

Phase 3 Study of Teclistamab in Combination With Lenalidomide and Teclistamab Alone vs Lenalidomide Alone in Newly Diagnosed Multiple Myeloma as Maintenance Therapy Following Autologous Stem Cell Transplantation: Safety Run-in Results From the EMN30/MajesTEC-4 Trial*

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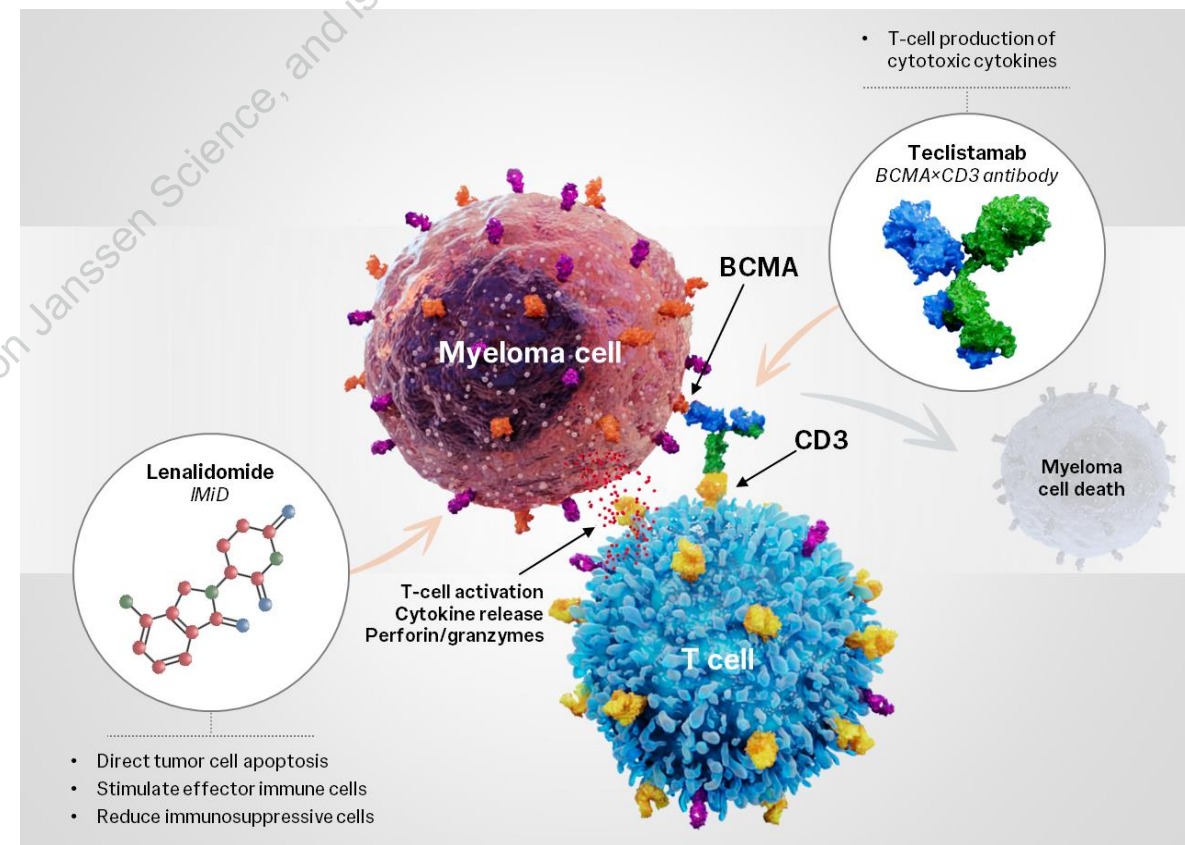
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EMN30/MajesTEC-4: Introduction

- Lenalidomide (Len) is a SoC maintenance therapy in NDMM following ASCT¹
- Teclistamab (Tec) is a first-in-class BCMA × CD3 BsAb approved in TCE RRMM, with promising efficacy in earlier-line RRMM²⁻⁷
- The combined cytotoxic and immunomodulatory properties of Tec and Len may lead to enhanced efficacy⁸
- In MajesTEC-2 (phase 1b), Tec-Len was safely combined and demonstrated promising efficacy in TCE MM⁹
- EMN30/MajesTEC-4 is a multicenter, open-label, phase 3 study evaluating Tec-Len, Tec, and Len maintenance therapy in NDMM
- We report initial results from the SRI



