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Talquetamab Outcomes From Practice Outside of Clinical Trials: The BiTAL study.

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Introduction

- Talquetamab (Tal) is the first bispecific antibody (BsAb) approved by both the FDA and EMA that targets the G-protein-coupled receptor, family C group 5 member D[1,2]. Since commercial availability across different countries, more than 7,700 patients worldwide have been treated with commercial talquetamab[3].
- Tal is intended for patients with relapsed refractory multiple myeloma (RRMM) who have previously received treatment with a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.
- Findings from the MonumenTAL-1 study indicate that Tal offers a new, effective, and manageable treatment option for this challenging patient group[4].
- Gathering real-world data is essential to assess its effectiveness and safety outside the rigorously defined clinical trial environments, helping to inform future enhancements in the clinical application of these therapies.

Aim

- This poster aims to characterize interim safety and effectiveness outcomes in a cohort of TCE RRMM pts who received Tal outside of clinical trials in Spain.

Methods

- This is an ongoing retrospective, non-interventional, observational study conducted currently at 68 Spanish sites at data cut-off (May 2025).
- Adult (≥18 years) patients with TCE RRMM, who had initiated treatment with Tal monotherapy outside clinical trials through PAA in Spain, were included in the study after reviewing for program eligibility based on specified PAA treatment guidelines and after signing an Informed Consent Form (ICF).
- Data were collected from patient medical records, including demographics, disease characteristics, prior therapies, effectiveness, and safety.
- Treatment outcomes were assessed based on response rates, progression free survival (PFS), and overall survival (OS). Responses were evaluated according to International Myeloma Working Group criteria.
- Quantitative variables are described using measures of central tendency and dispersion (mean, standard deviation [SD], median, range [min-max]). Qualitative variables are described using absolute and relative frequencies (N, %).

Results

Clinical and demographic characteristics

- At database cut-off, a total of 163 patients were evaluable and analyzed for this interim analysis. Of these, 129/147 (n/N) (87.8%) received a biweekly initial dosage regimen (Q2W) (**Table 1**), the rest weekly, following SmPC (summary of product characteristics).
- The population was heavily pre-treated with a median of 4 prior lines of therapy.
- Approximately 20-25% of the patients with ECOG ≥2 and Charlson ≥2.
- All patients were triple-class (PI+IMiD+CD38) exposed and refractory, and most (67.8%) were penta-class (2PI+2IMiD+CD38)) exposed **(Table 1**).

Table 1. Patients' demographic and clinical characteristics at talquetamab initiation

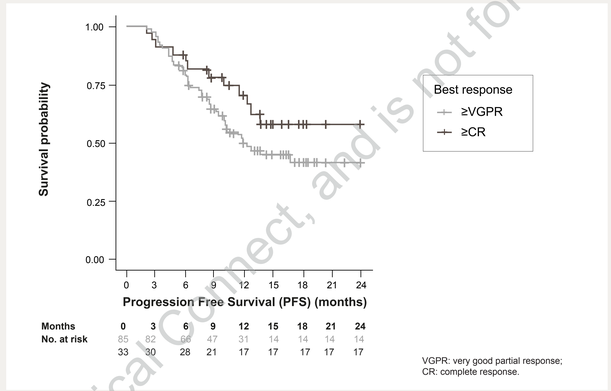
Characteristics	Overall population (N = 163)[a]	Biweekly (Q2W) (N = 129)[a]
Age (years), median (range)	66.0 (40.0-84.0)*	67.0 (40.0-84.0)
65-75 years, n/N (%)	63/153 (41.2)	50 (38.8)
> 75 years, n/N (%)	23/153 (15)	21 (16.3)
Female, n/N (%)	78/154 (50.6)	66 (51.2)
ECOG, n/N (%)		
0-1	104/130 (80.0)	89/110 (80.9)
≥2	26/130 (20)	21/110 (19.1)
Charlson Index, n/N (%)		
0-1	116/152 (76.3)	98 (76.0)
≥2	36/152 (23.7)	31 (24.0)
Frailty[b], n/N (%)		
Fit+Intermediate	81/129 (62.8)	69/110 (62.7)
Frail	48/129 (37.2)	41/110 (37.3)
CRAB, n/N (%)	135/149 (90.6)	114/127 (89.8)
ISS Stage, n/N (%)		
I	37/128 (28.9)	34/108 (31.5)
II	48/128 (37.5)	37/108 (34.3)
III	43/128 (33.6)	37/108 (34.3)
High risk cytogenetics[c], n/N (%)	15/52 (28.8)	15/43 (34.9)
Extramedullary[d] **plasmacytoma**, n/N (%)	22/76 (28.9)	18/63 (28.6)
Creatinine clearance, n/N (%)		
<30 mL/min	13/138 (9.4)	9/117 (7.7)
≥30 to <60 mL/min	27/138 (19.6)	25/117 (21.4)
Patients ineligible for MonumenTAL-1[e], n/N (%)	64/124 (51.6)	50/106 (47.2)
Years since diagnosis, median (range)	5.3 (0.7-25.3)[a]	5.4 (0.7-25.3)[a]
Previous lines of therapy, median (range)	4.0 (1.0-9.0)[§]	4.0 (1.0-9.0)
Triple-class exposed, n/N (%)	152/152 (100)	129/129 (100)
Penta-class exposed, n/N (%)	103/152 (67.8)	85 (65.9)
Triple refractory, n/N (%)	119/119 (100)	102/102 (100)
Penta refractory, n/N (%)	40/139 (28.8)	33/119 (27.7)
Autologous SCT, n/N (%)	110 (67.5)	91 (70.5)
Patients receiving prior BCMA, n/N (%)	54 (33.1)	47 (36.4)
CAR T	6 (3.7)	5 (3.9)
Belantamab	42 (25.8)	39 (30.2)
BCMA BsAbs	6 (3.7)	3 (2.3)

