ABBOTT **Statistical Analysis Plan**

Module 1
(Non-standard data and analyses)

Version 2.0, Date 06 Aug 18

Study: RACE3003

Multicenter, open-label, controlled, randomized clinical study to evaluate the efficacy and safety of Racecadotril in infants, children and adolescents with acute diarrhea

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Statistical Analysis Plan is based on the Abbott template for clinical studies. Template Version 4.0

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1. ABBREVIATIONS

1.1 Standard Abbreviations

AE	adverse event
ANCOVA	analysis of covariance
ATC	Anatomical Therapeutic Chemical (class)
AUC	area under the curve
BDR	blind data review
bpm	beats per minute
CRF	case report form
CRO	contract research organization
CV	coefficient of variation
DBP	diastolic blood pressure
DDT	data definition table
DSMB	data safety monitoring board
ECG	electrocardiogram
FA	Full Analysis
FDA	food and drug administration
Geo. mean	geometric mean
GOP	global standard operating procedure
HLGT	High Level Group Term
HLT	High Level Term
ICH	International Conference on Harmonization
LDA	day number of the last day of drug administration
LLOQ	lower level of quantification
LLT	Lowest Level Term
LOCF	last observation carried forward
max	maximum
MedDRA	Medical Dictionary for Regulatory Activities
min	minimum
N,n	number of observations
NA	not applicable
OC	observed cases
PD	pharmacodynamic
PK	pharmacokinetic
PP	Per Protocol
PT	Preferred Term
QOL	quality of life
SAE	serious adverse event
SAP	statistical analysis plan
SBP	systolic blood pressure
SD	standard deviation
S.I.	System International
SOC	System Organ Class

SOP	standard operating procedure
TARC	Therapeutic Area Review Committee
TEAE	treatment-emergent adverse event
TESAE	treatment-emergent serious adverse event
TLF/T,L,F	tables, listings and figures
ULOQ	upper limit of quantification
URL	upper reference limit
WC	windowing convention
WHO-DD(E)	World Health Organization – Drug Dictionary (enhanced)

2. Introduction

[redacted]

3. SUMMARY OF THE PROTOCOL

3.1 Overall Study Plan

This is a controlled, open-label, parallel-group study evaluating the efficacy and safety of Racecadotril in infants, children and adolescents with acute diarrhea. The number of subjects to be screened is 150 in order to enroll 124 subjects for either standard treatment (oral rehydration solution, ORS) alone or ORS plus Racecadotril.

1.5 mg/kg of Racecadotril will be administered, 3 times daily, via the oral route. Study drug intake will start either with the noon or the evening dose on day 1.

In infants less than 9 kg: one 10 mg sachet 3 times daily.
In infants from 9 kg to <13 kg: two 10 mg sachets 3 times daily.
In children from 13 kg to 27 kg: one 30 mg sachet 3 times daily.
In children from more than 27 kg to 60 kg: two 30 mg sachets 3 times daily.
In children or adolescents of 60 kg or higher: 100 mg capsule 3 times daily

Standard treatment is oral rehydration solution (ORS) according to the registered local label and the instruction of the investigator. The same brand of ORS and the same age-appropriate standardized treatment pattern for the subjects will be applied throughout the trial. ORS treatment and dosing will be documented in the CRF.

Screening and Enrolment (Day 1, Visit 1)
Subjects presenting with acute diarrhea will be evaluated for eligibility. They will undergo a physical examination including assessment of dehydration level, vital signs, a review of their medical history and concomitant medication. If the subjects are eligible for the study, demographics, number of stools during the last 24 hours will be assessed as baseline values. The subjects will be randomized to Racecadotril plus ORS or ORS alone. On Day 1 the subject will start with study treatment. The starting dose will either be the noon or the evening dose depending on the timing of Visit 1.

Treatment period (until recovery, maximally 5 days)
Subjects will be treated with Racecadotril tid according to the body weight dose requirement on an in- or out-patient basis for maximum 5 days. One arm will be treated with ORS alone as standard treatment, the other treatment arm will be treated with ORS (according to the registered local label and the instruction of the investigator) in addition to Racecadotril. ORS will be prescribed by the investigator and will be taken according to the product label and the instruction of the investigator. The parent(s)/caregiver(s) will be instructed to stop study drug treatment when the patient recovered. On each day, the parent(s)/caregiver(s) will fill in their diaries, documenting the date and time of each individual stool, the stool consistency of each stool (diarrheal/watery or normal), the amount of ORS and the study drug intake. After the occurrence of two consecutive normal stools, the parent(s)/caregiver(s) can stop recording of the diary and return to the study site for the end of treatment visit. The date of recovery is the day when the first of two consecutive normal stools were excreted. AEs are to be reported on an ongoing basis.

End of treatment (Day 6 or early recovery, Visit 2)
The last dose of study drug will be the morning dose of day 6, if not recovered earlier. The same day, or within 24 hours after recovery, the parent(s)/caregiver(s) will visit the site for the end of treatment visit of the child. Data on vital signs, AEs, physical examination and concomitant medication will be collected. Subjects will return their diaries and unused medication.

Safety follow-up
A phone call will be performed at 5-7 days after end of the treatment period for the safety follow-up.

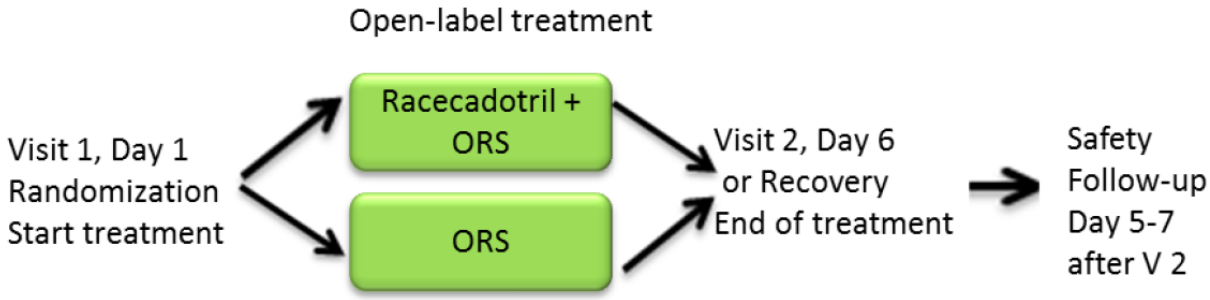

Figure 3-1 Study design

3.2 Study Flowchart

The flowchart of the study can be found in Appendix 9.1.

3.3 Study Objectives

Primary Objective(s)
The primary objective is to evaluate the efficacy of Racecadotril in addition to standard treatment oral rehydration solution (ORS) versus ORS alone in infants, children and adolescents (3 months until <18 years) with acute diarrhea measured as duration of diarrhea (hours) between the start of treatment until final diarrheal/watery stool before recovery or end of study treatment (treatment duration maximal 5 days).

