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Characteristics and Outcomes of Non-Transplanted Newly Diagnosed Multiple Myeloma Patients Treated with Daratumumab, Bortezomib, Lenalidomide, Dexamethasone (DVRd) with Once-Weekly Bortezomib Dosing

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Key Takeaway

Once-weekly bortezomib dosing is an effective treatment option for non-transplanted patients with newly diagnosed multiple myeloma treated with the daratumumab, bortezomib, lenalidomide, and dexamethasone (DVRd) regimen.

Conclusions

Data from this analysis indicate that the once-weekly bortezomib dosing schedule, as part of the daratumumab-based quadruplet regimen DVRd, is effectively used in the real-world setting and has a similar progression-free survival to that observed in the CEPHEUS trial.

This practice of weekly bortezomib dosing frequency among frontline DVRd-treated patients was observed regardless of age and disease risk and is feasible for the treatment of frailer patients.

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Introduction

- The phase 3 CEPHEUS trial of patients with newly diagnosed multiple myeloma (NDMM) who were transplant-ineligible (TIE) or transplant-deferred (TD) showed that after a median follow-up of 58.7 months, daratumumab, bortezomib, lenalidomide, and dexamethasone (DVRd) had several benefits compared with VRd, including:[1]
  - A significantly higher rate of overall minimal residual disease negativity (60.9% vs. 39.4%)[1]
  - A significantly longer progression-free survival (PFS; hazard ratio: 0.57, median PFS not reached for DVRd)[1]
- This has led to an increased adoption of DVRd as frontline (FL) treatment of TIE or TD NDMM in clinical practice.
- In the real-world, DVRd is typically dosed once weekly (instead of twice weekly as used in the CEPHEUS protocol) to optimize side effect management, decrease patient burden, and enhance quality of life.[2]
- **Study objective:** to characterize the patients receiving FL DVRd and evaluate real-world outcomes with once-weekly bortezomib dosing among non-transplanted NDMM patients.

Methods

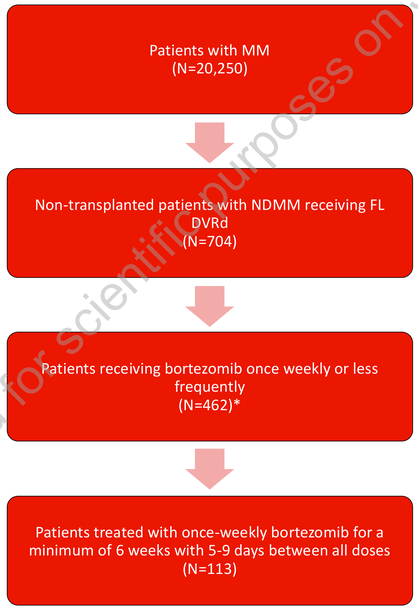
- Retrospective, single-arm, observational, cohort study.
- Data extracted from electronic health records of eligible patients from the Flatiron Health Research database.
- **Inclusion criteria:** NDMM patients aged ≥18 years treated with FL DVRd between January 1, 2019, and December 31, 2024.
- **Key dates and time periods**
  - **Index date:** the initiation date of DVRd
  - **Baseline period:** the 12 months preceding the index date
  - **Follow-up period:** from the index date to the earliest occurrence of death, last recorded activity, start of next line of treatment (LOT), or end of data availability
- **Exclusion criteria:**
  - Because transplant eligibility status was not recorded in the Flatiron database, hematopoietic stem cell transplantation (HSCT) was used as a proxy exclusion criterion, and all patients who had HSCT during the study period were excluded
  - Enrolment in a clinical trial, presence of other cancers, and diagnosis of amyloid light-chain amyloidosis prior to the index date
- **Once-weekly bortezomib dosing schedule:** if bortezomib was initiated and maintained for ≥6 weeks with 5-9 days between all doses.
- Frailty score was calculated based on age, Charlson-Comorbidity Index, and Eastern Cooperative Oncology Group performance status (ECOG PS).
- **Patient characteristics:** captured during the baseline period.
- **Clinical outcomes:** captured during the follow-up period:
  - **PFS** (time from the index date to either disease progression or death, whichever occurred first)
- Patient and disease characteristics were summarized using descriptive statistics, and time to event outcomes were analyzed using Kaplan-Meier methods.

