STASTICAL ANALYSIS PLAN

Document Date: Version 1.0, 22 Nov 2022

NCT #: NCT04182490

Statistical Analysis Plan

LMN-101

A Phase 2 Randomized, Double-Blind, Placebo-Controlled, Single Dose Regimen Study of LMN-101 in Healthy Volunteers Challenged with Campylobacter jejuni

Investigational Product:	LMN-101
Reference Product:	Placebo
Phase:	2
Document Type:	Statistical Analysis Plan
Version:	Final v1.0
Date of Issue:	22 Nov 2022

Statistical Analysis Plan Approval Form

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01F03BF4ED584FA99CBCAE6BC25D754D

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ABBREVIATIONS

AE	Adverse Event
AESIs	Adverse events of special interest
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BMI	Body Mass Index
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CV	Coefficient of Variation
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EOS	End of study
ET	Early Termination
HBsAg	Hepatitis B Surface Antigen
HCV Ab	Hepatitis C Virus Antibody
HIV	Human Immunodeficiency Virus
HR	Heart Rate
MedDRA	Medical Dictionary for Regulatory Activities
PI	Principal Investigator
PR	Time between the Start of the P Wave and the Start of the QRS Complex
PT	Preferred Term
PT	Prothrombin time
PTT	partial thromboplastin time
QT	Time between the Start of the Q Wave and the End of the T Wave
QTcF	QT Interval Corrected by the Fridericia Formula
RR	R-R interval
SAE	Serious Adverse Events
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
WHO	World Health Organization

1 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide details and specifications for statistical analyses of the study CAM02 "A Phase 2 Randomized, Double-Blind, Placebo-Controlled, Single Dose Regimen Study of LMN-101 in Healthy Volunteers Challenged with Campylobacter *jejuni*" as set forth in the clinical study protocol Version 2.0, dated December 7, 2021.

Data from the Pharmacology, if conducted, will be reported separately from the clinical study report (CSR) and are therefore not included in this SAP.

1.1 STUDY OBJECTIVES

1.1.1 PRIMARY OBJECTIVE

- To evaluate the frequency of solicited and unsolicited adverse events in subjects that received LMN-101 compared to placebo

1.1.2 SECONDARY OBJECTIVES

- To evaluate efficacy based on the proportion of subjects with campylobacteriosis in LMN-101 versus placebo recipients after challenge with Campylobacter *jejuni*
- To evaluate efficacy based on the proportion of subjects with specific solicited adverse events in LMN-101 versus placebo recipients after challenge with Campylobacter *jejuni*

1.1.3 EXPLORATORY OBJECTIVES

To evaluate in LMN-101 versus placebo recipients after challenge with C. *jejuni*:

- Duration of campylobacteriosis symptoms
- Duration of specific solicited adverse events
- Severity of campylobacteriosis symptoms
- Severity of specific solicited adverse events
- Frequency of recurrence of Campylobacter jejuni stool shedding
- Frequency of recurrence of campylobacteriosis clinical symptoms

1.2 STUDY ENDPOINTS

1.2.1 PRIMARY ENDPOINTS

- Safety: Frequency of solicited or unsolicited adverse events in subjects that received LMN-101 compared to placebo for the protocol-specified duration of collection for each type of adverse event

1.2.2 SECONDARY ENDPOINTS

- Efficacy: Proportion of subjects with campylobacteriosis after challenge with Campylobacter jejuni strain CG8421

- Efficacy: Proportion of subjects with specific solicited adverse events after challenge with Campylobacter jejuni strain CG8421
- "Campylobacteriosis" is defined as:
  - Moderate to severe diarrhea (≥ 4 loose stools or ≥ 401 g of loose stools in 24 hours); or
  - Fever (oral temperature ≥ 38.0°C present on at least two occasions, at least 20 minutes apart) plus at least one of the following symptoms of moderate severity: nausea, vomiting, abdominal cramps, tenesmus; or
  - Fever (oral temperature ≥ 38.0°C present on at least two occasions, at least 20 minutes apart) plus gross blood in ≥ 2 loose stools
- "Specific solicited adverse events" is defined as
  - diarrhea,
  - fever,
  - nausea,
  - vomiting,
  - abdominal pain,
  - abdominal cramping,
  - tenesmus,
  - mucoid or bloody stools,
  - constipation,
  - headache,
  - lightheadedness,
  - fatigue,
  - lack of appetite,
  - muscle aches,
  - chills,
  - joint pains

