Appendix 16.1.9 Documentation of Statistical Methods

- Statistical Analysis Plan, Version 1.0, dated 16 September 2021

A PHASE I/II STUDY OF HUMAN PLACENTAL HEMATOPOIETIC STEM CELL DERIVED NATURAL KILLER CELLS (CYNK-001) FOR THE TREATMENT OF ADULTS WITH COVID-19

Protocol Number: CYNK-001-COVID-19

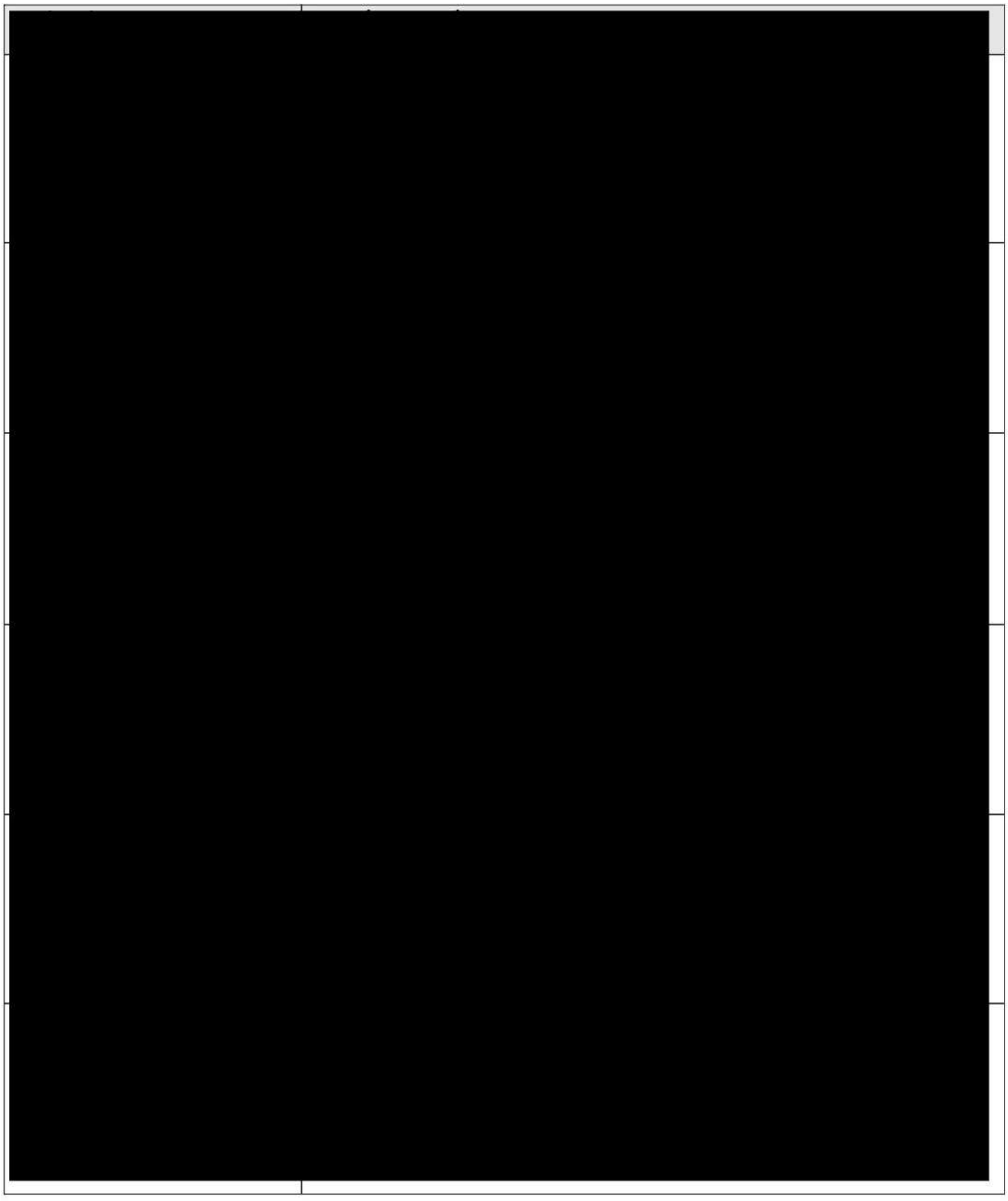
IND Number: 019650

Date of Protocol Version : 04 February 2021 (Amendment 5.1)

Sponsor Name: Celularity Inc.

Statistical Analysis Plan, Version 1.0

September 16, 2021



STUDY SUMMARY

Title:	A Phase I/II study of human placental hematopoietic stem cell derived natural killer cells (CYNK-001) for the treatment of adults with coronavirus disease (COVID-19)
Design:	A two-stage study, single arm at phase I and open-label two-arm 1:1 randomization with control at phase II, to investigate the safety, tolerability and efficacy of CYNK-001 on subjects with COVID-19
Investigational Drug:	CYNK-001
Reference Treatment:	Current standard of care for COVID-19 subjects
Population:	86 COVID-19 subjects in total (14 in phase I and 72 in phase II)
Study Duration:	The enrollment is expected for 5 months starting in May, 2020; each subject is expected to receive up to 3 doses in the first week and stay in the study for another 3 weeks. After that, each subject will be followed up to 6 months after randomization day.
Primary Objectives:	Phase I –To evaluate safety, tolerability and efficacy of CYNK-001 Phase II – To evaluate efficacy of CYNK-001
Primary Endpoints:	Phase I – Safety will be assessed by the frequency and severity of adverse events, changes in vital signs, laboratory assessments, Performance Status assessment, and immunological and inflammation assessments. Efficacy will be determined by time to clinical improvement at Day 15 using the Ordinal Scale for Clinical Improvement (OSCI), as defined by the World Health Organization (WHO). Phase II – Efficacy is determined by time to clinical improvement using the OSCI
Secondary Objectives:	Phase II – To determine A) safety and tolerability of CYNK-001 as measured by the frequency and severity of adverse events (AEs) using CTCAE 5.0, and B) overall clinical benefit of receiving CYNK-001 for COVID-19 as measured by rate of clinical improvement by OSCI, time to and rate of clinical improvement by NEWS2 Score, and all-cause mortality rate, time to and rate of clearance of SARS-CoV-2, time to and rate of pulmonary clearance, duration of

hospitalization, supplemental oxygen-free days, proportion of subjects requiring ventilation, SOFA score, and radiologic evaluation score.

