BISPECIFIC ANTIBODIES FOR EARLY RELAPSED MM… AND BEYOND.

Roberto Mina, MD

Associate Professor

Winship Cancer Institute, Emory University

EMORY WINSHIP CANCER INSTITUTE
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Disclosures

Consultant	Janssen, Sanofi
Honoraria	Amgen, Celgene-Bristol-Myers Squibb, Janssen, Takeda, Menarini-Stemline, Sanofi, Pfizer, GSK, Abbvie
Scientific Advisory Board	Amgen, Celgene-Bristol-Myers Squibb, Janssen, Takeda, Pfizer, Sanofi, GSK

Treatment options for patients with RRMM as early as second relapse: EHA-EMN 2025 guidelines

Cilta-cel [I,A]

BelaVd [I,A]
BelaPd [I,A]

Dara-Pd [I,A]
Isa-Pd [I,A]
DaraKd [I,A]
IsaKd [I,A]

3L, third-line; 4L, fourth-line; ADC, antibody-drug conjugate; B, belantamab mafodotin; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; d, dexamethasone; Dara, daratumumab; Elo, elotuzumab; GPRC5D, G-protein coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; Isa, isatuximab; K, carfilzomib; mAb, monoclonal antibody; MoA, mechanism of action; P, pomalidomide; PI, proteasome inhibitor; R, lenalidomide; RRMM, relapsed/refractory multiple myeloma; Sel, selinexor; TCE, triple class-exposed; V, bortezomib.

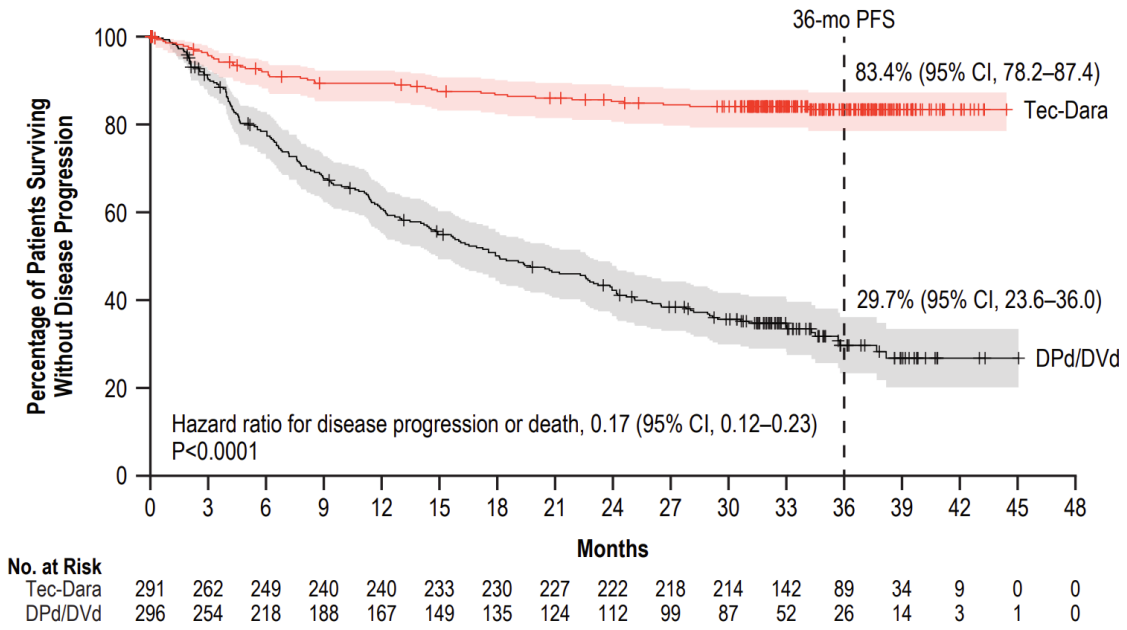
1. Dimopoulos M, et al. Nat Rev Clin Oncol 2025;22:680–700.

MajesTEC-3: Tec-Dara improved PFS and OS vs DPd/DVd[1,2]

Median follow-up: 34.5 months[1]

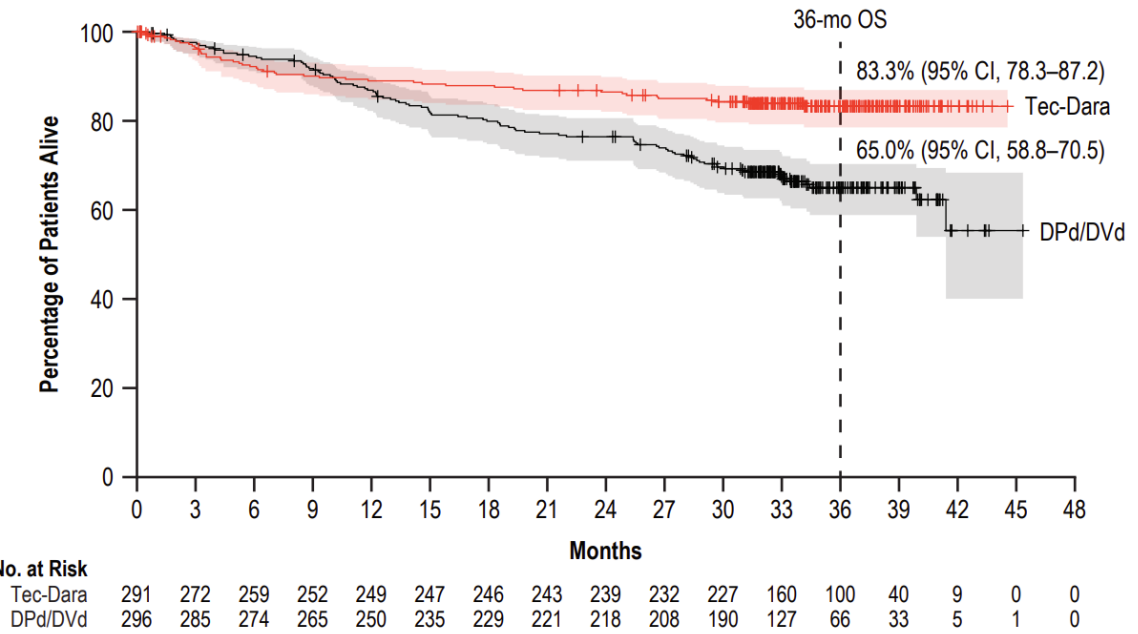
587 pts, 100% len exposed (83% refractory), 5% Anti-CD38 exposed