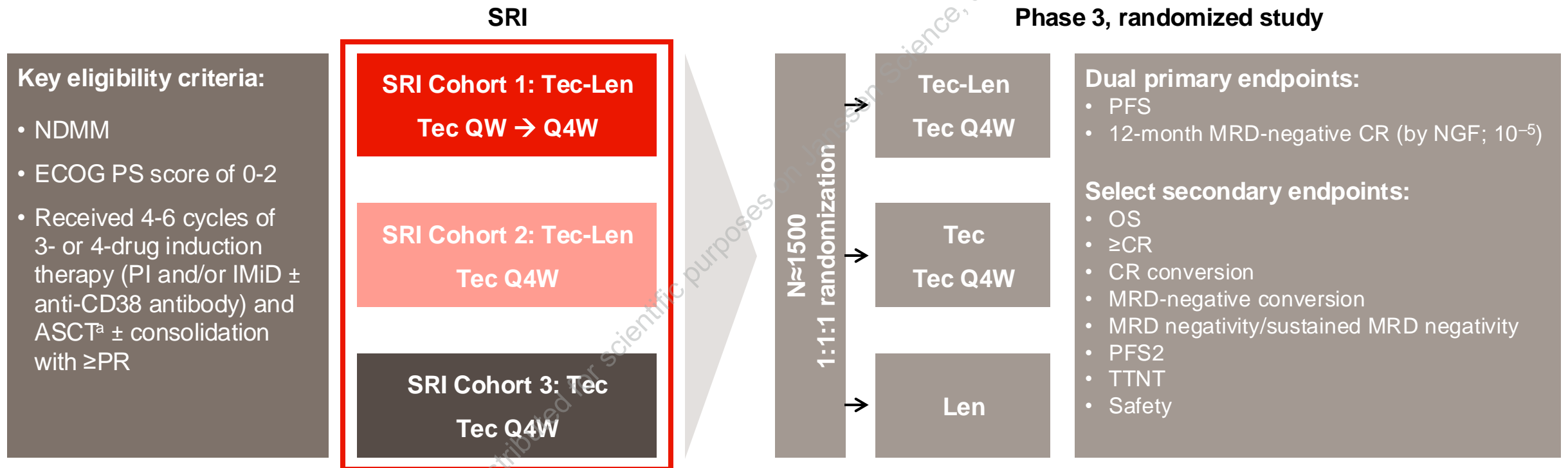
ASCT, autologous stem cell transplantation; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; EMN, Stichting European Myeloma Network; IMiD, immunomodulatory drug; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; RRMM, relapsed/refractory multiple myeloma; SoC, standard-of-care; SRI, safety run-in; TCE, triple-class-exposed.

1. McCarthy PL, et al. *J Clin Oncol*. 2017;35(29):3279-3289. 2. Moreau P, et al. *N Engl J Med*. 2022;387(6):495-505. 3. Garfall AL, et al. *J Clin Oncol*. 2024;42(16 suppl). Abstract 7540. 4. Touzeau C, et al. *J Clin Oncol*. 2024;42(16 suppl). Abstract 7506. 5. Raab MS, et al. Presented at: 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA. Presentation 493. 6. TECVAYLI® (teclistamab). Summary of product characteristics. Janssen Biologics BV; 2024. 7. TECVAYLI® (teclistamab-cqyv) injection [package insert]. Janssen Biotech, Inc.; 2024. 8. Cho SF, et al. *Blood Adv*. 2020;4(17):4195-4207. 9. Tan C, et al. *Hemasphere*. 2023;7(S3):1623-1624.

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EMN30/MajesTEC-4: Study Design



^aSingle or tandem ASCT permitted.

ASCT, autologous stem cell transplantation; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EMN, Stichting European Myeloma Network; IMiD, immunomodulatory drug; Len, lenalidomide; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGF, next-generation flow cytometry; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival after next line of therapy; PI, proteasome inhibitor; PR, partial response; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab; TTNT, time to next treatment.



