Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study

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Summary

Background Talquetamab is the first GPRC5D×CD3 bispecific antibody approved for relapsed or refractory multiple myeloma. In phase 1 of the MonumenTAL-1 study, initial results of subcutaneous talquetamab 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks showed preliminary clinical activity. We describe safety and activity results in patients treated with talquetamab, including patients who had received previous T-cell redirection therapy (TCR). This post-hoc analysis was done with more mature median follow-up to evaluate duration of response in patients treated with talquetamab 0·8 mg/kg every 2 weeks.

Methods MonumenTAL-1 is a multicentre, open-label, phase 1–2 study of talquetamab, phase 1 of which has previously been published. The 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks recommended subcutaneous doses identified in phase 1 were evaluated in phase 2 in patients who were 18 years of age or older, had at least three previous lines of therapy, had an Eastern Cooperative Oncology Group performance status of 0 to 2, and were naive or exposed to previous TCR. The primary endpoint was overall response rate assessed by independent review committee in all patients who received at least one dose of talquetamab. Safety was assessed in all patients who received at least one dose of talquetamab. This study was registered with ClinicalTrials.gov, NCT03399799 (phase 1) and NCT04634552 (phase 2).

Findings Between Jan 3, 2018, and Feb 20, 2023, 735 patients were screened across all phase 1–2 cohorts. Of these, 537 patients screened for inclusion were treated across phase 1 and 2 cohorts, of whom 198 (27%) patients were excluded from the study, most commonly due to not meeting eligibility criteria or not having measurable disease. As of Oct 11, 2023, 375 patients had received recommended talquetamab doses across three groups: 143 (0·4 mg/kg once a week group) and 154 (0·8 mg/kg every 2 weeks group) TCR-naive patients and 78 with previous TCR who received either recommended dose (previous TCR group). 217 (58%) of 375 patients were male and 158 (42%) were female. 325 (87%) of 375 patients were White and 32 (9%) patients were Black. Median follow-up was 25·6 months (IQR 8·5–25·9) in the 0·4 mg/kg once a week group, 19·4 months (9·2–20·7) in the 0·8 mg/kg every 2 weeks group, and 16·8 months (7·6–18·7) in the previous TCR group. Overall response rate was 74% (106 of 143 patients, 95% CI 66–81) in the 0·4 mg/kg once a week group, 69% (107 of 154 patients, 62–77) in the 0·8 mg/kg every 2 weeks group, and 67% (52 of 78 patients, 55–77) in the previous TCR group. Most common adverse events in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR groups were cytokine release syndrome (113 [79%] of 143 patients, 115 [75%] of 154 patients, and 57 [73%] of 78 patients), taste changes (103 [72%], 110 [71%], and 59 [76%]), and infections (85 [59%], 105 [68%], and 59 [76%]). Most common grade 3–4 adverse events were neutropenia (44 [31%], 33 [21%], and 37 [47%]), anaemia (45 [31%], 40 [26%], and 21 [27%]), and lymphopenia (37 [26%], 40 [26%], and 13 [17%]). Fatal adverse events occurred in five patients in the 0·4 mg/kg once a week group, seven patients in the 0·8 mg/kg every 2 weeks group, and no patients in the previous TCR group; none were related to treatment.

Interpretation Talquetamab continued to demonstrate high overall response rates in heavily pretreated patients with relapsed or refractory multiple myeloma with longer follow-up in this post-hoc analysis. Overall response rate was promising in patients with previous TCR, including therapies targeting BCMA. On-target, off-tumour adverse events were common but led to few treatment discontinuations.

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Research in context

Evidence before this study

We searched PubMed on May 21, 2024, with no date restriction, using the keywords "myeloma" and "GPRC5D," leading to 97 results. These included four articles on clinical trials, three of which described data from phase 1 or 2 studies evaluating GPRC5D-directed chimeric antigen receptor T-cell therapies; the fourth reported the results of the phase 1 portion of this current study (MonumenTAL-1), which evaluated intravenous talquetamab once a week and every 2 weeks (0·0005–0·180 mg/kg) doses or subcutaneous talquetamab once a week, every 2 weeks, and once a month (0·005–1·60 mg/kg) in patients with relapsed or refractory multiple myeloma who had progressed on or could not tolerate established therapies for multiple myeloma. The results showed that talquetamab 0·4 mg/kg once a week or 0·8 mg/kg every 2 weeks induced deep and durable responses in patients with heavily pretreated relapsed or refractory multiple myeloma; common adverse events reported were cytokine release syndrome, skin-related events, and dysgeusia.

Added value of this study

In phase 1 of the MonumenTAL-1 study, initial results of subcutaneous talquetamab 0·4 mg/kg once a week (n=30) and 0·8 mg/kg every 2 weeks (n=44) showed high rates of response. In this post-hoc analysis, we report phase 1–2 data on activity and safety for a larger number of patients, with longer follow-up, including a separate group of patients who had received previous T-cell redirection therapy (TCR), most of which were BCMA targeting. Among patients who had not been exposed to previous TCR, overall response rates were 74% with the 0·4 mg/kg once a week dose and 69% with the 0·8 mg/kg every 2 weeks dose, confirming the results from the phase 1 portion of the study. Among patients who had received previous TCR (0·4 mg/kg once a week or 0·8 mg/kg every 2 weeks dosing), overall response rate was 67%, which is promising in a patient population who represent an emerging unmet need. No new safety signals were identified. Robust evaluation methods to assess the severity and impact of taste changes on patients have not yet been established, and rates of grade 3 or worse infections appeared lower than those in published studies of BCMA-targeted bispecific antibodies.

Implications of all the available evidence

Talquetamab shows promising activity in patients with heavily pretreated relapsed or refractory multiple myeloma, including patients who had previous exposure to therapies that use T-cell redirection to other myeloma antigens as the mechanism of antitumour activity. Talquetamab has the potential to expand the current repertoire of multiple myeloma therapies as an off-the-shelf treatment option that can be administered subcutaneously. The lower rates of high-grade infections compared with BCMA-directed therapies, potentially due to limited expression of GPRC5D on B cells and normal plasma cells, support combining talquetamab with other myeloma therapies due to its distinct mechanism of action. Ongoing studies are evaluating talquetamab combinations in patients with multiple myeloma.

Introduction

Patients with multiple myeloma have cycles of remission and relapse on standard therapies,[1,2] with a poorer prognosis with each successive relapse.[3] Although anti-BCMA therapies are approved and have shown clinical benefit for patients with relapsed or refractory multiple myeloma,[4–7] relapses continue; thus, there is a need for novel therapies to expand treatment options.

GPRC5D is an orphan receptor highly expressed in malignant plasma cells but with little expression on normal plasma cells and normal human tissues.[8,9] Talquetamab is a first-in-class, off-the-shelf, T-cell-redirecting bispecific antibody targeting GPRC5D on myeloma cells and the CD3 receptor on T cells approved for triple-class exposed relapsed or refractory multiple myeloma.[10] In phase 1 of the MonumenTAL-1 trial, two recommended doses of subcutaneous talquetamab were identified: 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks.[8] With a median follow-up of 11·7 and 4·2 months, respectively, in patients treated with the 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks recommended doses, overall response rate was 70% and 64%, respectively, and median duration of response was 10·2 and 7·8 months, respectively.[8]

Here, we describe updated safety and activity results with longer follow-up from MonumenTAL-1 in patients treated with subcutaneous talquetamab 0·4 mg/kg once a week or 0·8 mg/kg every 2 weeks (median follow-up 25·6 and 19·4 months, respectively), including analyses in patients who had received previous T-cell redirection therapy (TCR; chimeric antigen receptor T-cell [CAR-T] therapies or bispecific antibodies [median follow-up 16·8 months]). Crucially, this post-hoc analysis was conducted with more mature median follow-up to evaluate duration of response in patients treated with talquetamab 0·8 mg/kg every 2 weeks.

