Talquetamab + Cetrelimab in Patients With Relapsed/Refractory Multiple Myeloma: Initial Safety and Efficacy Results From the Phase 1b TRIMM-3 Study

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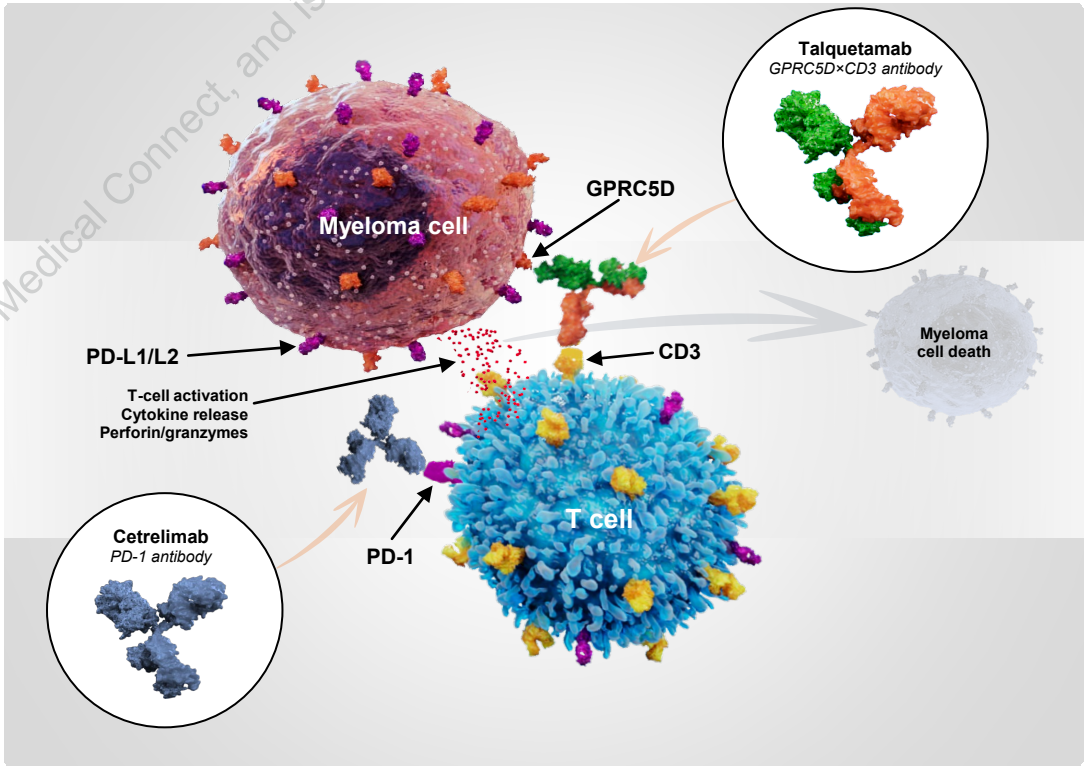
TRIMM-3 (Tal + Cet): Background

- Tal is the first approved GPRC5D-targeting bispecific antibody for RRMM[1-3]
  - Patients with prior exposure to BsAb therapy is a newly emerging patient population with a high unmet need
- Cet is a monoclonal antibody that inhibits PD-1 to enhance T-cell activity and antitumor immunity[4]
- Combining Cet with T-cell redirection therapy may lead to additive antimyeloma effects by reinvigorating T cells



We report initial safety and efficacy results of Tal + Cet from the TRIMM-3 study

TRIMM-3 ClinicalTrials.gov identifier: NCT05338775. BsAb, bispecific antibody; Cet, cetrelimab; GPRC5D, G protein–coupled receptor class C group 5 member D; PD-1, programmed cell death receptor-1; RRMM, relapsed/refractory multiple myeloma; tal, talquetamab. 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 5, 2025. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/talvey. 4. Rutkowski P, et al. *J Clin Oncol* 2019;37(8 Suppl):31.

