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Research paper

Real-world epidemiology, treatment patterns and survival of multiple myeloma patients in a large nationwide health plan

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ABSTRACT

Background: Survival of patients with multiple myeloma (MM) has improved significantly with access to autologous stem cell transplant (SCT) and new treatments. This study aims to describe epidemiology, treatment patterns, and outcomes of MM in Israel.

Methods: A retrospective observational study was conducted in Maccabi Healthcare Services, a 2-million-member nationwide health plan in Israel. MM was defined by cross-linking data on MM diagnoses, dispensed treatments, and serum free light-chain assays. Point prevalence (31/12/2016) and incidence (2012–2016) rates were age-standardized. Newly diagnosed and treated patients (2009–2015) were followed through 31/12/2016 for progression to second-line (L2), with death as a competing risk.

Results: MM prevalence and incidence rates were 26.2 and 4.6 per 100,000 population, respectively. In the treatment cohort (N = 552), mean ± SD) age was 65.6 ± 11.3) years (60.1% male) and median (95% CI) OS in years was 5.2 (4.3–6.1) overall and 6.5 (4.9–8.1) for first-line (L1) bortezomib (N = 421). In a multivariable analysis, OS was significantly higher among patients starting L1 in 2012–2015 vs. 2009–2011. Within a year, 38.4% underwent SCT. Cumulative incidence of L2 was 38.2% and 51.4% within 1 and 2 years, respectively, and was associated with older age (≥65y; $P < 0.001$).

Conclusion: These results from a large heterogeneous population demonstrate MM incidence and survival rates that are in line with the literature, together with a significant improvement in overall survival over time. Approximately half of newly treated patients progressed to L2 within two years. These results will serve as a baseline for further research to evaluate the clinical impact of new interventions.

1. Introduction

Multiple myeloma (MM) is the second most common hematologic malignancy [1]. Almost all cases of MM develop from monoclonal gammopathy of unknown significance (MGUS), with an estimated 1% rate of annual progression of MGUS to MM [1], which evolves from asymptomatic smoldering MM (SMM). Recent data from Sweden [2] and the US [3] suggest that approximately 14% of patients newly diagnosed with MM are smoldering at diagnosis. Age-standardized incidence rates of MM per 100,000 range from 3.3 to 4.7 in previous studies from Europe and the UK before 2015 [4–6], whereas data from 2015 suggest higher rates of 7.0 and 9.3 in the US [7] and UK [8], respectively. The median age at MM diagnosis is approximately 67–70 years [1]. MM incidence rises sharply with age and the male-to-female is approximately 13-15:10 [5,9].

Over past decades, survival rates have improved significantly due to the availability of autologous stem cell transplant (SCT) and the introduction of new drugs [1]. Whereas a study from the UK reported a median survival of 12 months in 2000 [4], data from the US indicate that the median overall survival increased from 4.6 years for patients diagnosed in 2001–2005, to 6.1 years for patients diagnosed in 2006–2010 [10]. In addition to the individual course of disease and treatment, patients' comorbidities, including renal impairment, have been shown to contribute to poorer prognosis [11]. MM remains an incurable disease, despite recent therapeutic advances, with progressive resistance to treatment due to a constant acquisition of new or additional molecular abnormalities. Consequently, there is a need for new agents to overcome the acquired resistance to drugs to which each

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Table 1
Inclusion of MM treatments in the National List of Health Services in Israel during the study period 2009-2016.

Year	Inclusion of MM treatments in the National List of Health Services in Israel[a]
< 2009	L1 Melphalan L1 Thalidomide L2 Bortezomib
2009	L1 Bortezomib restricted to patients with bone disease and/or renal failure
2010	L1 Bortezomib + thalidomide (combination)
2011	L1 Bortezomib L2 Lenalidomide
2014	L3 Pomalidomide or Carflilzomib

[a] The use of steroids (usually dexamethasone) is included in all treatment regimens.

patient has been exposed. Currently, initial myeloma treatment is based on proteasome inhibitors (PI) and immunomodulatory agents.

