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

Shaji Kumar[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], Laura Rosiñol[18], Koichi Onodera[19], Surabhi Bajpai[20], Vikram Kurra[20], Emma Scott[21], Christoph Heuck[21], Jenny Zhang[21], Todd Henninger[22], Lisa O'Rourke[21], Payal Thakkar[22], Mariacristina Festa[23], Lin Huang[21], Jiashen Lu[24], Nicholas Au[21], Maria Krevvata[21], Ashwini Kumar[21], Saad Z Usmani[25], Yaël C Cohen[26]

[1]Mayo Clinic Rochester, Rochester, MN, 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 Cener, 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]Hospital Clínic de Barcelona, IDIBAPS, Barcelona, Spain; [19]Tohoku University Hospital, Sendai shi, Miyagi, Japan; [20]Perceptive Imaging, Boston, MA, USA; [21]Johnson & Johnson, Spring House, PA, USA; [22]Johnson & Johnson, Raritan, NJ, USA; [23]Johnson & Johnson, Leiden, Netherlands; [24]Johnson & Johnson, Shanghai, China; [25]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [26]Tel Aviv Sourasky (Ichilov) Medical Center, Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel

Presented by S Kumar at the European Hematology Association (EHA) 2025 Hybrid Congress; June 12–15, 2025; Milan, Italy

Extramedullary Disease (EMD) is Associated With Poor Survival in Myeloma

BONE DEPENDENT

Paramedullary disease[1,2]
Plasmacytomas growing contiguously with bone and extending into soft tissue after cortical disruption

BONE INDEPENDENT

True EMD[1,2]
Soft tissue/organ-associated plasmacytomas noncontiguous with bony structures

Inferior outcomes vs patients with paramedullary plasmacytomas and patients with MM without EMD[3-13]

Patients with EMD are 87% less likely to respond to treatment vs patients without EMD
Poster PF768

Worse outcomes for patients with true EMD with real-world standard-of-care myeloma treatments[13]

Heavily pretreated, triple-class exposed RRMM	With EMD	Without EMD
ORR, %	24.1	33.3
mPFS, months	2.7	5.1
mOS, months	7.2	15.5

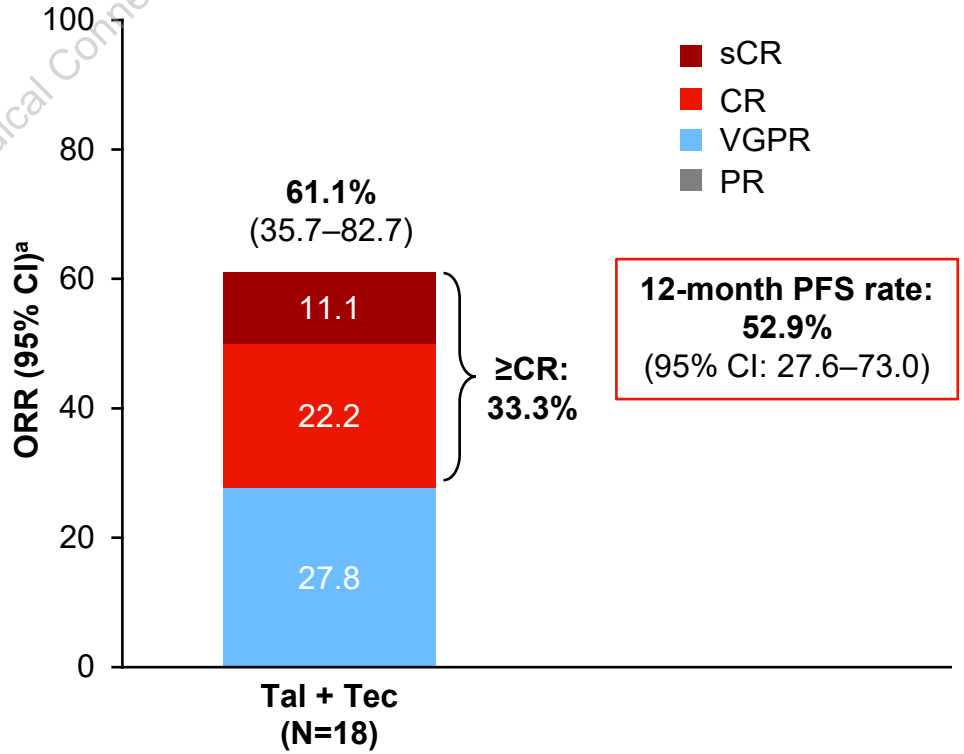
1. Ho M, et al. *Curr Oncol* 2025;32:182. 2. Bladé J, et al. *Blood Cancer J* 2022;12:45. 3. Rosiñol L, et al. *Br J Haematol* 2021;194:496-507. 4. Pour L, et al. *Haematologica* 2014;99:360-4. 5. Mangiacavalli S, et al. *Ann Hematol* 2017;96:73–80. 6. Rasche L, et al. *Ann Hematol* 2012;91:1031-7. 7. Richard S, et al. *Blood* 2022;140(Suppl 1):4301-2; 8. Pan D, et al. *Blood* 2023;142(Suppl 1):1006. 9. Dima D, et al. *Blood Cancer J* 2024;14:90. 10. Zanwar S, et al. *J Hematol Oncol* 2024;17:42. 11. Usmani SZ, et al. *Haematologica* 2012;97:1761-7. 12. Beksac M, et al. *Haematologica* 2020;105:201-8. 13. Moreau P, et al. *Clin Lymphoma Myeloma Leuk* 2025:S2152-2650(25)00106-5. mOS, median overall survival; mPFS, median progression-free survival; ORR, overall response rate; RRMM, relapsed/refractory multiple myeloma.

