P-050

Talquetamab vs Real-World Physician's Choice in Patients With Relapsed/Refractory Multiple Myeloma and Prior B-Cell Maturation Antigen Therapy: Analyses of MonumenTAL-1 vs LocoMMotion/MoMMent

María-Victoria Mateos[1], Andrzej Jakubowiak[2], Hermann Einsele[3], Carolina Schinke[4], Britta Besemer[5], Sébastien Anguille[6], Salomon Manier[7], Leo Rasche[8], Hartmut Goldschmidt[9], Niels WCJ van de Donk[10], Aurore Perrot[11], Raphael Teipel[12], Lionel Karlin[13], Christof Scheid[14], Jesús San-Miguel[15], Charlotte Pawlyn[16], Joaquín Martinez-Lopez[17], Michele Cavo[18], Joris Diels[19], Thomas Renaud[20], Oleksiy Orel[21], Jedelyn Cabrieto[19], Nolen Perualila[19], Katja Weisel[22], Philippe Moreau[23]

[1]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [2]University of Chicago, Chicago, IL, USA; [3]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany; [4]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [5]University of Tübingen, Tübingen, Germany; [6]Vaccine and Infectious Disease Institute, Center for Cell Therapy and Regenerative Medicine, Antwerp University Hospital, Edegem, Belgium; [7]University of Lille, CHU Lille, Lille, France; [8]University Hospital of Würzburg, Würzburg, Germany; [9]Internal Medicine V, GMMG-Study Group at University Hospital Heidelberg, Germany; [10]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [11]Centre Hospitalier Universitaire de Toulouse, Oncopole, Toulouse, France; [12]Medizinische Klinik und Poliklinik 1, Universitätsklinikum Carl Gustav Carus an der TU Dresden, Dresden, Germany; [13]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [14]University of Cologne, Cologne, Germany; [15]Clínica Universidad de Navarra, CCUN, CIMA; IDISNA, CIBERONC, Pamplona, Spain; [16]The Institute of Cancer Research, London, UK, and The Royal Marsden NHS Foundation Trust, London, UK; [17]Hematological Malignancies Clinical Research Unit, Hospital 12 de Octubre Universidad Complutense, Centro Nacional de Investigaciones Oncológicas, CIBERONC, Madrid, Spain; [18]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Seràgnoli Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; [19]Janssen Pharmaceutica NV, Beerse, Belgium; [20]Janssen Research & Development, Raritan, NJ, USA; [21]Janssen-Cilag GmbH, Neuss, Germany; [22]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [23]Hematology Clinic, University Hospital Hotel-Dieu, Nantes, France

Introduction

- T-cell redirection therapy (TCR), including B-cell maturation antigen (BCMA)-targeted chimeric antigen receptor (CAR)-T cells and bispecific antibodies (BsAbs), are new treatment options for patients with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM) but result in an unmet need for patients who relapse after TCR[1,2]
- Talquetamab is the first G protein–coupled receptor family C group 5 member D–targeting BsAb approved for the treatment of patients with TCE RRMM[3-5]
  - At a previous data cut-off (DCO), overall response rates (ORRs) with talquetamab were 72.9% and 56.5% in patients treated with prior BCMA CAR-T and prior BCMA BsAb therapy, respectively, in the MonumenTAL-1 study (NCT03399799/NCT04634552)[6]
- LocoMMotion (NCT04035226) and MoMMent (NCT05160584) are 2 prospective, consecutive, observational studies evaluating clinical outcomes with real-world physician's choice of treatment (RWPC) in patients with TCE RRMM[7,8]
- As MonumenTAL-1 was a single-arm study, adjusted comparisons can help determine the relative efficacy of talquetamab vs other treatments
- We present results of talquetamab vs RWPC in patients with prior BCMA TCR

