TALVEY® (talquetamab-tgvs) MonumenTAL-1 study

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MonumenTAL-1 study[1]

- MonumenTAL-1 (NCT03399799 and NCT04634552) is an ongoing, open-label, phase 1/2 study evaluating the efficacy and safety of TALVEY for RRMM after ≥3 prior LOTs, including a PI, an immunomodulatory drug, and an anti-CD38 mAb.

MonumenTAL-1 phase 2 study design[1,2]

Key eligibility criteria

- ≥18 years of age, measurable MM per IMWG criteria
- ≥3 prior LOTs, including a PI, an immunomodulatory drug, and an anti-CD38 mAb
- ECOG PS score 0-2

TCR naïve: Tal 0.4 mg/kg SC QW
(not previously exposed to TCR such as CAR-T or BsAbs [prior BCMA ADC allowed])
(n=143)

TCR naïve: Tal 0.8 mg/kg SC Q2W
(not previously exposed to TCRs [prior BCMA ADC allowed])
(n=154)

Prior TCR exposed: Tal 0.4 mg/kg SC QW or 0.8 mg/kg SC Q2W
(previously exposed to TCRs)
(n=78)

Endpoints

- **Primary:** ORR
- **Key secondary:** DOR, PFS, OS, safety, PK, PROs, and MRD

Results

- At a **data cutoff date of September 2024**, the efficacy and safety results from the MonumenTAL-1 study were presented at an extended median follow-up of 38.2 months for the 0.4 mg/kg SC QW cohort, 31.2 months for the 0.8 mg/kg SC Q2W cohort, and 30.3 months for the prior TCR-exposed (QW and Q2W) cohorts.[3]
- At a **data cutoff date of January 29, 2024**, the efficacy and safety results from the MonumenTAL-1 study were presented at a median follow-up of 29.8 months for the 0.4 mg/kg SC QW cohort, 23.4 months for the 0.8 mg/kg SC Q2W cohort, and 20.5 months for the prior TCR-exposed cohort.[4]
- At a **data cutoff date of October 11, 2023**, the efficacy and safety results from the MonumenTAL-1 study were published at a median follow-up of 25.6 months (IQR, 8.5-25.9) for the 0.4 mg/kg SC QW cohort, 19.4 months (IQR, 9.2-20.7) for the 0.8 mg/kg SC Q2W cohort, and 16.8 months (IQR, 7.6-18.7) for the prior TCR-exposed cohort from phases 1 and 2 of the MonumenTAL-1 study.[1]

CD, cluster of differentiation; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IQR, interquartile range; LOT, line of therapy; mAb, monoclonal antibody; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetic; PRO, patient-reported outcome; Q2W, every other week; QW, weekly; RP2D, recommended phase 2 dose; RRMM, relapsed or refractory multiple myeloma; SC, subcutaneous; Tal, talquetamab; TCR, T-cell-redirection therapy.

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- MonumenTAL-1 (NCT03399799, NCT04634552) is a phase 1/2 study of TALVEY in patients with RRMM.[1]

Phase 2 study design[1,5,6]

Eligibility criteria

Select inclusion criteria:

- Age ≥18 years
- Measurable MM per IMWG criteria
- ≥3 prior LOTs, including a PI, an immunomodulatory drug, and an anti-CD38 mAb
- ECOG PS score 0-2

Select exclusion criteria:

- Prior grade ≥3 CRS related to any TCR or any prior GPRC5D-targeting therapy
- CNS involvement or clinical signs of meningeal involvement of MM
- Received cumulative dose of corticosteroids equivalent to ≥140 mg of prednisone within 14 days prior to the study drug (not including premedication)

TCR naïve: Tal 0.4 mg/kg SC QW (not previously exposed to TCR such as CAR-T or BsAbs [prior BCMA ADC allowed]) (n=143)

TCR naïve: Tal 0.8 mg/kg SC Q2W (not previously exposed to TCRs [prior BCMA ADC allowed]) (n=154)

Prior TCR exposed: Tal 0.4 mg/kg SC QW or 0.8 mg/kg SC Q2W (previously exposed to TCRs) (n=78)

Dosing

- SUDs of TALVEY were administered as follows:
  - 0.4 mg/kg SC QW: 0.01 mg/kg and 0.06 mg/kg
  - 0.8 mg/kg SC Q2W: 0.01 mg/kg, 0.06 mg/kg, and 0.3 mg/kg
- Subsequent treatment doses: 0.4 mg/kg SC QW or 0.8 mg/kg SC Q2W until disease progression, unacceptable toxic effects, withdrawal of consent, or end of study.
- Patients were required to be hospitalized for at least 48 hours from the start of each SUD and the first full treatment dose of TALVEY.
- Premedication with a glucocorticoid (dexamethasone 16 mg or equivalent), an antihistamine, and an antipyretic was required for each SUD and for the first full treatment dose of TALVEY.

Primary endpoint

- ORR

Key secondary endpoints

- DOR
- PFS
- OS
- Safety
- PK
- PRO
- MRD

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- The median follow-up was 25.6 months (IQR, 8.5-25.9) for the 0.4 mg/kg SC QW cohort, 19.4 months (IQR, 9.2-20.7) for the 0.8 mg/kg SC Q2W cohort, and 16.8 months (IQR, 7.6-18.7) for the prior TCR-exposed cohort.[1]

Baseline demographics and clinical characteristics

MonumenTAL-1 study: baseline characteristics[1]

Characteristic	0.4 mg/kg SC QW[a] (n=143)	0.8 mg/kg SC Q2W[a] (n=154)	Prior TCR[a,b] (n=78)
Median age, years (IQR)	67 (58-72)	67 (58-74)	61 (55-68)
Sex, n (%)			
Female	65 (45)	64 (42)	29 (37)
Male	78 (55)	90 (58)	49 (63)
Race, n (%)			
White	128 (90)	126 (82)	71 (91)
Black	12 (8)	17 (11)	3 (4)
Asian	1 (1)	6 (4)	4 (5)
Native Hawaiian or other Pacific islander	0	1 (1)	0
Multiple	0	1 (1)	0
Unknown	0	1 (1)	0
Not reported	2 (1)	2 (1)	0
Bone marrow plasma cells ≥60%, n (%)[c]	17 (12)	34 (23)	11 (15)
Extramedullary plasmacytomas ≥1, n (%)[d]	33 (23)	41 (27)	25 (32)
High-risk cytogenetics, n (%)[e]	41 (31)	40 (30)	25 (37)
ISS stage, n (%)			
I	62 (43)	68 (44)[f]	38 (49)
II	53 (37)	48 (31)[f]	27 (35)
III	28 (20)	37 (24)[f]	13 (17)
ECOG PS, n (%)			
0	44 (31)	58 (38)	36 (46)
1	86 (60)	84 (55)	39 (50)
2	13 (9)	12 (8)	3 (4)
Median time since diagnosis, years (IQR)	6.7 (4.3-9.7)	6.3 (3.8-10.4)	6.3 (4.2-9.9)
Previous LOTs, n (IQR)	5 (4.0-6.0)	4.5 (4.0-6.0)	6 (5.0-8.0)
Previous stem cell transplantation, n (%)	113 (79)	121 (79)	69 (88)
Exposure status, n (%)			
Triple-class[g]	143 (100)	154 (100)	78 (100)
Penta-drug[h]	105 (73)	107 (69)	65 (83)
Belantamab mafodotin	22 (15)	17 (11)	11 (14)
BsAb	-	-	26 (33)
CAR-T	-	-	57 (73)
BsAb + CAR-T	-	-	5 (6)
Refractory status, n (%)			
PI[i]	116 (81)	129 (84)	71 (91)
Immunomodulatory drug	134 (94)	141 (92)	76 (97)
Thalidomide	12 (8)	20 (13)	6 (8)
Lenalidomide	115 (80)	110 (71)	69 (88)
Pomalidomide	110 (77)	106 (69)	60 (77)
Anti-CD38 mAb[j]	134 (94)	142 (92)	74 (95)
Triple-class[g]	107 (75)	110 (71)	66 (85)
Penta-drug[h]	45 (31)	39 (25)	34 (44)
Belantamab mafodotin	18 (13)	14 (9)	8 (10)
To the last LOT	134 (94)	145 (94)	45 (58)

[a]Received 2-3 SUDs.
[b]Prior TCR was primarily targeting BCMA (96%; n=75); other targets included CD38 (n=2) and MAGE-A1 (n=1).
[c]Maximum value was selected when results from both bone marrow biopsy and bone marrow aspirate were available. Evaluated in 138, 150, and 73 patients in the 0.4 mg/kg SC QW, 0.8 mg/kg SC Q2W, and prior TCR-exposed cohorts, respectively.
[d]Soft tissue plasmacytomas not associated with the bone were included.
[e]del(17p), t(4;14), or t(14;16); evaluated in 132, 133, and 67 patients in the 0.4 mg/kg SC QW, 0.8 mg/kg SC Q2W, and prior TCR-exposed cohorts, respectively.
[f]Evaluated in 153 patients.
[g]≥1 PI, ≥1 immunomodulatory drug, and ≥1 anti-CD38 mAb.
[h]≥2 PIs, ≥2 immunomodulatory drugs, and ≥1 anti-CD38 mAb.
[i]Bortezomib, carfilzomib, or ixazomib.
[j]Daratumumab, isatuximab, or an investigational anti-CD38 mAb.

BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor-T-cell therapy; CD, cluster of differentiation; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; ISS, International Staging System; mAb, monoclonal antibody; MAGE-A1, melanoma antigen gene family member A1; LOT, line of therapy; PI, proteasome inhibitor; Q2W, every other week; QW, weekly; SC, subcutaneous; SUD, step-up dose; TCR, T-cell-redirection therapy.

