Treatment patterns and effectiveness of patients with multiple myeloma initiating Daratumumab across different lines of therapy: a real-world chart review study

Shebli ATRASH1, Philippe THOMPSON-LEDUC2*, Ming-Hui TAI3, Shuchita KAILA3, Kathleen GRAY3, Isabelle GHELERTER2, Marie-Hélène LAFEUILLE2, Patrick LEFEBVRE2 and Adriana ROSSI4

Abstract

Background: Daratumumab, a CD38 monoclonal antibody, has demonstrated efficacy as monotherapy and combination therapy across several indications, both among newly-diagnosed and refractory patients with multiple myeloma (MM). However, there is limited evidence on treatment patterns and effectiveness of daratumumab in the real-world setting, particularly in first line (1 L). This study aimed to describe real-world treatment patterns and clinical outcomes among patients initiating daratumumab across different lines of therapy.

Methods: A retrospective chart review of adult patients with MM initiating daratumumab between November 2015 and March 2021 was conducted at two clinical sites in the United States. De-identified patient-level data were abstracted in an electronic case report form. Patient characteristics and treatment patterns were described. Clinical outcomes including overall response rate (ORR), progression-free survival, and time to next line of therapy were reported using descriptive statistics and stratified by line of therapy (1 L, second line [2 L] or third line or later [3 L+]). A sub-group analysis evaluated treatment patterns and ORR among patients re-treated with daratumumab.

Results: A total of 299 patients were included in the study (mean age: 68 years; 55% male). Among them, 26 were 1 L patients, 66 were 2 L patients, and 207 were 3 L+ patients; 110 patients (36.8%) received a stem cell transplant prior to daratumumab initiation. The mean duration of follow-up was 10 months among 1 L patients and 19 months among 2 L and 3 L+ patients. Patients who initiated daratumumab in 1 L had a 100% ORR, while those initiating in 2 L and 3 L+ had an ORR of 78.8 and 65.2%, respectively. Among re-treated patients, ORR was 66.7% during the first treatment segment, and 52.9% during the second treatment segment. Kaplan-Meier rates of progression-free survival at 12 months were 89.9, 75.2, and 53.1% among patients who initiated daratumumab in 1 L, 2 L, and 3 L+, respectively. Kaplan-Meier rates of time to next line of therapy at 12 months were 94.1, 73.4, and 50.0% among patients who initiated daratumumab in 1 L, 2 L, and 3 L+, respectively.

Conclusions: These findings suggest that daratumumab-based regimens are an effective treatment option across all lines of therapy, with highest response rate in 1 L.
Background
Multiple myeloma (MM) is characterized by the accumulation of neoplastic plasma cells in the bone marrow [1]. The incidence of MM is expected to account for 1.8% of all new cancer cases and for 2.0% of all cancer deaths in the United States (US) in 2021 [2]. Between 2011 and 2017, the average five-year survival rate of patients diagnosed with MM was 55.6% [2].

Daratumumab is a human monoclonal antibody targeting CD38 approved for the treatment of MM [3]. Daratumumab monotherapy was first approved by the Food and Drug Administration (FDA) for patients with relapsed and/or refractory MM who have received at least three prior treatments (including at least one proteasome inhibitor and an immunomodulatory agent) in November 2015 [4–6]. Daratumumab was subsequently approved for the treatment of MM in combination with lenalidomide and dexamethasone, [7] or bortezomib and dexamethasone [8] among patients who have received at least one prior therapy and in combination with pomalidomide and dexamethasone among patients with relapsed or refractory MM [9]. In May 2018, daratumumab was approved for use in front line among patients who are ineligible for autologous stem cell transplant (ASCT) [10] and among ASCT-eligible patients in September 2019 [11].

While the safety and efficacy of daratumumab in front line and later lines has been well documented in clinical trials, real-world insights on treatment patterns and outcomes among patients with MM initiated on daratumumab, including among patients treated and re-treated with daratumumab, [12] are limited. In light of the rapidly-evolving treatment landscape in MM, [13] there is a need to understand real-world outcomes associated with daratumumab among patients with newly-diagnosed and relapsed or refractory MM. Therefore, the goal of this study was to describe the real-world treatment patterns and clinical outcomes of adult patients with MM receiving daratumumab across different lines of therapy.

