Statistical Analysis Plan

Sponsor:	Lupin Research Inc.
Protocol No:	SYM-1219-401
Protocol Title:	A Multi-Center, Open-Label Study to Evaluate the Safety of a Single Oral Dose of Solosec™ (secnidazole) 2g Oral Granules for the Treatment of Adolescent Girls with Bacterial Vaginosis
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APPROVAL SIGNATURES

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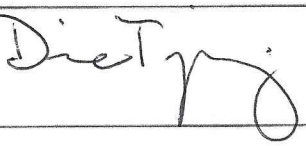
Vice President, Biostatistics	Diane Tipping		01-Apr-2019

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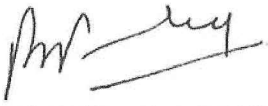
Medical Monitor	Brajesh Pandey, MD		01/APR/2019

DOCUMENT HISTORY

Rev No	Date	Description
1.0	22-Mar-2019	Original document

TABLE OF CONTENTS

List of Abbreviations

AE	Adverse Event
BV	Bacterial Vaginosis
CRF	Case Report Form
EOS	End of Study
FDA	Food and Drug Administration
ITT	Intent to Treat
KOH	Potassium Hydroxide
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent to Treat
SAP	Statistical Analysis Plan
SOC	System Organ Class
TOC	Test of Cure
WHO-DDE	World Health Organization Drug Dictionary

1. INTRODUCTION

1.1 Study Background

Solosec (secnidazole, SYM-1219) 2g oral granules is a Food and Drug Administration (FDA) approved treatment for bacterial vaginosis (BV) in adult women. Solosec™ is a potent, 5-nitroimidazole antibiotic with enhanced pharmacokinetic properties that enable delivery in a single dose that has been shown to be efficacious and well tolerated.

1.2 Study Design

This is a multi-center, open-label study to evaluate the safety of Solosec in adolescent girls with bacterial vaginosis. Approximately 40 patients will be enrolled. Patients determined to be eligible at the Baseline Visit (Day 1) will receive a single oral dose of Solosec™ granules (containing 2g of secnidazole) on Day 1. Patients will return to the site once between Days 7-14 for a "test of cure" (TOC) Visit, or at End of Study (EOS) if the final visit is not conducted between Study Day 7-14. A follow-up telephone call will be performed at Days 21-30 to assess the continued clinical response to treatment and adverse events.

1.3 Study Objectives

1.3.1 Primary Objectives

The objective of this study is to evaluate safety of single oral dose of Solosec™ (secnidazole) 2g oral granules for the treatment of adolescent girls with bacterial vaginosis.

1.3.2 Secondary Objectives

Secondary assessments of efficacy will be assessed.

2. STATISTICAL METHODOLOGY

2.1 General Principles

All analyses will be performed using SAS® software version 9.4. Adverse Events (AEs) will be coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 21.1. Prior and concomitant medications will be coded using World Health Organization Drug Dictionary Enhanced (WHO-DDE) March 2017.

All data collected will be presented in data listings. Continuous parameters will be summarized by N (number of non-missing observations), mean, standard deviation, median, minimum, and maximum. Categorical parameters will be summarized by count and percent (of non-missing observations).

2.2 Sample Size Determination

The sample size was chosen to provide observational safety data only. No formal sample size calculations were made.

2.3 Study Populations

Safety: The Safety population will be composed of all enrolled patients who received the study medication.

Intent-to-Treat (ITT): The ITT population will include all enrolled patients.

Modified Intent-To-Treat (mITT): The mITT population will include all enrolled patients who met all inclusion/exclusion criteria.

2.4 Subject Accounting and Baseline Characteristics

Baseline characteristics (demographics, BV history, vaginal assessments) will be summarized for the mITT and safety populations. Medical history, and prior and concomitant medications will be summarized for the safety populations. Study completion status and primary reason for discontinuation will be displayed overall and by site for the ITT population.

2.5 Efficacy Analyses

The mITT population will be used for summaries of efficacy endpoints. The number and percentage of patients will be summarized for each endpoint. The following efficacy endpoints will be evaluated at the TOC/EOS Visit:

- Clinical Outcome: A Clinical Outcome Responder is defined as a patient with all of the following:

  1) Resolution of abnormal vaginal discharge (vaginal discharge assessed as normal), and

  2) Negative 10% potassium hydroxide (KOH) Whiff test; and

3) Clue cells less than 20% of the total epithelial cells on microscopic examination of the vaginal wet mount using saline.

- Nugent Score: Score of 0-3 will be considered normal; a score of 4 and above will be considered abnormal.
- Investigator's Clinical Assessment: Investigator's opinion of the need for additional BV treatment (Yes or No).

The Patient's Continued Clinical Response (Yes or No) will be summarized based on the Investigator's opinion of the continued clinical response to treatment at the follow-up assessment (Day 21-30 telephone call).

2.6 Safety Analyses

Safety evaluations will be based on the incidence, intensity, and type of AE, and changes in vital signs, and clinical safety laboratory results. Safety variables will be tabulated and presented for all patients in the Safety population.

AEs will be summarized by System Organ Class (SOC), Preferred term, and intensity for treatment emergent AEs. Summaries will also be provided for study drug-related AEs, serious AEs, and AEs leading to discontinuation. Each patient will be counted only once for each of the incidence rates, regardless of the number of occurrences (events) the patient experiences. An event will be considered treatment-emergent AE if it occurs any time after administration of the study drug and through the final visit, or if it is considered study drug-related regardless of the start date of the event.

Changes in laboratory results and vital signs from baseline to the TOC/EOS visit will be summarized. Shifts from baseline will also be presented for laboratory parameters.

2.7 Interim Analyses

No interim analyses are planned.

3. DATA HANDLING

3.1 Baseline and Study Visits

Visits for all summaries will be as recorded on the Case Report Forms (CRFs). Baseline is defined as the last assessment prior to dosing. The day of dosing is considered Day 1.

3.2 Missing Data

Patients with any missing data at TOC/EOS will be imputed as a non-responder for the Clinical Outcome. No other imputation will be done.

4. CHANGES FROM THE PROTOCOL

None