PS1737

Updated Comparative Effectiveness of Talquetamab vs Real-World Physician's Choice of Treatment in LocoMMotion and MoMMent for Patients With Triple-Class Exposed Relapsed/Refractory Multiple Myeloma

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Key Takeaway

With longer follow-up, Tal QW and Q2W continued to show superior efficacy vs RWPC, demonstrating its clinical benefit in patients with TCE RRMM

Conclusions

Patients treated with Tal were significantly more likely to achieve clinical responses, especially deep responses, and had significantly improved PFS, TTNT, and OS vs patients receiving RWPC in contemporary, prospective, real-world studies

Outcomes of Tal vs RWPC were consistent in the USPI-aligned patient population (≥4 prior LOT), demonstrating effectiveness of Tal in a heavily pretreated patient population

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Poster

Supplementary material

https://www.congresshub.com/EHA2025/Oncology/Talquetamab/Einsele

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Introduction

- Talquetamab (Tal) is the first G protein–coupled receptor class C group 5 member D (GPRC5D)-targeting bispecific antibody (BsAb) approved for triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM) based on the MonumenTAL-1 study (NCT03399799/NCT04634552)[1-3]
- LocoMMotion (NCT04035226) and MoMMent (NCT05160584) are prospective, noninterventional, observational studies characterizing real-world physician's choice of treatment (RWPC) in patients with TCE RRMM[4,5]
- Previous adjusted comparisons showed superior efficacy of Tal vs RWPC in patients with TCE RRMM[6,7]

We report an updated adjusted comparison of Tal vs RWPC in patients with TCE RRMM with longer follow-up in MonumenTAL-1 and MoMMent

Methods

Data sources
- MonumenTAL-1 IPD, data cut-off, Sept 2024:
  - SC Tal 0.4 mg/kg QW (n=143; mFU, 38.2 mo)
  - SC Tal 0.8 mg/kg Q2W (n=154; mFU, 31.2 mo)
- LocoMMotion/MoMMent IPD meeting MonumenTAL-1 key eligibility criteria (n=175):
  - LocoMMotion: final data, data cut-off, Oct 2022; mFU, 26.4 mo
  - MoMMent: data cut-off, Aug 2024; mFU, 27.1 mo

MonumenTAL-1 key eligibility criteria
- TCE RRMM
- ≥3 LOT
- Progression ≤12 mo after last LOT
- No prior T-cell redirection therapy (chimeric antigen receptor-T or BsAb)
- Eastern Cooperative Oncology Group performance status ≤2
- Hemoglobin ≥8 g/dL
- Creatinine clearance ≥40 mL/min/1.73 m^2

Adjusted treatment comparison
- Analysis: inverse probability of weighting with ATT weights[a] to adjust for baseline characteristic imbalances; balance after adjustment assessed using SMDs[b]
- Outcomes assessed: ORR, ≥VGPR, ≥CR, DOR, PFS, TTNT, and OS

Statistical analysis
- Binary outcomes: weighted logistic regression estimated odds ratios and response ratios with 95% CIs
- Time-to-event outcomes: weighted Cox proportional hazards model estimated HRs and 95% CIs
- Sensitivity analyses: evaluated impact of alternative statistical methods and variable adjustment
- Subgroup analysis: evaluated USPI-aligned population of patients with ≥4 prior LOT

[a]The IPTW-ATT approach involved a multivariable logistic regression propensity score model to transform important prognostic baseline factors to ATT weights to balance cohorts.[7] [b]SMDs >0.25 indicate important differences between cohorts. ATT, average treatment effect in the treated; CR, complete response; DOR, duration of response; HR, hazard ratio; IPD, individual patient data; LOT, line of therapy; mFU, median follow-up; ORR, overall response rate; PFS, progression-free survival; Q2W, every other week; QW, weekly; SC, subcutaneous; SMD, standardized mean difference; TTNT, time to next treatment; USPI, US prescribing information; VGPR, very good partial response.

