Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Combination With Daratumumab and Lenalidomide in Patients With Newly Diagnosed Multiple Myeloma: Safety and Efficacy Results From the Phase 1b MonumenTAL-2 Study

Ajay K Nooka[1], Tara Cochrane[2], Anita D'Souza[3], Jeffrey V Matous[4], Peter M Voorhees[5], Karthik Ramasamy[6], Aurore Perrot[7], Andrew Spencer[8], Cyrille Hulin[9], Hang Quach[10], Deeksha Vishwamitra[11], Ashley Nguyen[11], Debopriya Ghosh[12], Elizabeth Shearin[11], Gary E Mason[11], Thomas Renaud[12], Gurdeep Parmar[13]

[1]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [2]Gold Coast University Hospital, Griffiths University, Southport QLD, Australia; [3]Medical College of Wisconsin, Milwaukee, WI, USA; [4]Colorado Blood Cancer Institute and Sarah Cannon Research Institute, Denver, CO, USA; [5]Atrium Health Levine Cancer Institute, Charlotte, NC, USA; [6]Oxford Translational Myeloma Centre, University of Oxford and Oxford University Hospitals, NHS Foundation Trust, Oxford, UK; [7]Centre Hospitalier Universitaire de Toulouse, Oncopole, Toulouse, France; [8]Alfred Health-Monash University, Melbourne, VIC, Australia; [9]Hôpital Haut Leveque, University Hospital, Pessac, France; [10]University of Melbourne, St. Vincent's Hospital, Melbourne, VIC, Australia; [11]Janssen Research & Development, Spring House, PA, USA; [12]Janssen Research & Development, Raritan, NJ, USA; [13]Wollongong Hospital, NSW, Wollongong, Australia

Presented by AK Nooka at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA

MonumenTAL-2 (Tal-Dara-Len): First Combination of Talquetamab in NDMM

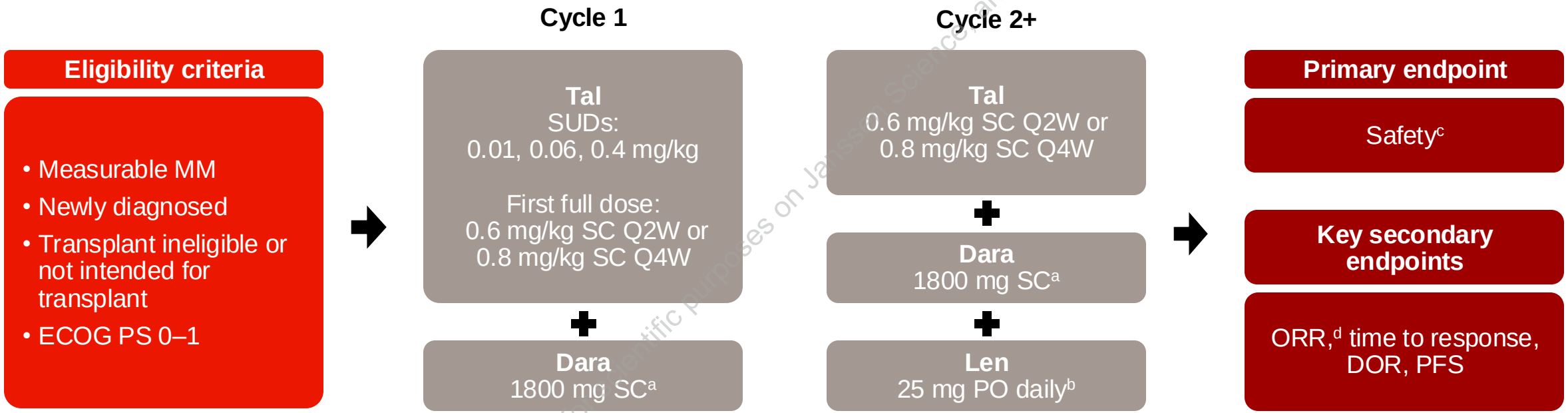
- Talquetamab (Tal) is the first approved GPRC5D-targeting bispecific antibody for the treatment of patients with relapsed/refractory MM[1-3]
- Daratumumab (Dara), an anti-CD38 monoclonal antibody, is a foundational therapy across all lines of MM therapy with direct on-tumor and immunomodulatory actions[4,5]
- Lenalidomide (Len) is an established immunomodulatory drug that has direct on-tumor apoptotic activity[6]
- Combining Dara and Len with T-cell redirection therapy may potentiate antimyeloma effects
- We report initial efficacy and safety results of the immune-based Tal-Dara-Len regimen in patients with NDMM from the MonumenTAL-2 study

