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Real-World Treatment Trends and Triple Class Exposed Status in Japanese Patients with Newly Diagnosed Multiple Myeloma: A Retrospective Claims Database Study

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Objectives

- To clarify patient characteristics, treatment trends, TCE patient status and treatment sequences in NDMM patients in a Japanese real-world setting.
- To evaluate treatment regimens for NDMM patients to bring to TCE

Conclusions

- Our study showed that in the real-world setting, transplantation was able to be performed in patients with favorable health conditions and aged up to 73 years.
- The present study showed that in both transplant and non-transplant groups receiving the 1st line treatment, most patients received doublet regimen consisting of Rd-based, as well as Vd-based, and triplet regimen consisting of RVd-based.
- Most TCE patients comprised DRd-based, RVd-based and DVd-based regimens. Increasing trends in the proportion of TCE patients were indicated after 2nd or later lines for both transplant-ineligible and eligible patients, and it was notably high in the transplant group.
- The major outcomes of this study will support the development of treatment strategies and policies for actual clinical practice for MM treatment in Japan.

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References: **1**. Uno, S, et al. J Med Econ 2020;23:166-173. **2**. Guan J, et al. Japan J Pharmacoepidemiol/Yakuzai Ekigaku 2020;25:43-53. **3**. Lee Y, et al. Blood 2022;140 (Supplement 1):5156-5157.

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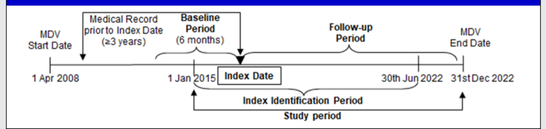
Background

- The treatment trends and sequences adopted for treating newly diagnosed multiple myeloma (NDMM) are not completely evaluated in real-world setting in the Japanese population at a large scale.
- Triple class exposed (TCE) patients with relapsed or refractory MM (RRMM) have a poor prognosis with worsening outcomes and limited treatment options.
- It is essential to identify the current real-world treatment trends and TCE patient population in each line for transplant ineligible and eligible Japanese patients with NDMM in large scale to establish a clinical consensus on standards of care and treatment strategies for TCE patients in an RRMM setting in near future.

Methods

- In the study period from Jan 1 2015, to Dec 31, 2022, MM patients were extracted from a hospital-based administrative claims data from Japanese hospitals.
- This study identified NDMM patients who were prescribed daratumumab, lenalidomide and/or bortezomib as the 1st line treatment during study period. The index date was defined as the earliest prescription date of the 1st line drugs in the same month or months after the 1st diagnosis of MM. Baseline period was considered as 6 months before the index date.
- Patients were excluded if they were prescribed anti-myeloma treatment drugs except steroids and subjected to stem cell transplantation (SCT) between April 1, 2008 and the day before index date, or were without any medical record before the index date for ≥3 years (**Figure 1**).
- The study population was divided into transplant and non-transplant patient groups based on whether they received autologous SCT or not after the index date, and the patient characteristics, treatment trends, TCE patient status and treatment sequences in NDMM patients were examined for transplant and non-transplant groups separately.

Figure 1: Study design



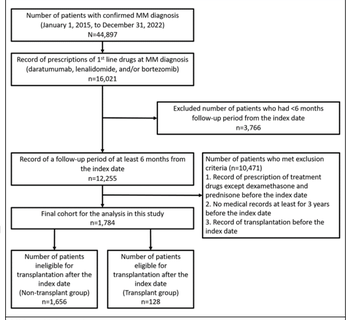
MDV, Medical Data Vision

Results

PATIENTS DISPOSITION AND CHARACTERISTICS

- As final cohort for the analysis, 1,784 patients were extracted. Of the 1784 patients, 1,656 and 128 patients were transplant-ineligible and transplant-eligible, respectively (**Figure 2**).
- Of 1,784 patients, 1,656 and 128 patients were transplant-ineligible (median age 75y [range: 37-94]) and transplant-eligible (median age 61y [range: 35-73]), respectively.
- In the non-transplant group, higher proportion of patients had different complex comorbidities including renal (16.2%) and cardiac (24.3%) dysfunctions, and vascular disorder (32.5%) compared to the transplant-group; renal (7.0%) and cardiac (6.3%) dysfunctions, and vascular disorder (9.4%) (**Table 1**).

