



Treatment Outcomes and Health Care Resource Utilization in Patients With Newly Diagnosed Multiple Myeloma Receiving Lenalidomide-only Maintenance, Any Maintenance, or No Maintenance: Results from the Connect MM Registry

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ABSTRACT

Purpose: Maintenance therapy after autologous stem cell transplantation (ASCT) improves clinical outcomes in multiple myeloma (MM), but the effect of continued treatment with lenalidomide-only maintenance, or any maintenance, on health care resource utilization (HCRU) is largely unknown.

Methods: Here we present an analysis of HCRU and clinical outcomes in a cohort of patients from the Connect MM registry, the largest, ongoing, observational, prospective US registry of patients with symptomatic newly diagnosed MM. In this study, patients with newly diagnosed MM who completed induction and single ASCT without subsequent consolidation received lenalidomide-only maintenance (n = 180), any maintenance (n = 256), or no maintenance (n = 165). HCRU (hospitalization, surgery/procedures, and concurrent medications [growth factors, bisphosphonates, or neuropathic pain medication]) was assessed starting from 100 days post-ASCT for up to 2 years.

Findings: Although the rates of hospitalization per 100 person-years were similar across groups at the end

of years 1 and 2, the median duration of hospitalization was numerically longer with no maintenance. The rates of use of growth factors, bisphosphonates, and neuropathic pain medication were generally similar in all 3 groups. The receipt of any maintenance was associated with significantly reduced use of neuropathic pain medications during year 1. Of note, lenalidomide-only maintenance was associated with significantly longer progression-free survival (54.5 vs 30.4 months; hazard ratio [HR] = 0.58; 95% CI, 0.43–0.79; $P = 0.0005$) and overall survival (OS) (median OS not reached in either group; HR = 0.45; 95% CI, 0.28–0.73; $P = 0.001$) compared with no maintenance. Likewise, the group treated with any maintenance had significantly longer median progression-free survival (44.7 vs 30.4 months; HR = 0.62; 95% CI, 0.47–0.82;

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$P = 0.0008$) and OS (median OS not reached in either group; HR = 0.50; 95% CI, 0.33–0.76; $P = 0.001$) than did the group that did not receive maintenance.

Implications: These findings suggest that in this largely community-based study population, post-ASCT maintenance therapy, including lenalidomide-only maintenance, improves clinical outcomes without negatively affecting HCRU. ClinicalTrials.gov identifier: NCT01081028. (*Clin Ther.* 2018;40:1193–1202) © 2018 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license. (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Key words: health care, maintenance therapy, newly diagnosed multiple myeloma.

INTRODUCTION

In the United States, multiple myeloma (MM) is the second most common hematologic malignancy, accounting for an estimated 30,300 new diagnoses in 2016.¹ In recent years, the prognosis in patients with newly diagnosed (ND) MM has improved considerably, with response rates of >80% and median progression-free survival (PFS) exceeding 40 months.^{2–6} New options for induction therapy, including the proteasome inhibitor bortezomib and the immunomodulatory drug lenalidomide, have changed the therapeutic paradigm of MM and offer hope for better clinical outcomes.^{3,7}

Autologous stem cell transplantation (ASCT) is the standard of care for NDMM.^{5,6,8–10} Despite improvements in treatment, ASCT is curative in only a subset of patients, with more than half of patients relapsing within 2 to 3 years of ASCT without post-ASCT treatment.^{2,4,9,11,12} Thus, a key treatment goal for transplant-eligible patients with NDMM is to extend post-ASCT remission. Several randomized studies have demonstrated significant clinical benefit among patients who received lenalidomide maintenance therapy post-ASCT.^{2,4,5} A recent meta-analysis of data from the studies CALGB 100104 (Cancer and Leukemia Group B), IFM 2005-02 (Intergroupe Franco-phonie du Myelome), and GIMEMA RV-209 (Gruppo Italiano Malattie Ematologiche dell'Adulto) found a significant improvement in median overall survival (OS) that was independent of post-ASCT response and was consistent across subgroups examined.¹³

Although the clinical benefits of lenalidomide maintenance are well documented, the effect of continued

lenalidomide treatment on health care resource utilization (HCRU) remains to be determined. HCRU data can be beneficial in characterizing the impact of various toxicities that may be associated with a continuous maintenance therapy and have the potential to affect the choice of maintenance therapy. Connect MM* is a large, noninterventional, US-based prospective registry of data on >3000 patients with NDMM from 250 academic-, government-, and community-based centers. Most patients (84%) were enrolled at community-based oncology centers. This registry was designed to examine diagnostic patterns, common first-line treatment regimens, and subsequent therapeutic strategies in patients with NDMM.^{14,15} The present study analyzed data from the Connect MM registry to assess the effects of any maintenance, lenalidomide-only maintenance, and no maintenance on treatment outcomes and HCRU after ASCT in patients with NDMM.