Secondary Endpoints: Phase II – A) Safety will be assessed by the frequency and severity of adverse events, changes in vital signs, laboratory assessments, Performance Status assessment, and immunological and inflammation assessments. B) The overall clinical benefit will be evaluated by the rate of clinical improvement by OSCI, time to and rate of clinical improvement by NEWS2 Score, duration of hospitalization, and all-cause mortality rate, time to and rate of clearance of SARS-CoV-2, time to and rate of pulmonary clearance, supplemental oxygen-free days, proportion of subjects requiring ventilation, SOFA score, and radiologic evaluation score.

LIST of ABBREVIATION and SPECIALIST TERM

Abbreviation and Specialist Term	Explanation
AE	Adverse event
AESI	Adverse events of special interest
ARDS	Acute Respiratory Distress Syndrome
CI	Confidence interval
CMV	Cytomegalovirus
COVID-19	coronavirus disease
CT	Computerized tomography
CTCAE	Common Terminology Criteria for Adverse Events
CRS	Cytokine release syndrome
CRP	C-reactive protein
CYNK-001	Investigational product under study; allogeneic off the shelf cell therapy enriched for CD56+/CD3- NK cells expanded from human placental CD34+ cells
DLT	Dose limiting toxicity
DM	Data management
DMC	Data Monitoring Committee
eCRF	Electronic case report form
IV	Intravenous
LOCF	Last observation carry-forward
MedDRA	Medical Dictionary for Regulatory Activities
NEWS2	National Early Warning Score 2
rRT-PCR	Real-time Reverse Transcriptase-Polymerase –Chain Reaction

RFR	Randomization request form
RS	Randomization statistician
RTSM	Randomization and Trial Supply Management System in Clinical One
SAP	Statistical analysis plan
SAE	Serious adverse event
SARS-Cov-2	Severe acute respiratory syndrome coronavirus 2
SOC	Standard of care
SOP	Standard procedure
SpO_2	Oxygen saturation
SUSAR	Suspected unexpected serious adverse drug reaction
TEAE	Treatment-emergent adverse event

TABLE OF CONTENTS

1. Introduction

This statistical analysis plan (SAP) expands the analysis plan in *Section 14 Statistics* of the study protocol "A Phase I/II Study of Human Placental Hematopoietic Stem Cell Derived Natural Killer Cells (CYNK-001) for the Treatment of Adults With COVID-19" authored by the sponsor (Celularity Inc) dated February 4, 2021. This is the first version of the SAP and there are no changes to track from a previous approved version. The first approved version of the SAP will be available before the interim analysis of Phase I prior to moving to Phase II. The final approval of SAP from the sponsor and FHI is planned prior to unblinding of the data in Phase II.

The scope of analysis provided in this SAP includes: 1) analysis plan for three scheduled DMC meetings; 2) plan of final analysis for both Phases I and II after trial completion. The analyses in Phase I will assess the tolerability, safety, and efficacy or CYNK-001. The analyses in Phase II will assess safety and efficacy of CYNK-001 in comparison to control (best supportive care).

2. Study Objectives

2.1 Primary Objective

Phase I Study

The primary objectives of the Phase I portion of the study are to evaluate the safety, tolerability, and efficacy of multiple CYNK-001 intravenous (IV) infusions administered with an initial dose of 150 x 10^6 cells on Day 1 followed by 600 x 10^6 cells on Days 4 and 7 in subjects with COVID-19.

Phase II Study

The primary objective of the phase II portion is to evaluate the efficacy of CYNK-001 on subjects with COVID-19 by using the Ordinal Scale for Clinical Improvement (OSCI) defined by the World Health Organization (WHO).

2.2 Secondary Objectives

The secondary objectives for the phase II study are:

1. To determine safety and tolerability of CYNK-001 as measured by the frequency and severity of AEs using Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.
2. To evaluate the overall clinical benefit of receiving CYNK-001 for COVID-19 as measured by rate of clinical improvement by OSCI, time to and rate of clinical improvement by NEWS2 Score,

medical discharge, hospital utilization, all-cause mortality rate, time to and rate of clearance of SARS-CoV-2, time to and rate of pulmonary clearance, supplemental oxygen-free days, proportion of subjects requiring ventilation, SOFA score, and radiologic evaluation score.

2.3 Exploratory Objectives

Exploratory objectives include detection of SARS-CoV-2 via rRT-PCR in various specimen types, cytokine and chemokine measurement, and immune monitoring, alloreactivity measurement.

3. Study Design and Procedures

The study includes two phases with safety and efficacy evaluation between phases to determine the implementation of phase II study.

In the Phase I portion, a total of 14 subjects will be enrolled to assess the safety and efficacy of CYNK-001. To evaluate the safety for potential dose limiting toxicities (DLTs), this phase will enroll 3 subjects initially treated with CYNK-001. If any DLT is observed in the first three subjects, the DMC will be convened for a recommendation. The safety data for these 3 subjects will be evaluated 24 hours after the final dose was provided to the 3rd subject. If deemed safe, the remaining 11 subjects will be enrolled and monitored per the safety stopping rule until Day 15 after the first CYNK-001 infusion.

