STATISTICAL ANALYSIS PLAN

Clinical Trial Protocol Identification No:	ITOLI-C19-02-I-00
Title:	A Multi-Centric, Open label, Two Arm Randomized, Pivotal Phase2 Trial to Study the Efficacy and Safety of Itolizumab in COVID-19 Complications.
Trial Phase:	Pivotal Phase II
Name of the Drug:	Itolizumab (ALZUMAb™)
Clinical Trial Protocol Date and Version:	3-June-2020/ Version 5.0
Statistical Analysis Plan Date and Version:	29-June-2020/ Final
Sponsor:	Biocon Biologics India Limited, Biocon House, Electronic City, Bengaluru – 560100, India

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List of abbreviations

ADR	Adverse Drug Reaction
AE	Adverse event
ALT/SGPT/ ALAT	Alanine Transaminase /Serum Glutamic Pyruvic Transaminase/ Alanine Aminotransferase
ANC	Absolute Neutrophil Count
AP	Alkaline Phosphatase
AST / SGOT/ASAT	Aspartate Transaminase/ Serum Glutamic Oxaloacetic Transaminase/Aspartate Aminotransferase
ART	Adverse Reaction Terminology
CRO	Contract Research Organization
CSR	Clinical Study Report
CRP	(C-Reactive Protein) Level
ECG	Electrocardiogram
EOS	End of Study
EoT	End of Trial
eCRF	Electronic case report form
FiO2	Fraction of Inspired Oxygen
i.v.	intravenous(ly)
IMP	Investigational Medical Product
IRC	Independent Review Committee
IE	In evaluable
MedDRA	Medical Dictionary for Regulatory Activities
PP	Per Protocol
PaO2	Partial Pressure of Oxygen
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SAP	Statistical Analysis Plan
UNK	Unknown
US	Ultrasound
V	Visit
Wk	Week

1 Purpose

The purpose of this statistical analysis plan (SAP) is to assess the efficacy and safety of Itolizumab administered in patients with COVID-19 complications in comparison with the Best of Care that will be included in the clinical study report. And this document is based on protocol version 5.0, 3rd June 2020. SAP will ensure that the data listings, summary tables and figures are complete; and the statistical methodologies used are appropriate to allow valid conclusions in line with the study's objectives. This document will be appended to the clinical study report (CSR). The statistical analyses will be performed in accordance with the ICH-E9 guidelines "Statistical Principles for Clinical Trials" and relevant guidelines from Central Drugs Standard Control organization (CDSCO). If circumstances arise during the study such that more appropriate analytic procedures become available, this statistical analysis plan (SAP) may be revised. Any revisions to the SAP (both alternative and additional methods) will be made prior to database lock and reasons for such revisions will be described in the final Clinical Study Report (CSR).

2 Responsibility

Biocon Biologics India Limited/Designated CRO will be responsible for the conduct of statistical analyses, and the production and quality control of all tables, figures and listings).

3 Study Objectives

Coronavirus disease 2019 (COVID-19) progresses to respiratory complications as consequence of the exaggerated immune response of the host, producing a pro-inflammatory cytokine storm syndrome (i.e.: IL-6, TNF) and cytopenia, with a high mortality rate. Emergency treatments aiming to reduce individual cytokines (IL-6 and IL-1) specifically [or indirectly (JAK inhibitors and CCR5 antagonists) have shown survival benefit in patients with hyperinflammation, without increased adverse events. However, not being sufficient to reduce the rising mortality by COVID-19 other interventions to immunomodulate the life-threatening hyperinflammation are urgently needed. Therefore, the proposal for use of an anti-CD6 monoclonal antibody (Itolizumab) for the treatment of the COVID-19 complications (cytokine storm syndrome).

3.1 Trial Objectives

3.1.1 Primary Objectives

To study the efficacy and safety of adding Itolizumab in patients with Moderate to Severe COVID-19 complications (Cytokine Release Syndrome).

3.1.2 Secondary Objectives

To study the effect of immunomodulation by Itolizumab and its correlation to clinical improvement by evaluating biomarker data (IL6, TNF-a, IL17, IL1, Interferon -A etc.) before and after Itolizumab treatment

3.2 Outcome Measures

3.2.1 Primary endpoint

1. Proportion of patients with deterioration of lung function as measured by*:
   - Stable SpO2 without increasing FiO2
   - Stable PaO2 without increasing FiO2
2. Reduction of endo-tracheal intubation rate, measured as rate of patients needing intubation*
3. Reduction in proportion of patients who need*
   - Non-invasive ventilation
   - Invasive mechanical ventilation
   - High flow nasal oxygen
4. Time of duration of mechanical ventilation or time to end of mechanical, measured as elapsed time from the start date of mechanical ventilation to the weaning date, for patients needing intubation*
5. One-month mortality rate between the two arms* [Time Frame: up to 1 month] 1-month mortality is defined as the ratio of patients who will live after 1month from study start out of those registered at baseline
6. Change in inflammatory markers like CRP (C-reactive protein) level, d-Dimer, ferritin etc. [Time Frame: Arm A; baseline, during treatment (Before every dose and 12 to 24 h after every dose) up to 1 month, Arm B: baseline, 12 to 24 h and approx. 7 and 14 days after randomization]

* Applicable for both the arm

3.2.2 Secondary endpoints

1. Biomarkers (IL-6, TNF-a, IL1, IL17, etc…) [Time Frame: Arm A; baseline, during treatment (Before every dose and 12 to 24 h post dose) up to 1 month, Arm B; baseline, 12 to 24 h and approx. 7 and 14 days after randomization]
2. Lymphocyte count [Time Frame: Arm A; baseline and before every dose up to 1 month, Arm B; baseline, approx. 7 and 14 days after randomization] Lymphocyte count assessed by routinely used determination of blood count
3. PaO2 (partial pressure of oxygen) / FiO2 (fraction of inspired oxygen, FiO2) ratio (or P/F ratio) [Time Frame: Arm A; baseline, during treatment (Before every dose and 48 h post dose) up to 1 month, Arm B: baseline, 48 h and approx. 7 and 14 days after randomization] calculated from arterial blood gas analyses (values from 300 to 100)
4. Number of participants with treatment-related side effects as assessed by Common Terminology Criteria for Adverse Event (CTCAE) version 5.0 [Time Frame: during treatment and up to 30 days after the last treatment dose]* graded according to CTCAE citeria (v5.0)
5. Radiological response [Time Frame: at baseline, after seven days and if clinically indicated (up to 1 month)]* Thoracic CT scan or Chest XR
6. Duration of hospitalization [Time Frame: from baseline up to patient's discharge (up to 1 month)]* Days of hospitalization and ICU