PATIENTS AND METHODS

Registry Design and Patient Eligibility

As previously described,¹⁵ Connect MM is an observational, prospective, multicenter registry (clinicaltrials.gov identifier: NCT01081028) that collects longitudinal data on patients with NDMM in the United States. Participation in the registry was voluntary, and to minimize bias, enrollment was competitive (ie, each consecutive patient was screened for enrollment). Medical treatment was administered per physician discretion, including all medications, follow-up visits, and any laboratory testing. Eligible patients were aged ≥ 18 years and were diagnosed with symptomatic previously untreated MM within 60 days before study entry. All patients who provided signed informed consent were eligible for registry inclusion. Patients were followed up quarterly for treatment and outcomes until study end or early discontinuation (eg, due to death, withdrawal of consent, or loss to follow-up). MM was evaluated per International Myeloma Working Group criteria.¹⁶

The registry comprises 2 cohorts. The analysis population in the present study included patients in cohort 1 ($n = 1493$), who enrolled between September 2009 and December 2011 (data cutoff, January 7, 2016) and underwent single ASCT. Median time from diagnosis to enrollment was 25 days. To reduce potential sources

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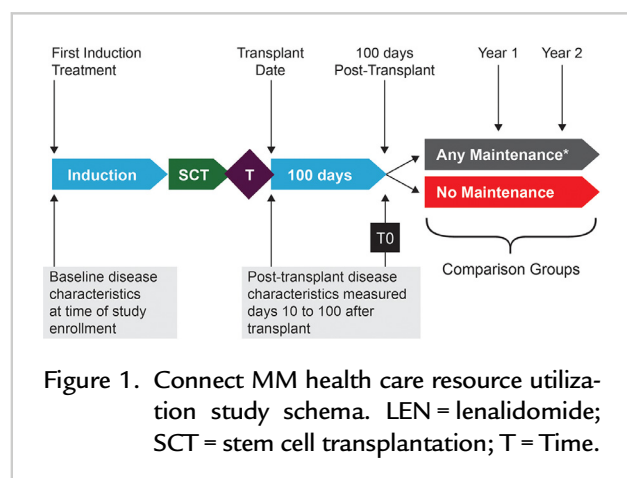
of bias, patients who received allogeneic and unknown-type transplant, tandem transplant, first transplant after first progression, or consolidation prior to maintenance in course 1, and patients in the top 5% of time to start of maintenance, were excluded. Thus, we did not expect a healthy survival effect.

Assessments

Three comparison groups were defined as no maintenance, any maintenance, and lenalidomide-only maintenance. The any-maintenance group included patients who received lenalidomide maintenance. The primary comparison in this study was lenalidomide-only maintenance versus no maintenance. Inclusion in maintenance groups required initiating maintenance treatment at >100 days after transplantation.

The clinical outcomes (PFS and OS) and HCRU (hospitalization; use of growth factors, bisphosphonates, or neuropathic pain medication; intensive care unit [ICU] admission; and surgery/procedures) were assessed.

HCRU periods are shown in **Figure 1**. In the no-maintenance group, the year-1 period began on the date of transplantation plus 100 days and ended on the date of transplantation plus 1 year and 100 days, or at the time of death, discontinuation, or data cutoff (whichever occurred first). In the maintenance groups, the year-1 period began on the date of transplantation plus 100 days or at the start of maintenance (whichever occurred later) and ended at the earlier of 1 year from either the date of transplantation plus 100 days or from the start of maintenance (whichever occurred later) or at the date of death, discontinuation, or data cutoff (whichever occurred first).



In the no-maintenance group, the year-2 period began with the date of transplantation plus 1 year and 101 days, ending on the date of transplantation plus 2 years and 101 days, or at the time of death, discontinuation, or data cutoff (whichever occurred first). In the maintenance group, the year-2 period began on the date of transplantation plus 100 days or at the start of maintenance (whichever occurred later) plus 1 year and 1 day, ending at the earlier of 2 years and 1 day from either the date of transplantation plus 100 days or from the start of maintenance (whichever occurred later) or on the date of death, discontinuation, or data cutoff (whichever occurred first).