Duration of diarrhea is defined by date and time of the evacuation of the final watery/diarrheal stool before recovery derived from the daily diary (see Figure 3-2 Duration of diarrhea and Time until recovery definition).

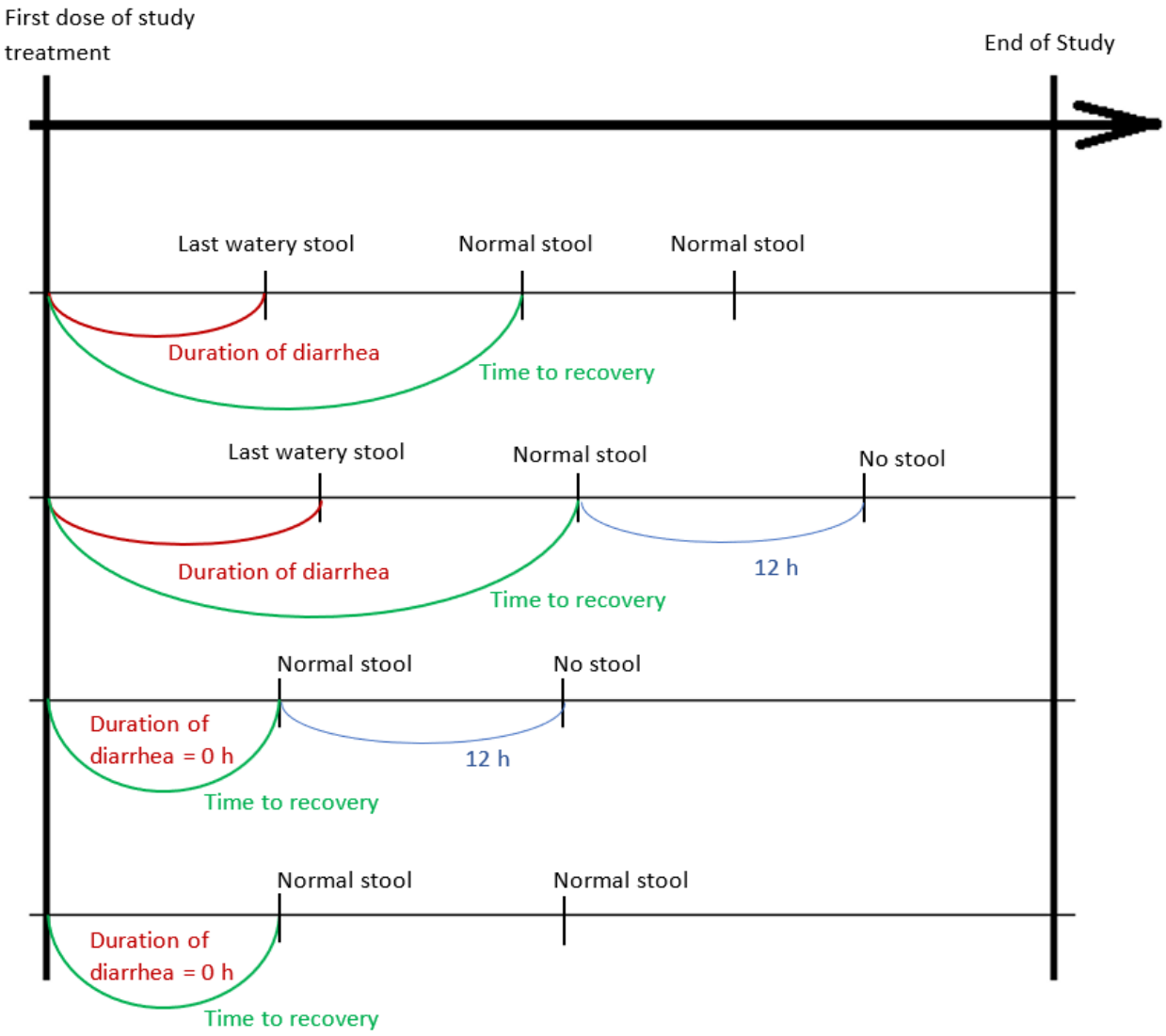

Figure 3-2 Duration of diarrhea and Time until recovery definition

Secondary Objective(s)

- Number of recovered subjects per treatment group in total and until each individual treatment day. Mean and median time until recovery per treatment group.
- Time until recovery, defined by date and time of the evacuation of the first of two consecutive normal stools or no stool within 12 hours after first normal stool (see Figure 3-2 Duration of diarrhea and Time until recovery definition).
- Global Physician Assessment at the end of treatment:
    - 1 = Complete relief of acute diarrhea,
    - 2 = marked improvement of acute diarrhea,

- 3 = moderate improvement of acute diarrhea,
- 4 =slight improvement of acute diarrhea,
- 5 = no change in acute diarrhea,
- 6 =worsening of acute diarrhea. (Treatment success = GPA score of 1 or 2).

- For toilet trained children and adolescents: number of stools per day as well as number of watery stools per day from start of treatment and until end of study treatment.

Safety Objective(s)
To evaluate the safety and tolerability of Racecadotril together with oral rehydration solution (ORS) versus ORS alone in infants, children and adolescents with acute diarrhea by adverse events, physical examination and vital signs.

4. STATISTICAL ANALYSIS

4.1 Subject samples

There will be five subject samples.

- The all subjects consented sample will consist of all subjects who:
  - Gave their informed consent.
- The all subjects allocated to treatment sample will consist of all subjects who:
  - Were in the all subjects consented sample; and
  - Were allocated to treatment.
- The safety sample will consist of all subjects who:
  - Were in the all subjects allocated to treatment sample; and
  - Had at least one dose of study medication administered.
- The full analysis (FA) sample will consist of all subjects who:
  - Were included in the safety sample; and
  - Had data for at least one post-baseline assessment of any efficacy measurement.
- The per-protocol (PP) sample will be defined through blind data review and will consist of all subjects who:
  - Were included in the FA sample; and
  - Did not present any major protocol violation (consideration about exclusion of patients from *the PP sample* will be performed at the Blind Data Review).

4.2 Efficacy analysis

The *FA subject sample* will be used for the analysis of the efficacy data. Additionally, primary efficacy results analysis will be conducted on the *PP sample* as the sensitivity analysis. Descriptive statistics will be presented by treatment arm and by stratification level (Age Category) for all planned efficacy endpoints.

All analyses will be based on available data only and no missing data will be imputed.

All parameters will be summarized using descriptive statistics and listed.

4.2.1 Primary Efficacy Analysis

The primary efficacy variable is the duration (hours) of diarrhea (treatment duration max 5 days). Duration of diarrhea is defined by date (“event” date) of the evacuation of the last diarrheal/watery stool before recovery.

