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POSTER ABSTRACTS

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Patterns of Cytokine Release Syndrome with Teclistamab in Relapsed/Refractory Multiple Myeloma with or without Prior T-Cell Redirection Therapy

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Introduction: Numerous therapeutic options with novel mechanisms of actions are currently available for treating patients with relapsed/refractory multiple myeloma (RRMM). Teclistamab (Tec) is a first-in-class BCMA X CD3 bispecific T-cell engager antibody that was recently approved for patients with RRMM who have received at least 4 lines of therapy (LOT). In the landmark MajesTEC-1 study, cytokine release syndrome (CRS) with Tec was reported at a rate of 72% (Usmani S, et al. *Lancet* 2021, Moreau P, et al. *N Engl J Med* 2022); however, patients who were previously treated with T-cell redirection therapies (TCRT) were excluded from the study [TCRT: chimeric antigen receptor (CAR) T-cells and/or other bispecific antibodies]. Given this knowledge gap, we investigated whether prior TCRT exposure impacts CRS rates with Tec in a real-world setting.
Methods: Our institutional plasma cell disorders database was queried to identify RRMM patients who received commercial Tec from November 2022 to July 2023. Patients who completed the Tec step-up dosing phase (first step-up, second step-up and first full doses) were divided into two cohorts based on prior TCRT exposure before treatment with Tec (prior TCRT exposure: **cohort 1** and no prior TCRT exposure: **cohort 2**). Data collection included patient demographics, disease characteristics, prior LOT, and rates/grades of CRS and immune effector cell-associated neurotoxicity syndrome (ICANS). The Chi-square/Fisher exact test was used to compare differences in CRS rates between the two cohorts. Univariate and multivariate logistic regression analyses were performed to assess impact of prior TCRT exposure on CRS rates with Tec. The results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). For **cohort 1**, the Mann-Whitney U-test was used to compare the median time elapsed from the last prior TCRT dose until the first Tec step-up dose between patients who developed CRS with Tec compared to those who did not. All statistical analyses were performed using SPSS software (version 29).
Results: 50 patients (cohort 1: 25 and cohort 2: 25) were included in the final analysis. Baseline characteristics were comparable between the two cohorts except for prior LOT, where patients in cohort 1 represented a more heavily pretreated population **(Table 1**). The CRS rates were significantly lower in cohort 1 (40%, n=10) compared to cohort 2 (76%, n=19, p=0.02; **Figure 1**). CRS grades 1 and 2 occurred in 32% (n=8) and 8% (n=2) of patients in cohort 1 and 48% (n=12) and 28% (n=7) of patients in cohort 2, respectively (p=0.40). Among the CRS events, 60% (6/10) and 68% (13/19) occurred following the first Tec step-up dose in cohorts 1 and 2, respectively. In univariate logistic regression analysis, no prior exposure to a TCRT was associated with about a 5-fold increase in the incidence of CRS with Tec (OR= 4.8, 95% CI: 1.5-17.1.2, p=0.02). After adjusting for age, extramedullary disease (EMD) and elevated LDH levels, the impact of prior exposure to TCRT remained significant with an OR of 4.5 (95% CI: 1.3-18.6, p=0.01). In cohort 1 (prior TCRT exposure), the median time elapsed between the last TCRT dose and the first Tec step-up dose was 321.5 days (range: 50-808 days) in patients who developed CRS with Tec compared to 265 days (range: 41-1617 days) in those who did not (p=0.90).

Conclusion: In our study, prior exposure to a TCRT was associated with a significantly lower incidence of CRS during the Tec step-up dosing phase, which may be suggestive of T-cell exhaustion. This observation will allow for optimization of CRS prophylactic strategies for RRMM patients receiving Tec treatment.

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Table 1. Baseline characteristics of cohorts 1 and 2.

Parameter	Cohort 1 (prior TCRT exposure, n=25)	Cohort 2 (no prior TCRT exposure, n=25)	P value
Median age, years	70 (range: 51-88)	67 (range: 39-88)	0.40
Gender, % (n)			0.40
- Male	60 (15)	44 (11)	
- Female	40 (10)	56 (14)	
Race, % (n)			0.90
- White	84 (21)	84 (21)	
- Black	8 (2)	16 (4)	
Weight, kg	72 (range: 47-122)	76 (range: 48-127)	0.85
MM type, % (n)			0.37
- FKLC	8 (2)	16 (4)	
- FLLC	12 (3)	8 (2)	
- IgA kappa	16 (4)	4 (1)	
- IgA lambda	16 (4)	16 (4)	
- IgG kappa	28 (7)	44 (11)	
- IgG lambda	20 (5)	12 (3)	
High risk cytogenetics*, % (n)	71 (15)	40 (8)	0.60
Median prior lines of therapy	8 (range: 4-13)	6 (range: 3-15)	0.20
EMD, % (n)	50 (10)	52 (11)	0.90
Elevated LDH (prior to teclistamab), % (n)	33 (8)	15(4)	0.27
Autologous transplant, % (n)	70 (14)	70 (14)	1.00
Allogeneic transplant, % (n)	14 (3)	0	0.23
T-cell redirection therapy**, % (n)		0	
- CAR T-cells			
. *BCMA-targeted*	67 (19)		
. *GPRC5D-targeted*	3 (1)		
. *CD38-targeted*	3 (1)		
- Bispecific antibodies			
. *BMCA-targeted*	10 (3)		
. *GPRC5D-targeted*	7 (2)		
. *FcRH5-targeted*	10 (3)		

*: High-risk cytogenetic abnormalities [t(4;14), t(14;16), t(14;20), *TP53* mutations, del 17p and 1q amplification]; **: 4 patients were treated with both CAR-T cells and bispecific antibodies.

Figure 1. Differences in rates of cytokine release syndrome based on prior exposure to T-cell redirection therapy.

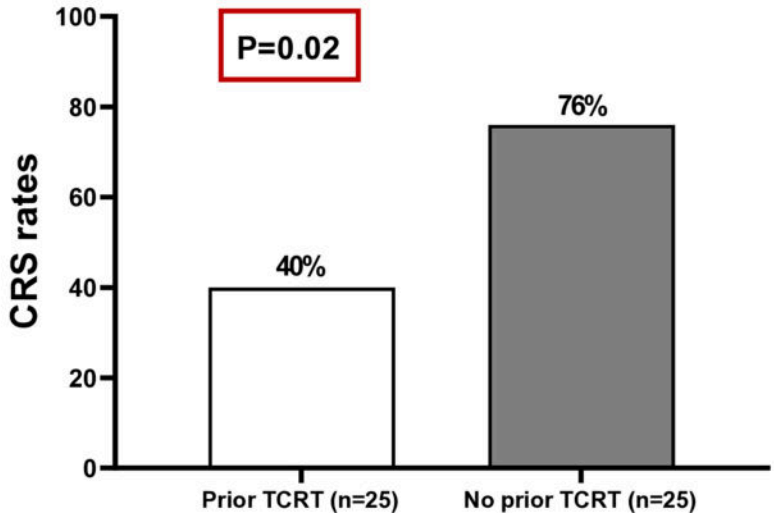

Figure 1

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