Real-World Evaluation of Teclistamab for the Treatment of Relapsed/Refractory Multiple Myeloma (RRMM)

Sireesha Asoori[1], Yi Lin[2], Larissa Brunaldi[2], Radhika Bansal[2], Andre De Menezes Silva Corraes[2], Saurabh Chhabra[3], Ricardo Parrondo[3], Sikander Ailawadhi[4], Efstathios Kastritis[5], Despina Fotiou[5], Meletios Dimopoulos[5], Joaquin Martinez-Lopez[6], and Thomas Martin[1].

University of California San Francisco

1. Division of Hematology and Oncology, University of California San Francisco, San Francisco, CA 2. Mayo Clinic Cancer Center, Rochester, MN 3. Mayo Clinic, Scottsdale, AZ, 4. Mayo Clinic, Jacksonville, FL, 5. Department of Clinical Therapeutics, Nathional and Kapodistrian University of Athens, Greece, 6. University of Complutense, Hospital 12 de Octubre, Madrid, Spain.

soho2023 ELEVENTH ANNUAL MEETING

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:

- 92 patients treated with Teclistamab at 6 academic centers from 3 countries (US, Greece, Spain), were included. Data was collected up until July 28, 2023.
- Overall response rate (ORR) was determined according to IMWG criteria[2]. Overall survival (OS) and progression-free survival (PFS) were summarized by Kaplan-Meier methods using SPSS 29.0

Results:

Table 1: Baseline characteristics

BASELINE CHARACTERISTICS	ALL PATIENTS (N=92)
Age (years) – Median (Range)	63 (33-91)
≥75 yrs - n (%)	15 (16.3%)
Gender, Male – n(%)	52 (56.5%)
Race – n (%)	
Caucasian	62 (67.3%)
Hispanic	12 (13%)
Asian	14 (15.2%)
African American	4 (4.34%)
Risk features	
High-risk cytogenetics/FISH abnormalities* – n (%)	27/76 (35.5%)
1q gain – n (%)	30/72 (41.6%)
Median no. of lines of previous therapy (range)	6 (1-16)
Triple class refractory – n (%)	41/52 (78.8%)
MajecTEC-1 Ineligibility – n (%)	57/76 (75%)
Prior BCMA exposure – n (CAR-T/ADC/BsAb)	45 (28/14/3)
CrCl <30ml/min - n	13 (14.13%)
Hemodialysis - n	3 (3.26%)

* High-risk MM was defined having one of the following cytogenetic abnormalities: del17p, t(4;14), t(14;16) or t(14; 20)

Results:

- CRS was seen in 47.8% (Gr 1-97.7%, Gr2-20.45%, Gr4-2.27%), generally resolved within 24 hrs and was managed with tocilizumab alone (54.5%) or dex alone (20.45%) or dex+toci (25%) **(Table 3).**
- Median number of hospital days was 8 (n= 60) but 32 patients were treated entirely as outpatients (Mayo clinic (MN, AZ, FL)).
- CRS was more common with inpatient (65%) vs outpatient (15.6%) TEC Rx **(Table 3).**
- CrCl <30 ml, did not appear to alter the incidence or severity of CRS (50%; 1 Gr4).
- ICANS was infrequent (n=5; 5.43%), 1 pt with Gr 4-Sz requiring HD-steroids and TEC discontinuation).
- Infections were common, seen in 48 (52.17%) of patients, the majority were viral URI or CMV reactivation (n=26; 3 pts receiving CMV Rx, 1 pt with CMV organ disease).
- IVIG was given in 39/56 pts (69.64%).