7. Remission of respiratory symptoms [Time Frame: up to 1 month]* time to independence from non-invasive mechanical ventilation calculated in days
8. Remission of respiratory symptoms [Time Frame: up to 1 month]* time to independence from oxygen therapy in days

* Applicable for both arms

4 TRIAL DESIGN AND DESCRIPTION

4.1 Trial Design

It is a Multi-Centric, Open label, Two Arm Randomized, Pivotal Phase 2 Trial to Study the Efficacy and Safety of Itolizumab in COVID-19 complications. Patients who have tested positive for virological diagnosis of SARS-CoV2 infection (PCR) are planned to be randomised for enrolment from various centres in India. All eligible patients entering into the study will be randomized in 2:1 ratio to receive the treatment A/ B respectively.

4.2 Subject Selection

Patients who have tested positive for virological diagnosis of SARS-CoV2 infection (PCR) are planned to be randomised for enrolment from various centres in India.

4.3 Inclusion Criteria

1. Male or female adults above 18 years (not tested in children yet)
2. Informed consent for participation in the study
3. Confirmed virological diagnosis of SARS-CoV2 infection (RT-PCR)
4. Hospitalized due to clinical worsening of COVID-19 infection
5. Oxygen saturation at rest in ambient air ≤94%
6. Patients who are in moderate to severe ARDS as defined by PaO2/Fio2 ratio of < 200 or more than 25% deterioration from the immediate previous value.
7. Baseline serum ferritin level ≥ 400 ng/mL or IL-6 levels greater than 4 times ULN, if known

Note: Either of Inclusion number 6 or 7 is required for inclusion of the patient into the study. Since there is logistical delay in getting results in time, biomarker data as inclusion criteria may be used if already known.

4.4 Exclusion Criteria

1. Known severe allergic reactions to monoclonal antibodies
2. Active tuberculosis (TB) infection
3. History of inadequately treated tuberculosis or latent tuberculosis

Note:. Latent tuberculosis should be excluded based on history, physical examination and chest x ray before dosing (day 1). QuantiFERON TB also should be performed, however considering criticality of patient condition, patient can be dosed without QuantiFERON TB test results. If

QuantiFERON TB test is positive, then continuation of patient in the study is investigator's discretion considering benefit-risk evaluation with the sponsor.

4. In the opinion of the investigator, progression to death is highly probable, irrespective of the provision of treatments
5. Patient on invasive mechanical ventilator support.
6. Have received oral anti-rejection or immune-suppressive drugs within the past 6 months

Note: Patient receiving oral anti-rejection or immune-suppressive drugs regularly in the last 6 months will be excluded. Patient will be included if received short course of steroids.

7. Participating in other drug clinical trials like using anti-IL-6 therapy like tocilizumab (participation in COVID-19 anti-viral trials may be permitted if approved by Sponsor)
8. Patient on treatment of anti-IL-6 or plasma therapy as a part of supportive care
9. Pregnant or breastfeeding, or positive pregnancy test in a pre-dose examination
10. Any serious medical condition or abnormality of clinical laboratory tests that, in the investigator's judgment, precludes the patient's safe participation in and completion of the study
11. Patients with known history of Hepatitis B, Hepatitis C or HIV
12. Absolute Neutrophils count (ANC) <1000 / mm3
13. Platelet count <50,000 / mm3
14. Absolute Lymphocyte count (ALC): <500/mm3

Note: ANC, ALC and platelet counts can be done in local lab in the hospital.

4.5 Sample Size, Treatment Assignment, Randomization

Approximately 30 patients are considered sufficient to explore the study objectives and will be included in this study (number of patients may be increased if there is benefit observed in initial cohort of patients. There is no formal sample size calculation estimated). All eligible patients entering into the study will be randomized in 2:1 ratio to receive the treatment A/ B respectively. A computer derived randomization schedule is planned to be generated using appropriate system e.g. SAS to assign patient to treatment groups. Randomization will be central and appropriate system (e.g. remote telephone based, computer-based email, sealed envelope) will be used to distribute randomization schedule to the site Note: If the patient is randomised to Arm A and is not initiated itolizumab or not administer one full infusion, is then not considered randomized. The same randomisation code will be used for the subsequent subject in that particular site.

5 Protocol Deviation

Deviations from the protocol, including deviations of inclusion/exclusion criteria will be assessed as 'major' or 'minor' in agreement with Medical Team. Refer to "Guidance Document for Protocol Deviation Reporting and Specifications" for details. All protocol deviations will be appropriately captured in CSR

6 General Aspects for Statistical Methods

In general, metric variables and derived parameters will be presented using descriptive summary statistics including arithmetic mean, standard deviation, median, minimum and maximum.

Categorical variables will be presented using descriptive summary statistics including number of patients and percentages. Percentages of patients will be based on non-missing values. The presentation will be by treatment group. Individual values as well as minimum and maximum will be presented with the same number of decimal places as the raw data. Derived parameter will have as many decimal places as the measured number with the smallest number of decimal places. Descriptive statistics, such as arithmetic/geometric mean and median will be presented with an additional decimal place and standard deviation with two additional decimal places as the raw or derived data. All relevant subject data will be included in the listings; and all subjects entered into the database will be included in subject data listings .SAS 9.4 or any other validated software will be used for analysis purpose and generating Tables, Listings & Figures. P-values less than 0.05 may be reported as statistically significant.

The formatting of the final version of a table, figure, or listing may differ from what is presented in the mock shell or the presentation of the results may be changed, however the key content will remain unchanged. dditional tables, figures, and listings may be generated to supplement the planned output.

