P-154

Clinical Outcomes of Teclistamab Among MajesTEC-1 Eligible and Ineligible Population in the Real-World Setting for the Treatment of Relapsed/Refractory Multiple Myeloma

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Conclusions

In this real-world study, teclistamab continues to demonstrate high ORR and deep and durable responses comparable to the MajesTEC-1 trial, despite a high proportion of patients who would have been excluded in the MajesTEC-1 trial

Real-world patients with similar characteristics to the MajesTEC-1 trial population demonstrated an impressive ORR of 86%, and strong DOR, PFS and OS results (all medians have not been reached at 12-month follow-up)

In patients who would not have met MajesTEC-1 eligibility criteria, including those with prior BCMA-directed therapy, despite significant disease burden and high-risk features, the clinical outcomes still appear to be comparable with the MajesTEC-1 trial

Rates of CRS and ICANS in our real-world population were comparable to the incidences reported in MajesTEC-1, with all CRS and the vast majority of ICANS being low grade. The rates appear similar based on MajesTEC-1 eligibility criteria. The rate of infection was also comparable to MajesTEC-1, with numerically higher rates observed in MajesTEC-1-eligible patients

Introduction

- Teclistamab is the first B-cell maturation antigen (BCMA) and CD3 bispecific antibody approved for triple class–exposed relapsed/refractory multiple myeloma (RRMM)
- Results from the MajesTEC-1 study indicated an overall response rate (ORR) of 63%, a median progression-free survival (PFS) of 11.4 months, and a median duration of response (mDoR) of 24.0 months at a median follow-up of 30.4 months[1]
- Existing evidence showed that the majority of the real-world patients in the US treated with teclistamab would not have met MajesTEC-1 eligibility criteria[2,3]
- Herein, we examined the real-world clinical outcomes of patients with RRMM treated with teclistamab, stratified by MajesTEC-1 eligibility criteria

Methods

- This was a retrospective study of patients with RRMM treated with teclistamab at Memorial Sloan Kettering Cancer Center from November 29, 2022, to July 5, 2024
- Data were collected until July 31, 2024
- MajesTEC-1 eligibility was determined based on clinical trial eligibility criteria. Key criteria include: Eastern Cooperative Oncology Group performance status of 0 or 1; no prior BCMA-targeted therapy; no prior T-cell redirecting therapy; absolute neutrophil count ≥1.0 x 10^9/L; hemoglobin ≥8 g/dL; and platelets ≥75 x 10^9/L
- Responses were evaluated according to the International Myeloma Working Group Uniform Response Criteria[4]
- Patient characteristics were summarized by frequency (percentage) for categorical variables or median (interquartile range [IQR]) for continuous variables
- PFS, duration of response (DOR), and overall survival (OS) were evaluated using the Kaplan-Meier method
- All statistical analyses were performed using *R*

