Patterns and Predictors of First-Line Therapy Use Among Newly Diagnosed Multiple Myeloma Patients Ineligible for Stem Cell Transplant in an Integrated Healthcare System

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Citation

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Abstract

Objective: To identify the treatment patterns of newly diagnosed multiple myeloma patients who were ineligible for stem cell transplant and initiated on a first line chemotherapy. Also to identify factors associated with first line treatment choice in an integrated healthcare delivery system in the U.S.

Methods: We identified a retrospective cohort of incident MM patients ineligible for stem cell transplant from January 1, 2006 to December 31, 2010 using the Kaiser Permanente Southern California (KPSC) cancer registry. First line therapy was identified and start date labeled as index date. Patients were >18 years old on the index date; and had at least 6 months of membership and drug eligibility prior to the index date. Patient and clinical characteristics were described and a multivariate stepwise logistic regression model was used to evaluate characteristics such as age, gender, race, comorbid conditions, and concomitant therapies to examine predictive factors associated with first line treatment choices.

Results: The final cohort consisted of 599 newly diagnosed MM patients (mean age 70 years, men 53%). First line therapy was identified, and the majority of the patients were initiated on either thalidomide containing regimens (39%), or conventional therapies (31%). Within this integrated system, factors such as age, comorbidity score, and renal function were factors that were associated with physicians' first line treatment choice as well as use of concomitant therapies.

Conclusion: Many new therapies are becoming available; however this work helps us understand some prescribing patterns prior to newer agents becoming available. Patient and clinical factors such as age, comorbidity score and renal function were associated with physicians' first line treatment choice and concomitant medication use. It is good to evaluate changes in treatment choices prior to newer therapies.

Multiple myeloma (MM) is an incurable malignant neoplasm that accounts for 1% of all cancers and 10% of hematological malignancies. In 2013, it was estimated that 22,350 new cases of MM were diagnosed and 10,710 patients died from MM in the United States [1]. MM affects older individuals; the median age at diagnosis is 70 years and two-thirds of MM patients are 65 years and older when diagnosed [2,3]. The increased life-expectancy of the general population is showing an increase in the number of elderly MM patients [2-5]. The common complications or symptoms that arise from MM are hypercalcemia, renal insufficiency, anemia, and lytic bone lesions [6,7].

Although MM remains incurable, significant advances have occurred over the past decade in treatments for MM, leading to a paradigm shift [8-10]. Increased survival is reflective from the novel therapies that have evolved, such as immunomodulatory agents: thalidomide, lenalidomide, pomalidomide; and protease inhibitors: bortezomib, carfilzomib. Through various clinical trials [9-15], these therapies have shown to improve overall survival as single agents and or in combination with standard conventional therapies containing chemotherapy (i.e cyclophosphamide, melphalan, doxorubicin), or corticosteroids (prednisone, dexamethasone). While standard of care was previously melphalan and prednisone; as a result of newer agents, clinicians are now in a position to choose from a variety of

treatment options for the management of newly diagnosed and relapsed MM patients [8-11]. Currently, initial treatment choices from physicians are based on clinical evidence (randomized clinical studies), guidelines [4,5,16,17], and patient characteristics (age, cyotgenetics, and presence of comorbidities).

Although current novel medications are showing great promise and scientific evidence is helping physicians make treatment choices, there are limited published studies on real-world treatment utilization and factors associated with first line treatment choices among patients with newly diagnosed MM. We conducted a retrospective database analysis to evaluate patient and clinical characteristics of newly diagnosed MM patients ineligible for stem cell transplant (SCT) and identify factors associated with first line treatment choices using an integrated healthcare system.

