

CONVEGNO INTERREGIONALE SIE

Delegazioni Umbria e Marche

Società Italiana di Ematologia

NOVITÀ TERAPEUTICHE NEI LINFOMI NON-HODGKIN E MIELOMA MULTIPLO: FOCUS SU ANTICORPI BISPECIFICI E CAR-T

Assisi, Sala Conciliazione, Comune di Assisi
4 Novembre 2026

Anticorpi bispecifici anti BCMA: Evidenze cliniche consolidate e loro impatto sulla pratica clinica

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Disclosures of Marino Brunori

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Astrazeneca						Yes	
JJ						Yes	
GSK						Yes	
Sanofi						Yes	
Menarini						Yes	

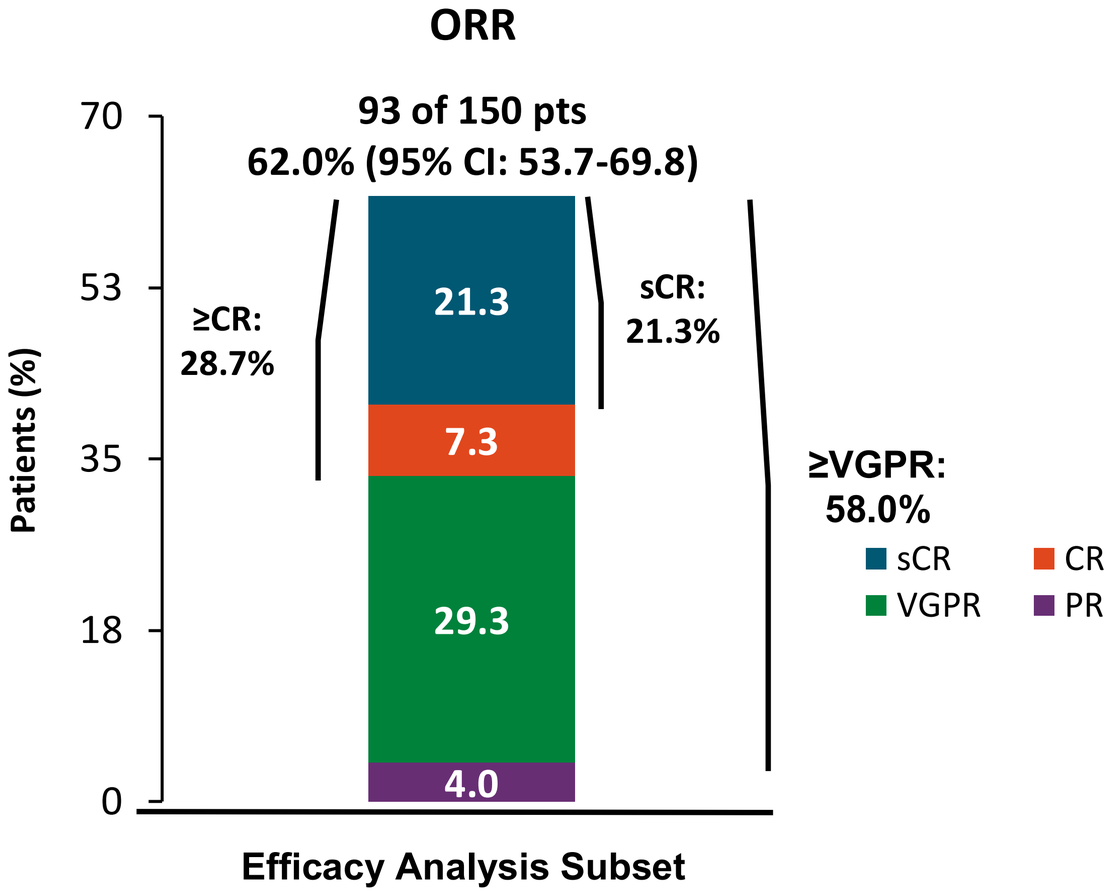






Prima evidenza clinica consolidata: Bispecici anti BCMA efficaci in linee avanzate?

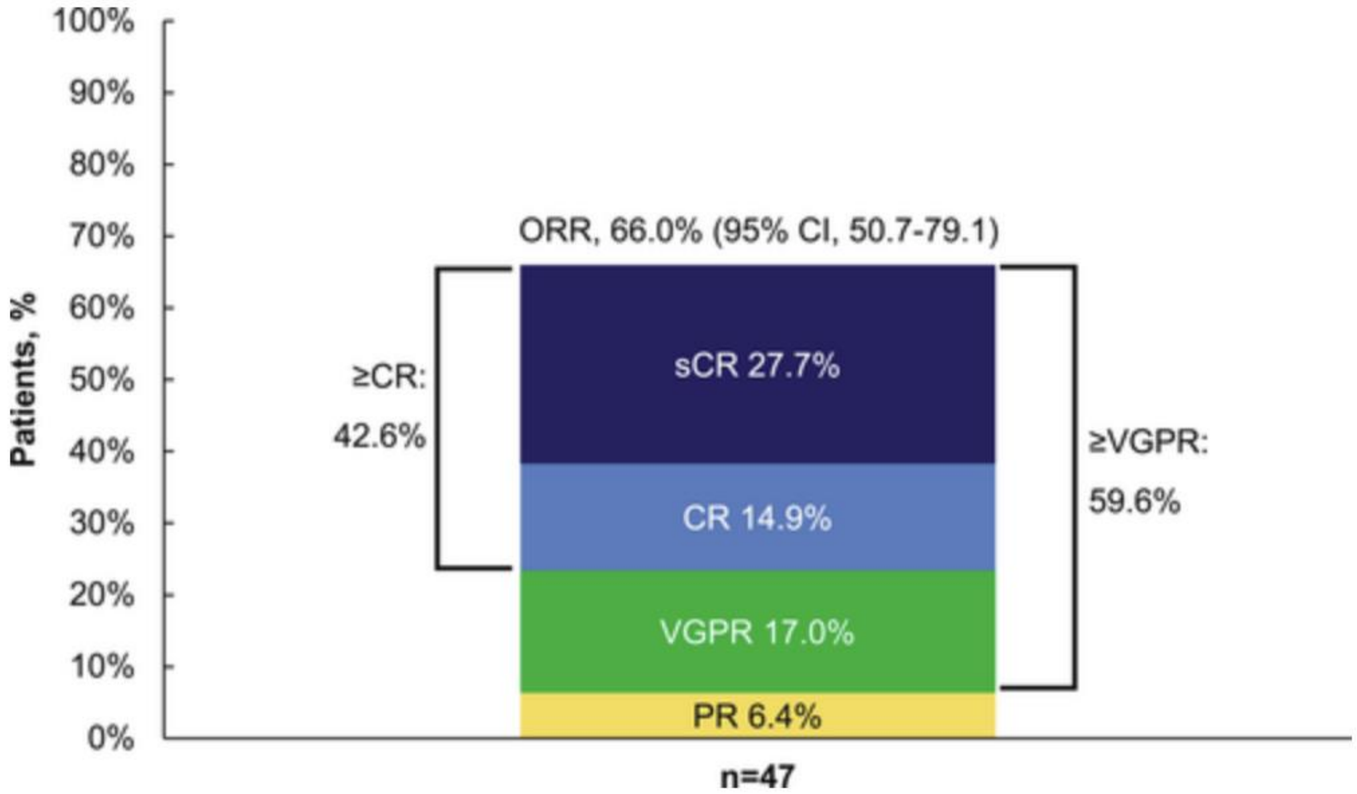
MajesTEC-1: > o = 3 linee precedenti e triplo esposti



Event	All Patients (N = 165)
MRD negativity, n (%, 95% CI)	(n = 150)
▪ At 10^{-5}	37 (24.7; 18.0-32.4)
▪ At 10^{-6}	25 (16.7; 11.1-23.6)
MRD negativity with ≥CR, %	41.9
Median TTR, mo (range)	1.2 (0.2-5.5)
Median DoR, mo	Not yet reached
EFS rates, % (95% CI)	
▪ 6-Mos	92.5 (80.6-97.2)
▪ 9-Mos	85.9 (70.0-93.7)
PFS rates, % (95% CI)	
▪ 6-Mos	64.4 (56.0–71.7)
▪ 9-Mos	58.5 (48.8–67.0)
Median OS	Not yet reached

Median follow-up: 7.8 mos (range: 0.5+ to 18)

