

Updates in Treatment in Multiple Myeloma

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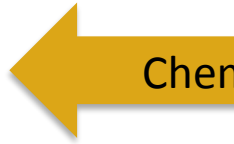
Disclosure Information

I have NO financial relationships to disclose

Myeloma Therapies



Daratumumab SQ



Chem

Melphalan
1958

Steroids
1962

1950

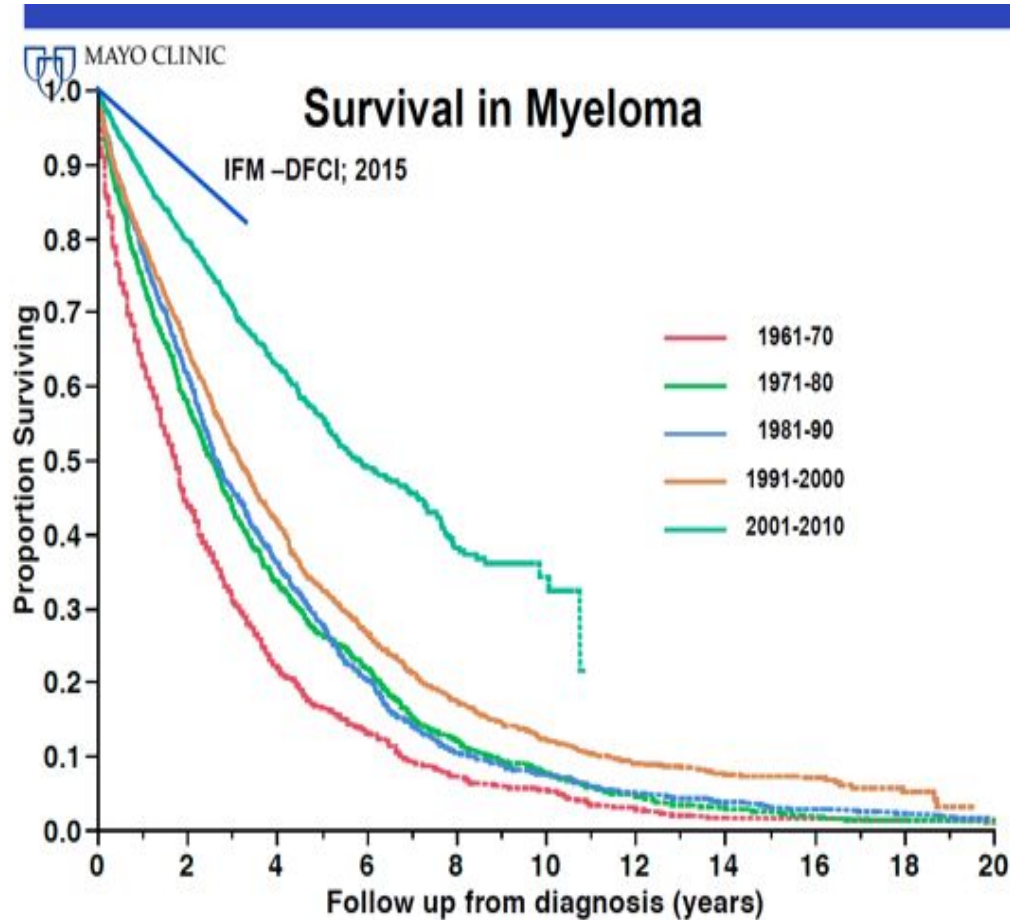
1960



Targeted Therapy

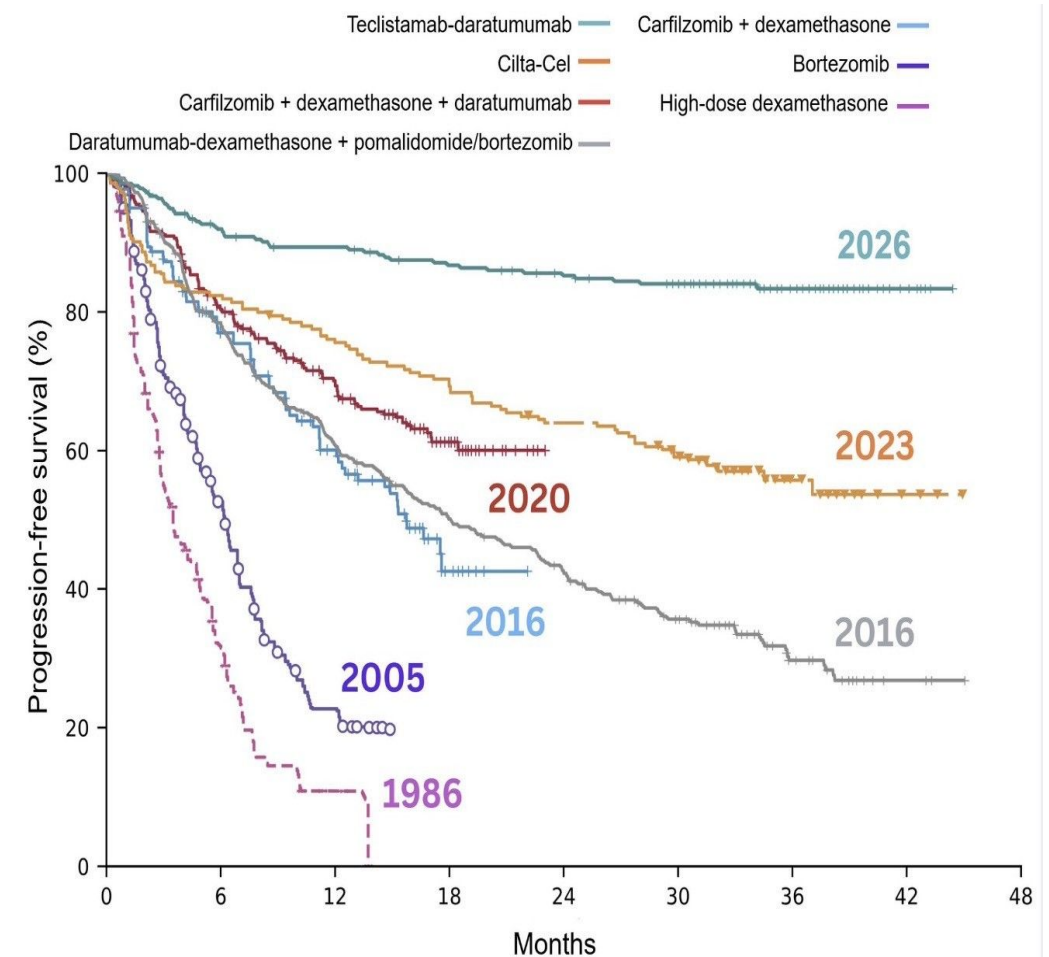
Car
Therapy

Myeloma Survival By Decades



Kumar S. Blood 2008;111: 2516 – 2520; Kumar S. Leukemia (2014) 28, 1122–1128.