In Israel, bortezomib was the first PI approved for inclusion for MM patients in the National List of Health Services (NLHS) in 2006, initially as second line (L2) and subsequently as first line (L1) treatment. Access to L1 bortezomib was restricted in 2009–2010 and expanded in 2011 to all MM patients. Table 1 summarizes treatments included in the NLHS during the study period. New MM treatments introduced to the NLHS in 2017 (after the study period) include an oral PI (ixazomib), as well as monoclonal antibodies: elotuzumab (anti-SLAMF7) and daratumumab (anti-CD318).

Furthermore, previous improvements in the treatment of MM were limited mostly to the younger patients, since older and more fragile patients had lower utilization of SCT and were less likely to be recruited to clinical trials evaluating new drugs [12]. It is important, therefore, to assess the recent advancement in care of MM among the elderly patients.

This study aims to harness real-world data from a nationwide health plan in Israel to provide updated data on MM epidemiology, including time to text treatment (TTNT) and overall survival (OS).

2. Methods

2.1. Data source

A retrospective cohort study was conducted using the computerized databases of Maccabi Healthcare Services (MHS), a nationwide healthcare insurer-provider representing a quarter of the population in Israel, with more than 2.1 million members. The MHS database contains longitudinal data that are automatically collected since 1993 for a stable population people (with less that 1% of members moving out each year), including laboratory results from a single central laboratory and pharmacy prescription and purchase data. MHS uses the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) coding systems, as well as internal coding systems to provide more granular diagnostic information. Procedures are coded using *Current Procedural Terminology* (CPT) codes.

2.2. Case ascertainment

To increase the validity of case ascertainment, MM diagnoses (ICD-9 203.0) were cross-linked with pharmacy data and free light chain (FLC) assays; abnormally high FLC ratios were considered relevant only when documented in combination with either MM diagnosis or treatment. Specifically, treated MM patients met the case definition if they met any of the following criteria during the period 1998-2016: (i) dispensed specific MM treatment + "MM diagnosis"; (ii) dispensed MM treatment + 2 measurements of abnormally high FLC ratio within 60 days; (iii) dispensed bortezomib + 1 measurement of abnormally high FLC ratio; where "MM diagnosis" was defined as ≥1 diagnosis recorded in the National Cancer Registry [13] or ≥1 inpatient diagnosis or ≥1 diagnosis from MHS Medication Approval Center records or ≥2 separate outpatient diagnoses. In addition, untreated patients were included in the analysis of incidence and prevalence according to the following criteria (iv): "MM diagnosis" + ≥2 measurements of abnormally high FLC ratio within 60 days. The date of the earliest MM-specific criteria (diagnosis or dispensed bortezomib) was defined as the MM diagnosis date.

2.3. Study population

2.3.1. Epidemiology of MM

The point prevalence of MM was assessed among all MHS members alive on 31/12/2016 (i.e. at the end of the study period) who had at least 12 months of prior continuous health plan enrolment. In order to describe the incidence of MM in recent years, data were obtained on newly diagnosed cases during the last five years of the study period (2012–2016), which was characterized by consistent criteria for L1 in the NLHS (Table 1). Incidence was defined by a period of at least 12 months of continuous enrolment prior to the MM diagnosis date.

2.3.2. Treatment patterns and survival

A cohort of newly diagnosed and newly treated patients was defined to include MHS members who met any of the case ascertainment criteria i-iii, with MM diagnosis date in 2009–2015, at least 12 months of prior enrolment, and MM treatment initiation in 2009–2015. The index date was defined as the first dispensed MM treatment. This index period was selected according to the changes to the NLHS for MM treatment in 2009, which marked the first inclusion of L1 bortezomib.

