ABSTRACT PF640

Multiple Myeloma Treatment Landscape From 2011 to 2017 in Alberta, Canada: Results From the Population-Based "Identifying Outcomes in Real-World Multiple Myeloma" (INFORMM) Study

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BACKGROUND

- The treatment landscape for patients with multiple myeloma (MM) has been evolving rapidly in recent years, with the availability of new therapeutic options leading to improved responses and survival rates[1-3]
- Use of autologous stem cell transplantation (ASCT) in combination with proteasome inhibitors and immunomodulatory agents as induction and consolidation/maintenance therapies has become an integral part of the treatment of newly diagnosed MM (NDMM)[4]
- It is important to examine treatment patterns and outcomes in the real-world setting to establish a benchmark for future therapies; however, very few such studies exist[5,6]
- The overall aim of the Identifying Outcomes in Real-World Multiple Myeloma (INFORMM) study is to describe the real-world NDMM population and treatment landscape in Alberta, Canada

OBJECTIVE

- **To describe baseline and clinical characteristics, and treatment patterns, including lines of therapy (LoT), duration of therapy (DoT), and time to next treatment (TTNT), in patients with NDMM from the INFORMM study**

METHODS

Study Design and Population

- This is a retrospective observational study in patients diagnosed with MM between April 1, 2011 and March 31, 2017 (2011–2016 Canada fiscal years), using several data sources from the Government of Alberta (Figure 1)
- The study population consisted of adult (aged ≥ 18 years) patients with NDMM from Alberta with ≥ 1 year of pre-index baseline data (Figure 2)

Treatment Regimen Grouping and LoT

- Treatment regimens were classified as lenalidomide (LEN)-based, bortezomib (BORT)-based, LEN + BORT-based, or other; and LoT were defined using an algorithm modified from Song et al. (2016),[5] based on whether patients had an ASCT in the first year of MM diagnosis (Figure 3)

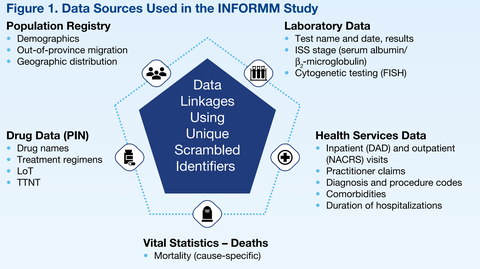
Statistical Analysis

- Descriptive statistics, including frequencies, means, and standard deviations (SDs), were used to describe demographic and clinical characteristics
- Frequencies and proportions were also used to describe the treatment regimens and patterns within the study cohort, while DoT and TTNT calculations are presented as the mean ± SD
- Comparisons between groups were performed using Student t-tests for continuous variables, whereas χ^2 tests were used for categorical variables
- All analyses were performed using SAS statistical software (SAS version 9.4; SAS Institute, Cary, NC, USA)

RESULTS

- 1,729 NDMM cases were identified between 2011 and 2017 in Alberta (Figure 4)

Figure 1. Data Sources Used in the INFORMM Study



DAD, discharge abstract data; FISH, fluorescence in situ hybridization; ISS, International Staging System; LoT, line of therapy; NACRS, National Ambulatory Care Reporting System; PIN, Pharmaceutical Information Network; TTNT, time to next treatment.

Figure 2. Study Timeline for the INFORMM Study

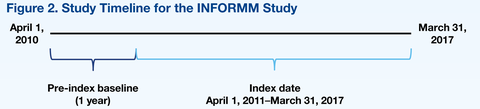
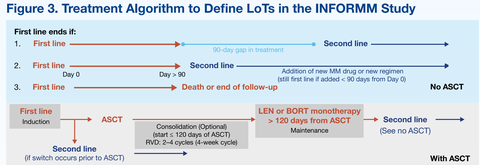
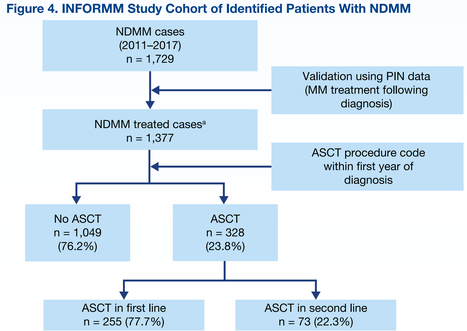


Figure 3. Treatment Algorithm to Define LoTs in the INFORMM Study



ASCT, autologous stem cell transplantation; BORT, bortezomib; LEN, lenalidomide; LoT, line of therapy; MM, multiple myeloma; RVD, LEN, BORT, and dexamethasone.