The starting dose is 150×10^6 cells on Day 1 followed by 600×10^6 cells on Days 4 and 7. The dose limiting toxicities (DLTs) will be evaluated for 28 days following the first dose of the CYNK-001 infusion (Day 1).

MTD is defined as the highest CYNK-001 dose level wherein it was deemed safe per the defined stopping rules or if the DMC recommends stopping the study due to DLTs suspected to be related to CYNK-001. In Phase I, any DLT finding will be forwarded to the DMC for recommendation, review and confirmation as to whether or not the MTD has been exceeded. If the MTD is confirmed by the DMC, no further CYNK-001 administration will occur within that dose level or at any higher dose level.

A de-escalation Dose level -1 will be initiated based on the study stopping rules and DLTs. Dose de-escalation is defined as reducing the frequency of doses by providing doses only on Days 1 and 7 due to potential safety concerns per the DMC recommendation. Once CYNK-001 is deemed safe per the stopping rule and if efficacy is established in at least 2 out of the 14 subjects by Day 15 of the CYNK-001 infusion, it will trigger the initiation of the Phase II of the study. If efficacy has not been demonstrated, the study may stop for futility.

The Phase II portion of the study is a randomized, open-label, multi-site study. 72 Subjects will be randomized to either CYNK-001 (n=36) or Control group (n=36) with best supportive care alone as defined by the hospital by 1:1 ratio, stratified by age (<45 vs. >=45 years old).

DMC will be convened at midpoint of Phase II (after 18 subjects have received treatment) to evaluate safety and adverse events of interest such as shock, ARDS, and death in the treatment group versus control group. Adverse events of special interest (AESI) will be identified in collaboration with the sponsor and medical monitor.

Each subject is expected to remain in the study for both, treatment period (Day 1 after first infusion to Day 28) and follow-up period (Day 29 to Month 6) with assessment at 3-month and 6-month after infusion.

The study is divided into 3 study periods: Screening Period, Treatment Period, and Follow-up Period, each with associated evaluations and procedures that must be performed at specific timepoints.

4. General Analytic Considerations

Analysis for Phase I and Phase II will be performed separately.

4.1 Data Sources

FHI data management (DM) plans are detailed in a separate study-specific document. In summary, DM will design the eCRF, edit checks and data cleaning.[redacted]

The collection and analysis source of lab data, biomarkers and immune monitoring refers to schedule of assessment table in the protocol; and the local lab data will be entered by the site into database. Data will be verified by study monitors and appraised for consistency by FHI 360 DM staff using automated logical checks. Adverse event (AE) will be centrally coded using the Medical Dictionary for Regulatory Activities (MedDRA Version 23.0). No formal adjudication will be performed by FHI 360. SAS datasets (version 9.4 or higher) will be created by FHI 360 DM for use by biostatisticians conducting analysis for DMC meeting purpose and final analyses.

4.2 Missing Data

For time to event data in the efficacy analysis, if the subject withdraws after randomization but before any measurement, the subject will be censored at the randomization date. For subjects who have an

early termination or death, the censoring rule will be described in the corresponding section for each outcome.

For the event rate data in the efficacy analysis, last observation carry-forward (LOCF) will be used if applicable.

The outcomes for safety assessment and assessment additional to efficacy analysis will not be imputed if data is missing.

Please refer to corresponding sections in this SAP for more detail about missing data handling.

Additional rules for imputation of missing data may be determined during blinded review of the data and documented prior to unblinding.

4.3 Analysis Scope of Data Monitoring Committee (DMC) Meeting and Final Analysis

The analysis plan for three scheduled DMC meetings for both phase I and phase II is written in the relevant section independently. The rest of the analysis plan applies to final analysis only after the end of the study, defined as all subjects satisfy the criteria of "End of Study" in the protocol. The analysis for protocol defined exploratory objective will be implemented by Celularity translational team, and thus is not included in the scope of this SAP.

4.4 Covariate Adjustment

For phase I study, no pre-specified set of covariates will be employed to adjust for analysis result.

For phase II study, the primary efficacy endpoint will be adjusted by the age groups (< 45 vs. >=45 years old). The summary of primary efficacy endpoint by the strata of age, will also be performed in the subgroup analysis. More details will be provided in the corresponding sections of this SAP.

4.5 Test Size and Confidence Levels

Unless otherwise noted, all reported confidence intervals will be computed at the 95% coverage level, and all p-values will be assessed at the two-sided 0.05 significance level, with no further adjustment for multiple testing.

4.6 Analysis of safety data

If not further specified, the system organ class (SOC) and preferred term for adverse events analysis will be summarized using Medical Dictionary for Regulatory Activities (MedDRA) Version 23.0 with severity grade defined by CTCAE Version 5.0.

4.7 Reporting Timeframe of Measurement for Analysis

For analyses of efficacy endpoints, the latest observation within the study day will be used. If the observations for Day 15 and Day 28 fall outside of the 24-hour window of the study day, the observation will be considered as missing and the imputation as described above will apply as appropriate.

For summary analyses of subject efficacy assessment and safety analysis, the latest observation within the study day during treatment period or within protocol defined time-windows during the follow-up period, will be used. No imputation will be made.

For safety analysis with adverse events, the observation with highest severity within the study day during treatment period or within protocol defined time-windows during the follow-up period, will be used. No imputation will be made.

