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ORIGINAL ARTICLE

Patterns of bisphosphonate treatment among patients with multiple myeloma treated at oncology clinics across the USA: observations from real-world data

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Abstract

Purpose Current guidelines recommend that intravenous bisphosphonates be initiated in all patients with multiple myeloma for management of bone disease. The objective of this study was to describe real-world bisphosphonate treatment patterns.

Methods This was a retrospective observational study using oncology electronic health record (EHR) data contained in Amgen's Oncology Services Comprehensive Electronic Records (OSCER) database, generated by Flatiron Health (New York, NY), representing over 1.5 million US oncology patients. Patients were newly diagnosed with multiple myeloma between January 1, 2009 and April 30, 2016. Timing of bisphosphonate administration, frequency, schedule, changes in dosing schedule, and discontinuations were calculated. Bisphosphonate treatment relative to renal function and anti-multiple myeloma therapy regimens were also assessed.

Results A total of 11,112 patients were enrolled in the study with a median follow-up of 687 days. Sixty-three percent received ≥ 1 bisphosphonate administration, primarily every 4 weeks (67.7%). Mean time from diagnosis to bisphosphonate administration was 106 days (median, 29). Most patients (58.2%) initiated treatment in first year after diagnosis and about half (51.9%) either discontinued or changed dosing. Patients with poorer renal function by estimated glomerular filtration rate (eGFR) stage at baseline were less likely to receive bisphosphonates (eGFR stage 5 vs 1: 24 vs 72%) and more likely to have delayed initiation of bisphosphonate treatment from diagnosis (eGFR stage 5 vs 1: median 70 vs 25 days).

Conclusions Real-world data from US oncology practices indicate that many patients with multiple myeloma may not receive optimal therapy for bone disease, particularly those with renal impairment.

Keywords Multiple myeloma · Bisphosphonates · Renal function · Dosing

Introduction

Multiple myeloma is a common hematologic cancer in the USA, with an annual incidence of 6.5 per 100,000 persons, which increases with age until approximately 74 years [1]. The median age at diagnosis is approximately 70 years, and the prevalence of multiple myeloma is increasing, likely due to increased life expectancy in the population [2]. Although

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multiple myeloma is incurable, it is a treatment-responsive cancer, and many patients achieve long-term asymptomatic remission [3].

Osteolytic bone disease is the hallmark of multiple myeloma and is present in approximately 75 to 80% of patients at diagnosis, depending on the detection method used [4, 5]. The severity of bone destruction typically correlates with disease burden and prognosis [4, 6]. Osteolytic lesions are caused by an imbalance between osteclastic and osteoblastic activities [4].

Bisphosphonates are the standard of care recommended for managing bone disease in patients with myeloma: the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), the Mayo Clinic, and European Myeloma Network panels advocate monthly treatment with intravenous pamidronate or zoledronic acid for patients with lytic bone disease [7]. Bisphosphonates inhibit osteoclastic activity while also possibly eliciting an indirect anti-myeloma effect [4]. Evidence from clinical trials indicates that the use of bisphosphonates is associated with fewer skeletal-related events (clodronate and pamidronate vs placebo; zoledronic acid vs clodronate or pamidronate) and possibly greater overall survival and progression-free survival (zoledronic acid vs clodronate) [7–10]. However, there is no clinical consensus on whether to continue, reduce, or stop bisphosphonates in patients who achieve a good response with primary myeloma therapies. Furthermore, bisphosphonates are associated with renal dysfunction; close monitoring of creatinine clearance (CrCl) with dose reductions in patients with reduced renal function is recommended [11, 12]. Patients with multiple myeloma are already at an increased risk of renal impairment: it has been estimated that 46% of patients with multiple myeloma have impaired renal function at the time of diagnosis and 61% of patients with multiple myeloma develop renal impairment at some point in the course of the disease [13, 14]. Thus, renal impairment needs to be considered when optimizing treatment of bone disease for patients with multiple myeloma.

Data are limited on the real-world use of intravenous bisphosphonates in patients with multiple myeloma. The primary objective of this analysis was to describe treatment patterns of bisphosphonate use in patients with multiple myeloma, with a focus on dosing, concomitant anti-myeloma therapy, and changes in dosing by renal function.

