

HIGHLIGHTS IN EMATOLOGIA

TREVISO
7-8 NOVEMBRE 2025



Ruolo e timing dei bispecifici

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REGIONE DEL VENETO



ULSS8
BERICA

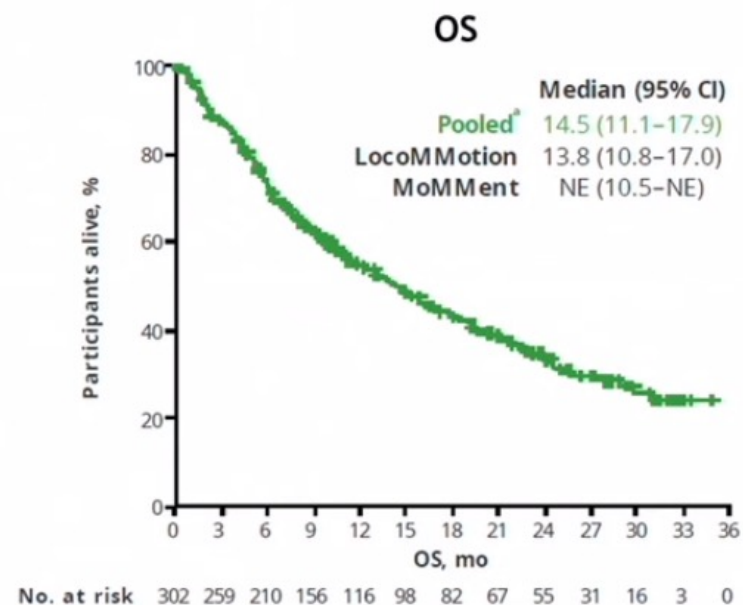
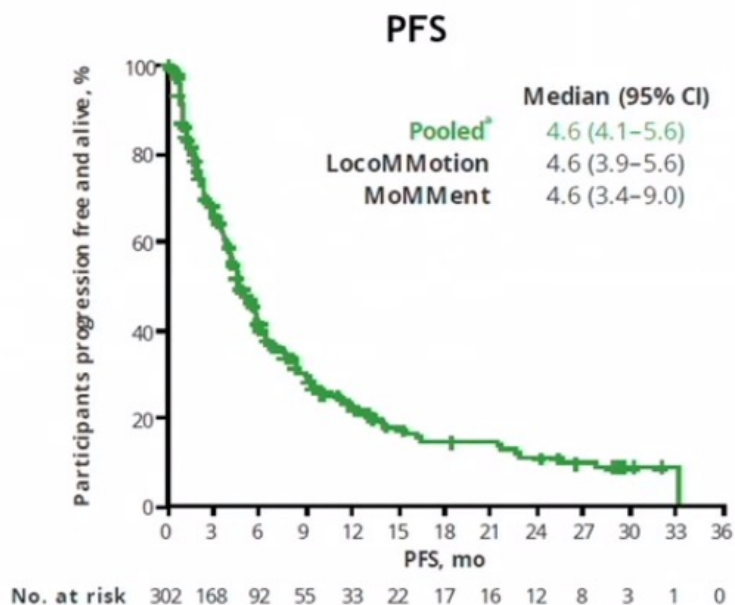


Disclosures of Gregorio Barilà

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Johnson & Johnson			X		X	X	
Amgen					X		
Pfizer			X		X	X	
BMS					X		
Sanofi			X		X	X	
Menarini Stemline					X	X	

PROGNOSI DEI PAZIENTI TCE/TCR

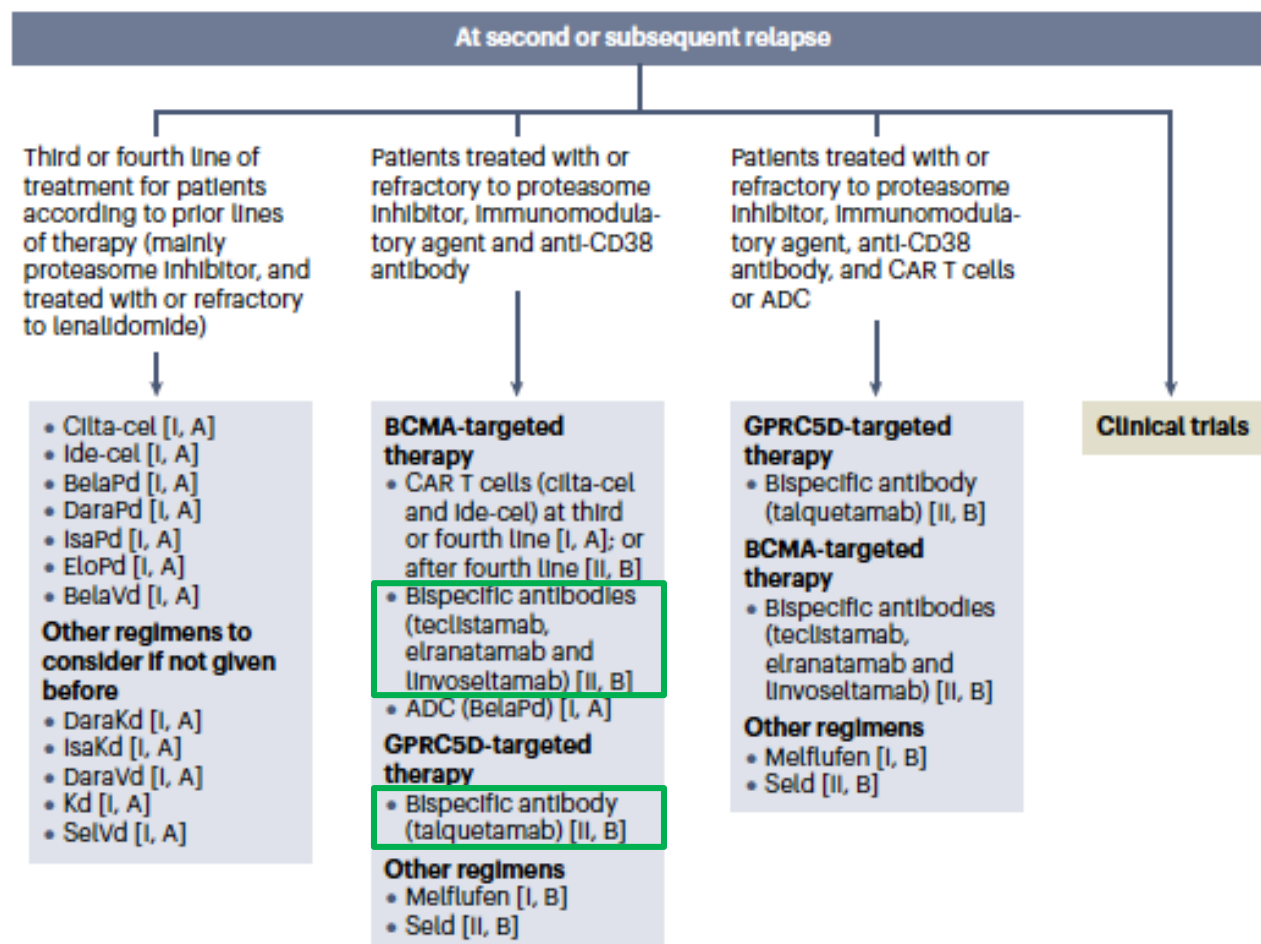
- 100% pazienti triplo-esposti
- 75.3% triplo refrattari
- Mediana di precedenti linee di terapia=4



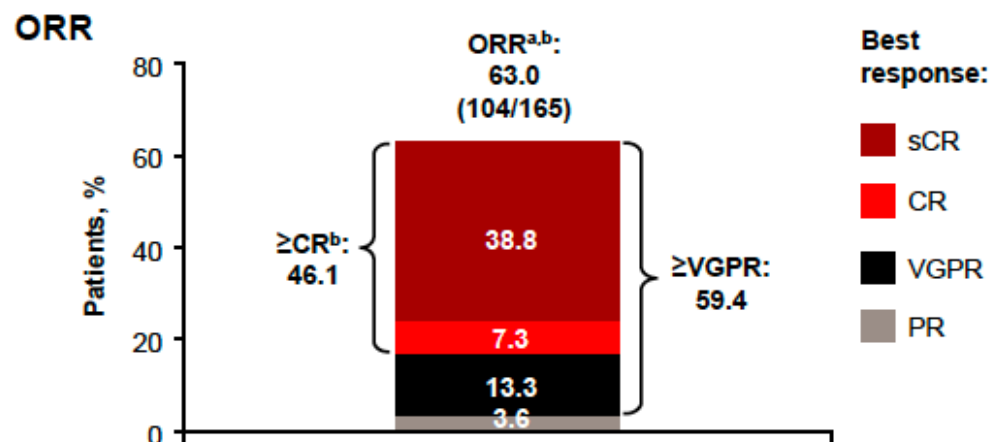
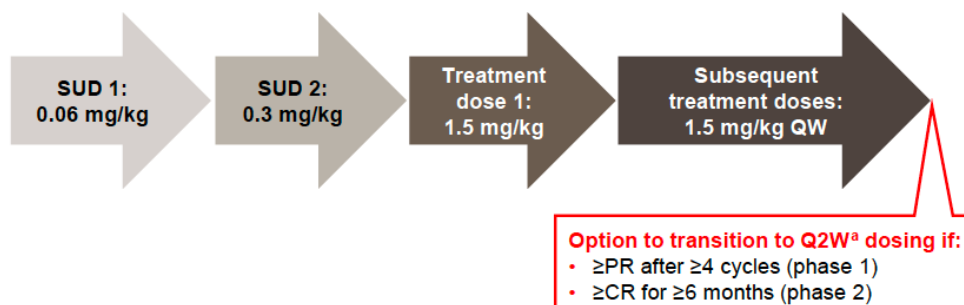
- **RUOLO E TIMING DEI BISPECIFICI NEL 2025**
 - **RUOLO E TIMING DEI BISPECIFICI NEL 202X**
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LINEE GUIDA EHA/EMN

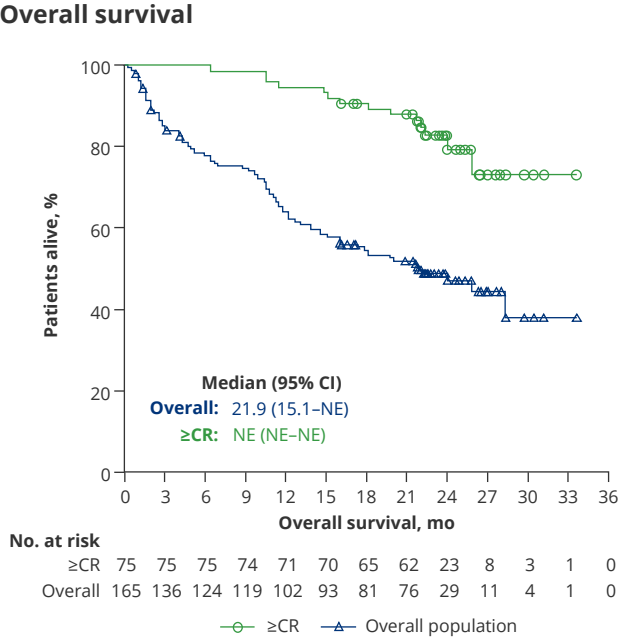
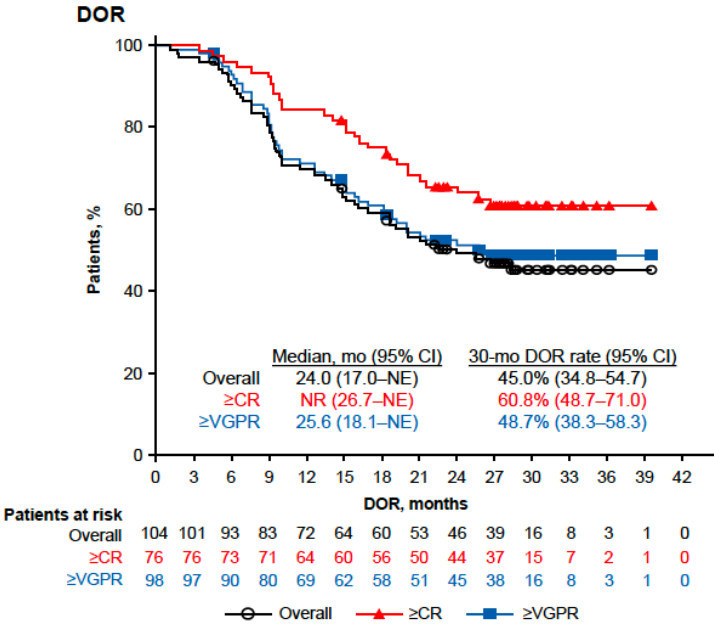
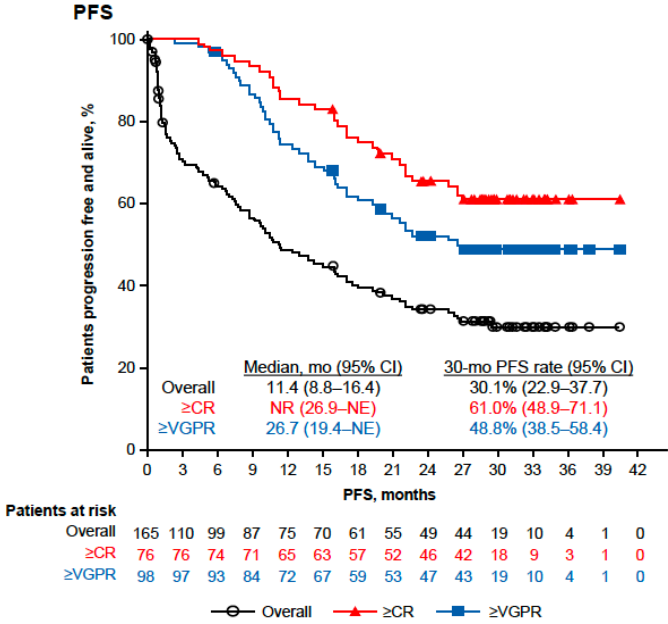


