City of Hope®

Southeastern Multidisciplinary Approaches to Cancer Symposium

Updates in Multiple Myeloma

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Disclosures

Consultant for Abbvie, ADC Therapeutics, Fate Therapeutics, Genmab, Iowa Oncology Society & Regeneron. On the Speaker's Bureau for Beigene, Genmab, & Peerview.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

The off-label/investigational use of anitocabtagene autoleuce will be addressed.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:
The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:
Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

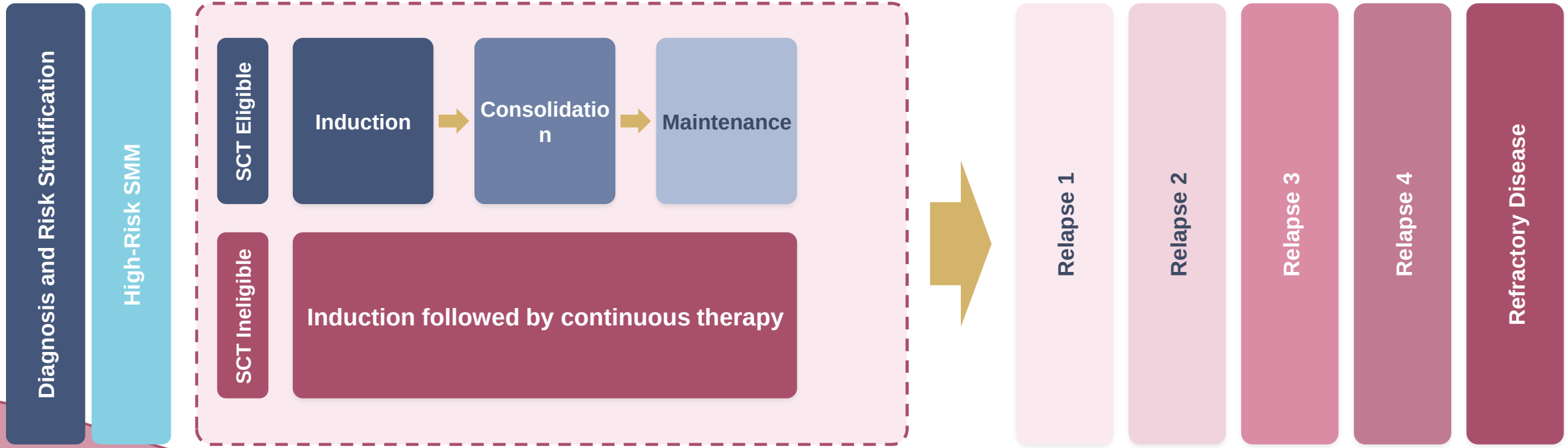
The following CLC & IB components will be addressed in this presentation:

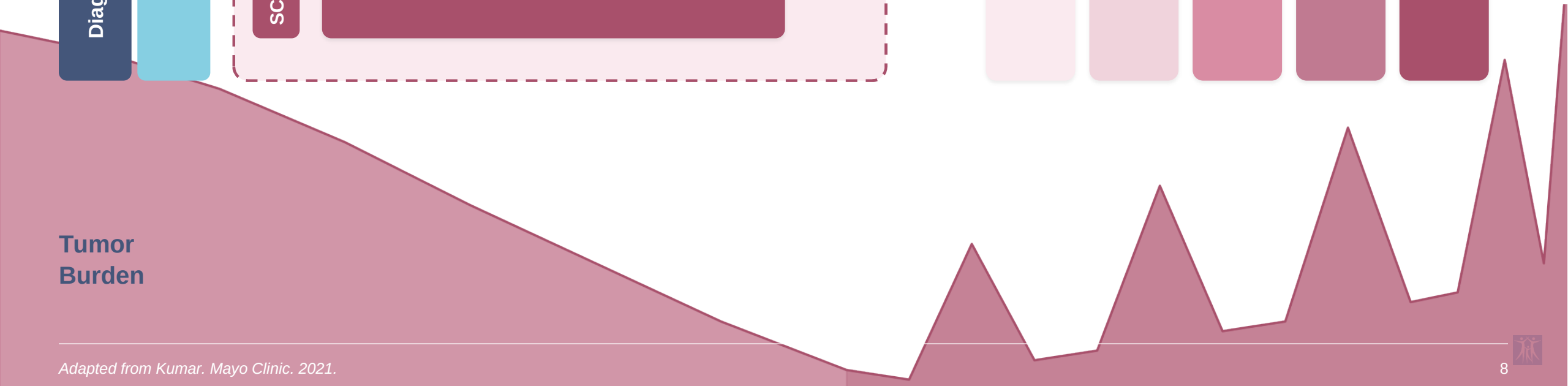
- *Disparities in Incidence and Outcomes in myeloma . Barriers to Equitable Care and Importance of Inclusive Clinical Trials*
- *Strategies to Reduce Implicit Bias*
- *Providing implicit bias and cultural humility training, Standardizing referral and treatment pathways and*
- *Expanding diverse clinical trial recruitment*

CONTENTS

Myeloma Treatment Paradigm

SCT-Eligible vs. SCT-Ineligible Pathways and Relapse Progression





Adapted from Kumar. Mayo Clinic. 2021.

Newly Diagnosed Multiple Myeloma

TRANSPLANT ELIGIBLE

Collect Stem Cells[b]

STANDARD RISK → **Dara-VRd** or **Isa-VRd** x ~4 cycles → **Autologous Stem Cell Transplant (ASCT)** → **Maintenance**: Len alone or with Anti-CD38 (Dara or Isa) till progression[a]

HIGH RISK → **Dara-VRd** or **Isa-VRd** x ~4 cycles → **Autologous Stem Cell Transplant (ASCT)** → **Doublet Maintenance**: Len + either bortezomib[c] or Anti-CD38 (Dara or Isa) till progression[a]

TRANSPLANT INELIGIBLE

STANDARD RISK → **Dara-VRd** or **Isa-VRd** induction For frail patients: **DRd** or **Isa-Rd**[a] → **Lenalidomide alone** or **Doublet Maintenance**: Len + Anti-CD38 (Dara or Isa)[a]

HIGH RISK → **Dara-VRd** or **Isa-VRd** induction, **DRd**, **Isa-Rd**, or **VRd** induction → **Doublet Maintenance**: Len + either bortezomib or Anti-CD38 (Dara or Isa)[a]

Dara-VRd, daratumumab + bortezomib + lenalidomide + dexamethasone; Isa-VRd, isatuximab + bortezomib + lenalidomide + dexamethasone; VRd, bortezomib + lenalidomide + dexamethasone; DRd, daratumumab + lenalidomide + dexamethasone; Isa-Rd, isatuximab + lenalidomide + dexamethasone; Dara, daratumumab; Isa, isatuximab; Len, lenalidomide; MRD, minimal residual disease.

Adapted from NCCN guidelines Ver 5.2026, https://www.msmart.org/mm-treatment-guidelines

Multiple Myeloma: Relapse & Refractory Treatment Algorithm

FIRST RELAPSE

NOT REFRACTORY TO ANTI-CD38		REFRACTORY TO ANTI-CD38	
Cellular therapy & bispecifics eligible **BCMA CAR-T[a] or Tec-Dara**	Unable to access cell therapy / bispecifics **Relapsed Triplet with Dara/Isa based[b]**	Cellular therapy & bispecifics eligible **BCMA CAR-T[a] or Tec-Dara**	Unable to access cell therapy / bispecifics **Relapsed Triplet with carfilzomib based[b]**

SECOND RELAPSE

Sensitive to both BCMA and Dara	BCMA sensitive; Dara refractory	Refractory to BCMA Bispecifics	Relapse after prior BCMA CAR-T
Tec-Dara, or **BCMA CAR-T[a]**	**BCMA CAR-T or Bispecifics[c]**, or Belantamab combination, or **RelapsedTriplet[b]**	**Relapsed Triplet[b]**, or Belantamab combination	**Relapsed Triplet[b]**, or Belantamab combination, or **Bispecifics[c]**

REFRACTORY MM

Refractory to Imid, PI, anti-CD38, and BCMA approaches

- Venetoclax if t(11;14)
- Talquetamab or Tec-Talq combination[d]
- Other non-BCMA immunotherapy
- Alkylator-based regimens (VCd, KCd, IV melphalan)
- Selinexor-based regimen
- High-dose cyclophosphamide (e.g., 1000–1500 mg/m² × 2 doses over 2 days)
- Combination chemo (DCEP, VDT-PACE, CVAD, DPACE)
- Bendamustine-based regimens
- Alternative BCMA-based therapy (CAR-T if bispecific-refractory, and vice versa)

[a] *Cilta-cel should be discussed with eligible patients; discuss pros/cons of a one-time CAR-T approach vs prolonged therapy.* [b] *Choice of standard triplet is based on refractoriness to Len, anti-CD38, and other drugs. Key options: DRd, KRd, KPd, Anti CD38-Pd, Anti CD38-Kd, EloPd, Dara-KPd, PI-Cd — choose a triplet with ≥ 2 drugs the patient is not refractory to. If t(11;14), Dara-Venetoclax-dex and Carfilzomib-Venetoclax-Dex are additional options.*

[c] *BCMA Bispecifics can be teclistamab, elranatamab, linvoseltamab, or the Tec-Dara combination.* [d] *Tec-Talq combination has shown efficacy in patients with relapsed MM plus EMD.*

Adapted from NCCN guidelines Ver 5.2026, https://www.msmart.org/mm-treatment-guidelines

High-Risk Multiple Myeloma

2025 IMS/IMWG Consensus Genomic Classification

HIGH-RISK DISEASE = ANY ONE of the four criteria below (single unified definition, no separate ISS staging required)

1 del(17p) and/or TP53 mutation

del(17p) with clonal cell fraction (CCF) **≥20%**, and/or a **TP53 mutation** — either alone is sufficient.

2 IgH translocation + 1q/1p lesion

t(4;14), t(14;16), or t(14;20) PLUS gain/amp(1q21) and/or del(1p32).
Translocation alone is no longer sufficient for HR.

3 Chromosome 1p burden

Monoallelic del(1p32) with concurrent 1q gain, **OR** a **biallelic del(1p32)** on its own.

4 β2-microglobulin (renal-adjusted)

β2-microglobulin ≥5.5 mg/L, counted **only when creatinine is normal** (excludes renal-impairment confounding).

Key shift from legacy criteria: old model (del17p OR t(4;14) OR t(14;16), any single hit → HR) treated IgH translocations as independently high-risk.
New model requires co-occurring 1q/1p abnormality — translocation alone → standard risk.

Avet-Loiseau H, et al. IMS/IMWG consensus recommendations on the definition of high-risk multiple myeloma. J Clin Oncol. 2025;43(24):2739–2751.

Bispecific Antibody Therapy

❑ "Off the shelf" immunotherapy with multiple binding domains

Target different tumor antigens like **BCMA**, **GPRC5D**, **FcRH5**

Also bind to immune cell targets, including CD3 (T cells)

Teclistamab*: CD3 x BCMA

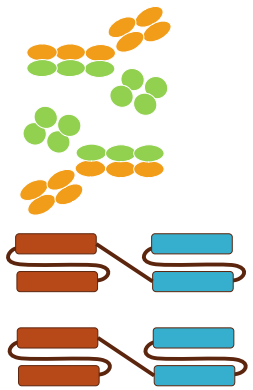
Elranatamab*: CD3 x BCMA

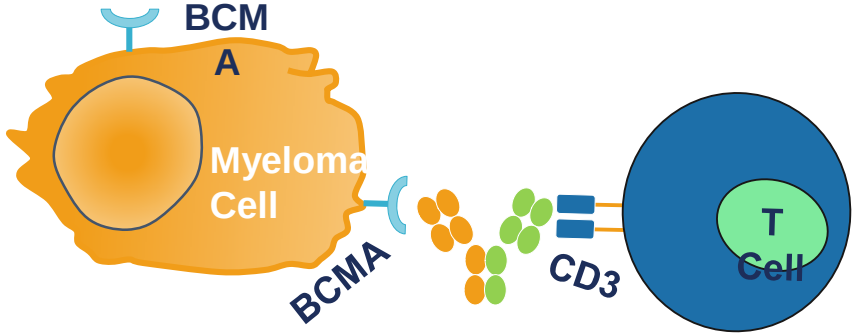
Linvoseltamab*: CD3 x BCMA

Talquetamab*: CD3 x GPRC5D

Cevostamab: CD3 x FcRH5

Etentamig: CD3 x BCMA





*FDA approved as monotherapy for treating adults with R/R MM after ≥4 prior lines of therapy, including a PI, IMiD, and anti-CD38 mAb.

❑ Variable administration: SC or IV options with required step-up dosing

Dual antigen engagement → Immune synapse activation → Polyclonal T cell activation → Cytokine release and lysis

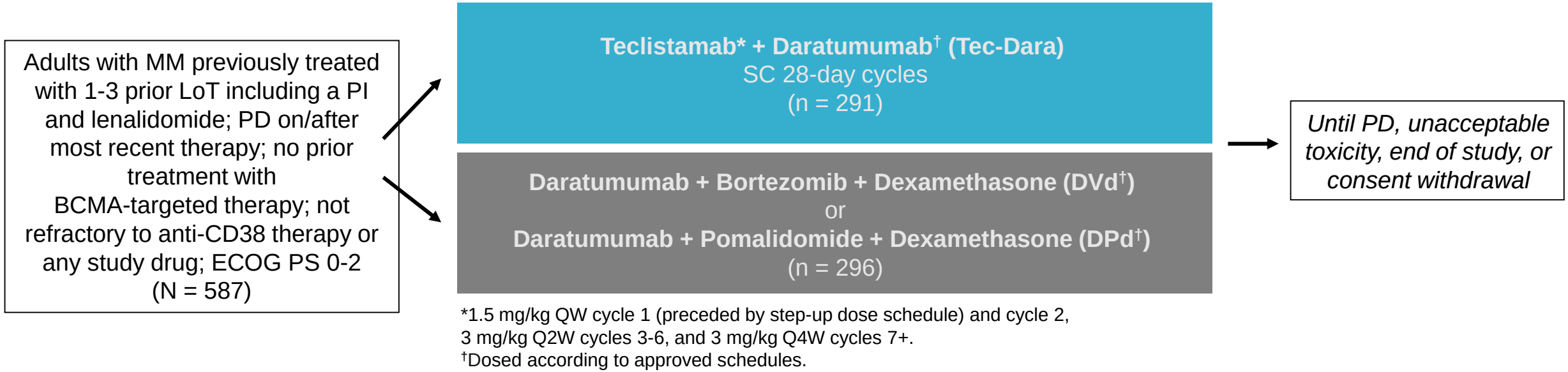
Elranatamab-bcmm PI. Linvoseltamab-gcpt PI. Talquetamab-tgvs PI. Teclistamab-cqyv PI. van de Donk. Lancet. 2023;402:142.

