Real World Evaluation of Teclistamab: A Focus on Infections in Patients with Relapsed Refractory Multiple Myeloma (RRMM)

University of California San Francisco

Sireesha Asoori, MBBS, MSPH[1]; Jeffrey Wolf, MD[1]; Alfred Chung, MD[1]; Shagun Arora, MD[1]; Thomas Martin, MD[2]

1. Division of Hematology and Oncology, Department of Medicine, University of California, San Francisco, San Francisco, CA 2. UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA.

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Background:

- : Teclistamab (TEC) is a bispecific BCMA-CD3 directed T-cell antibody (BsAb), which received EMA approval on 8/24/22 and subsequent FDA approval on 10/25/22, based on the MajesTEC-1 study showing high single agent response rates (≥PR in 63.0%) in heavily pretreated patients with relapsed/refractory multiple myeloma (RRMM)[1].
- Also reported were unique side effects including, cytokine release syndrome (CRS) and neurotoxicity (ICANS), and prompting the FDA/EMA to recommend inpatient monitoring during the initial step-up and first full-dose of TEC[1].
- In addition, a high incidence of infections (76.4%; ≥grade 3: 44.8%) have been reported. Thus, the IMF Immunotherapy subgroup embarked on this international analysis of real-word use of Teclistamab in RRMM[1].

Methods:

- We performed a single-center retrospective study of 46 patients treated with TEC at UCSF and data was collected until 7/28/2023.
- The incidence, type and severity of infections were reviewed. Viral infections including CMV reactivation were quantified. Patients were treated for infection according to local standard algorithms.
- Overall response rate (ORR) was determined according to IMWG criteria[2]. Overall survival (OS) and progression-free survival (PFS) were summarized using Kaplan-Meier methods.

Results:

Table 1: Baseline characteristics

BASELINE CHARACTERISTICS	ALL PATIENTS (N=46)
Age (years) – Median (Range)	71 (50-91)
≥75 yrs - n (%)	14 (30.43%)
Gender, Male – n(%)	23 (50%)
Race – n (%)	
Caucasian	23 (50%)
Hispanic	6 (13.04%)
Asian	14 (30.4%)
African American	2 (4.3%)
Risk features	
High-risk cytogenetics/FISH abnormalities – n (%)	13/34 (38.2%)
1q gain – n (%)	16/33 (48.4%)
Median no. of lines of previous therapy (range)	7 (4-14)
Triple class refractory – n (%)	41 (89.13%)
MajecTEC-1 Ineligibility – n (%)	31 (67.3%)
Prior BCMA exposure – n (CAR-T/ADC/BsAb)	16 (9/4/3)
CrCl <30ml/min - n	15 (32.6%)
Hemodialysis - n	2/37 (5.4%)

* High-risk MM was defined having one of the following cytogenetic abnormalities: del17p, t(4;14), or t(14;16)

Results:

- Infections were common and occurred in 39 (84.78%) of the patients; 23 patients (50%) had >1 infection **(Table 2).**
- The majority of infections were viral (n=50) with CMV reactivation being most common (n=24). Of note, serial CMV monitoring by PCR was performed in only 37 patients. Despite a median peak value of 2721 IU/ml (Range: 48-77655), antiviral therapy was used in only 4 patients. Infections were self limited with no organ infection identified.
- Infection was responsible for re-hospitalization in 7 (15.2%) patients **(Table 3).**
- There were 9 bacterial infections; 4 E. Coli (3 UTIs, 1 sepsis), 2 C.diff colitis, 1 Klebsiella Pneumoniae (UTI/sepsis) and 5 covid infections requiring treatment.
- There were 2 cases of parvovirus reactivation causing significant anemia and requiring high-dose IVIG.
- Hypogammaglobulinemia (IgG <400mg/dL) was common (n=32: 70%), and 10 patients had low serum IgG levels prior to TEC initiation. IVIG was administered in 34 (73.9%) patients as standard protocol per institution guidelines.
- Grade 3/4 neutropenia was seen in 20 (43.4%) but few (n=7) had prolonged neutropenia (>7 days) **(Table 3).**
- No fungal infections have occurred.
- The overall response rate in these 46 patients was 70%; (sCR/CR 6; VGPR 19; PR 7; SD 3; PD, 1 MR), similar to the entire population (64%).