TECLISTAMAB /MAJESTEC-1



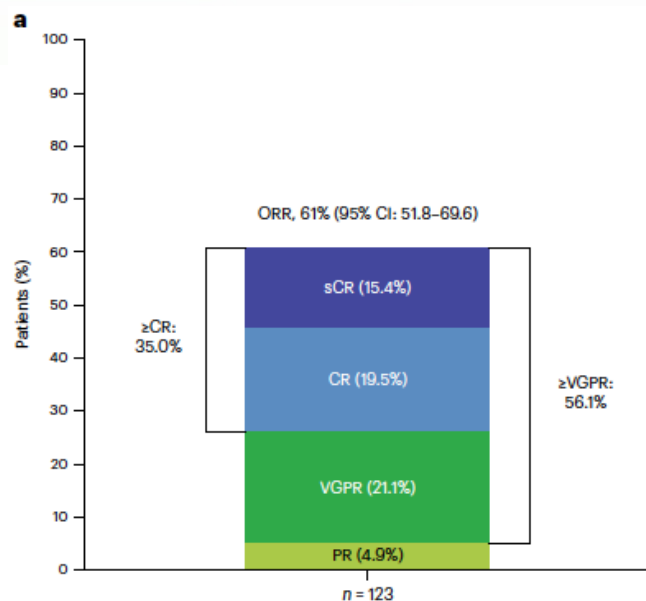
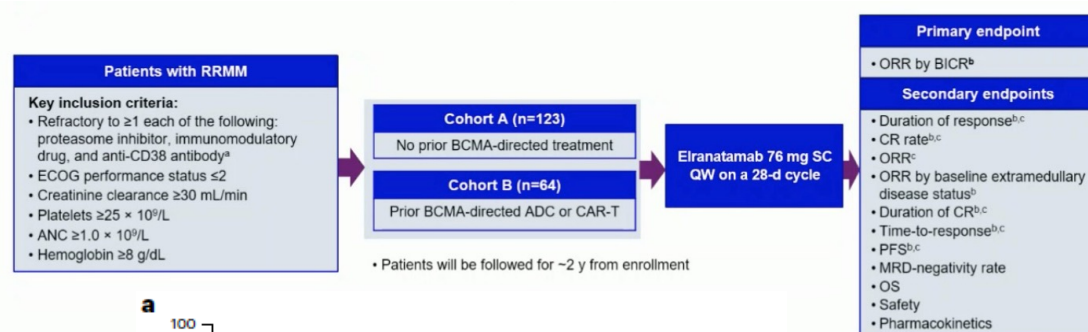
Characteristic	N=165
Age (years), median (range)	64 (33–84)
Male, n (%)	96 (58.2)
Race, n (%)	
White	134 (81.2)
Black/African American	21 (12.7)
Asian	3 (1.8)
Other	7 (4.2)
EMD, ^a n (%)	28 (17.0)
High-risk cytogenetics, n/N (%)	38/148 (25.7)
ISS stage, n/N (%)	
I	85/162 (52.5)
II	57/162 (35.2)
III	20/162 (12.3)
Time since diagnosis (years), median (range)	6.0 (0.8–22.7)
Number of prior LOT, median (range)	5 (2–14)
Prior stem cell transplant, n (%)	135 (81.8)
Exposure status, n (%)	
Triple-class ^b	165 (100)
Penta-drug ^c	116 (70.3)
Refractory status, n (%)	
Anti-CD38 mAb	148 (89.7)
Triple-class ^b	128 (77.6)
Penta-drug ^c	50 (30.3)

TECLISTAMAB /MAJESTEC-1



Popat R. et al, IMS, 2024; Van de Donk N et al, ASCO, 2023

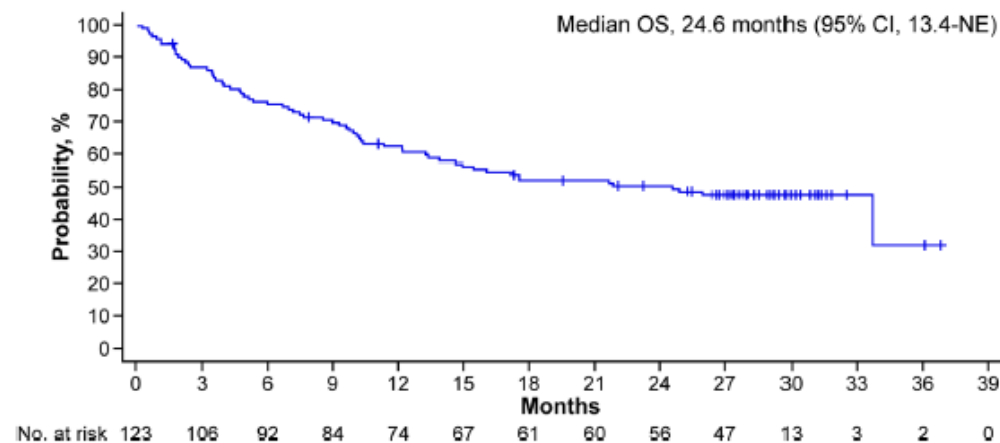
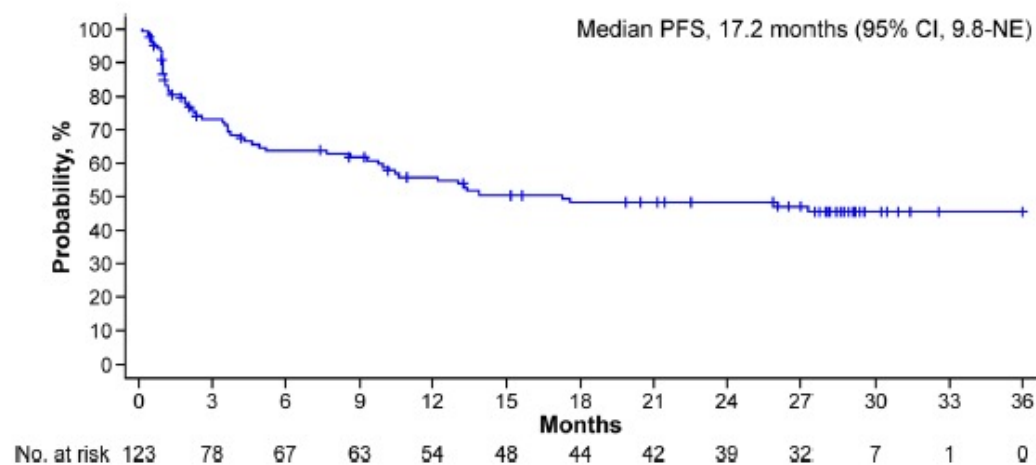
ELRANATAMAB /MAGNETISMM-1



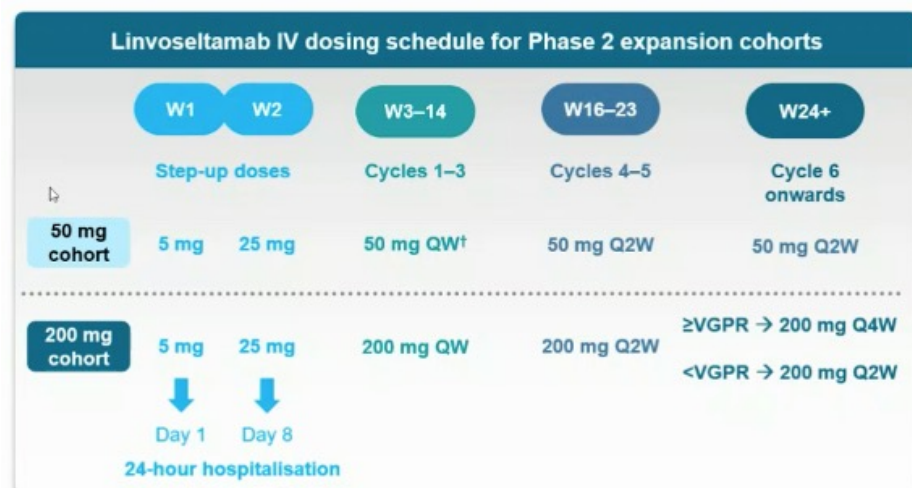
MRD negativity 91% (10^{-5})*

Extramedullary disease by BICR, n (%) ^c	39 (31.7)
Bone marrow plasma cells, n (%)	
<50%	89 (72.4)
≥50%	26 (21.1)
Missing	8 (6.5)
≥1 poor prognosis feature ^d	94 (76.4)
Median no. of prior antimyeloma lines of therapy (range)	5 (2–22)
Prior stem cell transplant, n (%)	87 (70.7)
Exposure status, n (%)	
Triple-class ^e	123 (100)
Penta-drug ^f	87 (70.7)
Refractory status, n (%)	
Triple-class ^e	119 (96.7)
Penta-drug ^f	52 (42.3)
Refractory to last line of therapy, n (%)	118 (95.9)

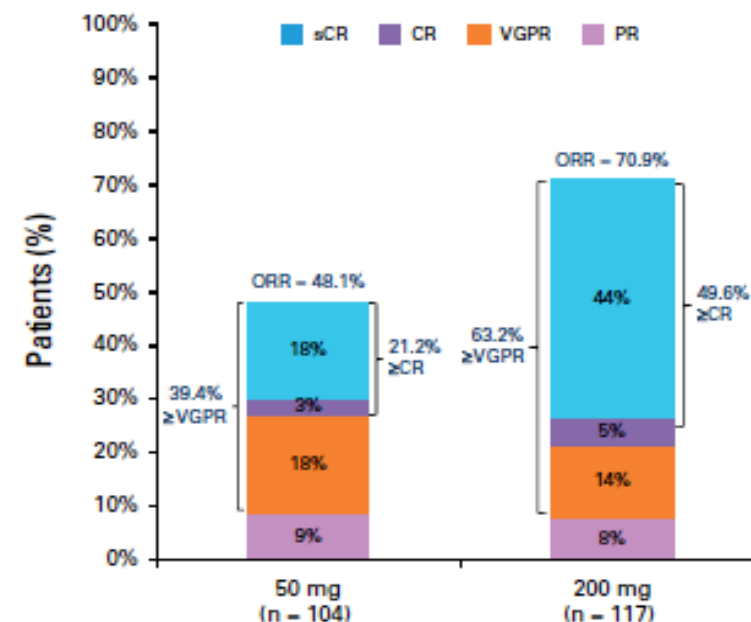
ELRANATAMAB /MAGNETISMM-1



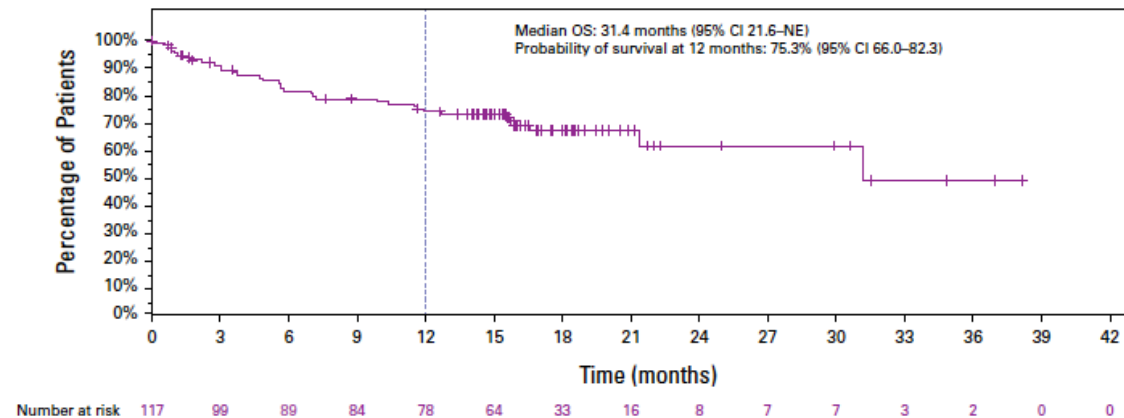
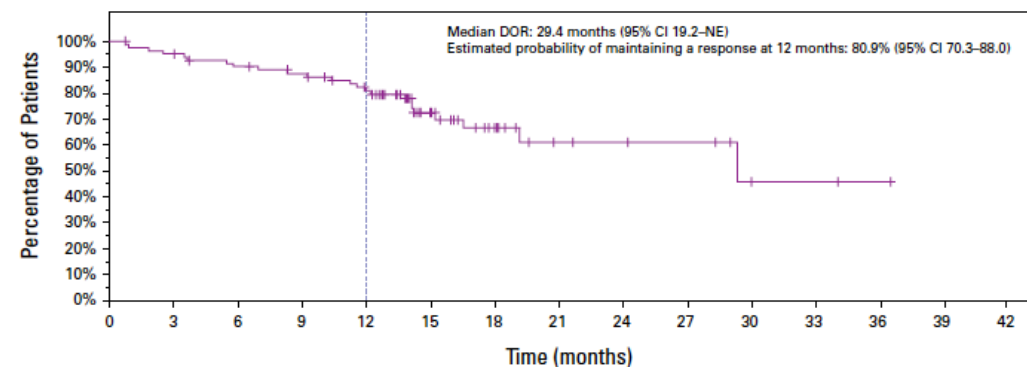
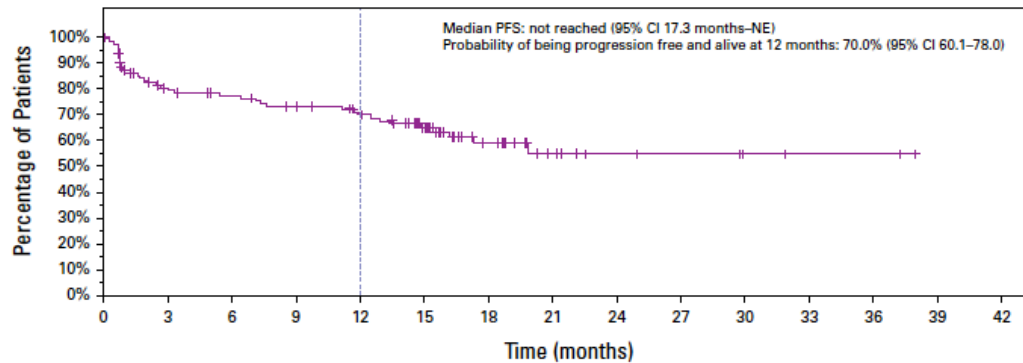
LINVOSELTAMAB/LINKER-MM1



