



2.0 Synopsis

Abbott Laboratories	Individual Study Table Referring to Part of Dossier: Volume: Page:	(For National Authority Use Only)
Name of Study Drug:		
Name of Active Ingredient: ABT-358 Zemplar [®] Capsules		
Title of Study: A Prospective, Multicenter Study to Evaluate the Safety of Vitamin D Receptor Activators as Determined by Hypercalcemia in Pediatric Patients ages 0 to 16 with Chronic Kidney Disease (CKD) Stage 5 Receiving Peritoneal Dialysis (PD) within Current Clinical Practice		
Investigator: Tamara Marshall, MD, [REDACTED]		
Study Sites: 21 sites in the United States North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) Dialysis Registry.		
Publications: There are no publications based on this study.		
Studied Period (Years): First Subject First Visit: 03 June 2010 Last Subject Last Visit: 17 May 2012	Phase of Development: Observational Study	
Objectives: The objective of this study is to observe the safety of paricalcitol utilization in pediatric subjects being treated for secondary hyperparathyroidism (SHPT). Incident rates of adverse events and serious adverse events, and the changes from Baseline in laboratory assessments, height, and weight were also to be measured. Safety was primarily measured by the proportion of subjects developing at least 1 episode of hypercalcemia (calcium > 10.2 mg/dL).		
Methodology: In this observational study, male and female pediatric subjects ages 0 to 16 years on peritoneal dialysis receiving paricalcitol or calcitriol were enrolled. The study was performed in 2 phases. An initial Screening/Enrollment Phase was followed by the Observational/Follow-Up Phase. The procedures performed in the screening phase were to collect an informed consent/assent, demographics, medical history (including history of tobacco and alcohol use), laboratory data, peritoneal dialysate (calcium concentration), height and weight, concomitant medications, and paricalcitol/calcitriol duration of treatment and dosing. The following information was collected at each routine peritoneal dialysis visit during the follow-up phase: height and weight, laboratory data, peritoneal dialysate (calcium concentration), safety data (AEs and SAEs), concomitant medications, and paricalcitol or calcitriol dosing.		



Number of Subjects (Planned and Analyzed): Approximately 40 subjects receiving paricalcitol and approximately 40 subjects receiving calcitriol were planned to be enrolled. Following enrollment of 21 subjects in the paricalcitol group and 40 subjects in the calcitriol group significant enrollment delays in the paricalcitol group were experienced and the study was subsequently closed.

Analysis was conducted using the All Treated Population that includes all subjects who received at least 1 dose of paricalcitol (paricalcitol group) or at least one dose of calcitriol (calcitriol group).

Diagnosis and Main Criteria for Inclusion: Main inclusion criteria included subjects male or female between 0 to 16 years of age (inclusive), on peritoneal dialysis for at least 30 days with a history of secondary hyperparathyroidism defined by having initiated a vitamin D receptor activator (VDRA) to treat an elevated parathyroid hormone (PTH) level, who are attending a site associated with NAPRTCS Dialysis Registry and have received paricalcitol or calcitriol for a minimum of 10 days.

Subjects were not eligible for study enrollment if they were scheduled for a kidney transplant within 3 months, expected to stop peritoneal dialysis or transfer to hemodialysis within 3 months, or planned to enroll in an investigational study where the drug and/or dose were unknown to the investigator within the first 3 months from the date of subject enrollment.

Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number: Paricalcitol or calcitriol were prescribed by each physician under the usual and customary practice of that physician.

Duration of Treatment: A minimum of 3 months and up to approximately 36 months.

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number: Not applicable.

Criteria for Evaluation

Safety: Safety was primarily measured by the proportion of subjects developing at least one episode of hypercalcemia (calcium > 10.2 mg/dL). Other safety measurements included incident rates of adverse events and serious adverse events, and the change from baseline in laboratory assessments, height and weight.

Statistical Methods

Safety: The known introduction of bias in this study design (no randomization mechanism) made direct between-group comparisons invalid. The sample size requirements for this study were not determined by a statistical power calculation.

Demographic and baseline characteristics were summarized for each treatment group and total (treatment groups combines). Concomitant medications were summarized by generic name as concomitant medications or prior medications. For each type of medication summary, the number and percentage of subjects who take at least one medication and the number and percentage of subjects who take at least one dose of a specific medication was presented by treatment group and total (combining treatment groups). An overall summary of the number and percentage of subjects experiencing one or more treatment-emergent adverse events for each treatment group and total (combining treatment groups) was generated. Treatment-emergent adverse events were also summarized by system organ class, preferred term, maximum relationship to study drug, and maximum severity.



Statistical Methods (Continued)

Safety (Continued):

Laboratory test results specified by protocol were summarized as follows: The mean change from Baseline in laboratory tests to each monthly visit and to the minimum, maximum, and final test results were summarized. Shift tables for laboratory test results were prepared by treatment group for reference range category shifts from Baseline to minimum value (related to the normal range), maximum value (related to the normal range), and final values during the study. The number and percentage of subjects developing at least 1 episode of hypercalcemia (calcium > 10.2 mg/dL) was summarized by treatment, by subgroups, and for each month.

Mean change from Baseline in weight was generated. The average daily mcg dose of paricalcitol or calcitriol (VDRA) was summarized over each month during the study.

Summary/Conclusions

Safety Results: Overall, the highest incidence of severe adverse events was reported in infections and infestations system organ class; severe adverse events in the infections and infestations system organ class were reported for 14 subjects (66.7%) in the paricalcitol and for 25 subjects (62.5%) in the calcitriol group. Eight subjects (38.1%) in the paricalcitol group and 26 subjects (65.0%) in the calcitriol group experienced a serious adverse event. There were no deaths in the paricalcitol group. Two subjects in the calcitriol group died following treatment-emergent adverse events that the investigator considered not related to study drug. One subject in the paricalcitol group and 3 subjects in the calcitriol group experienced an adverse event that led to discontinuation of study drug. The primary measurement of safety in this study was identified as the proportion of subjects developing at least 1 incidence of hypercalcemia (calcium > 10.2 mg/dL). A higher percentage of subjects in the calcitriol group experienced at least 1 incidence hypercalcemia than in the paricalcitol group (54.1% for calcitriol versus 36.8% for paricalcitol).

Conclusions: No paricalcitol-related safety signals were identified. Adverse events reported for subjects in the paricalcitol group were within the known safety profile of paricalcitol. The study was closed following consultation with the United States Food and Drug Administration (because of enrollment difficulties), and safety data were reported in this abbreviated clinical study report.