PFS[1]



Median PFS was NR for Tec-Dara vs 18.1 months for DPd/DVd (HR, 0.17; 95% CI, 0.12–0.23; p<0.0001)[1]

OS[1]



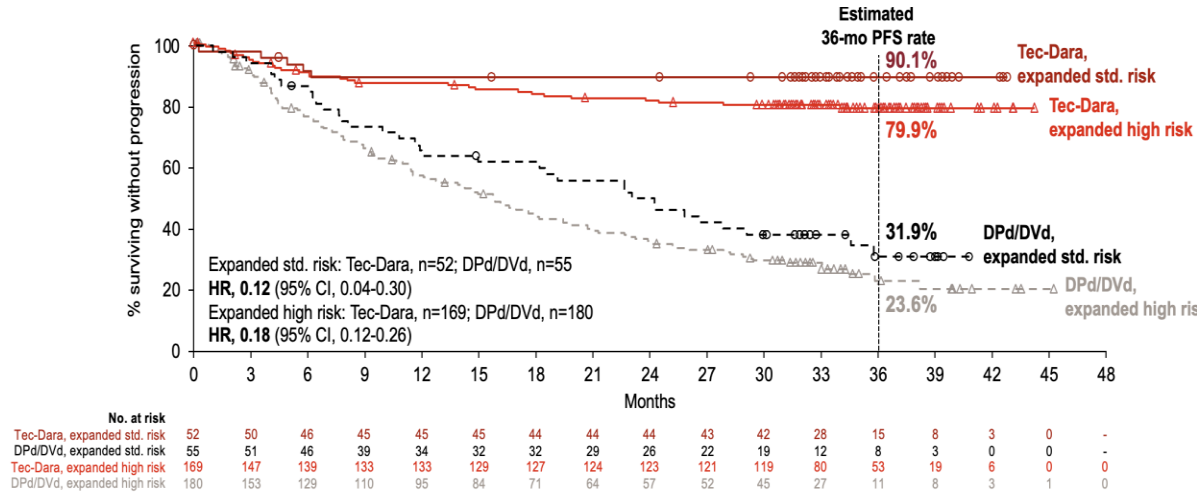
Median OS: NR in either treatment arm (HR, 0.46; 95% CI, 0.32–0.65; p<0.0001)[1,2]

CI, confidence interval; D/Dara, daratumumab; d, dexamethasone; HR, hazard ratio; NR, not reached; mo, month; OS, overall survival; P, pomalidomide; PFS, progression-free survival; Tec, teclistamab; V, bortezomib.

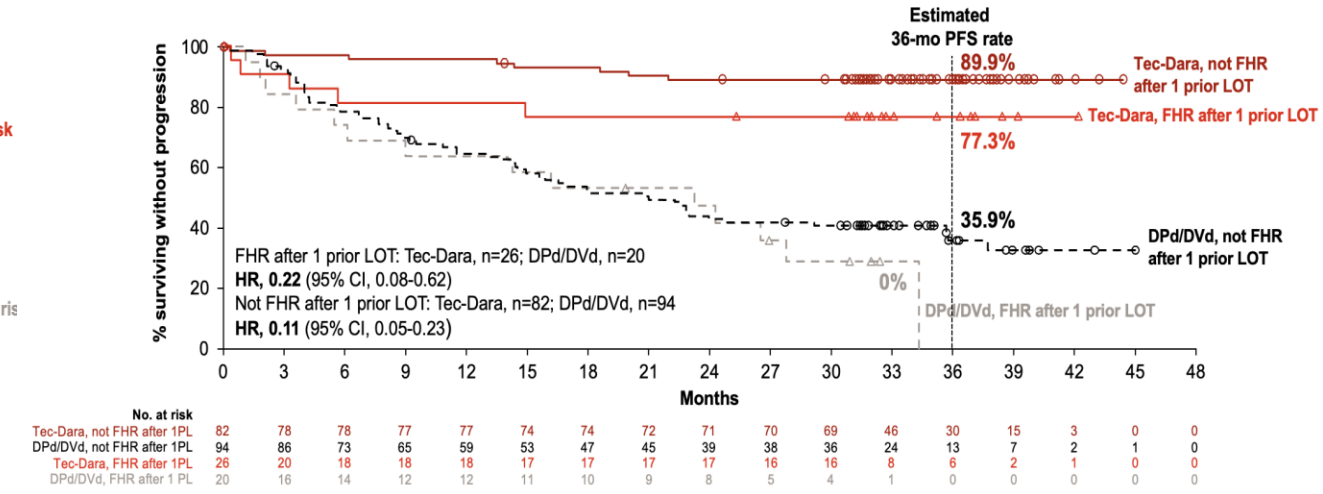
1. Costa LJ, et al. N Engl J Med. 2026;394:739–752; 2. Costa LJ, et al. N Engl J Med. 2026;394:739-752 (supplementary appendix).

