cohort
   - Exposure response analysis comparing steroid dose area under the curve (AUC) with ATYR1923 PK parameters through Week 24. This endpoint is not analyzed based on this analysis plan. A separate document is prepared for all PK related analyses.
2) Immunogenicity of multiple IV doses of ATYR1923 in patients with pulmonary sarcoidosis based on the following endpoints:
   - Incidence and titer of positive ADA (anti-ATYR1923) and anti-Jo-1 Ab.

4.2.3. Exploratory Endpoints

Change from baseline in clinical measures, including:

- FVC%
- DLco
- SUVmax as measured by ^{18}F-FDG-PET/CT
- Health-Related Quality of Life, as assessed by the SAT, KSQ, LCQ, FAS, and SAC BDI-TDI.
- Skin lesions in patients with cutaneous involvement utilizing SPGA, body surface area assessment, and the SASI.

Change from baseline in serum and tissue biomarkers, including but not limited to:

- ACE and sIL2R (disease serum biomarkers)
- Extracellular histidyl-tRNA synthetase (HARS), NRP2, and VEGFC (pathway serum biomarkers)
- State of immune cell anergy in peripheral blood mononuclear cells (PBMCs)
- Histopathology (skin biopsy)

5. STUDY METHODS

5.1. General Study Design and Plan

As background for the statistical methods presented below, this section provides an overview of the study design and plan of study execution. The protocol is the definitive reference for all matters discussed in what follows.

This randomized, double-blind, placebo-controlled, study will evaluate the safety, tolerability, immunogenicity, PK, and preliminary efficacy of multiple ascending doses of IV ATYR1923 in patients with pulmonary sarcoidosis undergoing a protocol-guided oral corticosteroid (OCS) tapering regimen.

This study will consist of 3 staggered multiple dose cohorts. Each eligible patient will participate in only one cohort during the study. Within each cohort, 12 patients will be randomized 2:1 (block size of 6) to ATYR1923 (N=8) or placebo (N=4). Study drug will be administered via IV infusion every 4 weeks for a total of 6 doses (20 weeks of treatment). The follow-up study visit is scheduled for 4 weeks after the last infusion. The ATYR1923 doses levels to be evaluated are 1.0 mg/kg, 3.0 mg/kg, and 5.0 mg/kg.

Day 1 is the calendar day of first infusion.

Starting on Day 15, patients will begin a taper (reduction) in OCS (per the ATYR1923-C-002 Oral Corticosteroid Taper Guidelines) from their starting dose of 10-25 mg/day of prednisone (or equivalent) to a target dose of 5 mg/day, to be completed on or before Day 50. The OCS dose will be tapered by 5.0 mg/day every 1 to 2 weeks, depending on the starting dose. Smaller incremental titrations to the target dose of 5 mg/day by Day 50 may be implemented per Investigator judgement. Patients will be maintained at the target dose of 5.0 mg/day (or equivalent) through Week 24/End-of-Study (EOS). Optionally, further titrations in the OCS dose to below 5 mg/day may be attempted after the Week 16 visit, if determined by the Investigator to be feasible.

Patients who develop an acute worsening of symptoms or are unable to adhere to the protocol-defined OCS tapering regimen may receive ‘rescue’ treatment with higher OCS doses as clinically indicated. Upon resolution of symptoms, the Investigator may choose to reinstitute a taper back down to the target maintenance dose of 5 mg/day. Patients who require rescue treatment following two attempts at tapering to 5 mg/day may remain on a higher stable dose of OCS as determined by the Investigator. Patients who require an increase in OCS dose at any time in the study should continue to receive blinded study drug and followed through to the end of the study.

Dose Escalation

Cohorts 1 through 3 will be enrolled sequentially in a staggered manner. After at least 6 patients of a given cohort have received at least 3 infusions of study drug (ATYR1923 or placebo), cumulative unblinded safety data (including but not limited to any reported adverse events (AEs), electrocardiogram (ECG) recordings, clinical laboratory values and vital signs) will be reviewed by the DSMB. Enrollment in the next scheduled (higher dose) cohort may commence after this review is completed, dose escalation is approved, and the remaining 6 patients have been randomized in the previous cohort. Dose escalation will continue in this manner until the highest planned dose level of ATYR1923 is reached, or the criteria for pausing enrollment have been met.

Criteria for Pausing Enrollment

In the event that a serious unexpected suspected adverse reaction (SUSAR) has occurred, the enrollment and initiation of study drug administration to new patients will be paused and the Sponsor will request an unblinded review by the DSMB, who will provide its recommendation to aTyr Pharma. Such recommendation may include, but is not limited to, stopping an ongoing cohort, stopping further dose escalation, continuing the study as planned, or continuing the study with modifications, such as evaluation of a lower or intermediate dose in the next cohort(s) to gain more information on safety and tolerability.

In addition, if unexpected, clinically significant trends or changes in other safety assessments are identified during routine blinded safety reviews the Sponsor may request the DSMB to similarly perform an unblinded review and provide recommendations.

The schedule for assessments and timing of events is presented in Table 1.

Table 1 Schedule of Time and Events

Study Period		Treatment													
Visit	Screen	1	1a	2	2a	3	3a, 3b, 3c	4	4a	5	5a	6	6a	7	EOS
Study Day	-28 to - 1	D1	W1/ D8	W2/ D15	W3/ D22	W4/ D29	W5, 6, 7	W8/ D57	W10/ D71	W12/ D85	W14/ D99	W16/ D113	W18/ D127	W20/ D141	WK24/ D169
Visit Window (Days)	-	-	-	±2	±3	±3	±2	±3	±3	±3	±3	±3	±3	±3	±3
Written informed consent	X														
Telephone Contact			X		X		X		X		X		X		
Eligibility check	X	X													
Demographics	X														
Medical history	X														
Height & weight[1]	X	X				X		X		X		X		X	
Modified MRC Dyspnea Scale	X														
Physical examination[2]	X									X					X
Vital signs[3]	X	X		X		X		X		X		X		X	X
Pulse oximetry[4]	X	X				X		X		X		X		X	X
12-lead ECG[5]	X	X[5]				X		X		X[5]		X		X[5]	X
Pulmonary Function Tests[6]	X	X				X		X		X		X		X	X
DL_{CO}[7]		X								X				X	X
Pregnancy test (females only)[8]	X (serum)	X						X				X			X (serum)
Serum FSH[9]	X														
Rheumatoid factor		X													
Jo-1 antibody (serum)	X			X		X		X		X		X		X	X
ADA sampling (serum) for anti-ATYR1923 antibodies[17]	X			X		X		X		X		X		X	X
Safety laboratory testing (hematology, clinical chemistry)	X	X		X		X		X		X		X		X	X
Urinalysis[10]	X	X		X		X		X		X		X		X	X
Coagulation laboratory testing (PT, INR, PTT)	X					X		X		X		X		X	X
Serology (HBsAg, anti-HCV, and anti-HIV 1/2 tests)	X														
Serum complement, serum tryptase, and IgE[11]		X													

Study Period		Treatment													
Visit	Screen	1	1a	2	2a	3	3a, 3b, 3c	4	4a	5	5a	6	6a	7	EOS
Study Day	-28 to - 1	D1	W1/ D8	W2/ D15	W3/ D22	W4/ D29	W5, 6, 7	W8/ D57	W10/ D71	W12/ D85	W14/ D99	W16/ D113	W18/ D127	W20/ D141	WK24/ D169
Visit Window (Days)	-	-	-	±2	±3	±3	±2	±3	±3	±3	±3	±3	±3	±3	±3
Plasma complement[11]		X													
^{18}F-FDG-PET/CT (optional)[12]	X											X			
Skin lesion visual assessments (if applicable)[13]	X			X		X		X		X		X		X	
Skin lesion biopsy (optional for patients at select sites)[14]	X									X					
AE assessment/Concomitant medications		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Randomization[15]		X													
King's Sarcoidosis Questionnaire		X				X		X		X		X		X	X
Leicester Cough Questionnaire		X				X		X		X		X		X	X
Baseline/Transitional Dyspnea Indices		X				X		X		X		X		X	X
Fatigue Assessment Scale		X				X		X		X		X		X	X
Sarcoidosis Assessment Tool		X				X		X		X		X		X	X
Blood sampling (serum) for ATYR1923 PK[16]		X[16]		X		X		X		X		X		X[16]	X
PBMC collection[18]		X								X					X
Serum biomarkers[19]		X								X				X	X
Infusion site examination[20]		X				X		X		X		X		X	
Study drug administration		X				X		X		X		X		X	
OCS Taper[21]				X											

ADA = anti-drug antibodies; AE = adverse event; BMI = body mass index; D = Day; ECG = electrocardiogram; EOI = end of infusion; EOS = End-of-Study; ET= Early Termination; FSH = follicle stimulating hormone; HBsAg = hepatitis B surface antigen; HCV = hepatitis C virus; HIV = human immunodeficiency virus; HRCT = high-resolution computed tomography; INR = international normalized ratio; OCS = Oral Corticosteroid; PBMC = peripheral blood mononuclear cell; PD = pharmacodynamics; PET = positron emission tomography; PK = pharmacokinetics; PT = prothrombin time; PTT = partial thromboplastin time; SOI=start of infusion; W = week(s).
On dosing days, all assessments will be performed pre-dose unless otherwise specified.

1. **Height** only at Screening.
2. P**hysical examination**. Full physical examinations are to be obtained at Screening, Week 12 and 24, abbreviated symptom-directed physical examination may be completed at other visits if needed.

