

La rivoluzione terapeutica nel linfoma e nel mieloma

Napoli, Hotel Royal Continental • 14-15 Maggio 2026

Come cambia la seconda linea di trattamento

Danilo De Novellis, AOU Ruggi D'Aragona

Salerno

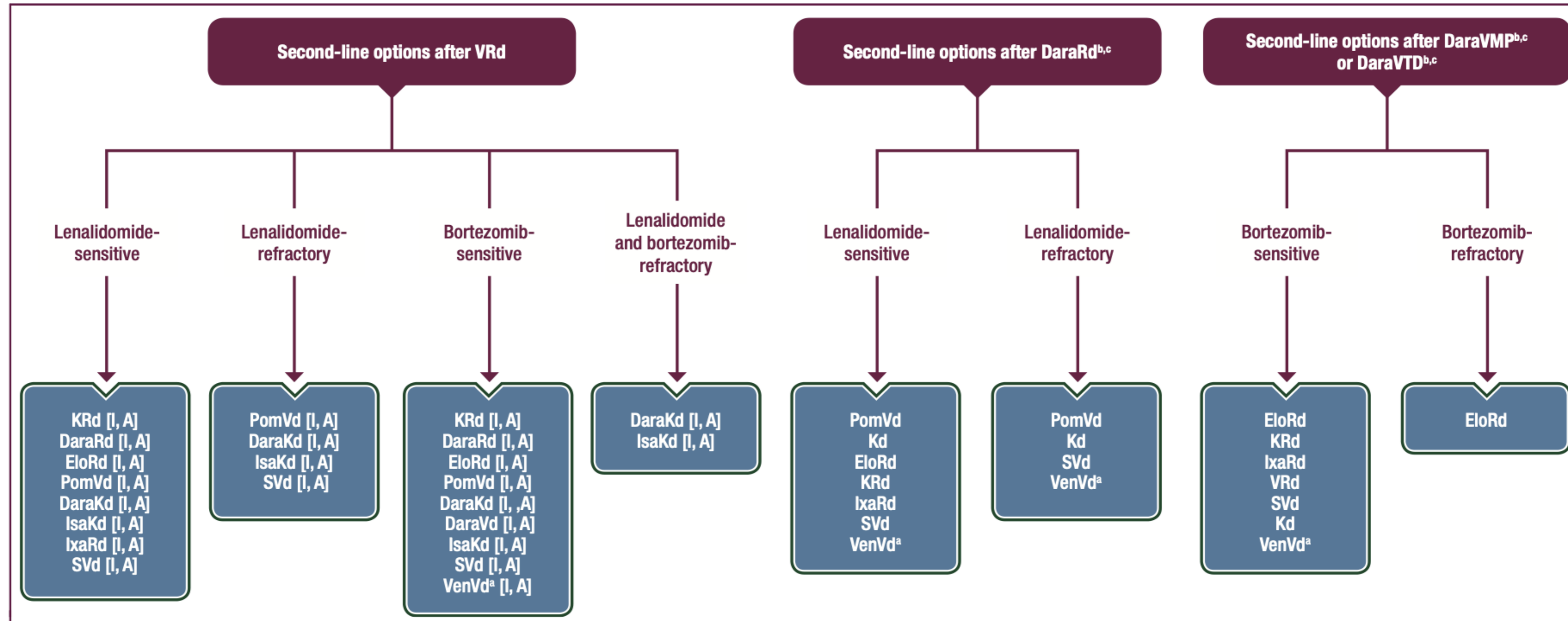


La rivoluzione terapeutica nel linfoma e nel mieloma

Disclosures of Danilo De Novellis

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Sanofi			x			x	
Amgen			x				
Johnson&Johnson			x				
GSK						x	
Pfizer						x	

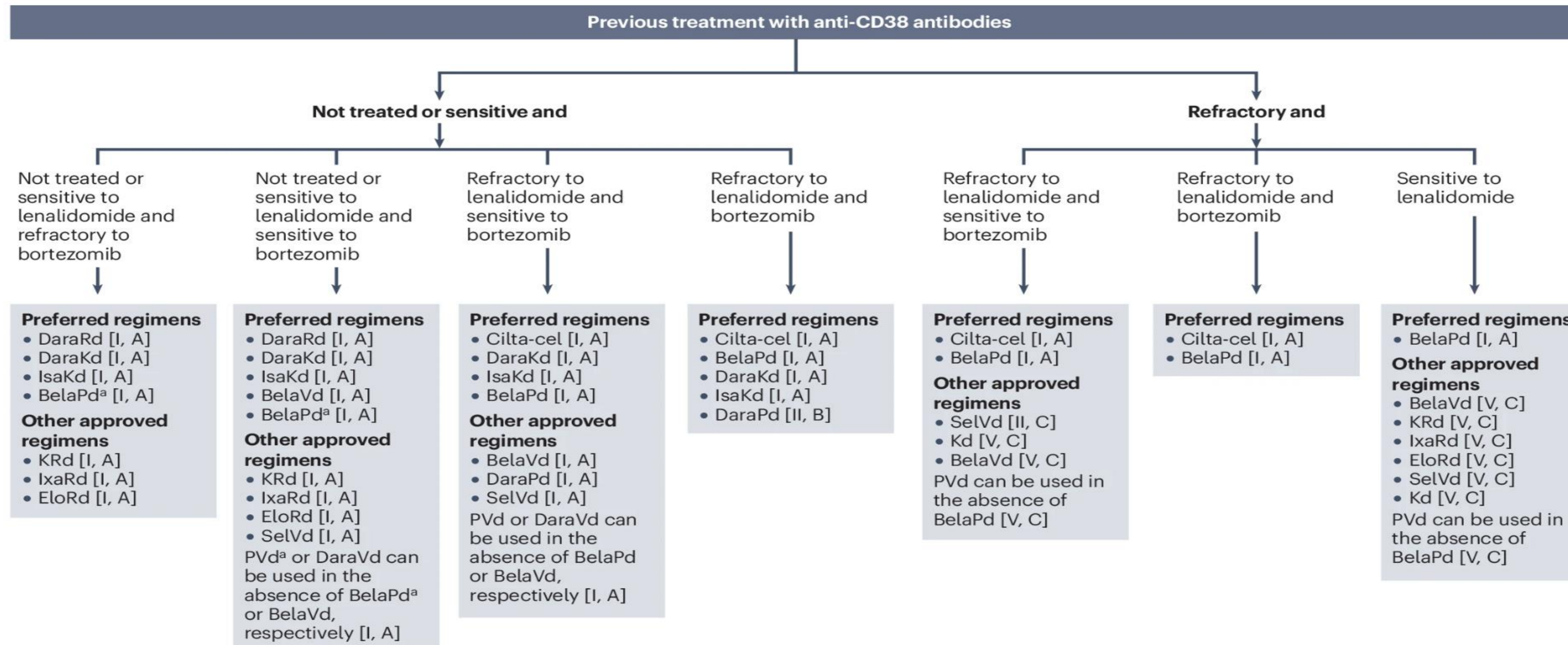
La II linea è già cambiata



Annals of Oncology

Linee guida 2021

La rivoluzione terapeutica nel linfoma e nel mieloma

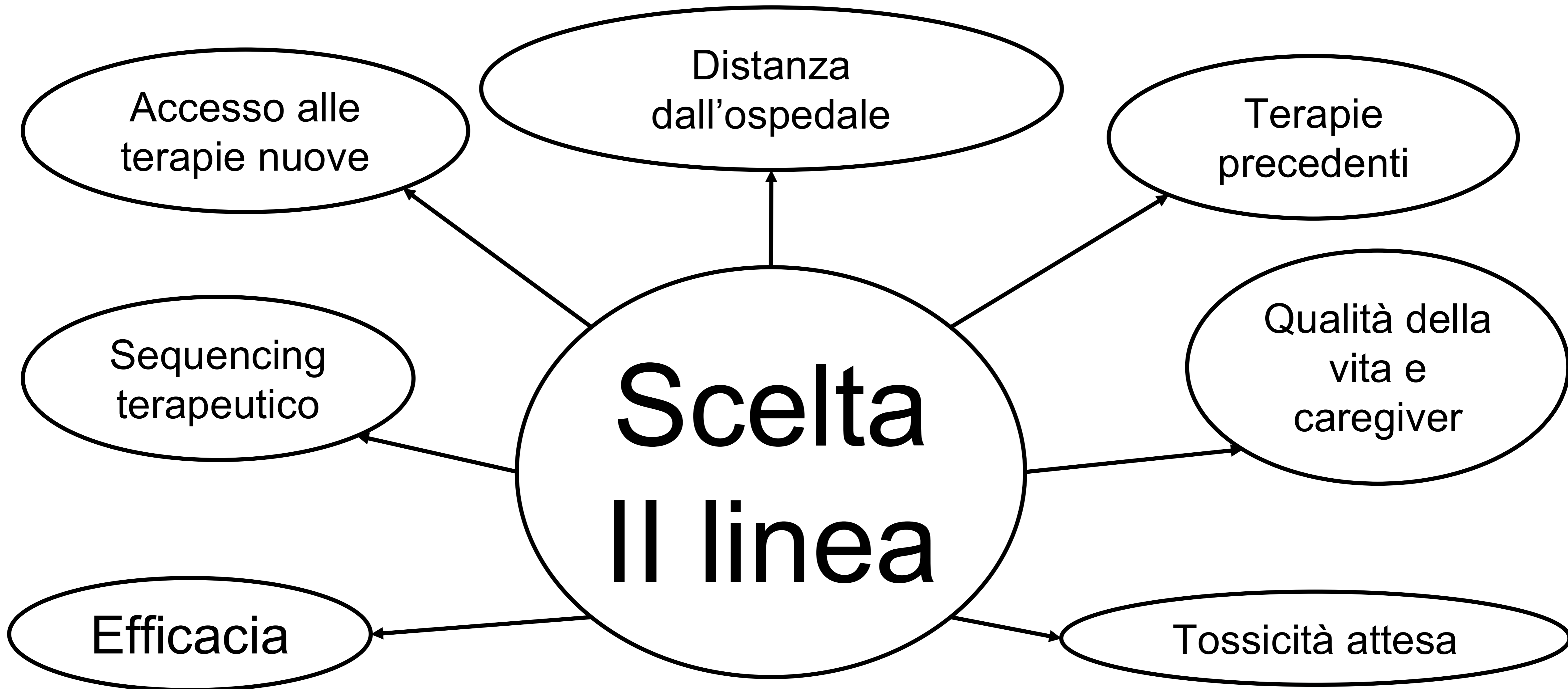


Linee guida 2025

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- Rispetto al passato, il paziente che recidiva oggi è virtualmente refrattario a lenalidomide
- Il cardine delle nuove linee guida è la valutazione della refrattarietà/esposizione ad anti-CD38 mAbs

Approccio alla seconda linea nel mieloma oggi

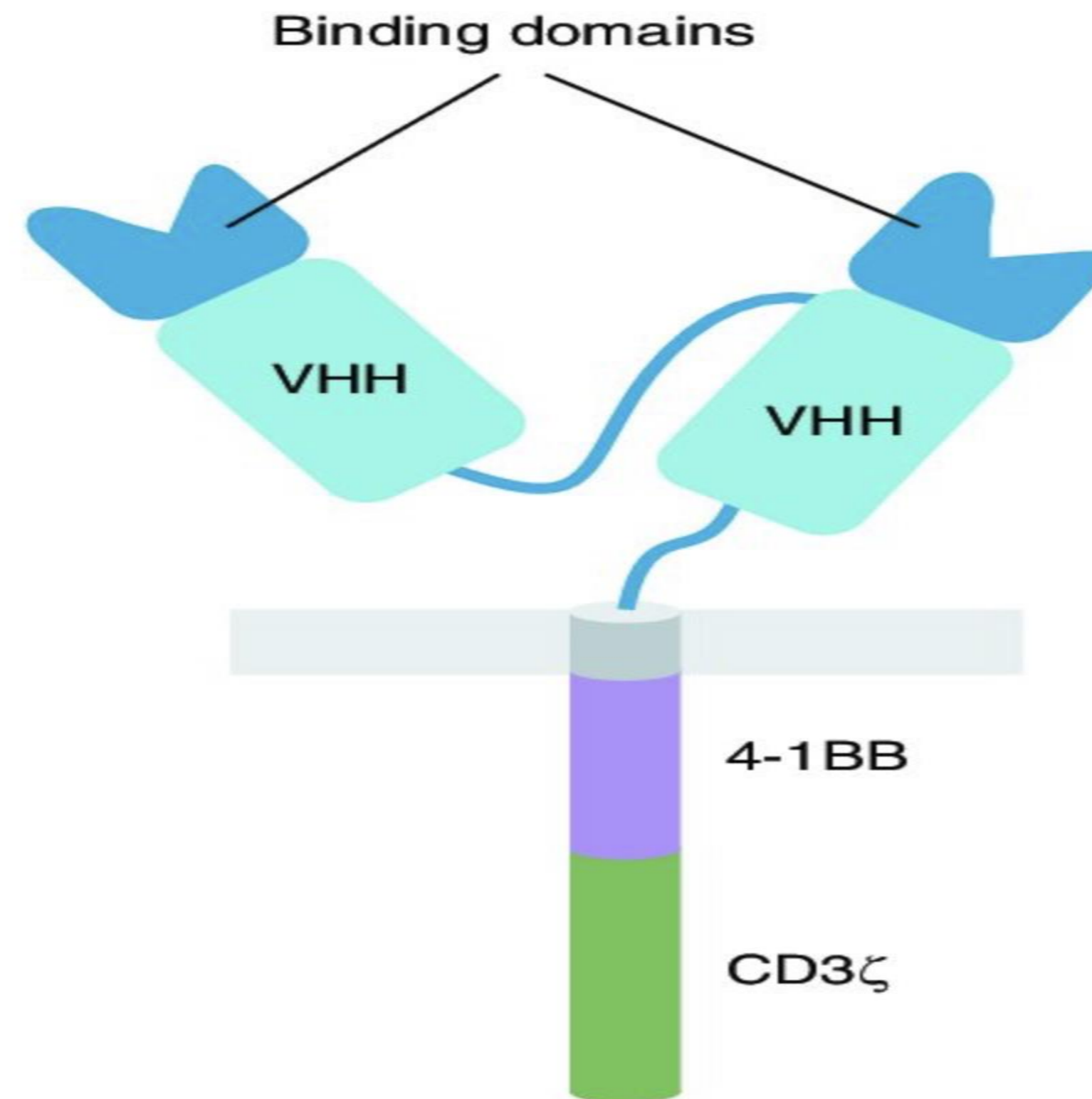


Approccio alla seconda linea nel mieloma oggi

La domanda è...

Il paziente, considerato tutti i fattori decisionali, è candidato da subito o lo sarà in linee successive a terapia CAR-T con target BCMA (cilta-cel)?