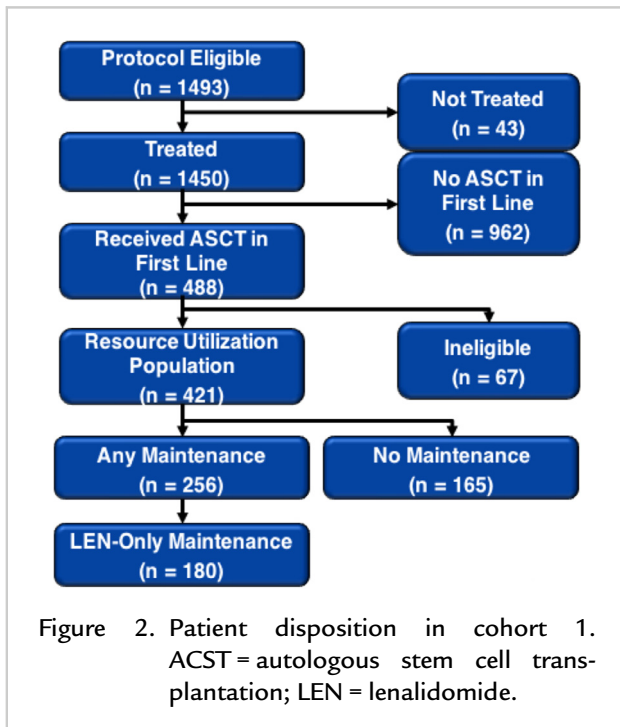
Statistical Analysis

Multivariate Cox regression was used to estimate PFS and OS across treatment groups, adjusted for the following covariates, which differed between groups: baseline creatinine level, stage on the International Staging System for MM,¹⁷ presence of del(17p), history of monoclonal gammopathy of unknown significance, and first-line triplet, lenalidomide, and bortezomib therapy use. The complete list of variables included in the analysis are listed in the **Supplemental Table** in the online version at doi:10.1016/j.clinthera.2018.05.017. HCRU end points were defined as the number of hospitalizations per patient, number of procedures and surgeries per patient, and whether the patient was taking any growth factor, bisphosphonate, or concurrent medication for neuropathic pain (all *yes* or *no*). Missing covariate data were imputed using an iterative regression, single-imputation method. Incidence rate ratios of hospitalizations and procedures/surgeries, 95% CI, and *P* values were calculated using a generalized linear model, with the negative binomial distribution and duration of exposure as offsets. Odds ratios (ORs) for other end points, 95% CIs, and *P* values were calculated using a logistic regression model.

RESULTS

Patient Characteristics

Between September 2009 and December 2011, 1493 patients in cohort 1 had enrolled in the Connect MM registry. Of the 1450 patients who received treatment, 1173 (80.9%) were from community-based sites, 259 (17.9%) were from academic-based sites, and 19 (1.2%) were from government-based sites. A total of 488 patients received ASCT in the first line, and the



HCRU population consisted of 421 patients (Figure 2). Among patients in the HCRU population, 256 (60.8%) received maintenance therapy (180 [42.8%], lenalidomide monotherapy; 76 [30%], other therapy [most commonly lenalidomide combination therapy (n = 41), bortezomib (n = 19), or bortezomib in combination with dexamethasone (n = 9)]), and 165 (39.2%) received no maintenance. The baseline characteristics of patients in the lenalidomide-only maintenance, no-maintenance, and any-maintenance groups were generally similar except for stage on the International Staging System for Multiple Myeloma, history of monoclonal gammopathy of unknown significance, presence of del(17p), and induction regimen (Table I). The median age in all 3 groups was 60 years (range, 24–78 years), with ~30% of patients being 65 years of age or older. Approximately 60% of patients were male and 86% were white.

Efficacy

The median duration of lenalidomide-only maintenance was 27.3 months, and the median duration of any maintenance was 25.8 months. After a median follow-up of 39.3 months, the group treated with lenalidomide-only maintenance had a significantly longer median PFS (54.5 vs 30.8 months; HR = 0.58; 95% CI, 0.43–0.79; $P = 0.0005$) (Figure 3A) and OS (median

OS not reached in either group; HR = 0.45; 95% CI, 0.28–0.73; $P = 0.001$) (Figure 3B) than did the group that did not receive maintenance. Likewise, the group treated with any maintenance had a significantly longer median PFS (44.7 vs 30.4 months; HR = 0.62; 95% CI, 0.47–0.82; $P = 0.0008$) (Figure 4A) and OS (median OS not reached in either group; HR = 0.50; 95% CI, 0.33–0.76; $P = 0.001$) (Figure 4B) than did the group that did not receive maintenance.