Methods
Data source
A retrospective study design using data from electronic medical records (EMR) and medical charts was employed. De-identified data were retrieved from two clinical sites, Levine Cancer Institute (Atrium Health) and Weill Cornell Medicine. Chart abstraction was conducted between July 2020 and February 2021. Charts were randomly selected among daratumumab-treated patients at each institution using an algorithm based on the first letter of the patients’ last name. Structured and unstructured data were entered into an electronic case report form (eCRF). This study was reviewed and approved by the institutional review board of each site involved (Atrium Health Institutional Review Board and Weill Cornell Medicine Institutional Review Board) prior to the initiation of data retrieval.

Patient inclusion
Patients were included if they had a confirmed diagnosis of MM by the treating physician in their patient record, were at least 18 years old at the time of daratumumab initiation, and had complete treatment history available between MM diagnosis and daratumumab initiation. Patients who accessed daratumumab through interventional clinical trials were excluded. Patients were followed from the initiation of daratumumab until death, loss to follow-up, or date of chart abstraction completion, whichever occurred first.

Study measures
Patient demographic characteristics were reported, including the age at time of daratumumab initiation, time between MM diagnosis and daratumumab initiation, sex, race, and primary insurance plan type. Patient clinical characteristics reported included MM stage at diagnosis based on the Revised International Staging System (R-ISS) for multiple myeloma [14], cytogenetic profile as of daratumumab initiation (high risk defined as del(17p), t(4;14) or t(14;16)), refractory disease on treatments prior to initiating daratumumab, and the year of daratumumab initiation.

Treatment patterns were described for patients’ first daratumumab-based regimen, including the number of lines of therapy and individual regimens received prior to daratumumab initiation (as per physician notes), the regimen, whether patient received a stem cell transplant prior to initiating the regimen, the regimen type (i.e., induction therapy, conditioning therapy, consolidation therapy, maintenance therapy post-stem cell transplant, bridging therapy), and the length of the regimen.

Treatment response to the first daratumumab-based regimen was reported, as per physician notes and according to the criteria from the International Myeloma Working Group [15] (i.e., stringent complete response, complete response, very good partial response, partial response, minimal response, stable disease, progressive disease, clinical relapse, other). Overall response was defined as “partial response” or better among patients with...
Table 1 Patient Characteristics