Figure 4. INFORMM Study Cohort of Identified Patients With NDMM



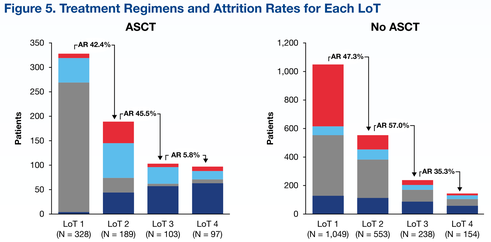
[a] NDMM cases that had ≥ 1 MM treatment.
NDMM, newly diagnosed MM; PIN, Pharmaceutical Information Network.

Table 1. Baseline Demographic and Clinical Characteristics, Stratified by ASCT Status

Characteristic	Overall	ASCT		*P* Value
		Yes	No	
Overall, n (%)	1,377 (100)	328 (23.8)	1,049 (76.2)	
Follow-up time, mean ± SD, years	2.3 ± 1.6	2.7 ± 1.5	2.1 ± 1.6	< 0.01[a]
Age, mean ± SD, years	68.9 ± 12.2	57.9 ± 7.3	72.3 ± 11.4	< 0.01[a]
Sex, n (%)				0.06[b]
Female	549 (39.9)	116 (35.4)	433 (41.3)	
Male	828 (60.1)	212 (64.6)	616 (58.7)	
Charlson Comorbidity Index, mean ± SD	4.7 ± 3.0	3.7 ± 2.4	5.0 ± 3.1	< 0.01[a]
ISS stage, n (%)				< 0.01[b]
I	278 (20.2)	111 (33.8)	167 (15.9)	
II	213 (15.5)	60 (18.3)	153 (14.6)	
III	325 (23.6)	71 (21.6)	254 (24.2)	
Missing	561 (40.7)	86 (26.2)	475 (45.3)	
ISS-FISH, n (%)				0.13[b]
I	300 (21.8)	86 (26.2)	214 (20.0)	
II	128 (9.3)	28 (8.5)	100 (9.5)	
III	59 (4.3)	21 (6.4)	38 (3.6)	
Missing	1,018 (73.9)	193 (58.8)	697 (66.4)	
Number of chromosomal abnormalities, n (%)[c]				0.03[b]
0	401 (29.1)	113 (34.5)	288 (27.5)	
1	127 (9.2)	40 (12.2)	87 (8.3)	
≥ 2	38 (2.8)	18 (5.5)	20 (1.9)	
Missing	811 (58.9)	157 (47.9)	654 (62.3)	
Diabetes at baseline, n (%)[d]				< 0.01[b]
No	1,127 (81.8)	290 (88.4)	837 (79.8)	
Yes	250 (18.2)	38 (11.6)	212 (20.2)	
Diabetes developed during follow-up, n (%)				0.45[b]
No	1,050 (77.6)	273 (94.1)	777 (92.8)	
Yes	77 (22.4)	17 (5.9)	60 (7.2)	
Metformin use (if diabetes at baseline), n (%)[e]				0.08[b]
No	98 (39.2)	10 (26.3)	88 (41.5)	
Yes	152 (60.8)	28 (73.7)	124 (58.5)	

[a] *P* value for Student t-test between ASCT and non-ASCT groups.
[b] *P* value for χ^2 tests between ASCT and non-ASCT groups.
[c] Number of chromosomal abnormalities based on a count of t(4;14), t(11;14), t(14;16) translocations and TP53 deletions; cytogenetic test results were available for only a subset of the cohort (patients from the Calgary zone).
[d] Diabetes at baseline was defined as having a diabetes diagnosis within 1 year prior to multiple myeloma diagnosis.
[e] Metformin use was defined as having a prescription dispensed for metformin within 1 year of diabetes diagnosis.
ISS, International Staging System; SD, standard deviation.

Figure 5. Treatment Regimens and Attrition Rates for Each LoT



[a] Other medications predominantly consisted of dexamethasone and prednisone.
AR, attrition rate; ASCT, autologous stem cell transplantation; BORT, bortezomib; LEN, lenalidomide; LoT, line of therapy.

Table 2. DoT[a] for First-Line Therapy in Patients by First-Line Treatment Regimen

First-Line Treatment Regimen	ASCT in First Line (n = 255)		No ASCT
	Maintenance[b]	No Maintenance	
Overall			
Patients, n	158 (136/22)[c]	97	1,049
DoT, mean ± SD, months	31.8 ± 17.6	10.8 ± 9.9	11.1 ± 10.0
LEN-based			
Patients, n	NR	NR	128
DoT, mean ± SD, months			9.3 ± 4.6
BORT-based			
Patients, n	130 (113/17)[c]	82	425
DoT, mean ± SD, months	32.8 ± 18.0	10.3 ± 9.4	8.9 ± 6.9
Other			
Patients, n	27 (23/NR)[c]	14	496
DoT, mean ± SD, months	26.0 ± 14.0	14.5 ± 12.1	13.4 ± 12.4