3. **Vital signs** are to be obtained at every visit. On study drug administration days, vital signs are to be measured pre-infusion and at 15 and 30 minutes (±5 minutes) and at 1, 2, and 4 hours (±15 minutes) after the start of infusion (SOI). Vital signs are to be measured before blood sample collection. Vital signs will include blood pressure (systolic and diastolic, recorded after lying supine for 5 min), heart rate, respiratory rate. Temperature is to be obtained at Screening and on dosing days at pre-dose, 60 minutes (±15 minutes) after the SOI, and again at 4 hours (±15 minutes) after the SOI.
4. **Pulse oximetry:** continuous pulse oximetry is to be measured on dosing days from 5 minutes pre-dose until EOI, and recorded at the same time points as vital signs. On non-dosing days pulse oximetry is to be obtained with vital sign assessments.
5. **12-lead ECG** is to be obtained at Screening, within 1-hour pre-dose on dosing days. At Day 1 and Weeks 12 and 20, an ECG is to be obtained at 4 hours (±30 minutes) after SOI. The ECG is to be obtained after patients have been lying supine for 5 minutes.
6. **Pulmonary Function Testing** is to be performed using the same spirometer throughout the study. Parameters include forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), FEV_1/FVC ratio at all specified visits. A minimum of 3 efforts should be obtained that meet the acceptance criteria of the American Thoracic Society or European Respiratory Society.
7. **DL_{CO}** measurements *should* be obtained after patients have been sitting quietly for 5 minutes.
8. **Pregnancy** serum tests are to be performed on all females at Screening and at Week 24/EOS. A urine pregnancy test is to be performed at other time points indicated.
9. **FSH** only required for all female patients.
10. **Urinalysis** (semi-quantitative by dipstick): microscopy is to be performed if indicated by an abnormal and clinically significant result.
11. **Serum Complement, Tryptase/Plasma Complement, and IgE** are to be collected at Day 1 pre-dose and again if an infusion related reaction (IRR) occurs.
12. **^{18}F-FDG-PET/CT scans are optional**; patients who elect to participate agree to have imaging performed within 4 weeks prior to Day 1, and within ±5 days of Week 16 or if early termination prior to Week 16.
13. **Skin lesion evaluation:** To be completed for patients with skin lesions present. Skin lesions will be evaluated by: Skin Physician Global Assessment (SPGA), body surface Area assessment, the Sarcoidosis Activity and Severity Index (SASI).
14. **Skin lesion biopsy:** Optional for patients with skin lesions present. A non-target lesion (ie, a lesion that is not being assessed by SASI over time) is to be selected by the Investigator for biopsy during Screening and confirmed by the patient that it had been identified by his or her private dermatologist as cutaneous sarcoidosis. Skin lesion biopsy may be obtained within 4 weeks prior to Day 1 for patients who are otherwise deemed eligible for the study and within ±5 days of Week 12 or if early termination prior to Week 12.
15. **Randomization** is to be performed within 0-3 days prior to Day 1 or on the day of dosing.
16. **ATYR1923 serum PK** samples are to be collected pre-dose on dosing days. On Day 1 and Week 20 visits, PK samples are also collected post start of infusion at: 1 hr (just prior to [i.e., within 0-10 minutes] EOI), and at any single time point between 4-6 hours.
17. **ADA** samples are to be collected pre-dose when obtained on dosing days.
18. **Blood for PBMC assessments** will be collected pre-dose when obtained on dosing days.
19. **Serum for biomarkers** are to be collected pre-dose when obtained on dosing days.
20. **Infusion site examination:** the IV infusion site should be examined at 0.5 and 1.5 hours (±10 minutes) after the end of infusion.
21. **OCS Taper:** OCS taper to start at Day 15 (Week 2) and continue through Day 50 (Week 7) per the ATYR1923-C-002 OCS Taper Guideline.

5.2. Inclusion – Exclusion Criteria and General Study Population

The general study population will include a total of at least 36 adult patients with pulmonary sarcoidosis, age 18 to 75 years, inclusive. The inclusion and exclusion criteria defined in the protocol apply to all patients regardless of age stratification and are not repeated herein the SAP. Reference is made to the final protocol for the specific inclusion and exclusion criteria for patients.

Patients withdrew for reasons other than treatment-related AEs may be replaced.

5.3. Randomization and Blinding

It is planned that 36 patients with pulmonary sarcoidosis will be randomized into one of 3 sequential cohorts, each comprising 12 patients allocated 2:1 (block size of 6) to ATYR1923:Placebo.

The master randomization schedule will be made of randomly permuted blocks of appropriate sizes, as determined by the unblinded study team member producing the schedule. The schedule will be generated electronically.

For patients who are replaced, the replacements should take the same treatment assignment as the original patient to ensure that the treatment groups stay balanced.

The randomization code will be produced within the interactive web response system (IWRS). The study center pharmacist will be provided access to the randomization code within the IWRS and through notifications generated by the IWRS. The laboratory where the PK samples are to be analyzed will also be provided access to distinguish between samples of patients dosed with ATYR1923 versus placebo.

Patients who withdraw for any reason without completing all screening evaluations successfully, will be considered “screen failures”.

Randomization will be performed using an IWRS. The patient will be issued a randomization number only after the patient has met all Inclusion and Exclusion criteria.

The following controls will be employed to maintain the double-blind status of the study:

- The infusion solution containing active drug and placebo will be indistinguishable in appearance.
- The study center pharmacist will have access to randomized treatment assignments via IWRS for dispensing purposes; treatment assignments will be accessible only to the pharmacist and authorized personnel and will be maintained in a blinded fashion.

Rules for unblinding a patient for safety reasons are fully described in the Protocol and not repeated herein this SAP.

6. SAMPLE SIZE

For this study, no prospective calculations of statistical power have been made. The sample size has been selected to provide information on safety, tolerability, immunogenicity, PK and efficacy following single doses of ATYR1923. Any p-values to be calculated will be interpreted in the perspective of the explorative character of this study.

7. GENERAL CONSIDERATIONS

7.1. Analysis Sets

7.1.1. Safety Set

The Safety Set will comprise all patients who receive any amount of study drug and will be based on the actual treatment received, if this differs from that to which the patient was randomized.

7.1.2. Modified Intent-to-Treat Set (mITT)

The mITT Set will comprise all patients who have received any amount of study drug and will be based on the randomized treatment, regardless of which treatment the patient actually received.

7.1.3. Efficacy Evaluable Set (EE)

The EE Set includes all subjects who have received at least four doses of study drug and no major protocol deviations that may affect the interpretation of efficacy. Decisions regarding exclusion of patients from the EE Set will be documented before unblinding of the treatment assignments. Treatment groups will be analyzed based on the randomized treatment.

7.2. Covariates and Subgroups

7.2.1. Planned Covariates

There are no planned covariates for the primary analysis (i.e. for endpoints based on safety data). Specific covariates used for efficacy endpoints are described within the respective efficacy endpoint definitions elsewhere in this document.

7.2.2. Planned Subgroups

There are no planned subgroup analyses (i.e. for endpoints based on safety data). Specific subgroups used for efficacy endpoints are described within the respective efficacy endpoint definitions elsewhere in this document.

7.3. Management of Analysis Data

7.3.1. Baseline Definition

Unless otherwise specified, baseline measures are the last measures assessed on or before the first dose date. If multiple measures are taken on Day 1 (e.g., vital signs, 12-lead ECG), then the last measure before the first dose will be used as baseline.

Baseline OCS dose is defined as the dose recorded in the OCS log prescribed for the day before the first dose of the study drug.

7.3.2. Data Handling

Unscheduled or repeated laboratory (with the exception of coagulation) and clinical test results will not be analyzed in the summary of continuous values unless used as baseline data, but will be included in the laboratory or clinical shift tables as follows:

- Unscheduled/repeated tests will be included with the nearest regularly scheduled test. If there is a scheduled test and one or more unscheduled tests assigned to the same time point, the most conservative test (i.e., a test with low or high results) will be used.

- If it is not obvious which repeated/unscheduled result is more abnormal, then the results closest to the scheduled target day would be summarized in shift tables.

For Coagulation parameters, PT, PTT and INR, any repeated parameter will replace original scheduled visit values in the prior scheduled visit, for both change from baseline summaries, as well as shift tables.

7.3.3. Missing Data

In general, missing data will not be imputed, unless methods for handling missing data are specified. All study related data that is collected will be included in data listings that will accompany the clinical study report.

7.3.3.1. Missing Date Values

The following conventions will be used to impute missing portions of dates for adverse events and concomitant medications, if warranted. Note that the imputed values outlined here may

not always provide the most conservative date. In those circumstances, the imputed value may be replaced by a date that will lead to a more conservative analysis.

A. Start Dates
   1) If the year is unknown, then the date will not be imputed and will be assigned a missing value.
   2) If the month is unknown, then:
      i) If the year matches the first dose date year, then impute the month and day of the first dose date.
      ii) Otherwise, assign 'January.'
   3) If the day is unknown, then:
      i) If the month and year match the first dose date month and year, then impute the day of the first dose date.
      ii) Otherwise, assign the first day of the month.

B. Stop Dates
   1) If the year is unknown, then the date will not be imputed and will be assigned a missing value.
   2) If the month is unknown, then assign 'December.'
   3) If the day is unknown, then assign the last day of the month.

7.3.3.2. Missing Baseline Data

Every effort will be made to ensure that accurate baseline information on the patients is collected. In the event that a patient is missing baseline data, the patient will be included in appropriate analysis sets per definition in Section 7.1 but excluded from change from baseline analyses.

7.3.3.3. Missing Relationship and Severity in Adverse Events

During final analysis, adverse event relationships and severity grades will not be imputed. At the end of the study, all missing relationships and severity grades will be queried and completed.