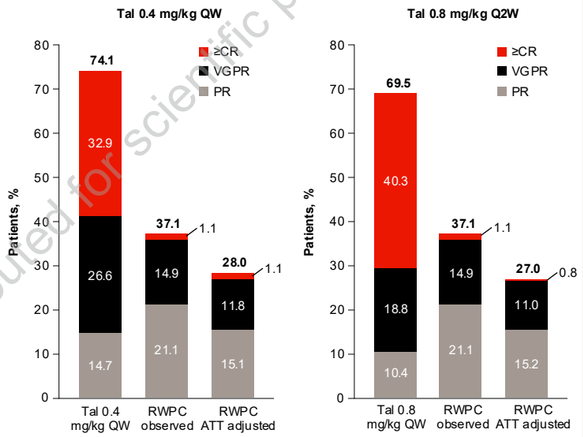
Results

After weighting, the RWPC cohort was well balanced vs Tal cohorts, with all SMDs <0.22 (Supplemental Figures 1 and 2). Most common therapies in the RWPC cohort are shown in the Supplemental Table

Table 1: Patients treated with Tal QW and Q2W had superior outcomes across all endpoints vs patients treated with RWPC. Results were consistent across all sensitivity analyses

Outcome	Tal 0.4 mg/kg QW vs RWPC		Tal 0.8 mg/kg Q2W vs RWPC	
	Response ratio (95% CI)	*P* value	Response ratio (95% CI)	*P* value
ORR	2.64 (1.90–3.69)	<0.0001	2.58 (1.79–3.72)	<0.0001
≥VGPR	4.61 (2.76–7.70)	<0.0001	5.01 (3.06–8.20)	<0.0001
≥CR	30.81 (7.39–128.47)	<0.0001	52.22 (12.52–217.78)	<0.0001
	HR (95% CI)	***P* value**	**HR (95% CI)**	***P* value**
DOR	0.77 (0.51–1.16)	0.2081	0.52 (0.35–0.77)	0.0011
PFS	0.54 (0.40–0.72)	<0.0001	0.47 (0.35–0.63)	<0.0001
TTNT	0.52 (0.40–0.68)	<0.0001	0.46 (0.35–0.60)	<0.0001
OS	0.39 (0.28–0.55)	<0.0001	0.35 (0.24–0.52)	<0.0001

Figure 1: ATT-adjusted ORRs were more than 40% higher with Tal QW and Q2W vs RWPC



PR, partial response.

Figure 2: Significantly improved PFS (top) and OS (bottom) in patients treated with Tal vs RWPC

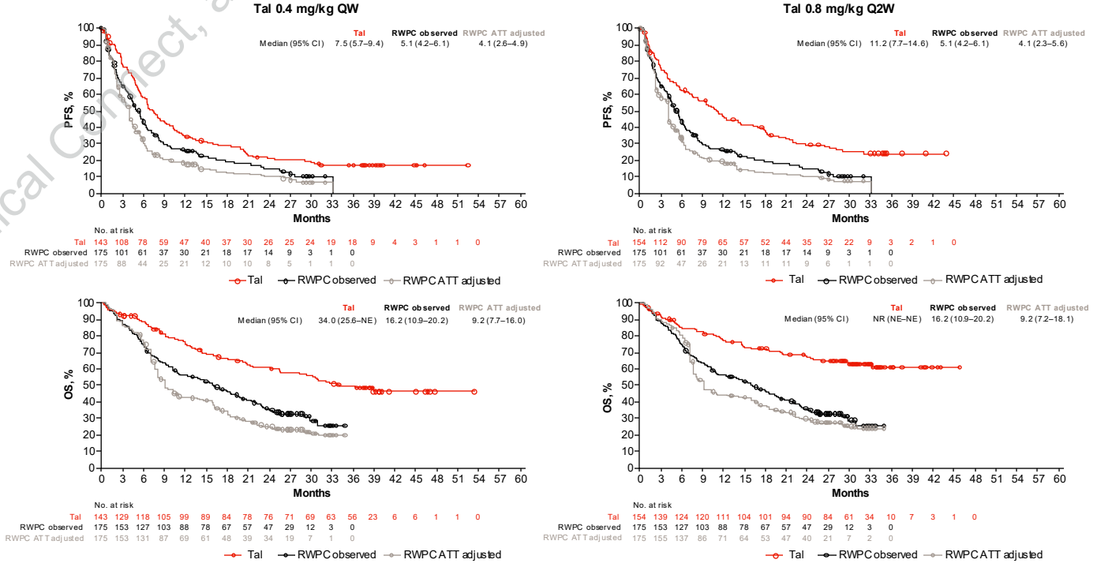


Table 2: Superior treatment outcomes with Tal vs RWPC were also observed in the subgroup analysis of the USPI-aligned patient population (≥4 prior LOT)

