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1 A Prospective Randomized Study Comparing Rituximab and Dexamethasone Vs Dexamethasone Alone in ITP: Results of Final Analysis and Long Term Follow up

Sunday, December 7, 2008: 2:00 PM
Halls B and C (Moscone Center)

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Introduction. Previous uncontrolled studies have highlighted the activity of rituximab in patients with idiopathic thrombocytopenic purpura (ITP) relapsed or refractory to standard treatments. To better address this effect, a prospective randomized (1:1), multicenter, phase III study comparing treatment with dexamethasone alone (arm A) vs dexamethasone plus rituximab (arm B) was conducted from July 2005 through June 2007 for adult patients with previously untreated ITP and a platelet (PLT) count ≤ 20 x10^9/L. **Material and methods.** Patients randomized to arm A received a single course of oral dexamethasone 40 mg on days +1, +2, +3, +4, while patients randomized to arm B received dexamethasone (as in arm A) in association with rituximab 375 mg/m^2 iv on days +7, +14, +21, +28. Patients in arm A who failed to achieve a sustained response and had a platelet count ≤ 20 x 10^9/L (from day +30 up to the end of 6 months) could receive salvage treatment with the experimental arm (dexamethasone plus rituximab). The primary objective of the study was to compare the sustained response (SR), i.e. PLT count ≥ 50 x 10^9/L at month + 6 of treatment. Secondary objectives were: evaluation of the safety, the initial response (PLT count ≥ 50 x 10^9/L) by day 30 after the initiation of treatment, the activity of salvage therapy with dexamethasone plus rituximab in patients non responding to dexamethasone monotherapy, the definition of clinical and laboratory factors predictive of response and to explore the pharmacokinetics parameters of rituximab and their potential relation with response. Results were analyzed by an intention to treat (ITT) and by a per-protocol (PP) analysis. **Results.** One-hundred-one patients (52 for arm A and 49 for arm B) and 64 patients (38 for arm A and 26 for arm B) represented the ITT and PP population, respectively. Demographic baseline data were in accordance to what expected for a population of ITP patients. No significant differences among the two groups of randomization were present. There was a female prevalence and the mean age was 47 and 49 years in arm A and B, respectively. Table 1 summarizes the ITT and PP efficacy results considering 3 different levels of response (i.e. PLT count ≥ 50 x 10^9/L, ≥ 100 x 10^9/L and ≥ 150 x 10^9/L). A significant advantage for arm B patients was documented.

Table 1

	Initial response			Initial response			Sustained response			Sustained response		
Analysis	Intention-to Treat			Per-Protocol			Intention-to Treat			Per-Protocol		

Treatment	**Arm A**	**Arm B**	P value	**Arm A**	**Arm B**	P value	**Arm A**	**Arm B**	P value	**Arm A**	**Arm B**	P value
Valuable patients	44	25		32	13		52	49		38	26	
PLT ≥ $50x10^9$/L	27%	68%	.001	31%	69%	.009	36%	63%	.004	39%	85%	<.001
PLT ≥ $100x10^9$/L	23%	48%	.015	28%	46%	.122	33%	53%	.019	37%	77%	<.001
PLT ≥ $150x10^9$/L	18%	36%	.178	22%	38%	.127	25%	43%	.029	29%	65%	.002

Twenty-seven patients initially allocated to arm A and who failed to achieve initial response or SR received salvage treatment with the dexamethasone plus rituximab. In this group, ITT and PP SR rate were 56% and 59%, respectively. No clinical or laboratory factors predictive of SR were identified. In arm B patients the serum concentrations of rituximab levels did not correlate with the rate of response. Twelve SR patients of arm A, 27 of arm B and 19 of salvage therapy group were systematically followed up beyond month 6 for a median period of observation of 18 months (range 10-34 months). The rate of SR loss (platelets < 50 x 10^9/L) in these three groups was 25 % (3/12), 11% (3/27) and 10.5% (2/19). The safety profile was good with no substantial difference between the two arms of randomization. No patient died during the study period.
Conclusion. The results of this study indicate that the association of dexamethasone plus rituximab improves patients outcome without worsening of the safety profile. This effect is characterized by prolongation of SR and reduction in relapse rate. The long period of relapse free survival registered in some patients suggests a possible curative effect. This treatment can be offered as an option before splenectomy, particularly in those patients where the surgical option is not well accepted or have higher risk of complications.

Disclosures: Off Label Use: Use of Rituximab in ITP. **Gamba:** *Roche - Italy:* Employment.

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