In order to compare the primary efficacy parameter, duration of diarrhea, between the treatment groups, a Kaplan Meier (KM) analysis will be performed. The KM algorithm will be applied to derive the median duration and the 95% confidence intervals for the median, Q1, Q3 and mean duration with Greenwood's estimator of standard deviation of Kaplan-Meier estimator.

The log-rank test will be used to test whether the difference between the duration of diarrhea between two treatment groups is statistically significant, i.e. p-value <0.05.

For duration estimation the date and time of first drug intake will be assumed as start time point and all subjects without "event" will be censored by 6 days (144 hours).

SAS code for the analysis:

PROC LIFETEST DATA = *[dataset name]*

METHOD=KM PLOTS=SURVIVAL

OUTSURV=SURV CONFTYPE=LOGLOG ATRISK;

TIME *[time variable]*[censor variable]*;

STRATA *[arm variable]*;

RUN;

The "OUTSURV=SURV" statement provides variables that contains the lower and upper limits of the pointwise confidence intervals for the survivor function ("SDF_LCL" and "SDF_UCL"), this confidence intervals should be transformed for tables as follows:

[Lower limit var name] = round(100*(1-SDF_UCL),.1);

[Upper limit var name] = round(100*(1-SDF_LCL),.1);

As a first sensitivity analysis, duration of diarrhea will be analyzed by age subgroups as follows:

- Racecadotril + ORS (age subgroup 3 to < 24 month) vs ORS (age subgroup 3 to < 24 month) comparison;
- Racecadotril + ORS (age subgroup >= 2 to <12 years) vs ORS (age subgroup >= 2 to <12 years) comparison;
- Racecadotril + ORS (age subgroup 12 to < 18 years) vs ORS (age subgroup 12 to < 18 years) comparison;

As a second sensitivity analysis, duration of diarrhea will be analyzed by weight/dosing subgroups as follows:

- Racecadotril + ORS (Infants less than 9 kg) vs ORS (Infants less than 9 kg) comparison;

- Racecadotril + ORS (Infants from 9 kg to < 13 kg) vs ORS (Infants from 9 kg to < 13 kg Infants from 9 kg to < 13 kg) comparison;
- Racecadotril + ORS (Children from 13 kg to 27 kg) vs ORS (Children from 13 kg to 27 kg) comparison;
- Racecadotril + ORS (Children from more than 27 kg to 60 kg) vs ORS (Children from more than 27 kg to 60 kg) comparison;
- Racecadotril + ORS (Children or adolescents of 60 kg or higher) vs ORS (Children or adolescents of 60 kg or higher) comparison;

SAS code for the analysis:

PROC LIFETEST DATA = *[dataset name]*
METHOD=KM PLOTS=SURVIVAL
OUTSURV=SURV CONFTYPE=LOGLOG ATRISK;
TIME *[time variable]*[censor variable]*;
STRATA *[arm variable]*;
BY *[age subgroup variable]*;
RUN;

PROC LIFETEST DATA = *[dataset name]*
METHOD=KM PLOTS=SURVIVAL
OUTSURV=SURV CONFTYPE=LOGLOG ATRISK;
TIME *[time variable]*[censor variable]*;
STRATA *[arm variable]*;
BY *[weight/dosing category variable]*;
RUN;

Description of the Cox regression model analysis is presented in the Section 4.2.3 of the SAP.

4.2.2 Secondary efficacy analysis

The secondary efficacy variables are

- Number of recovered subjects per treatment group in total and until each individual treatment day. Mean and median time until recovery per treatment group.
- Time until recovery, defined by date and time of the evacuation of the first of two consecutive normal stools.

Time until recovery, number of recovered subjects per treatment group in total and until each individual treatment day and mean and median time until recovery per treatment group will be estimated Kaplan Meier analysis as described for the primary endpoint.

- Global Physician Assessment at the end of treatment:
    - 1 = Complete relief of acute diarrhea,
    - 2 = marked improvement of acute diarrhea,
    - 3 = moderate improvement of acute diarrhea,
    - 4 =slight improvement of acute diarrhea,
    - 5 = no change in acute diarrhea,
    - 6 =worsening of acute diarrhea.

Frequencies table will be performed for the Global Physician Assessment at the end of treatment by GPA score and by success rating. Treatment will be rated as success when the GPA score equals 1 or 2.

Description of the subgroup analysis is presented in the Section 4.2.3 of the SAP.

The comparisons of treatment arms using Fisher exact test will be performed by proportion of patients with Global Physician Assessment success at the end of treatment.

SAS code for the analysis:

PROC FREQ DATA = *[dataset name]*;

WEIGHT *[GPA frequency] / ZEROS;*

TABLES *[GPA yes/no level]* * *[Arm]* / EXACT FISHER;

RUN;

If SAS code produces the “Row or column sum zero. No statistics computed for this table.” output due to insufficient memory available to complete the Fisher exact computations, then the p-value should be assumed as equal 1.0000.

- For toilet trained children and adolescents: number of stools per day as well as number of watery stools per day from start of treatment and until end of study treatment.

Number of stools and number of watery stools will be presented descriptively per treatment group and cumulatively until each day of treatment.

4.2.3 Other efficacy analysis

Additionally, duration of diarrhea and time to recovery will be analyzed using Cox regression model where treatment group, age group, and dosing/weight group will be included as covariates. Relative risk will be presented for each covariate with 95% confidence intervals (Relative risk is referred to as "Hazard ratio" in the output from PROC PHREG SAS procedure).

SAS code for the analysis:

PROC PHREG DATA = *[dataset name]*;

CLASS *[arm variable]* (ref=*[reference level]*)

[age group] (ref=*[reference level]*)

[weight/dosing category] (ref=*[reference level]*);

MODEL *[time variable]* * *[censor variable]* =

[arm variable] [age group] [weight/dosing category] / RL;

RUN;

The results of the exploratory analyses using Cox regression model will be provided in appropriate tables with the main results (see 10.1.4.1.2.1; 10.1.4.1.2.2; 10.1.4.1.5.1; 10.1.4.1.5.2; 10.1.4.2.2.1 and 10.1.4.2.2.2 table shells).

The comparisons by subgroup for GPA score success rating using Fisher exact test will be performed using the following SAS code:

PROC FREQ DATA = *[dataset name]*;

WEIGHT *[GPA frequency] / ZEROS;*

TABLES *[GPA yes/no level]* * *[Arm]* / EXACT FISHER;

BY *[age subgroup variable]*;

RUN;

If SAS code produces the "Row or column sum zero. No statistics computed for this table." output due to insufficient memory available to complete the Fisher exact computations, then the p-value should be assumed as equal 1.0000.

The results of the exploratory analyses will be provided in appropriate tables with the main results (see Table 10.1.4.2.3), no adjustment for multiplicity will be done due to the exploratory nature of analyses.

