PA-061

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

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Key Takeaway

With longer follow-up, Tal continued to demonstrate superior effectiveness, especially with the Q2W dosing schedule vs RWPC, demonstrating its clinical benefit in patients with TCE RRMM

Conclusions

- Patients treated with Tal QW and Q2W had significantly improved PFS, TTNT, and OS compared with patients treated with RWPC
- Efficacy outcomes of Tal vs RWPC were consistent in the USPI-aligned patient population (≥4 prior LOT), highlighting the effectiveness of Tal in heavily pretreated patients
- Clinical trials in earlier treatment lines are ongoing to evaluate the clinical benefit of Tal as part of combination therapy

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Poster

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Introduction

- Talquetamab (Tal), a G protein–coupled receptor class C group 5 member D (GPRC5D)-targeting bispecific antibody, is approved for the treatment of triple class exposed (TCE) relapsed/refractory multiple myeloma (RRMM) based on results from the MonumenTAL-1 study (NCT03399799/NCT04634552)[1-4]
- The US-based deidentified electronic health record-derived Flatiron Health Research Database[5] Multiple Myeloma cohort study (Flatiron) evaluated real-world physician's choice of treatment (RWPC) in patients with TCE RRMM
- A previous indirect treatment comparison showed improved efficacy outcomes with Tal vs RWPC[6]

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

Methods

Data sources

- MonumenTAL-1 patient-level data, 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)
- External control arm from the research database (data cut-off from Feb 2016 to July 2022 with follow-up until Oct 2024) for patients who met key MonumenTAL-1 eligibility criteria (N=1169[a]; mFU, 39.2 mo)

MonumenTAL-1 key eligibility criteria

- TCE RRMM
- ≥3 prior LOT
- Progression ≤12 mo after last LOT
- No prior T-cell redirection therapy (chimeric antigen receptor-T or bispecific antibody)
- Eastern Cooperative Oncology Group performance status ≤2
- Hemoglobin ≥8 g/dL
- Estimated glomerular filtration rate ≥40 mL/min/1.73 m^2

Adjusted treatment comparison

- Analysis: IPTW-ATT weights[7] to adjust for baseline characteristic imbalances; balance after adjustment assessed using SMDs[c]
- Outcomes assessed: PFS, TTNT, and OS

Statistical analysis

- Time-to-event outcomes: weighted Cox proportional hazards model estimated HRs and 95% CIs, and weighted Kaplan-Meier method estimated medians with 95% CIs
- Sensitivity analyses evaluated impact of alternative statistical methods and variable adjustment
- Subgroup analysis evaluated USPI-aligned population of phase 2 patients with ≥4 prior LOT

[a]629 patients with a total of 1169 eligible LOT. [b]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] [c]SMDs >0.2 indicate substantial differences between cohorts. ATT, average treatment effect in the treated; HR, hazard ratio; IPTW, inverse probability of treatment weighting; LOT, line of therapy; mFU, median follow-up; mo, month; OS, overall survival; PFS, progression-free survival; Q2W, every other week; QW, weekly; SC, subcutaneous; SMD, standardized mean difference; TTNT, time to next treatment; USPI, United States Prescribing Information.

Results

After reweighting, baseline characteristics were balanced between the RWPC and Tal cohorts, with all SMDs <0.1

Table 1: Most common treatment regimens in the RWPC cohort

Treatment regimen[a]	Frequency, n (%) (N=1169[b])
Daratumumab (±hyaluronidase-fihj), pomalidomide, dexamethasone	62 (5.3)
Elotuzumab, pomalidomide, dexamethasone	56 (4.8)
Clinical study drug[c]	43 (3.7)
Carfilzomib, dexamethasone	42 (3.6)
Carfilzomib, cyclophosphamide, dexamethasone	36 (3.1)
Carfilzomib, pomalidomide, dexamethasone	32 (2.7)
Daratumumab (±hyaluronidase-fihj), carfilzomib, dexamethasone	27 (2.3)
Belantamab mafodotin-blmf	23 (2.0)
Bortezomib, selinexor, dexamethasone	23 (2.0)
Elotuzumab, lenalidomide, dexamethasone	22 (1.9)
Daratumumab, dexamethasone	21 (1.8)
Selinexor, dexamethasone	21 (1.8)
Daratumumab, lenalidomide, dexamethasone	19 (1.6)
Pomalidomide, dexamethasone	19 (1.6)
Clinical study drug[c], dexamethasone	18 (1.5)
Daratumumab, bortezomib, dexamethasone	18 (1.5)