Magnetism-3: > o = 3 linee precedenti e triplo esposti



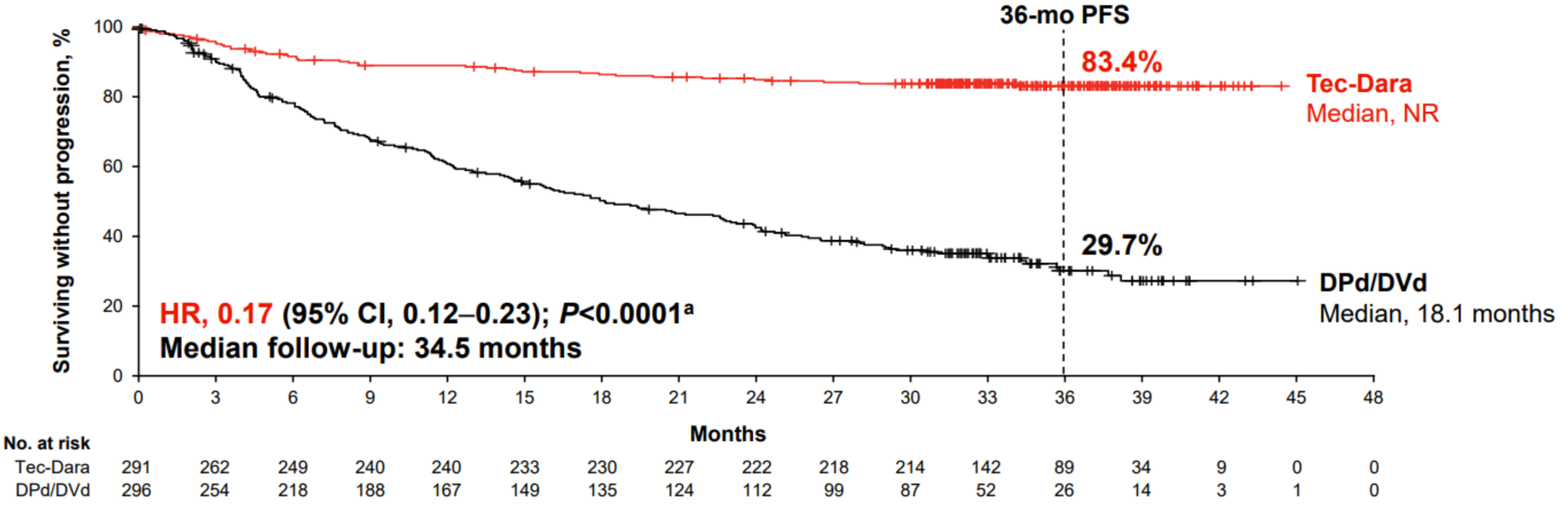
Prior lines of therapy, median (range)	5 (2–22)
Prior stem cell transplant, n (%)	87 (70.7)
Exposure status, n (%)	
Triple-class[g]	123 (100)
Penta-drug[h]	87 (70.7)
Refractory status, n (%)	
Triple-class[g]	119 (96.7)
Penta-drug[h]	52 (42.3)
Refractory to last line of therapy, n (%)	118 (95.9)

Prima evidenza clinica consolidata:
Bispecici anti BCMA efficaci in linee avanzate



Seconda evidenza clinica consolidata:
Bi-specifico anti BCMA efficace in seconda linea?

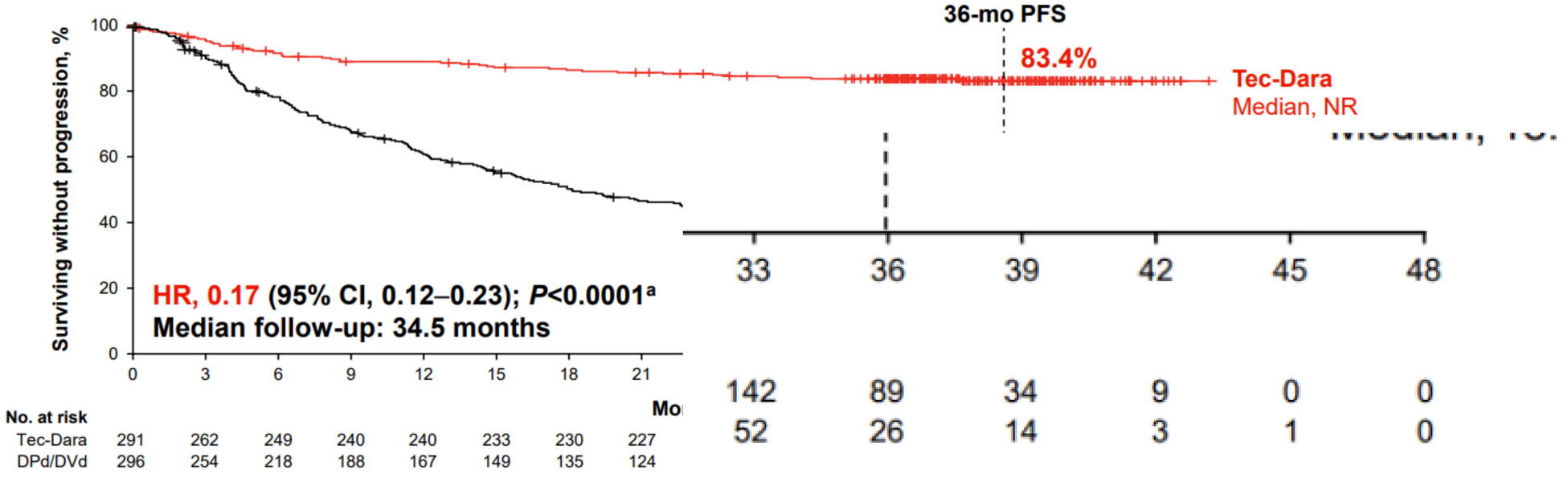
MajesTEC-3: PFS (Primary Endpoint)



Tec-Dara significantly improved PFS, with a plateauing curve after ~6 months and >90% of patients progression-free at 6 months sustaining such a benefit at 3 years

[a]The *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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MajesTEC-3: PFS (Primary Endpoint)



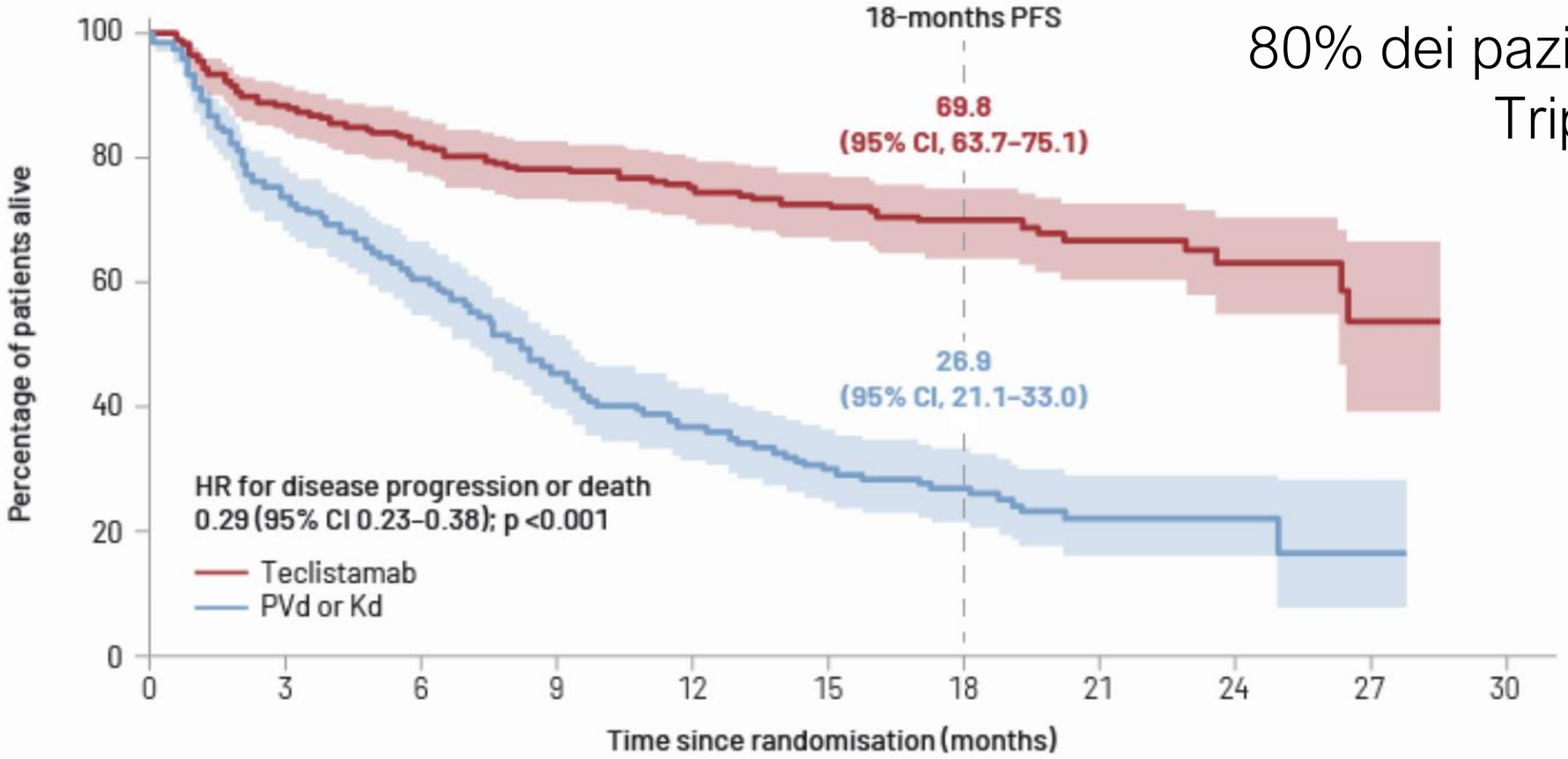
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TECVAYLI - MajesTEC-3/MMY3001 study summary

