PS1736

Talquetamab vs Real-World Physician's Choice in Patients With Relapsed/Refractory Multiple Myeloma and Prior B-Cell Maturation Antigen Therapy: Updated 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], Francesca Ghilotti[20], Bonnie W Lau[21], Thomas Renaud[21], Oleksiy Orel[22], Fenny Ong[19], Diogo F Ramos[23], Eric Ammann[21], Katja Weisel[24], Philippe Moreau[25]

[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, Hematology, Oncology and Rheumatology, GMMG Study Group, Heidelberg University Hospital and National Center for Tumor Diseases, 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 Carusan der TU Dresden, Dresden, Germany; [13]Centre Hospitalier Lyon Sud, Pierre-Bénite, France; [14]University of Cologne, Cologne, Germany; [15]Cancer Center Clínica Universidad de Navarra, CIMA, IDISNA, Pamplona, Spain; [16]The Institute of Cancer Research, London, UK, and The Royal Marsden NHS Foundation Trust, London, UK; [17]Hospital 12 de Octubre, Complutense University, CNIO, MIC, Madrid, Spain; [18]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Seràgnoli Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; [19]Janssen & Johnson, Beerse, Belgium; [20]Janssen & Johnson, Milano, Italy; [21]Janssen & Johnson, Raritan, NJ, USA; [22]Janssen & Johnson, Neuss, Germany; [23]Janssen & Johnson, Madrid, Spain; [24]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [25]University Hospital Hôtel-Dieu, Nantes, France

Key Takeaway

With longer follow-up, Tal continued to demonstrate superior efficacy vs real-world physician's choice of treatment in patients with triple-class exposed RRMM and prior BCMA T-cell redirection therapies, supporting Tal as an effective treatment option in this patient population

Conclusions

Patients with prior BCMA TCR receiving Tal were significantly more likely to achieve clinical responses, especially deep responses, and had significantly improved PFS and OS vs patients receiving RWPC

Similar results were observed with Tal vs RWPC in patients with ≥4 prior LOT, demonstrating effectiveness in a heavily pretreated population with prior BCMA TCR exposure

Clinical benefit was observed with Tal vs RWPC in patients who received prior BCMA CAR-T and/or prior BCMA BsAb therapy

Please scan QR code

Poster

https://www.congresshub.com/EHA2025/Oncology/Talquetamab/Mateos

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

Acknowledgments

We thank the patients who participated in the study and their families and caregivers, the physicians and nurses who cared for patients and supported this clinical trial, staff members at the study sites, and staff members involved in data collection and analyses. This study was funded by Johnson & Johnson. Medical writing support was provided by Lisa O'Brien, PharmD, of Eloquent Scientific Solutions and funded by Johnson & Johnson.

Disclosures

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

Introduction

- There is an unmet need for patients with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM) relapsing on novel T-cell redirection therapies (TCR), including B-cell maturation antigen (BCMA)-targeted chimeric antigen receptor (CAR)-T cell and bispecific antibody (BsAb) therapies[1-3]
- Talquetamab (Tal) is the first GPRC5D-targeting BsAb approved for TCE RRMM based on the MonumenTAL-1 study (NCT03399799/NCT04634552)[4-6]
- LocoMMotion (NCT04035226) and MoMMent (NCT05160584) are prospective, observational studies characterizing real-world physician's choice of treatment (RWPC) in patients with TCE RRMM[7,8]
- Previous adjusted comparisons showed superior efficacy of Tal vs RWPC in patients with prior BCMA TCR exposure[9]

We report an updated adjusted comparison of Tal vs RWPC in TCE RRMM with prior BCMA TCR exposure with longer follow-up in MonumenTAL-1 and MoMMent

Methods

Data sources
- MonumenTAL-1 IPD, data cut-off, Sept 2024:
  - SC Tal 0.4 mg/kg QW or 0.8 mg/kg Q2W with prior BCMA TCR (n=75; mFU, 30.3 mo)
- LocoMMotion/MoMMent IPD with prior BCMA TCR meeting MonumenTAL-1 key eligibility criteria (n=36):
  - LocoMMotion: final data, data cut-off, Oct 2022; mFU, 26.4 mo
  - MoMMent: data cut-off, Aug 2024; mFU, 27.1 mo

MonumenTAL-1 key eligibility criteria
- TCE RRMM
- ≥3 prior LOT
- Prior BCMA TCR
- ECOG PS ≤2
- Hemoglobin ≥8 g/dL
- Creatinine clearance ≥40 mL/min/1.73 m^2