1.2.3 EXPLORATORY ENDPOINTS

- Efficacy:
  - Duration of diarrhea, diarrhea amount (total weight) and stool grade
  - Duration of campylobacteriosis symptoms
  - Duration of specific solicited adverse events
  - Severity of campylobacteriosis symptoms
  - Severity of specific solicited adverse events
  - Frequency of recurrence of Campylobacter jejuni stool shedding

- Frequency of recurrence of campylobacteriosis clinical symptoms

1.3 STUDY DESIGN

1.3.1 GENERAL STUDY DESIGN AND PLAN

This is a randomized, double-blind, placebo-controlled, single dose regimen study of LMN-101 followed by Campylobacter jejuni challenge.

Subjects will initially, after documentation of informed consent, begin taking their assigned LMN-101 or placebo regimen three times daily. After two days, subjects will receive the C. jejuni challenge inoculum. Subjects will begin an appropriate antibiotic course upon meeting early treatment criteria or 144 hours following C. jejuni challenge, whichever is earlier.

Subjects will be allowed to leave the clinical research facility 3 days after antibiotics, when all symptoms have resolved or are resolving, and have had ≥ 2 consecutive stool cultures ≥ 12 hours apart negative for C. jejuni and are afebrile > 24 hours prior to release and off antipyretics within 24 hours of discharge. Subjects will continue taking their LMN-101 or placebo regimen three times daily for a total of 14 days. Subjects will be provided a diary card/memory aid and thermometer for at-home monitoring of solicited adverse events through Day 24. Subjects will be seen at research facility for protocol-specified evaluations and will also be contacted by telephone 6 months after challenge.

The schedule of events is provided in Table 1.

Error! Reference source not found.: Schedule of study visits and evaluations

	Screening		Inpatient														Follow-up						
Day	**-60 to 0**	**-21 to 0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**17**	**24**	**31**	**38**	**59**	**87**	**115**	**190**
Event	**Screen**	**Screen**	**Admit**		**Challenge**																			
Window (days)																	± 2	± 2	± 3	± 3	± 3	± 7	± 7	± 30
Informed consent	*X*																							
Comprehension test	*(X)*																							
Inclusion/exclusion		*X*	*X*																					
Medical/Surgical history, comorbidities	*X*		*X*																					
Concomitant medications	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	
Campylobacter prior-exposure test (IgA titer to *C. jejuni* glycine extract)	*X*																							
Urine tox screen	*X*		*X*															*X*						
Collect blood for IgA and HLA-B27	*X*																							
Collect blood for HbsAg, HCV, HIV		*X*																						
Serum/urine pregnancy test[1]		*X*	*X*															*X*						
Collect whole blood for hematology[3]		*X*	*X*									*X*						*X*						
Collect serum for chemistry [3]		*X*	*X*									*X*						*X*						
Collect blood for PT, PTT[3]		*X*																*X*						
Physical examination (focused PE)		*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*			*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	
Vital signs	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*			*X*	*X*	*X*	*X*	*X*	*X*	*X*	
Electrocardiogram[10]		*X*										*X*												
Height/weight		*X*	*X*																					
TID dosing of study drug[13]			*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*								
Approximate unit discharge day[7]														*X*										
Review memory/diary card			*X*	*X*													*X*	*X*						
***Campylobacter* challenge**					*X*																			
Serum for drug concentrations[2]			*XX*			*X*			*X*			*X*						*X*						

Collect serum for anti-drug antibodies			*X*														*X*							
Collect serum for biomarkers[9]			*X*			*X*	*X*	*X*	*X*	*X*	*X*	*X*												
Collect stool for biomarkers[9]			*X*			*X*	*X*	*X*	*X*	*X*	*X*	*X*												
Blood culture for T ≥ 39°C						*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*										
Collect stool for weighing and					*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*										
Collect stool for *Campylobacter* culture[5]					*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*			*X*	*X*	*X*	*X*	*X*	*X*	*(X)*	
Administer antibiotics[6]						*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	*(X)*	*(X)*								
AEs[8]			*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*			*X*	*X*	*X*	*X*	*X*			
SAEs			*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*			*X*	*X*	*X*	*X*	*X*	*X*	*X*	*X*
AESI assessments[8]																		*X*	*X*	*X*	*X*	*X*	*X*	*X*
Telephone Follow up/ Study completion																								*X*

[1]Serum beta-hCG or urine pregnancy test must be collected from women of childbearing potential within 14 days before receipt of first dose of investigational product and at Day 1. Serum beta-hCG is also collected on Day 24.