Costrutto CAR cilta-cel



Target = BCMA

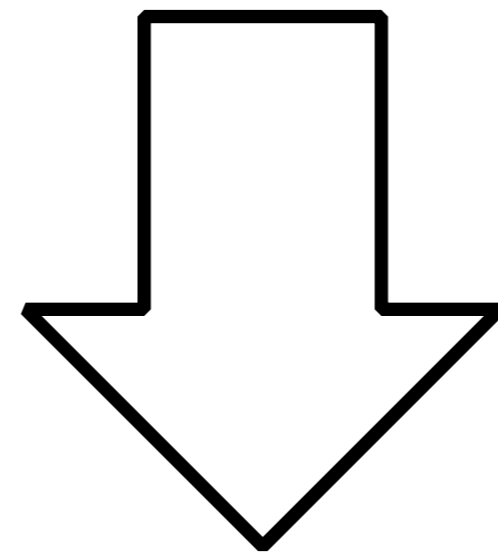
Due anticorpi a singolo dominio per potenziare l'avidità di legame

Criteri eleggibilità a cilta-cel

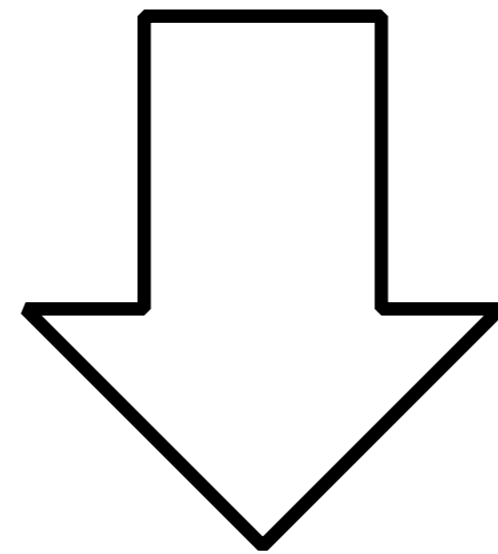
- Età
- Fitness e comorbidità (ECOG 0-1)
- No Disfunzione renale (clearance creatinina > 40 ml/min)
- Trattamenti precedenti (almeno 1 PI, IMiD, anti-CD38 → de facto si)
- No precente terapia anti-BCMA
- Aggressività e velocità della recidiva (biochimica, clinica EMD, etc)
- Logistica breve di accesso al prodotto

Scenario 1

Paziente triplo esposto o triplo refrattario

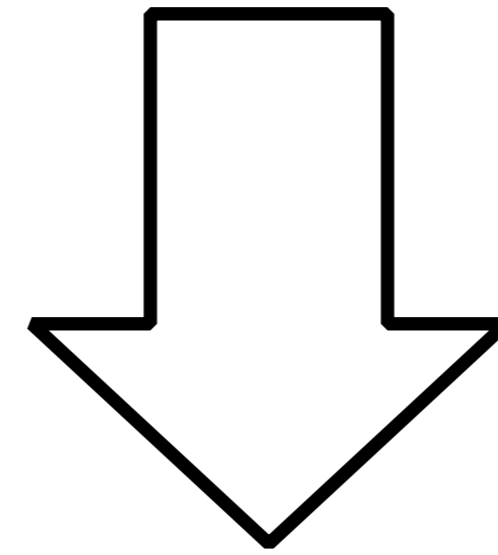


Se soddisfatte condizioni di eleggibilità a CAR-T



Allora cilta-cel

Ma... perché proprio cilta-cel?



Campionato a parte

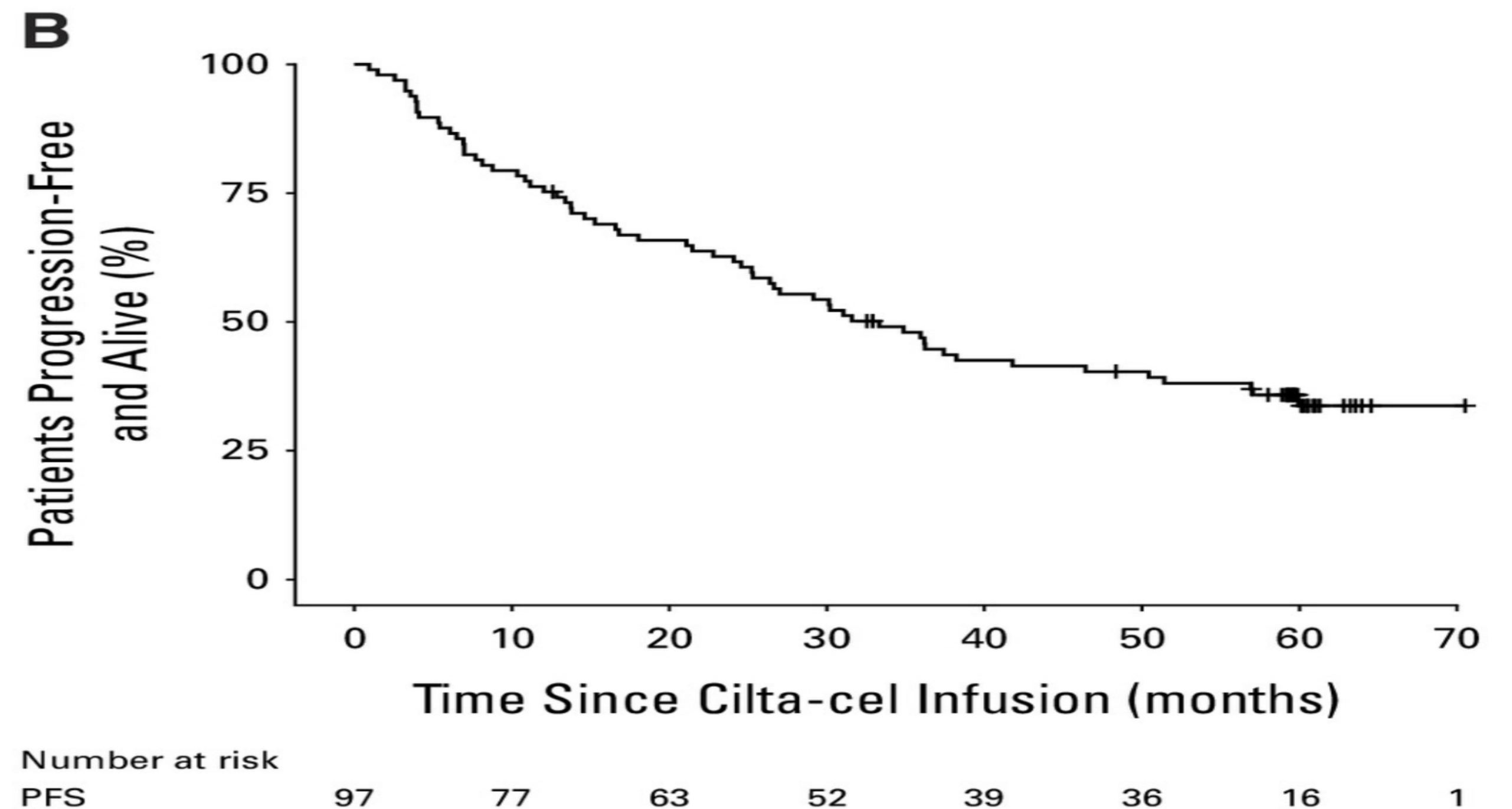
Sia nel plurirecidivato...

Studio Cartitude-1

Mediana linee precedenti 6 (3-18)

87% triple class refrattari

42% penta class refrattari



PFS mediana 34.9 mesi

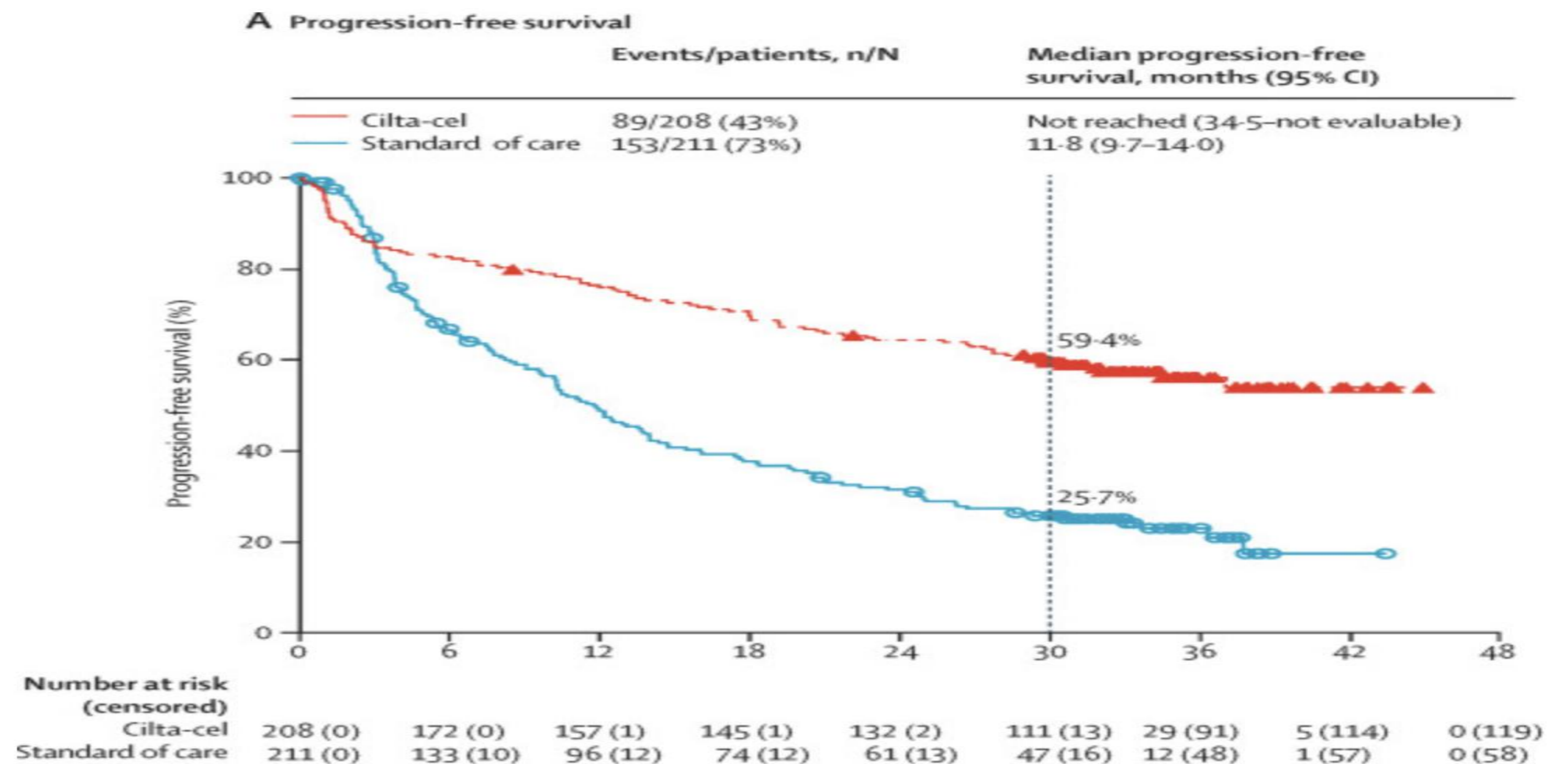
...che in linee più precoci

Studio Cartitude-4

Linee precedenti: 1 (32.7%), 2 (39.9%), 3 (27.4%)

25% triple class esposti

6.7% penta class exposure



PFS mediana non raggiunta vs 11.9 mesi

Efficace nei vari sottogruppi

Multiple Myeloma

MM-567 Ciltacabtagene Autoleucel vs Standard of Care in Lenalidomide-Refractory Multiple Myeloma: Phase 3 CARTITUDE-4 Subgroup Analysis by Cytogenetic Risk

Roberto Mina MD¹, Binod Dhakal MD², Jesus San-Miguel MD, PhD³, Mi Kwon MD^{4, 5}, Duncan Purtill MD⁶, Hila Magen MD^{7, 8}, Magdalena Dutka PhD⁹, Michel Delforge MD¹⁰, Ravi Vij MD, MBA¹¹, Stina Wichert N/A¹², Sung-Soo Yoon MD¹³, Monique C. Minnema MD, PhD¹⁴, Nikoletta Lendvai MD¹⁵, Carolina Lonardi N/A¹⁶, Ana Slaughter N/A¹⁷, Martin Vogel MD, PhD¹⁸, Katherine Li N/A¹⁹, Diana Chen MS²⁰, Man Zhao PhD²¹, Tzu-min Yeh MS¹⁵...
Joaquin Martinez-Lopez MD, PhD²⁷

EMN: POSTERS

P48 | LONG-TERM PROGRESSION-FREE SURVIVAL BENEFIT WITH CILTACABTAGENE AUTOLEUCEL IN STANDARD-RISK RELAPSED/REFRACTORY MULTIPLE MYELOMA

D. Dytfeld¹, L.J. Costa², A. Oriol³, S. Manier^{4|5}, P.M. Voorhees⁶, Y. Lin⁷, M. Htut⁸, W. Roeloffzen⁹, P. J. Ho^{10|11}, U. Shah^{12|13}, M. Zhao¹⁴, Q. Li¹⁵, A. Balogh¹⁵, K. Li¹⁵, A. Slaughter¹⁵, N. Benachour¹⁵, C. Lonardi¹⁵, A. Ghosh¹⁵, H. Sun¹⁵, N. Lendvai¹⁵, T. Lengil¹⁵, N. Patel¹⁶, M. Koneru¹⁶, E. Florendo¹⁶, O. Costa Filho¹⁶, V. Mahajan¹⁶, P. Rodríguez-Otero¹⁷, C. Strouse¹⁸, A.K. Stewart^{19|20}, S. Sidana²¹

Affiliations +

Vol. 111 No. s2 (2026): Abstract Book of the 7th European Myeloma Network Meeting, Prague, 16-18 April 2026
<https://doi.org/10.3324/haematol.2026.s2.14061>

Multiple Myeloma

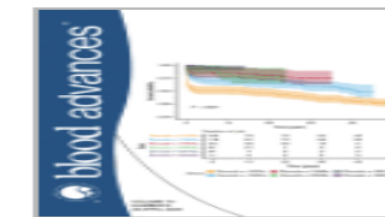
MM-549 Ciltacabtagene Autoleucel vs Standard of Care in Patients With Functional High-Risk Multiple Myeloma: CARTITUDE-4 Subgroup Analysis

Luciano Costa MD¹, Katja Weisel MD², Niels WCJ van de Donk MD, PhD³, Surbhi Sidana MD⁴, Yaël Cohen MD⁵, Duncan Purtill MD⁶, Cyrille Touzeau MD, PhD⁷, Carlos Fernández de Larrea MD, PhD⁸, Joaquin Martinez-Lopez MD⁹, Nikoletta Lendvai MD¹⁰, Ana Slaughter¹¹, Carolina Lonardi N/A¹², Man Zhao¹³, Katherine Li¹⁴, Martin Vogel MD, PhD¹⁵, Mythili Koneru MD, PhD¹⁶, Nitin Patel¹⁶, Erika Florendo MD¹⁶, Octavio Costa Filho MD¹⁶, Maria-Victoria Victoria MD, PhD¹⁷