Methods

Study design and participants

MonumenTAL-1 is a first-in-human, multicentre, open-label, phase 1–2 study of talquetamab, phase 1 of which has previously been published.[8] Briefly, phase 1 consisted of talquetamab dose escalation, initiated at talquetamab 0·5 µg/kg administered intravenously every 2 weeks, before investigating higher doses on once a week or every 2 weeks schedules via intravenous or subcutaneous administration; a monthly subcutaneous dose was also explored. In phase 1, eligible patients were aged 18 years

or older, had measurable myeloma according to the International Myeloma Working Group (IMWG) criteria,[11] and had disease that had progressed with established therapies or could not receive established therapies without unacceptable adverse events.[8] The objective of phase 1 was to select the recommended doses for phase 2, which were talquetamab 0·4 mg/kg once a week or 0·8 mg/kg every 2 weeks. We report results from patients treated with the two recommended phase 2 doses across phases 1 and 2 of the study. In phase 2, eligible patients were aged 18 years or older; had multiple myeloma (serum monoclonal paraprotein [M-protein] level ≥1·0 g/dL or urine M-protein level ≥200 mg/24 h; or serum immunoglobulin free light chain ≥10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio without serum or urine assessments) measurable per IMWG criteria;[11] had documented progressive disease based on IMWG 2016 criteria;[12] were required to have at least three previous lines of therapy that included a proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody; and had an Eastern Cooperative Oncology Group performance status of 0–2. Laboratory tests at screening met the following conditions, with no red blood cell transfusion, platelet-stimulating factor or growth factor support within the seven days prior to the laboratory test, haemoglobin of at least 80 g/L, platelets of at least 50×10^9 cells/L, absolute neutrophil count of at least 1×10^9 cells/L, aspartate or alanine aminotransferase levels no more than 3 times the upper limit of normal, creatinine clearance of at least 40 mL/min per 1·73 m², total bilirubin levels no more than 2 times the upper limit of normal, and corrected serum calcium of no more than 14 mg/dL or free ionised calcium of no more than 6·5 mg/dL. Previous exposure to antibody–drug conjugates was permitted. Previous TCR, including BCMA-targeting bispecific antibodies and CAR-T therapy, was only permitted in a separate phase 2 cohort that enrolled patients later. Patients were excluded if they received or planned to receive any live or attenuated vaccine within four weeks prior to the first dose, during treatment or within 4 weeks of the last dose of talquetamab, or any vaccine approved for emergency use (eg, COVID-19), received a cumulative dose of corticosteroids equivalent to more than 140 mg of prednisone within the 14-day period before the first dose of talquetemab, received an allogenic stem-cell transplantation within 6 months or an autologous stem-cell transplantation within 12 weeks before first dose of talquetamab. Patients were excluded if they had central nervous system involvement or clinical signs of meningeal involvement of multiple myeloma; had plasma cell leukaemia, Waldenström's macroglobulinemia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin abnormalities), or primary amyloid light chain amyloidosis; were seropositive for human immunodeficiency virus or acquired immune deficiency syndrome; hepatitis B or C virus infections; a serious active viral, bacterial, or uncontrolled systemic fungal infection; active autoimmune disease or a documented history of autoimmune disease; psychiatric conditions; severe dementia; or altered mental status.

This study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines of the International Council for Harmonization. Study protocol and amendments were approved by each site's institutional review board. All patients provided informed written consent. All authors affirm that the trial was conducted in accordance with the protocol. This study was registered with ClinicalTrials.gov, NCT03399799 (phase 1) and NCT04634552 (phase 2), and is ongoing.

Procedures

Patients included in this analysis were treated with the recommended doses of subcutaneous talquetamab in phase 1 and 2 of MonumenTAL-1: 0·4 mg/kg once a week or 0·8 mg/kg every 2 weeks in patients who had not received previous TCR therapy.[8] One group was treated with either dosing schedule and had received previous TCR therapy (hereafter referred to as previous TCR group). Switching to less frequent dosing (ie, a permanent change to a reduced dosing schedule) was permitted for patients who had a partial response or better (phase 1 only) or to mitigate adverse events. Step-up dosing was implemented to mitigate risk of severe cytokine release syndrome; patients received 0·01 mg/kg and 0·06 mg/kg for step-up doses 1 and 2, respectively, in both the 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks groups, and 0·3 mg/kg for step-up dose 3 in the 0·8 mg/kg every 2 weeks group. Pretreatment with a glucocorticoid (dexamethasone 16 mg or equivalent), antihistamine, and antipyretic was required before all step-up doses and initial full dose. Hospital admission for 48 h or more was required from the start of each step-up dose and first full dose, but was not required for repeat step-up doses, which were given per investigator discretion for patients who needed to repeat step-up dosing after dose delays. Patients received treatment until disease progression, unacceptable toxic effects, withdrawal of consent, or end of study. Disease and safety evaluations are described in the appendix (p 3).

See Online for appendix

Adverse events were graded by Common Terminology Criteria for Adverse Events (CTCAE) v4.03. Weight measurements were used to assess weight loss and the percentage change from baseline was graded per CTCAE criteria. Cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome events were reported according to American Society for Transplantation and Cellular Therapy criteria; immune effector cell-associated neurotoxicity syndrome was only reported in phase 2. Immune effector cell-associated neurotoxicity syndrome was not reported in phase 1 as immune effector cell-associated encephalopathy

assessments were not conducted during this portion of the study, although general neurotoxic effects were assessed using mini-mental state examinations. Patient immune profiles were characterised using flow cytometry from whole blood and bone marrow aspirate samples. This analysis was based on a post-hoc clinical cutoff date of Oct 11, 2023.

Outcomes

The primary endpoint in phase 2 was overall response rate per IMWG criteria,[11] based on independent committee review, which was defined as the proportion of patients who had a partial response or better. Secondary endpoints included duration of response (time from first documented partial response or better to progressive disease or death due to any cause, whichever occurred first), overall response rate in patients with high-risk molecular features, rate of very good partial response or better, rate of complete response or better, time from first study treatment to response (partial response or better), progression-free survival (time from first study treatment dose to progressive disease or death due to any cause, whichever occurred first), overall survival (time from first study treatment dose to death due to any cause), minimal residual disease, incidence of adverse events, patient-reported outcomes, and pharmacokinetics. Patient-reported outcomes and pharmacokinetics will be included in other publications.

Statistical analyses

In the phase 1 dose escalation portion of this study, at least one patient was enrolled at each dose level during dose escalation, with at least six patients enrolled at the identified recommended phase 2 doses; the total number of patients enrolled during this phase of the study was dependent on the frequency of dose-limiting toxic effects. In phase 1 dose expansion, up to 40 patients were to be treated with the recommended phase 2 doses to further assess safety and preliminary antitumour activity. For phase 2, approximately 120 patients were to be treated in the 0·4 mg/kg once a week group, approximately 100 patients were to be treated in the 0·8 mg/kg every 2 weeks group, and approximately 60–100 patients were to be treated in the previous TCR group with either 0·4 mg/kg once a week or 0·8 mg/kg every 2 weeks dosing. The sample size for the 0·4 mg/kg once a week group was determined by assuming that the overall response rate at this dose would be least 45%. If this assumption was true, there would be approximately 90% or greater power to declare that the overall response rate was higher than 30% at the one-sided significance level of 0·025. The sample size for the 0·8 mg/kg every 2 weeks group was determined on the assumption that the overall response rate would be at least 45%. If this assumption was true, there would be more than 85% power to declare that the overall response rate was higher than 30% at the one-sided significance level of 0·025.