RedirecTT-1: Dual-Targeting of GPRC5D and BCMA in Patients With True EMD

- EMD lesions are highly complex, with active T-cell infiltration and heterogenous expression of GPRC5D and BCMA[1]
- Tal (anti-GPRC5D) and Tec (anti-BCMA) are first-in-class BsAbs approved as monotherapies for triple-class exposed RRMM[2-6]
- In patients with EMD, ORR was 43.5% with Tal monotherapy and 43.4% with Tec monotherapy in MonumenTAL-1 and MajesTEC-1, respectively[7]

Preliminary data from phase 1 suggest that dual targeting of GPRC5D and BCMA led to higher ORR and greater depth and durability of response likely by mitigating antigen-related escape

RedirecTT-1 phase 1 results showed promising activity of the Tal + Tec RP2R in patients with true EMD[8,9]



ClinicalTrials.gov identifier: NCT04586426.

1. John M, et al. *Blood* 2024;144:2121-35. 2. Chari A, et al. *Lancet Hematol* 2025;e269-81. 3. Chari A, et al. *N Engl J Med* 2022;387:2232-42. 4. TALVEY (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 5. Moreau P, et al. *N Engl J Med* 2022;387:495-505. 6. TECVAYLI (teclistamab-cqyv). Prescribing information. Horsham, PA: Janssen Biotech, Inc; 2024. 7. Data on file. 8. Cohen Y, et al. *N Engl J Med* 2025;9;392:138-49. 9. Cohen YC, et al. Presented at IMS; September 25–28, 2024; Rio de Janeiro, Brazil.

[a]ORR was investigator-assessed; due to rounding, individual response rates may not sum to the ORR. BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CR, complete response; GPRC5D, G protein–coupled receptor family C group 5 member D; PR, partial response; PFS, progression-free survival; RP2R, recommended phase 2 regimen; sCR, stringent complete response; Tal, talquetamab; Tec, teclistamab; VGPR, very good partial response.

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RedirecTT-1 Phase 2 Tal + Tec: Largest Dedicated Phase 2 Study in Patients With True EMD

Key eligibility criteria

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

- MM per IMWG criteria
- Triple-class exposed[c] RRMM
- Prior CAR-T (≤20% patients) and BsAb therapy permitted
  - BsAbs could not target GPRC5D or BCMA
- Nonsecretory/oligosecretory disease permitted

Step up doses[d] 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[d] until disease progression

Primary endpoint

- ORR[e] (EMD response assessed by central radiology review of whole-body PET-CT scans)

Secondary endpoints

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

Option to reduce dosing frequency for both agents to monthly dosing after:

- ≥VGPR and minimum 4 cycles of therapy, *or*
- 6 cycles, per investigator discretion

[a]Patients may have had paraskeletal plasmacytomas in addition to true EMD. [b]Whole body MRI permitted with sponsor approval. [c]Prior PI, IMiD, and anti-CD38 monoclonal antibody. [d]Tal and Tec administered on the same day, 30 (±10) minutes apart, for all step-up and full treatment doses. [e]Response was assessed by independent review committee per IMWG criteria. CAR, chimeric antigen receptor; DOR, duration of response; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRI, magnetic resonance imaging; PET-CT, positron emission tomography/computed tomography; PI, proteasome inhibitor; PK, pharmacokinetics; Q2W, every other week; SC, subcutaneous.

RedirecTT-1 Phase 2 Tal + Tec: Most Patients With True EMD Were Triple-Class Refractory

Characteristic	Tal + Tec (N=90)
Median age, years (range)	64.5 (42–84)
Male, n (%)	57 (63.3)
Race, n (%)	
White	64 (71.1)
Black/African American	8 (8.9)
Asian	13 (14.4)
Not reported	5 (5.6)
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)

Characteristic	Tal + Tec (N=90)
ECOG performance status, n (%)	
0	32 (35.6)
1	50 (55.6)
2	8 (8.9)
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 (%)	
PI	86 (95.6)
IMiD	84 (93.3)
Anti-CD38 monoclonal antibody	85 (94.4)
Triple-class	76 (84.4)
Penta-drug	32 (35.6)
To last LOT	75 (83.3)

Data cut-off date: March 18, 2025.