Approved Bispecific Therapies for Myeloma

BsAb	Teclistamab[1]	Elranatamab[2]	Linvoseltamab[3]	Talquetamab[4]
Targets	BCMA x CD3	BCMA x CD3	BCMA x CD3	GPRC5D x CD3
Trial/phase/n treated	MajesTEC-1 phase I/II; n = 165	MagnetisMM-3 phase II; n = 123	LINKER-MM1 phase I/II; n = 117	MonumenTAL-1 phase I; n = 232
Patient population	≥3 LoT, including 1 PI, 1 IMiD, and 1 anti-CD38 mAb	Cohort A: refractory to ≥1 PI, 1 IMiD, and 1 anti-CD38 mAb	≥3 LoT, including 1 PI, 1 IMiD, and 1 anti-CD38 mAb	R/R MM with intolerance to or progressed on established therapies (data for all SC cohorts)
ECOG PS ≥1, %	67	63	85	NR (excluded PS ≥2)
Prior BCMA therapy allowed	Not allowed	Cohort A: no	No, except BCMA ADCs	Yes
Median age, yr (range)	64 (33-84)	68 (36-89)	70 (37-91)	64 (39-84)
• Age ≥75 yr, %	15	NR	27	30 for ≥70 yr
EMD, %	17	32	16	32
High-risk cytogenetics, %	26	25	39	16
Median LoT, n (range)	5 (2-14)	5 (2-22)	5 (2-16)	5.5 (2-17)
Triple-class refractory, %	78	97	82	75
Penta-drug refractory, %	30	42	28	25

1. Moureau. NEJM. 2022;387:495. 2. Lesokhin. Nat Med. 2023;29:2259. 3. Bumma. JCO. 2024;42:2702. 4. Chari. NEJM. 2022;387:2232.

MajesTEC-3: Teclistamab + Daratumumab in R/R MM



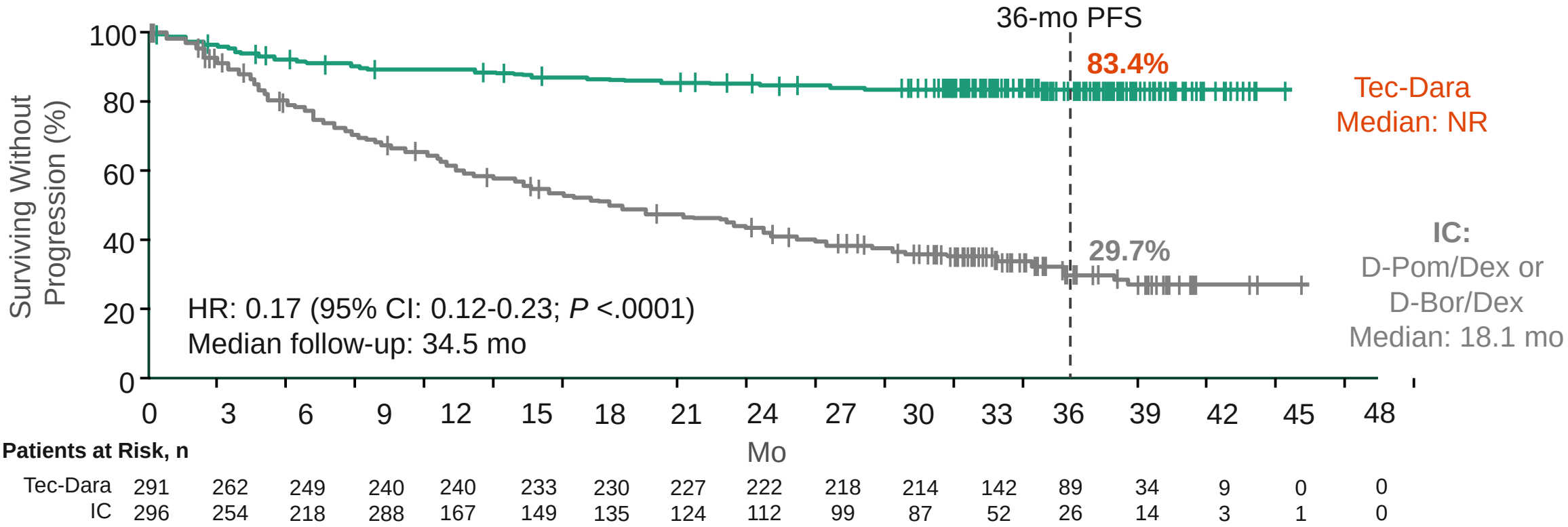
*1.5 mg/kg QW cycle 1 (preceded by step-up dose schedule) and cycle 2, 3 mg/kg Q2W cycles 3-6, and 3 mg/kg Q4W cycles 7+.
†Dosed according to approved schedules.

- **Primary endpoint: PFS by IRC**
- **Key secondary endpoints: CRR, ORR, MRD (10^{-5} by NGS), OS, safety, time to worsening of symptoms**

Study unblinded:
36-mo PFS HR: 0.17

Mateos. ASH 2025. Abstr LBA-6. Costa. NEJM. 2026;394:739.

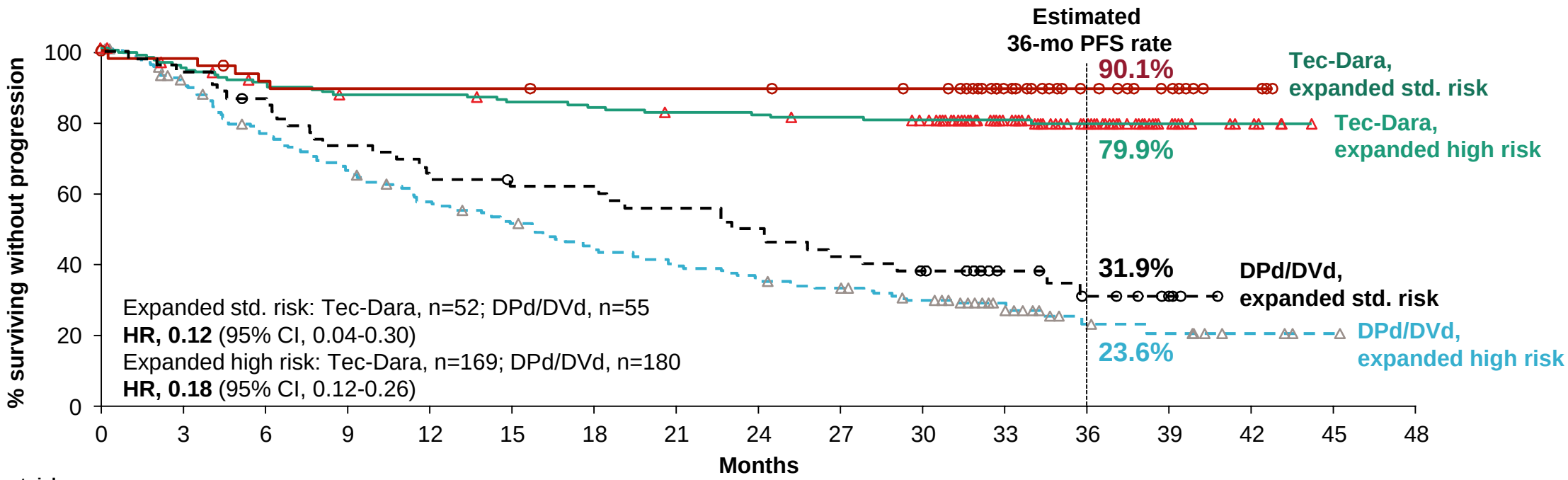
MajesTEC-3: PFS



On March 5, 2026, the FDA approved teclistamab in combination with daratumumab for adult patients with R/R MM who have received at least 1 prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, based on the results of the MajesTEC-3 trial

Costa. NEJM. 2026;394:739.

MajesTEC-3: PFS by Expanded Cytogenetic Risk



No. at risk																	
Tec-Dara, expanded std. risk	52	50	46	45	45	45	44	44	44	43	42	28	15	8	3	0	-
DPd/DVd, expanded std. risk	55	51	46	39	34	32	32	29	26	22	19	12	8	3	0	0	-
Tec-Dara, expanded high risk	169	147	139	133	133	129	127	124	123	121	119	80	53	19	6	0	0
DPd/DVd, expanded high risk	180	153	129	110	95	84	71	64	57	52	45	27	11	8	3	1	0

Tec-Dara maintained superior PFS vs DPd/DVd across expanded cytogenetic risk groups, consistent with the overall study effect[1]

Presented by R Banerjee at the 31st European Hematology Association (EHA) Annual Meeting; June 11-14, 2026; Stockholm, Sweden

MajesTEC - 9

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)

Primary endpoint

- PFS per IRC[b]

Key secondary endpoints

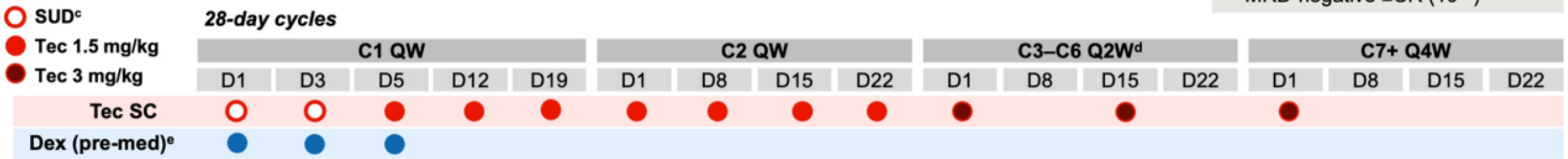
- ≥CR[b]
- OS
- MySIm-Q total symptom score

Other secondary endpoints

- ORR
- Safety
- PK and immunogenicity

Exploratory endpoints

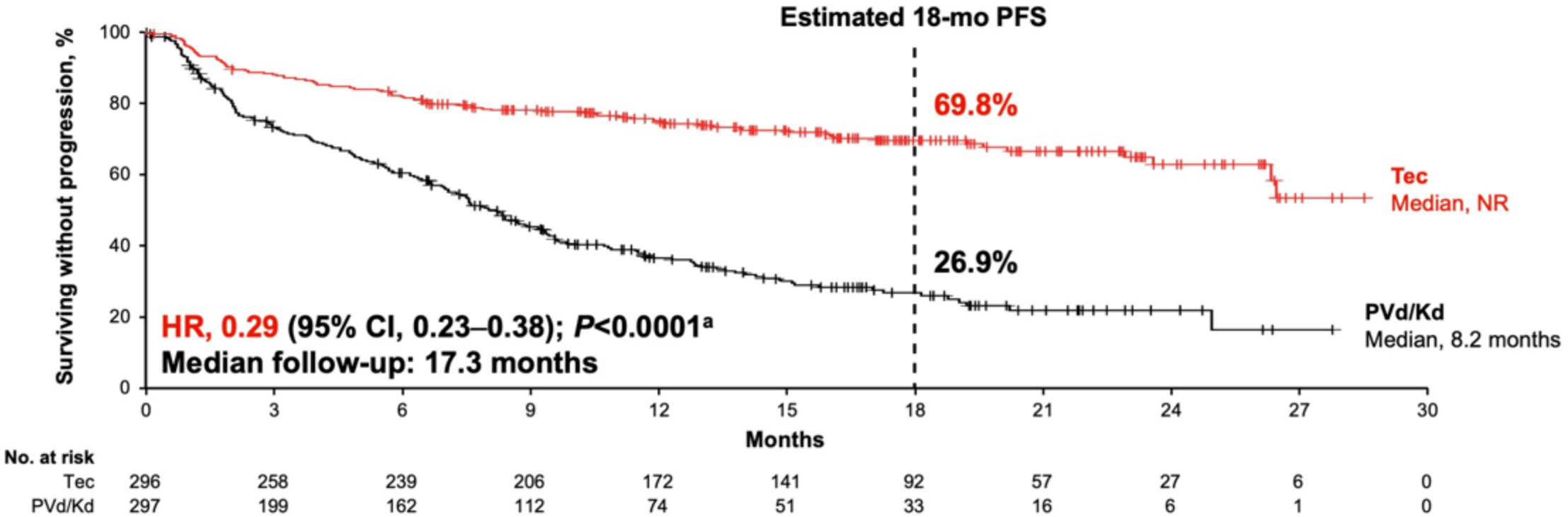
- MRD-negative ≥CR (10^{-5})



Monthly Tec dosing from C7 (earlier if ≥VGPR); steroid free after C1D5

Presented by R Mina at the American Society of Clinical Oncology (ASCO) Annual Meeting; May 29–June 2, 2026; Chicago, IL, USA.