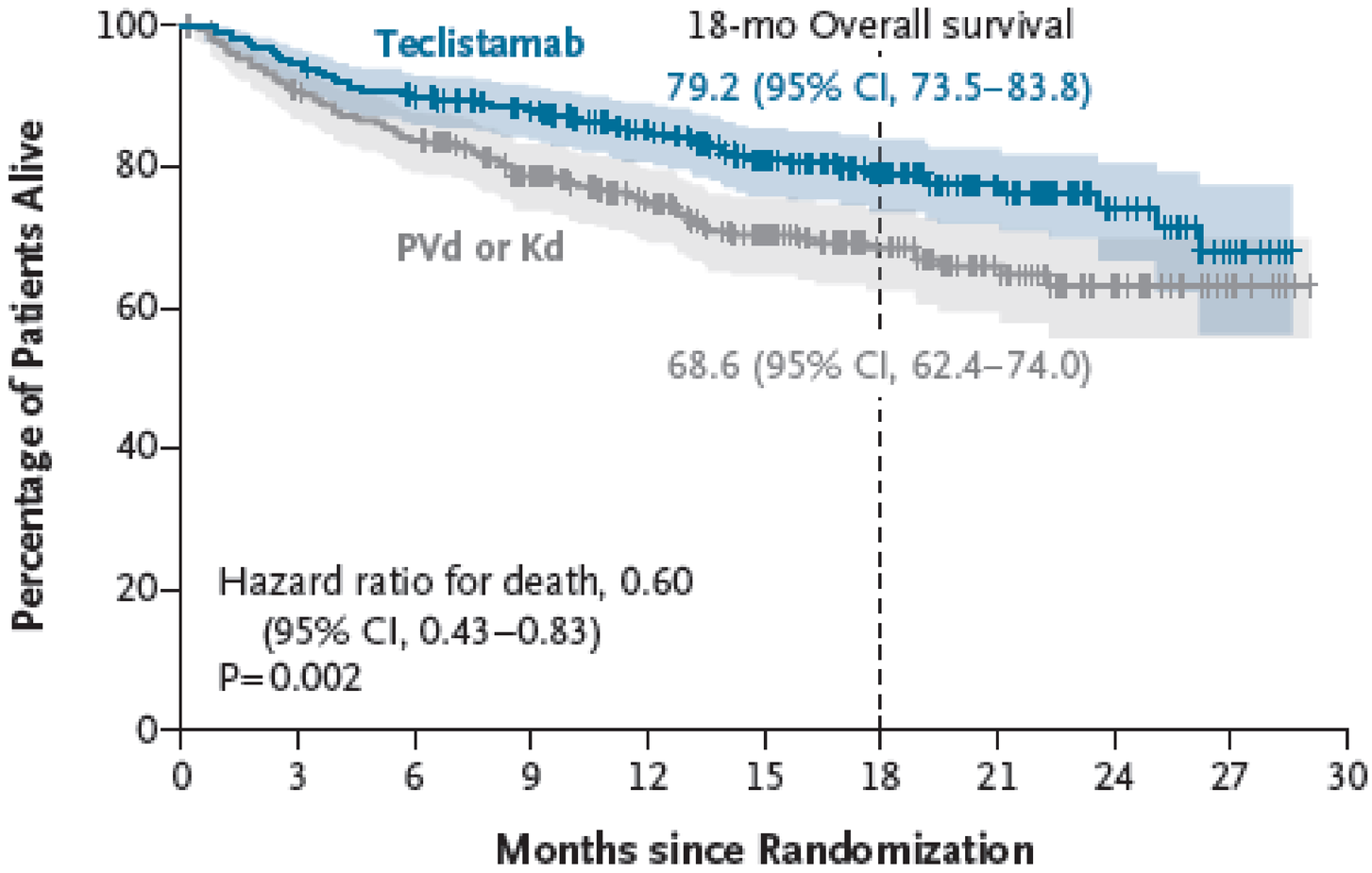
Median prior lines of therapy (range)	2 (1-3)
1 prior line of therapy, %	38
Prior exposure to lenalidomide, %	100
Prior exposure to a proteasome inhibitor, %	99.8
Refractory to lenalidomide, %	84
Prior autologous stem cell transplantation, %	74

MajesTEC-9



80% dei pazienti refrattari a DARA
Triple Ref 34%

MajesTEC-9


Teclistamab
18-mo Overall survival
79.2 (95% CI, 73.5–83.8)
PVd or Kd
68.6 (95% CI, 62.4–74.0)
Hazard ratio for death, 0.60
(95% CI, 0.43–0.83)
P=0.002
Percentage of Patients Alive
100
80
60
40
20
0
0
3
6
9
12
15
18
21
24
27
30
Months since Randomization

MajesTEC-9

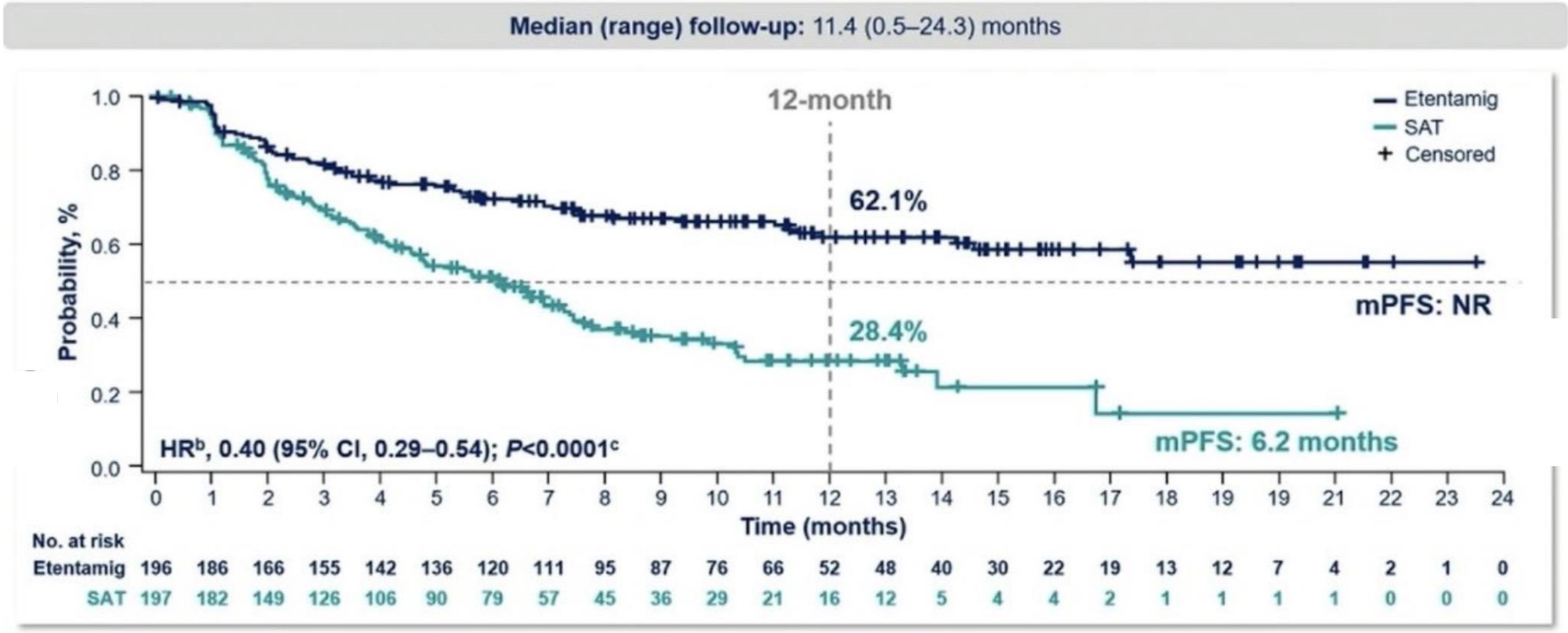
Characteristic	Tec (n=296)	PVd/Kd (n=297)
Prior LOTs, n (%)		
Median (range), n	**2 (1–3)**	**2 (1–3)**
1 prior LOT	64 (21.6)	64 (21.5)
2 prior LOTs	131 (44.3)	137 (46.1)
3 prior LOTs	101 (34.1)	96 (32.3)
Prior transplantation, n (%)	145 (49.0)	147 (49.5)
Autologous	145 (49.0)	146 (49.2)
Prior therapy exposure, n (%)		
PI	256 (86.5)	254 (85.5)
IMiD	296 (100)	297 (100)
Anti-CD38	296 (100)	297 (100)



We need dedicated first-relapse studies.

