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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Presented by S Manier at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA & Virtual

MajesTEC-7 Safety Run-In (SRI): Takeaway Messages

- 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 safety run-in cohort 1 of the phase 3 MajesTEC-7 study

- Rates of discontinuation were low, infections were common, and all CRS events were grade 1/2 with no new safety signals observed compared with each of the monotherapies[1,2]

- Almost all patients responded (92.3%), with >80% achieving ≥CR and no disease progressions; most patients remained on treatment as of clinical cut-off

- A debulking strategy to reduce CRS with 1 lead-in[a] cycle of DRd was employed in SRI cohorts 2 and 3, and resulted in a suboptimal safety profile; the randomized part of MajesTEC-7 is moving forward without use of a DRd lead-in[a] cycle

[a]DRd lead-in (dara SC 1800 mg QW; len oral 25 mg on days 1–21; dex oral/IV 20 mg QW) in cycle 1; Tec-DR or Tal-DR started in cycle 2.

ASCT, autologous stem cell transplant; CR, complete response; CRS, cytokine release syndrome; dara, daratumumab; dex, dexamethasone; DR, daratumumab and lenalidomide; DRd, daratumumab, lenalidomide, and dexamethasone; IV, intravenous; len, lenalidomide; NDMM, newly diagnosed multiple myeloma; QW, weekly; SC, subcutaneous; SRI, safety run-in; tal, talquetamab; tec, teclistamab.

1. Moreau P, et al. *N Engl J Med* 2022;387:495-505. 2. Schinke C, et al. Presented at ASCO 2023. Poster #8036.

MajesTEC-7: Background

- DRd was established by the MAIA study as the SOC in patients with transplant ineligible NDMM, with significant PFS and OS benefits[1]
  - However, many patients eventually relapse, highlighting a need for new frontline treatment options to improve patient outcomes[2]
- Teclistamab demonstrated deep and durable responses, with manageable safety in a late line setting and potential for improved outcomes in earlier LOT, in the phase 1/2 MajesTEC-1 study[3–5]
- The fully immune-based triplet of tec-DR showed promising early activity in patients with 1–3 prior LOT in the phase 1b MajesTEC-2 study, with no new safety signals observed vs each of the monotherapies[6]
- MajesTEC-7[a] is a phase 3 study exploring tec-DR and tal-DR vs DRd in patients with NDMM who are ineligible/not intended for ASCT; here, we present initial results from SRI cohort 1 (tec-DR)

[a]NCT05552222.

ASCT, autologous stem cell transplant; dara, daratumumab; dex, dexamethasone; DR, daratumumab and lenalidomide; DRd, daratumumab, lenalidomide, and dexamethasone; LOT, line of therapy; NDMM, newly diagnosed multiple myeloma; OS, overall survival; PFS, progression-free survival; SOC, standard of care; SRI, safety run-in; tal, talquetamab; tec, teclistamab.

1. Facon T, et al. *Lancet Oncol* 2021;22:1582-96. 2. Lemieux C, et al. *Bone Marrow Transplant* 2021;56:368-75. 3. Moreau P, et al. *N Engl J Med* 2022;387:495-505. 4. van de Donk NWCJ, et al. *J Clin Oncol* 2023;41(suppl 16):8011.
5. van de Donk NWCJ, et al. Presented at HEMO 2023. Poster #403. 6. Searle E, et al. Presented at ASH 2022. Oral #160.

MajesTEC-7: SRI Cohorts Inform Phase 3 Design

Key eligibility criteria[a]:

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

SRI cohort 1: Tec-DR

SRI cohort 2: Tec-DR + DRd lead-in[b]

SRI cohort 3: Tal-DR + DRd lead-in[b]

SRI period to establish safety prior to enrolling the randomized study

N=1500 1:1:1 Randomization

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

Dual primary endpoints:

- PFS
- 12-mo MRD-neg CR

Secondary endpoints:

- ≥CR
- OS
- Sustained MRD-neg CR
- PFS2
- Safety
- PROs
- PK

SRI cohort 1: Tec-DR	mFU	Cycle 1	Cycle 2	Cycle 3–6	Cycle 7+ until PD
	13.8 mo (range, 2.0–15.4)	Tec step-up[c] + D	Tec 1.5 mg/kg QW + DR	Tec 3 mg/kg Q2W + DR	Tec 3 mg/kg Q4W + DR

[a]SRI cohort 2 and SRI cohort 3 required an International Myeloma Working Group frailty score <2 (except when score is due to age a lone). [b]DRd lead-in (dara SC 1800 mg QW; len oral 25 mg on days 1–21; dex 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.