Outcome[a]	Tal 0.4 mg/kg QW vs RWPC in USPI-aligned population		Tal 0.8 mg/kg Q2W vs RWPC in USPI-aligned population	
	Rate, %	Response ratio (95% CI)	Rate, %	Response ratio (95% CI)
ORR	73.0 vs 29.4	2.48 (1.71–3.59); *P*<0.0001	71.1 vs 30.0	2.37 (1.64–3.43); *P*<0.0001
≥VGPR	57.0 vs 14.3	3.99 (2.21–7.20); *P*<0.0001	61.1 vs 13.9	4.39 (2.57–7.51); *P*<0.0001
	Median, mo (95% CI)	**HR (95% CI)**	**Median, mo (95% CI)**	**HR (95% CI)**
DOR	10.2 (6.6–15.7) vs 8.0 (4.0–13.9)	0.79 (0.47–1.33); *P*=0.3727	17.9 (12.5–26.0) vs 8.1 (5.8–18.2)	0.52 (0.31–0.87); *P*=0.0127
PFS	6.8 (5.5–10.4) vs 4.1 (2.7–5.6)	0.59 (0.42–0.84); *P*=0.0036	12.4 (9.6–18.2) vs 4.5 (2.9–6.5)	0.50 (0.35–0.71); *P*=0.0001
TTNT	9.5 (7.1–13.2) vs 4.7 (3.7–6.2)	0.51 (0.37–0.70); *P*<0.0001	12.8 (10.4–20.0) vs 4.7 (4.2–6.5)	0.47 (0.34–0.66); *P*<0.0001
OS	NR (21.7–NE) vs 9.2 (7.2–16.4)	0.39 (0.27–0.59); *P*<0.0001	NR (33.2–NE) vs 9.2 (7.2–17.9)	0.34 (0.22–0.53); *P*<0.0001

Data for talquetamab are reported from phase 2 only in patients with ≥4 prior LOT, consistent with the USPI.
[a]No patients had a ≥CR in the RWPC cohort. mo, month; NE, not evaluable; NR, not reached.

