7 October 2016

Press release

Rituximab effective in the treatment of membranous glomerulonephritis

A national trial on membranous glomerulonephritis in 80 patients was coordinated by Prof. Pierre Ronco, of the Department of Nephrology and Dialysis at Tenon Hospital AP-HP, of the Inserm Unit "Rare and common kidney diseases, matrix remodelling and tissue repair" [1] and Pierre and Marie Curie University, and by Dr Karine Dahan, of the Nephrology Day Hospital at Tenon Hospital AP-HP
This serious autoimmune disease is the most common cause of nephrotic syndrome in adults. In 30% of cases, it progresses to very severe renal failure.
Conducted in collaboration with Prof. Tabassome Simon, from the Department of Clinical Pharmacology and East Paris Clinical Research Centre at Saint Antoine Hospital, AP-HP, this trial shows, for the first time, the efficacy and safety of rituximab in treating the disease.
This work was published on 27 June 2016 in the *Journal of the American Society of Nephrology*.

Membranous glomerulonephritis is a rare autoimmune disease (one new case recorded per year per 100,000 inhabitants), in most cases caused by antibodies directed against a protein (PLA2R) located in the renal filter (the glomerulus). The immunosuppressive treatments – aimed at attenuating this immune reaction of the body – that have been used until now have shown some efficacy, associated, however, with considerable toxicity: risks of infection, fertility problems, subsequent development of cancer or impaired renal function.
Rituximab is a monoclonal antibody specifically directed against the B lymphocytes that produce the toxic antibodies. Until now, its safety and efficacy had not been demonstrated.

In this context, Prof. Pierre Ronco and Dr Karine Dahan conducted a study in 80 patients with a severe form of membranous glomerulonephritis at Tenon Hospital AP-HP. The patients were enrolled from January 2012 to July 2014 in 31 nephrology departments throughout France, including 9 departments of Paris public hospitals (AP-HP) [2], with annual follow-up for two years.

This randomised study made it possible to compare the efficacy of the standard treatment, known as "antiproteinuric," with the same treatment combined with 2 intravenous infusions of rituximab (375 mg/m2) given at a one-week interval. Patients were observed for the occurrence of immunological remission (disappearance of antibodies), clinical remission (reduction or disappearance of proteinuria) and adverse effects of the treatment.

Results showed that rituximab had a positive effect on immunological remission (50% from 3 months) and clinical remission (with 64% of patients entering remission before the end of the study), with corresponding values of only 12% and 34% respectively in patients given the antiproteinuric treatment alone.

The percentage of remission was similar to that obtained with other immunosuppressive treatments, but with a much lower therapeutic risk, since the number of adverse events was the same in both treatment groups (with or without rituximab).

"This study contributes a very important element to the debate surrounding immunosuppressive treatments in membranous glomerulonephritis," explains Prof. Pierre Ronco.
"In clinical terms, it favours the use of rituximab as a first-line treatment in severe forms, with very regular monitoring of the level of anti-PLA2R antibodies in these patients."

This study will provide a basis for other protocols aimed at increasing the percentage of clinical and immunological remission without increasing the rate of adverse effects. It is likely that some patients did not respond to the treatment because the rituximab leaked into the urine. These protocols will therefore include the use of higher or more frequent doses, and further IV infusions in patients who maintain high antibody levels.

Rituximab for severe membranous nephropathy: A 6-month trial with extended follow-up. Dahan K, Debiec H, Plaisier E, Cachanado M, Rousseau A, Wakselman L, Michel PA, Mihout F, Dussol B, Matignon M, Mousson C, Simon T and Ronco P; GEMRITUX Study Group. J Am Soc Nephrol. 2016

About AP-HP: *AP-HP is an internationally renowned university hospital system with a European dimension. Its 39 hospitals receive 8 million patients a year, in clinics, emergency departments, and through planned hospital admissions or home hospitalisation. It provides a public health service for all, on a 24-hour basis, which for AP-HP is a matter of both duty and pride. AP-HP is the biggest employer in Ile de France: 100,000 people – physicians, researchers, allied medical staff, administrative staff and other employees – work there. http://www.aphp.fr*

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