7.3.3.4. Imputation Methods for Missing OCS Dose Data

OCS dosage levels will not be imputed, and those that are recorded as "ongoing" or are missing an end date in the collected OCS information will be assumed to have been taken up to the date of last visit. The data listings will not show an end date.

7.3.3.5. Multiple Imputation for PFT Parameters

For PFT, sensitivity analyses will be performed to evaluate the impact of missing data. Where an analysis is specified as "Including Imputation", it will be performed using the Multiple Imputation (MI) Fully Conditional Specification (FCS), using the proc mi procedure from SAS. The endpoints listed as "Key PFT endpoints" in Table 2 will be imputed by regressing on non-missing values of these variables at other timepoints. The number of imputations will be the percentage number of missingness. The following pseudo code will be used.

```
proc mi data=&pftparm._wide (where=(_NAME_ eq "FEV1PP")) seed=1234
        out=imputed_&pftparm._wide nimpute=pctmissing;
        fcs reg;
        var BASELINE WEEK_4 WEEK_8 WEEK_12 WEEK_16 WEEK_20 WEEK_24;
run;
```

Imputed values for Percent Predicted endpoints are restricted to 0 to 150 to ensure imputed values are consistent with values for patients with sarcoidosis and ensuring that impossible values are not produced (e.g. imputation of negative values).

7.3.4. Study Day

In the analyses described in this SAP, whenever possible, actual study day based on calendar days relative to Day 1 will be used whenever "study day" is mentioned. In cases where calendar date is not available, e.g. imputed instances, nominal days will be used.

7.3.5. Pooling of Investigational Sites

The data from all study centers will be pooled together for all planned analyses.

7.3.6. Coding Conventions for Events and Medications

All adverse events, and medical history will be mapped to the Medical Dictionary for Regulatory Activities (MedDRA Version 24.0) system for reporting (preferred term and body system).

Prior and Concomitant medications will be coded using WHO-DD (Drug Dictionary) (Version C3 Format- Mar 1, 2021).

7.3.7. Analysis Software

Data manipulation, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will be performed primarily using SAS (release 9.4 or higher) for Windows. PK parameterization will be performed via WinNonlin®. If the use of other software is warranted, the final clinical study report will detail what software was used and for what purposes.

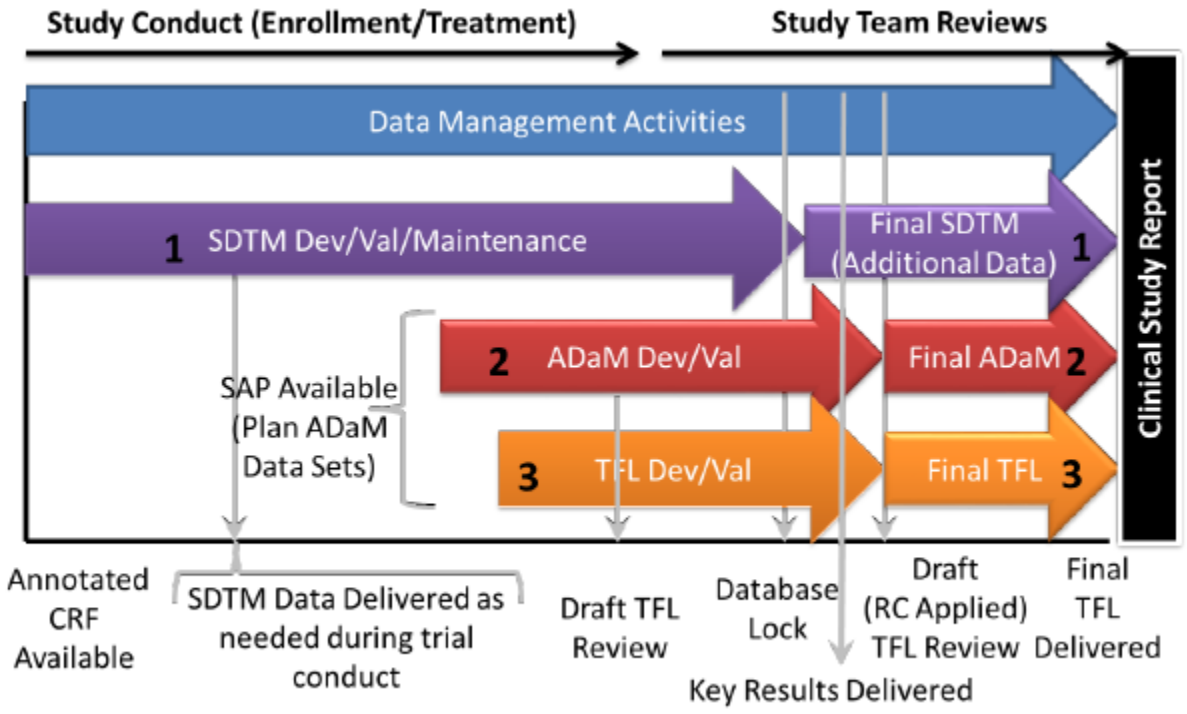
7.3.8. Study Data

Study data identified in the schedule for time and events (Table 1) are collected, and source verified, on the electronic data capture tool: Fusion eClinical Suites. Laboratory and efficacy data are provided from external laboratories and uploaded into the EDC.

Study data will be formulated into regulatory compliant data sets to provide transparency, traceability, and integrity of trial analysis results from the collection source. Observed study data will be mapped to the CDISC Study Data Tabulation Model (SDTM) and serve as the source data from the trial. All study analyses will be completed using analysis data sets that are derived from the SDTM and follow the CDISC Analysis Data Model (ADaM) architecture.

The methods for programming the CDISC SDTM and ADaM data sets are described in Figure 1.

Figure 1 SDTM, ADaM, and TFL Development and Validation



Where:

1. Development, Validation, and Maintenance of SDTM Domains
2. Development and Validation of Analysis Data Sets (ADaM), with input source the appropriate SDTM domains

3. Development and Validation of Tables, Figures, and Listings (TFL), with input data source the SDTM domains and analysis specific ADaM data sets

7.4. Planned Study Analyses

7.4.1. Statistical Summaries: Descriptive and Inferential

There will be no formal hypothesis testing for this study. All p-values shown from exploratory analyses will be rounded to and displayed in four decimals. If a p-value less than 0.0001 occurs it will be shown in tables as <0.0001.

Descriptive summaries of variables will be provided where appropriate. For continuous variables, the number of non-missing values (n), mean, standard deviation, median, minimum, and maximum will be tabulated by treatment. For categorical variables, the counts and proportions of each value will be tabulated by treatment. Expansion of descriptive table categories within each treatment may occur if such elaborations are thought to be useful.

7.4.2. Data Safety Monitoring Board (DSMB)

An independent DSMB will perform reviews of unblinded safety, tolerability, and immunogenicity data from each cohort and ad hoc, per Sponsor request, if a pattern of unexpected, clinically significant trends or changes in other safety assessments is identified through blinded safety data reviews. The analyses required by the DSMB will be detailed in the DSMB Charter.

7.4.3. Interim Analysis

No Interim analysis will be performed.

7.4.4. Criteria for Pausing Enrollment

In the event a serious unexpected suspected adverse reaction (SUSAR) has occurred, the enrollment and initiation of study drug administration to new patients will be paused and the Sponsor will request an unblinded review by the DSMB, who will provide its recommendation to aTyr Pharma. Such recommendation may include, but is not limited to, stopping an ongoing cohort, stopping further dose escalation, continuing the study as planned, or continuing the study with modifications, such as evaluation of a lower or intermediate dose in the next cohort(s) to gain more information on safety and tolerability.

7.4.5. Final Analysis and Publication of Study Results

The final analyses detailed in this document will be completed after all patients have terminated from this study.

7.5. Multiple Testing Procedures

Statistical tests performed in this study are exploratory, and no adjustments for multiplicity will be performed.

8. SUMMARY OF STUDY DATA

Unless otherwise specified, summaries will be presented by treatment arms, presenting all active arms individually, in addition to combined placebo arm and combined active arm.

8.1. Disposition

Patient disposition will be summarized and listed. All percentages will be based on the number of patients randomized in each arm.

The number of patients randomized by each site will be summarized. End of treatment and end of study information for all patients with a randomization number (randomized patients) will be summarized in this table, including the number of patients completing the study and the number of patients who terminated prematurely from the study, with reasons for withdrawal. The number of patients in each analysis set will also be summarized. The impact that COVID-19 had on patient disposition will also be summarized.

8.2. Protocol Deviations

Protocol deviations will be reported through EDC, and all information collected will be included in the SDTM.DV domain (deviations domain).

All patient-level protocol deviations will be presented in a data listing. A summary table will be generated based on the classification of patient-level protocol deviations.

8.3. Demographics and Baseline Characteristics

Patient demographic data as taken at screening, including age (continuous and categorical 18-64 and 65+), sex, ethnicity, and race will be summarized.

Baseline characteristics as collected on Day 1, including weight (kg), height (cm), BMI (kg/m^2), Baseline Dyspnea Index total score, Baseline Modified MRC Dyspnea scale score, key lung function variables, Sarcoidosis diagnosis at screening (all organ systems involved), and duration of disease will be summarized.

Also to be summarized are anti-sarcoidosis treatment at baseline (refer to Section 7.3.1 for baseline definition) including OCS type and dose categories (10 mg/day to <15 mg/day, 15 mg/day to <20 mg/day and 20 mg/day or higher), oral immunomodulator type at the time of baseline using the same baseline definition.

The demographic data and baseline characteristics will be summarized for the Safety, mITT and EE Sets. If they are the same, only mITT tables are needed.

A patient's age in years is calculated as (date of screening - date of birth)/365.25. BMI is calculated by dividing the weight of patient screening in kg by the square of their height in meters.

