

Talquetamab Versus Belgian Real-World Clinical Practice in Triple-Class Exposed and Refractory Multiple Myeloma Patients Using Adjusted Comparison

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Key Takeaway



Talquetamab was associated with significantly superior efficacy compared with treatments administered in RWCP in Belgian patients with TCE RRMM for each measure of clinical efficacy

Conclusions



Talquetamab demonstrates significant clinical benefits vs currently available treatments in RWCP and should be considered as a novel and effective treatment option for patients with TCE RRMM



Results were consistent across sensitivity analyses and are in line with previous indirect comparisons vs other RWCP cohorts¹⁰⁻¹²

Introduction

- Patients with relapsed/refractory multiple myeloma (RRMM) who are triple-class exposed (TCE) have a poor prognosis and limited treatment options,^{1,2} with recently introduced B-cell maturation antigen-targeting agents now expanding available options³⁻⁶
- Talquetamab is the first and only approved bispecific antibody targeting the novel antigen G protein-coupled receptor class C group 5 member D (GPC5D) and CD3 for the treatment of patients with RRMM^{7,8}
- In the phase 1/2 MonumentAL-1 trial (NCT03399799/NCT04634552), talquetamab 0.4 mg/kg weekly (QW) and 0.8 mg/kg every other week (Q2W) demonstrated deep and durable responses at 29.8 and 23.4 months median follow-up, respectively⁹:
 - Overall response rate (ORR) was 74.1% and 69.5%, with complete response or better in 32.9% and 40.3%
 - Median progression-free survival (PFS) was 7.5 and 11.2 months
 - Median duration of response was 9.5 and 17.5 months
- We assessed the relative efficacy of talquetamab vs Belgian real-world clinical practice (RWCP) using individual patient data from MonumentAL-1 and Belgium Comparator study in Multiple Myeloma (BELCOMM), a retrospective patient cohort from 7 academic and non-academic centers in Belgium

Methods

Data sources

- Patients treated with talquetamab in MonumentAL-1 were compared with an external control arm of patients with TCE RRMM treated with RWCP therapies from the BELCOMM cohort (Figure 1) to assess the comparative efficacy of talquetamab
 - Patients had an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 , had received ≥ 3 prior lines of therapy (LOT), and had ≥ 1 subsequent active multiple myeloma (MM) therapy after becoming TCE
 - Patients with multiple LOT initiated after fulfilling the inclusion criteria contributed multiple times to the analyses
 - Safety data were not collected or included in the present analyses

Figure 1: Summary of studies for comparison

MonumentAL-1		BELCOMM
Talquetamab 0.4 mg/kg QW SC N=143 Data cut-off Jan 17, 2023	Talquetamab 0.8 mg/kg Q2W SC N=145 Data cut-off Jan 17, 2023	RWCP 268 LOT N=123 Data collected March 2017 – May 2021

SC, subcutaneous.

Statistical analyses

- Inverse probability weighting was used to adjust for imbalances in baseline covariates, estimating the average treatment effect in the treated population (ATT) in the main analysis:
 - Age
 - Sex
 - Lactate dehydrogenase
 - Hemoglobin
 - Albumin
 - Refractory status
 - Extramedullary disease
 - Years since MM diagnosis
 - Number of prior LOT
 - Average duration of prior LOT
 - Time to progression on last regimen
- Sensitivity analyses also included MM type, cytogenetic risk, and ECOG performance status in addition to the main analysis variables
- Standardized mean differences were used to evaluate the balance of baseline characteristics between study cohorts
- Comparative efficacy of talquetamab vs RWCP was estimated for ORR, very good partial response rate or better (\geq VGPR), PFS, time to next treatment (TTNT), and overall survival (OS)
 - For binary endpoints (ORR and \geq VGPR), weighted logistic regression was used to estimate the relative effect of talquetamab vs RWCP with odds ratios (OR) transformed into response-rate ratios (RR) and 95% CIs
 - For time-to-event endpoints (PFS, TTNT, and OS), weighted Cox proportional hazards regression was used to estimate hazard ratios and 95% CIs

Results

Patient population and treatments

- Baseline characteristics were well balanced between MonumentAL-1 and BELCOMM after reweighting the RWCP cohort (Supplemental Tables 1 and 2; available by scanning the QR code below)
- In the BELCOMM cohort, >50 unique treatment regimens were initiated after patients became TCE (Supplemental Table 3)

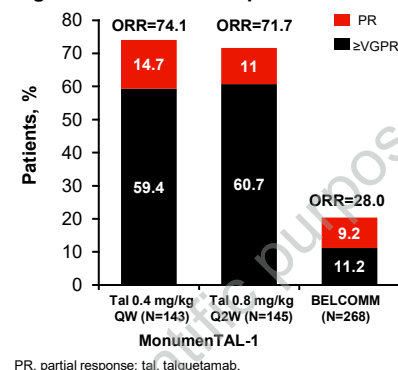
Comparative efficacy

- Patients had significantly better ORR and \geq VGPR rates with talquetamab vs RWCP in the BELCOMM cohort (Figure 2, Tables 1 and 2)
 - Patients were 2.5 and 2.3 times more likely to achieve a response (ORR) when treated with talquetamab 0.4 mg/kg QW SC and 0.8 mg/kg Q2W SC, respectively
 - Patients were 5.3 and 5.4 times more likely to reach \geq VGPR when treated with talquetamab 0.4 mg/kg QW SC and 0.8 mg/kg Q2W SC, respectively
- PFS, TTNT, and OS were significantly longer with talquetamab treatment vs RWCP in the BELCOMM cohort (Figure 3)

Sensitivity analysis

- Results of the sensitivity analyses for response outcomes, PFS, TTNT, and OS were consistent with those of the main analyses

Figure 2: Observed response rates



PR, partial response; tal, talquetamab.

