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Results From Safety Run-In Cohort 1 of the Phase 3 MajesTEC-7 Study in Patients With Transplant Ineligible/Not Intended Newly Diagnosed Multiple Myeloma

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Key Takeaway

Tec-DR demonstrates a manageable safety profile and promising efficacy in patients with NDMM who are transplant ineligible/not intended for ASCT at median follow-up >1 year from SRI cohort 1 of the phase 3 MajesTEC-7 study

Conclusions

- ORR was 92.3% (80.8% ≥CR; 92.3% ≥VGPR) with no disease progressions; 23 of 26 patients remain on treatment
- Infections occurred in all patients, with onset most common during cycles 1–3; 30.8% were grade 3/4. Cumulative exposure to tec-DR over time does not increase incidence of new grade 3/4 infections
- The randomized part of the MajesTEC-7 study is proceeding with len initiated in cycle 2 as informed by the SRI cohorts

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Poster

Supplementary material

https://www.congresshub.com/Oncology/EHA2024/Teclistamab/Donk

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Acknowledgments

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Disclosures

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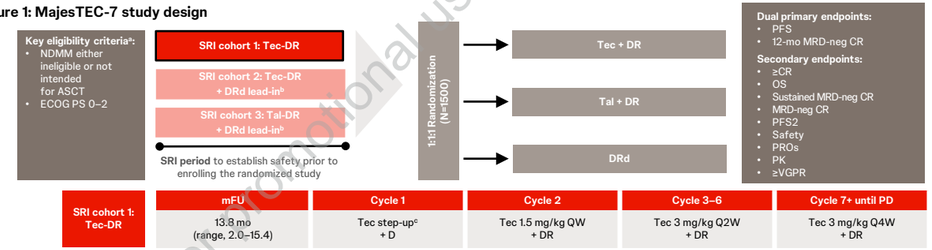
Introduction

- The MAIA study established daratumumab (dara), lenalidomide (len), and dexamethasone (DRd) as the standard of care in patients with transplant-ineligible newly diagnosed multiple myeloma (NDMM), with significant progression-free survival (PFS) and overall survival (OS) benefits[1]; however, many patients eventually relapse, highlighting a need for new frontline treatment options to improve patient outcomes[2]
- Teclistamab (tec) demonstrated deep and durable responses in the phase 1/2 MajesTEC-1 study, with manageable safety in a late-line setting and potential for improved outcomes in earlier lines of therapy (LOT)[3-5]
- In the phase 1b MajesTEC-2 study, the fully immune-based triplet of tec, dara, and len (tec-DR) showed promising early activity in patients with 1–3 prior LOT, with no new safety signals observed vs each of the monotherapies[6]
- MajesTEC-7 (NCT05552222) is a phase 3 study exploring tec-DR and talquetamab, dara, and len (tal-DR) vs DRd in patients with NDMM who are ineligible/not intended for autologous stem cell transplant (ASCT); here, we present initial results from safety run-in (SRI) cohort 1 (tec-DR)

Methods

- SRI cohort 1 study design (**Figure 1**)
- Randomized phase study design (**Supplemental Figure 1**)

Figure 1: MajesTEC-7 study design



[a]SRI cohort 2 and SRI cohort 3 required an IMWG frailty score <2 (except when the score is due to age alone). [b]DRd lead-in (dara SC 1800 mg QW; len oral 25 mg on days 1–21; dexamethasone oral/IV 20 mg QW) in cycle 1; Tec-DR or Tal-DR started in cycle 2. [c]0.06 and 0.3 mg/kg step-up doses on days 2 and 4 followed by treatment doses (1.5 mg/kg) on days 8, 15, and 22.
CR, complete response; D, daratumumab; DR, daratumumab and lenalidomide; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IV, intravenous; mFU, median follow-up; MRD, minimal residual disease; neg, negative; PD, progressive disease; PFS2, progression-free survival as time from randomization to first PFS event on first subsequent LOT; PK, pharmacokinetics; PRO, patient-reported outcome; Q2W, every other week; Q4W, every 4 weeks; QW, weekly; SC, subcutaneous.