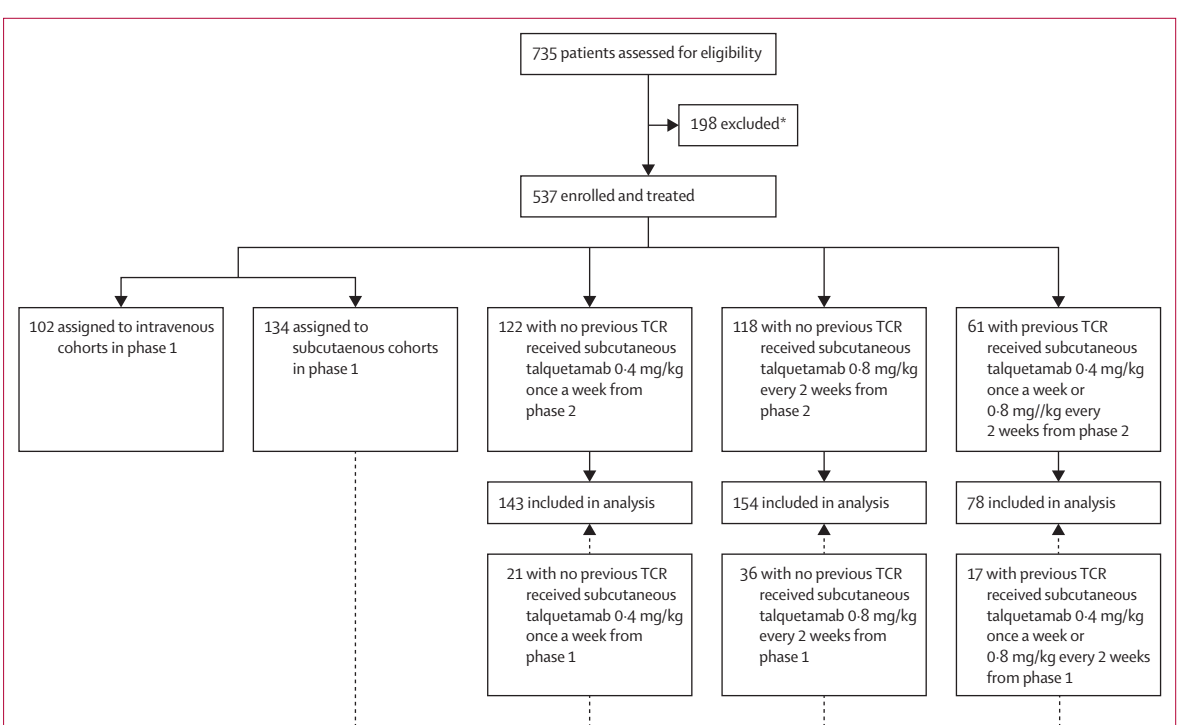


Figure 1: **Trial profile**
Only results for patients who received the recommended phase 2 doses of talquetamab across phases 1 and 2 of the study are reported. *Most common reasons were not meeting eligibility criteria or not having measurable disease.

The sample size for the previous TCR group was determined using a two-stage design to test the null hypothesis that the overall response rate was at most 15%, against the alternative that the overall response rate was at least 35%. With a one-sided significance level of 0·025 and a power of 80%, this cohort needed 34 response-evaluable patients. Assuming a non-evaluable rate of 10%, a total sample size required for this cohort was 38 patients. The sample size was increased to at least 60 patients to determine the overall response rate with more precision.

Safety and activity were analysed in patients across phases 1 and 2 who received at least one dose of talquetamab (all-treated analysis set). Response was calculated with two-sided exact 95% CIs (Clopper-Pearson method). The Kaplan-Meier method was used to estimate the time-to-event endpoints of duration of response, progression-free survival, and overall survival. Data were summarised using descriptive statistics; statistical methods for phase 1 have been published.[8]

Post-hoc exploratory analyses included overall response rate by baseline patient characteristics and previous therapy exposure subgroups in the talquetamab 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks groups; overall response rate by receipt of prior CAR-T versus bispecific antibodies (including analyses by time since last exposure and by line of therapy) in the previous TCR group; time to very good partial response or better; median progression-free survival by age, presence of extramedullary disease, cytogenetic risk, previous exposure to CAR-T or bispecific antibody therapy, and in patients who did and did not receive dose reductions; mean IgG levels during treatment in responders versus non-responders; and weight changes in patients with and without oral adverse events. Exploratory analyses of pharmacodynamics and talquetamab clinical activity and investigation of potential biomarkers of clinical activity or resistance to talquetamab were prespecified.

SAS studio (v3.8) was used to conduct analysis of clinical data. Correlative analyses were done in R (v4.0.5), and plots were generated using ggplot2 (v3.4.0).

Role of the funding source

The study sponsor, in collaboration with the authors, designed the trial; collected, analysed, and interpreted the data; and prepared the report. Medical writers assisted in manuscript preparation with funding from the sponsor.

Results

Between Jan 3, 2018, and Feb 20, 2023, 735 patients were screened across all phase 1–2 cohorts. In total, 537 patients screened for inclusion were treated across phase 1 and 2 cohorts, including during dose escalation and in other dosing cohorts. A total of 198 (27%) patients did not meet eligibility criteria. For the groups presented here, 143 patients without previous TCR received 0·4 mg/kg

	0·4 mg/kg talquetamab once a week* group (N=143)	0·8 mg/kg talquetamab every 2 weeks* group (N=154)	Patients with previous TCR* group (N=78)
Age, years	67 (58–72)	67 (58–74)	61 (55–68)
Sex			
Female	65 (45%)	64 (42%)	29 (37%)
Male	78 (55%)	90 (58%)	49 (63%)
Race			
White	128 (90%)	126 (82%)	71 (91%)
Black	12 (8%)	17 (11%)	3 (4%)
Asian	1 (1%)	6 (4%)	4 (5%)
Native Hawaiian or other Pacific Islander	0	1 (1%)	0
Multiple	0	1 (1%)	0
Unknown	0	1 (1%)	0
Not reported	2 (1%)	2 (1%)	0
Bone marrow plasma cells ≥60%†	17/138 (12%)	34/150 (23%)	11/73 (15%)
Extramedullary plasmacytomas ≥1‡	33 (23%)	41 (27%)	25 (32%)
High-risk cytogenetics§	41/132 (31%)	40/133 (30%)	25/67 (37%)
ISS stage			
I	62 (43%)	68/153 (44%)	38 (49%)
II	53 (37%)	48/153 (31%)	27 (35%)
III	28 (20%)	37/153 (24%)	13 (17%)
ECOG performance score			
0	44 (31%)	58 (38%)	36 (46%)
1	86 (60%)	84 (55%)	39 (50%)
2	13 (9%)	12 (8%)	3 (4%)
Time since diagnosis, years	6·7 (4·3–9·7)	6·3 (3·8–10·4)	6·3 (4·2–9·9)
Previous lines of therapy	5·0 (4·0–6·0)	4·5 (4·0–6·0)	6·0 (5·0–8·0)
Previous stem-cell transplantation	113 (79%)	121 (79%)	69 (88%)
Exposure status			
Triple-class¶	143 (100%)	154 (100%)	78 (100%)
Penta-drug‖	105 (73%)	107 (69%)	65 (83%)
Belantamab mafodotin	22 (15%)	17 (11%)	11 (14%)
Bispecific antibody	NA	NA	26 (33%)
CAR-T cell therapy	NA	NA	57 (73%)
Refractory status			
Proteasome inhibitor**	116 (81%)	129 (84%)	71 (91%)
Immunomodulatory drug	134 (94%)	141 (92%)	76 (97%)
Thalidomide	12 (8%)	20 (13%)	6 (8%)
Lenalidomide	115 (80%)	110 (71%)	69 (88%)
Pomalidomide	110 (77%)	106 (69%)	60 (77%)
Anti-CD38 monoclonal antibody††	134 (94%)	142 (92%)	74 (95%)
Triple-class¶	107 (75%)	110 (71%)	66 (85%)
Penta-drug‖	45 (31%)	39 (25%)	34 (44%)
Belantamab mafodotin	18 (13%)	14 (9%)	8 (10%)
To last line of therapy	134 (94%)	145 (94%)	45 (58%)

