



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

301.VASCULATURE, ENDOTHELIUM, THROMBOSIS AND PLATELETS: BASIC AND TRANSLATIONAL

Anti-GPIIb/IX Autoantibodies Are Associated with Poor Response to Dexamethasone Combined with Rituximab Therapy in Primary Immune Thrombocytopenia PatientsBingjie Ding¹, Hu Zhou², Mengjuan Li³, Xuewen Song³, Yuanyuan Zhang³¹Department of Hematology, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China²Department of Hematology, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China³The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China

This retrospective study aimed to evaluate whether anti-glycoproteins (GPs) autoantibodies can be used as predictors of response to high-dose dexamethasone combined with rituximab (DXM-RTX) in the treatment of primary immune thrombocytopenia (ITP) patients.

According to the screening criteria (Figure. 1), 126 ITP patients, including 85 (67.5 %) women and 41 (32.5 %) men, were included in the analyses, with a median age was 32 (10 - 80) years, the median duration of disease was 18 (0.1-228.0) months, and the median platelet count at baseline was $6.0 (0-28.0) \times 10^9/L$.

As shown in Table 1, 56.4% (71/126) of patients responded to DXM-RTX at four weeks, including 43 CR and 28 partial responses. The median time to response (TTR) of 71 responded patients was seven days (range: 4-28 days). The OR rate of ITP patients with anti-GPIIb/IX positivity was 47.6% (40/84), while that of anti-GPIIb/IX autoantibody-negativity was 73.8% (31/42) ($\chi^2 = 7.808$, $P = 0.005$). In line with the OR rate, a significant difference was found in the CR rate between ITP patients with anti-GPIIb/IX positivity and anti-GPIIb/IX autoantibody-negativity (26.2% vs. 50.0%, $\chi^2 = 7.061$, $P = 0.008$). At six months of DXM-RTX therapy, 54.0% (68/126) of patients responded to DXM-RTX, with 39 (31.0%) of CR. The CR and OR rates of anti-GPIIb/IX autoantibody-positive patients were also significantly lower than those of negative patients (CR: 45.2% vs. 71.4%, $\chi^2 = 7.731$, $P = 0.005$; OR: 25.0% vs. 42.9%, $\chi^2 = 4.178$, $P = 0.041$). No significant difference ($P > 0.05$) was found in OR and CR rates between anti-GPIIb/IIIa autoantibody positive and negative patients at four weeks and six months of DXM-RTX therapy.

At four weeks of DXM-RTX therapy, a significant difference in OR rate was found among the patients with anti-GPIIb/IX single-positivity (37.5%), double-positivity (51.7%), double-negativity (68.4%), and anti-GPIIb/IIIa single-positivity (78.3%) ($\chi^2 = 9.617$, $P = 0.022$) (Table 2). The further comparison revealed a higher resistance to DXM-RTX in patients with anti-GPIIb/IX single-positivity than patients with anti-GPIIb/IIIa single-positivity (OR: 37.5% vs. 78.3%; $P < 0.05$). A similar trend was also found in the six-month OR rate (29.2% vs. 78.3%, $P < 0.05$). An analysis of the CR rate at four weeks of therapy showed a significant difference among the four groups ($\chi^2 = 8.523$, $P = 0.036$) but no significant difference after Bonferroni's correction ($P > 0.05$). No significant difference ($P = 0.119$) was found in the CR rate among the four groups at six months of combined therapy. In addition, the NR rate of patients with anti-GPIIb/IX single-positivity also increased significantly in comparison with the patients with anti-GPIIb/IIIa single-positivity at four weeks (62.5% vs. 21.7%, $P < 0.05$) and six months (70.8% vs. 21.7%, $P < 0.05$) of combined therapy.

Multivariate logistic regression analyses revealed that age, sex, duration of disease, liver function, and baseline platelet count were not associated with patient response to DXM-RTX at 4 weeks and 6 months (Table 3). Anti-GPIIb/IX autoantibodies and megakaryocytes of DXM-RTX therapy at both 4 weeks and 6 months were associated with the OR rate of patients, with an odds ratio of 0.194 ($P = 0.003$, 95% CI: 0.065-0.575) at 4 weeks and 0.189 ($P = 0.003$, 95% CI: 0.064-0.563) at 6 months by comparing patients with anti-GPIIb/IX autoantibodies to those without anti-GPIIb/IX autoantibodies. The factorial design analyses revealed no interaction effect between autoantibodies and showed anti-GPIIb/IX autoantibodies at 4 weeks represented the only significant factor affecting OR rate with DXM-RTX therapy ($F = 9.128$, $P = 0.003$, Table 4).

Therefore, platelet anti-GPIIb/IX autoantibodies can predict poor response to DXM-RTX in ITP patients.

Disclosures No relevant conflicts of interest to declare.

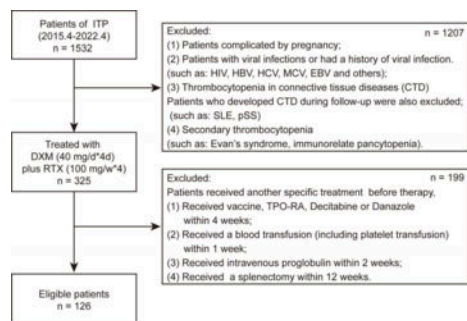


Figure 1. Flowchart of patient enrollment and screening.

Table 3. Multivariable logistic regression analysis of the effect of baseline characteristics and anti-GPs autoantibodies on the response to DXM-RTX treatment.