| Demographic characteristics | All patients | Frontline daratumumab patients | Daratumumab initiated in 2 L | Daratumumab initiated in 3 L+ | Re-treated patients
|-----------------------------|-------------|--------------------------------|-----------------------------|-----------------------------|---------------------|
| Age at daratumumab initiation, mean ± SD [median] | 67.7 ± 11.3 [69.0] | 68.2 ± 13.9 [72.0] | 68.4 ± 10.2 [68.0] | 67.4 ± 11.3 [68.0] | 67.2 ± 14.7 [66.0] |
| Time between MM diagnosis and daratumumab initiation (months), mean ± SD [median] | 35.4 ± 30.6 [29.6] | 2.1 ± 1.9 [1.8] | 24.2 ± 24.6 [15.1] | 43.2 ± 30.4 [36.7] | 53.3 ± 41.3 [45.3] |
| Sex, n (%) | | | | | |
| Male | 164 (54.8) | 15 (57.7) | 36 (54.5) | 113 (54.6) | 10 (52.6) |
| Female | 135 (45.2) | 11 (42.3) | 30 (45.5) | 94 (45.4) | 9 (47.4) |
| Race, n (%) | | | | | |
| White | 163 (54.5) | 15 (57.7) | 41 (62.1) | 107 (51.7) | 10 (52.6) |
| Black or African American | 89 (29.8) | 4 (15.4) | 11 (16.7) | 74 (35.7) | 7 (36.8) |
| Hispanic | 6 (2.0) | 0 (0.0) | 2 (3.0) | 4 (1.9) | 0 (0.0) |
| Asian | 4 (1.3) | 1 (3.8) | 1 (1.5) | 2 (1.0) | 0 (0.0) |
| Mixed | 9 (3.0) | 2 (7.7) | 3 (4.5) | 4 (1.9) | 1 (5.3) |
| Other | 1 (0.3) | 0 (0.0) | 1 (1.5) | 0 (0.0) | 0 (0.0) |
| Unknown | 27 (9.0) | 4 (15.4) | 7 (10.6) | 16 (7.7) | 1 (5.3) |
| Primary insurance plan type, n (%) | | | | | |
| Medicare | 181 (60.5) | 15 (57.7) | 37 (56.1) | 129 (62.3) | 13 (68.4) |
| Commercial insurance | 46 (15.4) | 4 (15.4) | 15 (22.7) | 27 (13.0) | 3 (15.8) |
| Medicaid | 8 (2.7) | 0 (0.0) | 0 (0.0) | 8 (3.9) | 0 (0.0) |
| Other | 35 (11.7) | 1 (3.8) | 7 (10.6) | 27 (13.0) | 1 (5.3) |
| Unknown | 29 (9.7) | 6 (23.1) | 7 (10.6) | 16 (7.7) | 2 (10.5) |
| Clinical characteristics | | | | | |
| MM stage as of MM diagnosis date (R-ISS) | | | | | |
| Stage I | 58 (19.4) | 8 (30.8) | 17 (25.8) | 33 (15.9) | 1 (53.0) |
| Stage II | 104 (34.8) | 8 (30.8) | 26 (39.4) | 70 (33.8) | 4 (21.1) |
| Stage III | 58 (19.4) | 2 (7.7) | 9 (13.6) | 47 (22.7) | 5 (26.3) |
| Unknown | 79 (26.4) | 8 (30.8) | 14 (21.2) | 57 (27.5) | 9 (47.4) |
| Cytogenetic profile as of daratumumab initiation | | | | | |
| Standard | 108 (36.1) | 19 (73.1) | 27 (40.9) | 62 (30.0) | 9 (47.4) |
| High | 55 (18.4) | 4 (15.4) | 9 (13.6) | 42 (20.3) | 2 (10.5) |
| Unknown | 136 (45.5) | 3 (11.5) | 30 (45.5) | 103 (49.8) | 8 (42.1) |
| Refractory disease prior to daratumumab initiation | | | | | |
| To any line of therapy prior to daratumumab initiation | 210 (76.9) | – | 35 (53.0) | 175 (84.5) | 15 (83.3) |
| To an immunomodulatory drug | 162 (59.3) | – | 25 (37.9) | 137 (66.2) | 10 (55.6) |
| To a proteasome inhibitor | 153 (56.0) | – | 14 (21.2) | 139 (67.1) | 13 (72.2) |
| To a proteasome inhibitor and an immunomodulatory drug | 111 (40.7) | – | 7 (10.6) | 104 (50.2) | 8 (44.4) |
| Year of daratumumab initiation, n (%) | | | | | |
| 2015 | 2 (0.7) | 0 (0.0) | 0 (0.0) | 2 (1.0) | 1 (5.3) |
| 2016 | 32 (10.7) | 0 (0.0) | 2 (3.0) | 30 (14.5) | 4 (21.1) |
| 2017 | 55 (18.4) | 0 (0.0) | 10 (15.2) | 45 (21.7) | 4 (21.1) |
known response rate. Response rate of “very good partial response” or better among patients with known response rate was also reported.

Clinical outcomes also included progression-free survival (PFS), time to next line of therapy, and overall survival. Disease progression was defined as a record of discontinuation due to progressive disease, progressive disease as a patient’s best response to a treatment regimen or death and was measured from the initiation of daratumumab onward. Patients not experiencing disease progression were censored at the time of the last follow-up, whichever occurred first. Time to next line of therapy was defined as the time between the initiation of the first daratumumab-based regimen and the initiation of the following line of therapy. Patients who did not initiate a subsequent line of therapy were censored at the end of follow-up. Overall survival was defined as the time between the initiation of the first daratumumab-based regimen and the date of death. Patients without a record of death were censored at the end of follow-up.

Study measures for the overall population were reported using descriptive statistics. As patients initiating daratumumab at different stages of treatment likely had different patterns and outcomes, results were stratified based on the line of therapy at daratumumab initiation (i.e., first line [1 L], second line [2 L], or third line and after [3 L+]).

Subgroup and sensitivity analyses

Treatment patterns and treatment response outcomes were also reported among patients who were re-treated at least once with daratumumab. Re-treatment was defined as the resumption of a daratumumab-based treatment regimen following a ≥90-day period during which daratumumab was not administered. Patients were excluded if they had a stem cell transplant during the gap between the daratumumab-based treatment regimens or during these regimens.

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number of patients were Stage I or Stage III (58 patients, 19.4%; see Table 1).

