

# Daratumumab Dosing Analysis Among Patients with Multiple Myeloma in a US Community Oncology Setting: A Retrospective Observational Study in the Integra Connect Network

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## Background

- Daratumumab was initially approved for the treatment of Multiple Myeloma (MM) in 2015 for the treatment of relapsed / refractory (RR) with expanded approval in additional combinations, as well as usage in newly diagnosed multiple myeloma (NDMM) in both transplant eligible and transplant ineligible settings
- Daratumumab is an anti-CD38 monoclonal antibody that has become the backbone of many MM treatment regimens following that initial approval as its indication has expanded
- Practices are increasingly focused on controlling the overall costs of care in cancer delivery with the advent of value-based care (VBC) and institutional VBC models such as the Oncology Care Model (OCM)
- OCM tracks the costs of care delivery at the cancer type level where the approval of daratumumab has largely driven MM costs overruns that outpace all other cancer types; as a result, cost containment in MM has become a focus of many community oncology practices
- This study sought to determine whether daratumumab costs were partially driven by over-compliance of the standard daratumumab dosing schedule
- The most common daratumumab dosing schedule with the highest overall compliance was selected for analysis

## Methods

### Study objectives

- Evaluate overall dosing compliance of daratumumab administered in the community oncology setting
- Analyze the cost impacts of overutilization of daratumumab beyond the FDA-approved label.

### Data collection

- Pts  $\geq$  18 years of age with MM identified by ICD-10 codes that were treated with daratumumab any time between January 1, 2016 through March 31, 2020
- Integra Connect (IC) database of electronic health records, practice management, and payer data from 13 large community networks and over 1000 physician caregivers
- Excluded were any patients whose first line of therapy (LOT) was ambiguous, in order to correctly identify the daratumumab-containing LOTs by correct sequence number
- Excluded were LOT 1 daratumumab containing transplant induction combination due to the wide variability in daratumumab dosing schedules in clinical trials in the transplant eligible patient
- LOTs were determined based on International Myeloma Working Group guidelines
- Data were collected on the date of each individual daratumumab administration, counting initial split dose, if utilized, as 1 dose.

### Compliance determination

- While there are minimal variations in the FDA-approved dosing schedule of daratumumab, the dosing schedule utilized to determine overall dosing compliance is documented in **Table 1** and is the dosing schedule for daratumumab when given in combination with lenalidomide, pomalidomide, or as monotherapy.
- This dosing schedule was chosen as it is not only the most commonly administered dosing for the timeframe that the study was conducted, but it also includes the largest volume of daratumumab doses in a one- and two-year timeframe to conduct a conservative compliance analysis.

**Table 1. Daratumumab dosing schedule for analysis**

Weeks	Dosing Frequency
Week 1 - 8	Weekly dosing for a total of 8 doses
Week 9 - 24	Bi-weekly dosing for a total of 8 doses
Week 25+	Every four weeks dosing until disease progression

## Results

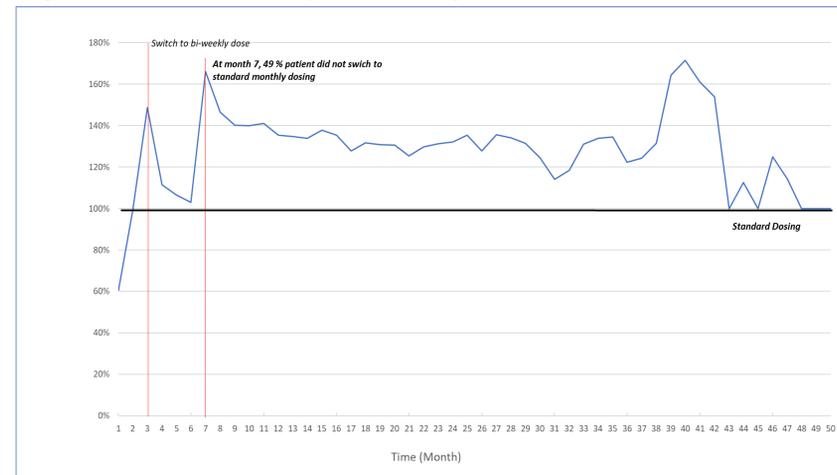
**Table 2** shows a total of 1,037 MM patients met the study inclusion criteria, including having at least 6 administrations of daratumumab to accurately represent overall compliance. Among these patients, the mean and median duration of therapy was 5.6 months and 9.8 months, respectively.

**Table 2. Overall patient counts by month and by daratumumab dosing frequency**

	Month 1	Month 3	Month 7	Month 12	Month 24	Month 36	Month 48
N=	1,037	945	671	569	331	83	3
Weekly Dose	776	572	51	62	22	5	0
Bi-weekly Dose	196	328	279	97	49	14	0
Monthly Dose	65	45	341	410	260	64	3

**Figure 2** shows monthly compliance as calculated as actual doses per month divided by expected doses per month from the **Table 1** schedule. This study found that compliance was consistently above 100%, implying a significant proportion of patients were receiving more frequent dosing than expected under the standard dosing schedule.

**Figure 2. Daratumumab compliance ratio by month**



Daratumumab over-compliance was consistent across lines of therapy (**Table 3**). The continuation of weekly and bi-weekly daratumumab dosing beyond the FDA-approved label also drives increased cost of care as calculated in **Table 4**.