Time	Variable	B	Standard error	Wald chi-square	P	Odds ratio	95% CI
Week 4	Constant	3.818	0.901	11.806	0.001		
	Age (years)	-0.010	0.014	0.449	0.503	0.991	0.963-1.018
	Gender						
	Male	-0.400	0.539	0.726	0.394	0.632	0.219-1.818
	Female						
	Disease course (months)	-0.006	0.005	1.666	0.199	0.994	0.985-1.003
	ALT (U/L)	-0.017	0.026	3.980	0.159	0.964	0.915-1.013
	AST (U/L)	-0.011	0.047	1.191	0.275	0.990	0.885-1.042
	Megakaryocyte	0.001	0.001	6.205	0.013	1.002	1.000-1.003
	Baseline PLTs ($\times 10^9/L$)	-0.007	0.036	3.522	0.061	0.935	0.872-1.003
Month 6	Constant	-1.641	0.554	8.759	0.003	0.194	0.065-0.573
	Anti-GPIIb/IIIa	0.875	0.493	1.156	0.276	2.399	0.914-6.301
	Age (years)	-0.011	0.014	0.628	0.428	0.989	0.963-1.017
	Gender						
	Male	-0.218	0.550	0.157	0.692	0.804	0.274-2.342
	Female						
	Disease course (months)	-0.004	0.005	0.874	0.350	0.996	0.986-1.005
	ALT (U/L)	-0.022	0.027	6.700	0.010	0.978	0.928-1.030
	AST (U/L)	-0.004	0.049	2.900	0.089	0.920	0.835-1.013
	Megakaryocyte	0.002	0.001	7.868	0.005	1.002	1.001-1.003

Table 1. Characteristics of ITP patients and response by anti-GPs autoantibodies status.

Terms	GPIIb/IIIa (+)	GPIIb/IIIa (-)	GPIb/IX (+)	GPIb/IX (-)	Total
Cases	83	43	84	42	126
Gender (female/male)	52/31	33/10	59/25	26/16	85/41
Median (range) age, years	32 (16-80)	32 (11-80)	36 (10-80)	30 (11-66)	32 (16-80)
Median (range) disease duration, months	20.0 (0-1-228)	12.0 (0-1-228)	17.5 (0-1-228)	19.0 (0-1-228)	18.0 (0-1-228)
Median (range) baseline platelet count, $\times 10^9/L$	6 (0-28)	6 (1-20)	6 (0-28)	6 (0-28)	6.0 (0-28)
Median (range) time to response (TTR), days	7 (4-28)	7 (4-14)	7 (4-28)	7 (4-20)	7 (4-28)
Response (4 weeks)					
OR (%)	49 (59.0%)	22 (51.2%)	40 (47.6%)	31 (73.8%)	71 (56.4%)
χ^2 (P)	0.714 (0.398)		7.308 (0.006)		
CR (%)	30 (36.1%)	13 (30.2%)	22 (26.2%)	21 (50.0%)	43 (34.1%)
χ^2 (P)	0.440 (0.507)		7.061 (0.008)		
Response (6 months)					
OR (%)	49 (59.0%)	19 (44.2%)	38 (45.2%)	30 (71.4%)	68 (54.0%)
χ^2 (P)	2.514 (0.113)		7.731 (0.005)		
CR (%)	28 (33.7%)	11 (25.0%)	21 (25.0%)	18 (42.9%)	39 (31.0%)
χ^2 (P)	0.881 (0.348)		4.178 (0.041)		

Table 2. ITP patients' response to DXM-RTX treatment with different anti-GPs autoantibodies.

Time	Response	GPIIb/IIIa (+), n=83	GPIIb/IIIa (-), n=43	χ^2	P	Total n=126
Week 4	CR	18 (21.6%)	12 (27.9%)	4	0.046	43 (34.1%)
	OR	31 (37.3%)	18 (41.9%)	13	0.002	71 (56.4%)
	NR	29 (34.9%)	15 (34.9%)	6	0.022	55 (43.7%)
	CR	17 (20.5%)	11 (25.6%)	7	0.007	39 (31.0%)
Month 6	CR	17 (20.5%)	11 (25.6%)	7	0.007	39 (31.0%)
	OR	31 (37.3%)	18 (41.9%)	13	0.002	71 (56.4%)
	NR	29 (34.9%)	15 (34.9%)	6	0.022	55 (43.7%)
	CR	17 (20.5%)	11 (25.6%)	7	0.007	39 (31.0%)

The different letters (a-b) at the same row indicate statistically significant differences (χ^2 test with Bonferroni's correction, $P < 0.05$).

Table 4. Factorial design analysis of anti-GPIIb/IIIa auto-antibodies and anti-GPIIb/IIIa auto-antibodies on the response to DXM-RTX treatment.

Time	Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Week 4	Corrected Model	9.462 ^a	3	3.154	3.36	0.021
	Intercept	343.443	1	343.443	365.919	0.000
	Anti-GPIIb/IIIa	8.568	1	8.568	9.128	0.003
	Anti-GPIIb/IIIa	1.493	1	1.493	1.59	0.210
	Anti-GPIIb/IIIa	0.048	1	0.048	0.052	0.821
	Error	114.507	122	0.939		
	Total	566	126			
	Corrected Total	123.968	125			
	Corrected Model	12.103 ^a	3	4.034	4.332	0.006
	Intercept	369.569	1	369.569	398.64	0.000
Month 6	Corrected Model	9.507	1	9.507	10.254	0.002
	Intercept	3.662	1	3.662	3.95	0.049
	Anti-GPIIb/IIIa	0.142	1	0.142	0.153	0.696
	Anti-GPIIb/IIIa	113.103	122	0.927		
	Error	990	126			
	Total	125.206	125			
	Corrected Total	125.206	125			

Dependent Variable: CR. ^a R Squared = 0.076 (Adjusted R Squared = 0.054). ^b R Squared = 0.097 (Adjusted R Squared = 0.074).

Figure 1

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