MajesTEC – 9- Improved PFS



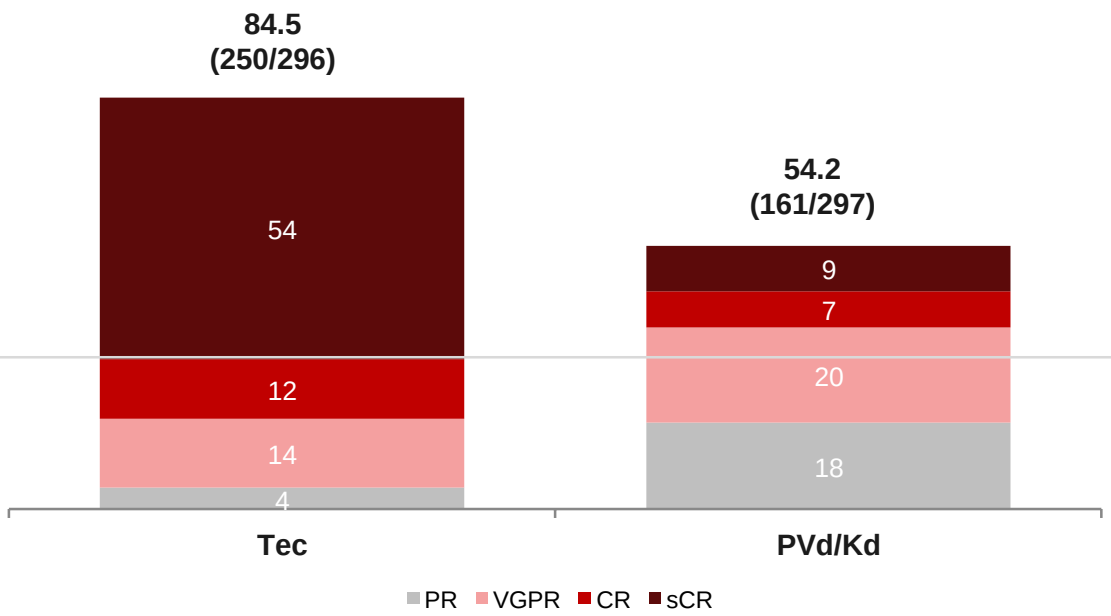
Tec significantly improved PFS, with a 71% reduction in the risk of disease progression or death in a highly refractory population

Presented by R Mina at the American Society of Clinical Oncology (ASCO) Annual Meeting; May 29–June 2, 2026; Chicago, IL, USA.

MajesTEC-9: Response, Duration, and MRD-Negativity

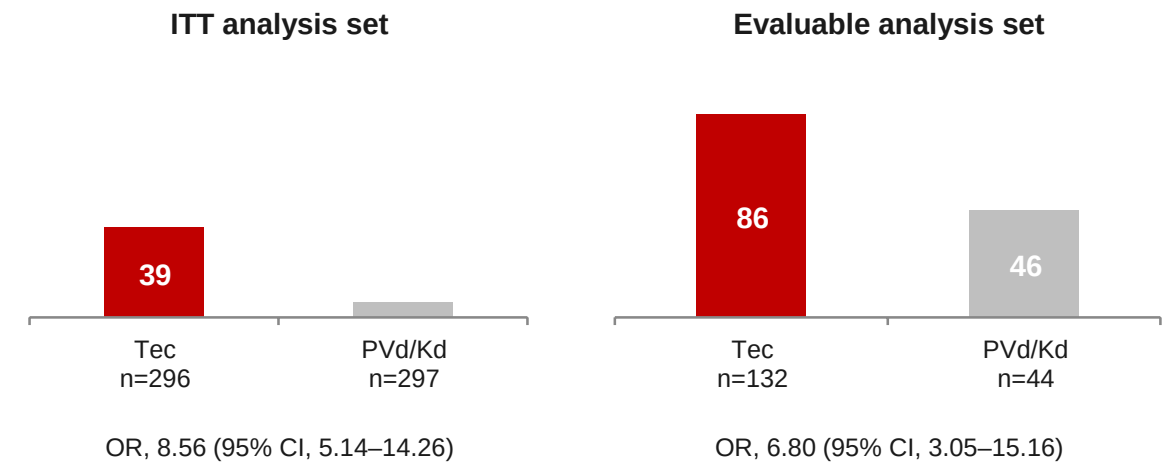
Tec vs PVd/Kd — Median follow-up 17.3 months

Treatment Response



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

MRD-Negative (10^{-5}) ≥CR Rate



Tec demonstrated significantly higher ORR, a ≥CR rate nearly 4× that of control, more durable responses, and an ~86% MRD-negative ≥CR rate among MRD-evaluable patients.

DOR, duration of response; ITT, intent-to-treat; MRD, minimal residual disease; NE, not estimable; NGF, next-generation flow cytometry; OR, odds ratio; PR, partial response; sCR, stringent complete response.

Presented by R Mina at the American Society of Clinical Oncology (ASCO) Annual Meeting; May 29–June 2, 2026; Chicago, IL, USA.

MonumenTAL-3: Talquetamab-Daratumumab in R/R Myeloma

Phase 3, multicenter, open-label study conducted at 182 sites in 18 countries

Patients

Key inclusion criteria
- RRMM*
- ≥1 prior LOT, including lenalidomide and a PI†
- ECOG PS score of 0-2

Key exclusion criteria
- Refractory to anti-CD38 mAbs
- Prior GPRC5D-directed therapy
- Prior pomalidomide therapy
- T-cell redirecting therapy ≤3 months before randomization

1:1:1 randomization N=864

Nov 4, 2022 to Mar 13, 2025

- Tal-DP N=287
- Tal-D N=287
- DPd N=290

93 (10.9%) patients were included from the United States

Endpoints

Primary endpoint
- PFS per IRC

Key secondary endpoints
- ORR
- ≥CR
- MRD-negative CR (10^{-5})
- OS

Additional secondary endpoints
- Safety
- PK and immunogenicity

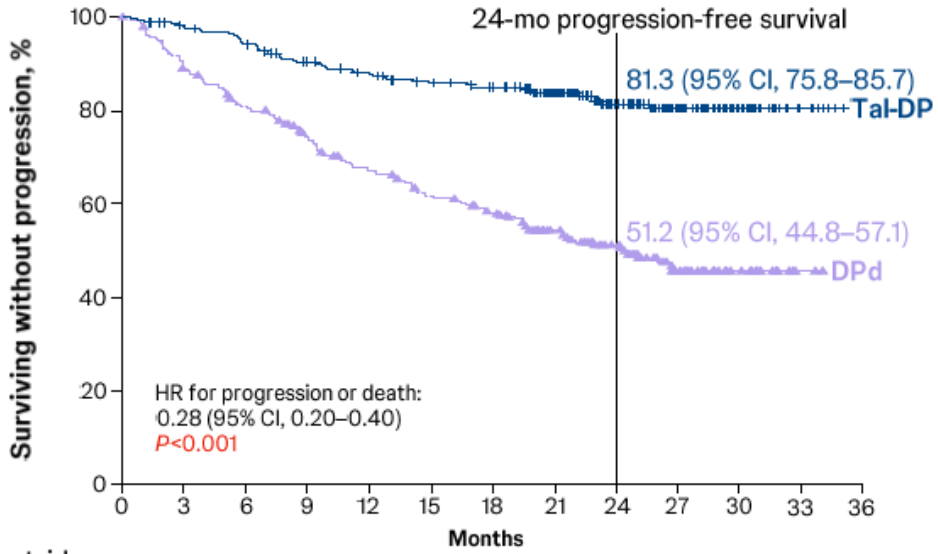
864 patients with RRMM and ≥1 prior LOT† were randomized to Tal-DP, Tal-D, or DPd; primary endpoint was PFS

Mina R, et al. *N Engl J Med*.DOI: 10.1056/NEJMoa2604657.

MonumenTAL-3: PFS

Median F/U : 24.6 months

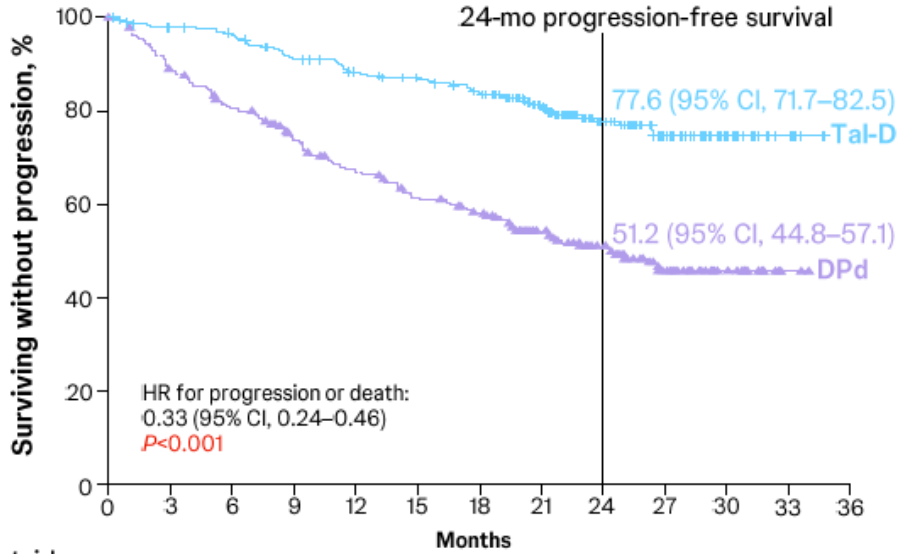
Tal-DP versus DPd



No. at risk

Tal-DP	287	266	255	240	229	218	212	169	116	74	32	8	0
DPd	290	249	223	198	175	158	146	113	81	44	22	2	0

Tal-D versus DPd



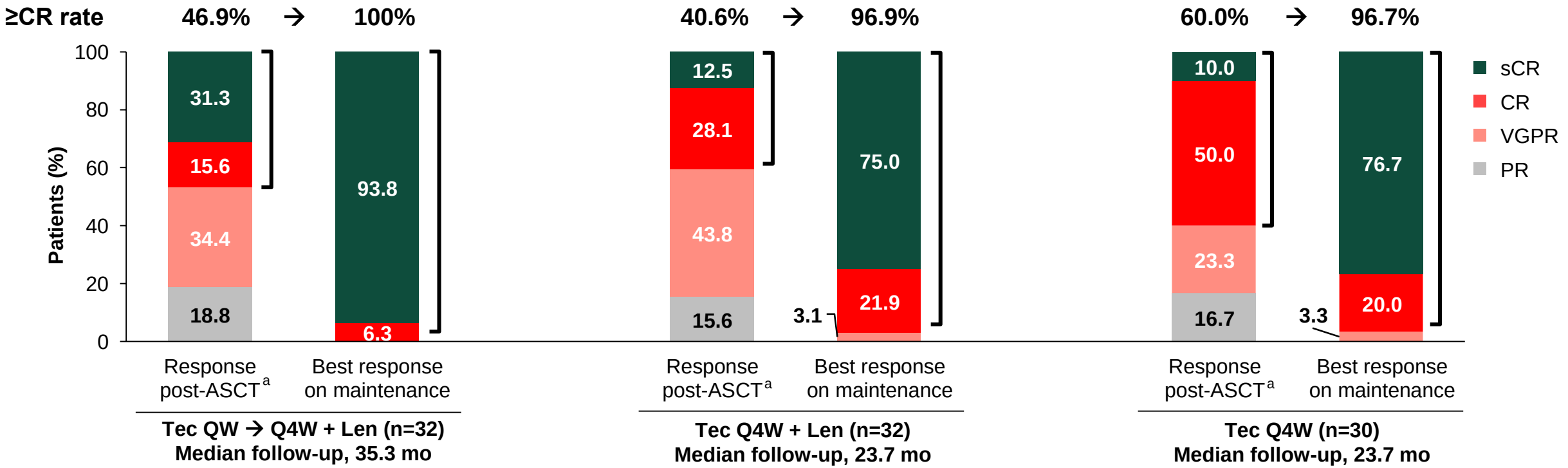
No. at risk

Tal-D	287	262	256	238	225	216	207	159	98	62	30	8	0
DPd	290	249	223	198	175	158	146	113	81	44	22	2	0

- **Tal-DP and Tal-D significantly improved PFS versus DPd, with 81% Tal-DP and 78% Tal-D patients alive and progression free at 2 years**
  - **Median PFS was not reached in the Tal-DP and Tal-D arms and was 24.4 months in the DPd arm**

Mina R, et al. *N Engl J Med*.DOI: 10.1056/NEJMoa2604657.

EMN30/MajesTEC-4 SRI: Teclistamab Post-ASCT and During Maintenance



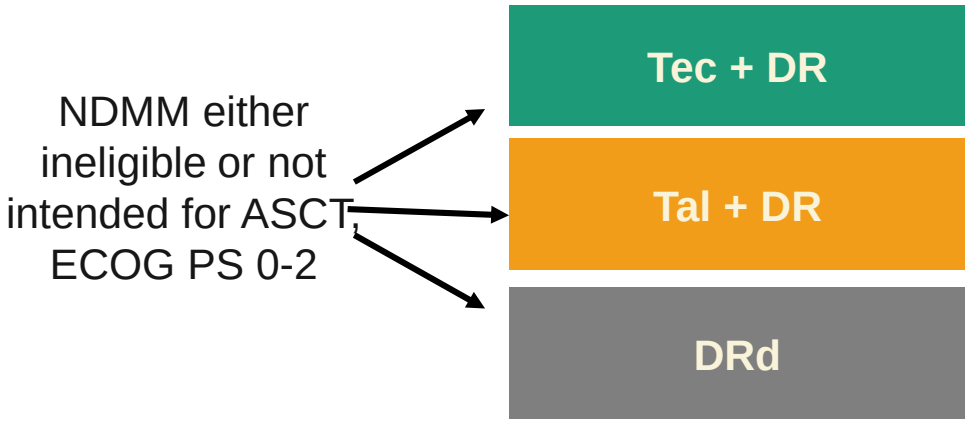
sCR, stringent complete response; VGPR, very good partial response.