EMN30/MajesTEC-4 SRI: Dosing

	Cycle 1	Cycle 2	Cycles 3-6	Cycles 7-26
Cohort 1: Tec-Len Tec QW → Q4W	Tec step up ^a + Tec 1.5 mg/kg on D8, D15, and D22	Tec 1.5 mg/kg QW + Len	Tec 3.0 mg/kg Q2W + Len	Tec 3.0 mg/kg Q4W + Len
Cohort 2: Tec-Len Tec Q4W	Tec step up ^a + Tec 1.5 mg/kg on D8 and D15	Tec 3.0 mg/kg Q4W + Len		
Cohort 3: Tec Tec Q4W	Tec step up ^a + Tec 1.5 mg/kg on D8 and D15	Tec 3.0 mg/kg Q4W		

- Len was initiated at 10 mg/day^b from Cycles 2 to 4, followed by 15 mg/day in Cycles 5 to 26, if tolerated
- 2-year fixed-duration maintenance regimen^c

^aPatients received step-up doses of 0.06 and 0.3 mg/kg. ^bIn 28-day cycles. ^cPatients who achieved CR on Tec-Len after 1 year discontinued Tec and continued Len for another year.
CR, complete response; D, Day; EMN, Stichting European Myeloma Network; Len, lenalidomide; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.



EMN30/MajesTEC-4 SRI: Demographic and Disease Characteristics

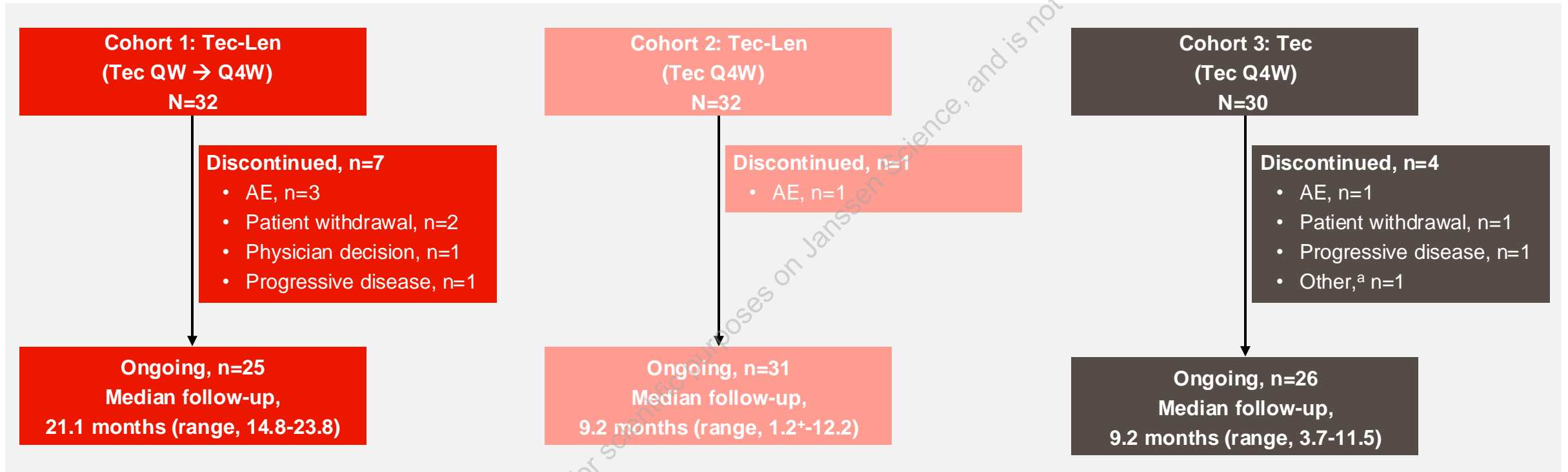
Characteristic	Cohort 1: Tec-Len (QW → Q4W) (N=32)	Cohort 2: Tec-Len (Q4W) (N=32)	Cohort 3: Tec (Q4W) (N=30)
Median age, y (range)	58.5 (31-73)	58.0 (38-73)	58.5 (34-72)
≥65, n (%)	12 (37.5)	5 (15.6)	9 (30.0)
Male, n (%)	21 (65.6)	21 (65.6)	22 (73.3)
White race, n (%)	32 (100)	32 (100)	30 (100)
ISS disease stage at diagnosis, n/N (%)			
I	18/32 (56.3)	8/32 (25.0)	9/28 (32.1)
II	7/32 (21.9)	9/32 (28.1)	11/28 (39.3)
III	7/32 (21.9)	15/32 (46.9)	8/28 (28.6)
High cytogenetic risk at diagnosis,^a n/N (%)	7/25 (28.0)	5/29 (17.2)	6/25 (24.0)
Induction regimen for MM, n (%)			
PI ^b + IMiD ^c	28 (87.5)	28 (87.5)	30 (100)
PI ^b + IMiD ^c + anti-CD38 ^d	11 (34.4)	19 (59.4)	20 (66.7)
Prior consolidation, n (%)	6 (18.8)	12 (37.5)	10 (33.3)