MATERIALS AND METHODS

Study Setting and Data

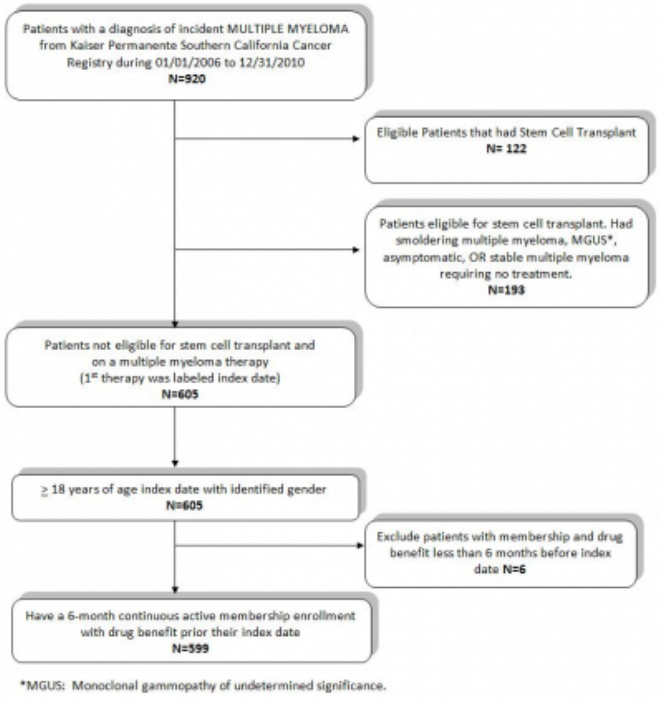
Kaiser Permanente Southern California (KPSC) is an integrated healthcare delivery system with approximately 3.6 million members located in Southern California. Data were derived from the KPSC Health Plan (KPSC HP) database and The Kaiser Permanente Regional Cancer Registry (CANREG) database. The KPSC HP database contains information on patient demographics, diagnoses, prescriptions, laboratory results, medical and hospital encounters from the 14 medical centers. KPSC HP has an electronic health medical record system (EMR) which allows for more detailed information to be accessed and included in studies. The CANREG database contains information on newly diagnosed patients or patients who received at least part of their first course of treatment for cancer at a KPSC facility. The CANREG data is provided to the Surveillance, Epidemiology, and End Results (SEER) program, of the National Cancer Institute, which collects cancer data in the U.S. and compiles national cancer statistics. The KPSC membership currently represents 15% of the underlying population in the Southern California region and this membership closely mirrors the Southern California population; it is racially diverse and includes the entire socioeconomic spectrum [18,19]. The institutional review board for KPSC approved this study.

Design and Study Population

A retrospective cohort database analysis was conducted during the study enrollment period of January 1, 2006 to December 31, 2010. Patients were selected from the KPSC CANREG database with diagnosis of MM. Patients with a history of SCT within 6 months prior were excluded. Only patients ineligible for SCT and received chemotherapy only were included in the analyses. Further exclusions were applied to patients not requiring any therapy such as smoldering, asymptomatic, or stable MM disease. These patients were further chart reviewed to ensure that they had smoldering, asymptomatic, or stable MM disease. The index date was defined as the start date of the first prescription to treat MM. Eligible patients were required to be aged ≥18 years on index date and have at least 6 months of continuous membership with drug eligibility prior to the index date. Enrollment gaps of ≤30 days were considered continuous enrollment. Patients were followed until there was a switch to a second line therapy, death, disenrollment from the health plan, or end of the study time period (December 31, 2012); whichever occurred first (Figure 1).

Figure 1

OVERVIEW OF THE STUDY COHORT



Covariates and Measures

We identified the patients' first line therapy between 2006 and 2010. We evaluated baseline characteristics such as age, sex, race, insurance plan, comorbid conditions, concomitant medication use, and renal function during the 6 month pre-index period. Renal function was evaluated using pre-index

period glomerular filtrate rate (GFR) lab values closest to the index date. Using the National Kidney Foundation stages for chronic kidney disease (CKD), we categorized CKD in the following stages based on GFR: (Stage 1: ≥90 ml/min, Stage 2: 60-89 ml/min, Stage 3: 30-59 ml/min, Stage 4: 15-29, and Stage 5: <15ml/min). International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes was used to identify MM related and other comorbidities from all health encounters. Bone disease consisted of lytic lesions, osteopenia, and fractures. Concomitant therapies were therapies identified using pharmacy claims that may have been used for management of MM symptoms or used for preventive care for side effects associated with some of the MM therapies were prescribed. Bisphosphonate therapies consisted of pamidronate or zoledronic acid. Treatments for peripheral neuropathy consisted of pregabalin, gabapentin, amitryptiline, venlafaxine, or duloxetine. Prophylaxis for herpes zoster consisted of antivirals (acyclovir, valacyclovir, and famciclovir). Antithrombotic therapies consisted of enoxaparin, low molecular weight heparin, warfarin, and aspirin.

