MM-349

Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Combination With Pomalidomide in Patients With Relapsed/Refractory Multiple Myeloma: Efficacy and Safety Results From the Phase 1b MonumenTAL-2 Study

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Key Takeaway

With longer follow-up, tal + pom showed promising efficacy and a manageable safety profile consistent with previously reported analyses, which further supports tal as a versatile combination partner in RRMM

Conclusions

- Tal + pom showed rapid, deep, and durable responses; a trend for longer DOR with deeper response was observed, which suggests that patients with a ≥VGPR may have more durable responses
- Neutropenia was worse with the combination than with tal monotherapy, but its frequency was comparable to pom monotherapy[4,6,8]; there was no evidence of additive hematologic or CRS toxicities
- Similar rates of GPRC5D-related AEs were observed as with tal monotherapy, and the majority were grade 1/2, with few discontinuations[4]; dose reductions were used to manage AEs

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Disclosures
ES has served in a consulting role for Sanofi and Shattuck Labs; and has received honoraria from AbbVie and Janssen.

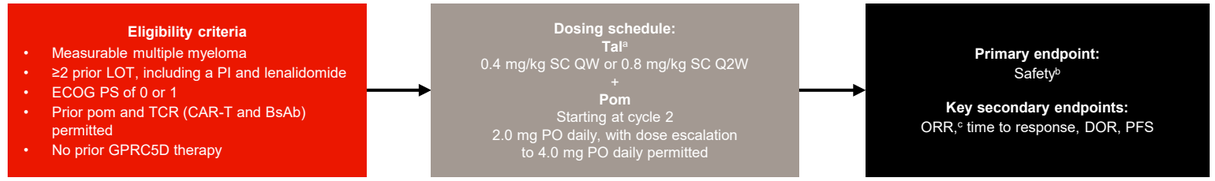
Introduction

- Talquetamab (tal) is the first approved G protein–coupled receptor family C group 5 member D (GPRC5D)-targeting bispecific antibody (BsAb) for the treatment of patients with relapsed/refractory multiple myeloma (RRMM)[1-3]
  - In the phase 1/2 MonumenTAL-1 study, tal showed overall response rates (ORRs) of >71% and a clinically manageable safety profile in patients with RRMM[4]
- Pomalidomide (pom), an established immunomodulatory drug, has direct on-tumor apoptotic activity and enhances immune activity[5,6]
- Initial MonumenTAL-2 results (clinical cut-off date: Oct 2023) showed that the combination of tal + pom led to rapid and deep responses in patients with RRMM[7]
- We report updated safety and efficacy results of tal + pom from MonumenTAL-2

Methods

- MonumenTAL-2 (NCT05050097) is a multiarm, phase 1b study of tal in combination with antimyeloma agents in patients with multiple myeloma
- The tal + pom treatment arm enrolled patients who were either naive or exposed to prior T-cell redirection therapy (TCR) or pom (**Figure 1**)

Figure 1: MonumenTAL-2 (tal + pom) phase 1b study design



[a]With 2–3 step-up doses. [b]AEs assessed per CTCAE v5.0, except for CRS and ICANS, which were graded per ASTCT guidelines. [c]Assessed per IMWG 2016 criteria.
AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMWG, International Myeloma Working Group; LOT, line of therapy; PFS, progression-free survival; PI, proteasome inhibitor; PO, by mouth; Q2W, every other week; QW, weekly, SC, subcutaneous.

Results

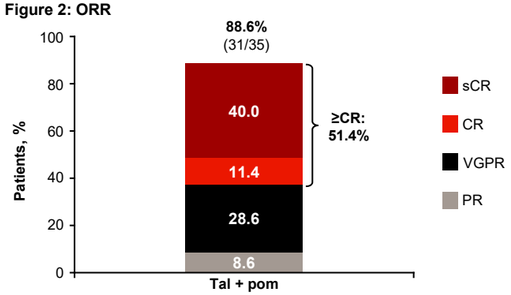
Baseline characteristics

- Baseline characteristics have been published previously[7]
- Briefly, the median age was 65.0 years, 39.1% of patients had high-risk cytogenetics, and 14.3% had extramedullary disease
- Prior treatments included CAR-T (8.6%), BsAb (2.9%), anti-CD38 antibody (74.3%), and pom (22.9%)

Efficacy

- As of April 22, 2024, ORR was 88.6% (**Figure 2**); additional efficacy outcomes are presented in **Table 1**
- High ORRs were observed in subgroups, including high-risk cytogenetics (77.8%) and prior CAR-T (100%) or pom (100%)
- Although numbers are small, a trend for longer DOR with deeper response was observed (**Table 2**)
- Responses deepened over time (**Figure 3**)

Figure 2: ORR



CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

Table 1: Efficacy outcomes

	Tal + pom (N=35)
Median follow-up, months (range)	16.8 (1.2–25.1)
Median time to first response, months (range)	1.1 (0.0–3.3)
Median DOR, months (95% CI)	NR (12.0–NE)
12-month DOR rate, % (95% CI)	74.4 (53.5–86.9)
Median PFS, months (95% CI)	NR (12.9–NE)
12-month PFS rate, % (95% CI)	72.6 (53.9–84.7)

NE, not estimable; NR, not reached.