4.8 General Rules for Summarizing Data

The general rules for summarizing the data, unless otherwise mentioned, are:

- Number of subjects in the defined population and numbers of subjects with available data will be provided
- Continuous variables will be summarized using descriptive statistics such as mean, standard deviation, median, minimum, and maximum.
- Categorical variables (e.g., gender, race, etc.) will be provided using frequency tabulations
- Analyses for Phase I portion and for Phase II portion will be performed separately. The analysis for Phase I will be based on safety analysis set. Analysis for Phase II will be performed by treatment group. The main analysis set for efficacy is the full analysis set, and the main analysis set for safety is the safety analysis set.

5. Randomization, Allocation Concealment and Blinding

5.1 Randomization

The Phase I study is a single-arm open label study and thus no randomization is planned.

At Phase II study, 72 subjects will be randomized to either one of the treatment arms below with randomization ratio 1:1.

- CYNK-001 with Standard of Care (SOC, also known as best supportive care) (n=36)
- SOC (n=36)

The randomization will be stratified by subject's age at baseline (less than 45 years; and greater or equal to 45 years).

The randomization sequence will be developed by a qualified FHI 360 Randomization Statistician (RS) who is not otherwise involved in the study using a validated program written in SAS®. A

[redacted]

The detail about randomization plan is documented in the randomization request form (RFR) which is prepared under FHI Standard of Procedure (SOP) Document #07002.

5.2 Allocation Concealment and Blinding

Since the randomized phase (phase II) of the study is open label, no blinding after randomization is involved. To assure unbiasedness, the study statisticians will remain blinded with no access to the data of treatment arm before completion of final data cleaning.

5.3 Blinded Data Review

Prior to scheduled unblinding and final data cleaning, the data may be reviewed in a blinded fashion. Based on analysis needs, the lead statistician will develop specific listings for this review and will document the sponsor or stakeholders' decisions prior to unblinding.

[redacted]

Blinded data review may also include clinical evaluation of safety data for reasonableness or to issue clinical queries to the site if needed. Any decisions affecting analysis will be described in internal documentation and the CSR.

6. Study Size and Power

Phase I Study

Fourteen (14) subjects will be treated with CYNK-001 in the Phase I portion. This sample size is determined to be adequate for the evaluation of safety and potential efficacy, based on clinical

judgement for this coronavirus disease and the current treatment status before starting Phase II portion. This number is not driven by hypothesis testing and power calculation.

Phase II Study

The primary efficacy endpoint is time to clinical improvement on the Ordinal Scale for Clinical Improvement (OSCI) defined by the World Health Organization (WHO), at Day 15. As preliminary purpose of proof of concept, without relevant data for the new coronavirus disease, no multiplicity will be adjusted and a 1-sided α of 0.05 will be used for the sample size consideration. With a sample size of 36 for each group (72 in total with 1:1 randomization ratio), a reduction of 50% for the time to event efficacy of CYNK-001 comparing with control can be detected with a power of at least 81% (assuming the time to clinical improvement is 8 days or earlier for CYNK-001 group, and 16 days or earlier for the control group with the same reduction rate of 50%) by using Log-rank test. This estimation is based on the study design with endpoint assessment at 28 days after infusion for each subject.

7. Analysis Populations

- Screened population – include the subjects who are screened.
- Safety Population – include all subjects who receive any amount of CYNK-001 in either phase or who enroll into the control group in phase II. Subjects will be analyzed according to the actual treatment they received for safety analysis.
- ITT Population– the definition of intent-to-treat population applies to phase II only. This population includes all randomized subjects. The subject will be analyzed according to the treatment arm they are randomized to.
- Per Protocol Population (PP) - the definition of per protocol (PP) population applies to phase II only. This population includes all randomized and treated subjects who have no major protocol violations/deviations that may affect the primary efficacy outcome. Protocol violations/deviations will be identified and reviewed before database lock.

8. Data Monitoring Committee (DMC)

Periodic safety monitoring will be conducted by the DMC. The recommendation whether to continue, de-escalate, stop the trial or move to Phase II for safety or futility will be reached by the DMC based on their review of safety and efficacy information. Specific details are provided in the DMC Charter.

9. Subject Disposition and Protocol Violation/Deviation

Subject disposition (analysis population allocation, enrolled, discontinued, primary reason for discontinuation) will be summarized using frequency and percent. A summary of subjects enrolled by site will be provided.

Protocol deviations will be identified before database lock. Major protocol deviations will be summarized.

10. Demographics and Baseline Characteristics

Demographic variables such as sex, race, ethnicity and age group will be summarized using number (n) and percentage (%). Descriptive statistics such as n, mean, standard deviation (SD), median, min and max will be calculated for age. Infection symptoms at baseline will be summarized.

Medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 23.0. System Organ Class (SOC) and Preferred Term (PT) will be summarized by number and percentage (%) of patients.

11. Analysis of Study Treatment Exposure

Exposure to study drug will be summarized with descriptive statistics for the number of doses received and the total cumulative dose. The number of dose interruptions will be summarized. The analysis will be based on safety population.

Individual listings will be provided.

12. Study Day Definition

Study Day 1 is defined as the day subject took the first dose of CYNK-001.

The study day of any given event is relative to Study Day 1. If an event is after the first dose, then study day is calculated as the event date minus the date of Study Day 1 + 1; if an event is before the first dose, then study day is calculated as the event date minus the date of Study Day 1.

13. Efficacy Analysis

13.1 Primary Efficacy Endpoint

13.1.1 Primary Efficacy Endpoint for Phase I

The efficacy analysis for Phase I will be based on the safety analysis population.

The primary efficacy endpoint for Phase I is clinical improvement by OSCI on or prior to Day 15. Clinical improvement by OSCI is defined as at least one patient state improvement compared to baseline. If clinical improvement by OSCI is demonstrated for at least 2 out of 14 subjects on or prior to Study Day 15, and CYNK-001 is deemed to be safe, the study will move to Phase II. Otherwise, the study will be terminated.