8.4. Concurrent Illness and Medical Conditions

The number and percentage of patients with individual concurrent illness and medical histories will be summarized. Individual patient listings will also be provided for concurrent illness and medical history.

Concurrent illness and medical history will be coded using the MedDRA Version 24.0. The number and percentage of patients with any medical history will be summarized overall and for each system organ class (SOC) and preferred term (PT). Percentages will be calculated based on number of patients in the Safety Set.

Patient medical history data including specific details will be presented in a listing.

8.5. Prior and Concomitant Medications

The number and percentages of concomitant medications and prior medications that are ongoing at the start of study drug will be summarized by Anatomical Therapeutic Chemical (ATC) level 2 and PT. The total number of prior/concomitant medications and the number and percentages of patients with at least 1 medication will be summarized. All summaries will be performed using the Safety Set. Similarly, non-OCS sarcoidosis medications will be summarized separately.

A listing will present all prior and concomitant medications. Non-OCS sarcoidosis medications will be presented in a separate listing.

A concomitant medication is defined as any medication taken on or after the day of first exposure to study drug up until 30 days after last dose of study drug.

A Prior medication is defined as any medication that the patient is started and stopped prior to the day of first exposure to study drug, collected from up to 30 days prior to Screening.

If a medication has a missing start date, then it is conservatively assumed to be both prior and concomitant only.

8.6. Non-Medication Therapies/Treatments

All non-medication therapies and treatments will be listed as collected using the Safety Set.

8.7. Treatment Administration and Exposure

Study drug will be administered at the study center. To ensure treatment compliance, administration of the study drug will be supervised by the Investigator or authorized designee.

The number of fully administered doses and total dose infused (as calculated by the sum of all administrated doses in mg) will be summarized and listed.

An exposure summary will be conducted using the Safety Set.

9. SAFETY ANALYSES

All Safety analyses will be conducted using the Safety Set.

9.1. Adverse Events

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 24.0. Adverse events will be recorded from the date of informed consent, throughout the clinical trial.

Treatment-emergent adverse events (TEAEs) are defined as any adverse event or worsening of an existing condition after initiation of the investigational product and through 30 days after the patient's last study visit (study completion or early termination).

If the onset of an AE is on Day 1, then the time of first dose, collected from the Study Drug Administration CRF, will be compared to the time of onset to determine if the AE is treatment-emergent. If the start time is reported as "unknown", the AE is classified as TEAE.

The number and percent of patients with any TEAEs as well as number of TEAEs will be summarized by system organ class and preferred term by treatment and overall. At each level of tabulation (ex. at the preferred term level) patients will be counted only once if they had more than one such event reported during the AE collection period.

Level of intensity will be assessed using the CTCAE grading.

The following summary tables and patient level listings will be presented for AE data:

- Overall summary of TEAEs, including the number and percentage of the following: any TEAEs, treatment-related TEAEs, Serious TEAEs, TEAEs leading to study drug withdrawal, leading to study drug interruption, TEAEs leading to deaths, Grade 3 or 4 TEAEs, TEAEs suspected to be infusion related;
- Summary table of TEAEs by SOC and PT;
- Summary table of TEAEs by PT;

- Summary table of TEAEs by highest relationship level to study drug by SOC and PT;
- Summary table of TEAEs by maximum intensity by SOC and PT;
- Summary table of serious TEAEs by SOC and PT;
- Summary table of suspected infusion related TEAEs by SOC and PT;
- Listing of suspected infusion related TEAEs;
- Listing of all Non-Treatment-Emergent AEs;
- Listing of all TEAEs;
- Listing of AEs leading to study drug interruption;
- Listing of AEs leading to study drug withdrawal;
- Listing of AEs leading to death;
- Listing of TEAEs of grade 3 or 4;
- Listing of Serious TEAEs.

In summary tables, missing data are imputed per rules established in Section 7.3.3.1.

9.2. Clinical Laboratory Evaluations

Clinical laboratory results will be summarized descriptively for each treatment group by timepoint for the observed value as well as for the change from baseline value. In addition, laboratory shift tables will be provided for all laboratory parameters where low/normal/high or abnormal/normal status can be ascertained. Listings of individual laboratory parameters by visit with normal ranges and abnormality assessments will also be provided.

In addition, since anticoagulation medication may affect coagulation parameters, each record will be examined by medical monitor. Coagulation parameters of Subjects with concomitant medications of warfarin sodium, apixaban, rivaroxaban between screening and end of treatment are excluded for all visits.

9.3. Vital Signs

Descriptive statistics of observed values will be presented for vital sign data by schedule study visit, including systolic blood pressure (mmHg), diastolic blood pressure (mmHg), oral temperature (℃), heart rate (bpm) and respiration (breaths/minute) by treatment group for patients. Changes from baseline to each scheduled post-baseline visit will be presented.

Listings of individual vital sign data will be provided.

9.4. 12-Lead ECG

PR interval, QRS duration, QTcF interval, QT interval and overall interpretation will be summarized in actual value and change from baseline by timepoint and treatment arm.

All 12-lead ECG data by patient will be presented in a listing.

9.5. Physical Examinations

A by-patient listing will be generated to display all physical examination information, including abbreviated.

10. SECONDARY ENDPOINT ANALYSES

The following analyses will be performed using the mITT Set. OCS and PFT related analyses will also be presented using the EE Set.

10.1. Potential Decrease in Background Oral Corticosteroid Dose

For analyses in this section, the data will be summarized in different ways if there are missing data values for OCS dose. For details see Section 7.3.3.4.

10.1.1. OCS Data Sources

The sources of OCS use are summarized in the table below.

Time of Use	Data Source	CRF Name	Comments
Historical and current use at Screening	OCS LOG	OCS Log - Prior and Current Use table	Historical use will be added here. An additional row for every change in steroid or dose
Steroid use beginning on Day 1	eDiary	Patient Diary	Patients will be entering a form every day and from that data we can pull out any dosing changes or changes in use
	OCS LOG (for subjects who do not have eDiary)	OCS Log - Prior and Current Use table	Study Coordinators will be responsible for recording any dosing changes or changes in steroid use in this table based on the paper diaries completed by the subject

Changes in Dose	eDiary and OCS LOG for subjects without eDiary	Patient Diary and OCS Log - Prior and Current Use table	

10.1.2. Steroid Dose Level Conversion

The dosage levels of OCS are collected as daily doses. For analysis purposes, the dose of any OCS other than prednisone or prednisolone will be converted to the prednisone equivalent dose using the following conversion factors:

Medication Term	Conversion factor
Prednisone	1
Prednisolone	1
Methylprednisolone	1.25
Triamcinolone	1.25
Dexamethasone	0.15
Betamethasone	0.12

10.1.3. Time adjusted OCS Burden

Time adjusted AUC is a measure of steroid burden and approximates the mean steroid usage post-baseline for each patient. For each patient, it is calculated and summarized as follows,

$$Time\ Adjusted\ AUC = \sum_{t=M}^{N-1} \frac{AUC}{N-M} = \sum_{t=M}^{N-1} \frac{(C_t + C_{t\prime})(t\prime - t)}{2(N-M)},$$

where

C_x is the OCS dose in mg on day x,

t' is the study day of the next known OCS daily dose after day t,

M and N are start and end study days of the analysis periods of interest. In this study, we are interested in the time periods a) Day 1 through end of dosing period (30 days after last dose) or day of last known OCS dose (if earlier than end of dosing period) and b) Day 51 through end of dosing period (30 days after last dose) or day of last known OCS dose (if earlier than end of dosing period).

Similarly, change from baseline and percent change from baseline at each diary entry will be used as C_x in the formula above, and analyses will be repeated.

In addition, active treatment arm for each cohort and combined active arm are compared to combined placebo using the following pseudo code.

```
proc glm data = auc;
       class treatment(ref=Placebo);
       model auc = treatment baselineOCS / solution;
       lsmeans treatment / pdiff=control("Placebo") adjust=T cl;
run;
```

The difference between LS means, 95% Confidence Intervals and p-values will be presented.

Time adjusted AUC for Day 1/51 through end of treatment periods will be summarized using density and box plots by treatment.

10.1.4. Study Drug Adjusted OCS Burden

Since a missed dose in study treatment is likely to affect OCS dose, in order to isolate the effect of treatment, the above mentioned OCS dose, change from baseline and percent change from baseline analyses will be repeated, but excluding a window around a missed dose of study treatment, where a window is defined as 30 days after the previous dose and restart on the day of the next administered dose. Active treatment and placebo will be compared in the same way as in time adjusted OCS burden in the previous section.

10.1.5. Achievement of Target Taper Dose of Prednisone 5 mg/day (or Equivalent) and Maintained Through Week 24

The number and percentage of patients who have achieved the following will be summarized.

1. **Ability to Taper:** Taper OCS dose level down to 5mg/day or less at any time and remained for at least 5 consecutive days.

2. **Maintain Taper:**

    a. Taper OCS dose level down to 5mg/day or less at any time and remained for at least 30 consecutive days.

    b. Taper OCS dose level down to 5mg/day or less at any time and remained for at least 60 consecutive days.

    c. Taper OCS dose level down to 5mg/day or less at any time and remained for at least 90 consecutive days.

    d. Taper OCS dose level down to 5mg/day or less at any time and remained for at least 115 consecutive days

e. Time to first relapse of taper for sarcoidosis. Defined as the duration from the first day of hitting 5mg (plus 5 consecutive days) to when >5mg is needed. If the reason for increase in OCS is unrelated to sarcoidosis (as identified from the eCRF) then that episode will not count as a relapse and counting of the duration will recommence on the next day on which 5mg is achieved. For patients who maintain 5mg after successful taper will be censored at 30 days after last dose or EOS (if earlier). Patients who never reach 5 mg will be assigned a duration of 1 day and be classified as a censored data point.

f. Proportion of days at 5mg or less ignoring diary days when OCS dose was increased >5mg for non-sarcoidosis events (i.e. same exclusion as the Time to First Relapse endpoint)

g. Proportion of days at 5mg or less including all diary days (i.e. even those when OCS dose was increased >5mg for non-sarcoidosis events)

In each of the above endpoints, when study drug dosing is missed, OCS diary data >30 days after previous study drug infusion will be ignored until dosing restarted as described in Section 10.1.4.

