LocoMMotion: A Prospective, Observational, Multinational Study of Real-Life Current Standards of Care in Patients With Relapsed/Refractory Multiple Myeloma—Final Analysis at 2-Year Follow-Up

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BACKGROUND

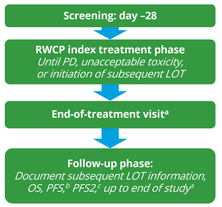
- Most patients with multiple myeloma (MM) relapse[1,2] and/or become treatment refractory[2] and cycle through standard drug classes
  - Patients with ≥3 prior lines of therapy (LOT) or who are refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD) represent an urgent unmet clinical need and are a major focus for development of new treatments
- LocoMMotion (NCT04035226) assessed effectiveness and safety of real-world clinical practice (RWCP) treatments in 248 heavily pretreated patients with relapsed/refractory MM (RRMM)
  - Previous results (16.1-months median follow-up) showed a low overall response rate (ORR; 31.5% [95% CI, 25.7–37.6]) and rapid disease progression (median progression-free survival [PFS], 4.6 months [95% CI, 3.9–5.6]) by response review committee (RRC), and short median overall survival (OS; 13.8 mo [95% CI, 10.8–18.5]) with first RWCP treatment after study enrollment, ie, index LOT[3]
- Here, we report final LocoMMotion results with a longer median study follow-up of 26.4 months and details of subsequent LOT

METHODS

Study design and treatment

- Prospective, observational study; patients were enrolled at 75 sites in Belgium, France, Germany, Italy, Netherlands, Poland, Russia, Spain, United Kingdom, and United States[4,5]; RWCP treatments were defined as those used in local clinical practice, as previously described.[4] Patients were enrolled August 2019 to October 2020
- Primary focus: effectiveness and safety of index treatment where progressive disease (PD)/responses were assessed by RRC, per International Myeloma Working Group (IMWG) criteria.[6] Responses with subsequent LOT were subject to investigator assessment
- Study composed of 3 sections: index treatment, presubsequent LOT, and subsequent LOT. Variables were summarized using descriptive statistics, ORR by RRC was reported using 95% Clopper-Pearson (exact) CIs, and time-to-event data were summarized using Kaplan-Meier methods (**Figure 1**)

FIGURE 1: LocoMMotion study design



[a]End-of-treatment visit: ~30 days after last index treatment dose. End of study: 24 months after first index treatment dosing of last patient enrolled, except where patient death ends study early; assessments planned periodically up to end of study. [b]By RRC. [c]Time to progression or death (whichever occurs first) from start of study through first subsequent LOT, determined by investigator assessment.

Key eligibility criteria

- Documented MM per IMWG criteria[6]
- Eastern Cooperative Oncology Group performance status of 0 or 1 at screening
- Measurable disease at screening
- ≥3 prior LOT or refractory to a PI and IMiD
- Prior treatment with a PI, IMiD, and anti-CD38 monoclonal antibody
- Disease progression during/after their last LOT

MULTIPLE MYELOMA

RESULTS

LocoMMotion patients and index RWCP treatments

- Study period was August 2019–October 2022. 248 patients were included; baseline characteristics have been previously reported[4]
- Patients had received a median of 4 prior LOT (range, 2–13); 73.4% were triple-class refractory, 92.3% were refractory to last prior LOT, and 64.5% had received a prior stem cell transplant (SCT)
- 91 unique treatment regimens were used in the index LOT; 162 (65.3%) patients received a combination of ≥3 drugs, and 6 (2.4%) had an SCT
- Median study follow-up was 26.4 months (95% CI, 25.0–28.1). ORR by RRC was 31.9% (95% CI, 26.1–38.0), median duration of treatment (DOT) was 4.0 months (range, 0.1–33.6), and median duration of response was 7.4 months (95% CI, 4.9–11.1)
- Median PFS by RRC was 4.6 months, median OS was 13.8 months (**Figure 2**), and 24-month PFS rate by RRC and OS rate were 10.5% and 33.7%, respectively (**Table 1**)