[2]Serum PK is collected before first dose of study drug; 2 ± 1 hours after first dose of study drug. Serum PK is also collected on Day 4; Day 7; Day 10; and Day 24.

[3]Selected clinical laboratory studies to include hemoglobin, platelet count, white blood cell count with differential, sodium, potassium, calcium, magnesium, phosphate, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin. Coagulations studies are prothrombin time (PT) and partial thromboplastin time (PTT).

[5]Stool culture for *Campylobacter jejuni* collected daily while in study center and at follow up clinic visits. If subject is not able to produce a sample on the planned Recrudescence day of the follow-up visit, then the visit should be postponed to a day within the window for that visit (e.g., + 2 days); if patient still cannot produce a sample, then a rectal swab may be taken. If there is no new recrudescence on Day 87 then no stool will be collected for *Campylobacter jejuni* culture on Day 115. If there is a new recrudescence on Day 87 then all subjects who have not recrudesced will have a *Campylobacter jejuni* stool culture completed on Day 115.

[6]Azithromycin 500 mg po daily and ciprofloxacin 500 mg po twice daily for five days will begin when a subject meets early treatment criteria or it has been 144 hours since the *Campylobacter jejuni* challenge, whichever is earlier.

[7]Subjects will be discharged from the clinical research facility when they have had 3 days of antibiotics, all symptoms have resolved or are resolving, and subjects have had ≥ 2 stool cultures ≥ 12 hours apart negative for *C. jejuni* and are afebrile > 24 hours prior to release and off antipyretics within 24 hours of discharge.

[8]Specific solicited adverse events following *Campylobacter jejuni* challenge include diarrhea, fever, nausea, vomiting, abdominal pain, abdominal cramping, tenesmus, mucoid or bloody stools, constipation, headache, lightheadedness, fatigue, lack of appetite, muscle aches, chills, and joint pains will be monitored through Day 24. Subjects will be provided a diary card/memory aid and thermometer for follow-up monitoring of specific solicited adverse events. Adverse events will be collected through Day 59. Adverse events of special interest (AESIs) following *Campylobacter jejuni* challenge include signs or symptoms of Guillain-Barre syndrome, neurodegenerative changes, uveitis, reactive arthritis, and myocarditis/pericarditis and will be collected through Day 190.

[9]Biomarkers (e.g., serum C-reactive protein, fecal total protein, fecal calprotectin, fecal lipocalin, fecal myeloperoxidase, fecal neopterin, fecal lactoferrin, fecal cytokines and/or fecal microbiome). Serum for biomarkers will be collected at aliquoted, and frozen on admission and on Days 4, 5, 6, 7, 8, 9, and 10. Stool for biomarkers will be collected on admission prior to challenge, and on Days 4, 5, 6, 7, 8, 9, and 10; the inability of a subject to produce a sample on these days will not be considered a protocol deviation.

[10]Electrocardiogram at screening and Day 10.

1.3.2 SAMPLE SIZE CONSIDERATIONS

The sample size for this study was selected to be large enough so that an adverse event that occurs with 5-10% frequency with LMN-101 administration in the context of Campylobacter jejuni exposure is likely to be observed in the study. However, practical and ethical considerations for this human challenge study were also important in limiting the size of the study. With 21 subjects receiving LMN-101, there is a 66% probability that an adverse event expected to occur in 5% of the population would occur in the study. An event with a 10% rate in the population is 89% likely to occur among the 21 LMN-101 subjects in the study.

While the sample size was not selected to provide a specific amount of statistical power to detect a statistically significant difference between the two treatment groups, assuming 18 subjects per treatment group complete the study, there is 80% power to detect a large risk reduction in attack rates (e.g., from 80% in the placebo group to 40.6% in the LMN-101 group) at the one-sided significance level of 0.05.

