Pharmacokinetics, Safety, and Efficacy of Teclistamab Administered in the Arm or Thigh of Patients With Relapsed/Refractory Multiple Myeloma in MajesTEC-1

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Key Takeaway

Overall, clinical data suggest that the arm and thigh are viable alternative injection sites to the abdomen for SC teclistamab administration in patients with RRMM

Conclusions

- Despite the small sample size in this analysis, teclistamab SC administration in the arm or thigh resulted in PK exposure and safety profiles comparable with those observed in patients receiving SC teclistamab in the abdomen in the phase 1 MajesTEC-1 RP2D population
- Although median PK parameters for teclistamab administered in the arm were slightly lower than those for the abdomen and thigh, PK parameters generally fall within the range observed at the RP2D
- Teclistamab administered in the arm and thigh demonstrated high ORRs; however, the sample size was small, and follow-up period was limited
- CRS events with arm or thigh administration were low grade, manageable, and generally comparable with the phase 1 MajesTEC-1 RP2D population
- No ISRs occurred in the thigh administration cohort. The arm administration cohort had a comparable rate of ISRs vs the phase 1 MajesTEC-1 RP2D population

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Disclosure
LK is an employee of Janssen.

Introduction

- Teclistamab (tec) is the first approved B-cell maturation antigen x CD3 bispecific antibody (BsAb) for the treatment of triple-class exposed relapsed/refractory multiple myeloma (RRMM), with weight-based dosing and the longest study follow-up of any BsAb in MM[1,2]
- In the pivotal phase 1/2 MajesTEC-1 study, the abdomen was the preferred injection site for patients receiving tec at the recommended phase 2 dose (RP2D)[3]
- Drug absorption and bioavailability can be influenced by regional differences in the hypodermis, blood and lymph flow, presystemic catabolism, and neonatal Fc receptor binding; however, immunoglobulins are less likely to show site-dependent pharmacokinetics (PK) compared with peptides/small proteins and non-immunoglobulin proteins[4]
  - Hence, we hypothesized that there would be no differences in tec exposure when administered in anatomic sites other than the abdomen
- The cohorts reported here were assessed for the impact of subcutaneous (SC) injection site on tec disposition

Methods

- Administration of SC tec in the arm or thigh was evaluated in specific cohorts in MajesTEC-1 (NCT03145181/NCT04557098; 1.5 mg/kg in cycles 1–3; **Figure 1**)
- Serum samples were collected to evaluate tec serum concentrations
- PK parameters were determined for cycles 1 and 3 using non-compartmental analysis (NCA)
- Cytokine release syndrome (CRS) was graded per Lee et al[5]
- Local injection-site reactions (ISRs) were graded per the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03[6]
- Rates of CRS and ISRs were evaluated through cycle 3 day 7, consistent with the period in which arm/thigh administration occurred
- Efficacy was analyzed in patients who received at least 1 dose of tec and had at least 1 post-baseline response evaluation
- Response rates were evaluated beyond the period of arm and thigh administration

Figure 1: Tec dosing schedule

[a]Less frequent dosing (eg, Q2W) starting in cycle 4 in the arm and thigh cohorts.
2–4 days were allowed between SUD 1, SUD 2, and treatment dose 1.
Q2W, every other week; QW, weekly; SUD, step-up dose.

Results

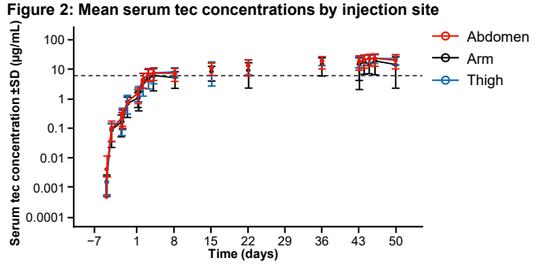
- Tec administration in the arm or thigh was evaluated in 12 patients (6 per cohort) as of December 9, 2023 (**Table 1**)
- Serum concentrations following tec administration in the arm or thigh during SUD and cycles 1–3 were comparable with those observed in patients who received tec in the abdomen at the RP2D in phase 1 (n=40; **Figure 2**)
- NCA PK parameters were generally within the range observed in patients who received tec in the abdomen at the RP2D in phase 1 (**Figure 3**)
  - Median values were slightly lower in the arm; however, this finding was not deemed clinically relevant given sample size and distribution overlap with the abdomen, arm, and thigh, and safety and efficacy observations. Additionally, exposure does not appear to be affected