For each of the first 4 taper maintenance endpoints above, 2-sided Fisher's exact test will be performed between each individual active treatment arm and combined placebo, using the pseudo code below.

```
proc freq data = taper (where=(treatment in ("Treatment A", "Placebo")));
       table taper_var*treatment / fisher;
run;
```

For the 5th of the "Maintain taper" endpoints (i.e. Time to first relapse of taper), Kaplan-Meier methods will be used to derive estimates of median (& 95% CI) of the time to first taper relapse. A log-rank test will be performed between each individual/combined active treatment arm and placebo to obtain p-values versus placebo. Kaplan-Meier curve will be presented as well. The following pseudo SAS code is used.

```
proc lifetest;
    time duration*status(0);
strata treatment / test=logrank;
run;

where 0 indicates no relapse.
```

For 6th and 7th of the "Maintain taper" endpoints (i.e. Proportion of days at 5mg or less) descriptive statistics (Mean, SD etc) will be used to informally compare groups. A Wilcoxon rank sum test will be performed between each individual/combined active treatment arm and placebo to obtain p-values versus placebo. The following pseudo SAS code will be used.

```
proc npar1way wilcoxon correct=no;
   class treatment;
   var days_at_5mg;
   exact wilcoxon;
run;
```

10.1.6. OCS Dose-Time Profiles

The dose of OCS taken by individual patients on each day according to the OCS diary will be plotted against study day, to show individual OCS dose-time profiles. Similarly, the average OCS dose across subjects for each day per dose group will be plotted against study day. The change from baseline OCS across subjects for each day per dose group will also be plotted against study day. These profile plots will be presented separately for each dose cohort.

One set of plots will have standard errors associated, while another without.

10.1.7. OCS Burden by Baseline characteristics

Each time adjusted AUC for Day 1/51 through end of treatment periods will be summarized using density and box plots against baseline characteristics by treatment. The following baseline parameter and categories will be used.

1. Density and box plots overall, not by treatment.
2. Baseline dyspnea as summarized by BDI total score, in categories of 5 or less and 6 or more.
3. Baseline dyspnea as summarized MRC grade 1 vs. grade 2 or higher.
4. Baseline OCS level (10mg/day vs. >10mg/day),
5. Baseline FEV1 PP 80% or higher vs. below 80%.
6. Baseline FVC PP 80% or higher vs. below 80%.
7. Baseline DLco PP 80% or higher vs. below 80%.
8. Disease duration (>= median duration vs. < median duration).
9. Sex
10. Race of African American vs. Non-African American (not including missing).

10.2. Immunogenicity

ADA and anti-Jo 1 analyses will use the mITT Set

10.2.1. Incidence and Titer of Positive ADA (anti-ATYR1923).

The number and percentage of patients with ADA titers at any visit (by maximum individual ADA titer), will be summarized, and all ADA data will be listed.

Analysis of ADA results according to published definitions (Shankar et al, 2014) will include

ADA Prevalence: The proportion of all individuals having drug reactive antibodies at any point in time (ATYR1923 and placebo subjects).

Baseline ADA Incidence: The proportion of pre-dose ADA-positive subjects as a percentage of total number of subjects (ATYR1923 and placebo subjects).

Treatment-induced ADA Incidence: The proportion of individuals with ADA any time after ATYR1923 treatment that were ADA negative at baseline.

Treatment-boosted ADA incidence: The proportion of individuals that were ADA positive at baseline who had significant increases in ADA after ATYR1923 treatment.
ADA may be analyzed by subgroup.

If warranted, kinetic analyses of ADA over time may be performed.

10.2.2. Incidence and Titer of Positive anti-Jo 1 Ab

The number and percentage of patients with negative (≤7 U/mL), equivocal (7-10 U/mL), or positive (>10 U/mL) maximum anti-Jo 1 Ab levels over all scheduled sampling visit will be summarized by treatment group. All anti-Jo 1 Ab data will be listed.

10.2.3. Relationship between Immunogenicity and Adverse Events

Post-hoc analyses may be performed to assess the difference in AE profiles among different immunogenicity titer levels.

11. EXPLORATORY ANALYSES

11.1. Clinical and Biomarker Measures

The following measures (continuous) will be summarized in actual values, change and percent change from baseline for each measured visit. If a parameter is missing at baseline, then the patient will not be included in the analysis of change and percent change from baseline for this parameter. If a post-baseline parameter is missing, then the patient will not be included for that visit in both actual values, change and percent change from baseline. The mITT Set will be used for the analyses below. In addition, all PFT and Quality of Life Questionnaire summaries will also be presented in the EE Set.

Additional exploratory analyses of biomarker data may be performed that is beyond the scope of this SAP and the results from such analyses will be described in a separate report and/or publications.

11.1.1. Pulmonary Function Tests (PFT)

Key PFT Endpoints

Due to patient-to-patient variability with observed values of PFT measurements (FEV1, FVC, DLco etc), the Percent Predicted ("PP") versions of these endpoints will be the key PFT endpoints for summary, statistical analyses and interpretation of lung function in ATYR1923-C-002. Additional key PFT endpoints are listed in Table 2 below.

PFT endpoints that are not classified as Key PFT endpoints will be termed "Supportive PFT endpoints". Where it is warranted, descriptive summaries and/or plots may be produced for some of the Supportive PFT endpoints. All PFT data will appear in the data listings.

Key PFT Timepoints
For tables and figures, all scheduled visits (Baseline, Weeks 4, 8, 12, 16, 20, 24. except DLco measures at Baseline, Weeks 12, 20 and 24) will be presented, though Baseline, Weeks 4, 16 and 24 are the main timepoints of interest for interpretation of the study.

Table 2 PFT Endpoint Classification with Planned Summaries and Statistical Analyses

Endpoint classification	Descriptive Statistics				Endpoint Derivations*			Statistical Modeling	
	Absolute value at each Visit	Change from Baseline at each Visit	% Change from Baseline at each Visit	Line Plot by Treat-ment	Categorized Change from Baseline at each Visit (+/- 5%)	Categorized Change from Baseline at each Visit (+/-10%)	Worsen-ing	MMRM (on Absolute Value with Baseline as covariate)	RCRM (on Absolute Value with Baseline as covariate)
Key PFT Endpoints									
PP FEV_1 (%)	x	x	x	x	x	x		x	x
PP FVC (%)	x	x	x	x	x	x	x	x	x
PP FEV_1/FVC (%)	x	x	x	x	x	x		x	x
PP DLco (%)	x	x	x	x	x	x		x	x
PP DLco adjusted for HgB (%)	x	x	x	x	x	x		x	x
DLco/VA adjusted for HgB	x	x	x	x	x	x		x	x
Supportive PFT Endpoints									
FEV_1 (L)	x	x	x	x					
FVC (L)	x	x	x	x					
FEV_1 /FVC	x	x	x	x					
DLco	x	x	x	x					

Endpoint classification	Descriptive Statistics				Endpoint Derivations*			Statistical Modeling	
	Absolute value at each Visit	Change from Baseline at each Visit	% Change from Baseline at each Visit	Line Plot by Treat-ment	Categorized Change from Baseline at each Visit (+/- 5%)	Categorized Change from Baseline at each Visit (+/-10%)	Worsen-ing	MMRM (on Absolute Value with Baseline as covariate)	RCRM (on Absolute Value with Baseline as covariate)
DLco adjusted for HgB	x	x	x	x					
VA	x	x	x	x					
DLco/VA	x	x	x	x					
PEF (L/min)	x	x	x	x					
IVC	x	x	x	x					

* Endpoint derivations:

Endpoint	Derivation rule	Handling of missing values	Statistical analysis
Categorized changes (+/- 5%, +/-10%)	Decrease >5%, Within +/-5%, Increase >5%. Similarly for 10%. For the first 5 key parameters, change here refers to post-baseline minus baseline in the percent predicted. For the DLco/VA adjusted for HgB, this change refers to post-baseline minus baseline divided by baseline.	Missing values are excluded from the "n" count in the summary table	Frequency tables by-visit. Mean PFT value by treatment is plotted against study day. No statistical hypothesis testing to be performed.
Worsening	Two consecutive values with decreases of >5% from baseline. The percent change	If there are 1 or more missed visits between 2 values below the 5% cutoff then classify the patient as Worsened. Rationale is that we	statistical analytical modeling will be performed as detailed in Sections 11.1.1.1 and11.1.1.2.

	here is calculated similarly as the row above.	implicitly assume that the patient has stayed below the cutoff during those missing visits	

11.1.1.1. Mixed Model Repeated Measures Analysis (MMRM)

The absolute values specific parameters specified in Table 2 will be analyzed using a mixed linear model. Treatment and baseline are included as fixed effects. Repeated effect is included for visit. Restricted maximum likelihood method and Kenward and Roger (1997) method for degrees-of-freedom will be used. If a subject's baseline value is missing for a given parameter, then the subject is removed from that parameter's analysis.

