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Characteristics, Treatment Patterns, and Outcomes of Patients with Multiple Myeloma Retreated with Daratumumab in Real-World Clinical Practice in the USA

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Key Takeaway

Retreatment with daratumumab may provide clinical benefit, regardless of whether patients are sensitive or refractory to daratumumab after first exposure.

Conclusions

This largest real-world study of retreatment with DARA showed that DARA retreatment is utilized frequently in real world clinical practice and suggests that it could be an effective strategy to reuse DARA in subsequent lines of therapy among patients with relapsed refractory multiple myeloma.

Based on the findings of this study, it could be hypothesized that DARA retreatment may be more effective when used as early as possible after first DARA-exposure. Although further research is warranted.

Ongoing clinical studies assessing the efficacy of retreatment with DARA in combination with novel drugs with different mechanisms of action will further demonstrate the benefit of DARA-retreatment.

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https://www.congresshub.com/ASH2024/Oncology/Daratumumab/Ailawadhi

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Introduction

- Daratumumab (DARA) has demonstrated clinical benefit in multiple myeloma (MM) and is approved for the treatment of both newly diagnosed MM (NDMM) and relapsed refractory MM (RRMM).[1,2]
- Single-center studies have shown the benefit of DARA retreatment in patients who became refractory to DARA (D-Ref).[3,4]
- However, there is a lack of real-world data on the characteristics of patients who are retreated with DARA across multiple lines of treatment (LOTs).
- This study sought to examine the characteristics of patients retreated with DARA, patterns of retreatment with DARA, and outcomes among patients who are D-Ref and those are sensitive to DARA (D-Sens) after the first DARA exposure in real-world clinical practice in the USA.

Methods

- This study used the Flatiron MM Core Registry data to identify patients with MM treated with a DARA-containing regimen in ≥2 separate LOTs between November 1, 2015, and March 31, 2024.[5]
- The first DARA-based LOT was defined as D1 and the second DARA-based LOT was defined as the retreatment LOT (D2).
- Criteria shown in **Figure 1**, developed by Janssen Scientific Affairs, were used to classify patients as DARA-retreated.
- Derived disease progression reported in the Flatiron data was used for this analysis.
- If disease progression was reported during D1, or within 60 days of discontinuing D1, the patient was considered D-Ref, otherwise the patient was considered as D-Sens.
- Kaplan-Meier (KM) analyses were conducted to evaluate the duration of D2 and progression-free survival (PFS) rates during D2.
- Time to next treatment (TTNT) was defined as time from initiation of D2 to the initiation of the next LOT, or death, whichever occurs first. Next LOT could be initiated due to adverse events or disease evaluation with or without meeting criteria of progressive disease.

Figure 1: DARA retreatment definition (any of the following).

Patients treated with the same DARA-containing regimens in consecutive LOTs, if there was a gap of >90 days between D1 and D2

Patients treated with different DARA-containing regimens in consecutive LOTs

Patients had ≥1 non-DARA-containing LOTs between D1 and D2, regardless of the gap between LOTs

Results

Patient and clinical characteristics

- This study included 201 patients retreated with DARA, of which 150 were D-Sens and 51 were D-Ref.
- Patient and clinical characteristics were measured at D2 initiation (unless otherwise specified; **Table 1**).
- Retreatment with DARA is more prevalent after 2020, than in earlier years.

Table 1: Patient and clinical characteristics of D-Sens and D-Ref patients.

	D-Sens (N=150)	D-Ref (N=51)
Female, n (%)	66 (44.0)	23 (45.1)
Age at D1 initiation, median (IQR) years	68 (13)	62 (12)
Race, n (%)[a]		
White	98 (65.3)	22 (43.1)
African American or Black	24 (16.0)	13 (25.5)
Asian	5 (3.3)	2 (3.9)
Other Race	8 (5.3)	5 (9.8)
Received treatment in community practice, n (%)	130 (86.7)	40 (78.4)
Follow-up from D2 initiation, median (IQR), months	12.9 (12.7)	6.2 (14.7)
ECOG PS[b], n (%)		
0	38 (25.3)	14 (27.5)
1	68 (45.3)	19 (37.3)
2	19 (12.7)	10 (19.6)
3-4	4 (2.7)	1 (2.0)
Frailty, n (%)[c]	97 (64.7)	31 (60.8)
Quan-Charlson Comorbidity Index ≥3, n (%)	84 (56.0)	27 (52.9)
Gain or amplification 1q21, n (%)	30 (20.0)	10 (19.6)
High cytogenetic risk[d], n (%)	47 (31.3)	16 (31.4)
Received transplant prior to D2, n (%)	63 (42.0)	25 (49.0)

[a]Unknown/missing for 9 D-Ref and 15 D-Sens patients. [b]Unknown/missing for 7 D-Ref and 21 D-Sens patients [c]Frailty was defined per the simplified IMWG frailty score (using age, ECOG and Quan-Charlson Comorbidity Index).[3,4] [d]High cytogenetic risk was defined as presence of markers in del17, t(4,14), t(14,16), t(14,20) or amplification 1q21. ECOG PS, Eastern Cooperative Oncology Group performance status. IQR, interquartile range.