Data are median (IQR), n (%), or n/N (%). CAR=chimeric antigen receptor. ECOG=Eastern Cooperative Oncology Group. ISS=International Staging System. NA=not applicable. TCR=T-cell redirection therapy. *With two to three step-up doses. †Maximum value from bone marrow biopsy or bone marrow aspirate was selected if both results were available. ‡Soft tissue plasmacytomas not associated with the bone were included. §del(17p), t(4;14), or t(14;16). ¶At least one proteasome inhibitor, at least one immunomodulatory drug, and at least one anti-CD38 monoclonal antibody. ‖At least two proteasome inhibitors, at least two immunomodulatory drugs, and at least one or more anti-CD38 monoclonal antibodies. **Bortezomib, carfilzomib, or ixazomib. ††Daratumumab, isatuximab, or an investigational anti-CD38 monoclonal antibody.

Table 1: **Patient demographics and baseline characteristics**

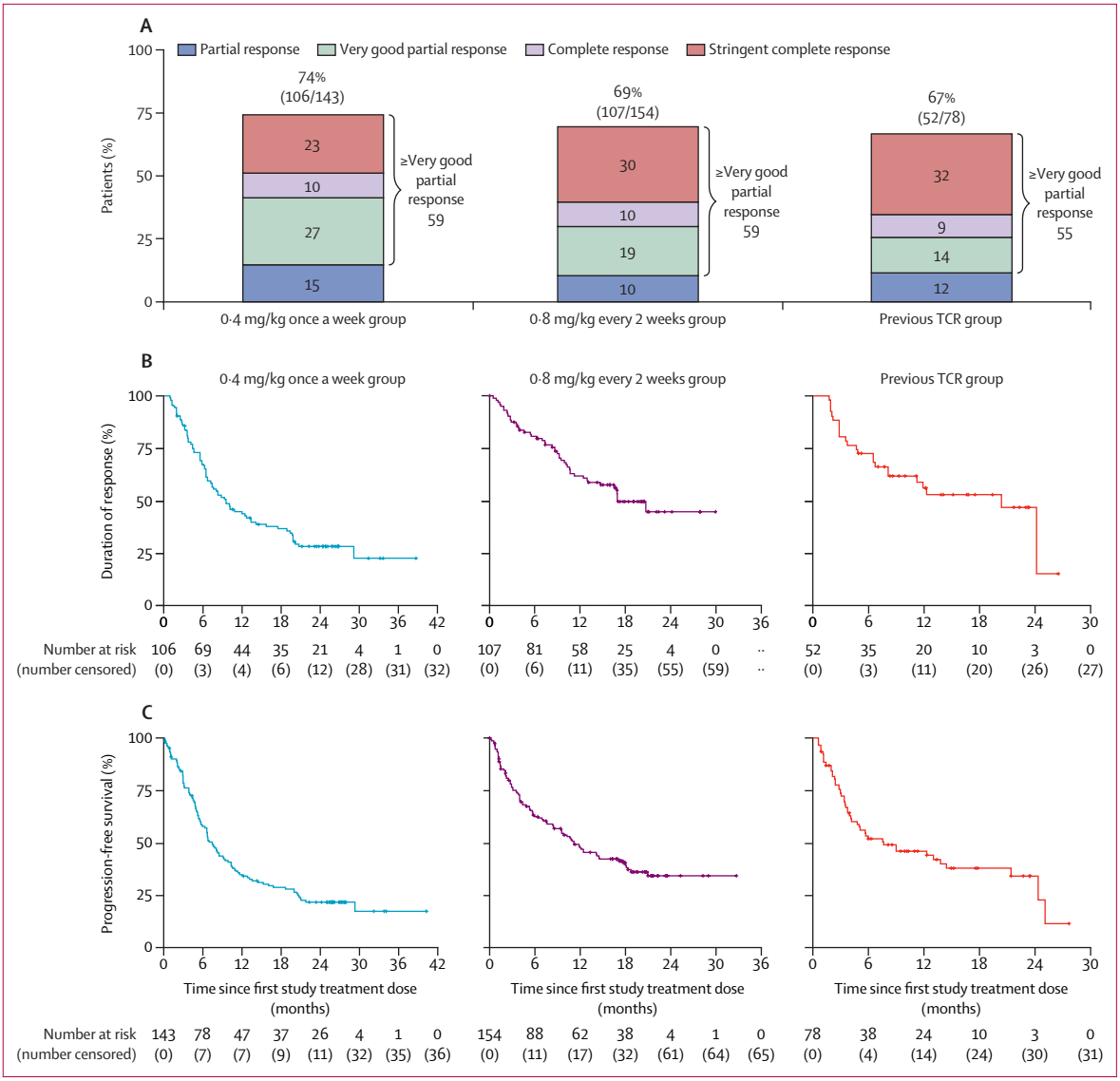


Figure 2: **Response to talquetamab, duration of response in responders, and progression-free survival**
(A) Response. (B) Duration of response. (C) Progression-free survival. Data are for both doses in patients with and without previous TCR. Independent review committee assessment of evaluable patients per 2016 International Myeloma Working Group response criteria; due to rounding, individual response rates might not sum to the overall response rate. Crosses denote censored patients. For the duration of response analysis, patients who had not progressed or died were censored at the last disease evaluation before the start of subsequent antimyeloma therapy. For the progression-free survival analysis, patients who had not progressed or died were censored at the last disease evaluation before the start of subsequent antimyeloma therapy; additionally, patients with no post-baseline disease assessments were censored at the date of the first dose of study treatment. Relapse from complete response or better was not considered as disease progression for the progression-free survival analysis. TCR=T-cell redirection therapy.

once a week and 154 patients without previous TCR received 0·8 mg/kg every 2 weeks; 78 patients received either dose schedule in the previous TCR group (figure 1). Patients with previous TCR received previous CAR-T therapy (57 [73%] of 78 patients), previous bispecific antibody therapy (26 [33%]), or both (five [6%]); most were BCMA-directed (75 [96%]; other antigen targets were CD38 [n=2] and MAGE-A1 [n=1]). Baseline demographics were generally well balanced across groups, although compared with patients in the 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks groups, patients in the previous TCR group were younger, had a higher prevalence of high-risk cytogenetics, had received more previous lines of therapy, and were less likely to be refractory to their last line of therapy (table 1). 217 (58%) of 375 patients were male and 158 (42%) were female. 325 (87%) of 375 patients were White and 32 (9%) of 375 patients were Black.