2.4. Study definitions and variables

MM treatment included all of the following drugs provided in MHS through 2016 ('study drugs'): bortezomib, thalidomide, melphalan, lenalidomide, carfilzomib and pomalidomide (Table 1). The use of steroids (usually dexamethasone [D]) was not analyzed, as they are included in all treatment regimens, and cyclophosphamide (C) use was not captured. Treatment lines including bortezomib but excluding any other of the study drugs were defined as 'bortezomib ± C/D' (per local guidelines and common treatment practices in Israel, this group consists primarily of bortezomib + C + D). Treatment lines including bortezomib in combination with one or more of the other study drugs mentioned previously were defined as 'bortezomib, other combination'. Treatment lines (L1-4) were defined at the patient level according to the sequence of dispensed medications. In order to capture combination regimens, L1 was defined by medication(s) purchased in the first month of treatment. Similarly, each new line of treatment was defined by medication(s) purchased within the first month of a new line, that is, after changes to the previous line. Addition of medication(s) to a previous line was considered the start of a new line, but dropping one component of a combination regimen was not considered a new line. Data were obtained on both allogenic and autologous SCTs (CPT codes 38240 and 38241).

Treatment and survival outcomes were assessed through 31/12/2016, allowing for at least 12 months of follow-up (and up to 8 years). Treatment patterns were described as changes from L1, including moving to L2 and treatment discontinuation. Among patients who did not move to L2 during follow-up, discontinuation was defined as a treatment gap > 120 days since run-out of the last L1 purchase (i.e. treatment gaps within L1 were considered to be treatment interruption rather discontinuation). The proportion of patients progressing to L3 or L4 within 12 months of index date was described. TTNT was defined as the time from index date until initiation of L2, based on time-to-event analyses. SCT rates were described within the first year since treatment initiation and through the end of follow-up. OS was assessed using all-

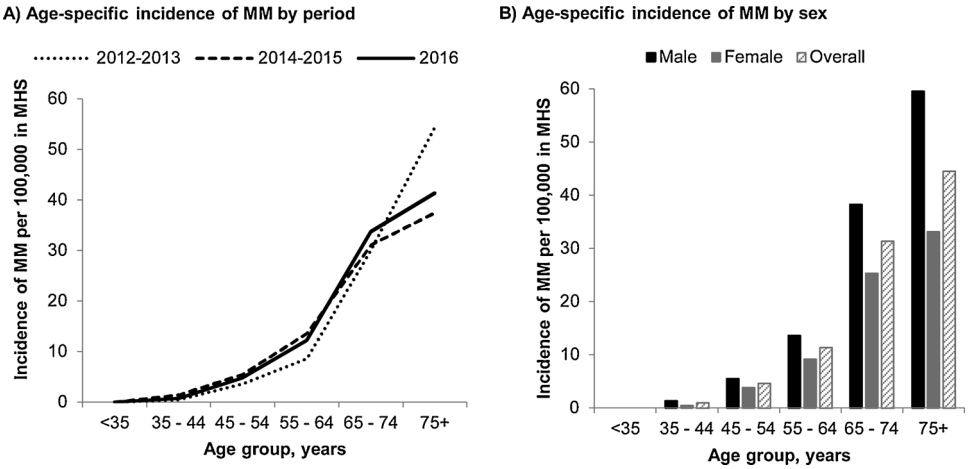

Fig. 1. Crude average annual incidence of MM in MHS (2012–2016, N = 531).

cause mortality data from the National Insurance Institute.

Patients were characterized according to demographic data (age, sex, residence area, and birth country). Socioeconomic status (SES) was based on a score ranked with 1 (lowest) to 10 built for commercial purposes by Points Location Intelligence using geographic information systems and data such as expenditures related to retail chains, credit cards and housing. This score is highly correlated with SES measured by the Central Bureau of Statistics [14]. SES was categorized into low (1–4), medium (5–6) and high (7–10) levels. Body mass index (BMI) was categorized using standard cut-points [15]. Comorbidities were assessed ever since 1998 unless otherwise specified. Baseline chronic diseases were identified using previously validated MHS automated chronic disease registries for diabetes [16], cardiovascular disease (CVD) [17], chronic kidney disease (CKD) [18] and hypertension [19]. Cancer history was obtained from National Cancer Registry [13] data available through 2015 and MHS cancer registry data which draws from pathology reports and diagnoses linked to cancer medication approvals through 2016. Data were extracted up to 5 years before treatment index date to describe baseline anemia, neutropenia, thrombocytopenia and hypercalcemia, defined by ≥ 2 separate diagnoses or ≥ 1 abnormal laboratory test result for hemoglobin (based on age-sex-specific cut-offs used in MHS), neutrophil count ($< 1.8 \times 109$/L), platelet count ($< 150 \times 109$/L) or calcium (> 10.4 mg/dL), respectively. Baseline pneumonia, cerebral bleeding, gastrointestinal (GI) bleeding and unspecified hemorrhage, were defined according to ≥ 2 separate diagnoses within a 5-year baseline period.