Among the study population, 19 patients were retreated with daratumumab after their initial daratumumab treatment. These patients had generally similar characteristics at the initiation of daratumumab as compared to the overall sample. However, the mean number of lines of treatment prior to the initiation of the first daratumumab regimen was 3.4, compared with 2.4 for the overall sample (median: 2, range: 0–10).

A total of 206 initiated daratumumab on or after 2018, including 22 1 L patients, 54 2 L patients, and 130 3 L+ patients.

**Treatment patterns of first daratumumab-based regimen**

The mean duration of follow-up was 18.4 months (standard deviation [SD]: 12.5) and was shorter among 1 L patients (9.7 months, SD: 6.7) than 2 L (19.2 months, SD: 11.6) or 3 L+ patients (19.3 months, SD: 12.9). Among patients who initiated daratumumab in 1 L, the

| Table 2 | Treatment Patterns of the First Daratumumab-Based Regimen |
|---------|----------------------------------------------------------|
|         | All patients N = 299                                      | Frontline daratumumab patients N = 26 | Daratumumab initiated in 2 L N = 66 | Daratumumab initiated in 3 L+ N = 207 |
| Duration of follow-up1 (months), mean ± SD [median] | 18.4 ± 12.5 [16.6] | 9.7 ± 6.7 [7.5] | 19.2 ± 11.6 [16.9] | 19.3 ± 12.9 [17.2] |
| Number of lines of therapy received prior to daratumumab initiation, mean ± SD [median] | 2.4 ± 1.6 [2.0] | 0.0 ± 0.0 [0.0] | 1.0 ± 0.0 [1.0] | 3.2 ± 1.4 [3.0] |
| Number of regimens2 received prior to daratumumab initiation, mean ± SD [median] | 3.2 ± 2.0 [3.0] | 0.0 ± 0.0 [0.0] | 1.8 ± 1.0 [1.0] | 4.1 ± 1.7 [4.0] |
| First daratumumab regimen3, n (%) | | | | |
| DPd | 113 (37.8) | 0 (0.0) | 16 (24.2) | 97 (46.9) |
| Daratumumab (monotherapy) | 51 (17.1) | 0 (0.0) | 6 (9.1) | 45 (21.7) |
| DRd | 49 (16.4) | 9 (34.6) | 18 (27.3) | 22 (10.6) |
| Dvd | 31 (10.4) | 3 (11.5) | 17 (25.8) | 11 (5.3) |
| DVMP | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Other regimens | 55 (18.4) | 14 (53.8) | 9 (13.6) | 32 (15.5) |
| Bortezomib + daratumumab + lenalidomide ± dexamethasone | 18 (6.0) | 12 (46.2) | 6 (9.1) | 0 (0.0) |
| Carfilzomib + daratumumab ± dexamethasone | 7 (2.3) | 0 (0.0) | 0 (0.0) | 7 (3.4) |
| Carfilzomib + daratumumab + pomalidomide ± dexamethasone | 3 (1.0) | 0 (0.0) | 1 (1.5) | 2 (1.0) |
| Daratumumab + ixazomib + pomalidomide ± dexamethasone | 2 (0.7) | 0 (0.0) | 0 (0.0) | 2 (1.0) |
| Other | 25 (8.4) | 2 (7.7) | 2 (3.0) | 21 (10.1) |
| Received a stem cell transplant prior to initiating daratumumab, n (%) | 110 (36.8) | 0 (0.0) | 19 (28.8) | 91 (44.0) |
| Regimen type of daratumumab-based therapy3, n (%) | | | | |
| Induction therapy | 140 (46.8) | 25 (96.2) | 32 (48.5) | 83 (40.1) |
| Conditioning therapy | 65 (21.7) | 1 (3.8) | 12 (18.2) | 52 (25.1) |
| Consolidation therapy | 23 (7.7) | 0 (0.0) | 6 (9.1) | 17 (8.2) |
| Maintenance therapy post-stem cell transplant | 9 (3.0) | 0 (0.0) | 1 (1.5) | 8 (3.9) |
| Bridging therapy | 2 (0.7) | 0 (0.0) | 1 (1.5) | 1 (0.5) |
| Unknown/non applicable | 80 (26.8) | 1 (3.8) | 17 (25.8) | 62 (30.0) |
| Length of regimen (months), mean ± SD [median] | 10.3 ± 10.7 [6.5] | 6.9 ± 5.8 [4.1] | 12.3 ± 10.5 [8.8] | 10.1 ± 11.1 [6.4] |

