Characteristics, Treatment Patterns, and Survival Outcomes of Patients With Relapsed/Refractory Multiple Myeloma in North America and Europe: Findings From the PREAMBLE Study

Ravi Vij,¹ Clara Chen,² Catherine Davis,² Hyang Kim,³ Brian Durie,⁴ Gordon Cook,⁵ Hartmut Goldschmidt⁶

¹Washington University School of Medicine, St Louis, MO; ²Bristol-Myers Squibb, Princeton, NJ; ³PAREXEL, Billerica, MA; ⁴Cedars-Sinai Medical Center, Los Angeles, CA;

⁵University of Leeds, Leeds, UK; ⁶University Clinic Heidelberg, Internal Medicine V and National Center for Tumor Diseases (NCT), Heidelberg, Germany

Background

- Most patients with multiple myeloma (MM) relapse or become refractory to treatment, meaning that 5-year survival rates remain low¹
- With improved treatment strategies and access to therapies with novel mechanisms of action, prolonging survival for patients with relapsed/refractory (RR) MM has become a realistic goal
- Proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and PI + IMiD combinations have become the standard of care in RRMM²
- In addition, the monoclonal antibodies elotuzumab and daratumumab are a relatively new class of approved agents²
 - In clinical trials, elotuzumab and daratumumab have prolonged progression-free survival among patients with RRMM^{3,4}
- Treatment selection in RRMM is becoming increasingly complex due to an expanding number of available regimens, and access to therapies may vary between North America and Europe, thereby affecting outcomes

Objective

- To evaluate the impact of regional treatment differences on outcomes in patients with RRMM enrolled in PREAMBLE, an ongoing, prospective, observational study

Methods

- Patients with RRMM from North America (US and Canada) and Europe (France, Germany, Italy, and the UK) were identified from PREAMBLE (NCT01838512) (**Figure 1**)

Figure 1. Overall PREAMBLE study design

*Newer agents included monoclonal antibodies and histone deacetylase inhibitors

Statistical analyses

- Baseline characteristics and length of follow-up were assessed using descriptive analysis
- Statistical comparisons were made using *t* tests, Mann–Whitney *U* tests (continuous variables), and chi-square tests (categorical variables); 2-sided *p*-values were obtained

- Overall survival (OS) was analyzed using Kaplan–Meier (K–M) methods, log-rank tests, and multivariate Cox regression (adjusted for covariates selected using stepwise regression including treatment option, disease status, age at MM diagnosis, sex, International Staging System [ISS] scoring, number of prior therapies, and baseline comorbidities of cardiac and gastrointestinal disorders)

Results

Baseline demographics

- At database lock (Nov 30, 2017), 1159 eligible patients with RRMM were identified; 381 (33%) from North America and 778 (67%) from Europe
- Baseline demographics were generally similar between patients enrolled in North America and Europe (**Table 1**)
 - Patients in North America were younger at diagnosis and at enrollment compared with patients in Europe

Table 1. Baseline demographics and disease characteristics

Characteristic	North America (n=381)	Europe (n=778)	p-value
Age at MM diagnosis, years			
Median (range)	61 (29–88)	65 (29–88)	<0.0001
Age at enrollment, years			
Median (range)	66 (37–91)	70 (34–92)	<0.0001
Male	225 (59)	440 (57)	0.4189
Disease status			0.5681*
Relapsed	292 (77)	603 (78)	
Refractory	84 (22)	159 (20)	
Unknown	5 (1)	16 (2)	
ISS stage			0.3057*
I	51 (13)	135 (17)	
II	57 (15)	120 (15)	
III	91 (24)	175 (22)	
Unknown	182 (48)	348 (45)	
Country			NA
US	364 (96)	–	
Canada	17 (4)	–	
France	–	231 (30)	
Germany	–	148 (19)	
Italy	–	228 (29)	
UK	–	171 (22)	

Data reported as n (%) unless stated otherwise. Percentages may not total 100% due to rounding
*Unknown values were excluded from statistical analysis
NA, not applicable

- The prevalence of comorbidities among patients in North America was significantly higher compared with those in Europe (94% vs 80%; *p*<0.0001) (**Table 2**)

Table 2. Common comorbidities

Characteristic	North America (n=381)	Europe (n=778)	p-value
Patients with ≥1 comorbidity	357 (94)	623 (80)	<0.0001
Most common comorbidities (among patients with ≥1 comorbidity)			
Vascular	225 (63)	259 (42)	<0.0001
Metabolism & nutrition	163 (46)	167 (27)	<0.0001
Musculoskeletal & connective tissue	149 (42)	138 (22)	<0.0001
Gastrointestinal	124 (35)	97 (16)	<0.0001
Nervous system	118 (33)	128 (21)	<0.0001
Cardiac	71 (20)	124 (20)	0.9953

Data reported as n (%)

Patient disposition

- Median (range) follow-up was 13 (7–27) months and 12 (6–25) months for patients in North America and Europe, respectively
- In total, 58% of patients in North America and 48% of patients in Europe withdrew from the study due to death or other reasons (**Table 3**)
 - Most deaths were due to disease progression (North America, 68%; Europe, 67%)