As of Oct 11, 2023, median follow-up was 25·6 months (IQR 8·5–25·9) in the 0·4 mg/kg once a week group

and 19·4 months (9·2–20·7) in the 0·8 mg/kg every 2 weeks group. Overall response rate was 74% (106 of 143 patients, 95% CI 66–81) in the 0·4 mg/kg once a week group and 69% (107 of 154 patients, 62–77) in the 0·8 mg/kg every 2 weeks group. The proportion of patients achieving very good partial response or better and complete response or better was high in both groups (figure 2A). Overall response rate was consistent across clinically relevant subgroups, with the exception of patients with baseline extramedullary plasmacytomas (appendix p 4).

At a median follow-up of 16·8 months (IQR 7·6–18·7) in the previous TCR group, overall response rate was 67% (52 of 78 patients, 95% CI 55–77), and the proportion of patients achieving very good partial response or better and complete response or better was high (figure 2A).

In post-hoc analyses, overall response rate was 72% (41 of 57 patients, 95% CI 59–83) in patients receiving previous CAR-T therapy and 58% (15 of 26 patients, 37–77) in patients receiving previous bispecific antibody therapy. Overall response rate was 74% (26 of 35 patients, 57–88) in patients who had received BCMA-targeting CAR-T as the immediate previous line of therapy, 68% (15 of 22 patients, 45–86) in patients who had received BCMA-targeting CAR-T before the last line of therapy, and 88% (14 of 16 patients, 62–98) in patients who received BCMA-targeting CAR-T less than 6 months before talquetamab, 100% (four of four patients, 40–100) in patients receiving BCMA-targeting CAR-T between 6 and 9 months before talquetamab, and 62% (23 of 37, 45–78) at least 9 months before talquetamab (post-hoc analysis). Overall response rate was 68% (13 of 19 patients, 43–87) in patients who had received BCMA-targeting bispecific antibodies before the last line of therapy and 29% (two of seven patients, 4–71) in patients who had received BCMA-targeting bispecific antibodies as the immediate previous line of therapy; overall response rate was 75% (six of eight patients, 35–97) in patients who received BCMA-targeting previous bispecific antibodies at least 9 months before talquetamab, versus 50% (three of six patients, 12–88) in patients receiving BCMA-targeting bispecific antibodies between 6 and 9 months before talquetamab, and 50% (six of 12 patients, 21–79) in patients who received BCMA-targeting bispecific antibodies less than 6 months before talquetamab (post-hoc analysis).

Median time to first response was 1·2 months (IQR 1·1–1·6), 1·3 months (1·2–1·7), and 1·2 months (1·1–1·7), and median time to very good partial response or better (post-hoc analysis) was 1·9 months (1·2–3·0), 2·2 months (1·2–4·0), and 1·4 months (1·1–2·7) in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR groups, respectively.

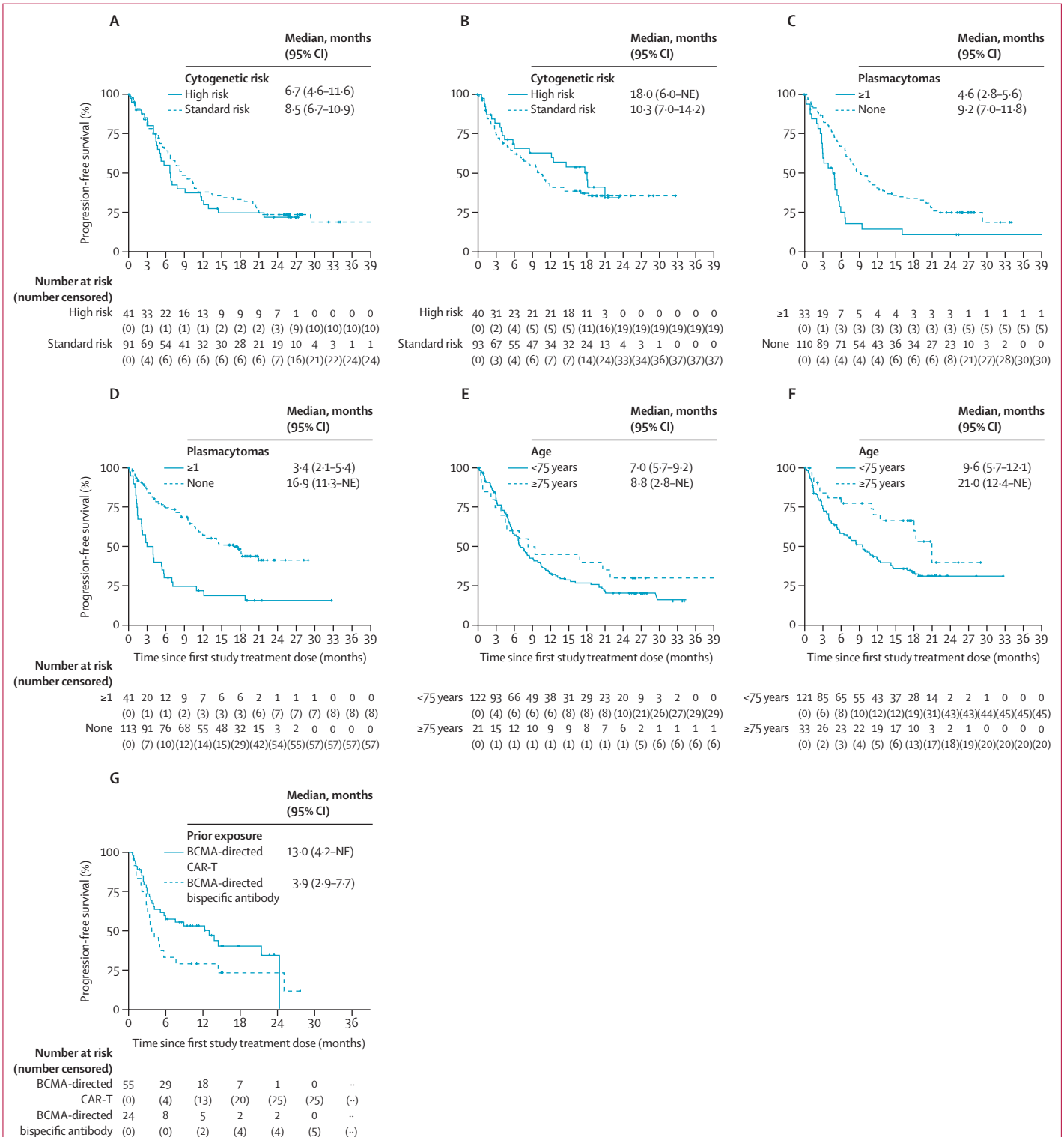
With 74 events in 106 responders in the 0·4 mg/kg once a week group and 48 events in 107 responders in the 0·8 mg/kg every 2 weeks group, median duration of response was 9·5 months in the 0·4 mg/kg once a week group (95% CI 6·7–13·4) and 16·9 months in the 0·8 mg/kg every 2 weeks group (12·9–not estimable) The 12-month duration of response rate was 56% (95% CI 41–69) in the previous TCR group (figure 2B).

