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RP2R dose selection of Tal + Tec for the treatment of EMD patients in the RedirecTT-1 study

Nicholas Au[1], Dongfen Yuan[1], Natalia Quijano Cardé[1], Elvis Danso[1], Yibo Wang[2], Yue Guo[1], Yaming Su[2], Nahor Haddish-Berhane[1], Emma Scott[1], Payal Thakkar[2], Todd Henninger[1], Mariacristina Festa[3], Lin Huang[1], Michelle Peterson[1], Christoph Heuck[1], Jenny Zhang[1], Indrajeet Singh[1]

[1]Johnson & Johnson, Spring House, PA, USA; [2]Johnson & Johnson, Raritan, NJ, USA; [3]Johnson & Johnson, Leiden, Netherlands

Key Takeaway

The totality of evidence demonstrates that the Tal + Tec RP2R (Q2W) regimen is a potentially effective treatment option for RRMM pts with EMD previously treated with a PI, an IMiD, and an anti-CD38 mAb, supporting its advancement for further clinical development. This regimen also allows flexibility to switch to Q4W dosing in responders.

Conclusions

- Dose optimization was conducted by evaluating several dosing regimens including QW, Q2W and Q4W at varying dose levels of Tal and Tec.
- The RP2R (Tal 0.8 mg/kg + Tec 3.0 mg/kg Q2W) generally provided higher and deeper responses (≥CR) in EMD pts compared to non-RP2R regimens (Figure 1).
- The efficacy E-R analysis demonstrated that the optimized RP2R resulted in Tal and Tec exposure levels associated with better efficacy in EMD pts (Figure 2 and 3).
- The overall safety profile of Tal + Tec at the RP2R was manageable and consistent with each agent as monotherapy (Table 1).

Acknowledgments

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Disclosures

All listed authors are employees of Johnson & Johnson and may hold stock in Johnson & Johnson.

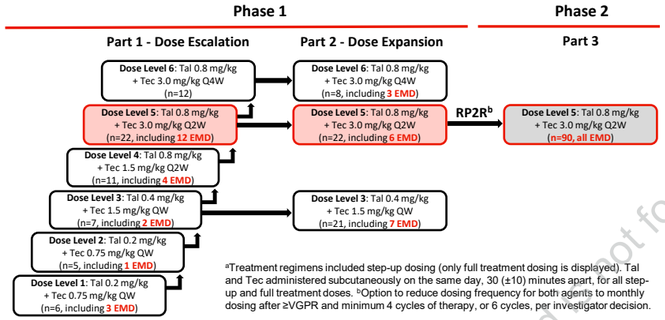
Introduction

- Patients (pts) with soft tissue plasmacytomas noncontiguous with bone (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 teclistamab (Tec), which targets B-cell maturation antigen (BCMA), are the most widely used T-cell engaging bispecific antibodies for the treatment of triple-class exposed relapsed/refractory multiple myeloma (RRMM)[5-9]
- RedirecTT-1 (NCT04586426) is a Phase 1b/2 dose escalation/expansion study evaluating Tal + Tec in RRMM pts including EMD

- **We present data supporting selection of the optimal recommended Phase 2 regimen (RP2R) for treatment of EMD pts, based on efficacy, safety, and exposure-response (E-R) analyses from Phase 1**
- **Pts with and without EMD were included, but the present analysis will only present EMD**

Methods

Study Design and RP2R Selection[a]



[a]Treatment regimens included step-up dosing (only full treatment dosing is displayed). Tal and Tec administered subcutaneously on the same day, 30 (±10) minutes apart, for all step-up and full treatment doses. [b]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.

Key eligibility criteria

- MM per IMWG criteria
- Triple-class exposed[a] RRMM with EMD
- Nonsecretory/oligosecretory disease permitted with EMD

EMD was defined as: ≥1 nonradiated bone-independent soft tissue plasmacytoma ≥2 cm in greatest dimension by PET-CT[b,c]

Pharmacokinetics CavgC1, CtrC1 → **Exposure-Response Analysis for Efficacy**

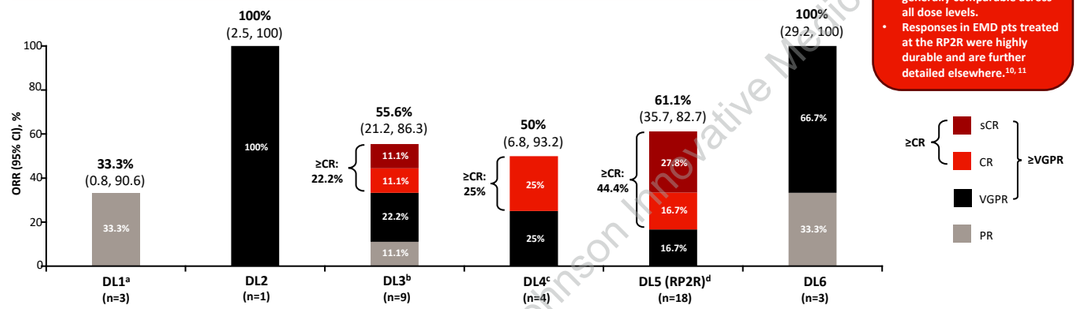
Efficacy ORR[e]

Safety Treatment-emergent AEs[f]

[a]Prior PI, IMiD, and anti-CD38 monoclonal antibody. [b]Pts may have had paraskeletal plasmacytomas in addition to true EMD. [c]Whole body MRI permitted with sponsor approval. [d]PK metrics were derived using established population PK models after passing external validation. [e]Investigator-assessed confirmed response per IMWG criteria was reported. [f]CRS and ICANS were graded by ASTCT criteria; all other AEs were graded by CTCAE v5.0. CavgC1, Cycle 1 average concentration; CtrC1, trough concentration before Cycle 2 Day 1 dose. AE; adverse event.