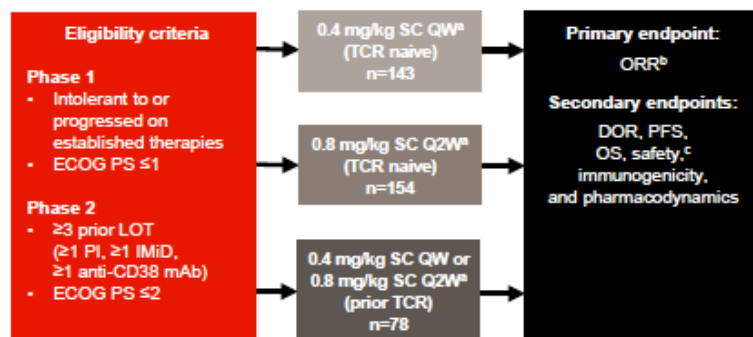
Prior treatments, n (%), unless otherwise stated	50 mg (n=104)	200 mg† (n=117)
Prior autologous transplant	81 (77.9)	74 (63.2)
Median prior lines of therapy, n (range)	6 (3–14)	5 (2–14)
Exposure status		
At least triple-exposed	104 (100.0)	117 (100.0)
At least quad-exposed	104 (100.0)	112 (95.7)
At least penta-exposed	95 (91.3)	88 (75.2)
Refractory status		
At least triple-refractory	91 (87.5)	86 (73.5)
At least quad-refractory	79 (76.0)	67 (57.3)
At least penta-refractory	52 (50.0)	28 (23.9)
Refractory to last line of therapy†	88 (84.6)	90 (76.9)



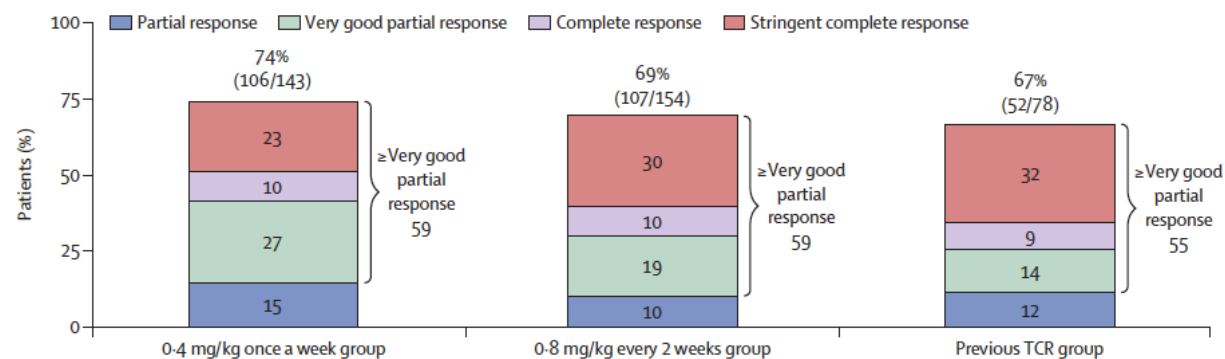
LINVOSELTAMAB/LINKER-MM1



TALQUETAMAB/MONUMENTAL-1

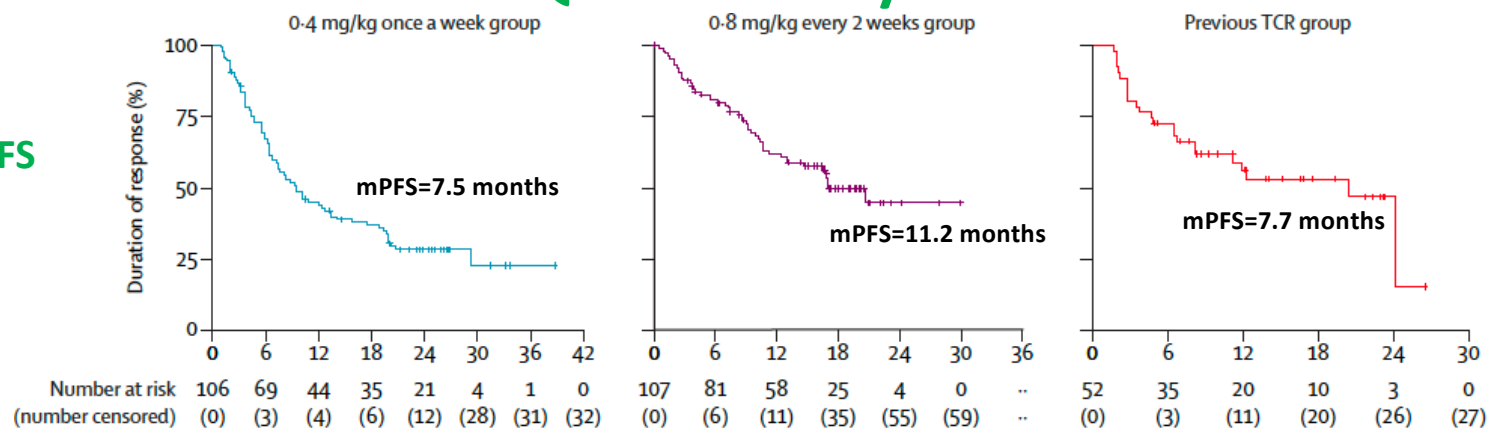


Characteristic	0.4 mg/kg SC QW and 0.8 mg/kg SC Q2W (n=162)
Age (years), median (range)	64.5 (42–81)
Male, n (%)	93 (57.4)
Extramedullary plasmacytomas ≥1, ^a n (%)	48 (29.6)
High-risk cytogenetics, ^b n (%)	38 (27.5)
Prior LOT, median (range)	5 (2–17)
Exposure status, n (%)	
Triple-class ^c	162 (100)
Penta-drug ^d	117 (72.2)
Belantamab	20 (12.3)
Refractory status, n (%)	
Triple-class ^c	122 (75.3)
Penta-drug ^d	47 (29.0)
To last prior LOT	154 (95.1)

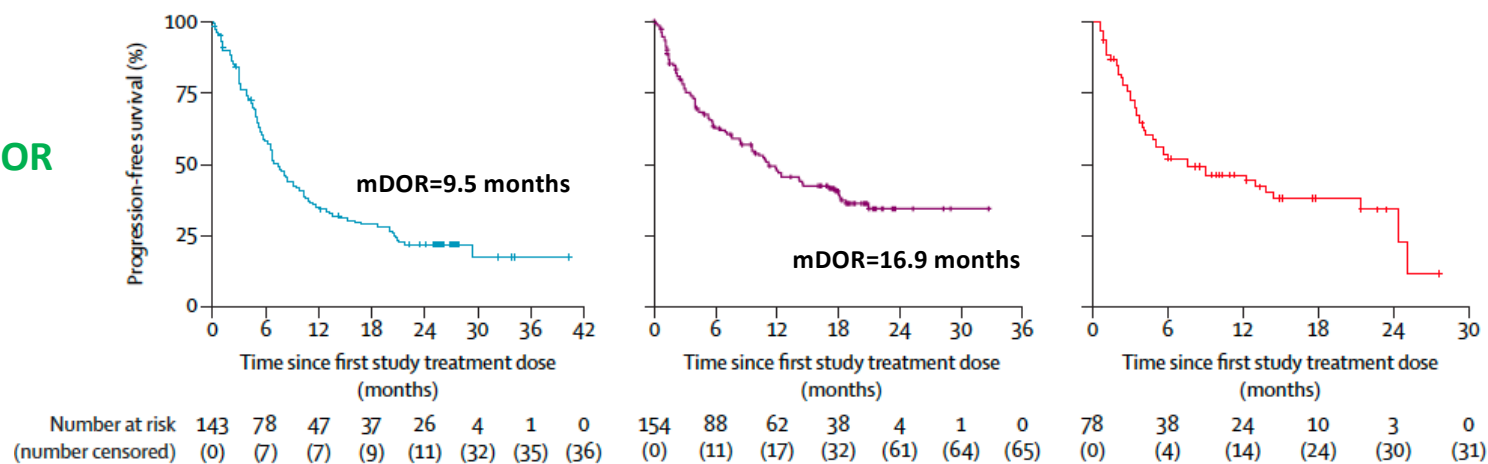


TALQUETAMAB/MONUMENTAL-1

PFS

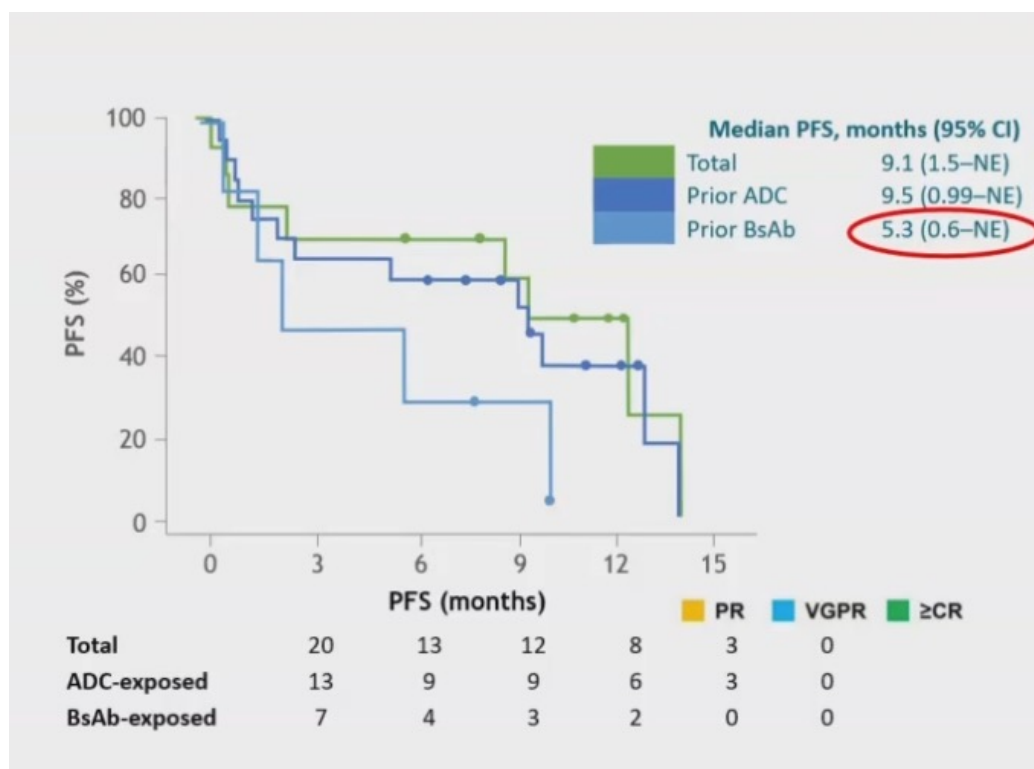


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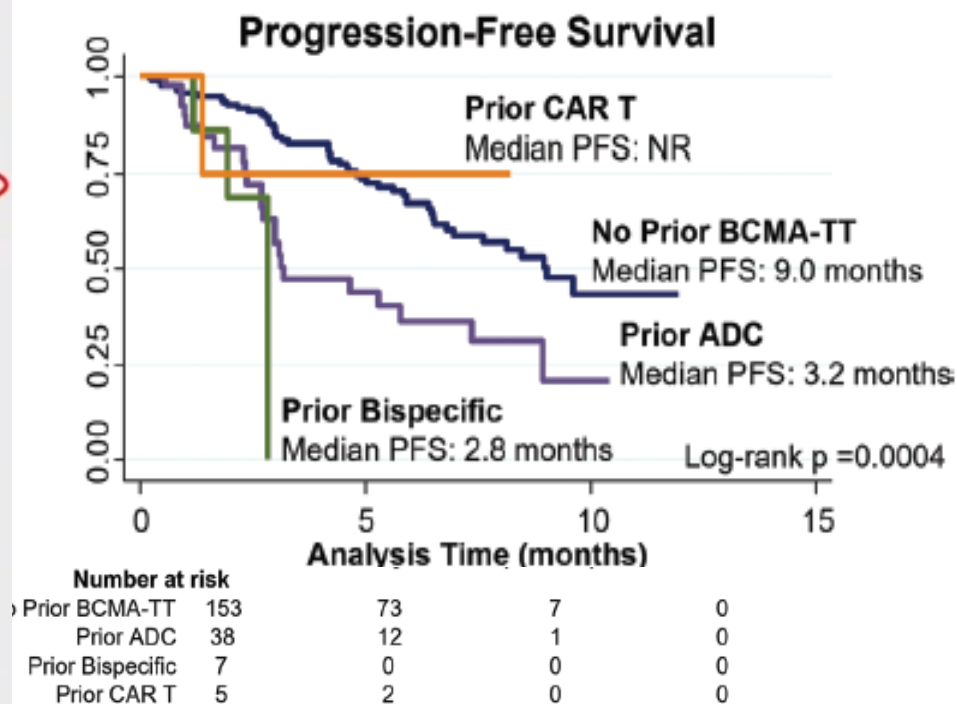