ASCT, autologous stem cell transplant; CR, complete response; D, daratumumab; dara, daratumumab; dex, dexamethasone; DR, daratumumab and lenalidomide; DRd, daratumumab, lenalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; len, lenalidomide; mFU, median follow-up; mo, months; MRD, minimal residual disease; neg, negative; NDMM, newly diagnosed multiple myeloma; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival as time from randomization to first PFS event on first subsequent line of therapy; PK, pharmacokinetics; PRO, patient-reported outcome; Q2W, every other week; Q4W; every 4 weeks; QW, weekly; SC, subcutaneous; SRI, safety run-in; tal, talquetamab; tec, teclistamab.

MajesTEC-7: SRI Cohorts 2 and 3 With DRd Lead-In

	mFU mo (range)	Cycle 1	Cycle 2	Cycle 3+
SRI cohort 2: Tec-DR N=23	**3.7** (1.7–4.9)	DRd lead-in[a]	Tec step-up + DR	Tec + DR
SRI cohort 3: Tal-DR N=22	**3.5** (2.8–5.3)	DRd lead-in[a]	Tal step-up + DR	Tal + DR

- SRI cohorts 2 and 3, with DRd lead-in strategy for debulking, were associated with an increased incidence of neutropenia, grade 3 CRS events, and serious/fatal infections (SRI cohort 2 only)
- Hypothesized that administering lenalidomide prior to and during the bispecific step-up schedule may have increased T-cell activation and bone marrow suppression
- SRI cohort 1 with the bispecific step-up schedule prior to the first dose of lenalidomide was not associated with similar risks
- DRd lead-in[a] strategy will not be adopted for the randomized phase of the study

[a]DRd lead-in (dara SC 1800 mg QW; len oral 25 mg on days 1–21; dex oral/IV 20 mg QW) in cycle 1; Tec-DR or Tal-DR started in cycle 2.
CRS, cytokine release syndrome; dara, daratumumab; dex, dexamethasone; DR, daratumumab and lenalidomide; DRd, daratumumab, lenalidomide, and dexamethasone; IV, intravenous; len, lenalidomide; mFU, median follow-up; mo, months; QW, weekly; SC, subcutaneous; SRI, safety run-in; tal, talquetamab; tec, teclistamab.

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MajesTEC-7 (Tec-DR) SRI Cohort 1: Baseline Demographics and Disease Characteristics

Characteristic	SRI Cohort 1 N=26
Median age, years (range)	72.5 (66–84)
≥70	21 (80.8)
≥75	7 (26.9)
Male, n (%)	17 (65.4)
Race, n (%)	
White	21 (80.8)
Median time from diagnosis, mo (range)	1.0 (0.13–4.8)
ECOG PS, n (%)	
0	14 (53.8)
1	9 (34.6)
2	3 (11.5)
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.

ECOG PS, Eastern Cooperative Oncology Group performance status; DR, daratumumab and lenalidomide; IMWG, International Myeloma Working Group; ISS, International Staging System; mo, months; SRI, safety run-in; tec, teclistamab.

MajesTEC-7 (Tec-DR) SRI Cohort 1: Safety

At median follow-up of 13.8 months

- 61.5% of patients had CRS, occurring mostly in cycle 1 (all cases resolved)
  - Grade 1, 57.7%; grade 2, 3.8%
- One case of ICANS (grade 1) occurred in cycle 1 (resolved)

- 26 patients received tec-DR (median, 15 cycles [range, 2–17])
- 23/26 (88.5%) remained on treatment[d]
- Median relative dose intensity[e] was 97.0% (tec), 95.8% (dara), and 58.6% (len; 17 patients dose reduced)

TEAE, n (%)	Safety population (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
Non-hematologic 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 maculo-papular 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 non-hematologic AEs in ≥25% of patients. [c]Maximum CTCAE grade is 2. [d]3 patients discontinued all study treatment due to grade 5 influenza pneumonia, second primary malignancy (bladder neoplasm), and withdrawal of consent. [e]Calculated as percentage of total dose received in all relevant cycles (including step-up and repeat step-up doses) divided by the sum of planned doses in those cycle s.