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- The median follow-up was 29.8 months for the 0.4 mg/kg SC QW cohort, 23.4 months for the 0.8 mg/kg SC Q2W cohort, and 20.5 months for the prior TCR-exposed cohort.[4]

Baseline demographics and clinical characteristics

MonumenTAL-1 study: baseline characteristics[4,5]

Characteristic	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=145)	Prior TCR (n=51)
Median age, years (range)	67.0 (46-86)	67.0 (38-84)	61.0 (38-78)
Median time since diagnosis, years (range)	6.7 (1.4-20.8)	6.4 (0.8-25.4)	6.3 (1.7-19.6)
Male, n (%)	78 (54.5)	83 (57.2)	31 (60.8)
Bone marrow plasma cells ≥60%[a], n (%)	17 (12.3)	32 (22.7)	8 (17.0)
Extramedullary plasmacytomas ≥1[b], n (%)	33 (23.1)	37 (25.5)	16 (31.4)
High-risk cytogenetics[c], n (%)	41 (31.1)	37 (28.9)	18 (40.9)
ISS stage[d], n (%)			
I	62 (43.4)	64 (44.4)	24 (47.1)
II	53 (37.1)	45 (31.3)	18 (35.3)
III	28 (19.6)	35 (24.3)	9 (17.6)
Median prior LOTs, n (range)	5 (2-13)	5 (2-17)	6 (3-15)
Exposure status, n (%)			
Triple-class[e]	143 (100)	145 (100)	51 (100)
Penta-drug[f]	105 (73.4)	101 (69.7)	40 (78.4)
BsAb	-	-	18 (35.3)[g]
CAR-T	-	-	36 (70.6)[h]
BsAb + CAR-T	-	-	3 (6.0)
Belantamab	22 (15.4)	16 (11.0)	6 (11.8)
Refractory status, n (%)			
Triple-class[e]	106 (74.1)	100 (69.0)	43 (84.3)
Penta-drug[f]	42 (29.4)	34 (23.4)	21 (41.2)
To the last LOT	134 (93.7)	137 (94.5)	31 (60.8)
PI[i]	114 (79.7)	120 (82.8)	46 (90.2)
Immunomodulatory drug[j]	133 (93.0)	130 (89.7)	49 (96.1)
Anti-CD38 mAb[k]	133 (93.0)	134 (92.4)	49 (96.1)
Belantamab	18 (12.6)	13 (9.0)	4 (7.8)

[a]Maximum value from bone marrow biopsy or bone marrow aspirate is selected if both the results are available. Percentages are calculated from n=138 for the 0.4 mg/kg SC QW cohort, n=141 for the 0.8 mg/kg SC Q2W cohort, and n=38 for the prior TCR-exposed cohort.
[b]Soft tissue plasmacytomas not associated with the bone were included.
[c]del(17p), t(4;14), and/or t(14;16); calculated from n=132 for the 0.4 mg/kg SC QW cohort, n=128 for the 0.8 mg/kg SC Q2W cohort, and n=44 for the prior TCR-exposed cohort.
[d]ISS staging is derived based on serum β2-microglobulin and albumin. Percentages calculated from n=144 for the 0.8 mg/kg SC Q2W cohort.
[e]≥1 PI, ≥1 immunomodulatory drug, and ≥1 anti-CD38 mAb.
[f]≥2 PIs, ≥2 immunomodulatory drugs, and ≥1 anti-CD38 mAb.
[g]Sixteen patients received a BCMA-directed BsAb.
[h]Thirty-four patients received a BCMA-directed CAR-T.
[i]Bortezomib, carfilzomib, and/or ixazomib.
[j]Thalidomide, lenalidomide, and/or pomalidomide.
[k]Daratumumab, isatuximab, and/or an investigational anti-CD38 mAb.

BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T-cell therapy; ISS, International Staging System; mAb, monoclonal antibody; LOT, line of therapy; PI, proteasome inhibitor; Q2W, once every other week; QW, weekly; SC, subcutaneous; TCR, T-cell redirection therapy

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- A total of 17 patients in the 0.4 mg/kg SC QW cohort, 27 patients in the 0.8 mg/kg SC Q2W cohort, and 18 patients in the prior TCR-exposed cohort remained on TALVEY as of September 2024. All patients were responders, and 2 patients subsequently progressed during this time.[3]

MonumenTAL-1 study: efficacy outcomes[3]

Response	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Median follow-up, months	38.2	31.2	30.3
ORR[a], %	74.1	69.5	66.7
sCR	23.1	31.2	33.3
CR	9.8	9.1	9.0
VGPR	26.6	18.8	12.8
PR	14.7	10.4	11.5
≥CR, %	32.9	40.3	42.3
Median DOR[b], months (95% CI)	9.5 (6.7-13.4)	17.5 (12.5-25.1)	19.2 (8.1-24.7)
Median PFS, months (95% CI)	7.5 (5.7-9.4)	11.2 (7.7-14.6)	7.7 (4.1-14.5)
Median OS[c], months (95% CI)	34.0 (25.6-NE)	NR (NE-NE)	28.3 (19.5-NE)
36-month OS rate, % (95% CI)	49.3 (40.4-57.6)	60.8 (51.5-68.8)	44.6 (31.4-57.0)
MRD-negativity (10^{-5})[d], % (95% CI)	64.3 (51.9-75.4)	65.2 (52.8-76.3)	57.1 (37.2-75.5)

Clinical data cutoff date of September 2024.
[a]Due to rounding, individual response rates may not sum to ORR. Since the previous disclosure, 1 patient in the prior TCR-exposed (QW and Q2W) cohort experienced a deepening in response (CR to sCR).
[b]Evaluated in 106 patients in the 0.4 mg/kg SC QW cohort, 107 patients in the 0.8 mg/kg SC Q2W cohort, and 52 patients in the prior TCR-exposed (QW and Q2W) cohort.
[c]Data not mature in the 0.8 mg/kg SC Q2W cohort.
[d]Assessed in patients with evaluable samples. Evaluated in 70 patients in the 0.4 mg/kg SC QW cohort, 69 patients in the 0.8 mg/kg SC Q2W cohort, and 28 patients in the prior TCR-exposed (QW and Q2W) cohort. Only MRD assessments (10-5) within 3 months of achieving CR or sCR until death, disease progression, or subsequent therapy are considered.

Efficacy outcomes in the USPI population

MonumenTAL-1 study: efficacy outcomes in the USPI population[a,3]

Response	0.4 mg/kg SC QW (n=100)	0.8 mg/kg SC Q2W (n=90)	Prior TCR QW and Q2W[b] (n=58)
ORR, %	73.0	71.1	72.4
CR	35.0	43.3	50.0
VGPR	22.0	17.8	8.6
PR	16.0	10.0	13.8
Median time to best response of ≥CR[c], month (range)	2.27 (1.1-12.7)	6.24 (1.2-16.8)	2.66 (1.2-17.5)
Median time to best response of VGPR[d], month (range)	1.97 (1.1-6.2)	3.06 (0.3-18.9)	2.04 (1.2-2.1)
Median time to best response of PR[e], month (range)	1.28 (1.1-2.9)	2.07 (1.2-2.8)	1.13 (1.1-3.0)
Median DOR[f], month (95% CI)	10.2 (6.6-15.7)	17.9 (12.5-26.0)	19.2 (6.7-NE)
≥CR[c]	28.8 (18.9-NE)	26.1 (18.0-NE)	24.7 (19.2-NE)
VGPR[d]	6.4 (4.4-9.5)	9.3 (7.4-15.2)	4.8 (2.1-NE)
PR[e]	3.0 (1.9-5.6)	5.5 (0.9-6.5)	2.4 (1.9-4.6)
Median PFS, month (95% CI)	6.8 (5.5-10.4)	12.4 (9.6-18.2)	11.3 (4.8-21.4)
36-month PFS, %	17.6 (10.7-26.0)	NE (NE-NE)	28.2 (16.0-41.7)
Median OS, month (95% CI)	NR (21.7-NE)	NR (33.2-NE)	30.6 (20.2-NE)
36-month OS, %	50.5 (40.0-60.0)	NE (NE-NE)	46.4 (29.2-61.9)

[a]Data are reported from phase 2 only.
[b]Phase 2 data include only the 0.4 mg/kg QW cohort.
[c]Evaluated in 35 patients in the 0.4 mg/kg SC QW cohort, 39 patients in the 0.8 mg/kg SC Q2W cohort, 29 patients in the prior TCR-exposed (QW and Q2W) cohort.
[d]Evaluated in 22 patients in the 0.4 mg/kg SC QW cohort, 16 patients in the 0.8 mg/kg SC Q2W cohort, 5 patients in the prior TCR-exposed (QW and Q2W) cohort.

CI, confidence interval; CR, complete response; DOR, duration of response; NE, not estimable; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; Q2W, every other week; QW, weekly; SC, subcutaneous; TCR, T-cell redirection therapy; USPI, US prescribing information; VGPR, very good partial response.

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Efficacy outcomes by prior TCR therapy in TCR-exposed cohort[4]

- In the TCR-exposed cohort, the median PFS was 12.3 months with prior CAR-T therapy and 4.1 months with prior BsAb therapy.
- In the TCR-exposed cohort, ORR was 71% (40 of 56) in patients with prior CAR-T therapy and 58% (15 of 26) in patients with prior BsAb therapy.