Tec-Dara for patients with high-risk MM: MajesTec-3 study

PFS by Expanded[a] Cytogenetic Risk



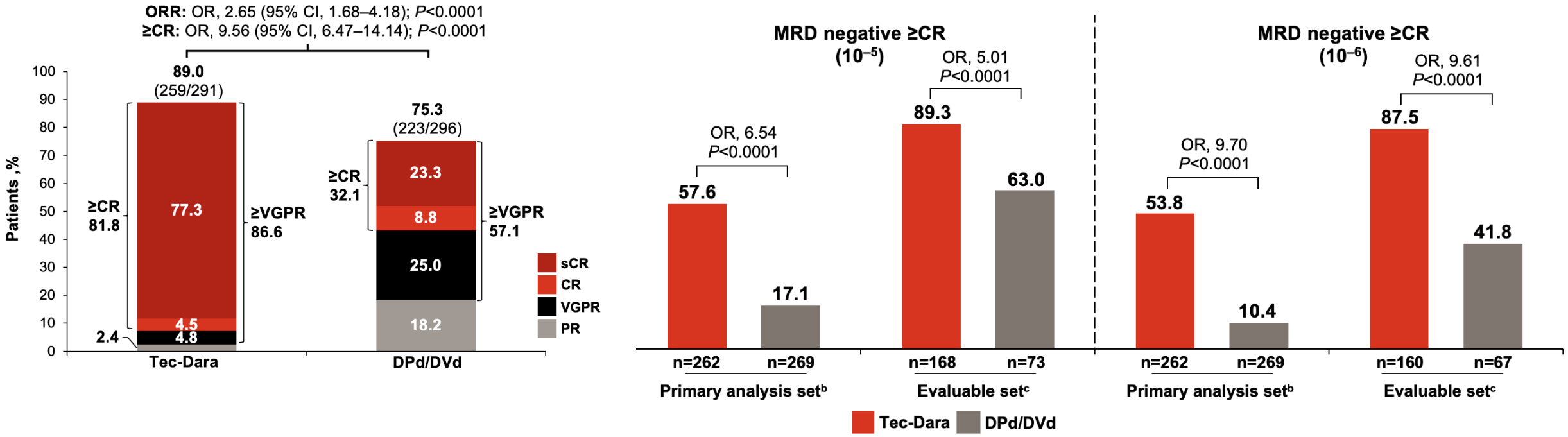
PFS by Functional High-Risk



[a]Expanded standard risk: none of del(17p), t(4;14), t(14;16), amp(1q21), or gain(1q21). Expanded high risk: ≥1 of del(17p), t(4;14), t(14;16), amp(1q21), or gain(1q21).

Banerjee R. et al, EHA26

MajesTEC-3: Tec-dara improved CR and MRD rates vs DPd/DVd



Costa L. et al, NEJM 2025

MajesTEC9: teclistamab monotherapy improved PFS and OS vs SOC in RRMM exposed and refractory to lenalidomide and anti-CD38 Ab

Key inclusion criteria

- RRMM
- 1–3 prior LOTs including an anti-CD38 mAb and lenalidomide
- ECOG PS score of 0–2

Key exclusion criteria

- Prior BCMA-directed therapy

1:1 randomization N=593

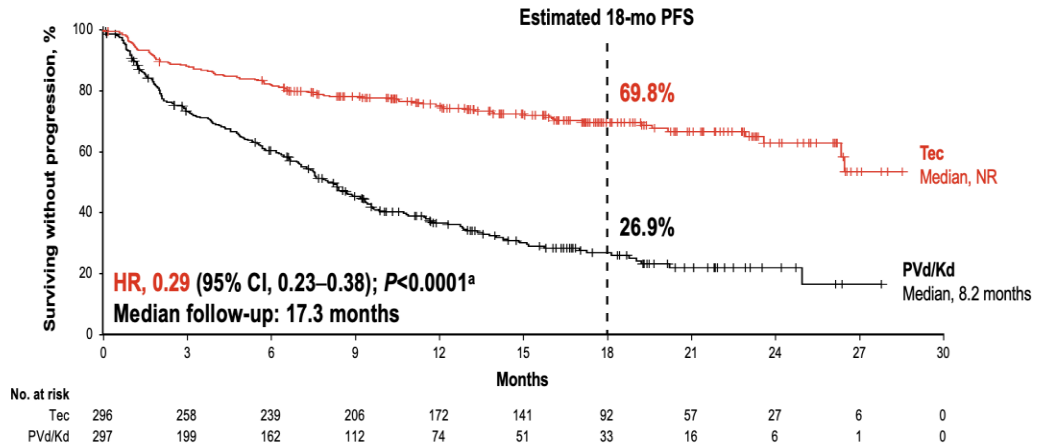
April 28, 2023–April 3, 2025

Tec n=296

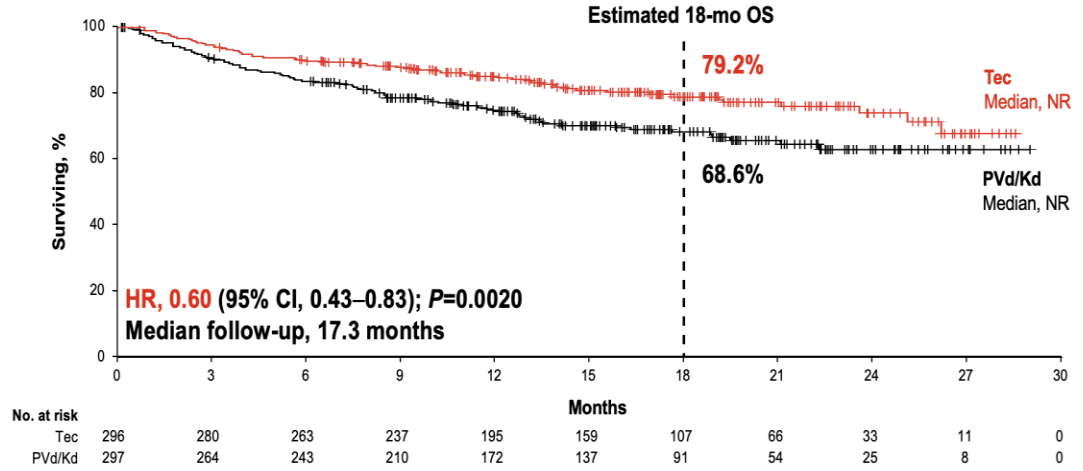
PVd/Kd[a] by investigator's choice n=297 (69% Kd)