AE, adverse event; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; dara, daratumumab; DR, daratumumab and lenalidomide; ICANS, immune effector cell–associated neurotoxicity syndrome; len, lenalidomide; N/A, not applicable; SRI, safety run-in; TEAE, treatment-emergent adverse event; tec, teclistamab; URTI, upper respiratory tract infection.

MajesTEC-7 (Tec-DR) SRI Cohort 1: Infection Profile

- COVID-19 was most common
- 1 death due to influenza pneumonia in cycle 3
- Hypogammaglobulinemia[b] occurred in 21 (80.8%) patients; 19 of 26 (73.1%) received at least one dose of IVIG

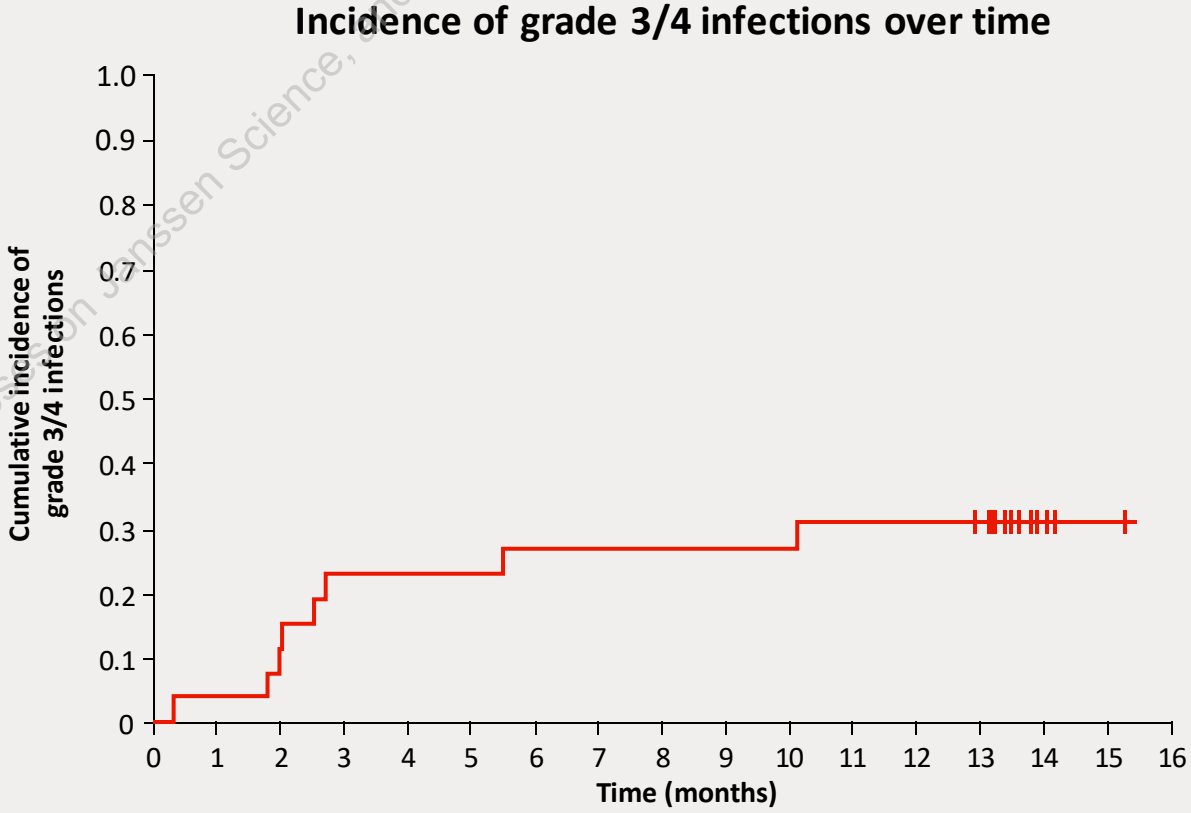
- Infection prophylaxis per institutional guidelines
  - Prophylactic Ig replacement recommended to maintain serum IgG levels ≥400 mg/dL
  - PCP/PJP, herpes zoster reactivation, and routine antibiotic prophylaxis were recommended

