CONFIDENTIAL

Statistical Analysis Plan (SAP)

Sponsor:	*CalciMedica through EMAS*
Study code:	*CM4620-202*
Study title:	*A Pharmacodynamic and Pharmacokinetic Study of CM4620 Injectable Emulsion in Patients with Acute Pancreatitis*
Date:	*Draft 1 – 14May2019* *Final – 29May2019*

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1 LIST OF ABBREVIATIONS

AE – Adverse Event

ALB - Albumin

ATC – Anatomical-Therapeutic-Chemical

CF – Clean File

CRF – Case Report Form

CSP – Clinical study protocol

FAS – Full Analysis Set

HCT - Hematocrit

MedDRA – Medical Dictionary for Regulatory Affairs

PPS – Per Protocol Set

SAE – Serious Adverse Event

SAP – Statistical Analysis Plan

SAS – Statistical Analysis System

SD – Standard Deviation

2 INTRODUCTION

This Statistical Analysis Plan (SAP) gives details regarding the statistical analyses and data presentation outlined in the final Clinical study protocol (CSP) for the study *CM4620-202.* Any changes from the final CSP are given in Section 8. This needs to be approved and signed prior to database lock.

This SAP will not cover the analysis of IL-6 and pharmacokinetic analyses-

3 CLINICAL STUDY DETAILS

3.1 Clinical Study Objectives

3.1.1 Primary objective

N/A

3.1.2 Primary endpoint

N/A

3.1.3 Secondary objectives

To assess the safety and tolerability of a single dose of CM4620-IE in patients with acute pancreatitis.

3.1.4 Secondary endpoints

The secondary efficacy endpoints are:

- Adverse events including SAE
- Vital signs
- Days in hospital
- Safety laboratory

3.2 Clinical Study Design

This open-label, dose-response, study will evaluate the pharmacodynamic and pharmacokinetic profile of CM4620-IE in patients with acute pancreatitis. The first 5 patients will receive ≤2.08 mg/kg of CM4620-IE by continuous IV infusion on Day 1. If necessary, up to an additional 4 patients may be treated at a different dose of CM4620-IE determined by the obtained PK and PD data. The infusion of CM4620-IE will start within 12 hours from the time the patient or LAR provides informed consent.

The decision to enroll additional patients will be made after CalciMedica reviews the available pharmacodynamic, pharmacokinetic, safety and tolerability data from the first 5 patients enrolled and discusses the data with the Principal Investigator.

A study physician or appropriately trained delegate will perform in all patients enrolled in the study who remain hospitalized, selected safety assessments daily through Day 10 and every 48 hours from Day 12 until Day 30, or until discharge if occurring earlier. Patients discharged prior to Day 30 will be asked to return on Day 30 to provide a blood draw for PK and PD determinations and to record any SAEs and readmissions to the hospital. For patients that cannot return to the hospital on Day 30, they will be contacted on Day 30 (± 2 days) to capture SAEs and any readmissions to the hospital. Patients will also be contacted on Day 90 (± 7 days) to assess mortality.

CalciMedica may submit modifications to the protocol to change the planned doses, the dosing schedule, the infusion time, the number of sites in the study and the total number of patients enrolled in the study for safety and/or tolerability considerations.

3.3 Number of Subjects

7 subjects

3.4 Methods of Assigning Subject to IMP

N/A

3.5 Blinding

N/A

4 STATISTICAL AND ANALYTICAL PLANS

4.1 Sample Size Justification

This open-label study will enroll 5 patients, with the possibility of enrolling 4 more patients. The sample size was selected based on practical considerations to initially evaluate the pharmacodynamic and pharmacokinetic profile of CM4620-IE in patients with acute pancreatitis. This study is not powered for analysis of study data with inferential statistics.

4.2 Definition of Analysis Sets

4.2.1 Full Analysis Set

The full analysis set includes all patients with acute pancreatitis who receive one complete administration of CM4620-IE.

4.2.2 Safety Analysis Set

The safety population includes all patients who receive any amount of study drug treatment

4.2.3 Per Protocol Set

N/A.

4.2.4 Use of analysis set

Safety analysis set will be used in the analyses described below. The FAS population will be used for IL-6 and pharmacokinetics.

4.3 Definition of Baseline

Baseline measurement is defined as the latest measurement prior to first dose of IMP.

4.4 Summary Statistics

No summary statistics will be used.

4.5 Significance Level

N/A

4.6 Multiple Comparisons/Multiplicity

N/A

4.7 Handling of Drop-outs, Missing Data and Outliers

N/A

4.8 Adjustment for Covariates

N/A

4.9 Multicenter Studies

N/A

4.10 Examination of Subgroups

N/A

4.11 Blind Review

N/A.

5 SUBJECTS

5.1 Subject Disposition

The number of subjects that entered the study, withdrawn subjects, completed subjects and the number of subjects at each visit will be summarized by treatment.

5.2 Baseline Characteristics and Demographics

All baseline and demographic data will be presented using listings

6 TREATMENT INFORMATION AND EXTENT OF EXPOSURE

6.1 Active Treatment

N/A

6.2 Prior and Concomitant Medications

Prior and concomitant medication data will be listed and by ATC code. Prior and concomitant medications will be coded according to the World Health Organization (WHO Drug Dictionary) classification system.

7 STATISTICAL METHODOLOGY

7.1 Secondary endpoint(s)

7.1.1 Adverse events

The adverse events will be presented using listings.

7.1.2 Vital signs

The vital signs parameters will be presented using listings together with absolute and relative change from baseline.

7.1.3 Days in hospital

Days in hospital will be presented using listings.

7.1.4 Safety laboratory

The safety laboratory parameters will be presented using listings together with absolute and relative change from baseline.

7.2 Discontinuation

Patients who discontinue from IMP treatment will be listed. The reason for discontinuation will be given. For discontinuation due to AE, the AEs will be given.

7.3 Interim Analysis

N/A

8 CHANGES FROM THE CSP

9 STATISTICAL DELIVERABLES

The following documents will be delivered:

- SAP
- Listings

10 SOFTWARE

All statistical analyses will be performed using SAS Version 9.4 (SAS institute, Cary, NC).

11 APPROVAL

Issued by:

_____ _____

Fredrik Hansson, Director Biometrics — Date (dd-Mmm-yyyy)

CTC Representative

Approved by:

_____ 02-Jul-2019

Sudarshan Hebbar — Date (dd-Mmm-yyyy)

CalciMedica Representative