REALiTEC: a multi-country observational retrospective study of teclistamab in patients with relapsed/refractory multiple myeloma outside of clinical trials

Katarina Uttervall,[1] K. Martin Kortüm,[2] Aurore Perrot,[3] Sarah Leeth Farmer,[4] Michele Cavo,[5] Bhuvan Kishore,[6] Caroline Jacquet,[7] Maria Casanova,[8] Markus Hansson,[9] Katja Weisel,[10] Hila Magen,[11] Carmine Liberatore,[12,13] Charlotte Toftmann Hansen,[14] Moshe E. Gatt,[15] Tamir Shragai,[16] Matteo Claudio Da Vià,[17] Teresa De Soto Alvarez,[18] Mathew Streetly,[19] Marc S. Raab,[20] Salomon Manier,[21] Jesper Aegesen,[22] Claire Albrecht,[23] Peter Hu,[24] Pavel Smirnov,[25] Diptendu Santra,[26] Eva Rubio-Azpeitia[27] and Rakesh Popat[28]

[1]Medical Unit Haematology, Karolinska University Hospital, Stockholm, Sweden; [2]Department of Medicine II, University Hospital of Würzburg, Würzburg, Germany; [3]Université de Toulouse, Centre Hospitalier Universitaire Service d'Hématologie, IUCT Oncopole CRCT, Toulouse, France; [4]Department of Haematology, Vejle Hospital, Vejle, Denmark; [5]Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy; [6]University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [7]Service d' Hématologie, CHU de Nancy, Vandoeuvre-lès-Nancy, France; [8]Hospital Costa del Sol, Marbella, Spain; [9]Section of Haematology, Sahlgrenska University Hospital, Gothenburg, Sweden; [10]Universitätsklinikum Hamburg-Eppendorf, Medizinische Klinik und Poliklinik, Hamburg, Germany; [11]Department of Haematology, Chaim Sheba Medical Center, Ramat Gan, Faculty of Medicine, Tel Aviv University, Tel-Aviv, Israel; [12]Department of Medicine and Aging Sciences, University G. d'Annunzio of Chieti-Pescara, Chieti, Italy; [13]Haematology Unit, Santo Spirito Hospital, Pescara, Italy; [14]Department of Haematology, Odense University Hospital, Odense, Denmark; [15]Department of Haematology, Hadassah Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel; [16]Department of Haematology, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; [17]Department of Oncology and Hematology-Oncology, University of Milan, Milan, Italy; Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [18]Haematology Department, La Paz University Hospital, IdiPAZ Research Institute, Madrid, Spain; [19]Department of Clinical Haematology, Guys Hospital, Guys and St. Thomas' NHS Foundation Trust, London, UK; [20]Heidelberg Myeloma Center, Department of Medicine V, University Hospital Heidelberg, Heidelberg, Germany; [21]Department of Haematology, University of Lille, Centre Hospitalier Universitaire Lille, Lille, France; [22]Department of Medicine, Ryhov County Hospital, Jönköping, Sweden; [23]Johnson & Johnson, Issy-les-Moulineux, France; [24]Statistics & Decision Science, Johnson & Johnson Innovative Medicine Research & Development, New Brunswick, NJ; USA; [25]Johnson & Johnson, Milan, Italy; [26]Parexel International, Uxbridge, UK; [27]Johnson & Johnson, Madrid, Spain and [28]NIHR UCLH Clinical Research Facility, University College London Hospitals NHS Foundation Trust, London, UK

Correspondence: K. Uttervall
katarina.uttervall@regionstockholm.se

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Abstract

Teclistamab is the first approved anti-B-cell maturation antigen (BCMA) bispecific antibody for patients with triple-class exposed relapsed/refractory multiple myeloma (RRMM), based on the results of the MajesTEC-1 clinical trial. Here, we first report the findings from REALiTEC, a retrospective observational study of patients who received teclistamab outside of clinical trials in Europe and Israel. The study included 113 patients from 23 sites in eight countries, with most (88.5%) accessing the medication through pre-approval access programs. The median age was 66 years, and patients had a median of 6 prior lines of therapy. Notably, 78.8% were triple-class refractory, 44.2% penta-class refractory, and 35.4% had previous anti-BCMA treatment. Overall response rate (ORR) was 60.2%, with 52.2% of patients achieving a very good partial response or better (≥VGPR). After a median follow-up of 20.7 months, median duration of response (DOR) was 20.3 months, median

progression-free survival (PFS) was 9.7 months, and median overall survival (OS) was 26.3 months. Patients attaining ≥VGPR experienced longer DOR (median 26.1 months), with 12-month PFS and OS rates of 71.2% and 83.1%, respectively. Subgroup analyses demonstrated consistent outcomes across different patient groups, even in those with historically poorer outcomes. Most common adverse events were infections (all grades 70.8%), cytokine release syndrome (55.8%), neutropenia (35.4%), and anemia (25.7%), with no new safety signals identified. Infection rates decreased over time, and immunoglobulin replacement therapy was used in up to 60% of patients. REALiTEC corroborates the efficacy observed in the MajesTEC-1 study, supporting teclistamab as an effective treatment option in heavily pre-treated RRMM patients.

Introduction

Multiple myeloma is characterized by a pattern of continuous relapses with worsening outcomes at each line of therapy.[1,2] In the relapsed/refractory MM (RRMM) setting, prognosis for patients exposed to the three main classes of drugs for MM (proteasome inhibitors [PI], immunomodulatory drugs [IMiD], and anti-CD38 monoclonal antibodies [CD38 mAb]) (triple-class exposed [TCE]) is especially poor, with a median progression-free survival (PFS) of 4.6 months and a median overall survival (OS) of 14.8 months reported when patients were treated with traditional standards of care.[3]

Teclistamab is the first approved B-cell maturation antigen/cluster of differentiation 3 (BCMA/CD3) bispecific monoclonal antibody, following the results of the recommended phase II dose (RP2D) of the pivotal phase Ib/II MajesTEC-1 trial (European Medicines Agency approval: July 2022; US Food & Drug Administration approval: October 2022).[4] The patient population was heavily pre-treated with a median of 5 prior lines of therapy.[5-8] After a median follow up of 30.4 months, teclistamab demonstrated deep and durable responses, with an overall response rate (ORR) of 63%, with 73% of those being complete response or better (46.1% ≥ complete response [CR] rate). Median duration of response (DOR) was 24 months and median PFS and OS were 11.4 and 22.2 months, respectively.[9] Notably, the recruitment period for MajesTEC-1 coincided with the highest peak of deaths worldwide in the COVID-19 pandemic, which adversely affected patient outcomes. Thus, a post-hoc analysis was conducted to adjust for the deaths related to COVID-19, yielding a median PFS and OS of 15.1 months and 28.3 months, respectively.[10] Additionally, a pooled analysis of three registrational studies of teclistamab monotherapy that included 217 patients showed consistent findings, with median DOR, PFS, and OS of 26.7, 15.1, and 26.3 months, respectively.[11] In the MajesTEC-1 subgroup analysis, teclistamab showed consistent response rates across different subgroups such as penta-refractory patients (resistant to all major drug classes [two PI, two IMiD, and CD38 mAb]), patients with high-risk cytogenetics, and patients aged over 75 years compared with the overall study population.[12] The most common adverse events (AE) reported in MajesTEC-1 were infections, hematologic toxicities, and cytokine release syndrome (CRS). Moreover, discontinuation rate due to AE in MajesTEC-1 was low (4.8%, with 3% attributable to infections).[5]

Prior to the commercialization of teclistamab, pre-approval access programs (PAA) were implemented in more than 20 countries worldwide to allow early access for patients with a justified unmet medical need. These were mainly heavily pre-treated patients with no other treatment options available or even eligible for ongoing clinical trials. Generating early data from patients treated outside of clinical trials is critical to complement clinical trial findings in broader patient populations to guide clinical practice and help define therapy management strategies. Here, we present the first report of results of REALiTEC, a retrospective observational study that describes the management and outcomes of patients with RRMM receiving teclistamab outside of clinical trials.