Adjusted treatment comparison
- Multivariable regression was used to adjust for imbalances in refractory status, ISS stage, time to progression on prior LOT, number of prior LOT, time since diagnosis, presence of extramedullary plasmacytomas, ECOG PS, lactate dehydrogenase levels, hemoglobin levels, and creatinine clearance

Statistical analysis
- ORR: multivariable logistic regression estimated odds ratios, relative risk, and 95% CIs
- PFS and OS: multivariable Cox proportional hazards regression estimated HRs and 95% CIs
- Sensitivity analyses: additional baseline characteristic adjustments,[a] receipt of TCR as last LOT
- Subgroup analysis: evaluated USPI-aligned population of patients with ≥4 prior LOT

[a]Age, sex, multiple myeloma type, average duration of prior LOT, and prior autologous stem cell transplantation. ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; IPD, individual patient data; ISS, International Staging System; LOT, line of therapy; mFU, median follow-up; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Q2W, every other week; QW, weekly; SC, subcutaneous; USPI, United States prescribing information.

Results

Table 1: Baseline patient characteristics in the Tal and RWPC cohorts were consistent with those previously reported[9]

Characteristic	Tal (n=75)	RWPC (n=36)
Age, years, n (%)		
≥65	28 (37.3)	16 (44.4)
Male, n (%)	48 (64.0)	27 (75.0)
Extramedullary plasmacytomas ≥1,[a] n (%)	25 (33.3)	4 (11.1)
ISS stage, n (%)		
III	13 (17.3)	15 (41.7)
Number of prior LOT, n (%)		
≤4	18 (24.0)	4 (11.1)
>4	57 (76.0)	32 (88.9)
Median time since last TCR, mo (range)	9.9 (0.8–59.8)	4.0 (0.0–36.8)
Exposure status, n (%)		
CAR-T	50 (66.7)	12 (33.3)
BsAb	20 (26.7)	21 (58.3)
CAR-T and BsAb	5 (6.7)	3 (8.3)
TCR in last LOT, n (%)		
CAR-T	33 (44.0)	9 (25.0)
BsAb	7 (9.3)	15 (41.7)
Refractory status,[b] n (%)		
Double- or triple-class	22 (29.3)	13 (36.1)
Quad	21 (28.0)	12 (33.3)
Penta-drug	32 (42.7)	11 (30.6)

[a]Only true extramedullary disease (soft tissue lesions)[10] were analyzed in MonumenTAL-1, while both paraskeletal lesions and/or true extramedullary disease were analyzed in LocoMMotion and MoMMent. [b]Refractoriness categories are defined as mutually exclusive.

Table 2: Treatment regimens received by the RWPC cohort included standard regimens and newer immunotherapies

Treatment regimen	Frequency, n (%) (n=36)
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)
Other regimens[a]	
PI regimens[b]	7 (19.4)
Single agents[c]	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[d]	1 (2.8)
IMiD regimen	1 (2.8)
PI and anti-CD38 mAb regimen	1 (2.8)

[a]Treatment regimens received by single patients are grouped by class. [b]1 patient received a PI regimen containing selinexor. [c]1 patient each received belantamab mafodotin, bendamustine, pomalidomide, and venetoclax. [d]CAR-T regimen comprised idecabtagene vicleucel, cyclophosphamide, and fludarabine. IMiD, immunomodulatory drug; mAb, monoclonal antibody; PI, proteasome inhibitor.

Table 3: Superior efficacy outcomes were observed in patients with prior BCMA TCR treated with Tal vs RWPC. Results were consistent in the USPI-aligned population (≥4 prior LOT) and across all sensitivity analyses

Outcome	All patients with prior BCMA TCR Tal (n=75) vs RWPC (n=36)			Subgroup analysis of USPI population with prior BCMA TCR Tal (n=56) vs RWPC (n=34)		
	Rate, %	RR (95% CI)	*P* value	Rate, %	RR (95% CI)	*P* value
ORR	65.3 vs 22.2	3.03 (1.66–5.54)	0.0003	71.4 vs 20.6	3.57 (1.81–7.03)	0.0002
≥VGPR	53.3 vs 11.1	4.88 (1.84–12.95)	0.0014	57.1 vs 11.8	5.06 (1.81–14.17)	0.002
	Median, mo (95% CI)	HR (95% CI)	*P* value	Median, mo (95% CI)	HR (95% CI)	*P* value
PFS	6.0 (4.0–14.5) vs 2.5 (1.9–3.5)	0.30 (0.17–0.52)	<0.0001	8.9 (4.2–20.9) vs 2.5 (1.9–3.5)	0.26 (0.14–0.48)	<0.0001
OS	27.6 (19.5–NE) vs 13.0 (5.4–15.0)	0.37 (0.20–0.70)	0.002	28.3 (19.7–NE) vs 8.9 (5.4–14.5)	0.32 (0.16–0.65)	0.0015

Data for talquetamab are reported from phase 2 only in patients with ≥4 prior LOT, consistent with the USPI.
NE, not estimable; RR, relative risk; VGPR, very good partial response.

