

Rituximab is an alternative to splenectomy in adults with chronic immune thrombocytopenic purpura: results of a multicenter prospective phase II study

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Origin of Study France

Type of Study MULTICENTER, PROSPECTIVE, PHASE II STUDY

Objectives Assess the safety and efficacy of rituximab (Rituxan) in patients with immune thrombocytopenic purpura (ITP) and a platelet count $\leq 30 \times 10^9/L$.

Study Design The team conducted the trial according to Fleming's single-stage procedure. Nonsplenectomized adults received 4 weekly intravenous infusions of 375 mg/m² of rituximab. All other treatments were stopped.

Success was defined as a platelet count $\geq 50 \times 10^9/L$, with at least a two-fold increase of the initial value at 1 year after the first rituximab infusion. Patients given another treatment during follow-up were considered nonresponders.

A sample size of at least 56 patients was calculated by Fleming's single-stage design to ensure 90% power for proving lack of efficacy if the true complete response rate was $< 25\%$.

Patients Patients were ≥ 18 years of age. In all, 40 women and 20 men with chronic ITP (mean age, 48 years) took part. Mean platelet count at inclusion was $16 \pm 10 \times 10^9/L$.

Observations All patients received 4 infusions except one patient with reversible serum sickness that was diagnosed after 2 infusions. Further, 15 others experienced transient side effects that did not lead to treatment discontinuation, and no patient was lost to follow-up.

Success was achieved in 40% of patients (see Table). Among 24 long-term responders, platelet count at 1 year was $\geq 150 \times 10^9/L$ in 18 patients and $50\text{--}150 \times 10^9/L$ in 6 patients. Two others had an incomplete response. Further, 34 patients failed to respond; 21 have since undergone splenectomy.

Initial and One-Year Response to Treatment

ONE-YEAR RESPONSE	INITIAL RESPONSE			
	FAILURE (n = 18)	INTERMEDIATE RESPONSE	GOOD RESPONSE $\geq 50 \times 10^9/L$	
		30–49 $\times 10^9/L$ (n = 6)	50–149 $\times 10^9/L$ (n = 15)	$\geq 150 \times 10^9/L$ (n = 21)
Failure	18	6	7	3
Intermediate response (30–49 $\times 10^9/L$)	0	0	2	0
Good response ($\geq 50 \times 10^9/L$)	0	0	6*	18*

* $P < 0.01$ between these groups of patients

Conclusions Rituximab appears to be a safe and good splenectomy-sparing strategy in adults with chronic ITP, leading to a significant, durable response in 40% of patients.

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Discussion

Current research suggests that about 50% of patients with ITP respond well to rituximab, and another 25% to 40% experience a sustained response. Based on these outcomes, a group of French investigators assessed the safety and efficacy of rituximab in an extended population of adults with chronic ITP and low platelet counts who were candidates for splenectomy.

“Splenectomy is an effective treatment for these patients, as more than 60% respond to it; however, it is invasive, with a risk of sepsis, and the long-term efficacy is not assured,” said Dr. Godeau.

The prospective multicenter study included 60 patients with chronic ITP (mean duration, 4.8 years) and platelet counts $< 30 \times 10^9/L$ (mean count, $15 \times 10^9/L$). Patients received four weekly intravenous infusions of rituximab at a dose of 375 mg/m^2 . All other ITP treatments were stopped. Treatment success was defined as a platelet count $\geq 50 \times 10^9/L$, with at least a two-fold increase over baseline 1 year after the first rituximab infusion.

Of the 60 patients, 36 patients initially responded to treatment with rituximab, for a 60% response rate. Of the 34 failures at 1 year, 21 patients underwent splenectomies, of which 11 were successful.

Initial response correlated significantly with long-term response among the 36 responders. Among the 21 patients with an initial response and with platelet counts of $> 150 \times 10^9/L$, 18 maintained a long-term response; of the 15 patients with platelet counts of $50\text{--}149 \times 10^9/L$, only 6 maintained a response at 1 year, for a statistically significant difference between these types of patients ($P < 0.01$). Patients who were younger and had undergone few previous treatments had significantly better responses as well.

Rituximab was well tolerated in this population. Five patients developed a rash, but only one case of serum sickness was reported, which resolved upon treatment interruption.

Key Points

- Rituximab is an effective treatment of chronic ITP in adults; patients respond rapidly to the drug.
- The 1-year response is correlated with initial response.
- The drug is well tolerated.

Reference

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