≥CR was reached in nearly 100% of patients during maintenance across cohorts

Presented by NWCJ van de Donk at the 31st European Hematology Association (EHA) Annual Meeting; June 11-14, 2026; Stockholm, Sweden

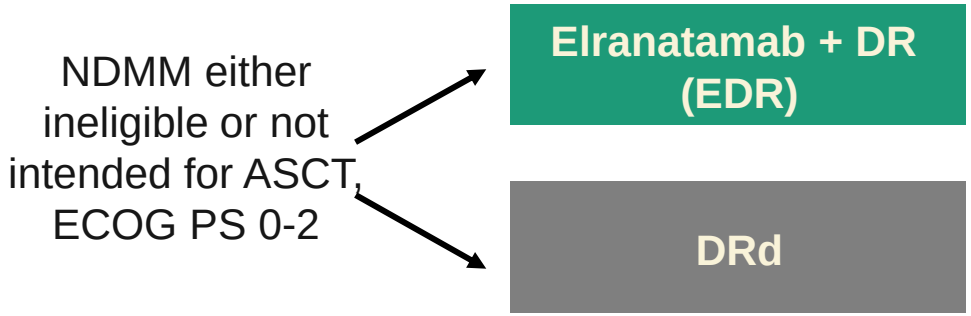
Bispecific in Newly diagnosed Multiple myeloma (ASCT ineligible)

MajesTEC-7
Phase III



Primary endpoints:
PFS and sustained MRD neg

MagnetisMM-6
Phase III



Primary endpoints:
PFS and sustained MRD neg

Facon. NEJM. 2019;380:2104. NCT05552222. Krishnan. Blood. 2022; 140:10148. NCT05623020. Byun. Blood. 2025;146:5845.

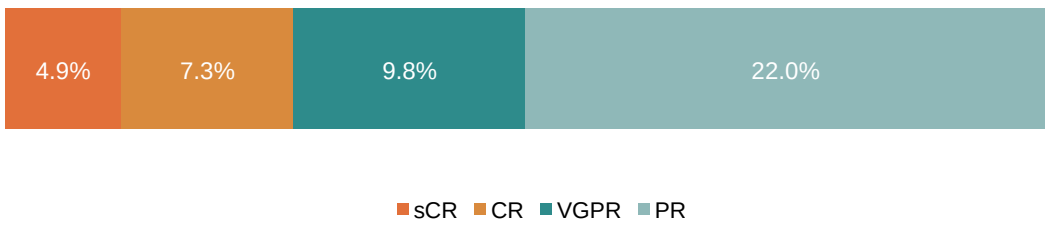
Cevostamab in Triple-Class Refractory MM After Prior BCMA CAR-T: Efficacy & Safety

Expansion results from the Phase I/II CAMMA 2 study (N=41)

EFFICACY

43.9%	34.1%	17.4 mo
ORR	VGPR+	MEDIAN DOR

RESPONSE DEPTH (N=41)



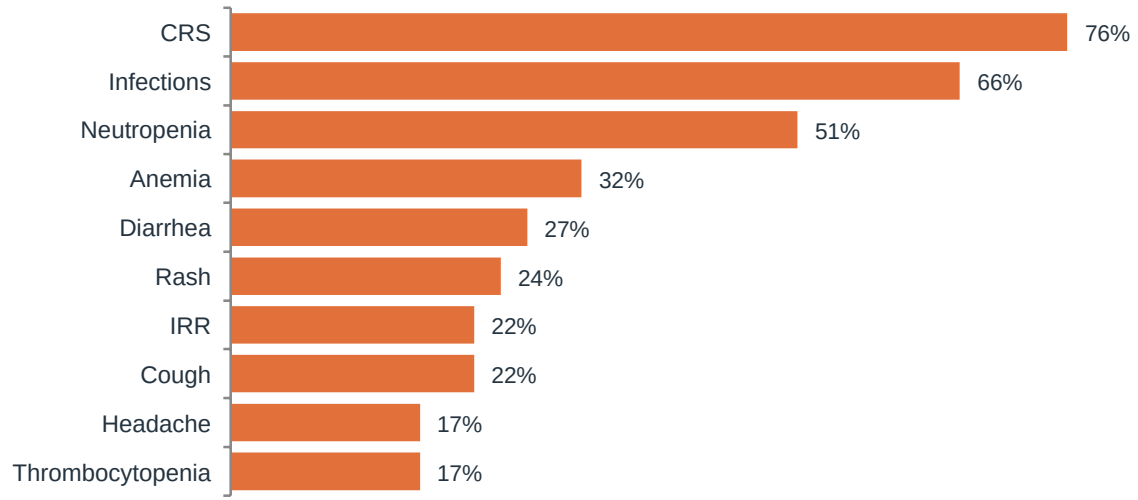
44.4% of responders (8/18) remain in remission at data cut-off

59.8% DOR rate at 15 months (95% CI: 36.7–83.0)

75.6% of patients received BCMA CAR-T as their last prior line; median 13.4 months since last anti-BCMA therapy.

SAFETY

MOST COMMON AEs, ANY GRADE (≥15% of patients)



CRS

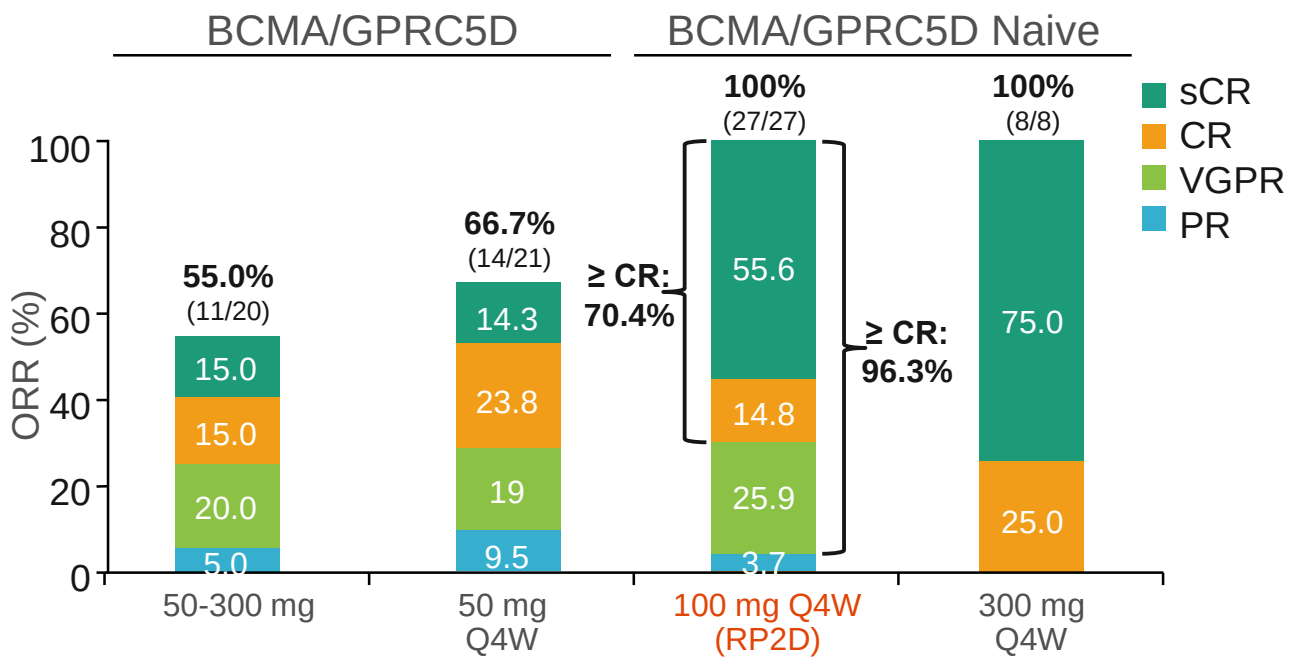
- All Grade 1–2
- 77% within 24h of infusion
- Managed w/ toci (51.6%) or steroids (51.6%); all resolved

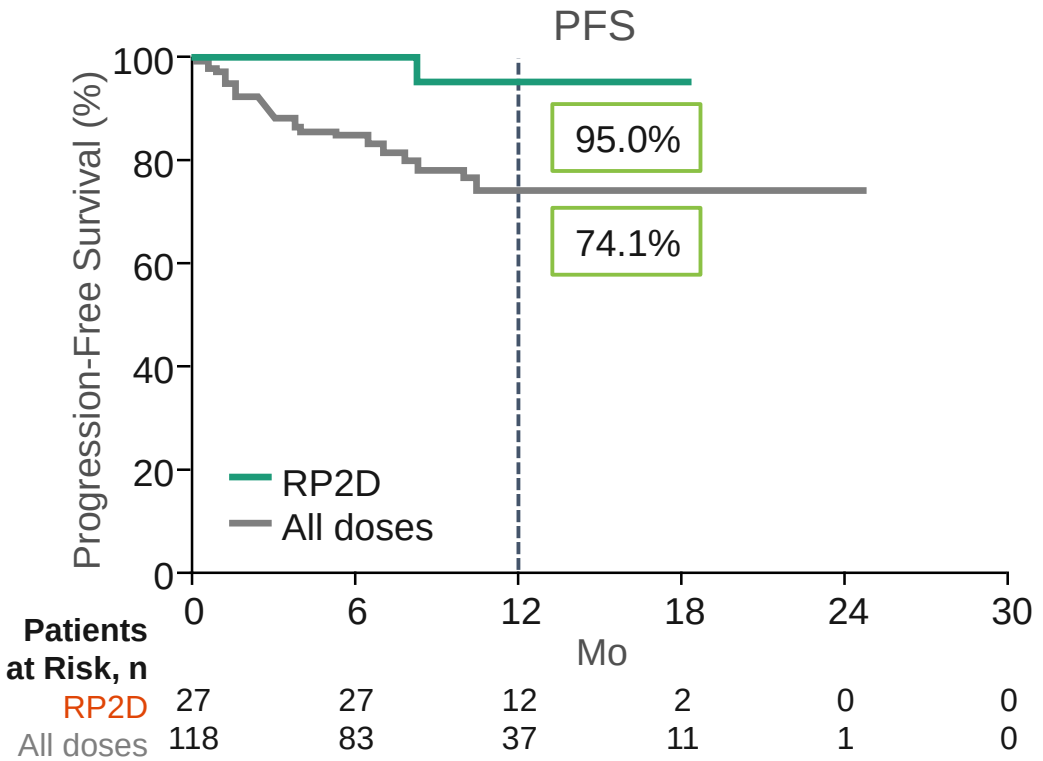
DISCONTINUATION

- Serious AEs in 68.3% of patients
- AE-related d/c in 1 pt (Gr 5 MDS, unrelated)
- No Gr 5 events among cytopenias

Phase I Study of Trispecific Antibody JNJ-5322 in R/R MM

RP2D: 100 mg SC Q4W with 1 step-up dose

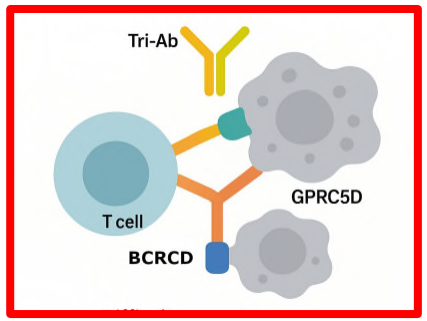




Safety: similar or lower incidence/severity of GPRC5D-associated AEs

Decreased incidence of taste AEs, weight loss

Similar incidence of skin and nail AEs



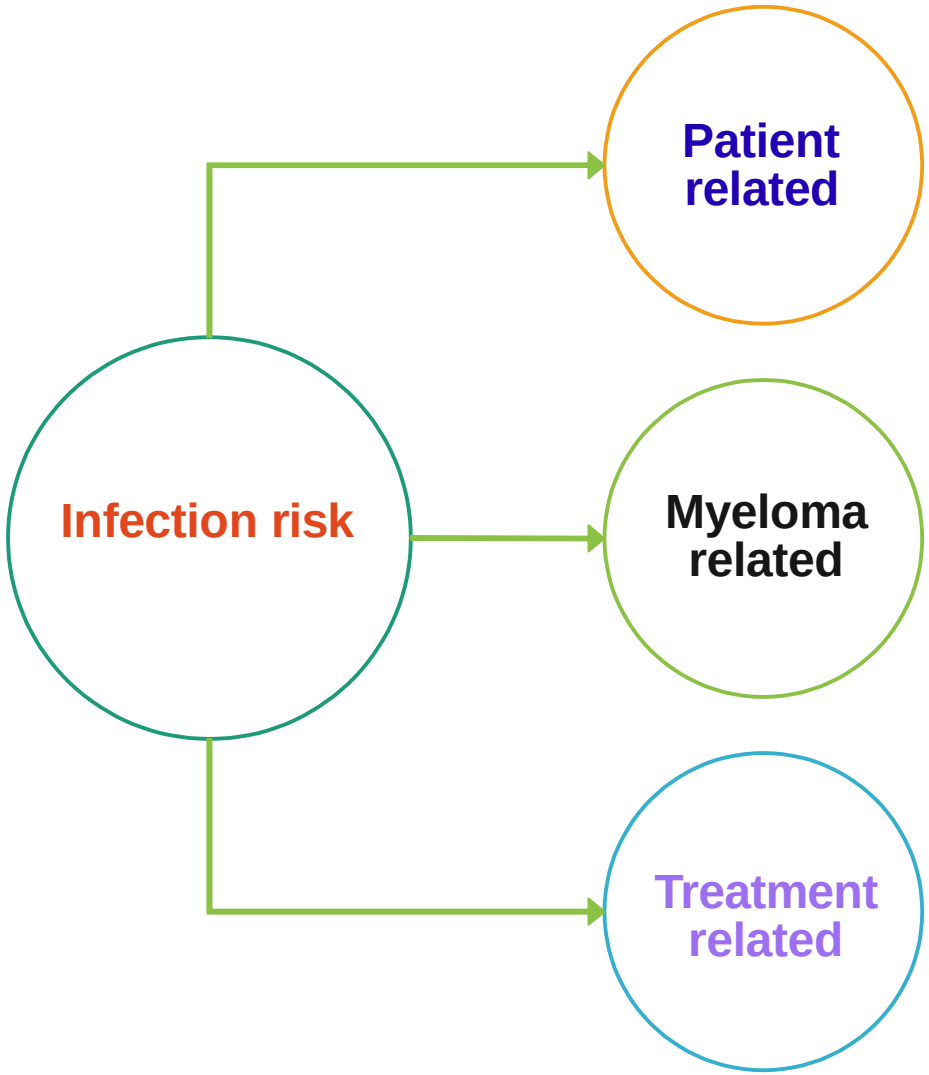
van de Donk. ASCO 2025. Abstr 7505.