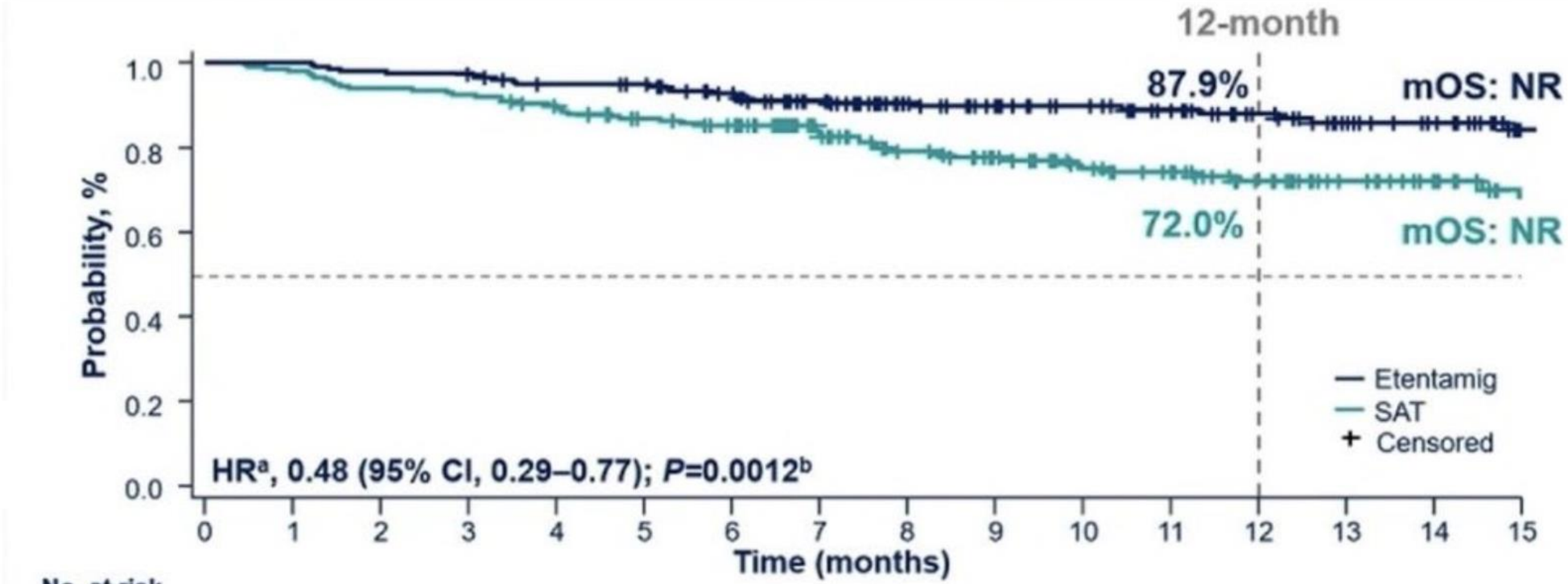
✓ Only ~22% had 1 prior line.

Cervino: Etentamig



Cervino

Median (range) follow-up: 11.4 (0.5–24.3) months



No. at risk																
Etentamig	196	196	192	190	182	179	166	151	130	121	111	97	82	71	64	46
SAT	197	193	185	182	174	162	155	127	111	100	84	77	62	51	42	30

- **NRM:**
  - **5.1%** for Etentamig vs **9.8%** for SAT
- **Infection NRM:**
  - **1.5%** for Etentamig vs **3.1%** for SAT
- **Relapse mortality:**
  - **9.2%** for Etentamig vs **15.0%** for SAT

Cervino

Characteristics	Etentamig (N=196)	SAT (N=197)
Median age, years (range)	69 (38–91)	70 (40–90)
≥65 years	127 (64.8)	141 (71.6)
≥75 years	60 (30.6)	66 (33.5)
Male	98 (50.0)	109 (55.3)
Region		
Europe	79 (40.3)	79 (40.1)
Japan and Asia-Pacific	53 (27.0)	45 (22.8)
North America (US only)	24 (12.2)	33 (16.8)
Other	40 (20.4)	40 (20.3)
Race[a]		
White	121 (61.7)	133 (67.5)
Asian	58 (29.6)	49 (24.9)
Black/African American	13 (6.6)	11 (5.6)
Proportion in US population	*8/24 (33.3)*	*8/33 (24.2)*
Site		
Academic[b]	143 (73.0)	159 (80.7)
Non-academic	53 (27.0)	38 (19.3)
Cytogenetic risk[c]		
High	41 (20.9)	51 (25.9)
Standard	94 (48.0)	88 (44.7)

Characteristics	Etentamig (N=196)	SAT (N=197)
Presence of soft tissue plasmacytomas[d]	41 (20.9)	47 (23.9)
Extramedullary	10 (5.1)	18 (9.1)
Paraskeletal	34 (17.4)	33 (16.8)
ECOG PS [at baseline][e]		
0	86 (43.9)	83 (42.1)
1	90 (45.9)	98 (49.7)
2	20 (10.2)	16 (8.1)
R-ISS [at baseline][e]		
I	33 (16.8)	37 (18.8)
II	150 (76.5)	141 (71.6)
III	13 (6.6)	19 (9.6)
Number of prior LoT, median (range)	3 (2–10)	3 (1–8)[f]
2 lines	89 (45.4)	86 (43.7)
3 lines	56 (28.6)	50 (25.4)
≥4 lines	51 (26.0)	60 (30.5)
Triple-class exposed	196 (100)	197 (100)
Penta-class exposed	45 (23.0)	42 (21.3)
Refractory to last prior LoT	175 (89.3)	179 (90.9)
Refractory to an anti-CD38	169 (86.2)	169 (85.8)
Refractory to an IMiD and anti-CD38	147 (75.0)	150 (76.2)
Triple-class refractory	101 (51.5)	103 (52.3)

CERVINO enrolled a diverse population, with a substantial proportion treated

Seconda evidenza clinica consolidata: Bi-specifico efficace in seconda linea



Terza evidenza clinica consolidata: Anticorpo monoclonale anti BCMA +/- Dara efficace anche nei pazienti esposti a Dara precedentemente?

MajesTEC-3, nel braccio sperimentale TEC-DARA (teclistamab + daratumumab), i pazienti precedentemente esposti a daratumumab erano 15 (pari al 5,2% dei 291 pazienti totali) del braccio

MajesTEC-9

15% pazienti
Non erano
Dara refractory

Characteristic	Tec (n=296)	PVd/Kd (n=297)
Refractory status, n (%)		
To last prior LOT	**274 (92.6)**	**273 (91.9)**
Any PI	122 (41.2)	128 (43.1)
Any IMiD	245 (82.8)	251 (84.5)
Lenalidomide	**234 (79.1)**	**240 (80.8)**
Any anti-CD38	**253 (85.5)**	**252 (84.8)**
Double refractory (IMiD and anti-CD38)	218 (73.6)	221 (74.4)
Triple refractory (IMiD, anti-CD38, and PI)	102 (34.5)	98 (33.0)

Cervino

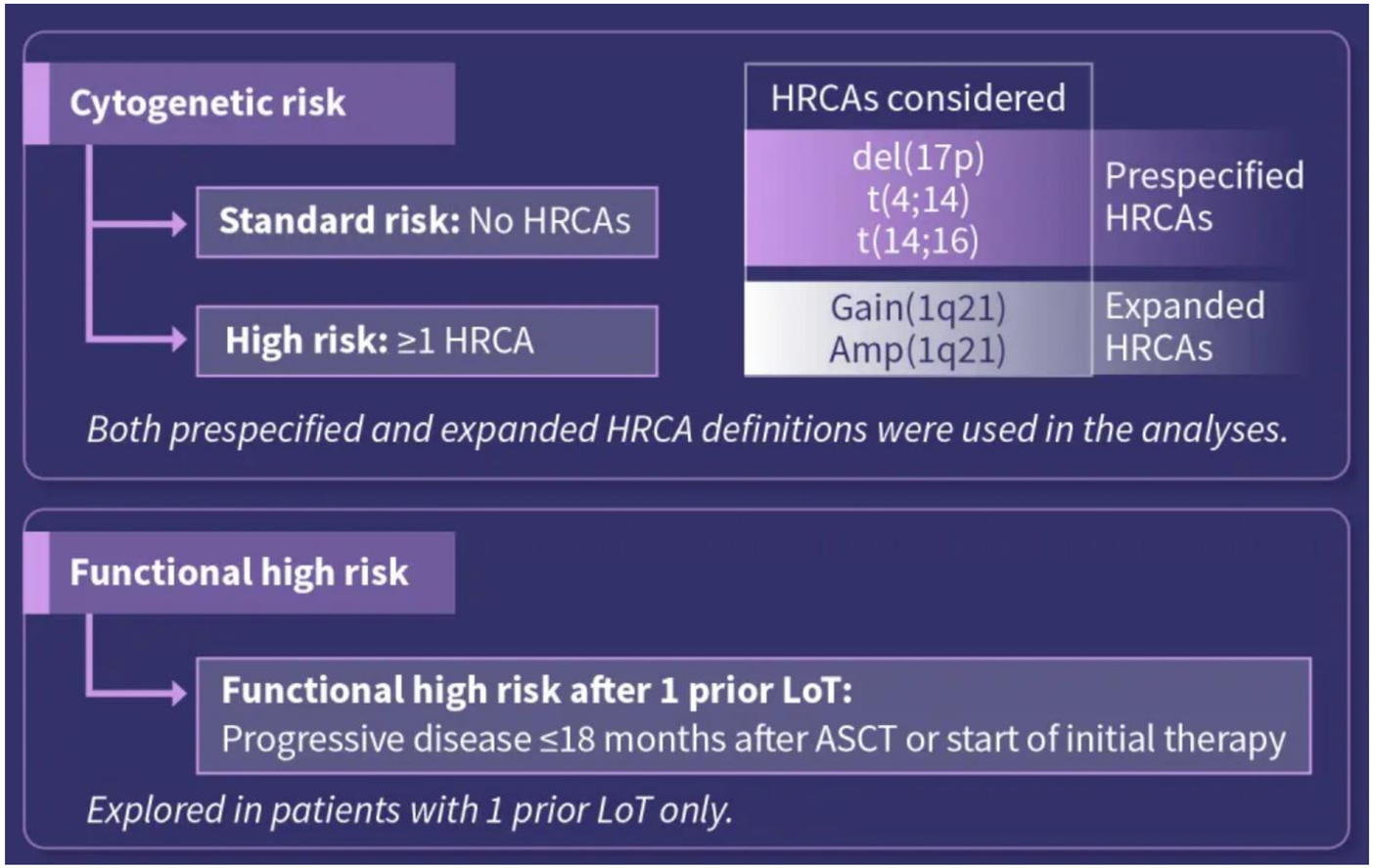
Circa la metà dei pazienti inseriti nello studio erano triplo refrattari