80% len refractory and 85% Anti-CD38 refractory

Progression-free survival



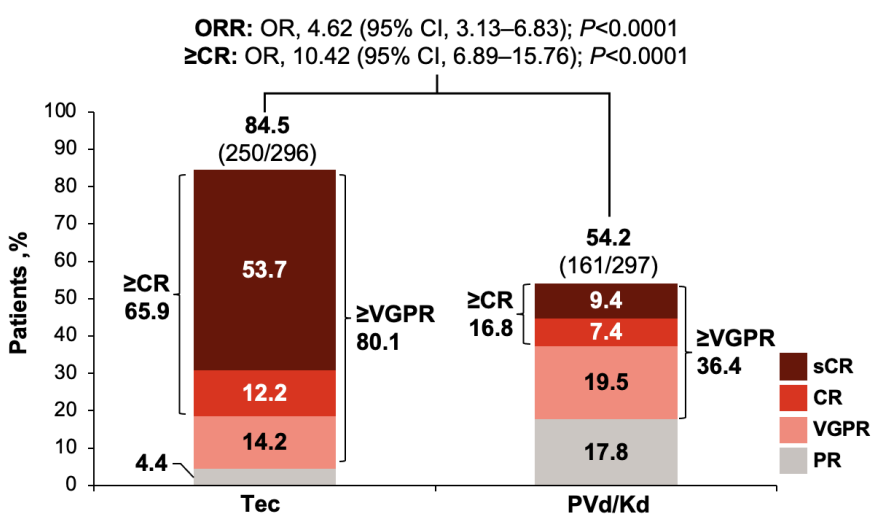
Overall survival

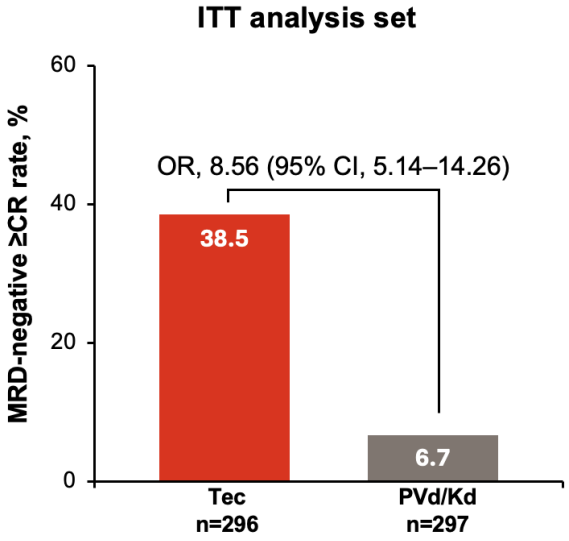


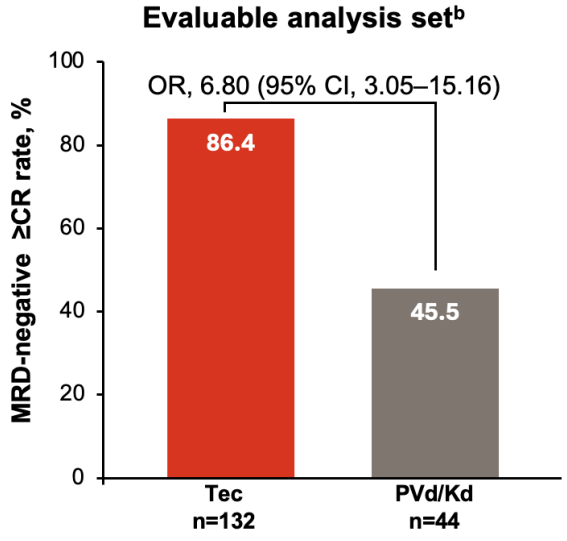
2/3 of pts received CART/bispecific antibodies in subsequent lines of therapying the SOC arm

Mina R. et al ASCO2026; Touzeau C et al, NEJM 2026

Teclistamab monotherapy improved responses and MRD negativity vs SOC in RRMM







Mina R. et al ASCO2026; Touzeau C et al, NEJM 2026

Safety profile of teclistamab and teclistamab-daratumumab

Majestec-9

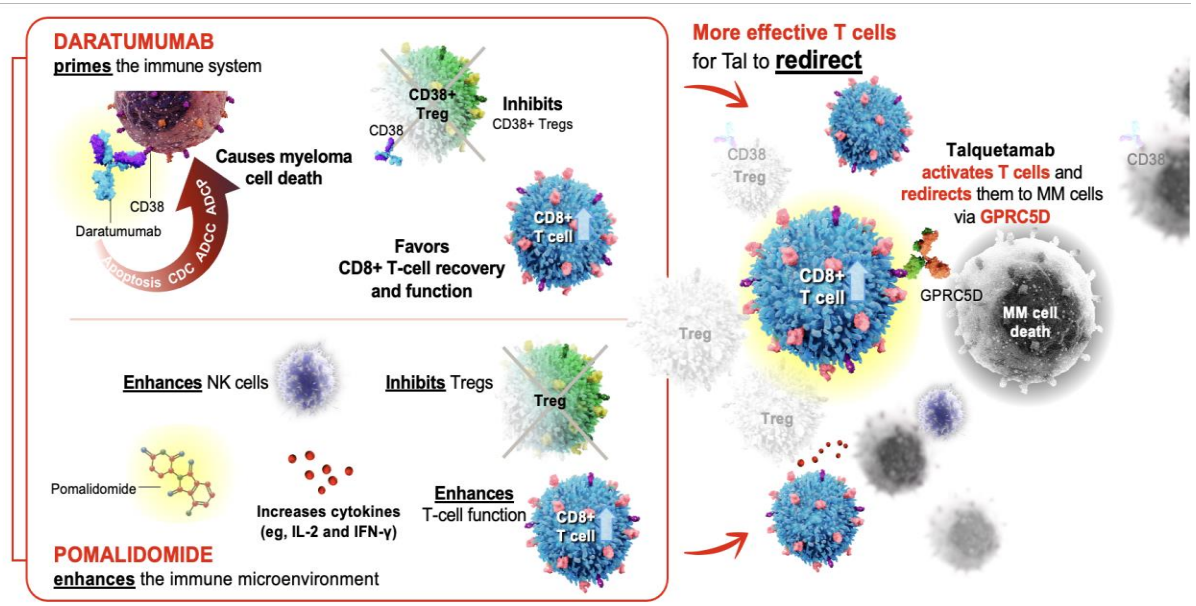
TEAE, n (%)[c]	Tec (n=291)		PVd/Kd (n=283)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	290 (99.7)	247 (84.9)	277 (97.9)	216 (76.3)
Hematologic				
Neutropenia	**182 (62.5)**	**158 (54.3)**	**81 (28.6)**	**63 (22.3)**
Anemia	110 (37.8)	52 (17.9)	119 (42.0)	46 (16.3)
Thrombocytopenia	80 (27.5)	31 (10.7)	110 (38.9)	60 (21.2)
Nonhematologic[d]				
CRS	**192 (66.0)**	**2 (0.7)**	**0**	**0**
Diarrhea	124 (42.6)	15 (5.2)	72 (25.4)	4 (1.4)
Hypertension	20 (6.9)	13 (4.5)	51 (18.0)	32 (11.3)
Any infection	241 (82.8)	121 (41.6)	193 (68.2)	82 (29.0)
URTI	77 (26.5)	7 (2.4)	58 (20.5)	6 (2.1)
Pneumonia	64 (22.0)	42 (14.4)	43 (15.2)	30 (10.6)