**Table 3. Daratumumab dosing compliance by line of therapy**

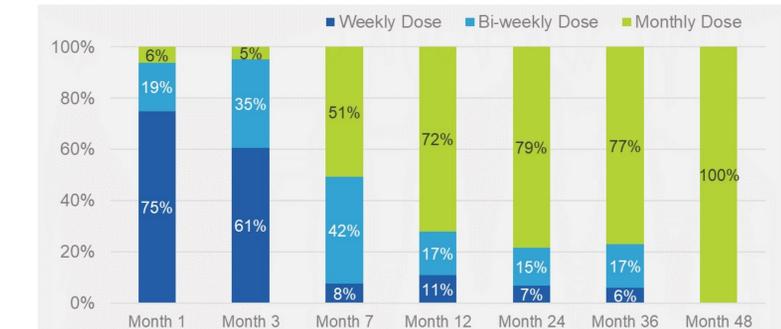
Daratumumab started at:	Patient Count	Average Compliance Dose Ratio*	95% CI	Observed Dose for a 52-weeks Treatment
LOT 1	60	1.09	[1.05, 1.13]	25.3
LOT 2	477	1.17	[1.12, 1.22]	26.9
LOT 3	288	1.23	[1.17, 1.29]	28.3
LOT 4+	212	1.20	[1.13, 1.27]	27.6
All	1037	1.19	[1.13, 1.25]	27.3

**Table 4. Estimated cost impact of daratumumab overcompliance assuming Medicare Part B reimbursement**

Daratumumab started at:	Patient Count	52-weeks Total Cost of Observed Dose	52-weeks Total Cost of Standard Dosing
LOT 1	60	\$190,979.19	
LOT 2	477	\$203,049.16	
LOT 3	288	\$213,610.39	\$173,628.60
LOT 4+	212	\$208,329.78	
All	1037	\$206,066.66	

**Table 2 and Figure 2** show that for patients reaching Month 7 of daratumumab treatment, 671 (64%) patients remained on daratumumab-containing regimens, with 330 (49%) patients continuing weekly or bi-weekly dosing, whereas the standard dosing schedule would employ a switch to every 4 week dosing

**Figure 1. Overall daratumumab dosing frequency by month**



## Conclusions

- In real-world community oncology practices, daratumumab is utilized in a more frequent dosing schedule than the FDA approved standard dosing schedule. At standard dosing, there are 23 daratumumab doses in the first 52 weeks. The compliance dose ratio found in our study implies 27.3 doses in the first year for the entire cohort and 26.9 and 28.3 doses in LOTs 2 and 3, respectively. Thus, significantly increased drug and administrative costs are incurred over those anticipated in respect to daratumumab dosing utilization.
- This study is limited to the EMR and administrative claims data of those individuals who are being treated in a community oncology setting. Residual confounding and bias may exist due to entry error and unobserved patient characteristics.

## References

- Gergely Varga, et al; Real World Data on the Efficacy and Safety of Daratumumab in Relapsed/Refractory Multiple Myeloma: Data Collected from the Hungarian Hematology Centers. Blood 2018; 132 (Supplement 1): 3257. doi: <https://doi.org/10.1182/blood-2018-99-115039>
- Rifkin R, Singer D, Aguilar KM, Baidoo B, Maiese EM. Daratumumab Split First Versus Single Dosing Schedule Among Patients With Multiple Myeloma Treated in a US Community Oncology Setting: A Retrospective Observational Study. Clin Ther. 2019;41(5):866-881.e7. doi:10.1016/j.clinthera.2019.03.013
- DARZALEX® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.
- Abdallah N, Kumar SK. Daratumumab in untreated newly diagnosed multiple myeloma. Ther Adv Hematol. 2019;10:2040620719894871. Published 2019 Dec 23. doi:10.1177/2040620719894871
- Rajkumar SV, Richardson P, San Miguel JF. Guidelines for determination of the number of prior lines of therapy in multiple myeloma. Blood. 2015;126(7):921-922. doi:10.1182/blood-2015-05-647636
- Cost Assumptions:

Assumption	Reference
Body weight 81.5kg	Talamo G et al. Retrospective Study of Body Weight in Patients with Multiple Myeloma through Different Stages of the Disease. Metab Nutr Oncol 2013; 1: e7-e11
Standard Dosage per Patient =1304 mg (16mg/kg with an 81.5kg body weight)	DARZALEX® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.
Drug cost \$56.06/10mg	Medicare Part B ASP Drug Cost for HCPCS Jcode : J9145, July 1, 2020 <a href="https://www.cms.gov/license/ama7files/zip/july-2020-asp-pricing-file.zip">https://www.cms.gov/license/ama7files/zip/july-2020-asp-pricing-file.zip</a>
Administration Time 7 hours for the first dose, 4.3 hours for the second dose, and 3.5 hours for the subsequent dose	King T, Jagger J, Wood J, et al. Best Practice for the Administration of Daratumumab in Multiple Myeloma: Australian Myeloma Nurse Expert Opinion. Asia Pac J Oncol Nurs. 2018;5(3):270-284. doi:10.4103/apjon.apjon_9_18
Administration Cost 1 <sup>st</sup> hour \$141.47 Additional hour: 30.68	CMS Physician Fee Schedule Search. HCPCS CPT Code: 96413 (Chemo iv infusion 1 hr); 96415 (Chemo iv infusion addl hr) <a href="https://www.cms.gov/physician-fee-schedule/search/results.aspx?Y=0&amp;T=0&amp;HT=0&amp;CT=3&amp;H1=96413&amp;M=1">https://www.cms.gov/physician-fee-schedule/search/results.aspx?Y=0&amp;T=0&amp;HT=0&amp;CT=3&amp;H1=96413&amp;M=1</a>
Calculation 23 doses per 52 weeks	Drug cost: \$168,135.15; assuming no drug wastage. \$56.06 x (1304mg/10mg) x 23 doses Administration Cost: \$5,493.45; First dose \$325.55, second dose: \$264.19; subsequent dose: \$233.51 Total Cost: \$173,628.60

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