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TRIMM-3 (Tal + Cet): Phase 1b Study Design

Eligibility criteria

- MM per IMWG criteria
- RRMM who may not be eligible for or expected to benefit from available therapies
- ECOG PS 0 or 1

Dosing schedule

Dose escalation cohorts
Tal 0.4 or 0.8 mg/kg SC Q2W[a]
+
Cet 80, 160, or 240 mg IV Q2W
(starting cycle 2 day 2)
(n=25)

Dose expansion cohort
Tal 0.8 mg/kg SC Q2W[a]
+
Cet 240 IV Q2W (starting cycle 2 day 2)
(n=19)

Primary endpoint:
Safety

Key secondary endpoints:
ORR,[b] DOR, time to response, and pharmacokinetics

- Tal and Cet dosing regimens were escalated to their respective RP2Ds (Tal 0.8 mg/kg Q2W; Cet 240 mg Q2W)
- All patients in the dose expansion cohort had prior exposure to BsAb therapy[c]

[a]2–3 step-up doses before first full dose. Premedication including glucocorticoid, antihistamine, and antipyretic at step-up and first full dose. [b]Assessed using the IMWG criteria. [c]Included CD3 redirecting antibody therapy.
Cet, cetrelimab; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IV, intravenous; MM, multiple myeloma; Q2W, every other week; RP2Ds, recommended phase 2 doses; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; Tal, talquetamab.

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TRIMM-3 (Tal + Cet): Baseline Characteristics

Characteristic	All patients (Tal + Cet) (N=44)
Age (years), median (range)	64 (45–87)
Male, n (%)	24 (54.5)
Race, n (%)	
White	22 (50.0)
Black/African American	2 (4.5)
Asian	1 (2.3)
Not reported	15 (34.1)
High cytogenetic risk,[a] n (%)	17 (43.6)
ISS stage, n (%)	
I	27 (61.4)
II	11 (25.0)
III	6 (13.6)
Time since diagnosis (years), median (range)	6.8 (1.0–16.8)

Characteristic	All patients (Tal + Cet) (N=44)
Prior LOT (n), median (range)	5 (2–11)
Prior stem cell transplantation, n (%)	34 (77.3)
Prior therapies, n (%)	
Triple class[b]	44 (100.0)
Penta drug[c]	29 (65.9)
BCMA-targeted therapy	31 (70.5)
CAR-T	9 (20.5)
Bispecific antibody	22 (50.0)
ADC	4 (9.1)
Refractory status, n (%)	
Triple class[b]	37 (84.1)
Penta drug[c]	15 (34.1)
Any prior BCMA	24 (54.5)
To last LOT	35 (79.5)

Data cut-off: April 2, 2025. [a]del(17p), t(4;14), and/or t(14;16); percentages calculated from n=39. [b]≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 mAb. [c]≥2 PIs, ≥2 IMiDs, and ≥1 anti-CD38 mAb. ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; Cet, cetrelimab; IMiD, immunomodulatory drug; ISS, International Staging System; LOT, line of therapy; mAb, monoclonal antibody; PI, proteasome inhibitor; Tal, talquetamab.

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TRIMM-3 (Tal + Cet): The Addition of Cet Did Not Exacerbate AEs Associated With Tal

AEs (≥25%),[a] n (%)	All patients (N=44)	
	Any Grade	Grade 3/4
Taste events[b]	36 (81.8)	0 (0)
Infections	36 (81.8)	13 (29.5)
Nail events[c]	33 (75.0)	0 (0)
Nonrash skin events[d]	31 (70.5)	0 (0)
CRS	27 (61.4)	0 (0)
Dry mouth	21 (47.7)	0 (0)
Weight decreased	15 (34.1)	1 (2.3)
Diarrhea	14 (31.8)	1 (2.3)
Rash events[e]	14 (31.8)	1 (2.3)
PD-1 immune-mediated events[f]	13 (29.5)[f]	3 (6.8)
Pyrexia	13 (29.5)	0 (0)

- GPRC5D-related AEs were mostly low grade with no discontinuations
- 6 (14%) patients had AEs that led to treatment discontinuation[g]
- 9 (20%) patients had AEs that led to Tal dose reductions
- Immune-mediated AEs associated with Cet were consistent with other anti-PD-1–related therapies[f]