Majestec-3

TEAE, n (%)[‡]	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	283 (100)	269 (95.1)	290 (100)	280 (96.6)
Hematologic				
Neutropenia	222 (78.4)	214 (75.6)	240 (82.8)	228 (78.6)
Anemia	111 (39.2)	58 (20.5)	103 (35.5)	50 (17.2)
Thrombocytopenia	103 (36.4)	55 (19.4)	126 (43.4)	68 (23.4)
Nonhematologic[§]				
Any infection	273 (96.5)	153 (54.1)	244 (84.1)	126 (43.4)
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)
CRS[¶]	170 (60.1)	0	-	-
Diarrhea	147 (51.9)	10 (3.5)	89 (30.7)	7 (2.4)

Mina R. et al ASCO2026; Touzeau C et al, NEJM 2026: Costa L. et al, NEJM 2025

MonumenTAL-3: Tal-D +/- Pom vs DPd in RRMM for patients with ≳ 1 prior line



Key inclusion criteria

- Age ≥18 years
- Measurable RRMM
- ≥1 prior LOT including Len and a PI
- ECOG PS 0 to 2

Key exclusion criteria

- Refractory to anti-CD38 mAb
- Prior GPRC5D, Pom, or T-cell redirecting therapy within 3 months before randomization

1:1:1 randomization N=864

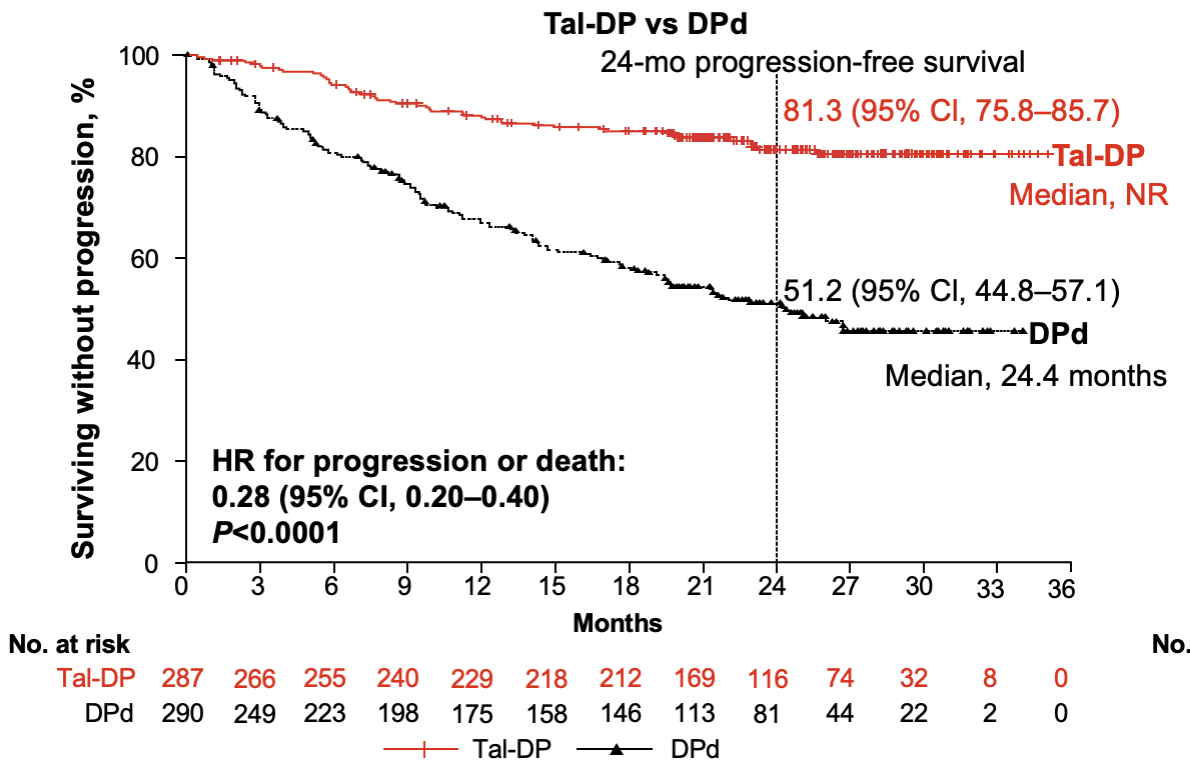
4 Nov 2022 to 13 Mar 2025

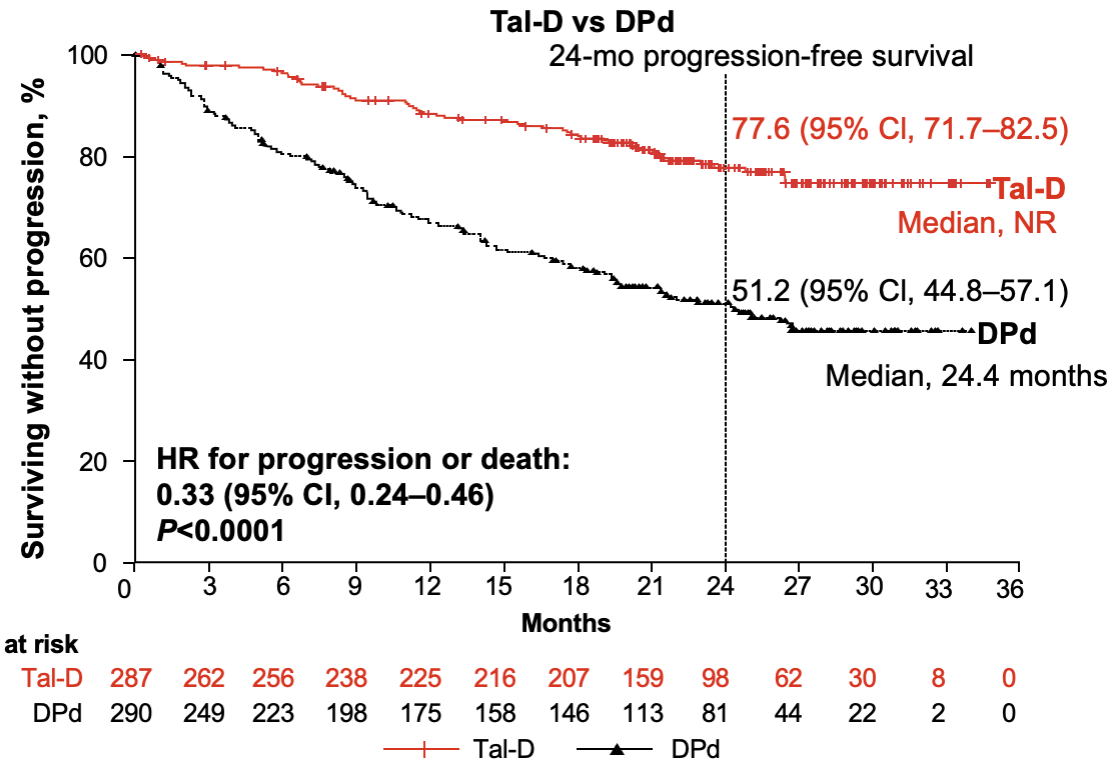
- **Tal-DP (n=287)**
- **Tal-D (n=287)**
- **DPd (n=290)**