Methods

Data sources

- An adjusted treatment comparison was performed using individual patient data (IPD) for patients with prior BCMA TCR and who received subcutaneous talquetamab 0.4 mg/kg weekly (QW) or 0.8 mg/kg every other week (Q2W) (MonumenTAL-1: DCO, Jan 2024) or RWPC therapies (LocoMMotion: final data; MoMMent: DCO, Aug 2023)
- IPD from talquetamab 0.4 mg/kg QW and 0.8 mg/kg Q2W dosing were pooled from patients with prior BCMA TCR who met MonumenTAL-1 eligibility criteria (**Figure 1**)

Adjusted treatment comparison

- For the base case analysis, multivariable regression was used to adjust for imbalances in refractory status, International Staging System (ISS) stage, time to progression on prior line of therapy (LOT), number of prior LOT, time since diagnosis, presence of extramedullary plasmacytomas, Eastern Cooperative Oncology Group performance status (ECOG PS), lactate dehydrogenase levels, hemoglobin levels, and creatinine clearance

Statistical analysis

- ORR was analyzed using multivariable logistic regression to estimate odds ratios, relative risk (RR), and 95% CIs
- Progression-free survival (PFS) and overall survival (OS) were analyzed using multivariable Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% CIs
- A sensitivity analysis, including additional adjustments for age, sex, multiple myeloma type, average duration of prior LOT, and prior autologous stem cell transplantation, was also performed
- An additional sensitivity analysis, adjusting for whether or not a TCR was received in last LOT, was also performed on top of the base case analysis

Figure 1: MonumenTAL-1 key patient eligibility criteria

MonumenTAL-1 (n=74) and RWPC (n=36)

- TCE RRMM
- ≥3 prior LOT
- Prior BCMA TCR
- ECOG PS ≤2
- Hemoglobin ≥8 g/dL
- Creatinine clearance ≥40 mL/min/1.73 m^2

Key Takeaway

These analyses demonstrate clinical benefit and superior efficacy of talquetamab vs RWPC in patients with TCE RRMM and prior BCMA TCR

Conclusions

Patients with prior BCMA TCR who were treated with talquetamab were significantly more likely to achieve responses, especially deep responses, and had significantly improved PFS and OS compared with patients treated with RWPC

Clinical benefit was observed with talquetamab vs RWPC in patients who received either prior BCMA CAR-T or prior BCMA BsAb therapy

These results support talquetamab as a novel, highly effective treatment option not only for BCMA-naive patients, but also for patients with prior exposure to BCMA TCR

Results

Baseline characteristics and treatments

- Among prior BCMA TCR received, more patients received CAR-T (n=49/74, 66.2%) vs BsAb (n=20/74, 27.0%) in the talquetamab cohorts, whereas more patients received BsAb (n=21/36, 58.3%) vs CAR-T (n=12/36, 33.3%) in the RWPC cohort; 5 (6.8%) patients in the talquetamab cohort and 3 (8.3%) patients in the RWPC cohort received both prior CAR-T and BsAb
- In last LOT prior to talquetamab, CAR-T and BsAb were received by 44.6% and 9.5% of patients, respectively; in last LOT prior to RWPC, CAR-T and BsAb were received by 25.0% and 41.7% of patients, respectively (**Table 1**)
- In the RWPC cohort, the most common regimens received were teclistamab and a combination of cyclophosphamide, pomalidomide, and dexamethasone (**Table 2**)

Table 1: Key baseline characteristics

Characteristic	Talquetamab (n=74)	RWPC (n=36)
Age, years, n (%)		
<65	46 (62.2)	20 (55.6)
≥65	28 (37.8)	16 (44.4)
Male, n (%)	48 (64.9)	27 (75.0)
Extramedullary plasmacytomas ≥1,[a] n (%)	24 (32.4)	4 (11.1)
ISS stage, n (%)		
I	37 (50.0)	9 (25.0)
II	24 (32.4)	12 (33.3)
III	13 (17.6)	15 (41.7)
Prior LOT, n (%)		
≤4	18 (24.3)	4 (11.1)
>4	56 (75.7)	32 (88.9)
Time since end of last TCR, months, median (range)	9.9 (0.76–59.8)	4.0 (0.03–36.8)
TCR in last LOT		
CAR-T	33 (44.6)	9 (25.0)
BsAb	7 (9.5)	15 (41.7)
Refractory status,[b] n (%)		
Double- or triple-class	22 (29.7)	15 (41.7)
Quad	21 (28.4)	10 (27.8)
Penta-drug	31 (41.9)	11 (30.6)