4.3 Safety analysis

The Safety Sample will be used for the analysis of the safety and tolerability data.

Descriptive statistics for all safety and tolerability data will be presented by treatment arm and by stratification level (Age Category).

AEs are considered treatment emergent (TE) if they start or worsen at or after the first administration of study drug and before or on the day of last administration of study drug plus a gap period of 1 day (24 hours).

AEs will be reported on a per-subject basis, i.e. counting subjects rather than events. This means that if a subject suffers the same AEs repeatedly during the applicable study period, the event will be counted only once for that period. Repeated events per subject will be summarized according to the following rule: if a subject suffered the same AE more than once, the event will be assigned the worst severity, the closest relationship to the study drug and the earliest starting date. Only treatment emergent AEs will be reported. In the listings, however, all occurrences of the AEs will be presented.

For each unique treatment, treatment emergent AEs will be summarized per primary SOC, per HLT by primary SOC and per PT by HLT and primary SOC. Severity and drug-event relationship of treatment emergent AEs are summarized separately. Non-TEAEs will be listed.

Vitals signs: Height (m), Weight (kg), Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg), Pulse (bpm), including changes from baseline will be summarized. A frequency table will be presented for markedly abnormal values (presented in the table categories includes “to high”, “to low” and “normal” levels based on normal ranges).

Temperature data will be presented in appropriate listing only.

RACE3003 clinical study was conducted with the involvement of local laboratories, thus local normal ranges have been used in each particular site (the ranges are presented below). Additional footnote (“Created <*table/listing*> based on site specific ranges.”) will be presented for appropriate tables and listings in the statistical analysis report.

Normal Heart Rate by Age (beats/minute)									
Site / Age	1	2	3	4	5	6	7	8	9
1-12 month	100-140	100-190	100-190	100-160	100-190	100-190	110-170	100-190	100-190
1-3 years	98-120	98-140	95-110	98-140	98-140	98-140	100-130	98-140	98-140
3-6 years	80-105	80-120	80-120	80-120	80-120	80-120	85-115	80-120	80-120
6-9 years	75-90	75-118	75-110	75-118	75-118	75-118	75-105	75-118	75-118
9-12 years	70-90	60-100	60-100	60-100	60-100	60-100	70-90	60-100	60-100
12-18 years	70-90	60-100	60-100	60-100	60-100	60-100	70-90	60-100	60-100

Normal Systolic Blood Pressure by Age (mm Hg)									
Site / Age	1	2	3	4	5	6	7	8	9
1-12 month	80-112	90-112	85-105	90-112	90-112	90-112	75-80	90-112	90-112
1-3 years	90-112	100-112	85-110	100-112	100-112	100-112	80-85	100-112	100-112
3-6 years	100-116	100-116	85-115	100-116	100-116	100-116	90-95	100-116	100-116
6-9 years	100-122	100-122	95-120	100-122	100-122	100-122	95-105	100-122	100-122
9-12 years	100-126	110-126	110-125	110-126	110-126	110-126	105-115	110-126	110-126

Normal Systolic Blood Pressure by Age (mm Hg)									
Age \ Site	1	2	3	4	5	6	7	8	9
12-18 years	110-120	110-136	110-130	110-136	110-136	110-136	110-120	110-136	110-136

Normal Diastolic Blood Pressure by Age (mm Hg)									
Age \ Site	1	2	3	4	5	6	7	8	9
1-12 month	50-74	50-74	45-60	50-74	50-74	50-74	50-74	50-74	50-74
1-3 years	60-74	60-74	50-60	60-74	60-74	60-74	50-55	60-74	60-74
3-6 years	60-76	60-76	55-60	60-76	60-76	60-76	50-60	60-76	60-76
6-9 years	60-78	60-78	55-70	60-78	60-78	60-78	65-70	60-78	60-78
9-12 years	70-82	60-82	55-70	70-82	70-82	70-82	70-75	70-82	70-82
12-18 years	70-86	60-86	55-70	70-86	70-86	70-86	70-80	70-86	70-86

Temperature (C)									
Age \ Site	1	2	3	4	5	6	7	8	9
Axillary	36,1-36,9	35,9-36,9	36,3-36,9	36,3-36,9	36,3-37,0	36,3-36,9	36,3-36,9	36,3-36,9	36,3-36,9
Oral	36,8-37,3	36,2-37,3	36,8-37,3	36,8-37,3	36,8-37,3	36,8-37,3	36,8-37,3	36,8-37,3	36,8-37,3
Rectal	37,1-37,9	36,9-37,9	37,3-37,7	37,3-37,7	37,3-38,0	37,3-37,7	37,3-37,7	37,3-37,7	37,3-37,7
Tympanic membrane	36,1-36,9	36,5-37,5	37,3-37,7	37,3-37,7	37,3-37,7	37,3-37,7	37,3-37,7	37,3-37,7	37,3-37,7
Skin / Temporary artery	36,1-36,9	36,3-36,9	36,3-36,9	36,3-36,9	36,3-36,9	36,3-36,9	36,3-36,9	36,3-36,9	36,3-36,9

Physical Examination will be summarized by subgroup (toilet trained, not toilet trained and overall).

4.4 Interim Analysis

No interim analysis is planned.

4.5 Data Safety Monitoring Board

Not applicable.

4.6 Safety Management Team

Not applicable.

5. DESCRIPTION OF NON-STANDARD DATA COLLECTED AND DERIVED VARIABLES

5.1 Other Non-Standard Baseline Characteristics

Other baseline characteristic collected in the study is Main Diagnosis. The main Main Diagnosis data will be tabulated using descriptive statistics and listed.

5.2 Non-Standard Disease History

Not applicable.

5.3 Efficacy data

The efficacy data collected are:

- Information about diarrheal/watery stool/stool from Subjects Diary (domain SS);
- Global physician assessment at the end of treatment (domain QS).

5.4 Non-standard Safety Data

The following non-standard safety data are collected*: Physical Examination (PE domain).*

5.5 Drug Accountability and Exposure

5.5.1 Drug Accountability

Treatment compliance/drug accountability is defined as the number of sachets /capsules that were actually taken relative to the number of sachets /capsules that should have been taken for the duration of actual treatment exposure. The overall compliance, assessed by sachet/capsule count, will be calculated as follows:

1. Racecadotril treatment:

$$\text{Compliance (\%)} = \frac{(\text{N of sachets /capsules dispensed} - \text{N of sachets /capsules returned})}{[(\text{Difference between Date/time of last dose and first dose in hours})/24 * \text{N of sachets /capsules prescribed per day}]}$$

2. ORS treatment:

$$\text{Compliance (\%)} = \frac{\text{Amount of ORS intake} * 100\%}{[(\text{Difference between Date/time of last dose and first dose in hours})/24 * \text{Amount prescribed per day}]}$$

For prescribed ORS dose if frequency coded as “7=prn” (when necessary) then compliance will be stated as 100%, else the formula for compliance will be used.