Median OS now exceeds 7-10 years for many patients



Stages of Myeloma Treatment/ The Iceberg Model

SCT
eligible

SCT
ineligible

Diagnosis & Risk
Stratification

Induction



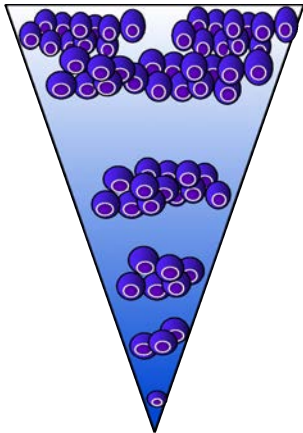
Consolidation



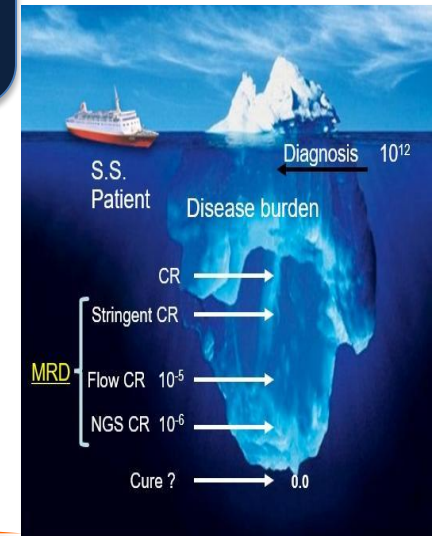
Maintenance

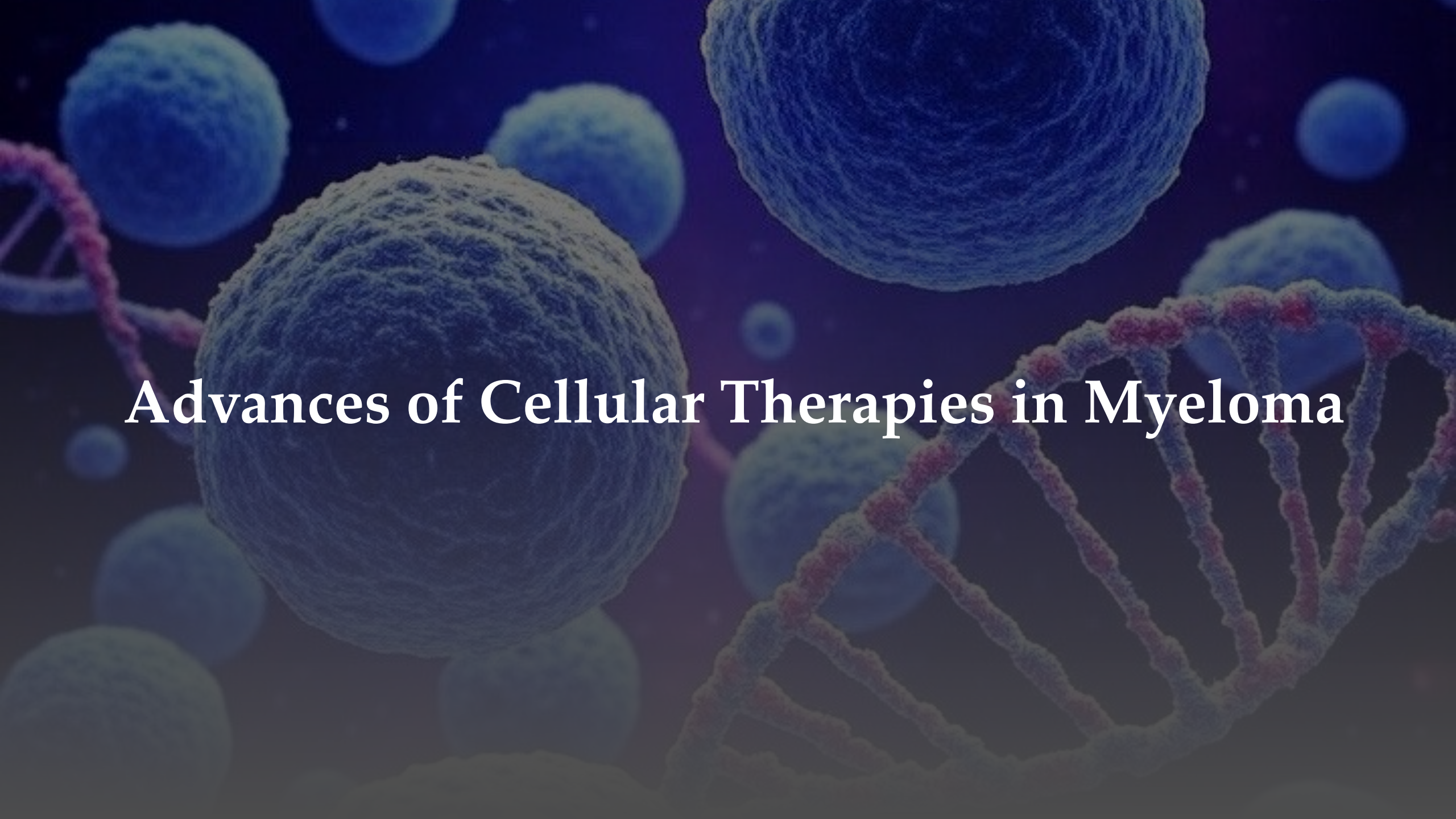
Induction followed by continuous therapy

Factors to be considered for ASCT
Age, performance status (PS), comorbidities (R-MCI
score, HCT-CI) and organ function



Tumor Burden



The background is a dark blue gradient. It features several large, textured blue spheres that resemble cells or molecules. A prominent DNA double helix structure is visible on the right side, rendered in a light blue and white color. The overall aesthetic is scientific and modern.