Phase I efficacy data will be summarized by descriptive analyses for the number and proportion of subjects who achieved clinical improvement by OSCI by Day 15.

The proportion of the clinical improvement by OSCI at Day 15 will be summarized with a point estimate, standard error and a 95% confidence interval.

Patients who do not achieve at least one patient state improvement will be considered as failure to improve by OSCI. No formal hypothesis testing will be carried out for this part of the analysis.

Subject listings of clinical status using OSCI will be provided.

13.1.2 Primary Efficacy Endpoint for Phase II

The primary endpoint is time to clinical improvement as measured by OSCI. Time to clinical improvement by OSCI is defined as the time from the date of randomization to the first date of clinical improvement measured by OSCI. Subjects who do not have clinical improvement on or before Study Day 28 will be censored at Study Day 28.

13.2 Efficacy Endpoints

The study includes the following efficacy endpoints:

1) Clinical status by OSCI at Day 28.
2) Clinical improvement by OSCI by Day 15.
3) Rate of clinical improvement by OSCI at Day 28. The rate is defined as the proportion of subjects who achieved clinical improvement by OSCI on or prior to Day 28.
4) Time to clinical improvement as measured by OSCI.
5) Time to clinical improvement by NEWS2. Time to clinical improvement by NEWS2 is defined as the time from the date of randomization (date of first dose of CYNK-001 for Phase 1) to the first date of clinical improvement by NEWS2. Clinical improvement by NEWS2 is defined as a 25% decrease compared to baseline in the NEWS2 Score. Subjects without clinical improvement by NEWS2 on or before Day 28 will be censored at Day 28.

6) Rate of clinical improvement by NEWS2 at Day 28. The rate is defined as the proportion of subjects who achieved clinical symptom improvement by NEWS2 Score on or prior to Day 28.

7) Rate of clearance of SARS-CoV-2 from mucosal specimens at Day 28. Rate is defined as the proportion of subjects with clearance of SARS-CoV-2 by rRT-PCR by two negative results at least 24 hours apart. Specimens included are nasopharyngeal swab and optional oropharyngeal swab.

8) Time to clearance of SARS-CoV-2 from mucosal specimens at Day 28. Clearance is defined as the time from the date of randomization to clearance of SARS-CoV-2 by rRT-PCR by two negative results at least 24 hours apart. Specimens included are nasopharyngeal swab and optional oropharyngeal swab.

9) Time to pulmonary clearance at Day 28. Clearance is defined as the time from randomization to the date of pulmonary clearance. This is defined as disappearance of virus from LRT specimen where it has previously been found (induced sputum and endotracheal aspirate if available).

10) Rate of pulmonary clearance at Day 28. Rate is defined as the proportion of subjects who had disappearance of virus from LRT specimens where it has previously been found.

11) Duration of hospitalization from date of hospitalization to date of medical discharge.

12) For subjects requiring supplemental oxygen, the days with supplemental oxygen-free up to Day 28.

13) Proportion of subjects who need invasive or non-invasive ventilation up to Day 28.

14) SOFA score for subjects admitted to the ICU from ICU admission to ICU discharge, up to Day 28.

15) Radiologic Evaluation Score at Day 28 using Chest x-ray and/or CT scans.

16) Proportion of subject who died up to Day 28 and up to Month 6.

13.2.1 Exploratory Endpoints

The exploratory outcomes of this study include:

1) Cytokine and Chemokine assessment measured serially until Month 6.

2) Immune monitoring as measured by chimerism and/or other differentiating methodologies of donor-derived natural killer cells for those treated with CYNK-001. Immune profiling and immunophenotyping including alloreactivity at Month 6.

3) Detection of SARS-CoV-2 via rRT-PCR in various specimens including peripheral blood at Month 6.

13.3 Analysis Methods

The primary endpoints will be analyzed with hypothesis testing procedures. No formal hypothesis will be carried out for secondary endpoints and the p-values are provided for informative purpose only.

Missing data and censoring will be handled as described below.

- **Primary Efficacy Analysis**

Phase II efficacy data will be analyzed for the ITT population based on randomized treatment group.

The primary efficacy endpoint is the time to clinical improvement on or before Day 28. Kaplan-Meier estimates of the survival curve, estimate of median survival time and its 95% CI will be calculated. Log-rank test will be used to test the difference between treatment groups while adjusting for pre-defined age strata.

Hazard ratio will be estimated via proportional hazard model using treatment as a factor stratified by age group.

Subjects who withdraw after randomization and before any measurements assessed will be censored at randomization date; subjects who terminate from the study before Day 28 without clinical improvement will be censored on the date of the last visit; and subjects who died without clinical improvement by OSCI will be censored on Day 28; subjects without clinical improvement ~~who have no event~~ on or before Day 28 will be censored on Day 28.

- **Secondary Endpoints Analyses**

The analysis will be based on the ITT population unless otherwise specified. Since the purpose of the analysis is for hypothesis generation, no multiplicity adjustment or adjustments for stratification covariates (age and site strata) will be made.

For the endpoints of event rate, including:

- Proportion of subjects who achieved clinical improvements by OSCI

- Proportion of subjects with clearance of SARS-CoV-2 by rRT-PCR
- Proportion of subjects who had pulmonary clearance by LRT specimens where it has previously been found
- Proportion of subjects who need invasive or non-invasive ventilation
- Proportion of subjects who died

The proportions and their two-side 95% CIs will be calculated. Fisher's exact test will be used to test the difference between treatment groups. If the subject has no data after baseline, the subject will be considered as failure in the analysis.