With 107 events in 143 patients in the 0·4 mg/kg once a week group, 89 events in 154 patients in the 0·8 mg/kg every 2 weeks group, and 47 events in 78 patients in the previous TCR group, median progression-free survival was 7·5 months (95% CI 5·7–9·4), 11·2 months (8·4–16·9), and 7·7 months (4·1–14·5), respectively (figure 2C). Median progression-free survival in post-hoc analyses by age (75 years or older *vs* younger than 75 years), presence of baseline extramedullary disease (with *vs* without), cytogenetic risk profile (high *vs* standard), and previous exposure to CAR-T versus bispecific antibody therapy are shown in figure 3. Progression-free survival in patients who did or did not have a dose reduction by day 300 is shown in the appendix (p 6). With 58 events in 143 patients, 44 events in 154 patients, and 27 events in 78 patients in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR groups, 12-month overall survival rates were 76% (95% CI 68–83), 77% (69–83), and 74% (62–82), respectively. Medians are not yet available, as the data are immature.

The most common adverse event was cytokine release syndrome in the 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks groups and taste changes in the previous TCR group (table 2 and appendix p 13). Haematological toxic effects were the most common grade 3–4 events (appendix pp 14–22), were generally reversible, and were limited to the first few cycles. Grade 3–4 neutropenia occurred in 44 (31%) of 143 patients in the 0·4 mg/kg once a week group, 33 (21%) of 154 patients in the 0·8 mg/kg every 2 weeks group, and 37 (47%) of 78 patients in the previous TCR group. In the three groups, adverse events resulted in treatment discontinuation in seven (5%) of 143 patients in the 0·4 mg/kg once a week group, 14 (9%) of 154 patients in the 0·8 mg/kg every 2 weeks group, and four (5%) of 78 patients in the previous TCR group (appendix p 23) and dose reductions in 22 (15%) of 143 patients in the 0·4 mg/kg once a week group, 13 (8%) of 154 patients in the 0·8 mg/kg every 2 weeks group, and nine (12%) of 78 patients in the previous TCR group (appendix p 24). 78 (55%) of 143 patients in the 0·4 mg/kg once a week group, 81 (53%) of 154 patients in the 0·8 mg/kg every 2 weeks group, and 40 (51%) of 78 patients in the previous TCR group had at least one serious adverse event. Fatal adverse events occurred in five patients in the 0·4 mg/kg once a week group (COVID-19 pneumonia, fungal sepsis, septic shock, general physical health deterioration, and pulmonary embolism), seven in the 0·8 mg/kg every 2 weeks group (COVID-19 pneumonia, infection, acute respiratory failure, respiratory failure, general physical health deterioration, acute myeloid leukaemia, and basilar artery occlusion), and no patients in the previous

TCR group (appendix pp 14–22). Three patients (two in the 0·4 mg/kg once a week group and one in the 0·8 mg/kg every 2 weeks group) were in response at the time of death. There were no treatment-related deaths.

Cytokine release syndrome events were largely confined to step-up and first full doses, with few events occurring at or after cycle 2 (appendix p 25). Grade 3 cytokine release syndrome events occurred in three patients in the



0·4 mg/kg once a week group and one patient each in the 0·8 mg/kg every 2 weeks and previous TCR groups; no grade 4–5 events were reported (table 2; appendix p 13). Median time to cytokine release syndrome onset and median duration are in the appendix (p 25). Overall, 46 (32%) of 143 patients in the 0·4 mg/kg once a week group, 51 (33%) of 154 patients in the 0·8 mg/kg every 2 weeks group, and 23 (29%) of 78 patients in the previous TCR group had more than one cytokine release syndrome event; a small proportion had a worse grade during the subsequent event (six [4%] of 143 patients in the 0·4 mg/kg once a week group, seven [5%] of 154 patients in the 0·8 mg/kg every 2 weeks group, and three [4%] of 78 patients in the previous TCR group). Supportive measures for cytokine release syndrome were given to 106 (74%) of 143 patients in the 0·4 mg/kg once a week group, 109 (71%) of 154 patients in the 0·8 mg/kg every 2 weeks group, and 54 (69%) of 78 patients in the previous TCR group; acetaminophen was the most common supportive measure and tocilizumab was also used often.

Other common adverse events included taste changes, non-rash skin-related, rash-related, and nail-related adverse events (defined as on-target, off-tumour adverse events); for applicable adverse events, these were predominantly low grade (table 2). Median duration and outcomes of these adverse events are shown in the appendix (p 26). Three patients discontinued treatment due to non-rash skin-related adverse events, two in the 0·4 mg/kg once a week group (both due to skin exfoliation) and one in the 0·8 mg/kg every 2 weeks group (dermatitis exfoliative generalised and dry skin). No patients discontinued due to nail-related or rash-related adverse events. Two patients discontinued due to taste changes (both in the 0·8 mg/kg every 2 weeks group). Dose modifications (dose delays, skips, or reductions) to manage taste changes occurred in 12 (8%) of 143 patients in the 0·4 mg/kg once a week group, nine (6%) of 154 patients in the 0·8 mg/kg every 2 weeks group, and six (8%) of 78 (8%) patients in the previous TCR group. Development of on-target, off-tumour adverse events that occurred in early treatment cycles was associated with a greater likelihood of response compared with patients who did not have these adverse events (appendix p 7).

Weight decrease occurred in 59 (41%) of 143 patients, 64 (42%) of 154 patients, and 29 (37%) of 78 patients in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR groups, respectively, which were grade 3 in three (2%) patients, eight (5%) patients, and one (1%) patient, respectively. Weight decreases were evident early but stabilised and then increased slightly over time, including in patients with oral adverse events (appendix p 8).

Infections occurred in 85 (59%) of 143 patients, 105 (68%) of 154 patients, and 59 (76%) of 78 patients, and grade 3–4 infections occurred in 29 (20%) of 143 patients, 28 (18%) of 154 patients, and 20 (26%) of 78 patients in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR

	0·4 mg/kg talquetamab once a week* group (N=143)			0·8 mg/kg talquetamab every 2 weeks* group (N=154)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Haematological						
Anaemia	19 (13%)	45 (31%)	0	26 (17%)	40 (26%)	0
Neutropaenia	6 (4%)	29 (20%)	15 (10%)	11 (7%)	24 (16%)	9 (6%)
Lymphopenia	3 (2%)	17 (12%)	20 (14%)	6 (4%)	14 (9%)	26 (17%)
Thrombocytopaenia	10 (7%)	15 (10%)	14 (10%)	17 (11%)	14 (9%)	14 (9%)
Leukopenia	12 (8%)	6 (4%)	5 (3%)	11 (7%)	14 (9%)	4 (3%)
Non-haematological						
Cytokine release syndrome	110 (77%)	3 (2%)	0	114 (74%)	1 (1%)	0
Taste-related changes†‡	103 (72%)	NA	NA	110 (71%)	NA	NA
Non-rash skin-related adverse events§	81 (57%)	0	0	113 (73%)	1 (1%)	0
Nail-related adverse events¶	79 (55%)	0	0	82 (53%)	0	0
Weight decreased	56 (39%)	3 (2%)	0	56 (36%)	8 (5%)	0
Rash-related adverse events‖	57 (40%)	2 (1%)	0	45 (29%)	8 (5%)	0
Dry mouth	38 (27%)	0	0	60 (39%)	0	0
Pyrexia	52 (36%)	4 (3%)	0	40 (26%)	2 (1%)	0
Diarrhoea	34 (24%)	3 (2%)	0	40 (26%)	2 (1%)	0
Fatigue	30 (21%)	5 (3%)	0	41 (27%)	1 (1%)	0
Decreased appetite	27 (19%)	2 (1%)	0	41 (27%)	2 (1%)	0
Dysphagia	34 (24%)	0	0	35 (23%)	3 (2%)	0
Cough	28 (20%)	0	0	32 (21%)	0	0
Headache	26 (18%)	1 (1%)	0	31 (20%)	1 (1%)	0
Nausea	29 (20%)	0	0	30 (19%)	0	0
Arthralgia	28 (20%)	2 (1%)	0	27 (18%)	0	0
Asthenia	36 (25%)	3 (2%)	0	16 (10%)	2 (1%)	0
Constipation	25 (17%)	0	0	31 (20%)	0	0
COVID-19	14 (10%)	2 (1%)	0	35 (23%)	4 (3%)	0