Advances of Cellular Therapies in Myeloma

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

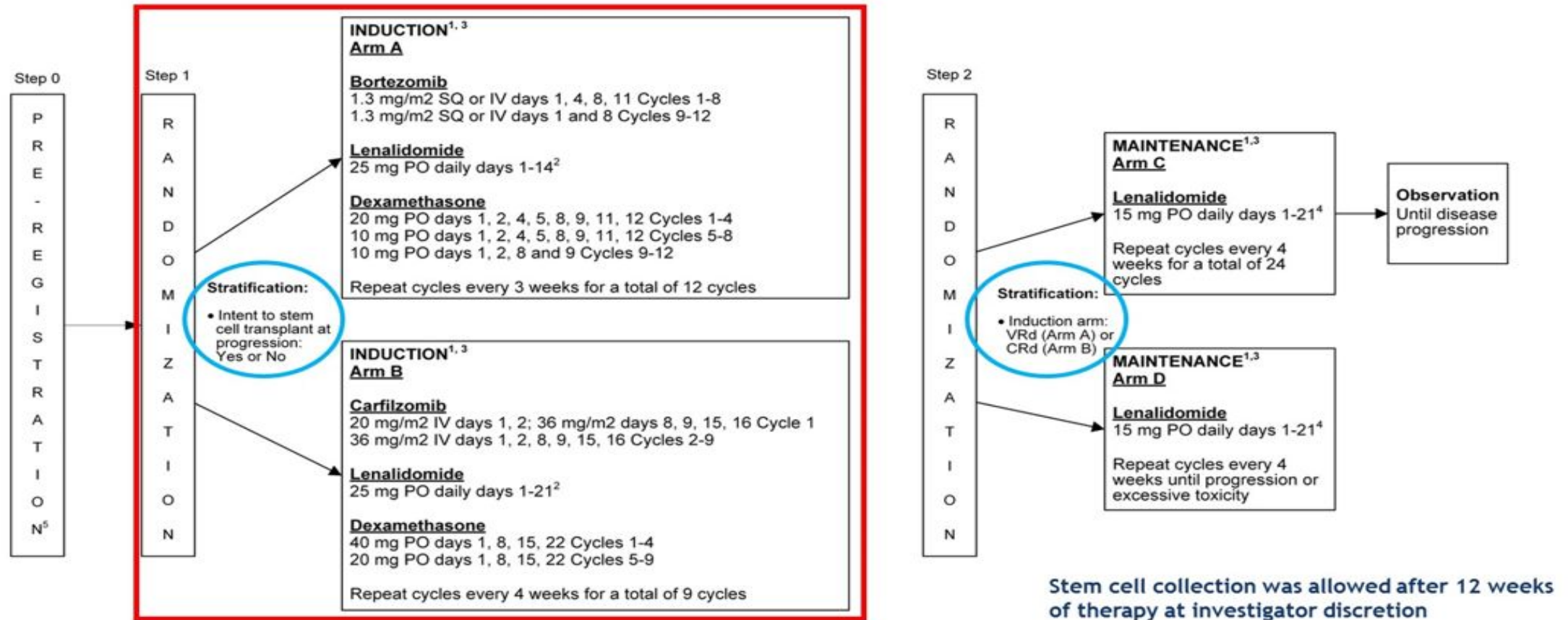
JULY 16, 2026

VOL. 395 NO. 3

Continuous or Fixed-Duration Maintenance Therapy in Multiple Myeloma

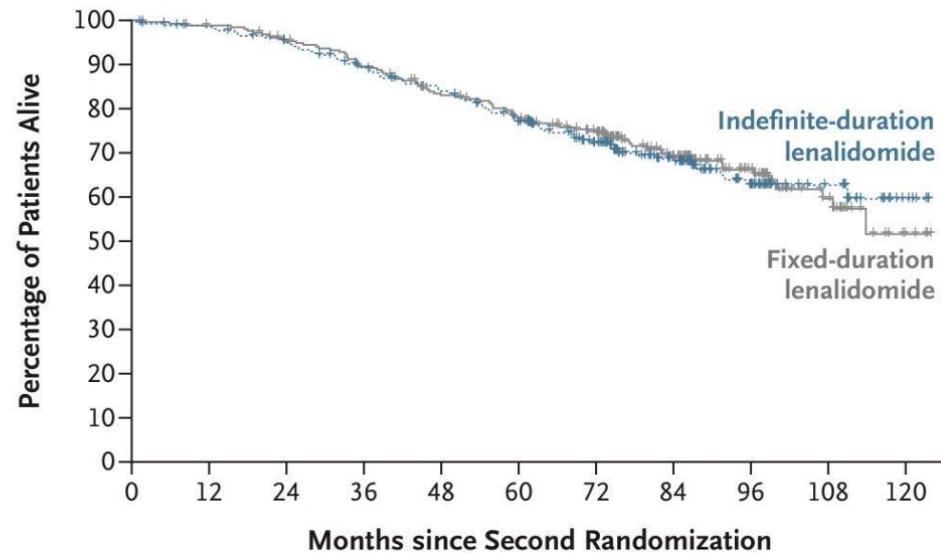
Shaji Kumar, M.D.,¹ Susanna Jacobus, M.Sc.,² Adam Cohen, M.D.,³ Matthias Weiss, M.D.,⁴ Natalie Callander, M.D.,⁵ Avina Singh, M.D.,⁶ Terri Parker, M.D.,⁷ Michael Green, M.D.,⁸ Raymond Thertulien, M.D.,⁹ Benjamin Parsons, M.D.,¹⁰ Pankaj Kumar, M.D.,¹¹ Prashant Kapoor, M.D.,¹ Aaron Rosenberg, M.D.,¹² Elie Dib, M.D.,¹³ Daniel Almquist, M.D.,¹⁴ Jeffrey Zonder, M.D.,¹⁵ Edward Faber, D.O.,¹⁶ Zihan Wei, M.S.P.H.,² Kenneth Anderson, M.D.,¹⁷ Sagar Lonial, M.D.,¹⁸ Paul Richardson, M.D.,¹⁷ Robert Orlowski, M.D., Ph.D.,¹⁹ Lynne Wagner, Ph.D.,²⁰ and S. Vincent Rajkumar, M.D.¹

Patient Randomization and Treatment Schedule



ENDURANCE trial:Efficacy

7-year OS: 68.6% vs 69.0% (P = 0.93)

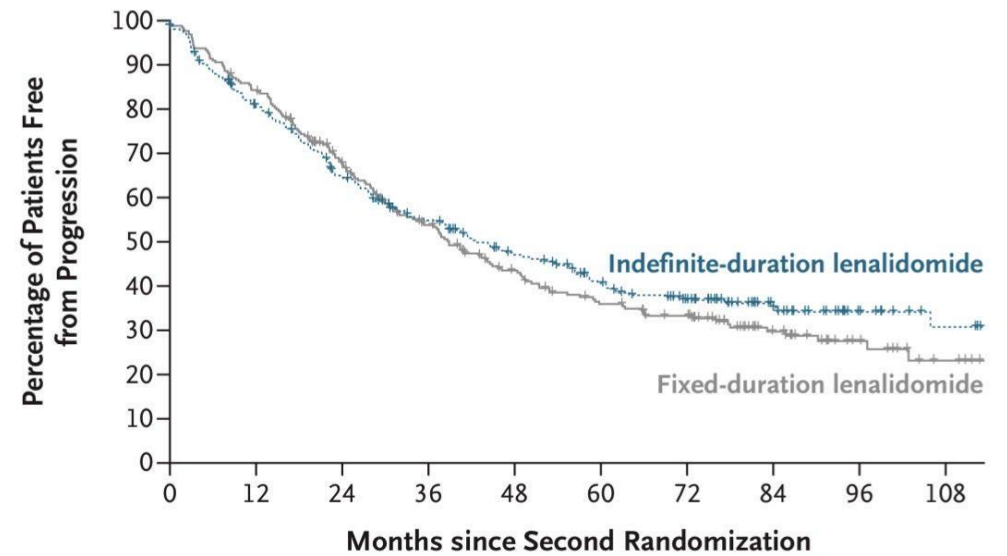


No. at Risk

Indefinite duration	260	251	240	220	203	180	143	97	52	24	6
Fixed duration	256	250	236	221	199	184	158	104	58	27	5

Median PFS: 42.5 vs 38.9 months

7-year PFS: 36.1% vs 29.7%



No. at Risk

Indefinite duration	260	200	156	125	99	78	61	38	17	9
Fixed duration	256	214	160	119	88	69	59	32	16	7

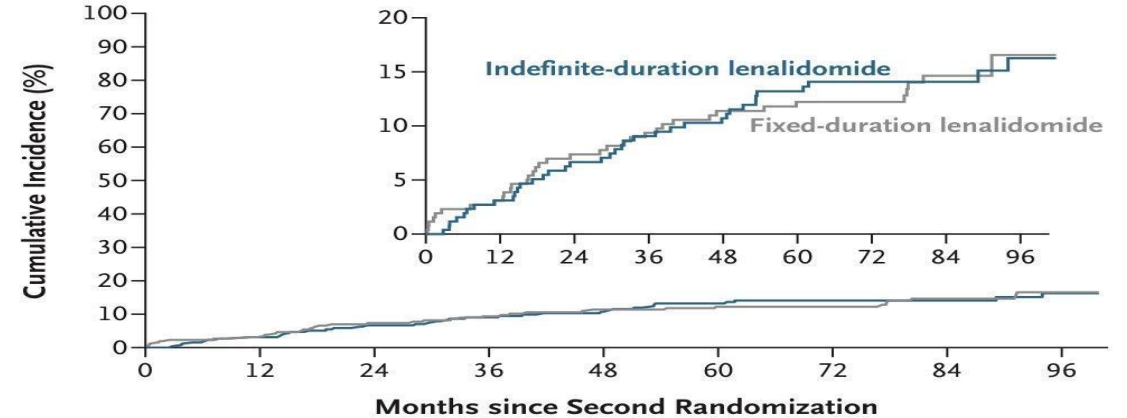
ENDURANCE Adverse events

second primary malignancies: 11.2% vs 8.3%

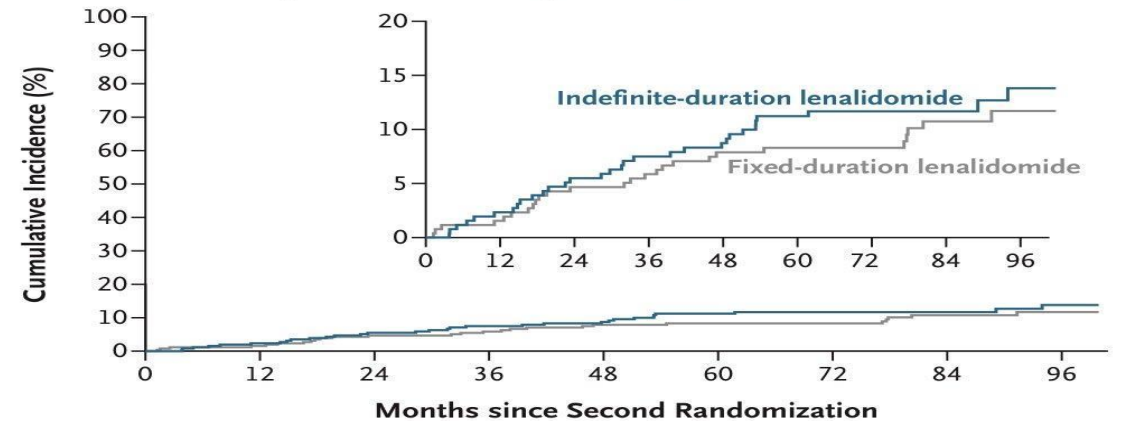
Table 3. Solicited Adverse Events, According to Grade.*