Figure 1: Improved PFS and OS were observed in patients with prior BCMA TCR treated with Tal vs RWPC

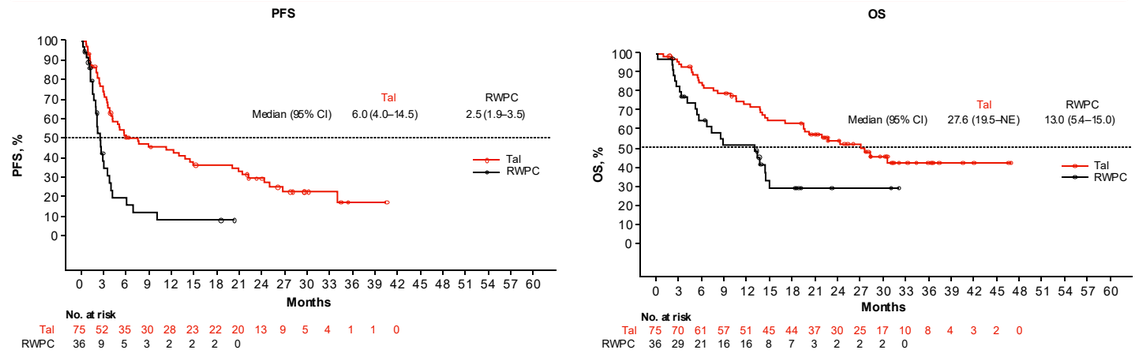
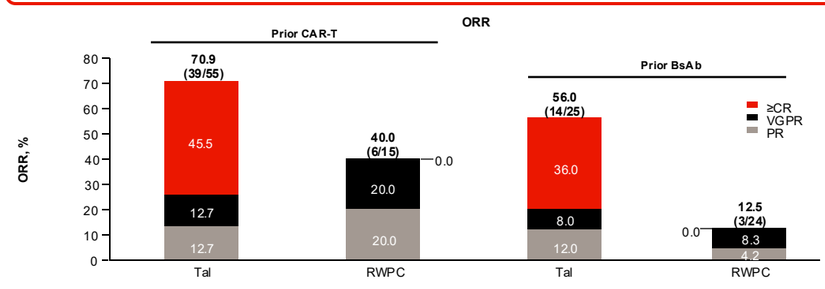


Figure 2: Subgroup analyses by type of prior TCR therapy demonstrated improved efficacy outcomes in patients treated with Tal vs RWPC



PFS/OS

In patients with prior BCMA CAR-T
- PFS (HR: 0.17 [95% CI: 0.06–0.46]) and OS (HR: 0.32 [0.11–0.95]) were longer with Tal vs RWPC

In patients with prior BCMA BsAb
- PFS (HR: 0.43 [95% CI: 0.15–1.26]) and OS (HR: 0.33 [0.09–1.17]) were longer with Tal vs RWPC

Patients who received both CAR-T and BsAb prior to Tal (n=5) or RWPC (n=3) are included in both exposure subgroups. CR, complete response; NE, not estimable; PR, partial response.

References

1. Gagelmann N, et al. *Haematologica* 2023;108:2799-802. 2. Swan D, et al. *Cancers (Basel)* 2023;15:1819. 3. Jakubowiak A, et al. Presented at ASH; December 9–12, 2023; San Diego, CA. USA. #3377. 4. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 5. TALVEY™ (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 6. European Medicines Agency. TALVEY™ (talquetamab). Accessed April 29, 2025. https://www.ema.europa.eu/en/documents/product-information/talvey-epar-product-information_en.pdf. 7. Mateos M, et al. *Leukemia* 2022;36:1371-6. 8. ClinicalTrials.gov, NCT05160584. 9. Mateos M-V, et al. Presented at IMS; September 25–28, 2024; Rio de Janeiro, Brazil. #P-050. 10. Bladé J, et al. *Blood Cancer J* 2022;12:45.

Multiple Myeloma

Presented by M-V Mateos at the European Hematology Association (EHA) 2025 Hybrid Congress; June 12–15, 2025; Milan, Italy