Results

SRI cohort 1 (tec-DR)

- At median follow-up of 13.8 months, 26 patients had received tec-DR (**Table 1**)

Table 1: SRI cohort 1 baseline demographics and disease characteristics

Characteristic	SRI cohort 1 (N=26)
Age, median (range), years	72.5 (66–84)
≥70	21 (80.8)
≥75	7 (26.9)
Male, n (%)	17 (65.4)
Race, n (%)	
White	21 (80.8)
Time from diagnosis, median (range), months	1 (0.13–4.8)
ECOG PS, n (%)	
0	14 (53.8)
1	9 (34.6)
2	3 (11.5)
Presence of soft tissue plasmacytomas,[a] n (%)	4 (15.4)
Transplant ineligible, n (%)	22 (84.6)
IMWG frailty score, n (%)	
Fit	16 (61.5)
Intermediate	7 (26.9)
Frail	3 (11.5)
ISS stage, n (%)	
I	2 (7.7)
II	22 (84.6)
III	2 (7.7)

Data cut-off date: March 18, 2024.
[a]All bone-related soft tissue plasmacytomas, no extramedullary soft-tissue plasmacytomas.
ISS, International Staging System.

SRI cohort 1 (tec-DR): Safety

At median follow-up of 13.8 months

- 61.5% of patients had CRS (**Table 2**), occurring mostly in cycle 1, and all cases resolved
  - Grade 1, 57.7%
  - Grade 2, 3.8%
- 1 case of immune effector cell–associated neurotoxicity syndrome (grade 1) in cycle 1 that resolved

26 patients received tec-DR with median of 15 cycles (range, 2–17); 23/26 (88.5%) remained on treatment at clinical cut-off (March 18, 2024)

- 3 patients discontinued all study treatment (grade 5 influenza pneumonia, second primary malignancy [bladder neoplasm], and withdrawal of consent)
- Median relative dose intensity (calculated as percentage of total dose received in all relevant cycles divided by the sum of planned doses in those cycles):
  - Tec: 97.0%; dara: 95.8%; len: 58.6% (17 patients dose reduced len)

Table 2: TEAEs in SRI cohort 1

TEAE, n (%)	SRI cohort 1 (N=26)	
	Any Grade	Grade 3/4
Any TEAE	26 (100.0)	24 (92.3)
Hematologic AEs,[a] n (%)	22 (84.6)	17 (65.4)
Neutropenia	15 (57.7)	15 (57.7)
Anemia	8 (30.8)	1 (3.8)
Thrombocytopenia	4 (15.4)	4 (15.4)
Febrile neutropenia	3 (11.5)	3 (11.5)
Eosinophilia	3 (11.5)	0
Nonhematologic AEs,[b] n (%)		
Diarrhea	18 (69.2)	1 (3.8)
CRS	16 (61.5)	0
Cough	14 (53.8)	0
Dysgeusia	10 (38.5)	N/A[c]
Constipation	9 (34.6)	0
Injection site erythema	9 (34.6)	0
Nausea	8 (30.8)	0
COVID-19	8 (30.8)	3 (11.5)
Muscle spasms	8 (30.8)	0
Bronchitis	7 (26.9)	0
URTI	7 (26.9)	1 (3.8)

Data cut-off date: March 18, 2024.
23.1% of patients had rash (1 occurred in cycle 1, 2 in cycle 2, 1 in cycle 3, and 2 in cycle 7; grade 3/4, 11.5%) and 23.1% of patients had maculopapular rash (1 occurred in cycle 1, 3 in cycle 2, 1 in cycle 3, and 1 in cycle 8; grade 3/4, 11.5%).
[a]Any-grade hematologic AEs in ≥10% of patients. [b]Any-grade nonhematologic AEs in ≥25% of patients. [c]Maximum CTCAE grade is 2.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.

SRI cohort 1 (tec-DR): Infection profile

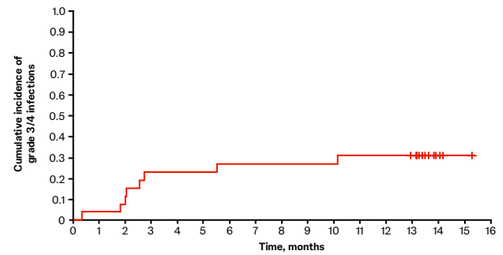
- COVID-19 was most common (**Table 3**)
- 1 death due to influenza pneumonia in cycle 3
- Hypogammaglobulinemia occurred in 21 (80.8%) patients (includes patients with ≥1 treatment-emergent hypogammaglobulinemia or post-baseline IgG value <500 mg/dL)
  - 19/26 (73.1%) patients received at least 1 dose of IV immunoglobulin (IVIG)
- Infection prophylaxis per institutional guidelines
  - Prophylactic Ig replacement was recommended to maintain serum IgG levels ≥400 mg/dL
  - Use of prophylaxis for *Pneumocystis carinii* pneumonia/*Pneumocystis jirovecii* pneumonia and herpes zoster reactivation recommended, as well as routine antibiotic prophylaxis
- 8/26 (30.8%) patients had grade 3/4 infections, most of which had first onset within the first 3 months (**Figure 2**)
- Cumulative exposure to tec-DR over time does not increase incidence of new grade 3/4 infections
- IVIG supplementation and infection prophylaxis should be initiated early and maintained throughout treatment