Data cut-off: April 2, 2025. [a]AEs were graded by CTCAE v5.0, except for CRS, which was graded per ASTCT criteria. AEs reported were treatment emergent. [b]Oral AEs include dysgeusia, ageusia, taste disorder, and hypogeusia. Per CTCAE, the maximum grade for dysgeusia is 2. [c]Nail AEs include nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [d]Skin AEs include skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysaesthesia syndrome. [e]Includes rash, maculopapular rash, erythematous rash, and erythema. [f]Immune-mediated class effects of PD-1 inhibitors include (but are not limited to) pruritus, diarrhea, hypothyroidism, hyperthyroidism, pneumonitis, amylase/lipase increased, and rash. In the current study, immune-mediated AEs due to Cet were investigator attributed and included skin-related (18.2%), hematologic (4.5%), gastrointestinal (4.5%), and pyrexia (2.3%). [g]2 patients discontinued both Tal and Cet (ataxia and pneumonia); 4 patients discontinued Cet only (pemphigoid, immune thrombocytopenia, diarrhea, and diarrhea/eosinophilia). AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; Cet, cetrelimab; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; GPRC5D, G protein–coupled receptor class C group 5 member D; PD-1, programmed cell death receptor-1; Tal, talquetamab.

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TRIMM-3 (Tal + Cet): The Addition of Cet Did Not Potentiate CRS

Characteristic	All patients (N=44)
Patients with CRS,[a] n (%) Grade 1 Grade 2	27 (61.4) 20 (45.5) 7 (15.9)
Time to onset (days),[b] median (range)	2 (1–11)
Duration (days), median (range)	2 (1–7)
Received supportive measures,[c] n (%) Tocilizumab Corticosteroids Other	24 (54.5) 15 (34.1) 1 (2.3) 19 (43.2)

- CRS mostly confined to step-up and cycle 1 dosing (prior to the addition of Cet) with no discontinuations
  - No grade ≥3 CRS
  - All events recovered
- ICANS[a] in 2 patients (both grade 1)

Data cut-off: April 2, 2025.
[a]CRS and ICANS were graded per ASTCT criteria. [b]Relative to most recent dose (day of most recent dose = day 1). [c]A patient could receive >1 supportive therapy.
ASTCT, American Society for Transplantation and Cellular Therapy; Cet, cetrelimab; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; Tal, talquetamab.

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TRIMM-3 (Tal + Cet): Grade 3/4 Infections Comparable With Tal Monotherapy in a Similar Patient Population[a]

AEs (≥10%),[b] n (%)	All patients (N=44)	
	Any Grade	Grade 3/4
Infections	36 (81.8)	13 (29.5)
COVID-19	10 (22.7)	1 (2.3)
Bronchitis	7 (15.9)	0 (0)
Nasopharyngitis	6 (13.6)	1 (2.3)
Pneumonia	6 (13.6)	2 (4.5)
Upper respiratory tract infection	5 (11.4)	0 (0)
Hematologic AEs		
Anemia	26 (59.1)	17 (38.6)
Neutropenia	24 (54.5)	19 (43.2)
Thrombocytopenia	16 (36.4)	7 (15.9)
Lymphopenia	12 (27.3)	12 (27.3)
Leukopenia	6 (13.6)	4 (9.1)

- Hypogammaglobulinemia (or IgG <400 mg/dL) occurred in 56.8% of patients
- 34.1% received ≥1 dose of IVIG
- 1 death occurred due to pneumonia

Data cut-off: April 2, 2025.
[a]Patients with prior TCR, including CAR-T and BsAbs in the MonumenTAL-1 study. [b]AEs were graded by CTCAE v5.0. AEs reported were treatment emergent.
AE, adverse event; BsAb, bispecific antibody; CAR, chimeric antigen receptor; Cet, cetrelimab; CTCAE, Common Terminology Criteria for Adverse Events; IgG, immunoglobulin G; IVIG, intravenous immunoglobulin; Tal, talquetamab; TCR, T-cell redirection therapy.