Abbreviations: 2 L: second-line; 3 L: third-line; DPd: daratumumab, pomalidomide, and dexamethasone; DRd: daratumumab, lenalidomide, and dexamethasone; Dvd: daratumumab, bortezomib, and dexamethasone; DVMP: daratumumab, bortezomib, melphalan, and prednisone; SD: standard deviation

Notes:
1] Follow-up was defined as the number of months between the index date and the latest of 1) the end date of the last regimen entered (or date of chart abstraction if the last regimen entered was ongoing at the time of entry), 2) the last recorded best response to a regimen, or 3) death
2] Regimens consisting of the same agents with or without dexamethasone were reported as the same regimen
3] Each daratumumab-based regimen may have > 1 regimen type
most common regimens were daratumumab with bortezomib and lenalidomide (± dexamethasone, DVRd, \( n = 12, 46.2\% \)) and daratumumab with lenalidomide (± dexamethasone, DRd, \( n = 9, 34.6\% \)). Among patients who initiated daratumumab in 2 L, the most common regimens were DRd (\( n = 18, 27.3\% \)), daratumumab with bortezomib (± dexamethasone, DVd, \( n = 17, 25.8\% \)) and daratumumab with pomalidomide (± dexamethasone, DPd, \( n = 16, 24.2\% \)). Among patients who initiated daratumumab in 3 L+, the most common regimens were DPd

![Diagram ofdaratumumab re-treatment patterns](image-url)

**Fig. 1** Daratumumab Re-Treatment Patterns. DPd: daratumumab, pomalidomide, and dexamethasone; D Rd: daratumumab, lenalidomide, and dexamethasone; DVd: daratumumab, bortezomib, and dexamethasone. **Notes:** [1] Other regimens include: bortezomib + daratumumab + dexamethasone + pomalidomide, bortezomib + cyclophosphamide + daratumumab + dexamethasone, carfilzomib + cisplatin + cyclophosphamide + daratumumab + dexamethasone + etoposide, carfilzomib + daratumumab, carfilzomib + daratumumab + pomalidomide, daratumumab + denosumab + pomalidomide + dexamethasone. [2] Other regimens include: bortezomib + daratumumab + dexamethasone + pomalidomide, bortezomib + cyclophosphamide + daratumumab + dexamethasone, carfilzomib + daratumumab, daratumumab + dexamethasone + selinexor, daratumumab + venetoclax, cyclophosphamide + daratumumab + dexamethasone + pomalidomide, carfilzomib + cisplatin + cyclophosphamide + daratumumab + dexamethasone + etoposide + doxorubicin + melphalan + thalidomide, carfilzomib + daratumumab + cyclophosphamide + doxorubicin + etoposide, bexar + carfilzomib + cisplatin + daratumumab + etoposide + liposomal doxorubicin + venetoclax, DPd + ixazomib. [3] Other agents include: cisplatin, doxorubicin, bortezomib, ixazomib, lenalidomide, thalidomide, selinexor, venetoclax, melphalan, panobinostat, and clinical trial/investigational agents.

Duration of first segment in days, mean [median] 14 (74%) patients received treatment during gap, including: Carfilzomib (N=7, 50%), Pomalidomide (N=7, 50%), Cyclophosphamide (N=6, 43%), Etoposide (N=5, 36%) Other agents (N=12, 85%)

Duration of second segment in days, mean [median] 103 [98]
Table 3  Treatment Response on First Daratumumab-Based Regimen