Tossicità neurologica

Rara ma distintiva

Tossicità neurologica tardiva Non -ICANS



Available online 30 March 2026

In Press, Journal Pre-proof ⓘ [What's this?](#)

Systematic Review

Non-ICANS Neurologic Toxicity after BCMA CAR T: A systematic review and meta-analysis of 4630 multiple myeloma patients *, †,

Herman van Besien *¹, Gwynne Ozkan *¹, Neela Easton¹, Tobias Tix², Mohammad Alhomoud^{1 3}, Roni Shouval^{1 3}, Kai Rejeski^{† 2 3}, Samuel Yamshon^{† 1 4}  

N= 4630 pts

Paralisi nervi cranici: 32.3%

Disturbi cognitivi e del movimento: 12%

Neuropatie periferiche: 7.5%

Parkinsonismo

5/60 pazienti trattati a Chicago

Tempo mediano di insorgenza: 26 giorni

Spesso associata a linfocitosi CAR nel liquor

Refrattarietà a steroide e levo dopa

MTX intratecale o ciclofosfamide ad alte dosi

Fattori di rischio e strategia di mitigazione

1. Alto burden di malattia all'infusione
2. CRS ≥ 2
3. ICANS
4. Picco di espansione CAR-T > 1000 cellule a giorno 14
5. Persistenza CART > 300 cellule al gg +56

1. Bridging therapy efficace
2. Trattamento intensivo di CRS ed ICANS
3. Riconoscimento precoce
4. Monitoraggio stretto

Scenario 2

Paziente

- Non candidato a cilta-cel nell'immediato ma che potrebbe esserlo in futuro
- Non ancora triplo esposto/refrattario (post dara-RD)
- Tempi logistici lunghi per l'accesso al prodotto (holding therapy)

Meeting Abstract: 2025 ASCO Annual Meeting I

FREE ACCESS | Hematologic Malignancies—Plasma Cell Dyscrasia | May 28, 2025 | Latest version



Disease response at apheresis and association with long-term outcomes following CAR-T cells for relapsed/refractory multiple myeloma (RRMM).

Authors: [Thomas Luo](#), [Luca Paruzzo](#), [Sandra P. Susanibar Adaniya](#), [Alfred L. Garfall](#), [Matthew Ho](#), [Shivani Kapur](#), [Marco Ruella](#), [Edward Allen Stadtmauer](#), [Federico Stella](#), [Dan T. Vogl](#), [Adam J. Waxman](#), and [Adam D. Cohen](#) | [AUTHORS INFO & AFFILIATIONS](#)

N=149

Follow up mediano: 14 mesi

CAR-T come consolidamento vs. CAR-T alla progressione

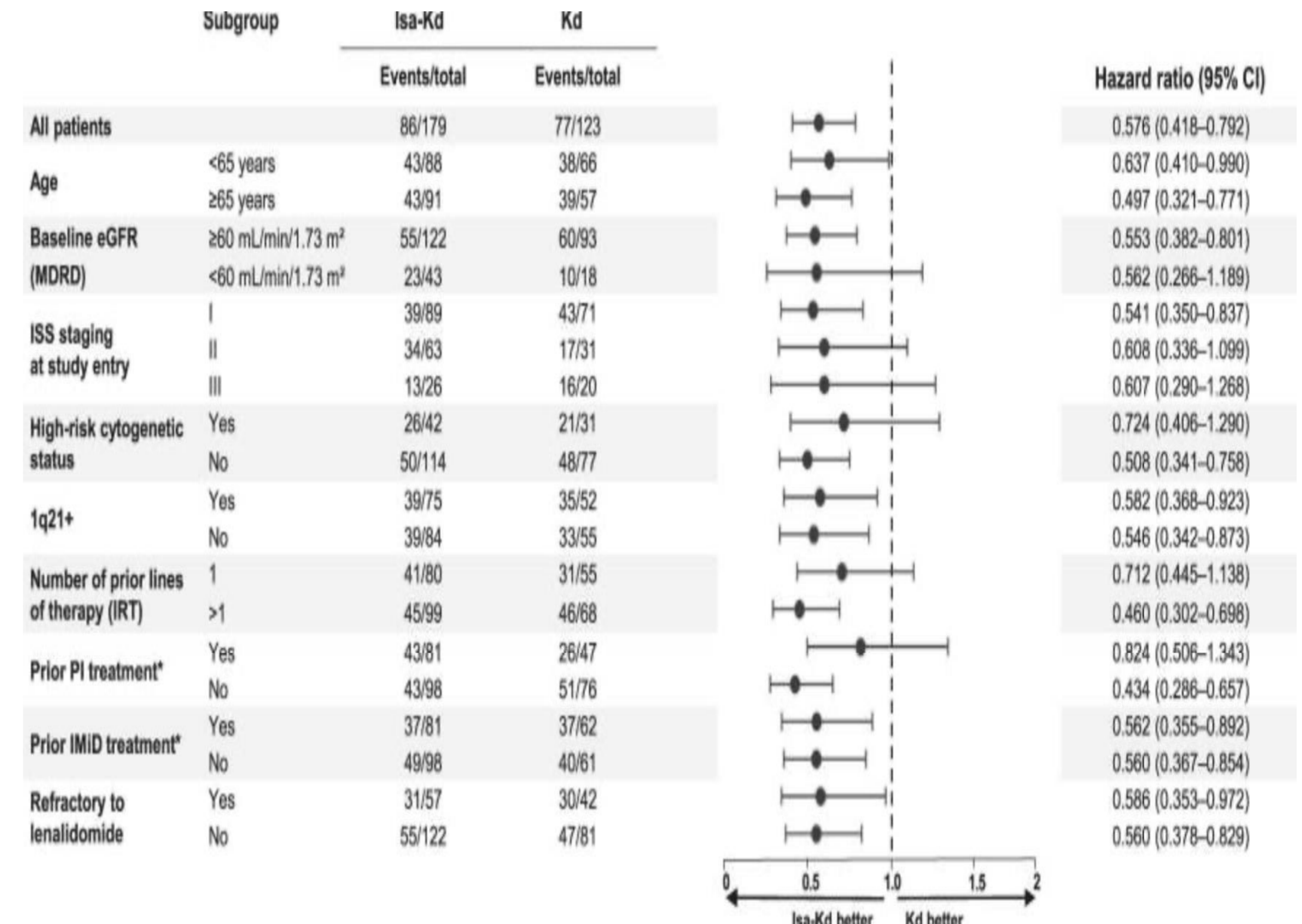
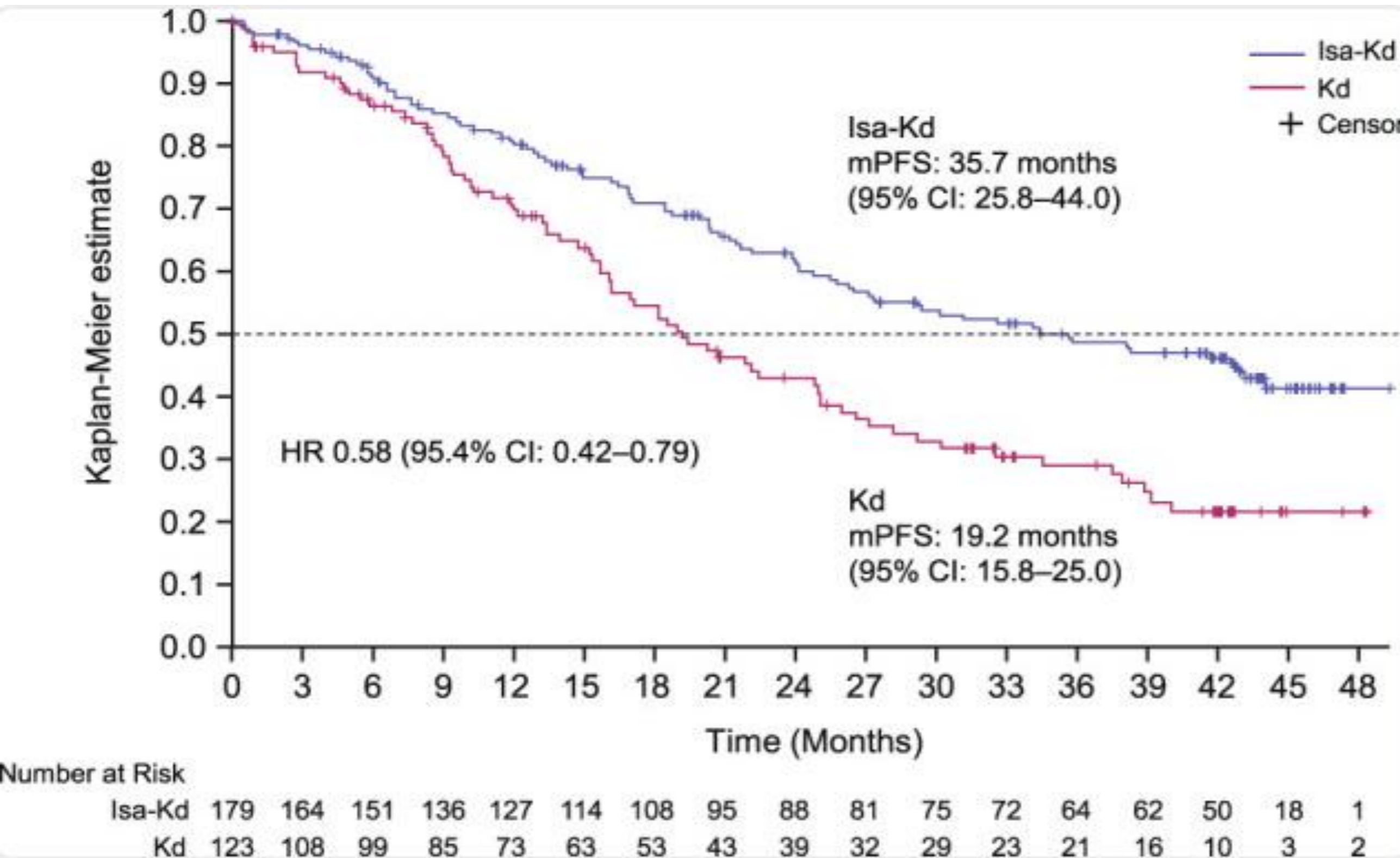
Nel gruppo CAR-T di consolidamento gli outcomes sono stati migliori (\geq VGPR, 86% vs. 66%; PFS mediana non raggiunta vs. 10 mesi)

Evitare altre terapie anti-BCMA → no regimi a base belantamab

Valutazione status verso anti-CD38:

- Se esposto → ISA-KD
- Se refrattario → SVD o KD56

Studio IKEMA



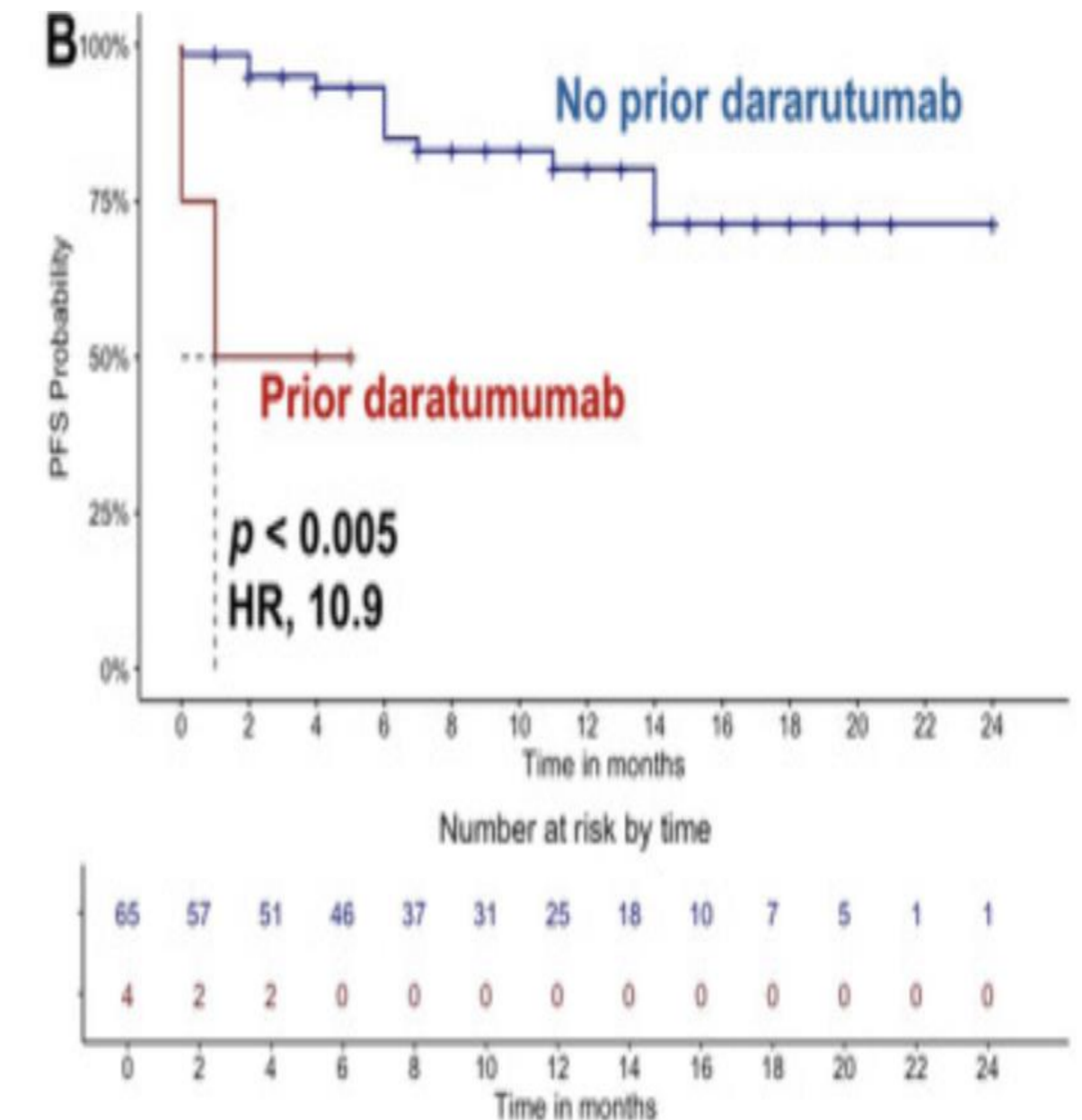
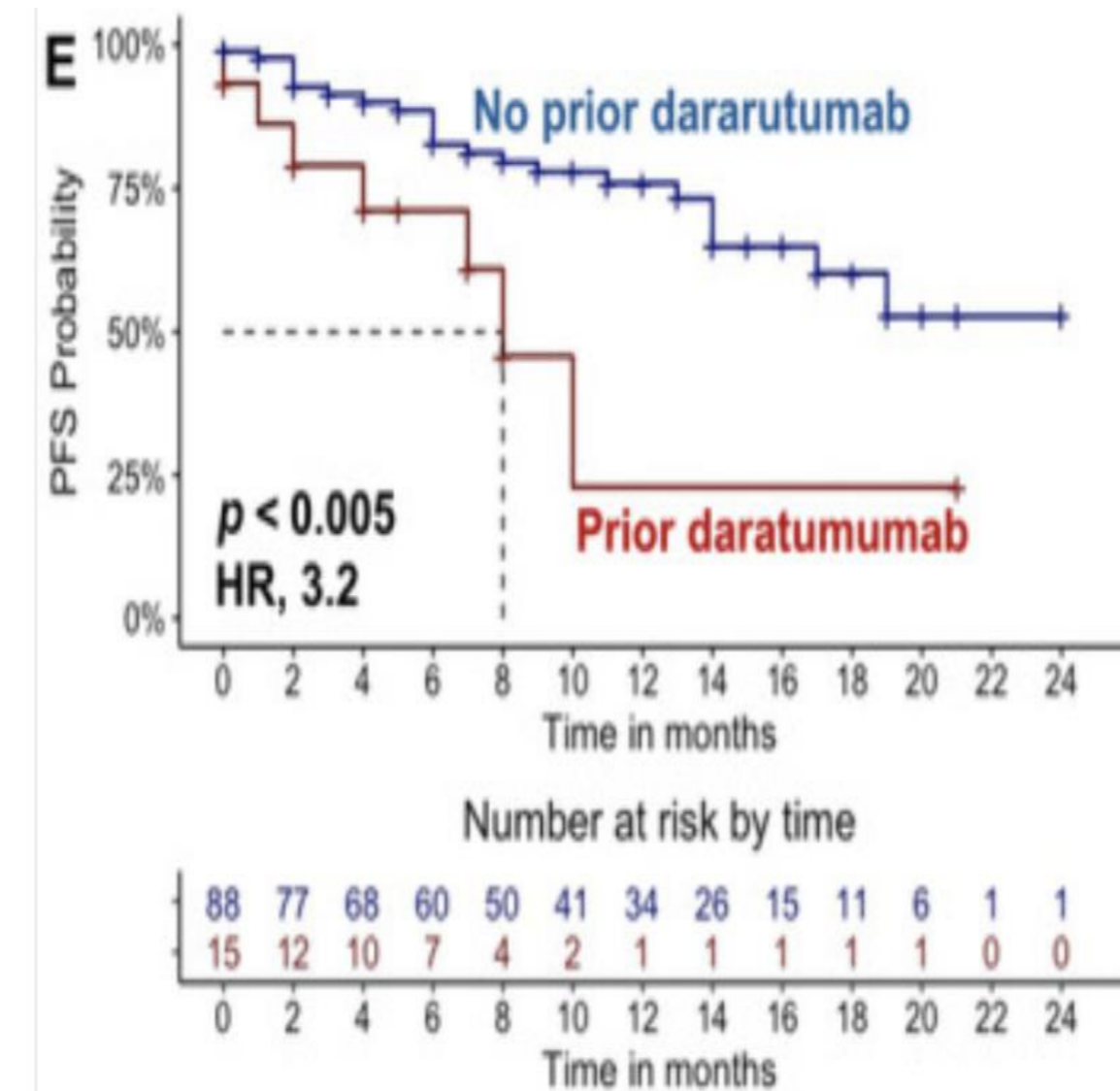
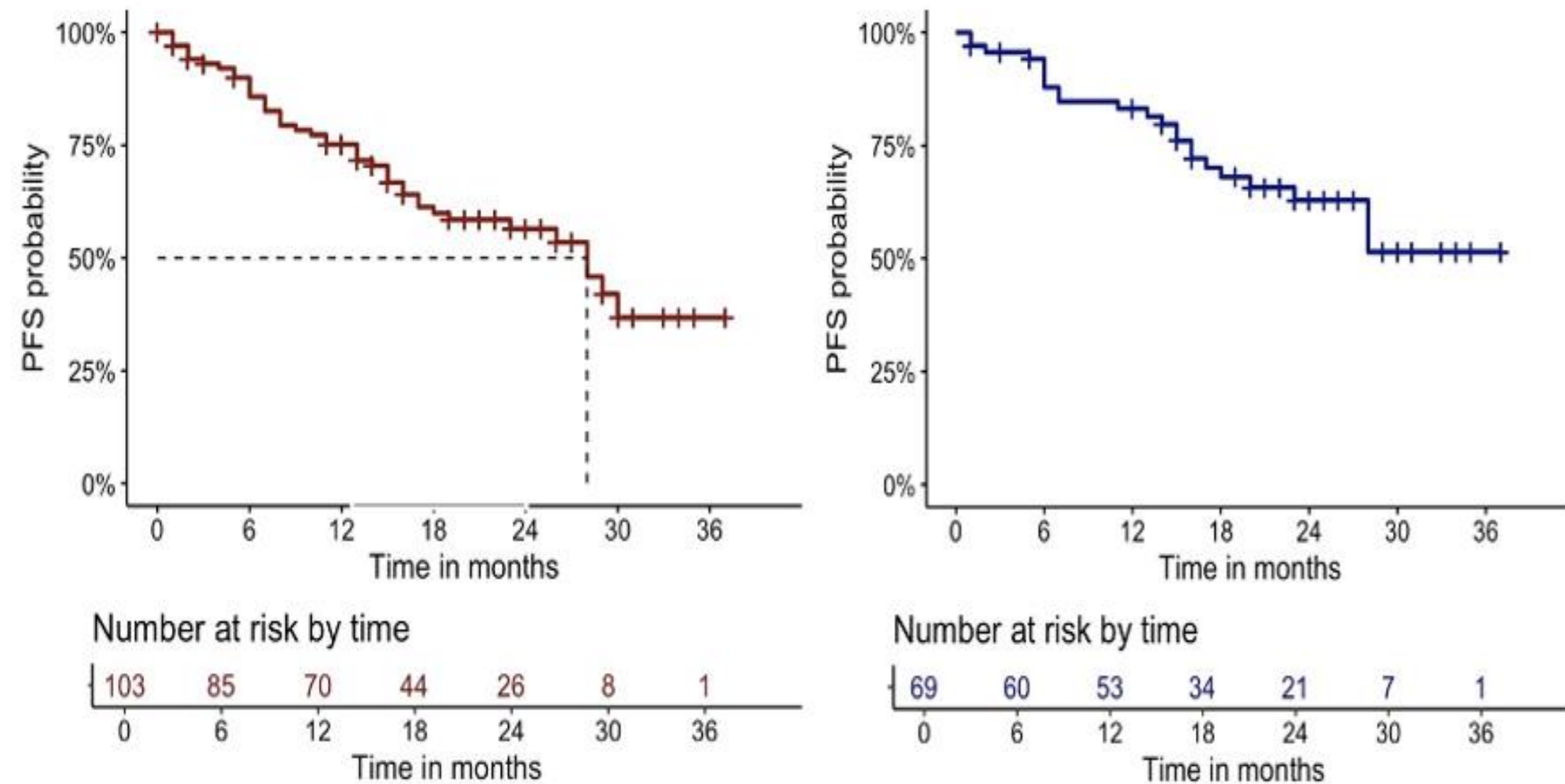
Scarsa rappresentazione pazienti refrattari a lenalidomide (32%)

No pazienti anti-CD38 esposti/refrattari

Real-life per colmare il gap dei trials clinici

► Eur J Haematol. 2024 Oct 6;114(1):105–114. doi: [10.1111/ejh.14314](https://doi.org/10.1111/ejh.14314)

Clinical Efficacy of Isatuximab Plus Carfilzomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma Patients

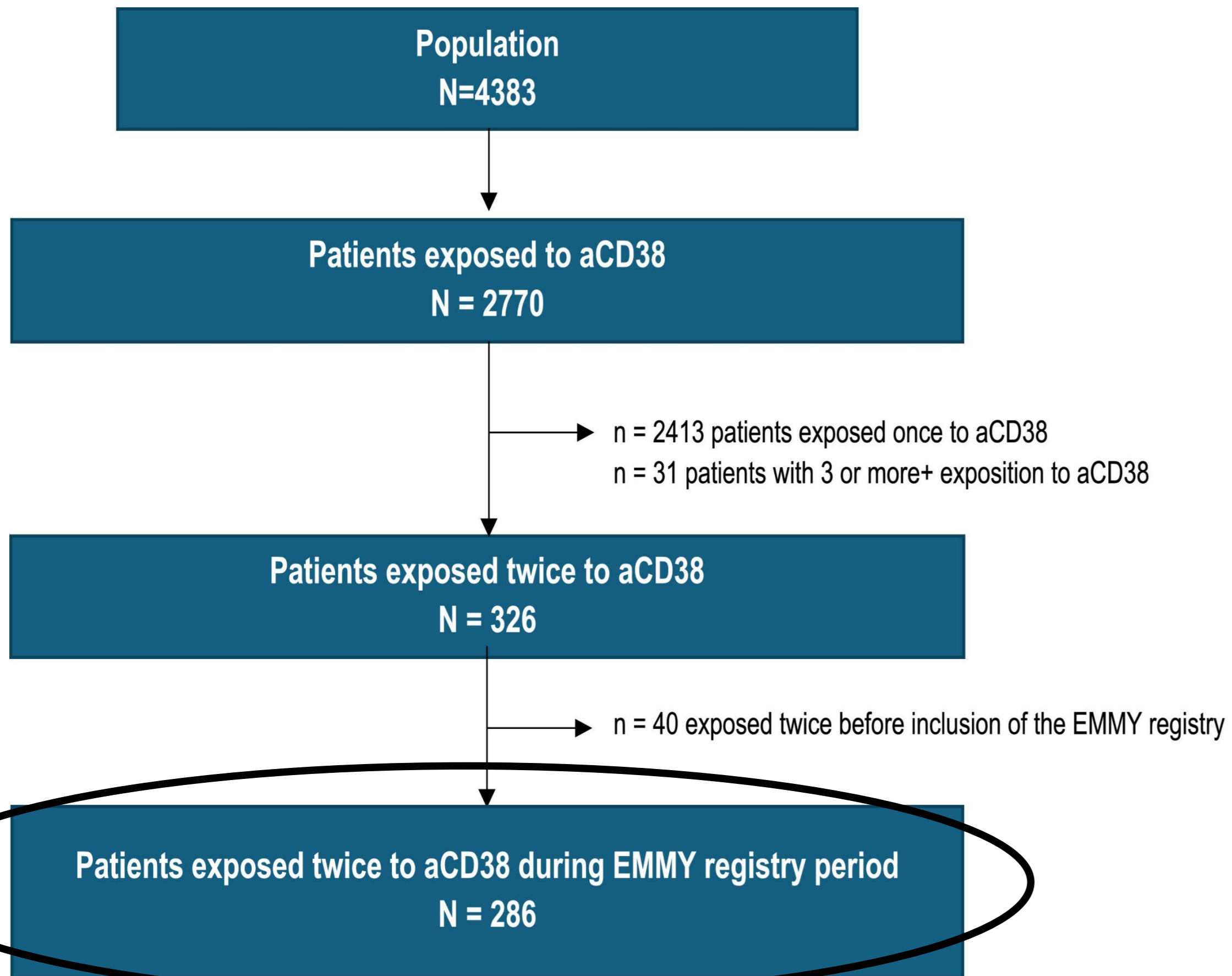


Mediana linee precedenti 1 (1-3)

Lenalidomide esposti/refrattari 19%-71%

Ritrattamento con anti-CD38

Studio EMMY



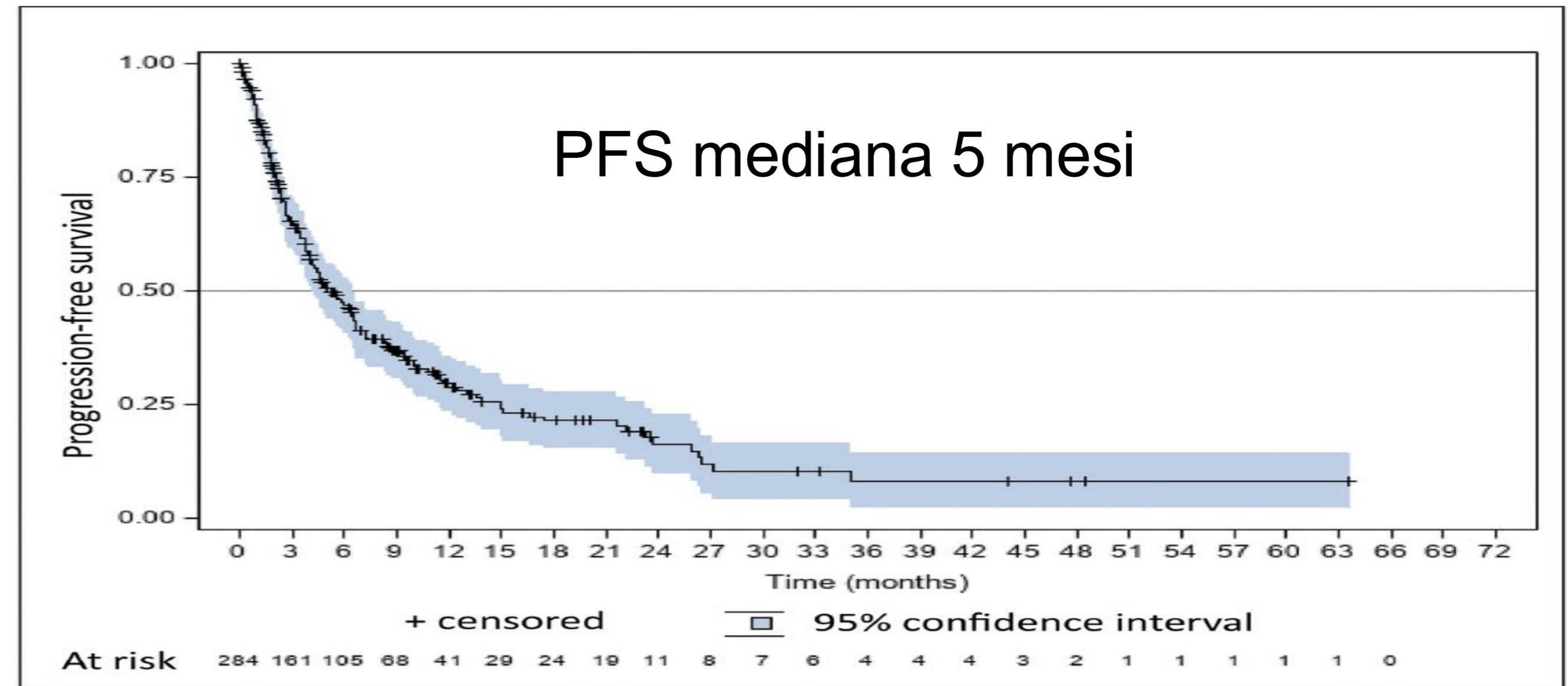
Exposure to aCD38	Yes	286 (100.0)
aCD38	Daratumumab	267 (93.4)
	Isatuximab	19 (6.6)
Refractory to aCD38	Yes	209 (73.1)
	No	76 (26.6)