7 Analysis Population

ITT/FAS population: Patients randomized (in Arm B) and received at least one full dose of Itolizumab (in Arm A)

Safety population: Patients randomized (in Arm B) and received partial or full dose of Itolizumab (in Arm A)

8 Demography other baseline Characterstics

Demographic characteristics including age, gender, race, and ethnicity will be summarized for ITT/FAS populations. Baseline is defined as the last observed value/data before the patient receives study drug for the first time or randomized (in Arm B)

Vital signs such as height, weight, pulse, temperature, respiratory rate, systolic blood pressure, diastolic blood pressure, PaO2/FiO2, FiO2, SpO2, mean arterial pressure & GCS score will be summarized.

Medical history, Physical Examination & concomitant medications will be summarized using counts and percentage. Additionally, prognostic markers and few key laboratory parameters will be summarized.

9 Efficacy Evaluation

Primary Efficacy Evaluation

Proportion of patients with deterioration of lung function as measured by Stable SpO2 without increasing FiO2 and Stable PaO2 without increasing FiO2 will be summarized using count and

percentage. The difference between two proportion with its 95% Confidence interval and associated p-values may be presented, if p-value is less than 0.05 it can be concluded that there is a statistically significant difference between two proportions.

Reduction of endo-tracheal intubation rate, measured as rate of patients needing intubation will be summarize using descriptive statistics.

Reduction in proportion of patients who need/ Non-invasive ventilation / Invasive mechanical ventilation/high glow nasal oxygen will be summarized using count & percentage.

One-month mortality rate between the two arms will be summarized. The difference between two rates with its 95% Confidence interval and associated p-values may be presented, if p-value is less than 0.05 it can be concluded that there is a statistically significant difference between two-rates.

Change in inflammatory markers like CRP (C-reactive protein) level, d-Dimer, ferritin etc will be summarize with descriptive statistics. Change from Baseline may be presented along with 95% CI.

Secondary Efficacy Evaluation

Biomarkers (IL-6, TNF-a, IL1, IL17, etc…) will be summarize using summary statistics.

Lymphocyte count will be summarized using count & percentage.

PaO2 (partial pressure of oxygen) / FiO2 (fraction of inspired oxygen, FiO2) ratio (or P/F ratio) calculated from arterial blood gas analyses. Radiological response will be summarized in descriptive manner.

Duration of hospitalization will be summarized using descriptive statistics.

Time to independence from non-invasive mechanical ventilation and from oxygen therapy will be summarize using summary statistics.

Biomarkers (IL-6, TNF-a, IL1, IL17, etc…) Lymphocyte count, CRP (C-reactive protein) level, PaO2 (partial pressure of oxygen) / FiO2 (fraction of inspired oxygen, FiO2) ratio (or P/F ratio), will be summarized with descriptive statistics. Change from Baseline will be presented along with 95% CI for the difference between two treatments will be reported.

Radiological response, Duration of hospitalization & Remission of respiratory symptoms will be summarized using descriptive statistics.

Number of participants with treatment-related side effects as assessed by Common Terminology Criteria for Adverse Event (CTCAE) version 5.0 graded according to CTCAE criteria (v5.0) will be summarized based on frequency and proportion of total subjects, by system organ class and preferred term. Proportion of subjects with IRR in both the arm will be presented. An overall summary of deaths will be presented by treatment arms.

10 Other Evaluations

Additional Safety Evaluation

Additional safety analysis will be provided by treatment group, by severity, by outcome and related to study drug. Events will be summarized with descriptive statistics (count & percentage).

Laboratory Evaluations

For haematology and biochemistry variables, descriptive summaries of observed values and changes from baseline will be presented by treatment arm. Numerical variables will be described by number of subjects, mean, standard deviation, median, minimum and maximum and categorical variables will be described by number and percentage.

Vital Signs and Physical examination

Descriptive statistics of each vital signs parameter will be presented for the Safety Population, showing the observed visit and change from baseline to each visit value. These summaries statistics (N, mean, SD, median and Min, Max) will be presented by visit for each treatment arm

11 Interim Study Report

Data will be provided to DSMB (constituted prior to first patient screened) on a periodic basis. Based on DSMB recommendation, interim clinical study report may be prepared and submitted to DCGI/regulatory agencies.

12 Key Definitions

For few assessments (weight, physical examination, vital signs haematology, biochemistry Chest X Ray/CT scan), screening assessments will be considered as baseline assessment (as day 1).

Stable SpO2:

- Stable SpO2: Defined as absence of increase in FiO2 to maintain Spo2 ≥ 92%
- Improvement of SpO2: Defined as decrease in FiO2 to maintain SpO2 >92%

Stable PaO2:

- Stable PaO2: Defined as up to 10% change in PaO2/FiO2 ratio from baseline
- Improvement of PaO2: Defined as > 10% improvement in PaO2/FiO2 ratio from baseline (including patients weaned off oxygen)

If assessment is missing on particular day then it should be captured from assessment available in next two days.
For lab parameters, if assessment is missing on particular day, then it should be captured from assessment available in ± 2 days.

13 Programming Considerations, Listing of Tables, Figures & Format, Software detail

All tables, data listings, figures (TLFs), and statistical analyses will be generated using SAS® for Windows, Release 9.4 (SAS® Institute Inc., Cary, NC, USA) or any other validated statistical software. One SAS program will be used to create several outputs / a separate SAS program will be created for each output. Output files will be delivered in Word / pdf format.

For few assessments (weight, physical examination, vital signs haematology, biochemistry Chest X Ray/CT scan), screening assessments will be considered as baseline assessment (as day 1).

Missing data:

All attempts will be made to collect all data per protocol. Any data point that appears to be erroneous or inexplicable based on clinical judgment will be investigated as a possible outlier. If data points are identified as outliers, sensitivity analyses may be performed to examine the impact of including or excluding the outliers. Subjects who meet fatal outcome during the observing period up to 30 days will be an event. Subjects lost to follow up or withdraw consent during the observing period, will be censored at last assessment. Patient data will be censored at the time of their last observed assessment in case of lost to follow up, withdrawal consent or after 30 days of enrolment.

