PA-060

Phase 2 Study of Talquetamab + Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma and Extramedullary Disease: RedirecTT-1

Saad Z Usmani[1], María-Victoria Mateos[2], Jing Christine Ye[3], Shebli Atrash[4], Hila Magen[5], Hang Quach[6], Michael P Chu[7], Suzanne Trudel[8], Joshua Richter[9], Paula Rodríguez-Otero[10], Hun Chuah[11], Moshe Gatt[12], Eva Medvedova[13], Shahzad Raza[14], Dok Hyun Yoon[15], Tadao Ishida[16], Jeffrey V Matous[17], Koichi Onodera[18], Emma Scott[19], Christoph Heuck[19], Payal Thakkar[20], Mariacristina Festa[21], Lin Huang[19], Shaji Kumar[22], Yaël C Cohen[23]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [3]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [4]Levine Cancer Institute-Atrium Health, Charlotte, NC, USA; [5]Chaim Sheba Medical Center, Ramat-Gan, Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel; [6]University of Melbourne, St Vincent's Hospital, Melbourne, VIC, Australia; [7]Alberta Health Services, Edmonton, AB, Canada; [8]Princess Margaret Cancer Centre, Toronto, ON, Canada; [9]Mount Sinai Medical Center, New York, NY, USA; [10]Cancer Center Clínica Universidad de Navarra, Cima, Pamplona, Spain; [11]Royal Perth Hospital, Perth, WA, Australia; [12]Hadassah Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel; [13]Knight Cancer Institute, Oregon Health and Science University, Portland, OR, USA; [14]Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, USA; [15]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [16]Japanese Red Cross Medical Center, Tokyo, Japan; [17]Colorado Blood Cancer Institute and Sarah Cannon Research Institute, Denver, CO, USA; [18]Tohoku University Hospital, Sendai shi, Miyagi, Japan; [19]Johnson & Johnson, Spring House, PA, USA; [20]Johnson & Johnson, Raritan, NJ, USA; [21]Johnson & Johnson, Leiden, Netherlands; [22]Mayo Clinic Rochester, Rochester, MN, USA; [23]Tel Aviv Sourasky (Ichilov) Medical Center, Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel

Key Takeaway

In the largest EMD study to date, Tal + Tec showed deep and durable responses, highlighting the clinical benefit of this combination in patients with RRMM and true EMD, a population with high unmet clinical need

Conclusions

Tal + Tec led to a high ORR and deep, durable responses in patients with true EMD; efficacy exceeded standard therapies and novel T-cell redirecting therapies

AEs were not exacerbated with the combination vs Tal and Tec monotherapies. The infection profile supports vigilant infection monitoring and management in this patient population

Please scan QR code

Poster

Supplementary material

https://www.congresshub.com/Oncology/IMS2025/Talquetamab/Usmani

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 Rachael Smith, PhD, of Eloquent, part of Envision Ignite, an Envision Medical Communications agency, a part of Envision Pharma Group, and funded by Johnson & Johnson. These data were previously presented at the European Hematology Association 2025 Annual Meeting; June 12–15, 2025; Milan, Italy.

Disclosures

SZU reports grants and personal fees from Johnson & Johnson.

Introduction

- Patients with soft tissue plasmacytomas noncontiguous with bone (true extramedullary disease [EMD]) have poor outcomes with standard therapies and rapid relapses[1-4]
- Talquetamab (Tal), which targets G protein–coupled receptor class C group 5 member D (GPRC5D) and CD3, and teclistamab (Tec), which targets B-cell maturation antigen (BCMA) and CD3, are the first bispecific antibodies (BsAbs) approved as monotherapies for triple-class exposed relapsed/refractory multiple myeloma (RRMM)[5-9]
- Preliminary data from phase 1 of RedirecTT-1 suggested that combination targeting of GPRC5D with talquetamab and BCMA with teclistamab led to higher response as well as greater depth and durability of response compared with each agent as monotherapy[10]

We report the efficacy and safety of Tal + Tec in the phase 2, RedirecTT-1 true EMD cohort

Methods

Phase 2 RedirecTT-1[a] study design

As of March 2025, median follow-up was 12.6 (range, 0.5–19.5) months

Key eligibility criteria

True EMD defined as:
≥1 nonradiated bone-independent soft tissue plasmacytoma ≥2 cm in greatest dimension confirmed by central review of PET-CT scans[b,c]

- MM per IMWG criteria
- Triple-class exposed[d] RRMM
- Prior CAR-T and BsAb therapy permitted
  - BsAbs could not target GPRC5D or BCMA
- Nonsecretory/oligosecretory disease permitted