Terza evidenza clinica consolidata: TEC +/- Dara efficace anche nei pazienti esposti a Dara precedentemente

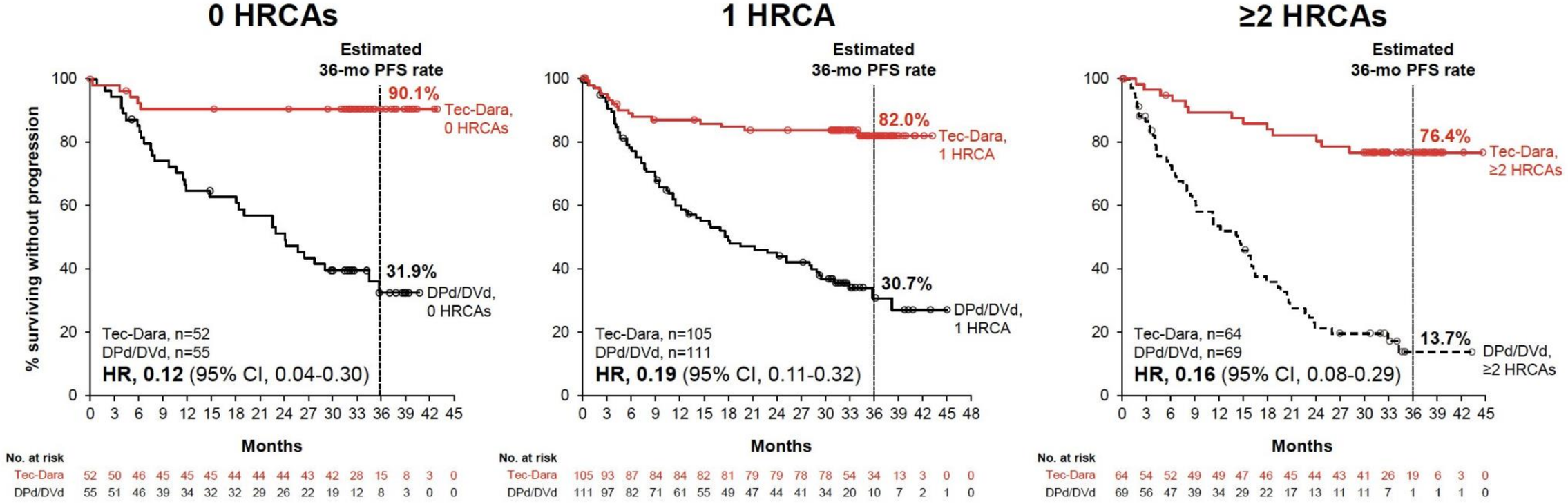


Quarta evidenza clinica consolidata: TEC-Dara efficace anche nei pazienti ad alto rischio citogenetico e nei pazienti Functionally HR

Majestec-3

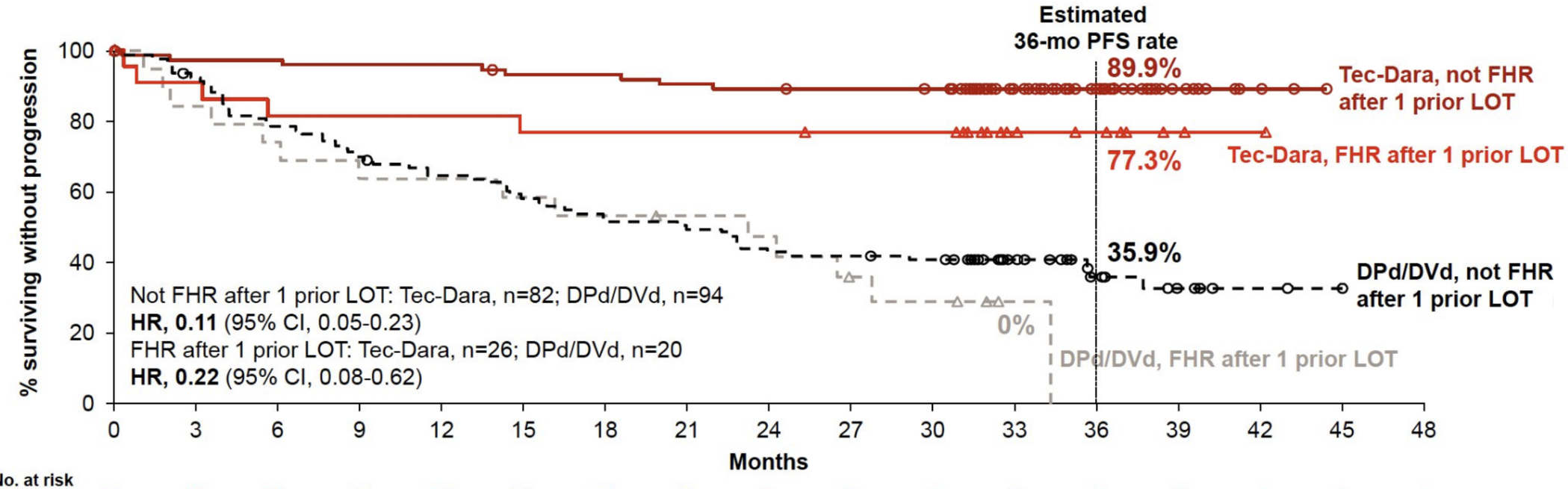

Cytogenetic risk
Standard risk: No HRCAs
High risk: ≥1 HRCA
HRCAs considered
del(17p)
t(4;14)
t(14;16)
Prespecified HRCAs
Gain(1q21)
Amp(1q21)
Expanded HRCAs
Both prespecified and expanded HRCA definitions were used in the analyses.
Functional high risk
Functional high risk after 1 prior LoT:
Progressive disease ≤18 months after ASCT or start of initial therapy
Explored in patients with 1 prior LoT only.

MajesTEC-3: PFS by Number of Expanded[a] HRCAs



Tec-Dara consistently improved PFS vs DPd/DVd, including in patients with ultra high-risk RRMM

MajesTEC-3: PFS by Functional High-Risk Status[a]

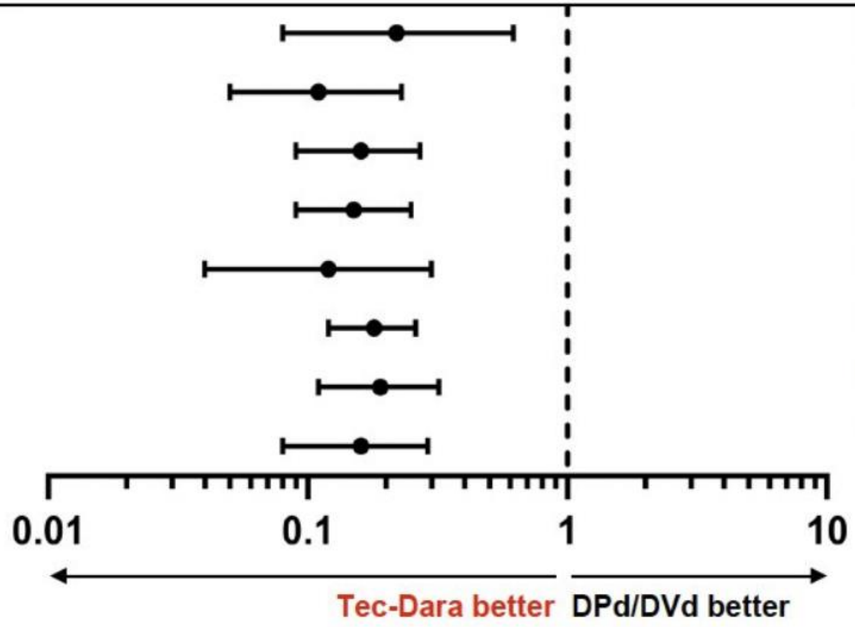


No. at risk																	
Tec-Dara, not FHR after 1PL	82	78	78	77	77	74	74	72	71	70	69	46	30	15	3	0	0
DPd/DVd, not FHR after 1PL	94	86	73	65	59	53	47	45	39	38	36	24	13	7	2	1	0
Tec-Dara, FHR after 1PL	26	20	18	18	18	17	17	17	17	16	16	8	6	2	1	0	0
DPd/DVd, FHR after 1 PL	20	16	14	12	12	11	10	9	8	5	4	1	0	0	0	0	0

Tec-Dara substantially prolonged PFS vs DPd/DVd in patients with FHR MM, surpassing inferior outcomes historically seen with traditional therapies[1]

MajesTEC-3: PFS By Risk Status (ITT)

