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Real-Life Outcomes in Triple-Class Exposed Relapsed/Refractory Multiple Myeloma Treated With Carfilzomib- and/or Pomalidomide-Based Regimens in the LocoMMotion and MoMMent Studies

María-Victoria Mateos[1], Katja Weisel[2], Maria Esther Gonzalez Garcia[3], Hermann Einsele[4], Joanna Lindsey-Hill[5], Valerio De Stefano[6], Britta Besemer[7], Laure Vincent[8], Suriya Kirkpatrick[9], Lionel Karlin[10], Hartmut Goldschmidt[11], Concetta Conticello[12], Wilfried Roeloffzen[13], Niels WCJ van de Donk[14], Michel Delforge[15], Pamella Villanova[16], Margaret Doyle[17], Kathleen Gray[18], Claire Albrecht[19], Vadim Strulev[20], Jozefien Buyze[20], Jonathan Squire[21], Philippe Moreau[22]

[1]Hospital Universitario de Salamanca, Instituto de Investigación Biomédica de Salamanca (IBSAL), Centro de Investigación del Cáncer (IBMCC-USAL,CSIC), Salamanca, Spain; [2]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [3]University Hospital Cabueñes, Gijón, Spain; [4]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany; [5]Nottinghamshire University Hospitals NHS Trust, Nottingham, UK; [6]Catholic University, Fondazione Policlinico A. Gemelli, IRCCS, Rome, Italy; [7]University of Tübingen, Tübingen, Germany; [8]Centre Hospitalier Universitaire de Montpellier, Montpellier, France; [9]University of the West of England, Bristol, UK; [10]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [11]Internal Medicine V, GMMG-Study Group at University Hospital Heidelberg, Heidelberg, Germany; [12]Azienda Policlinico-OVE, University of Catania, Catania, Italy; [13]University Medical Center Groningen, Groningen, Netherlands; [14]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [15]University of Leuven, Leuven, Belgium; [16]Janssen Research & Development, São Paulo, Brazil; [17]Janssen Ireland, Dublin, Ireland; [18]Janssen Research & Development, Bridgewater, NJ, USA; [19]Janssen-Cilag, Issy-les-Moulineaux, France; [20]Janssen Pharmaceutica NV, Beerse, Belgium; [21]IQVIA, Berkeley, CA, USA; [22]University Hospital Hôtel-Dieu, Nantes, France

Key Takeaway

Outcomes in patients with TCE RRMM remain poor, despite the use of carfilzomib and pomalidomide. New treatments, such as CAR-T cell therapies and BsAbs, are needed to address the remaining high unmet need for patients with TCE RRMM

Conclusions

55% of patients in LocoMMotion and MoMMent received carfilzomib- and/or pomalidomide-based regimens

Despite the use of carfilzomib- and/or pomalidomide-based regimens, overall outcomes (mPFS, 5.5 months) remain poor in patients with TCE RRMM

A high unmet need remains for new immunotherapies for patients with TCE RRMM

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Poster

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Disclosures

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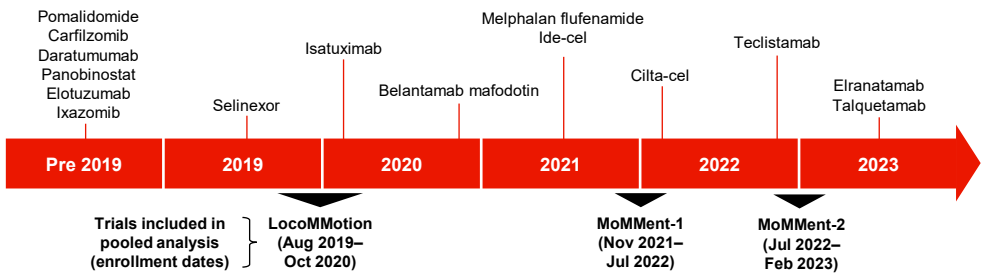
Introduction