[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]Paraskeletal 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. ECOG, Eastern Cooperative Oncology Group; FcRH5, Fc receptor-homolog 5; FISH, fluorescence in situ hybridization; ISS, International Staging System; LOT, line of therapy.

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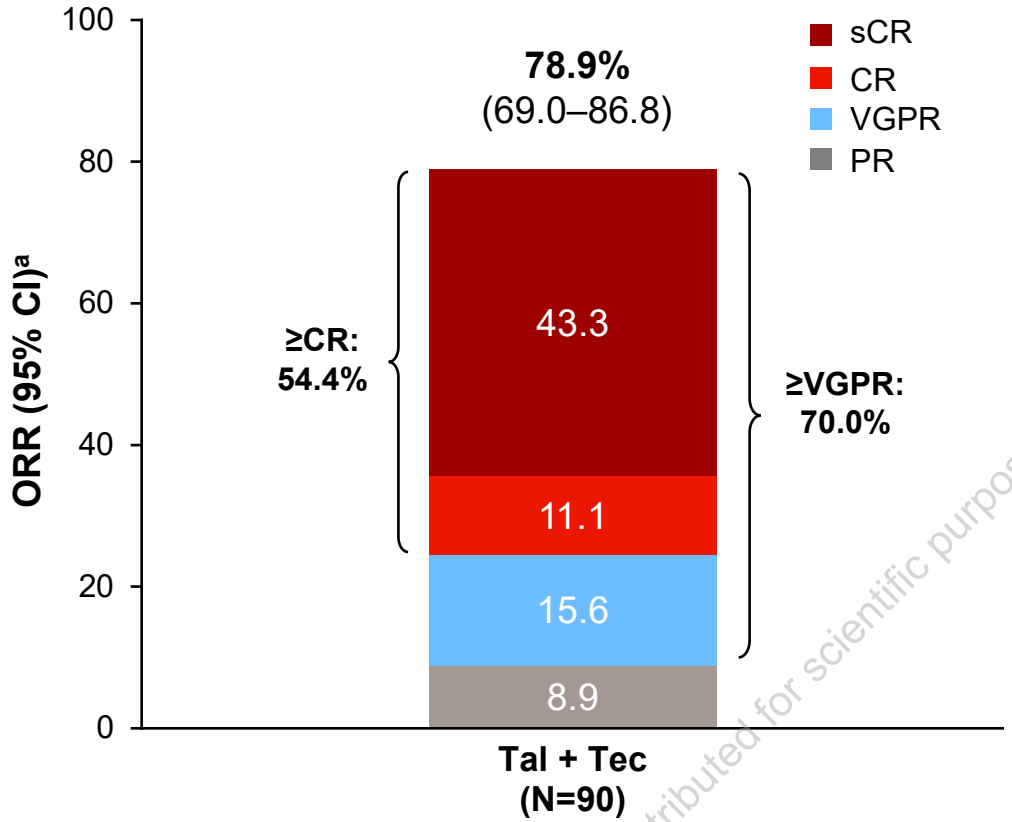
RedirecTT-1 Phase 2 Tal + Tec: High Response Rates in Patients With True EMD With Unmet Need



Parameter	Tal + Tec (N=90)
Median (range) follow-up, months	12.6 (0.5–19.5)
Median (range) time to first response, months	2.6 (1.0–5.8)
Median (range) time to best response, months	4.7 (1.0–11.9)

Prior therapy	ORR	95% CI
Anti-BCMA CAR-T, % (n/N)	83.3 (15/18)	58.6–96.4
Anti-FcRH5 BsAb, % (n/N)	75.0 (6/8)	34.9–96.8
Belantamab mafodotin, % (n/N)	90.9 (10/11)	58.7–99.8

High ORR (78.9%) and deep responses (≥CR: 54.4%) in patients with EMD

Data cut-off date: March 18, 2025.

[a]ORR was assessed by independent review committee per IMWG criteria; due to rounding, individual response rates may not sum to the ORR.