[a]True extramedullary disease is restricted to soft tissue plasmacytomas that arise due to hematogenous spread and have no contact with bony structures.[9] Only true extramedullary disease soft tissue lesions were analyzed in MonumenTAL-1, while both paraskeletal lesions and/or true extramedullary disease soft tissue lesions were analyzed in LocoMMotion and MoMMent. [b]Refractoriness categories are defined as mutually exclusive.

Table 2: Treatment regimens in the RWPC cohort

Treatment regimen	Frequency, n (%) (n=36)[a]
Teclistamab	5 (13.9)
Cyclophosphamide, pomalidomide, and dexamethasone	5 (13.9)
Isatuximab, pomalidomide, and dexamethasone	2 (5.6)
Pomalidomide and dexamethasone	2 (5.6)
Bortezomib, venetoclax, and dexamethasone	2 (5.6)
Regimens in single patients[b]	
PI regimens[c]	7 (19.4)
Single agents[d]	4 (11.1)
IMiD and anti-CD38 mAb regimens	2 (5.6)
Chemotherapy regimens	2 (5.6)
PI, IMID, and anti-CD38 mAb regimens	2 (5.6)
CAR-T therapy[e]	1 (2.8)
IMiD regimen	1 (2.8)
PI and anti-CD38 mAb regimen	1 (2.8)

[a]Percentages calculated with the number of patients in the all-treated analysis set as denominator (n=36). [b]Treatment regimens received by single patients are grouped by class. [c]1 patient received a PI regimen containing selinexor. [d]1 patient each received belantamab mafodotin, bendamustine, pomalidomide, and venetoclax. [e]CAR-T regimen comprised of idecabtagene vicleucel, cyclophosphamide, and fludarabine. IMiD, immunomodulatory drug; mAb, monoclonal antibody; PI, proteasome inhibitor.

Table 3: Treatment outcomes with talquetamab vs RWPC

Outcome	Talquetamab (n=74) vs RWPC (n=36)	
	RR (95% CI)	*P* value
ORR	6.42 (2.54–16.25)	<0.0001
VGPR	10.17 (2.45–42.24)	0.0012
	HR (95% CI)	*P* value
PFS	0.53 (0.29–0.98)	0.0423
OS	0.32 (0.17–0.63)	0.0008

VGPR, very good partial response.

Efficacy outcomes

- Base case analysis showed superior efficacy of talquetamab in patients with prior BCMA TCR across all endpoints (**Table 3**), vs RWPC
  - ORR was 64.9% for talquetamab vs 11.1% for RWPC
  - PFS (**Figure 2**) and OS (**Figure 3**) were also improved with talquetamab vs RWPC
- In subgroup analyses, efficacy outcomes were improved in patients who received talquetamab vs RWPC following BCMA CAR-T and BCMA BsAb, respectively:
  - ORR was 70.4% and 56.0% in patients treated with talquetamab and 20.0% and 4.2% in patients who received RWPC (**Figure 4**)
  - Median PFS (95% CI) was 12.3 (4.2–22.2) and 4.1 (2.9–7.7) months in patients treated with talquetamab and 2.3 (1.2–not estimable [NE]) and 2.1 (1.5–4.1) months in patients who received RWPC
  - Median OS (95% CI) was 27.1 (19.7–NE) and 14.0 (8.2–NE) months in patients treated with talquetamab and 7.4 (4.1–NE) and 8.9 (5.4–14.5) months in patients who received RWPC
- Results were generally consistent across sensitivity analyses