Table 2: DOR by depth of best response

Depth of response	12-month DOR rate, % (95% CI)
PR	0.0 (NE–NE) n=2
VGPR	78.8 (38.1–94.3) n=11
CR	80.4 (50.6–93.2) n=17

Safety

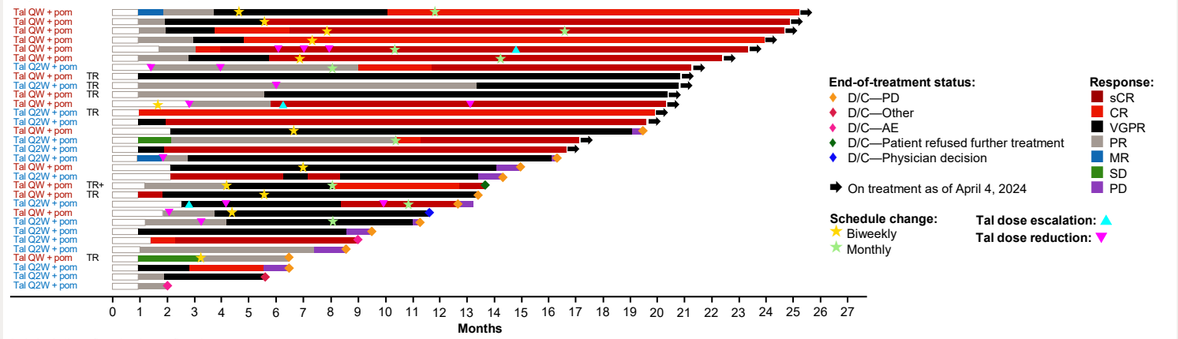
- The most common AEs were taste-related events, infections, and CRS (**Table 3**)
- Cytopenias were mostly grade 3/4 and generally limited to the first few cycles
- ICANS occurred in 3 patients; all were grade 1
- Taste-, skin-, nail-, and rash-related GPRC5D AEs were mainly grade 1/2, with few discontinuations
- 9 patients had AEs that led to treatment discontinuation
- AEs led to dose reduction of tal or pom in 37.1% and 48.6% of patients, respectively; 65.7% and 77.1% of patients skipped doses of tal and pom due to AEs, respectively
  - The most common AEs that led to dose reduction of pom included neutropenia, peripheral neuropathy, and fatigue
  - Dose reduction and schedule changes were used to manage AEs
- In patients with and without oral toxicities, weight loss was evident early but stabilized and improved over time; a more gradual trend of improvement was noted in patients with oral toxicities
- The most common infections were pneumonia, upper respiratory tract infections, and COVID-19; infections were mostly grade 1/2
  - First-onset infections generally occurred in the first few cycles of treatment
- Consistent with target expression, there was no reduction in total CD19+ B cells during treatment

Table 3: Hematologic and nonhematologic AEs

TEAE ≥25%, n (%)	All patients (N=35)	
	Any Grade	Grade 3/4
Hematologic AEs		
Neutropenia	22 (62.9)	20 (57.1)
Anemia	13 (37.1)	9 (25.7)
Thrombocytopenia	10 (28.6)	7 (20.0)
Nonhematologic AEs		
Taste related[a]	30 (85.7)	0
Infections	28 (80.0)	8 (22.9)
CRS	26 (74.3)	1 (2.9)
Skin related[b]	26 (74.3)	2 (5.7)
Nail related[c]	24 (68.6)	0
Dry mouth	19 (54.3)	0
Fatigue	19 (54.3)	5 (14.3)
Pyrexia	14 (40.0)	1 (2.9)
Nausea	13 (37.1)	0
Diarrhea	11 (31.4)	0
Headache	10 (28.6)	1 (2.9)
Rash related[d]	10 (28.6)	1 (2.9)
Back pain	9 (25.7)	1 (2.9)
Cough	9 (25.7)	0
Weight decreased	9 (25.7)	2 (5.7)

[a]Includes dysgeusia, ageusia, taste disorder, and hypogeusia. Per CTCAE v5.0, the maximum grade of dysgeusia is 2. [b]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [c]Includes nail discoloration, nail disorder, nail toxicity, nail dystrophy, nail ridging, onychoclasis, onycholysis, and onychomadesis. [d]Includes rash, maculopapular rash, erythematous rash, and erythema.
TEAE, treatment-emergent adverse event.

Figure 3: Treatment response in patients who had ≥PR with tal + pom



Includes both confirmed and unconfirmed responses.
+, penta-refractory; D/C, discontinued; MR, minimal response; PD, progressive disease; SD, stable disease; TR, triple-class refractory.

References
1. Verkleij CPM, et al. *Blood Adv* 2021;5:2196-215. 2. TALVEY™ (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 3. European Medicines Agency. TALVEY™ (talquetamab). Accessed May 2, 2024. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/talvey. 4. Schinke C, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8036. 5. Bazarbachi AH, et al. *Leukemia* 2019;33:2243-357. 6. POMALYST® (pomalidomide). Prescribing information. Summit, NJ: Celgene Corporation; 2020. 7. Matous J, et al. Presented at ASH; December 10–13, 2023; San Diego, CA, USA. #1014. 8. Dimopoulos MA, et al. *Blood* 2016;128:497-503.

Multiple Myeloma

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