Safety of Approved Bispecific Antibodies for Multiple Myeloma

Parameter	Teclistamab[1-3]	Elranatamab[4,5]	Linvoseltamab[6]	Talquetamab[7-10]
Target	CD3/BCMA	CD3/BCMA	CD3/BCMA	CD3/GPRC5D
CRS occurrence	72%: Grade 1: 50% Grade 2: 21%	58%: Grade 1: 44% Grade 2: 14%	46%: Grade 1: 35% Grade 2: 10%	76%: Grade 1: 57% Grade 2: 17%
ICANS occurrence	Grade 1/2: 3% Grade 3/4: 0%	Grade 1/2: 3% Grade 3/4: 0%	Grade 1/2: 5.4% Grade 3: 2.6%	Grade 1/2: 3% Grade 3/4: 3%
Neutropenia	Grade 3/4: 56%	Grade 3/4: 51%	Grade 3/4: 47%	Grade 3/4: 35%
Infection	Grade 3/4: 35%	Grade 3/4: 31%	Grade 3/4: 38%	Grade 3/4: 17%
Skin/nail toxicity	Not reported	26%	15%	62%
Oral toxicity	Not reported	Not reported	Not reported	80% (dysgeusia: 49%, dry mouth: 34%, dysphagia: 23%, ageusia: 18%)

1. Moreau. NEJM. 2022;387:495. 2. van de Donk. ASCO 2023. Abstr 8011. 3. Teclistamab-cqyv PI. 4. Lesokhin. Nat Med. 2023;29:2259. 5. Elranatamab-bcmm PI. 6. Linvoseltamab PI. 7. Chari. NEJM. 2022;387:2232. 8. Touzeau. EHA 2023. Abstr S191. 9. Talquetamab-tgvs PI. 10. Chari. Lancet. 2025;V12:E269.

BsAb Therapy's Infection Risk



Treatment target (BCMA > non-BCMA) leads to significant hypogammaglobulinemia as well as impaired humoral immunity

Treatment MoA (T-cell redirection)

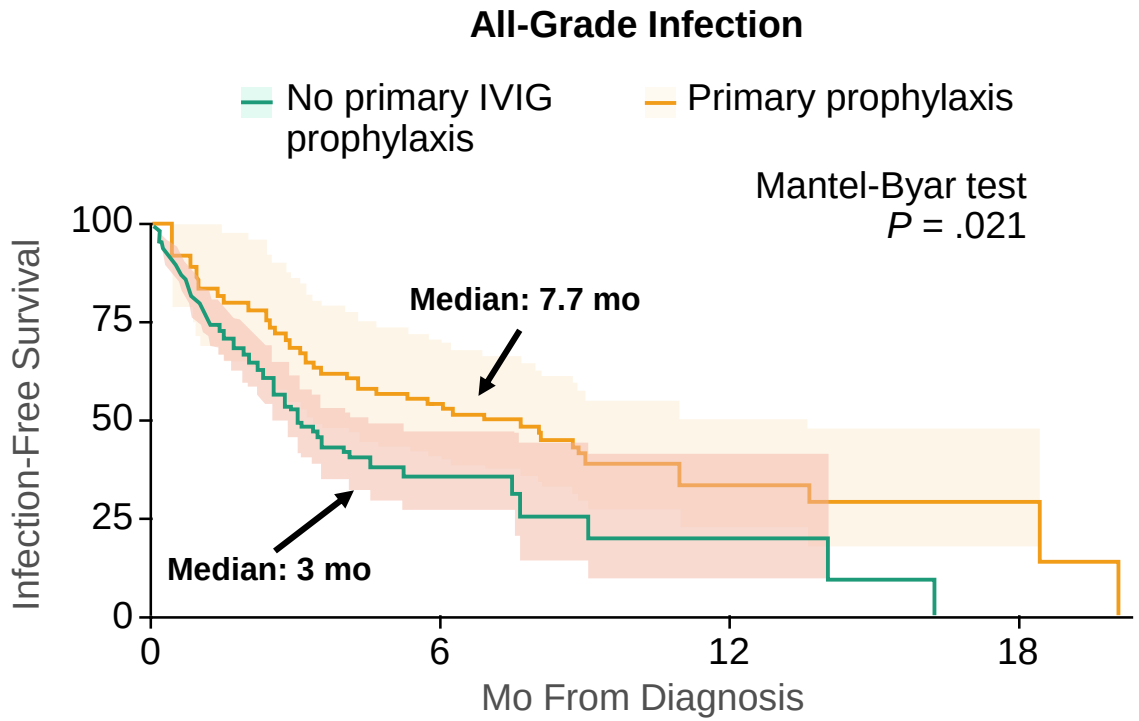
- T-cell dysfunction/exhaustion leads to impaired cellular immunity
- Activation of immunosuppressive T-regulatory cell subtypes
- CRS risk and related concomitant immunosuppressive supportive medications (corticosteroids, tocilizumab)

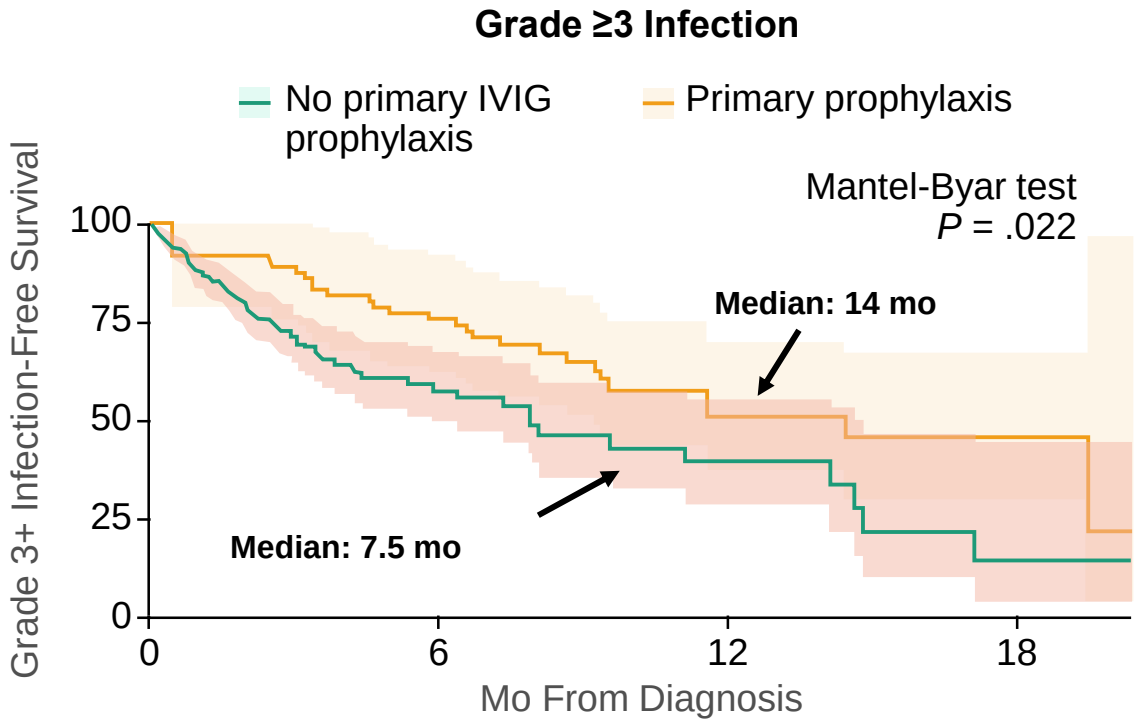
Cumulative therapeutic exposure (long)

- Continuous therapy by design in most protocols in already substantially pretreated patients
- Significant DoR compared with historic conventional therapies used in R/R MM → longer duration of therapy

Koristka. J Immunol. 2012;188:1551.

Effect of IVIG Prophylaxis on Infection-Free Survival in Recipients of BCMA-Directed BsAb for MM



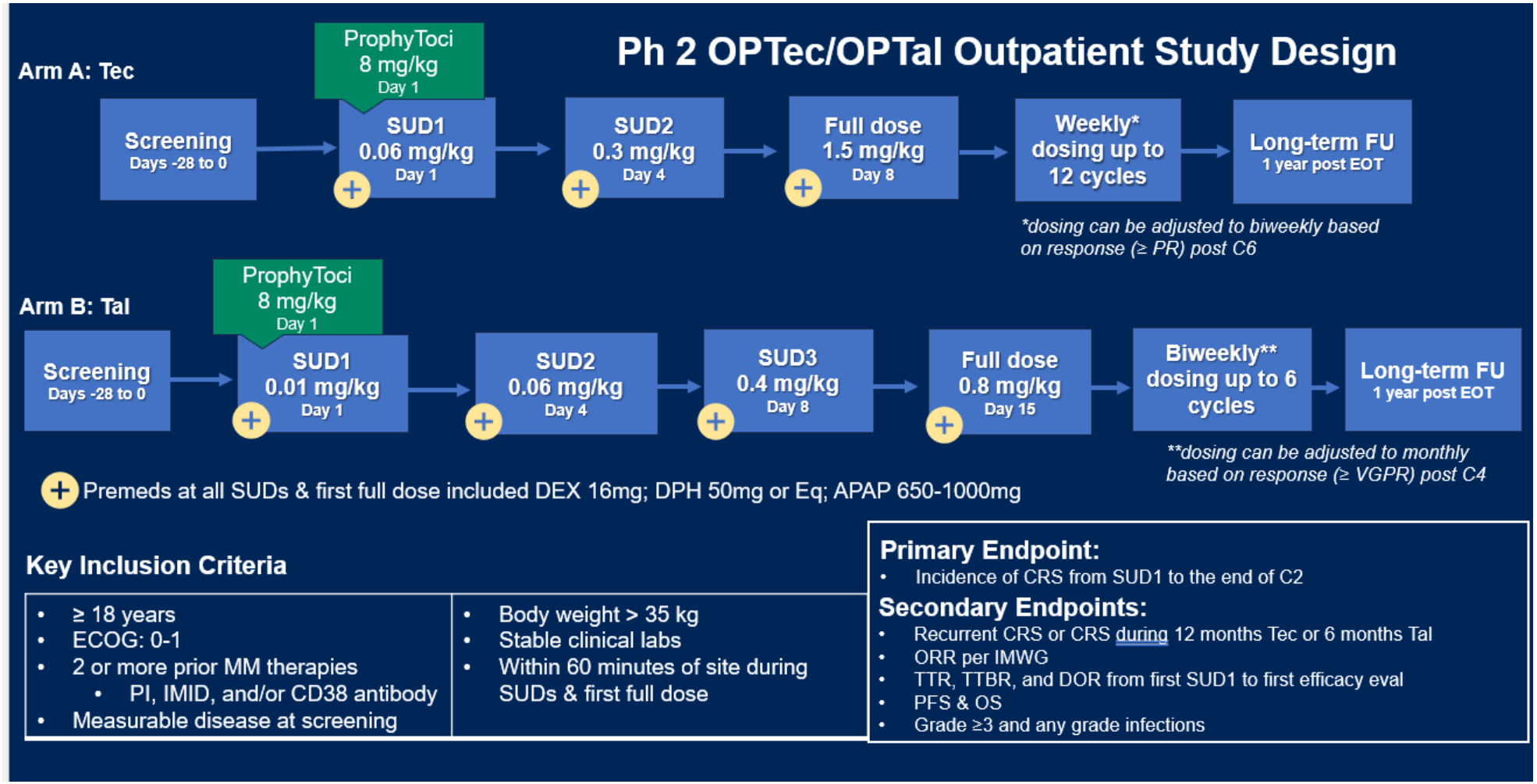


No primary IVIG prophylaxis				
At risk	221	12	2	0
Events	0	89	92	94
Primary prophylaxis				
At risk	13	41	10	2
Events	0	25	36	37

No primary IVIG prophylaxis				
At risk	223	33	9	2
Events	0	60	67	71
Primary prophylaxis				
At risk	13	48	13	2
Events	0	12	23	24

Mohan. Blood Cancer J. 2025;15:74.

OPTec/OPTal: A Phase 2 study to evaluate outpatient (OP) step-up administration of teclistamab (Tec) or talquetamab (Tal) with prophylactic tocilizumab (prophyToci) in patients (pts) with relapsed/refractory multiple myeloma (RRMM)



Peter Forsberg, MD; OPTec/OPTal ASCO 2026

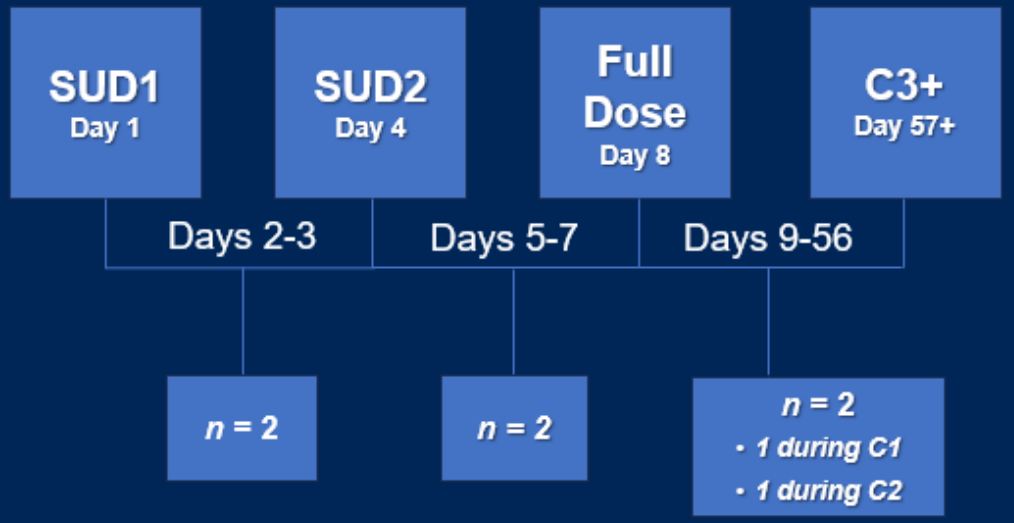
CRS/ICANS and Management in an Outpatient Setting*

Arm A: Tec

No reported ICANS • No Grade 3 or 4 CRS reported

CRS Events: *n* = 6 in 4 of 45 patients (8.9%)