The calculated percentage compliance will be categorized as:

- Too Low: $< 80\%$ compliance.
- Adequate: $\geq 80\%$ to $\leq 120\%$ compliance.
- Too High: $> 120\%$ compliance.

5.5.2 Exposure

Exposure analysis will be provided using EC domain. Descriptive statistics tables will be presented for:

- Mean duration of treatment[1] (in hours) by weight subgroups (less than 9 kg, from 9 kg to < 13 kg, from 13 kg to 27 kg, from more than 27 kg to 60 kg, 60 kg or higher) and overall;
- Mean duration of treatment (in hours) by age subgroup and overall;
- Cumulative dose divided by weight (mg/kg).

1 The duration of treatment will be assumed as 1 hour in case of single dose administration.

6. FURTHER SPECIFICATIONS TO THE STANDARD ANALYSES IN MODULE 2

6.1 Trial Design [2]

6.1.1 Trial Periods

The combination of trial arms and trial periods for the current trial is presented in the following diagram:

		Screening Period	Treatment Period	Follow-up Periods
Trial Arm A (RACE+ORS)	Subgroup A	Screen	Racecadotril + ORS	Follow-up
	Subgroup B	Screen	Racecadotril + ORS	Follow-up
	Subgroup C	Screen	Racecadotril + ORS	Follow-up
Trial Arm B (ORS)	Subgroup A	Screen	ORS	Follow-up
	Subgroup B	Screen	ORS	Follow-up
	Subgroup C	Screen	ORS	Follow-up

Subgroups are defined by age categories:

- Subgroup A (from 3 to < 24 month)
- Subgroup B (from >= 2 to <12 years)
- Subgroup C (12 to < 18 years),

6.1.2 Trial Elements

The start time of each intervention will be expressed relative to the first administration of investigational study drug closest to that intervention.

The Trial Elements are presented in the following diagram:

Trial Element	Description of Element	Rule for Start of Element	Rule for End of Element	Planned Duration of Element
Screen	Screening period	Date of Informed Consent	First dose of study treatment	
Racecadotril + ORS	Treatment period	First dose of Racecadotril + ORS	Last dose of Racecadotril + ORS	5 days or less
ORS	Treatment period	First dose of ORS	Last dose of ORS	5 days or less
Follow-up	Safety Follow-Up period	Last dose of study treatment	Investigator's phone call 5-7 days after end of treatment visit	5-7 days

6.1.3 Trial Arms

The trial arms for this study are made up of the following trial elements:

Trial Arm	Elements			
	Screen	Racecadotril + ORS	ORS	Follow-up
A	Y	Y	N	Y
B	Y	N	Y	Y

6.1.4 Visits and related definitions

Tests and examinations that were scheduled in the protocol will be related to the general time axis of the trial by relating the visit date on which a test or examination is performed to the start date of the trial element that describes the first administration of investigational study drug closest in time to the visit date of that test or examination (Reference Start Date/ Time).

Test / Examination	Visit name	Visit Label	Visit Number	Reference Start Date/Time	Relative Day Number
Informed consent/assent	Screening	Screening	1		
Randomization	Screening	Screening	1		
Demographic data	Screening	Screening	1		

Test / Examination	Visit name	Visit Label	Visit Number	Reference Start Date/Time	Relative Day Number
Medical history	Screening	Screening	1		
Physical examination	Screening	Screening	1		
In-or outpatient	Screening	Screening	1		
Stool frequency within the last 24 hours	Screening	Screening	1		
Inclusion/exclusion criteria	Screening	Screening	1		
Vitals signs	Screening	Screening	1		
Dispense study drug	Screening	Screening	1		
Concomitant medication	Screening	Screening	1		
Adverse events	Screening	Screening	1		
Dispense diary	Screening	Screening	1		
Collect diary	End of Treatment	End of Treatment	2	Date of last dose of study treatment	Day 6 (*)
Physical examination	End of Treatment	End of Treatment	2	Date of last dose of study treatment	Day 6 (*)
Compliance check	End of Treatment	End of Treatment	2	Date of last dose of study treatment	Day 6 (*)
Adverse events	End of Treatment	End of Treatment	2	Date of last dose of study treatment	Day 6 (*)
Collect study drug	End of Treatment	End of Treatment	2	Date of last dose of study treatment	Day 6 (*)

Test / Examination	Visit name	Visit Label	Visit Number	Reference Start Date/Time	Relative Day Number
Concomitant medication	End of Treatment	End of Treatment	2	Date of last dose of study treatment	Day 6 (*)
Adverse events	Follow-Up	Safety follow-up (phone call 5-7 days after Visit 2)	3	Investigator's phone call 5-7 days after end of treatment visit	Day 11-13
Concomitant medication	Follow-Up	Safety follow-up (phone call 5-7 days after Visit 2)	3	Investigator's phone call 5-7 days after end of treatment visit	Day 11-13

(*) or within 24 h after recovery if this occurs before day 6

6.2 Further Specifications to the Standard Tables in Module 2

Not applicable.

6.3 Other Further Specifications

Not applicable.

7. CHANGES TO PLANNED ANALYSES

No changes will be made to the final SAP

8. REFERENCE

1. Abbott SAP Module 2
2. CDISC terminology, see http://www.cdisc.org.

9. APPENDICES

9.1 Study Flowchart

Note: Any additional medical procedures not included into this study protocol can be performed within routine clinical practice in each medical institution.

Period	Screening	End of Treatment period	Safety follow-up (phone call 5-7 days after Visit 2)
Visit	1	2	3
Day	1	6 [2]	11-13
Informed consent	X		
Randomization	X		
Demographic data	X		
Medical history	X		
Pregnancy Test [4]	X		
Physical examination [3]	X	X	
In- or outpatient	X		
Stool frequency within the last 24 hours	X		
Inclusion/exclusion criteria	X		
Vitals signs	X	X	
Dispense study drug	X		
Concomitant medication	X	X	X if applicable
Compliance check		X	
Adverse events	X	X	X
Collect study drug		X	
Dispense diary	X [1]		
Collect diary		X	

[1] Subjects' parent/caregivers have to fill in their daily diaries continuously.

[2] or within 24 h after recovery if this occurs before day 6

[3] including assessment of dehydration level

[4] for females of child-bearing potential, urine test

9.2 Tables, Listings and Figures

9.2.1 Tables

For the shells of the non-standard tables, see Section 10.1.