1.3.3 RANDOMIZATION AND BLINDING

42 Subjects will be randomized in a 1:1 ratio to one of two treatment groups (LMN-101 or placebo) in 2 cohorts. Subjects who fulfill all inclusion/exclusion criteria and are eligible to participate will be assigned the next sequential treatment number by the Principal Investigator. The treatment number corresponds to a given treatment assignment known to the study pharmacist but blinded to the subject, the PI, and the remaining members of the clinical research site and collaborators.

Sealed, code-break envelopes will be provided to the research pharmacist if a given subject has a serious adverse event that requires unblinding of treatment assignment.

If a given subject drops out of the study or becomes ineligible before the Campylobacter jejuni challenge, they will be replaced on the study by a subject given the same treatment assignment.

Individual subject assignments to a given treatment group will remain blinded to investigators, subjects, and personnel involved in collecting, cleaning, and analyzing the data until completion of the trial phase and validation of the clinical and outcome data.

2 STATISTICAL CONSIDERATIONS

2.1 GENERAL CONSIDERATIONS

SAS version 9.4 or greater (SAS Institute Inc., Cary, NC, SAS System) will be used for analysis. For descriptive statistics, continuous variables will be summarized by the number of non-missing observations, mean, median, standard deviation, and minimum and maximum. Categorical variables will be summarized by presenting the frequency and percent.

Inferential statistics will not be used in the analysis of safety variables but will be applied to the secondary and exploratory efficacy endpoints using 1-sided tests of significance at the 0.05 level of significance and/or two-sided 90% confidence intervals. It is expected that the study will be

enrolled as two separate cohorts, and cohort will be used as a stratification factor in statistical tests when applicable.

Unscheduled results will not be included in the summary tables except for determining baseline, but will be presented in data listings.

All data listings will be sorted by group, subject and visit/timepoint where applicable. All dates will be displayed in DDMMMYYYY format. No algorithm for missing data imputation will be employed.

2.2 ANALYSIS SETS

The Safety Analysis Set will be based on all subjects who received study treatment (LMN-101 or Placebo). Subjects will be analyzed according to the treatment they received, even if this differs from the treatment they were randomized to (an as-treated approach).

The Efficacy Analysis Set will be based on all subjects who received study treatment and complete the Campylobacter jejuni challenge without significant protocol deviations (a per protocol approach). Subjects will be analyzed according to the treatment they received, even if this differs from the treatment they were randomized to.

3 DATA HANDLING CONVENTIONS

3.1 DERIVED AND TRANSFORMED DATA

3.1.1 BASELINE AND CHANGE FROM BASELINE DEFINITION

The baseline value of a variable is defined as the last value obtained on or before the date and time of the dose of LMN-101 and placebo, including unscheduled assessments.

Change from baseline will be derived for each subject as the post-baseline evaluation minus the baseline evaluation.

3.1.2 STUDY DAY

Study Day will be calculated from the reference start date (defined as the first day of administration of study drug), and will be used to show start/stop day of assessments/events:

- Study Day = (date of assessments/events - reference start date) if event/assessment is prior to the reference start;
- Study Day = (date of assessments/events - reference start date + 1) if event/assessment is on or after the reference start.

There is no study day 0.

3.1.3 LAB PARAMETER RESULTS WITH SPECIAL CHARACTERS

If any lab parameter results contain special characters such as ‘<’ or ‘>’, the numerical portion of the results will be used for descriptive summary.

3.2 ANALYSIS VISIT WINDOWS

For analysis of data over time (wherever specified), the nominal study days/visits will be used as analysis days/visits. No windowing algorithm will be used.

3.3 PREMATURE WITHDRAWAL AND MISSING DATA

Should withdrawals occur, efforts will be made to ensure subject safety. In case of subject withdrawal, for whatever reason, a final trial evaluation must be completed (if possible) stating the reasons. Withdrawals due to non-attendance must be followed-up by the Principal Investigator to the extent possible to obtain the reason for non-attendance. Subjects withdrawing from the study prior to receiving the challenge dose (Day 3) will stop taking the investigational product and be asked to complete a final visit for safety about 28 days (± 5 days) after the last dose. Subjects withdrawing after receiving the C. jejuni challenge dose will receive antibiotics (two days dosing under direct observation prior to discharge) for their own at-home treatment and will be educated on the importance of complying with treatment. Attempts will be made to follow all subjects for safety through Day 190.