- **Grade 1: 6**



Management of CRS Events During Treatment	
Grade 1	• No patients were admitted • All patients were managed with dexamethasone • Dexamethasone dose range: 8-20 mg

Arm B: Tal

No reported ICANS • No Grade 3 or 4 CRS reported

CRS Events: *n* = 4 in 2 of 7 patients (28.5%)

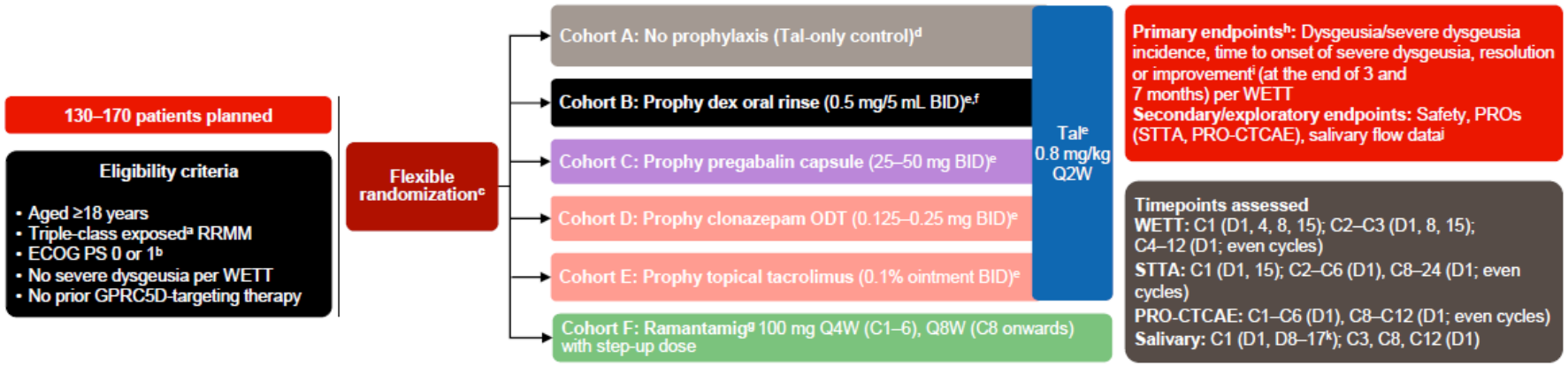
- **Grade 1: 3**
- **Grade 2: 1**

Management of CRS Events During Treatment	
Grade 1	**One patient experienced three Grade 1 CRS events (D34, D41, D53)** • Patient was admitted for all 3 events (SAEs) • Patient was given dexamethasone (8 mg) and/or antibiotics
Grade 2	• One patient hospitalized (SAE) • Patient given dexamethasone (10 mg), fluid hydration, & tocilizumab • Resolved within 3 days • Tal held for 1 week post resolution of CRS • Repeated SUD 2 (7 days after resolution of CRS) • No further CRS reported during time on treatment

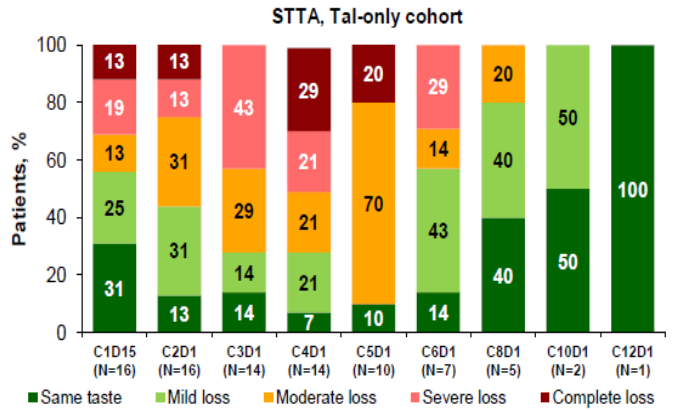
**Data updated: March 6, 2026*

Early Resolution of Talquetamab Oral Side Effects in Relapsed/Refractory Multiple Myeloma: Updated Waterless Empirical Taste Test and Patient-Reported Outcomes

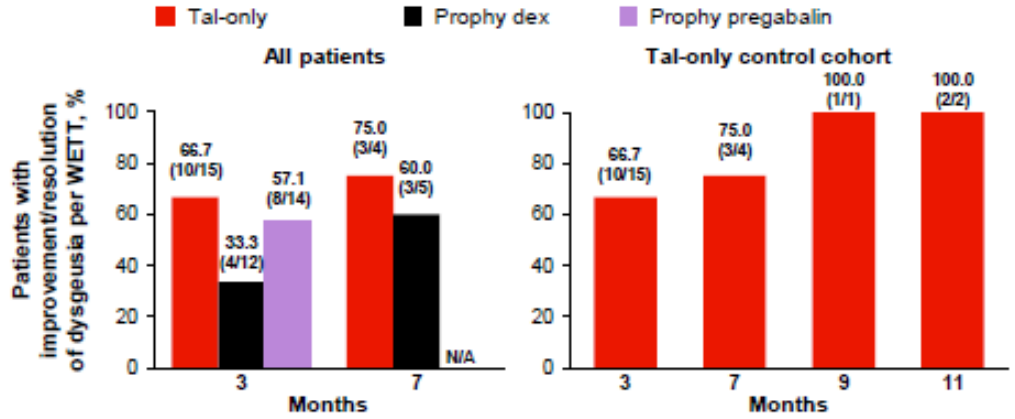
TALisman phase 2 study design



In the Tal-only cohort, severity of taste loss tended to stabilize or improve after peaking at 4–5 cycles per subjective STTA



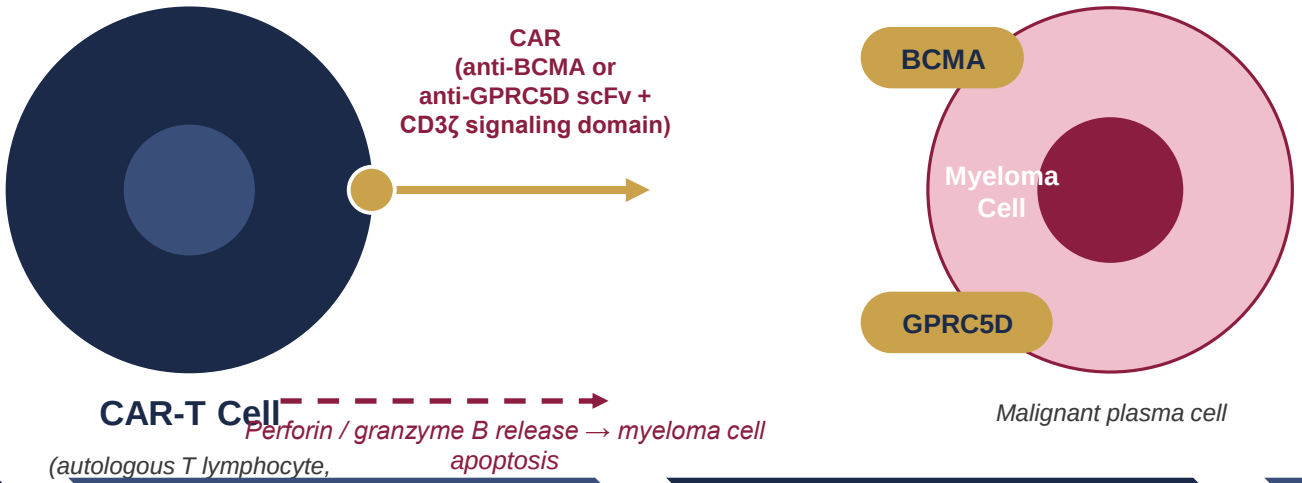
Dysgeusia per WETT resolved in most (10/15) patients after 3 months, resolving in (6/9 of patients after 7 months; prophylaxis did not improve outcomes



Presented by NWCJ van de Donk at the European Hematology Association (EHA) 2026 Congress; June 11–14, 2026; Stockholm, Sweden

CAR-T Cell Therapy in Myeloma

Chimeric Antigen Receptor T Cells Engineered Against BCMA or GPRC5D



1. Antigen recognition
2. Immune synapse formation
3. T-cell activation & expansion
4. Cytotoxic killing (apoptosis)

BCMA-Directed CAR-T — FDA Approved

Idecabtagene vicleucel (ide-cel, Abecma) and **ciltacabtagene autoleucel (cilta-cel, Carvykti)** — approved for relapsed/refractory MM after ≥1 prior line (cilta-cel) or ≥2 prior lines (ide-cel).

GPRC5D-Directed CAR-T — Investigational

Arlocabtagene autoleucel (arlo-cel, BMS-986393) — phase 3 trials ongoing (QUINTESSENTIAL) in R/R MM; not yet FDA approved. GPRC5D is not expressed on normal plasma cells.

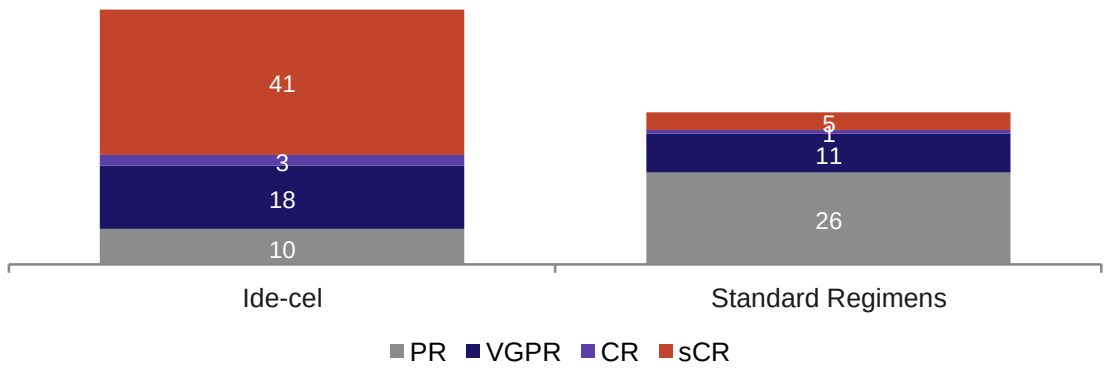
CAR T-Cell Therapy Moving Earlier in R/R Multiple Myeloma

KarMMa-3 (Ide-cel) vs CARTITUDE-4 (Cilta-cel): Phase III Head-to-Head Trial Data

	KarMMa-3 — Ide-cel (N = 254 treated)	CARTITUDE-4 — Cilta-cel (N = 208 treated)
Enrollment criteria	2–4 prior LoT, refractory to last regimen	1–3 prior LoT, refractory to lenalidomide
Triple-class refractory	65%	14.4%
ORR (95% CI)	71.0% (66–77)	84.6% (176/208)
≥ CR rate	~30%	76.9% (33.6-mo f/u)
Median PFS (95% CI)	13.8 mo (11.8–16.1)	NR (34.5–NE)
HR vs standard of care	0.49 (0.38–0.63)	0.29 (0.22–0.39), P < .0001
Median DoR / 30-mo PFS	16.6 mo (12.1–19.6)	30-mo PFS: 59.4% vs 25.7% (SoC)
CRS, %	88.0%	76.1%
Neurotoxicity, %	15.0%	20.5% (ICANS: 4.5%)

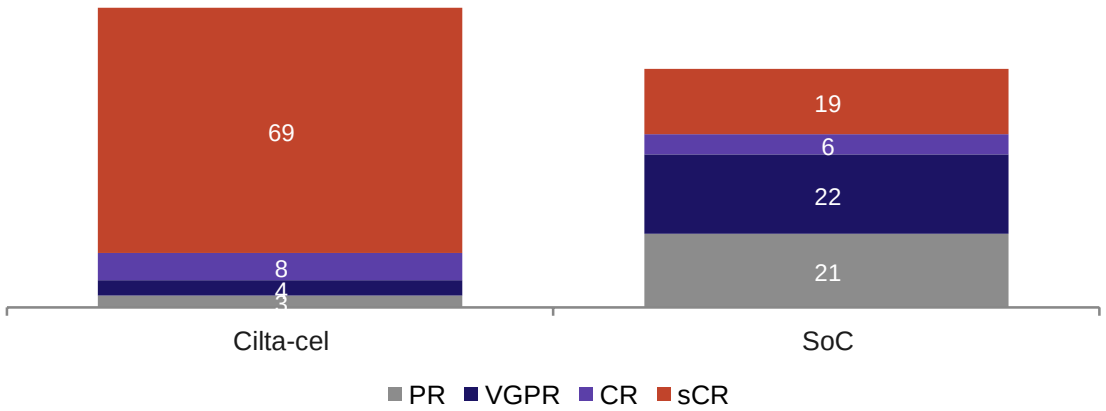
KarMMa-3: Depth of Response

ORR 71% vs 42% (SRs)



CARTITUDE-4: Depth of Response (33.6-mo f/u)

ORR 84.6% vs 67.3% (SoC)