Methods

Study design

REALiTEC (clinicaltrials.gov identifier NCT06285318) is a retrospective, non-interventional, multi-country study, that describes safety and effectiveness of teclistamab in RRMM patients treated outside of the clinical trial setting. Patients were eligible if they had a confirmed diagnosis of RRMM, were ≥18 years of age, and had received ≥1 dose of teclistamab prior to 31st December 2022 outside of an interventional clinical trial. The study was conducted in accordance with the Good Clinical Practice guidelines and the principles of the Declaration of Helsinki. The Institutional Review Board or Ethics Committee at each study site provided protocol approval. Patients on PAA programs were included according to their country's national regulations, and treated according to the summary of product characteristics (SMPC) and physician discretion.[13] Teclistamab treatment was administered by subcutaneous injection (SC) according to the SMPC (step-up doses of 0.06 mg/kg and 0.3 mg/kg, then 1.5 mg/kg weekly, with a possible 1.5 mg/kg SC every 2 weeks).[13] Informed consent was obtained for all alive patients prior to data collection; for deceased patients, informed consent waivers were obtained as applicable, based on country-/site-specific requirements.

Data collection and outcomes

Data collection was structured using a dedicated, detailed electronic case report form (eCRF), tailored and validated to

meet study requirements independently of PAA. Retrospective data were collected from available medical records from first dose of teclistamab through date of informed consent for patients still under treatment or follow-up, and up to the date of death for deceased patients. Baseline data collected included patient demographics, Eastern Cooperative Oncology Group (ECOG) performance status, comorbidities of clinical interest, hematologic and chemistry laboratory parameters, disease characteristics, and prior therapies.

Responses recorded were evaluated according to the International Myeloma Working Group (IMWG) classifications. Treatment outcomes were assessed based on response rates, time to first and best response, DOR, PFS, OS, PFS2, and time to next treatment (TTNT) (see *Online Supplementary Appendix* for further information). Exploratory subgroup analyses were conducted in a range of subgroups of patients of clinical interest. Safety outcomes were coded using Medical Dictionary for Regulatory Activities (MedDRA). All AE except CRS and immune cell-associated neurotoxicity syndrome (ICANS) were graded as per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0, with CRS and ICANS graded according to American Society for Transplantation and Cellular Therapy (ASTCT) guidelines.[14]

Statistical analysis

Data on patient demographics and disease characteristics were summarized using medians with a range for continuous variables, and as percentages with corresponding 95% confidence intervals (CI) as appropriate for categorical variables. Time-to-event variables (e.g., DOR, PFS, OS, PFS2, and TTNT) were analyzed using the Kaplan-Meier approach, with DOR calculated only among responders. Incidence and severity of all grades of CRS, ICANS, infections, and any other AE during treatment were summarized using categorical variables, with 95% Clopper-Pearson confidence intervals. Pre-specified univariate subgroup analyses were conducted for DOR, PFS, and OS. For each subgroup, hazard ratios (HR) and corresponding 95% CI were estimated using Cox proportional-hazards regression. Forest plots showing HR point estimates and 95% CI were created.

Ethics statement

The study was conducted in accordance with Good Clinical Practice guidelines and the principles of the Declaration of Helsinki. The Institutional Review Board or Ethics Committee at each study site approved the protocol and the consent process as applicable.

Results

Patient disposition

In total, 113 eligible patients who received teclistamab on/before the 31st December 2022 from 23 sites in eight different countries (Denmark, France, Germany, Israel, Italy, Spain, Sweden, and the United Kingdom) were included in the study. Of the 113 patients, 100 patients (88.5%) received teclistamab as part of PAA programs. Most patients (89.4%) were treated in academic centers whilst the rest were treated in smaller community centers. All patients were admitted to hospital for step-up dosing, and median inpatient length of stay during the step-up phase, including the first full dose, was eight days (2-41).

At time of consent, 36 patients were on treatment and 5 had their treatment on hold. Seventy-two patients (63.7%) had discontinued treatment primarily due to progressive disease in 42 patients (37.2%), AE in 18 patients (15.9%), and 6 deaths (5.3%). The 6 deaths were due to disease progression in 4 patients and due to unknown causes in 2 patients (*Online Supplementary Figure S1*).

Baseline characteristics

Median age was 66 years. Patients received a median of 6 (2-15) prior lines of therapy, and were all TCE; 88.5% penta-class exposed, and 78.8% and 44.2% patients were triple-class and penta-class refractory, respectively (Table 1). Of the patients with available data (N=62), 51.6% had high-risk cytogenetics defined as having one or more of the following abnormalities by fluorescent *in situ* hybridization: t(4;14), t(14;16), del17p13, and amp1q21. Of the 113 patients included, 80 (70.8%) would not have been eligible for the MajesTEC-1 trial because they met one or more of MajesTEC-1 trial exclusion criteria[9] (*Online Supplementary Table S1*). Notably, 40 patients (35.4%) had been previously exposed to prior BCMA-directed treatments: 32 to antibody-drug conjugates (ADC), 10 to CAR-T-cell therapies, and 3 to bispecific antibody. These patients had similar baseline characteristics but had a longer median time since diagnosis (9.3 years [2.1-18.5] *vs*. 6.1 years [0.7–24.2]) and a median of 6 (3-15) prior lines of therapy *versus* 5 (2-12), with most patients having ≥5 prior lines of therapy (90.0% *vs*. 58.9%). Of note, 20 of these patients received ≥1 lines of therapy in between prior BCMA and teclistamab treatment (median 2; range 1-4).