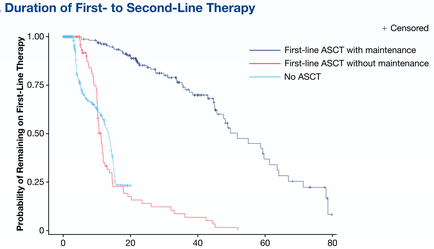
[a] DoT was determined using the start date of medication and the end date of one of the following: (a) date of subsequent LoT; (b) last date of medication or treatment; or (c) date of death.
[b] Maintenance monotherapy was defined as the presence of either LEN or BORT monotherapy 120 days post-ASCT.
[c] Number of patients on LEN or BORT maintenance monotherapy (LEN/BORT).
DoT, duration of therapy; NR, not reported (sample size < 5).

Table 3. TTNT[a]

Treatment Line	ASCT in First Line (n = 255)		No ASCT
	Maintenance[b]	No Maintenance	
First to second			
Patients, n	54	62	553
TTNT, mean ± SD, months	27.6 ± 16.5	15.3 ± 10.3	8.0 ± 4.5
Second to third			
Patients, n	35	45	237
TTNT, mean ± SD, months	4.4 ± 6.6	5.2 ± 1.9	4.9 ± 1.6
Third to fourth			
Patients, n	30	44	154
TTNT, mean ± SD, months	6.7 ± 2.9	4.6 ± 2.9	3.5 ± 0.9

[a] TTNT was restricted to only those advancing to the next LoT and was determined using the start date of medication and the end date of the start of the subsequent LoT.
[b] Maintenance monotherapy was defined as the presence of either LEN or BORT monotherapy within 120 days of ASCT.
TTNT, time to next treatment.

Figure 6. Duration of First- to Second-Line Therapy



	Number at Risk	Advanced to Second Line	Number Censored
First-line ASCT with maintenance	158	54	104
First-line ASCT without maintenance	97	62	35
No ASCT	1,049	553	496

- Patients in the non-ASCT group were older and had higher Charlson Comorbidity Index scores and International Staging System (ISS) stages versus patients in the ASCT group (Table 1)
- Among all treated patients, regardless of ASCT status, 742 (53.9%) patients advanced to second-line therapy, 341 (24.8%) advanced to third-line therapy, and 251 (18.2%) patients had ≥ 4 LoTs (Figure 5)
  - Most patients began on a BORT-based regimen in first-line therapy, with increased use of LEN- and LEN + BORT-based regimens in subsequent LoT
- Patients who received maintenance therapy post-ASCT had longer DoT compared with those who did not receive maintenance therapy post-ASCT and non-ASCT patients (Table 2)
- For patients receiving ASCT in second-line therapy, mean DoT of first-line regimen was 3.9 ± 0.7 months, indicating a treatment switch after 3–4 cycles of their initial treatment regimen (data not shown)
- Similar to DoT, the mean TTNT in ASCT patients receiving first-line maintenance monotherapy was substantially longer than those without maintenance monotherapy or non-ASCT patients (Table 3 and Figure 6)
- However, following ASCT, the mean TTNT becomes more comparable to non-ASCT patients in subsequent lines of therapy, regardless of whether patients were on maintenance monotherapy (Table 3)

LIMITATIONS

- No adjustments for patient baseline characteristics were performed when making comparisons between groups
- Inclusion of underrepresented racial/ethnic and socioeconomic groups, and reduced reliance on self-report in administrative data may result in under- or overestimation due to miscoding, data linkage, and algorithm errors
- To reduce potential bias, algorithms used in interpreting data need to be validated against good-quality reference standards

CONCLUSIONS

- **This study aimed to describe the MM treatment landscape in Alberta, Canada, by leveraging administrative data collected in databases in the clinical setting**
- **Findings showed that, among treated NDMM cases, around 24% of patients had ASCT**
- **ASCT patients appeared to be more "fit" as indicated by lower mean age, comorbidity index, and ISS stage compared with non-ASCT patients**
- **Treatment attrition rates were similar in both the ASCT and non-ASCT group from LoT 1 to LoT 2, although attrition rates were higher in the non-ASCT group in subsequent LoT**
- **Notably, patients benefited from post-ASCT maintenance therapy regardless of the induction regimens used**

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The interpretation and conclusions contained herein are those of the researchers and do not necessarily represent the views of the Government of Alberta. Neither the Government of Alberta nor Alberta Health expresses any opinion in relation to this study.

DISCLOSURES

V.H.J.-Z., J.T.: Celgene Corporation – honoraria. G.C., T.C., E.S., M.F.: Celgene Corporation – consultancy. F.F.L.: Celgene Corporation – employment.

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