All reasonable measures will be taken to ensure minimal missing data. Despite this, some data are likely to be missing at the end of the study. No imputation is planned for any endpoints in this study, and all data will be considered to be missing completely at random. Should observations indicate this is not likely to be true for a given endpoint, additional sensitivity analyses may be conducted, such as multiple imputation, to assess the impact of the missing data.

3.4 MULTIPLE COMPARISON/MULTIPLICITY

Not Applicable.

4 STATISTICAL ANALYSES

4.1 SUBJECT INFORMATION

4.1.1 DISPOSITION OF SUBJECTS

Subject disposition will be summarized for all screened subjects by group. The number and percentage of subjects in all Populations, as well as number and percentage of subjects who completed the study and discontinued the study will be summarized along with the primary reason for discontinuation. The percentages will be based on the number of subjects in the Safety Analysis Set.

A listing will present whether the subject is in the Safety, Efficacy Analysis Set, whether the subject completed the study, date of completion/withdrawal, and the primary reason for discontinuation of study, if applicable.

A subject eligibility listing will also be provided to describe if the subject meets all inclusion/exclusion criteria.

4.1.2 PROTOCOL DEVIATIONS

The study site will record all deviations that occurred during the conduct of the study. Protocol deviations will be classified as either minor or major by the Sponsor or designee prior to database lock.

The protocol deviation data with the verbatim description, the reason for the deviation and whether the deviation is classified as minor or major will be summarized by group and listed.

4.1.3 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Demographics and baseline characteristics (age, gender, race, height (cm), weight (kg) and body mass index (BMI) (kg/m2)) will be summarized descriptively by treatment group for the Safety Analysis Set as well as the Efficacy Analysis Set. Descriptive statistics will be presented for age, height, weight, and BMI. Frequency counts and percentage will be presented for sex, ethnicity origin, and race.

The demographic and baseline characteristics data will also be presented as data listings by group and subject.

4.1.4 SEROLOGY

The screening serology for hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (anti-HCV) and human immunodeficiency virus antibodies (anti-HIV) will be listed by group and subject for the Safety Analysis Set.

4.1.5 PREGNANCY

Serum beta-hCG or urine pregnancy test must be collected from women of childbearing potential within 14 days before receipt of first dose of investigational product and at Day 1. Serum beta-hCG is also collected on Day 24. All pregnancy test information will be listed by group and subject for all women in the Safety Analysis Set.

4.1.6 PRIOR AND CONCOMITANT MEDICATIONS

Concomitant medications will be coded using the World Health Organization (WHO) Drug Global latest version.

Prior medications will be those discontinued prior to the start of the study drug. Concomitant medications will be medications started prior to the start of the study drug and continued after administration of study drug or started during the study after administration of study drug.

Prior and concomitant medication information will be listed by group and subject with verbatim text given by the investigator, WHO Drug Dictionary PT, indication, whether it is related to AE/MH and associated AE/MH number, start and stop date/time, dosage, route, and frequency.

4.1.7 MEDICAL HISTORY

All medical history will be coded using Medical Dictionary for Regulatory Activities (MedDRA) 24.1. Medical history will be listed by group and subject for the Safety Analysis Set.

4.1.8 URINE TOXICOLOGY SCREEN

Urine toxicology screen including Amphetamines, Barbiturates, Cocaine metabolites, Opiates, Benzodiazepines, Cotinine, Methadone, Phencyclidine, Propoxyphene, Tricyclics

Antidepressants, Tricyclics and serum alcohol results will be listed by group and subject for the Safety Analysis Set.

4.1.8 IMMUNOGLOBULIN AND HLA-B27 TESTS

Immunoglobulin and HLA-B27 Tests information will be listed by group and subject for the Safety Analysis Set.

4.1.9 CAMPYLOBACTER PRIOR EXPOSURE TEST

Campylobacter prior exposure test information will be listed by group and subject for the Safety Analysis Set.

4.1.10 STUDY DRUG ADMINISTRATION

The study drug administration information will be listed by group and subject including date and time of dose, whether the drug was delayed and reason, dose point for the Safety Analysis Set.

4.1.11 COVID-19 SCREENING

COVID-19 Screening information will be listed by group and subject for the Safety Analysis Set.