Effectiveness

At the time of database lock, the median duration of follow-up was 20.7 months (range 0.7-35.8) with a median treatment duration of 9.4 months (range 0.26-35.8). Teclistamab led to an ORR of 60.2% (95% CI: 50.5-69.3%), with 52.2% of patients achieving very good partial response or better (≥VGPR) (95% CI: 42.6-61.7%), and a CR or better response (stringent CR + CR) was achieved in 26.5% of patients (95 % CI: 18.7-35.7%). A near CR (defined as a patient meeting all criteria for CR except for confirmatory bone marrow assessment) was reported in 17.7% of patients (95% CI: 11.2-26.0%) (*Online Supplementary Table S2*). Median time to first response was 1.6 months (95% CI: 1.2-1.9), with a median time to best response of 3.8 months (95% CI: 2.8-5.0). Median DOR was 20.3 months (95% CI: 14.8-not esti-

Table 1. Summary of baseline characteristics in REALiTEC (N=113 patients).[a]

Characteristic	N=113[b]
Age, years, median (range) <65 years, N (%) ≥65 to <75 years, N (%) ≥75 years, N (%)	66.0 (43-83) 47 (41.6) 49 (43.4) 17 (15.0)
Male, N (%)	57 (50.4)
Weight, kg, median (range)	71.9 (42.0-118.1)
Race, N (%) White Black Multiple Unknown/not reported	 83 (73.5) 3 (2.7) 1 (0.9) 26 (23.0)
ECOG PS ≥1, 49 evaluated, N (%)	27 (55.1)
LDH >245 U/L, 86 evaluated, N (%)[c]	28 (32.6)
Years since diagnosis, median (range)	7.4 (0.7-24.2)
Extramedullary plasmacytoma, 59 evaluated, N (%)	9 (15.3)
ISS stage, 94 evaluated, N (%) I II III	 32 (34.0) 41 (43.6) 21 (22.3)
High-risk cytogenetics,[d] 62 evaluated, N (%) t(4;14) t(14;16) del17p13 amp1q21	32 (51.6) 12 (19.4) 1 (1.6) 18 (29.0) 13 (21.0)
Previous lines of therapy, median (range) Triple-refractory, N (%) Penta-refractory, N (%) Refractory to the last line of therapy, N (%)	6 (2-15) 89 (78.8) 50 (44.2) 86 (76.1)
Prior autoSCT, N (%)	86 (76.1)
Prior alloSCT, N (%)	8 (7.1)
Prior BCMA, N (%)	40 (35.4)
Number of prior BCMA therapies CAR-T ADC BsAb	45 10 32 3
Patients ineligible for MajesTEC-1, N (%)	80 (70.8)
Creatinine clearance/GFR, mL/min or mL/min/1.73 m^2, 104 evaluated, N (%) <30 ≥30 to <40 ≥40	 3 (2.9) 11 (10.6) 90 (86.5)
Hb ≥80 g/L, 112 evaluated, N (%)	103 (92.0)
Platelet count ≥75x10^9 cells/L, 112 evaluated, N (%)	86 (76.8)
ANC ≥1x10^9 cells/L, 102 evaluated, N (%)	91 (89.2)

mable [NE]) (Figure 1A). Median PFS was 9.7 months (95% CI: 5.6-18.8) (Figure 1B), and median OS was 26.3 months (95% CI: 16.5-NE) (Figure 1C). PFS and OS estimates at 12 months were 47.4% (95% CI: 38.0-56.3%) and 61.9% (95% CI: 52.3-70.2%), respectively. Effectiveness was improved in patients achieving ≥VGPR, with a median DOR of 26.1 months (95% CI: 16.7-NE), and median PFS and OS were not reached (95% CI: 17.3-NE and 95% CI: 26.3-NE), with 12-month estimates of 71.2% (95% CI: 57.8-81.0%) and 83.1% (95% CI: 70.8-90.5%), respectively (Figure 1A-C). Median TTNT (95% CI: 24.4-NE) and median PFS2 (95% CI: NE-NE) were not reached (*Online Supplementary Figure S2*), with 12-month estimates of 74.3% (95% CI: 65.2-81.4%) and 80.5% (95% CI: 72.0-86.7%), respectively.

Subgroup analyses

Exploratory subgroup analyses showed response rates to be consistent between the overall patient cohort and selected subgroups, such as the penta-class refractory (N=50; ORR: 58.0% [95% CI: 43.2-71.8%]; ≥VGPR: 50.0% [95% CI: 35.5-64.5%), high-risk cytogenetics (N=32; ORR: 68.8% [95% CI: 50.0-83.9%]; ≥VGPR: 65.6% [95% CI: 46.8-81.4%]), patients aged ≥75 years (N=17; ORR: 64.7% [95% CI: 38.3-85.8%]; ≥VGPR: 64.7% [95% CI: 38.3-85.8%]), International Staging System III (N=21; ORR: 52.4% [95% CI: 29.8-74.3%]; ≥VGPR: 47.6% [95% CI: 25.7-70.2%]), and participants ineligible for MajesTEC-1 (N=80; ORR: 57.5% [95% CI: 45.9-68.5%], ≥VGPR: 51.3% [95% CI: 39.8-62.6%]) (Figure 2A). Patients without prior anti-BCMA exposure (N=73) had 63.0% ORR (95% CI: 50.9-74.0%) and 53.1% ≥VGPR (95% CI: 41.4-65.2%) as compared with 55.0% ORR (95% CI: 38.5-70.7%) and 50.0% ≥VGPR (95% CI: 33.8-66.2%) rates in those previously exposed to BCMA targeted agents (N=40). In the 32 patients previously exposed to ADC, ORR was 53.1% (95% CI: 34.7-70.9%) and the ≥VGPR rate was 46.9% (95% CI: 29.1-65.3%), while in those with prior CAR-T (N=10), ORR was 50.0% and the ≥VGPR rate was 50.0% (95% CI: for both, 18.7-81.3%) (Figure 2B). We did not find any notable differences in response rates in patients for whom more than six months had elapsed between prior anti-BCMA and teclistamab treatment compared with those with less than a 6-month interval between them. Patients without prior exposure to BCMA targeted agents had a median DOR of 20.3 months (95% CI: 12.4-NE), a median PFS of 13.8 months (95% CI: 7.5-NE), and a median OS that was not reached (95% CI: 26.3-NE), with a 12-month estimate of 65.8% (95% CI: 53.7-

[a]17 patients from 3 sites in the REALiTEC cohort overlap with the French EAP cohort (RetrosTECtive study, which enrolled patients from 14th October 2022 to 14th September 2023). Since REALiTEC only included patients treated prior to 31st December 2022, these patients had an overlap of approximately 3 months. Given the limited temporal window and the small number of patients from the overlapping sites, any duplication is expected to be minimal. [b]Data available added as denominators if some were missing and not available in the clinical chart for the whole cohort. [c]Baseline lactate dehydrogenase (LDH) stratification value of 245 U/L represents the institutional Upper Limit of Normal (ULN). [d]High-risk cytogenetics defined as having presence of t(4;14), t(14;16), del17p13, and amp1q21 by fluorescent *in situ* hybridization. ADC: antibody-drug conjugate; ANC: absolute neutrophil count; alloSCT: allogeneic stem cell transplant (SCT); autoSCT: autologous SCT; BCMA: B-cell maturation antigen; BsAb: bispecific antibody; CAR-T: chimeric antigen receptor T-cell therapy; ECOG: Eastern Cooperative Oncology Group performance status; GFR: glomerular filtration rate; Hb: hemoglobin; Ig: immunoglobulin; ISS: International Staging System;

75.4). Conversely, those previously exposed to anti-BCMA treatments had a median DOR of 17.4 months (95% CI: 6.6-NE), a median PFS of 3.4 months (95% CI: 2.6-18.8), and a median OS of 15.2 months (95% CI: 4.7-NE). Overall,