	Tec-Dara		DPd/DVd		HR (95% CI)
	Events n/N	Median PFS (mo)	Events n/N	Median PFS (mo)	
Functional high risk	5/26	NE	14/20	23.2	0.22 (0.08-0.62)
Non-functional high risk	8/82	NE	57/94	20.8	0.11 (0.05-0.23)
Prespecified std. risk[a]	15/126	NE	84/145	24.7	0.16 (0.09-0.27)
Prespecified high risk[a]	20/104	NE	78/104	14.4	0.15 (0.09-0.25)
Expanded std. risk[b]	5/52	NE	34/55	24.2	0.12 (0.04-0.30)
Expanded high risk[b]	30/169	NE	122/180	15.8	0.18 (0.12-0.26)
1 HRCA	17/105	NE	69/111	17.9	0.19 (0.11-0.32)
≥2 HRCAs	13/64	NE	53/69	14.4	0.16 (0.08-0.29)



Quarta evidenza clinica consolidata: TEC-Dara efficace anche nei pazienti ad alto rischio citogenetico e nei pazienti Functionally HR



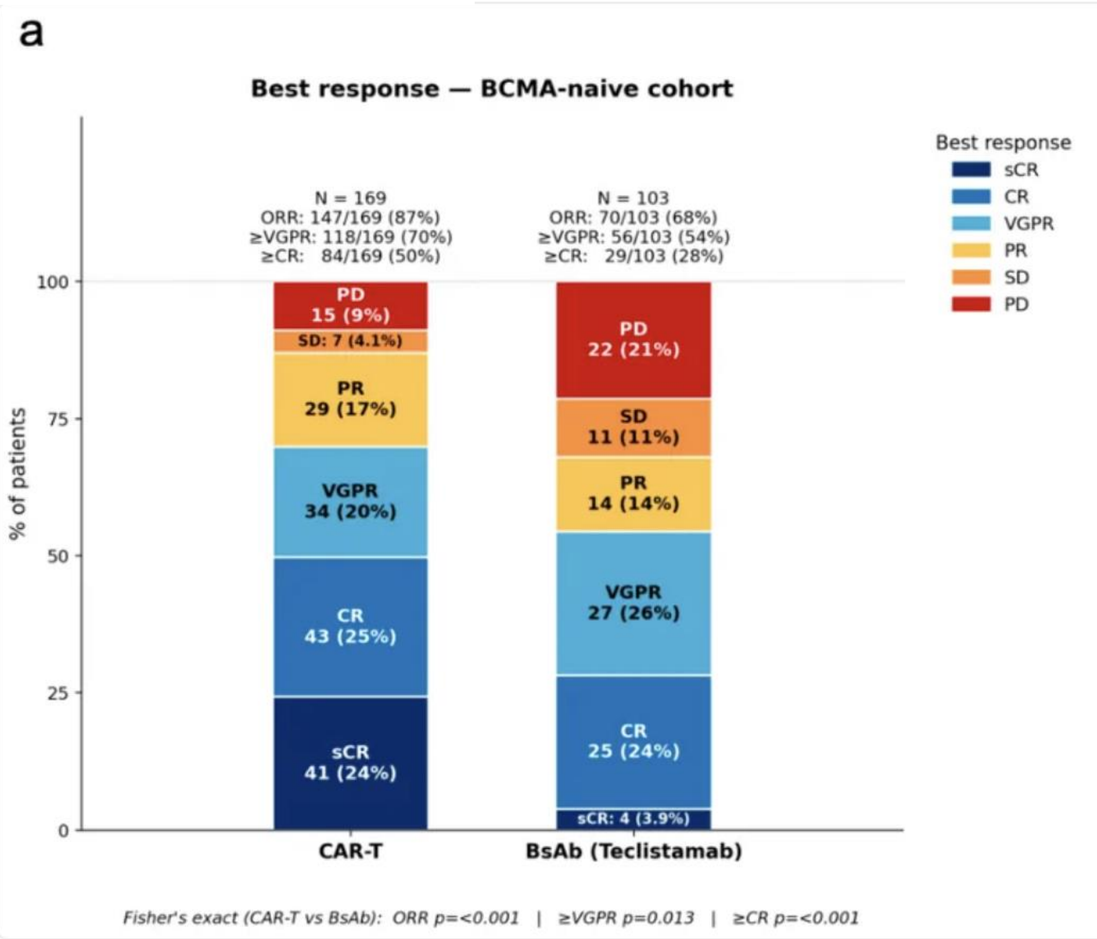
Quinta evidenza clinica consolidata: Importanza del Sequencing - Anticorpi bispecifici anti BCMA prima delle CART anti BCMA riducono l'efficacia

Sequencing

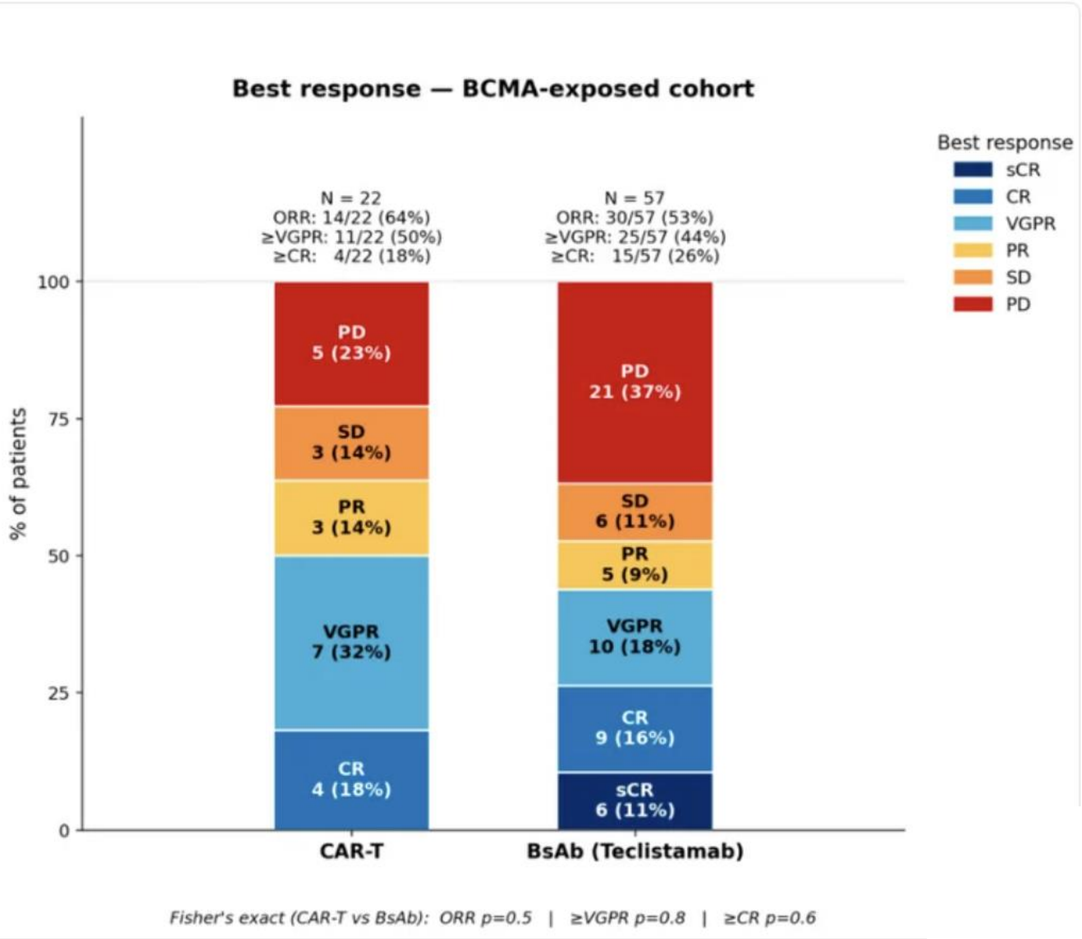
Sequencing BCMA-Directed Therapies in Relapsed/Refractory Multiple Myeloma: A Real-World Comparison of CAR T-Cell Therapy and Bispecific Antibodies

Osama M Younis [1], Sencer Goklemez [2], Carmel Awadallah [3], Shebli Atrash [4], Barry Paul [4], Hira Shaikh [5], Christopher Strouse [5], Andrew Vegel [5], Emily Struble [5], Anita Mazloom [6], Omar Alkharabsheh [2 6], Prerna Mewawalla [7], Mansi R Shah [8], Abhiraj Saxena [8], Zahra Mahmoudjafari [9], Jordan Snyder [9], Muhammad Umair Mushtaq [9], Jeries Kort [9], Alma Habib [9], Joseph McGuirk [9], Al-Ola Abdallah [9], Abdullah Mohammad Khan [10]

a



b





Quinta evidenza clinica consolidata: Importanza del Sequencing - Anticorpi bispecifici anti BCMA prima delle CART anti BCMA riducono l'efficacia

Quinta evidenza clinica consolidata: Importanza del Sequencing - Anticorpi bispecifici anti BCMA dopo delle CART o altro trattamento BDT?



Sesta evidenza clinica consolidata:
Problematica delle infezioni nei pazienti sottoposti a BDT e riduzione delle infezioni dopo profilassi con Ig e anticipando il farmaco in linee più precoci?