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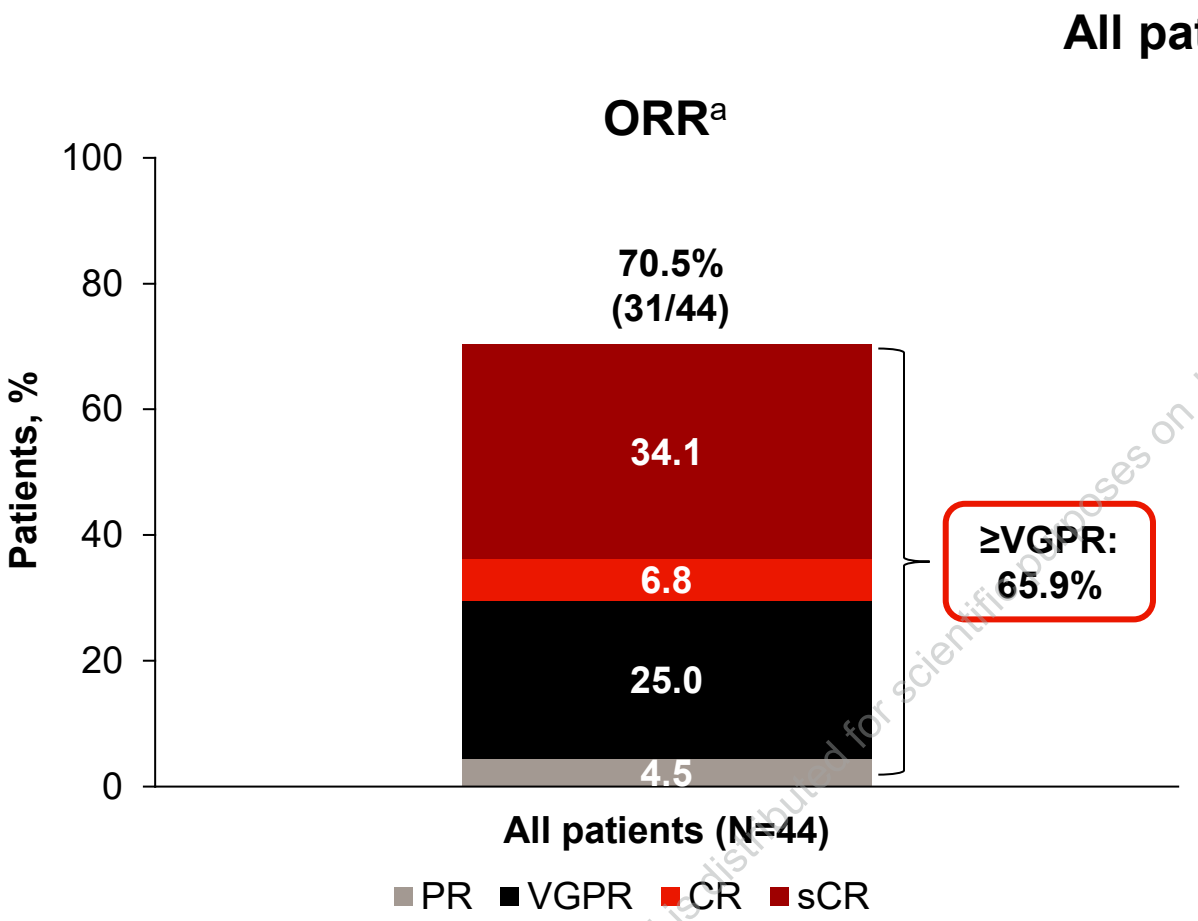
TRIMM-3 (Tal + Cet): Promising Efficacy in the Overall Population of Patients Who Were Heavily Pretreated



	All patients (N=44)
Median (range) follow-up, months	11.5 (1.5–32.3)
Median (range) time to first response, months	1.9 (0.8–17.5)
Median (range) time to best response, months	4.0 (1.1–22.8)
Median (range) DOR, months	16.8 (10.6–NE)
9-month DOR, %	72.6
6-month PFS, %	69.9

Data cut-off: April 2, 2025. [a]Response was assessed by IMWG criteria. Percentages are calculated with the number of patients in each group as denominator.
Cet, cetrelimab; CR, complete response; DOR, duration of response; IMWG, International Myeloma Working Group; NE, not evaluable; ORR, overall response rate; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; Tal, talquetamab; VGPR, very good partial response.