Efficacy outcomes in overall population

Time to first confirmed response in the Q2W cohort

ORR among high-risk subgroups

Efficacy outcomes in USPI population

MonumenTAL-1 study: efficacy outcomes in overall population[4]

Parameter	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Median follow-up, months	29.8	23.4	20.5
ORR[a], %	74.1	69.5	66.7
sCR	23.1	31.2	32.1
CR	9.8	9.1	10.3
VGPR	26.6	18.8	12.8
PR	14.7	10.4	11.5
≥VGPR, %	59.4	59.1	55.1
Median DOR[b], months (95% CI)	9.5 (6.7-13.4)	17.5 (12.5-NE)	NR[c]
Median DOR in patients with ≥CR, months (95% CI)	28.6 (19.4-NE)	NR (21.2-NE)	NR[c]
Median PFS, months (95% CI)	7.5 (5.7-9.4)	11.2 (8.4-14.6)	7.7 (4.1-14.5)
24-month OS rate, % (95% CI)	60.6 (51.7-68.4)	67.1 (58.3-74.4)	57.3 (43.5-68.9)
Median time to first response, months (range)	1.2 (0.2-10.9)	1.3 (0.2-4.9)	1.2 (0.2-7.5)
Median time to VGPR as best response, months (range)	2.2 (0.8-6.2)	2.3 (0.3-18.9)	1.8 (0.8-6.4)
Median time to ≥CR as best response, months (range)	3.0 (1.1-12.7)	5.8 (1.2-16.8)	2.7 (1.2-18.7)

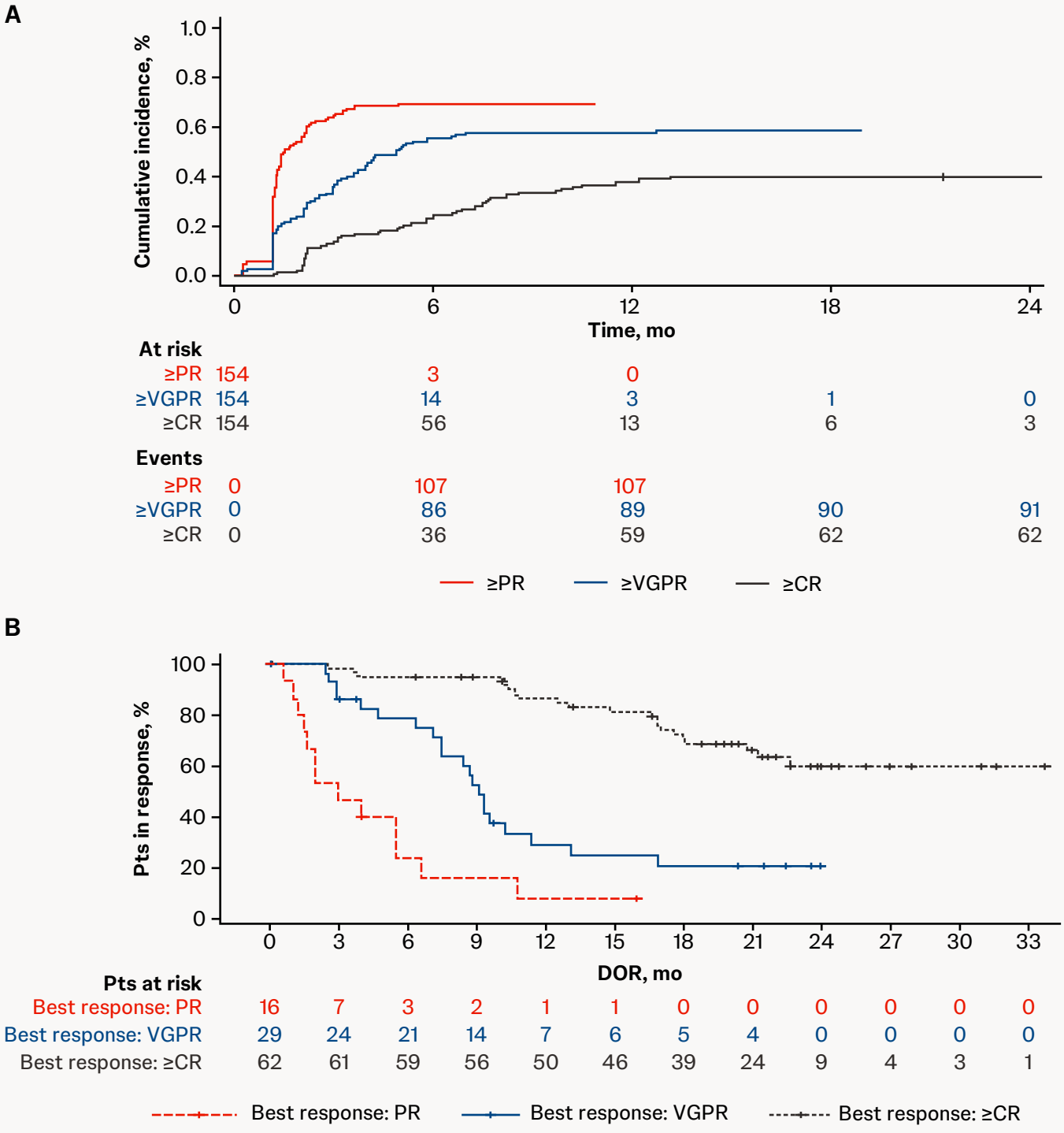
Clinical data cutoff date of January 29, 2024.
[a]Assessed by an independent review committee using IMWG criteria. Due to rounding, individual response rates may not sum to ORR.
[b]Evaluated in 106, 107, and 52 patients in the 0.4 mg/kg SC QW, 0.8 mg/kg SC Q2W, and prior TCR-exposed cohorts, respectively.
[c]NR due to heavy censoring from 12 to 20 months; the estimate may not be reliable at this time point.

CI, confidence interval; CR, complete response; DOR, duration of response; IMWG, International Myeloma Working Group; NA, not available; NE, not estimable; NR, not reported; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; Q2W, once every other week; QW, weekly; SC, subcutaneous; sCR, stringent complete response; TCR, T-cell redirection therapy; VGPR, very good partial response.

Efficacy outcomes in TCR naïve cohort[4]

- In the Q2W cohort, 40% of patients achieved ≥CR by approximately 12 months; patients with deeper responses achieved a longer DOR.

MonumenTAL-1 study: time to first confirmed response per independent review committee (A) and DOR by depth of response (B) in the Q2W cohort[4]



CR, complete response; DOR, duration of response; IRC, independent review committee; PR, partial response; Pts, patients; Q2W, once every other week; TCR, T-cell redirection therapy; VGPR, very good partial response; mo, months.

MonumenTAL-1 study: ORR among high-risk subgroups[4]

ORR in subgroups, % (95% CI)	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Median age ≥75 years	71.4 (47.8-88.7)	75.8 (57.7-88.9)	80.0 (28.4-99.5)
High-risk cytogenetics[a]	70.7 (54.5-83.9)	75.0 (58.8-87.3)	52.0 (31.3-72.2)
ISS stage III	64.3 (44.1-81.4)	59.5 (42.1-75.2)	76.9 (46.2-95.0)
Baseline renal function ≤60 mL/min/1.73 m²	65.0 (48.3-79.4)	65.2 (49.8-78.6)	63.2 (38.4-83.7)
Refractory status			
Triple-class[b]	72.9 (63.4-81.0)	67.3 (57.7-75.9)	65.2 (52.4-76.5)
Penta-drug[c]	71.1 (55.7-83.6)	69.2 (52.4-83.0)	58.8 (40.7-75.4)
Extramedullary plasmacytomas ≥1[d]	48.5 (30.8-66.5)	41.5 (26.3-57.9)	44.0 (24.4-65.1)

Note: Data are reported from only phase 2.
[a]Defined by del(17p), t(4;14), and/or t(14;16).
[b]≥1 PI, ≥1 immunomodulatory drug, and ≥1 anti-CD38 mAb.
[c]≥2 PIs, ≥2 immunomodulatory drugs, and ≥1 anti-CD38 mAb.
[d]Soft tissue plasmacytomas not associated with the bone were included.

CI, confidence interval; ISS, International Staging System; mAb, monoclonal antibody; ORR, overall response rate; PI, proteasome inhibitor; Q2W, once every other week; QW, weekly; SC, subcutaneous; TCR, T-cell redirection therapy.

MonumenTAL-1 study: efficacy outcomes in USPI population[4]

Parameter	0.4 mg/kg SC QW (n=100)	0.8 mg/kg SC Q2W (n=87)	Prior TCR[a] (n=32)
ORR, %	73.0	71.3	75.0
VGPR	22.0	18.4	12.5
PR	16.0	9.2	12.5
≥CR, %	35.0	43.7	50.0
Median time to first response[b], months (range)	1.2 (0.2-10.9)	1.3 (0.2-3.6)	1.1 (0.2-6.4)
Median time to best response[b], months (range)	2.1 (1.1-12.7)	4.7 (0.3-18.9)	2.1 (1.1-14.8)
≥CR[c]	2.3 (1.1-12.7)	6.4 (1.9-16.8)	4.4 (1.2-14.8)
VGPR[d]	2.0 (1.1-6.2)	3.1 (0.3-18.9)	2.0 (1.3-2.1)
PR[e]	1.3 (1.1-2.9)	2.1 (1.2-2.8)	1.1 (1.1-1.4)
Median DOR[b], months (95% CI)	10.2 (6.6-15.7)	18.0 (14.8-NE)	15.8 (3.7-NE)
≥CR[c]	28.6 (18.9-NE)	NR (21.2-NE)	24.1 (11.2-NE)
VGPR[d]	6.4 (4.4-9.5)	9.3 (7.4-16.8)	4.3 (2.1-NE)
PR[e]	3.0 (1.9-5.6)	4.2 (0.9-NE)	2.4 (1.9-NE)
Median PFS, months (95% CI)	6.8 (5.5-10.4)	12.5 (9.6-18.3)	6.8 (3.4-22.2)
24-month PFS rate, % (95% CI)	21.0 (13.4-29.7)	31.1 (20.1-42.8)	28.9 (13.9-45.9)
Median OS, months (95% CI)	32.1 (21.7-NE)	NR (24.4-NE)	24.3 (7.6-NE)
24-month OS rate, % (95% CI)	60.3 (49.8-69.4)	67.7 (55.2-77.4)	51.6 (32.7-67.6)

Note: Data are reported from only phase 2.
[a]Phase 2 data include only the 0.4 mg/kg QW cohort.
[b]n=73, QW; n=62, Q2W; and n=24, prior TCR.
[c]n=35, QW; n=38, Q2W; and n=16, prior TCR.
[d]n=22, QW; n=16, Q2W; and n=4, prior TCR.
[e]n=16, QW; n=8, Q2W; and n=4, prior TCR.