MonumenTAL-2 ClinicalTrials.gov identifier, NCT05050097. Dara, daratumumab; GPRC5D, G protein–coupled receptor class C group 5 member D; Len, lenalidomide; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; Tal, talquetamab.

1. TALVEY™ (talquetamab-tgvs). Prescribing information. Horsham, PA: Janssen Biotech, Inc.; 2023. 2. European Medicines Agency. TALVEY™ (talquetamab). Accessed October 8, 2024. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/talvey. 3. Schinke C, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. #8036. 4. DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj). Prescribing information. Horsham, PA. Janssen Biotech, Inc.; 2022. 5. van de Donk NWCJ, et al. *Immunol Rev* 2016;270:95-112. 6. REVLIMID (lenalidomide). Prescribing information. Summit, NJ. Celgene Corporation; 2013.

Presented by AK Nooka at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA

MonumenTAL-2 (Tal-Dara-Len): Phase 1b Study Design



[a]Administered QW (on days 1, 8, 15, and 22) during cycles 1 and 2, Q2W during cycles 3–6 (on days 1 and 15), and once (on day 1) during each subsequent 28-day cycle. [b]For 21 days of a 28-day cycle. [c]AEs assessed per CTCAE v5.0, except for CRS and ICANS, which were graded per ASTCT guidelines. [d]Assessed per IMWG 2016 criteria. AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; Dara, daratumumab; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMWG, International Myeloma Working Group; Len, lenalidomide; MM, multiple myeloma; ORR, overall response rate; PFS, progression-free survival; PO, by mouth; Q2W, every other week; Q4W, every 4 weeks; QW, weekly; SC, subcutaneous; SUD, step-up dose; Tal, talquetamab.

