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Citation: Kelly K, Gleeson M, Murphy PT. Slow responses to standard dose rituximab in immune thrombocytopenic purpura. Haematologica 2009; 94:443-444. doi: 10.3324/haematol.2008.001396

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Slow responses to standard dose rituximab in immune thrombocytopenic purpura. Author reply

We read the letter of Kelly *et al.*,[1] who report the results of their experience with standard dose rituximab (SD, *i.e.* 375 mg/m^2 weekly for four weeks) in patients with chronic immune thrombocytopenic purpura (ITP). Overall data are confirmatory to that previously reported by other authors: 6 out of 11 patients achieved a partial response (PR, platelet count > 50×10^9/L) and 3 a complete response (CR, > 100×10^9/L). The authors highlight that the time to CR was longer than expected (two months in 2 patients and six months in one), suggesting that a longer time of observation after rituximab therapy (at least six months) might be necessary before the decision regarding splenectomy.

Data from the literature indicate that in adult patients with ITP the response to SD rituximab develops more frequently early and often already within the fourth administration. Table 1 summarizes the results of some studies where data regarding the kinetic of response are available. In our previous study,[2] the median time to achieve PR and CR were 7 and 14 days respectively and only 3% and 10% of patients experienced PR and CR beyond the second and fourth month from the beginning of treatment.

In the reports of Stasi *et al.*[3] and Giagounidis *et al.*[4] all PRs and CRs were achieved within the first month of therapy. The paper of Cooper *et al.*,[5] on the contrary, showed 3 different timings of CR, suggesting that a significant proportion of patients may achieve CR much later (33% between month +4 and +6). Finally, in his systematic review, Arnold *et al.*[7] indicated a median time to response of 5.5 weeks from the first dose of rituximab in 123 valued patients with a range of 2-18 weeks. Different behavior can be seen with the use of low-dose rituximab (LD, *i.e.* 100 mg total dose weekly for four weeks), a very promising new therapeutic schedule for ITP.[6,8]

In our experience LD rituximab led to short and mid-term response rates similar to SD but with slower timing of response, with a median time to PR and CR of 31 and 44 days respectively[6] (Table 1). Taken together these data indicate that in ITP the time to response to rituximab may be different according to clinical, biological and therapeutic variables.

We agree that, when possible, a period of at least six months of observation from rituximab therapy may be necessary before undergoing splenectomy since at present we still don't have enough indicators predictive of brief and mid-term response.

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Key words: immune thrombocytopenic purpura, Rituximab, kinetic of response.

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Citation: Zaja F, Fanin R. Slow response to standard dose rituximab in immune thrombocytopenic purpura. Autoreply. Haematologica 2009; 94:444-445. doi:10.3324/haematol.2008.001974

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Table 1. Kinetic of response (complete and partial) after standard and low-dose rituximab.

	Zaja *et al.*[2]	Stasi et al.[3]	Giagounidis *et al.*[4]	Cooper *et al.*[5]	Zaja *et al.*[6]
Rituximab schedule	375 mg/m² weekly for 4 weeks	375 mg/m² weekly for 4 weeks	375 mg/m² weekly for 4 weeks	375 mg/m² weekly for 4 weeks	100 mg weekly for 4 weeks
Evaluable patients	25	11	7	31	16
Time to PR (days)					
≤7	17 (63%)	7 (64%)	6 (67%)	94% of patients	5 (31%)
> 7 ≤28	4 (15%)	4 (36%)	1 (11%)	within 8 weeks	2 (12%)
> 28 ≤60	3 (11%)	0	0	from rituximab	6 (37%)
> 60 ≤120	1 (3%)	0	0		3 (19%)
> 120 – 180	0	0	0		0
Evaluable patients	19	7	5	18	11
Time to CR (days)					
≤7	8 (42%)	2 (29%)	5 (56%)	7 (39%)	3 (27%)
> 7 ≤ 28	5 (26%)	5 (71%)	0		1 (9%)
> 28 ≤ 60	4 (21%)	0	0		5 (45%)
> 60 ≤120	2 (10%)	0	0	5 (28%)	2 (18%)
> 120 – 180	0	0	0	6 (33%)	0

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