Following Rules may be applied for the derivation of efficacy endpoints

- Patients who discharged from hospital (with improvement, Off O2), the status at discharge will be carried forward.
- Patients who lost to follow up will be considered as Non evaluable (NE)
- Patients who worsen or met fatal outcome, status at event will be carried forward.

Note: Telephonic improvement of weaning of O2 will be considered as improved.

These rules will be applied to analyse following endpoint:

Proportion of patients with deterioration of lung function as measured by:

- Stable SpO2 without increasing FiO2
- Stable PaO2 without increasing FiO2

Listing of Tables, Figures & Format

Table, figure, and listing shells are presented in Appendices 14. The formatting of the final version of a table, figure, or listing may differ from what is presented in the shell or the presentation of the results may be changed, however the key content will remain unchanged. Additional summaries/data points may be included in the final version of a table, figure, or listing, as well. Additional tables, figures, and listings may be generated to supplement the planned output.

Software Detail

SAS version 9.4 or any validated statistical software will be used to generate all tables, figures and listings.

14 Tables and mock shells

14.1.1 Screening Failures

	Overall N (%)
Total Screened Subjects	XX (XX.X %)
Screen Failures	XX (XX.X %)
Total Randomized Subject	XX (XX.X %)
Subject met Inclusion Criteria or met Exclusion Criteria	XX (XX.X %)
Subject not met Inclusion Criteria or met Exclusion Criteria	XX (XX.X %)
Others	XX (XX.X %)
• Withdrawal Informed Consent	XX (XX.X %)
• Lost to Follow-Up	XX (XX.X %)
…….	

Note: XX patients could not complete first dosing hence replaced as per the protocol.

14.1.2 Disposition of Patients

Disposition	**Arm A [n (%)]**	**Arm B [n (%)]**
Randomized	XX (XX.X %)	XX (XX.X %)
ITT/FAS Population	XX (XX.X %)	XX (XX.X %)
Safety Population	XX (XX.X %)	XX (XX.X %)
Completed the study	XX (XX.X %)	XX (XX.X %)
Completed 30 days follow up in hospital		
Early discharged*		
Discontinued	XX (XX.X %)	XX (XX.X %)
Reasons for Discontinuation		
Adverse event	XX (XX.X %)	XX (XX.X %)
Death	XX (XX.X %)	XX (XX.X %)
Physician decision	XX (XX.X %)	XX (XX.X %)
As per Protocol	XX (XX.X %)	XX (XX.X %)
Lost to follow up	XX (XX.X %)	XX (XX.X %)
Subject/Guardian decision	XX (XX.X %)	XX (XX.X %)
Diagnosis of COVID 19 by RT-PCR		
Positiive	XX (XX.X %)	XX (XX.X %)
Negative	XX (XX.X %)	XX (XX.X %)
Not Available	XX (XX.X %)	XX (XX.X %)

* Patients discharged early due to clinical improvement and government policy during the study.

14.1.3 Subject Disposition by Centre

Center Number	Arm A [n (%)]	Arm B [n (%)]
1	XX (XX.X %)	XX (XX.X %)
2	XX (XX.X %)	XX (XX.X %)
3	XX (XX.X %)	XX (XX.X %)
4	XX (XX.X %)	XX (XX.X %)

14.1.4 Summary of Demographic Characterstics

	Arm A [n (%)]	Arm B [n (%)]
Age (years)		
N	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Sex, n (%)		
Male	XX (XX.X %)	XX (XX.X %)
Female	XX (XX.X %)	XX (XX.X %)
Race, n (%)		
Asian	XX (XX.X %)	XX (XX.X %)
Black	XX (XX.X %)	XX (XX.X %)
Ethnicity		
Hispanic	XX (XX.X %)	XX (XX.X %)
East Asian	XX (XX.X %)	XX (XX.X %)

14.1.5 Summary of Concomitant Medication by treatment group

	Arm A (N=XX) [n (%)]	**Arm B (N=XX) [n (%)]**
Any medication taken		
Yes	XX (XX.X %)	XX (XX.X %)
No	XX (XX.X %)	XX (XX.X %)
ATC		
XXXXX	XX (XX.X %)	XX (XX.X %)
XXXXX	XX (XX.X %)	XX (XX.X %)
Medication Name	XX (XX.X %)	XX (XX.X %)
XXXXXXXXXX	XX (XX.X %)	XX (XX.X %)
XXXXXXXXXX	XX (XX.X %)	XX (XX.X %)
XXXXXXXXXX	XX (XX.X %)	XX (XX.X %)
XXXXXXXXXX	XX (XX.X %)	XX (XX.X %)
XXXXXXXXXX	XX (XX.X %)	XX (XX.X %)
XXXXXXXXXX	XX (XX.X %)	XX (XX.X %)

14.1.6 Summary of Medical History

	Arm A (N=XX) [n (%)]	**Arm B (N=XX) [n (%)]**
Diagnosis of COVID 19 by RT-PCR Positive , n (%)	XX (XX.X %)	XX (XX.X %)
Duration of COVID-19 related symptoms at enrolment		
N	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Patients with co-morbidities		
Diabetes Mellitus	XX (XX.X %)	XX (XX.X %)
Hypertension	XX (XX.X %)	XX (XX.X %)
Others	XX (XX.X %)	XX (XX.X %)
XXXX	XX (XX.X %)	XX (XX.X %)
XXXX	XX (XX.X %)	XX (XX.X %)

14.1.7 Summary of Vital Parameters and change from Baseline

Variable	Visit	**Arm A (N=XX) [n (%)]**	**Arm B (N=XX) [n (%)]**
Weight (kg)	Baseline		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
	48 hours		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
	Change from Baseline		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX

Note: *: repeated for Weight, Body Temperature, Pulse, Systolic, Diastolic, Respiratory Rate, PaO2/FiO2, FiO2, SpO2, Mean Arterial Pressure, Glasgow Coma Scale, PaO2 etc
Repeated for Day 7, Day 14, Day 21, Day 30 and EOS

14.1.8 Summary of Laboratory Test Results and Change from Baseline: Hematology

Test	Visit	**Arm A (N=XX) [n (%)]**	**Arm B (N=XX) [n (%)]**
Haematocrit* %	Baseline[&]		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
	Day 7		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
	Change from Baseline[&&]		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX

&: Repeat for day 14, Day 21, 30/EOS for all applicable parameters,

&&: Repeat for Day 14, Day 21, Day 30/EOS Change from Baseline

*: Haemoglobin, Total leukocyte count, Platelet count, Absolute lymphocyte count, Absolute neutrophil count, Basophils- Differential, Eosinophils- Differential, Lymphocytes- Differential, Monocytes- Differential and Neutrophils- Differential.etc

14.1.9 Summary of Laboratory Test Results and Change from Baseline: Biochemistry

Variable	Time point	Visit	**Arm A (N=XX) [n (%)]**	**Arm B (N=XX) [n (%)]**
Blood Urea*	Predose	Baseline[&]		
		N	XX	XX
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X
		Min, Max	XX, XX	XX, XX
		12-24 hours		
		N	XX	XX
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X
		Min, Max	XX, XX	XX, XX
		Change from Baseline		
		N	XX	XX
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X
		Min, Max	XX, XX	XX, XX
	12-24Hrs Post Dose	Day 7[&&]		
		N	XX	XX
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X
		Min, Max	XX, XX	XX, XX

&: Repeat for day 14, Day 21, 30/EOS for all applicable parameters , Change from Baseline, Week 3, Change from Baseline, Week 4 and Change from Baseline

&&: Repeat for Day 14, Day 21, Day30/EOS 2, Change from Baseline,

*: Serum Bilirubin, AST (SGOT), ALT (SGPT), ALP, Serum Albumin, LDH, HDL, LDL, Triglycerides, Total Cholesterol, Serum creatinine, Procalcitonin, d-Dimer, Trop-I, Ferritin etc.

14.1.10 Hospitalization

	Arm A (N=XX) [n (%)]	**Arm B (N=XX) [n (%)]**
Was patient hospitalized during study?		
Yes	XX (XX.X %)	XX (XX.X %)
No	XX (XX.X %)	XX (XX.X %)
Discharged During study		
Yes	XX (XX.X %)	XX (XX.X %)
No	XX (XX.X %)	XX (XX.X %)
N/A	XX (XX.X %)	XX (XX.X %)
Was patient in Intensive Care Unit during this hospitalization period		
Yes	XX (XX.X %)	XX (XX.X %)
No	XX (XX.X %)	XX (XX.X %)

14.1.11 Duration of hospitalization and ICU stay

	Arm A [n (%)]	**Arm B [n (%)]**
No of days of hospitalization		
N	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
No of days of hospitalization during study		
N	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
No of days of ICU		
N	Xxx	Xxx
Mean (SD)	Xxx	Xxx
Median	Xxx	Xxx
Min, Max	Xxx	Xxx
No of days of ICU during study		
N	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
Median	XX.X	XX.X
Min, Max	XX, XX	XX, XX
Time to independence from non-invasive mechanical ventilation calculated in days		
N	Xxx	Xxx
Mean	Xxx	Xxx
Median	Xxx	Xxx
Min, Max	Xxx	Xxx
Duration in Days for independence from oxygen therapy		
N	Xxx	Xxx
Mean	Xxx	Xxx
Median	xxx	Xxx
Min, Max	xxx	Xxx

14.1.12 Summary of Study Treatment: Itolizumab treatment details in Arm A

	Arm A
Dose	
N	XX
Mean (SD)	XX.X (XX.XX)
Median	XX.X
Min, Max	XX, XX
No of infusion received during study	
1	XX (XX.X %)
2	XX (XX.X %)
3	XX (XX.X %)
4	XX (XX.X %)
Infusion interrupted	
Yes	XX (XX.X %)
No	XX (XX.X %)
Reason for interruption	
XXXX	XX (XX.X %)
XXXX	XX (XX.X %)
XXXX	XX (XX.X %)
Regimen administered	
Weekly	XX (XX.X %)
Alternate weekly	XX (XX.X %)
Dose deferred	
Yes	XX (XX.X %)
No	XX (XX.X %)
Reason	
XXXX	XX (XX.X %)
XXXX	XX (XX.X %)
XXXX	XX (XX.X %)

14.1.13 Summary of BSC treatment details in both arms

	Arm A n (%)	Arm B n (%)
Antibiotics		
XXXX	XX (XX.X %)	XX (XX.X %)
XXXX	XX (XX.X %)	XX (XX.X %)
XXXX	XX (XX.X %)	XX (XX.X %)
Antivirals		
XXXX	XX (XX.X %)	XX (XX.X %)
XXXX	XX (XX.X %)	XX (XX.X %)
XXXX	XX (XX.X %)	XX (XX.X %)
HCQ	XX (XX.X %)	XX (XX.X %)
Heparin	XX (XX.X %)	XX (XX.X %)
Glucocorticoids		
Supplements	XX (XX.X %)	XX (XX.X %)
IV fluids	XX (XX.X %)	XX (XX.X %)
Others		
XXXX	XX (XX.X %)	XX (XX.X %)
XXXX	XX (XX.X %)	XX (XX.X %)
XXXX	XX (XX.X %)	XX (XX.X %)

14.2 Primary outcome measures

14.2.1 Primary Outcome Measures

Visit*		Arm A (N=XX)	Arm B (N=XX)
Baseline	patients with Stable SpO2 without increasing FiO2	XX (XX.X %)	XX (XX.X %)
	patients with Stable PaO2 without increasing FiO2	XX (XX.X %)	XX (XX.X %)

*day 7, day 14, day 21 and day 30/EOS or all available visits

14.2.2 Proportion of patients needed intubation during the study

	Arm A (N=XX)	Arm B (N=XX)
Patients needed intubation n(%)	XX (XX.X %)	XX (XX.X %)

14.2.3 Reduction in proportion of patients who need Non-invasive ventilation

Visit		Arm A (N=XX)	Arm B (N=XX)
	Patients on Non-invasive ventilation at baseline	XX	XX
Day 7	N	XX	XX
	Stable or improved (shifted to bag and mask, NRBM, FM, nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 14	N	XX	XX
	Stable or improved (shifted to bag and mask, NRBM, FM, nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 21	N	XX	XX
	Stable or improved (shifted to bag and mask, NRBM, FM, nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 30/EOS	N	XX	XX
	Stable or improved (shifted to bag and mask, NRBM, FM, nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)