| Best response achieved per IMWG criteria, n (%) | All patients N = 299 | Frontline daratumumab patients N = 26 | Daratumumab initiated in 2 L N = 66 | Daratumumab initiated in 3 L+ N = 207 |
|------------------------------------------------|----------------------|--------------------------------------|-----------------------------------|-------------------------------------|
| Stringent complete response                      | 16 (5.4)             | 5 (19.2)                             | 6 (9.1)                           | 5 (2.4)                             |
| Complete response                                 | 25 (8.4)             | 4 (15.4)                             | 4 (6.1)                           | 17 (8.2)                            |
| Very good partial response                        | 99 (33.1)            | 10 (38.5)                            | 28 (42.4)                         | 61 (29.5)                           |
| Partial response                                  | 71 (23.7)            | 7 (26.9)                             | 14 (21.2)                         | 50 (24.2)                           |
| Minimal response                                  | 4 (1.3)              | 0 (0.0)                              | 2 (3.0)                           | 2 (1.0)                             |
| Stable disease                                    | 38 (12.7)            | 0 (0.0)                              | 5 (7.6)                           | 33 (15.9)                           |
| Progressive disease                               | 43 (14.4)            | 0 (0.0)                              | 7 (10.6)                          | 36 (17.4)                           |
| Clinical relapse                                  | 0 (0.0)              | 0 (0.0)                              | 0 (0.0)                           | 0 (0.0)                             |
| Unknown/not available                             | 3 (1.0)              | 0 (0.0)                              | 0 (0.0)                           | 3 (1.4)                             |

Patients with known response rate, n (%)  
Overall response rate, n (%)  
Very good partial response or better, n (%)  
Months from regimen start to best response date, mean ± SD [median]

Abbreviations: 2 L: second-line; 3 L: third-line; IMWG: International Myeloma Working Group; SD: standard deviation

Notes

[1] Kumar S, Paiva B, Anderson KC, Durie B, Landgren O, Moreau P et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol. 2016 Aug;17 [15]:e328-e346

Table 4  Treatment Response among Re-Treated Patients

| Best response achieved per IMWG criteria, n (%) | Daratumumab re-treated patients N = 19 | Second treatment segment N = 19 |
|------------------------------------------------|--------------------------------------|----------------------------------|
| Stringent complete response                      | 0 (0.0)                              | 0 (0.0)                          |
| Complete response                                 | 0 (0.0)                              | 1 (5.3)                          |
| Very good partial response                        | 5 (26.3)                             | 2 (10.5)                         |
| Partial response                                  | 7 (36.8)                             | 6 (31.6)                         |
| Minimal response                                  | 0 (0.0)                              | 1 (5.3)                          |
| Stable disease                                    | 5 (26.3)                             | 1 (5.3)                          |
| Progressive disease                               | 1 (5.3)                              | 6 (31.6)                         |
| Clinical relapse                                  | 0 (0.0)                              | 0 (0.0)                          |
| Other                                             | 0 (0.0)                              | 0 (0.0)                          |
| Unknown/not available                             | 1 (5.3)                              | 2 (10.5)                         |

Patients with known response rate, n (%)  
Overall response rate, n (%)  
Very good partial response or better, n (%)  
Months from regimen start to best response date, mean ± SD [median]

Abbreviations: IMWG: International Myeloma Working Group; SD: standard deviation

Notes

[1] Re-treatment was defined as the resumption of a daratumumab-based treatment regimen following a ≥ 90-day period during which daratumumab was not administered. Patients were excluded if they had a stem cell transplant during the gap between the daratumumab-based treatment regimens or during these regimens.

[2] Kumar S, Paiva B, Anderson KC, Durie B, Landgren O, Moreau P et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol. 2016 Aug;17 [15]:e328-e346

[3] Overall response rate defined as partial response or better among patients with known response rate.
A total of 110 patients (36.8%) received a stem cell transplant prior to initiating daratumumab, including 19 patients (28.8%) who had initiated daratumumab in 2 L, and 91 patients (44.0%) who had initiated daratumumab in 3 L+ (see Table 2).

Among re-treated patients, all but one patient had their first treatment segment in 3 L+. The most common regimen used for the first treatment segment was daratumumab monotherapy (± dexamethasone, n = 6, 31.6%), while the most common regimen used for the second treatment segment was DPd (n = 5, 26.3%). The mean length of the gap between treatment segments was 258 days (range: 93–644 days). The majority of patients (14/19, 73.7%) had a non daratumumab-based regimen during the ≥90-day gap. Six patients (31.6%) remained on the same regimen before and after the ≥90-day gap. Among these, four patients did not receive any treatment during the gap. The length of the gap for these four patients ranged between 112 and 195 days. Among the two who did, one patient was treated with bortezomib, dexamethasone and lenalidomide. The other patient received 8 regimens during the gap, 7 of which were carfilzomib-based and 1 of which was an investigational antibody-drug conjugate (see Fig. 1).

Treatment response was similar for patients who initiated daratumumab on or after 2018 (see Supplementary Table 1).