This same analysis will be performed with and without multiple imputation as described in Section 7.3.3.5 Each individual/combined active arm will be compared with combined placebo arm.

Unstructured covariance structure will be used, but if convergence is not achieved, then compound symmetry (type=cs) covariance structure will be used.

The following pseudo code will be used.

```
proc mixed data = imputed method=reml;
       by _imputation_;
       class trt01p(ref='Placebo')  avisit usubjid;
       model FEV1PP = trt01p avisit trt01p*avisit base / ddfm=kr;
       repeated / subject=usubjid type=un;
       lsmeans  trt01p*avisit /pdiff=all cl;
       ods output diffs=lsmdiffs1;
run;

proc mianalyze parms(classvar=full)=lsmdiffs1;
       class trt01p _trt01p avisit _avisit;
       modeleffects trt01p*avisit;
       ods output ParameterEstimates=lsmdiffEstimate;
run;
```

11.1.1.2. Random Coefficient Regression Model (RCRM)

Table 2 lists key variables that will also be analyzed in RCRM. This model will include treatment, baseline value and treatment-by-time interaction as fixed effects. Both intercept and continuous time in days are included as random effects. Unstructured covariance structures will be used for slope and intercept. If convergence is not achieved, then compound symmetry covariance structure (type=cs) is used and/or the random intercept may be removed. Restricted maximum likelihood and Kenward Rogers (1997) method for degrees-of-freedom will be used.

This same analysis will be performed with and without multiple imputation as described in Section 7.3.3.5. Each individual/combined active arm will be compared with combined placebo arm.

Pseudo code below will be used.

For comparing individual arms with placebo:

```
proc mixed data=imputed method=reml;
     class TRT01P(ref='Placebo') usubjid;
     by _imputation_;
     model &pftparm.=TRT01P BASE TRT01P*ady/noint  solution ddfm=kr;
     random intercept ady/subject=usubjid type=un; *unstructured covariance
     structure had half of the trials not converge;
     estimate 'A_V_P' TRT01P*ady 1 0 0 -1/ CL;
     estimate 'B_V_P' TRT01P*ady 0 1 0 -1/ CL;
     estimate 'C_V_P' TRT01P*ady 0 0 1 -1/ CL;
     estimate 'T_V_P' TRT01P*ady 1 1 1 -3/ CL divisor=3;
     ods output Estimates=ran_coef_est(rename=(label=effect));
run;

proc mianalyze parms(classvar=full)=ran_coef_est;
     *class A_V_P B_V_P B_V_P A_V_B B_V_C A_V_C;
     modeleffects A_V_P B_V_P C_V_P A_V_B B_V_C A_V_C;
     ods output ParameterEstimates=rcrm_est;
run;
```

For combined active vs. placebo:

```
proc mixed data=imputed method=reml;
     class TRT01P(ref='Placebo') usubjid;
     by _imputation_;
     model &pftparm.=TRT01P BASE TRT01P*ady/noint  solution ddfm=kr;
     random intercept ady/subject=usubjid type=un; *unstructured covariance
     structure had half of the trials not converge;
     estimate 'A_V_P' TRT01P*ady 1 0 0 -1/ CL;
     ods output Estimates=ran_coef_est(rename=(label=effect));
run;

proc mianalyze parms(classvar=full)=ran_coef_est;
     class A_V_P;
     modeleffects A_V_P;
     ods output ParameterEstimates=rcrm_est;
run;
```

11.1.2. Whole body 18F-FDG-PET/CT

SUV_{max} as measured by whole body ^{18}F-FDG-PET/CT at screening and week 16/early termination visits. Patients with glucose levels above 11 mmol/L (200 mg/dL) have their scan delayed or be rescheduled as appropriate. Patients who did not have measures both at screening and at Week 16 (+/- 3 days) will not be included in change from baseline calculations, but will be included in by absolute value summaries. The measure may also be performed during an unscheduled visit within 3 days of the week 16 visit. If a patient has no

measures at Week 16/early termination visit, but has an unscheduled visit within 3 days of week 16/early termination visit, then the unscheduled visit will be used.

The three end points for PET scan will be as follows –

- Change from baseline in the highest SUVMax for an entire region - lung
- Change from baseline in the highest SUVMax for an entire region - lymph nodes
- Change from baseline in the highest SUVMax for an entire region - extra thoracic

Baseline SUV Max is the highest SUV max for all the focal lesions in a given region (e.g. lung). Post baseline SUV max is the highest SUV max for all the focal lesions in a given region (e.g. lung). It is noted that the baseline and post baseline highest SUV max may not be in the same focal lesion but will be in the same region.

Boxplots will also be created for SUV max by treatment by timepoint. Separate plots will be created for each region.

11.1.3. Health-Related Quality of Life

Health-Related Quality of Life, as assessed by the SAT, SAC BDI-TDI, KSQ, LCQ, and FAS. Scores and change from baseline for each questionnaire are summarized and listed using the mITT and EE Set.

For the change from baseline for each subscore or total score below, individual/combined active treatment arm will be compared to placebo using the pseudo code below. The integer scores are treated as continuous. Restricted maximum likelihood and Kenward Rogers (1997) method for degrees-of-freedom will be used.

```
proc mixed data = score method=reml;
       class trt01p(ref='Placebo') avisit usubjid;
       model change_from_baseline = trt01p avisit trt01p*avisit base / ddfm=kr;
       repeated / subject=usubjid type=un;
       lsmeans  trt01p*avisit /pdiff=all cl;
run;
```

11.1.3.1. Sarcoidosis Assessment Tool (SAT)

The SAT is a sarcoidosis-specific patient-reported outcome developed for use in sarcoidosis clinical studies to measure the patient's assessment of impact of disease and response to therapy. It utilizes Item Response Theory to allow the use of a short questionnaire.

The questionnaire contains 8 subscales:

1. Physical Functioning (daily activities) (6 Questions)
2. Satisfaction with Roles and Activities (5 Questions)

3. Pain Interference (5 Questions)
4. Sleep Disturbance (5 Questions)
5. Fatigue (5 Questions)
6. Sarcoidosis-Lung Concerns (10 Questions)
7. Sarcoidosis-Skin Concerns (10 Questions)
8. Sarcoidosis-Stigma (embarrassment) (5 Questions)

The scoring of this questionnaire is done via a SAS macro provided by Victorson *et al* (2013).

Each instance of a subscale needs to contain at least 4 valid responses in order to be scored. Subscale scores will be rounded to the first decimal place. All subscale scores and change from baseline will be summarized by treatment and listed. No total score will be calculated.

This tool is currently experimental, and the results will also be treated as exploratory.

11.1.3.2. The Self-Administered Computerized Baseline and Transitional Dyspnea Indices (SAC BDI-TDI)

The BDI measures the severity of dyspnea at the baseline (or the beginning of a clinical study), and the TDI measures changes from this baseline (transition period) at subsequent visits. The BDI and TDI each contain 3 domains including functional impairment, magnitude of task, and magnitude of effort. The lower the score on the BDI, the worse the severity of dyspnea at baseline and the lower the score on the TDI, the more deterioration in the severity of dyspnea. The minimal clinically important difference of the TDI is a total score of 1.

The BDI is administered on Day 1, while the TDI is administered at Weeks 4, 8, 12, 16, 20 and 24/Early Termination visits.

The total score for BDI will be the summation of all 3 domains. TDI total scores are the summation of all 3 domains divided by 2. If any individual item is missing, then the total score is missing. If the BDI for a subject is missing, the TDI can still be included in analyses. BDI and TDI domains and total scores will be summarized separately by visit and treatment. Individual items for BDI and TDI will be listed together.

11.1.3.3. King’s Sarcoidosis Questionnaire (KSQ)

The KSQ is a 29-item questionnaire to be completed by patients, with 5 domains:

1. General health status (GHS),
2. Lungs,
3. Medication,

4. Skin, and

5. Eyes.

The KSQ is administered on Day 1 and Weeks 4, 8, 12, 16, 20 and 24/Early Termination Visits. All 5 domains and the GHS-Lung score, scored using logit scores with each logit score ranging from 0 and 100 (except the GHS-Lung score which is the sum of the GHS and Lungs scores and ranges from 0 to 200), and change from baseline will be summarized by visit and treatment. The domains and the GHS-Lung score will be listed. See Appendix 1: King's Sarcoidosis Questionnaire (KSQ) scoring information for further details on KSQ scoring.

11.1.3.4. Leicester Cough Questionnaire (LCQ)

The LCQ is a 19-item self-completed quality of life measure of chronic cough. Items on the scale are divided into 3 domains, physical, psychological, and social. Items are scored on a 7-point Likert scale. The individual domain scores are averages of all questions within the domain (ranging 1-7). A total score (range 3 to 21) is also calculated by adding the domain scores together, with higher scores indicating better quality of life. The minimal clinically important difference (MCID) for chronic cough is 1.3. The LCQ is administered on Day 1 and Weeks 4, 8, 12, 16, 20 and 24/Early Termination Visits. The total and 3 domain scores and change from baseline will be summarized by visit and treatment, as well as being listed with domain scores.

If a question is missing, then the corresponding domain score is set to missing, and the total score is also missing.

11.1.3.5. Fatigue Assessment Scale (FAS)

The FAS contains 10 fatigue questions rated from 1=never to 5=always (about everyday). Missing individual scores are not permitted. Scores on questions 4 and 10 should be recoded (1=5, 2=4, 3=3, 4=2, 5=1). Subsequently, the total FAS score can be calculated by summing the scores on all questions (the recoded scores for question 4 and 10). The sum of questions 3 and 6–9 indicates mental fatigue, and the sum of the questions 1, 2, 4, 5 and 10 indicates physical fatigue. The minimal score is 10, and the maximal score is 50. Scores of ≥22 are considered to represent substantial fatigue (Drent *et al*, 2012). A change in the FAS score of 4 points is considered to be the MCID. The FAS is administered on Day 1 and Weeks 4, 8, 12, 16, 20 and 24/Early Termination Visits.