- The median time from ASCT to maintenance treatment for all patients was 4.7 months (range, 1.8-7.4)
- All patients had an ECOG PS score of 0 or 1
- More patients in Cohorts 2 and 3 received anti-CD38 during induction compared with in Cohort 1

^aHigh cytogenetic risk is defined as the presence of ≥1 of the following abnormalities: del(17p), t(4;14), or t(14;16). ^b93/94 (98.9%) received bortezomib, 3/94 (3.2%) carfilzomib. ^c53/94 (56.4%) received Len, 39/94 (41.5%) thalidomide, 1/94 (1.1%) pomalidomide. ^d49/94 (52.1%) received daratumumab and 1/94 (1.1%) isatuximab as part of a triplet regimen; 1/94 (1.1%) received daratumumab with lenalidomide as part of a doublet regimen. ASCT, autologous stem cell transplantation; ECOG PS, Eastern Cooperative Oncology Group performance status; EMN, Stichting European Myeloma Network; IMiD, immunomodulatory drug; ISS, International Staging System; Len, lenalidomide; MM, multiple myeloma; PI, proteasome inhibitor; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.



EMN30/MajesTEC-4 SRI: Treatment Disposition and Exposure



- As of September 9, 2024, 81 of 94 patients (86.2%) remained on treatment

+ = censored observation. ^aPatient decision.

AE, adverse event; EMN, Stichting European Myeloma Network; Len, lenalidomide; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.



EMN30/MajesTEC-4 SRI: Hematologic TEAEs

	Cohort 1: Tec-Len (QW → Q4W) (N=32)		Cohort 2: Tec-Len (Q4W) (N=32)		Cohort 3: Tec (Q4W) (N=30)	
Median follow-up, mo	21.1		9.2		9.2	
TEAEs, ^a n (%)	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	32 (100)	32 (100)	32 (100)	27 (84.4)	30 (100)	17 (56.7)
Hematologic Aes						
Neutropenia	30 (93.8)	30 (93.8)	21 (65.6)	20 (62.5)	17 (56.7)	14 (46.7)
Leukopenia	9 (28.1)	3 (9.4)	1 (3.1)	0	1 (3.3)	1 (3.3)
Lymphopenia	2 (6.3)	1 (3.1)	4 (12.5)	4 (12.5)	4 (13.3)	4 (13.3)
Thrombocytopenia	6 (18.8)	2 (6.2)	0	0	2 (6.7)	0
Febrile neutropenia	3 (9.4)	3 (9.4)	3 (9.4)	3 (9.4)	0	0
Anemia	3 (9.4)	0	1 (3.1)	1 (3.1)	1 (3.3)	0
Eosinophilia	1 (3.1)	1 (3.1)	1 (3.1)	1 (3.1)	0	0

- Cumulative incidence of grade 3/4 neutropenia at 6 months:
 - Cohort 1: 81.3%
 - Cohort 2: 56.3%
 - Cohort 3: 40.0%
- Median relative dose intensity:
 - 95.5% to 99.7% for Tec
 - 58.4% to 61.5% for Len
- Low rates of treatment discontinuation due to TEAEs (5.3% overall)

Teclistamab every 4 weeks from Cycle 2 had a lower cumulative incidence of grade 3/4 neutropenia than teclistamab weekly → every 4 weeks

Data cutoff date: September 9, 2024.