14.2.4 Reduction in proportion of patients who need NRBM

Visit		Arm A (N=XX)	Arm B (N=XX)
	Patients on NRBM at baseline	XX	XX
Day 7	N	XX	XX
	Stable or improved (shifted to FM, nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 14	N	XX	XX
	Stable or improved (shifted to FM, nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 21	N	XX	XX
	Stable or improved (shifted to FM, nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 30/EOS	N	XX	XX
	Stable or improved (shifted to FM, nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)

14.2.5 Reduction in proportion of patients who need Face Mask

Visit		Arm A (N=XX)	Arm B (N=XX)
	Patients on FM at baseline	XX	XX
Day 7	N	XX	XX
	Stable or improved (shifted to nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 14	N	XX	XX
	Stable or improved (shifted to nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 21	N	XX	XX
	Stable or improved (shifted to nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)
Day 30/EOS	N	XX	XX
	Stable or improved (shifted to nasal canula or off O2)	XX (XX.X %)	XX (XX.X %)

14.2.6 Reduction in proportion of patients who need High Flow Nasal Oxygen

Visit		Arm A (N=XX)	Arm B (N=XX)
	Patients on High flow nasal oxygen at baseline	XX	XX
Day 7	N	XX	XX
	Stable or improved (off O2)	XX (XX.X %)	XX (XX.X %)
Day 14	N	XX	XX
	Stable or improved (off O2)	XX (XX.X %)	XX (XX.X %)
Day 21	N	XX	XX
	Stable or improved (off O2)	XX (XX.X %)	XX (XX.X %)
Day 30/EOS	N	XX	XX
	Stable or improved (off O2)	XX (XX.X %)	XX (XX.X %)

14.2.7 One-month Mortality Rate

	Arm A [n (%)]	**Arm B [n (%)]**
Number of patients died	XX (XX.X %)	XX (XX.X %)
95% CI Difference between Rate	XX (XX , XX)	
p-value	XX	

14.2.8 Change in inflammatory markers before and after dosing in Treatment ARM A

	Before dose	12-24 hrs after dosing
Serum ferritin		
First dose (n)		
Mean change		
Second dose (n)		
Mean change		
Third Dose (n)		
Mean change		
Fourth Dose (n)		
Mean change		
Programming Note: Repeat for other inflammatory markers: Serum LDH, Serum CRP, Serum d-Dimer etc Repeat Table for first , second, third and fourth infusion (dose) of Itolizumab		

14.2.9 Survival status

	Arm A (N=XX) [n (%)]	Arm A (N=XX) [n (%)]
Survival Status	XX (XX.X %)	XX (XX.X %)
Alive	XX (XX.X %)	XX (XX.X %)
Dead	XX (XX.X %)	XX (XX.X %)
Unknown	XX (XX.X %)	XX (XX.X %)

14.2.10 Summary of Oxygen and SOFA analysis

Variable		**Arm A (N=XX) [n (%)]**	**Arm B (N=XX) [n (%)]**
Oxygen requirement (L/min)	Week 1*		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
	Week2		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
	Change from Week 1		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
SOFA score	Week 1*		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
	Week2		
	N	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX
	Change from Week 1		
	N	XX	XX

	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X
	Min, Max	XX, XX	XX, XX

*Repeated for Day 7, day 14, day 21 and Day 30/EOS

14.2.11 Ordinal Scale: No and Proportion of patient reduced by 1 or more points

		Day 7 n (%)	Day 14 n (%)	Day 21 n (%)	Day 30/EOS n (%)
Arm A (n=XX)					
Arm B (n=XX)					

14.2.12 Respiratory rate over time

Sr. No.	Arm A (N=xx)		Arm B (N=xx)	
	Up to 20	> 20	Up to 20	> 20
Baseline	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Day 2/3	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Day 7	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Day 14	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Day 21	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Day 30/EOS	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)

14.3 Safety Analysis

14.3.1 Summary of Subjects with TEAEs by treatment group

Description	ARM A (N=XX) [n (%)]	No of events	ARM B (N=XX) [n (%)]	No of events
At least one TEAE	XX (XX.X %)	XX	XX (XX.X %)	XX
At least one related TE AE	XX (XX.X %)	XX	XX (XX.X %)	XX
At least one Severe/Grade 3 or above TEAE	XX (XX.X %)	XX	XX (XX.X %)	XX
At least one related Severe/Grade 3 or above TE AE	XX (XX.X %)	XX	XX (XX.X %)	XX
At least one IRR	XX (XX.X %)	XX	XX (XX.X %)	XX
At least one TE SAE	XX (XX.X %)	XX	XX (XX.X %)	XX
At least one related TE SAE	XX (XX.X %)	XX	XX (XX.X %)	XX
Fatal TEAEs	XX (XX.X %)	XX	XX (XX.X %)	XX
Fatal AE related to study drug	XX (XX.X %)	XX	XX (XX.X %)	XX
Number of patients with dose temporarily stopped at least once	XX (XX.X %)	XX	XX (XX.X %)	XX
Number with dose permanently stopped	XX (XX.X %)	XX	XX (XX.X %)	XX
Seriousness criteria		XX		XX
Death	XX (XX.X %)	XX	XX (XX.X %)	XX
Life threatening	XX (XX.X %)	XX	XX (XX.X %)	XX
Requires in-patient hospitalization or prolongation of existing hospitalization	XX (XX.X %)	XX	XX (XX.X %)	XX
Significant disability	XX (XX.X %)	XX	XX (XX.X %)	XX
Congenital anomaly or birth defect Other medically important serious event	XX (XX.X %)	XX	XX (XX.X %)	XX

Note1 : TEAE are defined as any AE which started or deteriorated at or after first dose of study treatment

Note2: Includes related AE.

Note 3: n=number of subjects with AEs. Percentages are based on the number of subjects in safety population (N).