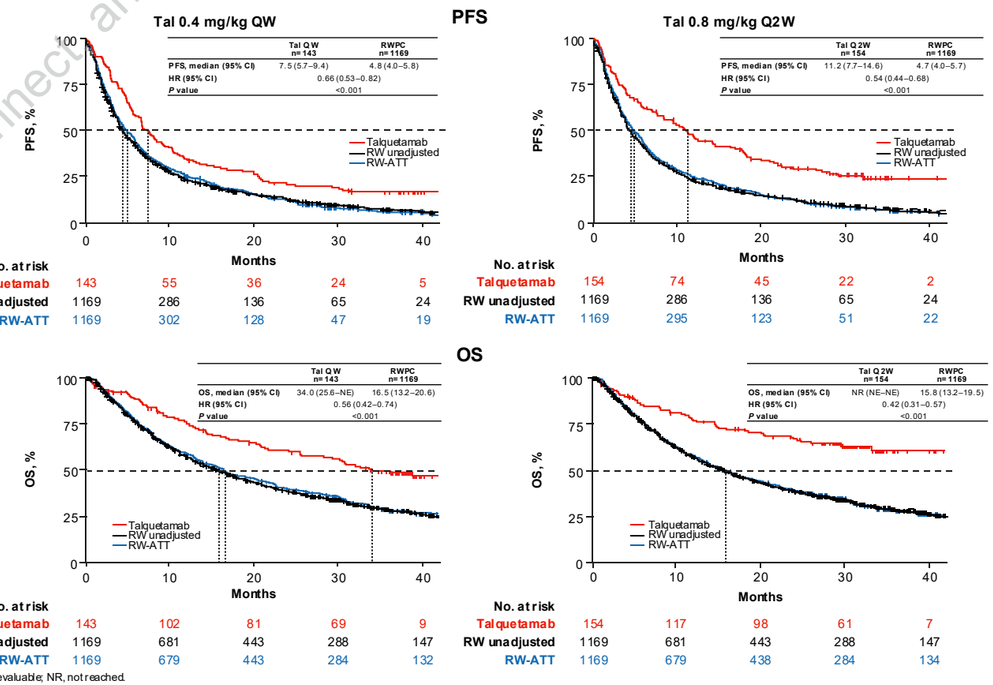
[a]Only treatments used in ≥18 patients are presented. [b]629 patients with 1169 eligible LOT. Percentages are calculated with the number of eligible LOT in the all-treated analysis set as denominator (N=1169). Patients can be counted in ≥1 regimen if they have received ≥1 combination in their treatment before progression or death. [c]Details on the specific drug(s) being used in the context of a clinical trial were unavailable in the research database.

Table 2: Patients treated with Tal QW and Q2W showed significantly improved efficacy outcomes vs patients treated with RWPC. Results were generally consistent across all sensitivity analyses

Outcome	Tal 0.4 mg/kg QW vs RWPC			Tal 0.8 mg/kg Q2W vs RWPC		
	Median, mo	HR (95% CI)	*P* value	Median, mo	HR (95% CI)	*P* value
PFS						
Primary analysis	7.5 vs 4.8	0.66 (0.53–0.82)	<0.001	11.2 vs 4.7	0.54 (0.44–0.68)	<0.001
Fully adjusted analysis	7.5 vs 4.7	0.70 (0.54–0.90)	0.005	11.2 vs 4.6	0.58 (0.46–0.73)	<0.001
TTNT						
Primary analysis	9.1 vs 5.1	0.57 (0.47–0.69)	<0.001	11.8 vs 5.1	0.49 (0.40–0.60)	<0.001
Fully adjusted analysis	9.1 vs 5.1	0.59 (0.48–0.73)	<0.001	11.8 vs 5.1	0.51 (0.42–0.63)	<0.001
OS						
Primary analysis	34.0 vs 16.5	0.56 (0.42–0.74)	<0.001	NR vs 15.8	0.42 (0.31–0.57)	<0.001
Fully adjusted analysis	34.0 vs 17.9	0.60 (0.44–0.81)	0.001	NR vs 17.1	0.45 (0.33–0.61)	<0.001

NR, not reached.

Figure 1: Significantly improved PFS (top) and OS (bottom) in patients treated with Tal vs patients treated with RWPC



NE, not evaluable; NR, not reached.

Table 3: Among the USPI-aligned subgroup of patients with ≥4 prior LOT, superior treatment outcomes with Tal vs RWPC were also observed

Outcome	Tal 0.4 mg/kg QW vs RWPC			Tal 0.8 mg/kg Q2W vs RWPC		
	Median, mo	HR (95% CI)	*P* value	Median, mo	HR (95% CI)	*P* value
PFS						
Primary analysis	6.8 vs 4.4	0.62 (0.47–0.81)	<0.001	12.4 vs 4.4	0.48 (0.37–0.63)	<0.001
Fully adjusted analysis	6.8 vs 4.4	0.66 (0.48–0.91)	0.012	12.4 vs 4.3	0.49 (0.37–0.65)	<0.001
TTNT						
Primary analysis	9.5 vs 5.1	0.54 (0.42–0.69)	<0.001	12.8 vs 4.9	0.46 (0.36–0.59)	<0.001
Fully adjusted analysis	9.5 vs 5.2	0.57 (0.44–0.75)	<0.001	12.8 vs 5.0	0.46 (0.35–0.59)	<0.001
OS						
Primary analysis	NR vs 16.5	0.50 (0.35–0.71)	<0.001	NR vs 15.7	0.39 (0.27–0.58)	<0.001
Fully adjusted analysis	NR vs 17.0	0.55 (0.37–0.80)	0.002	NR vs 16.5	0.41 (0.27–0.61)	<0.001

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Multiple Myeloma

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