Methods

Study design

This retrospective observational study used oncology electronic health record (EHR) data contained in Amgen's Oncology Services Comprehensive Electronic Records (OSCER) database, generated by Flatiron Health (New York, NY, April 30, 2016). OSCER represents a longitudinal, demographically and geographically diverse database containing data from over 250 cancer clinics representing over 1.5 million active US patients treated at community-based hematology/oncology practices and from three academic centers in the USA. Patients represent all payer types (commercial, Medicare, Medicaid, self-pay, and other). The de-identified patient-level data include structured (diagnostic details, laboratory values, and prescribed drugs) and unstructured data collected via technology-enabled chart abstraction from physician's notes and other unstructured documents. The Institutional Review Board of each oncology practice approved collaboration to contribute data to a large longitudinal EHR database; informed patient consent was waived per the US framework for retrospective noninterventional studies. Individual patient-level data were protected against breach of confidentiality consistent with the final Health Insurance Portability and Accountability Act (HIPAA) Security Rule from the US Department of Health and Human Services.

Eligibility criteria

Eligible patients were those newly diagnosed with multiple myeloma between January 1, 2009, and April 30, 2016. Diagnosis was defined as International Classification of Diseases, Ninth Revision (ICD-9) diagnosis of 203.00 or ICD-10 diagnosis of C90.00, with an available diagnosis date, and an office visit or treatment recorded within 1 month of diagnosis. Patients were excluded if they received anti-multiple myeloma therapy or a bisphosphonate before diagnosis. Patients were followed from the index date (initial diagnosis date for multiple myeloma) until the end of the study period (April 30, 2016) or loss to follow-up or death.

Objectives

The primary study objectives were to estimate the proportion of patients with multiple myeloma receiving bisphosphonates, to estimate the average time from diagnosis to treatment with bisphosphonates, to describe dosing schedules with bisphosphonates, and to understand when bisphosphonates are administered relative to therapy lines and regimens for multiple myeloma. Secondary objectives were to identify predictors of initiation of treatment with bisphosphonates and to conduct additional analyses stratified by chronic kidney disease stage (per Kidney Disease Outcomes Quality Initiative [KDOQI]) classification.

Analysis

Bisphosphonate treatment was defined by the intravenous administration of pamidronate or zoledronic acid, including dates of administration for each patient. The dosing schedules

analyzed for the bisphosphonates were less than every 4 weeks (< Q4W), Q4W, > Q4W and < Q12W, Q12W, and > Q12W, which were calculated as the time between two administrations of bisphosphonate. Gaps greater than 100 days (with patient alive and present in the database for the entire 100 days) were considered discontinuations. Switched dosing schedules were described as follows: the patient was initially on one dosing schedule and the next administered doses were more/less spaced apart; the date of the switch was the date of the first bisphosphonate administration on the new schedule. Reinitiation was defined as a patient restarting treatment after a discontinuation. The duration of treatment was calculated from the date of initiation to the end of treatment, less any time discontinued.

Timing of bisphosphonates, ever receipt of bisphosphonates, and the frequency of bisphosphonate treatment were summarized by time from diagnosis, anti-myeloma therapy, and CKD stage (measured by estimated glomerular filtration rate [eGFR]) [15]. eGFR was calculated as outlined by Levey et al. [16]. Patient counts, percentages, means, and medians were calculated for relevant endpoints. Renal impairment at baseline was defined by the Cockcroft-Gault formula for estimated creatinine clearance rate < 60 mL/min.

Anti-myeloma line of therapy and regimen were established based on the 90-day window upon the first administered treatment. All drugs administered in the first 90 days would be considered as a regimen. A line of therapy would end after a 90-day gap for all drugs in that regimen. Alternatively, the initiation of a new drug that was not adjunctive to the existing regimen would be considered as starting a new line.

To assess predictors of receiving bisphosphonates, a multivariate Cox regression analysis was used to assess demographic and clinical covariates. Additionally, a sensitivity analysis using only patients with at least 2 years of follow-up was conducted to assess the robustness of the analysis.

