

A Pharmacokinetic, Pharmacodynamic and Safety Study of Single and Multiple Doses of Rabeprazole in Pediatric Subjects with GERD 1 to 11 Months Old, Inclusive (RAB-GRD-1003)

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Synopsis:

Objective(s): The objective of this study is to evaluate the pharmacokinetics, pharmacodynamics (intraesophageal/intragastric pH, clinical global impressions, formulation palatability and GERD daily symptom diary) and safety of rabeprazole after single and multiple daily administration at 2 dose levels in children between the ages of 1 and 11 months, inclusive (up to 11 months 29 days), with GERD. As this study is an exploratory assessment of the pharmacokinetics, pharmacodynamics and safety of rabeprazole in children, no formal hypothesis testing is applied.

Study Design: This is an open-label, multicenter, Phase 1 study, consisting of 2 parts. Each part consists of 3 phases, a pretreatment phase (screening of up to 21 days before the beginning of treatment), a treatment phase, and a posttreatment phase lasting at least 2 weeks after the final drug administration. The first part of the study (12 subjects) will be nonrandomized, all subjects will receive the same dose. In the second part of the study (24 subjects), subjects will be randomized into 2 dose groups (12 subjects per dose group). Subjects who withdraw early will also undergo an evaluation at least 2 weeks after the time of withdrawal. The total study length for each subject is approximately 6 weeks.

Subjects will have a diagnosis of GERD based on the below main criteria for inclusion. During the screening phase, medical history and evaluation of symptoms will be recorded. During the treatment phase subjects will receive single daily doses of rabeprazole in the morning for 5 days. Single dose pharmacokinetic and pharmacodynamic evaluations will be done after the dose on Day 1. Multiple dose pharmacokinetic and pharmacodynamic evaluations will be done at the presumed steady state after the 5th dose on Day 5.

Subjects in the first part of the study (pilot dose group cohort) will receive single and multiple daily q24h doses of 0.14 mg/kg, using increments of 1 mg dose. After the first cohort has completed (Part 1 of the study) at the initial rabeprazole sodium dose, the J&JPRD study physician will discuss the safety/tolerability data with the investigators and the medical monitors at the individual sites. Serious adverse events, drug related events, and pharmacokinetic data will be reviewed. When it is agreed by the J&JPRD study physician, the investigators, and the medical monitors that the drug is considered well-tolerated, enrollment will begin for Part 2 of the study. The pharmacokinetic and pharmacodynamic results from the first cohort of subjects (Part 1 of the study) will be assessed prior to commencement of the dosing in the second part of the study to determine the 2 dosages to be studied. These 2 dosages will be chosen to target the level of exposure (AUC) observed in adults from a 10 mg (AUC=400 ng·h/mL) and 20 mg (AUC=800 ng·h/mL) dose.

For the second part of the study subjects will be assigned to 1 of the 2 dose groups based on a computer-generated randomization schedule. The randomization will be balanced using randomly permuted blocks and will be stratified by age group. Based on their age group, subjects will be centrally randomized via a call center into one of the two dose groups.

A minimum of 36 subjects (one cohort of 12 for the first part of the study(pilot dose group), and one cohort of 24 for the second part of the study (randomized to 2 dose groups of 12)) will complete the study.