Rituximab promotes long-term response for patients with immune destruction of platelets

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A new analysis concludes that rituximab, a drug commonly used to treat blood cancers, leads to treatment responses lasting at least five years in approximately one quarter of patients with low platelet counts and a risk of bleeding due to chronic immune thrombocytopenic purpura (ITP). In study results published online today in *Blood*, the Journal of the American Society of Hematology (ASH), investigators at Weill Cornell Medical College provide the very first long-term outcome data for patients with chronic ITP treated with rituxamab.

Approximately 200,000 Americans suffer from ITP, a bleeding disorder in which the immune system destroys blood cells called platelets that are necessary for normal blood clotting, which can result in excessive bleeding and heavy bruising.[1] Common treatment options for increasing platelet counts in the majority of patients with ITP include corticosteroid drug therapy, used to suppress a patient's immune system in order to help bring platelet counts back to normal; splenectomy, the surgical removal of the spleen, to halt the destruction of antibody-coated platelets found in the organ; and newer thrombopoietin (TPO)-mimetic agents to help stimulate platelet production. While these treatments are successful in many patients, all are associated with side effects: corticosteroids are associated with bone loss, cataracts, and other serious toxicity with long-term use; splenectomy can increase a patient's risk of infection; and TPO-mimetic agents can result in blood clots, and their long-term response in patients is not well-studied. In addition to their reported side effects, some patients with ITP stop responding or have insufficient response to these therapies.

More than ten years ago, researchers identified rituximab as an alternative treatment for patients with chronic ITP who have failed at least one other therapy. Rituximab specifically destroys B-cells – the cells responsible for producing antibodies that coat platelets and lead to their destruction – with low toxicity and decreased risk of infection compared to other treatments. Previous studies have shown that rituximab treatment resulted in normalized platelet counts lasting longer than one year in some patients with chronic ITP. Despite these encouraging reports, long-term data were previously lacking, and the durability and long-term safety of this treatment were largely unknown.

"While rituximab therapy for chronic ITP has been an exciting development, until now, due to a lack of sufficient patient numbers and follow-up in previous studies, we have only known how this treatment will affect ITP patients in the short term," said Vivek L. Patel, PhD, the study's first author and Research Associate at Weill Cornell Medical College in New York. "By utilizing the longest follow-up and the largest number of responders to the drug, our study sought to determine how children and adults with chronic ITP treated with rituximab would fare three, four, and five years down the road."

In this follow-up study, Dr. Patel's team reviewed 18 published clinical trials assessing rituximab treatment in children and adults with ITP and calculated initial and one-year response rates for 138 patients treated in 2000-2007 from seven clinical centers in the United States and Europe. Seventy-two adults with ongoing response one year from first treatment and 66 children with partial or complete response of any duration were included in the long-term analysis. The investigators calculated five-year response rates of 26 percent for children and 21 percent for adults. The researchers also analyzed the relationship of other clinical variables in response to rituximab and found no difference in projected five-year outcomes in children and adults who had undergone prior splenectomy versus those who had not. Age, gender, prior ITP duration, and response

to other ITP treatment were also not predictive of duration of response.

Results are particularly encouraging for ITP patients and their physicians who now have more substantial long-term data to help them decide whether and when to treat with rituximab. "The results from this study provide clinicians and patients with accurate and realistic expectations of the long-term effect of rituximab and its potential to become a first-line treatment for ITP," said James B. Bussel, MD, senior author and Professor of Pediatrics at Weill Cornell Medical College. "Our next step is to try to augment the effect of rituximab by combining it with dexamethasone, a common steroid therapy for ITP, in order to determine its effect in conjunction with known treatment strategies."

More information: [1]About ITP. Platelet Disorder Support Association. www.pdsa.org/media-center/press-kit/about-itp.html . Accessed April 30, 2012.

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