FIGURE 2: PFS by RRC and OS at median study follow-up 26.4 months

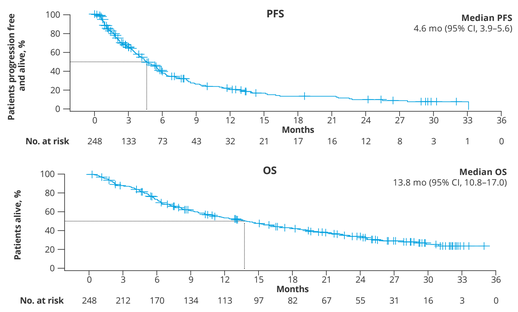


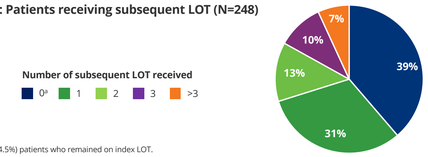
TABLE 1: PFS by RRC and OS rates up to 24 months

	N=248	
	%	95% CI
Survival outcomes		
12-month PFS by RRC	21	15.3–27.3
12-month OS	53.4	46.7–59.6
24-month PFS by RRC	10.5	6.1–16.3
24-month OS	33.7	27.3–40.2

Subsequent LOT

- 152 (61.3%) patients had subsequent LOT; 78 had only 1 subsequent LOT, and 74 had ≥2 subsequent LOT (**Figure 3**)
- Median PFS2 by investigator assessment was 10.8 months (95% CI, 8.4–13.0). PFS2 includes PD events after start of subsequent LOT 1 and deaths from start of index LOT (ie, not PD events during index LOT) and censors patients who withdrew before subsequent LOT 1, allowing some potential bias selecting for better responders
- 79 different treatment regimens were used in subsequent LOT 1; median DOT was 2.8 months (range, <1–29.7)
- Most common subsequent LOT regimens are shown in **Table 2**
- Use of B-cell maturation antigen (BCMA)-targeted therapy increased to 24.2% in subsequent LOT from 2.8% in index LOT

FIGURE 3: Patients receiving subsequent LOT (N=248)



[a]Includes 36 (14.5%) patients who remained on index LOT.

TABLE 2: Treatment regimens used in index and subsequent LOT (N=248)

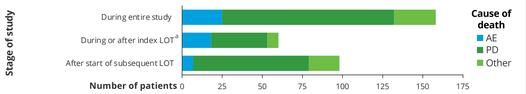
	No. regimens	No. patients	Most common regimens,[a,b] %
Index LOT	91	248	Kd (14.1), CPd (14.1), Pd (11.7)
Subsequent LOT 1	79	152	blmf (6.5), CPd (4.0)
Subsequent LOT 2	47	74	blmf (5.6), KCd (1.6), Kd (1.6)
Subsequent LOT 3	30	42	blmf (3.2), IPd (2), DKd (0.8)
Subsequent LOT 4+	34	17	blmf (1.2)

[a]Patients can be counted in more than one regimen. [b]Percentage calculated out of N=248; for subsequent LOT, the percentage does not account for patients who died or were lost to follow-up. blmf, belantamab mafodotin; CPd, cyclophosphamide, pomalidomide, and dexamethasone; DKd, daratumumab, carfilzomib, and dexamethasone; IPd, isatuximab, pomalidomide, and dexamethasone; KCd, carfilzomib, cyclophosphamide, and dexamethasone; Kd, carfilzomib and dexamethasone; Pd, pomalidomide and dexamethasone.

Safety

- During index LOT, 86.7% of patients experienced an adverse event (AE)
  - Most common AEs were cytopenias
  - A second primary malignancy was reported in 13 (5.2%) patients (index LOT, n=5; after index LOT, n=8)
- 158 (63.7%) patients died during the study, predominantly from PD regardless of stage of study (**Figure 4**)

FIGURE 4: Deaths and causes of death



[a]These patients did not receive subsequent LOT.