CI, confidence interval; CR, complete response; DOR, duration of response; NE, not estimable; NR, not reached; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; Q2W, once every other week; QW, weekly; SC, subcutaneous; TCR, T-cell redirection therapy; USPI, United States Prescribing Information; VGPR, very good partial response.

TALVEY® (talquetamab-tgvs) MonumenTAL-1 study

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MonumenTAL-1 study: efficacy[4]

Parameter	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Median follow-up (range), months	25.6 (8.5-25.9)	19.4 (9.2-20.7)	16.8 (7.6-18.7)
ORR, % (95% CI)	74 (66-81)	69 (62-77)	67 (55-77)
sCR, %	23	30	32
CR, %	10	10	9
VGPR, %	27	19	14
PR, %	15	10	12
≥VGPR, %	59	59	55
Median time to first response (IQR), months	1.2 (1.1-1.6)	1.3 (1.2-1.7)	1.2 (1.1-1.7)
Median time to ≥VGPR (IQR), months[a]	1.9 (1.2-3.0)	2.2 (1.2-4.0)	1.4 (1.1-2.7)
Median DOR (95% CI), months[b]	9.5 (6.7-13.4)	16.9 (12.9-NE)	-
12-month DOR rate, % (95% CI)	-	-	56 (41-69)
Median PFS (95% CI), months[c]	7.5 (5.7-9.4)	11.2 (8.4-16.9)	7.7 (4.1-14.5)
12-month OS rate, % (95% CI)[d]	76 (68-83)	77 (69-83)	74 (62-82)

[a]As per post hoc analysis.
[b]A total of 74 events in 106 responders and 48 events in 107 responders were reported in the 0.4 mg/kg SC QW and 0.8 mg/kg SC Q2W cohorts, respectively.
[c]A total of 107 events in 143 patients, 89 events in 154 patients, and 47 events in 78 patients were reported in the 0.4 mg/kg SC QW, 0.8 mg/kg SC Q2W, and prior TCR-exposed cohorts, respectively.
[d]A total of 58 events in 143 patients, 44 events in 154 patients, and 27 events in 78 patients were reported in the 0.4 mg/kg SC QW, 0.8 mg/kg SC Q2W, and prior TCR-exposed cohorts, respectively. Medians are NA since the data are immature.

TALVEY® (talquetamab-tgvs)
MonumenTAL-1 study

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MonumenTAL-1 study: hematologic and nonhematologic AEs (≥30% in any cohort)[3]

AE, n (%)	0.4 mg/kg SC QW (n=143)		0.8 mg/kg SC Q2W (n=154)		Prior TCR QW and Q2W (n=78)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Hematologic AEs						
Anemia	65 (45.5)	46 (32.2)	67 (43.5)	39 (25.3)	38 (48.7)	22 (28.2)
Neutropenia	50 (35.0)	44 (30.8)	44 (28.6)	33 (21.4)	40 (51.3)	37 (47.4)
Thrombocytopenia	39 (27.3)	29 (20.3)	46 (29.9)	28 (18.2)	30 (38.5)	22 (28.2)
Nonhematologic AEs						
CRS	113 (79.0)	3 (2.1)	116 (75.3)	1 (0.6)	57 (73.1)	1 (1.3)
Dysgeusia[a]	103 (72.0)	NA	111 (72.1)	NA	59 (75.6)	NA
Infections[b]	87 (60.8)	33 (23.1)	109 (70.8)	33 (21.4)	61 (78.2)	20 (25.6)
Skin related[c]	85 (59.4)	0	113 (73.4)	1 (0.6)	53 (67.9)	0
Nail related[d]	80 (55.9)	0	84 (54.5)	0	47 (60.3)	0
Weight decreased	59 (41.3)	3 (2.1)	64 (41.6)	9 (5.8)	29 (37.2)	1 (1.3)
Rash related[e]	57 (39.9)	2 (1.4)	48 (31.2)	8 (5.2)	25 (32.1)	2 (2.6)
Pyrexia	57 (39.9)	4 (2.8)	44 (28.6)	2 (1.3)	27 (34.6)	0
Dry mouth	38 (26.6)	0	60 (39.0)	0	34 (43.6)	0
Fatigue	36 (25.2)	5 (3.5)	44 (28.6)	1 (0.6)	25 (32.1)	1 (1.3)

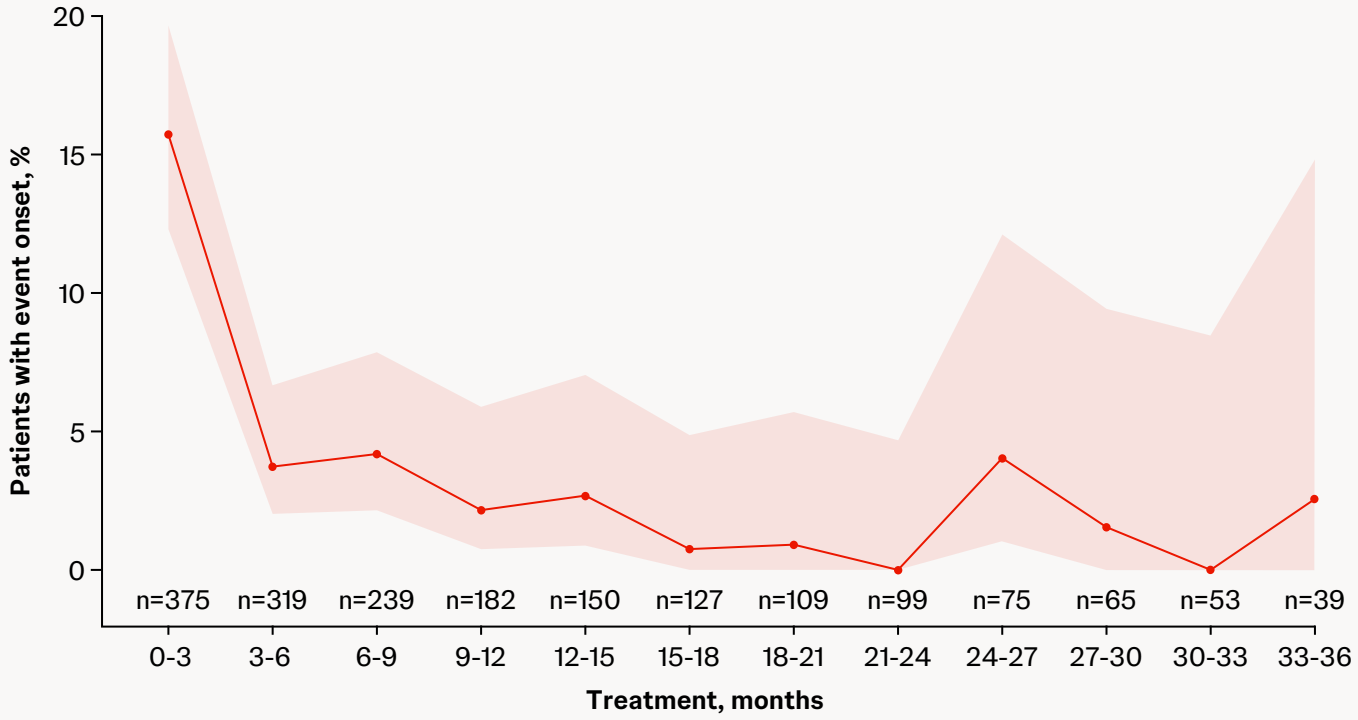
[a]Includes ageusia, dysgeusia, hypogeusia, and taste disorder. Per CTCAE, the maximum possible grade of dysgeusia was 2.
[b]Infections were reported as a system organ class.
[c]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome.
[d]Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging.
[e]Includes rash, maculopapular rash, erythematous rash, and erythema.

Weight loss and treatment discontinuation due to GPRC5D-related AEs[6]

- All patients initially lost weight before stabilizing and improving; patients with a baseline "healthy-weight" body mass index who remained on treatment returned to their baseline weight over time.
- No new discontinuations occurred due to GPRC5D-related AEs.

New-onset grade ≥3 infections

MonumenTAL-1 study: new-onset grade ≥3 infections[3]



Note: Shaded areas represent 95% confidence intervals. Data were plotted if ≥25 patients remained on treatment.

TALVEY® (talquetamab-tgvs) MonumenTAL-1 study

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GPRC5D-associated AEs and weight loss[4]

- Weight loss initially occurred but later stabilized and improved over time, even in patients with oral toxicities.
- One additional patient discontinued treatment due to GPRC5D-associated AEs since the earlier follow-up.
- Weight loss, as assessed using vital signs, was observed in 39%, 34%, and 39% of patients in the 0.4 mg/kg SC QW, 0.8 mg/kg SC Q2W, and prior TCR-exposed cohorts, respectively.