- A pooled analysis from the prospective, noninterventional, multinational LocoMMotion (NCT04035226) and MoMMent (NCT05160584) studies demonstrated suboptimal outcomes in patients with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM)[1]
  - Overall response rate (ORR): 31.8%; median progression-free survival (PFS) and overall survival (OS): 4.6 and 14.5 months, respectively
  - The results highlighted the lack of a single standard of care (SOC) with >100 different regimens used
- The RRMM treatment landscape is rapidly evolving (**Figure 1**), and continuous assessments of the changing SOC and TCE patient profiles are needed to further elucidate unmet needs in clinical practice[2]
- Here, we evaluate outcomes in patients from LocoMMotion and MoMMent treated with carfilzomib- and/or pomalidomide-based regimens as observed during the period from 2019–2022, preceding the era of chimeric antigen receptor (CAR)-T cell therapies and bispecific antibodies (BsAbs)

Figure 1: Evolving treatment landscape in MM[a]



[a]Representative of initial regulatory approval across the US and EU.
cilta-cel, ciltacabtagene autoleucel; ide-cel, idecabtagene vicleucel; MM, multiple myeloma.

Methods

- Data were pooled from LocoMMotion (final analysis: October 27, 2022) and MoMMent (clinical cut-off: August 18, 2023)
- LocoMMotion and MoMMent have the same study design and data collection methods, with most patients enrolled from the same sites
- Both studies included patients with:
  - ≥3 prior lines of therapy (LOT; LocoMMotion allowed <3 prior LOT if patients were double-refractory to a proteasome inhibitor [PI] and an immunomodulatory drug [IMiD])
  - Eastern Cooperative Oncology Group performance status (ECOG PS) score of 0 or 1 at screening
  - TCE RRMM
  - Measurable disease and documented progressive disease since last LOT
- The primary endpoint was ORR, evaluated per International Myeloma Working Group criteria by the same review committee in both studies
- Continuous variables were summarized using descriptive statistics; ORR was reported with 95% exact CIs
- Time-to-event data were summarized by Kaplan-Meier methods

Results

- The current pooled analysis (median follow-up, 24.4 months [range, 0.1–33.6]) included 166 patients (LocoMMotion, n=131; MoMMent, n=35) treated with either a carfilzomib- and/or pomalidomide-based regimen
- Patient baseline characteristics are described in **Table 1**
- Overall, 36 unique carfilzomib- and/or pomalidomide-based regimens were used as SOC (**Table 2**)
  - The most common (≥5% of patients) were pomalidomide-cyclophosphamide-dexamethasone (24.7%); carfilzomib-dexamethasone (20.5%); pomalidomide-dexamethasone (12.7%); and elotuzumab-pomalidomide-dexamethasone (5.4%)

Table 1: Baseline characteristics of patients who received carfilzomib- and/or pomalidomide-based SOC regimens in LocoMMotion and MoMMent

Characteristic	Carfilzomib (n=76)	Pomalidomide (n=96)	Pooled (N=166)
Age, years, median (range)	70.0 (52–89)	68.5 (45–86)	69.0 (45–89)
Male, n (%)	38 (50.0)	58 (60.4)	94 (56.6)
ECOG PS score, n (%)			
0	19 (25.0)	25 (26.0)	41 (24.7)
1	57 (75.0)	70 (72.9)	124 (74.7)
2	0	1 (1.0)	1 (0.6)
Time since diagnosis, years, median (range)	6.0 (0.3–18.5)	6.1 (0.8–16.0)	6.0 (0.3–18.5)
Number of prior LOT, median (range)	4.0 (2–11)	4.0 (2–12)	4.0 (2–12)
Number of prior LOT, n (%)			
2	7 (9.2)	7 (7.3)	14 (8.4)
3	18 (23.7)	30 (31.3)	46 (27.7)
4	23 (30.3)	25 (26.0)	47 (28.3)
≥5	28 (36.8)	34 (35.4)	59 (35.5)
Prior exposure, n (%)			
PI	76 (100)	96 (100)	166 (100)
Carfilzomib	18 (23.7)	37 (38.5)	54 (32.5)
IMiD	76 (100)	96 (100)	166 (100)
Pomalidomide	49 (64.5)	21 (21.9)	67 (40.4)
PI and IMiD	76 (100)	96 (100)	166 (100)
Pomalidomide or carfilzomib	52 (68.4)	46 (47.9)	94 (56.6)
Pomalidomide and carfilzomib	15 (19.7)	12 (12.5)	27 (16.3)
Alkylating agents	60 (78.9)	74 (77.1)	130 (78.3)
Anthracyclines	18 (23.7)	15 (15.6)	33 (19.9)
Anti-CD38 antibodies	76 (100)	96 (100)	166 (100)
BsAb	1 (1.3)	3 (3.1)	4 (2.4)
BCMA-targeted	1 (1.3)	3 (3.1)	4 (2.4)
GPRC5D-targeted	1 (1.3)	1 (1.0)	2 (1.2)
ADC	1 (1.3)	1 (1.0)	2 (1.2)
BCMA-targeted	1 (1.3)	1 (1.0)	2 (1.2)
CAR-T	0	0	0
Refractory status, n (%)			
Triple-class[a]	51 (67.1)	72 (75.0)	121 (72.9)
Penta-drug[b]	9 (11.8)	10 (10.4)	19 (11.4)
Carfilzomib	12 (15.8)	27 (28.1)	39 (23.5)
Pomalidomide	45 (59.2)	16 (16.7)	59 (35.5)
Pomalidomide or carfilzomib	45 (59.2)	35 (36.5)	78 (47.0)
Pomalidomide and carfilzomib	12 (15.8)	8 (8.3)	20 (12.0)