Results

Figure 1. Responses were observed in patients with EMD across all dose levels, but the proportion of patients achieving a deeper response (≥CR) is highest in DL5 (RP2R) compared with all other Phase 1 cohorts



[a]MR, SD, or PD; n=2. [b]MR, SD, or PD; n=3, NE; n=1. [c]MR, SD, or PD; n=2. [d]MR, SD, or PD; n=4, NE; n=3. DL, dose level; ORR, overall response rate; sCR, stringent complete response; CR, complete response; VGPR, very good partial response; PR, partial response; MR, minimal response; SD, stable disease; PD, progressive disease; NE, not evaluable.

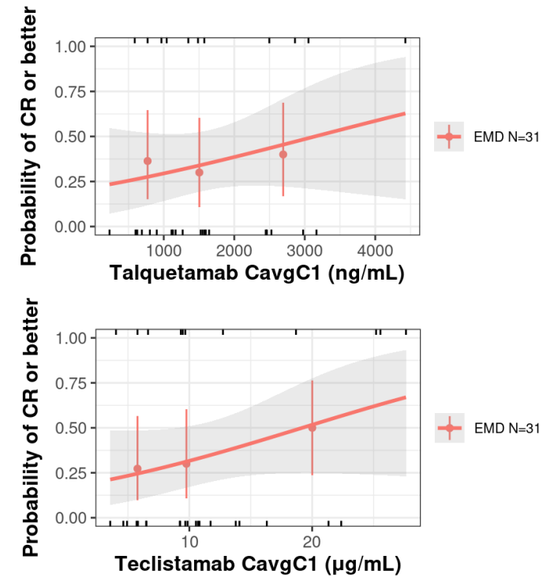
- **As of March 18, 2025, median follow-up across dose levels was 31.6 (0.5-49.0) months.**
- **Pt demographics were generally comparable across all dose levels.**
- **Responses in EMD pts treated at the RP2R were highly durable and are further detailed elsewhere.[10,11]**

Table 1. Common adverse events of interest across all dose levels - adverse events were not exacerbated with the combination compared to Tal and Tec monotherapies[5,8]

Hematologic AEs,[a] n (%)	DL1 (n=3)		DL2 (n=1)		DL3 (n=9)		DL4 (n=4)		DL5 (n=18)		DL6 (n=3)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Neutropenia	1 (33.3%)	1 (33.3%)	1 (100.0%)	1 (100.0%)	6 (66.7%)	6 (66.7%)	3 (75.0%)	3 (75.0%)	12 (66.7%)	11 (61.1%)	3 (100.0%)	2 (66.7%)
Anemia	3 (100.0%)	3 (100.0%)	1 (100.0%)	1 (100.0%)	6 (66.7%)	5 (55.6%)	3 (75.0%)	1 (25.0%)	8 (44.4%)	5 (27.8%)	2 (66.7%)	2 (66.7%)
Thrombocytopenia	2 (66.7%)	2 (66.7%)	1 (100.0%)	1 (100.0%)	3 (33.3%)	2 (22.2%)	3 (75.0%)	2 (50.0%)	8 (44.4%)	4 (22.2%)	1 (33.3%)	0
Nonhematologic AEs,[a] n (%)												
CRS	3 (100.0%)	0	1 (100.0%)	0	7 (77.8%)	1 (11.1%)	2 (50.0%)	0	13 (72.2%)	0	2 (66.7%)	0
ICANS	0	0	0	0	1 (11.1%)	1 (11.1%)	0	0	2 (11.1%)	0	0	0
Infections[b]	3 (100.0%)	2 (66.7%)	1 (100.0%)	1 (100.0%)	8 (88.9%)	7 (77.8%)	4 (100.0%)	4 (100.0%)	17 (94.4%)	10 (55.6%)	3 (100.0%)	2 (66.7%)
Taste Changes[c]	2 (66.7%)	0	1 (100.0%)	0	8 (88.9%)	0	1 (25.0%)	0	7 (38.9%)	0	1 (33.3%)	0

[a]Data presented on a treatment-emergent basis. [b]The most common infections were pneumonia and COVID-19. [c]Includes dysgeusia, ageusia, hypogeusia, and taste disorder; maximum grade for taste changes is 2 per CTCAE. CRS, cytokine release syndrome; ICANS, Immune Effector Cell-Associated Neurotoxicity Syndrome.

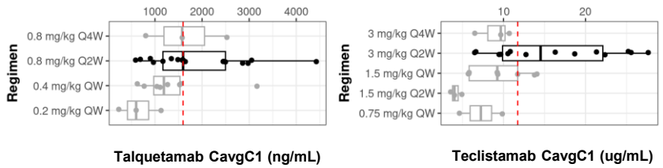
Figure 2. A positive relationship was observed between Tal and Tec exposure and CR or better in patients with EMD



The dots and error bars represent the observed complete response or better rate and its 95% CI (by Wilson method) in the respective exposure tertile groups. Lines and shaded areas represent the model-predicted response rate and 95% CI via logistic regression.

Other PK metrics including CtrC1 were highly correlated with CavgC1 and showed the same trend. Therefore, only CavgC1 is shown.

Figure 3. The RP2R achieved the deepest responses at the highest rate, likely driven by increased exposure to both antibodies



Plots above includes EMD (n=31) pts only and show the distribution of simulated exposure based on individual parameter estimates and actual dose records (black: RP2R; grey: non-RP2R). Red-dashed vertical lines indicate minimum of the 3rd tertile of exposures across Dose Levels 1 to 6 in Phase 1.

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Multiple Myeloma

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