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Safety Results From REALiTEC: A Multi-Country Observational Retrospective Study of Teclistamab in Relapsed/Refractory Multiple Myeloma Outside of Clinical Trials

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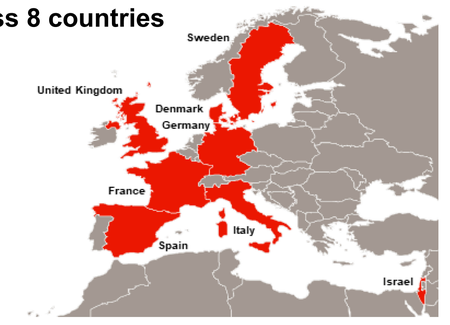
INTRODUCTION

- Teclistamab is the first approved bispecific monoclonal antibody targeting B-cell maturation antigen (BCMA) and CD3 for the treatment of patients with triple-class exposed relapsed/refractory multiple myeloma[1-3]
- With a median follow-up of 30.4 months, the pivotal phase 1/2 MajesTEC-1 trial (N=165) showed deep and durable responses with teclistamab in patients without prior BCMA-targeted treatment[1,4]
  - Overall response rate (ORR) was 63% with a complete response or better rate of 46.1% and a very good partial response or better (≥VGPR) rate of 59.4%[4]
  - Median duration of response (DOR) was 24 months, and median progression-free survival (PFS) and overall survival (OS) were11.4 and 22.2 months, respectively[4]
  - When censored for COVID-19 deaths, median PFS and OS were 15.1 and 28.3 months, respectively[5]
- Here, we report the safety results of the REALiTEC study, a retrospective study of patients receiving teclistamab outside of clinical trials

METHODS

- REALiTEC is a retrospective, international, noninterventional study that aims to describe the management and outcomes of patients treated with teclistamab outside of clinical trials
  - Informed consent was obtained for all patients
- Data were collected from patient medical records, including demographics, disease characteristics, prior therapies, effectiveness, and safety
- Treatment outcomes measured included response rates, adverse events (AEs; cytokine release syndrome [CRS], immune effector cell–associated neurotoxicity syndrome [ICANS], infections, and other AEs), and subsequent treatments
- REALiTEC included 23 sites across 8 countries (**Figure 1**)

Figure 1: 23 sites across 8 countries in REALiTEC



RESULTS

Patients

- Overall, 113 patients were included; 100 from preapproval access programs and 13 treated with commercial teclistamab
- Patient baseline characteristics are shown in **Table 1**

Table 1: Baseline demographics and disease characteristics

Characteristic	N=113[a]
Age, years, median (range)	66 (43–86)
<65 years, n (%)	47 (41.6)
≥65 to <75 years, n (%)	49 (43.4)
≥75 years, n (%)	17 (15.0)
Male, n (%)	57 (50.4)
ECOG PS ≥1, n (%)	27/49 (55.1)
ISS stage, n (%)	
I	32/94 (34.0)
II and III	62 (54.8)
High-risk cytogenetics,[b] n (%)	32/62 (51.6)
Extramedullary plasmacytoma, n (%)	9/59 (15.3)
Patients ineligible for MajesTEC-1, n (%)	78 (69.0)
Years since diagnosis, median (range)	6.88 (0.7–24.2)
Previous lines of therapy, median (range)	6 (2–12)
Penta-class exposed, n (%)	100 (88.5)
Triple-class exposed, n (%)	113 (100)
Triple-refractory, n (%)	89 (78.8)
Penta-refractory, n (%)	50 (44.2)
Refractory to the last line of therapy, n (%)	86 (76.1)
Patients receiving prior BCMA, n (%)[c]	38 (33.6)
No. of therapies	43
CAR-T	10
ADC	32
BsAbs	1

[a]Data available added as denominators if some were missing and not available in the clinical chart for the whole cohort. [b]High risk defined as having presence of t(4;14), t(14;16), del17p13, and amp1q21. [c]38 patients received 43 prior BCMA-directed therapies. ADC, antibody-drug conjugate; BsAB, bispecific antibody; CAR, chimeric antigen receptor; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System.