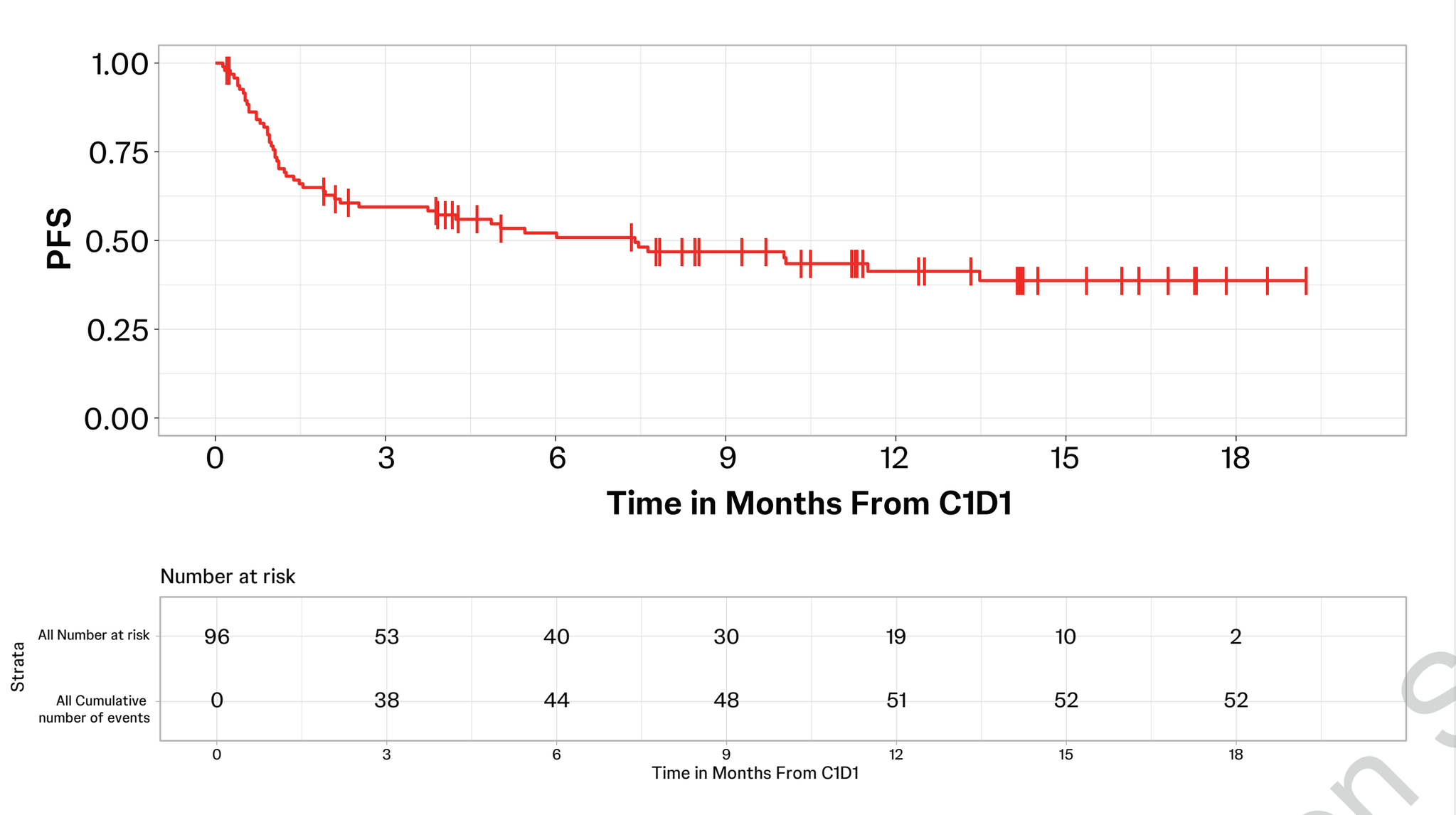
Results

- There were 96 patients with RRMM who received ≥1 dose of teclistamab who were included in this analysis

Overall Population

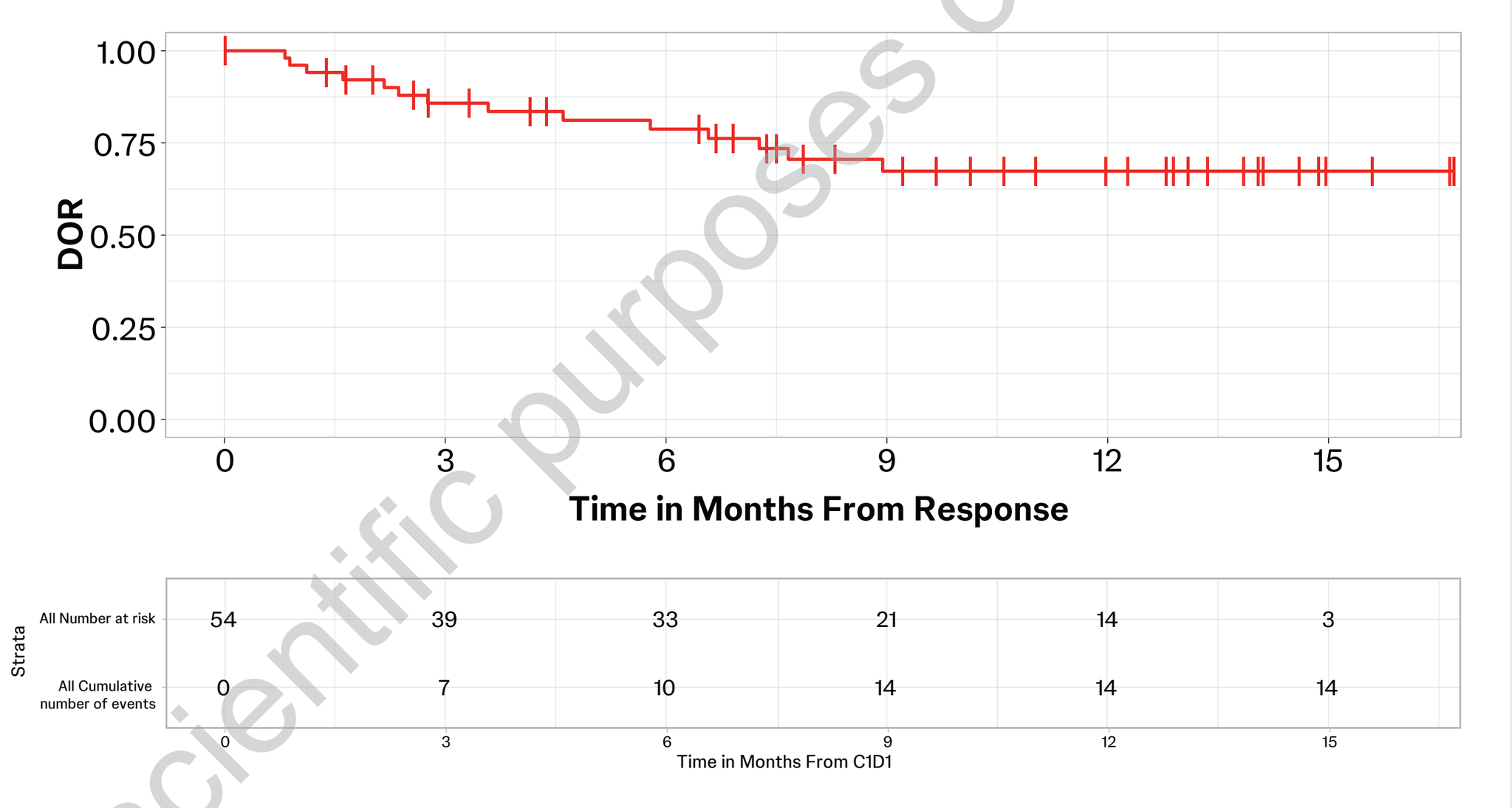
- Known high-risk cytogenetic abnormalities were noted in 72% of patients before initiation of treatment with teclistamab
- The median time from diagnosis to start of treatment with teclistamab was 6.2 years (range, 0.7-29.2 years)
- Thirty-seven patients (39%) had prior BCMA-directed therapy, including antibody drug conjugate, chimeric antigen receptor T-cell therapy, and other bispecific antibodies (**Table 1**)
- The ORR was 61% for 88 response-evaluable patients, including 48% with responses that were a very good partial response (VGPR) or better
  – The ORR for patients with prior BCMA-directed therapy was 44%
- The median time to first response was 1.3 months (IQR, 0.9-2.9 months)
- After a median follow-up of 12.4 months, the 6-month PFS rate was 52.1% (95% CI, 42.8%-63.5%); the 12-month PFS rate was 41.3% (95% CI, 31.6%-53.9%)
- The median PFS was 7.4 months (95% CI, 3.75-not reached)
- The 6-month DOR rate was 78.8% (95% CI, 67.8%-91.5%); the mDOR was not reached
- The 6-month OS rate was 66.6% (95% CI, 57.4%-77.2%); the 12-month OS rate was 61.6% (95% CI, 51.9%-73.2%). The median OS was not reached

FIGURE 1. PFS in overall patients receiving real-world treatment with teclistamab



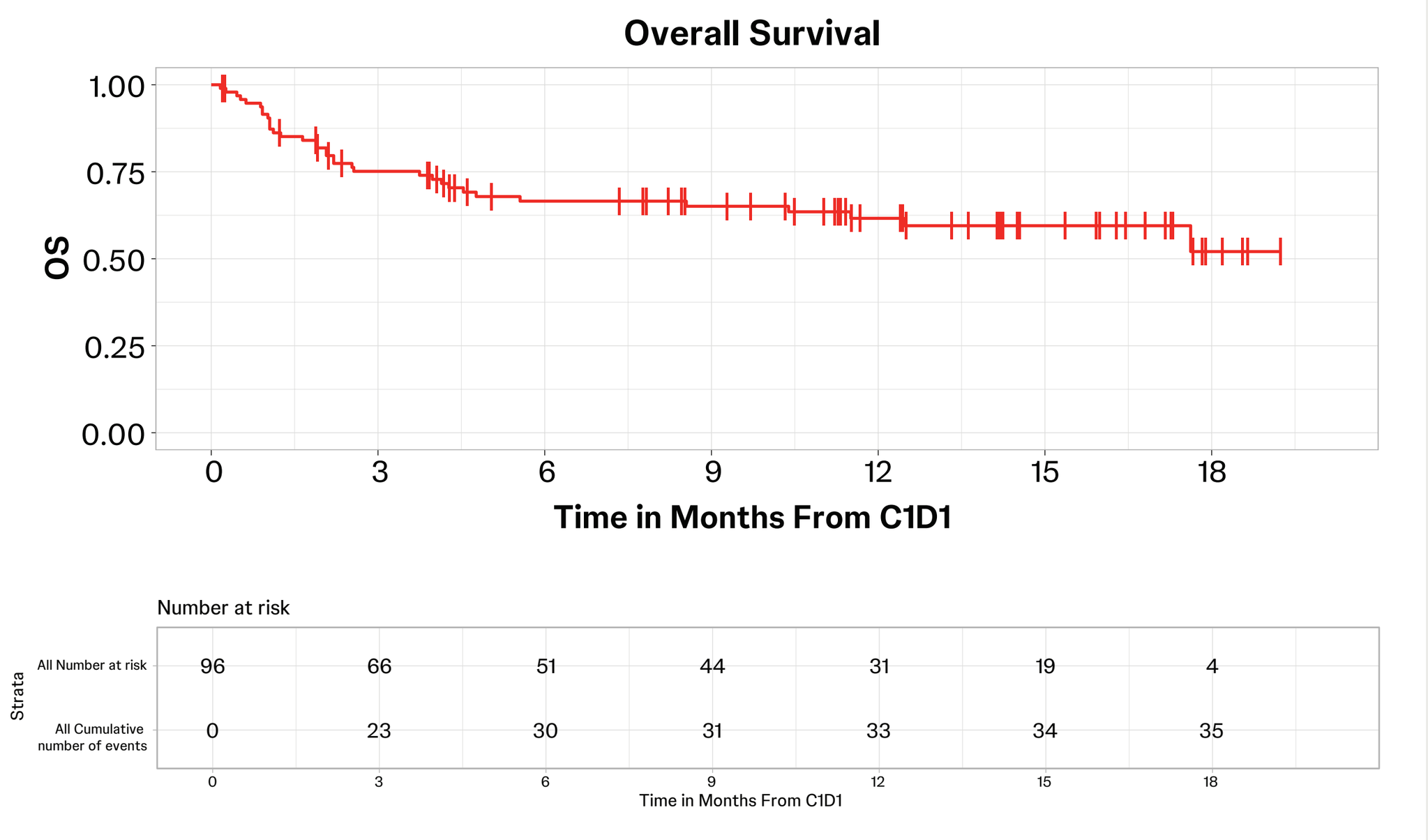
C1D1, cycle 1 day 1; PFS, progression-free survival.

FIGURE 2. DOR in overall patients receiving real-world treatment with teclistamab



DOR, duration of response.

FIGURE 3. OS in overall patients receiving real-world treatment with teclistamab



C1D1, cycle 1 day 1; OS, overall survival.