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
DST001	Subject Disposition	10.1.1.1	Subject Disposition - All Subjects Allocated to Treatment Subject Sample			
DVT001	Protocol Deviations	10.1.1.2	Protocol Deviations – All Subjects Allocated to Treatment Subject Sample			
DVT002	Protocol Deviations	10.1.1.3	Subject Samples - All Subjects Allocated to Treatment Subject Sample			
DMT002	Demographic Data	10.1.1.5	Demographics – Safety Sample			
DMT002	Demographic Data	10.1.1.6	Demographics –Full Analysis Subject Sample			
VST003	Vital Signs	10.1.1.8	Other Baseline Characteristics – Safety Sample			
VST003	Vital Signs	10.1.1.9	Other Baseline Characteristics – Full Analysis Subject Sample			
MHT001	Medical History	10.1.1.10	Medical History – All Subjects Allocated to Treatment Subject Sample			
MHT001	Medical History	10.1.1.11	Medical History – Safety Sample			
MHT001	Medical History	10.1.1.12	Medical History – Full Analysis Subject Sample			
NST001	Medical History	10.1.1.13	Main Diagnosis - All Subjects Allocated to Treatment Subject Sample			
NST002	Medical History	10.1.1.14	Main Diagnosis - Safety Sample			
NST003	Medical History	10.1.1.15	Main Diagnosis - Full Analysis Subject Sample			
CMT001	Concomitant Medications	10.1.1.16	Concomitant Medications – All Subjects Allocated to Treatment Subject Sample			
CMT001	Concomitant Medications	10.1.1.17	Concomitant Medications – Safety Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
CMT001	Concomitant Medications	10.1.1.18	Concomitant Medications – Full Analysis Subject Sample			
DAT001	Treatment Compliance	10.1.1.19	Compliance to Study Drug – All Subjects Allocated to Treatment Subject Sample			
DAT001	Treatment Compliance	10.1.1.20	Compliance to Study Drug – Safety Sample			
DAT001	Treatment Compliance	10.1.1.21	Compliance to Study Drug – Full Analysis Subject Sample			
AET001	Adverse Events	10.1.3.1.1	Overall Summary of Adverse Events – Safety Sample			
AET002	Adverse Events	10.1.3.1.2	Incidence of TEAEs – Safety Sample			
AET005	Adverse Events	10.1.3.1.3	Incidence of TEAEs With a Reasonable Possibility for a Causal Relationship (Investigator's Judgment) – Safety Sample			
AET006	Adverse Events	10.1.3.1.4	Incidence of TEAEs by Maximum Severity (Investigator's Judgment) – Safety Sample			
AET007	Adverse Events	10.1.3.1.5	Incidence of TESAEs – Safety Sample			
AET008	Adverse Events	10.1.3.1.6	Incidence of TEAEs Leading to Study Termination – Safety Sample			
VST001	Vital Signs	10.1.3.2.1	Summary of Vital Signs – Safety Sample			
VST002	Vital Signs	10.1.3.2.2	Incidence of Markedly Abnormal Vital Signs – Safety Sample			
NST004	Physical Examination	10.1.3.3.1	Physical Examination by subgroup (Toilet trained / Not toilet trained) – Safety Sample			
NST005	Exposure	10.1.3.4.1	Treatment duration – Safety Sample			
NST006	Exposure	10.1.3.4.2	Cumulative dose by weight (mg/kg) – Safety Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
NST007	Subject Status	10.1.4.1.1	Duration of diarrhea: time to last diarrheal/watery stool before recovery by days. Kaplan-Meier analysis – Full Analysis Subject Sample			
NST008	Subject Status	10.1.4.1.2.1	Duration of diarrhea. Descriptive statistics (in hours) and comparison results – Full Analysis Subject Sample			
NST009	Subject Status	10.1.4.1.2.2	Duration of diarrhea. Cox Regression Model – Full Analysis Subject Sample			
NST010	Subject Status	10.1.4.1.3.1	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from 3 to < 24 month – Full Analysis Subject Sample			
NST011	Subject Status	10.1.4.1.3.2	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from >= 2 to <12 years – Full Analysis Subject Sample			
NST012	Subject Status	10.1.4.1.3.3	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from 12 to < 18 years – Full Analysis Subject Sample			
NST013	Subject Status	10.1.4.1.3.4	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category infants less than 9 kg – Full Analysis Subject Sample			
NST014	Subject Status	10.1.4.1.3.5	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category infants from 9 kg to < 13 kg – Full Analysis Subject Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
NST015	Subject Status	10.1.4.1.3.6	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children from 13 kg to 27 kg – Full Analysis Subject Sample			
NST016	Subject Status	10.1.4.1.3.7	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children from more than 27 kg to 60 kg – Full Analysis Subject Sample			
NST017	Subject Status	10.1.4.1.3.8	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children or adolescents of 60 kg or higher – Full Analysis Subject Sample			
NST018	Subject Status	10.1.4.1.3.9	Duration of diarrhea. Number of stools during the study - Full Analysis Subject Sample			
NST019	Subject Status	10.1.4.1.4	Duration of diarrhea: time to last diarrheal/watery stool before recovery by days. Kaplan-Meier analysis – Per Protocol Subject Sample			
NST020	Subject Status	10.1.4.1.5.1	Duration of diarrhea. Descriptive statistics (in hours) and comparison results – Per Protocol Subject Sample			
NST021	Subject Status	10.1.4.1.5.2	Duration of diarrhea. Cox Regression Model – Per Protocol Subject Sample			
NST022	Subject Status	10.1.4.1.6.1	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from 3 to < 24 month – Per Protocol Subject Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
NST023	Subject Status	10.1.4.1.6.2	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from >= 2 to <12 years – Per Protocol Subject Sample			
NST024	Subject Status	10.1.4.1.6.3	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from 12 to < 18 years – Per Protocol Subject Sample			
NST025	Subject Status	10.1.4.1.6.4	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category infants less than 9 kg – Per Protocol Subject Sample			
NST026	Subject Status	10.1.4.1.6.5	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category infants from 9 kg to < 13 kg – Per Protocol Subject Sample			
NST027	Subject Status	10.1.4.1.6.6	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children from 13 kg to 27 kg – Per Protocol Subject Sample			
NST028	Subject Status	10.1.4.1.6.7	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children from more than 27 kg to 60 kg – Per Protocol Subject Sample			
NST029	Subject Status	10.1.4.1.6.8	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children or adolescents of 60 kg or higher – Per Protocol Subject Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
NST030	Subject Status	10.1.4.1.6.9	Duration of diarrhea. Number of stools during the study - Per Protocol Subject Sample			
NST031	Subject Status	10.1.4.1.7	Number of stools per day (toilet trained subgroup) – Full Analysis Subject Sample			
NST032	Subject Status	10.1.4.1.8	Number of watery stools per day (toilet trained subgroup) – Full Analysis Subject Sample			
NST033	Subject Status	10.1.4.1.9	Cumulative number of stools until recovery or end of treatment by days – Full Analysis Subject Sample			
NST034	Subject Status	10.1.4.2.1	Time to recovery: time to evacuation of the first of two consecutive normal stools or no stool after first normal stool within 12 hours by days. Kaplan-Meier analysis – Full Analysis Subject Sample			
NST035	Subject Status	10.1.4.2.2.1	Time to recovery. Descriptive statistics (in hours) and comparison results – Full Analysis Subject Sample			
NST036	Subject Status	10.1.4.2.2.2	Time to recovery. Descriptive statistics (in hours) and comparison results – Full Analysis Subject Sample			
NST037	Subject Status	10.1.4.2.2.3	Time to recovery. Descriptive statistics (in hours) and comparison results for age group from 3 to < 24 month – Full Analysis Subject Sample			
NST038	Subject Status	10.1.4.2.2.4	Time to recovery. Descriptive statistics (in hours) and comparison results for age group from >= 2 to <12 years – Full Analysis Subject Sample			
NST039	Subject Status	10.1.4.2.2.5	Time to recovery. Descriptive statistics (in hours) and comparison results for age group from 12 to < 18 years – Full Analysis Subject Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
NST040	Subject Status	10.1.4.2.2.6	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Infants less than 9 kg – Full Analysis Subject Sample			
NST041	Subject Status	10.1.4.2.2.7	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Infants from 9 kg to < 13 kg – Full Analysis Subject Sample			
NST042	Subject Status	10.1.4.2.2.8	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Children from 13 kg to 27 kg – Full Analysis Subject Sample			
NST043	Subject Status	10.1.4.2.2.9	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Children from more than 27 kg to 60 kg – Full Analysis Subject Sample			
NST044	Subject Status	10.1.4.2.2.10	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Children or adolescents of 60 kg or higher – Full Analysis Subject Sample			
NST045	Questionnaires	10.1.4.2.3	Global Physician Assessment at the end of treatment – Full Analysis Subject Sample			
NST046	Questionnaires	10.1.4.2.4.1	Global Physician Assessment at the end of treatment for weight/dosing category Infants less than 9 kg – Full Analysis Subject Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
NST047	Questionnaires	10.1.4.2.4.2	Global Physician Assessment at the end of treatment for weight/dosing category Infants from 9 kg to < 13 kg – Full Analysis Subject Sample			
NST048	Questionnaires	10.1.4.2.4.3	Global Physician Assessment at the end of treatment for weight/dosing category Children from 13 kg to 27 kg – Full Analysis Subject Sample			
NST049	Questionnaires	10.1.4.2.4.4	Global Physician Assessment at the end of treatment for weight/dosing category Children from more than 27 kg to 60 kg – Full Analysis Subject Sample			
NST050	Questionnaires	10.1.4.2.4.5	Global Physician Assessment at the end of treatment for weight/dosing category Children or adolescents of 60 kg or higher – Full Analysis Subject Sample			