4.1.12 ANTIBIOTICS TREATMENT

Antibiotics treatment information will be listed by group and subject including day of treatment, date and time of dose, antibiotic name, prescribed dose, dosing frequency and comments for the Safety Analysis Set.

4.2 EFFICACY ANALYSIS

4.2.1 ANALYSIS OF THE SECONDARY EFFICACY ENDPOINT

Proportion of subjects with campylobacteriosis after challenge with Campylobacter jejuni strain CG8421 will be summarized using frequencies and percentages by treatment group as well as 90% confidence intervals around the percentages based on Efficacy Analysis Set. The campylobacteriosis risk ratio (LMN-101 / placebo) will be presented. P-value and 90% confidence interval for risk ratio will be both provided based on Cochrane-Mantel-Haenszel stratified by enrollment cohort.

Proportion of subjects with specific solicited adverse events after challenge with Campylobacter jejuni strain CG8421 will be summarized using frequencies and percentages by treatment group as well as 90% confidence intervals around the percentages based on Efficacy Analysis Set. The solicited adverse events risk ratio (LMN-101 / placebo) will be presented. The risk ratio will be tested using the method of Cochrane-Mantel-Haenszel stratified by enrollment cohort to determine if the risk ratio is statistically significantly different from 1; similar methodology will be used to construct a 90% asymptotic confidence interval around the risk ratio.

4.3 SAFETY ANALYSIS

4.3.1 ADVERSE EVENTS (AES)

AEs will be coded by system organ class (SOC) and preferred term (PT) according to MedDRA latest version. The Severity of the following adverse events (grades 0-4) should be assessed as defined in Table 2 below to ensure consistency with previous experimental

infection studies with other enteric pathogens by Lumen Bioscience, Inc.. Adverse Events not represented in the below criteria will be coded according to Common Terminology Criteria for Adverse Events (CTCEA), Version 5.0.

Table 2: Adverse Event definitions and parameters for in unit setting

Adverse Event		**Parameter**
Diarrhea	1	2-3 or more grade 3-5 stools in a 48-hour period totalling 200-400 g or more or a single grade 3-5 stool of 300 g in 24 hours
	2	4-5 grade 3-5 stools in 24 hours or 401-800 g of grade 3-5 stools for total episode
	3	> 6 grade 3-5 stools in 24 hours or > 800 g of grade 3-5 stools for total episode
	4	Life-threatening
Body Temperature	1	100.4-101.1°F (38.0-38.4°C)
	2	101.2-102.0°F (38.5-38.9°C)
	3	102.1-104.9°F (39.0-40.5°C)
	4	Life-threatening hyperthermia
Vomiting	1	One episode within any 24-hour period
	2	Two episodes within any 24-hour period
	3	More than two episodes within any 24-hour period
	4	Life-threatening consequence of emesis
1 = mild; 2 = moderate; 3 = severe; 4 = life-threatening		

Treatment-emergent AEs (TEAEs) are those that occur at the time of and following the administration of study drug. If the time of the AE is not available, then TEAEs will be those occurring on or after the day of study treatment. AEs occurring before the administration of study drug will not be included in the summary but will be listed.

All the AE analyses will be based on Safety Analysis Set.

4.3.1.1 Overview of Adverse Events

An overview of the number and percentage of subjects with at least one

- AE
- TEAE
- Serious TEAE
- unsolicited TEAE
    - study related (Causality of AE is defined as Study Drug, Campylobacter jejuni Infection and Alternate etiology) unsolicited TEAE
    - study drug related (Causality of AE is defined as Study Drug) unsolicited TEAE
    - Grade ≥3 study related unsolicited TEAE

  - Grade ≥3 study drug related unsolicited TEAE
  - serious study related unsolicited TEAE
  - serious study drug related unsolicited TEAE
  - unsolicited TEAE leading to discontinuation from study
  - unsolicited TEAE leading to death
- solicited TEAE
  - study related solicited TEAE
  - study drug related solicited TEAE
  - Grade ≥3 study related solicited TEAE
  - Grade ≥3 study drug related solicited TEAE
  - serious study related solicited TEAE
  - serious study drug related solicited TEAE
  - solicited TEAE leading to discontinuation from study
  - solicited TEAE leading to death
- AESI
  - study related AESI
  - study drug related AESI
  - Grade ≥3 study related AESI
  - Grade ≥3 study drug related AESI
  - serious study related AESI
  - serious study drug related AESI
  - AESI leading to discontinuation from study
  - AESI leading to death

All information pertaining to AEs will be listed by subject and all the details collected on the eCRF, including solicited, AESI, verbatim term given by the investigator, PT, SOC, onset date/time, end date/time, course, severity, seriousness, serious AE definition (congenital abnormality or birth defect, significant disability, death, hospitalization or prolongation of hospitalization, life threatening, other medically important event), autopsy performed and date of death if died, relationship to study drug, action taken with study drug, withdraw from study, treatment required and outcome.