TEAE, n (%)	Safety population 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.
Vaccinations allowed per local guidelines (including annual influenza and inactivated COVID-19 vaccines). Live, attenuated vaccines were not permitted.
[a]All-grade infections in ≥20% or grade 3/4 infections in ≥1 patient. [b]Includes patients with ≥1 treatment-emergent hypogammaglobulinemia or post-baseline IgG value <500 mg/dL.
DR, daratumumab and lenalidomide; Ig, immunoglobulin; IVIG, intravenous immunoglobulin; PCP, *Pneumocystis carinii* pneumonia; PJP, *Pneumocystis jirovecii* pneumonia; SRI, safety run-in; TEAE, treatment-emergent adverse event; tec, teclistamab; URTI, upper respiratory tract infection.

MajesTEC-7 (Tec-DR) SRI Cohort 1: Cumulative Incidence of Infections

- Grade 3/4 infections occurred in 8/26 (30.8%) patients, most of which had first onset within the first 3 cycles
- Incidence of grade 3/4 infections does not increase over time with cumulative exposure to tec-DR
- IVIG supplementation and infection prophylaxis should be initiated early and maintained throughout treatment

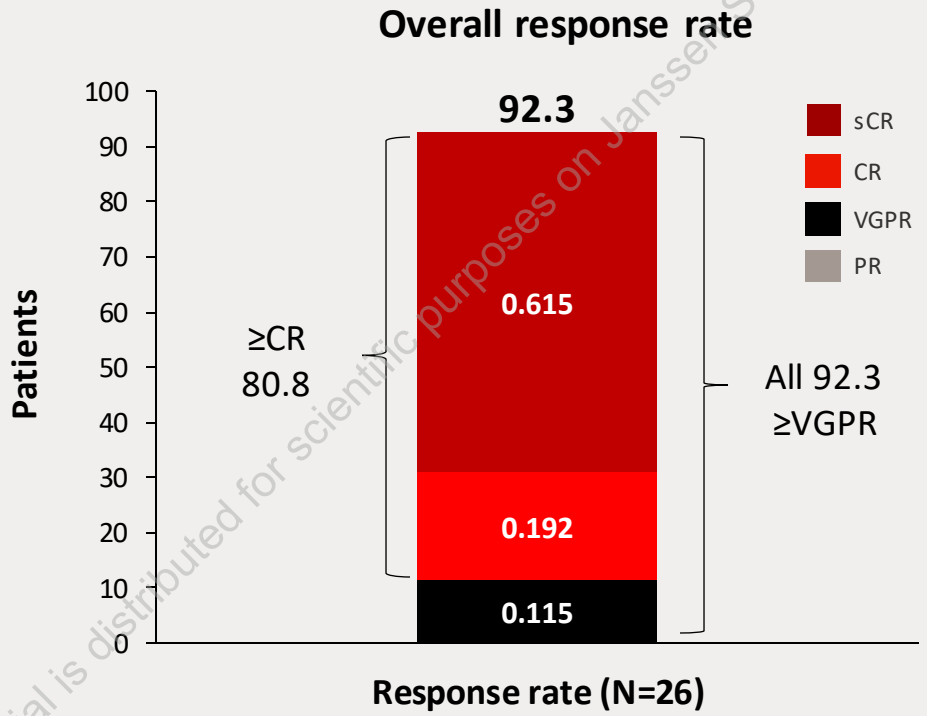


Data cut-off date: March 18, 2024.
Vaccinations allowed per local guidelines (including annual influenza and inactivated COVID-19 vaccines). Live, attenuated vaccines were not permitted.
DR, daratumumab and lenalidomide; IVIG, intravenous immunoglobulin; SRI, safety run-in; tec, teclistamab.

