STATISTICAL ANALYSIS PLAN (ABBREVIATED)

Version: 1.0

DATE OF PLAN:

April 7, 2024

STUDY DRUG: OMS721

PROTOCOL NUMBER: OMS721-HUS-002 AMENDMENT 01

(DATED 26 MAY 2017)

STUDY TITLE:

A Phase 3 Study to Evaluate the Safety and Efficacy of OMS721 for the Treatment of Atypical Hemolytic Uremic Syndrome (aHUS) in Adults and Adolescents

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This study is being conducted in compliance with good clinical practice, including the archiving of essential documents.

SIGNATURE PAGE

This document has been reviewed and accepted by:

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1. LIST OF ABBREVIATIONS

Table 1: List of Abbreviations

Abbreviation	Explanation
AE	Adverse event
aHUS	Atypical hemolytic uremic syndrome
BMI	Body mass index
BP	Blood pressure
ECG	Electrocardiogram
eGFR	Estimated glomerular filtration rate
Kg	Kilogram

2. INTRODUCTION

This abbreviated statistical analysis plan (SAP) is based on:

- Protocol No. OMS721-HUS-002, Amendment 01, dated 26 May 2017
- ICH guideline E9 (Statistical Principles for Clinical Trials)

OMS-721-HUS-002 was discontinued due before a meaningful number of patients could be enrolled. The purpose of this document is to provide guidance for the analyses that will be performed on the available data.

3. STUDY DESIGN

For a detailed description of the proposed methodology for OMS271-HUS-002, please refer to the study protocol.

The study procedures and assessments are presented in Section 10 of the same document.

4. ANALYZED OBJECTIVES

4.1. Primary Objective

The primary objective of this study was to evaluate the effect of OMS721 in subjects with aHUS on platelet count change from baseline. As a sufficient number of patients were not enrolled, data for the primary objective will be not analyzed.

4.2. Secondary Objective(s)

The secondary objectives of this study were to evaluate the effect of OMS721 in subjects with aHUS on a variety of parameters. Parameters that will be analyzed include:

- Safety as assessed by AEs, SAEs, vital signs, ECGs, physical examinations, and laboratory measures
- Serum creatinine change from baseline
- Serum LDH change from baseline
- Serum haptoglobin change from baseline

4.3. Exploratory Endpoints

Not applicable as the study was terminated due to incomplete recruitment.

5. DEFINITIONS AND CALCULATION ALGORITHMS

5.1. Calculations Using Dates

Age at informed consent is calculated as the integer part of (date of informed consent – date of birth)/365.25.

Duration of treatment (weeks) is defined as (last dose date – first dose date + 1)/7.

Study day is defined as

- Event Date – First Dose Date + 1 if the event date is on or after the first dose date
- Event Date – First Dose Date if the event date is before the first dose date

5.2. Baseline

Prior to the first OMS721 treatment, subjects had two platelet count samples collected. The second platelet count sample was collected between 1 and 4 hours following the first platelet count sample. These samples were sent to the central laboratory and the mean value was be used as the baseline platelet count for analyses. Visit 1 and Visit 2 may be combined for plasma therapy-resistant subjects. If Visit 1 and Visit 2 are combined, laboratory measures collected for Visit 1 will serve as the laboratory measures for Visit 2 as well.

For all the other variables, the baseline value will be the last recorded value prior to the administration of the first dose of study treatment.

5.3. Day 1

Study Day 1 is defined as the first dose date of the study drug.

5.4. Visit Windows Relative to the First Dose of Study Treatment

No windows will be defined for this study. Data collected at scheduled post-baseline visits will be analyzed at the visit where the values were collected. Data collected at unscheduled post-baseline visits and early termination visits will be analyzed at the closest planned visit if data were not collected at one of the two planned visits adjacent to this unscheduled or early termination visit. For example, if a subject early terminated from the study at Visit 35, and ECG was collected at Visit 35, then the ECG parameters collected at Visit 35 will be analyzed at Visit 36.

5.5. Analysis Populations

5.5.1. Safety Analysis Set

All presented analysis will be done using the safety analysis set which includes all subjects who receive any amount of study treatment.

6. DATA PRESENTATIONS AND DATA MANAGEMENT

6.1. Data Presentations

The plan for tabular presentations and analysis of the data, in general, is divided into five categories:

1. Subject disposition using the safety analysis set.
2. Baseline and demographic profile using the safety analysis set.
3. Safety and tolerability using the safety analysis set.

6.2. Data Management

All statistical analyses will be performed using SAS version 9.4 or later (SAS Institute Inc., Cary, NC).

7. SUBJECT DISPOSITION

The number of subjects treated, completing the protocol specified duration of study drug, discontinuing study drug early, completing the study, and early withdrawal from the study will be summarized by cohort. The reason(s) for early discontinuation of study drug and early withdrawal from the study will be summarized. A list of subjects failing any eligibility criteria will be provided.