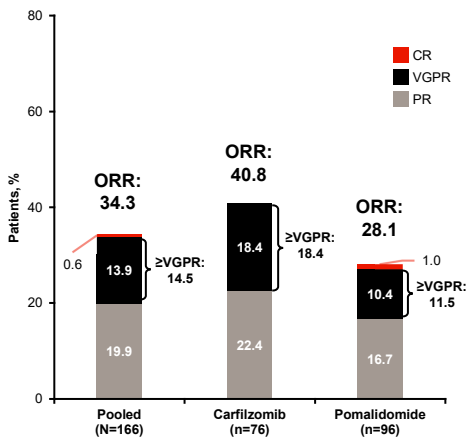
[a]1 each of PI + IMiD + anti-CD38 antibody. [b]2 PIs + 2 IMiDs + 1 anti-CD38 mAb.
ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; GPRC5D, G protein–coupled receptor class C group 5 member D; mAb, monoclonal antibody.

Table 2: Number of SOC regimens in patients who received carfilzomib- and/or pomalidomide-based regimens

SOC antimyeloma regimen,[a] n (%)	Pooled (N=166)
Carfilzomib-based regimens	76 (45.8)
As bridging to ide-cel	2 (1.2)
In combination with anti-CD38 antibodies (daratumumab or isatuximab)	15 (9.0)
Pomalidomide-based regimens	96 (57.8)
As bridging to ide-cel	2 (1.2)
In combination with anti-CD38 antibodies (daratumumab or isatuximab)	8 (4.8)
SOC antimyeloma regimens in ≥5% patients, n (%)	**Pooled (N=166)**
Pomalidomide-cyclophosphamide-dexamethasone	41 (24.7)
Carfilzomib-dexamethasone	34 (20.5)
Pomalidomide-dexamethasone	21 (12.7)
Elotuzumab-pomalidomide-dexamethasone	9 (5.4)

[a]6 patients received antimyeloma regimens which included both carfilzomib and pomalidomide.

Figure 2: ORR in patients who received carfilzomib- and/or pomalidomide-based regimens



CR, complete response; PR, partial response; VGPR, very good partial response.

Figure 3: PFS in patients who received carfilzomib- and/or pomalidomide-based regimens

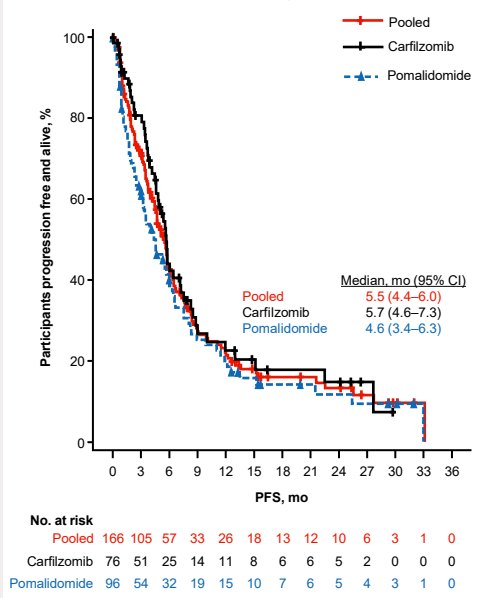


Figure 4: OS in patients who received carfilzomib- and/or pomalidomide-based regimens