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Multiple Myeloma

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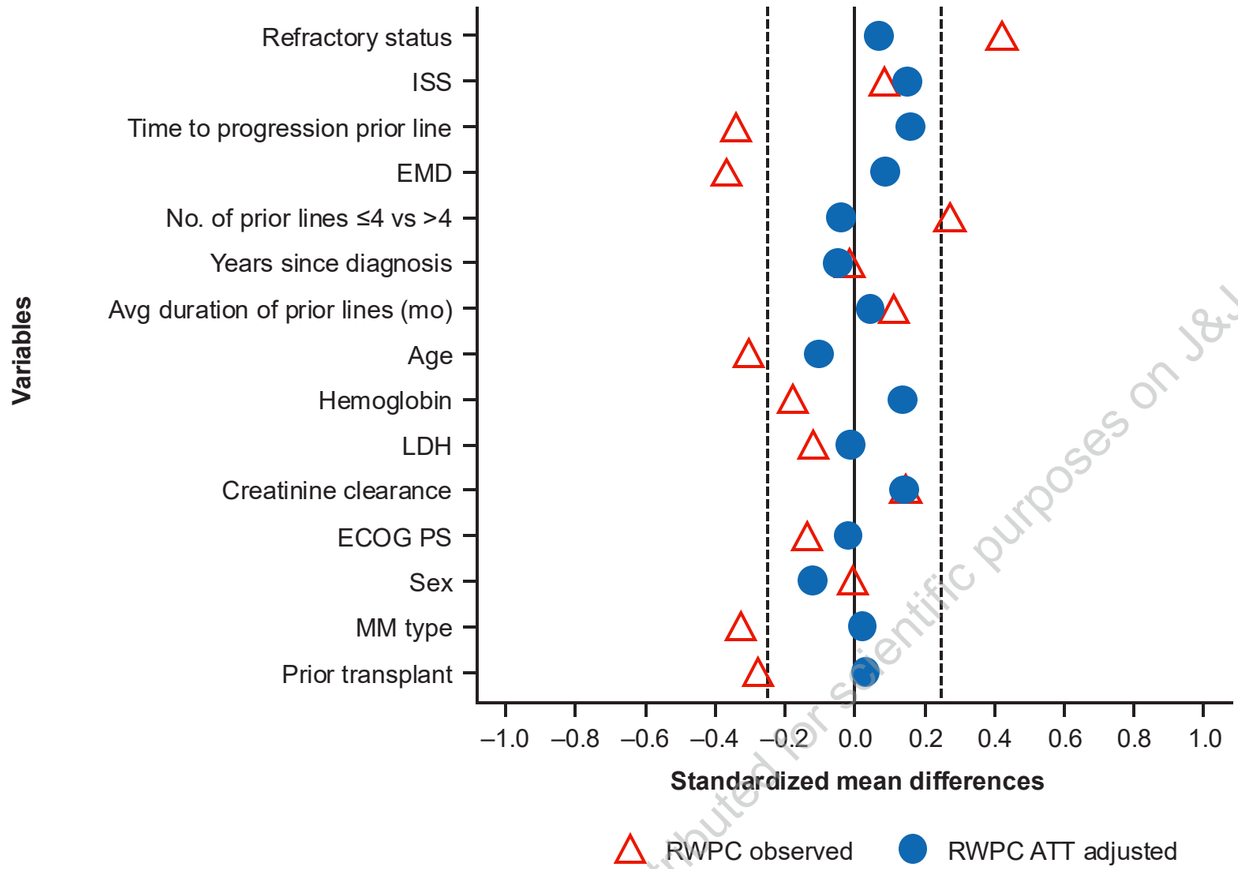
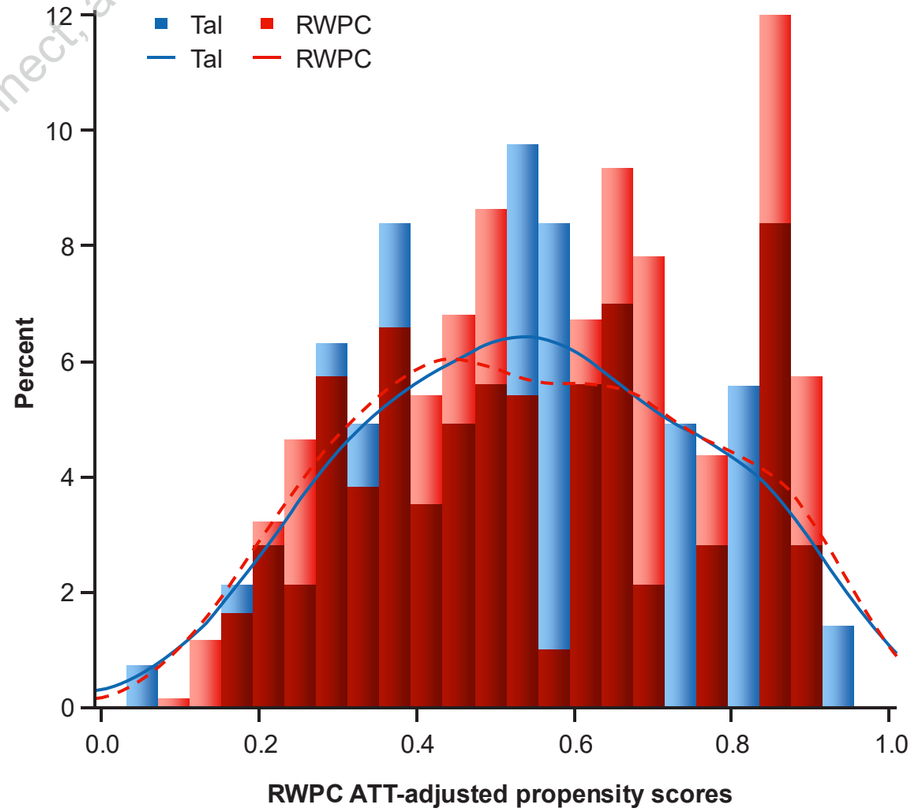
Supplemental Table: Treatment Regimens in the RWPC Cohort