For endpoints of time to event, including:

- Time to clinical improvement measured by NEWS2 Score
- Time to clearance of SARS-CoV-2 by rRT-PCR testing
- Time to disappearance of virus from LRTI specimen
- Time from randomization to medical discharge
- Duration of hospitalization (from time from hospitalization to medical discharge up to Day 28)

The Kaplan-Meier method will be used for estimating the survival curves, the median survival time and its two-sided 95% confidence interval will be estimated. [redacted]

[redacted]

Mortality rate will be provided and be compared using Fisher's Exact Test.

For the endpoint of proportion of subjects who achieved clinical symptom improvement by NEWS2 Score by Day 28, clinical improvement is defined as a 25% reduction in NEWS2 Score. The proportions

and their two-sided 95% CIs will be calculated. Fisher's exact test will be used to test the difference between groups. If the subject has no data after baseline, the subject will be considered as failure in the analysis.

1) Calculation

    a. Respiratory rate, oxygen saturation, temperature, systolic blood pressure, and heart rate will be collected on the Vital Signs and Oxygen Saturation eCRF forms.

    b. Consciousness score will be based on the Physical Exam eCRF form. If Neurological is normal, then NEWS2 Consciousness will be scored as zero. If Neurological is abnormal, then the score will be determined based on the comments. A clinical review of the comments from the abnormal neurological findings will be required.

    c. Air or Oxygen will be based on the eCRF form Prior and Concomitant Procedure and Surgeries. If a subject had Preferred Term "Oxygen Therapy" then the NEWS2 Air or Oxygen Score will be 2 for the days from the start day through the end day of the procedure.

    d. Calculation of overall NEWS2 Score for a given day will be the sum of the scores from respiratory rate, oxygen saturation, temperature, systolic blood pressure, heart rate, consciousness, and air or oxygen categories. For infusion days, data for Vital Signs and Oxygen Saturation are collected 3 separate times. For infusion days, a separate overall score will be calculated for each time the Vital Signs and Oxygen Saturation is collected, and the worst overall score will be used as the NEWS2 Score for that day.

2) Missing data handling:

    a. If a measure for vital signs and oxygen saturation is missing, corresponding NEWS2 score will be set as missing, and the overall NEWS2 score takes the form ≥ xx. If all categories from vital signs and oxygen saturation is missing, the overall NEW2 score will be set as missing.

    b. If the result for Neurological in Physical Exam is missing or not assessed, then corresponding NEWS2 score will be set as 0.

    c. NEW2 score for "Air or Oxygen" is based on the presence of oxygen therapy in the prior and concomitant procedure page, so NEWS2 will not be considered as missing.

Ordinal data endpoints, including Clinical status by OSCI and SOFA score, will be summarized descriptively with number and percentage in each treatment arm and overall. LOCF will be used to impute missing data.

13.4 Sensitivity Analysis

The analysis for the time to clinical improvement by OSCI, and time to clinical improvement by NEWS2 will also performed on the PP population as sensitivity analysis.

13.5 Additional Efficacy Analysis

For either phase, the Karnofsky performance status assessment will be summarized over time by the frequencies and proportions of presence and assessment status for symptom present subjects. The proportions and the 95% confidence interval of the proportions will be provided if applicable. The descriptive statistics, including mean, standard deviation, range and 95% confidence interval of body temperature will be provided. No hypothesis testing will be performed for this part of analyses.

For phase II study, the clinical status by OSCI will be summarized overall and by each attrition over time. Mann-Whitney-Wilcoxon test will be used to compare between groups at Day 28. This analysis will be based on the ITT population without missing data imputation strategy planned.

The proportion of subjects who need invasive and non-invasive ventilation support and its 95% confidence interval will be summarized over time. Organ support related days will be also summarized by mean, standard deviation, median, range and 95% confidence interval.

14. Safety Analysis

Safety analysis will be based on the safety analysis population. For Phase I, the analysis will be performed by cohort, including an overall column. For Phase II, the analysis will be performed by treatment arms.

14.1 Adverse Events

All AEs will be coded using the MedDRA dictionary Version 23.0 or higher. The severity of toxicities for AEs will be graded 1 to 5 according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0 whenever possible. AEs with missing severity will be presented in the summary table as missing category.

A treatment-emergent adverse event (TEAE) is defined as an AE which started on or after the first dosing date of the study drug or an existing condition being worse on or after the first dosing date of the IP.

Adverse events with unknown onset date and with end date after first dosing date will be counted in the TEAE.

A treatment-related AE is defined as an AE which is considered to be of suspected relationship to the study drug. Adverse events with missing relationship to study drug will be assessed as treatment-related.

The following summaries will be provided:

- A table for overall summary and a listing of all AEs by SOC and PT will be provided for AEs that occurred during the screening period.
- Separate summaries will be provided for the treatment period (Day 1 – Day 28) and follow-up period (Day 29 to 6 months). The following summary tables will be generated:
    - Overall summary
    - All TEAEs by SOC and PT
    - TEAEs that satisfy the DLT criteria (Phase I treatment period only)
    - TEAEs leading to discontinuation of treatment
    - TEAEs with toxicity grade >=3
    - Drug-related TEAEs
    - Serious TEAE
    - TEAEs that led to death
    - Summary of CRS

If a subject experiences multiple AEs under the same PT (SOC), then the subject will be counted only once for that PT (SOC). If a subject experiences the same AE more than once with different toxicity grade, the event with the highest grade will be tabulated in “by maximum toxicity grade” tables.

14.2 Laboratory assessment

Laboratory results including chemistry and hematology, will be summarized over time. Absolute change from baseline to each study day up to 6-month follow-up, will be summarized descriptively with mean, standard deviation, median, range and 95% confidence interval by visit.