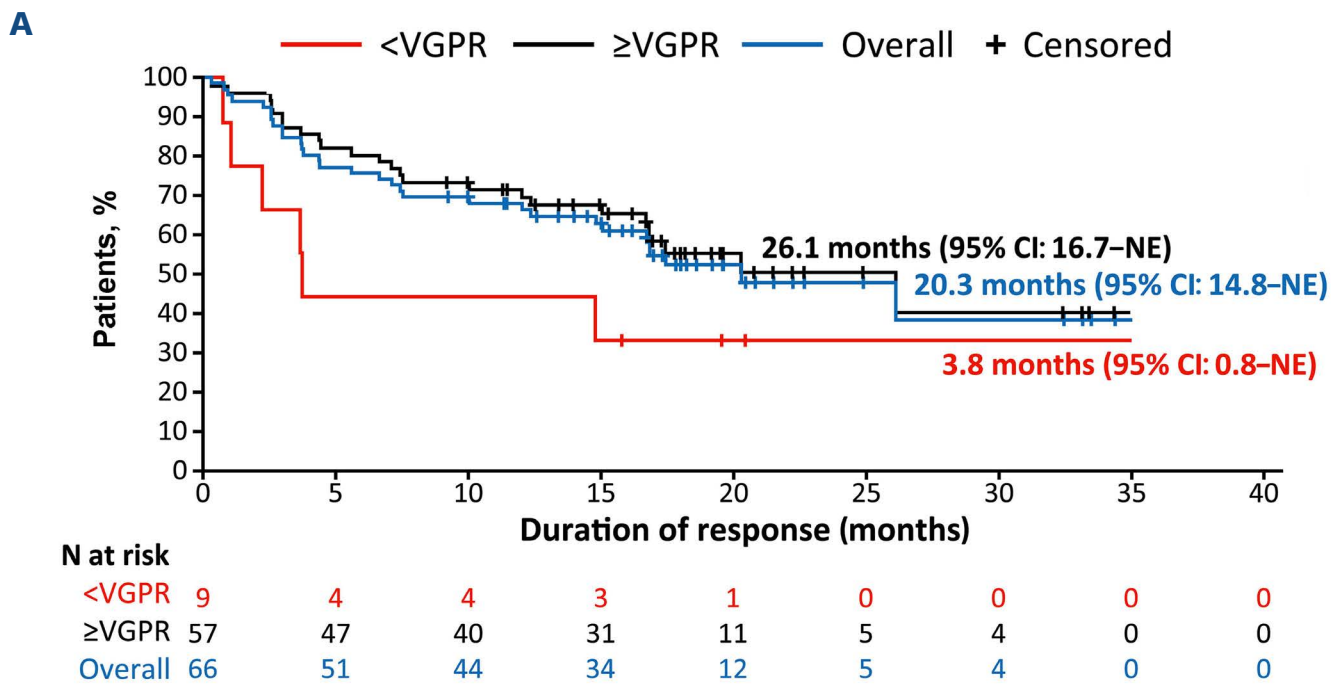


Figure 1. Kaplan-Meier plots in the overall REALiTEC patient population and in patients achieving more than very good partial response and less than very good partial response. (A) Duration of response (DOR), (B) progression-free survival (PFS), and (C) overall survival (OS). Summary data shown are median (95% Confidence Interval [CI]). N: number; NE: not estimable; NR: not reached; VGPR: very good partial response.

DOR, PFS, and OS were consistent across subgroups, with significant results observed when analyzed according to prior BCMA exposure, more specifically, prior BCMA ADC, depth of response (≥VGPR) achieved, and MajesTEC-1 eligibility (*Online Supplementary Figure S3*).

Patients with a change in dosing schedule

In our cohort, 45 (39.8%) patients switched to biweekly dosing after a median of 7.0 months of treatment (range 0-18); the main reason to switch was achievement of deep responses (≥VGPR: 62.2%). Other reasons listed were patient preference in 13.3% of cases, AE in 8.9%, convenience in 6.7%, and other in 26.7%. Moreover, 26 (23.0%) patients switched to monthly administration after a median of 10.5 months of treatment (range 1-22); the main reason for switching here was achievement of ≥VGPR in 80.8% of cases. Other reasons listed were patient preference in 11.5% of cases, convenience in 7.7%, and other in 19.2%. In the 45 patients who switched from weekly to biweekly dosing, an ORR of 82.2% (95% CI: 67.9-92.0%) was observed, with 80.0% (95% CI: 65.4-90.4%) of patients achieving ≥VGPR (*Online Supplementary Table S3*). In this biweekly cohort, median DOR (95% CI: 20.3-NE), PFS (95% CI: 22.2 months-NE), and OS (95% CI: 26.3-NE) were not reached. The 12-month estimates for DOR, PFS, and OS were 85.7% (95% CI: 68.9-93.8%), 86.7% (95% CI: 72.7-93.8%), and 97.8% (95% CI: 85.3-99.7%), respectively. In the 26 patients who switched to monthly dosing, an ORR of 88.5% (95% CI: 69.8-97.6%) was reported, with 84.6% (95% CI: 65.1-95.6%) achieving ≥VGPR (*Online Supplementary Table S3*). In these patients, median DOR (95% CI: 20.3-NE), PFS (95% CI: 22.2-NE), and OS (95% CI: NE-NE) were also not reached. The 12-month estimates for DOR, PFS, and OS were 95% (95% CI: 69.5-99.3%), 92.3% (95% CI: 72.6-98.0%), and 96.2% (95% CI: 75.7-99.4%), respectively.