ANTI-BCMA CAR-T AFTER ANTI BCMA TREATMENT

CILTACEL

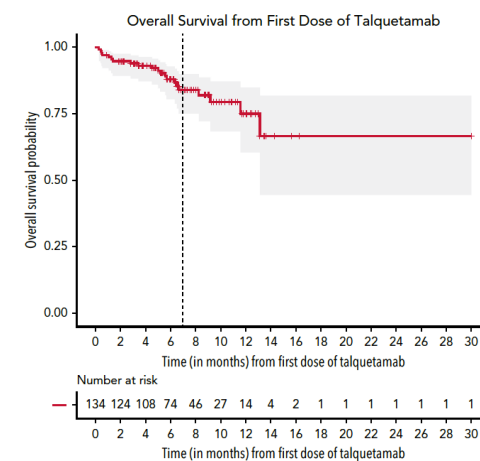
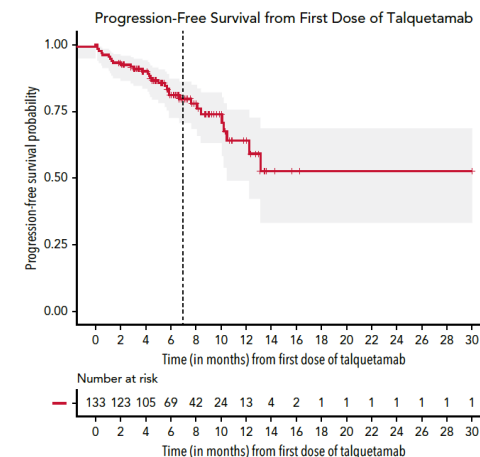
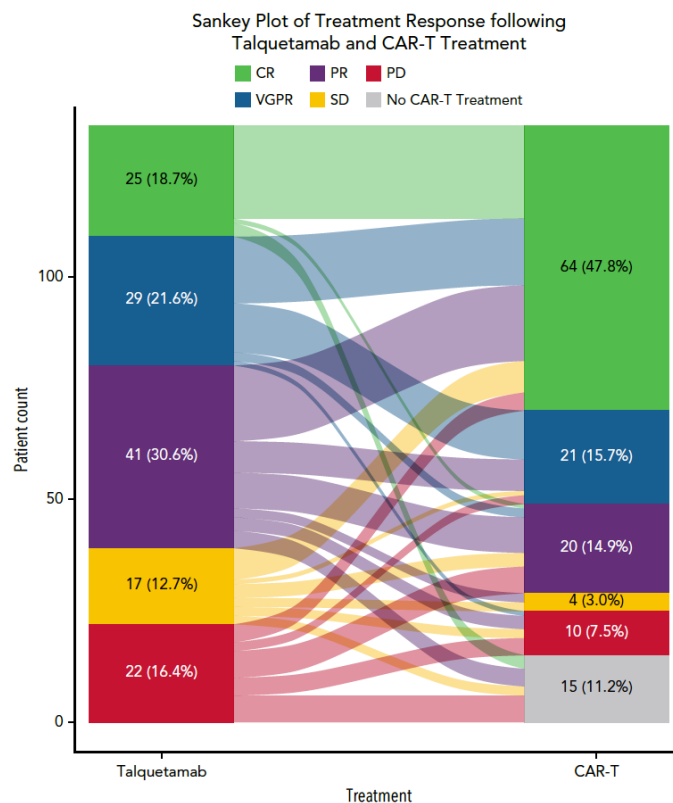


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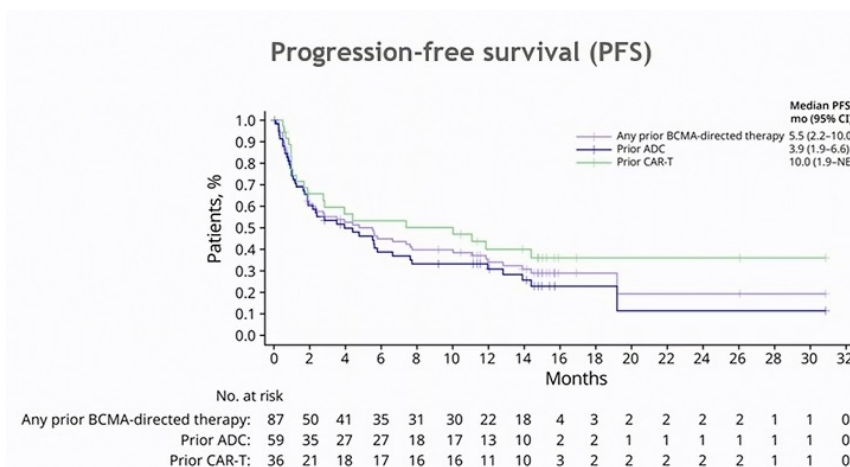
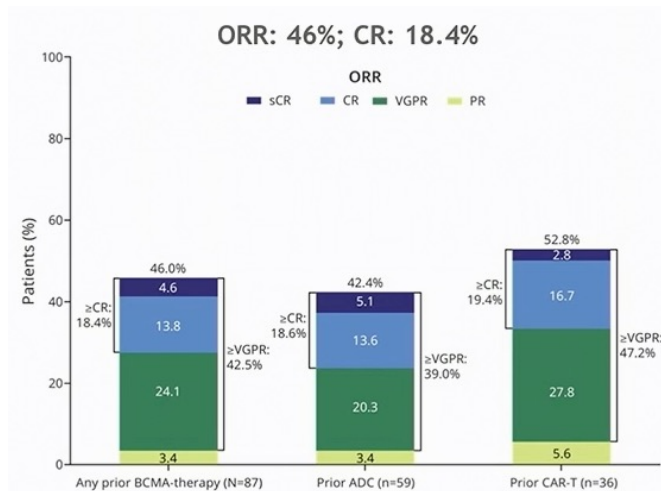
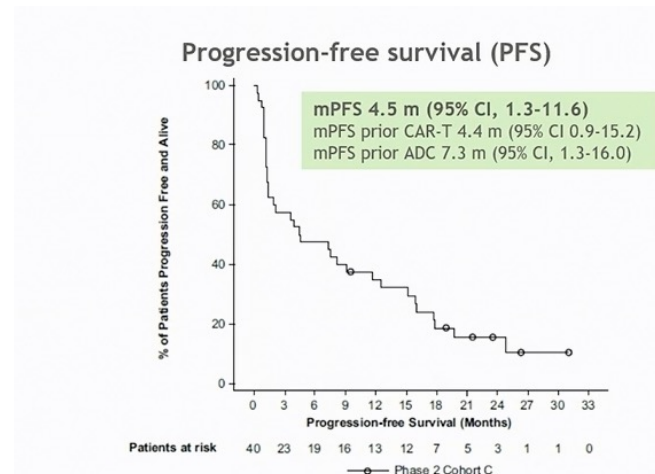
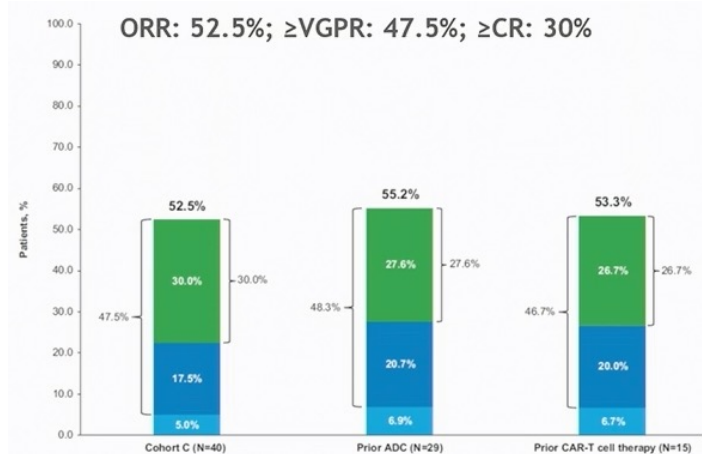


TALQUETAMAB- BRIDGING THERAPY

Characteristics	N = 134 (%)
Age, median (range), y	65 (59-72)
Sex, female	68 (51)
Race	
White	109 (81)
Black	13 (10)
Asian	6 (4)
Other	6 (4)
ECOG, ≤2	132 (99)
High-risk cytogenetics	59 (44)
EMD	55 (41)
Prior BCMA targeted therapy	13 (10)
Ferritin, baseline ≥400 ng/mL	57 (43)
Prior lines of therapy, median (range)	5 (4-6)
Triple class refractory	102 (76)
Penta refractory	46 (34)
Not meeting Cartitude-1 or KarMMA eligibility	114 (85)

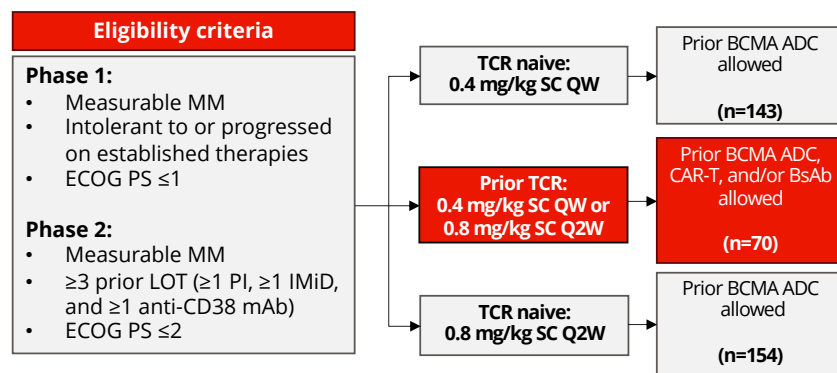
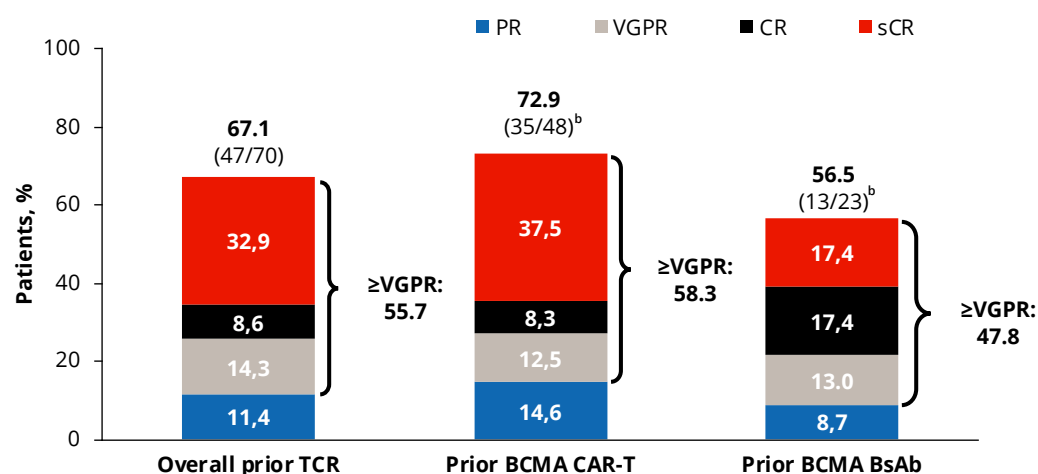
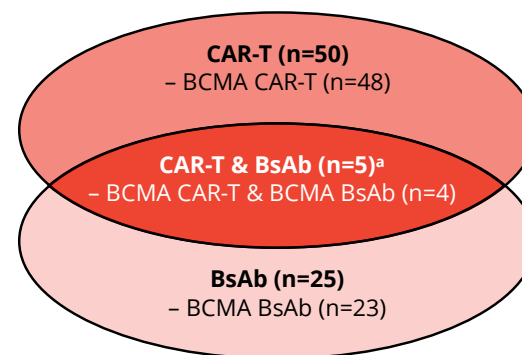