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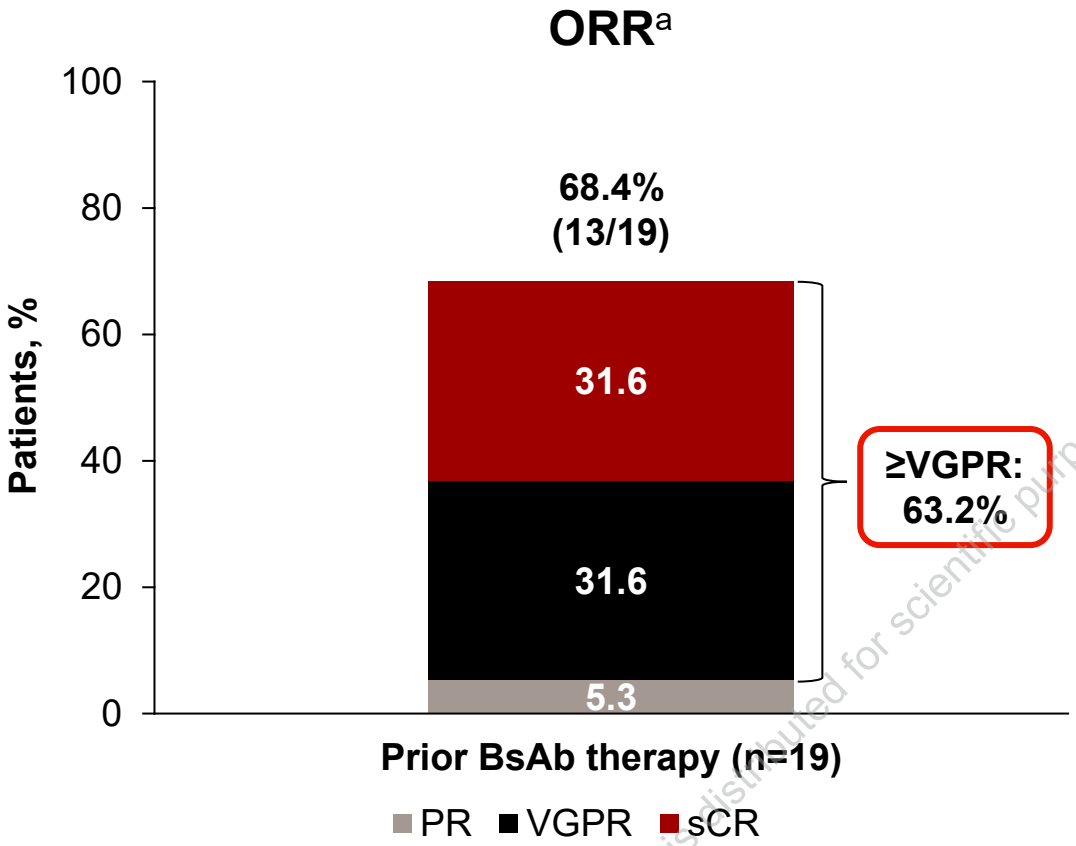
TRIMM-3 (Tal + Cet): Deep and Durable Responses in Patients With Prior BsAb Therapy

Dose expansion cohort



	Patients with prior BsAb therapy (n=19)
Median (range) follow-up, months	10.9 (1.5–17.5)
Median (range) time to first response, months	1.9 (0.8–3.7)
Median (range) time to best response, months	3.7 (1.8–7.4)
Median (range) DOR, months	12.0 (8.9–NE)
9-month DOR, %	65.9
6-month PFS, %	61.5

- 18 patients with BCMA-targeted BsAb therapy[b]
- 95% of patients with BsAb therapy as their immediate prior LOT
- Median of 39 days since prior exposure

Data cut-off: April 2, 2025.
[a]Response was assessed by IMWG criteria. Percentages are calculated with the number of patients in each group as denominator. [b]1 patient received cevostamab.
BCMA, B-cell maturation antigen; BsAb, bispecific antibody; Cet, cetrelimab; CR, complete response; DOR, duration of response; IMWG, International Myeloma Working Group; LOT, line of therapy; ORR, overall response rate; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; Tal, talquetamab; VGPR, very good partial response.

