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Real-world Treatment Patterns, Efficacy, and Safety of Daratumumab-based Regimens in Chinese Patients With Multiple Myeloma: An Updated Analysis of the MMY4032 Study

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Key Takeaway

In this RW study, which is one of the largest and first of its kind to investigate patient characteristics, treatment patterns, and clinical outcomes in Chinese patients with MM who received DARA-based therapy in RW routine clinical practice, clinical outcomes were favorable, with a greater benefit observed when DARA was initiated in earlier lines of therapy

Conclusions

This updated analysis of the RW MMY4032 study continues to provide insight into treatment decisions in routine clinical practice for Chinese patients with MM

Most patients received DARA in combination with a PI and/or IMiD

The rate of ≥VGPR was higher when DARA was given with a PI and/or IMiD or with other agents, although survival rates were generally consistent across regimens; outcomes were most favorable when DARA was initiated in earlier lines of therapy

With additional follow-up, DARA-based regimens continued to demonstrate efficacy and a good safety profile, further supporting the use of DARA-based regimens as a standard of care in this patient population

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Disclosure
LW has no competing interests to declare.

Introduction

- Daratumumab (DARA) is a human IgGκ monoclonal antibody targeting CD38 with a direct on-tumor[1-4] and immunomodulatory[5-7] mechanism of action and has been established by several pivotal randomized controlled trials (RCTs) as a standard of care for patients with newly diagnosed or relapsed/refractory multiple myeloma (MM)[8-10]
  - DARA was first approved in China in 2019, and clinical trials in Chinese patients have since reported the efficacy and tolerability of DARA in patients with MM[11-13]
- Real-world (RW) studies provide important complementary data to RCTs and additional insight into routine clinical practice
- The first interim analysis of the MMY4032 study (ChiCTR2200055491) described RW treatment patterns, patient characteristics, and preliminary DARA effectiveness and safety in Chinese patients with MM who received DARA-based regimens[14]
  - Here, we present an updated analysis of RW treatment patterns, treatment response, survival outcomes, and safety in Chinese patients with MM who were treated with DARA-based regimens in routine clinical practice

Methods

Study design and patients

- This is an ongoing, multicenter, noninterventional, observational study across 13 participating sites in China
- All patients were aged ≥18 years, had symptomatic newly diagnosed or relapsed/refractory MM, and had either started DARA after August 1, 2019, and were to continue DARA at the time of study initiation (November 3, 2021), or started DARA after study initiation
- Patients who had received ≥4 prior lines of MM therapy before starting DARA-based treatment, who had a diagnosis of other cancers (prior to MM diagnosis), or who were currently participating in another investigational study were excluded
- The decision to treat with DARA must have been made prior to and independently of the patient's inclusion in the study, and treatment was administered in accordance with local clinical practice

Data collection

- For patients who started DARA after August 1, 2019, but before study initiation, data were collected retrospectively using medical chart reviews; data were collected prospectively thereafter
- For patients who started DARA after study initiation, data were collected prospectively
- Prospective data collection was intended for every 2 months within the first 12 months after enrollment and every 6 months thereafter until the end of the study
- Baseline was defined as the latest status prior to the first dose of DARA within the study

Study endpoints

- The primary objectives of this study were to describe treatment patterns and clinical outcomes in routine clinical practice among Chinese patients with MM who were treated with DARA
  - The secondary objective of this study was to assess the safety and tolerability of DARA in Chinese patients with MM
- Key parameters collected and reported here include:
  - Patient demographics, disease characteristics, and treatment patterns
  - Clinical outcomes, such as treatment response (per International Myeloma Working Group response criteria), survival outcomes (progression-free survival [PFS], overall survival [OS]), and time to next treatment (TTNT)
  - Safety outcomes, such as the incidence of adverse drug reactions (ADRs) and serious treatment-emergent adverse events (TEAEs)
- Continuous and categorical variables were summarized using descriptive statistics, and time-to-event variables were estimated using the Kaplan–Meier method

