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

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Key Takeaway

With longer follow-up, talquetamab (Tal) + pomalidomide (Pom) continued to elicit deep and durable responses in patients with relapsed/refractory multiple myeloma (RRMM), consistent with previously reported analyses

Conclusions

The combination of Tal + Pom demonstrated a clinically manageable safety profile, consistent with individual agents, with no new safety signals identified with longer follow-up

These findings continue to support the phase 3 MonumenTAL-6 study, which compares the efficacy of Tal + Pom vs investigator's choice of elotuzumab + Pom + dexamethasone or Pom + bortezomib + dexamethasone in patients with RRMM who had 1–4 prior lines of therapy (LOT)

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Introduction

- Tal is the first G protein–coupled receptor class C group 5 member D (GPRC5D) × CD3 bispecific antibody (BsAb) approved for treatment of patients with RRMM[1-3]
- Pom is an established immunomodulatory drug with direct on-tumor apoptotic activity[4,5]
- Initial results of the phase 1b MonumenTAL-2 study (NCT05050097) combining Tal and Pom showed rapid and deep responses in patients with RRMM, with a safety profile consistent with the individual agents[6]

We report updated safety and efficacy results of Tal + Pom from MonumenTAL-2 with longer median follow-up of 20.7 months (range, 1.2–38.7). Data cut-off: March 2025

Methods

MonumenTAL-2[a] phase 1b study design

Eligibility criteria
- Measurable multiple myeloma
- ≥2 prior LOT, including a PI and lenalidomide
- ECOG PS of 0 or 1
- Prior BsAbs, CAR-T, and Pom permitted
- No prior GPRC5D therapy

→ **Dosing schedule**
Tal[b]
0.4 mg/kg SC QW (n=16) or
0.8 mg/kg SC Q2W (n=19)
+
Pom
Starting at cycle 2, days 1–21 of a 28-day cycle
2.0 mg PO daily with dose escalation to 4.0 mg PO daily permitted[c]

→ **Primary endpoint:**
Safety[d]

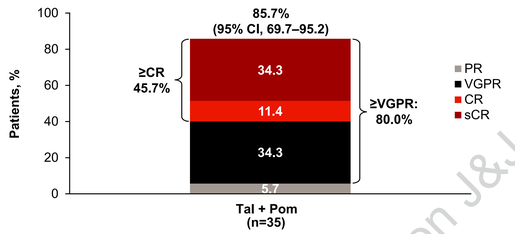
Key secondary endpoints:
Overall response rate (ORR)[e], time to response, duration of response (DOR), progression-free survival (PFS)

[a]NCT05050097. [b]With step-up doses. [c]Based on safety evaluation team recommendation. [d]AEs assessed per CTCAE v5.0, except for CRS and ICANS, which were graded per ASTCT guidelines. [e]Assessed by investigator 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; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMWG, International Myeloma Working Group; PI, proteasome inhibitor; PO, by mouth; Q2W, every other week; QW, weekly, SC, subcutaneous.

Results

Baseline characteristics have been previously presented[6]; median age was 65 years, median prior LOT was 3, 45.0% had high-risk cytogenetics, and 20.0% had extramedullary disease. Prior treatment exposure included Pom, B-cell maturation antigen CAR-T, and BsAbs

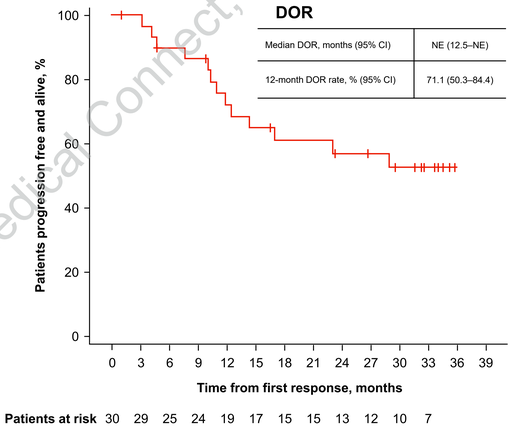
Figure 1: Treatment with Tal + Pom elicited a high ORR and deep responses in patients with RRMM with a median follow-up of 20.7 months

