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**NAME OF SPONSOR/COMPANY:**

Genzyme Corporation, 500 Kendall Street, Cambridge, MA 02142  
SangStat Medical Corporation, Menlo Park, CA 94025 (SangStat Medical Corporation was acquired by Genzyme Corporation September 2003)

**TITLE OF STUDY:**

**SMC-101-1002:** A Prospective, Open Label, Multicenter, Phase IIB Clinical Trial of Thymoglobulin® as Induction Immunosuppression for the Prevention of Acute Rejection in Pediatric Renal Transplant Recipients

**INVESTIGATORS AND STUDY CENTERS:**

This was a multicenter study conducted at 3 sites in the United States.

**STUDIED PERIOD:**

5 October 1998 (first patient enrolled) to  
30 November 2000 (last patient completed)

**PHASE OF DEVELOPMENT:**

Phase 2b

**OBJECTIVES:**

To assess the safety, efficacy, pharmacokinetics, and pharmacodynamics of Thymoglobulin in an induction protocol in pediatric renal allograft recipients.

**METHODOLOGY:**

Prospective, open-label, multicenter study with follow up for 12 months. Patients were given quadruple sequential immunosuppression consisting of induction with Thymoglobulin followed by maintenance with cyclosporine, mycophenolate mofetil, and prednisone. Prophylactic anti-infectives were prescribed according to the site's routine.

**NUMBER OF PATIENTS (PLANNED AND ANALYZED):**

In all, 24 patients were planned, but 16 were enrolled and analyzed as shown below.

Group	Age	Patients	
		Planned	Enrolled and Analyzed
Infants	1 month up to 2 years	4	1
Children	2 years up to 12 years	10	9
Adolescents	12 years up to 16 years	10	6

**DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION:**

Male and female patients 1 month to 16 years of age receiving primary or subsequent living-related or cadaver donor kidneys. Adolescent females of childbearing potential had to have negative pregnancy tests on admission.

**TEST PRODUCT, DOSE, AND MODE OF ADMINISTRATION:**

Thymoglobulin® 2.0 mg/kg administered intravenously (IV).

**REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION:**

Not applicable.

**DURATION OF TREATMENT:**

Up to 10 days

**CRITERIA FOR EVALUATION:**

**Criteria for Evaluation – Efficacy (Secondary Endpoints):**

- Patient and graft survival rates.
- Incidence, severity, and timing of acute rejection.

**Criteria for Evaluation – Safety (Primary Endpoint):**

Drug-related adverse events (AEs), infections, and malignancy assessed 12 months after transplantation.

**STATISTICAL METHODS:**

**Statistical Methods - Patients:**

Demographic information and baseline characteristics were summarized using descriptive statistics (mean, median, standard deviation, minimum, and maximum) for continuous variables, and counts and percents for categorical variables. For the analysis of efficacy, patients not able to complete a full course of Thymoglobulin therapy were excluded.

**Statistical Methods - Efficacy:**

Patient and graft survival rates were tabulated. Twelve months after transplant, the acute rejection rate was calculated and summarized descriptively using the Kaplan-Meier method, and two-sided 95% confidence intervals (CI) were generated.

**Statistical Methods - Safety:**

Initially, AEs were coded by the modified COSTART dictionary, but later MedDRA 4.0 was used for system organ class because of an upgrade in the safety department data collection system. AEs were summarized by relationship to study drug and by severity. Infections and malignancies were AEs of particular interest. Serious adverse events (SAEs), AEs leading to discontinuation, and deaths were summarized.

**SUMMARY / CONCLUSIONS**

**Summary / Conclusions - Patients:**

A total of 16 patients were enrolled and studied. Two patients failed to complete the 12-month follow up: 1 died and 1 suffered graft loss.

The mean age of patients at the time of transplantation was 10.9 years (range: 1.2 – 17.8 years), 63% of patients were male, and 88% were Caucasian.

**Summary / Conclusions - Efficacy Results:**

Data set analyzed: all patients who completed the full course of Thymoglobulin therapy (n=14). One patient was excluded because the patient missed the fourth infusion, and another was excluded because the patient discontinued after the second infusion on account of hyperacute rejection unrelated to study drug.

One patient died on study (see Safety Results for additional information). One patient had a graft loss due to infection that resulted in retransplantation. Nine patients had at least 1 rejection episode; the rejection episode(s) for 8 of these patients were confirmed by kidney biopsy. All rejection episodes were mild or moderate in severity.

Variable	Result as n (%)	Confidence Interval (%)
Patient survival at 1 year*	13 (93)	59 - 99

Graft survival at 1 year*	13 (93)	59 - 99
Patients with at least 1 episode of acute rejection	9 (64)	not available
Cumulative risk of acute rejection 1 year after transplant*	not applicable (69)	55 - 90
*Kaplan-Meier estimate based on 14 subjects who completed the full course of Thymoglobulin therapy.		

**Summary / Conclusions - Safety Results:**

Data set analyzed: all patients enrolled (n=16).

All but 2 patients, described in the section above, received the number of doses the protocol specified. However, 73% of patients had to reduce the amount of the Thymoglobulin dose because of leukopenia or thrombocytopenia.

The safety profile that emerged was similar to what was in the product's safety labeling.

-All patients had at least 1 AE.

-Most of the AEs were mild or moderate and most were judged as unlikely or not related to study drug.

-One patient had an SAE (hospitalization for urinary tract infection) that was considered unrelated to study drug. A second patient had 3 SAEs ("difficulty with oxygenation," a *Staphylococcus* infection, and death) that were considered at least possibly related to study drug.

-Twelve of 15 patients (80%) had at least 1 infection (1 patient had missing data). Twenty of 48 infections (42%) were considered related to study drug. The infections were viral, bacterial or fungal; there were no protozoal infections. In all, 73% of the infections were resolved by the end of the study.

-No patient had any malignancies during the 12-month study period.

**Based on report prepared on:** 27 February 2004

**Synopsis prepared on:** 31 August 2006