2.5. Statistical analyses

Descriptive statistics were presented as frequency n (%), mean ± SD or median (interquartile range, IQR), as appropriate. Differences between proportions across groups were evaluated using the χ^2 test, and Student's *t*-test was used to compare means. Crude incidence and point prevalence rates were calculated among the general population in MHS enrolled in the relevant calendar year, by age group and sex. Crude annual incidence rates were averaged over the period 2012-2016. Incidence and prevalence rates were also age-adjusted to the WHO World Standard population [20,21], as well as annual Israel population counts [22]. Kaplan-Meier (KM, unadjusted) and Cox regression (adjusted) were used for time-to-event analyses. For the analysis of TTNT, death was considered a competing risk event. The Gray model, a modified KM methods adjusting for competing risk, was used to define TTNT as the cumulative incidence of moving to L2 ('cmprisk' package in R v.3.2.2). Analyses other than competing risk were performed in SPSS v.24. The study was approved by the local Institutional Review Board (IRB) of Bayit Balev Hospital in Israel. As this is a retrospective observational study using data that were automatically collected as part of the routine computerized data collection in a large healthcare provider, informed consent was not required by the IRB.

3. Results

3.1. Epidemiology

A total of 663 prevalent MM patients were identified in MHS on 31/12/2016, corresponding to a crude point prevalence rate of 3.2 per 10,000 population (male-to-female ratio: 14:10). The age-adjusted prevalence per 10,000 was 2.6 based on the standard World population (and 3.2 applied to the Israeli national population). The mean age was 68.1 ± 11.0 years (55.4% male), with a mean time since MM diagnosis of 4.6 ± 4.0 years. Overall, 88.5% ever had a record of dispensed MM treatment and 64.4% were treated in 2016. The last treatment line dispensed in 2016 (N = 427) was: L1 (43%), L2 (30%), L3 (18%), L4 (8%) and L5 (1%).

In 2012–2016, 531 patients were newly diagnosed with MM in MHS, corresponding to an average of 106 new cases per year and a crude annual incidence rate of 5.1 per 100,000 population. The male-to-female incidence ratio was 14:10 and incidence increased with age (Fig. 1).

The average annual age-adjusted incidence of MM per 100,000 (2012–2016) was 4.6 based on the standard World population and 5.7 based on the Israeli population. Extrapolating results to the national level, there were an estimated 485 new cases of MM in 2016.

3.2. Treatment patterns and outcomes

Among 629 patients newly diagnosed in 2009–2015, a total of 552 patients initiated treatment in 2009–2015 and were included in the cohort. The mean age at treatment initiation was 65.6 ± 11.3 years (60.1% male), with a median of 6.0 (3.0–15.8) weeks since MM diagnosis. A total of 91.5% were treated within a year of MM diagnosis. Baseline anemia, thrombocytopenia and neutropenia were frequent. Detailed patient characteristics and comorbidities at the time of treatment initiation are presented in Table 2.

The age-specific prevalence of CKD and osteoporosis at MM diagnosis was significantly higher among younger patients (35–74 years), compared to the general population in MHS. In addition, younger men diagnosed with MM at age 50–74 had relatively higher burden of chronic diseases such as CVD.

The predominant L1 treatment was 'bortezomib ± C/D' (76.3%). Treatment with 'bortezomib, other combination' accounted for 8.5% of

Table 2
Baseline characteristics at treatment initiation in 2009–2015 (N = 552).