GPRC5D-associated AEs

Weight loss

Infections[4]

- No increase in grade 3/4 infections was observed with a longer follow-up duration.
- IVIG was required in 16%, 14%, and 24% of patients in the QW, Q2W, and prior TCR-exposed cohorts, respectively.

Dose reductions, discontinuations and deaths due to adverse events[4]

- Overall, rates of dose reductions due to AEs were 15%, 10%, and 12% and rates of discontinuations due to AEs were 5%, 10%, and 5% in the QW, Q2W, and prior TCR-exposed cohorts, respectively.
- No treatment-related deaths were reported.

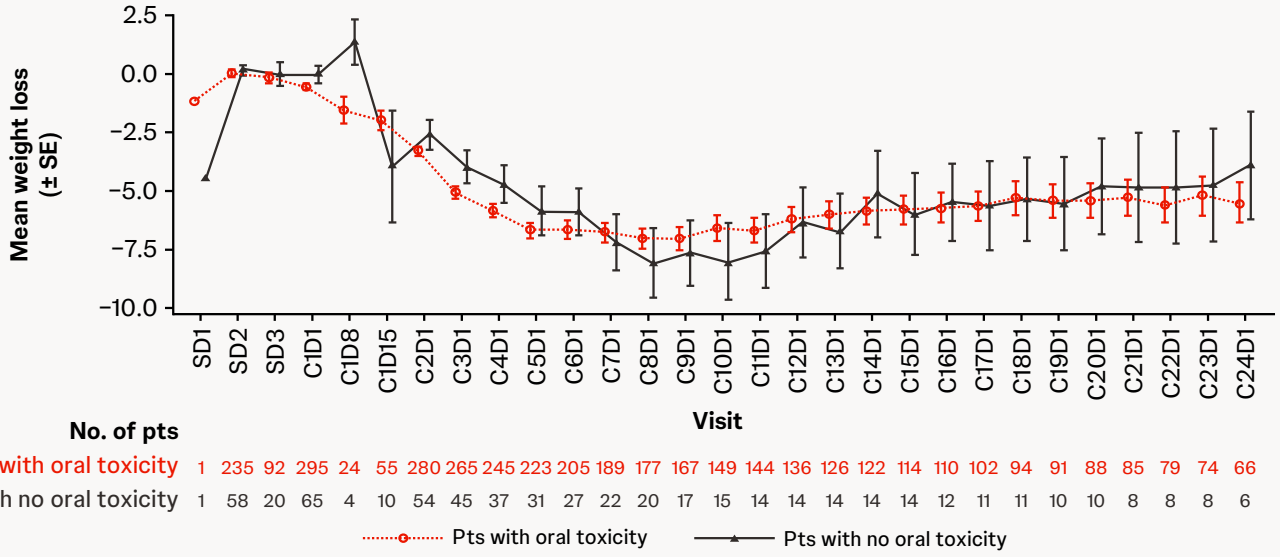
MonumenTAL-1 study: GPRC5D-associated AEs[4]

AE (any grade), n (%)	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Taste-related[a]			
Total	103 (72.0)	110 (71.4)	59 (75.6)
Leading to dose reduction	10 (7.0)	6 (3.9)	4 (5.1)
Leading to discontinuation	0 (0.0)	3 (1.9)	0 (0.0)
Skin-related[b]			
Total	81 (56.6)	113 (73.4)[c]	50 (64.1)
Leading to dose reduction	5 (3.5)	1 (0.6)	2 (2.6)
Leading to discontinuation	2 (1.4)	1 (0.6)	0 (0.0)
Nail-related[d]			
Total	79 (55.2)	82 (53.2)	46 (59.0)
Leading to dose reduction	1 (0.7)	1 (0.6)	1 (1.3)
Leading to discontinuation	0 (0.0)	0 (0.0)	0 (0.0)
Rash-related[e]			
Total	57 (39.9)[f]	46 (29.9)[g]	25 (32.1)[h]
Leading to dose reduction	1 (0.7)	1 (0.6)	0 (0.0)
Leading to discontinuation	0 (0.0)	0 (0.0)	0 (0.0)

[a]Includes ageusia, dysgeusia, hypogeusia, and taste disorder.
[b]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome.
[c]Includes 1 (0.6%) grade 3/4 event.
[d]Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging.
[e]Includes rash, maculopapular rash, erythematous rash, and erythema.
[f]Includes 2 (1.4%) grade 3/4 events.
[g]Includes 8 (5.2%) grade 3/4 events.
[h]Includes 2 (2.6%) grade 3/4 events.

AE, adverse event; GPRC5D, G protein-coupled receptor class C group 5 member D; Q2W, once every other week; QW, weekly; SC, subcutaneous; TCR, T-cell redirection therapy.

MonumenTAL-1 study: weight loss in patients with oral toxicitya in the QW and Q2W cohorts[4]



No. of pts																												
Pts with oral toxicity	1	235	92	295	24	55	280	265	245	223	205	189	177	167	149	144	136	126	122	114	110	102	94	91	88	85	79	74	66
Pts with no oral toxicity	1	58	20	65	4	10	54	45	37	31	27	22	20	17	15	14	14	14	14	14	12	11	11	10	10	8	8	8	6

Pts with oral toxicity Pts with no oral toxicity

[a]Includes dysgeusia, ageusia, taste disorder, hypogeusia, dry mouth, dysphagia, cheilitis, glossitis, glossodynia, mouth ulceration, oral discomfort, oral mucosal erythema, oral pain, stomatitis, swollen tongue, tongue discomfort, tongue erythema, tongue edema, and tongue ulceration.
C, cycle; D, day; No, number; Pts, patients; Q2W, once every other week; QW, weekly; SD, step-up dose; SE, standard error.

TALVEY® (talquetamab-tgvs) MonumenTAL-1 study

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Serious and fatal AEs[1]

- Overall, 55% of patients (n=78) in the 0.4 mg/kg SC QW cohort, 53% of patients (n=81) in the 0.8 mg/kg SC Q2W cohort, and 51% of patients (n=40) in the prior TCR-exposed cohort experienced ≥1 serious AE.
- Fatal AEs were reported in 5 patients in the 0.4 mg/kg SC QW cohort, 7 patients in the 0.8 mg/kg SC Q2W cohort, and no patients in the prior TCR-exposed cohort.
- Three patients (0.4 mg/kg SC QW cohort, n=2; 0.8 mg/kg SC Q2W cohort, n=1) were in response at the time of death. No treatment-related deaths were reported.

Weight loss[1]

- Weight loss occurred early but stabilized, and weight increased slightly over time, even in patients with oral AEs.

On-target, off-tumor AEs, and overall response[1]

- Patients who developed on-target, off-tumor AEs in early treatment cycles had a greater likelihood of experiencing response vs those who did not.

Hematologic and nonhematologic AEs

Treatment discontinuation and dose modification

CRS and neurotoxic AEs[1]

- CRS events primarily occurred during administration of SUDs and first full doses, with few events occurring at or after treatment cycle 2.
- One patient in the 0.8 mg/kg SC Q2W cohort had grade 2 cerebellar toxicity (reported as ataxia), which led to treatment discontinuation.

CRS

ICANS

Infection[1,7]

- The polyclonal IgG level/titer transiently dropped for the first 2 to 3 months of therapy but gradually increased above the baseline value as patients continued TALVEY therapy. IgG patterns were similar between responders and nonresponders.
- In the 0.4 mg/kg QW, 0.8 mg/kg Q2W, and prior TCR-exposed cohorts, IVIG (before TALVEY or for posttreatment hypogammaglobulinemia) was administered to 8% (n=12), 9% (n=14), and 19% (n=15) of patients, respectively.
- A total of 5 patients died due to infections (0.4 mg/kg SC QW cohort, n=3; 0.8 mg/kg SC Q2W cohort, n=2). COVID-19 pneumonia led to death in 2 patients (0.4 mg/kg SC QW cohort, n=1; 0.8 mg/kg SC Q2W cohort, n=1).

Infection

Skin-, nail-, rash-, and taste-related AEs

MonumenTAL-1 study: hematologic and nonhematologic AEs[1,7]