Table 1 Patient demographics and disease characteristics

Characteristic	Patients, *n* (%)
Sex, *n* (%)	
Female	4944 (44.5)
Male	6168 (55.5)
Age at diagnosis, years	
18–39	101 (0.9)
40–49	511 (4.6)
50–64	3168 (28.5)
65–74	3603 (32.4)
≥ 75	3729 (33.6)
Insurance type	
Commercial	3152 (28.4)
Medicare	5244 (47.2)
Medicaid	144 (1.3)
Other	1102 (9.9)
Unknown	1470 (13.2)
Multiple myeloma stage at diagnosis	*N* = 2897
Stage I	532 (18.4)
Stage II	743 (25.6)
Stage III	1612 (55.6)
Unknown	10 (0.3)
Analgesic use	
Yes	3021 (27.2)
No	8091 (72.8)
Renal impairment[a]	*N* = 8168
Yes	3779 (46.3)
No	4389 (53.7)
CKD stage (eGFR)	*N* = 7,445[b]
Stage 1 (> 90)	1304 (17.5)
Stage 2 (60–89)	2749 (36.9)
Stage 3A (45–59)	1276 (17.1)
Stage 3B (30–44)	1041 (14.0)
Stage 4 (15–29)	677 (9.1)
Stage 5 (< 15)	398 (5.3)

CKD chronic kidney disease, *eGFR* estimated glomerular filtration rate, mL/min/1.73m^2

[a] Renal impairment was calculated only for those with available data and was defined by Cockcroft-Gault formula estimated creatinine clearance rate < 60 mL/min; renal impairment status unknown in 2944 patients

[b] CKD stage unknown in 3667 patients

Results

Patients

Patient demographics and baseline characteristics are shown in Table 1. The majority of patients were men (55.5%) and aged ≥ 65 years (66.0%); accordingly, about one half of the patients had Medicare insurance. Under half (46.3%) of the patients had renal impairment. Overall, most patients (85.6%) were classified as CKD stages 1–3 (Table 1).

Overall bisphosphonate use

The median (Q1, Q3) length of follow-up was 687 (293, 1208) days; the average follow-up time was 818 days (Table 2). A total of 7013 (63%) patients received any bisphosphonate during follow-up; 6180 patients received zoledronic acid only and 489 patients received pamidronate only. The median (Q1, Q3) time from diagnosis to first bisphosphonate administration was 29 (11, 78) days (mean = 106 days). The median (Q1, Q3) duration of |bisphosphonate treatment was 380 (180, 716) days (mean = 498 days). Among initiators of bisphosphonates, 58% of patients started treatment in the first

Table 2 Patients who received bisphosphonate treatment, time from diagnosis, and duration of treatment

	Overall		Time after diagnosis, days					
			1–365		366–730		731+	
	N/mean	%	*N*/mean	%	*N*/mean	%	*N*/mean	%
Newly diagnosed cases with follow-up	11,112	100	11,112	100	7759	70	5331	48
Patients who received any bisphosphonate	7013	63	7013	63	5288	68	3677	69
Timing of first administration	NA	NA	6463	58	334	4	216	4
Ever discontinued or changed dosing	5766	52	4673	42	3021	39	2037	38
Total number of administration events	87,319	100	44,006	100	24,113	100	19,200	100
< Q4W dosed administrations	1802	2.1	1031	2.3	417	1.7	354	1.8
Q4W dosed administrations	59,108	67.7	30,535	69.4	17,523	72.7	11,050	57.6
> Q4W and < Q12W	10,361	11.9	4189	9.5	3226	13.4	2946	15.3
Q12W	4186	4.8	697	1.6	1191	4.9	2298	12.0
> Q12W	1040	1.2	194	0.4	285	1.2	561	2.9

Q4W every 4 weeks, *Q12W* every 12 weeks

year after diagnosis. Supplemental Fig. 1 shows the distribution of time between sequential administrations of bisphosphonates; close to one half of all administrations were given 28 days apart, consistent with 68% of all doses administered Q4W (Table 2). The average number of doses given in the first year was 6.8.