ANTI-BCMA BsAb AFTER ANTI-BCMA TREATMENT



Touzeau C. et al Blood, 2022;
Nooka AJ. et al, ASCO, 2023

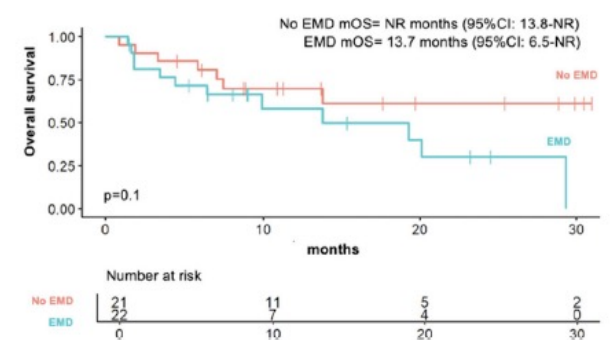
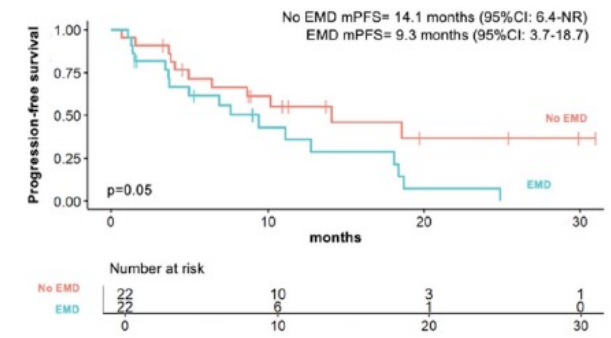
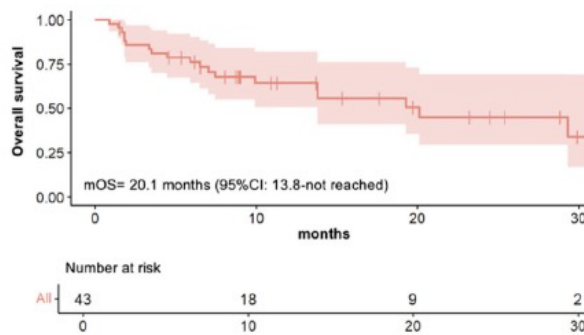
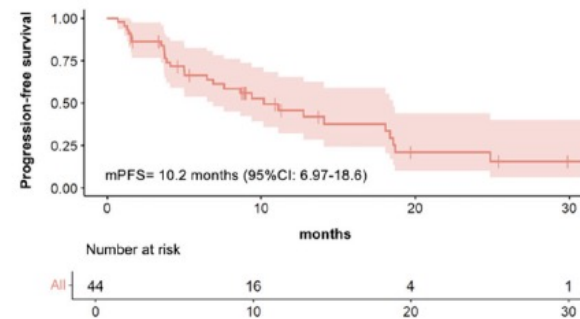
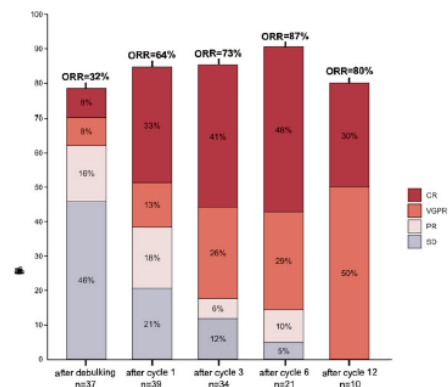
TALQUETAMAB AFTER ANTI-BCMA TREATMENT

ORR^a

Time from last dose of prior BCMA TCR to first dose of talquetamab		ORR, % (n/N)	12-mo DOR rate, % (95% CI)
BCMA CAR-T	<9 mo	93.8 (15/16)	57.1 (27.5–78.5)
	≥9 mo	62.5 (20/32)	53.0 (28.6–72.4)
BCMA BsAb	<9 mo	50.0 (8/16)	50.0 (15.2–77.5)
	≥9 mo	71.4 (5/7)	26.7 (1.0–68.6)

DEBULKING PRE-BISPECIFICO

n(%)	N = 44 patients
Median age, years-old	66 (min-max: 45-82)
Female, n(%)	22 (50)
Median of prior lines	4 (min-max : 2-9)
Triple class refractory, n(%)	41 (93)
ISS score III, n(%)	20 (48)
Cytogenetic abnormalities, n(%)	22 (50)
17p deletion	9 (20)
1q21 gain	5 (11)
t(4; 14)	3 (7)
t(14; 16)	2 (4)
Del1p32	2 (4)
1q21 amplification	1 (2)
Extramedullary disease, n(%)	22 (50)
Number of involved sites, n(%)	
1	4 (9)
2	5 (11)
≥3	10 (23)



- RUOLO E TIMING DEI BISPECIFICI NEL 2025
 - **RUOLO E TIMING DEI BISPECIFICI NEL 202X**
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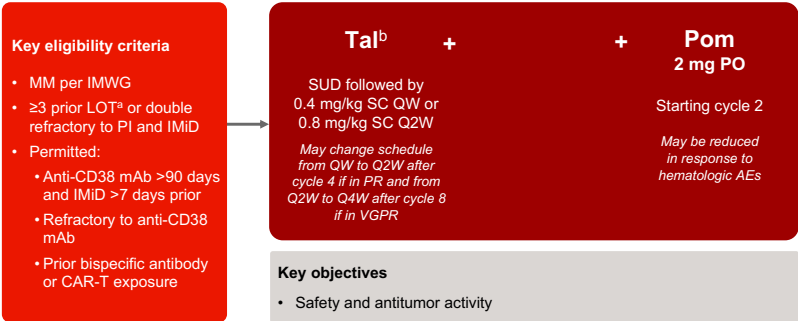
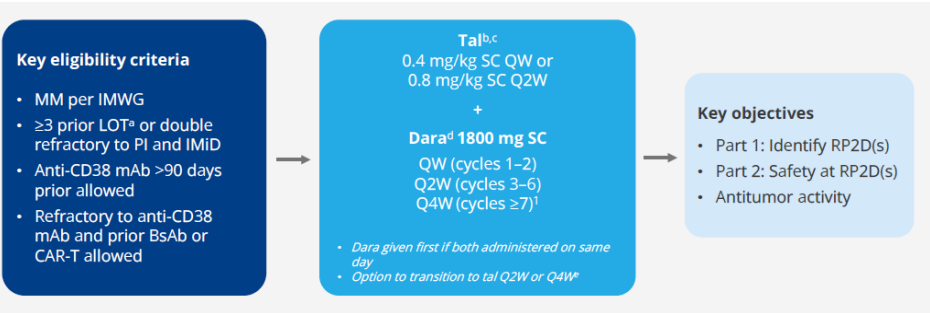
HIGHLIGHTS IN EMATOLOGIA

TREVISO, 7-8 NOVEMBRE 2025

Patients	Study	Phase	Experimental Therapy
R/R MM	MajesTEG1; MMY1001 (NCT04557098)	I	Teclistamab monotherapy
	MajesTEG1; MMY1001-P3 (NCT04557098)	II	Teclistamab monotherapy
	MajesTEG3; MMY3001 (NCT05083169)	III	Teclistamab + daratumumab SC vs DPd or DVd
	MajesTEG9; MMY3006 (NCT05572519)	III	Teclistamab vs. Pvd or Kd
	TRIMM-2; MMY1002 (NCT04108199)	I	Teclistamab or talquetamab + daratumumab S&P
	TRIMM-3; MMY1005 (NCT05338779)	Ib	Teclistamab or talquetamab + PD1 inhibitor
	RedirectT-1; MMY1003 (NCT04586426)	Ib/2	Teclistamab + talquetamab ± daratumumab SC
NDMM	MajesTEG4; MMY3003 (NCT05243797)	III	Teclistamab ± R vs. R (posttransplant maintenance)
	MajesTEG5; MMY2003 (NCT05695508)	II	Teclistamab + DRd ± V (induction) Teclistamab + DR (posttransplant maintenance)
	MajesTEG7; MMY3005 (NCT05552222)	III	Teclistamab + daratumumab SC + R vs DRd
R/R MM and NDMM	MajesTEG2; MMY1004 (NCT04722146)	I	Teclistamab + daratumumab SC + P Teclistamab + daratumumab SC + VR Teclistamab + nirogacestat Teclistamab + R Teclistamab + daratumumab + R

Patients	Study	Phase	Experimental Therapy
R/R MM	MonumenTAL-3 (NCT05455320)	III	Talquetamab + daratumumab SC + P
	MonumenTAL-1 (NCT04634552)	II	Talquetamab monotherapy
	MonumenTAL-1 (NCT03399799)	I	Talquetamab monotherapy
	TRIMM-3; MMY1005 (NCT05338775)	Ib	Talquetamab or teclistamab + PD-1 inhibitor
	TRIMM-2; MMY1002 (NCT04108195)	I	Talquetamab + daratumumab SC ± P
	RedirectT-1; MMY1003 (NCT04586426)	Ib/2	Talquetamab + teclistamab Talquetamab + teclistamab + daratumumab SC
	MonumenTAL-6; MMY3009 (NCT06208150)	III	Talquetamab SC + P PO ± d PO/IV Talquetamab SC + teclistamab SC ± d PO/IV Elotuzumab IV + P PO + d PO or bortezomib SC + P PO + d PO
MM	MonumenTAL-2; MMY1004 (NCT05050097)	Ib	Talquetamab + K Talquetamab + daratumumab + K Talquetamab + R Talquetamab + daratumumab + R Talquetamab + P
	Talisman; MMY2006 (NCT06500884)	II	Talquetamab monotherapy SC Talquetamab SC + prophylaxis A/B/C PO

TAL+DARA±POMA/TRIMM-2

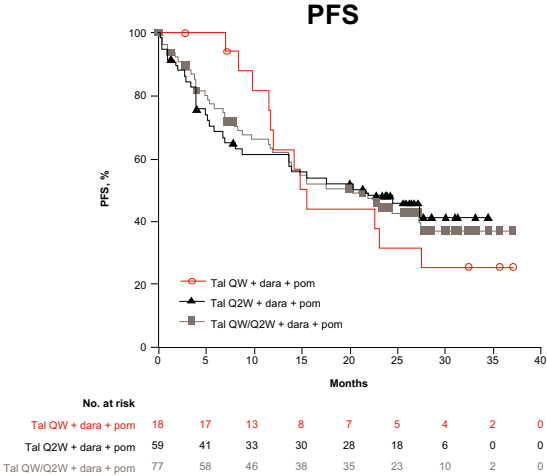
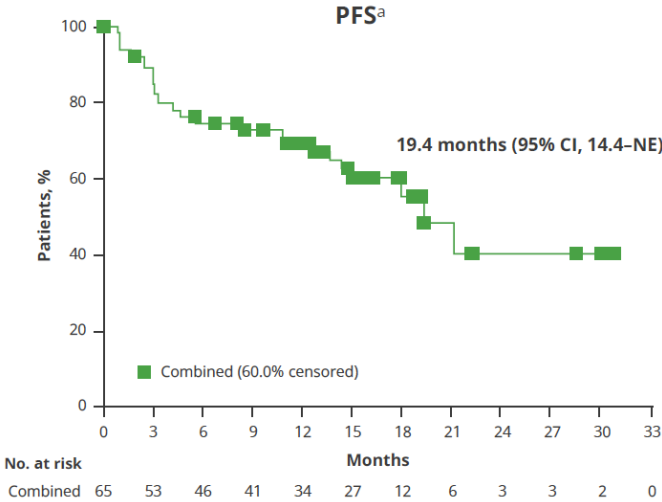
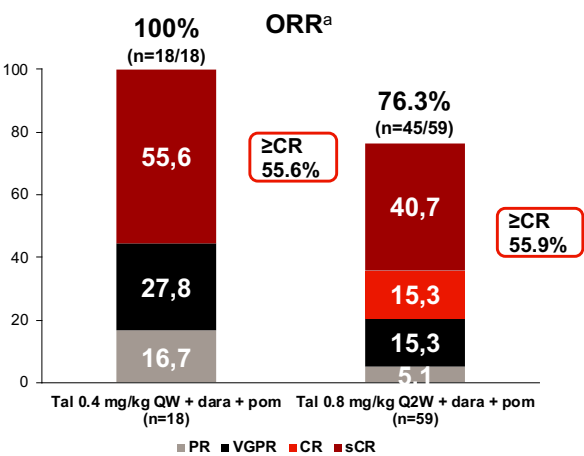
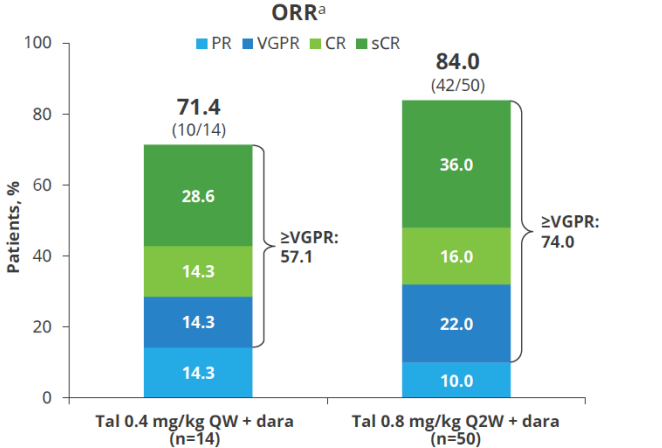


Parameter	Tal 0.4 mg/kg QW + dara (n=14)	Tal 0.8 mg/kg Q2W + dara (n=51)
Median (range) follow-up, mo	16.8 (1.9–31.0)	15.0 (1.0–23.3)
Median (range) time to first response, mo	1.0 (0.9–2.4)	1.0 (0.9–8.3)
ORR in anti-CD38, n (%)		
Naïve	3/3 (100.0)	5/5 (100.0)
Exposed	7/11 (63.6)	37/45 (82.2)
Refractory	7/11 (63.6)	32/40 (80.0)
ORR in T-cell redirection therapy ^b exposed, n (%)	4/6 (66.7) ^c	15/19 (78.9)
CAR-T	1/2 (50.0)	8/9 (88.9)
BsAb	4/5 (80.0)	7/10 (70.0)