4.3.1.2 Incidence of TEAEs, unsolicited, solicited TEAEs and AESI

A summary of the frequency (number and percentage of subjects) of TEAEs, unsolicited, solicited TEAEs and AESI will be presented by SOC and PT.

Multiple occurrences of the same AE (SOC or PT) will be counted only once when calculating the number and percentage of subjects. This summary will be sorted in decreasing order of frequency of SOC in all columns, and then in decreasing order of frequency of PT within the SOC.

Number and percentage of subjects with TEAEs, unsolicited, solicited TEAEs and AESI will also be presented by PT only. This summary will be sorted in decreasing order of frequency in all columns.

4.3.1.3 Incidence of TEAEs, unsolicited, solicited TEAEs and AESI by Worst Severity

The number and percentage of subjects reporting an TEAEs, unsolicited, solicited TEAEs and AESI will be tabulated by SOC, PT and the worst severity.

4.3.1.4 Incidence of study and study drug related TEAEs, unsolicited, solicited TEAEs and AESI by Worst Severity

The number and percentage of subjects reporting a study and study drug related TEAEs, unsolicited, solicited TEAEs and AESI will be also tabulated by SOC, PT, and severity.

4.3.1.5 Serious TEAEs, unsolicited, solicited TEAEs and AESI

Serious TEAEs, unsolicited, solicited TEAEs and AESI will be summarized and listed in the same manner described above for TEAEs (Section 4.3.1.2) .

4.3.1.6 TEAEs, Unsolicited, solicited TEAEs and AESI Leading to Death

TEAEs , Unsolicited, solicited TEAEs and AESI Leading to Death will be listed in the same manner described above for TEAEs (Section 4.3.1.2).

4.3.1.7 TEAEs, Unsolicited, solicited TEAEs and AESI Leading to Discontinuation of Study

TEAEs , Unsolicited, solicited TEAEs and AESI Leading to Discontinuation of Study in the same manner described above for TEAEs (Section 4.3.1.2).

4.3.2 SAFETY LABORATORY TESTS

All tests listed will be performed as per the Schedule of Assessments (Table 1).

Clinical laboratory results and changes from baseline in clinical laboratory results will be summarized by treatment group and visit. Shift tables will be constructed to tabulate categorical shifts in laboratory values from baseline to the minimum and maximum post-baseline values by treatment group. For shift tables, all post-baseline data including unscheduled visit will be included. Categories will be based on the laboratory normal ranges and CTCAE Grade 3 toxicity thresholds.

Individual listings of laboratory values for each subject by visit will be provided with all out-of-range values flagged.

4.3.4 VITAL SIGNS

Vital signs will include single measurements of oral temperature, respiratory rate, systolic blood pressure, diastolic blood pressure, and heart rate. Vital signs will be measured as per the Schedule of Assessments (Table 1).

Vital signs and their change from baseline will be tabulated using descriptive statistics by treatment group, visits and time point.

All vital signs including vital sign parameters and overall interpretations will be listed by subject.

4.3.5 ECGS

ECGs will be measured as per the Schedule of Assessments (Table 1). The results will include heart rate (HR), R-R interval (RR), PR interval, QRS interval, QT interval, QTc and QTcF interval. The corrected QT interval will be corrected for heart rate according to the following formula:

Fridericia's formula: $QTcF = QT/RR^{0.33}$

ECGs and their change from baseline will be tabulated using descriptive statistics by visits and time point.

Additionally, QTc measures (Fridericia's formula) will be summarized in the following categories:

- QTc >450 to ⩽480 msec
- QTc >480 to ⩽500 msec
- QTc >500 msec
- QTc increase of >30 and ⩽ 60 msec from baseline
- QTc increase of >60 msec from baseline

The listing will be provided for ECG including individual parameters, ECG interpretation and comments on findings if applicable.