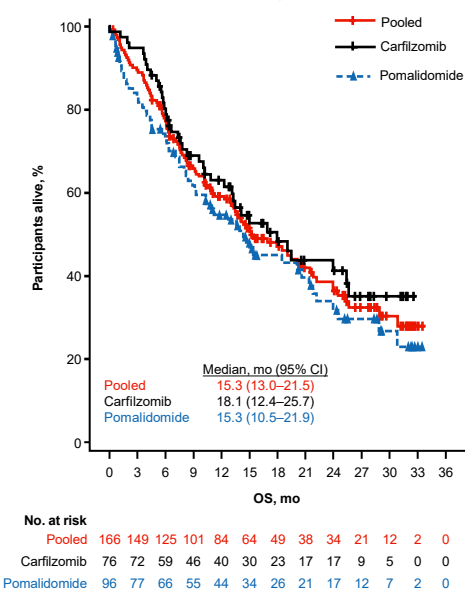


Figure 5: DOR in patients who received carfilzomib- and/or pomalidomide-based regimens

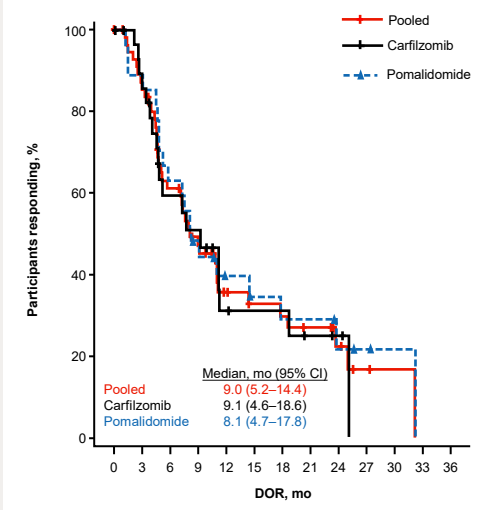
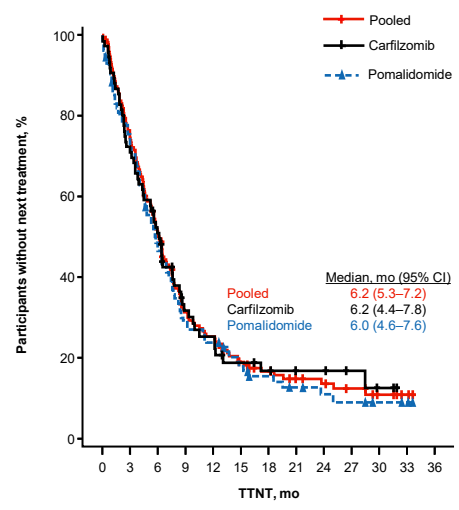


Figure 6: TTNT in patients who received carfilzomib- and/or pomalidomide-based regimens



Response to carfilzomib- and/or pomalidomide-based regimens

- In the pooled analysis, ORR was 34.3% (95% CI, 27.2–42.1; **Figure 2**)
- Median PFS (mPFS) was 5.5 months (95% CI, 4.4–6.0; **Figure 3**), median OS was 15.3 months (95% CI, 13.0–21.5; **Figure 4**), median duration of response (DOR) was 9.0 months (95% CI, 5.2–14.4; **Figure 5**), and median time-to-next treatment (TTNT) was 6.2 months (95% CI, 5.3–7.2; **Figure 6**)

References

1. Weisel K, et al. Presented at IMS; September 27–30, 2023; Athens, Greece. Poster #P325. 2. Tanenbaum B, et al. *Ann Hematol* 2023;102:1-11.

Multiple Myeloma

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