Table 3. Patient status

Status	North America (n=381)	Europe (n=778)	p-value
Still on study	107 (28)	342 (44)	<0.0001
Completed study	54 (14)	64 (8)	0.0017
Died	130 (34)	265 (34)	0.9841
Due to disease progression	89 (68)	177 (67)	0.7396
Discontinuation other than death	90 (24)	107 (14)	<0.0001

Data reported as n (%)

Treatment patterns prior to enrollment

- Median (range) number of prior therapies was 2 (1–11) in patients in North America and 2 (1–14) in Europe (**Table 4**)

Table 4. Number of prior therapies

Number of prior therapies	North America (n=381)	Europe (n=778)	p-value
1	143 (38)	371 (48)	
2	100 (26)	193 (25)	
3	65 (17)	91 (12)	
≥4	73 (19)	123 (16)	

Data reported as n (%)

- A greater proportion of patients in North America than Europe received PI + IMiDs (29% vs 16% of patients; *p*<0.0001) and newer agents (3% vs 1%; *p*=0.0390) (**Figure 2**)

Figure 2. Therapies received prior to enrollment

Percentages do not total 100% as patients may have received more than one line of therapy. Non-novel therapies include chemotherapy and steroids (dexamethasone/prednisolone) only
p*<0.05; **p*<0.001
NS, not significant

Treatment patterns at enrollment

- A greater proportion of patients in North America than Europe received PIs, PI + IMiDs, and newer agents
 - By contrast, patients in Europe versus North America were more likely to receive IMiDs (**Table 5**)

Table 5. Treatment type received at enrollment

Treatment type	North America (n=381)	Europe (n=778)	p-value
IMiD	90 (24)	429 (55)	<0.0001
PI	186 (49)	290 (37)	
PI + IMiD	65 (17)	50 (6)	
Newer agent	40 (10)	9 (1)	

Data reported as n (%)

Treatment patterns after enrollment

- A greater proportion of patients in North America than Europe received PIs (56% vs 46%), PI + IMiDs (29% vs 9%), and newer agents (21% vs 5%; *p*<0.001 for all) (**Figure 3**)
 - Conversely, patients in Europe were more likely to receive IMiDs (67% vs 38%; *p*<0.0001)

Figure 3. Therapies received after enrollment

Percentages do not total 100% as patients may have received more than one line of therapy. Non-novel therapies include chemotherapy and steroids (dexamethasone/prednisolone) only
****p*<0.001

Survival analysis

- Median (95% CI) OS was 37 (29, not estimable) months in North America and 31 (27, 38) months in Europe
- In a multivariate analysis, risk of death was 17% lower in patients in North America versus Europe (hazard ratio [95% CI]: 0.83 [0.66, 1.04]; *p*=0.110)
- There was no difference in OS across the entire follow-up period (*p*=0.4709). However, from 18 months onwards, patients in North America had a survival advantage over those in Europe (*p*=0.0402) (**Figure 4**)

Figure 4. K–M curves of OS

Summary/Conclusions

- Real-world data suggest that patients with RRMM in North America had greater access to newer agents and PI + IMiD combination regimens than patients in Europe
- Multivariate analysis identified a potential but non-significant reduction in the risk of death for patients in North America versus Europe
- OS was significantly higher from 18 months onward for patients in North America versus Europe
 - A survival advantage after 18 months in patients enrolled in North America could be partly due to possible benefits from newer agents, which are often reserved for later lines of therapy
- In this analysis, novel agents were largely restricted to therapy at or after enrollment, although this may have been due to the timing of approvals for the use of these agents
- Further analysis is warranted to contextualize these results and to fully understand the impact of regional treatment differences on outcomes in RRMM

References

- Siegel RL et al. *CA Cancer J Clin* 2016;66:7–30
- National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 4. 2018. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf
- Lonial S et al. *N Engl J Med* 2015;373:621–31
- Dimopoulos MA et al. *N Engl J Med* 2016;375:1319–31

Acknowledgments

This study was funded by Bristol-Myers Squibb. Professional medical writing assistance was provided by Simon Wigfield, Caudex, and was funded by Bristol-Myers Squibb.

Disclosures

RV: research funding: Celgene, Onyx; honoraria: Celgene, Janssen, Millennium, Novartis, Onyx, Sanofi. CC, CD: employment and/or stock ownership: Bristol-Myers Squibb. HK: employment: PAREXEL. BD: consultancy: Celgene, Johnson & Johnson, Onyx, Takeda. GC: consultancy: Amgen, Bristol-Myers Squibb, Celgene, Chugai, Janssen, Jazz Pharma, Takeda; research funding: Celgene; honoraria: Amgen, Bristol-Myers Squibb, Celgene, Chugai, Janssen, Sanofi, Takeda; speakers bureau: Amgen, Celgene, Chugai, Janssen, Sanofi, Takeda. HG: advisory committee, speakers bureau, and/or institutional research support: Amgen, ArtTempi, Bristol-Myers Squibb, Celgene, Chugai, Janssen, Mundipharma, Novartis, Sanofi, Takeda.

Copies of this poster obtained through Quick Response (QR) code are for personal use only and may not be reproduced without permission from the authors