Results

Patients and study disposition

- As of the cutoff date (December 1, 2023), 212 patients who had a diagnosis of MM and received ≥1 DARA treatment after August 1, 2019, were eligible for this analysis
- A summary of patient demographic and disease characteristics overall and by DARA-based regimen is presented in **Table 1**
  - For the overall population, the median (range) age at baseline was 64 (29-89) years and the median time since MM diagnosis to DARA initiation was 1 (0-12) year
  - Baseline characteristics were generally similar across DARA-based regimens, except that patients who received DARA + proteasome inhibitor (PI) ± dexamethasone or DARA + other agents were more likely to have International Staging System stage III disease
- At the data cutoff, 113 patients were ongoing in the study and 99 patients had discontinued (due to withdrawal [n = 51], death [n = 33], participation in another trial [n = 8], and lost to follow-up [n = 7])

Table 1: Patient demographic and baseline disease characteristics[a]

Characteristic	Overall (N = 212)	DARA monotherapy (n = 24)	DARA + dexa (n = 20)	DARA + PI ± dexa (n = 61)	DARA + IMiD ± dexa (n = 73)	DARA + PI + IMiD ± dexa (n = 28)	DARA + other agents (n = 6)
Age, median (range), y	64 (29-89)	66 (46-81)	64.5 (42-83)	63 (37-89)	65 (29-82)	59.5 (41-76)	56.5 (46-69)
Time from diagnosis to DARA initiation							
n	211	24	20	61	72	28	6
Median (range), y	1 (0-12)	2 (0-8)	1 (0-9)	0 (0-6)	1.5 (0-12)	0 (0-12)	2 (0-5)
Sex, n (%)							
Male	122 (57.5)	13 (54.2)	10 (50.0)	42 (68.9)	39 (53.4)	14 (50.0)	4 (66.7)
Female	90 (42.5)	11 (45.8)	10 (50.0)	19 (31.1)	34 (46.6)	14 (50.0)	2 (33.3)
ISS disease stage, n (%)							
n	141	15	12	36	55	20	3
I	30 (21.3)	3 (20.0)	2 (16.7)	3 (8.3)	16 (29.1)	6 (30.0)	0
II	53 (37.6)	7 (46.7)	6 (50.0)	11 (30.6)	19 (34.5)	9 (45.0)	1 (33.3)
III	58 (41.1)	5 (33.3)	4 (33.3)	22 (61.1)	20 (36.4)	5 (25.0)	2 (66.7)
ECOG PS, n (%)							
n	131	17	12	36	44	18	4
0	30 (22.9)	3 (17.6)	2 (16.7)	10 (27.8)	12 (27.3)	2 (11.1)	1 (25.0)
1	76 (58.0)	9 (52.9)	6 (50.0)	20 (55.6)	24 (54.5)	14 (77.8)	3 (75.0)
2	16 (12.2)	4 (23.5)	3 (25.0)	3 (8.3)	4 (9.1)	2 (11.1)	0
≥3	9 (6.9)	1 (5.9)	1 (8.3)	3 (8.3)	4 (9.1)	0	0

DARA, daratumumab; dexa, dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug; ISS, International Staging System; ECOG PS, Eastern Cooperative Oncology Group performance status.
[a]Data from the safety population (defined as all enrolled patients who received ≥1 dose of DARA; patients were included in the analysis according to the dose received).