Identification of First Line Therapy

A first line therapy (oral and injectable) was identified based on pharmacy claims during the study period and the start date was labeled as the index date. To ensure the patient was not on a prior MM therapy, we looked at a maximum of 24 months prior to the index date. Treatment regimens were categorized into bortezomib containing regimens (BCR), lenalidomide containing regimens (LCR), thalidomide containing regimens (TCR), immunomodulatory drug (IMiD) plus protease inhibitor (IMiD/PI) combination regimens which contained either lenalidomide or thalidomide with bortezomib; and conventional standard therapies which did not contain bortezomib, thalidomide, lenalidomide or IMiD/PI combinations. Conventional standard therapies consisted of any of the following: chemotherapy (carmustine, cisplatin, cyclophosphamide, dacarbazine, etoposide, melphalan, vincristine, doxorubicin); or corticosteriods (prednisone, dexamethasone).

Statistical methods

Descriptive statistics were used to summarize patient and clinical characteristics of the study population and their initial therapies. Differences between the patient groups were tested using two-sided t test for continuous variables and the chi squared statistic for categorical variables. Comorbidities were categorized into patients with one comorbidity, two comorbidities, and three or more comorbidities which could be applied into the regression. Predictors were assessed using multivariate stepwise regression. We identified potential predictors that were selected based on clinical significance with an emphasis on factors associated with comorbidities and concomitant therapies as-well-as other factors that may impact treatment choice. The significance level for deciding when to enter a predictor into the stepwise model was kept at 0.15. All data were analyzed using SAS version 9.2 (SAS Institute, Cary, NC). P-values <0.05 were considered to be statistically significant.

RESULTS

There were 920 patients identified from the KPSC Cancer Registry with newly diagnosed MM. After applying the inclusion and exclusion criteria (Figure 1), the final cohort identified was 599 patients with newly diagnosed MM (mean age 70 years, men 53%). Table 1 summarizes baseline characteristics of the final cohort and their respective first line therapies. First line therapy was identified for each patient, categorizing patients into the following groups: bortezomib containing regimens (BCR, N=80), lenalidomide containing regimens (LCR, N=97), thalidomide containing regimens (TCR, N=232), immunomodulatory drug plus protease inhibitor combination regimen (IMiD/PI, N=4), and conventional therapies (CON, N=186). The majority of patients were on either TCR (39%) or CON therapies (31%). Table 1 summarizes baseline characteristics of the final cohort and their respective first line therapies. The average duration of follow up was 2.4 (±1.2) years from index date, and patients were predominantly White (49%) with the majority of patients being 65 years and older in age (72%). All patients had at least 1 comorbidity. The most common comorbidities were hypertension (HTN, 70%), diabetes (DM, 41%), and chronic obstructive pulmonary disease (COPD, 20%). The mean baseline GFR was 55.1 (±24.3) ml/min, with the majority of patients categorized into either CKD stage 2 (31%) or CKD stage 3 (26%) with GFRs of 60-89 mL/min or 30-59 mL/min, respectively. The majority of the patients were prescribed a therapy for peripheral neuropathy (55%), with a few on bisphosphonates (5%) or antithrombotic therapies (5%).