Presented by AK Nooka at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA

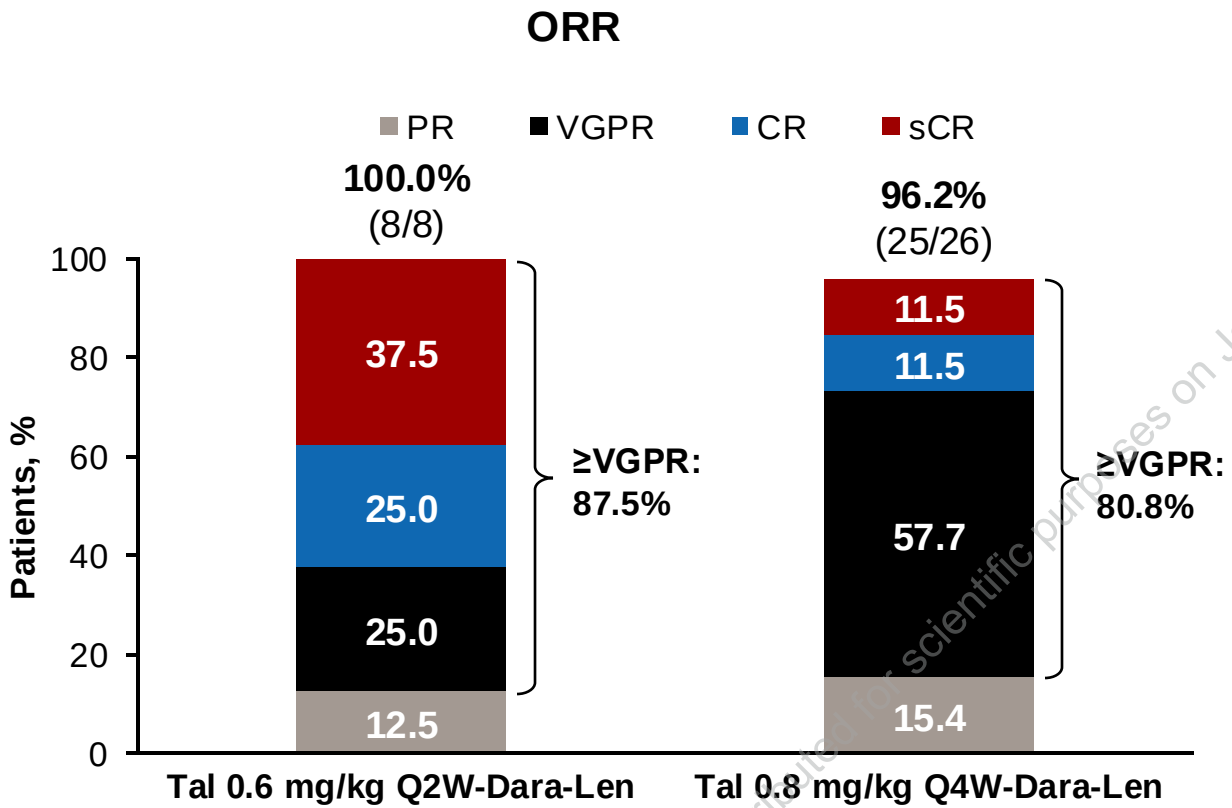
MonumenTAL-2 (Tal-Dara-Len): Baseline Characteristics

- Patients were mostly White, male, and had an ISS stage of I/II with a median age of 68.5 years (Q2W) and 74.0 years (Q4W)
- A higher proportion of patients with high-risk cytogenetics and/or extramedullary plasmacytomas were in the Q4W vs Q2W cohort, although numbers are small in the Q2W cohort

Dara, daratumumab; ISS, International Staging System; Len, lenalidomide; Q2W, every other week; Q4W, every 4 weeks; Tal, talquetamab.