Ritrattamento con anti-CD38

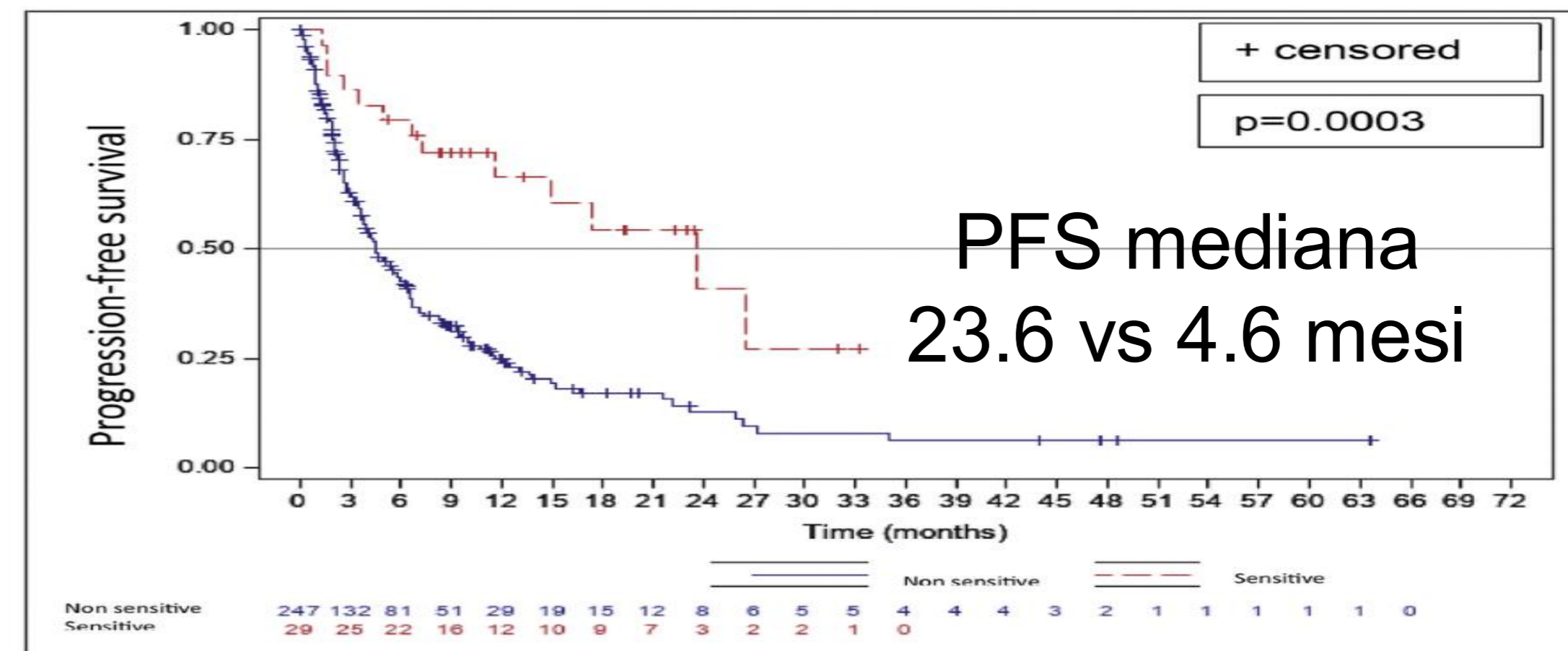
Refrattarietà < 90 giorni

Non refrattarietà e no sensibilità: tra 90 giorni e 11 mesi

Sensibilità > 12 mesi



A

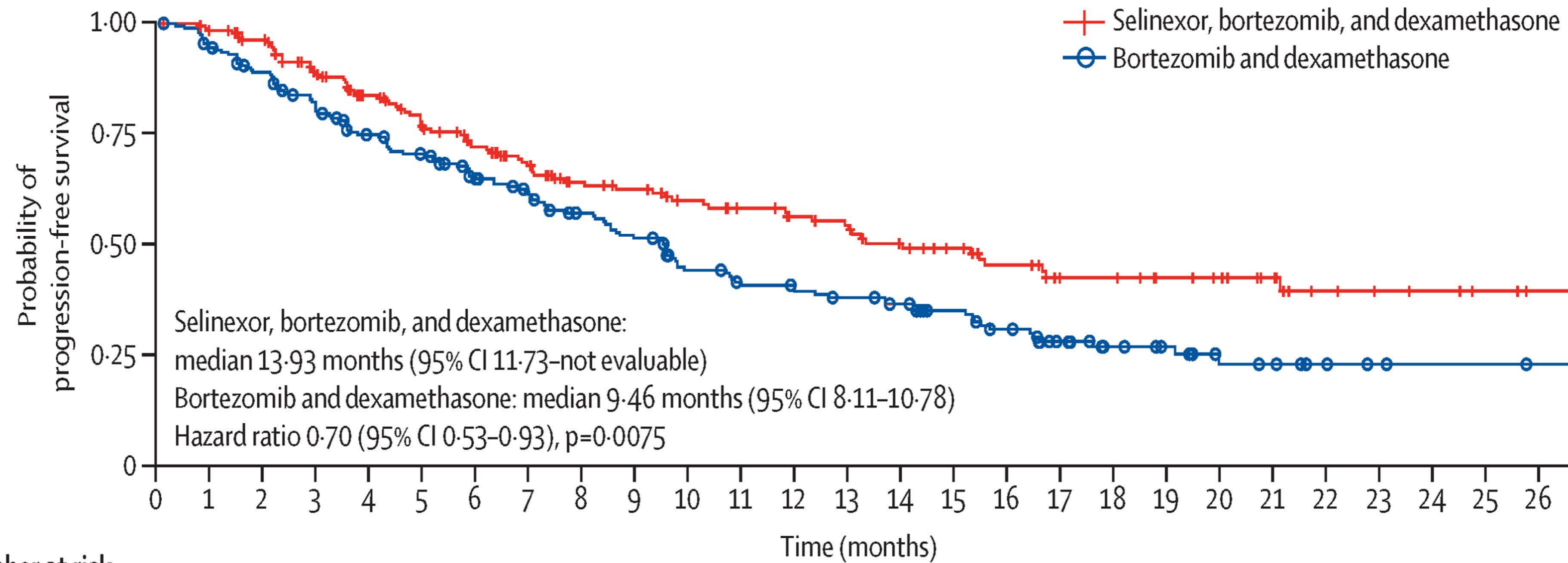


Ritrattamento con anti-CD38

Complessivamente pochi dati disponibili, provenienti da studi perlopiù osservazionali

Ritrattare con anti-CD 38 come holding therapy permette di controllare la malattia per un periodo anche breve, sufficiente per avere accesso a cilta-cel

Studio Boston

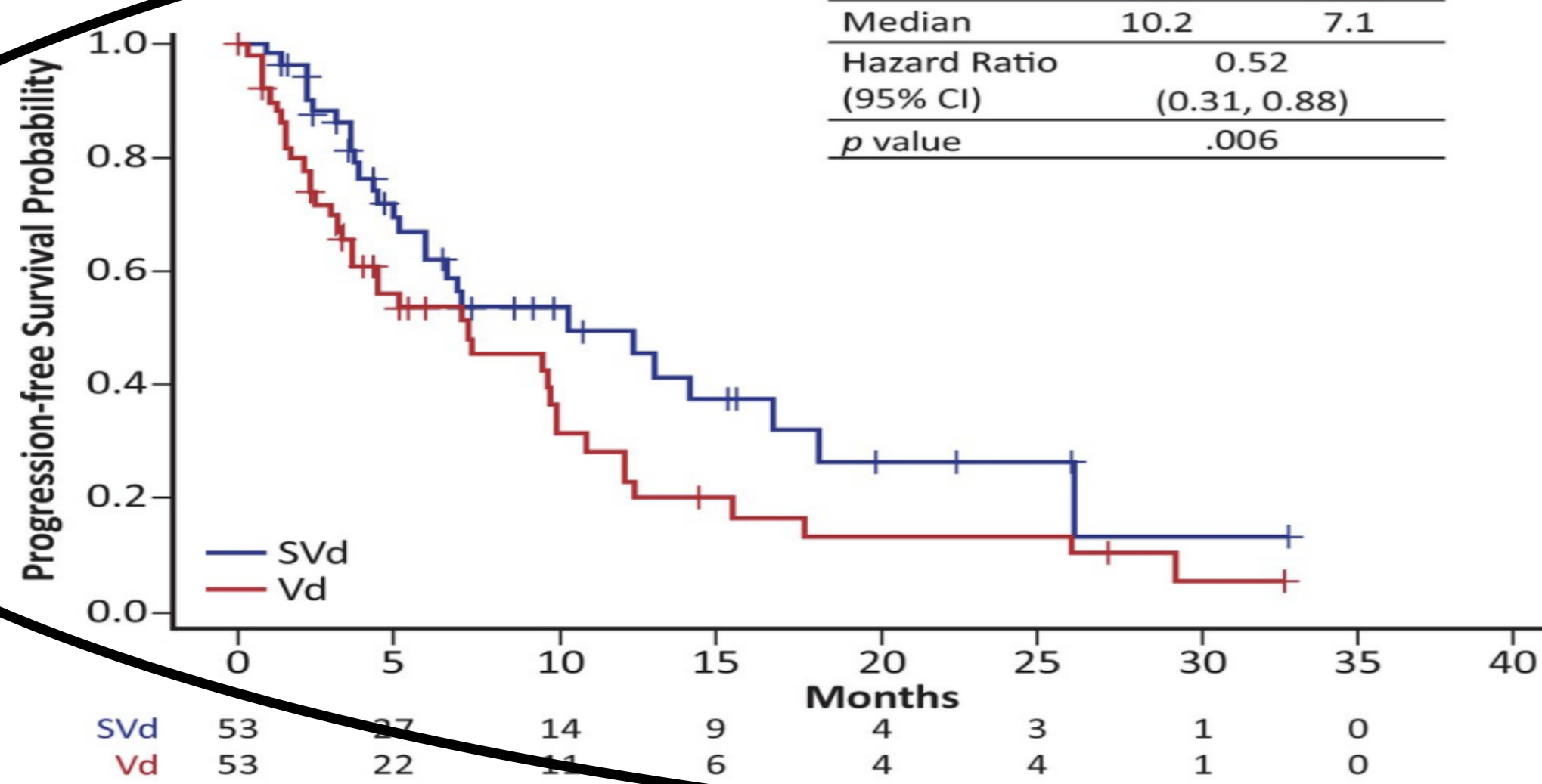


	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Number at risk	195	187	175	152	135	117	106	89	79	76	69	64	57	51	45	41	35	27	26	22	19	14	9	7	6	4	2
(number censored)	(0)	(5)	(12)	(21)	(31)	(37)	(42)	(50)	(57)	(59)	(63)	(66)	(71)	(73)	(76)	(80)	(83)	(89)	(90)	(94)	(97)	(102)	(106)	(108)	(109)	(111)	(113)
Bortezomib and dexamethasone	207	187	175	152	138	127	111	100	90	81	66	59	56	53	49	42	35	26	20	16	10	8	5	4	3	3	2
	(0)	(8)	(10)	(15)	(20)	(22)	(29)	(32)	(37)	(37)	(41)	(43)	(44)	(45)	(47)	(52)	(55)	(60)	(65)	(69)	(73)	(75)	(78)	(79)	(80)	(80)	(81)