Table 1

Patients Characteristics	Multiple Myeloma Patients Ineligible For Stem Cell Transplant	BORTEZOMIB THERAPY (BCR)	LENALIDOMIDE THERAPY (LCR)	THALIDOMIDE THERAPY (TCR)	IMiD/PI** COMBINATION THERAPY (IMiD/PI)	CONVENTIONAL THERAPY (CON)
Characteristics	Total Patients					
	N = 599	N = 80	N = 97	N = 232	N= 4	N= 186
Duration of Follow-up, mean, years	2.4±1.2	1.5±0.8	2.3±1.4	2.8±1.7	2.4±1.7	2.5±1.8
Duration of Treatment, mean, days	184.5±122.4	94.7±96.4	186.2±115.7	189.2±129.5	113.8±134.2	157.7±151.7
Male patients, n (%)	319 (53.3%)	44 (55.0%)*	58 (59.8%)*	120 (51.8%)	3 (75.0%)	89 (47.8%)
Patients Age, mean, SD	69.9±11.3	69±10.3*	69.9±9.7*	69.4±11.7*	55.1±15.9*	71.9±10.8
BMI (kg/m^2)	27.8±6	28.2±5.5	27.4±5.7	27.2±5.4	25.8±3.9*	28.7±6.3
Radiation prior 6 months, n (%)	73 (11.7%)	9 (11.3%)	12 (12.4%)	26 (11.2%)	1 (25.0%)*	22 (11.8%)
Patient Age Categories, n(%)	N = 599	N = 80	N = 97	N = 232	N= 4	N= 186
44 and less	6 (1.0%)	1 (1.3%)	–	3 (1.3%)	–	2 (1.1%)
45 to 54	42 (7.0%)	9 (11.3%)*	9 (9.3%)*	12 (5.2%)	2 (50.0%)*	10 (5.4%)
55 to 64	122 (20.4%)	16 (20.0%)*	16 (16.5%)	57 (24.6%)*	1 (25.0%)*	32 (17.2%)
65 or more	429 (71.6%)	54 (67.5%)*	72 (74.2%)	160 (69.0%)*	1 (25.0%)*	142 (76.3%)
Race, n(%)	N = 599	N= 80*	N=97*	N= 232*	N= 4*	N= 186
White	293 (48.9%)	37 (46.3%)	53 (54.6%)	97 (41.8%)	3 (75.0%)	103 (55.4%)
Black	137 (22.9%)	13 (16.3%)	20 (20.6%)	60 (25.9%)	1 (25.0%)	43 (23.1%)
Hispanic	120 (20.0%)	20 (25.0%)	17 (17.5%)	51 (22%)	–	32 (17.2%)
Asian/Pacific Islander	37 (6.2%)	7 (8.8%)	7 (7.2%)	18 (7.8%)	–	5 (2.7%)
Other	12 (2.0%)	3 (3.8%)	–	6 (2.6%)	–	3 (1.6%)
Insurance Type, n (%)	N = 599	N = 80	N = 97	N = 232	N= 4	N= 186
Commercial	599 (100%)	80 (100%)	97 (100%)	232 (100%)	4 (100%)	186 (100%)
Medicare	403 (67.3%)	49 (61.3%)*	63 (64.9%)*	155 (66.8%)*	–	136 (73.1%)
Renal Function Lab Data, n (%)	N = 599	N = 80	N = 97	N = 232	N= 4	N= 186
GFR (mL/min/1.73m2), mean, SD	55.8±24.35	62.46±21.96*	49.33±26.42*	53.55±23.9*	48.5±26.69*	56.91±24.5
CKD stage 1	87 (14.5%)	6 (7.5%)*	42 (43.3%)*	19 (8.2%)*	1 (25%)*	19 (10.2%)
CKD stage 2	186 (31.1%)	25 (31.3%)	25 (25.8%)*	79 (34.1%)*	1 (25%)*	57 (30.6%)
CKD stage 3	158 (26.4%)	21 (26.3%)*	10 (10.3%)*	74 (31.9%)*	–	53 (28.5%)
CKD stage 4	56 (9.3%)	13 (16.3%)*	6 (6.2%)	26 (11.2%)*	–	11 (5.9%)
CKD stage 5	42 (7.0%)	10 (12.5%)*	2 (2.1%)*	16 (6.9%)	–	13 (7.0%)
Other Comorbidities, n (%)	N = 599	N = 80	N = 97	N = 232	N= 4	N= 186
Cerebrovascular disease	41 (6.8%)	6 (7.5%)	8 (8.2%)*	13 (5.6%)*	–	14 (7.5%)
Chronic pulmonary disease	118 (19.7%)	22 (27.5%)*	22 (22.7%)	31 (13.4%)*	1 (25.0%)*	42 (22.6%)
Congestive heart failure	69 (11.5%)	9 (11.3%)*	8 (8.2%)*	24 (10.3%)*	–	28 (15.1%)
Diabetes	245 (40.9%)	47 (58.8%)*	34 (35.1%)*	84 (36.2%)*	–	80 (43.0%)
Dyslipidemia	114 (19%)	19 (23.8%)*	21 (21.6%)	31 (13.4%)*	4 (100.0%)*	39 (21.0%)
Hypertension	420 (70.1%)	66 (82.5%)	94 (96.9%)	150 (64.6%)	4 (100.0%)	92 (49.5%)
Myocardial infarction	54 (9%)	5 (6.3%)*	10 (10.3%)	17 (7.3%)*	–	22 (11.8%)
Peripheral vascular disease	38 (6.3%)	7 (8.8%)	4 (4.1%)*	11 (4.7%)*	–	16 (8.6%)
Peripheral Neuropathy	42 (7.0%)	4 (5.0%)	21 (21.6%)	7 (3.0 %)	–	10 (5.4%)
Pneumonia Infection	176 (29.4%)	10 (12.5%)	9 (9.3%)	89 (38.3%)	–	68 (36.6%)
Year of Initial Treatment Prescribed n (%)	N = 599	N = 80	N = 97	N = 232	N= 4	N= 186
2006	161 (26.9%)	4 (5%)	11 (11.3%)	90 (38.8%)	1 (25%)	55 (29.6%)
2007	119 (19.9%)	4 (5%)	13 (13.4%)	64 (27.6%)	1 (25%)	37 (19.9%)
2008	98 (16.4%)	10 (12.5%)	17 (17.5%)	34 (14.7%)	1 (25%)	36 (19.4%)
2009	99 (16.5%)	15 (18.8%)	26 (26.8%)	27 (11.6%)	1 (25%)	30 (16.1%)
2010	122 (20.4%)	47 (58.8%)	30 (30.9%)	17 (7.3%)	–	28 (15.1%)
Concomitant Therapies, n (%)	N = 599	N = 80	N = 97	N = 232	N= 4	N= 186
Bisphosphonate Therapies	33 (5.5%)	15 (18.8%)*	5 (5.2%)*	6 (2.6%)*	–	7 (3.8%)
Therapies for peripheral neuropathy	330 (55.1%)	78 (97.5%)*	40 (42.8%)*	116 (58.8%)	2 (50.0%)	94 (50.5%)
Therapies for Herpes Zoster	22 (3.7%)	15 (18.8%)*	5 (5.2%)*	2 (1.0%)*	–	2 (1.1%)
Antithrombotic Therapies	32 (5.3%)	2 (2.5%)*	5 (5.2%)*	23 (9.9%)*	–	2 (1.1%)