9.2.2 Listings

For the shells of the non-standard listings, see Section 10.2.

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
DSL001	Subject Disposition	12.2.1.1	Subjects Who Prematurely Terminated the Study Prior to Treatment Allocation - All Subjects Consented Subject Sample			
DSL002	Subject Disposition	12.2.1.2	Subjects Allocated to Treatment - All Subjects Allocated to Treatment Subject Sample			
DSL003	Subject Disposition	12.2.1.3	Subjects Allocated to Treatment Who Prematurely Terminated the Study - All Subjects Allocated to Treatment Subject Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
DVL001	Protocol Deviations	12.2.2.1	Subjects With Protocol Deviations - All Subjects Allocated to Treatment Subject Sample			
IEL002	Inclusion/Exclusion	12.2.2.2	Subjects With Deviations from Inclusion or Exclusion Criteria - All Subjects Consented Subject Sample			
DVL002	Protocol Deviations	12.2.3.1	Subjects Excluded From the Subject Samples - All Subjects Allocated to Treatment Subject Sample			
DML002	Demographic Data	12.2.4.1	Demographics - All Subjects Allocated to Treatment Subject Sample			
NSL001	Vital Signs	12.2.4.2	Other Baseline Characteristics - All Subjects Allocated to Treatment Subject Sample			
NSL002	Reproductive System Findings	12.2.4.3	Urinary Pregnancy Test / Childbearing Potential - All Subjects Allocated to Treatment Subject Sample			
MHL001	Medical History	12.2.4.4	Medical History: General - All Subjects Allocated to Treatment Subject Sample			
MHL002	Medical History	12.2.4.5	Medical History: MedDRA Coding - All Subjects Allocated to Treatment Subject Sample			
CML001	Concomitant Medications	12.2.4.6	Concomitant Medication: General - All Subjects Allocated to Treatment Subject Sample			
CML002	Concomitant Medications	12.2.4.7	Concomitant Medication: WHO-DD Coding - All Subjects Allocated to Treatment Subject Sample			
NSL003	Medical History	12.2.4.7	Main Diagnosis - All Subjects Allocated to Treatment Subject Sample			
DAL001	Drug Accountability	12.2.5.1	Drug Accountability and Compliance - All Subjects Allocated to Treatment Subject Sample			

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline Results	SMT	Interim Analysis
AEL008	Adverse Events	12.2.7.1	AEs: General - All Subjects Consented Subject Sample			
AEL002	Adverse Events	12.2.7.2	AEs: MedDRA Coding - All Subjects Consented Subject Sample			
AEL010	Adverse Events	10.1.3.1.9	Listing of Other SAEs - All Subjects Consented Subject Sample			
AEL011	Adverse Events	10.1.3.1.11	Listing of TEAEs Leading to Study Termination – Safety Sample			
AEL012	Adverse Events	10.1.3.1.12	Listing of TEAEs Leading to Discontinuation of Study Drug – Safety Sample			
VSL004	Vital Signs	12.2.8.8	Markedly Abnormal Vital Signs – Safety Sample			
VSL005	Vital Signs	12.2.8.9	Vital Signs - All Subject Allocated to Treatment Subject Sample			
SVL001	Subject Visits	12.2.8.15	Subject Visits – All Subject Allocated to Treatment Subject Sample			
NSL004	Physical Examination	12.2.9.1	Physical Examination - All Subject Allocated to Treatment Subject Sample			
NSL005	Questionnaries	12.2.9.2	Global Physician Assessment - All Subject Allocated to Treatment Subject Sample			
NSL006	Subject Status	12.2.9.3	Stool Evacuation- All Subject Allocated to Treatment Subject Sample			

9.2.3 Figures

For the shells of the non-standard figures, see Section 10.3.