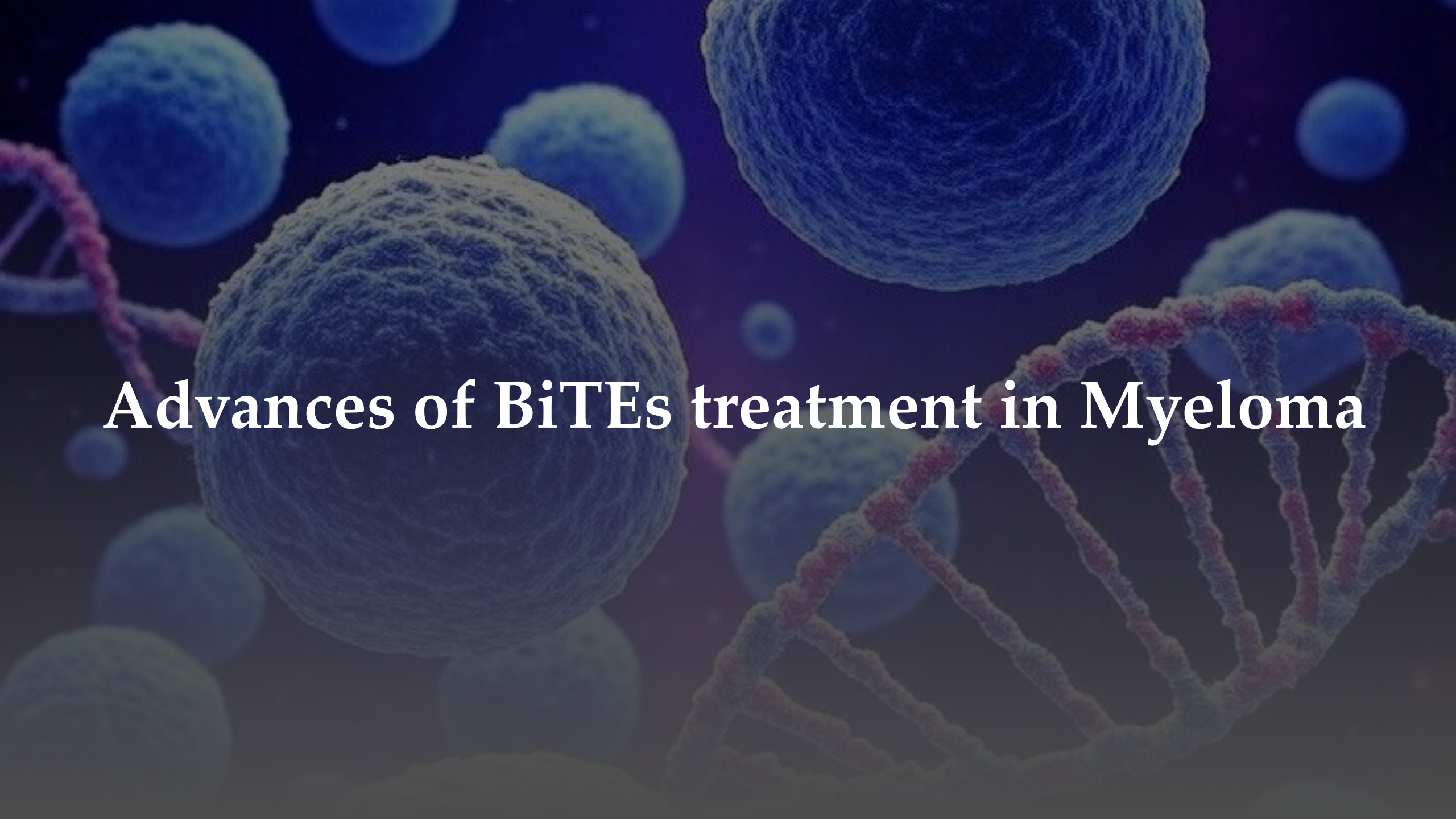
Event	Indefinite-Duration Lenalidomide (N=255)		Fixed-Duration Lenalidomide (N=254)	
	Grade 1 or 2	Grade 3 or 4	Grade 1 or 2	Grade 3 or 4
	<i>number of patients (percent)</i>			
Anemia	126 (49.4)	7 (2.7)	109 (42.9)	9 (3.5)
Diarrhea	109 (42.7)	14 (5.5)	90 (35.4)	5 (2.0)
Dyspnea	57 (22.4)	4 (1.6)	50 (19.7)	1 (0.4)
Edema in the limbs	80 (31.4)	1 (0.4)	64 (25.2)	1 (0.4)
Fatigue	146 (57.3)	15 (5.9)	120 (47.2)	6 (2.4)
Fever	18 (7.1)	1 (0.4)	19 (7.5)	0
Hyperglycemia	93 (36.5)	6 (2.4)	73 (28.7)	3 (1.2)
Insomnia	69 (27.1)	1 (0.4)	46 (18.1)	1 (0.4)
Irritability	10 (3.9)	0	15 (5.9)	0
Lymphocyte count decreased	91 (35.7)	22 (8.6)	77 (30.3)	15 (5.9)
Muscle weakness in the trunk	20 (7.8)	2 (0.8)	22 (8.7)	1 (0.4)
Nausea	58 (22.7)	3 (1.2)	45 (17.7)	2 (0.8)
Neutrophil count decreased	68 (26.7)	72 (28.2)	71 (28.0)	45 (17.7)
Peripheral motor neuropathy	40 (15.7)	0	23 (9.1)	1 (0.4)
Peripheral sensory neuropathy	121 (47.5)	2 (0.8)	101 (39.8)	4 (1.6)
Platelet count decreased	97 (38.0)	7 (2.7)	75 (29.5)	5 (2.0)
Rash, acneiform	26 (10.2)	3 (1.2)	27 (10.6)	3 (1.2)
Vomiting	20 (7.8)	2 (0.8)	20 (7.9)	2 (0.8)

A All Second Primary Cancers



B All Second Primary Cancers Excluding Nonmelanoma Skin Cancer



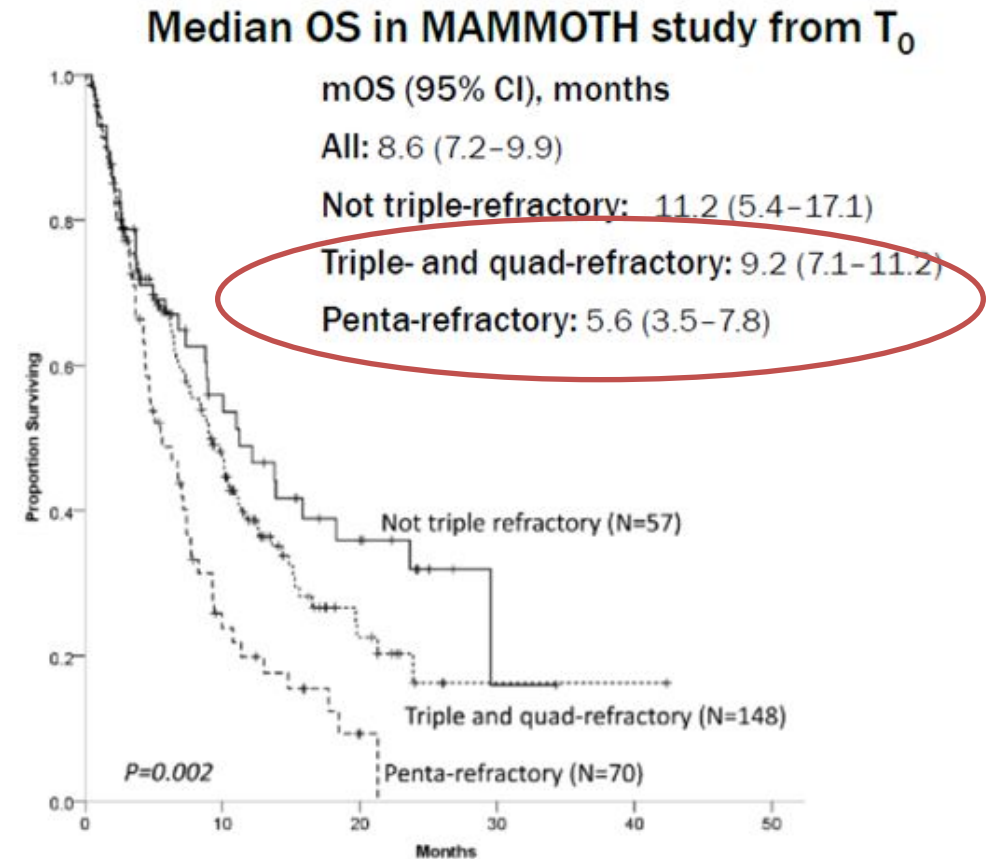
The background is a dark blue gradient. It features several large, textured blue spheres that resemble cells or molecules. A prominent DNA double helix structure is visible on the right side, rendered in a light blue and white color. The overall aesthetic is scientific and modern.