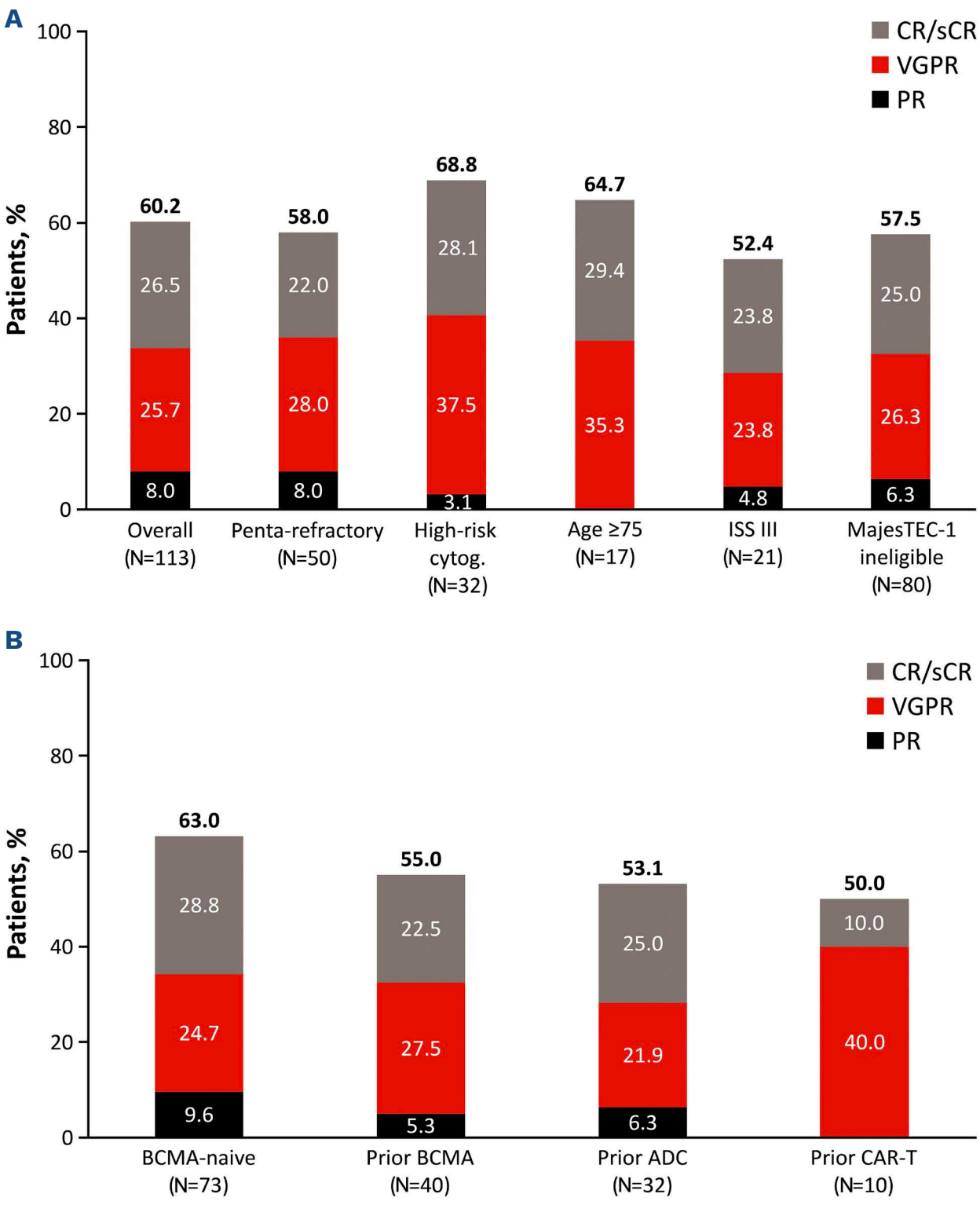


Figure 2. Overall response rates, very good partial response or better, and partial response across selected subgroups of patients in the REALiTEC study. (A) Patients with high-risk subgroups and (B) with prior B-cell maturation antigen (BCMA) (antibody-drug conjugate [ADC] and chimeric antigen receptor T-cell therapy [CAR-T]). CR: complete response; PR: partial response; cytog.: cytogenetics; ISS: International Scoring System; N: number; ORR: overall response rate; PR: partial sCR: stringent CR; VGPR: very good partial response.

Safety findings

The most common all-grade AE (≥20% of patients) were infections (70.8%), CRS (55.8%), neutropenia (35.4%), and anemia (25.7%) (Table 2). Overall, 18 (15.9%) patients discontinued therapy, 53 (46.9%) delayed a dose, 34 (30.1%) skipped a dose, and one (0.9%) reduced dose due to AE. 13 patients experienced grade 5 AE, 5 of which were considered to be related to teclistamab (*Online Supplementary Table S4*).

Ninety CRS events occurred in 63 patients (55.8%), with 19 patients (16.8%) experiencing multiple CRS events. Events were grade 1-2 in most patients (98.2%), with grade 3 events occurring in 2 patients. Most CRS events (94.4%) occurred after a step-up dose or the first maintenance dose and had a median duration of two days (range 1-23); all of them resolved. CRS was managed with antipyretics in 33 patients (29.2%), tocilizumab in 17 patients (15%), corticosteroids in 11 patients (9.7%), intravenous fluids in 6 patients (5.3%), vasopressors in one patient (0.9%), and other treatments in 18 patients (15.9%). No prophylactic tocilizumab was reported in our cohort. Six grade 1-2 ICANS events were observed in 4 (3.5%) patients, with one patient experiencing multiple ICANS events that did not worsen with subsequent episodes. No grade ≥3 ICANS events were observed. Two ICANS events were concurrent with CRS. All ICANS events occurred after a step-up dose or the first maintenance dose and lasted a median of 1.5 days (range 1-6). No patients discontinued teclistamab due to either CRS or ICANS.

Eighty (70.8%) patients experienced 261 infections, with 29 patients (25.7%) experiencing maximum grade 1-2 events, 44 (38.9%) had maximum grade 3-4 events, and 6 patients (5.3%) had grade 5 events. A total of 60 patients (53.1%) had multiple infectious events. Fatal infections were 3 cases of septic shock and 3 cases of pneumonia (Table 3, *Online Supplementary Table S4*). Among the classified infections, most infections were viral or bacterial (N=70 and N=66, respectively), with only 5 fungal infection events reported. Bacterial infections (grade 3-4) generally had an earlier onset than viral infections (63.5 days *vs.* 148.0 days), with a median duration of 14.0 (range 1-181) and 15.5 (range 1-273) days, respectively (Table 3). Median time to infection of any grade was 128.0 days (range 1-1062), and median time to grade 3-4 was 99.0 days (range 2-820).

Table 2. Summary of safety outcomes in REALiTEC (N=113 patients).

TEAE, N (%)	N=113	
	Any grade, N (%)	Grade 3/4, N (%)
Patients with any TEAE	108 (95.6)	83 (73.5)
Infections	80 (70.8)	49 (43.4)
Pneumonia	24 (21.2)	16 (14.2)
SARS-CoV2 virus (COVID-19)	17 (15.0)	8 (7.1)
Infection (unknown)	12 (10.6)	2 (1.8)
Upper respiratory tract infection	11 (9.7)	0
CMV reactivation	3 (2.7)	1 (0.9)
Hematologic TEAE		
Neutropenia	40 (35.4)	37 (32.7)
Anemia	29 (25.7)	19 (16.8)
Thrombocytopenia	21 (18.6)	17 (15.0)
Non-hematologic TEAE		
CRS	63 (55.8)	2 (1.8)
Diarrhea	17 (15.0)	0
Neurologic TEAE of interest		
Peripheral sensory neuropathy	5 (4.4)	0
ICANS	4 (3.5)	0
Motor dysfunction	1 (0.9)	0
Encephalopathy[a]	3 (2.7)	1 (0.9)

[a]Includes toxic encephalopathy and encephalopathy. CMV: cytomegalovirus; CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome; N: number; TEAE: treatment-emergent adverse event.

Table 3. Summary of infections in the REALiTEC study (N=113 patients).

Infections	Total	Bacterial[a]	Viral[a]
Patients with any event, N (%)	80 (70.8)	36 (31.9)	36 (31.9)
Patients with multiple events, N (%)	60 (53.1)	18 (15.9)	17 (15.0)
Patients with grade 3/4, N (%)	44 (38.9)	25 (22.1)	14 (12.4)
Patients with grade 5, N (%)	6 (5.3)	2 (1.8)	1 (0.9)
N of infection events	261	66[a]	70[a]
Time to onset, median N of days to event (range)	128.0 (1-1062)	101.0 (2-1062)	126.0 (1-859)
Grade 3/4 infection onset, median N of days to event (range)	99.0 (2-820)	63.5 (2-734)	148.0 (4-820)
Duration event, days, median (range)	15.0 (1-300)	14.0 (1-181)	15.5 (1-273)
Patients with AE leading to dose interruption, N (%)	52 (46.0)	19 (16.8)	25 (22.1)
Patients with AE leading to discontinuation, N (%)	10 (8.8)	2 (1.8)	4 (3.5)
Events recovering, recovered or resolved,[b] N (%)	236/261 (90.4)	62/66 (93.9)	64/70 (91.4)

[a]Classifications of some infections (N=120) were not recorded due to unavailability of medical records; 5 fungal infections were also reported. [b]Includes recovered/resolved, recovered/resolved with sequelae, recovering/resolving. AE: adverse events.