14.3.2 Treatment Emergent Adverse Event (TEAE) by SOC and PT

System Organ Class	Preferred term	ARM A (N=XX) [n (%)]	ARM B (N=XX) [n (%)]
No of Subjects with at least one TEAE		XX (XX.X %)	XX (XX.X %)
Any SOC		XX (XX.X %)	XX (XX.X %)
	PT1	XX (XX.X %)	XX (XX.X %)
	PT2	XX (XX.X %)	XX (XX.X %)
SOC1		XX (XX.X %)	XX (XX.X %)
	PT1	XX (XX.X %)	XX (XX.X %)
	PT2	XX (XX.X %)	XX (XX.X %)
	PT3	XX (XX.X %)	XX (XX.X %)
		XX (XX.X %)	XX (XX.X %)

TEAE are defined as any AE which started or deteriorated at or after first dose of study treatment
n=number of subjects with AEs. e=number of events. Percentages are based on the number of subjects in safety population
Note: System Organ Class and Preferred Term coded as per MedDRA version XX

14.3.3 Treatment Emergent Adverse Event (TEAE) by severity

System Organ Class	Preferred term	ARM A (N=XX) [n (%)]					ARM B (N=XX) [n (%)]				
		Mild	Moderate	Severe	Life threatening	Death	Mild	Moderate	Severe	Life threatening	Death
Any SOC		XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
SOC1		XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT3	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)

14.3.4 Treatment Emergent Adverse Event (TEAE) related to study drug

System Organ Class	Preferred term	ARM A (N=XX) [n (%)]		ARM B (N=XX) [n (%)]	
		Related	Not related	Related	Not related
Any SOC		XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
SOC1		XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	PT3	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Note: System Organ Class and Preferred Term coded as per MedDRA version XX					

14.3.5 Treatment Emergent Adverse Event (TEAE) by Outcome

ARM	System Organ Class	Preferred term	Recovered/resolved	Recovering/resolving	Not recovered/not resolved	Recovered/resolved with sequelae	Fatal	Unknown

Arm A (N=XX)	Any SOC		XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	SOC1		XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT3	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
Arm B (N=XX)	Any SOC		XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	SOC1		XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		PT3	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)

15. Supplementary Tables

Table S1: Mean Lymphocyte count

	Baseline	Day 2/3	Day 7	Day 14	Day 21	Day 30/EOS
n						
Arm A						
Arm B						

Table S2: Mean PaO2/FiO2 ratio

	Baseline	Day 2/3	Day 7	Day 14	Day 21	Day 30/EOS
n						
Arm A						
Arm B						

Table S3: Mean PaO2 / FiO2 ratio in Arm A

	Before dose	48 hrs after dose
First dose (n)		
PaO2 / FiO2 ratio		
Mean change		
Second dose (n)		
PaO2 / FiO2 ratio		
Mean change		
Third dose (n)		
PaO2 / FiO2 ratio		
Mean change		
Fourth dose (n)		

PaO2 / FiO2 ratio		
Mean change		

Table S4: Mean PaO2

	Baseline	Day 2/3	Day 7	Day 14	Day 21	Day 30/EOS
Arm A						
Arm B						

Table S5: Mean FiO2 (%)

	Baseline	Day 2/3	Day 7	Day 14	Day 21	Day 30/EOS
Arm A						
Arm B						

Table S6: Mean SpO2 (%)

	Baseline	Day 2/3	Day 7	Day 14	Day 21	Day 30/EOS
Arm A						
Arm B						

16. Listings

Listing 16.1.1 Subjects Inclusion

Treatment Group	Subject ID	Is the subject eligible for study enrolment based on satisfying all inclusion and exclusion criteria requirement?	INC 1	INC 2	INC 3	INC 4	INC 5	INC 6	INC 7
XXXXX	XXX	XXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
XXXXX	XXX	XXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Listing 16.1.2 Subjects Exclusion

Treatment Group	Subject ID	Is the subject eligible for study enrolment based on satisfying all inclusion and exclusion criteria requirement?	EXC 1	EXC 2	EXC 3	EXC 4	EXC 5	EXC 6	EXC 7	EXC 8	EXC 9	EXC 10	EXC 11	EXC 12

XXXXXX	XXX	XX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Listing 16.1.3 Demographic data

Treatment Group	Subject ID	Age	Was written informed consent obtained?	Date of Informed Consent	Gender	Date of birth	Is subject of child bearing status	Race	Ethnicity
XXXXXX	XXX	XX	XXX	XXX	XXXX	XXXX	XXX	XXX	XXX
XXXXXX	XXX	XX	XXX	XXX	XXXX	XXXX	XXX	XXX	XXX

Listing 16.1.4 Medical History

Treatment Group	Subject ID	Diagnosis of COVID 19 by RT-PCR	Date	Result	Is there any Medical History to be reported	Serial Number	Medical history term	Start Date	Stop Date	Ongoing
XXXXXX	XXX	XX	XXXX	XXXX	XXX	XXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XX	XXXX	XXXX	XXX	XXX	XXX	XXX	XXX	XXX

Listing 16.1.5 Concomitant Medication

Treatment Group	Subject ID	Were any medication(s) taken?	Medication Name	Indication	Start Date	End Date	Ongoing at final exam	Frequency	Route	Dose	Dose units
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX	XX	XXX
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX	XX	XXX

Listing 16.1.6 Disposition of Subjects

Treatment Group	Subject ID	Is the subject eligible to participate in treatment phase?	Did the subject complete study?	If No, primary reason for discontinuation	Date of last contact	Date of consent withdrawn	Diagnosis of COVID 19 by RT-PCR	Date	Result
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXXX
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXXX

Listing 16.1.7 Vital Parameters

Treatment Group	Subject ID	Date of assessment	Time of assessment	Visit	Was assessment performed?	Height	Weight	Body Temperature	Pulse	Blood Pressure	Respiratory Rate	PaO2/FiO2	FiO2	SpO2	MAP	GCS	PaO2
XXXXXX	XXX	XXXX	XX	XXX	XXXX	XXX	XX	XXX	XXX	XXX	XXX	XX.X	XXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XXXX	XX	XXX	XXXX	XXX	XX	XXX	XXX	XXX	XXX	XX.X	XXX	XXX	XXX	XXX	XXX