Table 2: Incidence and Severity of Infection

	N= 46 (ALL PATIENTS)
Any-grade infection, n (%)	39 (84.78%)
Grade 3/4 infection, n (%)	14 (35.8%)
>1 infection, n (%)	23 (50%)
Discontinuation due to infection, n (%)	1 (2.17%)
Death due to infection, n (%)	0
Median time to first onset of infection (months)(range)	1 (0.06-4)

Table 3: Type of Infection

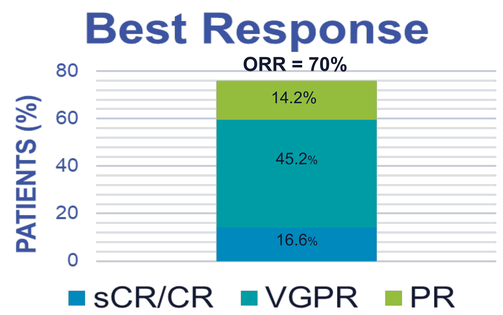
Type of Infection	N=46
Bacterial, n	**9**
Blood	0
Pneumonia	2
Urine	5
Other[a]	2
Viral, n	**54**
URI	16
Pneumonia	3
COVID-19	7
CMV viremia	24
Other[b]	4
Antiviral treatment	15
Grade 3/4 neutropenia, n (%)	20 (43.4%)
Prolonged neutropenia (>7 days), n (%)	6 (13%)
Re-hospitalizations, n (%)	7 (15.2%)

a = Clostridium Difficile, b = 2 Parvo, 1 VZV, 1 Herpes

Table 4: Hypogammaglobulinemia and IVIG use

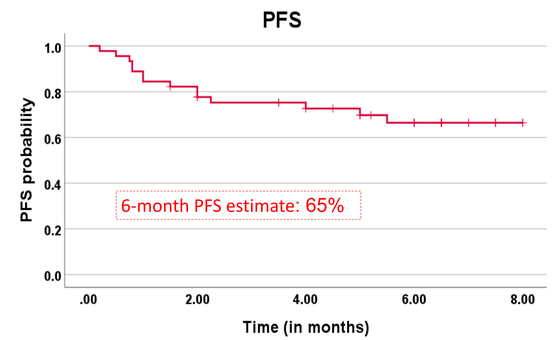
	N=46
Hypogammaglobulinemia (IgG <400mg/dL), n (%)	32 (69.56%)
IgG <400mg/dL prior to TEC initiation, n(%)	10 (21.73%)
IVIG administration, n(%)	34 (73.9%)

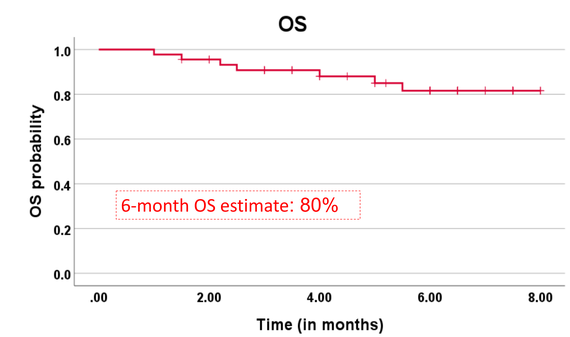
Figure 2: ORR



Results: Outcomes

Figure 1: PFS and OS curves





Conclusions:

- In this Real-World evaluation of Teclistamab, a high ORR was seen (70%) and the treatment was generally well-tolerated.
- Infections were common, but generally low grade (Gr1-2 53.8%, Gr3 35.8%) with viral infections including CMV reactivation and URIs being the most common.
- CMV reactivation although common, infrequently required anti-microbial treatment (n= 4/24).
- Incidence and types of infection may change with longer follow-up.

References:

1. Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in relapsed or refractory multiple myeloma. N Engl J Med 2022;387:495-505
2. Kumar S, Paiva B, Anderson KC, Durie B, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol. 2016 Aug;17(8):e328-e346.