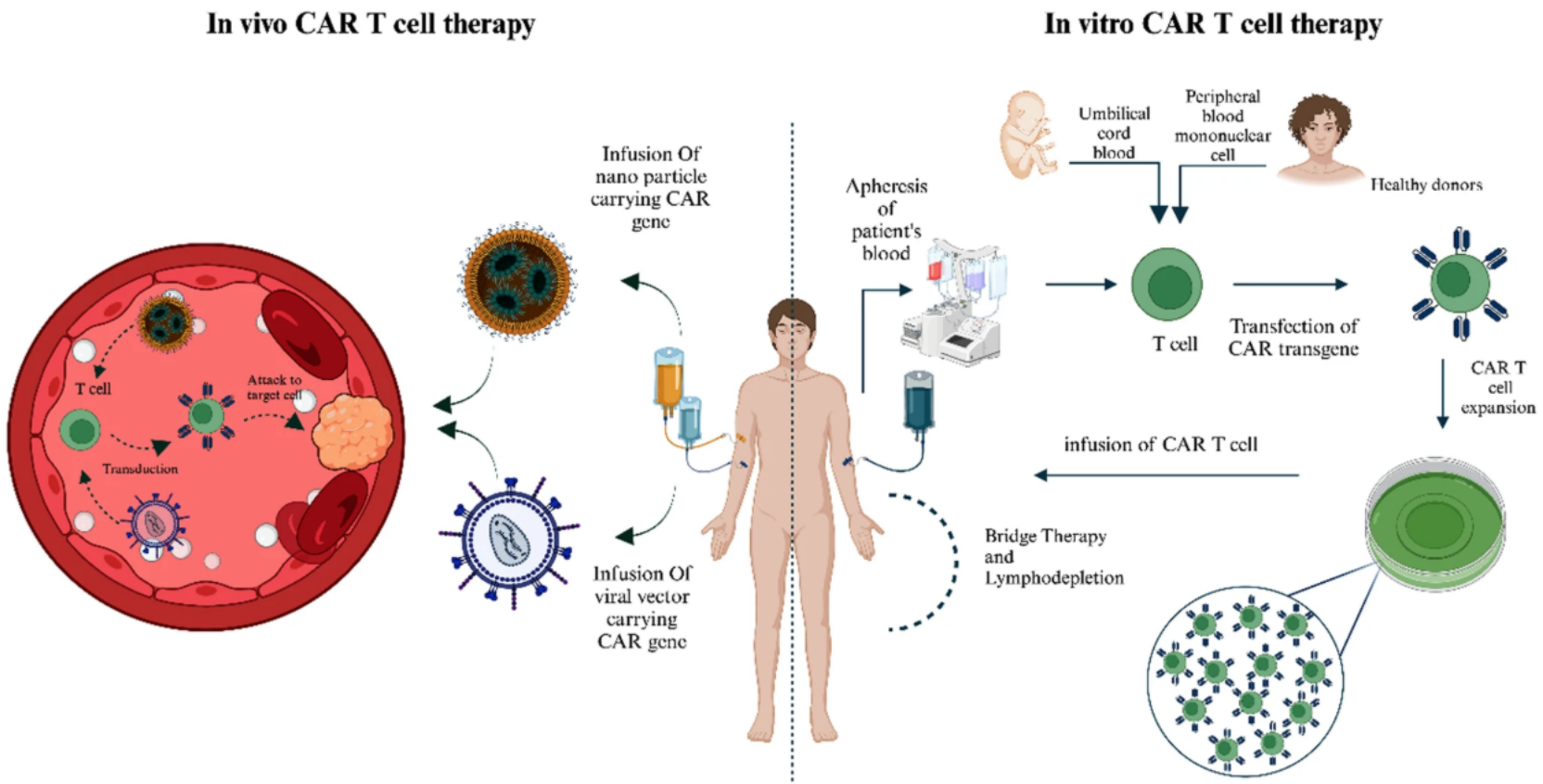
1. Rodriguez-Otero. NEJM. 2023;388:1002. 2. Ailawadhi. Blood. **2024;144:2389**. 3. San-Miguel. NEJM. 2023;389:335. 4. Einsele. Lancet Oncol. 2026;27:254.

Investigational CAR T-Cell Therapies in R/R MM

Parameter	ARI0002h CARTBCMA-HCB-01[1,2] (n = 60)	AZD0120 PGC0008[3] (n = 29)	Arlocabtagene autoleucel NCT04674813[4] (n = 84)	ESO-T01[5] (n = 5)
Phase	I/II	I/II	I	I
Target (MoA)	BCMA	BCMA/CD19 dual targeting CAR T	GPRC5D	**In vivo anti-BCMA** CAR T (nanobody directed lentiviral vector encoding an anti-BCMA CAR)
scFv origin	Humanized	FasTCAR	Human	Human
Co-stim	4-1BB	4-1BB	4-1BB	4-1BB
Specificity	Autologous	Autologous	Autologous	Allogeneic
Median age, yr (range)	58 (36-74)	57 (27-76)	63 (39-80)	52 (52-68)
Median no. of prior lines	3	5	5 (3-15)	3 (3-5)
With HR cytogenetics, %	28	90	42	40
With EMD, %	18	28	45	20
With triple-R, %	67	NA	35 (penta)	--
ORR, %	**95**	**93.1**	**87**	**4/5 (80)**
CR/sCR, %	58	82.8	53	3/4 (60)
MRD-neg (10^{-5}), n/N (%)	--	--	--	4/4 (100) by Day 60
PFS, mo	20	38	18.3	Not reached

1. Oliver-Caldes. ASH 2023. Abstr 1026. 2. de Larrea. ASCO 2024. Abstr 7544. 3. Du. ASCO 2023. Abstr 8005.
4. Bal. ASH 2024. Abstr 922. 5. An. Nat Med. 2026;32:1257.

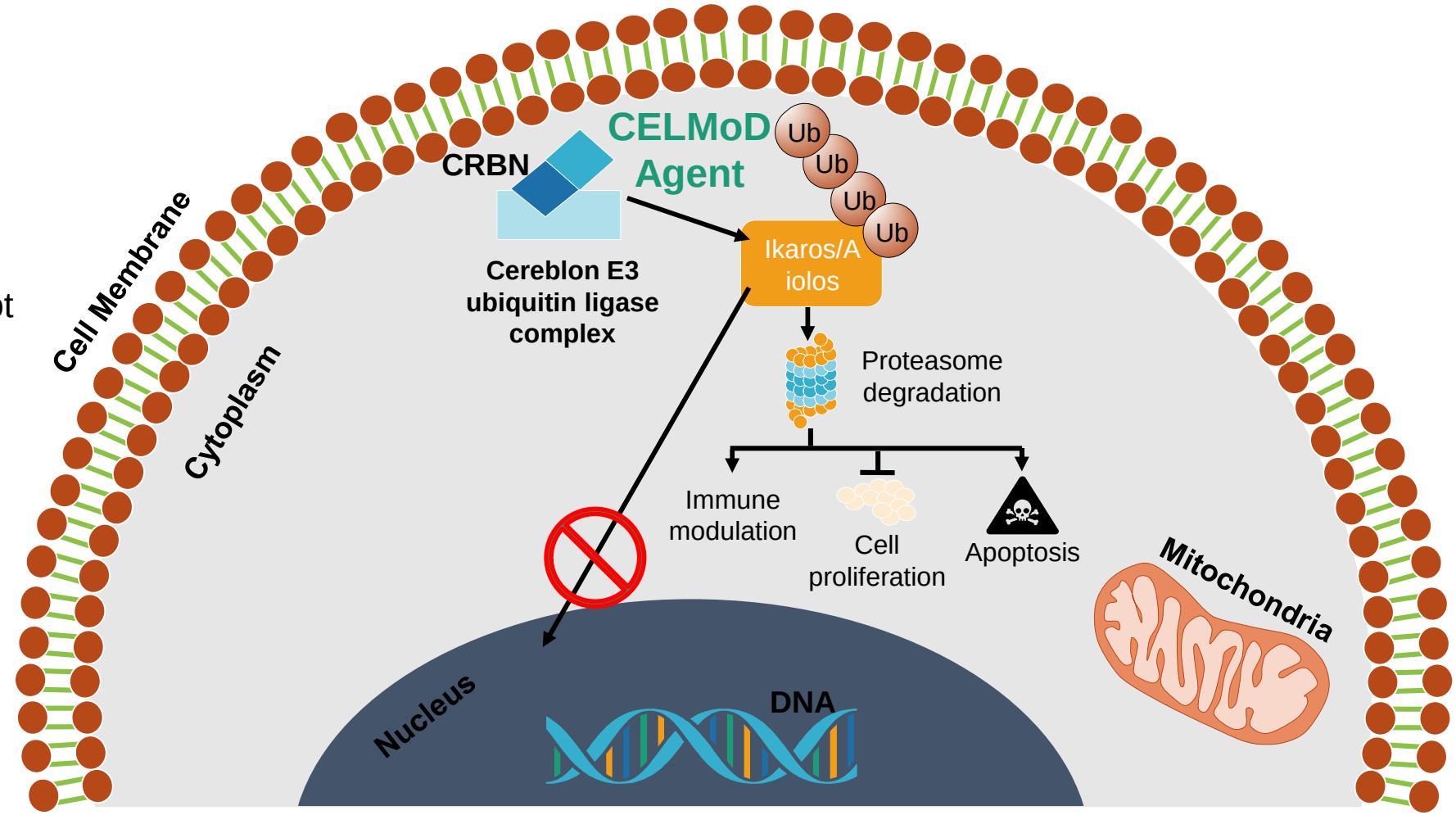
Next Gen CARs



State of the art in CAR-based therapy: In vivo CAR production as a revolution in cell-based cancer treatment, Cellular Oncology (2025) 48:859–883

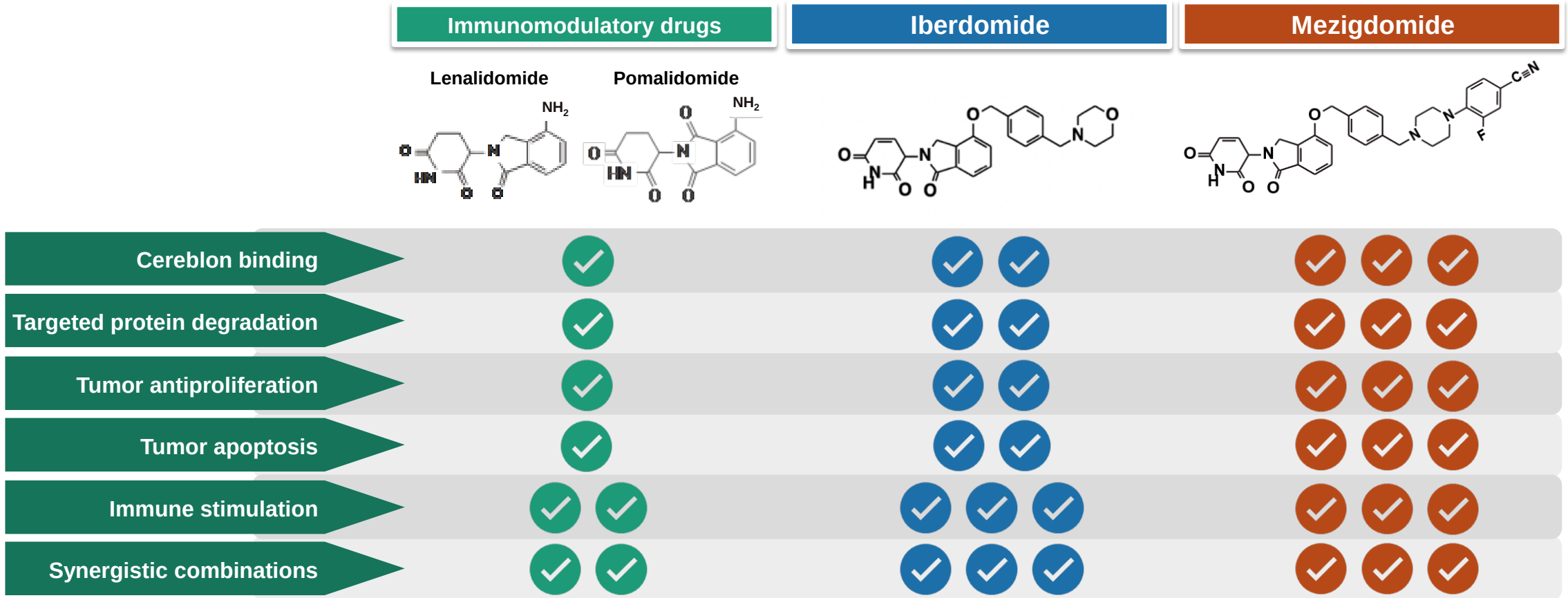
Protein Degradation in MM

- The ubiquitin-proteasome system tags proteins for proteasomal degradation with ubiquitin
- IMiD agents and novel CELMoD agents alter the target protein-binding properties of CRBN to promote interaction with protein substrates that otherwise would not be candidates for degradation



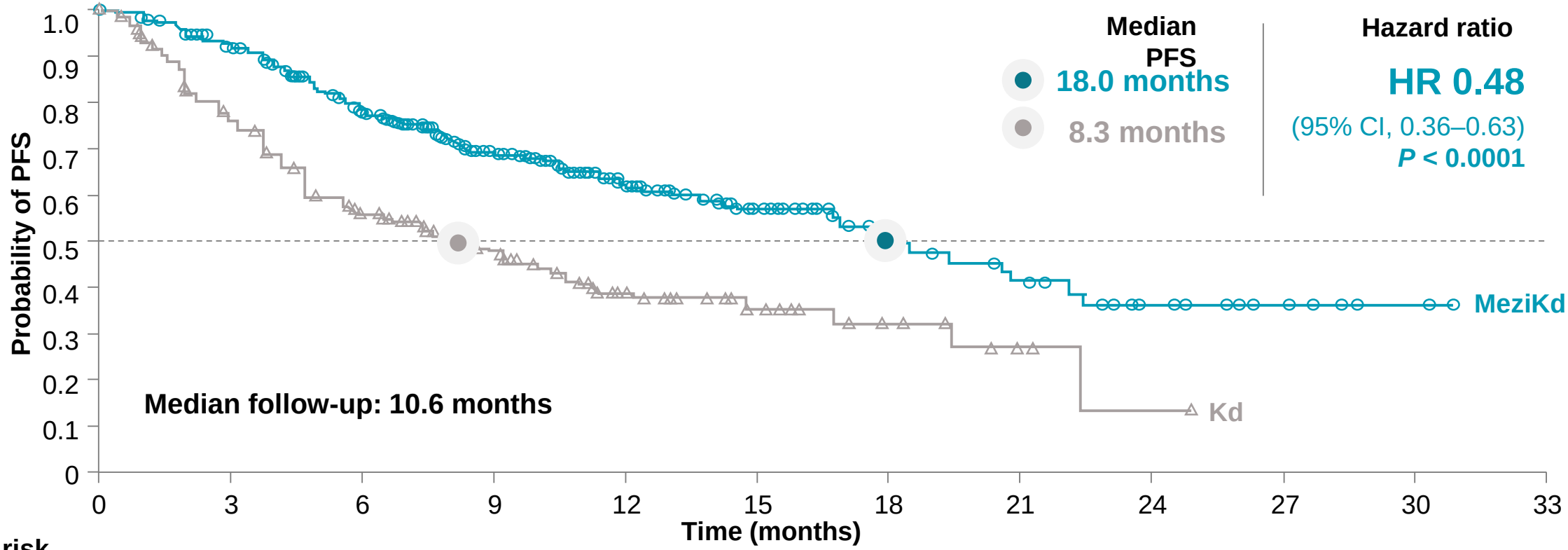
Charlinski. Cancers. 2021;13:4666. Ito. Int J Hematol. 2016;104:293.