Majestec-1

Table 2. Adverse Events in 165 Patients (Safety Population).*

Event	Any Grade	Grade 3 or 4
	no. of patients (%)	
Any adverse event	165 (100)	156 (94.5)
Hematologic		
Neutropenia	117 (70.9)	106 (64.2)
Anemia	86 (52.1)	61 (37.0)
Thrombocytopenia	66 (40.0)	35 (21.2)
Lymphopenia	57 (34.5)	54 (32.7)
Leukopenia	29 (17.6)	12 (7.3)
Nonhematologic		
Diarrhea	47 (28.5)	6 (3.6)
Fatigue	46 (27.9)	4 (2.4)
Nausea	45 (27.3)	1 (0.6)
Injection-site erythema	43 (26.1)	0
Pyrexia	45 (27.3)	1 (0.6)
Headache	39 (23.6)	1 (0.6)
Arthralgia	36 (21.8)	1 (0.6)
Constipation	34 (20.6)	0
Cough	33 (20.0)	0
Pneumonia	30 (18.2)	21 (12.7)
Covid-19	29 (17.6)	20 (12.1)
Bone pain	29 (17.6)	6 (3.6)
Back pain	27 (16.4)	4 (2.4)
Cytokine release syndrome†	119 (72.1)	1 (0.6)
Neurotoxic event	24 (14.5)	1 (0.6)

* Listed are adverse events of any grade that were reported in at least 15% of the patients, as well as neurotoxic events. Covid-19 denotes coronavirus disease 2019.
† In this analysis, events associated with cytokine release syndrome were graded according to the criteria of the American Society for Transplantation and Cellular Therapy.

Pneumonia	30 (18.2)	21 (12.7)
Covid-19	29 (17.6)	20 (12.1)
Bone pain	29 (17.6)	6 (3.6)
Back pain	27 (16.4)	4 (2.4)

Majestec-3

TEAE, n (%)	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any infection	273 (96.5)	153 (54.1)	244 (84.1)	126 (43.4)
Treatment-emergent infection or infestation[e]				
COVID-19	124 (43.8)	17 (6.0)	97 (33.4)	6 (2.1)
URTI	115 (40.6)	12 (4.2)	88 (30.3)	7 (2.4)
Pneumonia	65 (23.0)	47 (16.6)	53 (18.3)	43 (14.8)
Nasopharyngitis	62 (21.9)	0	57 (19.7)	0
Sinusitis	52 (18.4)	5 (1.8)	17 (5.9)	3 (1.0)
Rhinovirus infection	44 (15.5)	5 (1.8)	10 (3.4)	1 (0.3)
Bronchitis	40 (14.1)	2 (0.7)	31 (10.7)	6 (2.1)
Influenza	38 (13.4)	8 (2.8)	43 (14.8)	10 (3.4)
COVID-19 pneumonia	34 (12.0)	32 (11.3)	12 (4.1)	7 (2.4)
UTI	29 (10.2)	4 (1.4)	27 (9.3)	1 (0.3)

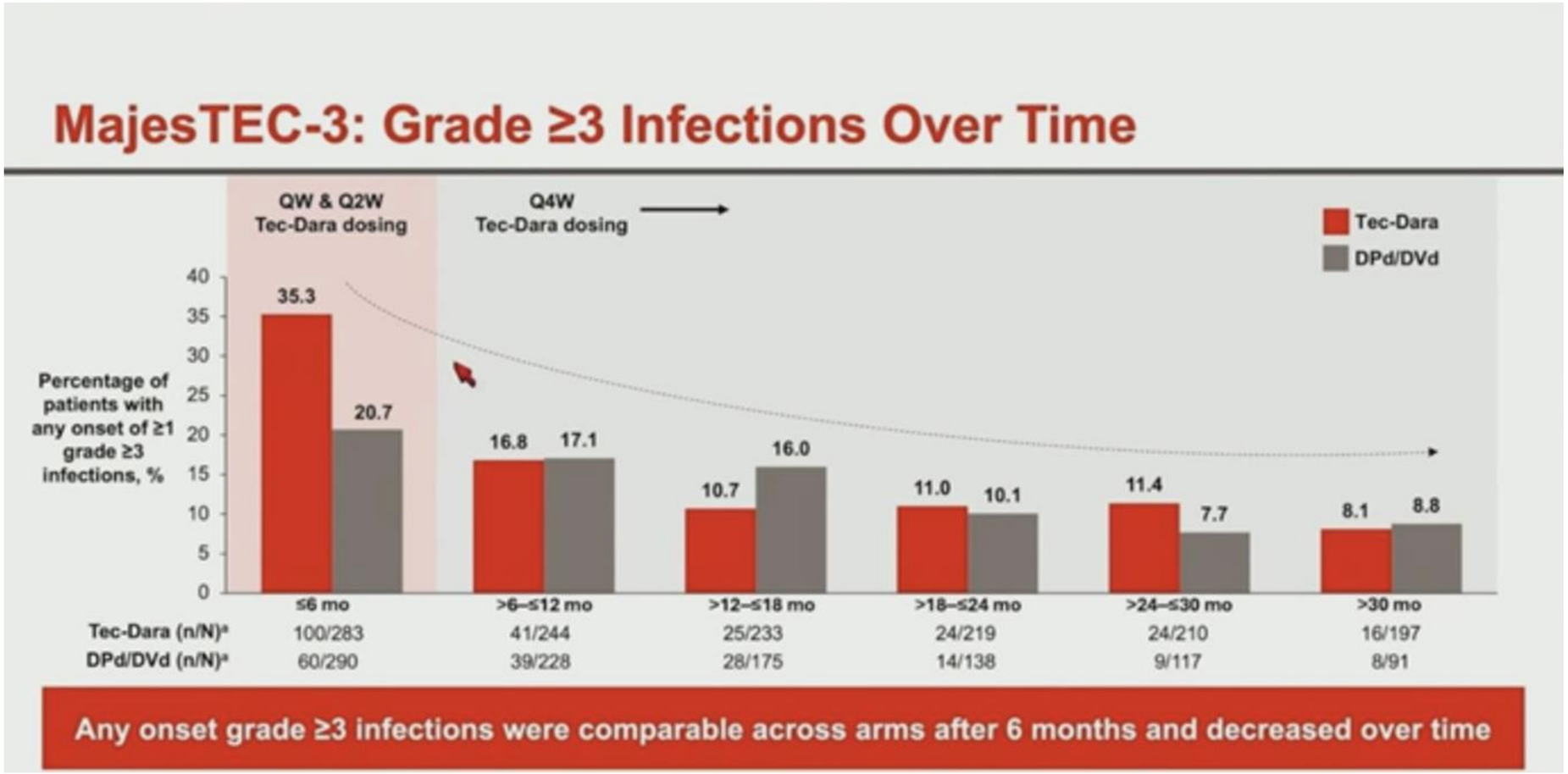
Majestec-9

Table 3. Most Common Adverse Events (Safety Population).*

Event	Teclistamab (N=291)		PVd or Kd (N=283)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients with event (percent)			
Any adverse event	290 (99.7)	247 (84.9)	277 (97.9)	216 (76.3)
Hematologic event				
Neutropenia	182 (62.5)	158 (54.3)	81 (28.6)	63 (22.3)
Anemia	110 (37.8)	52 (17.9)	119 (42.0)	46 (16.3)
Thrombocytopenia	80 (27.5)	31 (10.7)	110 (38.9)	60 (21.2)
Lymphopenia	71 (24.4)	59 (20.3)	49 (17.3)	32 (11.3)
Nonhematologic event				
Cytokine release syndrome	192 (66.0)	2 (0.7)	0	0
Diarrhea	124 (42.6)	15 (5.2)	72 (25.4)	4 (1.4)
Hypogammaglobulinemia†	124 (42.6)	7 (2.4)	46 (16.3)	1 (0.4)
Cough	80 (27.5)	2 (0.7)	39 (13.8)	0
Upper respiratory tract infection	77 (26.5)	7 (2.4)	58 (20.5)	6 (2.1)
Injection-site erythema	71 (24.4)	0	8 (2.8)	0
Pneumonia	64 (22.0)	42 (14.4)	43 (15.2)	30 (10.6)
Hypertension	20 (6.9)	13 (4.5)	51 (18.0)	32 (11.3)

Cervino

TEAEs	Etentamig (N=195)		
	Any grade	Grade 3/4	Grade 5
Any TEAE	191 (97.9)	138 (70.8)	5 (2.6)
Hematologic TEAEs (any grade >25% in etentamig arm)			
Neutropenia[a]	91 (46.7)	75 (38.5)	0
Thrombocytopenia[b]	51 (26.2)	21 (10.8)	0
Anemia[c]	50 (25.6)	28 (14.4)	0
Nonhematologic (any grade >20% in etentamig arm)			
Diarrhea	47 (24.1)	3 (1.5)	0
CRS (N=113)[d]	32 (28.3)	0	0
ICANS (N=113)[d,e]	1 (0.9)	0	0
Infections (any grade >15% in etentamig arm)	136 (69.7)	54 (27.7)	3 (1.5)
Upper respiratory tract infection	43 (22.1)	5 (2.6)	0
Pneumonia[f]	39 (20.0)	27 (13.8)	2 (1.0)
Opportunistic infections[e,g]	7 (3.6)	2 (1.0)	0
Cytomegalovirus-related infections[h]	3 (1.5)	1 (0.5)	0
COVID-19 related events[e]	14 (7.2)	2 (1.0)	0