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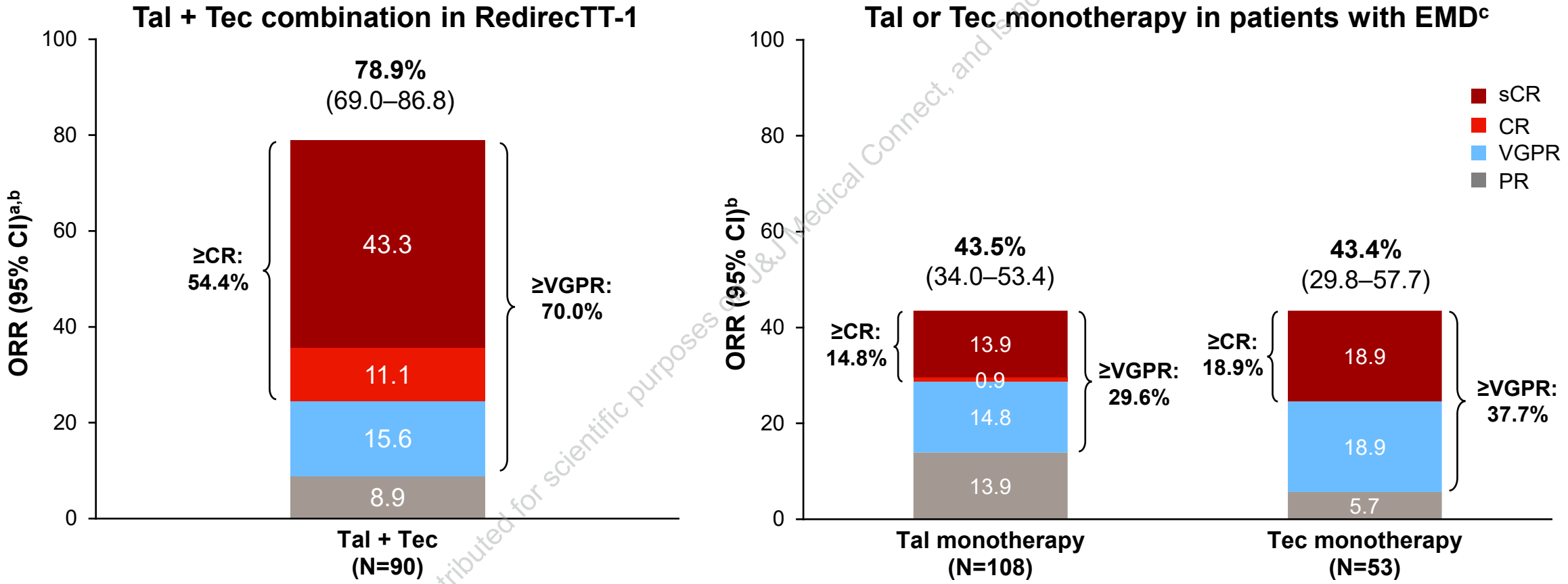
RedirecTT-1 Phase 2 Tal + Tec: Dual-Antigen Targeting in Patients With True EMD Led to Higher ORR and ≥CR Rate



Higher ORR and deeper responses in patients with EMD with Tal + Tec combination vs Tal or Tec monotherapy

Data cut-off date: March 18, 2025.

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

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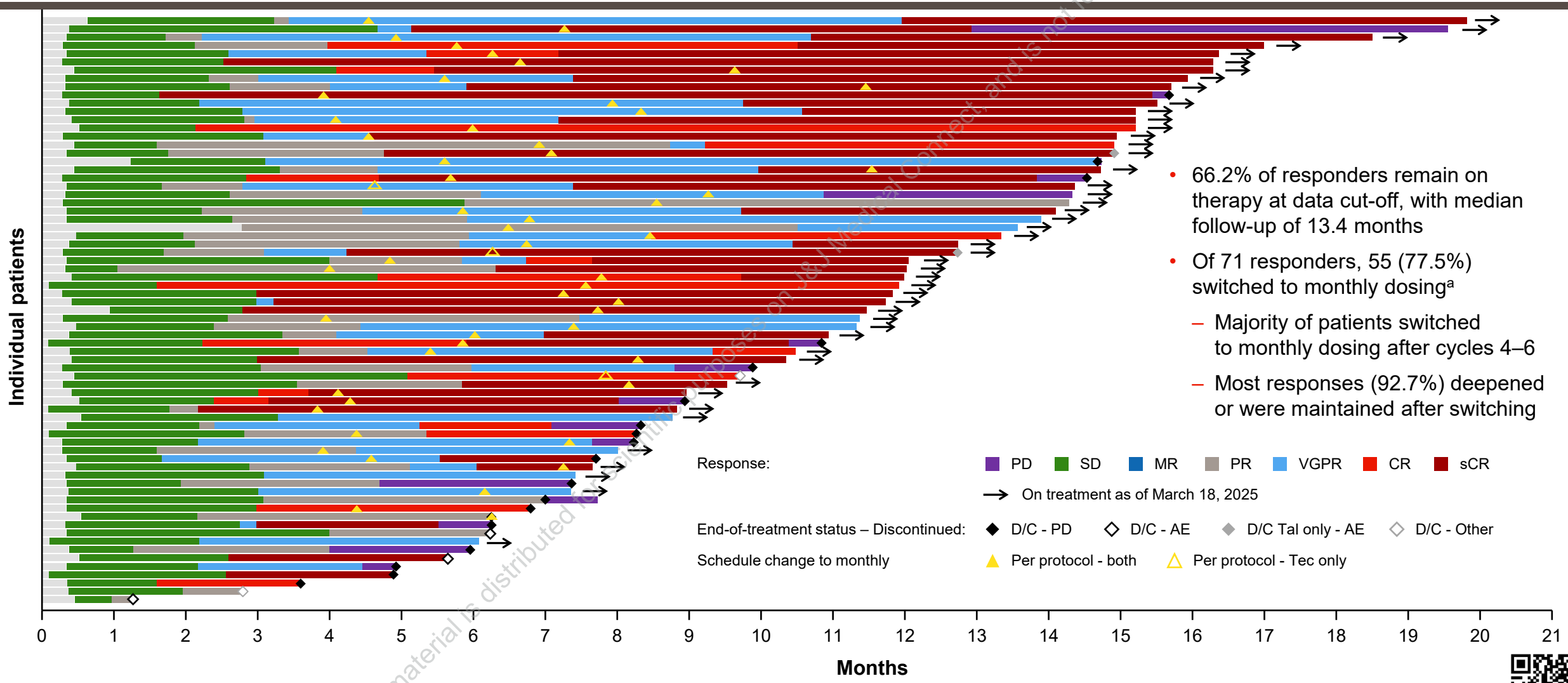
RedirecTT-1 Phase 2 Tal + Tec: Responses Deepened or Maintained in Most Patients With True EMD