*p-value <0.05 considered statistically significant. Comparing each therapy versus conventional therapy as the reference group by Students test/Chi-squared test/ Fisher Exact Test
** IMiD/PI stands for immunomodulatory drug (Lenalidomide or Thalidomide)/proteasome inhibitor (Bortezomib)

Across all identified first line therapies, more than 50% of the patients were male. Patients on IMiD/PI combination were the youngest in age (mean age 55 years) while patients on CON therapy were older in age (mean age 72 years). There were more black patients in the TCR (26%) and CON groups (23%), however there were more hispanic patients in the BCR group. 73% of the CON group had medicare insurance. Patients prescribed LCR or IMiD/PI therapies had numerically lower mean GFRs, 49.3 ml/min and 48.5 ml/min respectively (Table 1); however patients prescribed BCR had a mean GFR of 62.5 ml/min. The majority of patients initiating BCR had HTN and DM. Patients initiating BCR had the most prior bisphosphonate use (18.8%), peripheral neuropathy therapies (97.5%), and herpes zoster therapies (18.8%). Antithrombotic therapies were prescribed mostly to patients with a TCR or LCR therapy (9.9% and 5.2% respectively).

Evaluating the year the patients initiated their first line therapy, there was a decrease in utilization of thalidomide containing regimens and conventional therapies from 2006 to 2010, while there was an increase in utilization of bortezomib and lenalidomide containing regimens. Using stepwise multivariable analyses, we identified factors that were associated with first line treatment choice (Table 2). Factors associated with patients initiating BCR included being male, older than 65 years of age, hispanic or asian/pacific islander, have more severe CKD, higher comorbidity score, and a higher likelihood of using bisphosphonate, peripheral neuropathy, or herpes zoster therapies. Patients who initiated LCR were more likely to be male, younger in age, have 2 comorbidities, be on antithrombotic therapies, and be less likely to have severe renal dysfunction. Patients initiating TCR were more likely to be female, older in age, Black, have more severe CKD, on antithrombotic therapies, and less likely to have 3 or more comorbidities. Patients on conventional standard therapies were more likely to have 3 or more comorbidities, and less likely to be on concomitant therapies (Table 2).