A sensitivity analysis was undertaken for patients with at least 2 years (731 days) of follow-up, which included 5331 patients with a median (Q1, Q3) follow-up time of 1241 (957, 1637) days (mean = 1345 days). Overall, 69% of patients received any bisphosphonate, largely consistent with the primary analysis.

Discontinuations and dose changes of bisphosphonates

Most patients (5766/7013; 82%) who received bisphosphonate therapy either discontinued or changed dosing at least once during the study period (Table 2). Of these patients, 4325 (62%) patients discontinued treatment and 4554 (65%) patients restarted or switched dosing schedules during the study period (Table 2). The median (Q1, Q3) duration of bisphosphonate treatment for patients who discontinued was 219 (128, 412) days (mean = 318 days). Of the 19,760 restarted/switching events, 46% were to a less frequent dosing schedule and 46% were to a more frequent dosing schedule. The percentage of patients with a less frequent dosing schedule (> Q4W to < Q12W) increased by year since diagnosis, from 9.5% during the first year since diagnosis to 15.3% during the third year since diagnosis. Similarly, the percentage of patients on Q12W dosing increased from 1.6% for the first year since diagnosis to 12.0% for the third year since diagnosis. When examining discontinuation or dose change by time since diagnosis of multiple myeloma (i.e., 1, 2, or 3 years), proportions were roughly equivalent across the categories: 69% for those diagnosed between 2009 and 2010, 63% for those diagnosed between 2011 and 2012, and 58% for those diagnosed between 2013 and 2014.

Concomitant therapy

Table 3 lists the numbers and types of concomitant therapies for multiple myeloma that patients received during bone-targeting therapy. In this cohort, all patients received first-line anti-multiple myeloma therapy; 43% received second-line therapy, and 19% received third-line therapy. The most common first-line regimens for multiple myeloma included bortezomib, bortezomib + lenalidomide, and lenalidomide. Of all the lines examined, concomitant bisphosphonates began primarily during first-line anti-multiple myeloma therapy. Few patients received bisphosphonates between lines of therapy for multiple myeloma. Overall, 52% of patients received a concomitant bisphosphonate during first-line therapy for multiple myeloma; concomitant use during the second and third lines was similar, at 52 and 48%, respectively (Table 3).

Effects of renal dysfunction

The cumulative incidences of bisphosphonate treatment by baseline CKD stage are presented in Fig. 1. Patients with poorer renal function (i.e., higher CKD stage) at baseline were less likely to receive a bisphosphonate compared with patients with worse CKD stage at baseline. Receipt of

Table 3 Concomitant bisphosphonate treatment with anti-multiple myeloma treatment

Timing of bisphosphonate administration	Patients who received anti-multiple myeloma therapy, *n*	Patients who received a concomitant bisphosphonate, *n* (%)	Patients who received a bisphosphonate for the first time, *n* (%)
Prior to anti-multiple myeloma treatment	11,112	1426 (13)	1426 (13)
First-line treatment	11,112	5767 (52)	4675 (42)
Between first and second lines	11,110	1985 (18)	289 (3)
Second-line treatment	4752	2473 (52)	210 (4)
Between second and third line	4749	814 (17)	37 (1)
Third-line treatment	2111	1017 (48)	45 (2)
First-line regimens[a]			
Single agent[a]			
Bortezomib	3344	1764 (53)	1418 (42)
Lenalidomide	2180	848 (39)	563 (26)
Carfilzomib	107	45 (42)	30 (28)
Multiple agents[a]			
Bortezomib + lenalidomide	2497	1731 (69)	1507 (60)
Bortezomib + cyclophosphamide	1394	787 (56)	704 (51)
Bortezomib + cyclophosphamide + lenalidomide	170	118 (69)	102 (60)

[a] First-line regimens were all assumed to include dexamethasone, as OSCER does not adequately capture oral medications

bisphosphonates was delayed among patients with worse CKD stage compared with patients with better classification among patients who received bisphosphonates (Table 4). Patients with poorer renal function during follow-up (CKD stages 4–5) were less likely to receive a bisphosphonate within the next 6 months compared with patients with a better function (CKD stages 1–3).