14.3 Vital signs

Vital signs and the changes from baseline will be summarized descriptively with mean, standard deviation, median, range and 95% confidence interval by infusion time point at Day 1, Day 4 and Day 7. The clinically significant status of vital signs will also be tabulated. During the infusion day, the summary of vital signs will be summarized separately by infusion time point as pre-infusion, 30 minutes post-infusion and 4-hours post infusion.

14.4 Physical exams

Physical exams will be listed.

14.5 Immunological / Inflammation Assessments

High sensitivity C-reactive protein (CRP), ferritin, and D-dimer results and the change from baseline will be summarized over time descriptively with mean, standard deviation, median, range and 95% confidence interval.

14.6 Chest X-ray

The assessment of pulmonary infiltrate and pleural effusion over time will be tabulated separately for pre-specified age strata and overall population.

14.7 Infectious Symptom Assessment

The infectious symptom assessment will be tabulated over time with the proportion of clinical status assessment as defined in the CRF. The descriptive statistics, including the proportion and its 95% confidence interval will be provided.

No missing data will be imputed for this part of analysis nor formal hypothesis testing will be performed.

Subject level listing of AEs, vital signs, laboratory assessments and inflammation assessments will be provided.

15. Changes in Conduct or Planned Analyses from the Protocol

Description of change of conduct: Early termination of the study by the company.

In review of the current status and enrolment challenges of the CYNK-001-COVID-19 clinical trial and given the current landscape of the COVID-19 pandemic and the rollout COVID-19 vaccine, a decision by

Celularity has been made to close the CYNK-001-COVID-19 clinical trial. As a result of this early termination, only 7 patients were enrolled and dosed in the Phase I portion.

Due to this change, a brief clinical study report will be provided instead of a full CSR. Based on this change, only the following analysis will be provided for Phase I along with supporting listings:

- Summary of Subject disposition
- Summary of major protocol deviations
- Summary of demographics and baseline characteristics
- Analysis of time to clinical improvement by NEWS2 score
- Analysis of rRT-PCR tests and time to clearance of SARS-CoV-2 by rRT-PCR results (if enough data available)
- Analysis of SOFA scores (if enough data available)
- Summaries of adverse events
- List of deaths
- Summaries of laboratory results, shift from baseline and abnormal laboratory values
- Summaries of vitals signs, oxygen saturation and ECG and shifts from baseline
- Summary of abnormal post-baseline QTc results

16. Analysis of Concomitant Medication and Concomitant Procedure

16.1 Analysis of Prior and Concomitant Medication

Prior medicine is defined as the medication that was given prior to the day of the first dose

Concomitant Medicine is defined as medication which is given on or after the date of first dose.

Frequency summaries of prior and concomitant medications coded with WHO drug dictionary (version Mar2020) will be provided by treatment group.

At each level of subject summarization, a subject is counted once if the subject reported one or more medications. Complete listing, including reason for use, duration, frequency and dosage of concomitant and prior medication will be provided.

16.2 Analysis of Prior and Concomitant Procedure

Prior procedures are defined as procedures that occurred before the date of first dose

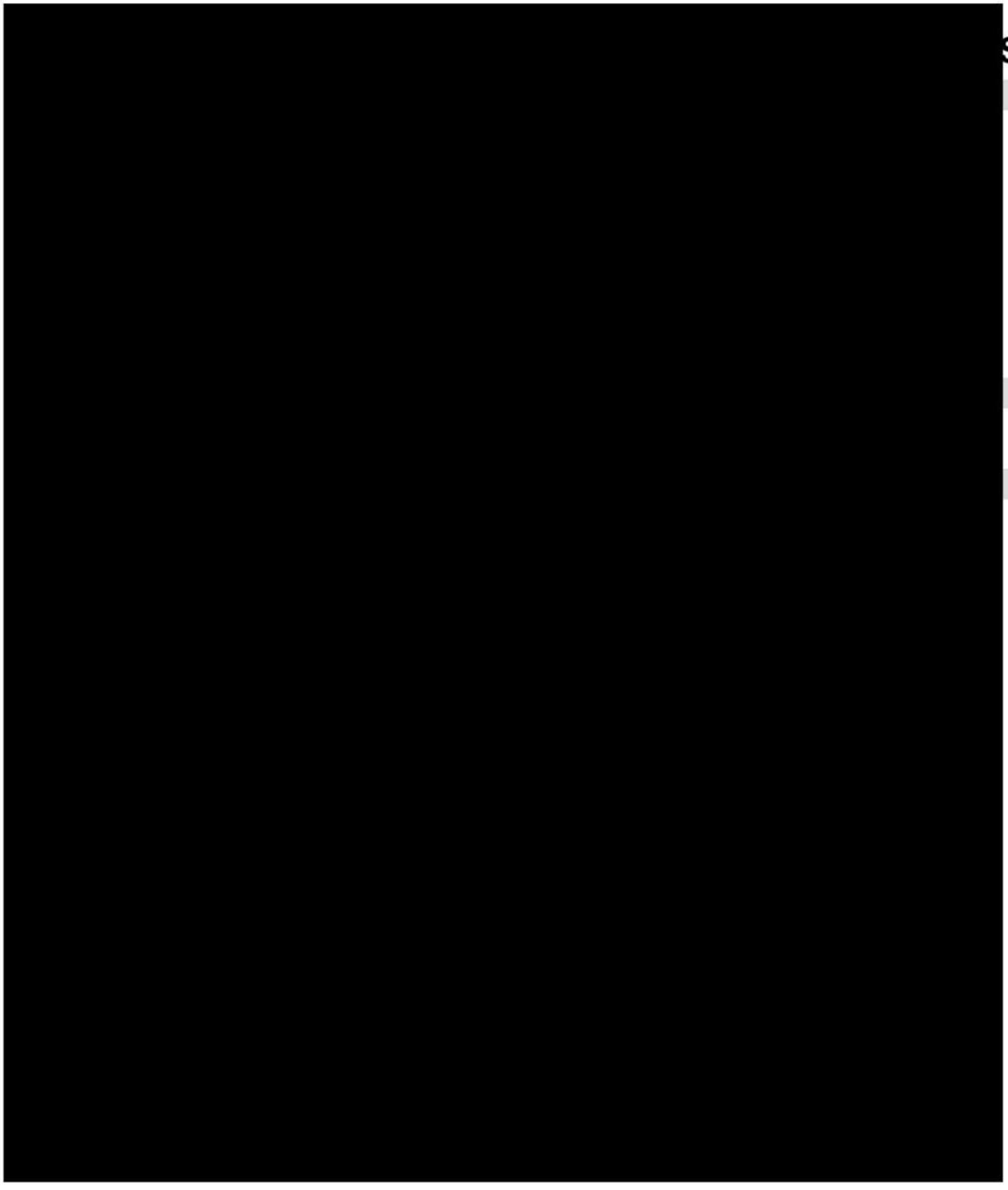
Concomitant procedures are defined as procedures which are given after the date of first dose.