Among re-treated patients, overall response rate was 66.7% during the first treatment segment, and 52.9% during the second treatment segment (see Table 4).

The median time to disease progression was not reached among patients who initiated daratumumab in 1 L. Among patients who initiated daratumumab in 2 L, median time to disease progression was 27.8 months. Among patients who initiated daratumumab in 3 L+, median time to disease progression was 12.0 months. Kaplan-Meier rates of PFS at 12 months were 89.8, 75.2 and 53.1% among patients who initiated daratumumab in 1 L, 2 L, and 3 L+, respectively (see Fig. 2).

### Table 1: Progression-Free Survival by Treatment Segment

| Treatment Segment | Patients at risk, n | Median time disease progression (months) |
|-------------------|--------------------|-----------------------------------------|
| Frontline daratumumab patients 1 | 26 (Not reached) | 23 (88.5) 16 (61.5) 12 (46.2) 10 (38.5) 1 (3.8) |
| Kaplan-Meier rates | 100.0 89.9 89.9 89.9 89.9 |
| Daratumumab initiated in 2L | 66 | 27.8 58 (87.9) 51 (77.3) 43 (65.2) 36 (54.5) 11 (16.7) |
| Kaplan-Meier rates | 90.6 84.2 79.0 75.2 61.1 |
| Daratumumab initiated in 3L+ | 207 | 12.0 152 (73.4) 118 (57.0) 80 (38.6) 68 (29.2) 20 (14.0) |
| Kaplan-Meier rates | 77.8 66.1 54.6 51.1 39.4 |

Fig. 2 Progression-Free Survival 1: Abbreviations: 2 L: second-line; 3 L: third-line. Notes: [1] Disease progression was defined as a record of discontinuation due to progressive disease, progressive disease as a patient’s best response to a treatment regimen, or death and was measured from the index date onward. Patients were censored at the earliest between initiation of a new line of therapy or end of follow-up, whichever occurred fir
The median time to next line of therapy was not reached among patients who initiated daratumumab in 1 L. Among patients who initiated daratumumab in 2 L, median time to next line of therapy was 31.3 months. Among patients who initiated daratumumab in 3 L+, median time to disease progression was 12.1 months. Kaplan-Meier rates of time to next line of therapy at 12 months were 94.1, 73.4 and 50.0% among patients who initiated daratumumab in 1 L, 2 L, and 3 L+, respectively (see Fig. 3).

Kaplan-Meier rates of overall survival at 12 months were 93.3, 86.9, and 79.3% among patients who initiated daratumumab in 1 L, 2 L, and 3 L+, respectively, although these results should be interpreted with caution due to the small sample size.

Discussion

This study reports the treatment patterns of patients initiating daratumumab across several lines of treatment in the real-world in the United States, including in first line and including daratumumab re-treatment. Most other real-world studies have focused on heavily pretreated patients [5, 18–21] or had relatively small sample sizes [22, 23].

In this study, daratumumab was used both in monotherapy and in combination with a variety of different agents. This is consistent with other reports of how daratumumab is used in the real world [24]. While a majority of patients initiated daratumumab in third line or after, the proportion of patients initiating daratumumab in earlier lines increased in the subset of patients initiating in 2018 or later. This is in line with the date of FDA approval of daratumumab for frontline treatment and illustrates a shift in treatment patterns over time.

Overall treatment response observed in this study (1 L: 100.0%, 2 L: 78.8%, 3 L+: 65.2%) show an overall favorable effectiveness profile, notably in earlier lines of treatment. Among patients initiating daratumumab in 1 L, 73% had a very good partial response or better. In recent trials of daratumumab among newly-diagnosed patients, the proportion of patients achieving very good partial response or better ranged from 73 to 83% [10, 11, 25]. However, it is challenging to directly compare these results with the current study, given differences in backbone agents, patient populations (stem cell transplant eligible vs. ineligible) and timing of the treatment response assessment. Nevertheless, the findings from this study provide real-world evidence that daratumumab is an effective treatment option in frontline.