Baseline characteristics at treatment initiation		L1 regimen				P value
		Bortezomib ± C/D (N = 421)	Bortezomib, other comb. (N = 47)	Other (N = 84)	Total (N = 552)	
Treatment initiation year	2009	6.4%	2.1%	29.8%	9.6%	< 0.001
	2010	6.7%	21.3%	25.0%	10.7%	
	2011	9.0%	8.5%	10.7%	9.2%	
	2012	16.4%	12.8%	15.5%	15.9%	
	2013	15.2%	12.8%	3.6%	13.2%	
	2014	21.4%	17.0%	9.5%	19.2%	
	2015	24.9%	25.5%	6.0%	22.1%	
Weeks since MM diagnosis	Median (IQR)	6.0 (3.0–16.0)	7.0 (3.0–14.0)	4.5 (2–14.5)	6.0 (3.0–15.5)	0.343
Sex	Male	60.3%	61.7%	58.3%	60.1%	0.919
Age group at treatment, y	Mean (SD)	67.9 (10.9)	70.8 (11.9)	76.4 (11.6)	69.4 (11.5)	< 0.001
SES group	Low (1-4)	12.4%	12.8%	22.6%	13.9%	0.222
	Medium (5-6)	40.4%	42.6%	29.8%	38.9%	
	High (7-10)	46.8%	44.7%	47.6%	46.7%	
	Missing	0.5%	0.0%	0.0%	0.4%	
Chronic comorbidities	CVD	27.3%	36.2%	45.2%	30.8%	0.004
	Diabetes	21.6%	25.5%	17.9%	21.4%	0.572
	Hypertension	55.8%	63.8%	67.9%	58.3%	0.090
	CKD	39.2%	42.6%	36.9%	39.1%	0.816
	ESRD	1.2%	2.1%	1.2%	1.3%	0.859
	COPD	5.9%	6.4%	3.6%	5.6%	0.671
	Obesity history	22.1%	10.6%	8.3%	19.0%	0.004
	Osteoporosis	27.8%	25.5%	39.3%	29.3%	0.090
	Warfarin use	6.9%	14.9%	11.9%	8.3%	0.074
Smoking history	Never	84.8%	80.9%	90.5%	85.3%	0.070
	Ever	14.0%	19.1%	6.0%	13.2%	
	Missing	1.2%	0.0%	3.6%	1.4%	
Other comorbidities[a]	Anemia	74.1%	87.2%	82.1%	76.4%	0.054
	Thrombo-cytopenia	27.6%	19.1%	31.0%	27.4%	0.342
	Neutropenia	20.9%	21.3%	31.0%	22.5%	0.129
	Hypercalcemia	12.6%	14.9%	13.1%	12.9%	0.903
	Pneumonia	15.7%	19.1%	17.9%	16.3%	0.760
	Bleeding[b]	9.5%	12.8%	20.2%	11.4%	0.018
	- GI	9.3%	12.8%	19.0%	11.1%	0.031
	- Cerebral	0.7%	0.0%	0.0%	0.5%	0.625
Cancer history	Diagnosed before MM[c]	16.9%	17.0%	22.6%	17.8%	0.448

[a] Based on 5-year baseline diagnosis and/or laboratory data.
[b] Cerebral, gastrointestinal (GI), or unspecified hemorrhage.
[c] Any prior cancer, ever, except hematologic neoplasms.

L1 overall and was comprised of combinations with the following study drugs: melphalan (4.0%), thalidomide (2.9%), melphalan and thalidomide (0.4%), and lenalidomide (1.3%). By the end of follow-up, 61% of patients moved to L2, 163 moved to L3 (48% of L2), and 58 moved to L4 (36% of L3). Within a year of treatment initiation, 38.2% of patients moved to L2, 33.0% continued L1 during Y1, 20.7% discontinued all treatment and survived, 7.8% died while on L1, and 0.4% died after discontinuation. In the competing risk analysis (N = 552), the cumulative incidence of moving to L2 within 1 and 2 years of L1 index was 38.2% and 51.4%, respectively. Patients who initiated L1 bortezomib ± C/D (N = 421) had a cumulative incidence of moving to L2 of 37.3% and 50.4% within 1 and 2 years, respectively, similar to patients on any other L1 regimen (P = 0.194). Older age (≥65 years) was significantly associated with a faster progression to L2, with a 1-year cumulative incidence of 44.5% vs. 29.6% (P < 0.001).