Data are n (%). Adverse events are listed by frequency on an any-grade basis. Adverse events listed are grade 1–2 events occurring in at least 20% of patients in either group or grade 3 or worse occurring in at least 10% of patients in either group. A comprehensive table of grade 3–5 adverse events is provided in the appendix (pp 14–22). NA=not applicable. *With two to three step-up doses. †Includes dysgeusia, ageusia, hypogeusia, and taste disorder. ‡Per Common Terminology Criteria for Adverse Events, the maximum grade for these events is 2. §Includes skin exfoliation, dry skin, pruritus, and palmar-plantar erythrodysesthesia syndrome. ¶Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. ‖Includes rash, maculopapular rash, erythematous rash, and erythema.

Table 2: **Haematological and non-haematological adverse events**

Figure 3: **Progression-free survival in high-risk subgroups (post-hoc analysis)**
Subgroups are as follows: (A) Cytogenic risk in the 0·4 mg/kg once a week group. (B) Cytogenic risk in the 0·8 mg/kg every 2 weeks group. (C) Presence of baseline extramedullary disease in the 0·4 mg/kg once a week group. (D) Presence of baseline extramedullary disease in the 0·8 mg/kg every 2 weeks group. (E) Patient age in the 0·4 mg/kg once a week group. (F) Patient age in the in the 0·8 mg/kg every 2 weeks group. (G) Previous CAR-T therapy or bispecific antibody therapy exposure in the previous TCR group. Progression-free survival is presented for both doses in patients without previous TCR (A–F) and for both doses in patients with previous TCR (G). Crosses denote censored patients. Patients who had not progressed or died were censored at the last disease evaluation before the start of subsequent antimyeloma therapy; additionally, patients with no post-baseline disease assessments were censored at the date of the first dose of study treatment. Relapse from complete response or better was not considered as disease progression. BCMA=B-cell maturation antigen. CAR-T=chimeric antigen receptor T cell. NE=not estimable. TCR=T-cell redirection therapy.

groups, respectively. Five patients died due to infections, three in the 0·4 mg/kg once a week group and two in the 0·8 mg/kg every 2 weeks group. Opportunistic infections, defined as either oesophageal candidiasis, adenovirus, herpesvirus 6, ophthalmic herpes, varicella zoster, cytomegalovirus, fungal sepsis, or viral retinitis, occurred in five (3%) of 143 patients, nine (6%) of 154 patients, and three (4%) of 78 patients in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR groups, respectively. 16 (11%) of 143 patients, 39 (25%) of 154 patients, and 11 (14%) of 78 patients in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR groups, respectively, had COVID-19 (table 2; appendix p 13). COVID-19 pneumonia led to death in two patients (one patient each in the 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks group). Polyclonal IgG transiently decreased for the first 2–3 months of therapy and then steadily rose above baseline values as patients continued talquetamab therapy; IgG results were similar for responders and non-responders (appendix p 9). Intravenous immunoglobulin (before talquetamab therapy or posttreatment hypogammaglobulinaemia) was given to 12 (8%) of 143 patients, 14 (9%) of 154 patients, and 15 (19%) of 78 patients in the 0·4 mg/kg once a week, 0·8 mg/kg every 2 weeks, and previous TCR groups, respectively.

Immune effector cell-associated neurotoxicity syndrome occurred in 13 (11%) of 122 patients in the 0·4 mg/kg once a week group, 12 (10%) of 118 patients in the 0·8 mg/kg every 2 weeks group, and two (4%) of 61 patients in the previous TCR group; most events were low grade and often occurred concurrently with cytokine release syndrome (appendix p 27). Median time to onset and duration were longer in the previous TCR group than in the 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks groups. One patient in the 0·8 mg/kg every 2 weeks group had grade 2 cerebellar toxicity (reported as ataxia), which led to discontinuation.

Numerically fewer median CD8 T-cell counts were found in patients in the previous TCR group compared with the 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks groups, although there was overlap in absolute counts between the cohorts. Low sample numbers precluded assessments of $CD8^+$ T-cell counts in patients who received previous bispecific antibody or CAR-T therapy. Numerically greater frequencies of PD-1/LAG-3-expressing $CD8^+$ T cells, TIM-3-expressing $CD8^+$ T cells, CD38-expressing $CD8^+$ T cells, and regulatory T cells were observed in the previous TCR group compared with the 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks groups, although there was overlap in the frequency of regulatory T cells and $CD8^+$ T cells expressing these markers between the cohorts (appendix p 10). Patients with previous CAR-T therapy had numerically greater max-fold induction of TIM-3-expressing and LAG-3-expressing $CD8^+$ T cells in the first cycle compared with patients with previous bispecific antibody therapy, although there was overlap between the cohorts and the sample sizes were small (appendix p 11). Responders had a tendency for higher T-cell counts and lower frequencies of LAG-3-expressing and CD38-expressing CD8-expressing T cells than non-responders (appendix p 12).

Discussion

In this post-hoc analysis with longer follow-up, talquetamab continued to show promising activity in TCR-naive patients with heavily pretreated relapsed or refractory multiple myeloma. Promising activity was also observed in the previous TCR group (majority BCMA-targeting), which is an emerging class of patients with a high unmet medical need. Responses were similar at both 0·4 mg/kg once a week and 0·8 mg/kg every 2 weeks doses and were rapid and deep, although median duration of response and progression-free survival were longer in the 0·8 mg/kg every 2 weeks group than the 0·4 mg/kg once a week group. Median progression-free survival was promising with the 0·8 mg/kg every 2 weeks dose in older patients aged 75 years and older. Importantly, and uncommon in multiple myeloma, similar progression-free survival was observed irrespective of cytogenetic risk profile. In patients who switched to a reduced dose after response, responses were maintained, supporting flexibility to adjust talquetamab dosing in responders to potentially improve patient experience while maintaining activity.

Talquetamab demonstrated an overall response rate of 67% in the previous TCR group. Median progression-free survival was promising in the previous TCR cohort, similar to results with the 0·4 mg/kg once a week group. It should be noted that most patients in the previous TCR group received the 0·4 mg/kg once a week dosing schedule, which had a shorter median progression-free survival than the 0·8 mg/kg every 2 weeks schedule in TCR-naive patients. Results in the previous TCR group were consistent with results in the 0·4 mg/kg once a week group despite patients in the previous TCR group having a more exhausted T-cell phenotype at baseline. Overall response rate was lower and progression-free survival was shorter in patients receiving previous bispecific versus CAR-T therapy, which is supported by analyses showing that patients with previous CAR-T therapy had greater T-cell activation (*vs* bispecific antibody-exposed patients). Additionally, overall response rate was 68% in patients who had received BCMA-targeting bispecific antibodies before the last line of therapy compared with 29% as the immediate previous line of therapy. Although numbers were small, there were no differences in baseline patient characteristics between these two populations. Taken together, talquetamab could be a viable option for BCMA-exposed patients, and studies evaluating outcomes with BCMA-directed therapies after talquetamab treatment will further inform potential sequencing strategies.