864 pts, 2 prior lines (median), 85% len refractory, 11% dara exposed

Mina R et al, NEJM2026

Tal-dara and Tal-dara-poma improved PFS compared to DPd in RRMM

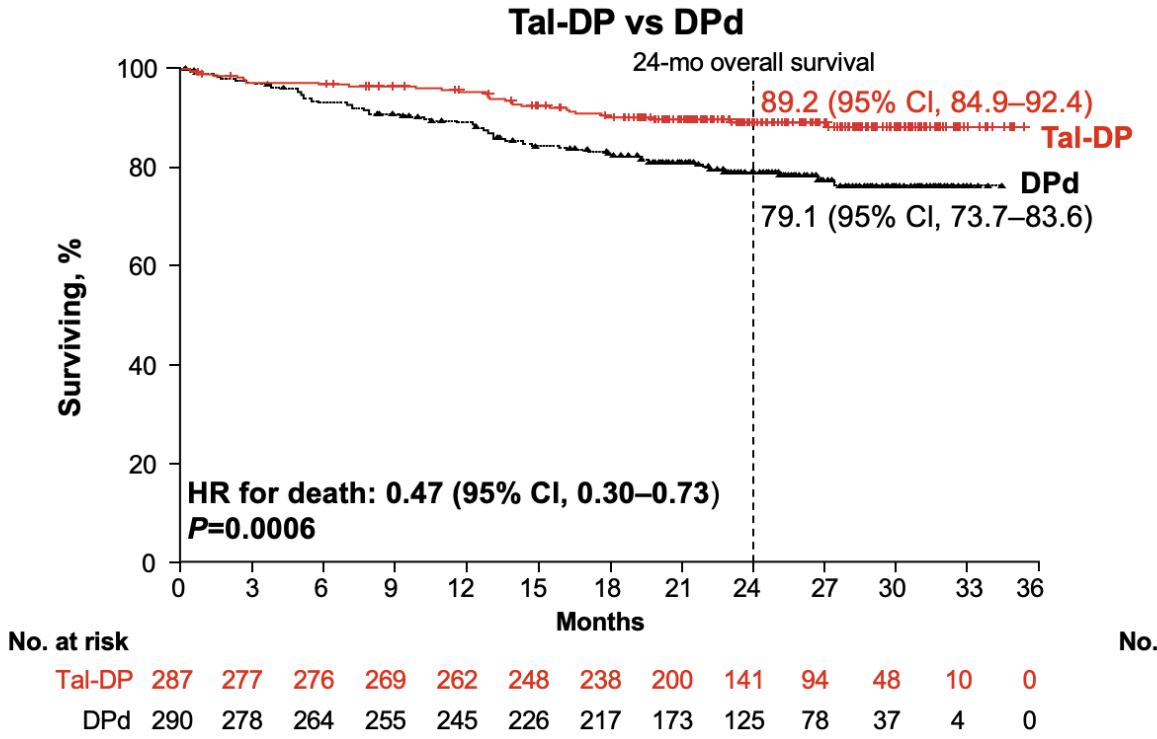


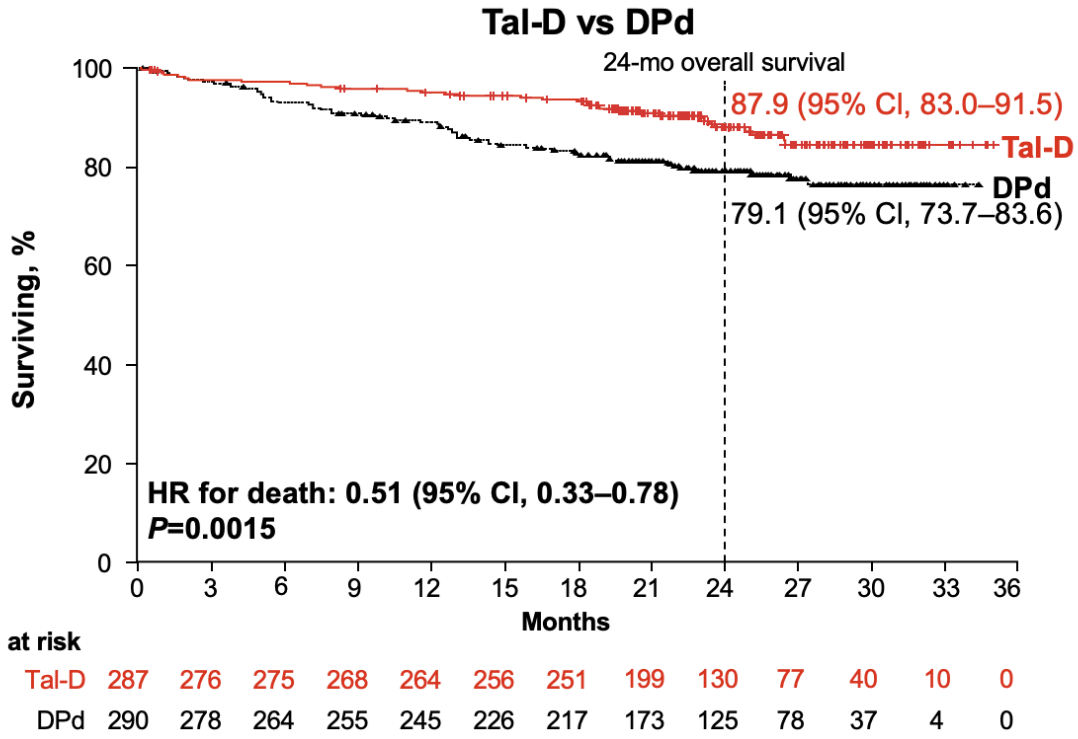


Tal-DP and Tal-D significantly improved PFS vs DPd

Voorhees P. et al, EHA2026; Mina R et al, NEJM2026

Tal-dara and Tal-dara-poma improved OS compared to SoC in RRMM





Tal-DP and Tal-D resulted in clinically meaningful OS improvement vs DPd, with >87% of patients alive at 2 years; *P*-values did not cross the prespecified boundary for superiority (0.0001)

Voorhees P. et al, EHA2026; Mina R et al, NEJM2026

Safety profile of Talquetamab-combinations in the Monumental-3 trial

	TEAE, n (%)	Tal-DP (n=276)		Tal-D (n=274)		DPd (n=283)	
		Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic	Neutropenia	232 (84.1)	211 (76.4)	112 (40.9)	80 (29.2)	255 (90.1)	244 (86.2)
	Anemia	136 (49.3)	66 (23.9)	107 (39.1)	41 (15.0)	117 (41.3)	45 (15.9)
	Thrombocytopenia	136 (49.3)	66 (23.9)	93 (33.9)	36 (13.1)	108 (38.2)	39 (13.8)
Non-hematologic	Infections	241 (87.3)	104 (37.7)	231 (84.3)	80 (29.2)	235 (83.0)	120 (42.2)
	Taste changes[b]	201 (72.8)	–	205 (74.8)	–	11 (3.9)	–