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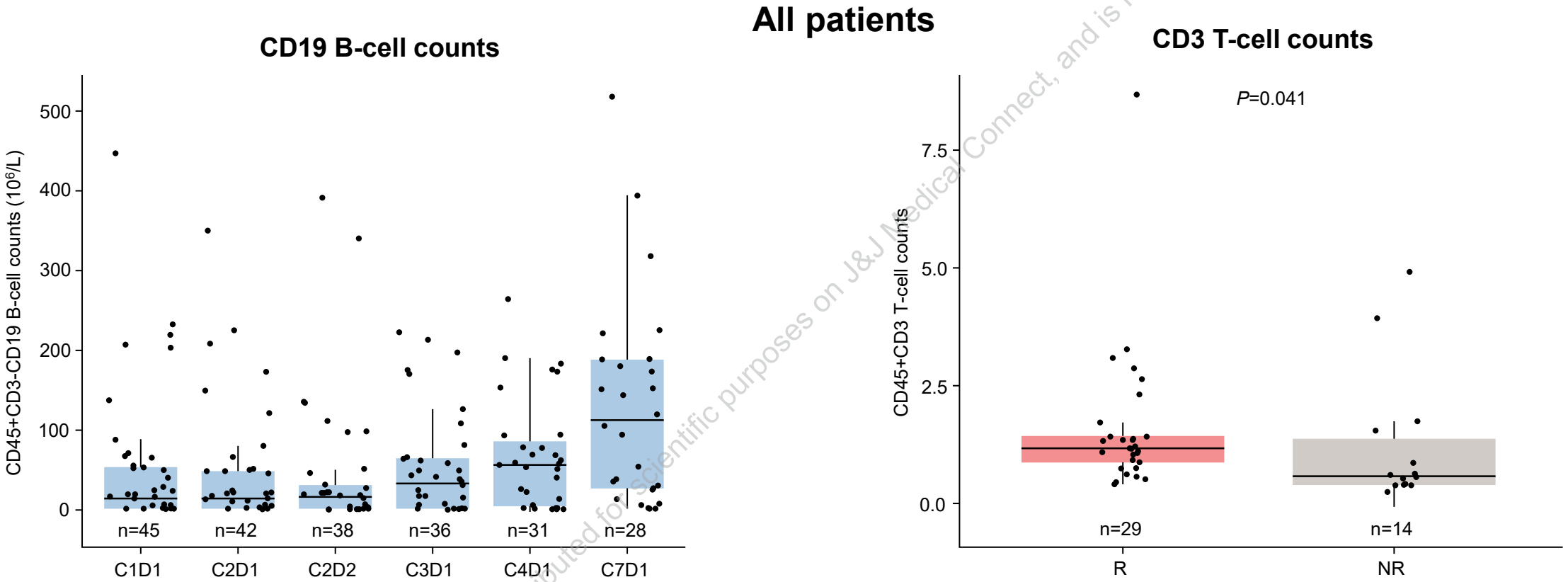
TRIMM-3 (Tal + Cet): No Reduction in B cells, and Greater T-cell Expansion in Responders vs Nonresponders



Data cut-off: April 2, 2025. B-cell counts assessed by flow cytometry. CD3 T cells show the maximum fold change from baseline to C7D1, assessed by flow cytometry.
C, cycle; Cet, cetrelimab; D, day; NR, nonresponders; R, responders; Tal, talquetamab.