Event, n (%)	0.4 mg/kg SC QW[a,b] (n=143)			0.8 mg/kg SC Q2W[a,b] (n=154)			Prior TCR[a,c] (n=78)		
	Grade 1/2	Grade 3	Grade 4	Grade 1/2	Grade 3	Grade 4	Grade 1/2	Grade 3	Grade 4
Hematologic AEs									
Neutropenia	6 (4)	29 (20)	15 (10)	11 (7)	24 (16)	9 (6)	3 (4)	18 (23)	19 (24)
Anemia	19 (13)	45 (31)	0	26 (17)	40 (26)	0	17 (22)	21 (27)	0
Thrombocytopenia	10 (7)	15 (10)	14 (10)	17 (11)	14 (9)	14 (9)	9 (12)	11 (14)	10 (13)
Leukopenia	12 (8)	6 (4)	5 (3)	11 (7)	14 (9)	4 (3)	3 (4)	8 (10)	6 (8)
Lymphopenia	3 (2)	17 (12)	20 (14)	6 (4)	14 (9)	26 (17)	2 (3)	4 (5)	9 (12)
Febrile neutropenia	-	-	-	-	-	-	0	4 (5)	0
Nonhematologic AEs									
Taste-related changes[d]	103 (72)	-	-	110 (71)	-	-	59 (76)	-	-
CRS	110 (77)	3 (2)	0	114 (74)	1 (1)	0	56 (72)	1 (1)	0
Nonrash skin-related AEs[e]	81 (57)	0	0	113 (73)	1 (1)	0	49 (63)	0	0
Nail-related AEs[f]	79 (55)	0	0	82 (53)	0	0	45 (58)	0	0
Dry mouth	38 (27)	0	0	60 (39)	0	0	34 (44)	0	0
Weight decreased	56 (39)	3 (2)	0	56 (36)	8 (5)	0	28 (36)	1 (1)	0
Fatigue	30 (21)	5 (3)	0	41 (27)	1 (1)	0	24 (31)	1 (1)	0
Pyrexia	52 (36)	4 (3)	0	40 (26)	2 (1)	-	25 (32)	0	0
Rash-related AEs[g]	57 (40)	2 (1)	0	45 (29)	8 (5)	0	23 (29)	2 (3)	0
Cough	28 (20)	0	0	32 (21)	0	0	21 (27)	0	0
Arthralgia	28 (20)	2 (1)	0	27 (18)	0	0	18 (23)	0	0
Decreased appetite	27 (19)	2 (1)	0	41 (27)	2 (1)	0	17 (22)	1 (1)	0
Dysphagia	34 (24)	0	0	35 (23)	3 (2)	0	18 (23)	0	0
Constipation	25 (17)	0	0	31 (20)	0	0	17 (22)	0	0
Diarrhea	34 (24)	3 (2)	0	40 (26)	2 (1)	0	16 (21)	0	0
Pain in extremity	-	-	-	-	-	-	16 (21)	0	0
Dyspnea	-	-	-	-	-	-	13 (17)	1 (1)	0
Nausea	29 (20)	0	0	30 (19)	0	0	14 (18)	0	0
Headache	26 (18)	1 (1)	0	31 (20)	1 (1)	0	13 (17)	0	0
Stomatitis	-	-	-	-	-	-	13 (17)	0	0
URTI	-	-	-	-	-	-	13 (17)	0	0
Hypophosphatemia	-	-	-	-	-	-	10 (13)	2 (3)	0
ALT increased	-	-	-	-	-	-	8 (10)	3 (4)	0
COVID-19	14 (10)	2 (1)	0	35 (23)	4 (3)	0	10 (13)	1 (1)	0
Asthenia	36 (25)	3 (2)	0	16 (10)	2 (1)	0	9 (12)	1 (1)	0
Injection-site erythema	-	-	-	-	-	-	10 (13)	0	0
Oropharyngeal pain	-	-	-	-	-	-	10 (13)	0	0
Chills	-	-	-	-	-	-	9 (12)	0	0
Back pain	-	-	-	-	-	-	9 (12)	0	0
Hypokalemia	-	-	-	-	-	-	9 (12)	0	0
Hypotension	-	-	-	-	-	-	9 (12)	0	0
Hypertension	-	-	-	-	-	-	3 (4)	4 (5)	0

Clinical data cutoff date of October 11, 2023.
[a]Received 2-3 SUDs.
[b]AEs are listed by frequency on an any-grade basis. AEs listed are grade 1-2 events occurring in at least 20% of patients in either group or grade 3 or worse events occurring in at least 10% of patients in either cohort.
[c]AEs included are grade 1/2 events occurring in ≥10% of patients or grade ≥3 events occurring in ≥5% of patients. AEs are listed by frequency on an any-grade basis.
[d]Includes dysgeusia, ageusia, hypogeusia, and taste disorder. Per Common Terminology Criteria for Adverse Events, the maximum grade for these events was 2.
[e]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome.
[f]Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging.
[g]Includes rash, maculopapular rash, erythematous rash, and erythema.

AE, adverse event; ALT, alanine aminotransferase; COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome; Q2W, every other week; QW, weekly; SC, subcutaneous; SUD, step-up dose; TCR, T-cell-redirection therapy; URTI, upper respiratory tract infection.

MonumenTAL-1 study: AEs leading to treatment discontinuation and dose modification[1,7]

Event, n (%)	0.4 mg/kg SC QW[a] (n=143)	0.8 mg/kg SC Q2W[a] (n=154)	Prior TCR[a] (n=78)
Treatment discontinuation	7 (5)	14 (9)	4 (5)
Dysgeusia	0	2 (1)	0
ICANS	2 (2)[b]	1 (1)[b]	0
Ataxia	0	1 (1)	0
Skin-related disorders[c]	2 (1)	2 (1)	0
Nail-related AEs	0	0	0
Rash-related AEs	0	0	0
Taste change	0	2 (-)	0
Administration-site conditions[d]	2 (1)	2 (1)	0
Infections[e]	2 (1)	0	1 (1)
Cardiac disorders[f]	0	2 (1)	0
Weight decreased	1 (1)	2 (1)	1 (1)
GI disorders[g]	2 (1)	0	0
CRS	0	1 (1)	0
Graft vs host disease	0	0	1 (1)
Hypercalcemia	0	1 (1)	0
AML	0	1 (1)	0
Myelodysplastic syndrome	0	0	1 (1)
Renal failure	0	1 (1)	0
Dose reduction	22 (15)	13 (8)	9 (12)
Taste disorder	10 (7)	5 (3)	4 (5)
Weight decreased	7 (5)	4 (3)	2 (3)
Decreased appetite	2 (1)	1 (1)	1 (1)
Dry mouth/dysphagia	1 (1)	4 (3)	4 (5)
Other GI disorders[i]	2 (1)	1 (1)	0
Parosmia	1 (1)	0	0
Skin and rash disorders[j]	7 (5)	3 (2)	4 (5)
Nail disorders[k]	2 (1)	1 (1)	1 (1)
General disorders and administration-site conditions[l]	4 (3)	0	2 (3)
CRS	1 (1)	1 (1)	0
ICANS	1 (1)[b]	0	0
Malnutrition	1 (1)	0	0
CMV infection	0	1 (1)	0
Myalgia	0	0	1 (1)
Sinusitis	0	0	1 (1)
Multisystem inflammatory syndrome	0	0	1 (1)

Clinical data cutoff date of October 11, 2023.
[a]Received 2-3 SUDs.
[b]Assessed only in phase 2, with percentage calculated based on n=122 for the 0.4 mg/kg SC QW cohort and n=118 for the 0.8 mg/kg SC Q2W cohort.
[c]Includes skin exfoliation, dry skin, and generalized exfoliative dermatitis.
[d]Includes asthenia, general physical health deterioration, and mucosal inflammation.
[e]Includes fungal sepsis, pneumonia, and rash pustular.
[f]Includes cardiac arrest and sinus bradycardia.
[g]Includes colitis and oral AEs.
[h]Includes dysgeusia, ageusia, and taste disorder.
[i]Includes glossitis, nausea, and oral AEs.
[j]Includes dry skin, palmar-plantar erythrodysesthesia syndrome, maculopapular rash, hyperkeratosis, mucocutaneous toxicity, pruritus, rash, skin exfoliation, skin ulcer, and skin fissures.
[k]Includes nail disorder, nail hypertrophy, nail onycholysis, and nail onychomadesis.
[l]Includes asthenia, chills, fatigue, and malaise.

AE, adverse event; AML, acute myeloid leukemia; CMV, cytomegalovirus; CRS, cytokine release syndrome; GI, gastrointestinal; ICANS, immune effector cell-associated neurotoxicity syndrome; Q2W, every other week; QW, weekly; SC, subcutaneous; SUD, step-up dose; TCR, T-cell-redirection therapy.

MonumenTAL-1 study: CRS events[7]

Event, n (%)	0.4 mg/kg SC QW[a] (n=143)	0.8 mg/kg SC Q2W[a] (n=154)	Prior TCR[a] (n=78)
Patients with CRS, n (%)	113 (79)	115 (75)	57 (73)
Grade 1	89 (62)	88 (57)	39 (50)
Grade 2	21 (15)	26 (17)	17 (22)
Grade 3	3 (2)	1 (1)	1 (1)
CRS symptoms (>10% in any cohort), n (%)			
Pyrexia	113 (79)	114 (74)	56 (72)
Hypotension	19 (13)	20 (13)	15 (19)
Chills	13 (9)	21 (14)	11 (14)
Hypoxia	11 (8)	9 (6)	8 (10)
Median time to onset[b], hours (IQR)	25.9 (17.8-31.9)	27.8 (21.0-34.6)	27.4 (21.2-34.5)
Median duration[c], hours (IQR)	14.5 (4.0-32.0)	17.0 (5.6-33.8)	20.6 (6.6-31.5)
Patients with CRS up to first full dose, n (%)			
SUD 1	48 (34)	41 (27)	23 (29)
SUD 2	70 (49)	63 (41)	34 (44)
SUD 3	-	55 (36)	1 (1)
First full dose	38 (27)	22 (14)	22 (28)
Patients with CRS cycle 2+, n (%)	5 (3)	5 (3)	2 (3)
Patients receiving supportive measures[d], n (%)	106 (74)	109 (71)	54 (69)
Acetaminophen	80 (56)	81 (53)	42 (54)
Tocilizumab[e]	50 (35)	57 (37)	37 (47)
Corticosteroids	5 (3)	6 (4)	11 (14)
Oxygen	8 (6)	10 (6)	7 (9)
Nasal cannula low flow (≤6 L/min)	8 (6)	9 (6)	6 (8)
Face mask	0	0	1 (1)
Venturi mask	1 (1)	0	0
Other	0	1 (1)	0
Vasopressor[f]	2 (1)	1 (1)	1 (1)
Patients with >1 CRS event, n (%)	46 (32)	51 (33)	23 (29)
Grade worsened at subsequent event	6 (4)	7 (5)	3 (4)

Clinical data cutoff date of October 11, 2023.
[a]Received 2-3 SUDs.
[b]Relative to the most recent dose.
[c]CRS with both start and end dates available.
[d]Patients could receive more than 1 supportive therapy.
[e]Tocilizumab was advised for grade 2 and higher but allowed for grade 1; the protocol did not recommend prophylactic tocilizumab use.
[f]Only single vasopressor used

CRS, cytokine release syndrome; IQR, interquartile range; Q2W, every other week; QW, weekly; SC, subcutaneous; SUD, step-up dose; TCR, T-cell-redirection therapy.