Step-up doses[e] administered 2–4 days apart

- Tal 0.4 mg/kg Tec 1.5 mg/kg
- Tal 0.06 mg/kg Tec 0.3 mg/kg
- Tal 0.01 mg/kg Tec 0.06 mg/kg

Tal 0.8 mg/kg Q2W SC + Tec 3.0 mg/kg Q2W SC[e,f] until disease progression

Primary endpoint
- ORR[g]

Secondary endpoints
- ≥VGPR, ≥CR, and sCR rate[g]
- Time to response,[g] DOR,[g] PFS, and OS
- Safety
- PK and immunogenicity

[a]NCT04586426. [b]Patients may have had paramedullary plasmacytomas in addition to true EMD. [c]Whole body MRI permitted with sponsor approval. [d]Prior PI, IMiD, and anti-CD38 monoclonal antibody. [e]Tal and Tec administered on the same day, 30 (±10) minutes apart, for all step-up and full treatment doses. [f]Option to reduce dosing frequency for both agents to monthly dosing after ≥VGPR and minimum 4 cycles of therapy, or 6 cycles, per investigator decision. [g]Response was assessed by independent review committee per IMWG criteria.
CAR, chimeric antigen receptor; CR, complete response; DOR, duration of response; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRI, magnetic resonance imaging; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PET-CT, positron emission tomography-computed tomography; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; Q2W, every other week; SC, subcutaneous; sCR, stringent complete response; VGPR, very good partial response.

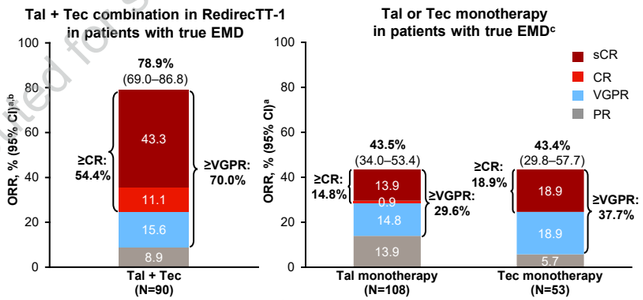
Results

Table 1: Patients with true EMD had a high disease burden and were heavily pretreated. 4.4% and 34.4% had nonsecretory and oligosecretory disease, respectively, and 8.9% had prior exposure to T-cell redirection therapies

Characteristic	Tal + Tec (N=90)
Median age, years (range)	64.5 (42–84)
Male, n (%)	57 (63.3)
True extramedullary plasmacytomas ≥1,[a] n (%)	90 (100)[b]
Number of extramedullary plasmacytomas,[a] median (range)	2 (1–7)
Number of extramedullary plasmacytomas,[a] n (%)	
1	38 (42.2)
2–3	29 (32.2)
≥4	23 (25.6)
High-risk cytogenetics,[c] n (%)	14 (21.5)
Measurable disease,[d] n (%)	
Nonsecretory	4 (4.4)
Oligosecretory	31 (34.4)
Years since diagnosis, median (range)[e]	4.7 (0.7–21.4)
Median prior LOT, n (range)	4.0 (1–10)
Exposure status, n (%)	
Belantamab mafodotin	11 (12.2)
Anti-BCMA CAR-T therapy	18 (20.0)
BsAb therapy[f]	8 (8.9)
Triple-class	90 (100)
Penta-drug	51 (56.7)
Refractory status, n (%)	
Triple-class	76 (84.4)
Penta-drug	32 (35.6)
To last LOT	75 (83.3)

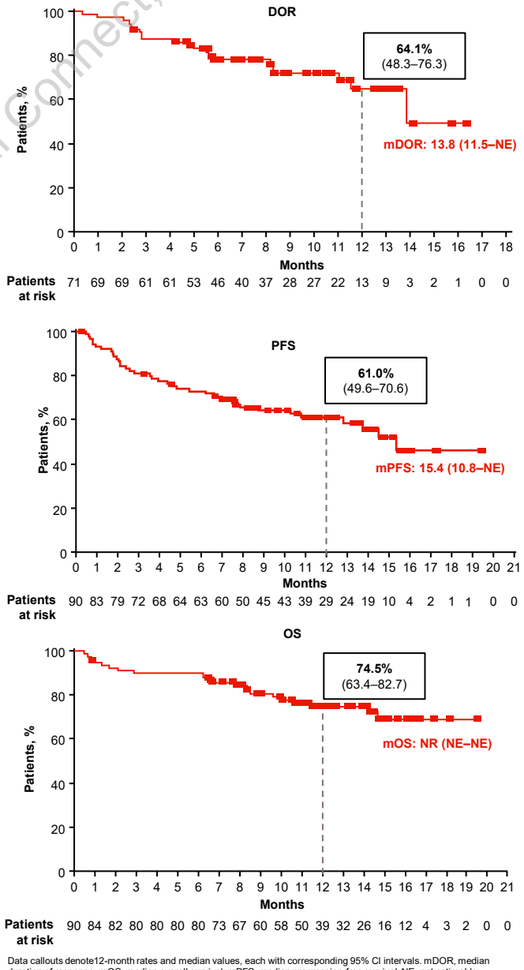
[a]≥1 nonradiated bone-independent soft tissue plasmacytoma (≥2 cm in greatest dimension) confirmed by PET-CT scans. 6 patients had data on the number of EMD lesions based on investigator assessment only. [b]Paramedullary lesions were also present in 19 patients. [c]FISH or karyotype testing in n=65; defined as del(17p), t(4;14), or t(14;16). [d]Per IMWG criteria. [e]Calculated in n=89. [f]All patients received anti-FcRH5 BsAbs. FcRH5, Fc receptor-homolog 5; FISH, fluorescence in situ hybridization.