Results

Patient and clinical characteristics

- A total of 113 non-transplanted NDMM patients treated with FL DVRd with once-weekly bortezomib were included in this analysis (Figure 1).
- Baseline patient and clinical characteristics are summarized in Table 1.
- Thirty-eight (33.6%) patients were considered to be frail (frailty score ≥2). Over half of patients (67.3%) had an ECOG PS of 0-1, and 14.2% had an ECOG PS of 2 (Table 1).
- Almost half (46.9%) had at least one of the high-risk cytogenetic biomarkers, defined as the presence of t(4;14), t(14;16), t(14;20), del(17p), and 1q gain/amplification, and 11.5% of patients had ≥2 of these high-risk cytogenetic biomarkers (Table 1).

Figure 1: Patients included in the analysis from the Flatiron database



*349 patients received inconsistent (alternating between once and twice weekly) or less frequent (>9 days between doses) dosing of bortezomib and were excluded from the final analysis.
DVRd, daratumumab, bortezomib, lenalidomide, and dexamethasone. FL, frontline. MM, multiple myeloma. NDMM, newly diagnosed multiple myeloma.

Table 1: Patient and clinical characteristics

Characteristics	Overall cohort (N=113)
Age, median (IQR) years	67 (58-73)
Gender, n (%)	
Female	50 (44.2)
Male	63 (55.8)
Race, n (%)	
White	71 (62.8)
African American	21 (18.6)
Asian	1 (0.9)
Other/unknown	20 (17.7)
Frailty score, n (%)	
0	37 (32.7)
1	38 (33.6)
2	24 (21.2)
3	10 (8.8)
4	2 (1.8)
5	2 (1.8)
Cytogenetic risk, n (%)	
High[a]	53 (46.9)
Non-high	45 (39.8)
Missing	15 (13.3)
ECOG PS, n (%)	
0	34 (30.1)
1	42 (37.2)
2	16 (14.2)
Missing	21 (18.6)
ISS, n (%)	
Stage I	32 (28.3)
Stage II	26 (23.0)
Stage III	18 (15.9)
Unknown	37 (32.7)
Comorbidities, n (%)	
Hypercalcemia	17 (15.0)
Renal impairment	17 (15.0)
Anemia	41 (36.3)
Bone disease	11 (9.7)

[a]High cytogenetic risk was defined as the presence of t(4;14), t(14;16), t(14;20), del(17p), and 1q gain/amplification. ECOG PS, Eastern Cooperative Oncology Group performance status. ISS, International Staging System. IQR, interquartile range.

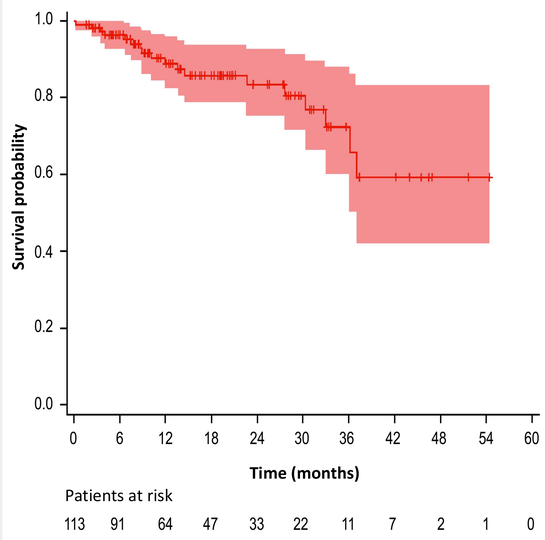
Treatment characteristics

- Median duration of follow-up was 19.1 months.
- Median duration of once-weekly bortezomib was 14 weeks (range: 6-58 weeks).
- Most patients (n=104; 92.0%) received bortezomib both intravenously and subcutaneously, while one patient (0.9%) received intravenous administrations only and eight patients (7.1%) received subcutaneous administrations only.

Clinical outcomes

- Median PFS was not reached (95% confidence interval [CI]: 36.1 months, not reached), with 18 disease progression or death events observed (Figure 2).
- The PFS rates at 12 and 24 months were 87.4% and 80.6%, respectively.

Figure 2: Progression-free survival



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2. Hoff FW, Banerjee R, Khan AM, McCaughan G, Wang B, Wang X, et al. Blood Cancer J 2024;14(1):52.

Multiple Myeloma

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