- 66.2% of responders remain on therapy at data cut-off, with median follow-up of 13.4 months
- Of 71 responders, 55 (77.5%) switched to monthly dosing[a]
  - Majority of patients switched to monthly dosing after cycles 4–6
  - Most responses (92.7%) deepened or were maintained after switching

Data cut-off date: March 18, 2025.

[a]Tal 0.8 mg/kg Q4W + Tec 3.0 mg/kg Q4W or Tec 3.0 mg/kg Q4W only, following discontinuation of Tal. AE, adverse event; D/C, discontinued; MR, minimal response; PD, progressive disease; SD, stable disease.

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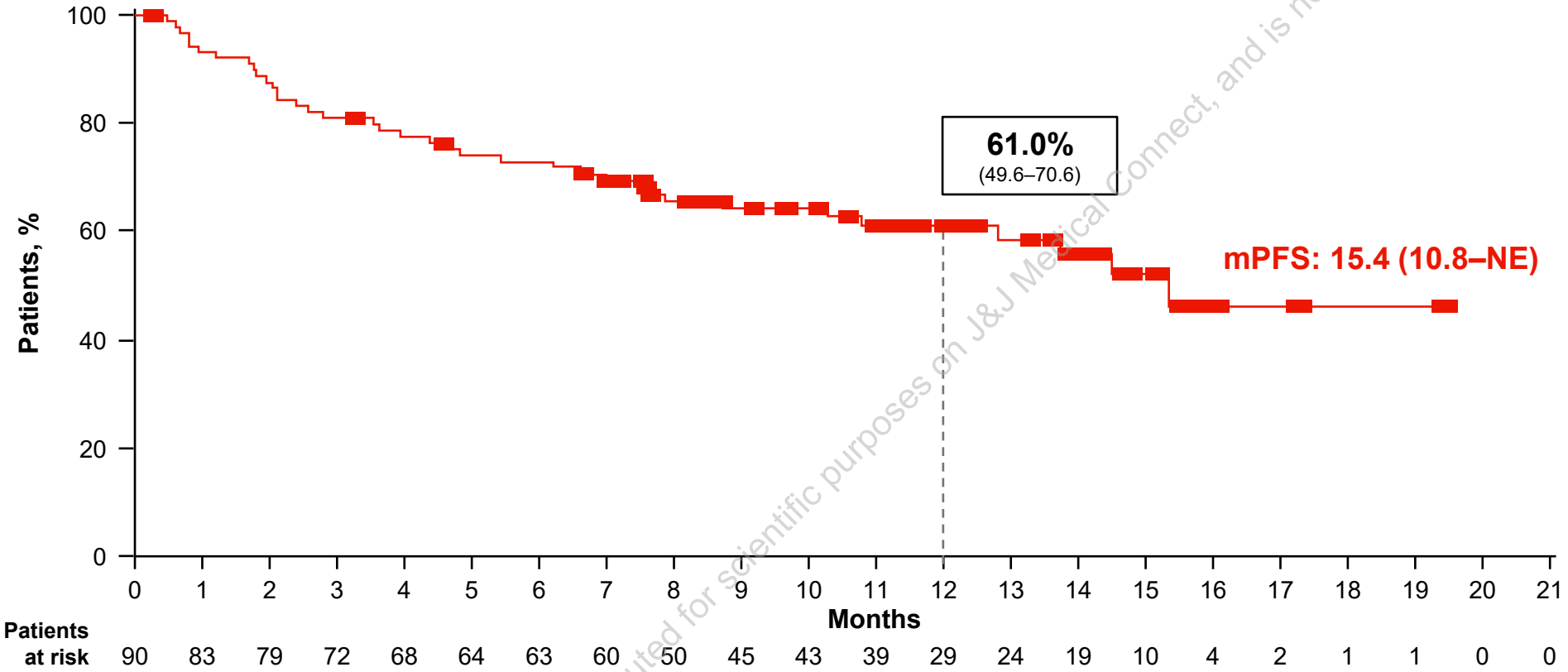
RedirecTT-1 Phase 2 Tal + Tec: Promising mPFS in Patients With True EMD After 13 Months of Follow-up