Table 2

Table 2: Multivariate Logistic Regression Evaluating Factors Associated with 1st Therapy Treatment Choice

Study Covariates	Patients initiated on BCR versus all other therapies	Patients initiated on LCR versus all other therapies	Patients initiated on TCR versus all other therapies	Patients initiated on Conventional Therapies versus all other therapies
Covariates	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)
Male vs females	1.05 (0.82,1.81)	1.15 (0.52,1.89)	0.95 (0.32,1.84)	0.78 (0.42,1.22)
< 65 years of age vs > 65 years	0.88 (0.78,1.11)	**1.73 (1.38,1.98)***	0.82 (0.58,1.08)	0.74 (0.31,1.38)
Race				
White (reference)	1.00	1.00	1.00	1.00
Black	0.71 (0.28,1.78)	1.02 (0.51,2.08)	**1.26 (1.09,2.35)**	1.12 (0.59,2.15)
Hispanic	**1.51 (1.05,2.09)**	0.93 (0.87,1.25)	1.03 (0.78,1.45)	0.91 (0.74,1.34)
Asian/Pacific Islander	**2.52 (1.89,2.78)**	0.91 (0.75,1.77)	0.88 (0.40,1.53)	0.33 (0.10,1.12)
Renal Function Lab Data				
CKD Stage 1-2 (reference)	1.00	1.00	1.00	1.00
CKD Stage 3	**2.21 (1.93,2.62)**	0.86 (0.65,1.79)	**1.84 (1.29-3.02)**	1.12 (0.84,1.93)
CKD Stage 4	**3.53 (2.82,4.23)**	**0.43 (0.21,0.86)**	**1.92 (1.02-2.89)**	0.71 (0.28,1.75)
Comorbidity				
1	0.97 (0.82,1.45)	1.02 (0.63,1.53)	1.59 (0.92,2.54)	0.98 (0.42,1.36)
2	1.25 (0.80,1.83)	**1.92 (1.02,2.57)**	1.11 (0.78,1.89)	1.02 (0.63,1.68)
3+	**1.89 (1.37,2.05)**	0.92 (0.24,1.28)	**0.58 (0.12,0.92)**	**2.25 (1.26,3.62)**
History of Concomitant Therapies				
Bisphosphonate Therapies	**1.54 (1.10,1.84)**	0.88 (0.57,1.02)	0.84 (0.78,1.12)	**0.35 (0.12,0.97)**
Therapies for peripheral neuropathy	**2.12 (1.28,2.61)**	0.63 (0.31,1.06)	1.43 (0.53,1.84)	0.73 (0.43,1.24)
Therapies for Herpes Zoster	**2.54 (1.95,2.82)**	0.55 (0.32,1.21)	0.69 (0.56,1.10)	**0.27 (0.11,0.87)**
Antithrombotic Therapies	0.65 (0.39,1.09)	**1.92 (1.04,2.86)**	**3.54 (1.26,4.01)**	**0.37 (0.14,0.99)**

*bolded numbers mean statistically significant

DISCUSSION

In this study we had the opportunity to evaluate newly diagnosed MM patients and their first line treatments using real world data in an integrated healthcare system. Physicians use guidelines [4,5,16,17] to facilitate the best treatment strategy for each of their patients. Guidelines [4,5] are used to aid physicians in daily clinical practice and ensure optimal care for patients with MM, as well as guidelines for supportive care [20]. Supportive care plays an increasingly important role in the modern management of MM. While modern treatments have significantly prolonged overall and progression free survival through disease control, the disease remains incurable and patients live with the burden of the disease itself along with the cumulative side effects of treatments [8]. In our study, we indirectly see how physicians might be using scientific evidence and guidelines to tailor treatments around a patient's age, number of comorbidities, and the expected toxicity profile of different regimens. The current MM treatment options offer the physicians the opportunity to tailor treatment approaches based on individual patient characteristics.

The elderly population is a heterogeneous group with a spectrum of physical frailty and multiple comorbid conditions (i.e diabetes, renal dysfunction, cardiovascular disease). Tolerability to treatments is also important factor to consider in this elderly population as the efficacy and safety profiles of newer agents are evaluated. For unfit elderly patients, dose adjustments are the key to improving tolerability [5, 11, 21-23]. Even though we did not evaluate dose adjustments in this study, this is a very important item to evaluate in future studies. Therefore, physicians treating the elderly population need to optimize the supportive care treatment with bisphosphonates, antibiotics, antivirals, anticoagulants, and other concomitant medications.