- At the time of consent, 36 patients were continuing treatment and 5 had their treatment on hold
  - 72 patients had discontinued treatment (42 due to progressive disease, 18 due to AEs, 6 due to death, and 6 due to patient/physician decision or other reasons)
- All patients were admitted to the hospital for step-up dosing, and median inpatient length of stay during the step-up phase, including the first maintenance dose, was 8 days (range, 2–41)
- With a median follow-up of 20.7 months (range, 0.7–35.8), median treatment duration was 9.4 months (range, 0.3–35.8)
- After a median of 7 months (range, 0–18), 45 (39.8%) patients switched from weekly to every-other-week dosing, with disease response included as the most common reason for switching in 62.2% of patients

Efficacy

- ORR for all patients was 60.2%, with most (52.2%) achieving ≥VGPR
- Median DOR, PFS, and OS were 20.3 months (95% CI, 14.8–not estimable [NE]), 9.7 months (95% CI, 5.5–18.8), and 26.3 months (95% CI, 16.5–NE), respectively
  - Survival outcomes were improved in patients achieving ≥VGPR, with median DOR 26 months (95% CI, 16.7–NE), median PFS and OS not reached (NR; 95% CI, 17.2–NR and 95% CI, 26.2–NE, respectively), and 12-month estimates of 71.2% and 83.1% for PFS and OS, respectively

Safety

- The overall safety profile is shown in **Table 2**
- The most common AEs were infections (70.8%), CRS (55.8%), and hematologic AEs (neutropenia [35.4%] and anemia [25.7%])
- 18 (15.9%) patients discontinued therapy, 53 (46.9%) delayed a dose, 34 (30.1%) skipped a dose, and 1 (0.9%) reduced dose due to AEs
- 13 patients had grade 5 AEs, 5 of which were considered related to teclistamab (febrile neutropenia, septic shock, hyponatremia, pneumonia, and toxic encephalopathy)

Table 2: Summary of TEAEs of interest

TEAE, n (%)	N=113	
	Any Grade, n (%)	Grade 3/4, n (%)
Patients with any TEAE, n (%)	108 (95.6)	85 (75.2)
Infections	80 (70.8)	44 (38.9)
Pneumonia	24 (21.2)	16 (14.2)
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 TEAEs		
Neutropenia	40 (35.4)	37 (32.7)
Anemia	29 (25.7)	19 (16.8)
Thrombocytopenia	21 (18.6)	17 (15.0)
Nonhematologic TEAEs		
CRS	63 (55.8)	2 (1.8)
Diarrhea	17 (15.0)	0
Neurologic TEAEs 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; TEAE, treatment-emergent adverse event.