^aAEs (graded according to the NCI-CTCAE Version 5.0); any grade occurring in >25% of patients or grade 3/4 in >1 patient.

AE, adverse event; EMN, Stichting European Myeloma Network; Len, lenalidomide; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; TEAE, treatment-emergent adverse event; Tec, teclistamab.



EMN30/MajesTEC-4 SRI: Nonhematologic TEAEs

	Cohort 1: Tec-Len (QW → Q4W) (N=32)		Cohort 2: Tec-Len (Q4W) (N=32)		Cohort 3: Tec (Q4W) (N=30)	
Median follow-up, mo	21.1		9.2		9.2	
TEAEs, ^a n (%)	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Nonhematologic AEs^b						
CRS	16 (50.0)	0	13 (40.6)	0	13 (43.3)	0
URTI	20 (62.5)	1 (3.1)	13 (40.6)	0	8 (26.7)	0
Cough	15 (46.9)	0	6 (18.8)	0	8 (26.7)	0
Diarrhea	13 (40.6)	3 (9.4)	9 (28.1)	1 (3.1)	6 (20.0)	0
Injection-site erythema	7 (21.9)	0	12 (37.5)	0	8 (26.7)	0
COVID-19	12 (37.5)	1 (3.1)	5 (15.6)	0	9 (30.0)	1 (3.3)
Fatigue	10 (31.3)	1 (3.1)	8 (25.0)	1 (3.1)	5 (16.7)	0
Pneumonia	9 (28.1)	4 (12.5)	3 (9.4)	0	2 (6.7)	1 (3.3)

- Among the most common nonhematologic TEAEs, rates of grade 3/4 events were low
- All CRS events were grade 1/2, mostly occurring during Tec step-up dosing
 - 37.2% after Step-up Dose 1
 - 8.5% after Step-up Dose 2
 - 5.3% after Treatment Dose 1
 - No discontinuations due to CRS
- No ICANS

Data cutoff date: September 9, 2024.

^aAEs (graded according to the NCI-CTCAE Version 5.0); any grade occurring in >25% of patients or grade 3/4 in >10% of patients. ^bHypogammaglobulinemia based on TEAE reporting also met the ≥25% threshold and is reported separately.

AE, adverse event; CRS, cytokine release syndrome; EMN, Stichting European Myeloma Network; ICANS, immune effector cell-associated neurotoxicity syndrome; Len, lenalidomide; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection.



EMN30/MajesTEC-4 SRI: Infections and Hypogammaglobulinemia

	Cohort 1: Tec-Len (QW → Q4W) (N=32)		Cohort 2: Tec-Len (Q4W) (N=32)		Cohort 3: Tec (Q4W) (N=30)	
Median follow-up, mo	21.1		9.2		9.2	
TEAEs, ^a n (%)	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Any infection	30 (93.8)	12 (37.5)	25 (78.1)	9 (28.1)	23 (76.7)	6 (20.0)
Most common infections^b						
URTI	20 (62.5)	1 (3.1)	13 (40.6)	0	8 (26.7)	0
COVID-19	12 (37.5)	1 (3.1)	5 (15.6)	0	9 (30.0)	1 (3.3)
Pneumonia	9 (28.1)	4 (12.5)	3 (9.4)	0	2 (6.7)	1 (3.3)
Nasopharyngitis	6 (18.8)	0	0	0	3 (10.0)	0

- Hypogammaglobulinemia^c reported in:
 - Cohort 1: 31 (96.9%) patients
 - Cohort 2: 25 (78.1%) patients
 - Cohort 3: 28 (93.3%) patients
 - All received ≥1 dose of IVIg or SCIg
- One grade 5 COVID-19 TEAE occurred in Cohort 2
- Infection prophylaxis, including Ig replacement, was strongly recommended^d

Data cutoff date: September 9, 2024.

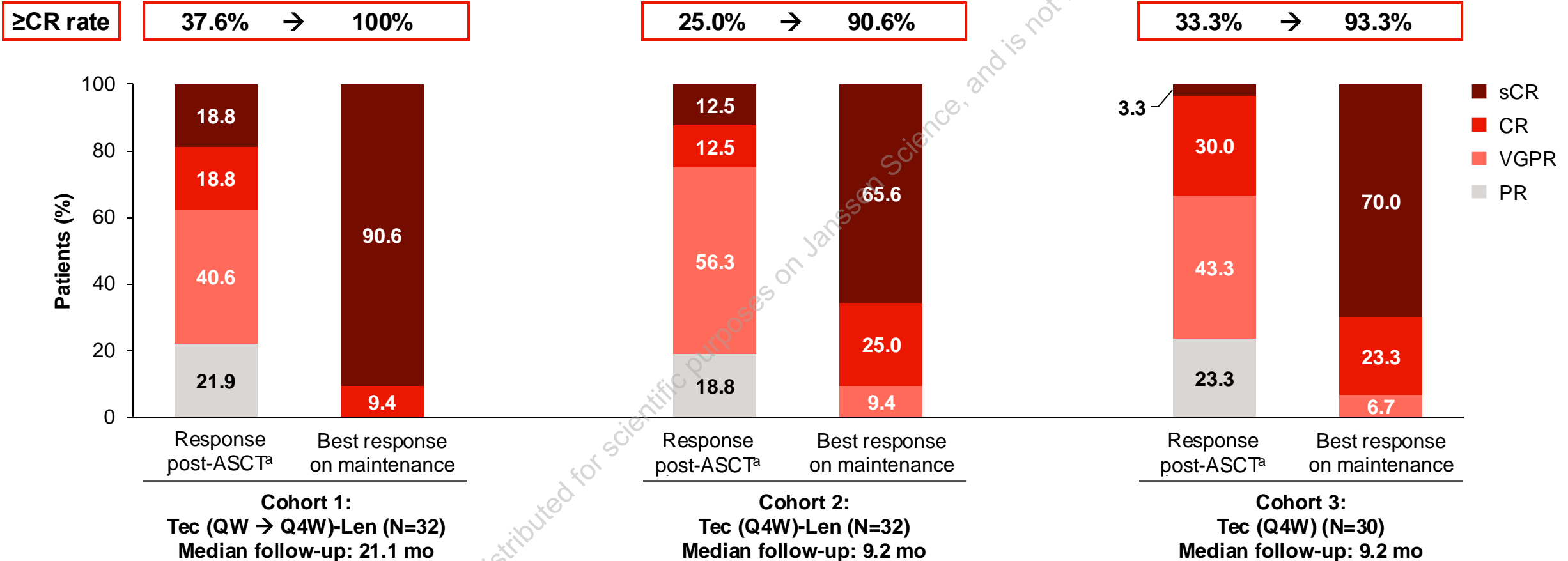
^aAEs (graded according to the NCI-CTCAE Version 5.0). ^bAny grade occurring in >10% of patients in any arm. ^cIncludes patients with ≥1 TEAE of hypogammaglobulinemia or post-baseline IgG value <400 mg/dL.

^dProphylactic IVIg replacement advised to maintain serum IgG levels of ≥400 mg/dL. Prophylaxis for *Pneumocystis jirovecii* pneumonia and herpes zoster reactivation was recommended, as well as routine antibiotic and antiviral prophylaxis.

AE, adverse event; EMN, Stichting European Myeloma Network; Ig, immunoglobulin; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; Len, lenalidomide; QW, weekly; Q4W, every 4 weeks; SCIg, subcutaneous immunoglobulin; SRI, safety run-in; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection.



EMN30/MajesTEC-4 SRI: Response Rates Post-ASCT and During Maintenance



Responses deepened during maintenance in all treatment cohorts

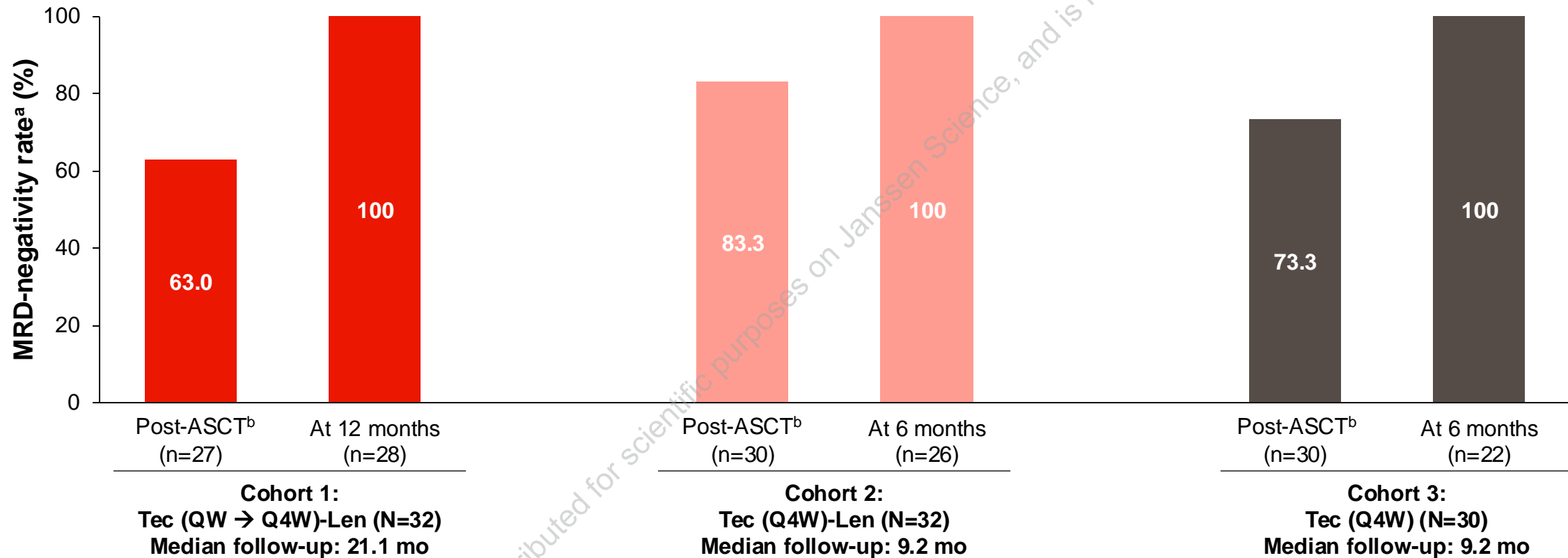
Data cutoff date: September 9, 2024.

^aPost-ASCT ± consolidation.

ASCT, autologous stem cell transplantation; CR, complete response; EMN, Stichting European Myeloma Network; Len, lenalidomide; PR, partial response; QW, weekly; Q4W, every 4 weeks; sCR, stringent complete response; SRI, safety run-in; Tec, teclistamab; VGPR, very good partial response.



EMN30/MajesTEC-4 SRI: MRD Negativity (10^{-5}) in Evaluable Patients Post-ASCT and During Maintenance



100% of evaluable patients were MRD negative during maintenance

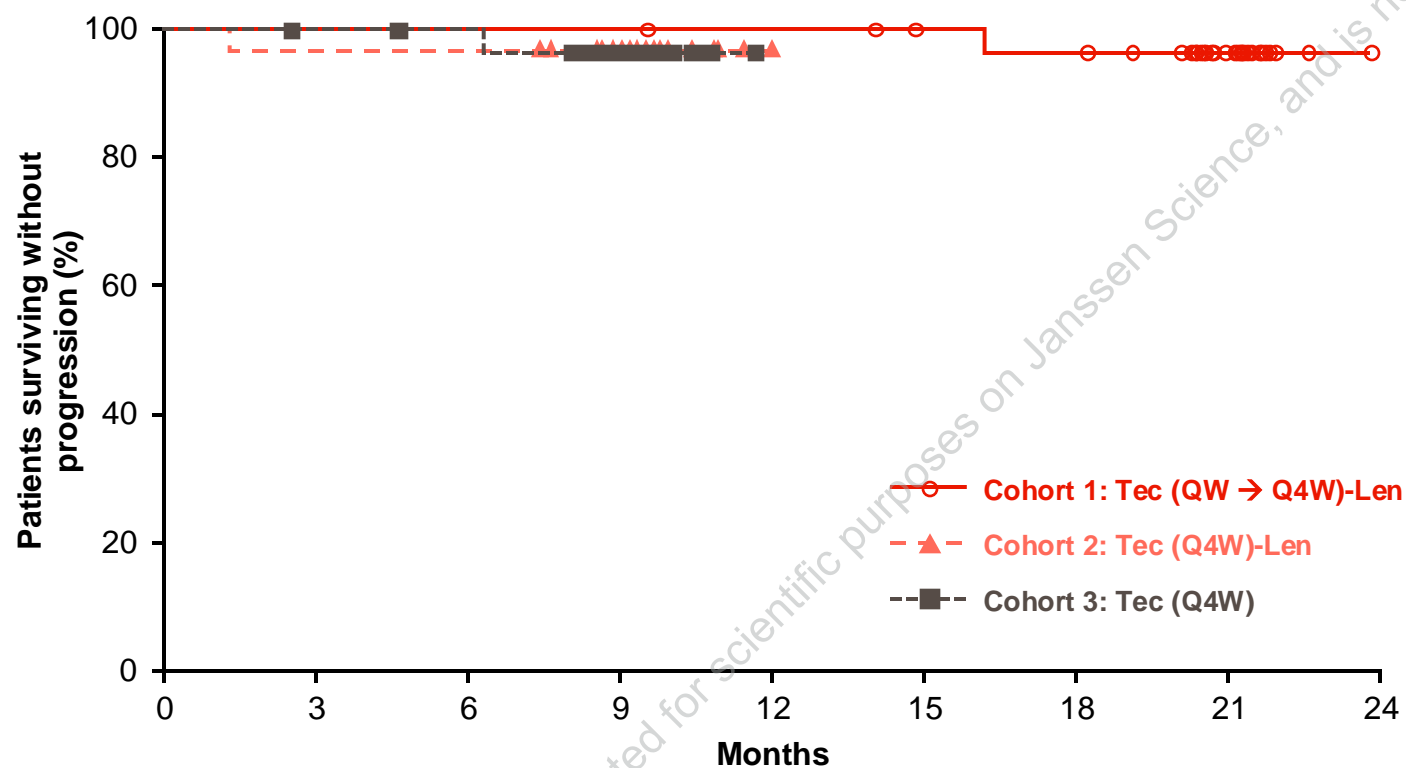
Data cutoff date: September 9, 2024.

^aMRD-negativity rate was defined as the proportion of patients who achieved MRD negativity (10^{-5}), regardless of response. Percentages are out of evaluable patients. Among 87 evaluable patients, 23 patients were MRD positive at screening (Cohort 1, n=10; Cohort 2, n=5; Cohort 3, n=8). All patients who were MRD positive at study entry and had an assessment during treatment were MRD negative during treatment. One patient in Cohort 1 was MRD positive at 18 months. ^bPost-ASCT ± consolidation.

ASCT, autologous stem cell transplantation; EMN, Stichting European Myeloma Network; Len, lenalidomide; MRD, minimal residual disease; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.



EMN30/MajesTEC-4 SRI: PFS



- Median PFS was not reached in all cohorts

Patients at risk:

Cohort 1: Tec (QW → Q4W)-Len	32	32	32	32	31	29	28	14	0
Cohort 2: Tec (Q4W)-Len	32	31	31	17	0	0	0	0	0
Cohort 3: Tec (Q4W)	30	29	28	14	0	0	0	0	0

Responses were maintained in all cohorts



EMN30/MajesTEC-4 SRI: Conclusions

- Tec as monotherapy or in combination with Len as fixed duration could be safely administered to approximately 90 patients with NDMM following ASCT
- Discontinuation rates due to TEAEs were low
- The most common hematologic toxicity was neutropenia, which was lower with Tec 3.0 mg/kg Q4W from Cycle 2
- Grade 3/4 infections occurred in ~30% of patients, and infection prophylaxis, including Ig replacement, was strongly recommended
- Unprecedented efficacy was observed, with all evaluable patients achieving MRD negativity during maintenance
- The randomized portion of the EMN30/MajesTEC-4 study is evaluating Tec-Len, Tec, and Len as maintenance with Tec dosing at 3 mg/kg Q4W



EMN30/MajesTEC-4: Participating Countries



Acknowledgments

- Patients who are participating in this study and their families
- Staff members at the study sites
- Data and safety monitoring committee
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