This may be of particular relevance, as a recent retrospective analysis of three large US-based database found that approximately 57% of newly-diagnosed patients with MM received only one line of therapy. Therefore, treating patients with the most effective treatment regimens

### Table 1: Treatment Patterns of Patients Initiating Daratumumab in First Line

| Patients at risk, n | Median time to next line of therapy (months) | 3 Months | 6 Months | 9 Months | 12 Months | 24 Months |
|---------------------|---------------------------------------------|----------|----------|----------|-----------|----------|
| **Frontline daratumumab patients** | | 26 (Not reached) | 23 (88.5) | 16 (61.5) | 12 (46.2) | 10 (38.5) | 1 (3.8) |
| Kaplan-Meier rates | | 100.0 | 94.1 | 94.1 | 94.1 | 94.1 |
| **Daratumumab initiated in 2L** | | 66 | 31.3 | 60 (90.9) | 52 (78.8) | 44 (66.7) | 36 (54.5) | 11 (16.7) |
| Number of patients at risk, n (%) | | 93.8 | 85.9 | 78.9 | 73.4 | 62.5 |
| Kaplan-Meier rates | | 84.2 | 68.4 | 55.1 | 50.0 | 33.9 |

**Fig. 3** Time to Next Line of Therapy

**Abbreviations:** 2 L: second-line; 3 L: third-line. **Notes:** [1] Time to next line of therapy was defined as the time between the initiation of the first daratumumab-based regimen (index date) and the initiation of the following line of therapy. Patients not initiating a subsequent line of therapy were censored at the end of follow-up.
at diagnosis rather than reserving them for later lines of therapy may increase clinical benefit [17].

Among patients initiating daratumumab in later lines of treatment, treatment response and PFS were sustained, despite more advanced stage of MM, the refractoriness of patients who initiate multiple lines of treatment, and the heterogeneity of the treatment patterns [26]. Furthermore, re-treatment with daratumumab appeared to be effective, with a response rate for the second segment comparable for that of the first daratumumab treatment segment (treatment response following second segment: 52.9%). These findings supplement those of a study that found that some patients may respond to DPd even if they had been refractory to a prior exposure to daratumumab and/or pomalidomide [12].

The findings of this study should be interpreted in light of certain limitations. First, data were restricted to what was available in patients’ medical charts and EMR at the treatment sites. Elements of disease history or progression recorded outside of the sites were not captured in this study. Second, clinical outcomes measures including overall survival should be interpreted with caution due to the relatively small sample size and short duration of follow-up. Third, even if data were entered in a standardized eCRF by data abstractors at both sites who had received training on how to use the eCRF, data are subject to data entry mistakes or omissions. Finally, both sites participating in this study are research facilities, both of which are highly experienced treating patients with daratumumab. Therefore, results of this study may not be generalizable to other settings or less experienced clinical centers.

Conclusion

In this study, patients initiating daratumumab across different lines of therapy had high response rates and long PFS. Patients treated with front line daratumumab showed the greatest clinical benefit, with response rates comparable to those observed in recent clinical trials of newly-diagnosed patients. Patients initiating daratumumab in later lines and patients re-treated with daratumumab also had high response rates. These findings suggest that daratumumab-based regimens are an effective treatment option across all lines of therapy in real-world practice, with the greatest benefit observed in 1 L.

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Authors’ contributions

PTL, IG, MHL, and PL contributed to the design of the study and interpretation of the data. PTL, KG, and MHL contributed to the data collection and data analysis. All authors critically revised the draft manuscript and approved the final content.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to restrictions but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the institutional review board of each site involved (Atrium Health Institutional Review Board and Weill Cornell Medicine Institutional Review Board) prior to the initiation of data retrieval. Patients were not contacted at any point during the course of this study. Patient information was fully de-identified at each site prior to being sent for analysis. Confidentiality of patient records was maintained at all times. All study reports contain aggregate data only and do not identify individual patients or physicians. The experiment protocol for involving human data was in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

PTL, IG, MHL, and PL are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Janssen Scientific Affairs, LLC to conduct this study. MT, SK, and KG are employees and stockholders of Johnson & Johnson.

Author details

1Levine Cancer Institute, Charlotte, NC, USA. 2Analysis Group, Inc, 1190 avenue des Canadiens-de-Montréal, Deloitte Tower, Suite 1500, Montreal, QC H3B 0G7, Canada. 3Janssen Scientific Affairs, LLC, Horsham, PA, USA. 4Division of Hematology and Medical Oncology, Weill Cornell Medicine, New York, NY, USA.

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Additional file 1: Supplementary Table 1. Treatment Response on First Daratumumab-Based Regimen among Patients Initiating Daratumumab in 2018 or Later.
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