

## Rituximab, a clinical update

Since the discovery that the drug rituximab could hold potential as a rescue therapy for patients affected by steroid resistant and dependent forms of FSGS and nephrotic syndrome (NS) there has been growing interest to learn more about it by both the scientific and lay communities.

Researchers have long suspected that T cells, a type of white blood cell important in immune response, plays a role in the development of NS <sup>1</sup> and now, there is increasing evidence that B cells, another category of white blood cells, may play an important role in NS as well<sup>2</sup>.

Rituximab is an antibody directed against an antigen (receptor) found on B cells. When administered, it results in reduction of the number of B cells. Treatment with rituximab has been successful in B cell lymphomas, resulting when B cells are mutated and become cancerous, as well as in patients with autoimmune diseases<sup>3</sup>.

In an effort to further examine the efficacy of rituximab on patients diagnosed with idiopathic NS, Dr. Prytula and colleagues collected data from questionnaires provided by members of the International Society of Paediatric Nephrology. The researchers received 70 questionnaires and divided the data into three groups. Group 1 was comprised of steroid dependent and frequently relapsing patients, group 2 included those diagnosed with steroid resistant NS and group 3 were children treated with rituximab for recurrence following transplantation. Within these categories, researchers found that 82% of the patients in group 1 experienced a good initial response with 61% experiencing a complete remission. Group 2 was less positive with 44% of these patients having an initially positive response and 22% achieving complete remission. Finally, in the patients diagnosed with post-transplant recurrence of NS, treatment with rituximab resulted in an initial positive response in 60% while 40% achieved full remission<sup>4</sup>.

A separate study evaluated the efficacy of rituximab in five patients with FSGS with variable results. The objective of the study by Dr. Printza and colleagues was to assess the efficacy of rituximab in five children diagnosed with steroid resistant FSGS all of whom had failed conventional therapies and did not have a genetic form of the disease. Rituximab was provided at a dose of 375mg/m<sup>2</sup> and the patients were followed up weekly to evaluate B cell depletion. Patients who did not have an initial decrease in their B cell count or who failed to achieve remission



were given up to four additional doses of rituximab. The researchers found that 2 of these five patients achieved and maintained a complete remission of FSGS. Another two patients experienced partial remission, however one was not responsive at follow up. The final patient presented did not respond to rituximab treatment<sup>5</sup>. These results are further indication of the variability in treatment with rituximab but also indicate the potential for its use in some patients with difficult to treat FSGS.

Another study of note was presented at the European Society of Paediatric Nephrology conference in the United Kingdom this year. Dr. Strologo and colleagues evaluated the use of rituximab in patients diagnosed with FSGS following a relapse after kidney transplantation. The authors presented the effects of rituximab on seven children who experienced a relapse of disease following transplantation and who had failed to respond to intensive plasmapheresis. The team found that leakage of protein was halted in three patients receiving treatment with rituximab, while another patient experienced a 70% decrease in protein leakage and yet another had a 50% decrease. Of the remaining patients, one did not respond to treatment and reached kidney failure within three months and the final patient had a severe reaction a few minutes following treatment with rituximab<sup>6</sup>.

To date, information is available from only a small number of patients and the positive results may be overestimated due to publication bias. Overall, the review of the literature suggests that while rituximab may provide physicians with another option as a rescue treatment for patients with NS, larger, controlled trials are needed to determine the true value and efficacy of rituximab. More information is needed in order to determine which patients are likely to benefit and what the risks of treatment may be.

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2. Benz K, Dittrich K, Campean V, Dotsch J, Amann K. Does the analysis of infiltrating cells in kidney biopsies from pediatric patients with idiopathic nephrotic syndrome help to stratify patients for Rituximab therapy? Presented at the World Congress of Nephrology, Milan, Italy, May 22-26, 2009.
3. Kemper M et al. Rituximab (RTX) for refractory steroid sensitive nephrotic syndrome (SSNS): registry of German pediatric nephrology association. Presented at the American Society of Nephrology, Philadelphia, Pennsylvania, November 4-9, 2008.



4. A. A. Prytula, K. Iijima, K. Kamei, E. Gottlich, A. Majid, M. Taylor, S. D. Marks, G. Filler, G. Smith, K. Tullus. Rituximab in the Treatment of Idiopathic and Post Transplant Recurrence of Nephrotic Syndrome: a Multicenter Retrospective Study. Presented at the European Society for Paediatric Nephrology conference, September 2-5, 2009 in Birmingham, United Kingdom.
5. N. Printza, K. Kollios, M. Pampouka, A. Taparkou, E. Farmaki, F. Papachristou. The Efficacy of Rituximab in the Treatment of Focal Segmental Glomerulosclerosis. Presented at the European Society for Paediatric Nephrology conference, September 2-5, 2009 in Birmingham, United Kingdom.
6. L. Dello Strologo, I. Guzzo, C. Laurenzi, M. Vivarelli, A. Parodi, G. Barbano, C. Roberta, F. Scozzola, A. Amore, F. Ginevri, L. Murer. Use of Rituximab in Focal Glomerulosclerosis Relapses After Renal Transplantation. Presented at the European Society for Paediatric Nephrology conference, September 2-5, 2009 in Birmingham, United Kingdom.