Advances of BiTEs treatment in Myeloma

Triple/Penta Class RRMM

- MAMMOTH Study

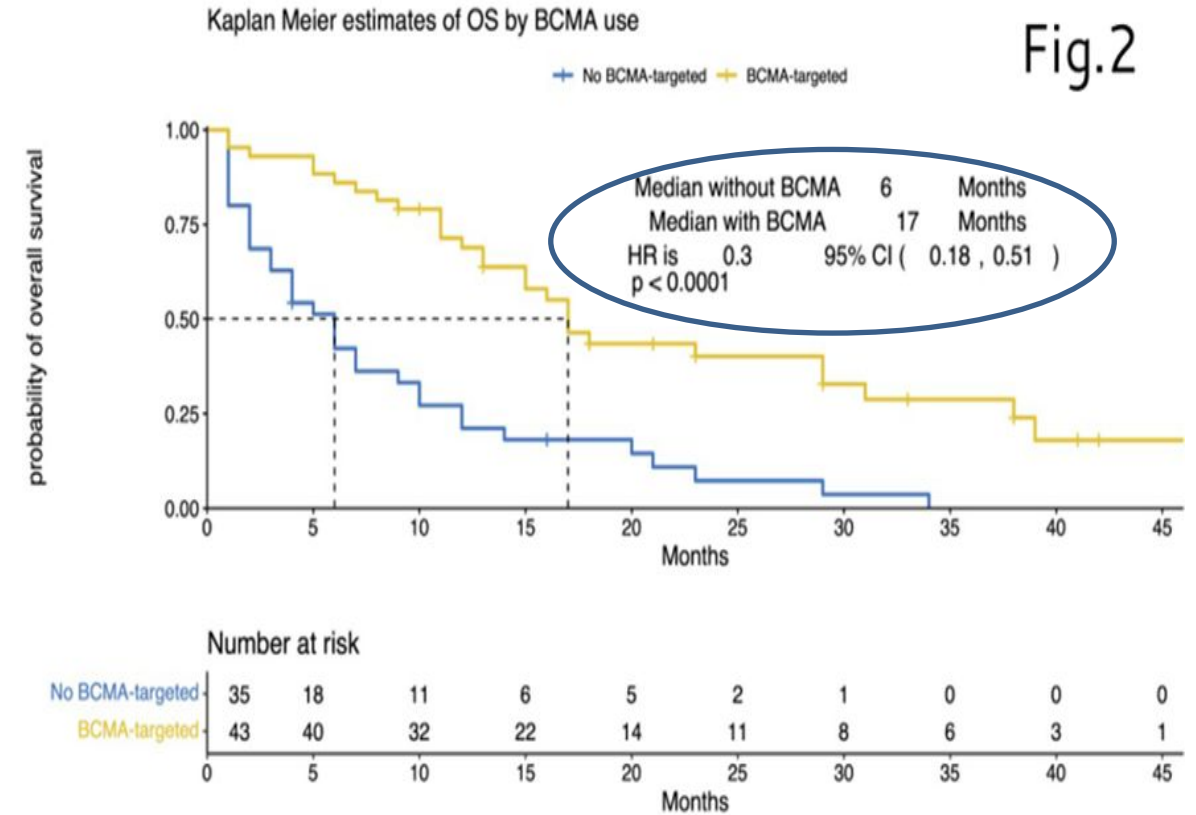
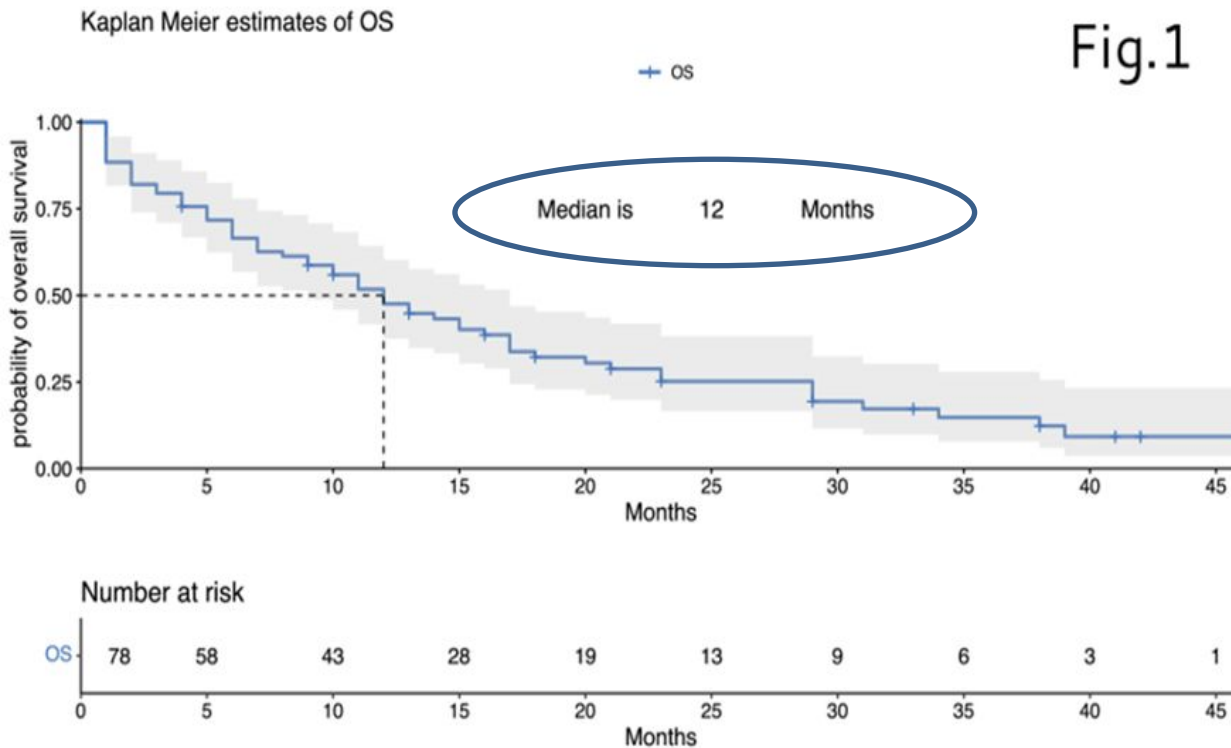
- Retrospective review of R/R MM
 - 275 patients
 - PI, IMiD, and CD38 exposed
- Median OS was **< 9 months** in MAMMOTH in patients with disease refractory to anti-CD38 mAbs
- Median OS was < 6 months if penta-refractory
- **Current treatment options** include conventional chemotherapy, salvage ASCT, recycling previous regimens, selinexor + dexamethasone, belantamab mafodotin and clinical trials



Gandhi. Leukemia. 2019;33:2266.

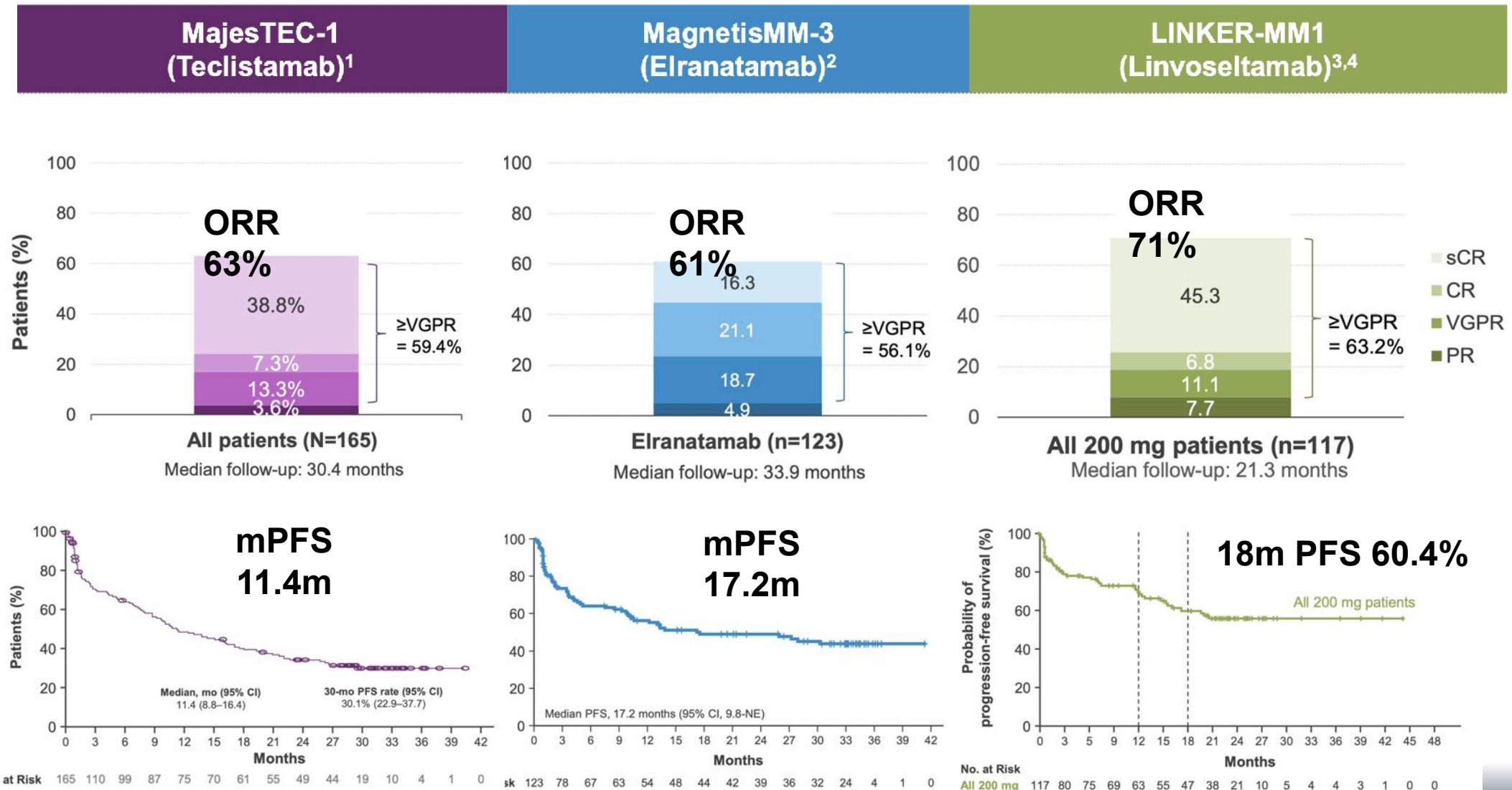
Why we need BCMA directed therapy?