The total score, mental fatigue score and physical fatigue score, as well as their change from baseline will be summarized by visit and treatment. A shift table for total score (Substantial fatigue vs. Moderate fatigue or lower) will be produced by visit and treatment. Individual item scores will be listed.

11.1.4. Skin Lesions Assessments

Skin lesion assessments are conducted at Screening (Baseline) and Weeks 2, 4, 8, 12, 16, 20.

Skin Physician Global Assessment (SPGA), scored 0 to 10 using visual analogue scale, with 0 being No Disease, and 10 being as severe as it could be. SPGA information will be listed.

The Sarcoidosis Activity and Severity Index (SASI) is an instrument that will be used to evaluate a lesion prospectively identified as the 'target' lesion, located anywhere on the body. The Investigator will score the extent of erythema and induration of this lesion, each on a scale ranging from 0 (none) to 4 (very severe). At each instance, erythema, induration and total score (erythema + induration) will be listed. . If either subscore is missing, the total score is set as missing.

All skin lesion assessments will be listed.

11.1.5. Serum and Tissue Biomarkers

The following biomarkers will be summarized for change from baseline and listed by treatment.

- ACE, neopterin, and sIL2R (disease serum biomarkers) collected on Day 1, Weeks 12, 20 and End of Study Visits.
- Extracellular histidyl-tRNA synthetase (HARS), NRP2, and VEGFC (pathway serum biomarkers) collected on Day 1, Weeks 12, 20 and End of Study Visits.
- State of immune cell anergy in peripheral blood mononuclear cells (PBMCs) collected on Day 1, Week 12 and End of Study Visits.
- Histopathology (skin biopsy) at screening and week 12, and only for selected sites.

12. PHARMACOKINETIC (PK) ANALYSES

Full details on all PK analyses will be provided in separate analysis plans.

13. REFERENCES

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APPENDIX 1: KING'S SARCOIDOSIS QUESTIONNAIRE (KSQ) SCORING INFORMATION

Calculating the logit scores in KSQ as obtained directly from vendor.

Notes

1. Example below is for the General Health Status domain. Use the same principle for other domains and combinations of domains.
2. The most useful scores are the 5 domain scores GHS, Lung, Skin, Eyes and Medications. Combination of domain scores are possible but usually not necessary (GHS-Lung is best when a single combined score is required rather than individual domain scores).
3. If more than 50% of the answer of a given module is missing, then the module score is considered missing. Combined score of multiple modules is then also considered missing.
4. If 50% or fewer of the questions have missing or invalid results, then the missing scores are replaced with module averages in the original score before re-score.

Step 1: Check the raw item responses as completed by the patient

Quality of life-QOL Domain (General health status)

	In the last 2 weeks...	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	Hardly any of the time	None of the time
1	I have felt frustrated	1	2	3	4	5	6	7
2	I have had trouble concentrating	1	2	3	4	5	6	7
3	I have lacked motivation	1	2	3	4	5	6	7
4	I have felt tired	1	2	3	4	5	6	7
5	I have felt anxious	1	2	3	4	5	6	7
6	I have felt aches and pains in my muscles/joints	1	2	3	4	5	6	7
7	I have felt embarrassed	1	2	3	4	5	6	7
8	I have worried about my weight	1	2	3	4	5	6	7
9	I have worried about my sarcoidosis	1	2	3	4	5	6	7

	In the last 2 weeks...	A huge amount	Considerable amount	A moderate amount	A Modest amount	A small amount	A tiny amount	None at all
10	Tiredness has interfered with my normal social activities such as going out with friends/family	1	2	3	4	5	6	7

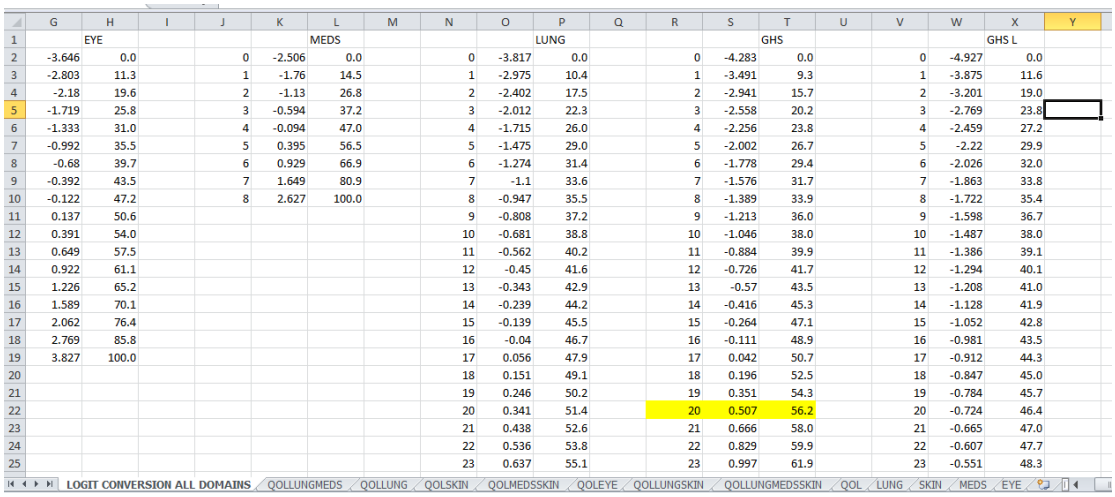
Step 2: Convert these raw individual scores into the re-scores using the Recoding Matrix.

For example, as patient responded to item 1 with "4", look up rescore value in QOL TAB. This score now is converted to "3." See screenshot below.

	A	B	C	D	E	F	G	H	I	J	K
1	Item	Max Score	Rescored	1	2	3	4	5	6	7	
2	I0001	4	Y	0	1	2	3	3	4	4	
3	I0002	6		0	1	2	3	4	5	6	
4	I0003	3	Y	0	1	1	2	2	3	3	
5	I0004	6		0	1	2	3	4	5	6	
6	I0005	3	Y	0	1	2	2	3	3	3	
7	I0006	2	Y	0	0	1	1	1	2	2	
8	I0007	3	Y	0	0	0	1	2	2	3	
9	I0008	2	Y	0	0	1	1	1	2	2	
10	I0009	2	Y	0	0	1	1	1	2	2	
11	I0010	2	Y	0	0	1	1	1	2	2	
12											
13		33									
14											
15											

Therefore, re-score total is 20.

Step 3: Convert the re-score total into the logit 0-100 scale by using the logit conversion list and looking up the appropriate domain, e.g. GHS.



	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
1		EYE				MEDS				LUNG				GHS				GHS L	
2	-3.646	0.0		0	-2.506	0.0		0	-3.817	0.0		0	-4.283	0.0		0	-4.927	0.0	
3	-2.803	11.3		1	-1.76	14.5		1	-2.975	10.4		1	-3.491	9.3		1	-3.875	11.6	
4	-2.18	19.6		2	-1.13	26.8		2	-2.402	17.5		2	-2.941	15.7		2	-3.201	19.0	
5	-1.719	25.8		3	-0.594	37.2		3	-2.012	22.3		3	-2.558	20.2		3	-2.769	23.8	
6	-1.333	31.0		4	-0.094	47.0		4	-1.715	26.0		4	-2.256	23.8		4	-2.459	27.2	
7	-0.992	35.5		5	0.395	56.5		5	-1.475	29.0		5	-2.002	26.7		5	-2.22	29.9	
8	-0.68	39.7		6	0.929	66.9		6	-1.274	31.4		6	-1.778	29.4		6	-2.026	32.0	
9	-0.392	43.5		7	1.649	80.9		7	-1.1	33.6		7	-1.576	31.7		7	-1.863	33.8	
10	-0.122	47.2		8	2.627	100.0		8	-0.947	35.5		8	-1.389	33.9		8	-1.722	35.4	
11	0.137	50.6						9	-0.808	37.2		9	-1.213	36.0		9	-1.598	36.7	
12	0.391	54.0						10	-0.681	38.8		10	-1.046	38.0		10	-1.487	38.0	
13	0.649	57.5						11	-0.562	40.2		11	-0.884	39.9		11	-1.386	39.1	
14	0.922	61.1						12	-0.45	41.6		12	-0.726	41.7		12	-1.294	40.1	
15	1.226	65.2						13	-0.343	42.9		13	-0.57	43.5		13	-1.208	41.0	
16	1.589	70.1						14	-0.239	44.2		14	-0.416	45.3		14	-1.128	41.9	
17	2.062	76.4						15	-0.139	45.5		15	-0.264	47.1		15	-1.052	42.8	
18	2.769	85.8						16	-0.04	46.7		16	-0.111	48.9		16	-0.981	43.5	
19	3.827	100.0						17	0.056	47.9		17	0.042	50.7		17	-0.912	44.3	
20								18	0.151	49.1		18	0.196	52.5		18	-0.847	45.0	
21								19	0.246	50.2		19	0.351	54.3		19	-0.784	45.7	
22								20	0.341	51.4		20	0.507	56.2		20	-0.724	46.4	
23								21	0.438	52.6		21	0.666	58.0		21	-0.665	47.0	
24								22	0.536	53.8		22	0.829	59.9		22	-0.607	47.7	
25								23	0.637	55.1		23	0.997	61.9		23	-0.551	48.3	