Potential factors associated with bisphosphonate treatment

We also examined if year of diagnosis had an influence on whether patients received treatment with a bisphosphonate. From 2009 to 2010, of the patients diagnosed, 874 (72%) received bisphosphonates, with a median of 1986 days of

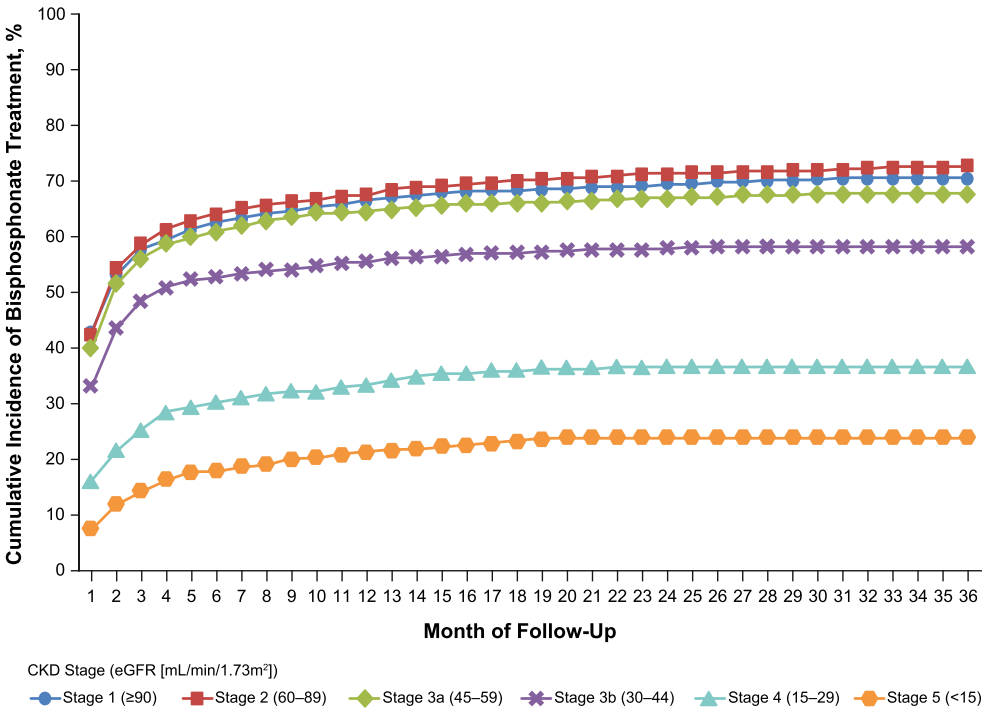

Fig. 1 Cumulative incidence of intravenous bisphosphonate treatment by CKD classification stage at baseline. CKD chronic kidney disease, eGFR estimated glomerular filtration rate

Table 4 Patients who received intravenous bisphosphonates by CKD stage

Lowest CKD stage (eGFR in mL/min/1.73m^2)	N^a	Patients who received a bisphosphonate, *n* (%)	Median (Q1, Q3) time to bisphosphonate, days	Percentage of patients who received a bisphosphonate, %	
				6 months prior to lowest eGFR	6 months after lowest eGFR
Stage 1 (> 90)	1304	942 (72)	25 (11, 65)	48	82
Stage 2 (60–89)	2749	2028 (74)	25 (10, 66)	51	79
Stage 3A (45–59)	1276	871 (68)	23 (9, 59)	51	76
Stage 3B (30–44)	1041	610 (59)	25 (10, 63)	56	73
Stage 4 (15–29)	677	250 (37)	39 (11, 110)	61	63
Stage 5 (< 15)	398	96 (24)	70 (23, 190)	54	43

CKD chronic kidney disease, *eGFR* estimated glomerular filtration rate, *Q1* first quartile, *Q3* third quartile

[a] Includes patients with known CKD stage; 3667/11,112 (33.1%) patients had unknown CKD stage

follow-up. From 2011 to 2012, of the patients diagnosed, 1905 (68%) received bisphosphonates, with a median of 1344 days of follow-up. From 2013 to 2014, of the patients diagnosed, 2517 (63%) received bisphosphonates, with a median of 754 days of follow-up. Some patients may receive bisphosphonates more than 2 years after diagnosis, although that number is relatively low. The time from diagnosis to treatment was similar regardless of year of diagnosis: patients diagnosed 2009–2010, 2011–2012, and 2013–2014 had similar median (Q1, Q3) times to starting bisphosphonates, which were 31 (9, 176), 29 (11, 103), and 29 (12, 81) days, respectively. Patients diagnosed in 2015 or 2016 had an insufficient length of follow-up and thus were excluded in this analysis. The impact of baseline factors and disease characteristics on receiving an intravenous bisphosphonate was also examined; these results are listed in Table 5.