8. BASELINE SUBJECT DATA

8.1. Baseline Demographic and Subject Characteristics

The following demographic characteristics and baseline values will be summarized by cohort: Age at informed consent, gender, ethnicity, race, childbearing potential, weight, BMI, systolic blood pressure, diastolic blood pressure, duration of disease, history of kidney transplantation for aHUS, platelet count, serum lactate hydrogenase, serum creatinine, and eGFR.

Concomitant medications used at baseline will be listed.

8.2. Medical History and Physical Examination

Medical and surgical history, history of aHUS and comprehensive and symptom-directed physical examinations will be presented in listings.

9. EFFICACY ANALYSIS

9.1. General Considerations

This study was discontinued due to the inability to recruit a meaningful number of subjects; therefore, no efficacy analyses will be performed. Analyses that will be performed are outlined in this SAP.

10. SAFETY AND TOLERABILITY

10.1. Overall Summary of Safety

An overall summary of treatment-emergent adverse events, which is defined as the AEs occurring or worsening after the start of study treatment, will be provided by cohort. All AEs will be coded by MedDRA. The following items will be included in the overall summary:

- Subject incidence of treatment-emergent AEs
- Subject incidence of treatment-related AEs (defined as probable or possible related to study drug)
- Subject incidence of treatment-emergent AEs by maximum CTCAE grade
- Subject incidence of treatment-emergent serious AEs (SAEs)
- Subject incidence of treatment-emergent AEs leading to discontinuation of study drug
- Subject incidence of treatment-emergent AEs leading to discontinuation of study
- Subject incidence of treatment-emergent fatal AEs
- Total number of unique treatment-emergent AE MedDRA preferred terms
- Median number of unique treatment-emergent AE MedDRA preferred terms per subject
- Total number of unique treatment-emergent SAE MedDRA preferred terms
- Median number of unique treatment-emergent SAE MedDRA preferred terms per subject

10.2. Adverse Event Preferred Term and Body/Organ System Summary Tables

Subject incidence of the following treatment-emergent AEs will be provided by cohort:

- Pre-treatment AEs will be summarized by MedDRA SOC and preferred term (pre-treatment AEs are those AEs that occurred prior to the start of study treatment)
- treatment-emergent AEs by MedDRA SOC, and preferred term
- treatment-emergent AEs by MedDRA preferred term
- treatment-related AEs by MedDRA SOC, and preferred term
- treatment-emergent AEs by MedDRA preferred term, and maximum CTCAE grade
- AEs leading to study drug discontinuation by MedDRA SOC, and preferred term
- AEs leading to study discontinuation by MedDRA SOC, and preferred term
- treatment-emergent SAEs by MedDRA SOC, and preferred term
- treatment-related SAEs by MedDRA SOC, and preferred term

- AEs leading to death by MedDRA SOC, and preferred term

10.3. Study Treatment Adherence and Extent of Exposure

Intravenous doses of the study drug are to be administered by study personnel.

To ensure good treatment adherence for study drug administered subcutaneously, investigative site personnel has prepared and administered the first SC injection at Visit 2 to train the subject or subject's caregiver on the proper techniques for dose preparation and injection. During Visit 3 (Day 2), Visit 4 (Day 3), and Visit 5 (Day 4) investigative site personnel observed and ensured that the subject is trained on the proper way to prepare and administer OMS721 SC. If deemed necessary, the site continued to instruct and observe SC injections by subject or subject's caregiver after Visit 5 (Day 4).

The following exposure items will be summarized with descriptive statistics by route (IV and SC) and cohort using the safety analysis set:

- Cumulative doses in milligrams taken by treatment period (the Treatment Induction Period, the Treatment Maintenance Period and the entire treatment period).
- Duration of treatment in weeks by treatment period, which is defined as (the last dose date of the treatment period – the first dose date of the treatment period + 1)/7.

10.4. Concomitant and Other Medications

Subject incidence of concomitant medications will be provided by WHODrug preferred term and cohort.

10.5. Routine Laboratory Data

Summary statistics for actual values and for change from baseline will be tabulated as appropriate for laboratory results by scheduled visit and cohort. Subjects with laboratory values outside of the normal reference range at any post-baseline safety assessment will be listed by cohort.

Shifts from baseline laboratory values (normal/abnormal) will be tabulated by cohort.

10.6. Vital Signs

Summary statistics for actual values and change from baseline will be tabulated for vital signs by cohort and scheduled visit.

10.7. Electrocardiogram

The ECG parameters (heart rate, PR interval, QRS interval, QT interval, and QTcF interval) at each time recorded as well as the change from baseline will be summarized with descriptive statistics by cohort. These parameters will be determined electronically by the ECG machine at the clinical site. QTcF will be calculated using Fridericia's formula.