In context of other therapies

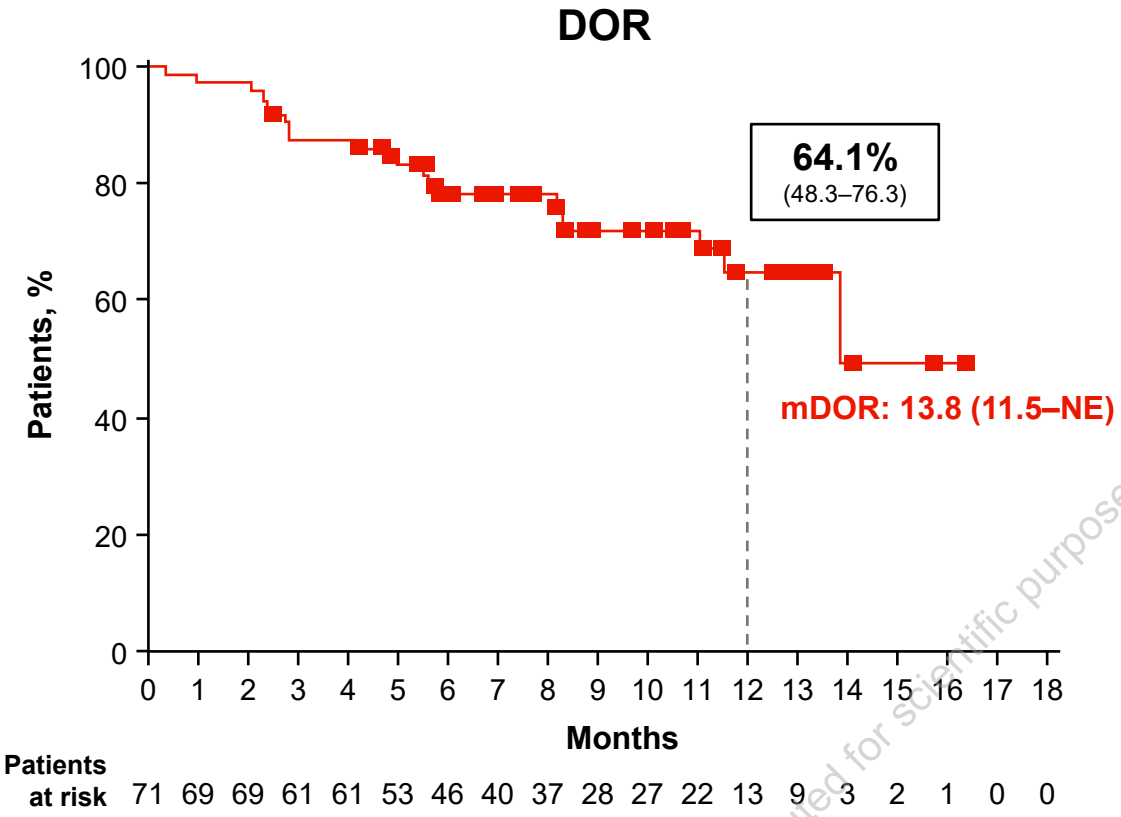
mPFS in patients with triple-class exposed RRMM with EMD:

- Standard-of-care therapies[a]: **<3 months**[1]
- Approved BsAbs[b]: **<6 months**[2]