Median duration of infectious events was 15.0 days (range 1-300). Overall, 90.3% of infections resolved or were resolving at data cut-off. Generally, infection rates declined over time (Figure 3).

Overall, 80.5% of patients received any prophylactic medication before teclistamab initiation, including 19 (16.8%) for management of CRS, 2 (1.8%) for management of ICANS, and 46 (40.7%) for management of infections. A total of 45.1% of patients received ≥1 growth factors during treatment; 22.1% were reported as prophylaxis. Eleven patients (9.7%) received ≥1 cycle of radiotherapy during teclistamab treatment.

Immunoglobulin replacement therapy (IgRT) was prescribed in 68 patients (60.2%), with most of these patients receiving it as primary prophylaxis (70.6%). Median start time of IgRT was 78.0 days (range 0-391). Most patients (N=59) received intravenous IgG whilst some received SC IgG (N=13). Other infectious prophylaxis strategies reported before initiation of teclistamab were antibiotics in 23.0% of patients, antivirals in 29.2%, and antifungal agents in 5.3%. Treatments for infections were reported in 74 patients (65.5%), including antibiotics in 72 patients (63.7%), antivirals in 26 (23.0%), antifungals in 11 (9.7%), and IVIg used as treatment in 55 (48.7%) and intravenous fluids in 11 (9.7%). AE led to teclistamab discontinuation in 20 patients (17.7%), 10 (8.8%) of which were due to infections.

Subsequent treatments

Overall, 39 (34.5%) patients received ≥1 subsequent treatments, of which 5 patients (4.4%) received one subsequent line of therapy, one patient (0.9%) each received 2 and 3 lines of therapy, and 32 patients (28.3%) received ≥4 lines of therapy. Fifteen patients received talquetamab, 13/15 patients as monotherapy. Other treatments were combinations based on PI (N=22; 19.5%), alkylating agents (N=17 [15.0%]; most commonly cyclophosphamide), IMiD (NN=13 [11.5%]; most commonly pomalidomide), and anti-CD38 (N=9; 8.0%). Overall, 19 patients (16.8%) had subsequent treatment regimens containing glucocorticoids (dexamethasone, prednisone, and other corticosteroids). Six patients (5.3%) received BCMA CAR-T.

In patients for whom responses were reported, the ORR to subsequent treatments (as monotherapy or in combination) were: 45.5% (5/11) with talquetamab (all of them being ≥VGPR), 80.0% (4/5) with BCMA CAR-T (of which 20% were ≥VGPR), and 37.5% (6/16) with PI-based combinations (of which 12.5% were ≥VGPR).

Discussion

The REALiTEC study aimed to comprehensively describe clinical outcomes in RRMM patients treated with teclistamab outside of clinical trials across several European countries. The novelty of this study lies in a long follow-up (median 20.7 months), the enrolment of a difficult-to-treat patient population (consistent with the expected characteristics of PAA patients), and the use of a detailed electronic case report form (eCRF) modelled on clinical trial case report forms that facilitated the collection of extensive data. Teclistamab showed notable effectiveness results and a safety profile consistent with reported.[7,9]

We reported an ORR of 60.2% with most responses being ≥VGPR (52.2%), consistent with the ORR reported in the MajesTEC-1 long-term follow-up (30.4 months). In REALiTEC, ≥CR rates were lower compared with MajesTEC-1 (46.1%), was lower than in the MajesTEC-1 (46.1%), because confirmatory bone marrow assessments were not frequently

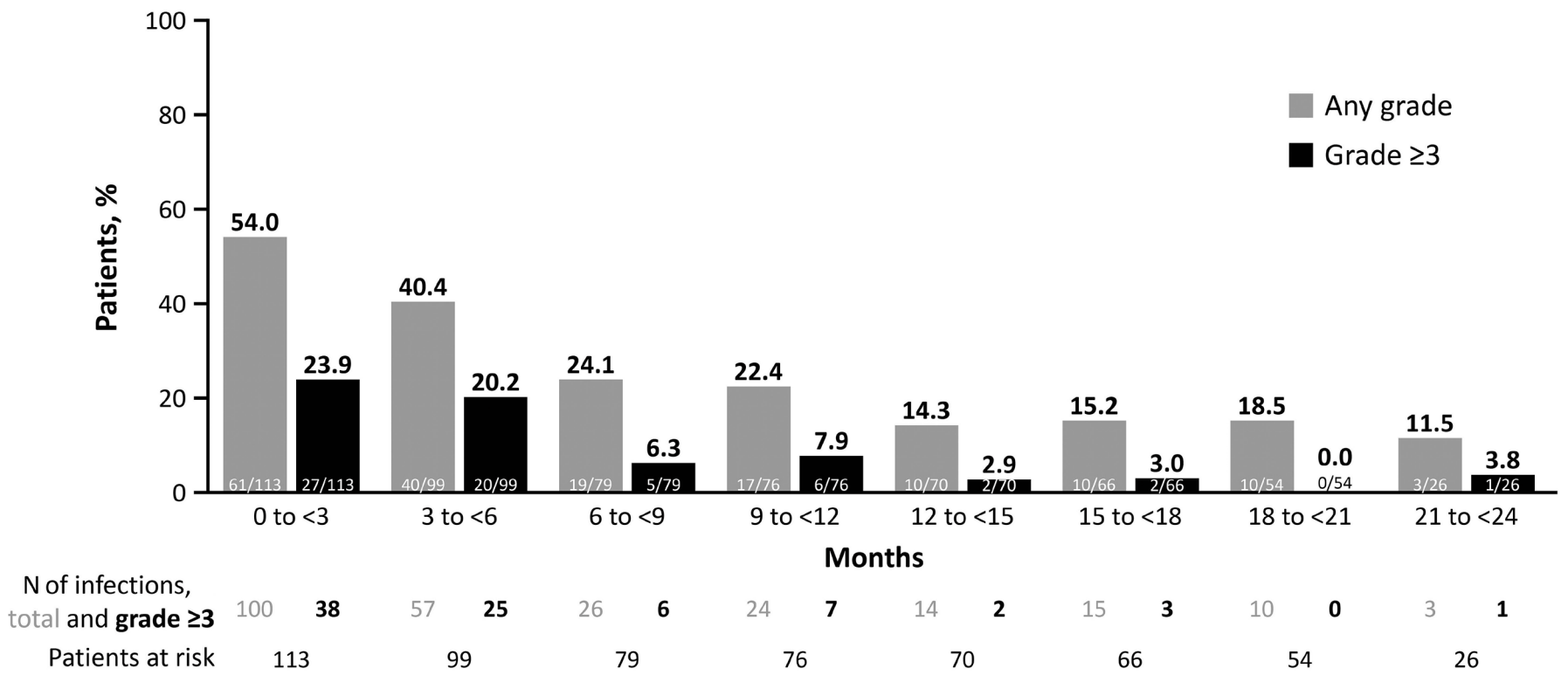


Figure 3. Incidence of infections over time in the overall REALiTEC population. Number of patients with infections / number of patients at risk.