Characteristic	Tal 0.4 mg/kg QW + dara + pom (n=18)	Tal 0.8 mg/kg Q2W + dara + pom (n=59)
Prior LOT (n), median (range)	6 (3–11)	6 (1–17)
Prior stem cell transplantation, n (%)	16 (88.9)	50 (84.7)
Prior therapies, n (%)		
Anti-CD38	17 (94.4)	55 (93.2)
IMiD	18 (100.0)	59 (100.0)
Triple class ^d	17 (94.4)	55 (93.2)
Penta drug ^e	12 (66.7)	41 (69.5)
BCMA-targeted therapy	13 (72.2)	40 (67.8)
CAR-T	5 (27.8)	19 (32.2)
Bispecific antibody ^f	6 (33.3)	17 (28.8)
ADC	3 (16.7)	12 (20.3)
Refractory status, n (%)		
Anti-CD38 ^g	15 (83.3)	49 (83.1)
Pom	13 (72.2)	45 (76.3)
Triple class ^d	15 (83.3)	45 (76.3)
Penta drug ^e	4 (22.2)	20 (33.9)
Any prior bispecific antibody	7 (38.9)	22 (37.3)
To last line of therapy	17 (94.4)	53 (89.8)

Bahilis N. et al, EHA, 2023; Bahilis N. et al, IMS, 2024

TAL+DARA±POMA/TRIMM-2

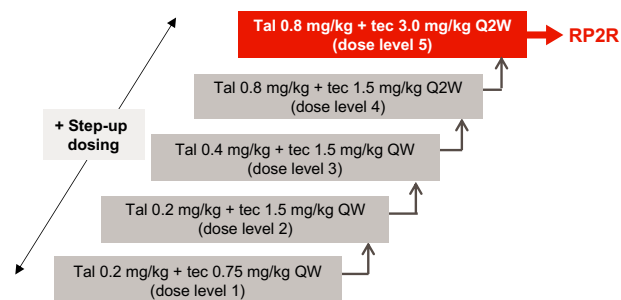


Parameter	Tal 0.4 mg/kg QW + dara + pom (n=18)	Tal 0.8 mg/kg Q2W + dara + pom (n=59)
Median (range) follow-up, months	15.8 (3.2–37.9)	17.5 (0.2–37.7)
Median PFS, months (95% CI)	15.4 (11.5–27.5)	20.3 (7.9–NE)
12-month PFS, % (95% CI)	62.7 (35.1–81.3)	61.1 (47.1–72.4)

Bahilis N. et al, EHA, 2023; Bahilis N. et al, IMS, 2024

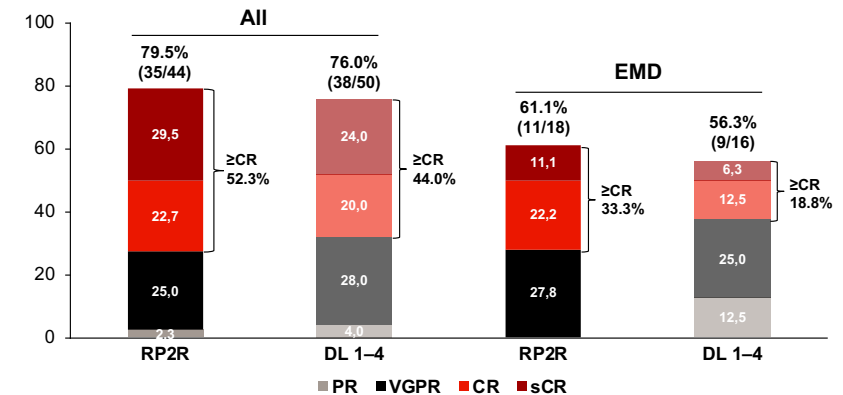
REDIRECTT-1

Phase 1 dose escalation

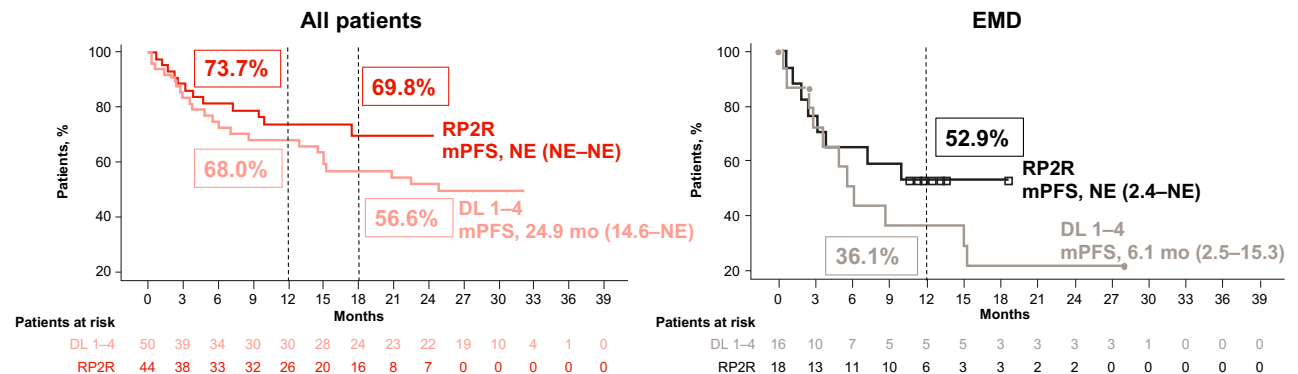


Characteristic	RP2R (n=44)	All doses (N=94)
Median prior LOT, n (range)	4.0 (2–10)	4.0 (1–11)
Exposure status, n (%)		
Belantamab mafodotin	5 (11.4)	18 (19.1)
CAR-T therapy ^d	2 (4.5)	4 (4.3)
Bispecific antibody ^e	2 (4.5)	7 (7.4)
Any BCMA-directed therapy	9 (20.5)	27 (28.7)
Triple-class	44 (100.0)	94 (100.0)
Penta-drug	28 (63.6)	61 (64.9)
Refractory status, n (%)		
Proteasome inhibitor	41 (93.2)	85 (90.4)
Immunomodulatory drug	41 (93.2)	91 (96.8)
Anti-CD38	43 (97.7)	93 (98.9)
Triple-class	37 (84.1)	81 (86.2)
Penta-drug	13 (29.5)	31 (33.0)
To last line of therapy	39 (88.6)	87 (92.6)

ORR (all treated patients)^b



Progression-free survival



REDIRECTT-1- Phase 2

Key eligibility criteria

EMD defined as:
 ≥ 1 nonradiated bone-independent soft tissue plasmacytoma ≥ 2 cm in greatest dimension confirmed by central review of PET-CT scans^{a,b}

- MM per IMWG criteria
- Triple-class exposed^c RRMM
- Prior CAR-T ($\leq 20\%$ patients) and BsAb therapy permitted
 - BsAbs could not target GPRC5D or BCMA
- Nonsecretory/oligosecretory disease permitted

**Step up doses^d
 administered
 2–4 days apart**

Tal 0.4 mg/kg
 Tec 1.5 mg/kg

Tal 0.06 mg/kg
 Tec 0.3 mg/kg

Tal 0.01 mg/kg
 Tec 0.06 mg/kg

**Tal 0.8 mg/kg
 Q2W SC +
 Tec 3.0 mg/kg
 Q2W SC^d
 until disease
 progression**

Primary endpoint

- ORR^e (EMD response assessed by central radiology review of whole-body PET-CT scans)

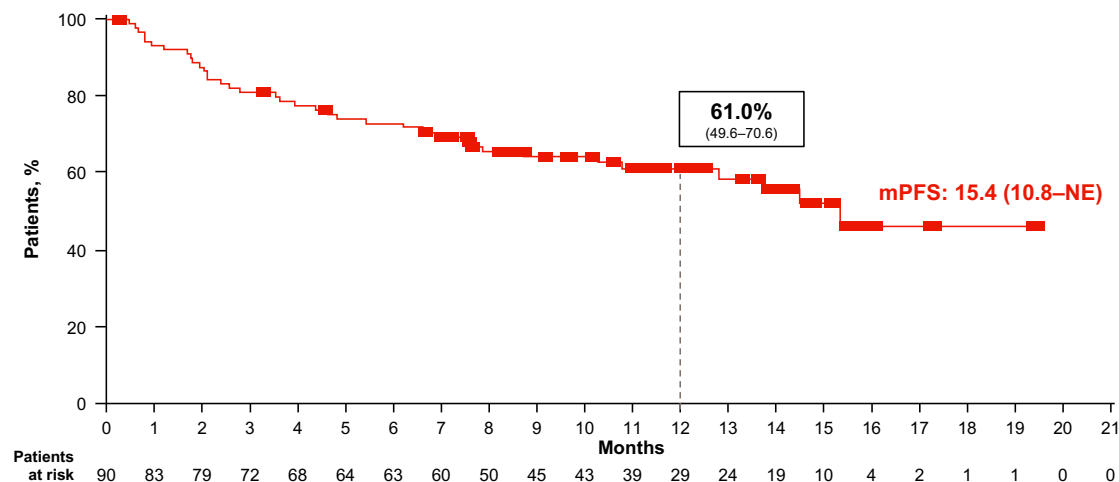
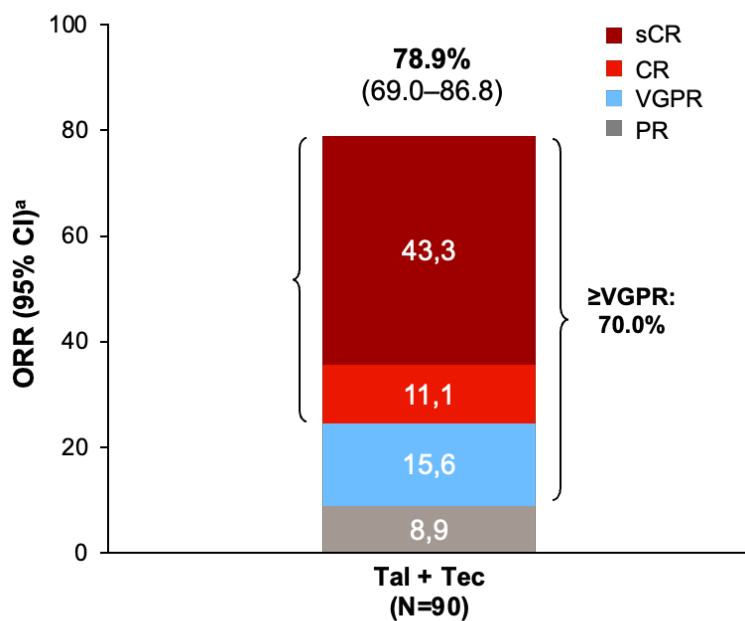
Secondary endpoints

- $\geq$ VGPR, $\geq$ CR, and sCR rate^e
- Time to response,^e DOR,^e PFS, and OS
- Safety
- PK, immunogenicity

Characteristic	Tal + Tec (N=90)
Median age, years (range)	64.5 (42–84)
Male, n (%)	57 (63.3)
Race, n (%)	
White	64 (71.1)
Black/African American	8 (8.9)
Asian	13 (14.4)
Not reported	5 (5.6)
True extramedullary plasmacytomas ≥ 1 , ^a n (%)	90 (100) ^b
Number of extramedullary plasmacytomas, ^a median (range)	2 (1–7)
Number of extramedullary plasmacytomas, ^a n (%)	
1	38 (42.2)
2–3	29 (32.2)
≥ 4	23 (25.6)
High-risk cytogenetics, ^c n (%)	14 (21.5)
Measurable disease, ^d n (%)	
Nonsecretory	4 (4.4)
Oligosecretory	31 (34.4)

Characteristic	Tal + Tec (N=90)
ECOG performance status, n (%)	
0	32 (35.6)
1	50 (55.6)
2	8 (8.9)
Years since diagnosis, median (range) ^e	4.7 (0.7–21.4)
Median prior LOT, n (range)	4.0 (1–10)
Exposure status, n (%)	
Belantamab mafodotin	11 (12.2)
Anti-BCMA CAR-T therapy	18 (20.0)
BsAb therapy ^f	8 (8.9)
Triple-class	90 (100)
Penta-drug	51 (56.7)
Refractory status, n (%)	
PI	86 (95.6)
IMiD	84 (93.3)
Anti-CD38 monoclonal antibody	85 (94.4)
Triple-class	76 (84.4)
Penta-drug	32 (35.6)
To last LOT	75 (83.3)

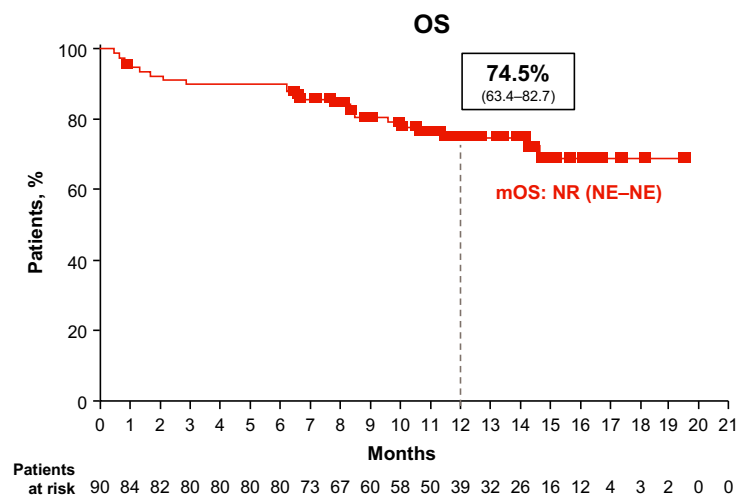
REDIRECTT-1- Phase 2



In context of other therapies

mPFS in patients with triple-class exposed RRMM with EMD:

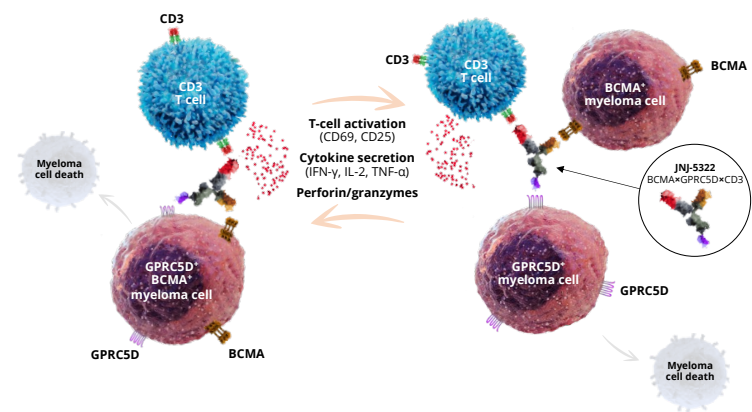
- Standard-of-care therapies^a: **<3 months¹**
- Approved BsAbs^b: **<6 months²**



HIGHLIGHTS IN EMATOLOGIA

TREVISO, 7-8 NOVEMBRE 2025

TRISPECIFICO ANTI-CD3/BCMA/GPR5D



N=147 all doses investigated (all SC)	
Dose Escalation	Dose Optimization
5 mg → 40–120 mg Q4W	5 mg → 50 mg Q4W
3.6/5.0 mg → 10–30 mg Q2W	5 mg → 100 mg Q4W
MABEL 0.4–10 mg Q2W	5 mg → 100 mg → 300 mg Q4W
	Loading Dose/Schedule Optimization
	5 mg → 200 mg Q4W ^b → 100 mg Q4W
	5 mg → 100 mg Q8W
	5 mg → 200 mg Q8W ^c → 100 mg Q8W

Optimization for Outpatient Dosing
Lower (2.5 mg) vs higher (10 mg) SUD
2–4 vs 6–8 days between step-up and full dose
Prophylactic tocilizumab

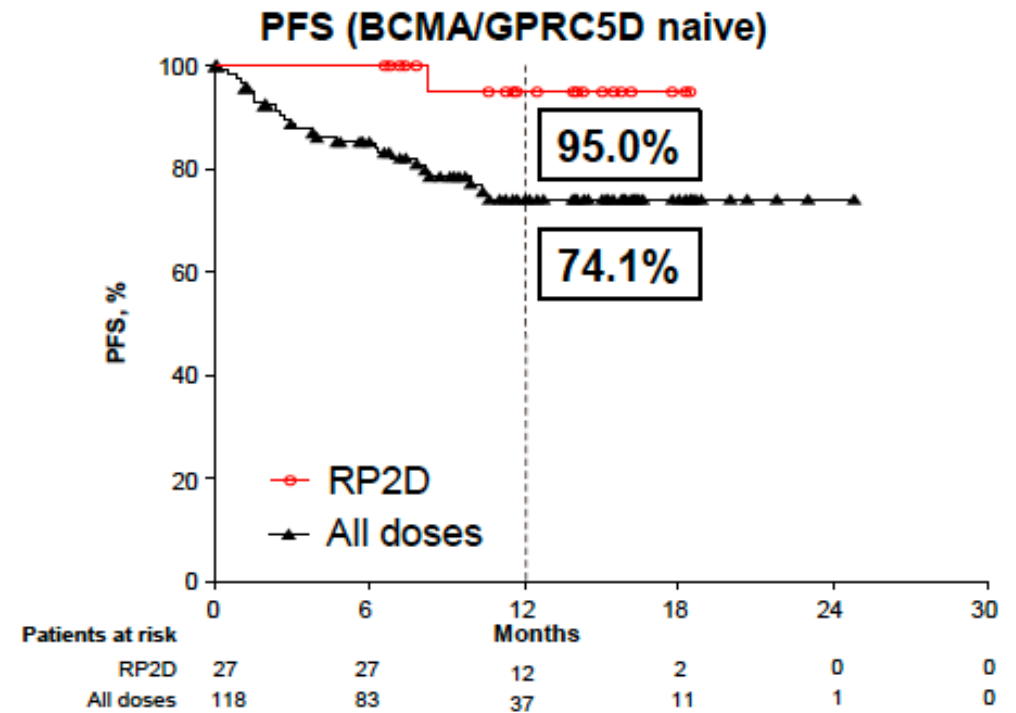
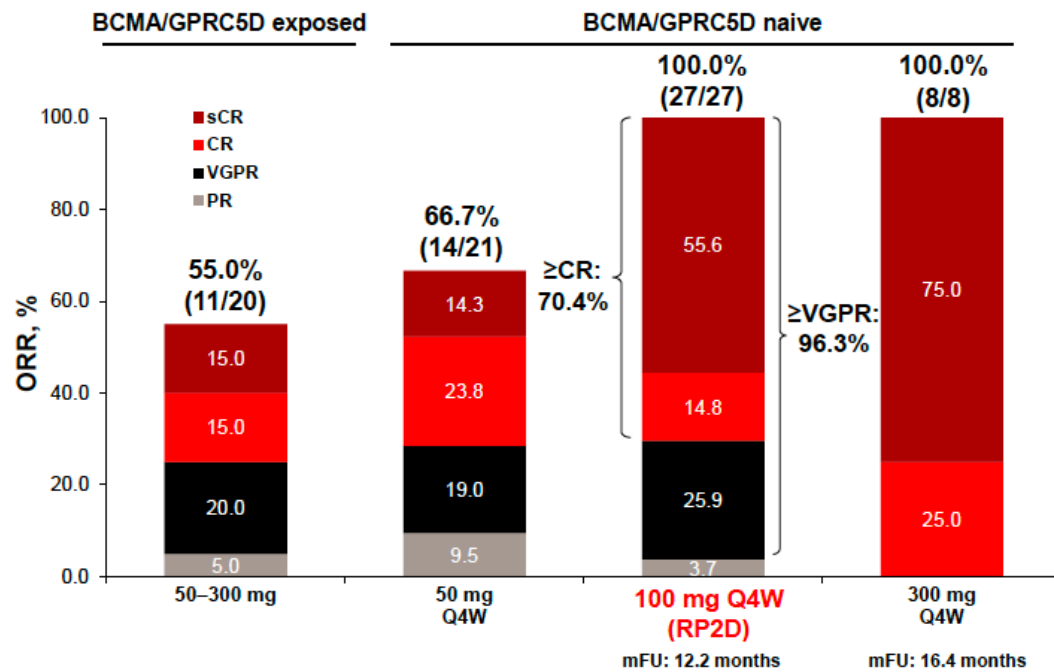
RP2D identification

5 mg SC → 100 mg Q4W SC

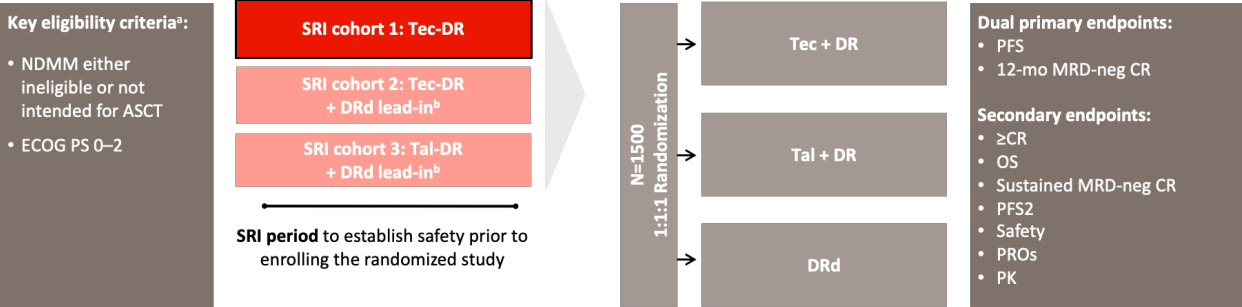
Characteristic	RP2D (n=36)	All doses (N=147)
Median follow-up, months (range)	11.6 (0.4–18.6)	9.3 (0.3–25.8)
Median age, years (range)	67.5 (43–87)	64.0 (39–87)
Male, n (%)	22 (61.1)	87 (59.2)
Race, n (%)		
White	28 (77.8)	110 (74.8)
Black/African American	1 (2.8)	13 (8.8)
Asian	1 (2.8)	7 (4.8)
Multiple	2 (5.6)	2 (1.4)
Unknown/not reported	4 (11.1)	15 (10.2)
Extramedullary plasmacytomas ≥1, ^a n (%)	3 (8.3)	16 (10.9)
High-risk cytogenetics, ^b n (%)	9 (27.3)	39 (31.2)
ISS stage, ^c n (%)		
I	19 (52.8)	77 (53.1)
II	12 (33.3)	50 (34.5)
III	5 (13.9)	18 (12.4)
Years since diagnosis, ^d median (range)	7.0 (0.9–18.7)	6.9 (0.7–31.9)

Characteristic	RP2D (n=36)	All doses (N=147)
Median prior LOT, n (range)	4.0 (2–11)	4.0 (1–11)
Exposure status, n (%)		
Triple-class ^a	36 (100.0)	147 (100.0)
Penta-drug ^f	15 (41.7)	72 (49.0)
BCMA/GPRC5D exposed	9 (25.0)	29 (19.7)
Prior BCMA	8 (22.2)	26 (17.7)
Prior GPRC5D	1 (2.8)	5 (3.4)
BCMA/GPRC5D naive	27 (75.0)	118 (80.3)
Antibody-drug conjugate	2 (5.6)	7 (4.8)
CAR-T therapy	4 (11.1)	12 (8.2)
Bispecific antibody	6 (16.7)	16 (10.9)
Refractory status, n (%)		
PI	19 (52.8)	86 (58.5)
IMiD	36 (100.0)	136 (92.5)
Anti-CD38	36 (100.0)	138 (93.9)
Triple-class ^a	19 (52.8)	79 (53.7)
Penta-drug ^f	2 (5.6)	10 (6.8)
To last LOT	34 (94.4)	132 (89.8)

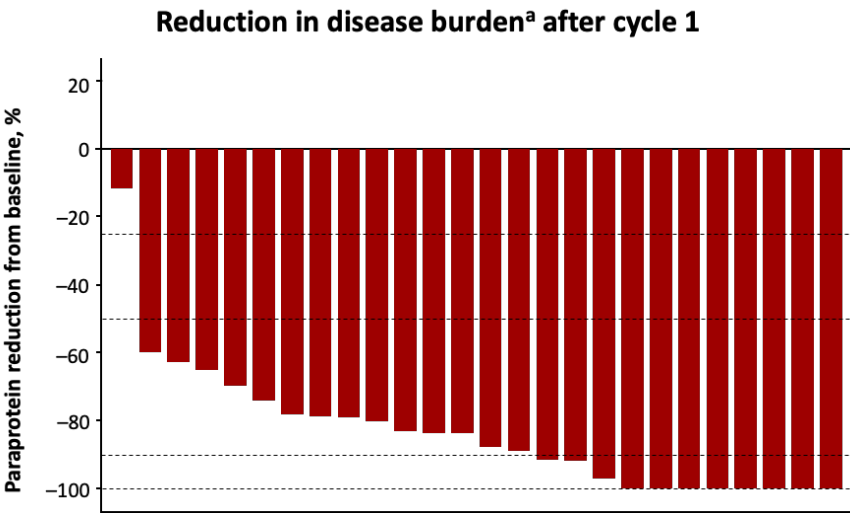
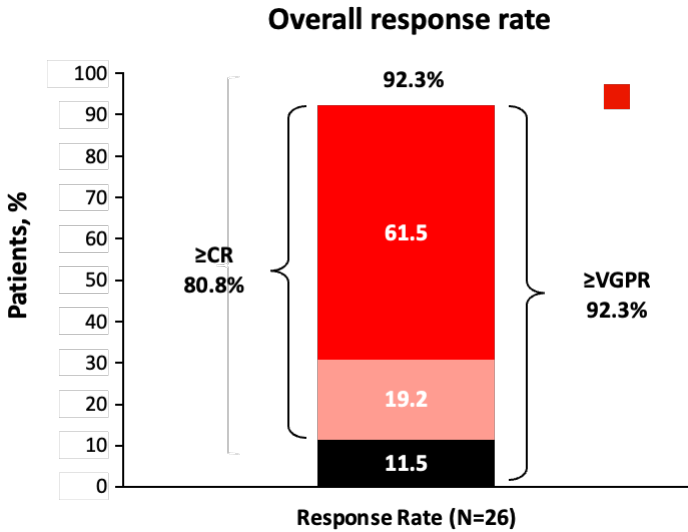
TRISPECIFICO ANTI-CD3/BCMA/GPR5D



