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652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Real-World Clinical Outcomes in Patients with Relapse and Refractory Multiple Myeloma Received VTD-PACE Treatment in the Era of Monoclonal Antibody

Moe Yogo[1], Taku Kikuchi, MD[2], Nobuhiro Tsukada, MD PhD[3], Kodai Kunisada[4], Yuki Okda[5], Kota Sato, MD[5], Mizuki Ogura[6], Tomomi Takei, MD[3], Yu ABE[6], Kenshi Suzuki, MD PhD[7], Tadao Ishida[5]

[1] Haematology, Japanese Red Cross Medical Center, Shibuya-Ku, Japan
[2] hematology, Japanese Red Cross Medical Center, Tokyo, JPN
[3] Japanese Red Cross Medical Center, Tokyo, JPN
[4] Hematology, Japanese Red Cross Medical Center, Shibuyaku, JPN
[5] Japanese Red Cross Medical Center, Tokyo, Japan
[6] Japanese Red Cross Medical Center, Shibuya-Ku, JPN
[7] Myeloma/Amyloidosis Center, Japanese Red Cross Medical Center, Tokyo, Japan

The treatment outcomes of multiple myeloma (MM) have drastically improved with the use of novel agents, including proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and monoclonal antibodies. However, ultimately, the disease relapses and results in a fatal outcome. Even in cases of relapse, treatment outcomes have improved with the use of novel agents. However, in situations where novel agents have been exhausted or when the disease rapidly progresses, bortezomib (Velcade), thalidomide, dexamethasone, platinum (cisplatin), adriamycin (doxorubicin), cyclophosphamide, and etoposide (VTD-PACE) is frequently utilized, with reported effectiveness. However, its outcomes in the era of monoclonal antibodies remain unclear. Therefore, this retrospective cohort study assessed the clinical outcomes of 60 patients with RRMM (median four prior treatment lines) administered VTD-PACE at the Japanese Red Cross Medical Center between June 2016 and April 2023. The characteristics of the 60 patients are shown in Table 1. The VTD-PACE regimen consisted of 1 mg/m^2 of bortezomib on days 1, 4, 8, and 11 administered subcutaneously; 200 mg of thalidomide administered orally on days 1-4; 40 mg of dexamethasone administered orally on days 1-4; and a 4-day continuous intravenous infusion of 10 mg/m^2 cisplatin, 40 mg/m^2 cyclophosphamide, 40 mg/m^2 etoposide, and 10 mg/m^2 doxorubicin. The cisplatin dose was adjusted based on renal function, as determined by the treating physician. The responses were evaluated according to the International Myeloma Working Group response criteria. High-risk cytogenetic abnormalities (HRCA) included del (17p), t(4;14), and t(14;16). Double-class refractory disease was defined as refractoriness to PIs and IMiDs, whereas triple-class refractory disease was defined as refractoriness to PIs, IMIDs, and anti-CD38 monoclonal antibodies. Penta-drug refractory disease was defined as refractoriness to bortezomib, carfilzomib, lenalidomide, pomalidomide, and anti-CD38 antibodies. The median follow-up period was 11.1 months (range, 0.5-72.0 months), during which they received a median of two cycles of VTD-PACE. The overall response (ORR), stringent complete response, complete response, and very good partial response rates were 66.7% (40 patients), 13.3% (8 patients), 5% (3 patients), and 20% (12 patients), respectively. The results of univariate analysis for factors associated with response rate are shown in Table 2. The ORRs in patients with ≥4 and ≤3 prior lines were 53.1% and 82.1%, respectively ($P = 0.027$). Extramedullary disease (EMD), refractoriness to anti-CD38 antibody, HRCA, and triple-class/penta-drug refractory disease did not significantly reduce the ORR. The median overall survival (OS) was 17 months with a median progression-free survival (PFS) of 9.8 months. The median PFS in patients with and without receiving hematopoietic stem cell transplantation (HSCT) or chimeric antigen receptor T-cell therapy (CART) following VTD-PACE were 9.8 and 5.1 months, respectively ($P = 0.023$). The median OS in patients with and without renal dysfunction were 10.7 months and 21.5 months, respectively ($P = 0.0091$). A trend for longer OS was observed in patients with HSCT or CART following VTD-PACE ($P = 0.18$). Therefore, VTD-PACE is useful as a bridging therapy for HSCT or CART, as a response is expected regardless of organ damage, disease risk, or history of anti-CD38 antibody use. However, the response rate decreased in late lines; therefore, its use in early lines is recommended.