Health Care Resource Utilization Analyses

The numbers of patients with any hospitalization, hospitalization rates per 100 patient-years (PYs), and hospitalization incidence rate ratios during years 1 and 2 were similar across all 3 groups (Table II). Figure 5 provides the percentages of patients with 0 to 5 hospitalizations; no significant between-group differences were found. In the no-maintenance, lenalidomide-only maintenance, and any-maintenance groups, the median durations of hospitalization were 10.5, 5.0, and 5.5 days, respectively, during year 1. During year 2, the median durations of hospitalization were 9.0, 7.0, and 6.0 days, respectively. The differences did not reach statistical significance. Moreover, the numbers of patients who underwent any procedure/surgery (see Supplemental Figure in the online version at doi:10.1016/j.clinthera.2018.05.017), procedure and surgery rates per 100 PYs, and incidence rate ratios during years 1 and 2 were similar across the 3 groups (Table II).

Although the rates of use of growth factors, bisphosphonates, and neuropathic pain medications were generally similar across the 3 groups (Table II), the group that received any maintenance had a significant reduction in neuropathic pain medication use during year 1 (OR = 0.50; 95% CI, 0.27–0.94; $P = 0.03$). Lenalidomide-only maintenance was associated with a nonsignificant reduction in the use of neuropathic pain medication during year 1 (OR = 0.57; 95% CI, 0.29–1.12; $P = 0.10$).

DISCUSSION

To the best of our knowledge, this is the first report that has addressed HCRU associated with maintenance therapy in NDMM. This analysis of data from the Connect MM patient registry shows that the use of maintenance therapy generally, and lenalidomide maintenance specifically, significantly improved

Table 1. Patient and disease characteristics at baseline. Data are given as number (%) of patients unless otherwise noted.

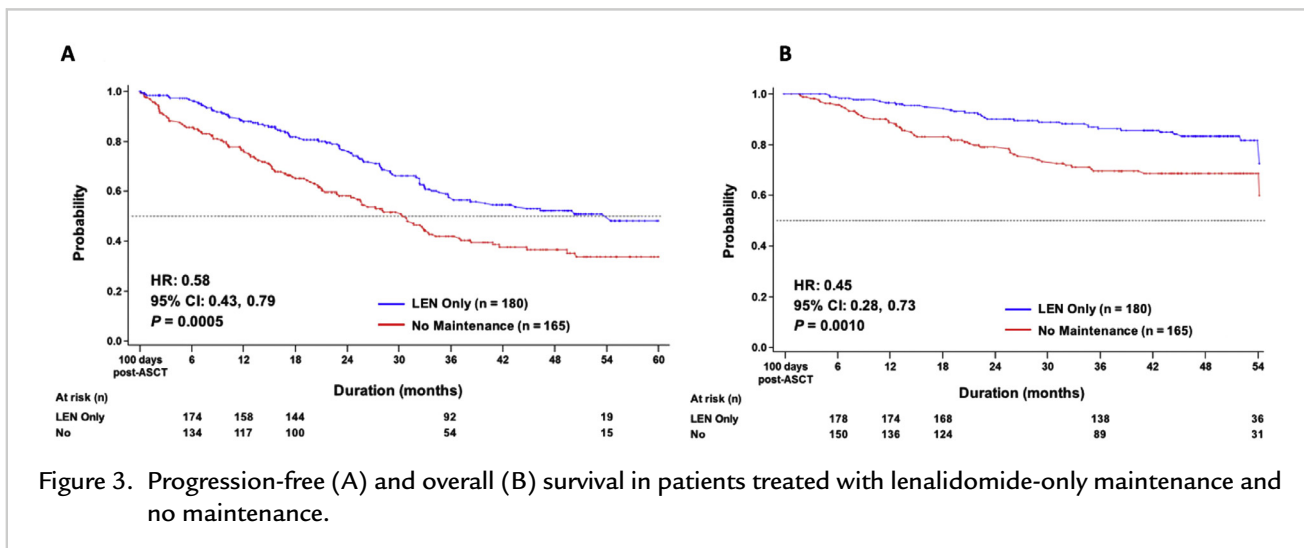
Characteristic	No Maintenance (n = 165)	Maintenance	
		LEN Only* (n = 180)	Any (n = 256)
Age			
Median (range), y	60 (27–75)	60 (24–74)	60 (24–78)
Group			
<65 y	113 (68)	127 (71)	171 (67)
65–<75 y	51 (31)	53 (29)	82 (32)
Male	93 (56)	108 (60)	159 (62)
Race			
White	139 (84)	152 (84)	221 (86)
Black	18 (11)	22 (12)	27 (11)
Asian	1 (1)	0	1 (<1)
Other	1 (1)	2 (1)	2 (1)
Not specified	6 (4)	4 (2)	5 (2)
ECOG PS			
0 or 1	113 (68)	123 (68)	163 (64)
2 or 3	7 (4)	9 (5)	21 (8)
Not specified	45 (27)	48 (27)	72 (28)
ISS stage			
I	50 (30)	51 (28)	73 (29)
II	36 (22)	56 (31)	72 (28)
III	44 (27)	37 (21)	58 (23)
Not specified	35 (21)	36 (20)	53 (21)
Serum creatinine			
>2.0 mg/dL	31 (19)	19 (11)	28 (11)
≤2.0 mg/dL	134 (81)	161 (89)	228 (89)
History of MGUS	19 (12)	9 (5)	13 (5)
Del(17p)			
Yes	9 (5)	5 (3)	15 (6)
No	67 (41)	87 (48)	111 (43)
Not provided	89 (54)	88 (49)	130 (51)
Induction			
Bortezomib in first regimen	130 (79)	154 (86)	226 (88)
Triplet treatment	85 (52)	117 (65)	160 (63)
Lenalidomide in first regimen	83 (50)	111 (62)	144 (56)