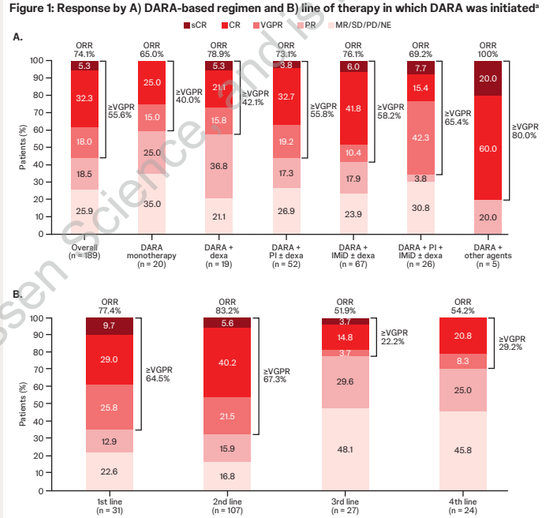
Treatment patterns

- Most patients (n = 177 [83.5%]) had received ≥1 line of therapy before initiating DARA
  - Prior PI use was reported for 175 (82.5%) patients, with bortezomib (n = 171 [80.7%]) the most common PI
  - Prior immunomodulatory drug (IMiD) use was reported for 125 (59.0%) patients, with lenalidomide (n = 111 [52.4%]) the most common IMiD
- The majority (n = 115 [54.2%]) of patients initiated DARA as 2nd-line therapy; DARA + IMiD ± dexamethasone (n = 73) and DARA + PI ± dexamethasone (n = 61) were the most frequently reported DARA-based combinations
  - DARA/pomalidomide/dexamethasone (D-Pd, n = 42/73 [57.5%]) was the most common DARA + IMiD ± dexamethasone regimen
  - DARA/bortezomib/dexamethasone (D-Vd, n = 50/61 [82.0%]) was the most common DARA + PI ± dexamethasone regimen
- The median (range) duration of DARA exposure was 8.2 (0-49.1) months overall and was longest when DARA was initiated in earlier lines of therapy: 9.7 (0.3-37.0) months in the 1st line, 8.1 (0-49.1) months in the 2nd line, 7.5 (0.1-31.5) months in the 3rd line, and 4.7 (0.5-28.7) months in the 4th line

Clinical outcomes

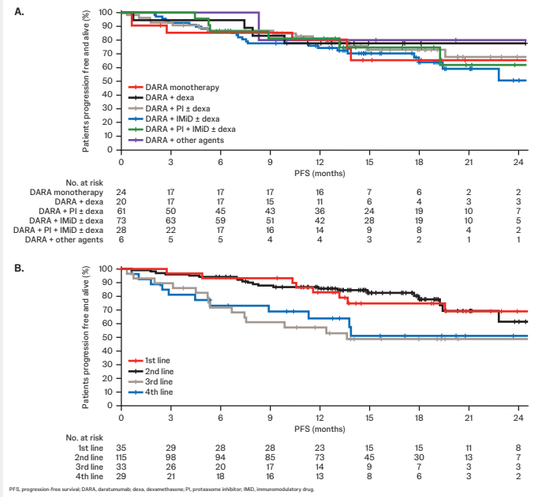
- At a median follow-up of 16.2 months, the overall response rate was 74.1% and the rate of very good partial response or better (≥VGPR) was 55.6%
  - The rate of ≥VGPR was similar for patients receiving DARA + PI ± dexamethasone (55.8%) and DARA + IMiD ± dexamethasone (58.2%) but higher for those receiving DARA + PI + IMiD ± dexamethasone (65.4%) and DARA + other agents (80.0%; **Figure 1A**)
  - Higher response rates were observed when DARA was initiated in earlier lines of therapy (**Figure 1B**)
- Median PFS and OS were 32.8 (95% confidence interval, 27.1-not estimable) months and not reached, respectively, and estimated 12-month rates were 77.9% and 87.8% (**Table 2**)
  - Across all DARA-based regimens, the highest estimated 12-month PFS and OS rates were observed in patients receiving DARA + PI + IMiD ± dexamethasone, 81.3% and 96.3%, respectively (**Figure 2A**)
- PFS and OS rates at 12 months were higher when DARA was initiated in earlier lines of therapy (**Table 3** and **Figure 2B**)
- Median TTNT was not reached across most DARA-based regimens, and 51 (24.1%) patients received subsequent non-DARA therapy (**Table 4**)

Figure 1: Response by A) DARA-based regimen and B) line of therapy in which DARA was initiated[a]



DARA, daratumumab; sCR, stringent complete response; CR, complete response; VGPR, very good partial response; PR, partial response; MR, minimal response; SD, stable disease; PD, progressive disease; NE, not evaluable; ORR, overall response rate; dexa, dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug.
[a]In patients with available post-DARA disease assessment.