Figure 2. Patients disposition



MM, multiple myeloma

Table 1. Patients' characteristics

Characteristics	Non-transplant group (n=1,656)	Transplant group (n=128)
Age, (years)		
Mean (SD)	74.7 (8.8)	59.4 (8.1)
Median (min–max)	75.0 (37–94)	61.0 (35–73)
Q1–Q3	70.0–81.0	54.0–65.5
Age category (years), n (%)		
<18	0 (0.0)	0 (0.0)
18–64	178 (10.7)	91 (71.1)
65–74	561 (33.9)	37 (28.9)
75–84	723 (43.7)	0 (0.0)
≥85	194 (11.7)	0 (0.0)
Sex, n (%)		
Male	870 (52.5)	62 (48.4)
Female	786 (47.5)	66 (51.6)
Comorbidities, n (%)		
Renal dysfunction	269 (16.2)	9 (7.0)
Liver dysfunction	112 (6.8)	6 (4.7)
Cardiac dysfunction	402 (24.3)	8 (6.3)
Pulmonary dysfunction	64 (3.9)	0 (0.0)
Vascular disorder	539 (32.5)	12 (9.4)
Back pain	263 (15.9)	17 (13.3)
Dementia	9 (0.5)	0 (0.0)
Hospital scale, n (%)		
≤199 beds	46 (2.8)	0 (0.0)
200–499 beds	824 (49.8)	51 (39.8)
≥500 beds	786 (47.5)	77 (60.2)
Hospital category, n (%)		
University hospital	82 (5.0)	10 (7.8)
Public hospital	1,365 (82.4)	110 (85.9)
Private hospital	209 (12.6)	8 (6.3)
Follow-up period (months)		
Mean (SD)	28.0 (18.6)	34.7 (19.7)
Median (min–max)	23.0 (5.9–94.3)	30.9 (7.7–95.2)
Q1–Q3	13.2–38.6	18.5–48.1

max, maximum; min, minimum; Q1, 1st quartile; Q3, 3rd quartile; SD, standard deviation

TREATMENT DUATION AND PREFFERED REGIMENS

Table 2. Duration of treatment in non-transplant and transplant groups

Treatment line	Duration of treatment (months)					
	Non-transplant group			Transplant group		
	Overall	Patients with subsequent line treatment		Overall	Patients with subsequent line treatment	
		Prescribed	Not prescribed		Prescribed	Not prescribed
	n=1,656	n=605	n=1,051	n=128	n=76	n=52
1st line	10.86 (0.03–95.08)	6.90 (0.03–70.67)	14.32 (0.03–95.08)	11.76 (0.43–76.06)	4.80 (0.43–66.60)	18.96 (4.70–76.06)
2nd line	7.56 (0.03–82.46)	6.46 (0.03–44.85)	8.51 (0.03–82.46)	8.08 (0.10–67.12)	2.92 (0.69–56.21)	9.91 (0.10–67.12)
3rd line	4.48 (0.03–66.60)	4.07 (0.07–40.67)	4.76 (0.03–66.60)	8.23 (0.46–47.77)	4.01 (0.46–15.80)	10.02 (1.97–47.77)
4th line	5.29 (0.03–43.89)	3.45 (0.23–15.61)	7.00 (0.03–43.89)	4.47 (0.10–30.55)	3.25 (0.72–6.44)	7.54 (0.10–30.55)

Duration of treatment in months expressed as median (minimum—maximum)

Figure 3. Treatment regimen in each line in (a) non-transplant and (b) transplant groups

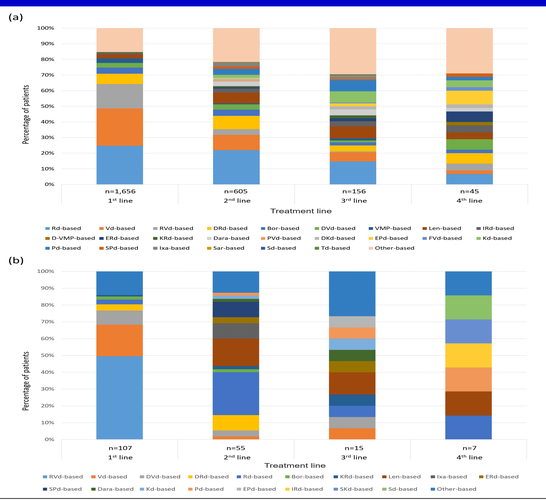


Table 3. Proportion of patients per treatment regimen by age and comorbidities in 1st line in the non-transplant group (≥1% in any group)

