
CTS Collaborative Transplant Study

Newsletter 2:2006

May 1, 2006

Nearly two-thirds of all participating centers have already returned the completed "**Cancer Confirmation Questionnaire**". We are aware that the effort required for obtaining accurate data on tumors in transplant patients is time-consuming. **Your support** of this part of the international study is therefore **especially appreciated**. If you have not yet returned the questionnaire, please do so soon. To reduce the likelihood of under-reporting, centers are included in the CTS analysis of tumors **only** if the "Cancer Confirmation Questionnaire" is completed and **returned**. Incidentally, it is our experience that if you inquire about tumors regularly at the time of documenting transplant outcome, completion of the yearly confirmation questionnaires will require little extra effort.

An example of the **clinical relevance** of the CTS **cancer data** is illustrated in the following 2 graphs. Currently, the two most commonly used methods for **antibody induction** therapy in renal transplantation are the administration of IL-2 receptor (IL-2R) antibodies or thymoglobulin.

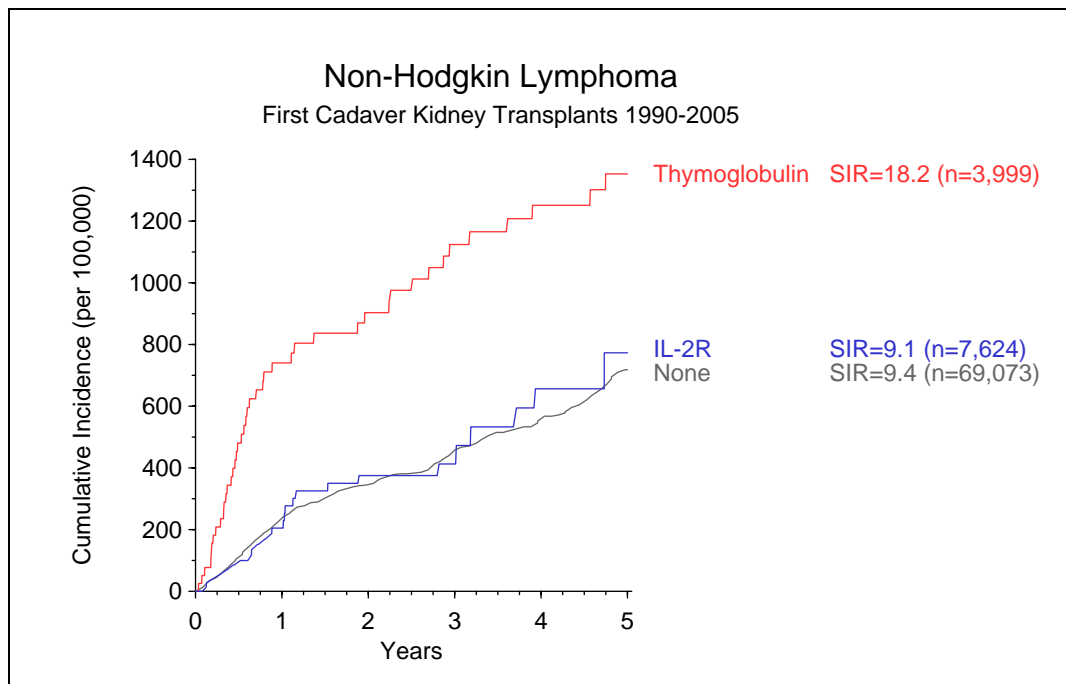


Figure 1

As shown in Figure 1, these products are associated with **strikingly different** rates of posttransplant **non-Hodgkin lymphoma**. Whereas IL-2R antibodies are associated with a lymphoma rate identical to patients without any antibody treatment, recipients receiving thymoglobulin show a rate approximately twice as high. The difference between the two treatments develops during the **first posttransplant year**. Compared to a normal background population standardized for age, gender, and geographical origin, all patient groups show an increased tumor incidence. The standardized incidence ratio (SIR) is 9.4 times higher in patients without antibody induction than in a matched non-transplant population, and the ratio is very similar, at 9.1, in patients receiving IL-2R antibodies. In patients receiving **thymoglobulin**, it is **much higher at 18.2**.

Analysis of **graft survival** rates shows that transplant success rates associated with the use of thymoglobulin or IL-2R antibodies are virtually **identical** (Figure 2). Thus, an increased occurrence of lymphomas is not necessarily a consequence of increased immunosuppressive efficacy against graft rejection.