MajesTEC-1 Eligible and Ineligible Cohorts

- Within our real-world cohort, 22 patients (23%) met eligibility criteria for MajesTEC-1; 74 (77%) did not (Baseline characteristics, **Table 1**)
- Among the 74 ineligible patients, the most common reasons for ineligibility were cytopenias (69%), prior BCMA-directed therapy (50%), creatinine clearance <40 mL/min (28%), and prior non–BCMA T-cell redirecting therapy (16%)
- The MajesTEC-1 ineligible cohort had more patients with high-risk cytogenetic abnormalities (81% vs 45%) and more prior lines of therapy (median 6 [4-9] vs 4 [4-5]) compared with the eligible cohort

TABLE 1. Patient characteristics based on MajesTEC-1 eligibility

Characteristics	Overall Patient Population (N = 96)	MajesTEC-1 Eligible Subgroup (n = 22)	MajesTEC-1 Ineligible Subgroup (n = 74)
Median age, years (IQR)	71 (63-78)	70 (64-78)	71 (64-77)
Male, %	48	36	51
Race, n (%)			
White	68 (71)	17 (77)	51 (69)
Black	20 (21)	5 (23)	15 (20)
Other	8 (8)	0	8 (11)
ISS stage			
I	27/69 (39)	10/16 (63)	17/53 (32)
II	21/69 (30)	5/16 (31)	16/53 (30)
III	21/69 (30)	1/16 (6)	20/53 (38)
Missing	27	6	21
HRCA,[a] n/N (%)	65/90 (72)	10/22 (45)	55/68 (81)
Extramedullary disease,[b] n/N (%)	35/86 (41)	5/18 (28)	30/68 (44)
Median # prior LOT, n (IQR)	6 (4-8)	4 (4-5)	6 (4-9)
Triple-class refractory,[c] n (%)	78 (81)	18 (82)	60 (81)
Penta-drug refractory,[d] n (%)	31 (32)	6 (27)	25 (34)
Prior BCMA exposure, n/N (%)	37/96 (39)	0	37/74 (50)
ADC alone	13/37 (35)	N/A	13/37 (35)
BCMA-bispecific antibody alone	1/37 (3)	N/A	1/37 (3)
CAR T-cell therapy alone	14/37 (38)	N/A	14/37 (38)
ADC + CAR T-cell therapy	7/37 (19)	N/A	7/37 (19)
ADC + CAR T-cell therapy + a bispecific antibody	2/37 (5)	N/A	2/37 (5)

[a]del(17p), t(4:14), t(14;16), t(14;20), and/or gain or amp 1q.
[b]Included soft-tissue plasmacytomas not associated with bone and extraosseous soft tissue.
[c]≥1 PI, ≥1 IMiD, ≥1 anti-CD38 mAb.
[d]≥2 PIs, ≥2 IMiDs, ≥1 anti-CD38 mAb.
ADC, antibody drug conjugate; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; HRCA, high-risk cytogenetic abnormality; IMiD, immunomodulatory drug; IQR, interquartile range; ISS, International Staging System; LOT, line of therapy; mAb, monoclonal antibody; N/A, not applicable; PI, proteasome inhibitor.

- After a median follow-up of 12.4 months for the overall population, the ORR was 86% and 54% in the 21 and 67 evaluable patients in the eligible and ineligible cohorts, respectively. The 12-month DOR was 78% and 61% in both cohorts, respectively (**Table 2**)
- Unadjusted 12-month PFS rates were 64.2% (95% CI, 45.6%-90.3%) and 33.7% (95% CI, 23.5%-48.5%), and the unadjusted 12-month OS rates were 81.3% (95% CI, 66.4%-99.7%) and 55.5% (95% CI, 44.3%-69.5%) in the eligible and ineligible cohorts, respectively (**Table 2**)
- At the analysis cut-off time point, 68% of the eligible patients and 32% of the ineligible patients were able to transition to less frequent dosing schedules (eg, every 2 weeks) based on reaching at least a partial response (PR) and/or for management of adverse events