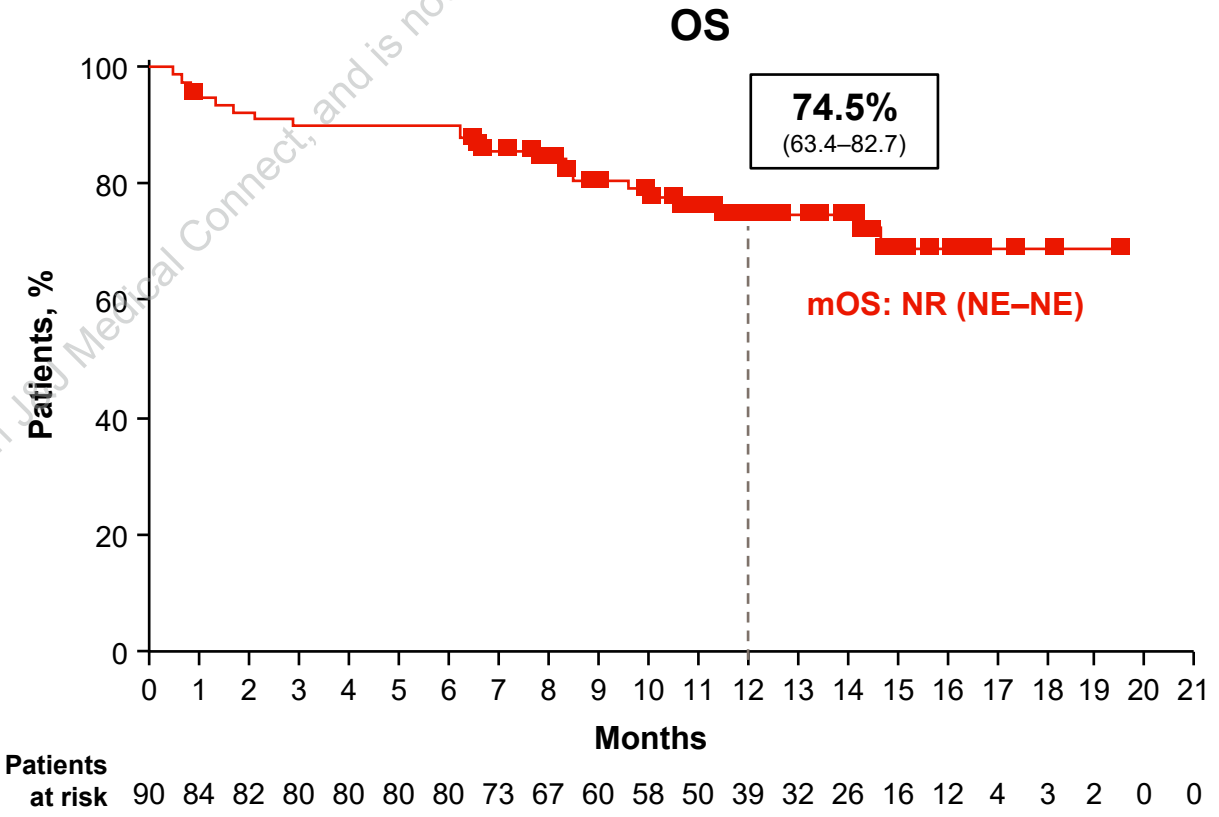
Estimated PFS rate at 1 year was 61%

Data cut-off date: March 18, 2025. Median follow-up: 12.6 months.
Medians and rates shown with 95% CIs. [a]Including anti-CD38-based doublets and triplet regimens. [b]Including Tal and Tec; PFS data not yet reported for elranatamab or linvoseltamab in patients with EMD. NE, not estimable.
1. Moreau P, et al. *Clin Lymphoma Myeloma Leuk* 2025;S2152-2650(25)00106-5. 2. Ho M, et al. *Curr Oncol* 2025;32:182.

RedirecTT-1 Phase 2 Tal + Tec: Durable Responses and Prolonged Survival in Patients With True EMD



Estimated 12-month freedom from progression rate was 64%



Estimated 12-month OS rate was 75%

Data cut-off date: March 18, 2025. Median follow-up: 12.6 months.
Medians and rates shown with 95% CIs. NR, not reported.

RedirecTT-1 Phase 2 Tal + Tec: CRS and ICANS Mostly Low Grade

CRS	Tal + Tec (N=90)
Patients with CRS,[a] n (%)	70 (77.8)
Grade 1	53 (58.9)
Grade 2	17 (18.9)
Grade 3	0 (0)
Occurrence of CRS,[b] n (%)	
Step-up dose 1	40 (44.4)
Step-up dose 2	51 (56.7)
Step-up dose 3	24 (26.7)
Cycle 1	5 (5.6)
Cycle 2 onwards	1 (1.1)
Days to onset,[c] median (range)	2 (1–29)
Duration, days, median (range)	2 (1–8)

ICANS	Tal + Tec (N=90)
Patients with ICANS,[a] n (%)	11 (12.2)
Grade 1	5 (5.6)
Grade 2	4 (4.4)
Grade 3	1 (1.1)
Grade 4	1 (1.1)
Occurrence of ICANS,[b] n (%)	
Step-up dose 1	2 (2.2)
Step-up dose 2	4 (4.4)
Step-up dose 3	7 (7.8)
Cycle 1	2 (2.2)
Cycle 2 onwards	0
Days to onset,[c] median (range)	3 (1–7)
Duration, days, median (range)	2 (1–7)

- CRS[d] was managed with tocilizumab (56.7%), acetaminophen (56.7%), corticosteroids (18.9%), and IV fluids (17.8%)
- ICANS[d] was managed with corticosteroids (10.0%), levetiracetam (4.4%), anakinra (2.2%), and tocilizumab (1.1%)

CRS and ICANS consistent with Tal and Tec monotherapy

Data cut-off date: March 18, 2025. Median follow-up: 12.6 months.
[a]CRS and ICANS were graded per ASTCT criteria. [b]Patients could experience ≥1 CRS event. [c]Relative to the most recent dose. [d]Patients could receive ≥1 supportive therapy. ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; IV, intravenous.