Discussion

This study examined patterns of treatment with intravenous bisphosphonates in patients with multiple myeloma from a large US-based EHR database. We found that less than two thirds of patients with multiple myeloma received treatment with a bisphosphonate, typically within the first year of diagnosis. Patients mostly received bisphosphonates on a Q4W schedule; however, most patients experienced at least one interruption in dosing. The majority of patients started their bisphosphonate during first-line therapy for multiple myeloma. Renal dysfunction and CKD stage were associated with a lower likelihood of receiving a bisphosphonate. Guidelines generally recommend bisphosphonates in all patients with multiple myeloma or all patients with bone disease [7, 17, 18]; therefore, the two thirds of patients with multiple myeloma who received treatment with bisphosphonates in our analysis is suboptimal based on clinical guidelines. The treatment rate in our study is higher than in a previous study that found that approximately 40% of patients with multiple myeloma received intravenous bisphosphonates [19]; this difference is likely due to varying inclusion criteria, particularly the requirement in our study that patients were seen in the oncology clinic within 1 month of diagnosis, thus insuring active follow-up in the database. Of interest, few patients received denosumab ($n = 155$), but its use was sporadic and minimal; therefore, these patients were not included in the main analysis.

Among patients that received a bisphosphonate, 92% received this treatment within 1 year after myeloma diagnosis. With respect to timing of bisphosphonates with multiple myeloma therapy, most patients received bisphosphonates concomitant with first-line anti-myeloma therapy. Most bisphosphonates were dosed Q4W as recommended, but the majority of patients had interruptions in their dosing, leading to an average of 6.8 administrations in the first year of multiple myelomas diagnosis. Additionally, many patients moved to a less frequent dosing schedule over time, particularly in the 2 years after multiple myeloma diagnosis. The duration of administration of bisphosphonates was consistent with the current guidelines by the International Myeloma Working Group (IMWG), which recommend that bisphosphonates be administered for at least 12 to 24 months, and then at the physician's discretion, because the optimal treatment duration remains unclear [7, 20].

Although the alterations in dosing represent deviations from the current guidelines, the dosing patterns observed in this study are aligned with a recent study investigating Q4W versus Q12W dosing in patients with metastatic breast cancer, prostate cancer, or multiple myeloma, which found that the longer dosing interval did not increase the risk of skeletal-related events over the course of the 2-year study [21].

Table 5 Baseline covariate predictors associated with receiving intravenous bisphosphonates

Parameter	Reference class value	Class value	HR (95% CI)
Age at diagnosis			0.997 (0.994–0.999)
Gender	Male	Female	1.112 (1.060–1.167)
Race	White	Black	0.833 (0.771–0.899)
		Asian	0.794 (0.630–1.000)
		Hispanic	1.205 (0.683–2.128)
		Other	0.910 (0.829–0.999)
		Unknown	1.043 (0.905–1.202)
Region	Northeast	Midwest	0.948 (0.872–1.030)
		South	0.933 (0.874–0.997)
		West	0.993 (0.909–1.086)
		Unknown	0.952 (0.729–1.244)
Insurance type	Commercial	Medicare	1.019 (0.960–1.080)
		Medicaid	0.950 (0.772–1.168)
		Other	0.964 (0.884–1.050)
		Unknown	0.721 (0.573–0.909)
BMI	< 25	25–29	1.050 (0.984–1.120)
		≥ 30	0.950 (0.887–1.018)
		Unknown	0.886 (0.771–1.019)
Stage of MM diagnosis	Stage I	Stage II	1.464 (1.275–1.681)
		Stage III	1.584 (1.399–1.794)
Analgesic use	No	Yes	1.492 (1.416–1.573)
Renal impairment[a]	No	Yes	0.852 (0.788–0.922)
		Unknown	0.700 (0.600–0.815)
CKD stage (eGFR)[b]	Stage 1 (≥ 90)	Stage 2 (60–89)	1.015 (0.936–1.101)
		Stage 3A (45–59)	0.968 (0.872–1.074)
		Stage 3B (30–44)	0.751 (0.665–0.849)
		Stage 4 (15–29)	0.364 (0.311–0.427)
		Stage 5 (< 15)	0.222 (0.178–0.277)
		Unknown	0.824 (0.699–0.972)
Hypercalcemia	No	Yes	1.893 (1.740–2.058)
		Unknown	1.182 (1.074–1.301)
Anemia	No	Yes	1.039 (0.976–1.107)
		Unknown	1.005 (0.906–1.115)