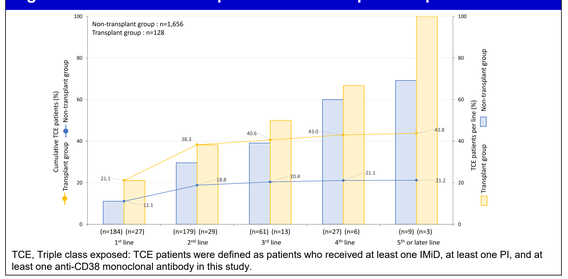
Treatment regimen	Total	Age			
		<65 years n (%)	65-74 years n (%)	75-84 years n (%)	≥85 years n (%)
		178	561	723	194
Rd-based	409	23 (12.9)	98 (17.5)	204 (28.2)	84 (43.3)
Vd-based	394	47 (26.4)	138 (24.6)	164 (22.7)	45 (23.2)
RVd-based	259	57 (32.0)	109 (19.4)	82 (11.3)	11 (5.7)
DRd-based	110	5 (2.8)	41 (7.3)	58 (8.0)	6 (3.1)
Bor-based	65	13 (7.3)	26 (4.6)	23 (3.2)	3 (1.5)
DVd-based	49	9 (5.1)	21 (3.7)	15 (2.1)	4 (2.1)
VMP-based	47	0 (0.0)	18 (3.2)	26 (3.6)	3 (1.5)
Len-based	43	1 (0.6)	16 (2.9)	18 (2.5)	8 (4.1)
IRd-based	13	0 (0.0)	1 (0.2)	12 (1.7)	0 (0.0)
KRd-based	4	2 (1.1)	2 (0.4)	0 (0.0)	0 (0.0)

Treatment regimen	Total	Comorbidities				
		Renal dysfunction n (%)	Liver dysfunction n (%)	Cardiac dysfunction n (%)	Pulmonary dysfunction n (%)	Vascular disorder n (%)
		269	112	402	64	539
Rd-based	409	68 (25.3)	26 (23.2)	116 (28.9)	20 (31.3)	140 (26.0)
Vd-based	394	88 (32.7)	26 (23.2)	115 (28.6)	15 (23.4)	155 (28.8)
RVd-based	259	21 (7.8)	19 (17.0)	39 (9.7)	10 (15.6)	48 (8.9)
DRd-based	110	17 (6.3)	9 (8.0)	24 (6.0)	1 (1.6)	35 (6.5)
Bor-based	65	17 (6.3)	7 (6.3)	21 (5.2)	3 (4.7)	21 (3.9)
DVd-based	49	10 (3.7)	3 (2.7)	14 (3.5)	1 (1.6)	16 (3.0)
VMP-based	47	6 (2.2)	3 (2.7)	6 (1.5)	3 (4.7)	13 (2.4)
Len-based	43	4 (1.5)	1 (0.9)	12 (3.0)	1 (1.6)	19 (3.5)
IRd-based	13	1 (0.4)	0 (0.0)	4 (1.0)	1 (1.6)	2 (0.4)

- Duration of treatment was longest (18.96 months) in patients in 1st line in the transplant group followed by patients (14.32 months) in 1st line in the non-transplant group when subsequent line of treatment was not prescribed (**Table 2**).
- The transplant-ineligible patients received Rd-based (24.7%), Vd-based (23.8%) and RVd-based (15.6%), and transplant-eligible patients received RVd-based (49.5%), Vd-based (18.7%) and DVd-based (8.4%) in 1st line.
- Daratumumab-containing regimens (D-VMP-based, DRd-based, DVd-based and DKd-based) or daratumumab-based therapies were prescribed to 10.0%, 16.2%, 10.9% and 20.0% patients in the 1st, 2nd, 3rd, and 4th line treatments, respectively (**Figure 3**).
- Of 128 patients in the transplant group, 107 (83.6%), 20 (15.6%) and 1 (0.8%) patients received transplantation in the 1st, 2nd and 4th lines, respectively. The top three regimens as induction therapy before SCT were RVd-based (49.5%), Vd-based (18.7%) and DVd-based (8.4%) in the 1st line and bortezomib-based (25.0%), Rd-based (20.0%) and KRd-based/Kd-based (each 10.0%) in the 2nd line (**Figure S1**).
- In the non-transplant group, the commonly prescribed treatment regimens were Rd-based for patients aged ≥75 years, Vd-based for patients aged 65 to 74 years and RVd-based for patients aged <65 years.
- Patients with renal dysfunction commonly received Vd-based, patients with liver dysfunction received each of Rd-based and Vd-based, patients with cardiac dysfunction received Rd-based, patients with pulmonary dysfunction received Rd-based and patients with vascular disorder received Vd-based (**Table 3**).

TCE PATIENTS

Figure 4. Cumulative TCE patients and TCE patients per line



TCE, Triple class exposed: TCE patients were defined as patients who received at least one IMiD, at least one PI, and at least one anti-CD38 monoclonal antibody in this study.

- Cumulative total TCE patients by 5th line were 351 (21.2%) and 56 (43.8%) for all transplant ineligible and transplant eligible patients, respectively. TCE ratio at each line gradually increased from 1st to 5th line, 11.1-69.2% in the non-transplant group and 21.1-100% in the transplant group, respectively (**Figure 4**).
- Of 184 TCE patients in 1st line in the non-transplant group, 89.7% received sequencing treatments including DRd, RVd and DVd, and 10.3% received D-RVd in 1st line. The TCE rate highly increased from 4% (3/73) to 45% (50/111) after D-VMP approval for NDMM (**Table S6**).