Figure 1: Tal + Tec elicited higher ORR and deeper responses in patients with true EMD vs either agent as monotherapy; ORR remained high in patients treated with the combination with prior exposure to BCMA-targeting and T-cell redirecting therapies (data not shown)



[a]Due to rounding, individual response rates may not sum to the ORR. [b]ORR was assessed by independent review committee per IMWG criteria. [c]Data on file. PR, partial response.

Figure 2: Tal + Tec elicited durable responses, promising PFS and prolonged OS in patients with true EMD after approximately 13 months of follow-up; most responses deepened or were maintained after switching to monthly dosing (Supplemental Figure 1)



Data callouts denote12-month rates and median values, each with corresponding 95% CI intervals. mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; NE, not estimable; NR, not reached.

Table 2: Safety profile of Tal + Tec was consistent with known profiles of each monotherapy; incidence and severity of adverse events (AEs) were not exacerbated with the combination. 10 (11.1%) patients had grade 5 AEs, including 5 infections

Hematologic AEs (≥30%),[a] n (%)	Tal + Tec (N=90)	
	Any Grade	Grade 3/4
Neutropenia	65 (72.2)	56 (62.2)
Anemia	46 (51.1)	28 (31.1)
Thrombocytopenia	34 (37.8)	23 (25.6)
Nonhematologic AEs (≥30%),[a] n (%)		
Taste changes[b]	71 (78.9)	NA
CRS	70 (77.8)	0
Non-rash skin AEs[c]	62 (68.9)	0
Nail-related AEs[d]	50 (55.6)	0
Weight decrease	48 (53.3)	10 (11.1)
Dry mouth	40 (44.4)	0
Cough	33 (36.7)	0
Diarrhea	30 (33.3)	3 (3.3)
Pyrexia[e]	28 (31.1)	1 (1.1)
Hypokalemia	27 (30.0)	7 (7.8)
Fatigue	27 (30.0)	3 (3.3)
Nausea[e]	27 (30.0)	0

[a]AEs graded by CTCAE v5.0; CRS per ASTCT criteria. [b]Includes dysgeusia, ageusia, hypogeusia, and taste disorder; maximum grade for taste changes is 2 per CTCAE. [c]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [d]Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [e]Excludes symptoms of CRS or immune effector cell–associated neurotoxicity syndrome. ASTCT, American Society of Transplantation and Cellular Therapy; CTCAE, Common Terminology Criteria for Adverse Events; NA, not applicable.

Table 3: Rates of severe infections with Tal + Tec were similar to each agent as monotherapy, underscoring the importance of vigilant infection prophylaxis and management. 70.0% of patients had posttreatment hypogammaglobulinemia[a] and 86.7% received ≥1 dose of intravenous immunoglobulin

Most common AEs (≥10% overall), n (%)	Tal + Tec (N=90)	
	Any Grade	Grade 3/4[b]
Infections	71 (78.9)	28 (31.1)
Upper respiratory tract infection	22 (24.4)	3 (3.3)
COVID-19	20 (22.2)	5 (5.6)
Pneumonia	16 (17.8)	4 (4.4)
Urinary tract infection	12 (13.3)	3 (3.3)
Viral upper respiratory tract infection	9 (10.0)	2 (2.2)

[a]Posttreatment immunoglobulin G <400 mg/dL or hypogammaglobulinemia treatment-emergent AE. [b]Mostly limited to early cycles.