BMI body mass index, *CrCl* creatinine clearance, *eGFR* estimated glomerular filtration rate, *HR* hazard ratio, *MM* multiple myeloma

[a] Defined by Cockcroft-Gault formula for estimated creatinine clearance rate < 60 mL/min

[b] Expressed as mL/min/1.73m^2

Patient CKD stage strongly influenced bisphosphonate treatment, which is consistent with guidelines for multiple myeloma, indicating that bisphosphonates are not recommended in patients with eGFR < 30 mL/min/1.73m^2 (CKD stages 4–5) [7]. Patients with worse CKD stage at baseline were less likely to receive bisphosphonates than patients with better classification. Up to 72% of patients with baseline CKD stage 1–3 received bisphosphonates versus 32% of patients with CKD stages 4–5. Generally, these patterns were inconsistent with NCCN and ASCO guidelines, which recommend that all patients with adequate renal function to receive bisphosphonate treatment [7, 18].

Patients with multiple myeloma are at risk for impaired renal function, primarily due to excess monoclonal light chain production and hypercalcemia [22]. Impaired renal function has been associated with reduced survival [13, 23]. Improvement in renal function may increase survival; however, survival remains inferior to patients with normal renal function at diagnosis [13, 24]. In addition to intravenous bisphosphonates, anti-multiple myeloma drugs such as lenalidomide require dose adjustments in patients

with impaired renal function [25]. In this study, we found that renal function significantly affected the likelihood of receiving treatment with an intravenous bisphosphonate. These results suggest that therapies that do not adversely affect kidney function are needed to prevent skeletal-related events in this patient group.

A notable strength of this study was the large population of patients with multiple myeloma. This population represents health-related encounters from oncology practices across the USA and represents geographic diversity as well as multiple EHR systems, payer types, and clinical pathways. These patient-level data are captured systematically and electronically from the same EHR used by practitioners to track patient care at each of the participating centers, which results in improved consistency. Our analysis was limited by unknown or missing information in some fields such as stage and ECOG at diagnosis (data not shown), which limited our model estimation for those covariates. We did not collect information on reasons for discontinuation or changes in dosing of bisphosphonates. The major limitation of this study is that a patient's history and incidence of skeletal-related events relative to bone-targeting treatment and interruption of treatment could not be assessed in this database. Future analyses will focus on assessing skeletal-related events at multiple myeloma diagnosis and during follow-up. Lastly, there are several known risks associated with bisphosphonate use [26, 27] that were not captured in the OSCER database, and therefore cannot be reported in our study.

In conclusion, this retrospective study, using a large real-world oncology database, showed that many patients with multiple myeloma might not receive optimal therapy for bone disease, particularly those with renal dysfunction.

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Compliance with ethical standards

The Institutional Review Board of each oncology practice approved collaboration to contribute data to a large longitudinal EHR database; informed patient consent was waived per the US framework for retrospective noninterventional studies.

Conflict of interest CK, RKH, and AL are current employees of and own stock in Amgen Inc. CK was provided travel expense to ASH conference for presentation of this work. PCC is a former employee of Amgen Inc. and is currently employed by Kite Pharma Inc. LC has no conflict of interest to disclose.

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