[a]Data available added as denominators (n/N) if some were missing or not available in the clinical chart for the whole cohort. [b]Fragility assessment was performed retrospectively using age, CCI and ECOG PS score, Facon et al. Leukemia 2020;34:224–33. [c]"del(17p)", "t(4;14)" or "t(14;16)". [d]Extramedullary disease was defined exclusively by the presence of extramedullary soft tissue lesions. [e]Main reasons for ineligibility were non-measurable disease, creatinine clearance <40 mL/min and hemoglobin level <8g/dL. ECOG: Eastern Cooperative Oncology Group; ISS: International Staging System; SCT: stem cell transplant; BsAbs: bispecific antibodies; del: deletion; t: translocation. *N=153; [§]N=144; [-]N=126; [‡]N=151.

Efficacy analysis

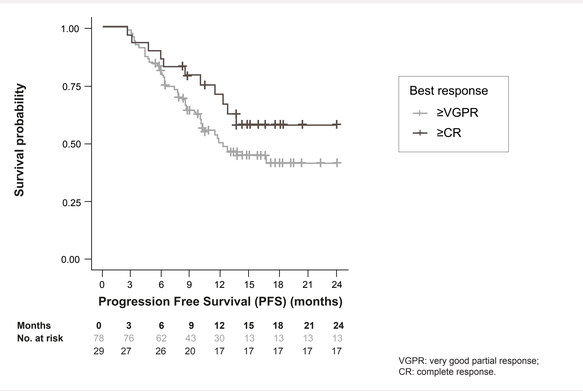
- With median follow-up of 10.9 (CI 95% 0.1–26.2) months overall, and 12.2 months (0.1–26.2) for Q2W group, ORR in the disease-response evaluated population was 83.8% and 84.7% (Table 2), with ≥VGPR in 65.4% and 66.1%, respectively. Median time to first response was 1.6 (1.25-2.04) for both overall and Q2W groups.
- Median PFS was 8.6 (6.5–10.7) and 9.9 (7.6–12.1) months (**Figure 1a and b**); median OS was 26.2 (15.6–36.7) and 26.2 (17.4–35.0) months (**Figure 2a and b**) for overall and Q2W groups (**Table 2**).
- The depth of response has influenced outcomes, as demonstrated in Figures 1 and 2, where achieving ≥VGPR and ≥CR correlated with extended progression-free survival (PFS) and overall survival (OS).
  - » PFS for best response ≥CR vs ≥VGPR, median NR (CI 95% NE-NE) vs 8.3 months (6.3-10.3) p<0.001, overall group. Best response ≥CR vs ≥VGPR, median NR (NE-NE) vs 8.4 months (6.3-10.4) p=0.001, Q2W group.
  - » OS for best response ≥CR vs ≥VGPR, median 26.2 (NE-NE) vs 20 months (13.9-26.1) p=0.012, overall group. Best response ≥CR vs ≥VGPR, median 26.2 (NE-NE) vs 20 months (13.9-26.1) p=0.013, Q2W group.