Table 3: Infections in SRI cohort 1

TEAE, n (%)	SRI cohort 1 (N=26)	
	Any Grade	Grade 3/4
Infections[a]	26 (100.0)	8 (30.8)
COVID-19	8 (30.8)	3 (11.5)
Bronchitis	7 (26.9)	0
URTI	7 (26.9)	1 (3.8)
Rhinitis	6 (23.1)	0
Pneumonia	3 (11.5)	1 (3.8)
Influenza pneumonia	1 (3.8)	1 (3.8)
Pneumonia pneumococcal	1 (3.8)	1 (3.8)
Pneumonia viral	1 (3.8)	1 (3.8)
Staphylococcal sepsis	1 (3.8)	1 (3.8)

Data cut-off date: March 18, 2024.
[a]All-grade infections in ≥20% or grade 3/4 infections in ≥1 patient.

Figure 2: Cumulative incidence of infections



Data cut-off date: March 18, 2024.
Vaccinations allowed per local guidelines (including annual influenza and inactivated COVID-19 vaccines). Live, attenuated vaccines were not permitted.

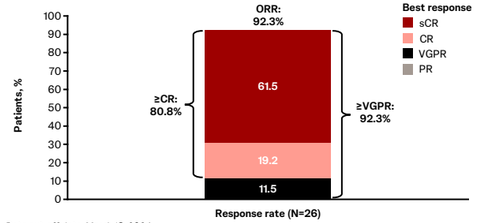
SRI cohort 1 (tec-DR): Efficacy

- ORR was 92.3% (**Figure 3**; ≥CR, 80.8%; all responses were very good partial response [VGPR] or better)
  - No disease progressions
- Disease burden decreased after cycle 1 (**Figure 4**)
- Median time to first response: 1.0 month (range, 0.9–4.6)
- Median time to best response: 6.5 months (range, 1.0–12.1)
- 1 PFS event occurred (**Figure 5**)
  - Estimated duration of response and PFS at 12 months: 100.0% and 96.2%, respectively

SRI cohorts 2 and 3 with DRd lead-in

- A debulking strategy to reduce CRS with 1 lead-in cycle of DRd was employed in SRI cohorts 2 and 3 and resulted in a suboptimal safety profile and will not be pursued further[7]

Figure 3: SRI cohort 1 ORR



Data cut-off date: March 18, 2024.
ORR, overall response rate; PR, partial response; sCR, stringent complete response.

Figure 4: Reduction in disease burden[a] after cycle 1

Data cut-off date: March 18, 2024.
[a]Disease burden represents the type of measurable disease: serum M protein, urine M protein, or difference between involved and uninvolved free light chain.

Figure 5: SRI cohort 1 PFS

Data cut-off date: March 18, 2024.
MRD analyses were not performed in the SRI cohorts.

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Multiple Myeloma

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Supplemental Figure 1: Randomized Phase Study Design

Key eligibility criteria:

- NDMM either ineligible or not intended for ASCT
- ECOG PS 0–2

1:1:1 Randomization (N=1500)

- **Tec + DR**
- **Tal + DR**
- **DRd**

Dual primary endpoints:
- PFS
- 12-mo MRD-neg CR

Secondary endpoints:
- ≥CR
- OS
- Sustained MRD-neg CR
- MRD-neg CR
- PFS2
- Safety
- PROs
- PK
- ≥VGPR

Randomized part of the study is proceeding with lenalidomide initiated in cycle 2 as informed by the SRI cohorts

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ASCT, autologous stem cell transplant; CR, complete response; DR, daratumumab and lenalidomide; DRd, daratumumab, lenalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; LOT, line of therapy; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; neg, negative; OS, overall survival; PFS2, progression-free survival as time from randomization to first PFS event on first subsequent LOT; PFS, progression-free survival; PK, pharmacokinetics; PRO, patient-reported outcome; SRI, safety run-in; tal, talquetamab; tec, teclistamab; VGPR, very good partial response.