	Non-rash skin AE[c]	191 (69.2)	6 (2.2)	177 (64.6)	7 (2.6)	24 (8.5)	0
	CRS	187 (67.8)	2 (0.7)	160 (58.4)	2 (0.8)	–	–
	Nail-related AE[d]	155 (56.2)	1 (0.4)	157 (57.3)	1 (0.4)	1 (0.4)	0
	Decreased weight	126 (45.7)	21 (7.6)	105 (38.3)	13 (4.7)	21 (7.4)	1 (0.4)
	Fatigue	83 (30.1)	14 (5.1)	60 (21.9)	8 (2.9)	69 (24.4)	9 (3.2)

AE, n (%)	Tal-DP (n=276)	Tal-D (n=274)
Taste changes[a]	201 (72.8)	205 (74.8)
Grade 3 or 4	–	–
Leading to discontinuation of Tal	11 (4.0)	6 (2.2)
Non-rash skin[b]	191 (69.2)	177 (64.6)
Grade 3	6 (2.2)	7 (2.6)
Leading to discontinuation of Tal	5 (1.8)	2 (0.7)
Nail related[c]	155 (56.2)	157 (57.3)
Grade 3	1 (0.4)	1 (0.4)
Leading to discontinuation of Tal	3 (1.1)	0
Rash-related[d]	105 (38.0)	107 (39.1)
Grade 3	5 (1.8)	7 (2.6)
Leading to discontinuation of Tal	1 (0.4)	2 (0.7)
Ataxia/balance disorders[e]	40 (14.5)	34 (12.4)
Grade 3	8 (2.9)	6 (2.2)
Leading to discontinuation of Tal	13 (4.7)	6 (2.2)
Weight decreased	126 (45.7)	105 (38.3)
Grade 3	21 (7.6)	13 (4.7)
Leading to discontinuation of Tal	6 (2.2)	5 (1.8)

Voorhees P. et al, EHA2026; Mina R et al, NEJM2026

Treatment options for patients with RRMM as early as second relapse

Cilta-cel [I,A]

BelaVd [I,A]
BelaPd [I,A]