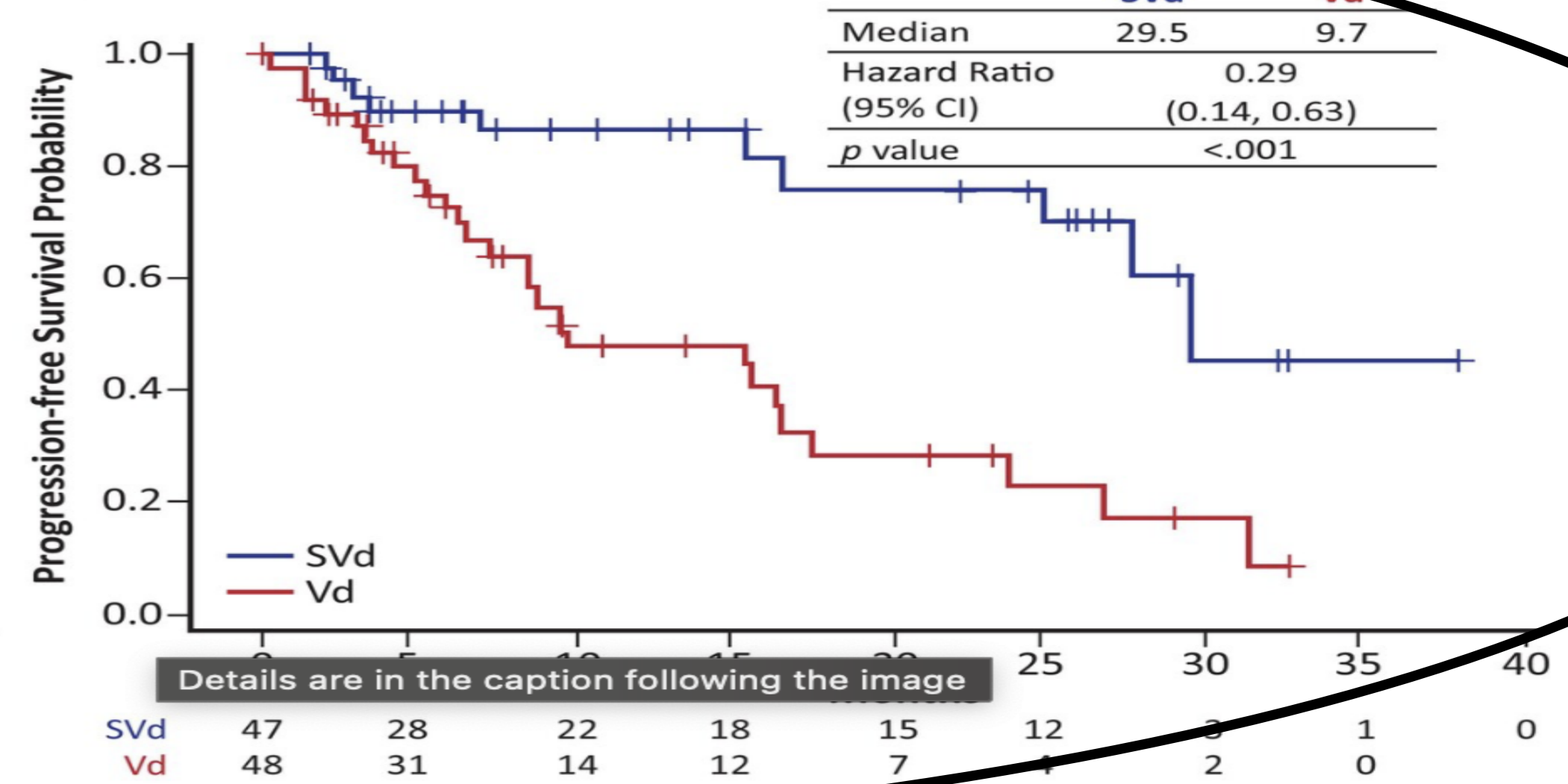
PFS mediana 13.93 mesi

La rivoluzione terapeutica nel linfoma e nel mieloma

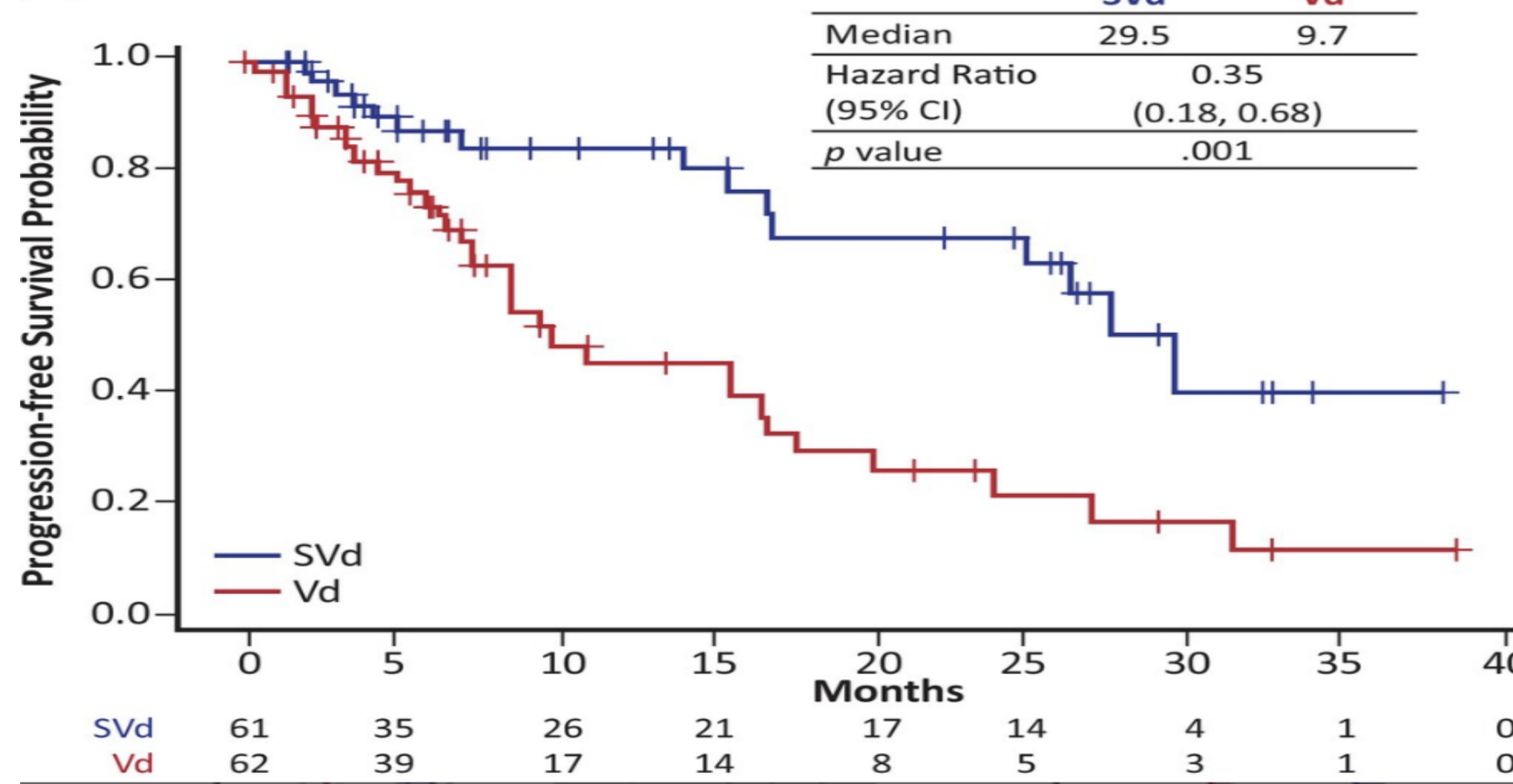
(A) Lenalidomide-refractory



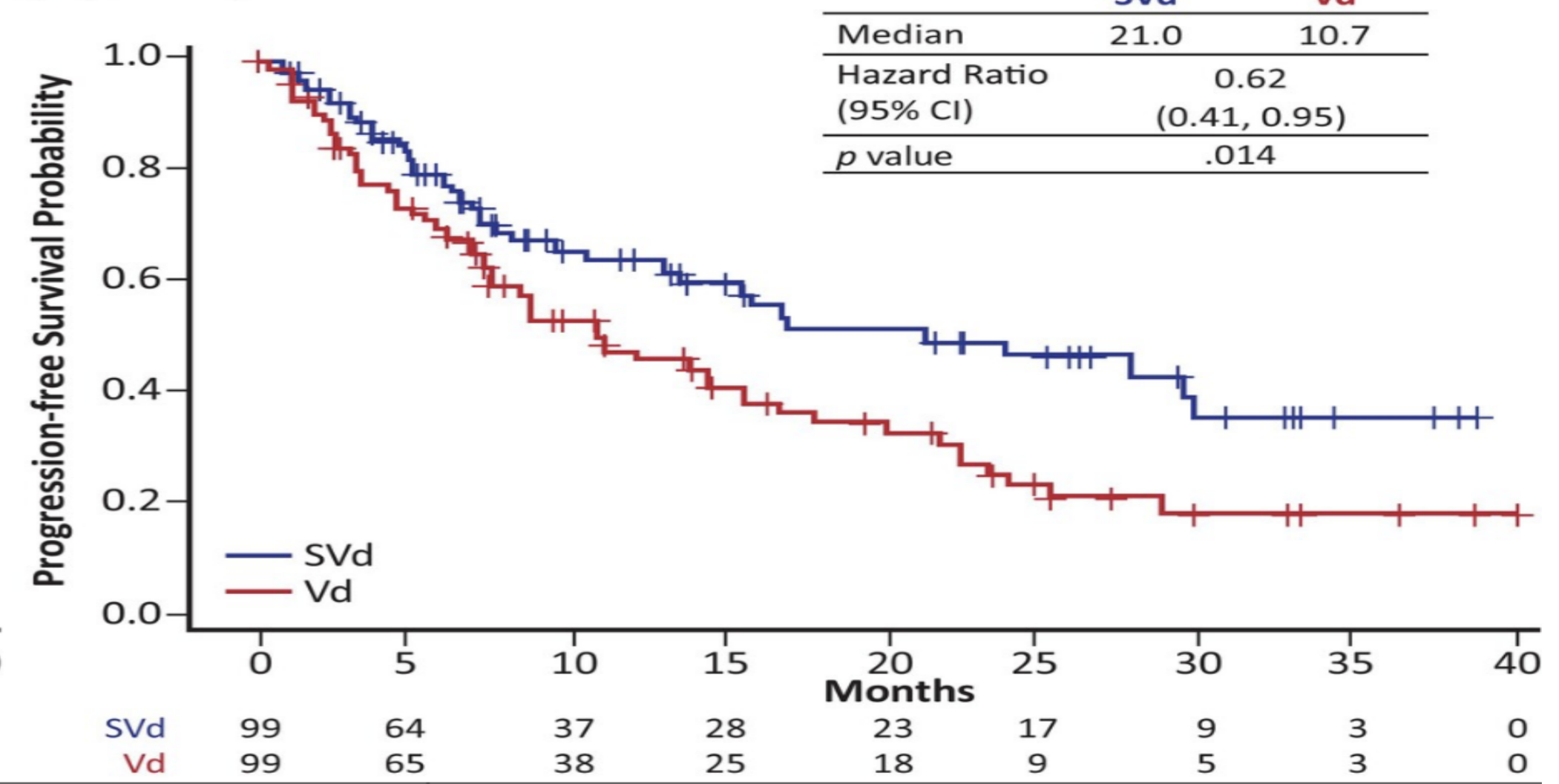
(B) PI-naïve



(C) Bortezomib-naïve



(D) One prior LOT

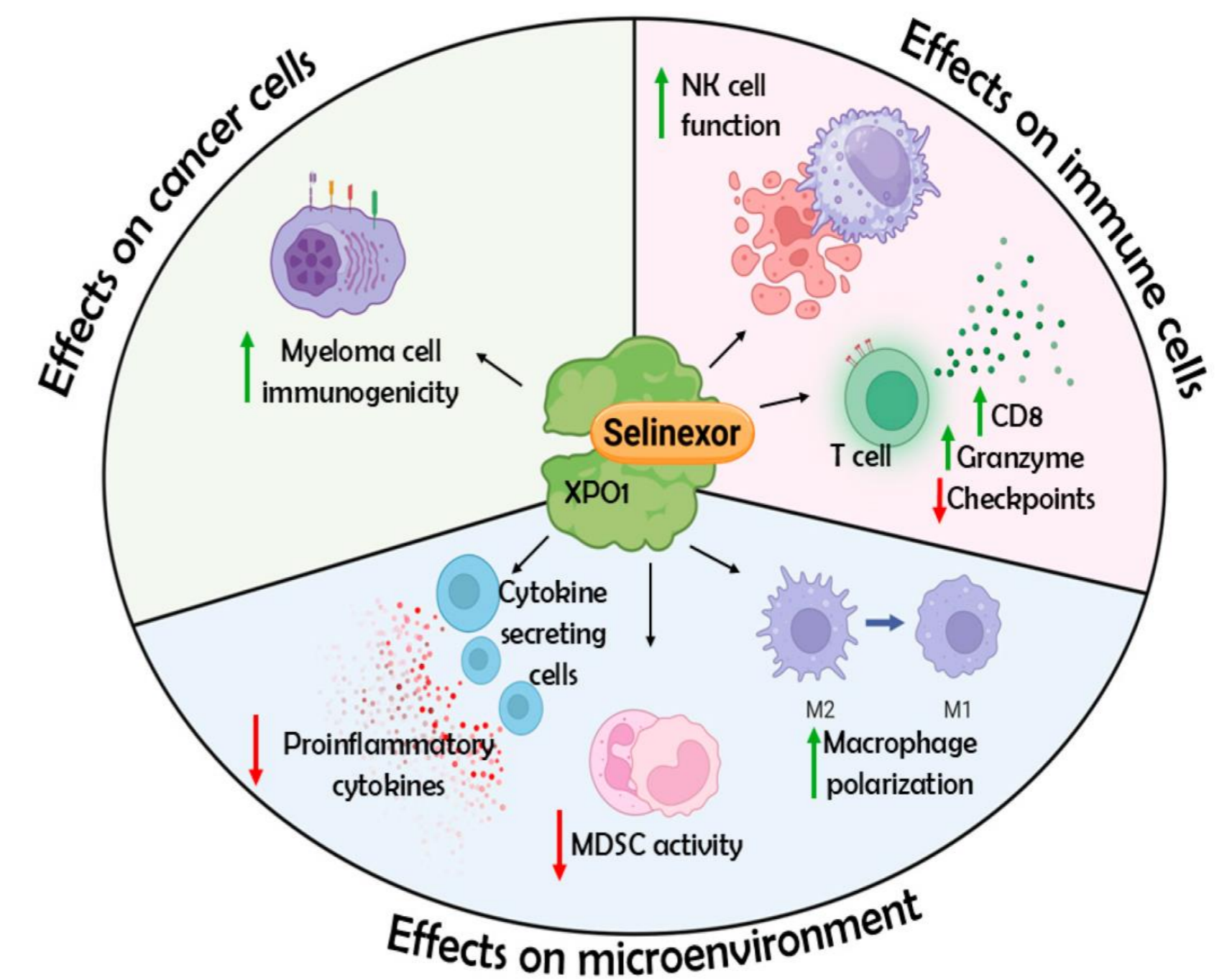


Selinexor ed immunoterapia

Focusing on Selinexor for Holding and Bridging Prior to CAR-T in Relapsed/Refractory Multiple Myeloma

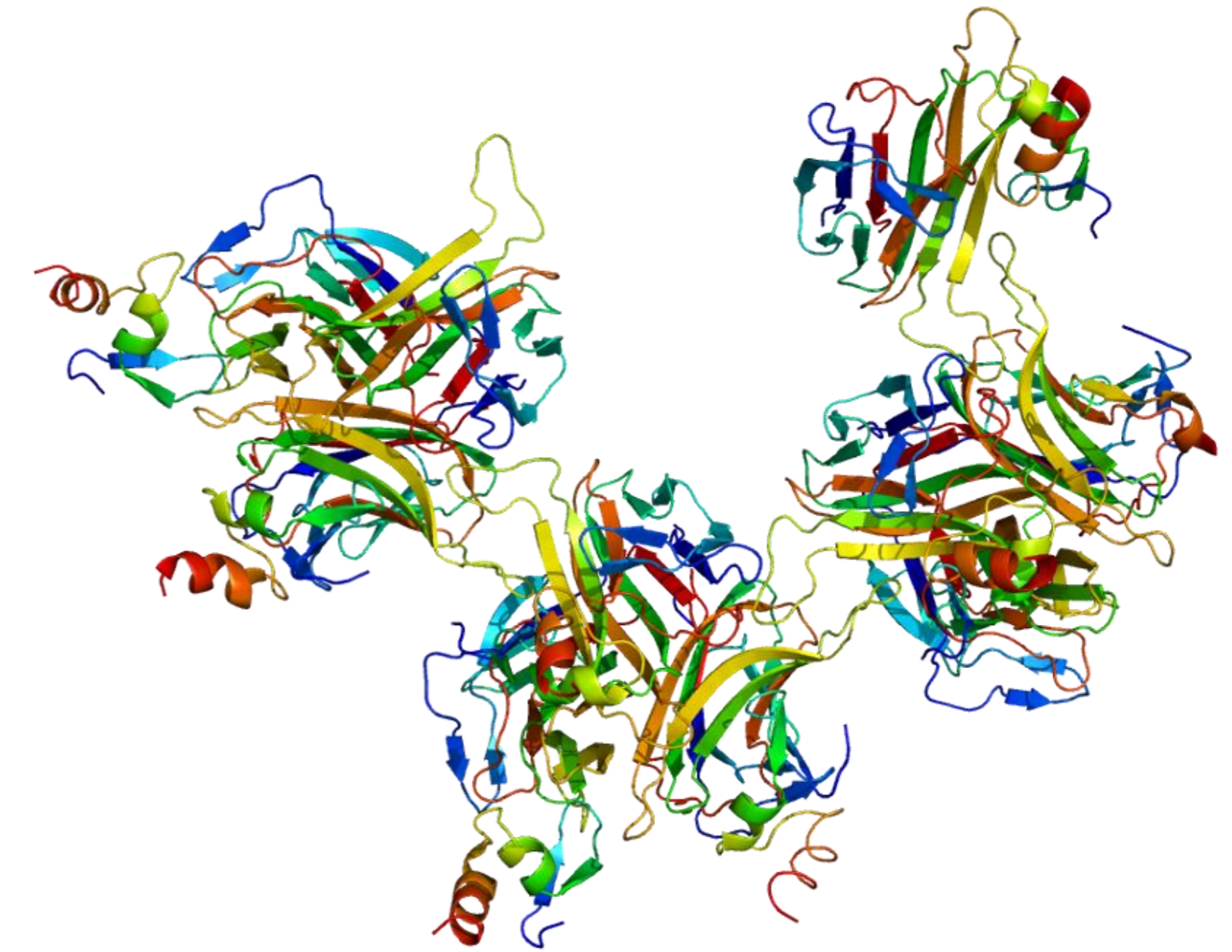
by Jack Khouri ¹ ✉ , Douglas Sborov ² ✉ , Adriana Rossi ³ ✉ , Thomas Martin ⁴ ✉ ,
Trinayan Kashyap ⁵ ✉, Tomer Mark ⁵ ✉ and Muhamed Baljevic ^{6,*} ✉