Presented by AK Nooka at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA

MonumenTAL-2 (Tal-Dara-Len): High ORR With Rapid and Deep Responses

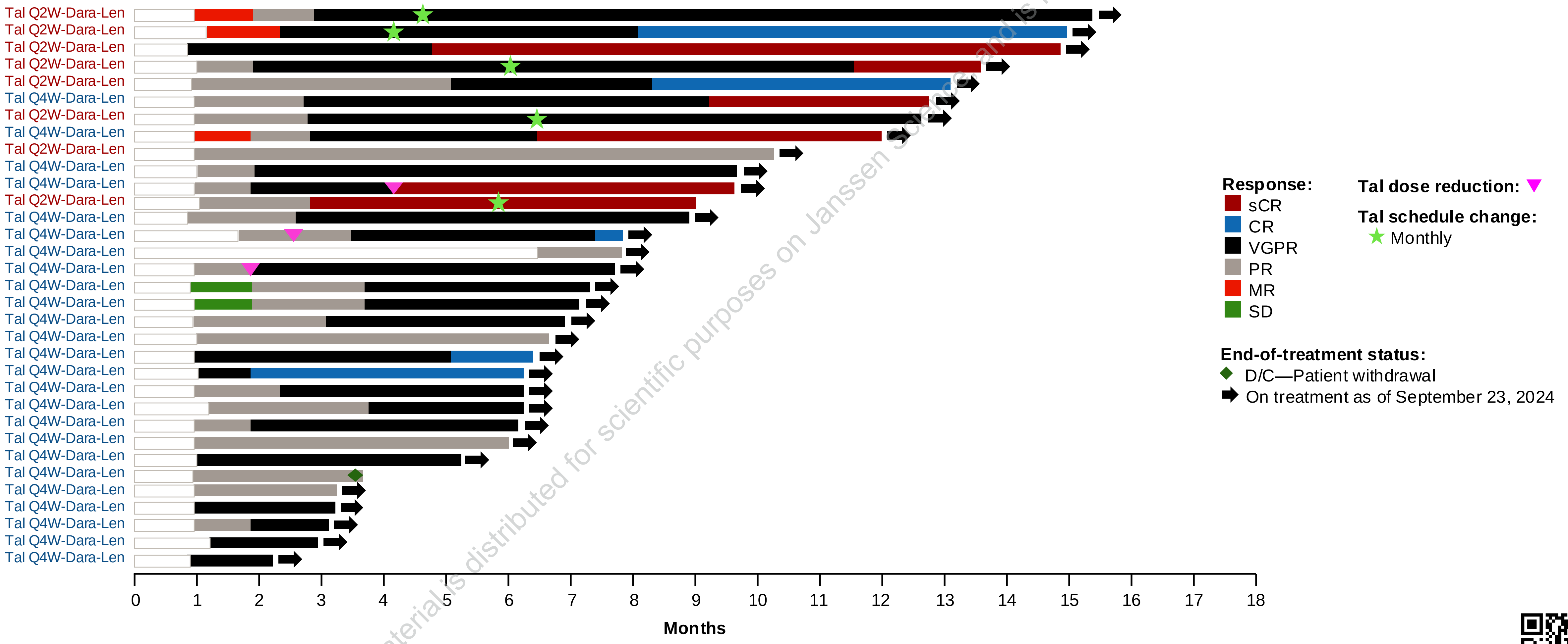


	Tal 0.6 mg/kg Q2W-Dara-Len (n=8)	Tal 0.8 mg/kg Q4W-Dara-Len (n=26)
Median follow-up, months (range)	13.2 (10.0–14.6)	5.8 (1.7[a]–12.0)
Median time to first response, months (range)	1.0 (0.9–2.3)	1.0 (0.9–1.9)
Median time to best response, months (range)	3.8 (1.0–11.6)	1.9 (0.9–9.2)
6-month DOR rate, % (95% CI)	100.0 (100.0–100.0)	100.0 (100.0–100.0)
6-month PFS rate, % (95% CI)	100.0 (100.0–100.0)	95.8 (73.9–99.4)

Median DOR and PFS were not reached in either cohort; data are still maturing. [a]Denotes patients who died. CR, complete response; Dara, daratumumab; DOR, duration of response; Len, lenalidomide; ORR, overall response rate; PFS, progression-free survival; PR, partial response; Q2W, every other week; Q4W, every 4 weeks; sCR, stringent complete response; Tal, talquetamab; VGPR, very good partial response.

Presented by AK Nooka at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA

MonumenTAL-2 (Tal-Dara-Len): Responses Deepened Over Time



CR, complete response; Dara, daratumumab; D/C, discontinued; Len, lenalidomide; MR, minimal residual; PR, partial response; Q2W, every other week; Q4W, every 4 weeks; sCR, stringent complete response; SD, stable disease; Tal, talquetamab; VGPR, very good partial response.