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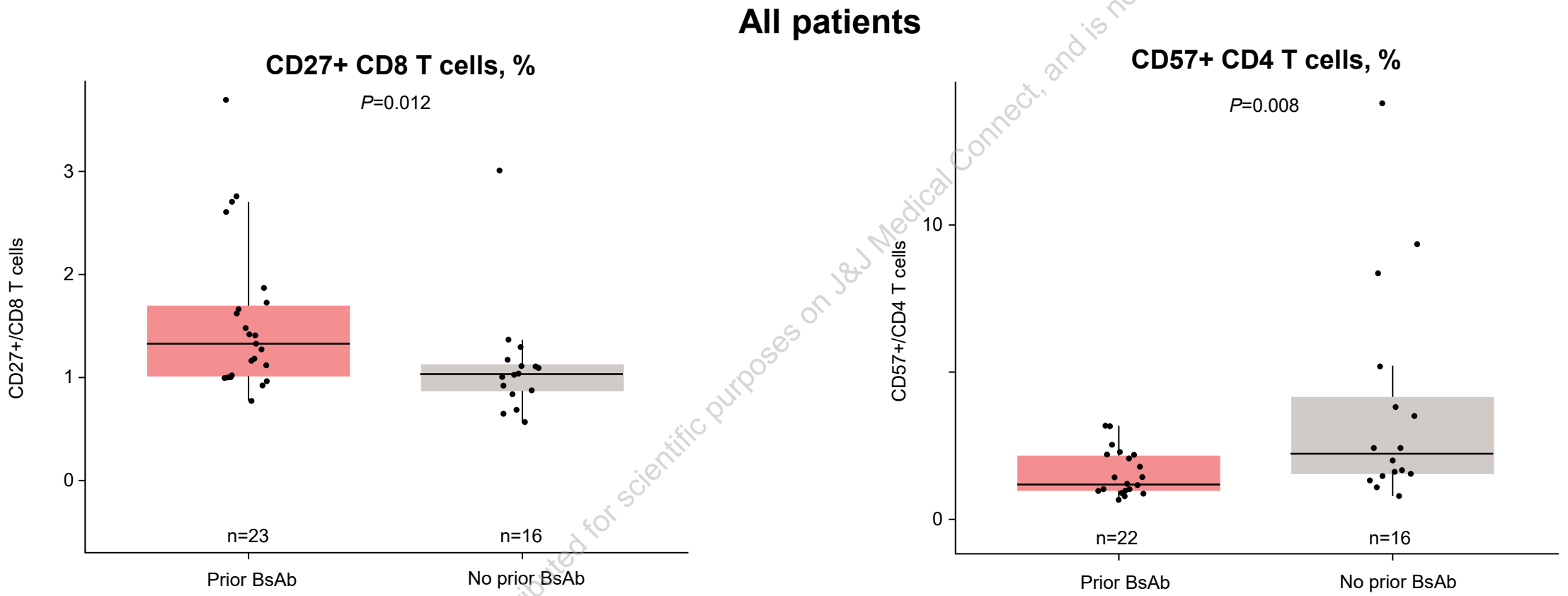
TRIMM-3 (Tal + Cet): Greater T-Cell Reinvigoration Potential in Patients With Prior BsAb Therapy



- In patients with prior BsAb, higher induction of costimulatory molecule CD27 (associated with T-cell survival and expansion) and lower expression of marker CD57 (associated with terminally differentiated T cells and replicative senescence) was observed
- Pharmacokinetic profile was comparable with Tal monotherapy

Data cut-off: April 2, 2025. Figures show maximum fold change from baseline to C7D1, assessed by flow cytometry. BsAb, bispecific antibody; C, cycle; Cet, cetrelimab; D, day; Tal, talquetamab.

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TRIMM-3 (Tal + Cet): Conclusions

- **Tal + Cet elicited deep and durable responses in patients with RRMM and prior BsAb therapy, similar to results with Tal + Dara in patients with prior T-cell redirection therapy including BsAbs[1]**
  - ORR was 68% (≥VGPR 63%) in patients with prior BsAb therapy
  - Median DOR of 12 months and 9-month DOR rate of 66% in patients with prior BsAb therapy
- **Safety profile was generally consistent with each individual agent,[2-4] supporting combinability of Tal**
  - Taste, skin, rash, and nail AEs were low grade, with no discontinuations of Tal
  - Grade 3/4 infections were comparable with Tal monotherapy in patients with prior CAR-T/BsAb therapy[1]
- **Higher induction of CD27 and lower expression of CD57 on CD8 T cells suggest greater T-cell reinvigoration potential, which may lead to improved outcomes in patients with prior BsAb therapy**
- **Together, in patients with prior BsAb therapy who may have altered T-cell function following treatment, Cet may potentiate Tal by reinvigorating T cells**

These data support Tal as a versatile combination partner and suggest potential activity of PD-1 inhibitors in RRMM

AE, adverse event; BsAb, bispecific antibody; CAR, chimeric antigen receptor; Cet, cetrelimab; Dara, daratumumab; DOR, duration of response; ORR, overall response rate; PD-1, programmed cell death receptor-1; RRMM, relapsed/refractory multiple myeloma; Tal, talquetamab; VGPR, very good partial response. 1. Dholaria B, et al. Presented at ASCO; June 2–6, 2023, Chicago, IL, USA & Virtual. 2. Chari A, et al. *Lancet Haematol* 2025;12:e269-81. 3. Rutkowski P, et al. *J Clin Oncol* 2019;37(8 Suppl):31. 4. Cohen YC, et al. *Clin Lymphoma Myeloma Leuk* 2021;21:46-54.e4.

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