4.3.6 PHYSICAL EXAMINATION

Physical examination and focused Physical examination will be done as per the Schedule of Assessments (Table 1).

All physical examinations will include, at a minimum, assessment of the following systems: Head , Eyes, Ears, Nose, Oropharynx, Neck, Chest, Lymph nodes, Abdomen, Musculoskeletal, Skin, Neurological and Other.

All subjects with any abnormal physical examination findings will be listed.

4.4 ANALYSIS OF THE EXPLORATORY ENDPOINTS

The duration of campylobacteriosis symptoms (including diarrhea, fever, nausea, vomiting, abdominal cramps and tenesmus) will be estimated with Kaplan-Meier survival analysis methodology and compared between treatment groups using the log-rank test based on Efficacy Analysis Set. Duration of campylobacteriosis symptoms is the number of days with one or more symptoms of campylobacteriosis until resolution in the period from challenge through discharge in a participant with a diagnosis of campylobacteriosis within 144 hours from challenge . Onset for the duration of campylobacteriosis is the onset of any campylobacteriosis symptoms; and

date of resolve all the campylobacteriosis symptoms before discharge is the end date of duration of campylobacteriosis. Censoring for the duration of campylobacteriosis symptoms will be assigned on the time of the last visit, death and discharge whichever is earlier from challenge through discharge if the end of campylobacteriosis symptoms can't be identified.

The duration of specific solicited adverse events will be estimated with Kaplan-Meier survival analysis methodology and compared between treatment groups using the log-rank test based on Safety Analysis Set. Duration of specific solicited adverse events is defined as the count of the number of days with the specific solicited AE until resolution in the period from challenge thru discharge in a participant with at least one specific solicited AE. Onset of the first specific solicited AE post challenge is the start date of duration of specific solicited AE; and date of resolve all the specific solicited AE before discharge is the end date of duration of specific solicited AEs. Censoring for the duration of specific solicited adverse events endpoint will be assigned on the time of the last visit, death and discharge whichever is earlier if the end of the specific solicited adverse events can't be identified.

The geometric mean total weight of diarrhea stools within 144 hours of challenge will be calculated for each treatment group and compared using Wilcoxon rank sum test with terms for treatment group and enrollment cohort. Subjects with zero diarrhea stool output will be imputed as the logarithm of half the smallest quantifiable output.

The Severity of campylobacteriosis symptoms and specific solicited adverse events from challenge through discharge will each be calculated and compared between treatment groups using the Cochran-Mantel-Haenszel row mean score test stratified by enrollment cohort. Since Grades of severity of Campylobacteriosis symptoms are only collected in AE form in EDC, all Campylobacteriosis symptoms will be selected from AE dataset.

Summary tables will also be created to detail quantitative and temporal features of the illness within 144 hours of challenge including diarrhea stool frequency and volume, maximum temperature observed.

Rates of recurrence of Campylobacter jejuni stool shedding and campylobacteriosis symptoms will be calculated and compared between treatment groups using the Cochrane-Mantel-Haenszel test stratified by enrollment cohort. If a subject has C jejuni isolated is "Yes" after Day 24 and beyond, the subject will be considered as the recurrence of Campylobacter jejuni stool shedding.

5 INTERIM ANALYSIS

The first interim analysis will include the initial cohort comprised of 21 subjects. After the initial cohort has completed the in-center portion of the study, an unblinded statistician will perform an interim analysis including safety analysis to allow a data safety monitoring board to determine if the trial should continue based on safety.

The second interim analysis will include through Study Day 24 for both cohorts. An unblinded statistician will perform the second interim analysis including safety and preliminary efficacy analysis to report data safety monitoring board. The purpose of this is to summarize the safety data and provide preliminary efficacy data for sponsor through Study Day 24 for both cohorts in a timely manner.

6 SUMMARY OF MAJOR CHANGES IN THE PLANNED ANALYSES

The second interim analysis which wasn't mentioned in protocol is included in the SAP.

7 PROGRAMMING SPECIFICATIONS

Programming specifications will be provided in the SAP table, listing, and figures shells document.

8 TABLES, LISTINGS, AND FIGURES SHELLS

The Tables, Listing, and Figures Shells will be provided as a separate document.

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