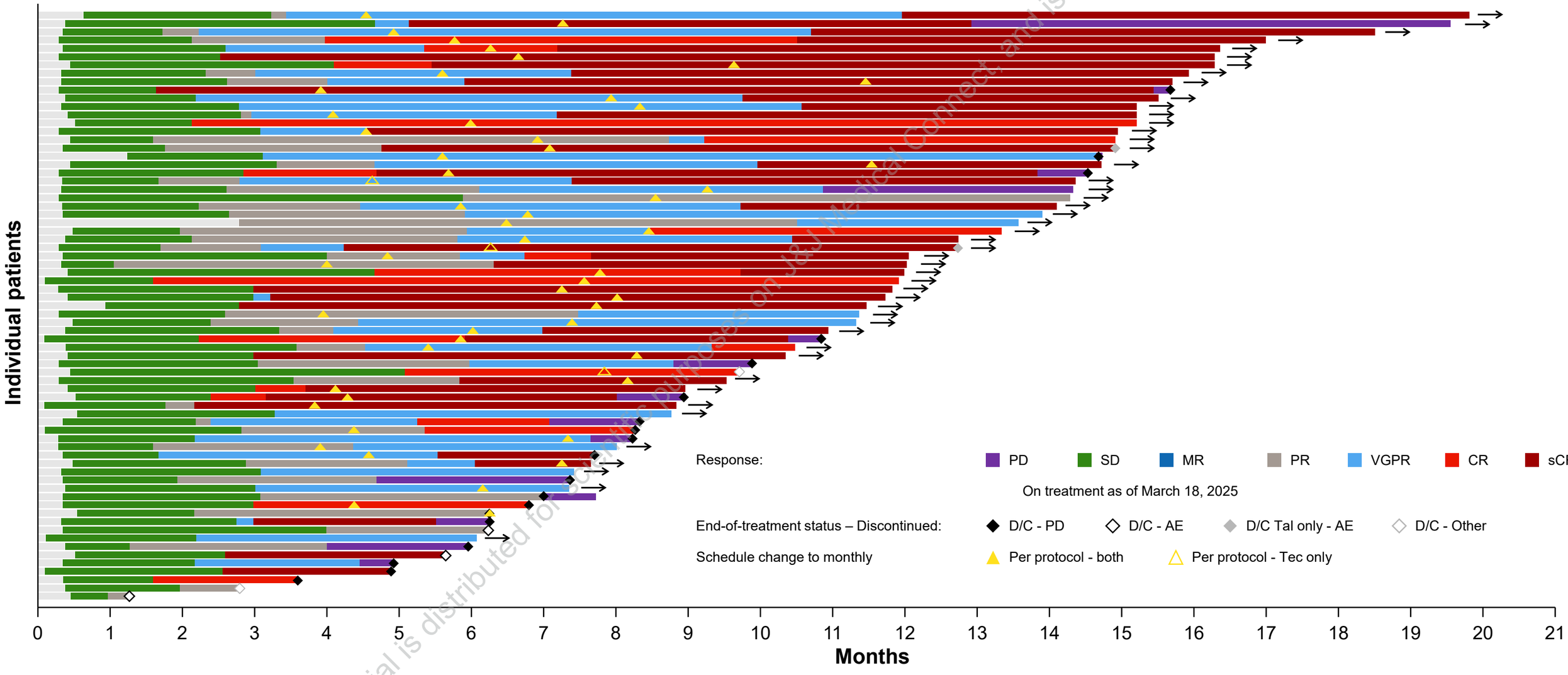
References

1. Rosiñol L, et al. *Br J Haematol* 2021;194:496-507. 2. Ho M, et al. *Curr Oncol* 2025;32:182. 3. Bladé J, et al. *Blood Cancer J* 2022;12:45. 4. Pour L, et al. *Haematologica* 2014;99:360-4. 5. Chari A, et al. *Lancet Hematol* 2025;e269-81. 6. Chari A, et al. *N Engl J Med* 2022;387:2232-42. 7. TALVEY (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 8. Moreau P, et al. *N Engl J Med* 2022;387:495-505. 9. TECVAYLI (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2024. 10. Cohen Y, et al. *N Engl J Med* 2025;9;392:138-49.

Multiple Myeloma

Presented by SZ Usmani at the 22nd International Myeloma Society (IMS) Annual Meeting & Exposition; September 17–20, 2025; Toronto, ON, Canada

Supplemental Figure 1: Responses Deepened or Were Maintained in Most Patients With True EMD



AE, adverse event; CR, complete response; D/C, discontinued; EMD, extramedullary disease; MR, minimal response; PD, progressive disease; PR, partial response; sCR, stringent complete response; SD, stable disease; Tal, talquetamab; Tec, teclistamab; VGPR, very good partial response.