TEC-DR/TAL-DR : MAJESTEC-7

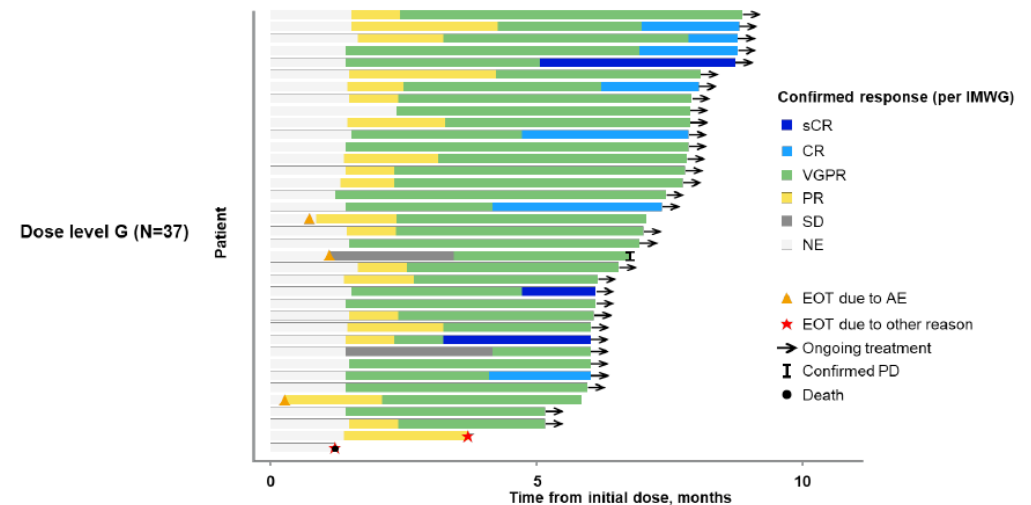
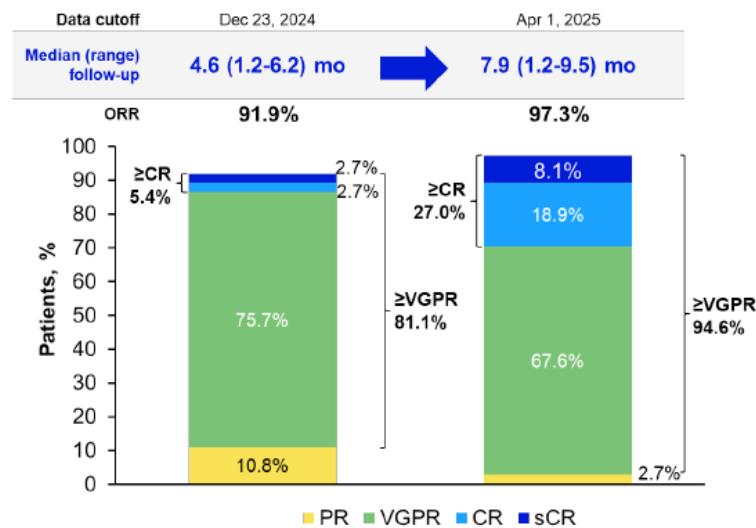
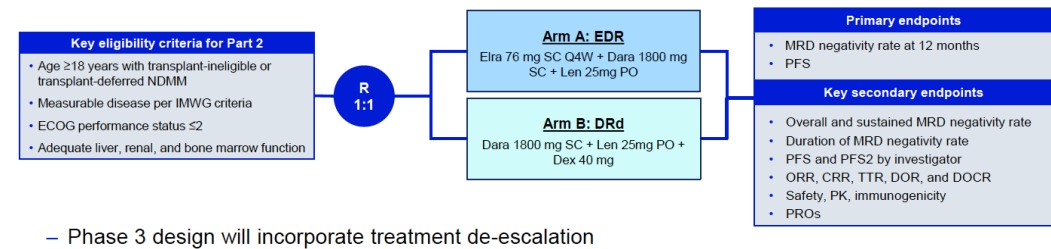
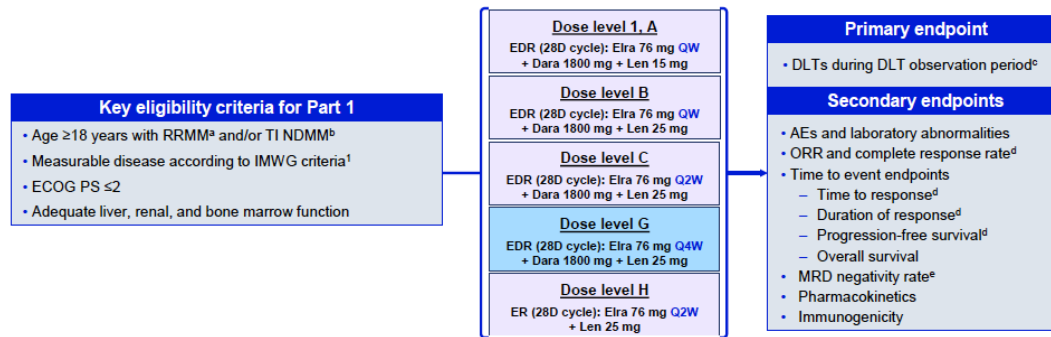


SRI cohort 1: Tec-DR	mFU	Cycle 1	Cycle 2	Cycle 3–6	Cycle 7+ until PD
	13.8 mo (range, 2.0–15.4)	Tec step-up ^c + D	Tec 1.5 mg/kg QW + DR	Tec 3 mg/kg Q2W + DR	Tec 3 mg/kg Q4W + DR



Touzeau C. et al, ASCO, 2024

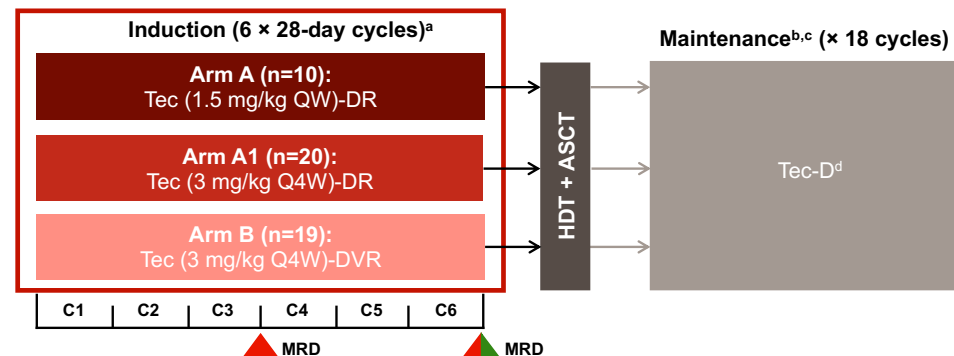
ELRA-DRD /MAGNETISMM-6



MAJESTEC-5/ GMMG-HD10/DSMM-XX

Key eligibility criteria:

- TE NDMM
- ECOG PS score of 0-2
- Aged 18-70 years



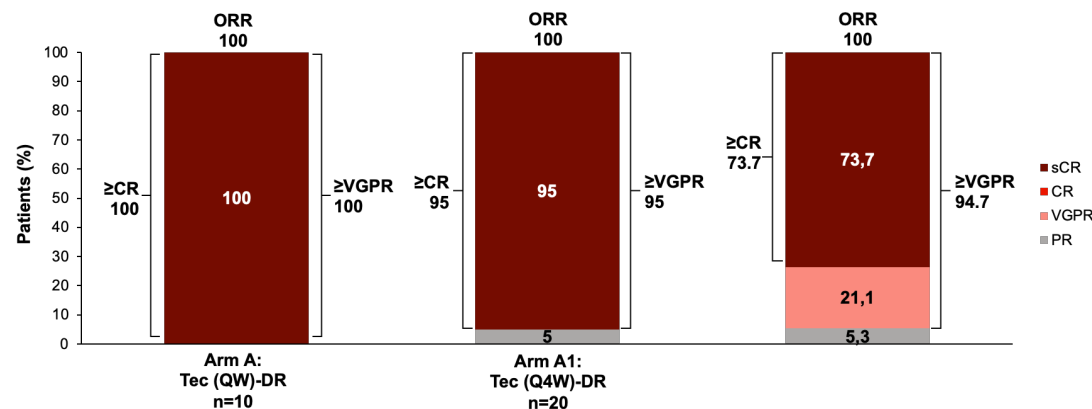
Primary endpoints:

- AEs, SAEs

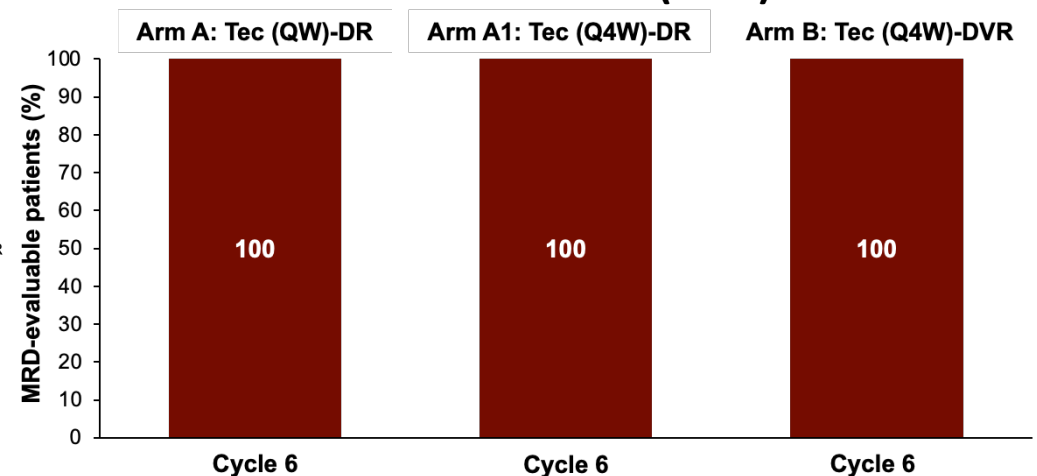
Select secondary endpoints:

- MRD negativity (10^{-5} and 10^{-6})
- ORR
- $\geq$ CR
- $\geq$ VGPR
- Stem cell yield

- ▲ MRD 10^{-5} via NGF
- ▲ MRD 10^{-6} via NGS



MRD: 10^{-6} (NGS)



MAJESTEC-4/EMN30

SRI

Key eligibility criteria:

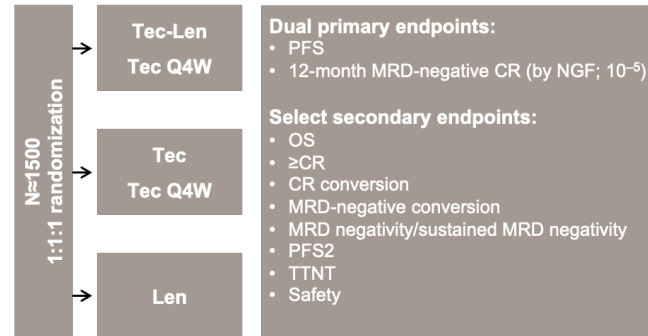
- NDMM
- ECOG PS score of 0-2
- Received 4-6 cycles of 3- or 4-drug induction therapy (PI and/or IMiD ± anti-CD38 antibody) and ASCT^a ± consolidation with ≥PR

SRI Cohort 1: Tec-Len
Tec QW → Q4W

SRI Cohort 2: Tec-Len
Tec Q4W

SRI Cohort 3: Tec
Tec Q4W

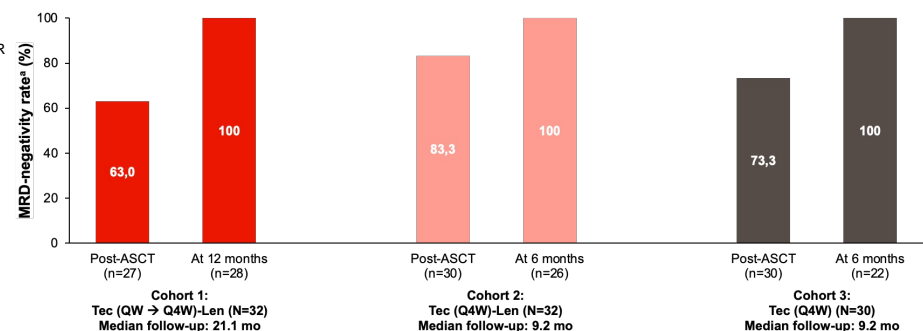
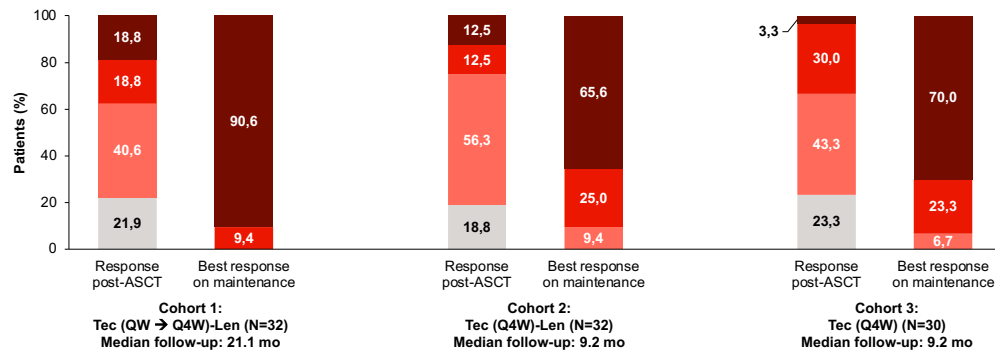
Phase 3, randomized study



≥CR rate 37.6% → 100%

25.0% → 90.6%

33.3% → 93.3%



CONCLUSIONI

- Anticorpi bispecifici rappresentano insieme ai CAR-T la terapia di prima scelta nei pazienti TCE/TCR
- Importante un sequencing adeguato
 - Tal → CAR-T anti BCMA
 - BsAb → BsAb (adeguato intervallo libero)
- Futuro degli anticorpi bispecifici:
 - studi di combinazione → TEC+TAL, anticorpi trispecifici
 - terapia di prima linea (mantenimento)