MajesTEC-3: Grade ≥3 Infections Over Time
QW & Q2W Tec-Dara dosing
Q4W Tec-Dara dosing
Tec-Dara
DPd/DVd
Percentage of patients with any onset of ≥1 grade ≥3 infections, %
40
35
30
25
20
15
10
5
0
35.3
20.7
16.8
17.1
10.7
16.0
11.0
10.1
11.4
7.7
8.1
8.8
≤6 mo
>6–≤12 mo
>12–≤18 mo
>18–≤24 mo
>24–≤30 mo
>30 mo
Tec-Dara (n/N)[a] 100/283 41/244 25/233 24/219 24/210 16/197
DPd/DVd (n/N)[a] 60/290 39/228 28/175 14/138 9/117 8/91
Any onset grade ≥3 infections were comparable across arms after 6 months and decreased over time

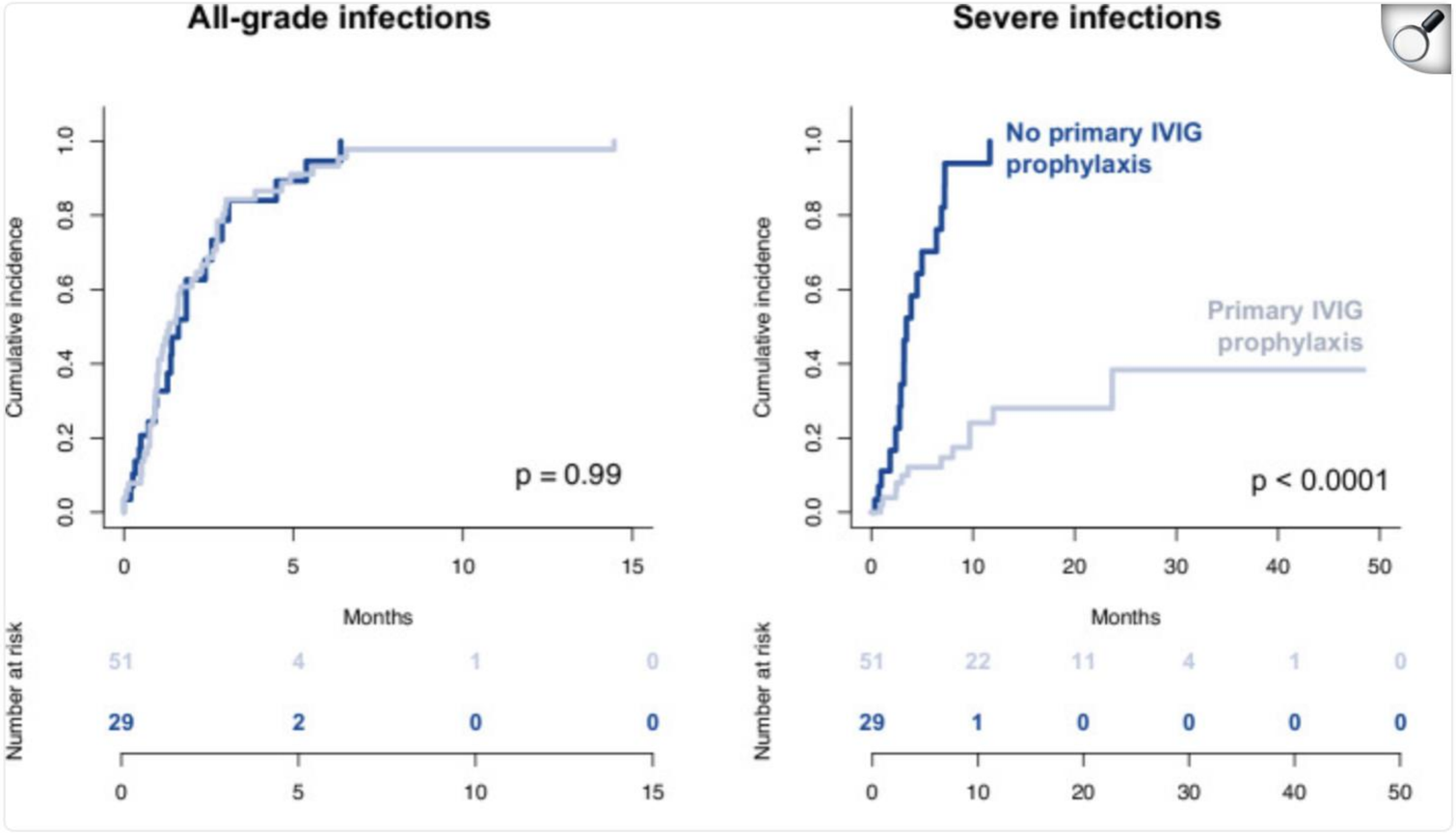
Blood Cancer J. 2026 Feb 21;16(1):26. doi: 10.1038/s41408-026-01451-9

Immunoglobulin supplementation and longer dosing intervals reduce risk of infections in patients with RRMM treated with teclistamab

Febe Smits [1,2,3], Kaz Groen [1,2], Charlotte L B M Korst [1,2], Kris A Frerichs [1,2], Ilse Kuipers [1,2], Sandy Kruyswijk [1,2], Maaike E M de Ruijter [1,2], Kazem Nasserinejad [4,5], Sonja Zweegman [1,2], Niels W C J van de Donk [1,2,✉]

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Sesta evidenza clinica consolidata: Problematica delle infezioni nei pazienti sottoposti a BDT e riduzione delle infezioni dopo profilassi con Ig e anticipando il farmaco in linee più precoci

Sesta evidenza clinica consolidata: Probabilmente l'insorgenza delle infezioni cala con il tempo



Settima evidenza clinica consolidata: Gestione della BDT in OUTPATIENT?

ORIGINAL ARTICLE OPEN ACCESS

European Expert Panel Consensus on Outpatient Administration of Teclistamab and Talquetamab in Patients With Multiple Myeloma: Feasibility, Key Considerations, and Future Directions

Thomas Lund[1,2] | Cyrus Khandanpour[3] | Sébastien Anguille[4] | Jens Kisro[5] | Maria Theresa Krauth[6] | Johan Lund[7] | Inger Nijhof[8] | Enrique M. Ocio[9] | Elena Zamagni[10] | Matthieu Javelot[11] | Claire Albrecht[11] | Cristina Entrala Cerezo[12] | Aurore Perrot[13]

OUT PTS

Outpatient preparation and patient selection

Infrastructure preparation

- Experience administering BsAbs in an inpatient setting
- Access to a hematology department/hematologist familiar with CRS, ICANS, and infections
- Access to emergency department and ICU
- Robust protocols put in place to guide HCPs with outpatient administration
- All relevant HCPs trained on the new process
- On-duty onco-hematologist ready to be contacted by outpatients receiving BsAbs if needed

Patient eligibility criteria†

- ECOG performance status score 0–2
- No high tumor burden or rapidly progressive disease
- If comorbidities, these must be well controlled; no active infection
- Presence of a caregiver residing at the same home as the patient to monitor for AEs
- Patient lives within 30–60 minutes of the hospital
- Patient/caregiver can be considered "reliable"

No difference in eligibility criteria expected for those receiving teclistamab vs talquetamab

Treatment initiation

Actions **prior** to SUD

- Administer mandatory premedications (paracetamol, antiallergic, dexamethasone[‡])
- Provide patients/caregivers with simple education on the signs and symptoms of CRS and ICANS
- Provide patient notices and cards to patients/caregivers
- Provide patients/caregivers with anticipated prescriptions (paracetamol, dexamethasone[‡])
- Provide patients/caregivers with a prescription for a thermometer, blood pressure monitor, and pulse oximeter

No changes to the preferred SUD schedule are likely to be needed in an outpatient setting

Post SUD management

AE monitoring

- Patients/caregivers to monitor patient temperature, blood pressure, and oxygen saturation 2–3 times a day
- Patients/caregivers to contact on-duty onco-hematologist if experiencing AEs

AE management

- HCPs must follow a predefined infection management strategy (IMWG and EMN guidelines)[1,‖]
- Patients to follow the directions of on-duty onco-hematologist when needed
- Patients who develop a fever should take paracetamol
- If patient develops signs and symptoms of grade 2 CRS, the anticipated prescription of dexamethasone can be taken following telephone instructions from the on-duty onco-hematologist
- Patients should be prepared to travel to the hospital within 1 hour if experiencing signs of persistent grade 2 CRS

Settima evidenza clinica consolidata: Gestione della BDT in OUTPATIENT



Comparare con real life

Ottava evidenza clinica consolidata:
Il paziente real life è quello degli studi?

Pazienti con RRMM trattati con anticorpi bispecifici anti BCMA nei trial clinici

	MagnetisMM-3	**MajesTEC-1**	**MajesTEC-9**	**MajesTEC-3**
Median age	68 (36-89)	64 (33-84)	70 (34-85)	64 (36-88)
ECOG <= 1	94 %	33 % ECOG 0 66 % >= 1	93 %	94,5 %

Comparare con real life

Ottava evidenza clinica consolidata:
Il paziente real life NON è quello degli studi



Conclusioni: evidenze cliniche consolidate
Anticorpi bi specifici anti BCMA



3



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