Figure 2: PFS

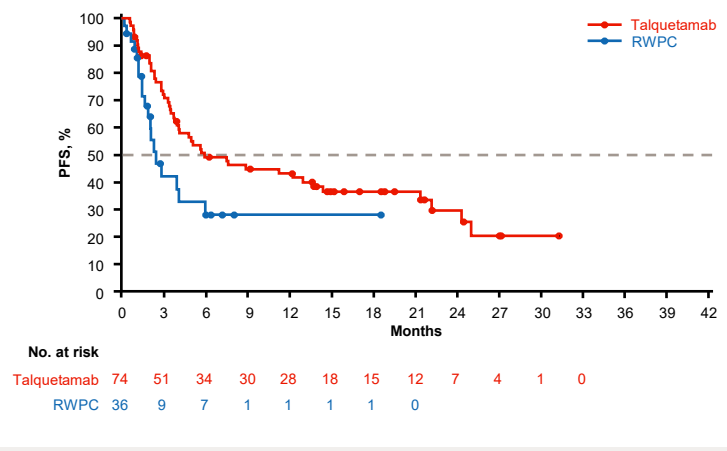


Figure 3: OS

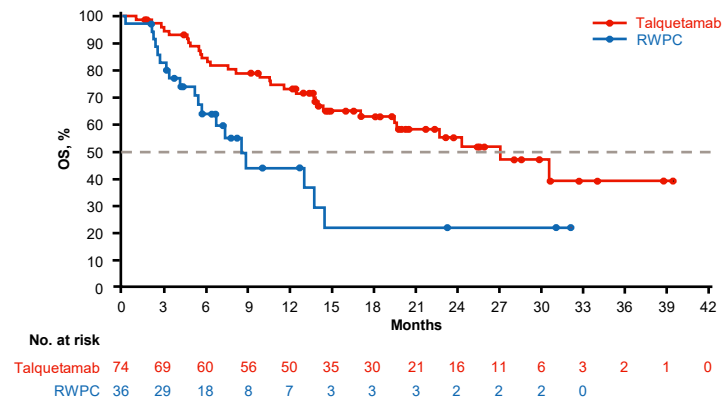
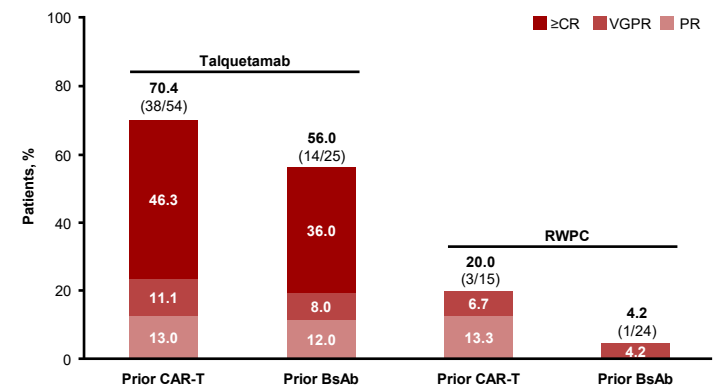


Figure 4: ORR[a]



[a]Patients who received both CAR-T and BsAb prior to talquetamab (n=5) or RWPC (n=3) are included in the respective ORR columns. CR, complete response. PR, partial response.

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Poster

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Acknowledgments

This study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Rachael Smith, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Disclosures

M-VM has received honoraria from AbbVie, Amgen, Celgene, GSK, Janssen, Kite, Oncopeptides, Pfizer, Regeneron, Roche, Sanofi, and Stemline; and has participated in a data safety monitoring board or advisory board for AbbVie, Amgen, GSK, Janssen, Kite, Pfizer, Roche, and Stemline.

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Multiple Myeloma

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil