SUPPLEMENTARY MATERIAL

Comparative Efficacy of Talquetamab vs. Real-World Physician's Choice of Treatment in Triple-Class-Exposed Relapsed/Refractory Multiple Myeloma: Updated Analyses of MonumenTAL-1 vs. LocoMMotion/MoMMent

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APPENDIX S1. DATA SOURCES

Patients Treated With Talquetamab in MonumenTAL-1

MonumenTAL-1 is an ongoing, first-in-human, open-label, single-arm phase 1/2 clinical trial studying the safety and efficacy of talquetamab in adult patients with triple-class exposed relapsed/refractory multiple myeloma (RRMM).[1] Eligible patients must have received a diagnosis of MM under International Myeloma Working Group (IMWG) diagnostic criteria. In phase 2, patients were required to have previous exposure to ≥ 1 proteasome inhibitor (PI), ≥ 1 immunomodulatory inhibitor (IMiD), and ≥ 1 anti-CD38 monoclonal antibody, as well as an Eastern Cooperative Oncology Group performance status score of 0 to 2. This study consists of three distinct parts, registered as two unique clinical trials: Parts 1 and 2 represent the phase 1 portion of the study (NCT03399799) and Part 3 represents the phase 2 portion (NCT04634552). The phase 1 portion assessed dose escalation and expansion of talquetamab, whereas the phase 2 portion examined efficacy and safety at the recommended phase 2 doses (RP2Ds) identified in phase 1. Patients in phase 1 were treated with intravenous or subcutaneous (SC) talquetamab, with doses ranging from 0.5 to 180 μg/kg and 5 to 1600 μg/kg, respectively.[1] The RP2Ds were determined to be SC talquetamab 0.4 mg/kg weekly (preceded by step-up doses of 0.01 and 0.06 mg/kg) and 0.8 mg/kg every other week (preceded by step-up doses of 0.01, 0.06, and 0.3 mg/kg).

Patients Receiving Treatments From Real-world Clinical Practice in LocoMMotion

LocoMMotion (NCT04035226) is the first prospective, multinational, non-interventional study assessing real-world physician's choice of treatment (RWPC) in patients with triple-class exposed RRMM and has been described elsewhere in detail.[2] A total of 76 centers from nine European countries and the United States enrolled a total of 248 patients between August 2019 and October 2020. Response and progression events were assessed by a response review committee. The data used for analyses in this study included final data from LocoMMotion as of October 27, 2022, with a median duration of patient follow-up of 26.4 months.

Patients Receiving Treatments From Real-World Clinical Practice in MoMMent

MoMMent (NCT05160584) is a prospective, multinational, non-interventional study assessing RWPC in patients with triple-class–exposed RRMM and was designed to be identical to LocoMMotion and to continue documenting current RWPC and associated outcomes. The study consists of two consecutive enrollment periods relevant to this report. Period 1 enrolled 54 patients who had received a PI, IMiD, and anti-CD38 monoclonal antibody to further complement the LocoMMotion cohort. Period 2 enrolled 38 patients who had received a PI, IMiD, and anti-CD38 monoclonal antibody, as well as BCMA-targeted therapy, to document clinical practice in a patient population exposed to BCMA-targeted therapy. Patients were enrolled at 51 sites across Europe between November 2021 and July 2022; follow-up of Periods 1 and 2 was completed in 2024. The analyses in this study included data from MoMMent, with a clinical cut-off of August 2024 and a median duration of follow-up of 27.1 months. An additional enrollment period (Period 3) is ongoing and not included in the present report.

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[1]Chari A, et al. N Engl J Med. 2022;387(24):2232–44
[2]Mateos MV, et al. Leukemia. 2022;36(5):1371–6

SUPPLEMENTARY TABLES

Table S1 Baseline characteristics in patients with prior T-cell redirection therapy

	Talquetamab, *n* (%) (*n* = 75)	**RWPC cohort, *n* (%) (*n* = 36)**
Prior exposure		
BsAb	17 (22.7)	19 (52.8)
CAR-T	46 (61.3)	8 (22.2)
BsAb and CAR-T	4 (5.3)	3 (8.3)
Refractory status[a]		
≤Triple[b]	22 (29.3)	13 (36.1)
Quadruple[c]	21 (28.0)	12 (33.3)
Penta[d]	32 (42.7)	11 (30.6)
ISS stage		
I	37 (49.3)	9 (25.0)
II	25 (33.3)	12 (33.3)
III	13 (17.3)	15 (41.7)
Time to progression in previous line (months)		
< 3	25 (33.3)	14 (38.9)
≥ 3	50 (66.7)	22 (61.1)
Extramedullary disease[e]		
Yes	25 (33.3)	4 (11.1)
No	50 (66.7)	32 (88.9)
Number of previous LOTs		
≤ 4	18 (24.0)	4 (11.1)
> 4	57 (76.0)	32 (88.9)
Median time since last TCR therapy (months [range])	9.9 (0.8–59.8)	4.0 (0.0–36.8)
TCR in last LOT, *n* (%)		
CAR-T	33 (44.0)	9 (25.0)
BsAb	7 (9.3)	15 (41.7)
Years since diagnosis (months)		
< 6	35 (46.7)	15 (41.7)
≥ 6	40 (53.3)	21 (58.3)
Average duration of prior lines (months)		
< 10	27 (36.0)	11 (30.6)
10–14	21 (28.0)	14 (38.9)
≥ 15	27 (36.0)	11 (30.6)
Age (years)		
< 65	47 (62.7)	20 (55.6)
≥ 65	28 (37.3)	16 (44.4)

	Talquetamab, *n* (%) (*n* = 75)	**RWPC cohort, *n* (%) (*n* = 36)**
Hemoglobin (g/dL)		
< 10	27 (36.0)	15 (41.7)
≥ 10	48 (64.0)	21 (58.3)
LDH (units/L)		
< 280	57 (76.0)	28 (77.8)
≥ 280	18 (24.0)	8 (22.2)
Creatinine clearance (mL/min)		
< 60	19 (25.3)	14 (38.9)
60 to < 90	35 (46.7)	12 (33.3)
≥ 90	21 (28.0)	10 (27.8)
ECOG PS		
0	34 (45.3)	7 (19.4)
1 or 2	41 (54.7)	29 (80.6)
Sex		
Male	48 (64.0)	27 (75.0)
Female	27 (36.0)	9 (25.0)
MM type		
IgG	24 (32.0)	16 (44.4)
Non-IgG	51 (68.0)	20 (55.6)
Prior transplant		
Yes	66 (88.0)	30 (83.3)
No	9 (12.0)	6 (16.7)

BsAb bispecific antibody, *CAR-T* chimeric antigen receptor T-cell, *ECOG PS* Eastern Cooperative Oncology Group performance status, *IgG* immunoglobulin G, *ISS* International Staging System, *LDH* lactate dehydrogenase, *LOT* line of therapy, *MM* multiple myeloma, *RWPC* real-world physician's choice of treatment, *TCR* T-cell redirection

[a]Refractoriness was defined as progressive disease/relapse (physician's choice cohort) and by International Myeloma Working Group consensus criteria (MonumenTAL-1)

[b]Refractory to 1 immunomodulatory agent (IMiD,) 1 proteasome inhibitor (PI,) and 1 anti-CD38 monoclonal antibody (mAb); or less than triple-class refractory

[c]Refractory to ≥ 2 IMiDs, 1 PI, and 1 anti-CD38 mAb; or ≥ 2 PIs, 1 IMiD, and 1 anti-CD38 mAb

[d]Refractory to ≥ 2 IMiDs, ≥ 2 PIs, and 1 anti-CD38 mAb

[e]True extramedullary disease is restricted to soft-tissue plasmacytomas that arise due to hematogenous spread and have no contact with bony structures.[3] Only true extramedullary disease soft-tissue lesions were analyzed in MonumenTAL-1, while both paraskeletal lesions and/or true extramedullary disease soft-tissue lesions were analyzed in LocoMMotion and MoMMent

[3]Bladé J, et al. Blood Cancer J. 2022;12:45

Table S2 Treatment regimens in patients naïve to T-cell redirection therapy in the RWPC cohort

Treatment regimen, *n* (%)	***N* = 175**
Cyclophosphamide, pomalidomide, dexamethasone	29 (16.6)
Pomalidomide, dexamethasone	20 (11.4)
Carfilzomib, dexamethasone	17 (9.7)
Belantamab mafodotin-blmf	10 (5.7)
Bortezomib, panobinostat, dexamethasone	8 (4.6)
Carfilzomib, cyclophosphamide, dexamethasone	8 (4.6)
Elotuzumab, pomalidomide, dexamethasone	7 (4.0)
Carfilzomib, lenalidomide, dexamethasone	6 (3.4)
Ixazomib, lenalidomide, dexamethasone	6 (3.4)
Bendamustine, bortezomib, dexamethasone	4 (2.3)
Carfilzomib, pomalidomide, dexamethasone	4 (2.3)
Lenalidomide, dexamethasone	4 (2.3)
Bortezomib, daratumumab, dexamethasone	3 (1.7)
Cyclophosphamide, dexamethasone	3 (1.7)
Daratumumab, pomalidomide, dexamethasone	3 (1.7)
Melphalan, dexamethasone	3 (1.7)
Idecabtagene vicleucel	3 (1.7)
Melphalan	3 (1.7)

Only treatments used in ≥ 3 patients are presented. Patients can be counted in multiple regimens if they have received different combinations in a single line of treatment. Percentages calculated with the number of patients in the all-treated analysis set as denominator (*N* = 175)

RWPC real-world physician's choice of treatment

Originally presented at EHA2025 and published in the EHA2025 Abstract Book.

Table S3 Treatment regimens in patients with prior T-cell redirection therapy in the RWPC cohort

Treatment regimen, *n* (%)	***N* = 36**
Cyclophosphamide, pomalidomide, dexamethasone	5 (13.9)
Teclistamab	5 (13.9)
Bortezomib, venetoclax, dexamethasone	2 (5.6)
Isatuximab, pomalidomide, dexamethasone	2 (5.6)
Pomalidomide, dexamethasone	2 (5.6)
Belantamab mafodotin-blmf	1 (2.8)
Bendamustine	1 (2.8)
Bendamustine, prednisone	1 (2.8)
Bortezomib, cisplatin, cyclophosphamide, etoposide, dexamethasone	1 (2.8)
Bortezomib, cisplatin, cyclophosphamide, etoposide, doxorubicin	1 (2.8)
Bortezomib, daratumumab, pomalidomide, doxorubicin, dexamethasone	1 (2.8)
Bortezomib, panobinostat, dexamethasone	1 (2.8)
Bortezomib, selinexor, dexamethasone	1 (2.8)
Carfilzomib, cisplatin, cyclophosphamide, daratumumab, etoposide	1 (2.8)
Carfilzomib, cyclophosphamide, dexamethasone	1 (2.8)
Carfilzomib, dexamethasone	1 (2.8)
Carfilzomib, venetoclax, dexamethasone	1 (2.8)
Cisplatin, cyclophosphamide, doxorubicin, etoposide	1 (2.8)
Cyclophosphamide, isatuximab, pomalidomide, dexamethasone	1 (2.8)
Cyclophosphamide, fludarabine, idecabtagene vicleucel	1 (2.8)
Daratumumab, ixazomib, thalidomide, dexamethasone	1 (2.8)
Daratumumab, lenalidomide, dexamethasone	1 (2.8)
Pomalidomide	1 (2.8)
Pomalidomide, prednisone	1 (2.8)
Venetoclax	1 (2.8)

Patients can be counted in multiple regimens if they have received different combinations in a single line of treatment. Percentages calculated with the number of patients in the all-treated analysis set as denominator (*N* = 36)

RWPC real-world physician's choice of treatment

Table S4 Treatment regimens in patients in the USPI-aligned population in the RWPC cohort

Treatment regimen, *n* (%)	***N* = 130**
Cyclophosphamide, pomalidomide, dexamethasone	22 (16.9)
Pomalidomide, dexamethasone	15 (11.5)
Carfilzomib, dexamethasone	12 (9.2)
Bortezomib, panobinostat, dexamethasone	7 (5.4)
Carfilzomib, cyclophosphamide, dexamethasone	6 (4.6)
Belantamab mafodotin-blmf	5 (3.8)
Elotuzumab, pomalidomide, dexamethasone	5 (3.8)
Ixazomib, lenalidomide, dexamethasone	5 (3.8)
Bendamustine, bortezomib, dexamethasone	4 (3.1)
Carfilzomib, lenalidomide, dexamethasone	4 (3.1)
Bortezomib, daratumumab, dexamethasone	3 (2.3)
Lenalidomide, dexamethasone	3 (2.3)
Melphalan	3 (2.3)

Only treatments used in ≥ 3 patients are presented. Patients can be counted in multiple regimens if they have received different combinations in a single line of treatment. Percentages calculated with the number of patients in the all-treated analysis set as denominator (*N* = 130)

RWPC real-world physician's choice of treatment, *USPI* US prescribing information

Table S5 Sensitivity analyses results for ORR, ≥ VGPR, and ≥ CR in patients naïve to T-cell redirection therapy

Outcome/ Analysis[a]	Talquetamab 0.4 mg/kg QW		Talquetamab 0.8 mg/kg Q2W	
	RR (95% CI)	*p* value	RR (95% CI)	*p* value
ORR				
ATT all variables	2.46 (1.50–4.03)	0.0004	2.03 (1.38–2.98)	0.0003
Multivariable regression	2.30 (1.85–2.86)	< 0.0001	2.03 (1.63–2.53)	< 0.0001
ATO	2.27 (1.79–2.89)	< 0.0001	2.05 (1.61–2.60)	< 0.0001
ATE	2.24 (1.72–2.91)	< 0.0001	2.25 (1.73–2.92)	< 0.0001
ATC	1.98 (1.51–2.61)	< 0.0001	2.03 (1.61–2.54)	< 0.0001
PS matching	2.96 (2.05–4.27)	< 0.0001	1.94 (1.47–2.58)	< 0.0001
≥ VGPR				
ATT all variables	4.35 (1.88–10.06)	0.0006	4.22 (2.22–8.01)	< 0.0001
Multivariable regression	4.54 (3.14–6.57)	< 0.0001	4.06 (2.83–5.83)	< 0.0001
ATO	4.30 (2.90–6.38)	< 0.0001	3.99 (2.72–5.87)	< 0.0001
ATE	4.23 (2.82–6.35)	< 0.0001	4.45 (2.98–6.63)	< 0.0001
ATC	3.98 (2.66–5.95)	< 0.0001	4.06 (2.79–5.91)	< 0.0001
PS matching	4.50 (2.60–7.80)	< 0.0001	3.87 (2.37–6.31)	< 0.0001
≥ CR				
ATT all variables	33.76 (5.34–213.43)	0.0002	50.56 (8.57–298.40)	< 0.0001
Multivariable regression	34.79 (8.67–139.64)	< 0.0001	39.71 (10.05–156.90)	< 0.0001
ATO	27.18 (6.68–110.63)	< 0.0001	37.72 (9.32–152.65)	< 0.0001
ATE	31.43 (7.68–128.59)	< 0.0001	43.59 (10.72–177.34)	< 0.0001
ATC	31.89 (7.75–131.24)	< 0.0001	38.24 (9.41–155.42)	< 0.0001
PS matching	NE	NE	41.00 (5.76–291.95)	0.0002

ATC average treatment effect in the control, *ATE* average treatment effect, *ATO* average treatment effect in the overlap, *ATT* average treatment effect in the treated, *CI* confidence interval, ≥ *CR* complete response or better, *NE* not evaluable, *ORR* overall response rate, *PS* propensity score, *Q2W* every other week, *QW* once weekly, *RR* response ratio, ≥ *VGPR* very good partial response or better

[a]Propensity score matching (caliper = 0.2) The total number of patients assessed for the 0.4 mg/kg cohort: multivariable regression (MonumenTAL-1, *N* = 143; RWPC, *N* = 175), ATO (MonumenTAL-1 and real-world physician's choice of treatment [RWPC], *N* = 65), ATE (MonumenTAL-1, *N* = 144; RWPC, *N* = 175), ATC (MonumenTAL-1, *N* = 143; RWPC, *N* = 175), and PS matching (MonumenTAL-1 and RWPC, *N* = 87)

The total number of patients assessed for the 0.8 mg/kg Q2W cohort: multivariable regression (MonumenTAL-1, *N* = 154; RWPC, *N* = 175), ATO (MonumenTAL-1 and RWPC, *N* = 67), ATE (MonumenTAL-1, *N* = 154; RWPC, *N* = 178), ATC (MonumenTAL-1, *N* = 154; RWPC, *N* = 175), and PS matching (MonumenTAL-1 and RWPC, *N* = 94)

Table S6 Sensitivity analyses results for DOR, PFS, TTNT, and OS in patients naïve to T-cell redirection therapy

Outcome/ Analysis[a]	Talquetamab 0.4 mg/kg QW		Talquetamab 0.8 mg/kg Q2W	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
DOR				
ATT all variables	0.76 (0.42–1.37)	0.3531	0.45 (0.29–0.72)	0.0009
Multivariable regression	0.66 (0.42–1.04)	0.0741	0.45 (0.29–0.72)	0.0008
ATO	0.79 (0.54–1.15)	0.2166	0.51 (0.34–0.76)	0.0009
ATE	0.77 (0.53–1.13)	0.1863	0.49 (0.33–0.74)	0.0007
ATC	0.76 (0.50–1.16)	0.2043	0.48 (0.30–0.75)	0.0016
PS matching	0.88 (0.53–1.47)	0.6268	0.47 (0.29–0.77)	0.0024
PFS				
ATT all variables	0.54 (0.35–0.84)	0.0062	0.49 (0.35–0.70)	< 0.0001
Multivariable regression	0.55 (0.41–0.73)	< 0.0001	0.45 (0.34–0.61)	< 0.0001
ATO	0.60 (0.45–0.79)	0.0002	0.50 (0.38–0.67)	< 0.0001
ATE	0.62 (0.46–0.84)	0.0021	0.47 (0.35–0.63)	< 0.0001
ATC	0.68 (0.47–1.00)	0.0477	0.47 (0.34–0.66)	< 0.0001
PS matching	0.59 (0.42–0.84)	0.0033	0.49 (0.35–0.70)	< 0.0001
TTNT				
ATT all variables	0.58 (0.41–0.84)	0.0040	0.52 (0.38–0.72)	< 0.0001
Multivariable regression	0.52 (0.39–0.68)	< 0.0001	0.46 (0.35–0.61)	< 0.0001
ATO	0.56 (0.43–0.73)	< 0.0001	0.51 (0.39–0.67)	< 0.0001
ATE	0.59 (0.44–0.79)	0.0004	0.48 (0.37–0.63)	< 0.0001
ATC	0.64 (0.44–0.93)	0.0195	0.50 (0.37–0.68)	< 0.0001
PS matching	0.55 (0.39–0.77)	0.0005	0.52 (0.37–0.72)	< 0.0001
OS				
ATT all variables	0.37 (0.25–0.56)	< 0.0001	0.36 (0.24–0.53)	< 0.0001
Multivariable regression	0.42 (0.29–0.59)	< 0.0001	0.35 (0.24–0.51)	< 0.0001
ATO	0.47 (0.33–0.66)	< 0.0001	0.39 (0.27–0.57)	< 0.0001
ATE	0.51 (0.34–0.75)	0.0008	0.36 (0.24–0.53)	< 0.0001

ATC	0.62 (0.38–1.02)	0.0583	0.37 (0.24–0.58)	< 0.0001
PS matching	0.45 (0.30–0.68)	0.0001	0.36 (0.23–0.56)	< 0.0001

ATC average treatment effect in the control, *ATE* average treatment effect, *ATO* average treatment effect in the overlap, *ATT* average treatment effect in the treated, *CI* confidence interval, *DOR* duration of response, *HR* hazard ratio, *OS* overall survival, *PFS* progression-free survival, *PS* propensity score, *Q2W* every other week, *QW* once weekly, *TTNT* time to next treatment

[a]PS matching (caliper = 0.2)

For DOR, the total number of patients assessed for the 0.4 mg/kg QW cohort: multivariable regression (MonumenTAL-1, *N* = 106; real-world physician's choice of treatment [RWPC], *N* = 65), ATO (MonumenTAL-1, *N* = 50; RWPC, *N* = 22), ATE (MonumenTAL-1, *N* = 106; RWPC, *N* = 58), ATC (MonumenTAL-1, *N* = 105; RWPC, *N* = 65), and PS matching (MonumenTAL-1, *N* = 68; RWPC, *N* = 23)

The total number of patients assessed for the 0.8 mg/kg Q2W cohort: multivariable regression (MonumenTAL-1, *N* = 107; RWPC, *N* = 65), ATO (MonumenTAL-1, *N* = 49; RWPC, *N* = 24), ATE (MonumenTAL-1, *N* = 111; RWPC, *N* = 57), ATC (MonumenTAL-1, *N* = 116; RWPC, *N* = 65), and PS matching (MonumenTAL-1, *N* = 70; RWPC, *N* = 36)

For PFS, TTNT, and OS, the total number of patients assessed for the 0.4 mg/kg QW cohort: multivariable regression (MonumenTAL-1, *N* = 143; RWPC, *N* = 175), ATO (MonumenTAL-1 and RWPC, *N* = 65), ATE (MonumenTAL-1, *N* = 144; RWPC, *N* = 175), ATC (MonumenTAL-1, *N* = 143; RWPC, *N* = 175), and PS matching (MonumenTAL-1 and RWPC, *N* = 87)

The total number of patients assessed for the 0.8 mg/kg Q2W cohort: multivariable regression (MonumenTAL-1, *N* = 154; RWPC, *N* = 175), ATO (MonumenTAL-1 and RWPC, *N* = 67), ATE (MonumenTAL-1, *N* = 154; RWPC, *N* = 178), ATC (MonumenTAL-1, *N* = 154; RWPC, *N* = 175), and PS matching (MonumenTAL-1 and RWPC, *N* = 94)

Table S7 Efficacy outcomes across all endpoints in patients with prior T-cell redirection therapy in the USPI-aligned patient subgroup (≥ 4 prior lines of therapy and phase 2 only)

	Talquetamab (*n* = 56) vs. RWPC (*n* = 34)		
	Response, %	**RR (95% CI)**	***p* value**
ORR			
Unadjusted	71.4 vs. 20.6	3.47 (1.76–6.85)	0.0003
Base case analysis	NA	3.57 (1.81–7.03)	0.0002
Fully adjusted analysis	NA	3.17 (1.66–6.07)	0.0005
≥ VGPR			
Unadjusted	57.1 vs. 11.8	4.86 (1.88–12.43)	0.0011
Base case analysis	NA	5.06 (1.81–14.17)	0.0020
Fully adjusted analysis	NA	4.48 (1.64–12.22)	0.0034
	Median, mo	**HR (95% CI)**	***p* value**
DOR			
Unadjusted	19.2 vs. 3.3	0.30 (0.11–0.83)	0.0197
Base case analysis	NA	0.07 (0.02–0.29)	0.0002
Fully adjusted analysis	NA	0.09 (0.02–0.45)	0.0035
PFS			
Unadjusted	8.9 vs. 2.5	0.33 (0.19–0.57)	< 0.0001
Base case analysis	NA	0.26 (0.14–0.48)	< 0.0001
Fully adjusted analysis	NA	0.29 (0.14–0.58)	0.0004
TTNT			
Unadjusted	8.2 vs. 2.9	0.28 (0.17–0.47)	< 0.0001
Base case analysis	NA	0.24 (0.13–0.43)	< 0.0001
Fully adjusted analysis	NA	0.25 (0.13–0.48)	< 0.0001
OS			
Unadjusted	28.3 vs. 8.9	0.33 (0.18–0.61)	0.0004
Base case analysis	NA	0.32 (0.16–0.65)	0.0015
Fully adjusted analysis	NA	0.37 (0.17–0.79)	0.0106

CI confidence interval, *DOR* duration of response, *HR* hazard ratio, *NA* not available, *ORR* overall response rate, *OS* overall survival, *PFS* progression-free survival, *RR* response ratio, *RWPC* real-world physician's choice of treatment, *TTNT* time to next treatment, *USPI* US prescribing information, ≥ *VGPR* very good partial response or better

Table S8 Efficacy outcomes across time-to-event endpoints in patients with prior CAR-T vs. bispecific antibody therapy

	Talquetamab vs. RWPC		
	CAR-T HR (95% CI)	**Bispecific antibody HR (95% CI)**	***p* value**
PFS			
Unadjusted	0.35 (0.16–0.79)	0.59 (0.29–1.21)	0.3534
Base case analysis	0.17 (0.06–0.46)	0.43 (0.15–1.26)	0.1210
TTNT			
Unadjusted	0.28 (0.14–0.56)	0.39 (0.18–0.81)	0.4155
Base case analysis	0.14 (0.06–0.33)	0.26 (0.09–0.74)	0.0627
OS			
Unadjusted	0.44 (0.19–1.05)	0.58 (0.26–1.30)	0.7560
Base case analysis	0.32 (0.11–0.95)	0.33 (0.09–1.17)	0.5911

Duration of response comparisons were excluded from this table as only 3 patients in the RWPC cohort were included in the analysis.

CAR-T chimeric antigen receptor T-cell, *CI* confidence interval, *HR* hazard ratio, *OS* overall survival, *PFS* progression-free survival, *RWPC* real-world physician's choice of treatment, *TTNT* time to next treatment

Table S9 Efficacy outcomes across all endpoints in patients with prior BCMA therapy (CAR-T, bispecific antibody, and antibody–drug conjugate) across the three MonumenTAL-1 cohorts

	Talquetamab QW, Q2W, and prior TCR (*n* = 114) vs. RWPC (*n* = 57)	
	RR (95% CI)	***p* value**
ORR		
Unadjusted	2.68 (1.67–4.30)	< 0.0001
Base case analysis	2.80 (1.76–4.48)	< 0.0001
Fully adjusted analysis	2.68 (1.66–4.33)	< 0.0001
≥ VGPR		
Unadjusted	4.83 (2.22–10.52)	< 0.0001
Base case analysis	5.10 (2.37–10.97)	< 0.0001
Fully adjusted analysis	4.99 (2.29–10.87)	< 0.0001
	HR (95% CI)	***p* value**
DOR		
Unadjusted	0.41 (0.20–0.83)	0.0131
Base case analysis	0.46 (0.21–1.00)	0.0512
Fully adjusted analysis	0.41 (0.18–0.92)	0.0314
PFS		
Unadjusted	0.44 (0.30–0.65)	< 0.0001
Base case analysis	0.41 (0.27–0.63)	< 0.0001
Fully adjusted analysis	0.40 (0.26–0.62)	< 0.0001
TTNT		
Unadjusted	0.37 (0.25–0.53)	< 0.0001
Base case analysis	0.32 (0.21–0.49)	< 0.0001
Fully adjusted analysis	0.30 (0.20–0.46)	< 0.0001
OS		
Unadjusted	0.43 (0.28–0.66)	0.0001
Base case analysis	0.36 (0.22–0.58)	< 0.0001
Fully adjusted analysis	0.37 (0.23–0.61)	< 0.0001

CI confidence interval, *DOR* duration of response, *HR* hazard ratio, *ORR* overall response rate, *OS* overall survival, *PFS* progression-free survival, *Q2W* every other week, *QW* weekly, *RR* response ratio, *RWPC* real-world physician's choice of treatment, *TCR* T-cell redirection, *TTNT* time to next treatment, ≥ *VGPR* very good partial response or better

Table S10 Efficacy outcomes across all endpoints in patients with prior BCMA therapy (CAR-T, bispecific antibody, and antibody–drug conjugate) across the three MonumenTAL-1 cohorts and USPI-aligned patient subgroup (≥ 4 prior lines of therapy and phase 2 only)

	Talquetamab QW, Q2W, and prior TCR (*n* = 90) vs. RWPC (*n* = 55)	
	RR (95% CI)	***p* value**
ORR		
Unadjusted	3.01 (1.84–4.93)	< 0.0001
Base case analysis	3.17 (1.93–5.21)	< 0.0001
Fully adjusted analysis	3.11 (1.85–5.22)	< 0.0001
≥ VGPR		
Unadjusted	4.89 (2.24–10.66)	< 0.0001
Base case analysis	5.28 (2.46–11.32)	< 0.0001
Fully adjusted analysis	5.39 (2.45–11.86)	< 0.0001
	HR (95% CI)	***p* value**
DOR		
Unadjusted	0.42 (0.20–0.86)	0.0171
Base case analysis	0.48 (0.21–1.06)	0.0683
Fully adjusted analysis	0.42 (0.18–0.96)	0.0386
PFS		
Unadjusted	0.40 (0.26–0.60)	< 0.0001
Base case analysis	0.37 (0.23–0.58)	< 0.0001
Fully adjusted analysis	0.35 (0.22–0.57)	< 0.0001
TTNT		
Unadjusted	0.35 (0.23–0.52)	< 0.0001
Base case analysis	0.28 (0.18–0.44)	< 0.0001
Fully adjusted analysis	0.26 (0.16–0.41)	< 0.0001
OS		
Unadjusted	0.36 (0.22–0.57)	< 0.0001
Base case analysis	0.31 (0.18–0.52)	< 0.0001
Fully adjusted analysis	0.31 (0.18–0.53)	< 0.0001

CI confidence interval, *DOR* duration of response, *HR* hazard ratio, *ORR* overall response rate, *OS* overall survival, *PFS* progression-free survival, *Q2W* every other week, *QW* weekly, *RR* response ratio, *RWPC* real-world physician's choice of treatment, *TCR* T-cell redirection, *TTNT* time to next treatment, ≥ *VGPR* very good partial response or better

Table S11 Ethics committees/Institutional Review Boards in MonumenTAL-1

Country	Ethics Committee/ Institutional Review Board Site	Approval date	Site ID Ref #
Belgium	J43-BE10003	20 Apr 2021	3680010
Belgium	U77-BE10004	07 Apr 2021	3680010
Belgium	U77-BE10002	23 Apr 2021	3680010
Belgium	U77-BE10001	30 Apr 2021	3680010
Belgium	U77-BE10003	07 Apr 2021	3680010
China	U77-CN10005	24 Jan 2022	60868387
China	U77-CN10007	16 Mar 2022	151734838/42909810
China	U77-CN10008	19 Dec 2022	4578301
China	U77-CN10002	21 Feb 2022	67081757
China	U77-CN10011	28 Jun 2023	296960146
China	U77-CN10001	07 Jan 2022	60868406
China	U77-CN10003	04 Mar 2022	107910421
China	U77-CN10004	25 Jan 2022	60890218/60868387
France	U77-FR10001	23 Feb 2021	109642093
France	U77-FR10002	15 Apr 2021	109642093
France	U77-FR10003	20 Apr 2021	109642093
France	U77-FR10006	19 Apr 2021	109642093
France	U77-FR10004	23 Feb 2021	109642093
France	U77-FR10005	14 Apr 2021	109642093
Germany	U77-DE10001	10 May 2021	3619686
Germany	U77-DE10005	04 Jun 2021	143018264/3619686
Germany	U77-DE10003	20 Apr 2021	65501442/3619686
Germany	U77-DE10002	11 Jun 2021	1966647/3619686
Israel	U77-IL10003	30 Mar 2021	67104354
Israel	U77-IL10001	16 Mar 2021	65304579
Israel	U77-IL10002	17 Mar 2021	214624638
Israel	U77-IL10004	11 Apr 2021	65304587
Israel	U77-IL10005	20 Apr 2021	65304587
Japan	U77-JP10008	04 Jul 2022	24221094
Japan	U77-JP10004	19 Jul 2022	61088794
Japan	U77-JP10012	20 Sep 2022	233581552
Japan	U77-JP10005	05 Sep 2022	4607595
Japan	U77-JP10011	20 Jul 2022	50981609
Japan	U77-JP10013	08 Nov 2022	112622177
Japan	U77-JP10009	11 Jul 2022	61088673
Japan	U77-JP10003	14 Jun 2022	200315467

Japan	U77-JP10010	22 Sep 2022	4607379
Japan	U77-JP10014	23 Aug 2023	290626781
Japan	U77-JP10006	31 Jul 2022	2454817
Japan	U77-JP10015	12 Sep 2023	162750144
Japan	U77-JP10007	19 Sep 2022	214786450
Netherlands	J43-NL10001	05 Sep 2019	67390905/61279424
Netherlands	J43-NL10002	11 Feb 2019	61279424
Netherlands	U77-NL10001	08 Jan 2021	2671572
Netherlands	U77-NL10002	29 Jan 2021	2671572
Poland	U77-PL10003	12 Apr 2021	295430681
Poland	U77-PL10001	13 Apr 2021	295430681
Poland	U77-PL10004	13 Apr 2021	295430681
Poland	U77-PL10005	13 Apr 2021	295430681
Poland	U77-PL10002	13 Apr 2021	295430681
Republic of Korea	U77-KR10003	07 Apr 2021	87655320
Republic of Korea	U77-KR10006	07 Apr 2021	9933063
Republic of Korea	U77-KR10002	07 Apr 2021	3267750
Republic of Korea	U77-KR10004	07 Apr 2021	3763615
Republic of Korea	U77-KR10001	07 Apr 2021	3268760
Republic of Korea	U77-KR10005	17 Apr 2021	3267957
Spain	J43-ES10001	24 May 2018	7830447
Spain	J43-ES10006	23 Apr 2021	7830447
Spain	J43-ES10004	23 Jul 2019	7830447
Spain	J43-ES10002	28 Feb 2019	7830447
Spain	J43-ES10003	26 Apr 2018	7830447
Spain	U77-ES10006	02 Mar 2021	102343062
Spain	U77-ES10002	08 Feb 2021	102343062
Spain	U77-ES10003	17 Feb 2021	102343062
Spain	U77-ES10009	18 Mar 2021	102343062
Spain	U77-ES10001	03 Mar 2021	102343062
Spain	U77-ES10010	11 Feb 2021	102343062
Spain	U77-ES10005	04 Jun 2021	102343062
Spain	U77-ES10011	19 Feb 2021	102343062
Spain	U77-ES10004	16 Feb 2021	102343062
Spain	U77-ES10007	10 Mar 2021	102343062
Spain	U77-ES10008	28 Apr 2021	102343062
US	J43-US10005	11 Jul 2018	75157813
US	J43-US10009	02 Mar 2018	117606562
US	J43-US10003	16 Dec 2017	18210329

US	J43-US10007	28 Oct 2020	246139841
US	J43-10001	05 Feb 2018	246139841
US	U77-US10011	15 Apr 2021	246139841
US	U77-US10015	27 Apr 2021	72485809
US	U77-US10005	23 Jul 2021	4475249
US	U77-US10026	31 Mar 2021	3615478
US	U77-US10013	18 Feb 2021	3615478
US	U77-US10016	09 Jun 2021	2630545
US	U77-US10022	28 Jun 2021	3615478
US	U77-US10024	01 Apr 2021	28196129
US	U77-US10007	14 Apr 2021	3615478
US	U77-US10014	13 May 2021	4783017
US	U77-US10009	14 Jan 2021	61089064/117606562
US	U77-US10003	28 Jan 2021	60967175
US	U77-US10025	07 May 2021	3615478

Table S12 Ethics committees/Institutional Review Boards in LocoMMotion

Country	Ethics Committee/ Institutional Review Board address	Approval date	Ref #
US	The James/ A054 Starling Loving Hall 320 W. 10th Ave, Columbus, OH 43210	15 Nov 2019	OSU-19288
US	Columbia Research 615 West 131st St. 3rd floor, New York, NY 10027	21 Nov 2019	IRB-AAAS7369 or 7571412
US	Washington University in St. Louis 660 South Euclid Ave. Campus Box 8089, St. Louis MO 63110	19 Dec 2019	201912009
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	10 Oct 2019	IRB ID 7513-PDEisenberg
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	29 Oct 2019	IRB ID 7513-Amazumder
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	19 Nov 2019	IRB ID 7513-KSJahangir
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	21 Oct 2019	IRB ID 7513-MEBednar
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	13 Nov 2019	IRB ID 7513-Cchen
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	3 Dec 2019	IRB ID 7513-DHuang
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	30 Sep 2019	IRB ID 7513-Zmalik
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	30 Oct 2019	IRB ID 7513-Lshunyakov
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	21 Jan 2020	IRB ID 7513-Hterebolo
US	St. Francis Hospital The Heart Center	5 Dec 2019	IRB #19-34
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	4 Dec 2019	IRB ID 7513-RRCaradonna
US	Sterling IRB 6300 Powers Ferry Road Suite 600-351, Atlanta GA 30339	5 Nov 2019	IRB ID 7513-Mbajaj
Germany	EC Universiaet Heidelberg, Ethik-Kommission I der Medizinischen Fakultät Heidelberg, Alte Glockengiesserei 11/1, 69115 Heidelberg	16 Aug 2019	S-549/2019
Germany	Tuebingen Ethik-Kommission an der Medizinischen Fakultät der Eberhard-Karls-Universität und am Universitätsklinikum Tübingen Gartenstraße 47, 72074 Tübingen	16 Sep 2019	548/2019BO2
Germany	EC medizinische Hochschule Hannover Ethik-Kommission d. Medizinischen Hochschule Hannover Carl-Neuberger-Str. 1, 3623 Hannover	20 Sep 2019	8672_B0_K_2019
Germany	EC Aertzekammer Hamburg Ethikkommission der Ärztekammer Hamburg; Körperschaft des öffentlichen Rechts Weidestr. 122b, 22083 Hamburg	21 Oct 2019	PV7092
Germany	EC Universitaet Wuerzburg Josef-Schneider-Str. 4, Bau C15, 97080 Wuerzburg	17 Jan 2020	172/19-me
Germany	EC Universiaet Koeln Geschäftsstelle der ethik-kommission der medizinischen fakultät der universität zu köln Kerpenerstr 62, 50937 Köln	18 Feb 2020	19-1545_1
Spain	Comité Coordinador de Ética de la Investigación Clínica de Andalucía Avda. de la Innovación, s/n. Edificio Arena 1, 41080 Sevilla	2 Oct 2019	N/A
Spain	Comité Coordinador de Ética de la Investigación Clínica de Andalucía Avda. de la Innovación, s/n. Edificio Arena 1, 41080 Sevilla	7 Oct 2019	N/A
Spain	Comité Coordinador de Ética de la Investigación Clínica de Andalucía Avda. de la Innovación, s/n. Edificio Arena 1, 41080 Sevilla	7 Oct 2029	N/A
Spain	Comité de Ética de la Investigación de Cadiz Avda. Ana de Viya, 21, 11009 Cadiz	23 Jul 2020	N/A

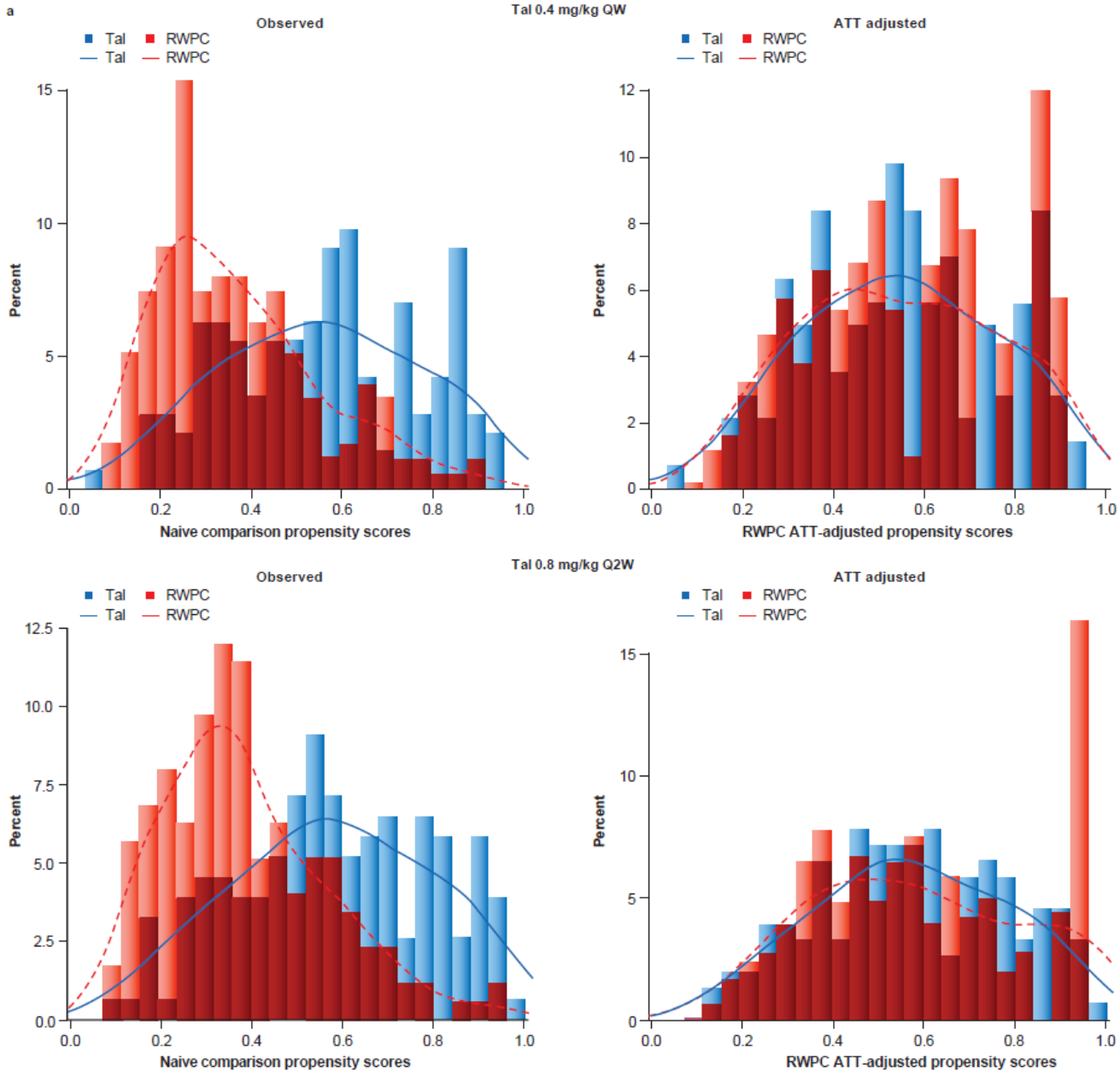
Spain	Comité Coordinador de Ética de la Investigación Clínica de Andalucía Avda. de la Innovación, s/n. Edificio Arena 1, 41080 Sevilla	30 Jul 2020	N/A
UK	Tayside medical science centre Residency block level 3, George Pirie way, Ninewells hospital and medical school, Dundee, DD1 9SY	29 Jul 2019	DL/19/ES/0088
Italy	Comitato Etico Area 3 ASL Lecce, Via Miglietta 5,73100	19 Sep 2019	CE150036
Italy	Comitato Etico Regione Liguria Largo Rosanna Benzi 10, 16132 Genova	24 Jan 2020	CE150193
Italy	Comitato etico dell'IRCCS casa sollievo della sofferenza di s. giovanni rotondo Viale Cappuccini, 71013 SGR	17 Jul 2019	CE150037
Italy	Comitato Etico Indipendente Azienda Ospedaliera Universitaria Policlinico S. Orsola-Malpighi di Bologna Via Albertoni 15, 40138 Bologna	3 Oct 2019	CE150192
Italy	Comitato Etico della Fondazione Policlinico Universitario Agostino Gemelli IRCCS Università Cattolica del Sacro Cuore Largo Agostino Gemelli 8, 00168 Roma	22 Jul 2019	CE150057
Italy	Comitato Etico Catania 1 c/o AOU Policlinico Vittorio Emanuele Via Santa Sofia 78, Catania	30 Oct 2019	CE150101
Italy	Comitato Etico "La Sapienza" Azienda Policlinico Umberto I Via Del Policlinico 155, 00161 Roma	24 Sep 2019	CE150031
Italy	Comitato Etico interaziendale aou citta' della salute e della scienza di Torino Corso Bramante 88/90, 10126 Torino	25 Oct 2019	CE150115
Italy	CESC della Provincia di Padova Via Giustininani 1, 35128 Padova	25 Jun 2020	CE150028
Italy	Comitato Etico Palermo 2 IRB-EC Viale Strasburgo 233, 90136 Palermo	14 Oct 2019	CE150125
Italy	Comitato etico referente per l'area di Pavia Viale Golgi 19, 27100 Pavia	5 Sep 2019	CE150183
Italy	Comitato Etico Unico Regionale per la Basilicata IRB-EC Via Potito Petrone 1, 85100 Potenza	16 Oct 2019	CE150051
Italy	Comitato Etico Interregionale c/o A.O.U. Policlinico Consorziale Piazza Giulio Cesare 11, 70124 Bari	8 Oct 2019	CE150162
Italy	Comitato Etico IRCCS Istituto Tumori "Giovanni Paolo II" Viale orazio flacco 65, 70124 Bari	23 Apr 2020	CE150168
Italy	Comitato Etico della Romagna CEROM Via Piero Maroncelli 40, 47014 Meldola	8 May 2020	CE150190
Italy	Comitato Etico Regione Toscana - Area Vasta Centro c/o Azienda Ospedaliera Universitaria Careggi Largo Brambilla 3, 50134 Firenze	11 May 2020	CE150071
Belgium	Etische Commissie, Onderzoek UZ/KU Leuven Herestraat 49, 3000 Leuven	13 Sep 2019	S62984
The Netherlands	METC van de stichting BEBO Dr. Nassaulaan 10, 9401 HK Assen	16 Jul 2019	19.084/IH
Poland	Komisja Bioetyczna przy, Uniwersytecie Medycznym im. Karola Marcinkowskiego w Poznaniu, Collegium Maius Dział Badań Naukowych; ul. Bukowska 70, 60-812 Poznań	07 Nov 2019	991/19
France	CPP EST III, Hopital de Brabois Rue du Morvan, 54511 Vandoeuvre-les-Nancy Cedex	5 Sep 2019	Numéro ID RCB: 2019-A01716-51
Russia	Independent Interdisciplinary Committee on Ethics Expertise of Clinical Trials, 51 Leningradskiy prospect, 125468 Moscow	4 Oct 2019	15

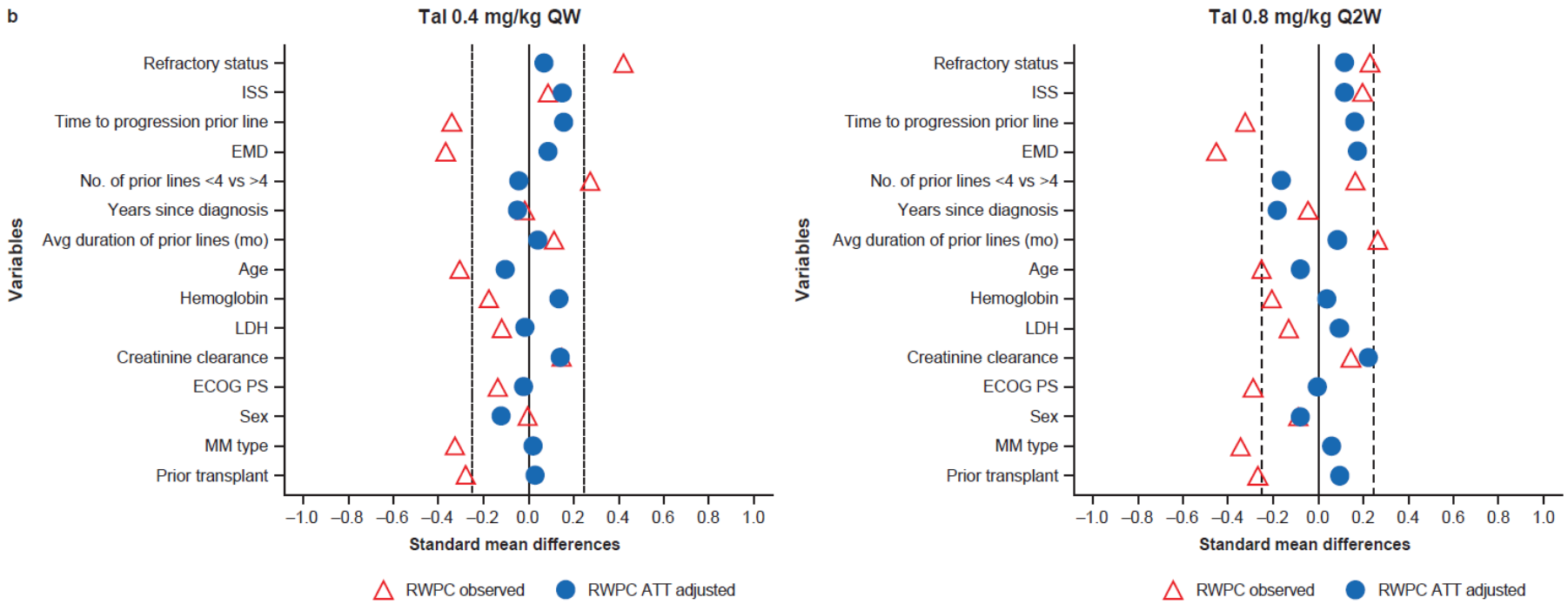
Table S13 Ethics committees/Institutional Review Boards in MoMMent

Country	Ethics Committee/ Institutional Review Board Site	Approval date	Ref #
Belgium	BE10002-Delforge	14 Dec 2021	S66063
Germany	DE10001-Besemer	21 Dec 2021	822/2021 BO
Germany	DE10002-Bittrich	03 Mar 2022	297/21
Germany	DE10003-Goldschmidt	24 Nov 2021	S-832/2021
Spain	ES10006-Ocio	2 Nov 2021	20/2021
Spain	ES10007-Perez	30 Dec 2021	2021-0113
Spain	ES10011-Gonzalez Garcia	14 Jan 2022	2021.612
France	FR10002-Perrot	23 Nov 2021	2022T3-03 HPS
France	FR10003-Karlin	24 Nov 2021	2022T3-03 HPS
France	FR10006-Moreau	25 Nov 2021	2022T3-03 HPS
France	FR10008-Vincent	26 Nov 2021	2022T3-03 HPS
UK	GB10006-Kirkpatrick	4 Feb 2022	21/WA/0349
UK	GB10009-Willis	16 Dec 2021	21/WA/0349
UK	GB10011-Benjamin	17 Dec 2021	21/WA/0349
UK	GB10013-Pawlyn	10 Mar 2022	21/WA/0349
UK	GB10016-Lindsey-Hill	18 Nov 2021	21/WA/0349
Italy	IT10001-Cangialosi	25 Jan 2022	242 AOR 2021
Italy	IT10003-Cavo	29 Dec 2021	4456/2021
Italy	IT10004-Cerchione	22 Dec 2021	10292/2021 - I.5/252
Italy	IT10005-De Stefano	18 Jan 2022	4535
Italy	IT10006-Di Raimondo	27 Dec 2021	61037
Italy	IT10008-Mangiacavalli	23 Dec 2021	0108695/21
The Netherlands	NL10001-Roeloffzen	17 Dec 2021	W21.255/NWMO21.10.039
The Netherlands	NL10002-van de Donk	17 Dec 2021	W21.255/NWMO21.10.039

SUPPLEMENTARY FIGURES

Fig. S1 Propensity score distributions for unadjusted and ATT-adjusted analysis (a) and standardized mean difference plots before and after ATT weighting[a] (b) in patients naïve to T-cell redirection therapy in the fully adjusted analysis



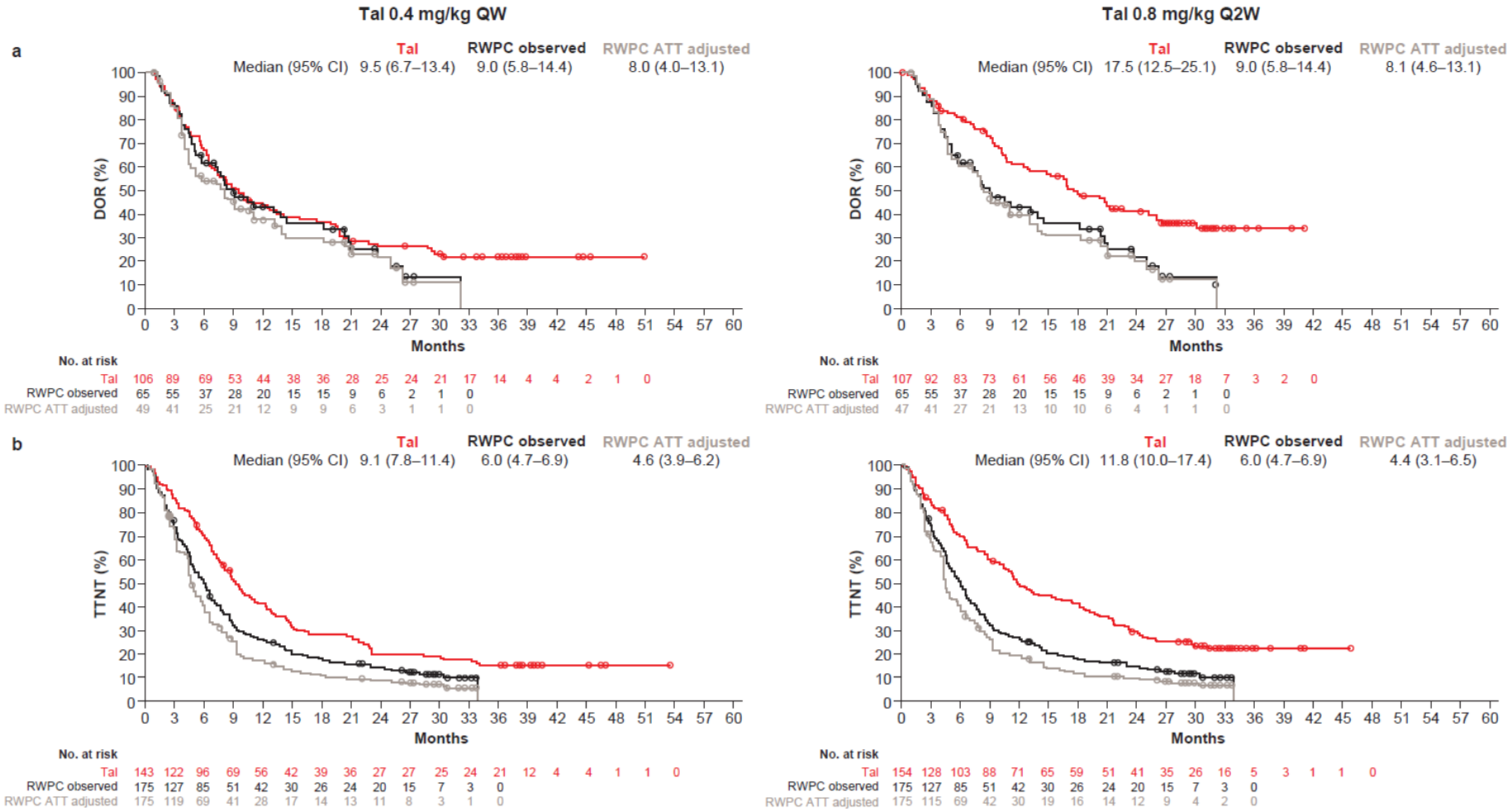


ATT average treatment effect in the treated population, *ECOG PS* Eastern Cooperative Oncology Group performance status, *EMD* extramedullary disease, *ISS* International Staging System, *LDH* lactate dehydrogenase, *MM* multiple myeloma, *mo* months, *RWPC* real world physician's choice, *Q2W* every other week, *QW* weekly, *RWPC* real-world physician's choice of treatment, *Tal* talquetamab

[a]Main analysis adjusted for refractory status, ISS stage, time to progression on last regimen, extramedullary plasmacytomas, number of previous LOTs, years since MM diagnosis, average duration of previous lines, age, hemoglobin levels, LDH levels, creatinine clearance, ECOG PS, sex, type of MM, and previous hematopoietic stem cell transplant

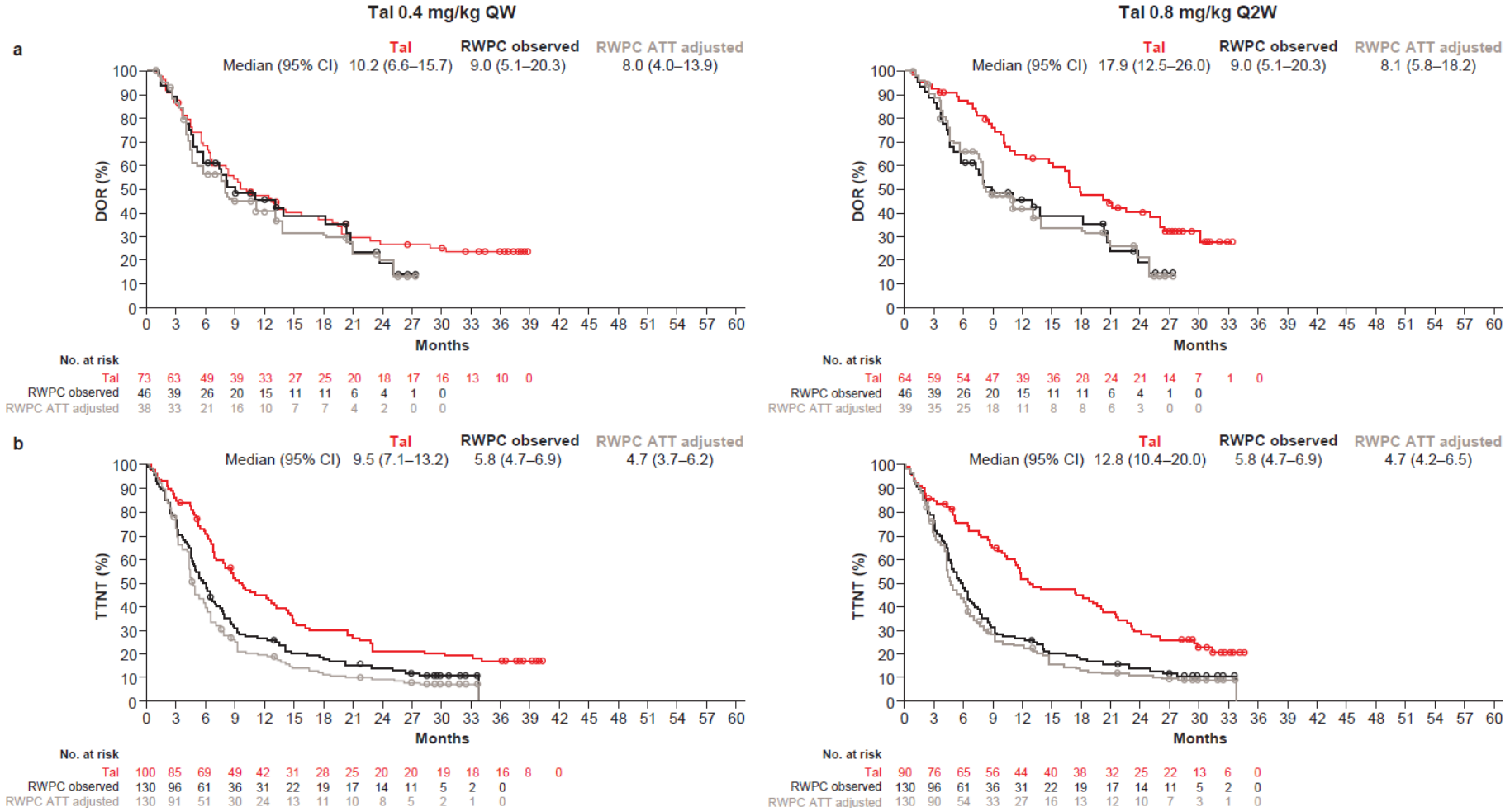
Originally presented at EHA2025 and published in the EHA2025 Abstract Book.

Fig. S2 Observed and ATT-adjusted Kaplan–Meier curves for a) DOR and b) TTNT in patients naïve to T-cell redirection therapy



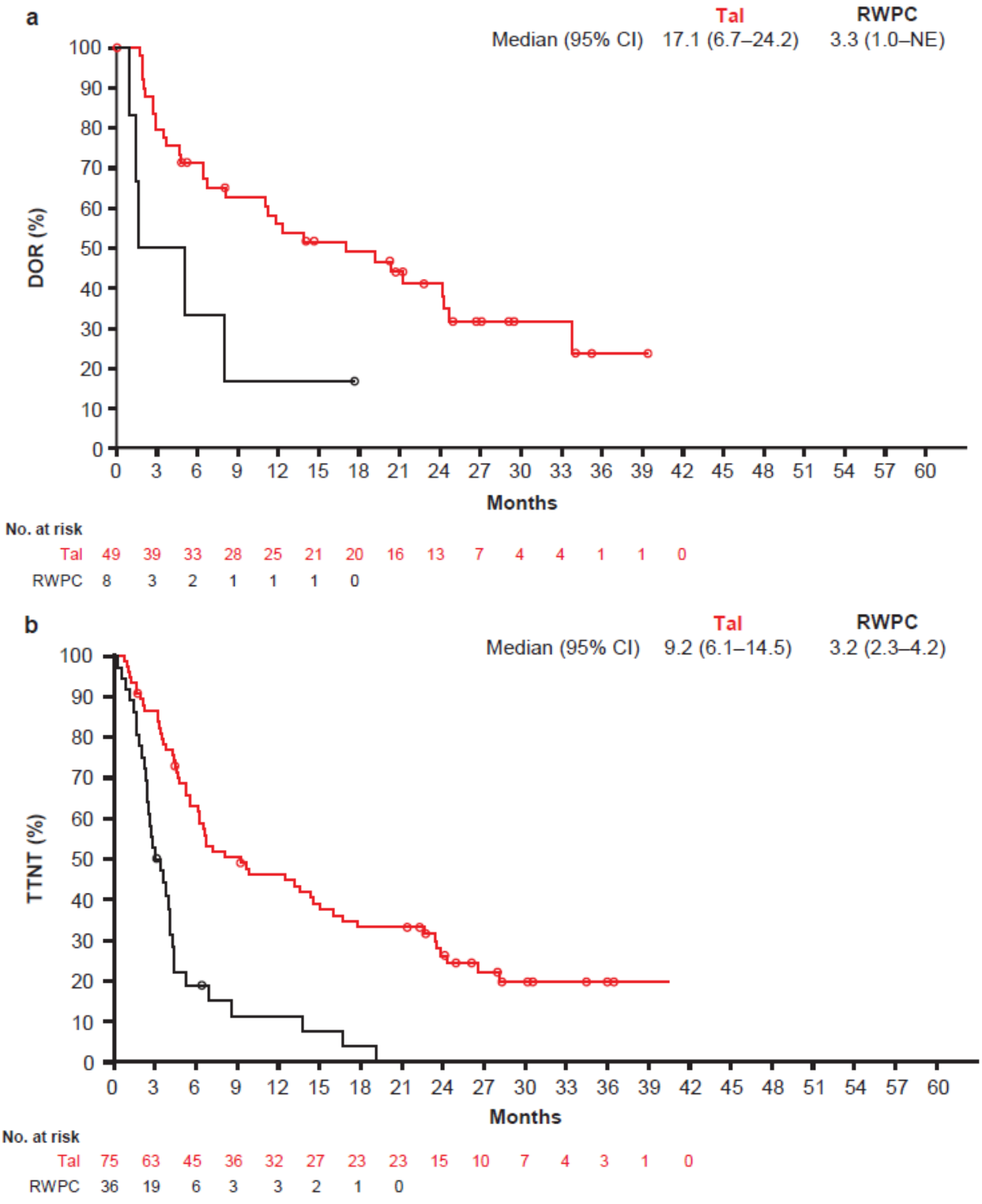
ATT average treatment effect in the treated, *CI* confidence interval, *DOR* duration of response, *Q2W* every other week, *QW* weekly, *RWPC* real-world physician's choice of treatment, *TTNT* time to next treatment

Fig. S3 Observed and ATT-adjusted Kaplan–Meier curves for a) DOR and b) TTNT in the USPI-aligned patient subgroup (≥ 4 prior lines of therapy and phase 2 only) in patients naïve to T-cell redirection therapy



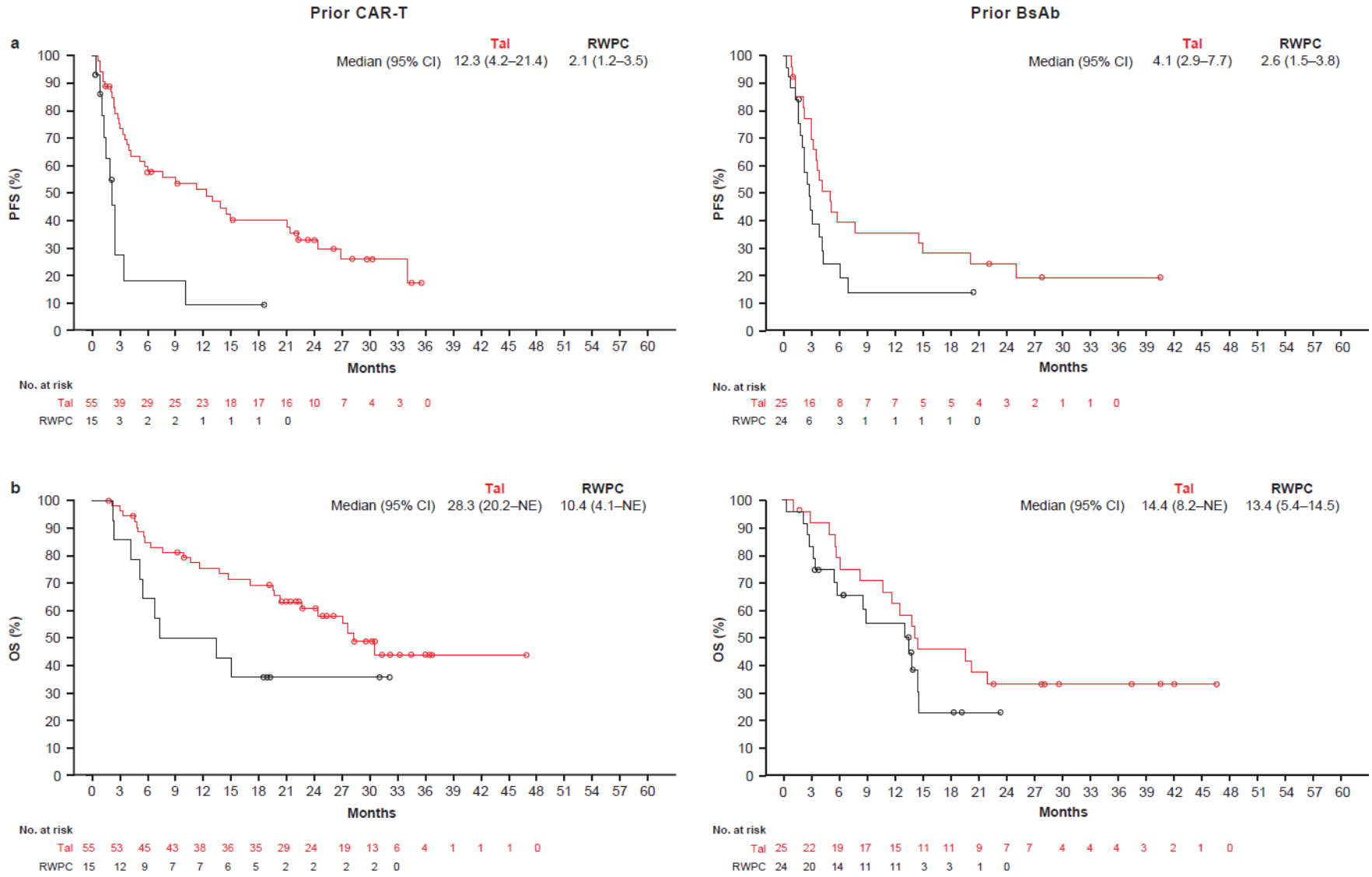
ATT average treatment effect in the treated, *CI* confidence interval, *DOR* duration of response, *Q2W* every other week, *QW* weekly, *TTNT* time to next treatment, *RWPC* real-world physician's choice of treatment, *USPI* US prescribing information

Fig. S4 Kaplan–Meier curves for a) DOR and b) TTNT in patients with prior T-cell redirection therapy



CI confidence interval, *DOR* duration of response, *NE* not evaluable, *RWPC* real-world physician's choice of treatment, *TTNT* time to next treatment

Fig. S5 Kaplan–Meier curves for a) PFS and b) OS in patients with prior CAR-T and with bispecific antibody therapy



CAR-T chimeric antigen receptor T-cell, *CI* confidence interval, *NE* not evaluable, *OS* overall survival, *PFS* progression-free survival, *RWPC* real-world physician's choice of treatment

SUPPLEMENTARY REFERENCES

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