performed. However, if we account for at least CR and near CR rates, we observed a rate of 44.2%, which is in line with the results of the pivotal MajesTEC-1 trial. Moreover, the ORR of 60.2% and the 52.2% ≥VGPR rate observed fall within the range of ORR and ≥VGPR rates reported in other real-world studies.[12,15-20]

The 20.7 month follow-up was substantially longer than other teclistamab real-world studies, where median follow-ups range between 3.8 and 16 months.[21-23] We observed a median DOR of 20.3 months, a median PFS of 9.7 months, and a median OS of 26.3 months. In the MajesTEC-1 study, median DOR was 24 months, median PFS was 11.4 months, and median OS was 22.2 months. Nevertheless, comparisons with MajesTEC-1 should be made with BCMA naïve patients, as this was an exclusion criterion for the trial. Thus, in our cohort's subgroup of BCMA-naive patients, we observed a median DOR of 20.3 months, a median PFS of 13.8 months, and a median OS that was not reached, which compares favorably with the outcomes of the MajesTEC-1 overall RP2D cohort, especially considering the harder-to-treat patient population of our study. In other real-world cohorts, median PFS ranged from 5.4 to not reached, but due to the short median follow-up of those studies and variable patient characteristics, any comparisons should be made with caution.[12,22] Moreover, consistent with prior findings, we observed that achieving deep responses (≥VGPR) had a significant impact on DOR, PFS, and OS. This was also observed in MajesTEC-1, where achieving deep responses was crucial for prolonged long-term survival outcomes, with a median DOR of 25.6 months, median PFS of 26.7 months, and median OS not reached in patients achieving ≥VGPR. When considering subgroup analyses, we observed similar response rates in subgroups with historically poorer outcomes as compared with the overall cohort. This is concordant with MajesTEC-1, where response rates were close between the overall RP2D population and penta-class refractory patients, patients with high-risk cytogenetics, and patients aged over 75 years. When we considered prior BCMA treatment, we found that teclistamab led to clinically meaningful responses in BCMA exposed patients, with 55.0% ORR and ≥VGPR rates of 50.0%. These results are consistent with those reported in MajesTEC-1 cohort C, in which an ORR of 52.5% and a ≥VGPR of 47.5% were observed. Patients treated with prior ADC and prior CAR-T also had similar response rates in REALiTEC as compared with the MajesTEC-1 cohort C; however, comparison of those results need to be made with caution as only 10 patients were treated with prior BCMA CAR-T in our cohort and of those, 5 were also treated with BCMA ADC. Interestingly, we found significantly impaired outcomes in patients treated with prior ADC. Tan *et al*. also found a significant impact of prior BCMA-targeting therapies on PFS, but no significant differences according to type of prior treatment.[17] In contrast with our findings, a recent large US real-world study (N=509) showed that an independent predictor of impaired responses and shorter PFS included BCMA-directed CAR-T therapy in the previous nine months, but not prior ADC exposure, which exhibited a comparable response rate to those without prior BCMA-directed therapy.[18] Taken together, patient characteristics and prior immunotherapies resulting in T-cell exhaustion, as well as BCMA downregulation and shorter washout intervals between BCMA-directed therapies may reduce immune engagement with teclistamab, raising the question about the optimal sequencing of BCMA agents and its management.

As in MajesTEC-1, in REALiTEC, responses were sustained when patients were switched to less frequent dosing after they achieved deep responses.[9] In our cohort, 45 patients switched to biweekly dosing and 26 to monthly dosing after a median of 7.0 and 10.5 months, respectively. These patients were deep responders with high response rates from therapy initiation that were maintained over time; this enabled switching to less frequent dosing even in a heavily pre-treated patient population.

The safety profile in REALiTEC is also consistent with MajesTEC-1, where the most common any-grade AE were cytopenia (neutropenia 71.5% and anemia 55.2%), infections (78.8%), and CRS (72.1%). In our cohort, most CRS events were low grade, a common feature of the safety profile of BCMA bispecifics that was also observed in MajesTEC-1[9,10,15] and real-world cohorts.[10-12,16-18,21,22] Similarly, ICANS events were generally mild. No patients discontinued treatment due to CRS or ICANS, consistent with previously reports.[9,10,15]

Infections are a common complication within the broader setting of RRMM and with BCMA-bispecific antibodies, and still the main cause of death in patients with myeloma.[24] In our study, infections were common, with grade 3-4 events occurring in 38.9% of patients and grade 5 events in 5.3%. In the long-term follow-up of MajesTEC-1, all-grade infections were observed in 78.8% of patients, 55.2% of which were grade 3-4. Grade 5 infections occurred in 22 patients (13.3%), but 18 of those were due to COVID-19. Lower rates of grade 3-4 infection and hematologic toxicities in REALiTEC compared with MajesTEC-1 have also been observed in other real-world cohorts.[17] These likely reflect improved awareness and more proactive supportive care, as well as differences in reporting and monitoring as real-world clinical management studies have inherently less intensive AE capture than clinical trials.[25] Also, consistent with MajesTEC-1, the incidence of infections in our study declined over time, coinciding with the switch to less frequent dosing (after months 7 and 10 corresponding to switching to biweekly and monthly dosing) and implementation of IgG supplementation (although no causality was examined).

To help prevent infection, patients receiving teclistamab should undergo comprehensive viral screening, keep vaccinations up to date, and receive tailored prophylaxis as well as routine IgRT. The importance of IgRT has been established; primary prophylaxis with IVIg is associated with a significantly lower risk of serious infections (5.3%

incidence at 6 months with IVIg *vs*. 54.8% with observation in MajesTEC-1). Likewise, in a retrospective, real-world study, it was observed that primary IVIg prophylaxis significantly improved all-grade and grade ≥3 infection-free survival.[21] In our cohort, we observed 60.2% of patients receiving IgG replacement with most patients receiving it as primary prophylaxis. All this emphasizes how critical it is to use IgG replacement to avoid infections and maintain patients on treatment to achieve the best outcomes.[26]

Limitations of our study are its retrospective design, evaluation without a comparator and without longer-term clinical outcomes. Other limitations of REALiTEC are those typical of real-world studies and include differences in patient selection, prior therapies, supportive care, treatment algorithms, and management, as well as variations in toxicity and response assessments. The absence of data for some assessments (e.g., measurable residual disease negativity rates) and key prognostic variables, such as cytogenetics and detailed IgG levels over time, has also impeded further detailed analysis. Accordingly, in some subgroup analyses, only a small number of patients could be considered for the analysis. On the other hand, the study's strengths include its design and the use of the detailed eCRF, which was capable of capturing diverse patient populations who are not routinely included in clinical trials, and including many early teclistamab-treated patients.

Overall, our findings provide robust data to support treatment decisions around the use of teclistamab in patients with hard-to-treat RRMM. More than 20,800 patients have been treated worldwide to date with commercial teclistamab (Johnson & Johnson, 2025, data on file). Data generation in the subsequent cohort of REALiTEC, REALiTEC-2, will help inform optimal patient management, sequencing, and outcomes in the real world.

REALiTEC demonstrates comparable effectiveness and safety to those reported in MajesTEC-1 in patients treated outside of clinical trials. Overall, these findings further validate teclistamab as an effective standard of care in this difficult-to-treat patient population.