Outcomes of Patients Who Are BCMA Directed Therapy Exposed Vs BCMA Naïve in Penta-RRMM



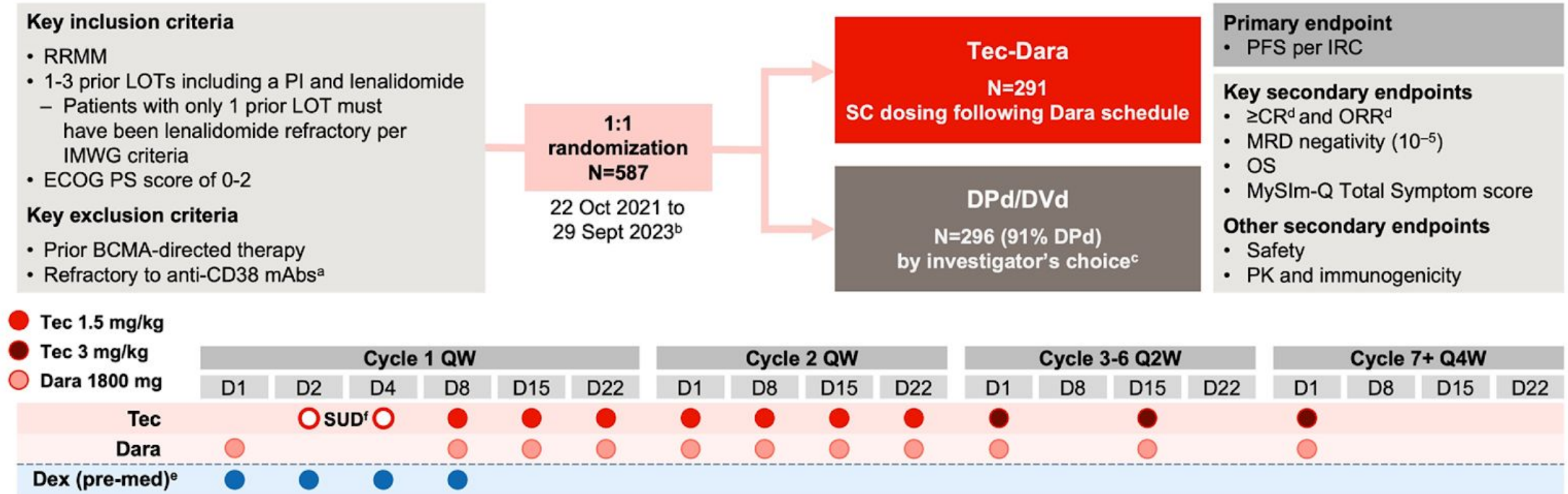
Atrash, S et al. Outcomes of Penta-Refractory Multiple Myeloma Patients Treated with or without BCMA-Directed Therapy. *Cancers* **2023**, 15, 2891.

Approved BCMA BsAbs in RRMM: Efficacy



1. Moreau P et al. N Engl J Med. 2022;387:495-505. 2. Lesokhin AM et al. Nat Med. 2023;29(9):2255-2267. 3. Lee HC et al. ASCO 2023. Abstract 8006. 4. Bumma N et al. J Clin Oncol. 2024;42:2702-2712.

MajesTEC-3: Teclistamab/Daratumumab in Early relapse



^aPrior exposure to anti-CD38 mAbs was permitted. ^bDuring the COVID-19 pandemic. ^cDPd/DVd were administered per the approved schedules. ^dResponse and disease progression were assessed by a blinded IRC per IMWG criteria. ^eDexamethasone, acetaminophen, and diphenhydramine pre-medication was required for the first 2 weeks; subsequent dexamethasone was not required thereafter. ^fPatients received SUD of 0.06 mg/kg and 0.3 mg/kg on Days 2 and 4, respectively.
CR, complete response; D, day; Dex, dexamethasone; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IRC, independent review committee; MRD, minimal residual disease; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; pre-med, pre-medication; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; SUD, step-up dosing.

Mateos, M-V et al, ASH 2025

MajesTEC-3: Baseline Demographics and Disease Characteristics

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Age		
Median (range), years	64 (36–88)	63 (25–84)
≥75 years, n (%)	31 (10.7)	25 (8.4)
Sex, n (%)		
Male	156 (53.6)	169 (57.1)
Female	135 (46.4)	127 (42.9)
Race, n (%)		
White	190 (65.3)	194 (65.5)
Asian	68 (23.4)	63 (21.3)
Black or African American	13 (4.5)	20 (6.8)
Other ^a	20 (6.9)	19 (6.4)

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Baseline ECOG PS score, n (%)		
0	167 (57.4)	160 (54.1)
1	108 (37.1)	127 (42.9)
2	16 (5.5)	9 (3.0)
ISS stage, n/N (%)		
I	182 (62.5)	185 (62.5)
II	85 (29.2)	88 (29.7)
III	24 (8.2)	23 (7.8)
BMPCs ≥60%, ^b n/N (%)	28/286 (9.8)	24/293 (8.2)
Presence of soft-tissue plasmacytomas, n (%)	41 (14.1)	41 (13.9)
Extramedullary plasmacytomas ^c	14 (4.8)	17 (5.7)
Paraskeletal plasmacytomas	32 (11.0)	31 (10.5)
High-risk cytogenetics, ^d n/N (%)	104/285 (36.5)	104/294 (35.4)

^a“Other” includes Native Hawaiian or Pacific Islander (Tec-Dara, n=1 [0.3%]; DPd/DVd, n=0; total, n=1 [0.2%]), American Indian or Alaska Native (Tec-Dara, n=0; DPd/DVd, n=1 [0.3%]; total, n=1 [0.2%]), not reported (Tec-Dara, n=14 [4.8%]; DPd/DVd, n=16 [5.4%]; total, n=30 [5.1%]), and unknown (Tec-Dara, n=5 [1.7%]; DPd/DVd, n=2 [0.7%]; total, n=7 [1.2%]). ^bMaximum value from bone marrow biopsy or bone marrow aspirate was selected if both results were available. ^cFrom metastatic or hematogenous spread involving only soft tissues. ^dPresence of ≥1 of del(17p), t(4;14), or t(14;16).
BMPC, bone marrow plasma cell; ISS, International Staging System.

MajesTEC-3: Treatment History

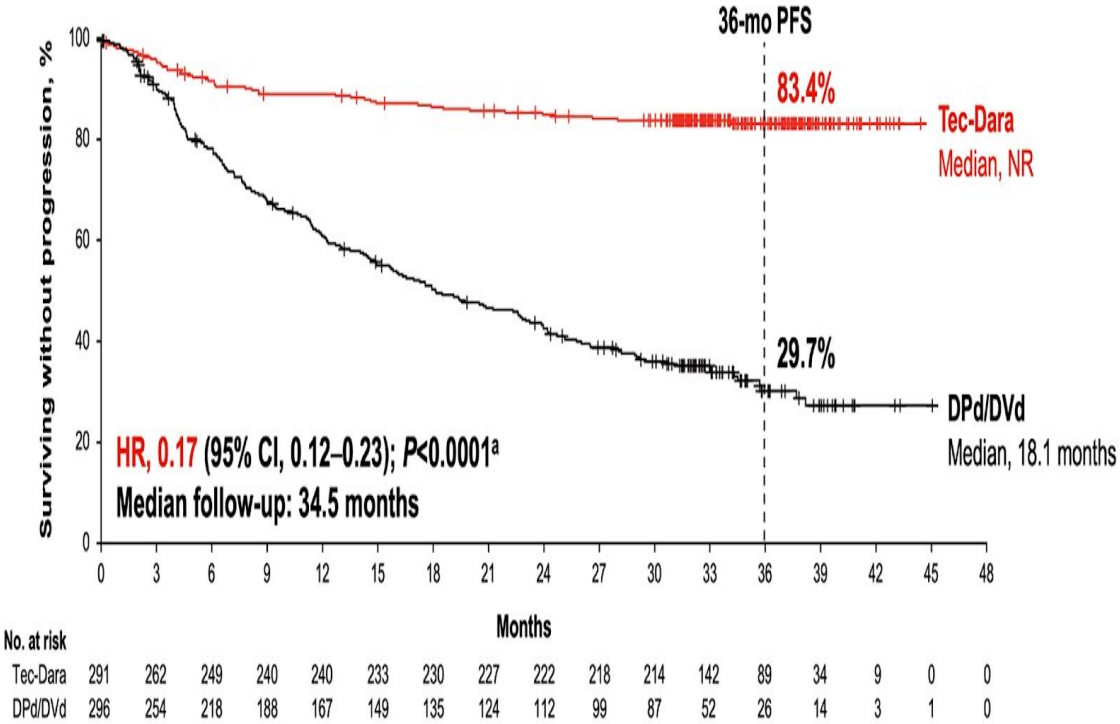
Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Prior LOTs		
Median (range), n	2 (1–3)	2 (1–3)
1 prior LOT	108 (37.1)	114 (38.5)
2 prior LOTs	134 (46.0)	134 (45.3)
3 prior LOTs	49 (16.8)	48 (16.2)
Prior transplantation, n (%)	210 (72.2)	226 (76.4)