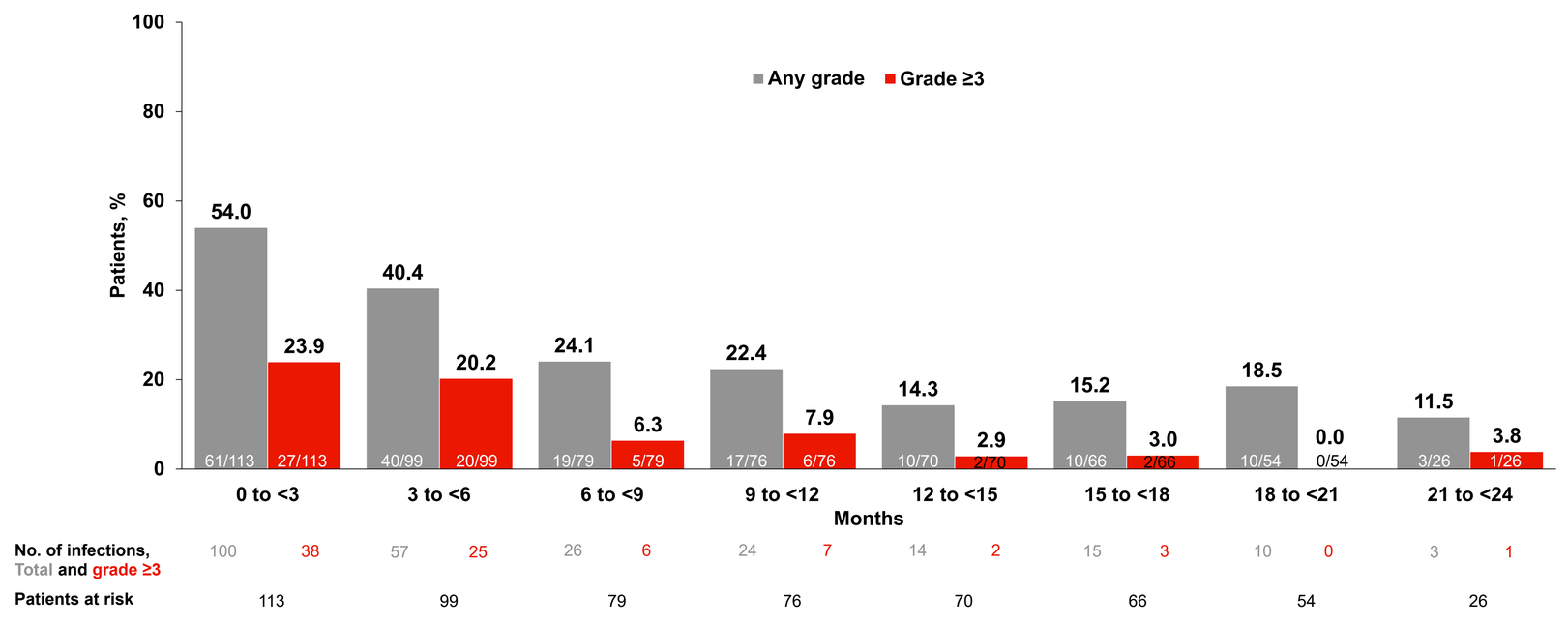
CRS and ICANS

- CRS and ICANS were mostly low grade, with only 2 (1.8%) patients experiencing a grade 3 CRS event and none with a grade 4 event (**Table 3**)
  - All events resolved, and no patients discontinued due to CRS or ICANS
  - 15% received tocilizumab as treatment for CRS; none received prophylactic tocilizumab
- ICANS was observed in 4 (3.5%) patients with no grade ≥3 events

Table 3: CRS events and management

Patients, n	CRS AEs N=113
Patients with any event, n (%)	63 (55.8)
No. of events, n	90
Grade 3 events, n (%)	2 (1.8)
Duration, days, median (range)	2.0 (1–23)
Resolved, n (%)	90 (100)
Management	
Antipyretics	33 (29.2)
Tocilizumab	17 (15.0)
Corticosteroids	11 (9.7)
Intravenous fluids	6 (5.3)
Vasopressor	1 (0.9)
Oxygen	0
Other	18 (15.9)

Figure 2: Incidence of infections over time



Infections

- 80 patients experienced 261 infections; 236 of 261 (90.1%) infections resolved or were resolving at data cut-off (**Table 4**)
  - 44 (38.9%) were grade 3/4
  - 6 patients had a fatal infection (3 septic shock and 3 pneumonia)
- Infection rates declined over time (**Figure 2**)
- Among the classified infections with type of infection data available, 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 (64 days vs 148 days), with a median duration of 14 (range, 1–81) and 15.5 (range, 1–273) days, respectively
- 60.2% (68/113) of patients received intravenous immunoglobulin (IVIg), with most (70.6% [48/68]) patients receiving IVIg as primary prophylaxis

Table 4: Infections

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)
Number of infection events	261	70	66
Time to onset, median days to event (range)	128.0 (1-1062)	101.0 (2-1062)	126.0 (1-859)
Grade 3/4 infection onset, median days to event (range)	99.0 (2-820)	63.5 (2-734)	148.0 (4-820)
Duration, median event days (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]Classification of some infections were not recorded due to unavailability of medical records. [b]Includes recovered/resolved, recovered/resolved with sequelae, recovering/resolving.

CONCLUSIONS

- Teclistamab demonstrated deep and durable responses with a similar safety profile as that shown in the MajesTEC-1 study in patients treated outside of clinical trials, including 69% of patients who would have been ineligible for the clinical trial
- Treatment discontinuations due to AEs were not common (n=18 [15.9%]) and no new safety signals were observed in this heavily pretreated, difficult-to-treat population
- CRS and ICANS were generally mild and manageable, and all events resolved
- Incidence of infections declined with time, and events typically resolved within 2 weeks
- Intravenous immunoglobulin was used in up to 60% of patients, highlighting the significance of supportive care to keep patients on treatment to achieve deep and durable responses
- More than 15,900 patients have been treated worldwide to date with commercial teclistamab. Data generation in subsequent REALiTEC cohorts in these patients will further inform optimal patient management and outcomes in the real world

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