ECOG PS = Eastern Cooperative Oncology Group performance status; ISS = International Staging System for Multiple Myeloma¹⁷; LEN = lenalidomide; MGUS = monoclonal gammopathy of unknown significance.

* Subset of any maintenance group.

survival outcomes relative to no maintenance treatment. In general, the use of maintenance therapy or not, had no appreciable effect on HCRU as measured in this study.

Hospitalization rates were similar across patients receiving lenalidomide-only maintenance, any maintenance, and no maintenance, although the median duration of hospitalization was numerically longer in



patients not receiving maintenance therapy versus the other groups. In addition, there were similar rates of procedures and surgeries, and use of growth factors, bisphosphonates, and neuropathic pain medication in both years 1 and 2. Of note, the only HCRU factor analyzed that reached significance was neuropathic pain medication use, which was significantly reduced in the any-maintenance group during year 1.

Several randomized trials have demonstrated that post-ASCT lenalidomide maintenance significantly extends the duration of remission compared to no maintenance.^{2,4,5} A recent meta-analysis of these 3 Phase III trials showed a significant survival benefit with lenalidomide compared to no maintenance (OS: HR = 0.75; log-rank $P = 0.001$).¹⁸ The results of our

analysis (OS: HR = 0.45; $P = 0.001$), in a primarily community-based setting, are aligned with previous findings.^{2,4,5,19–21} The present analysis demonstrated significant increases in PFS and OS in patients with NDMM receiving lenalidomide-only maintenance and any maintenance relative to no maintenance.

While current treatments have demonstrated improved clinical outcomes among patients with MM, increased treatment costs on relapse are making it increasingly important to evaluate economic outcomes associated with maintenance therapy.^{22,23} Among the few studies that have addressed HCRU in MM, one by Fonseca et al⁷ reported that in patients with NDMM, including those who did and did not undergo ASCT, non-drug-related costs, primarily outpatient services

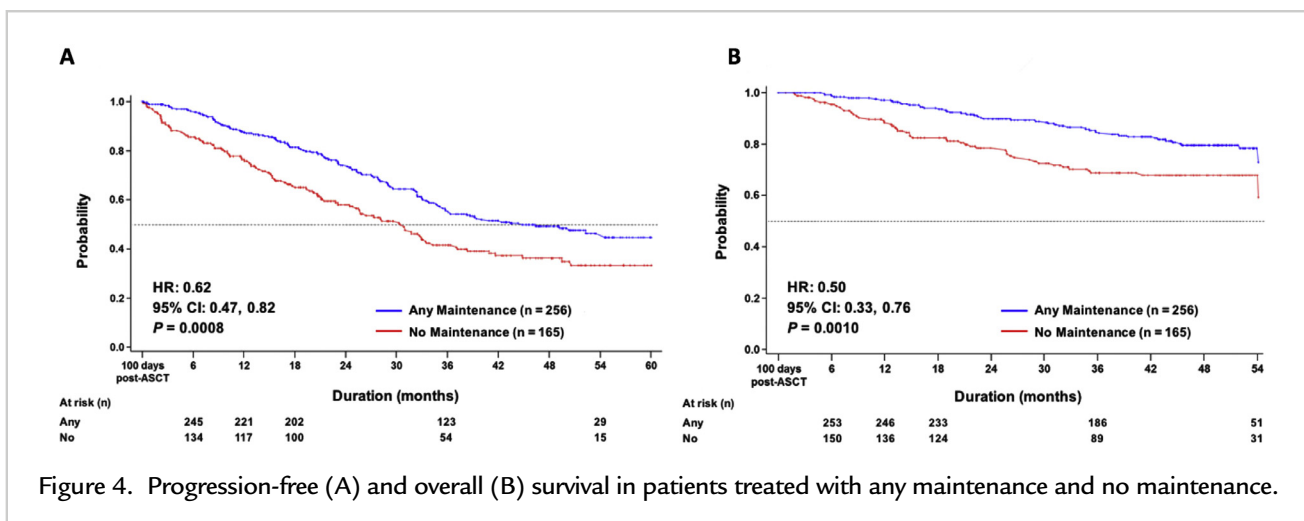


Table II. Health care resource utilization during years 1 and 2 after autologous stem cell transplantation.