- Effetto immunomodulante e di promozione dell'espressione di BCMA
- Selinexor non solo opzione terapeutica per MMRR ma anche potenziale strumento per gestire il paziente pre-CAR-T (terapia holding/bridging)



Scenario 3

Paziente non candidato a cilta-cel



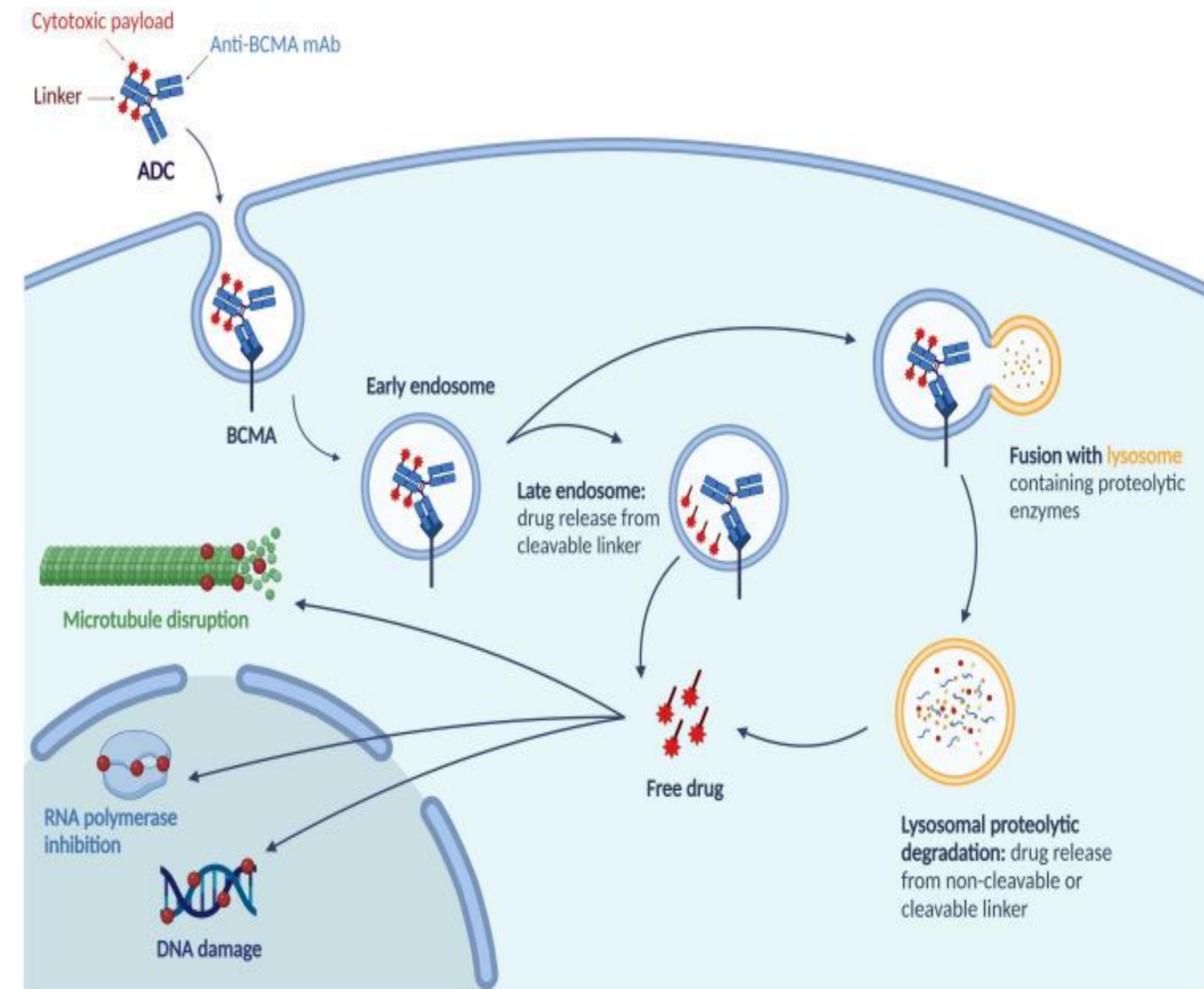
All'assalto del BCMA

Belantamab mafodotin

Anticorpo coniugato al composto citotossico monomethyl auristatina F (MMAF)

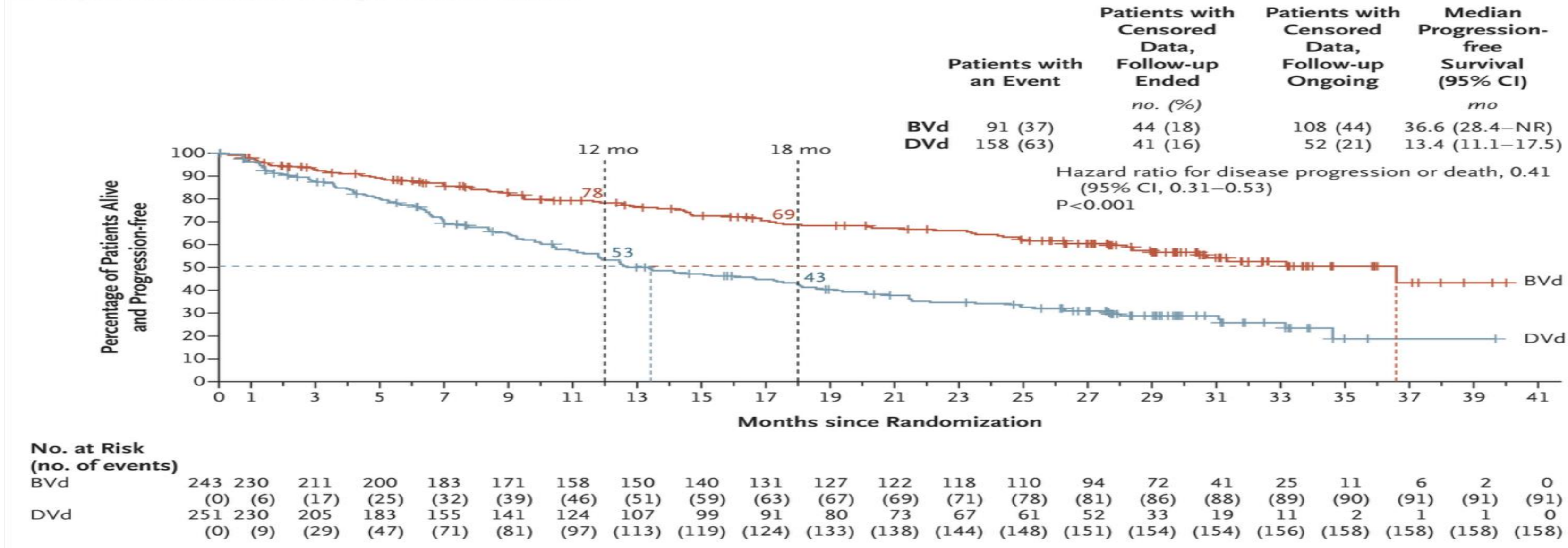
Una volta legato al BCMA sulle cellule MM, l'ADC viene internalizzato attraverso un processo di endocitosi mediata da recettore e trasportato ai lisosomi

Nell'ambiente acido dei lisosomi, viene rilasciato MMAF che si lega alla tubulina, interrompendo la formazione dei microtubuli, con arresto del ciclo cellulare ed innesco dell' apoptosi



Studio DREAMM-7

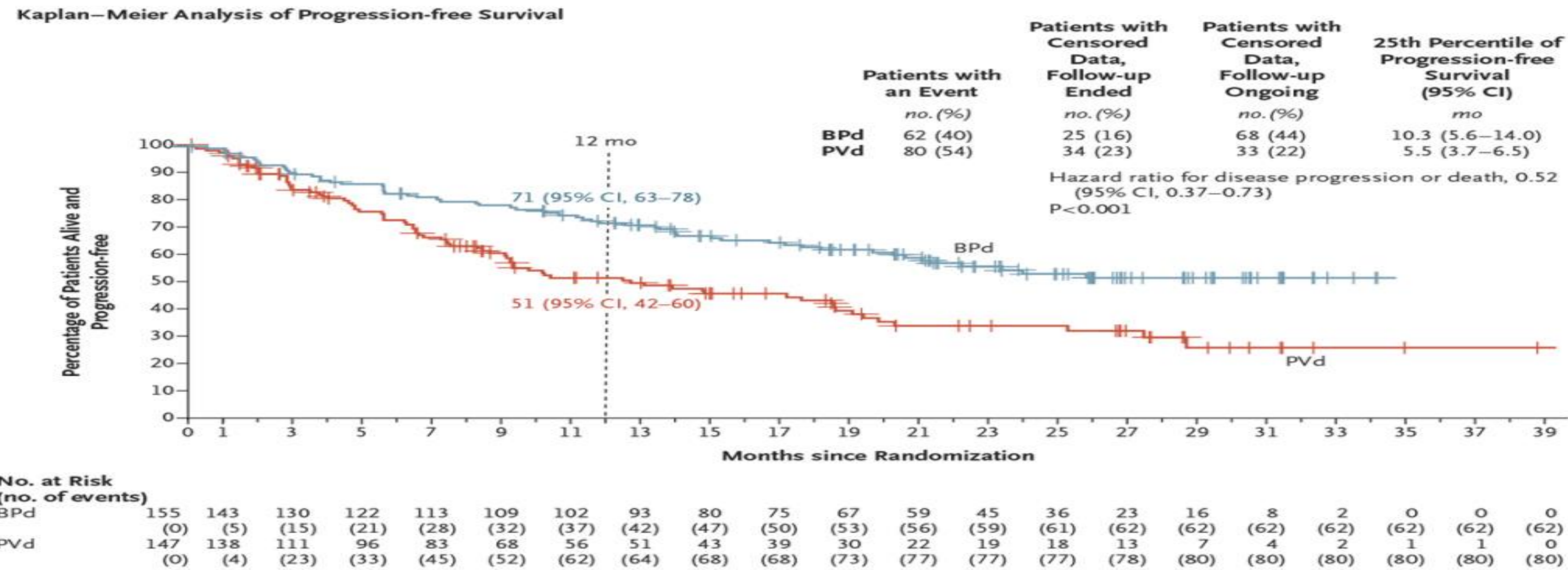
A Kaplan–Meier Analysis of Progression-free Survival



PFS mediana 36.6 mesi

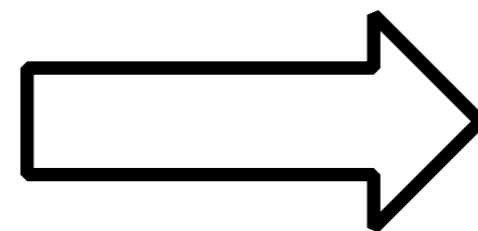
Coorte anti-CD38 naive a causa del braccio di controllo

Studio DREAMM-8



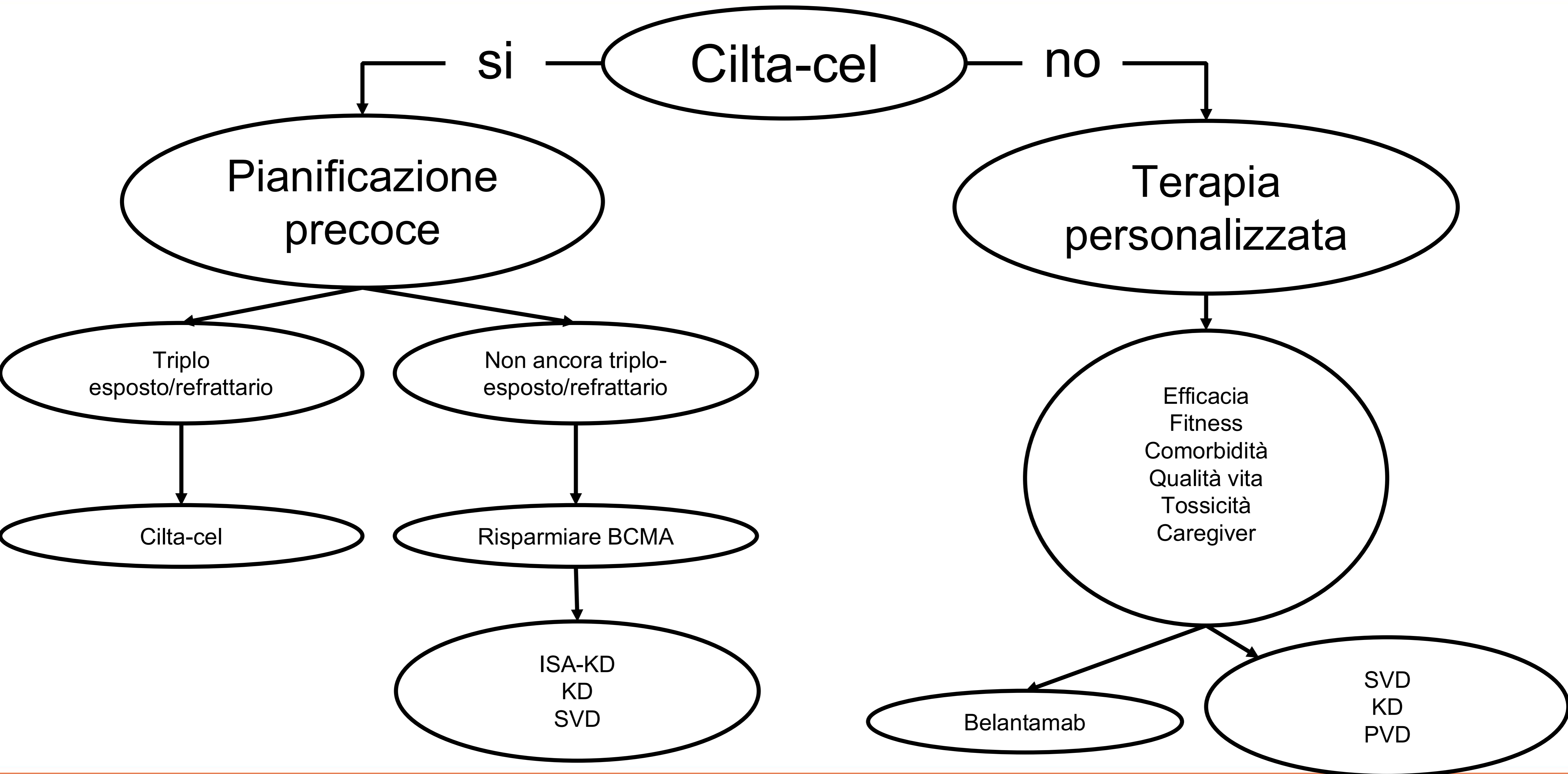
PFS mediana 32.6 mesi

25% and 29% dei pazienti con progresso trattamento anti-CD 38



Più rappresentativa dei pz provenienti da dara-RD

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Take home messages

La seconda linea è un momento cardine in cui si decide il futuro del paziente (attrition rate)