Taste changes were common, although it should be noted that these events are highly subjective and the

mechanism of taste changes with talquetamab remains unclear.[8] Standard classification tools, such as CTCAE classification, may not adequately describe the severity of these events, and a robust evaluation method to assess the severity and impact of taste changes on patients has not yet been established. Additionally, patients were found to be at similar risk for weight decreases regardless of whether they experienced oral adverse events, with weight stabilising and then increasing slightly over time in both cohorts. Management of weight requires patient education; close monitoring, especially for patients with a low starting bodyweight; early referral to a dietician or nutritionist; management of calorie deficits; and potential adjustments to weight-based medications. Non-rash skin-related adverse events were managed through topical treatments, nail-related adverse events were managed with emollients, and rash-related adverse events were treated using topical steroids and prompt short-course oral steroids. Guidance on managing adverse events during talquetamab has been published.[13] On-target, off-tumour adverse events were predominately low grade and led to few treatment discontinuations. Although adverse events can affect quality of life, particularly in early treatment cycles, it should be noted that a previous analysis showed that talquetamab led to meaningful improvements from baseline in multiple myeloma symptoms, physical function, and overall health-related quality of life.[14] Finally, although cerebellar toxicity has been identified as a safety signal with GPRC5D-targeting CAR-T therapies, only one event (grade 2 ataxia) was reported during this study at this data cutoff.[9]

Although most patients responded to therapy, early onset of on-target, off-tumour adverse events was associated with greater likelihood of response, which is an association not previously seen in multiple myeloma. However, early onset of these events should not be considered a proxy for response, especially as prophylactic and adverse event management strategies improve. Work is ongoing to assess associations between dose intensity reductions (after achieving a confirmed partial response or better) and the severity or resolution of oral, skin (rash and non-rash), and nail adverse events, as well as weight decreases.[15]

Infections occurred in more than half of the patients, which resulted in death in five patients. Rates of grade 3–4 infections were 26% or less across cohorts; combined with the low incidence of COVID-19–related deaths, these results are promising in the context of rates reported for other bispecific antibodies despite lower use of intravenous immunoglobulin and contemporaneous enrolment of similar patients during the omicron wave of the COVID-19 pandemic.[16–18] A modest effect on neutropenia was also observed, typically early during treatment. Unlike BCMA and FcRH5, which are expressed on normal plasma cells and B cells,[19,20] GPRC5D expression is restricted to normal and malignant plasma cells,[21] with lower expression on normal versus malignant plasma cells[22] and with minimal to no expression on B cells or B-cell precursors.[21–25] This might explain the lower incidence of grade 3–4 infections seen with talquetamab versus the BCMA-targeted bispecific antibodies elranatamab (40%; median follow-up 14·7 months)[18] and teclistamab (55%; median follow-up 30·4 months).[26] This intrinsic B-cell–sparing quality with no decreases in polyclonal IgG and non-overlapping safety profile with other treatment modalities makes talquetamab a suitable combination partner, which has been demonstrated by encouraging preliminary data with daratumumab, teclistamab, and pomalidomide.[27–30] These data further validate GPRC5D as a therapeutic target for relapsed or refractory multiple myeloma.[9,31]

Limitations to this study include that only 537 of 735 patients screened for inclusion were treated across phase 1–2 cohorts and the absence of comparator therapies assessed against talquetamab. However, additional phase 1 studies (NCT04586426; NCT04108195; NCT05050097; NCT05338775) and phase 3 studies (NCT05455320; NCT06208150) of talquetamab in combination with other agents in patients with relapsed or refractory multiple myeloma are ongoing, with phase 3 studies using the more convenient 0·8 mg/kg every 2 weeks dosing schedule. It should be noted that this study was not designed to assess the effectiveness of adverse event mitigation or management measures, including the effect of tocilizumab on the incidence or severity of cytokine release syndrome. Although the study population was representative of patients with relapsed or refractory multiple myeloma in terms of the expected age profile and ratio of male to female patients, there was a low proportion of Black patients enrolled. Finally, assessments of progression-free survival in patients who did and did not have dose reductions might be biased as dose reduction occurred after treatment.

In conclusion, talquetamab continued to show deep and durable responses with longer follow-up in TCR-naive, heavily pretreated patients with relapsed or refractory multiple myeloma in this post-hoc analysis. Activity results were promising in patients with previous TCR exposure, which is a population of patients with an emerging unmet need; most of these therapies were BCMA-targeting. Rates of high-grade neutropenia and high-grade and fatal infections remained low with longer follow-up compared with BCMA-directed bispecific antibodies, and although on-target, off-tumour adverse events were frequent, there were few treatment discontinuations due to these adverse events.

Contributions

AC, CT, CS, MCM, JGB, AO, NWCJvdD, PR-O, DM, CM-C, M-VM, LJC, JC, LR, AK, JCY, LK, BL, JS-M, and PM contributed to the study design, study conduct, and data analysis and interpretation. DV, SS, RV, XM, XQ, and HL contributed to data acquisition, analysis, and interpretation. MC, TM, BH, JT, TR, JDG, CK, and CH contributed to the study design, study conduct, and data acquisition and interpretation. All authors

participated in drafting or revising the manuscript, and all approved the final version for submission. All authors had full access to all of the data in the study and accept full responsibility for the decision to submit for publication. AC and TR accessed and verified the data in the study.

Declaration of interests

AC reports consulting fees from AbbVie, Adaptive, Amgen, Antengene, Bristol Myers Squibb, Forus, Genetech/Roche, GlaxoSmithKline, Janssen, Karyopharm, Millenium/Takeda, and Sanofi/Genzyme; and support for attending meetings or travel expenses from Antengene, Janssen, and Sanofi/Genzyme. CT support for attending meetings or travel expenses from Janssen. CS reports consulting fees from Janssen; payment or honoraria from MJH Life Sciences, OncLive, and Pfizer; and participation on a data safety monitoring board or advisory board for Janssen. MCM reports consulting fees from GlaxoSmithKline and Janssen; payment or honoraria from Bristol Myers Squibb, Janssen, and Siemens; support for attending meetings or travel expenses from Janssen; and participation on a data safety monitoring board or advisory board for Bristol Myers Squibb and Galapagos. 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XM and JDG were employees of Johnson & Johnson at the time the work was performed. DV, SS, XQ, TM, TR are employees of Johnson & Johnson and have stock or stock options in Johnson & Johnson. HL, MC, and JT are employees of Johnson & Johnson. BH, CK, and CH are employees of Johnson & Johnson; report planned, issued, or pending patents with Johnson & Johnson; and have stock or stock options in Johnson & Johnson. JS-M reports payment or honoraria from AbbVie, Bristol Myers Squibb, Celgene, GlaxoSmithKline, Haemalogix, Janssen, Karyopharm, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Sanofi, SecuraBio, and Takeda. PM reports payment or honoraria from AbbVie, Amgen, Celgene, GlaxoSmithKline, Janssen, Pfizer, Sanofi, and Takeda.

Data sharing

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://innovativemedicine.jnj.com/our-innovation/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at http://yoda.yale.edu.

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