Parameter/ Time Point/Statistic	No Maintenance	Maintenance	
		LEN Only*	Any
Hospitalization			
Year 1	n = 165	n = 180	n = 256
No. (%) of patients with any hospitalization	30 (18)	33 (18)	52 (20)
Rate per 100 PY	32.9	28.7	30.7
Incidence rate ratio (95% CI)	1 (Ref)	0.82 (0.44–1.52)	0.86 (0.50–1.46)
<i>P</i>	Ref	0.53	0.57
Duration, median (IQR), d	10.5 (5.0–18.0)	5.0 (4.0–14.0)	5.5 (4.0–13.5)
<i>P</i>	Ref	0.91	0.71
Year 2	n = 134	n = 173	n = 242
No. (%) of patients with any hospitalization	31 (23)	31 (18)	47 (19)
Rate per 100 PY	45.2	32.0	33.4
Incidence rate ratio (95% CI)	1 (Ref)	0.65 (0.34–1.24)	0.72 (0.41–1.28)
<i>P</i>	Ref	0.19	0.27
Duration, median (IQR), d	9.0 (5.0–19.0)	7.0 (4.0–11.0)	6.0 (4.0–12.0)
<i>P</i>	Ref	0.62	0.79
ICU admissions			
Year 1	n = 165	n = 180	n = 256
No. (%) of patients with any ICU admission	2 (1)	3 (2)	6 (2)
Duration, median (IQR), d	14.0 (10.0–18.0)	2.0 (1.0–5.0)	4.0 (2.0–6.0)
Year 2	n = 134	n = 173	n = 242
No. (%) of patients with any ICU admission	3 (2)	4 (2)	8 (3)
Duration, median (IQR), d	4.0 (2.0–17.0)	2.5 (1.5–4.0)	2.5 (1.5–3.5)
Procedures and surgeries			
Year 1	n = 165	n = 180	n = 256
No. (%) of patients with any procedure/surgery	27 (16)	29 (16)	42 (16)
Rate per 100 PY	30.9	28.1	30.7
Incidence rate ratio (95% CI)	1	0.91 (0.47–1.75)	1.00 (0.55–1.79)
<i>P</i>	Ref	0.77	0.99
Year 2	n = 134	n = 173	n = 242
No. (%) of patients with any procedure/surgery	16 (12)	23 (13)	39 (16)
Rate per 100 PY	27.3	23.4	26.7
Incidence rate ratio (95% CI)	1	0.72 (0.32–1.62)	0.86 (0.44–1.68)
<i>P</i>	Ref	0.42	0.66
Growth factor use			
Year 1	n = 165	n = 180	n = 256
No. (%) of patients with any growth factor use	15 (9.1)	14 (7.8)	24 (9.4)
Odds ratio (95% CI)	1	0.74 (0.34–1.65)	0.99 (0.49–2.00)
<i>P</i>	Ref	0.47	0.97
Year 2	n = 134	n = 173	n = 242
No. (%) of patients with any growth factor use	14 (10.4)	10 (5.8)	19 (7.9)
Odds ratio (95% CI)	1	0.51 (0.22–1.22)	0.79 (0.37–1.66)
<i>P</i>	Ref	0.13	0.53

(continued)

Table II. (Continued)

Parameter/ Time Point/Statistic	No Maintenance	Maintenance	
		LEN Only*	Any
Bisphosphonate use			
Year 1	n = 165	n = 180	n = 256
No. (%) of patients with any bisphosphonate use	28 (17.0)	39 (21.7)	51 (19.9)
Odds ratio (95% CI)	1	1.38 (0.79–2.42)	1.19 (0.71–2.01)
<i>P</i>	Ref	0.26	0.51
Year 2	n = 134	n = 173	n = 242
No. (%) of patients with any bisphosphonate use	20 (14.9)	18 (10.4)	25 (10.3)
Odds ratio (95% CI)	1	0.64 (0.32–1.29)	0.60 (0.31–1.15)
<i>P</i>	Ref	0.21	0.13
NP pain medication use			
Year 1	n = 165	n = 180	n = 256
No. (%) of patients with any pain medication use	26 (15.8)	17 (9.4)	22 (8.6)
Odds ratio (95% CI)	1	0.57 (0.29–1.12)	0.50 (0.27–0.94)
<i>P</i>	Ref	0.10	0.03
Year 2	n = 134	n = 173	n = 242
No. (%) of patients with any pain medication use	6 (4.5)	8 (4.6)	12 (5.0)
Odds ratio (95% CI)	1	0.92 (0.30–2.81)	1.00 (0.36–2.81)
<i>P</i>	Ref	0.89	1.00

P values are versus no-maintenance group.