MonumenTAL-1 study: ICANS events[7]

Event	0.4 mg/kg SC QW[a,b] (n=122)	0.8 mg/kg SC Q2W[a,b] (n=118)	Prior TCR[a,b] (n=61)
Patients with ICANS, n (%)	13 (11)	12 (10)	2 (3)
Grade 1	4 (3)	4 (3)	2 (3)
Grade 2	7 (6)	4 (3)	0
Grade 3	2 (2)	3 (3)	0
Grade 4	0	1 (1)	0
ICANS symptoms (≥2% in any cohort), n (%)			
Confusional state	6 (5)	5 (4)	0
Disorientation	3 (2)	2 (2)	0
Somnolence	3 (2)	2 (2)	0
Depressed level of consciousness	3 (2)	1 (1)	0
Median time to onset (IQR), hours[c]	23.6 (15.0-53.7)	31.9 (14.7-52.0)	81.6 (47.6-115.5)
Median duration (IQR), hours	15.5 (2.7-23.9)	7.8 (3.5-24.9)	25.3 (2.0-48.5)
Number of ICANS events	21	15	2
Recovered or resolved, n (%)	18 (86)	12 (80)	2 (100)
Not recovered or not resolved, n (%)	2 (10)	2 (13)	0
Recovering or resolving, n (%)	1 (5)	0	0
Unknown, n (%)	0	1 (7)	0
Concurrent CRS, n (%)[d]			
Yes	14 (67)	10 (67)	2 (100)
No	7 (33)	5 (33)	0

Clinical data cutoff date of October 11, 2023.
[a]Received 2-3 SUDs.
[b]ICANS was only measured in phase 2.
[c]Relative to the most recent dose.
[d]Concurrent CRS includes ICANS events that occur simultaneously with CRS or within 7 days after its resolution.

CRS, cytokine release syndrome; IQR, interquartile range; Q2W, every other week; QW, weekly; SC, subcutaneous; SUD, step-up dose; TCR, T-cell-redirection therapy.

MonumenTAL-1 study: infections[1,7]

Event, n (%)	0.4 mg/kg SC QW[a] (n=143)	0.8 mg/kg SC Q2W[a] (n=154)	Prior TCR[a] (n=78)
Any infection	85 (59)	105 (68)	59 (76)
Grade 3-4 infections	29 (20)	28 (18)	20 (26)
Opportunistic infections[b]	5 (3)	9 (6)	3 (4)
COVID-19 cases	16 (11)	39 (25)	11 (14)

Clinical data cutoff date of October 11, 2023.
[a]Received 2-3 SUDs.
[b]Includes esophageal candidiasis, adenovirus infection, herpesvirus 6 infection, ophthalmic herpes, varicella-zoster virus infection, cytomegalovirus infection, fungal sepsis, and viral retinitis.

COVID-19, corona virus disease 19; Q2W, every other week; QW, weekly; SC, subcutaneous; SUD, step-up dose; TCR, T-cell-redirection therapy.

MonumenTAL-1 study: duration and outcomes of skin-, nail-, rash-, and taste-related AEs[7]

Event	0.4 mg/kg SC QW[a] (n=143)	0.8 mg/kg SC Q2W[a] (n=154)	Prior TCR[a] (n=78)
Nonrash skin-related AEs[b]			
Total, n (%)	81 (57)	113 (73)	49 (63)
Leading to dose modification, n (%)	12 (8)	2 (1)	4 (5)
Median duration, days (IQR)	37.5 (20.5-74.5)	40.0 (16.0-98.0)	31.0 (20.0-57.0)
Outcome			
Number of events	157	195	99
Recovered or resolved, n (%)	95 (61)	112 (57)	66 (67)
Not recovered or not resolved, n (%)	58 (37)	76 (39)	33 (33)
Recovered or resolved with sequelae, n (%)	1 (1)	0	0
Recovering or resolving, n (%)	1 (1)	1 (1)	0
Unknown, n (%)	0	0	0
Missing, n (%)	2 (1)	6 (3)	0
Nail-related AEs[c]			
Total, n (%)	79 (55)	82 (53)	45 (58)
Leading to dose modification, n (%)	1 (1)	1 (1)	2 (3)
Median duration, days (IQR)	106.0 (61.0-190.0)	99.0 (59.0-203.0)	83.0 (18.5-151.5)
Outcome			
Number of events	100	105	57
Recovered or resolved, n (%)	36 (36)	33 (31)	20 (35)
Not recovered or not resolved, n (%)	63 (63)	67 (64)	34 (60)
Recovered or resolved with sequelae, n (%)	0	0	0
Recovering or resolving, n (%)	0	0	0
Unknown, n (%)	1 (1)	0	1 (2)
Missing, n (%)	0	5 (5)	2 (4)
Rash-related AEs[d]			
Total, n (%)	57 (40)	45 (29)	25 (32)
Leading to dose modification, n (%)	9 (6)	6 (4)	2 (3)
Median duration, days (IQR)	27.5 (11.5-50.5)	28.5 (13.0-57.0)	14.0 (7.0-28.0)
Outcome, n (%)			
Number of events	75	68	42
Recovered or resolved, n (%)	67 (89)	52 (76)	31 (74)
Not recovered or not resolved, n (%)	7 (9)	15 (22)	11 (26)
Recovered or resolved with sequelae, n (%)	0	0	0
Recovering or resolving, n (%)	1 (1)	1 (1)	0
Unknown, n (%)	0	0	0
Missing, n (%)	0	0	0
Taste-related AEs[e]			
Total, n (%)	103 (72)	110 (71)	59 (76)
Leading to dose modification, n (%)	12 (8)	9 (6)	6 (8)
Median duration, days (IQR)	119.5 (51.0-232.0)	168.5 (84.0-325.0)	132.0 (37.0-303.0)
Outcome			
Number of events, n (%)	127	126	68
Recovered or resolved	65 (51)	50 (40)	26 (38)
Not recovered or not resolved, n (%)	59 (46)	67 (53)	40 (59)
Recovered or resolved with sequela[e], n (%)	0	0	0
Recovering or resolving, n (%)	2 (2)	1 (1)	0
Unknown, n (%)	1 (1)	0	0
Missing, n (%)	0	8 (6)	2 (3)

Clinical data cutoff date of October 11, 2023.
[a]Received 2-3 SUDs.
[b]Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome.
[c]Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging.
[d]Includes rash, maculopapular rash, erythematous rash, and erythema.
[e]Includes dysgeusia, ageusia, hypogeusia, and taste disorder.

AE, adverse event; IQR, interquartile range; Q2W, every other week; QW, weekly; SC, subcutaneous; SUD, step-up dose; TCR, T-cell-redirection therapy.

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- In the phase 1 portion of the MonumenTAL-1 study in patients with RRMM[6]:
  - Patients received IV TALVEY at doses ranging from 0.5 to 180 µg/kg (median follow-up: 4.0 months) or SC TALVEY at 0.4 mg/kg QW or 0.8 mg/kg Q2W. The first RP2D for IV TALVEY was 405 µg/kg in the SC QW cohort (median follow-up: 11.7 months), and the second RP2D was 800 µg/kg in the SC Q2W cohort (median follow-up: 4.2 months). Additional IV and SC doses were evaluated in order to select RP2Ds.

Safety

- The most common any-grade hematologic AEs were neutropenia (0.4 mg/kg SC QW, 67% [n=20]; 0.8 mg/kg SC Q2W, 36% [n=16]), anemia (0.4 mg/kg SC QW, 60% [n=18]; 0.8 mg/kg SC Q2W, 43% [n=19]), and lymphopenia (0.4 mg/kg SC QW, 40% [n=12]; 0.8 mg/kg SC Q2W, 39% [n=17]).[6]
- The most common any-grade nonhematologic AEs were CRS (77% [n=23], 0.4 mg/kg SC QW; 80% [n=35], 0.8 mg/kg SC Q2W), skin-related events (0.4 mg/kg SC QW, 67% [n=20]; 0.8 mg/kg SC Q2W, 70% [n=31]), and dysgeusia (0.4 mg/kg SC QW, 63% [n=19]; 0.8 mg/kg SC Q2W, 57% [n=25]).[6]

Efficacy

- ORR was 70% (95% CI, 51-85) in the 0.4 mg/kg SC QW cohort and 64% (95% CI, 48-78) in the 0.8 mg/kg SC Q2W cohort.[6]
- The median time to response was 0.9 months (range, 0.2-3.8) in the 0.4 mg/kg SC QW cohort and 1.2 months (range, 0.3-6.8) in the 0.8 mg/kg SC Q2W cohort.[6]
- The median DOR was 10.2 months (95% CI, 3.0-NR) in the 0.4 mg/kg SC QW cohort and 7.8 months (95% CI, 4.6-NR) in the 0.8 mg/kg SC Q2W cohort.[6]
- Median time to ≥CR was 9.3 months (range, 1.7-17.1) in the 0.4 mg/kg SC QW cohort and 2.3 months (range, 2.1-6.8) in the 0.8 mg/kg SC Q2W cohort.[6]

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MonumenTAL-1 study

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- Patients were treated at the RP2Ds and reduced dose once they achieved a response.[8]
- Patients were included in the responsive dose intensity reduction cohorts or the prospective dose intensity reduction cohorts[8]:
  - **Responsive dose intensity reduction cohorts (n=50)**; after treatment at the RP2Ds, patients with ≥PR, treatment-emergent AE mitigation or both received a reduced or less frequent dose[8]:
    - In TCR-naïve TALVEY 0.4 mg/kg QW cohort: 25 patients received a reduced dose or a less frequent dose.
    - In TCR-naïve TALVEY 0.8 mg/kg Q2W cohort: 15 patients received a reduced dose or a less frequent dose.
    - In the prior TCR cohort: 10 patients received a reduced dose or less frequent dose.
  - **Prospective dose intensity reduction cohorts (n=19)[8]:**
    - TALVEY 0.8 mg/kg Q2W was reduced to 0.4 mg/kg Q2W in 9 patients who had ≥PR.
    - TALVEY 0.8 mg/kg Q2W was reduced to 0.8 mg/kg once every 4 weeks in 10 patients who had ≥PR.