Figure 2: PFS by A) DARA-based regimen and B) line of therapy in which DARA was initiated



PFS, progression-free survival; DARA, daratumumab; dexa, dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug.

Table 2: Survival outcomes by DARA-based regimen

Survival outcome	Overall (n = 212)	DARA monotherapy (n = 24)	DARA + dexa (n = 20)	DARA + PI ± dexa (n = 61)	DARA + IMiD ± dexa (n = 73)	DARA + PI + IMiD ± dexa (n = 28)	DARA + other agents (n = 6)
PFS							
Median (95% CI), mo	32.8 (27.1-NE)	NE (13.6-NE)	NE (NE-NE)	NE (19.6-NE)	27.1 (18.0-NE)	32.8 (13.2-NE)	NE (8.3-NE)
12-mo PFS, %	77.9	80.4	77.8	80.6	74.3	81.3	80.0
OS							
Median (95% CI), mo	NE (NE-NE)	NE (NE-NE)	NE (13.3-NE)	NE (26.0-NE)	NE (NE-NE)	NE (23.8-NE)	NE (8.3-NE)
12-mo OS, %	87.8	87.3	84.1	88.1	86.3	96.3	83.3

DARA, daratumumab; dexa, dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug; PFS, progression-free survival; CI, confidence interval; NE, not estimable; OS, overall survival.

Table 3: Survival outcomes by line of therapy in which DARA was initiated

Survival outcome	1st line (n = 35)	2nd line (n = 115)	3rd line (n = 33)	4th line (n = 29)
PFS				
Median (95% CI), mo	NE (19.6-NE)	27.1 (22.8-NE)	13.6 (6.7-NE)	NE (8.9-NE)
12-mo PFS, %	83.0	85.7	57.5	64.0
OS				
Median (95% CI), mo	NE (26.0-NE)	NE (NE-NE)	NE (NE-NE)	NE (13.9-NE)
12-mo OS, %	97.1	90.4	76.4	78.6

DARA, daratumumab; PFS, progression-free survival; CI, confidence interval; NE, not estimable; OS, overall survival.

Table 4: TTNT and subsequent therapy by DARA-based regimen

	Overall (n = 212)	DARA monotherapy (n = 24)	DARA + dexa (n = 20)	DARA + PI ± dexa (n = 61)	DARA + IMiD ± dexa (n = 73)	DARA + PI + IMiD ± dexa (n = 28)	DARA + other agents (n = 6)
TTNT							
Median (95% CI), mo	NE (32.8-NE)	NE (17.7-NE)	NE (NE-NE)	NE (23.1-NE)	NE (19.4-NE)	32.8 (23.3-NE)	NE (8.3-NE)
12-mo TTNT, %	82.1	87.3	78.8	84.5	77.5	87.5	83.3
Subsequent non-DARA therapy, n (%)	51 (24.1)	2 (8.3)	5 (25.0)	13 (21.3)	21 (28.8)	10 (35.7)	0
Most common (≥5 patients)							
KPd	7 (3.3)	0	0	1 (1.6)	4 (5.5)	2 (7.1)	0
P	6 (2.8)	0	0	0	6 (8.2)	0	0
KCd	5 (2.4)	0	0	1 (1.6)	3 (4.1)	1 (3.6)	0
R	5 (2.4)	0	0	1 (1.6)	1 (1.4)	3 (10.7)	0
Reason for subsequent non-DARA therapy[a]							
n	51	2	5	13	21	10	0
Physician recommendation	27 (52.9)	1 (50.0)	3 (60.0)	7 (53.8)	10 (47.6)	6 (60.0)	0
Disease progression	16 (31.4)	2 (100)	0	2 (15.4)	8 (38.1)	4 (40.0)	0
Patient request	2 (3.9)	0	1 (20.0)	0	1 (4.8)	0	0
Other	13 (25.5)	0	1 (20.0)	4 (30.8)	5 (23.8)	3 (30.0)	0
Unknown	7 (13.7)	0	2 (40.0)	3 (23.1)	0	2 (20.0)	0