KEY TAKEAWAY

Results of the LocoMMotion study highlight an urgent need for new treatment options for heavily pretreated patients with RRMM. There is a lack of well-established standard of care; these patients show rapid disease progression and poor survival despite the wide range of treatments used during the study, including subsequent LOT

CONCLUSIONS

- Final analysis at >2-year median study follow-up in heavily pretreated patients with RRMM confirms a lack of well-established standard of care
- Disease progression is rapid, even in subsequent LOT; median PFS2 by investigator assessment was 10.8 months
- Survival rates are low: 24-month PFS by RRC and OS rates were 10.5% and 33.7%, respectively

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DISCLOSURES

PM has received honoraria and/or served on advisory boards for AbbVie, Amgen, Celgene, Janssen, Sanofi, and Takeda. **KW** has served as a consultant and received honoraria from Adaptive Biotechnologies, Karyopharm, and Takeda; has received honoraria from Roche; and has received honoraria and served in a member on boards of directors and/or advisory committees for Amgen, BMS, Celgene, GSK, Janssen, OncoPeptides, and Sanofi. **VDS** has served on an advisory board or speakers' bureau and received honoraria from AbbVie, Alexion, AOP Health, argenx, BMS, GSK, Grifols, Leo Pharma, Novartis, Novo Nordisk, Sanofi, SOBI, and Takeda. **HG** has served as a consultant for Amgen, Novartis, and Takeda; has served as a consultant and received honoraria, grants, and/or provision of investigational medicinal product and research funding from Amgen, BMS, Celgene, Chugai, Janssen, and Sanofi; received research funding from Incyte, Molecular Partners, MSD, Mundipharma, and Novartis; and received other grants from Dietmar Hopp Foundation. **MD** has received honoraria from Amgen, BMS, GSK, and Janssen; and has served on the speakers' bureau for Janssen. **MM** has received honoraria from Adaptive Biotech, Amgen, Astellas, BMS, Gilead, Novartis, Pfizer, and Takeda; and has received honoraria/research funding from Celgene and Sanofi. **JL-H** has no relationships to disclose. **DD** is an employee/consultant/honoraria/member of board of directors/advisory committees for Janssen Cilag; and a member of the board of directors/advisory committees/received research funding from Celgene. **EÁ** has no relationships to disclose. **LV** has served on the advisory board of BMS, Janssen and Takeda. **AP** has received honoraria from or has served in a consulting/advisory role for AbbVie, Amgen, BMS, Janssen, Pfizer, Sanofi, and Takeda. **RB** has received honoraria/research funding from Allogene, BMS, Gilead, Janssen, and Servier. **NWCJvdD** has received research funding from Amgen, BMS, Celgene, Cellectis, Janssen Pharmaceuticals, and Novartis; and has served in a consulting/advisory role for Adaptive, Amgen, Bayer, BMS, Celgene, Janssen, Novartis, Roche, Servier, and Takeda. **EMO** has received honoraria from or has served in a consulting/advisory role for AbbVie, Amgen, BMS, GSK, Janssen, Karyopharm, Menarini, Oncopeptides, Pfizer, Sanofi, and Takeda. **EiG-D**, **TR**, **JMS**, **IH**, **VS**, **LM**, **JB**, and **SS** are employees of Janssen. **OCF** is an employee of Legend Biotech USA Inc. **HE** has received research funding or honoraria and has served in a consulting/advisory role for Amgen, BMS/Celgene, GSK, Janssen, and Sanofi. **M-VM** has received honoraria from or served on the board of directors or on an advisory committee for AbbVie, Adaptive Biotechnologies, Amgen, BMS/Celgene, GSK, Janssen, Oncopeptides, Pfizer, Regeneron, Roche, Sanofi, Sea-Gen, and Takeda.

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