ICU = intensive care unit; IQR = interquartile range; LEN = lenalidomide; NP = neuropathic; PY = patient-year.

* Subset of any maintenance group.

and inpatient admissions, accounted for the majority of treatment costs. Similarly, costs during treatment of relapsed/refractory MM were largely attributable to hospital admissions.^{23,24} Another study conducted in the relapsed/refractory setting found that maintenance therapy may reduce total costs by lengthening the period of lower-cost treatment.²² HCRU was analyzed in the present study since the Connect MM registry did not collect cost information. All information collected in the registry is either patient- or physician-reported, which has limitations. For example, generally patients provide out-of-pocket costs, not insurance-company payments, and physicians are unaware of the costs incurred by health care system visits. In addition, it is challenging to accurately estimate the costs of oral versus infusional treatment, and not all adverse events were collected, making the estimation of costs due to toxicities difficult. With maintenance therapy, there are expected to be additional costs of the actual treatment, but in the absence of a negative impact on quality of life²⁵ and taking into account the significant survival

benefit, patients have the potential to benefit from maintenance therapy.

Although this observational registry study provides insight into baseline factors, treatment patterns and a variety of outcomes in clinical practice, in patients treated largely at community-based oncology centers, limitations of registries should be acknowledged. These limitations include the nonrandomized nature of the study, the lack of mandate for specific treatments (investigator selection) or response assessments, and the variations in treatment duration and intensity. As in any observational study, there is also a potential for missing and erroneous data. However, a strength of this registry is the ability to query sites for more information on questionable data. Furthermore, by applying multiple imputation methods in the analyses, the impact of missingness should be substantially mitigated. The present analysis was limited by the small sample size. Also, HCRU measures were limited to those items collected by the registry with sufficient data for reliable analysis, and cost data were not collected. Despite these limitations,

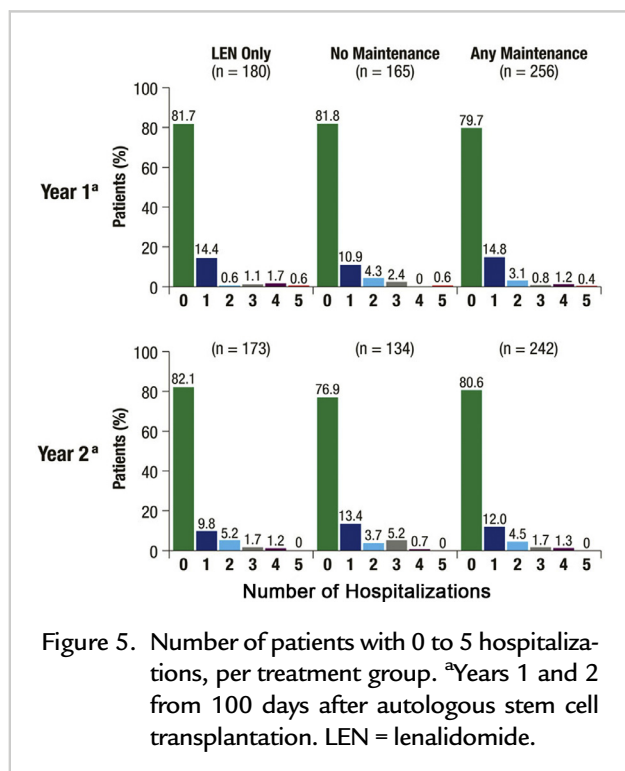


Figure 5. Number of patients with 0 to 5 hospitalizations, per treatment group. ^aYears 1 and 2 from 100 days after autologous stem cell transplantation. LEN = lenalidomide.

the present study provides new information regarding the impact of maintenance therapy on HCRU.

CONCLUSIONS

Findings from the present study indicate that lenalidomide-only maintenance and any maintenance significantly improved survival outcomes relative to no maintenance after ASCT, without increasing HCRU in this population of patients with NDMM in clinical practice. The results of the present study require further validation in a larger-scale cohort.

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CONFLICT OF INTEREST

This study and editorial assistance were supported by research funding from Celgene Corporation, the manufacturer of lenalidomide.

R.M. Rifkin owns stock options in McKesson and has received consultant's fees from Amgen, Boehringer Ingelheim, Celgene, EMD Serono, Sandoz, and Takeda. S. Jagannath has received consultant's fees from Bristol-Meyers Squibb, Celgene, Merck, and Novartis and has been a member of the speakers' bureaus at Multiple Myeloma Research Foundation (MMRF) and Medicom. B.G.M. Durie has received consultant's fees from Janssen and Takeda. M. Narang has received consultant's fees from Celgene and has been a member of the speakers' bureaus at Celgene and Janssen. H.R. Terebello has received consultant's fees from Celgene and has been a member of the speakers' bureaus at AbbVie, Janssen, Pharmacylics, and Takeda. C.J. Gasparetto has received consultant's fees from Celgene, Janssen, and Takeda; research funding from Celgene; and travel expenses from Celgene and Janssen. K. Toomey has received consultant's fees from Celgene, has been a member of the speakers' bureau at Myriad Genetics, and has received travel expenses from Dava Oncology. J.W. Hardin has received consultant's fees from Celgene. L. Wagner has received consultant's fees from EveryFit, Gilead, and Janssen. K. Parikh, S. Abouzaid, A. Kitali, and F. Zafar own equity in Celgene. S. Srinivasan holds patent ownership at Celgene. R. Abonour has received research funding from Celgene, Prothena, and Takeda. The authors have indicated that they have no other conflicts of interest with regard to the content of this article.

Study sponsors were involved in study design; in the collection, analysis, and interpretation of data; and in the writing of the manuscript.

SUPPLEMENTAL MATERIAL

Supplemental material accompanying this article can be found in the online version at doi:[10.1016/j.clinthera.2018.05.017](https://doi.org/10.1016/j.clinthera.2018.05.017).

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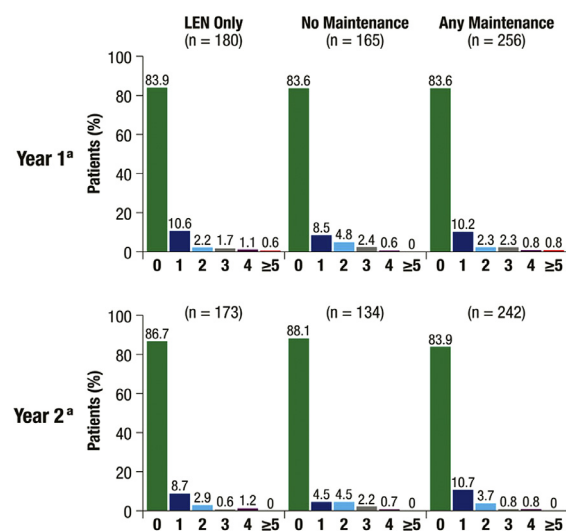
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Supplementary Table. Variables From Multivariable Cox Regression Analysis of PFS and OS Across Treatment Groups.

Variable	P-value
Multiple myeloma bone involvement	0.6564
Calcium category	0.3116
Neutropenia (ANC)	0.3655
Platelet count categories	0.7391
Creatinine categories	0.032
ANC category within SCT+100 days	0.8358
Creatinine category within SCT+100 days	0.8775
day 100 ECOG PS derived, 0,1 vs ≥ 2	0.9823
Hemoglobin category within SCT+100 days	0.1596
Platelet category within SCT+100 days	0.2747
Sex	0.494
Del17 (FISH)	0.1439
Hyperdiploidy, new defined	0.7417
Subgroup of t(4;14), new defined	0.4226
Hemoglobin category	0.9087
IMWG risk	0.3705
Insurance (public vs private)	0.2556
Novel therapies	0.0023
Radiation therapy for myeloma	0.8252
Age group	0.6762
Use of alkylator in first course first regimen	0.7937
History of MGUS?	0.0271
History of smoldering myeloma?	0.4771
History of asymptomatic myeloma?	0.6644
ECOG PS derived, 0,1 vs ≥ 2	0.749
Calculated ISS stage	0.1407
History of amyloidosis	0.9028
History of diabetes	0.6274
History of hypertension requiring treatment	0.8541
History of peripheral neuropathy	0.2032
Additional relevant medical history	0.8806
Non-secretory multiple myeloma	0.5868
Lenalidomide in first regimen	0.034
Bortezomib in first regimen	0.1015
Triplet therapy	0.0114
Past history or active treatment for VTE	0.8686
White vs non-white	0.9588

ECOG PS, Eastern Cooperative Oncology Group performance group; IMWG, International Myeloma Working Group; ISS, International Staging System; MGUS, monoclonal gammopathy of undetermined significance; PFS, progression-free survival; OS, overall survival; SCT, stem cell transplant; VTE, venous thromboembolism.



^a Year 1 and Year 2 are from 100 days post-ASCT.
LEN, lenalidomide

Supplemental Figure.