SCT was documented among 236 patients (42.8%) during follow-up from treatment index, with 212 patients (38.4%) having undergone a planned SCT in their first year. A total of 6.7% of patients underwent SCT after their first year (including first-time and second SCTs). A total of 142 patients received the same regimen combination as prior to SCT (of which 108 were on L1), and 47 patients received a different regimen (of which 40 were defined as having moved from L1 to L2 and 7 as having moved to L3 or L4). Among those treated with the same regimen before and after SCT (any line, n = 142), the median time from SCT to restarting treatment was 95 (IQR: 43–132) days, indicating that these patients went on to receive consolidation and/or maintenance standard care for myeloma. Among those who progressed to a new line after their first SCT (from any line, n = 47), 74.5% did so after more than 120 days.

Overall, 35.9% of patients died during follow-up, with a median (95% CI) OS of 5.2 (4.3–6.1) and an estimated 2-year survival rate of 78%. L1 bortezomib patients (N = 421) had a median OS of 6.5 (4.9–8.1) years. In the unadjusted analysis, L1 treatment with bortezomib ± C/D (compared to 'bortezomib, other combination' or other regimens) was significantly associated with longer OS (Fig. 2, P = 0.013).

In the multivariable analysis, there was no statistically significant association between the L1 regimen and OS after adjusting for treatment initiation year, end-stage renal disease and potential confounders. In this model adjusted for L1 regimen, patients who started L1 treatment in 2009, 2010 or 2011 had an over 2-fold higher risk of death, compared to patients who started in L2 in 2015 (Table 3).

4. Discussion

The results of this study indicate age-standardized prevalence and incidence rates of 2.6 per 10,000 and 4.6 per 100,000 population, respectively. Despite the heterogeneity of this population, these results are in line with incidence rates reported worldwide [1,5,6,9]. In the cohort treated in 2009–2015, of which 85% received L1 bortezomib (either as part of 'bortezomib ± C/D' or 'bortezomib, other combination' regimens), the median OS from treatment initiation was 5.2 (95% CI 4.3–6.1) years, with an estimated 2-year survival rate of 78%. Patients treated with L1 'bortezomib ± C/D' had a median OS of 6.5