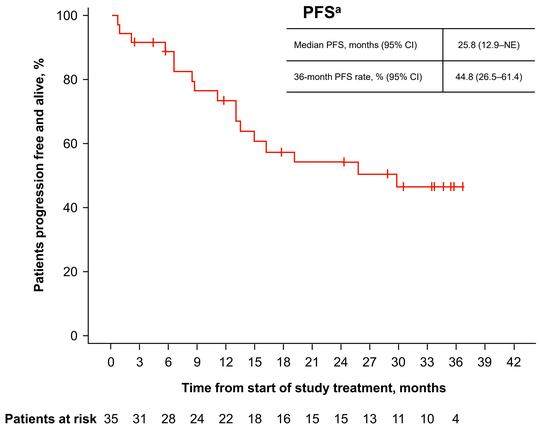


CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

High ORRs were observed across patient groups, including those with prior exposure to CAR-T (100%, 3/3) or Pom (100.0%, 8/8)

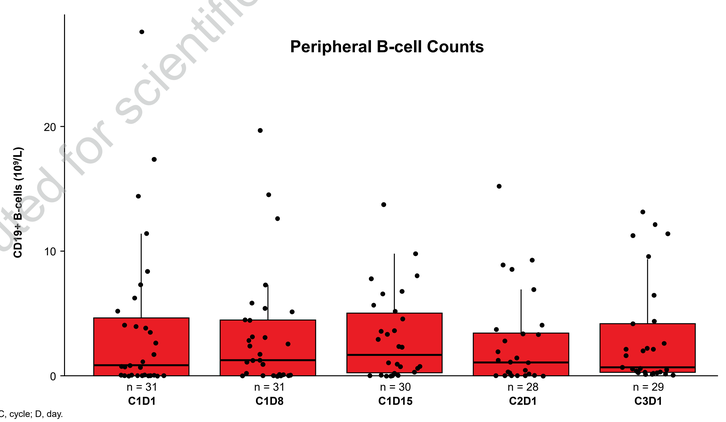
Figure 2: Tal + Pom elicited sustained DOR and PFS outcomes demonstrating long-term efficacy with longer follow-up; median DOR was not reached and nearly half of patients remained progression free at 3 years





[a]Early PFS events due to 3 deaths in the Q2W subgroup; 1 participant died due to a nonrelated serious AE (pulmonary embolism), while the other 2 died due to pulmonary disease after study day >100. No deaths were reported in the QW subgroup. NE, not evaluable.

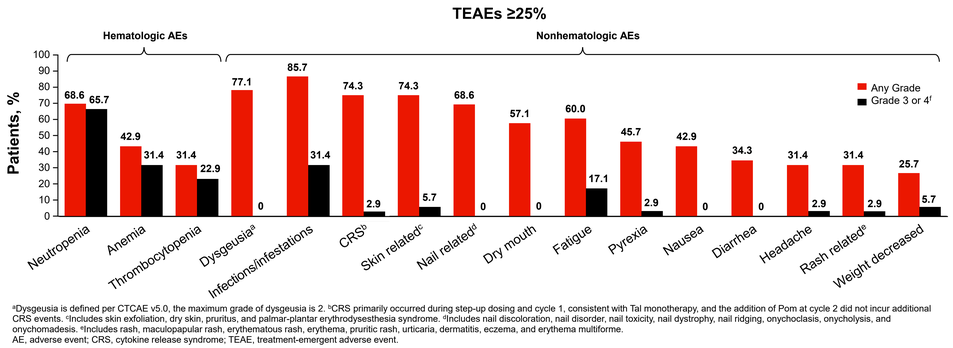
Figure 3: B-cells were retained across the first several cycles of treatment, consistent with prior findings and supporting the B-cell–sparing mechanism of Tal



C, cycle; D, day.

AEs led to dose reduction of Tal or Pom in 25.7% and 48.6% of patients, respectively, to dose omissions in 65.7% and 80.0%, and to dose delays in 77.1% and 22.9%. No further discontinuation of any study treatment due to AEs was observed vs the initial report (3 patients, 8.6%), indicating the absence of cumulative toxicity

Figure 4: The safety profile of Tal + Pom with longer treatment duration was comparable with previously reported data



[a]Dysgeusia is defined per CTCAE v5.0, the maximum grade of dysgeusia is 2. [b]CRS primarily occurred during step-up dosing and cycle 1, consistent with Tal monotherapy, and the addition of Pom at cycle 2 did not incur additional CRS events. [c]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. [d]Includes nail discoloration, nail disorder, nail toxicity, nail dystrophy, nail ridging, onycholysis, onycholysis, and onychomadesis. [e]Includes rash, maculopapular rash, erythematous rash, erythema, pruritic rash, urticaria, dermatitis, eczema, and erythema multiforme.
AE, adverse event; CRS, cytokine release syndrome; TEAE, treatment-emergent adverse event.

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Multiple Myeloma

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