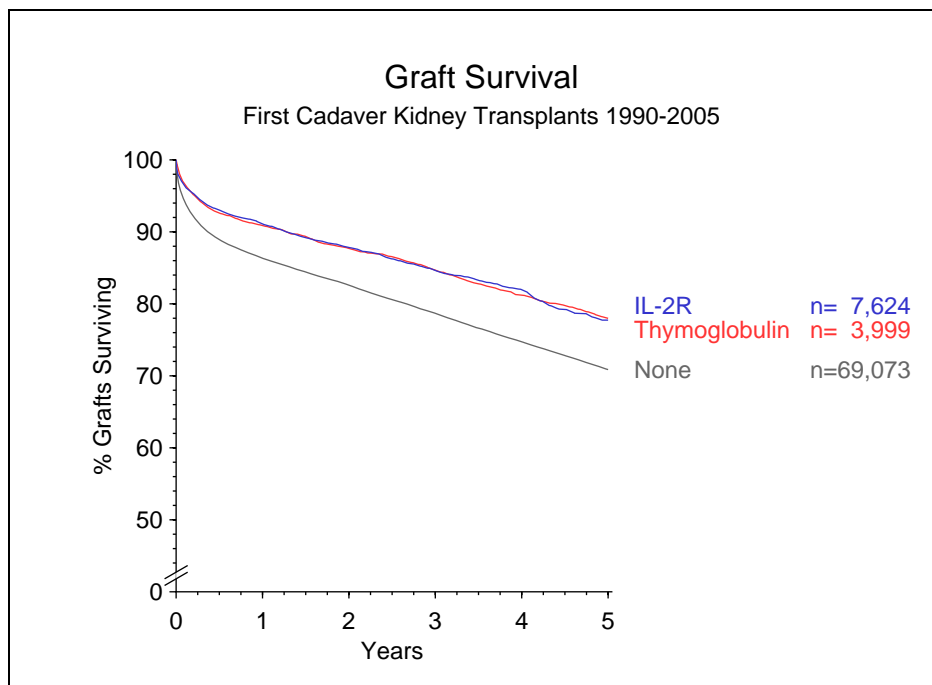


Figure 2

Please support our efforts to obtain high-quality data for the analysis of effects such as those shown in Figures 1 and 2. There are many more areas in which the CTS cancer data are of great interest. Due to the relatively rare occurrence of tumors, it is an indispensable prerequisite for valid cancer studies to analyze very large numbers of patients. The contribution of **each individual center** is therefore **extremely valuable**. Your support of the CTS tumor study is greatly appreciated!

The CTS **Prospective Serum Study** is beginning to yield interesting results. So far, we have received some **4,500 sera on 1,000 patients**. The preliminary data show:

1. Approximately **5%** of patients develop *de novo* HLA antibodies during the **first** post-transplant year.
2. About **20%** of patients with pre-transplant antibodies **turn negative** during post-transplant follow up.

The latter effect may be due to antibodies being **absorbed** by the transplanted organ. It will be very interesting to study potential **consequences** of this effect on graft outcome. We have also noticed preliminary evidence for **fluctuation** of *de novo* antibodies, the relevance of which is currently unknown. The most important goal of the prospective study is to elucidate the true frequency and temporal relationship of *de novo post-transplant* HLA antibodies with **chronic allograft deterioration**.

Studying a large number of patients increases the likelihood for obtaining statistically meaningful results aiding in the resolution of many of the **controversies** surrounding this challenging area of research. If you are not already participating in the Prospective Serum Study, **please join and enroll your new transplant patients**. As a benefit of your participation you will receive the **results of serum tests** on your patients **free** of charge, and you will make an **important contribution** to a timely research area in clinical immunology. Attached you will find the schedule for obtaining serum samples and the brief questionnaire which is requested only once (at the end of month 3). **Thank you for your cooperation!**

The next **shipping** date for the CTS serum and DNA studies is

May 29/30, 2006

As always, please inform us by e-mail, fax, or phone of the shipping details so that we can investigate in the event that shipments become delayed.

For those just joining the serum study: we will have another shipping date in November (date to be announced). Please **freeze and store** your sera for shipment in November.

Thank you for your support!

Sincerely yours,

Gerhard Opelz