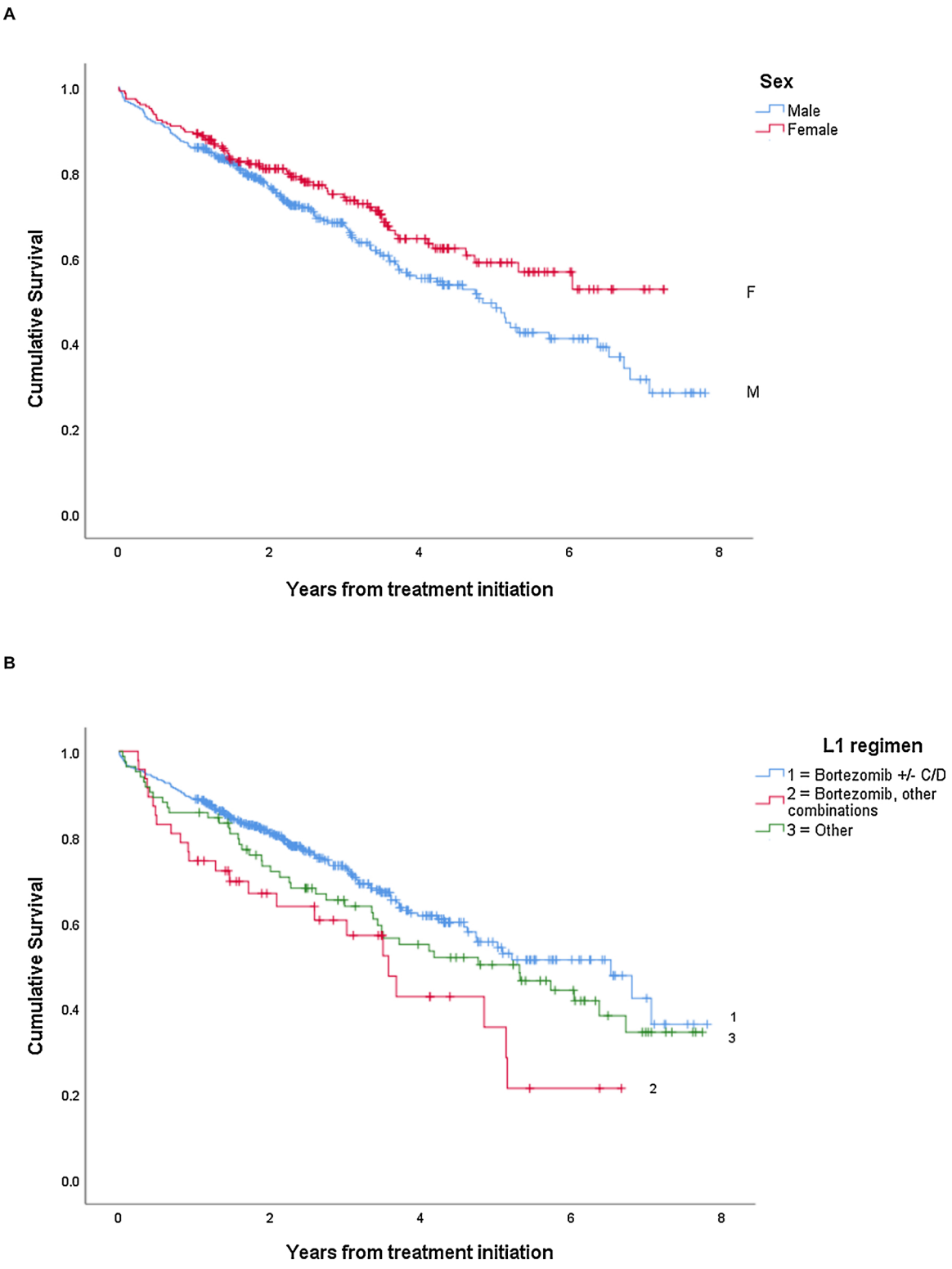

Fig. 2. Overall survival of newly diagnosed patients from treatment initiation (N = 552). **A) By sex** (Log Rank P = 0.032); **B) By L1 treatment** (Log Rank P = 0.013).

(4.9–8.1) years. Overall, these results are consistent with estimates from a US cohort of patients diagnosed in 2006–2010 [10]. Of note, although the median time to from diagnosis to treatment in our cohort was only 6 weeks, the median OS from MM diagnosis was 6.3 (5.4–7.2) years. However, when excluding 47 patients (8.5%) with delayed treatment initiation of 1 year or more since MM diagnosis, the median OS from diagnosis (5.2; 95% CI 4.3–6.2 y) was similar to median OS since treatment. This suggests that those patients with delayed treatment initiation may have been smoldering at MM diagnosis.

As demonstrated in previous studies [1,10], a significant improvement in OS was noted over time. After adjusting for L1 treatment regimen and patient characteristics and comorbidities, patients who started L1 in 2009–2011 ha d an over 2-fold higher risk of death compared to those who started in 2015. The apparent association between

Table 3
Factors associated with overall survival from treatment initiation (N = 552).