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Responsive dose intensity-reduction cohorts[8]

- At a data cutoff date of October 11, 2023, most patients with dose reductions were in response. Relative to treatment start, dose reduction occurred at a median of 3.2 months (range, 1.8-27.0) in the QW cohort, 4.5 months (range, 1.2-28.9) in the Q2W cohort, and 4.7 months (range, 2.3-9.7) in the prior TCR cohort.

Prospective dose intensity-reduction cohorts[8]

- At a data cutoff of October 2, 2023, patients with dose reductions had to be in response (n=19). Relative to treatment start, dose reduction occurred at a median of 3.1 months (range, 2.3-4.2).

Responsive dose intensity-reduction cohort: DOR

Prospective dose intensity-reduction cohort: efficacy

MonumenTAL-1 study: DOR (responsive dose intensity-reduction cohorts)[8]

	Responders with dose reduction		
	0.4 mg/kg SC QW[a] (n=24)	0.8 mg/kg SC Q2W[b] (n=13)	Prior TCR[c] (n=10)
Median follow-up (range), months	27.6 (2.7-41.2)	20.8 (12.3±33.6)	21.3 (9.2-29.4)
Median DOR (95% CI), months	19.8 (12.7-NE)	NE (12.5-NE)	24.2 (20.4-NE)
12-month DOR rate, % (95% CI)	78.3 (55.4-90.3)	84.6 (51.2-95.9)	100.0 (100.0-100.0)

[a]Patients who underwent dose reduction due to AEs, n=21; patients who underwent dose reduction only due to response, n=3.
[b]Patients who underwent dose reduction due to AEs, n=11; patients who underwent dose reduction only due to response, n=2.
[c]Patients who underwent dose reduction due to AEs, n=9; patients who underwent dose reduction only due to response, n=1.

AE, adverse event; CI, confidence interval; DOR, duration of response; NE, not estimable; Q2W, once every other week; QW, weekly; TCR, T-cell redirection therapy.

MonumenTAL-1 study: efficacy (prospective dose intensity-reduction cohorts)[8]

Parameter	Prospective cohorts (n=19)
Median follow-up (range), months[a]	13.2 (4.0±16.1)
Median PFS (95% CI), months[a]	13.2 (8.8-NE)
12-month PFS rate, % (95% CI)[a]	50.1 (27.9-68.7)
Median DOR (95% CI), months	NE (8.3-NE)
ORR, n (%)	19 (79.2)[a]
sCR, %	25.0[a]
CR, %	29.2[a]
VGPR, %	20.8[a]
PR, %	4.2[a]
≥VGPR, %	75.0[a]

Clinical data cutoff date of October 2, 2023.
[a]Based on all patients included in the cohorts (N=24).

CI, confidence interval; CR, complete response; DOR, duration of response; NE, not estimable; ORR, overall response rate; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

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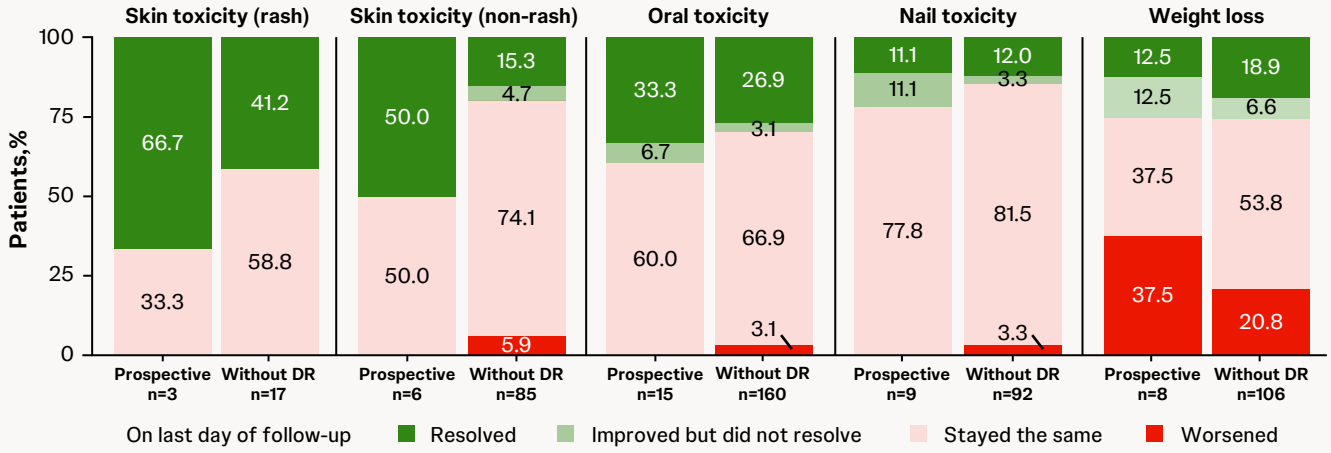
- Onset of GPRC5D-related AEs after switching was evaluated at a data cutoff of October 2, 2023.[8]

Prospective cohorts with change in AE status after switch vs matched cohort without dose reduction[8,a]



[a]Patients included had ≥PR before day 200 and were included from the prospective dose intensity-reduction cohorts (n=18) and from the MonumenTAL-1 cohort that did not undergo dose reduction (n=206). Each category shows only patients who had the respective AE on day 100. Color signifies how that respective AE grade changed from day 100 to the last day of follow-up (within 30 days of the last treatment; capped at 500 days).

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Immune fitness in dose-reduced cohorts[8]

- As of October 2, 2023, maintenance of CD3+ T-cell recovery was comparable between dose-reduced and non-dose-reduced cohorts between cycle 3 day 1 and cycle 7 day 1 of TALVEY (12/68 patients from the RP2D group included in the analysis had dose reductions outside the cycle 3 day 1 and cycle 7 day 1 timeframe).
- Reduction in coinhibitory receptor expression in dose-reduced vs sustained expression in non-dose-reduced cohorts between cycle 3 and cycle 7 of TALVEY was observed.

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ADC	Antibody-drug conjugate	**MRD**	Minimal residual disease
AE	Adverse event	**NA**	Not available
BCMA	B-cell maturation antigen	**NE**	Not estimable
BsAb	Bispecific antibody	**NR**	Not reached
CAR-T	Chimeric antigen receptor-T-cell therapy	**ORR**	Overall response rate
CD	Cluster of differentiation	**OS**	Overall survival
CI	Confidence interval	**PFS**	Progression-free survival
CNS	Central nervous system	**PI**	Proteasome inhibitor
COVID 19	Coronavirus disease 2019	**PK**	Pharmacokinetics
CR	Complete response	**PRO**	Patient-reported outcomes
CRS	Cytokine release syndrome	**PR**	Partial response
CTCAE	Common Terminology Criteria for Adverse Events	**Pts**	Patients
DR	Dose reduction	**Q2W**	Every other week
DOR	Duration of response	**QW**	Weekly
ECOG PS	Eastern Cooperative Oncology Group performance status	**RP2D**	Recommended phase 2 dose
GPRC5D	G protein-coupled receptor class C group 5 member D	**RRMM**	Relapsed or refractory multiple myeloma
IgG	Immunoglobulin G	**SC**	Subcutaneous
IMWG	International Myeloma Working Group	**sCR**	Stringent complete response
IQR	Interquartile range	**SD**	Standard deviation
ISS	International Staging System	**SE**	Standard error
IV	Intravenous	**SUD**	Step-up dose
IVIG	Intravenous immunoglobulin	**TCR**	T-cell-redirection therapy
LOT	Line of treatment	**Tal**	Talquetamab
mAb	Monoclonal antibody	**USPI**	United States prescribing information
MM	Multiple myeloma	**VGPR**	Very good partial response

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A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) was conducted on 06 February 2026.

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1. Chari A, Touzeau C, Schinke C, et al. Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1-2 study. *Lancet Haematol*. 2025;12(4):e269-e281.
2. Jakubowiak AJ, Anguille S, Karlin L, et al. Updated results of talquetamab, a GPRC5D×CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma with prior exposure to T-cell redirecting therapies: results of the phase 1/2 MonumenTAL-1 study. Poster presented at: the 65th American Society of Hematology (ASH) Annual Meeting; December 9-12, 2023; San Diego, CA/Virtual.
3. Rasche L, Schinke C, Touzeau C, et al. Efficacy and safety from the phase 1/2 MonumenTAL-1 study of talquetamab, a GPRC5D×CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma: analyses at an extended median follow-up. Poster presented at: the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting; May 30-June 3, 2025; Chicago, IL/Virtual.
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8. Chari A, Oriol A, Krishnan A, et al. Efficacy and safety of less frequent/lower intensity dosing of talquetamab in patients with relapsed/refractory multiple myeloma: results from the phase 1/2 MonumenTAL-1 study. Oral Presentation presented at: the 65th American Society of Hematology (ASH) Annual Meeting; December 9-12, 2023; San Diego, CA.

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Last updated: 19 February 2026.