Figure 1a. PFS (months) of talquetamab treatment in the overall population (N=163) and according to best response.



VGPR: very good partial response; CR: complete response.

Figure 1b. PFS (months) of talquetamab treatment in the Q2W population (N=129) and according to best response.



VGPR: very good partial response; CR: complete response.

Figure 2a. OS (months) of talquetamab treatment in the overall population (N=163) and according to best response.

VGPR: very good partial response; CR: complete response.

Figure 2b. OS (months) of talquetamab treatment in the Q2W population (N=129) and according to best response.

VGPR: very good partial response; CR: complete response.

Table 2. Efficacy outcomes and response.

Outcome (months)	Overall population (N = 123)	Biweekly (Q2W) (N = 106)
Follow-up, median (range)	10.9 (0.1-26.2)	12.2 (0.1-26.2)
PFS, median (95% CI)	8.6 (6.5-10.7)	9.9 (7.6-12.1)
OS, median (95% CI)	26.2 (15.6-36.7)	26.2 (17.4-35)
ORR, n/N (%)	109/130* (83.8)	100/118* (84.7)
ITT	109/163 (66,9)	100/129 (77,5)

*Patients with documented disease-response evaluation. ITT: intention to treat; CI: confidence interval; ORR: overall response rate; PFS: progression-free survival; OS: overall survival.

Safety analysis

- Median treatment duration with Tal was 7.8 (0.1–24.0) and 8.2 (0.1-24.0) months, overall and Q2W groups, respectively. Most patients completed first treatment dose after initial step-up doses: 126 out of 147 overall (85.7%) and 113 out of 129 Q2W group (85.7%).
- Five patients (5/94, 5.3%) discontinued due to treatment-emerged adverse events (TEAEs) (all Q2W), and five (5/163, 3.1%) had Tal dose reductions to manage AEs.
- A 54% (88/163) of the patients were alive at last follow-up,, (61% in Q2W group) and disease progression was the most frequent cause of death (30.7%, 50/163 overall group; 31.8%, 41/129 Q2W group). TEAEs were the cause of death for 3.7% (6/163) and 4.7% (6/129) patients in overall and Q2W groups, respectively.
- No new safety signals were identified.

Table 3. Adverse events characteristic of GPRC5D T-cell redirection therapy.

AEs, n (%)*	Overall population (N = 163)	
	Any grade	Grade ≥ 3
CRS event	101 (62.0)	5 (3.1)
ICANS event	13 (8.0)	3 (1.8)
Infection event	90 (55.2)	22 (13.5)
Weight loss event	17 (10.4)	2 (1.2)
Dysgeusia event	78 (47.9)	0 (0)
Skin-related event[$]	123 (75.5)	4 (2.5)
Nail-related event[^]	73 (44.8)	0 (0)

Grade according to ASTCT scales for CRS and ICANS. For the rest of the AEs, grade according to NCI-CTCAE v5.0. *Patients with at least one event. $Considering any of the following events (at least one): Skin rash: maculopapular rash, erythema, erythematous rash; and non-eruptive skin reactions: skin exfoliation, dry skin, pruritus and palmo-plantar erythrodysesthesia syndrome, alopecia. ^Considering any of the following events (at least one): Nail discoloration, nail disorders, onycholysis, onychomadesis, onycholysis, nail dystrophy, nail toxicity, and nail ridges. AE: adverse event; CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome.

Conclusions

- The BiTAL study shows efficacy and safety outcomes comparable to those of MONUMENTAL-1.
- Despite being a difficult-to-manage population, high ORR and survival underscore its effectiveness. Notably, most patients achieved ≥VGPR, showing even better outcomes.
- Depth of response in real-world setting has also been shown to impact survival outcomes, reinforcing its importance as an objective of RRMM therapy in clinical practice.
- The safety profile was favorable was favorable, with low discontinuation rate and few severe infections and GPRC5D related events.
- While the retrospective nature of this study imposes some limitations, this close to real-world data reflects the talquetamab use outside clinical trials, supporting its integration into routine clinical practice.

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Multiple myeloma