MajesTEC-7 (Tec-DR) SRI Cohort 1: Efficacy

Median follow-up of 13.8 months

- 92.3% ORR (80.8% ≥CR); all patients achieved ≥VGPR
- No disease progressions occurred



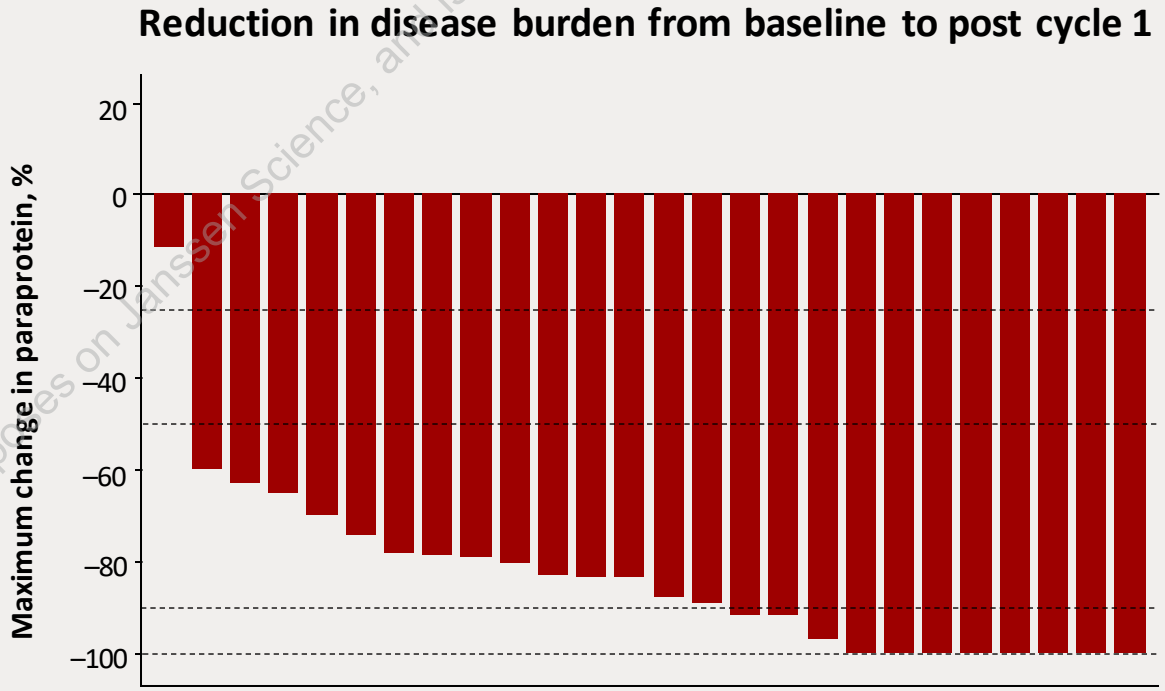
Data cut-off date: March 18, 2024.

CR, complete response; DR, daratumumab and lenalidomide; ORR, overall response rate; PR, partial response; sCR, stringent complete response; SRI, safety run-in; tec, teclistamab; VGPR, very good partial response.