Teclistamab-daratumumab

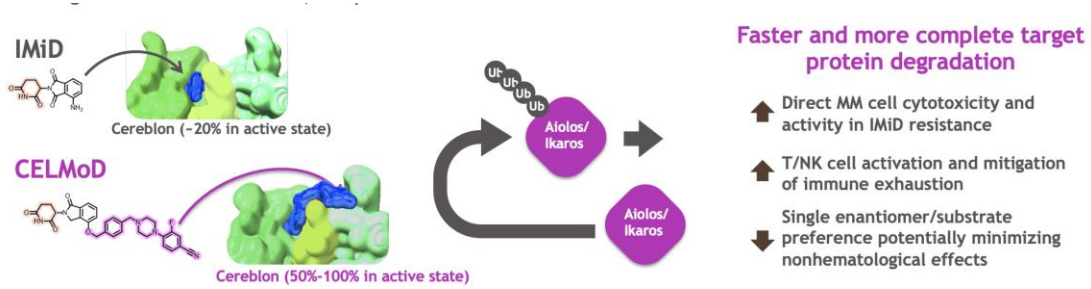
Teclistamab

Talquetamab-daratumumab ± pomalidomide

Dara-Pd [I,A]
Isa-Pd [I,A]
DaraKd [I,A]
IsaKd [I,A]

3L, third-line; 4L, fourth-line; ADC, antibody-drug conjugate; B, belantamab mafodotin; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; d, dexamethasone; Dara, daratumumab; Elo, elotuzumab; GPRC5D, G-protein coupled receptor class C group 5 member D; IMiD, immunomodulatory drug; Isa, isatuximab; K, carfilzomib; mAb, monoclonal antibody; MoA, mechanism of action; P, pomalidomide; PI, proteasome inhibitor; R, lenalidomide; RRMM, relapsed/refractory multiple myeloma; Sel, selinexor; TCE, triple class-exposed; V, bortezomib.

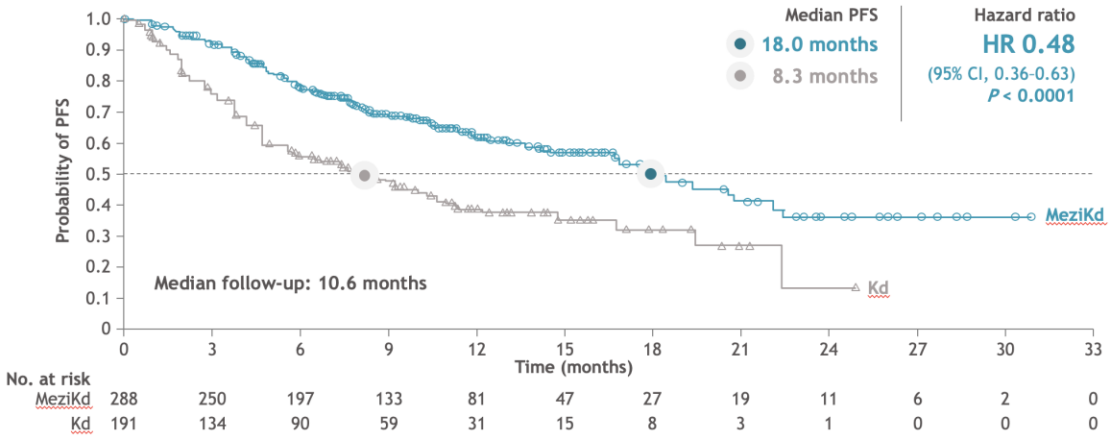
Beyond T-cell redirecting therapy: Celmods

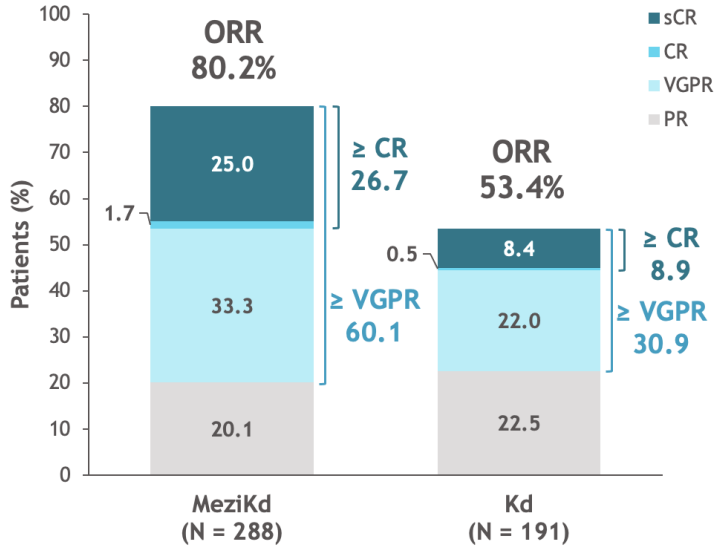


Mezigdomide-Kd vs Kd in RRMM: phase 3 SUCCESSOR-2 trial

N=479, prior therapies, 2 (median); 92% 3 –class exposed (IMiD, PI, anti-CD38); 8% BCMA exposed

Progression-free survival





Richardson PG et al, Lancet 2026

Conclusions

- BsAb, either monotherapy or in combinations, demonstrated to be superior to SOC therapy in early lines
- Tec and Tal + dara in dara-naive or exposed pts showed unprecedented MRD and PFS results, being the strongest combinations at 1° relapse.
- In double refractory (CD38/Len) pts, teclistamab monotherapy improved PFS and OS → new SoC as 2° line;
  - Tec-Tal combo (MonumenTAL-6) to come (PFS HR 0.11!)
- BCMA and GPRC5D targeting offer distinct safety profile
- BsAb have an established, predictable and safe toxicity profile, with effective mitigation strategies (e.g. ppx tocilizumab, IVIg)
- BsAb can be used in a wide patient population, including old and frail, with consistent efficacy and safety profile.
- BsAb offer simple logistic and readiness to use also in the community setting.

TRANSLATIONAL MYELOMA RESEARCH AT WINSHIP