Listing 16.1.8 Biomarker

Treatment Group	Subject ID	Visit	Was blood sample collected pre dose?	Date of sample collected Pre-Dose	Time of sample collected pre dose	Was blood sample collected 12-24 Hours post dose?	Date of sample collected Post-Dose	Time of sample collected 24 Hours post dose
XXXXXX	XXX	XXX	XXXX	XXXX	XX	XXX	XXXX	XX
XXXXXX	XXX	XXX	XXXX	XXXX	XX	XXX	XXXX	XX

Listing 16.1.9 Haematology

Treatment Group	Subject ID	Visit	Was blood sample collected pre dose	Date of sample collected Pre-Dose	Time of sample collected pre dose	Was blood sample collected 12 Hours post dose	Date of Sample collected Post dose	Time of sample collected 12 Hours post	Test Parameter	Result-PRE-DOSE	Result-12Hrs POST DOSE	Lower Reference Range	Upper Reference Range	Unit (SI)
XXXXXX	XXX	XXX	XXX	XXXX	XX	XXX	XXXX	XX	XXXX	XXX	XXX	XXX	XXX	XX
XXXXXX	XXX	XXX	XXX	XXXX	XX	XXX	XXXX	XX	XXXX	XXX	XXX	XXX	XXX	XX

Note: provide the listing for Haematology parameters as per available data

Listing 16.1.10 Biochemistry

Treatment Group	Subject ID	Visit	Was blood sample collected pre dose	Date of sample collected Pre-Dose	Time of sample collected pre dose	Was blood sample collected 12 Hours	Date of Sample collected Post dose	Time of sample collected 12 Hours post	Test Parameter	Result-PRE-DOSE	Result-12Hrs POST DOSE	Lower Reference Range	Upper Reference Range	Unit (SI)

						post dose								
XXXXXX	XXX	XXX	XXX	XXXX	XX	XXX	XXXX	XX	XXXXX	XXX	XXX	XXX	XXX	XX
XXXXXX	XXX	XXX	XXX	XXXX	XX	XXX	XXXX	XX	XXXXX	XXX	XXX	XXX	XXX	XX

Note: provide the listing for Haematology parameters as per available data

Listing 16.1.11 Study Treatment - Itolizumab

Treatment Group	Subject ID	Date of dose	Dose	Frequency	Route	Start Time of infusion	End Time of infusion	Was Infusion interrupted?	Reason for infusion interruption	Stop Time of infusion interruption	Restart Time of infusion	Type of change	Reason for change	Was premedication Hydrocortison administered?
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX	XXXX	XXXX	XXXX
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX	XXXX	XXXX	XXXX

Listing 16.1.12 Study Treatment - Supportive Care/Oxygen Therapy

Treatment Group	Subject ID	Name of treatment	Start date of Dose	End date of Dose	Dose	Frequency	Route	Start Time of infusion	Was infusion interrupted	Reason for infusion interruption	Stop time of infusion interruption	Restart Time of infusion	Delivery mode for inhalation	Date of intubation	Start Time of intubation	Date of extubation	Start Time of extubation	Was weaning from mechanical ventilation done?	Date of weaning	Time of weaning	Reason for change
												S									
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XX XX	XXXX	XX XX	XX XX	XXXXX	XX XX	XXXX	XX XX	XXXX	XXXXX	XXXXX	XXXX
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XX XX	XXXX	XX XX	XX XX	XXXXX	XX XX	XXXX	XX XX	XXXX	XXXXX	XXXXX	XXXX

Listing 16.1.13 Chest X Ray/CT Scan

Treatment Group	Subject ID	Was CHEST X RAY performed?	Date of assessment	CHEST X RAY	comments	CT SCAN	comments
XXXXXX	XXX	XXX	XXXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XXX	XXXX	XXX	XXX	XXX	XXX

Listing 16.1.14 Adverse Event (Part1)

Treatment Group	Subject ID	Were any adverse events reported?	Adverse event number	Adverse event term	Does this AE meet definition of SAE?	Seriousness criteria	Severity of event as per CTCAE ver 4.03	Reasonable possibility that AE related to Study Drug	Start Date	End date
XXXXXX	XXX	XXX	XXX	XXXX	XXX	XXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XXX	XXX	XXXX	XXX	XXX	XXX	XXX	XXX	XXX

Listing 16.1.15 Adverse Event (Part-2)

Treatment Group	Subject ID	Is it a study drug infusion site reaction?	Relationship to study drug	If "Unlikely/Unrelated" to study drug, alternative etiology	Action taken on Study Drug	Did this AE lead to discontinuation from the study	Was any concomitant medication taken for this AE?	Outcome
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Listing 16.1.16 Hospitalization

Treatment Group	Subject ID	Was patient hospitalized during study?	Date of Admission	Date of Discharge	Ongoing at final examination	Was patient in Intensive Care Unit during this hospitalization period	Date of admission to ICU	Date of discharge from ICU	If yes, number of days in Intensive care unit	Primary reason for hospitalization	Were these additional organ support needed?
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX

Listing 16.1.17 Survival Status

Treatment Group	Subject ID	Date of assessment	Survival Status	Last known date subject alive	If Subject died, kindly record- Date of Death	Time of death
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX

Listing 16.1.18 SOFA Score

Treatment Group	Subject ID	Respiratory system (PaO2/FiO2)	Central Nervous system (Glasgow Coma Scale)	Cardiovascular system (Mean arterial pressure (MAP) OR administration of vasopressors required)	Liver (Bilirubin (mg/dl) [µmol/L])	Coagulation (Platelets ×103/ml)	Kidney (Creatinine (mg/dl) [µmol/L]; urine output)
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Listing 16.1.19 Ordinal Scale

Treatment Group	Subject ID	Patient state	Descriptor	Score
XXXXXX	XXX	XXX	XXX	XXX
XXXXXX	XXX	XXX	XXX	XXX

Graphs

- Figure 1: Disposition by centres: Bar Graph
- Figure 2: PaO2/FiO2 ratio: Line Graph
- Figure 3: change from baseline for Key Lab parameters: Ferrtin, d-dimer, LDH, CRP, Lymphocyte counts
- Figure 4: KM Curve for time to event endpoints