MajesTEC-7 (Tec-DR) SRI Cohort 1: Efficacy

Median follow-up of 13.8 months

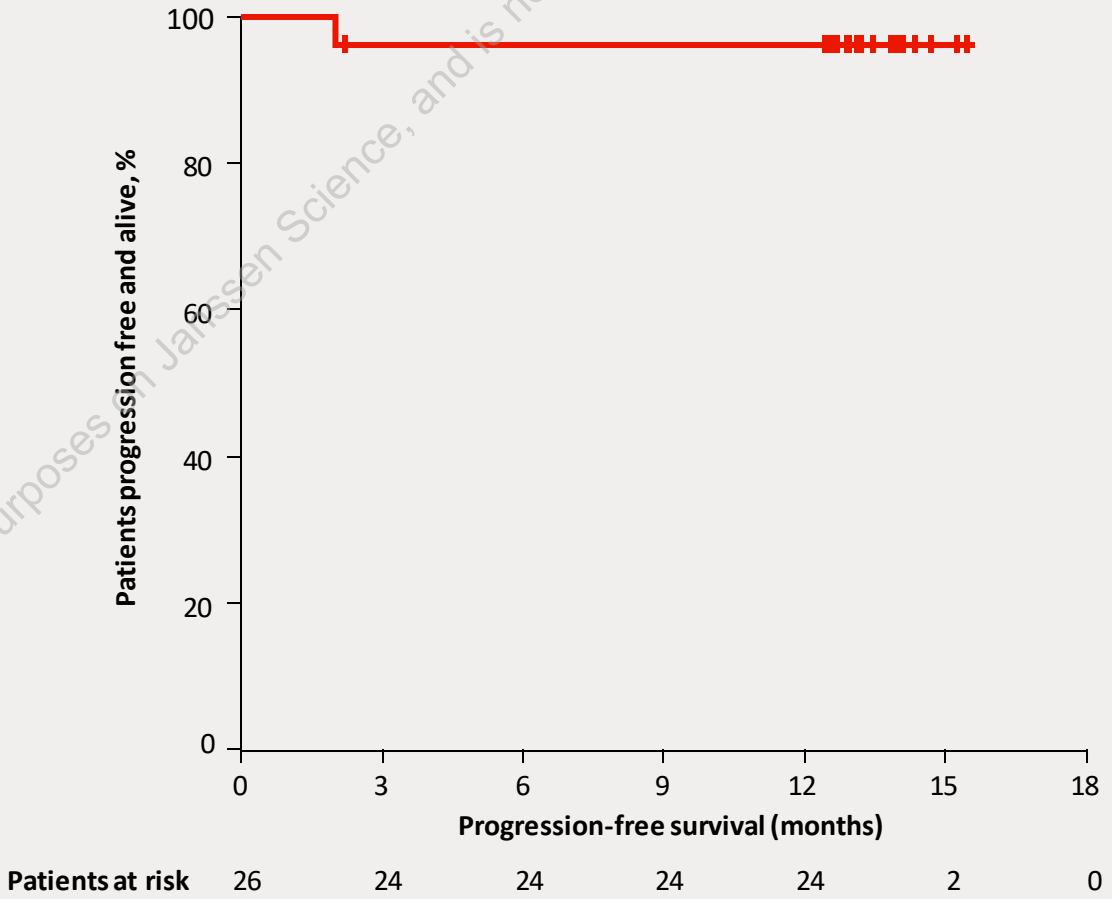
- Median time to first and best response was 1.0 month (range, 0.9–4.6) and 6.5 months (range, 1.0–12.1), respectively



Data cut-off date: March 18, 2024.
DR, daratumumab and lenalidomide; SRI, safety run-in; tec, teclistamab; tec, teclistamab.

MajesTEC-7 (Tec-DR) SRI Cohort 1: Progression-free Survival

- At median follow-up of 13.8 months, one PFS event has occurred
- Estimated 12-month DOR and PFS were 100.0% and 96.2%, respectively



Data cut-off date: March 18, 2024.
MRD analyses were not performed in the safety run-in cohorts.
DOR, duration of response; DR, daratumumab and lenalidomide; MRD, minimal residual disease; PFS, progression-free survival; SRI, safety run-in; tec, teclistamab.

MajesTEC-7: Conclusions

- Tec-DR with lenalidomide initiated in cycle 2 (after step-up schedule) demonstrated a manageable safety profile and promising efficacy at a median follow-up of 13.8 months in the SRI period
  - ORR was 92.3% (80.8% ≥CR; 92.3% ≥VGPR)
  - No disease progressions occurred
  - Infections occurred in all patients (grade 3/4, 30.8%), with onset most common during cycles 1–3
  - 23 of 26 patients remain on treatment

- A debulking strategy to reduce CRS with 1 lead-in[a] cycle of DRd was employed in SRI cohorts 2 and 3 and resulted in a suboptimal safety profile; the randomized part of MajesTEC-7 is moving forward without use of a DRd lead-in[a] cycle