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RedirecTT-1 Phase 2 Tal + Tec: Safety Consistent With Known Profiles of Tal and Tec

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 (0)
Non-rash skin AEs[c]	62 (68.9)	0 (0)
Nail-related AEs[d]	50 (55.6)	0 (0)
Weight decrease	48 (53.3)	10 (11.1)
Dry mouth	40 (44.4)	0 (0)
Cough	33 (36.7)	0 (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 (0)

- Low rates of discontinuations due to AEs (n=5)[f]
  - Tal + Tec (n=3; all nonfatal): pseudomonal pneumonia and pseudomonal sepsis (n=1), dry mouth, dysphagia, decreased weight (n=1), and ICANS (n=1)
  - Tal only (n=2; all nonfatal): dysgeusia and dysphagia (n=1), and hypohidrosis (n=1)
- 10 (11.1%) grade 5 AEs, including 5 infections[f]
  - Noninfectious
    - Related: aspiration (n=1)
    - Unrelated: respiratory failure, euthanasia, general physical health deterioration, and cerebellar hemorrhage (each n=1)

Data cut-off date: March 18, 2025. Median follow-up: 12.6 months.
[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 ICANS. [f]Data presented on a treatment-emergent basis. CTCAE, Common Terminology Criteria for Adverse Events; NA, not applicable.

RedirecTT-1 Phase 2 Tal + Tec: Rates of Infection

Most common AEs (≥10% overall),[a] 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)

- Grade 3/4 infections mostly limited to early cycles
- Grade 5 infections (5.6%): COVID-19 pneumonia, *Klebsiella* sepsis, pneumonia, *Klebsiella* pneumonia, pseudomonal sepsis (each n=1)
- 96.7% received antiviral prophylaxis
- 70.0% had posttreatment hypogammaglobulinemia[c]
- 86.7% received ≥1 dose of IVIG

Rates of severe infections were similar to monotherapy, underscoring the importance of vigilant infection prophylaxis and management

Data cut-off date: March 18, 2025. Median follow-up: 12.6 months.
[a]AEs were graded by CTCAE v5.0. [b]Maximum toxicity. [c]Posttreatment IgG <400 mg/dL or hypogammaglobulinemia treatment-emergent AE. Ig, immunoglobulin; IVIG, intravenous immunoglobulin.

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RedirecTT-1 Phase 2 Tal + Tec: Transformative Efficacy in Largest Dedicated EMD Study to Date

- **Deep and durable responses in true EMD myeloma with an off-the-shelf, dual-targeting regimen, showcasing enhanced efficacy in a difficult-to-treat disease**
  - ORR of 78.9% (≥CR, 54.4%)
  - 12-month PFS rate of 61.0%
  - 12-month OS rate of 74.5%
- **Combination of Tal + Tec demonstrated efficacy exceeding that of standard therapies and novel T-cell redirecting therapies**[1-5]
- **AEs were not exacerbated with combination vs Tal or Tec monotherapy in the setting of EMD**
  - Q2W to monthly dosing schedules may contribute to improved tolerability vs phase 1
  - Infection profile supports vigilant infection monitoring and management

Results from phase 2 of RedirecTT-1 showed deep and durable responses in a population with significant unmet need, highlighting the clinical benefit of dual-antigen targeting with Tal + Tec

1. Dima D, et al. *Blood Cancer J* 2024;14:90. 2. Zanwar S, et al. *J Hematol Oncol* 2024;17:42. 3. Martin T, et al. *J Clin Oncol* 2023;41:1265-74. 4. Zhao WH, et al. *J Hematol Oncol* 2022;15:86. 5. Moreau P, et al. *Clin Lymphoma Myeloma Leuk* 2025:S2152-2650(25)00106-5.

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Acknowledgments

- We thank the patients who are participating in this study and their caregivers, the physicians and nurses who care for them, the staff at study sites, and the staff involved in data collection and analyses
- We thank all the phase 2 RedirecTT-1 study investigators
- This study was funded by Johnson & Johnson
- Medical writing support was provided by Rachael Smith, PhD, of Eloquent Scientific Solutions and funded by Johnson & Johnson

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