Oggi tutti i pazienti sono virtualmente refrattari a lenalidomide e la maggior parte esposti/refrattari ad anti-CD38

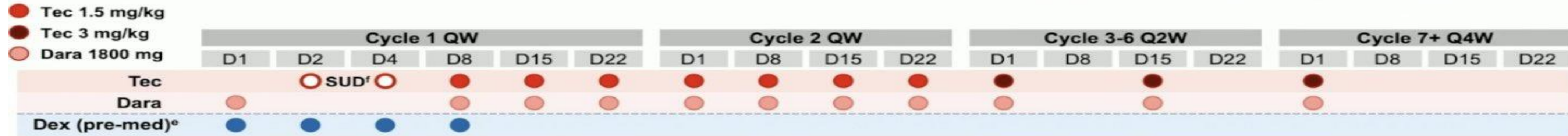
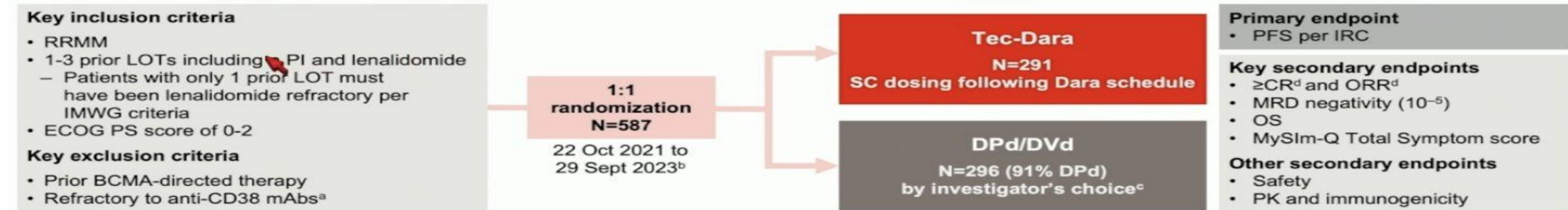
Valutare eleggibilità a CAR-T è essenziale nella scelta terapeutica

Se CAR-T → richiesta pianificazione anticipata con preservazione del target BCMA

Se non CAR-T → scelta terapeutica personalizzata

«Come cambierà la seconda linea di trattamento»

MajesTEC-3: Phase 3 Study Design



SC dosing aligned with Dara schedule, with monthly dosing after 6 cycles; steroid sparing after Cycle 1 Day 8

^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.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.



Caratteristiche PZs

Characteristic	Tec-Dara (n = 291)	DPd/DVd (n = 296)
Age		
Median, years (range)	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)

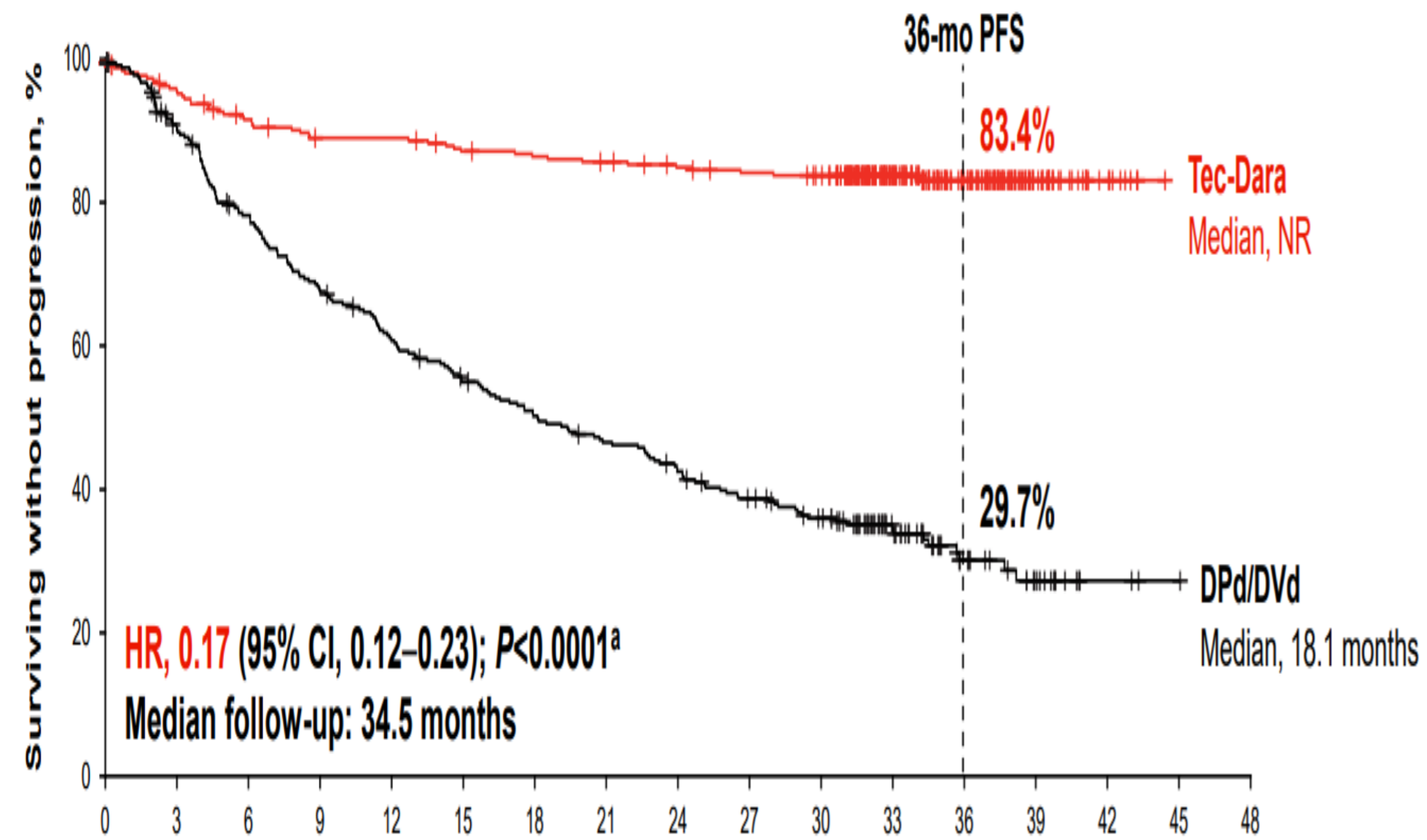
Characteristic	Tec-Dara (n = 291)	DPd/DVd (n = 296)
Baseline ECOG PS score, n (%)		
0	167 (57.4)	160 (54.1)
1	108 (37.1)	127 (42.9)
2	16 (5.5)	9 (3.0)
ISS stage, n/N (%)		
I	182 (62.5)	185 (62.5)
II	85 (29.2)	88 (29.7)
III	24 (8.2)	23 (7.8)
BMPCs ≥60% ^b n/N (%)	28/286 (9.8)	24/293 (8.2)
Presence of soft-tissue plasmacytomas, n (%)	41 (14.1)	41 (13.8)
Extramedullary plasmacytomas	14 (4.8)	17 (5.7)
High-risk cytogenetics, ^c n/N (%)	104/285 (36.5)	104/294 (35.4)

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

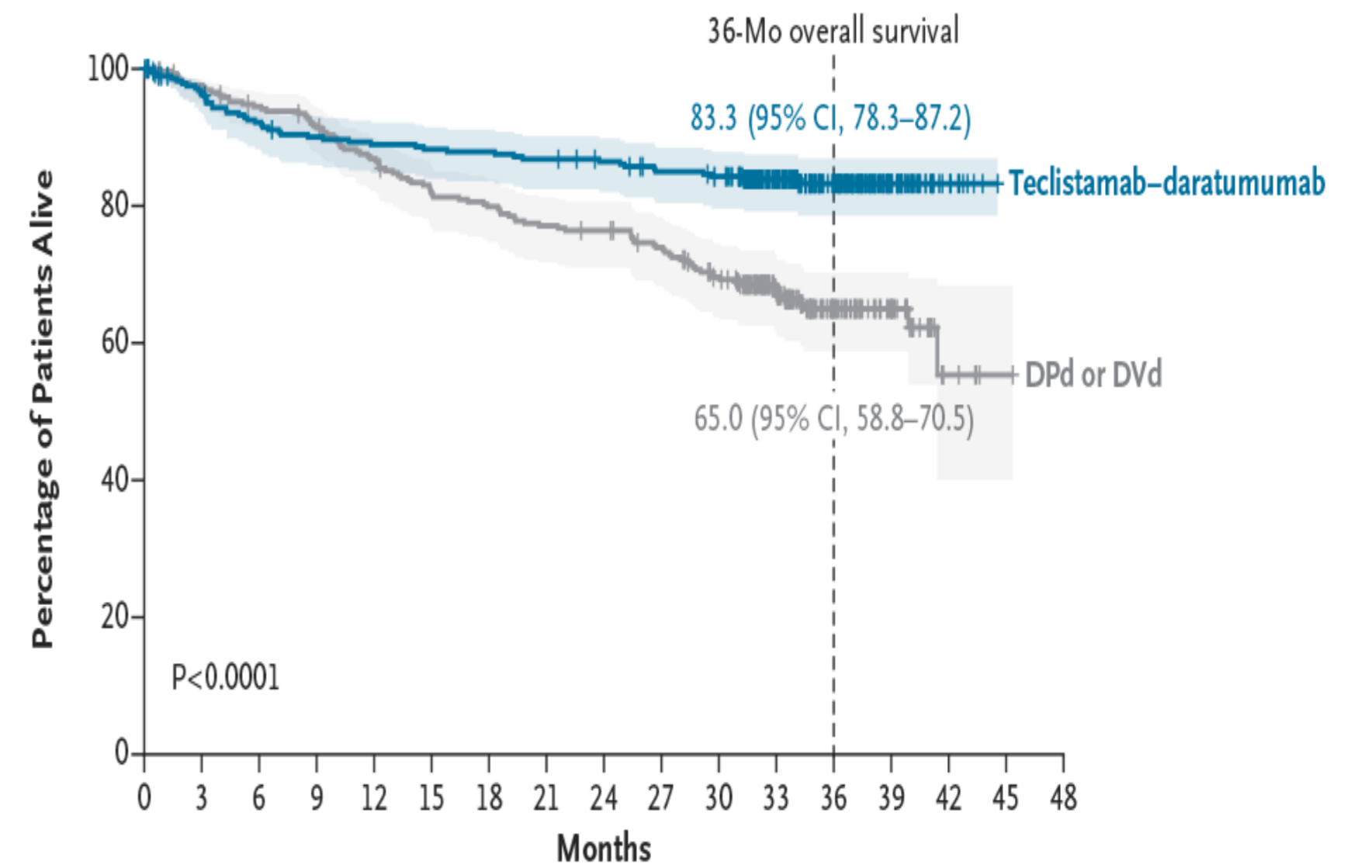
- Median prior LOT was 2
- The number of patients with prior anti-CD38 exposure was low
- >80% of patients were lenalidomide-refractory

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	15 (5.2)	16 (5.4)
Refractory status, n (%)		
To last line of prior therapy	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)

PFS&OS



No. at risk	Months																
	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
Tec-Dara	291	262	249	240	240	233	230	227	222	218	214	142	89	34	9	0	0
DPd/DVd	296	254	218	188	167	149	135	124	112	99	87	52	26	14	3	1	0



No. at Risk	Months																
	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
Teclistamab–daratumumab	291	272	259	252	249	247	246	243	239	232	227	160	100	40	9	0	0
DPd or DVd	296	285	274	265	250	235	229	221	218	208	190	127	66	33	5	1	0

Pfizer's ELREXFIO Significantly Improves Progression-Free Survival for Double-Class Exposed Patients with Relapsed or Refractory Multiple Myeloma

Wednesday, April 29, 2026 - 06:45am | 12 min read

- *Primary endpoint met at the interim analysis in MagnetisMM-5 trial demonstrating a statistically significant and clinically meaningful improvement in progression-free survival*
- *Safety was consistent with the known ELREXFIO profile, with no new safety signals identified*
- *Trial remains ongoing to assess overall survival, a key secondary endpoint*
- *Interim efficacy results further strengthen confidence in development strategy for ELREXFIO as monotherapy and in combination, across multiple lines of therapy*

NEW YORK--(BUSINESS WIRE)-- [Pfizer Inc.](#) (NYSE: PFE) today announced positive topline results from the Phase 3 MagnetisMM-5 study evaluating ELREXFIO® (elranatamab) as monotherapy in adults with relapsed or refractory multiple myeloma (RRMM) who received at least one prior line of treatment. The study demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of progression-free survival (PFS), as assessed by blinded independent central review (BICR), versus standard-of-care daratumumab plus pomalidomide and dexamethasone (DPd). The safety and tolerability of ELREXFIO was consistent with its known safety profile.

La seconda linea verso il futuro

Ruolo sempre più crescente
dell'immunoterapia



Cilta-cel

Bispecifici in associazione
Bispecifici in monoterapia



Quali criteri useremo per scegliere?
Quale terapia a chi?



La rivoluzione terapeutica nel linfoma e nel mieloma



Grazie per l'attenzione!

Napoli, Hotel Royal Continental • 14-15 Maggio 2026