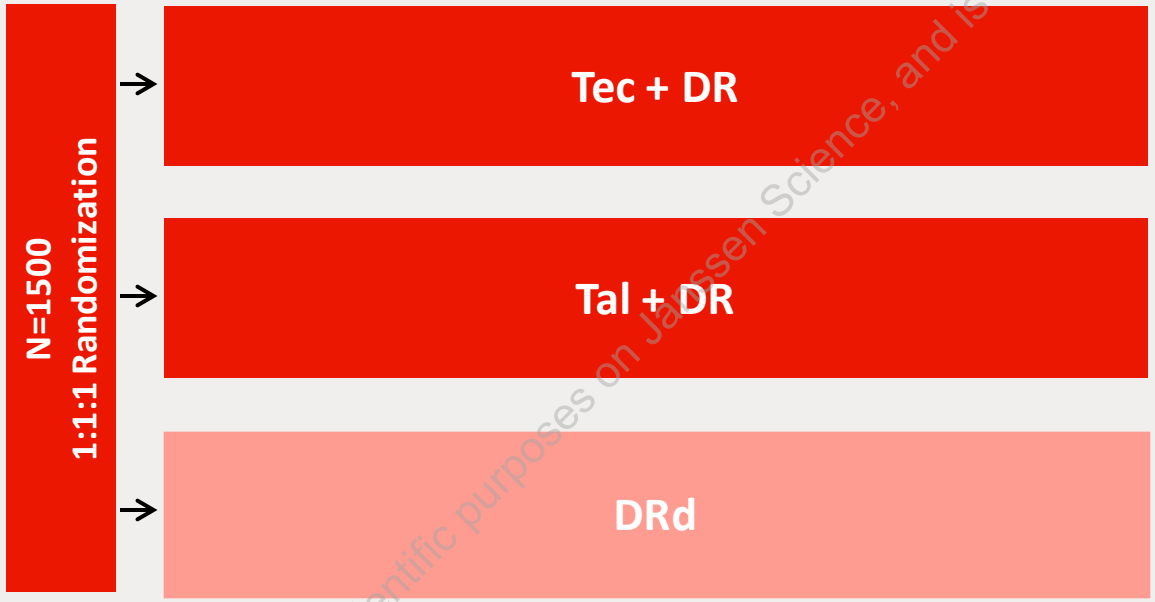
- MajesTEC-7 randomization is proceeding with lenalidomide initiated in cycle 2 as informed by the SRI cohorts

[a]DRd lead-in (dara SC 1800 mg QW; len oral 25 mg on days 1-21; dex oral/IV 20 mg QW) in cycle 1; Tec-DR or Tal-DR started in cycle 2.
CR, complete response; CRS, cytokine release syndrome; dara, daratumumab; dex, dexamethasone; DR, daratumumab and lenalidomide; DRd, daratumumab, lenalidomide, dexamethasone; IV, intravenous; len, lenalidomide; ORR, overall response rate; QW, weekly; SC, subcutaneous; SRI, safety run-in; tal, talquetamab; tec, teclistamab; VGPR, very good partial response.

MajesTEC-7: Phase 3 Design

Key eligibility criteria:

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



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

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; len, lenalidomide; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; neg, negative; OS, overall survival; PFS, progression-free survival PFS2; progression-free survival as time from randomization to first PFS event on first subsequent line of therapy; PK, pharmacokinetics; PRO, patient-reported outcome; SRI, safety run-in; tal, talquetamab; tec, teclistamab; VGPR, very good partial response.

Acknowledgments

- We thank the patients who are participating in this study and their caregivers, the physicians and nurses who care for them, the staff at study sites, and the staff involved in data collection and analyses

- This study was funded by Janssen Research & Development, LLC

- Medical writing support was provided by Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC

Phase 1b Data on Tec-R Combinations in RRMM: MajesTEC-2 Study

	Cycle 1	Cycle 2+
Tec-R	Tec step-up	Tec + **R**
Tec-DR	Tec step-up + Dara	Tec + Dara + **R**

R was initiated in cycle 2 to minimize potential interactions during CRS risk window[a]

Tec-R in ≥2 prior LOT (N=31; mFU, 10.8 mo)[1]

- ORR 74.2% (≥CR 35.5%)
- 1 grade 3 CRS event
- 45.2% grade 3/4 infections
- 2 infectious deaths (COVID-19, sepsis)

Tec-DR in 1–3 prior LOT (N=32; mFU, 8.4 mo)[2]

- ORR 93.5% (≥CR 54.8%)
- No grade 3 or 4 CRS events
- 37.5% grade 3/4 infections
- 2 infectious deaths (COVID-19, sepsis)

[a]Talquetamab combination studies with lenalidomide follow similar dosing schedules.
CR, complete response; CRS, cytokine release syndrome; dara, daratumumab; DR, daratumumab and lenalidomide; LOT, line of therapy; mo, months; ORR, overall response rate; R, lenalidomide; RRMM, relapsed/refractory multiple myeloma; tec, teclistamab.
1. Tan C, et al. Presented at EHA 2023. Poster #P865. 2. Searle E, et al. Presented at ASH 2022. Oral #160.