Disclosures Yogo: *Janssen:* Other: advisory fee; *Takeda:* Other: Remuneration for lecture . **Kikuchi:** *Abbvie:* Other: Remuneration for lecture; *Janssen:* Other: Remuneration for lecture ; *Takeda Pharmaceutial Company Limited:* Other: Remuneration for lecture ; *Sanofi:* Other: Remuneration for lecture; *Bristol-Myers Squibb:* Other: Remuneration for lecture. **Tsukada:** *Sanofi*

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Table 1. Patient characteristics at the time of VTD-PACE initiation (n = 60)

Variable	
Age (years), median (range)	57.5 (37–73)
Sex, n (%)	
Female	29 (48.3)
Male	31 (51.7)
MM subtype, n (%)	
IgG	30 (50.0)
IgA	9 (15.0)
IgD	2 (3.3)
IgM	1 (1.7)
Bence-Jones	18 (30.0)
ISS stage at diagnosis, n (%)	
Stage I	19 (31.7)
Stage II	16 (26.7)
Stage III	19 (31.7)
Unknown	6 (6.7)
LDH level, n (%)	
>ULN	25 (41.7)
≤ULN	35 (58.3)
Estimated glomerular filtration rate, n (%)	
≥60 mL/min/1.73m^2	38 (63.3)
<60 mL/min/1.73m^2	22 (36.7)
Cytogenetic risk, n (%)	
High-risk	24 (40.0)
del(17p)	16 (26.7)
t(4;14)	14 (23.3)
t(14;16)	3 (5.0)
Standard-risk	28 (46.7)
Unknown	8 (13.3)
1q gain	16 (26.7)
1q amplification	16 (26.7)
Number of prior lines of therapy, median (range)	4 (1–10)
Prior therapy, n (%)	
PI	60 (100.0)
IMiDs	59 (98.3)
Elotuzumab	16 (26.7)
Anti-CD38 antibody	39 (65.0)
Autologous stem cell transplantation	38 (63.3)
Allogeneic stem cell transplantation	1 (1.7)
Refractory status, n (%)	
PI refractory	45 (75.0)
IMiDs refractory	51 (85.0)
Anti-CD38 antibody refractory	37 (61.7)
Elotuzumab refractory	15 (25.0)
Double-class refractory	44 (73.3)
Triple-class refractory	28 (46.7)
Penta-drug refractory	8 (13.3)

Ig: immunoglobulin, IMiDs: immunomodulatory drugs, ISS: international scoring system, LDH: lactate dehydrogenase, MM: multiple myeloma, PI: proteasome inhibitor, ULN: upper limit of normal

Table 2. Factors affecting response rate in univariate analysis

Variable		N	≥VGPR (%)	P	≥PR (%)	P
Subtype	Non IgG	30	53.3	0.033	80	0.054
	IgG	30	23.3		53.3	
Estimated glomerular filtration rate	≥60 ml/min1.73m^2	38	39.5	1	68.4	0.78
	<60	22	36.4		63.6	
ISS	1,2	36	27.8	0.063	61.1	0.36
	3	18	55.6		77.8	
LDH level	≤ULN	35	34.3	0.59	65.7	1
	>ULN	25	44		68	
Extra-medullary disease	No	40	30	0.091	57.5	0.044
	Yes	20	55		85	
Previous treatment lines	<3	17	58.8	0.075	82.4	0.14
	≥3	43	30.2		60.5	
Previous treatment lines	<4	28	53.6	0.034	82.1	0.027
	≥4	32	25		53.1	
Cytogenetic risk	Standard-risk	28	42.9	1	57.1	0.14
	High-risk	24	41.7		79.2	
del17p	No	39	43.6	0.77	64.1	0.54
	Yes	16	37.5		75	
1q amplification	No	18	33.3	0.30	61.1	0.27
	Yes	16	56.3		81.3	
Double-class refractory	No	16	43.8	0.77	62.5	0.76
	Yes	44	36.4		68.2	
Triple-class refractory	No	32	37.5	1	68.8	0.79
	Yes	28	39.3		64.3	
Quad-class refractory	No	50	40	0.73	68	0.72
	Yes	10	30		60	
Penta-refractory	No	52	42.3	0.14	69.2	0.42
	Yes	8	12.5		50	

Figure 1

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