Treatment patterns

- Patterns of treatment of patients retreated with DARA are described in **Table 2**.
- The most common regimen used in D1 was DARA + lenalidomide + dexamethasone (dex; 18.7%) and DARA + bortezomib + dex (18.7%) among D-Sens patients, and DARA + pomalidomide + dex (23.5%) among D-Ref patients.
- The most common regimen used in D2 was DARA mono (31.3%) in D-Sens patients, and DARA mono (17.6%) and DARA + carfilzomib + dex (17.6%) in D-Ref patients.
- Overall, 32.0% of D-Sens and 35.3% of D-Ref patients received agents from the same drug class in D1 and D2.
- The median gap between D1 and D2 was 9.3 months in D-Sens patients and 9.0 in D-Ref patients, however, more D-Sens patients received D1 and D2 in consecutive LOTs compared with D-Ref patients (62.0% vs 51.0%).
- The KM median duration of D2 was 7.4 months (95% CI: 5.5-9.5) among D-Sens patients **(Figure 2A)** and 6.4 months (95% CI: 3.8-23.5) among D-Ref patients **(Figure 2B)**.
- Fewer D-Sens patients received D1 in the third LOT or later compared with D-Ref patients (30.0% vs 45.1%). The median number of LOTs before D2 was three in both groups **(Table 2)**.

Outcomes

- The percentage of patients that had not received subsequent treatment after D2 was 38.7% and 29.5% at 12 months in D-Sens and D-Ref patients, respectively.
- The median time to next treatment was 7.0 months (95% CI:4.1-9.7) for D-Sens patients and 3.3 months (95% CI: 1.1-10.8) for D-Ref patients.
- More D-Sens patients were alive or progression-free after initiation of D2 at 12 months than D-Ref patients (77.1% vs 49.4%; **Figure 3**).

Figure 2: Duration of treatment of D2 in (A) D-Sens and (B) D-Ref patients.

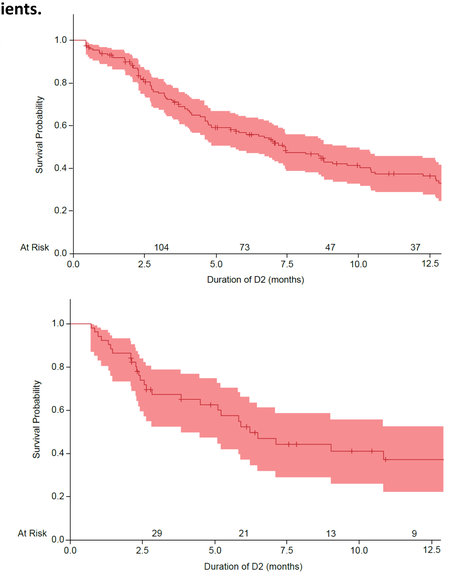
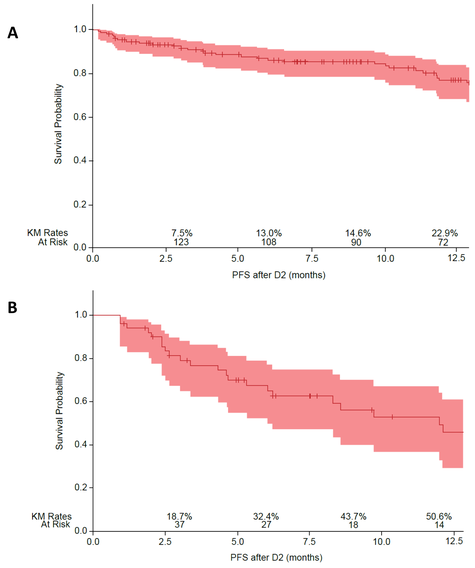


Table 2: Treatment patterns of D-Sens and D-Ref patients.

	D-Sens (N=150)	D-Ref (N=51)
Median time from diagnosis to start of D1, median (IQR) months	10.8 (49.9)	18.4 (33.4)
Median time from diagnosis to start of D2, median (IQR) months	44.4 (52.7)	34.9 (39.3)
Index DARA LOT number, n (%)		
1	35 (23.3)	9 (17.6)
2	70 (46.7)	19 (37.3)
3	25 (16.7)	11 (21.6)
4	20 (13.3)	12 (23.5)
DARA retreatment LOT number, n (%)		
2	8 (15.7)	26 (17.3)
3	11 (21.6)	46 (30.7)
4+	32 (62.7)	78 (52.0)
Median gap between D1 and D2, median (IQR) months	9.3 (13.1)	9.0 (15.4)
Number of lines between D1 and D2, n (%)		
0	93 (62.0)	26 (51.0)
1	39 (26.0)	16 (31.4)
2	15 (10.0)	5 (9.8)
3+	3 (2.0)	4 (7.8)

IQR, interquartile range. LOT, line of treatment.

Figure 3: PFS after D2 in (A) D-Sens and (B) D-Ref patients.



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