Treatment regimen[a]	Frequency, n (%) (N=175[b])
Cyclophosphamide, pomalidomide, dexamethasone	29 (16.6)
Pomalidomide, dexamethasone	20 (11.4)
Carfilzomib, dexamethasone	17 (9.7)
Belantamab mafodotin	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)

[a]Only treatments used in ≥3 patients are presented. [b]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.

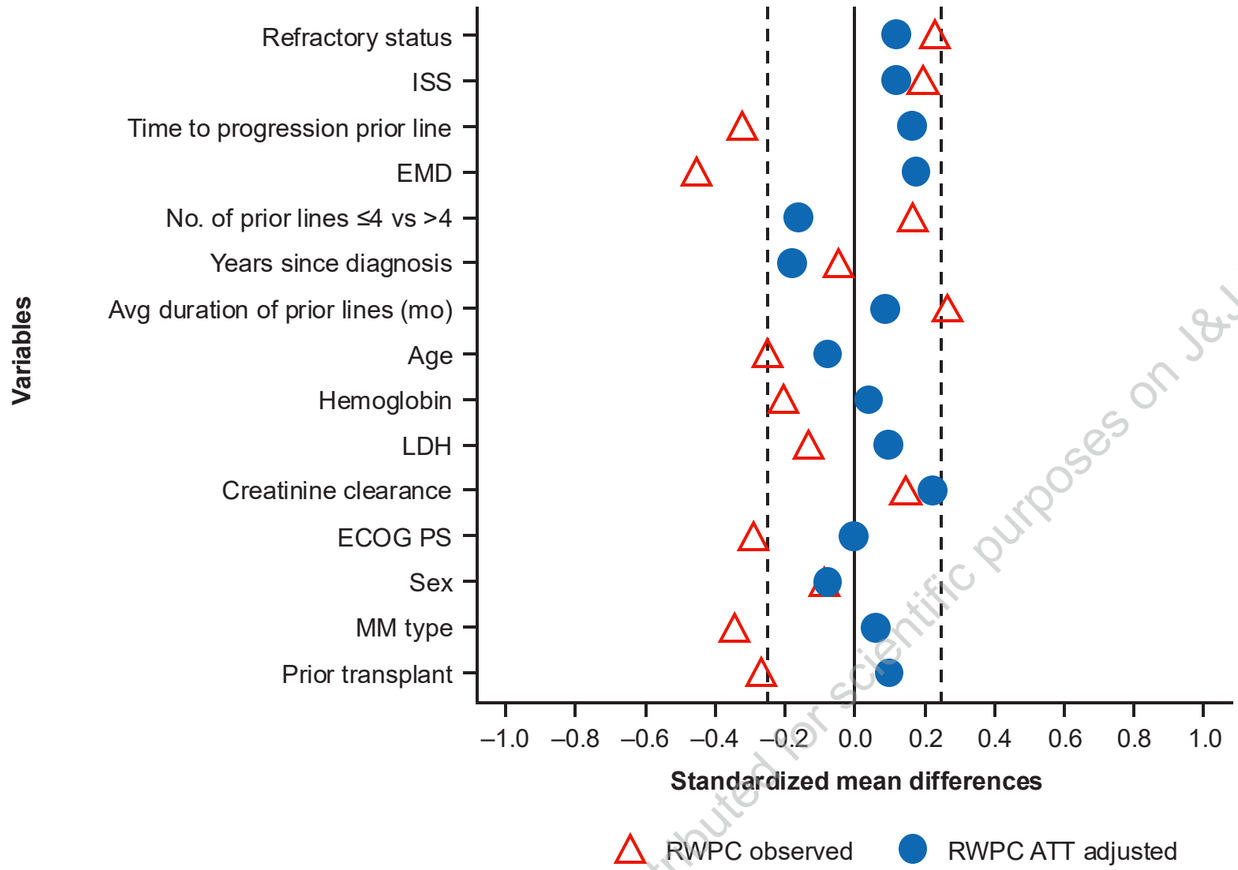
Supplemental Figure 1: SMD Plot and Distribution of Propensity Scores Before and After Adjustment in Tal 0.4 mg/kg QW Cohort