Presented by AK Nooka at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA

MonumenTAL-2 (Tal-Dara-Len): Safety Profile Consistent With Individual Agents

AEs ≥30%, n (%)	Tal 0.6 mg/kg Q2W-Dara-Len (n=8)		Tal 0.8 mg/kg Q4W-Dara-Len (n=26)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic AEs				
Neutropenia	6 (75.0)	6 (75.0)	12 (46.2)	11 (42.3)
Anemia	5 (62.5)	3 (37.5)	8 (30.8)	3 (11.5)
Thrombocytopenia	4 (50.0)	1 (12.5)	8 (30.8)	2 (7.7)
Nonhematologic AEs				
Taste related[a]	8 (100.0)	0	24 (92.3)	1 (3.8)
CRS	7 (87.5)	0	20 (76.9)	0
Skin related[b]	6 (75.0)	2 (25.0)	20 (76.9)	1 (3.8)
Infections[c]	8 (100.0)	3 (37.5)	13 (50.0)	1 (3.8)
Rash related[d]	5 (62.5)	3 (37.5)	15 (57.7)	3 (11.5)
Diarrhea	7 (87.5)	0	11 (42.3)	1 (3.8)
Nail related[e]	5 (62.5)	0	13 (50.0)	0
Dry mouth	5 (62.5)	0	12 (46.2)	0
Constipation	3 (37.5)	0	13 (50.0)	0
Pyrexia	5 (62.5)	0	10 (38.5)	0
Cough	6 (75.0)	0	8 (30.8)	0
Fatigue	5 (62.5)	1 (12.5)	9 (34.6)	2 (7.7)
Nausea	5 (62.5)	0	9 (34.6)	2 (7.7)
Weight decreased	2 (25.0)	0	11 (42.3)	1 (3.8)

- Most common infections were COVID-19, rhinovirus, and other upper respiratory tract infections; all infections were mostly grade 1/2
- Hypogammaglobulinemia was reported in 63% (Q2W) and 54% (Q4W) of patients; 50% (Q2W) and 19% (Q4W) received ≥1 dose of intravenous immunoglobulin during treatment
- AEs led to Tal dose reductions in 38% (Q2W) and 23% (Q4W), Tal skipped doses in 75% (Q2W) and 31% (Q4W), and Tal dose delays in 88% (Q2W) and 15% (Q4W) of patients
- No patients discontinued any study treatments due to AEs
- 1 patient had a grade 5 AE in the Q4W cohort (large intestine perforation due to sigmoid mass; not drug related)
- Translational and immune outcomes for this regimen are presented in **Poster 4653**

All AEs were treatment emergent. No patients had ICANS in either cohort. [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]Grade 3/4 infections included gastroenteritis, influenza, pneumonia, and COVID-19 pneumonia in the Q2W cohort and esophageal candidiasis in the Q4W cohort. [d]Includes rash, maculopapular rash, erythematous rash, and erythema. [e]Includes nail discoloration, nail disorder, nail toxicity, nail dystrophy, nail ridging,onychoclasis, onycholysis, and onychomadesis. AE, adverse event; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; Dara, daratumumab; ICANS, immune effector cell–associated neurotoxicity syndrome; Len, lenalidomide; Q2W, every other week; Q4W, every 4 weeks; Tal, talquetamab.

Presented by AK Nooka at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA

MonumenTAL-2 (Tal-Dara-Len): Conclusions

- The novel, immune-based combination regimen of Tal-Dara-Len elicited high and rapid responses that were deep in patients with NDMM with 6–13 months of follow-up
- The safety profile was consistent with the individual agents, with no evidence of additive hematologic AEs and no discontinuations due to AEs
- These data support further investigation in the MajesTEC-7 study (NCT05552222; Tal-Dara-Len or Teclistamab [Tec]-Dara-Len vs Dara-Len-Dexamethasone in NDMM), given the promising data here and initial results with the Tec (BCMA bispecific antibody) arm[1]

This first study combining Tal with Dara and Len in NDMM showed >96% ORRs and a manageable safety profile that continue to support Tal as a versatile combination partner, including in NDMM

AE, adverse event; BCMA, B-cell maturation antigen; Dara, daratumumab; Len, lenalidomide; NDMM, newly diagnosed multiple myeloma; ORR, overall response rate; Tal, talquetamab; Tec, teclistamab.

1. Touzeau C, et al. Presented at ASCO; May 31–June 4, 2024; Chicago, IL, USA & Virtual. #7506.

Presented by AK Nooka at the 66th American Society of Hematology (ASH) Annual Meeting; December 7–10, 2024; San Diego, CA, USA