MM is most prevalent in males, and African Americans are 2 times more likely to be diagnosed with MM [3]. In our study, the majority of MM patients were male, and more patients were White. Younger patients were prescribed LCR as their first line therapy, while patients older than 65 years of age were prescribed BCR, TCR, or conventional therapies. Per guidelines [5], elderly patients who are fit and without comorbidities or disabilities have treatment options of BCR, TCR, or conventional; however, high doses of TCR (thalidomide + dexamethasone) is not well tolerated by the elderly population [21-23]. Since BCR and TCR are better tolerated by patients with renal disease, and LCR is not well tolerated or needs dose adjustment, in this study we saw patients with worsening renal function were using more BCR and TCR versus LCR, [24]. Patients with a higher comorbidity score were initiated on BCR, or conventional therapy. In contrast, patients with a lower comorbidity score were initiated LCR or TCR. In addition to the comorbidity score, the type of comorbidities identified could potentially have an impact on the initiated treatment. Per guidelines and clinical trials, patients with cardiovascular disease or at high risk for venous thromboembolism or thromboembolic events were not prescribed LCR or TCR, however, patients who initiated TCR or LCR were started on antithrombotic or anticoagulation therapies [25,26].

Current available treatment options have different toxicity profiles [5,11]. The use of baseline antithrombotic agents for patients on LCR or TCR is likely to be prophylactic to prevent patients from developing thromboembolism [11,26]. There has been a reduction in thromboembolisms with the concomitant use of anticoagulation therapies along with TCR and LCR. Patients on BCR and TCR were using peripheral neuropathy agents, and this is likely for preventing the development of peripheral neuropathy [11,26]. Unlike LCR, TCR is associated with an increased risk of developing peripheral neuropathy. BCR is associated with an increased risk of herpes zoster virus reactivation and antiviral prophylaxis is required in patients who have no contraindications to such therapy. In our study, the most use of antivirals was in the BCR group. The patients initiated on BCR had a shorter follow up overall (1.5 years, + 0.8) as well as a shorter time on therapy (94.7 + 96.4 days) versus patients in other treatment regimens. One possibility for this may be due to patients in the BCR group being sicker when they initiated BCR; another possibility is the treatment of BCR being a finite treatment course versus TCR or LCR being treated to progression [7].

Within elderly patients or patients ineligible for SCT, melphalan and prednisone may be preferred because of its ease of administration and low toxicity [5,21-23]. Initial treatment of MM has changed markedly since there is increased availability of BCR, LCR and TCR gents since 2007 [3-5]. In our study we saw there was a decline in the use of TCR and conventional therapies within the 5 year time span, however, there was an increase in use of BCR and LCR. Most patients are receiving IMiDs and PI regimens instead of traditional chemotherapy [3-5]. Prior to development of current therapies such as IMiDs and PI, patients ineligible for SCT typically received oral melphalan and prednisone, however these patients are now being treated with a novel agent in conjunction with a corticosteroid.

With a retrospective database analysis, there are some limitations to this study. We are depending on data inputted from various health care providers, and using this information for our data. There is the potential for human error while inputting data into the system. We used lab values to identify renal function for our patients, however, the lab values were inputted into the system as well. Our healthcare system is an integrated system, and this may be generalizable to other integrated health systems but not to all. Even though we are trying to capture predictors of first line therapy within this MM population, we may not have captured all the predictors such as reasons from physicians for choosing certain therapies versus others. We did not have any patients on pomalidomide or carfilzomib, and thus we could not identify factors associated with these therapy choices. We understand that this data presented in this study

is prior to newer therapies becoming available; however, this is a study that can add information on how patients are being initiated on the MM therapies during 2006 to 2010. There is a need for future studies to evaluate the utilization of newer therapies after 2010, but due to the study period available in this dataset we see differences in treatment use post 2010 when data is available.

In our study we evaluate how there is a relationship between patients' clinical characteristics and prescribing patterns amongst physicians when prescribing first line therapy in newly diagnosed MM patients. The advent of thalidomide, lenalidomide, and bortezomib highlights the clinical advances for patients with newly diagnosed and relapsed MM. This has stimulated continued efforts to bring other compounds into the clinical setting. This cancer is known to predominantly be diagnosed in the elderly population. Due to increased life expectancy of the general population and the improved survival arising from these current agents, the number of MM patients is going to increase. Thus, there is always a need to create newer therapies that are safe and can be effectively used in combination to control the disease that will help MM patients preserve quality of life, especially managing the burden of symptoms associated with the disease or relieving adverse events from the therapies.

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