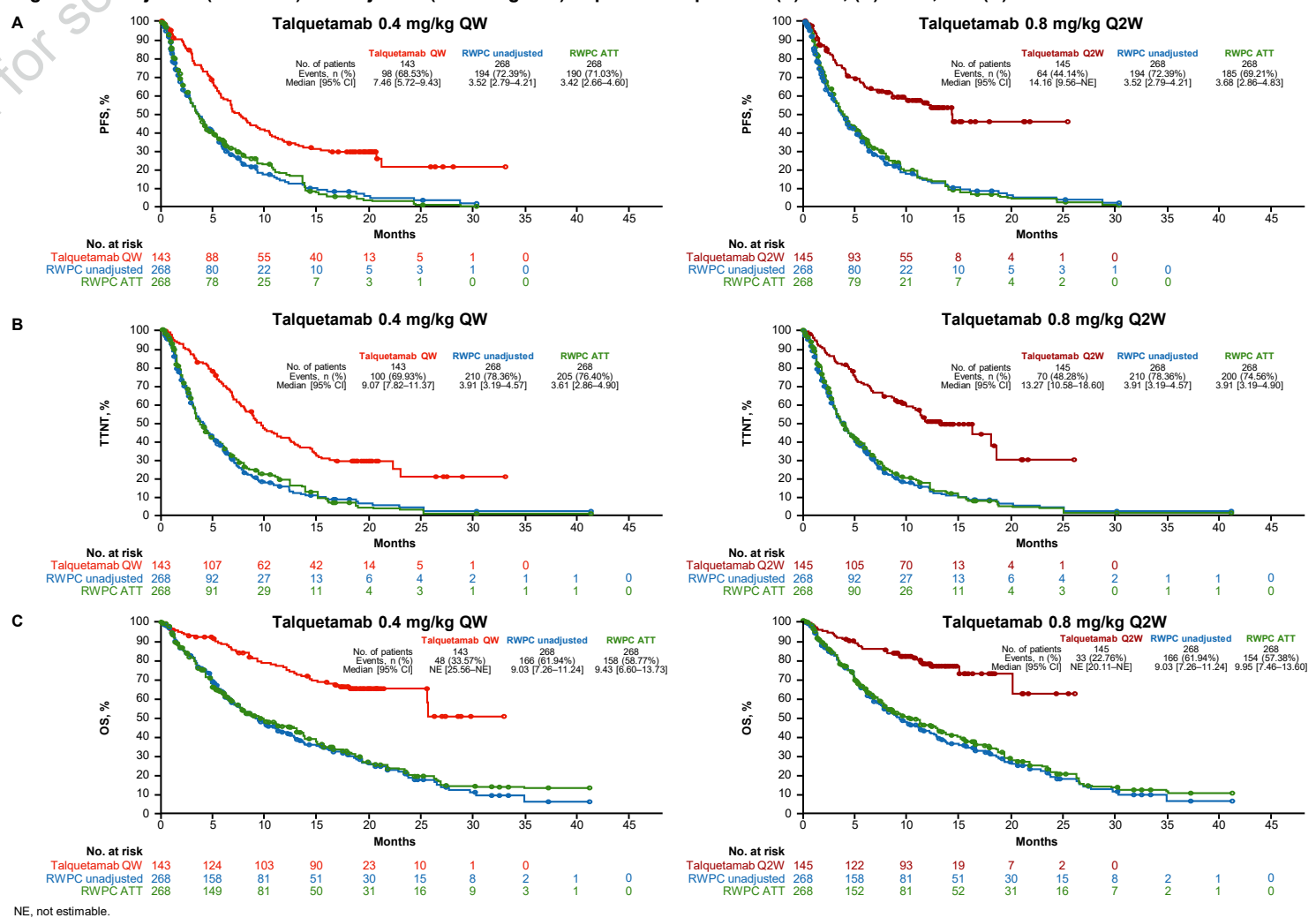
Table 1: Unadjusted (observed) and adjusted (ATT weighted) response outcomes 0.4 mg/kg population

Analysis	Talquetamab vs BELCOMM	
	OR (95% CI)	RR (95% CI)
ORR		
Unadjusted	7.37 (4.66–11.67)	2.65 (1.97–3.56)
Adjusted	6.84 (4.33–10.81)	2.51 (1.88–3.36)
\geqVGPR rate		
Unadjusted	11.63 (7.01–19.28)	5.31 (3.50–8.05)
Adjusted	11.65 (7.02–19.32)	5.32 (3.51–8.07)

Table 2: Unadjusted (observed) and adjusted (ATT weighted) response outcomes 0.8 mg/kg population

Analysis	Talquetamab vs BELCOMM	
	OR (95% CI)	RR (95% CI)
ORR		
Unadjusted	6.53 (4.17–10.23)	2.56 (1.90–3.45)
Adjusted	5.75 (3.68–8.97)	2.34 (1.75–3.13)
\geqVGPR rate		
Unadjusted	12.25 (7.39–20.30)	5.42 (3.58–8.21)
Adjusted	12.24 (7.38–20.28)	5.42 (3.58–8.20)

Figure 3: Unadjusted (observed) and adjusted (ATT weighted) Kaplan-Meier plots for (A) PFS, (B) TTNT, and (C) OS



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Multiple Myeloma