Table 1: Baseline characteristics and demographics

Characteristic	RP2D (Phase 1; n=40)	Arm (n=6)	Thigh (n=6)
Median age, y (range)	62.5 (39–84)	66.5 (64–71)	73.0 (68–85)
Male, n (%)	26 (65.0)	5 (83.3)	3 (50.0)
Race, n (%)			
White	34 (85.0)	6 (100.0)	5 (83.3)
Median time from diagnosis to first dose, y (range)	5.6 (0.8–17.4)	4.2 (2.5–9.7)	10.9 (3.7–18.0)
Weight (kg), median (range)	76.1 (50.0–103.5)	84.1 (68.0–110.0)	91.1 (58.0–94.0)
Type of myeloma by immunofixation or serum FLC assay			
IgG	17 (42.5)	3 (50.0)	3 (50.0)
IgA	8 (20.0)	2 (33.3)	3 (50.0)
IgD	2 (5.0)	0	0
Light chain	11 (27.5)	1 (16.7)	0
Kappa	7 (17.5)	1 (16.7)	0
Lambda	4 (10.0)	0	0
Biclonal	2 (5.0)	0	0
Type of measurable disease per IMWG			
Serum only	15 (37.5)	3 (50.0)	0
Serum and urine	4 (10.0)	0	1 (16.7)
Urine only	4 (10.0)	0	0
Serum FLC	16 (40.0)	3 (50.0)	5 (83.3)
Not evaluable	1 (2.5)	0	0
ISS stage, n (%)			
I	24 (61.5)	3 (50.0)	4 (66.7)
II	11 (28.2)	2 (33.3)	2 (33.3)
III	4 (10.3)	1 (16.7)	0
Baseline ECOG PS score, n (%)			
0	17 (42.5)	3 (50.0)	3 (50.0)
1	23 (57.5)	3 (50.0)	3 (50.0)
≥1 extramedullary plasmacytoma, n (%)	8 (20.0)	0	1 (16.7)
High-risk cytogenetics, n (%)	12 (32.4)	1 (20.0)	1 (20.0)

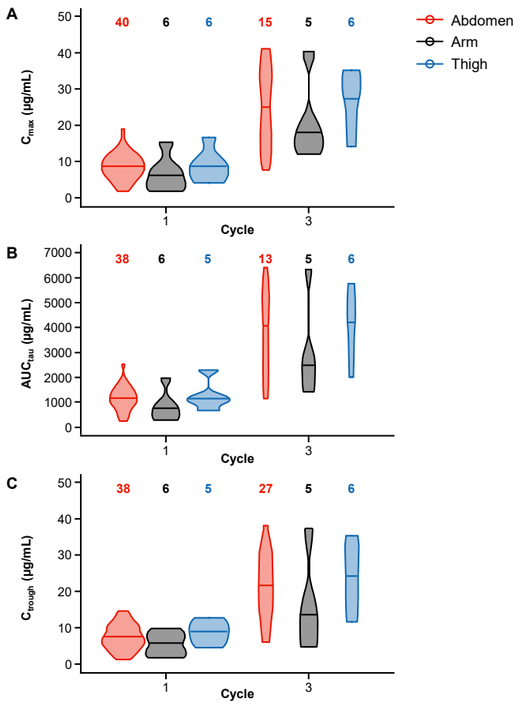
ECOG PS, Eastern Cooperative Oncology Group performance status; FLC, free light chain; Ig, immunoglobulin; IMWG, International Myeloma Working Group; ISS, International Staging System.

Figure 2: Mean serum tec concentrations by injection site



n=40 for abdomen, n=6 for arm, and n=6 for thigh. Events observed after cycle 3 day 7 have been excluded from this analysis.

Figure 3: NCA A) C_{max}, B) AUC_{tau}, and C) C_{trough} by injection site



Events observed after cycle 3 day 7 have been excluded from this analysis. Violin plots show the distribution of the data and are truncated at minimum and maximum values for each group. Solid horizontal lines represent the median values. The numbers in the plots represent sample sizes (n).
AUC_{tau}, area under the curve from time 0 to time tau; C_{max}, maximum concentration; C_{trough}, trough concentration.

Efficacy

- At median follow-up, overall response rate (ORR) was 83.3% in the arm cohort (median follow-up 15.1 mo) and 100.0% in the thigh cohort (median follow-up 14.1 mo; **Table 2**)

Safety

- Incidence of CRS was 66.7% (4/6 patients) in the arm cohort and 83.3% (5/6 patients) in the thigh cohort (**Table 3**)
  - Most CRS events were grade 1 (no grade ≥3 events were observed; median duration 2 days)
- ISRs were observed in 50% (3/6 patients; all grade 1) of patients who received tec in the arm cohort and 0% of patients in thigh cohort

Table 2: Summary of efficacy endpoints by injection site

Endpoint	RP2D (Phase 1; n=40)	Arm (n=6)	Thigh (n=6)
Median follow-up, mo (range)	36.7 (1.2–44.4)	15.1 (13.5–15.4)	14.1 (3.5–14.7)
ORR, n (%)	26 (65.0)	5 (83.3)	6 (100.0)
sCR	18 (45.0)	4 (66.7)	2 (33.3)
CR	3 (7.5)	0	1 (16.7)
VGPR	4 (10.0)	1 (16.7)	2 (33.3)
PR	1 (2.5)	0	1 (16.7)
SD	8 (20.0)	1 (16.7)	0

Efficacy analyses extended beyond the period of arm/thigh administration.
CR, complete response; PR, partial response; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

Table 3: Treatment-emergent CRS and ISRs by injection site

TEAE	RP2D (Phase 1; n=40)	Arm (n=6)	Thigh (n=6)
CRS, n (%)	28 (70.0)	4 (66.7)	5 (83.3)
Maximum grade			
Grade 1	19 (47.5)	3 (50.0)	5 (83.3)
Grade 2	9 (22.5)	1 (16.7)	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Median duration of CRS, days (range)	2.0 (1–8)	2.0 (1–2)	2.0 (1–3)
ISR, n (%)	19 (47.5)	3 (50.0)	0
Maximum grade			
Grade 1	18 (45.0)	3 (50.0)	0
Grade 2	1 (2.5)	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Evaluation of CRS and ISRs were based on limited data due to small sample size. Events observed after cycle 3 day 7 have been excluded from this analysis.
TEAE, treatment-emergent adverse event.

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