Output Code	Clinical Domain	Output Number	Title	Produced for:		
				Headline results	SMT	Interim analysis
DSF001	Subject Disposition	10.1.4.1	Flowchart of Subject Disposition			
DSF002	Subject Disposition	10.1.4.2	Flowchart of Subject samples			
NSF001	Subject Status	10.1.4.1.1	Kaplan-Meier Plot of duration of diarrhea – Full Analysis Subject Sample			
NSF002	Subject Status	10.1.4.1.2	Kaplan-Meier Plot of duration of diarrhea– Per Protocol Subject Sample			
NSF003	Subject Status	10.1.4.1.3	Kaplan-Meier Plot for time to recovery – Full Analysis Subject Sample			

9.3 Non-standard Tables, Listings and Figures Shells

9.3.1 Non-Standard Tables

Table code	Comment
10.1.1.13	Main Diagnosis – All Subjects Allocated to Treatment Subject Sample
10.1.1.14	Main Diagnosis – Safety Sample
10.1.1.15	Main Diagnosis – Full Analysis Subject Sample
10.1.3.3.1	Physical Examination by subgroup (Toilet trained / Not toilet trained) – Safety Sample
10.1.3.4.1	Treatment duration – Safety Sample
10.1.3.4.2	Cumulative dose by weight (mg/kg) – Safety Sample
10.1.4.1.1	Duration of diarrhea: time to last diarrheal/watery stool before recovery by days. Kaplan-Meier analysis – Full Analysis Subject Sample
10.1.4.1.2.1	Duration of diarrhea. Descriptive statistics (in hours) and comparison results – Full Analysis Subject Sample
10.1.4.1.2.2	Duration of diarrhea. Cox Regression Model – Full Analysis Subject Sample
10.1.4.1.3.1	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from 3 to < 24 month – Full Analysis Subject Sample
10.1.4.1.3.2	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from >= 2 to <12 years – Full Analysis Subject Sample
10.1.4.1.3.3	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from 12 to < 18 years – Full Analysis Subject Sample
10.1.4.1.3.4	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category infants less than 9 kg – Full Analysis Subject Sample
10.1.4.1.3.5	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category infants from 9 kg to < 13 kg – Full Analysis Subject Sample
10.1.4.1.3.6	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children from 13 kg to 27 kg – Full Analysis Subject Sample

10.1.4.1.3.7	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children from more than 27 kg to 60 kg – Full Analysis Subject Sample
10.1.4.1.3.8	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children or adolescents of 60 kg or higher – Full Analysis Subject Sample
10.1.4.1.3.9	Duration of diarrhea. Number of stools during the study - Full Analysis Subject Sample
10.1.4.1.4	Duration of diarrhea: time to last diarrheal/watery stool before recovery by days. Kaplan-Meier analysis – Per Protocol Subject Sample
10.1.4.1.5.1	Duration of diarrhea. Descriptive statistics (in hours) and comparison results – Per Protocol Subject Sample
10.1.4.1.5.2	Duration of diarrhea. Cox Regression Model – Per Protocol Subject Sample
10.1.4.1.6.1	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from 3 to < 24 month – Per Protocol Subject Sample
10.1.4.1.6.2	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from >= 2 to <12 years – Per Protocol Subject Sample
10.1.4.1.6.3	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for age group from 12 to < 18 years – Per Protocol Subject Sample
10.1.4.1.6.4	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category infants less than 9 kg – Per Protocol Subject Sample
10.1.4.1.6.5	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category infants from 9 kg to < 13 kg – Per Protocol Subject Sample
10.1.4.1.6.6	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children from 13 kg to 27 kg – Per Protocol Subject Sample
10.1.4.1.6.7	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children from more than 27 kg to 60 kg – Per Protocol Subject Sample
10.1.4.1.6.8	Duration of diarrhea. Descriptive statistics (in hours) and comparison results for weight/dosing category children or adolescents of 60 kg or higher – Per Protocol Subject Sample
10.1.4.1.6.9	Duration of diarrhea. Number of stools during the study - Per Protocol Subject Sample

10.1.4.1.7	Number of stools per day (toilet trained subgroup) – Full Analysis Subject Sample
10.1.4.1.8	Number of watery stools per day (toilet trained subgroup) – Full Analysis Subject Sample
10.1.4.1.9	Cumulative number of stools until recovery or end of treatment by days – Full Analysis Subject Sample
10.1.4.2.1	Time to recovery: time to evacuation of the first of two consecutive normal stools or no stool after first normal stool within 12 hours by days. Kaplan-Meier analysis – Full Analysis Subject Sample
10.1.4.2.2.1	Time to recovery. Descriptive statistics (in hours) and comparison results – Full Analysis Subject Sample
10.1.4.2.2.2	Time to recovery. Descriptive statistics (in hours) and comparison results – Full Analysis Subject Sample
10.1.4.2.2.3	Time to recovery. Descriptive statistics (in hours) and comparison results for age group from 3 to < 24 month – Full Analysis Subject Sample
10.1.4.2.2.4	Time to recovery. Descriptive statistics (in hours) and comparison results for age group from >= 2 to <12 years – Full Analysis Subject Sample
10.1.4.2.2.5	Time to recovery. Descriptive statistics (in hours) and comparison results for age group from 12 to < 18 years – Full Analysis Subject Sample
10.1.4.2.2.6	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Infants less than 9 kg – Full Analysis Subject Sample
10.1.4.2.2.7	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Infants from 9 kg to < 13 kg – Full Analysis Subject Sample
10.1.4.2.2.8	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Children from 13 kg to 27 kg – Full Analysis Subject Sample
10.1.4.2.2.9	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Children from more than 27 kg to 60 kg – Full Analysis Subject Sample
10.1.4.2.2.10	Time to recovery. Descriptive statistics (in hours) and comparison results for weight/dosing category Children or adolescents of 60 kg or higher – Full Analysis Subject Sample
10.1.4.2.1	Time to recovery: time to evacuation of the first of two consecutive normal stools or no stool after first normal stool within 12 hours by days. Kaplan-Meier analysis – Full Analysis Subject Sample
10.1.4.2.2	Time to recovery. Descriptive statistics (in hours) and comparison results – Full Analysis Subject Sample

10.1.4.2.3	Global Physician Assessment at the end of treatment – Full Analysis Subject Sample
10.1.4.2.4.1	Global Physician Assessment at the end of treatment for weight/dosing category Infants less than 9 kg – Full Analysis Subject Sample
10.1.4.2.4.2	Global Physician Assessment at the end of treatment for weight/dosing category Infants from 9 kg to < 13 kg – Full Analysis Subject Sample
10.1.4.2.4.3	Global Physician Assessment at the end of treatment for weight/dosing category Children from 13 kg to 27 kg – Full Analysis Subject Sample
10.1.4.2.4.4	Global Physician Assessment at the end of treatment for weight/dosing category Children from more than 27 kg to 60 kg – Full Analysis Subject Sample
10.1.4.2.4.5	Global Physician Assessment at the end of treatment for weight/dosing category Children or adolescents of 60 kg or higher – Full Analysis Subject Sample