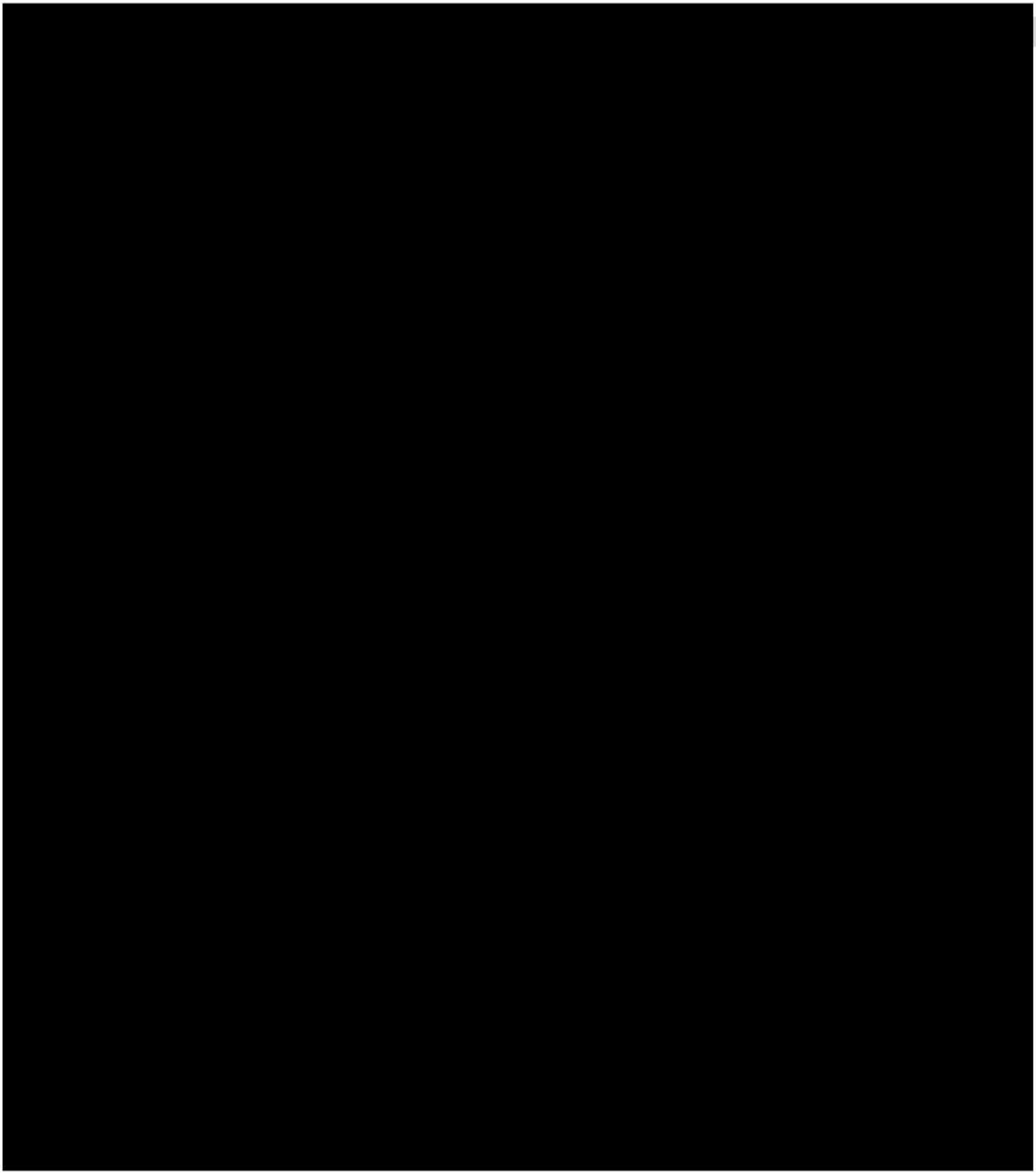
Frequency summaries of prior and concomitant procedures coded using MedDRA (version 23.0) along with the surgery necessity will be provided by treatment group. At each level of subject summarization, a subject is counted once if the subject reported one or more procedures. Complete listing, including necessity of surgery and duration of concomitant and prior procedure will be provided.

17. Subgroup Analysis

For phase II study, the primary efficacy endpoint

time to clinical improvement as measured by OSCI and other symptoms, will be further summarized by the subgroup of gender (male/female), severity of disease (definition pending), and time from symptom onset to enrollment (cut-off pending), protocol defined strata, and site for both treatment arms and overall population. Included in the summary will be hazard ratios and their 95% confidence intervals as a forest plot. No hypothesis testing will be performed.





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