Baseline characteristics at treatment index		N	Adj. HR (95% CI)	P value
L1 treatment category	Bortezomib ± C/D	421	1.0 (Ref.)	
	Bortezomib, other combination	47	1.5 (1.0–2.4)	0.077
	Other	84	0.7 (0.5–1.1)	0.162
Index year	2015 (Ref.)	122		
	2009	53	2.5 (1.3–4.8)	0.007
	2010	59	2.3 (1.2–4.5)	0.011
	2011	51	2.1 (1.1–4.1)	0.033
	2012	88	1.3 (0.7–2.5)	0.355
	2013	73	1.8 (0.9–3.6)	0.086
	2014	106	1.5 (0.8–3.0)	0.206
Sex	Male vs. Female	332	1.3 (0.9–1.7)	0.131
Age	Years	552	1.0 (1.0–1.1)	< 0.001
Smoking[a]	Ever vs. never	73	2.1 (1.4–3.1)	< 0.001
ESRD	Yes vs. no	7	6.2 (2.4–15.7)	< 0.001
CVD	Yes vs. no	170	1.5 (1.1–2.1)	0.009
Thrombocytopenia[b]	Yes vs. no	151	1.5 (1.1–2.0)	0.014
Cerebral bleeding[b]	Yes vs. no	3	5.7 (1.6–20.1)	0.007

[a] N = 8 missing smoking status (not shown).
[b] 5-year baseline period. Thrombocytopenia was based on diagnosis and/or laboratory data.

OS and L1 treatment with newer agents (bortezomib) was not clear from our multivariable analysis, likely due to differences in patients' baseline health characteristics associated with the changing treatment indications during the study period (including unmeasured factors such as bone metastases). In addition to changes in L1 treatment policy, the inclusion of lenalidomide (2011) and pomalidomide and carfilzomib (2014) for more advanced treatment lines should be taken into account when interpreting the improvement in OS over time.

Our study indicates that more than half of MM patients progressed to the next treatment line within two years. Older patients who initiated MM treatment at age ≥65 years had a significantly faster progression to L2.

The policy for SCT was to transplant all MM patients deemed to be fit. Accordingly, almost 40% of patients underwent SCT within a year of treatment initiation. There is evidence suggesting that earlier SCT allows for longer cancer remission compared to late SCT, but there is, as yet, no evidence of a difference in OS [23].

Our results suggest that patients diagnosed with MM at a younger age had a higher burden of chronic diseases compared to the general population, indicating perhaps an older physiological age. In addition, higher rates of CKD and osteoporosis at MM diagnosis could potentially be indicative of a delayed diagnosis. Further research is warranted to characterize comorbidities and their association with MM development and progression.

Several limitations of the study should be taken into consideration. Our case ascertainment criteria may not have captured all MM patients in the database, particularly in the case of untreated MM who were diagnosed more recently (i.e. not yet treated in the study period) and/or did not have documentation of 2 abnormal FLC ratio measurements within 60 days. Identifying SMM in epidemiologic studies is limited by the last of ICD codes differentiating SMM from active MM. Nonetheless, the percentage of untreated patients included in the incidence analysis is consistent with reports from US and Swedish population-based studies suggesting that approximately 14% of cases may be SMM at diagnosis [2,3]. Information on participation in clinical trials and treatment through private insurance plans was not available and could potentially lead to misclassification of treatment lines. Our definition of treatment lines was limited in its ability to capture consolidation/maintenance treatment after SCT; it is possible that patients who were treated with a different combination after SCT within 100 days, for example, were receiving consolidation/maintenance treatment rather than having moved to L2. However, this occurrence was very rare in this study. Data on metastases, immunoglobulin levels, classification by International Staging System (ISS), and IMWG treatment response measures were not available. Dexamethasone or cyclophosphamide use in combination with L1 regimens was not captured in this analysis, due to incomplete data from hospital sources as a result of reimbursement policies.

4.1. Conclusions

The results of this real-world analysis in a large heterogeneous population demonstrate MM incidence and survival rates that are in line with the literature, together with a significant improvement in overall survival over time. Approximately half of newly treated patients progressed to the next treatment line within two years and older patients, in particularly, progressed significantly faster. These data provide valuable background information regarding the treatment patterns and survival of MM patients which will serve as a baseline for further research to evaluate the clinical impact of new drugs and future interventions.

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Declaration of Competing Interest

None.

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