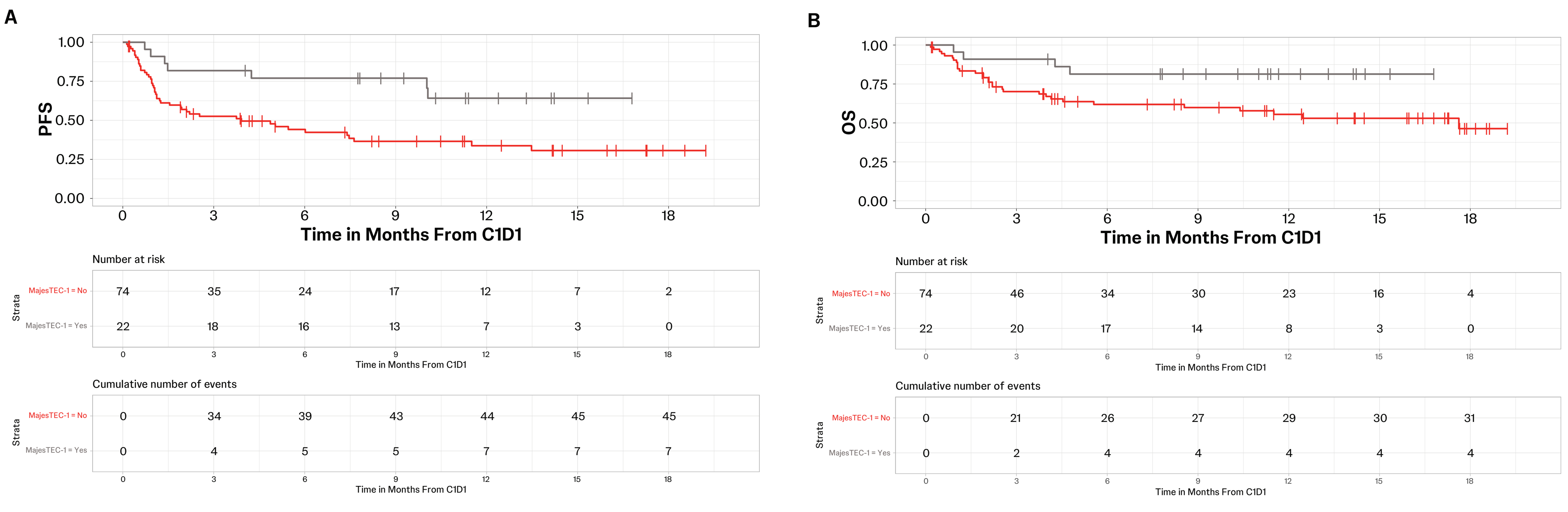
TABLE 2. Effectiveness and safety in real-world patients treated with teclistamab for RRMM

Outcomes	Overall Patient Population (N = 96)	MajesTEC-1 Eligible Subgroup (n = 22)	MajesTEC-1 Ineligible Subgroup (n = 74)
Median follow-up post-index, months (95% CI)	12 (11-15)	12 (10-15)	14 (11-16)
ORR, n/N (%)	54/88 (61)	18/21 (86)	36/67 (54)
12-month DOR, % (95% CI)	67.3 (54.3-83.5)	78 (58-100)	61 (45-83)
12-month PFS, % (95% CI)	41.3 (31.6-53.9)	64.2 (45.6-90.3)	33.7 (23.5-48.5)
12-month OS, % (95% CI)	61.6 (51.9-73.2)	81.3 (66.4-99.7)	55.5 (44.3-69.5)
Patients with any CRS, n (%)	52 (54)	14 (64)	38 (51)
Patients with recurrent CRS, n (%)	6 (7)	2 (9)	4 (6)
Patients with any ICANS, n (%)	12 (13)	1 (5)	11 (15)
Patients with any infection, n (%)	66 (69)	19 (86)	47 (64)
Patients with grade ≥3 infection, n (%)	37 (39)	10 (45)	27 (36)

CI, confidence interval; CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.

- Cytokine release syndrome (CRS) events were observed in 52 (54%) of patients overall and limited to grades 1 and 2 for all events in both the MajesTEC-1 eligible and ineligible cohorts (**Table 2**)
- Immune effector cell-associated neurotoxicity syndrome (ICANS) events were predominantly grades 1 and 2, except for one grade 4 event in the ineligible group. The patient with grade 4 ICANS received levetiracetam, tocilizumab, and methylprednisolone and the symptoms resolved. The patient received teclistamab later without the recurrence of ICANS (**Table 2**)

Figure 4. PFS (A) and OS (B) in patients receiving real-world treatment with teclistamab, stratified by MajesTEC-1 eligibility criteria



C1D1, cycle 1 day 1; PFS, progression-free survival; OS, overall survival.

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Poster

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Disclosures

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