- 5% of patients were Dara exposed
- In real-world data sets, 70% of patients in 2L are Dara naïve or exposed¹

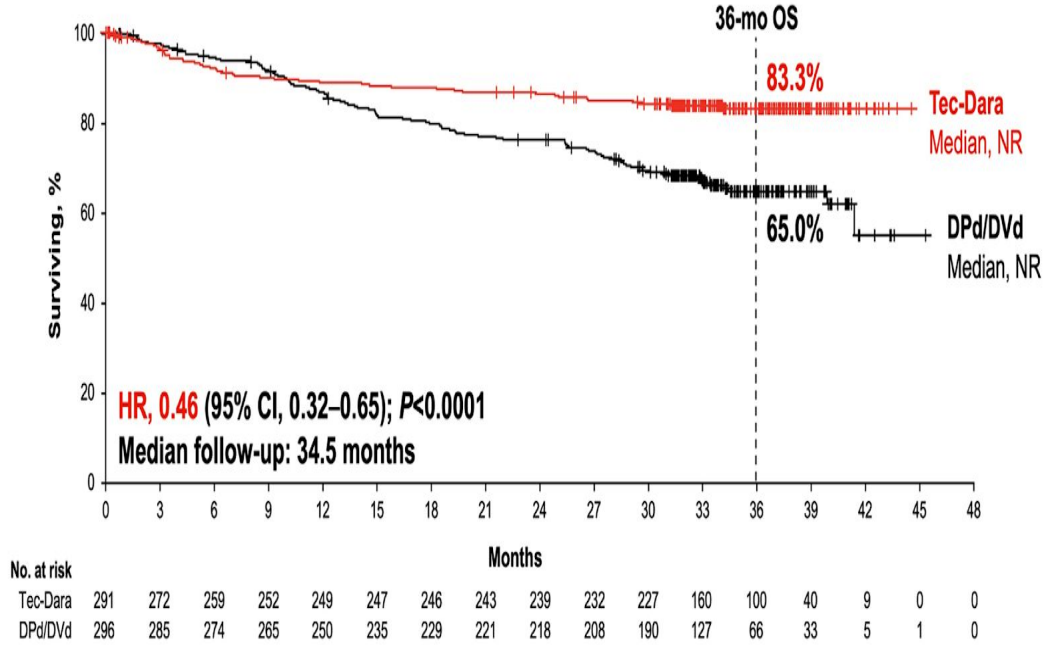
Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Prior therapy exposure, n (%)		
PI	290 (99.7)	296 (100)
IMiD	291 (100)	296 (100)
Anti-CD38, n (%)	15 (5.2)	16 (5.4)
Refractory status, n (%)		
To last prior LOT	250 (85.9)	251 (84.8)
Any PI	117 (40.2)	104 (35.1)
Any IMiD	247 (84.9)	253 (85.5)
Lenalidomide	240 (82.5)	251 (84.8)
Double (PI and IMiD)	99 (34.0)	88 (29.7)

Mateos, M-V et al, ASH 2025

MajesTEC-3: Efficacy



^aThe P value crossed the prespecified stopping boundary for superiority for the first interim analysis ($P=0.0139$).
CI, confidence interval; HR, hazard ratio; NR, not reached.
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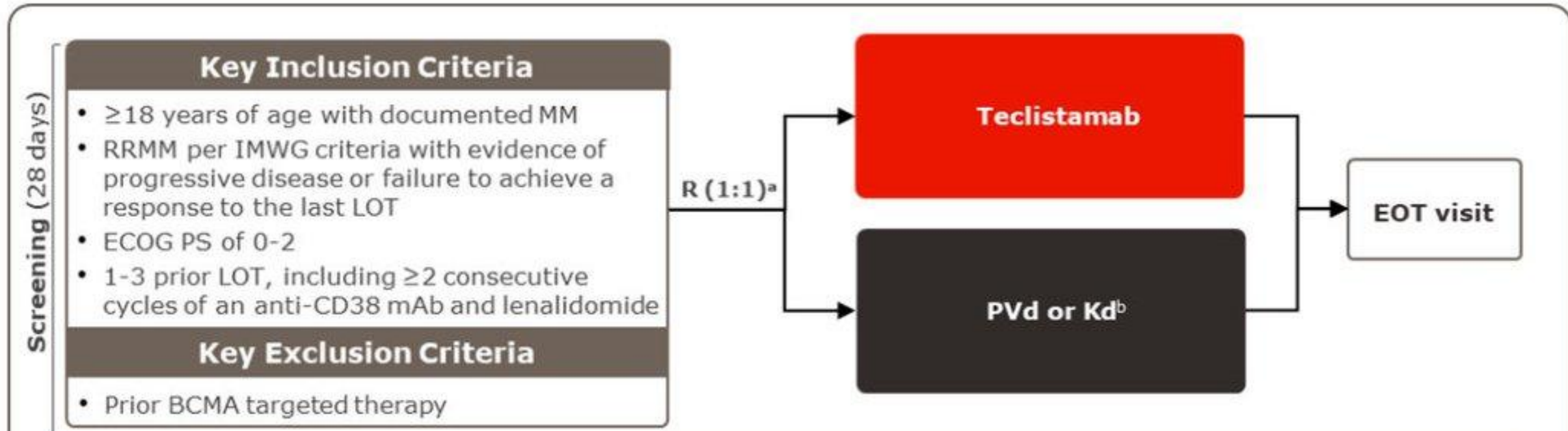
Analysis of RMST demonstrated an OS benefit for Tec-Dara versus DPd/DVd (RMST difference, 2.15 months; $P=0.0088$).
RMST, restricted mean survival time.

ORIGINAL ARTICLE

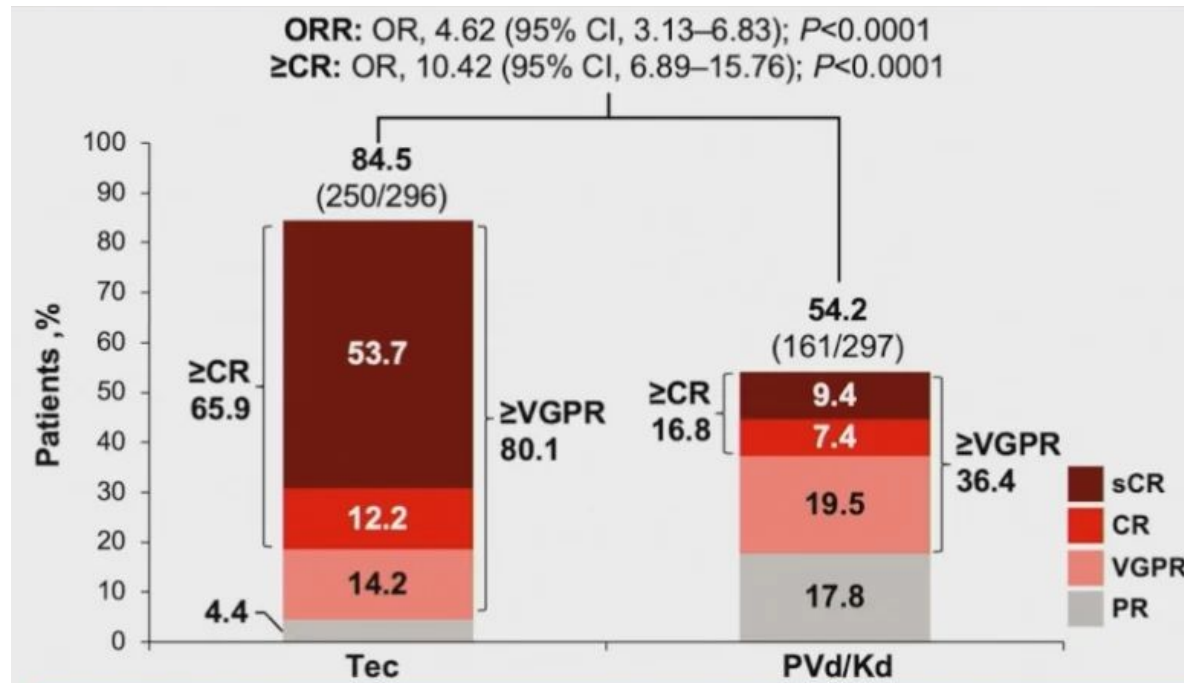
Teclistamab in Multiple Myeloma with One to Three Previous Lines of Therapy

C. Touzeau,¹ R. Mina,^{2,3} H. Quach,⁴ V. Hungria,⁵ D. Bhutani,⁶ W. Chen,⁷ S. Kumar,⁸ C. Chaulagain,⁹ M.A. Dimopoulos,^{10,11} N.J. Bahlis,¹² S. Maral,¹³ N.W.C.J. van de Donk,¹⁴ J. Schmidt Filho,¹⁵ K. Saja,¹⁶ R. Teipel,¹⁷ M. Ando,¹⁸ W. Roeloffzen,¹⁹ O. Annibali,²⁰ B. Augustson,²¹ C. Botta,²² M. Delforge,²³ E. Bourgeois,²⁴ G. Buda,²⁵ M. Hus,²⁶ A. Perrot,²⁷ M. Preis,^{28,29} M. Beksac,³⁰ L. Pour,³¹ S. Farmer,³² M. Nunes,³³ A. Oriol,³⁴ T. Melchardt,³⁵ Y. Hu,³⁶⁻³⁸ M. Flogegård,³⁹ D. Wang,⁴⁰ L. Pei,⁴⁰ S. Wroblewski,⁴¹ I.M. Ariës,⁴² N.A. Quijano Cardé,⁴¹ T. Perova,⁴¹ T. de Jager,⁴³ T.-M. Yeh,⁴⁰ V. Vanquickenberghe,⁴⁴ P. Shah,⁴⁵ K. Chastain,⁴⁰ R. Kobos,⁴⁰ R. Carson,⁴¹ and O. Landgren,⁴⁶ for the MajesTEC-9 Trial Investigators*

MajesTEC-9



MajesTEC-9: Efficacy

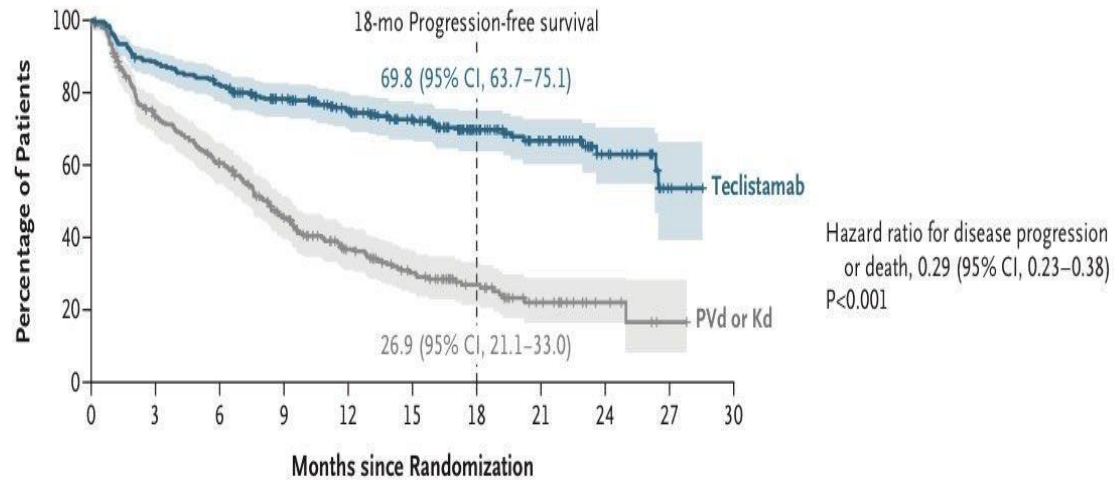


	Tec (n=250)	PVd/Kd (n=161)
Median (range) time to first response, months	1.2 (0.9–7.9)	1.1 (0.7–11.1)
Median (range) time to first $\geq$ CR, months	5.8 (1.0–23.0)	5.6 (0.9–16.3)
Median (95% CI) DOR, months	NE (25.2–NE)	13.4 (10.4–17.3)
Estimated 18-month DOR, % (95% CI)	80.6 (74.1–85.5)	40.1 (30.8–49.1)

MajesTEC-9: Efficacy

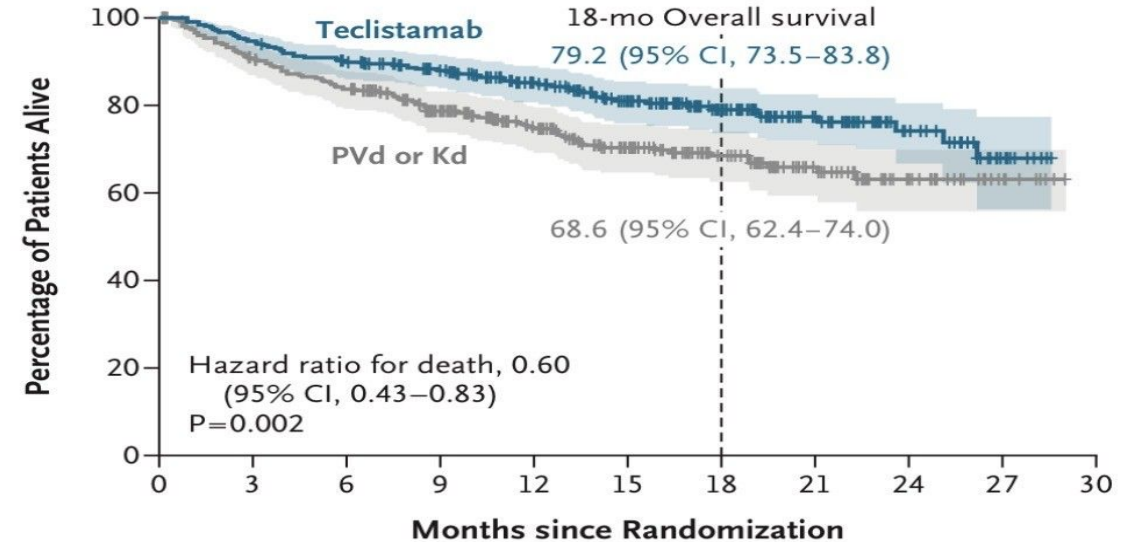
- **71% reduction** in the risk of **progression or death** HR = 0.29
- **40% reduction** in the risk of **death** OS HR = 0.60

A Progression-free Survival



No. at Risk

Teclistamab	296	258	239	206	172	141	92	57	27	6	0
PVd or Kd	297	199	162	112	74	51	33	16	6	1	0



No. at Risk

Teclistamab	296	280	263	237	195	159	107	66	33	11	0
PVd or Kd	297	264	243	210	172	137	91	54	25	8	0

Teclistamab in RRMM

Characteristic	MajesTEC-1 (Tec)	MajesTEC-9 (Tec)	MajesTEC-3 (Tec-Dara)
Prior lines	Median 5	1–3	1–3
High-risk cytogenetics	25.7%	35.7 %	36.5 %
Extramedullary disease	17.0%	6.4 %	NA
Triple-class refractory	77.6%	34.5%	NA
Penta-refractory	30.3%	NA	NA
ORR	63.0%	84.5%	89.0%
≥CR	39.4%	65.9%	81.8%
MRD negativity	26.7%	38.5%	58.4%
PFS	11.3 mo	18-mo PFS 69.8%	36-mo PFS 83.4%
OS	NR	18-mo OS 79.2%	36-mo OS 83.3%
Grade 3/4 infections	44.8%	41.6%	54.1%
CRS	72.1%	66.0%	60.1%
ICANS	3.0%	4.1%	1.1%

Take-Home Messages:

- Continuous lenalidomide maintenance improved PFS but did not improve overall survival, suggesting that longer therapy delays progression without extending life expectancy.
- The PFS benefit must be balanced against increased cumulative toxicity and a higher incidence of second primary malignancies, supporting an individualized approach to maintenance duration.
- MajesTEC-3 and MajesTEC-9 established teclistamab-based combinations (Tec-Dara and Tec-containing regimens) as superior to standard-of-care therapy, demonstrating significant improvements in clinical outcomes
- Community adoption of teclistamab remains challenging, highlighting the need for greater awareness and optimized infection prophylaxis and supportive care



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