LOGIT CONVERSION ALL DOMAINS | QOLLUNGMEDS | QOLLUNG | QOLSKIN | QOLMEDSSKIN | QOLEYE | QOLLUNGSKIN | QOLLUNGMEDSSKIN | QOL | LUNG | SKIN | MEDS | EYE

Therefore, the 0-100 logit score is 56.2 in this case. This is the GHS domain final score. (Range of all domains is 0-100)

Recoding Matrix

Original Score	Recoded Score						
	1	**2**	**3**	**4**	**5**	**6**	**7**
1	0	1	2	3	3	4	4
2	0	1	2	3	4	5	6
3	0	1	1	2	2	3	3
4	0	1	2	3	4	5	6
5	0	1	2	2	3	3	3
6	0	0	1	1	1	2	2
7	0	0	0	1	2	2	3
8	0	0	1	1	1	2	2
9	0	0	1	1	1	2	2
10	0	0	1	1	1	2	2
11	0	1	2	3	4	4	5
12	0	1	2	3	4	5	6
13	0	1	2	3	4	5	6
14	0	1	2	3	4	5	6
15	0	1	2	3	4	5	6
16	0	1	2	3	4	4	5
17	0	1	2	2	2	3	3
18	0	1	2	2	2	3	3
19	0	0	1	1	1	1	2
20	0	1	2	2	2	3	4
21	0	1	1	2	2	2	3

22	0	0	1	1	1	2	2
23	0	0	1	1	1	2	2
24	0	1	2	2	2	2	3
25	0	1	2	2	2	3	3
26	0	0	1	1	1	2	2
27	0	0	1	1	1	2	2
28	0	0	0	1	1	2	3
29	0	0	1	1	1	1	2

Logit Conversion:

GHS	Logit	Lung	Logit	Med	Logit
0	0	0	0	0	0
1	9.3	1	10.4	1	14.5
2	15.7	2	17.5	2	26.8
3	20.2	3	22.3	3	37.2
4	23.8	4	26	4	47
5	26.7	5	29	5	56.5
6	29.4	6	31.4	6	66.9
7	31.7	7	33.6	7	80.9
8	33.9	8	35.5	8	100
9	36	9	37.2		
10	38	10	38.8		
11	39.9	11	40.2		
12	41.7	12	41.6		
13	43.5	13	42.9		
14	45.3	14	44.2		
15	47.1	15	45.5		
16	48.9	16	46.7		
17	50.7	17	47.9		
18	52.5	18	49.1		
19	54.3	19	50.2		
20	56.2	20	51.4		
21	58	21	52.6		
22	59.9	22	53.8		
23	61.9	23	55.1		
24	63.9	24	56.4		
25	66.1	25	57.8		
26	68.4	26	59.3		
27	70.9	27	61		
28	73.6	28	62.9		
29	76.7	29	65.2		
30	80.3	30	68		

31	84.7	31	71.7
32	91	32	77.1
33	100	33	85.8
		34	100

Skin	Logit	Eye	Logit	GHS L	Logit
0	0	0	0	0	0
1	13.7	1	11.3	1	11.6
2	25.4	2	19.6	2	19
3	35.4	3	25.8	3	23.8
4	44.7	4	31	4	27.2
5	53.8	5	35.5	5	29.9
6	63.3	6	39.7	6	32
7	73.7	7	43.5	7	33.8
8	86.1	8	47.2	8	35.4
9	100	9	50.6	9	36.7
		10	54	10	38
		11	57.5	11	39.1
		12	61.1	12	40.1
		13	65.2	13	41
		14	70.1	14	41.9
		15	76.4	15	42.8
		16	85.8	16	43.5
		17	100	17	44.3
				18	45
				19	45.7
				20	46.4
				21	47
				22	47.7
				23	48.3
				24	48.9
				25	49.5
				26	50.1
				27	50.7
				28	51.2
				29	51.8
				30	52.4
				31	52.9
				32	53.5
				33	54.1
				34	54.6
				35	55.2
				36	55.8

37	56.4
38	56.9
39	57.5
40	58.1
41	58.7
42	59.3
43	59.9
44	60.5
45	61.2
46	61.8
47	62.5
48	63.2
49	63.9
50	64.7
51	65.4
52	66.2
53	67.1
54	68
55	68.9
56	69.9
57	71
58	72.1
59	73.3
60	74.7
61	76.2
62	77.9
63	80
64	82.6
65	86.1
66	91.5
67	100

GHS S	Logit	GHS E	Logit	GHS LS	Logit
0	0	0	0	0	0
1	9	1	9.1	1	8.5
2	15	2	15.3	2	14.1
3	19.2	3	19.5	3	17.9
4	22.3	4	22.8	4	20.6
5	25	5	25.5	5	22.8
6	27.3	6	27.8	6	24.6
7	29.3	7	29.8	7	26.2
8	31.1	8	31.7	8	27.5

9	32.8	9	33.4	9	28.7
10	34.3	10	34.9	10	29.8
11	35.8	11	36.4	11	30.7
12	37.1	12	37.7	12	31.6
13	38.4	13	39	13	32.4
14	39.6	14	40.2	14	33.1
15	40.8	15	41.4	15	33.8
16	41.9	16	42.5	16	34.5
17	43	17	43.5	17	35.1
18	44.1	18	44.5	18	35.6
19	45.1	19	45.5	19	36.2
20	46.1	20	46.5	20	36.7
21	47.2	21	47.5	21	37.2
22	48.2	22	48.4	22	37.7
23	49.2	23	49.3	23	38.2
24	50.2	24	50.2	24	38.7
25	51.2	25	51.1	25	39.1
26	52.2	26	52	26	39.5
27	53.2	27	52.9	27	40
28	54.3	28	53.8	28	40.4
29	55.4	29	54.8	29	40.8
30	56.5	30	55.7	30	41.2
31	57.7	31	56.6	31	41.6
32	59	32	57.6	32	42
33	60.4	33	58.6	33	42.4
34	62	34	59.6	34	42.8
35	63.7	35	60.7	35	43.2
36	65.6	36	61.8	36	43.6
37	67.9	37	62.9	37	44
38	70.6	38	64.1	38	44.4
39	74.2	39	65.3	39	44.8
40	79.1	40	66.7	40	45.2
41	87.1	41	68.1	41	45.6
42	100	42	69.6	42	46
		43	71.2	43	46.4
		44	73	44	46.8
		45	75.1	45	47.2
		46	77.6	46	47.7
		47	80.6	47	48.1
		48	84.6	48	48.6
		49	90.7	49	49
		50	100	50	49.5
				51	50
				52	50.5
				53	51

54	51.5
55	52.1
56	52.6
57	53.2
58	53.9
59	54.5
60	55.2
61	56
62	56.8
63	57.6
64	58.6
65	59.6
66	60.7
67	61.9
68	63.3
69	64.8
70	66.6
71	68.8
72	71.4
73	74.8
74	79.6
75	87.3
76	100

GSH LM	Logit	GSH SM	Logit	GSH LSM	Logit
0	0	0	0	0	0
1	8.8	1	10.2	1	9
2	14.7	2	17.2	2	15.2
3	18.6	3	22	3	19.5
4	21.7	4	25.6	4	22.6
5	24.1	5	28.3	5	25.1
6	26.2	6	30.7	6	27.1
7	28.1	7	32.7	7	28.8
8	29.7	8	34.6	8	30.2
9	31.1	9	36.2	9	31.5
10	32.5	10	37.8	10	32.7
11	33.7	11	39.2	11	33.7
12	34.9	12	40.5	12	34.7
13	36	13	41.7	13	35.6
14	37	14	42.9	14	36.4

15	38	15	43.9	15	37.1
16	38.9	16	44.9	16	37.8
17	39.8	17	45.8	17	38.4
18	40.7	18	46.7	18	39
19	41.6	19	47.6	19	39.6
20	42.4	20	48.4	20	40.1
21	43.2	21	49.1	21	40.6
22	44	22	49.9	22	41.1
23	44.8	23	50.6	23	41.5
24	45.5	24	51.3	24	42
25	46.2	25	51.9	25	42.4
26	47	26	52.6	26	42.8
27	47.7	27	53.3	27	43.2
28	48.4	28	53.9	28	43.6
29	49.1	29	54.6	29	44
30	49.8	30	55.3	30	44.3
31	50.5	31	56	31	44.7
32	51.2	32	56.7	32	45.1
33	51.8	33	57.5	33	45.4
34	52.5	34	58.3	34	45.8
35	53.2	35	59.2	35	46.2
36	53.9	36	60	36	46.5
37	54.6	37	61	37	46.9
38	55.3	38	62	38	47.2
39	56	39	63.1	39	47.6
40	56.7	40	64.2	40	47.9
41	57.4	41	65.5	41	48.3
42	58.2	42	66.9	42	48.7
43	59	43	68.5	43	49
44	59.8	44	70.3	44	49.4
45	60.6	45	72.4	45	49.7
46	61.5	46	75	46	50.1
47	62.5	47	78.4	47	50.5
48	63.5	48	83	48	50.8
49	64.5	49	89.9	49	51.2
50	65.7	50	100	50	51.5
51	66.9			51	51.9
52	68.2			52	52.3
53	69.7			53	52.7
54	71.3			54	53.1
55	73.2			55	53.4
56	75.3			56	53.8
57	77.8			57	54.3
58	81			58	54.7
59	85			59	55.1

60	91.1
61	100

60	55.6
61	56.1
62	56.6
63	57.1
64	57.6
65	58.2
66	58.8
67	59.4
68	60.1
69	60.9
70	61.6
71	62.5
72	63.4
73	64.3
74	65.4
75	66.5
76	67.8
77	69.3
78	71
79	73.1
80	75.6
81	78.9
82	83.5
83	90.1
84	100