TTNT, time to next treatment; DARA, daratumumab; dexa, dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug; CI, confidence interval; NE, not estimable; KPd, carfilzomib/cyclophosphamide/dexamethasone; R, lenalidomide.
[a]Multiple reasons may have been provided for each patient.

Safety

- No new safety concerns were observed with additional follow-up
- ADRs and serious TEAEs were reported in 43 (20.3%) and 33 (15.6%) patients, respectively (**Table 5**)
- Among the 33 reported deaths, progressive disease (n = 12) and other/unknown (n = 13) were the most common primary causes
  - A total of 8 deaths were reported due to adverse events; only 1 was DARA related (acute-onset chronic liver failure)

Table 5: Safety outcomes by DARA-based regimen

Safety outcome, n (%)	Overall (n = 212)	DARA monotherapy (n = 24)	DARA + dexa (n = 20)	DARA + PI ± dexa (n = 61)	DARA + IMiD ± dexa (n = 73)	DARA + PI + IMiD ± dexa (n = 28)	DARA + other agents (n = 6)
ADRs	43 (20.3)	5 (20.8)	1 (5.0)	10 (16.4)	21 (28.8)	5 (17.9)	1 (16.7)
Events in ≥5% of patients[a]							
Leukopenia	17 (8.0)	1 (4.2)	0	2 (3.3)	12 (16.4)	2 (7.1)	0
Neutropenia	15 (7.1)	1 (4.2)	0	1 (1.6)	12 (16.4)	1 (3.6)	0
Lymphopenia	12 (5.7)	1 (4.2)	0	1 (1.6)	8 (11.0)	2 (7.1)	0
Hypogammaglobulinemia	11 (5.2)	2 (8.3)	0	3 (4.9)	5 (6.8)	1 (3.6)	0
Serious TEAEs	33 (15.6)	4 (16.7)	3 (15.0)	13 (21.3)	7 (9.6)	5 (17.9)	1 (16.7)
Events in ≥1% of patients[a]							
Pneumonia	12 (5.7)	1 (4.2)	1 (5.0)	4 (6.6)	2 (2.7)	3 (10.7)	1 (16.7)
COVID-19	4 (1.9)	2 (8.3)	0	2 (3.3)	0	0	0
No. of patient-reported TEAEs leading to discontinuation	29 (13.7)	6 (25.0)	1 (5.0)	10 (16.4)	8 (11.0)	3 (10.7)	1 (16.7)
Deaths	33 (15.6)	4 (16.7)	4 (20.0)	9 (14.8)	12 (16.4)	3 (10.7)	1 (16.7)
Primary cause of death							
PD	12 (36.4)	3 (75.0)	1 (25.0)	2 (22.2)	4 (33.3)	1 (33.3)	1 (100)
AE	8 (24.2)	0	1 (25.0)	4 (44.4)	2 (16.7)	1 (33.3)	0
Other/unknown	13 (39.4)	1 (25.0)	2 (50.0)	3 (33.3)	6 (50.0)	1 (33.3)	0

DARA, daratumumab; dexa, dexamethasone; PI, proteasome inhibitor; IMiD, immunomodulatory drug; ADR, adverse drug reaction; TEAE, treatment-emergent adverse event; PD, progressive disease; AE, adverse event.
[a]Events occurring in the indicated proportion of patients within any treatment group.

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Multiple Myeloma

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