Table 4: ICANS

ICANS	N=5
Patients with ICANS, n(%)	5 (5.43%)
Grade 1	1
Grade 2	2
Grade ≥ 3	2
Time to onset (days), median (range)	4 (3-55)
Duration (days), median (range)	2 (1 – 9)
Treatment, n (%)	
Tocilizumab only	1 (20%)
Dexamethasone only	0
Toci + Dex	4 (80%)

Table 2: Overall Safety

EVENT AND GRADE	N = 92
Hematologic:	
Gr 3/4 Neutropenia	39 (42.3%)
Gr 3/4 Thrombocytopenia	27 (29.3%)
Non-Hematologic:	
Cytokine Release Syndrome (CRS)	44 (47.8%)
Neurotoxicity (ICANS)	5 (5.43%)
COVID-19	8 (8.69%)
Hypogammaglobulinemia	37/52 (71%)

Table 3: Cytokine Release Syndrome (CRS)

CRS	N=44
Patients with CRS, n(%)	44 (47.8%)
Grade 1	43
Grade 2	9
Grade ≥ 3	1
Patients with ≥2 CRS events, n (%)	9 (9.78%)
Incidence: Inpatient (n=60) vs Outpatient (n=32)	39 (65%) vs 5 (15.6%)
Time to onset (days), median	
Step-up dose 1	1
Step-up dose 2	1
First full dose	2
Duration (days), median	
Step-up dose 1	1
Step-up dose 2	1
First full dose	1
Treatment, n (%)	
Tocilizumab only	24 (54.5%)
Dexamethasone only	9 (20.45%)
Toci + Dex	11 (25%)

Results: Outcomes

Figure 1: PFS

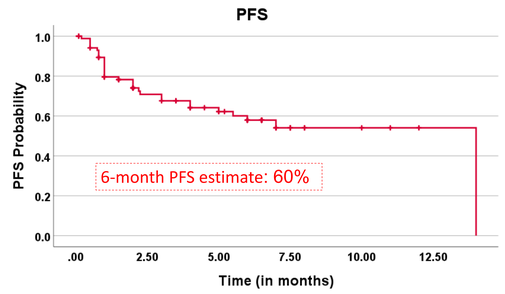
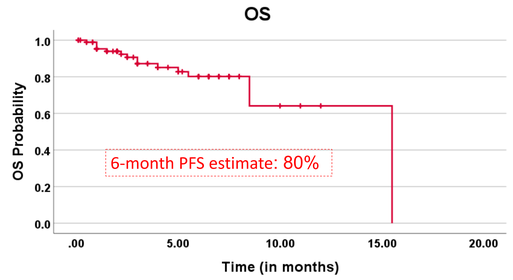
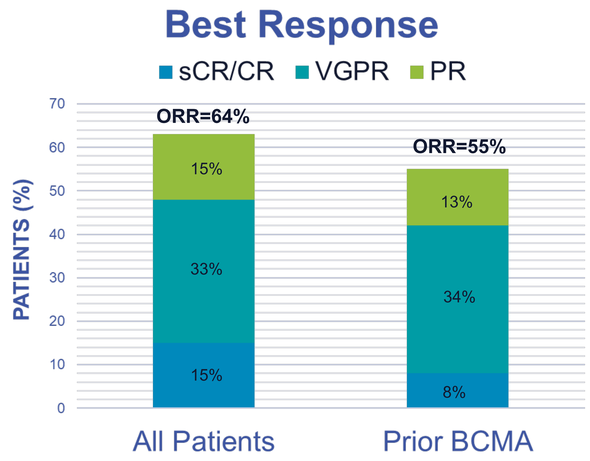


Figure 2: OS



Results: Outcomes

Figure 3: ORR



- The overall response rate for evaluable patients (n=80) was 64%; (sCR/CR 12; VGPR 26; PR 12; MR 1, SD 15; PD 14). In evaluable pts treated with prior BCMA (n=39), the ORR was 55% (sCR/CR 3; VGPR 13; PR 5; MR 1; SD 8; PD 9) **(Figure 3).**
- The most common reason for treatment discontinuation was PD (15.2%). 15 pts have died by the time of data cut-off (7/28/23), with the most common cause of death being disease progression.

Conclusions:

- In this Real-World evaluation of TEC, a high ORR was seen, similar to the MajesTEC-1 study.
- Responses were rapid and are expected to deepen over time (median f/u 3m).
- CRS rates were similar to MajesTEC-1 and no new toxicity signal was noted.
- The rates of infection appear low, but the incidence will likely increase 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.