Disclosures

KMK and MSR received financing of scientific research and honoraria from Johnson & Johnson; MCDV served as advisory board member for Takeda, Johnson & Johnson, Sanofi, Pfizer, Amgen and Menarini-Stemline, on a Speakers Bureau for Johnson & Johnson, Sanofi, Pfizer, Menarini-Stemline and GSK, and received scientific research funding from Johnson & Johnson and Pfizer; CA, PH, PS, DS and ERA are employees of Johnson & Johnson. All the other authors have no conflicts of interest to disclose.

Contributions

KU, KMK, AP and RP served as steering committee members; KU, KMK, AP, RP, CA, DS and ERA contributed to study conception and design; KU, KMK, AP, SLF, MC, BK, CJ, MC, MH, KW, HM, CL, CTH, MEG, TS, MCDV, TDSA, MS, MSR, SM, JA and RP recruited patients and collected data; KU, KMK, AP, CA, PH, PS, DS, ERA and RP analyzed and interpreted the data. All authors revised the manuscript for important intellectual content, had access to the study data, and reviewed and approved the final manuscript for publication.

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Data-sharing statement

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. Requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at http://yoda.yale.edu.

References

1. Yong K, Delforge M, Driessen C, et al. Multiple myeloma: patient outcomes in real-world practice. Br J Haematol. 2016;175(2):252-264.
2. Rodriguez-Otero P, Paiva B, San-Miguel JF. Roadmap to cure multiple myeloma. Cancer Treat Rev. 2021;100:102284.
3. Weisel K, Mateos M-V, Brittich M, et al. Outcomes in patients (PTS) with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM) treated with real-life standard of care (SOC) therapies in LocoMMotion and MoMMent final data. Hemasphere. 2025:2025:PS1783.
4. U.S. Food & Drug Administration. FDA approves teclistamab-cqyv for relapsed or refractory multiple myeloma. 2022 10 Dec. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-teclistamab-cqyv-relapsed-or-refractory-multiple-myeloma#:~:text=On%20October%2025%2C%202022%2C%20the%20Food%20and%20Drug,an%20immunomodulatory%20agent%2C%20and%20an%20anti-CD38%20monoclonal%20antibody. Accessed January 27, 2026.
5. TECVAYLI® (teclistamab-cqyv) injection fsu. Prescribing information. 2024. https://www.janssenlabels.com/package-

insert/product-monograph/prescribing-information/TECVAYLI-pi.pdf. Accessed January 27, 2026.
6. TECVAYLI® solution for injection. Summary of product characteristics. 2024. https://ec.europa.eu/health/documents/community-register/2022/20220823157360/anx_157360_en.pdf. Accessed January 27, 2026.
7. Usmani SZ, Karlin L, Benboubker L, et al. Durability of responses with biweekly dosing of teclistamab in patients with relapsed/refractory multiple myeloma achieving a clinical response in the majesTEC-1 study. J Clin Oncol. 2023;41(16_suppl):8034-8034.
8. Moreau P, San Miguel J, Sonneveld P, et al. Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017;28(suppl_4):iv52-iv61.
9. Garfall AL, Nooka AK, van de Donk NWCJ, et al. Long-term follow-up from the phase 1/2 MajesTEC-1 trial of teclistamab in patients with relapsed/refractory multiple myeloma. J Clin Oncol. 2024;42(Suppl 16):7540.
10. van de Donk N, Bahlis N, Costa LJ, et al. Impact of COVID-19 on outcomes with teclistamab in patients with relapsed/refractory multiple myeloma in the phase 1/2 MajesTEC-1 study. Blood Cancer J. 2024;14(1):186.
11. Martin TG, Mateos MV, van de Donk NWCJ, et al. Pooled efficacy and safety of teclistamab with 217 patients with triple-class exposed relapsed/refractory multiple myeloma from 3 registrational clinical studies. Blood. 2024;144(Suppl 1):3331.
12. Dima D, Davis JA, Ahmed N, et al. Safety and efficacy of teclistamab in patients with relapsed/refractory multiple myeloma: a real-world experience. Transplant Cell Ther. 2024;30(3):308.e301-308.e313.
13. European Medicines Agency: Science Medicine Health. Tecvayli: EPAR - Product Information. 2025 10 Dec. https://www.ema.europa.eu/en/documents/product-information/tecvayli-epar-product-information_en.pdf. Accessed January 27, 2026.
14. Lee DW, Santomasso BD, Locke FL, et al. ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant. 2019;25(4):625-638.
15. Mohan M, Monge J, Shah N, et al. Teclistamab in relapsed refractory multiple myeloma: multi-institutional real-world study. Blood Cancer J. 2024;14(1):35.
16. Riedhammer C, Bassermann F, Besemer B, et al. Real-world analysis of teclistamab in 123 RRMM patients from Germany. Leukemia. 2024;38(2):365-371.
17. Tan CR, Asoori S, Huang CY, et al. Real-world evaluation of teclistamab for the treatment of relapsed/refractory multiple myeloma (RRMM): an International Myeloma Working Group study. Blood Cancer J. 2025;15(1):53.
18. Razzo BM, Midha S, Portuguese AJ, et al. Real-world experience with teclistamab for relapsed/refractory multiple myeloma from the US Myeloma Immunotherapy Consortium. Blood Cancer Discov. 2025;6(6):561-571.
19. Dima D, Vazquez-Martinez MA, Davis JA, et al. Outcomes of teclistamab in patients with relapsed/refractory multiple myeloma with prior exposure to BCMA-directed therapy: a multicenter study from the U.S. Multiple Myeloma Immunotherapy Consortium. Blood Cancer J. 2025;15(1):111.
20. Pasvolsky O, Dima D, Feng L, et al. Outcomes of elderly patients with relapsed refractory multiple myeloma (RRMM) treated with teclistamab: a multicenter study from the U.S. Multiple Myeloma Immunotherapy Consortium. Blood Cancer J. 2025;15(1):92.
21. Touzeau C, Krishnan AY, Moreau P, et al. Efficacy and safety of teclistamab in patients with relapsed/refractory multiple myeloma after BCMA-targeting therapies. Blood. 2024;144(23):2375-2388.
22. Qureshi Z, Jamil A, Altaf F, Siddique R, Ahmed F. Efficacy and safety of teclistamab in relapsed or refractory multiple myeloma: a systematic review and meta-analysis. Ann Hematol. 2024;103(12):4901-4912.
23. Costa LJ, Bahlis NJ, Usmani SZ, et al. MM-328 Efficacy and safety of teclistamab in patients with relapsed/refractory multiple myeloma (RRMM) with high-risk (HR) features: a subgroup analysis from the phase 1/2 MajesTEC-1 study. Clin Lymphoma Myeloma Leuk. 2024;24(Suppl 1):S546-S547.
24. Dimopoulos MA, Terpos E, Boccadoro M, et al. EHA-EMN evidence-based guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma. Nat Rev Clin Oncol. 2025;22(9):680-700.
25. Costa LJ, Banerjee R, Mian H, et al. International myeloma working group immunotherapy committee recommendation on sequencing immunotherapy for treatment of multiple myeloma. Leukemia. 2025;39(3):543-554.
26. Banerjee R, Mohan M, Rejeski K, et al. IVIG prophylaxis should be initiated following bispecific antibody therapy in multiple myeloma regardless of IgG levels. Blood Adv. 2025;9(18):4720-4726.