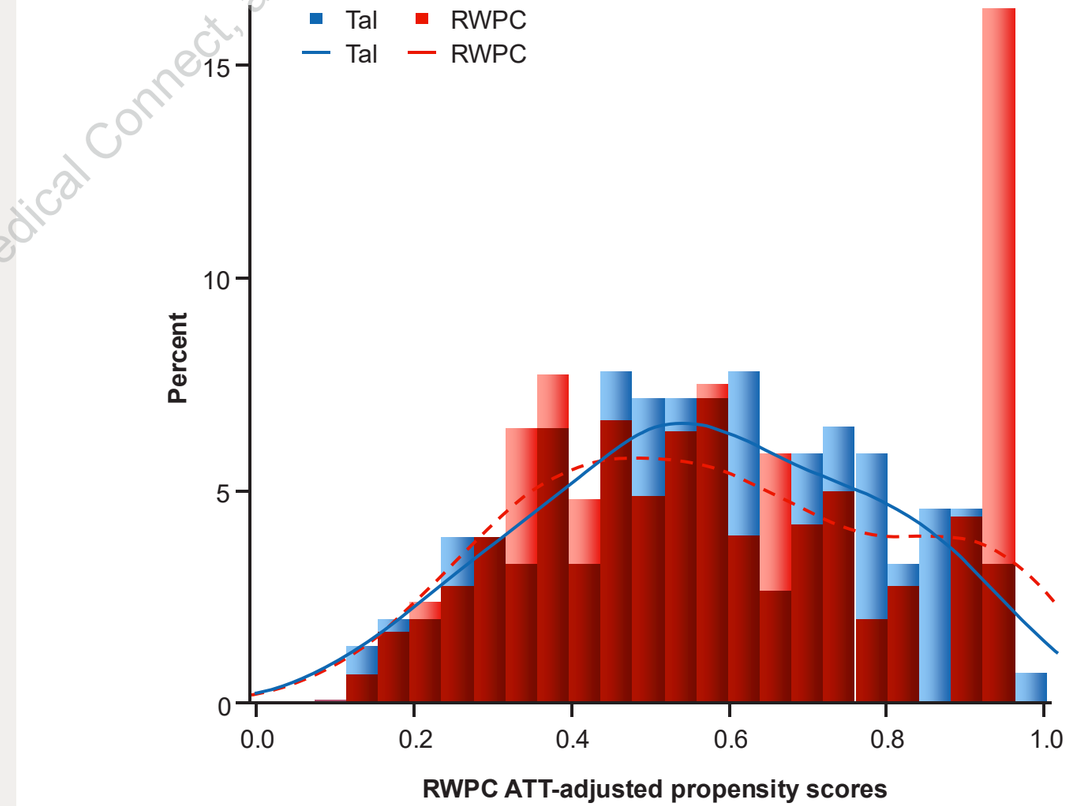




ATT, average treatment effect in the treated; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EMD, extramedullary disease; ISS, International Staging System; LDH, lactate dehydrogenase; MM, multiple myeloma; mo, month; RWPC, real-world physician's choice of treatment; SMD, standardized mean difference; Tal, talquetamab.

Supplemental Figure 2: SMD Plot and Distribution of Propensity Scores Before and After Adjustment in Tal 0.8 mg/kg Q2W Cohort





ATT, average treatment effect in the treated; ECOG, Eastern Cooperative Oncology Group Performance Status; EMD, extramedullary disease; ISS, International Staging System; LDH, lactate dehydrogenase; MM, multiple myeloma; mo, month; RWPC, real-world physician's choice of treatment; SMD, standardized mean difference; Tal, talquetamab.