Chemical Structures and Relative Preclinical Properties of IMiDs,



Hartley-Brown. Cancers (Basel). 2024;16:1166.

Mezigdomide, carfilzomib, and dexamethasone vs carfilzomib and dexamethasone in relapsed/refractory multiple myeloma: results from the phase 3 SUCCESSOR-2 trial



No. at risk

MeziKd	288	250	197	133	81	47	27	19	11	6	2	0
Kd	191	134	90	59	31	15	8	3	1	0	0	0

In anti-CD38 mAb- and LEN-exposed patients who had received ≥ 1 prior LOT (range 1–9), MeziKd significantly reduced the risk of progression or death by 52%

Richardson et al, ASCO 2026

KEY TAKEAWAYS

Immune-based therapy is reshaping every line of myeloma care.

01

Treatment algorithm & high-risk disease

Anti-CD38 quadruplets (Dara/Isa-VRd) anchor frontline induction, and the 2025 IMS/IMWG consensus unifies high-risk disease — an IgH translocation now counts only alongside a co-occurring 1q/1p lesion.

02

Bispecific antibody therapy

Off-the-shelf BCMA and GPRC5D bispecifics drive deep, durable responses; MajesTEC-3 establishes Tec-Dara as a new standard after ≥1 prior line, with IVIG prophylaxis central to managing infection risk.

03

CAR-T cell therapy

BCMA CAR-T (cilta-cel and ide-cel) is moving into earlier relapse with a marked PFS advantage over standard of care, while next-generation constructs such as anito-cel advance in trials.

04

Emerging therapies

CELMoDs (mezigdomide, iberdomide) and novel combinations such as MeziKd extend meaningful options for anti-CD38– and lenalidomide-exposed relapsed/refractory myeloma.

Ongoing Clinical trials at COH Atlanta

- **A Phase 3, Randomized, Open-Label Study to Compare the Efficacy and Safety of Anitocabtagene Autoleucel Versus Standard of Care Therapy in Participants With R/R MM**
- **A Phase 3 Randomized Study Comparing Teclistamab in Combination with Daratumumab SC and Lenalidomide (Tec-DR) and Talquetamab in Combination with Daratumumab SC and Lenalidomide (Tal-DR) versus Daratumumab SC, Lenalidomide, and Dexamethasone (DRd) in Participants with Newly-Diagnosed MM Who are Either Ineligible or Not Intended for Autologous Stem Cell Transplant as Initial Therapy**
- **First-in-Human, Open Label Study Evaluating Safety, Tolerability, PK and Preliminary Efficacy of ABBV-438 in Adult Subjects With Relapsed or Refractory Multiple Myeloma (R/R MM)**
- **A Phase III, Multicenter Study to Evaluate Treatment with AZD0120 versus ASCT in Transplant Eligible Newly Diagnosed Multiple Myeloma Patients (DURGA-6)**
- **Testing the Utility of Whole Genome Sequencing in Immunotherapy Exposed Multiple Myeloma Patients**
- **Retrospective and prospective database study designed to collect data from patients receiving immunotherapies at participating International Myeloma Working Group sites globally.**
- **A Multicenter Prospective Observational Cohort Study Evaluating the Impact of Cancer-Directed Treatment and Medication Use, including Cannabis Use, in Multiple Myeloma Patients**

Questions

Thank You

Email : sayyappan@coh.org

@SabarishMD

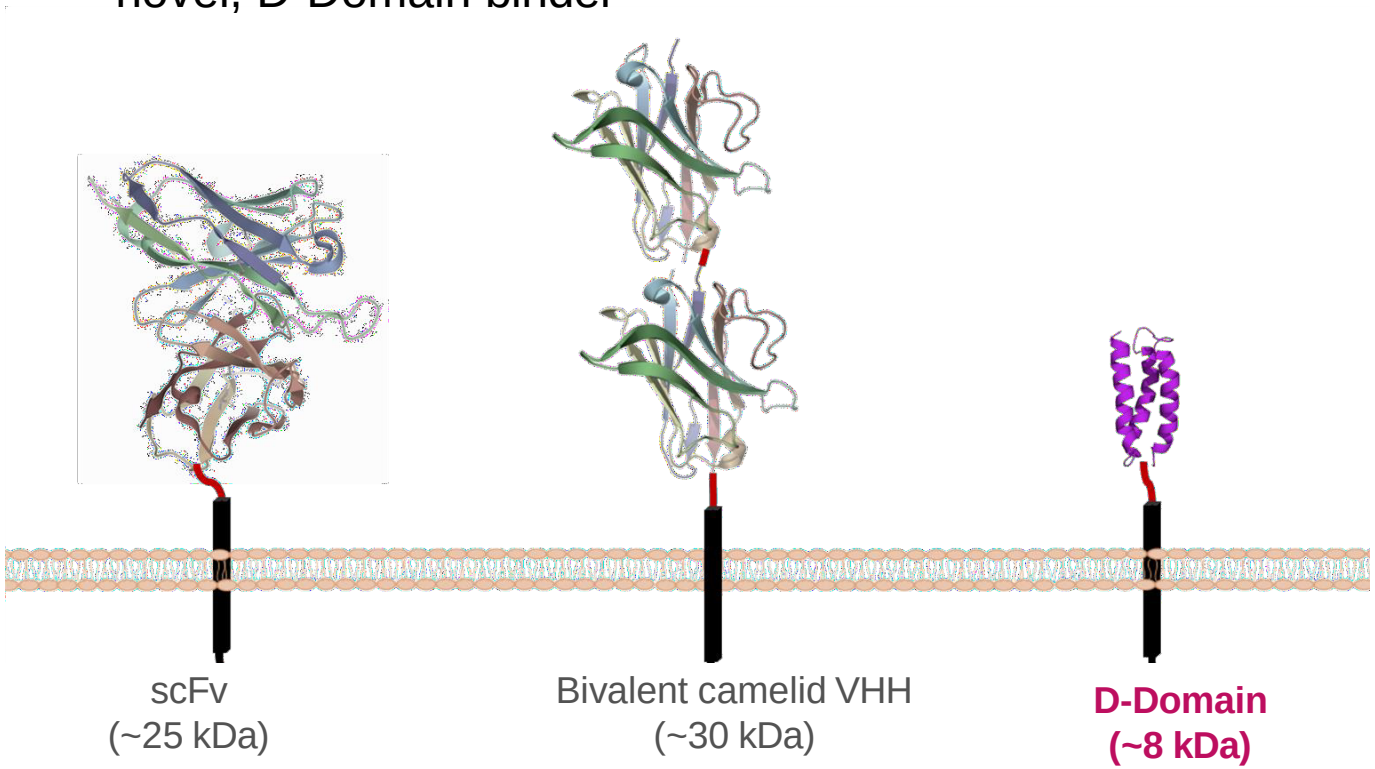
City of Hope®

BACKUP

01	Additional bispecific antibody trial & safety data
02	Additional CAR-T program data
03	Additional emerging therapy (CELMoD) data
04	For reference / Q&A only — not part of the 20-min talk

Anitocabtagene autoleucel (anito-cel/CART-ddBCMA)

Autologous BCMA-directed CAR T-cell therapy using a novel, D-Domain binder[1,2]



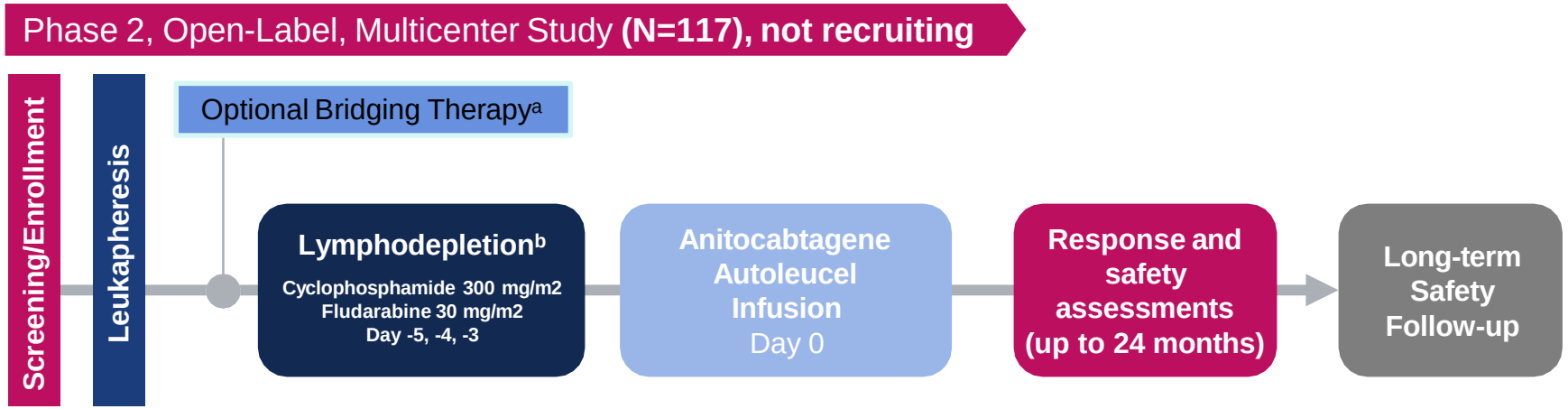
D-Domain Attributes:

Non-Antibody Derived Synthetic Protein[1,2]

Size	Small D-Domain construct facilitates high transduction efficiency and CAR positivity[2-4] resulting in a low total cell dose
Structure & Stability	D-Domain CARs are stable and lack tonic signaling[4,6] due to the rapid folding, lack of disulfide bonds, and hydrophobic core[5,6] of the D-Domain
Binding	The D-Domain binder has a fast off-rate[4] and high CAR surface expression[4]. This combination may allow optimal tumor cell killing without prolonged inflammation

[1]Rotte, et al. Immuno-Oncology Insights 2022; 3(1), 13–24; [2]Frigault, et al. Blood Adv. 2023; 7(5):768-777; [3]Cante-Barrett, et al. BMC Res. Notes 2016; 9:13; [4]Buonato, et al. Mol. Cancer Ther. 2022; 21(7):1171-1183; [5]Zhu, et al. Proc. Nat. Acad. Sci. 2003; 100(26): 15486-15491; [6]Qin, et al. Mol. Ther. 2019; 27(7): 1262-1274.

iMMagine-1 (phase 2): Anitocabtagene Autoleucel in Patients With RRMM[1,2]



Key Eligibility Criteria
• Prior IMiD, PI, and CD38-targeted therapy • Received ≥3 prior lines of therapy • Refractory to the last line of therapy • ECOG PS of 0 or 1 • Evidence of measurable disease Target Dose of 115 x 10^6 CAR+ T cell

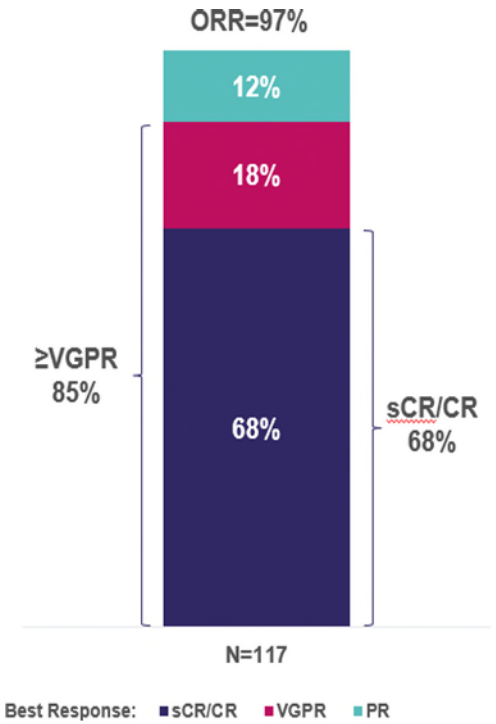
Primary Endpoint	Select Secondary Endpoints	
• ORR per 2016 IMWG criteria	• sCR/CR rate, per 2016 IMWG criteria • ORR in patients limited to 3 prior LoT, per 2016 IMWG criteria	• MRD-negative • Sustained MRD negativity • DoR • OS • TEAE

1. Hosoya H, et al. *Am Soc Clin Oncol Educ Book*. 2023;43:e389860. 2. Ahmed N, et al. *Front Oncol*. 2023;13:1206715. 3. Buonato JM, et al. *Mol Cancer Ther*. 2022;21(7):1171-1183. 4. Rotte A, et al. *Immuno-Oncology Insights*. 2022;3:13-24. 5. Snyder S, et al. *Adv Ther*. 2021;(38):4541-4555. 6. Adkins S et al. *J Adv Pract Oncol*. 2019;10(suppl_3):21-28. 7. Dhakal B et al. *Hematologist.* 2024;21(3):202432. 8. Rendo MJ, et al. *Blood Lymphat Cancer*. 2022;12:119–136. 9. The EBMT/EHA CAR-T Cell Handbook. Accessed October 2024. https://www.ncbi.nlm.nih.gov/books/NBK584164/.

iMMagine-1 (phase 2): Anitocabtagene Autoleucel in Patients With RRMM[1,2]

Overall Response Rate and MRD Negativity (N=117)

Efficacy Evaluable Patients, N=117



- At a median follow-up of 12.6 months, ORR was 97% and sCR/CR rate was 68%
- 93% (n=70/75) of evaluable patients were MRD negative at minimum of 10^{-5} sensitivity

	Evaluable Patients	Months (min - max)
Median time to first response	114	1.0 (0.9 – 13.4)
Median time to MRD negativity of ≤10^{-5}	70	1.0 (0.9 – 6.4)

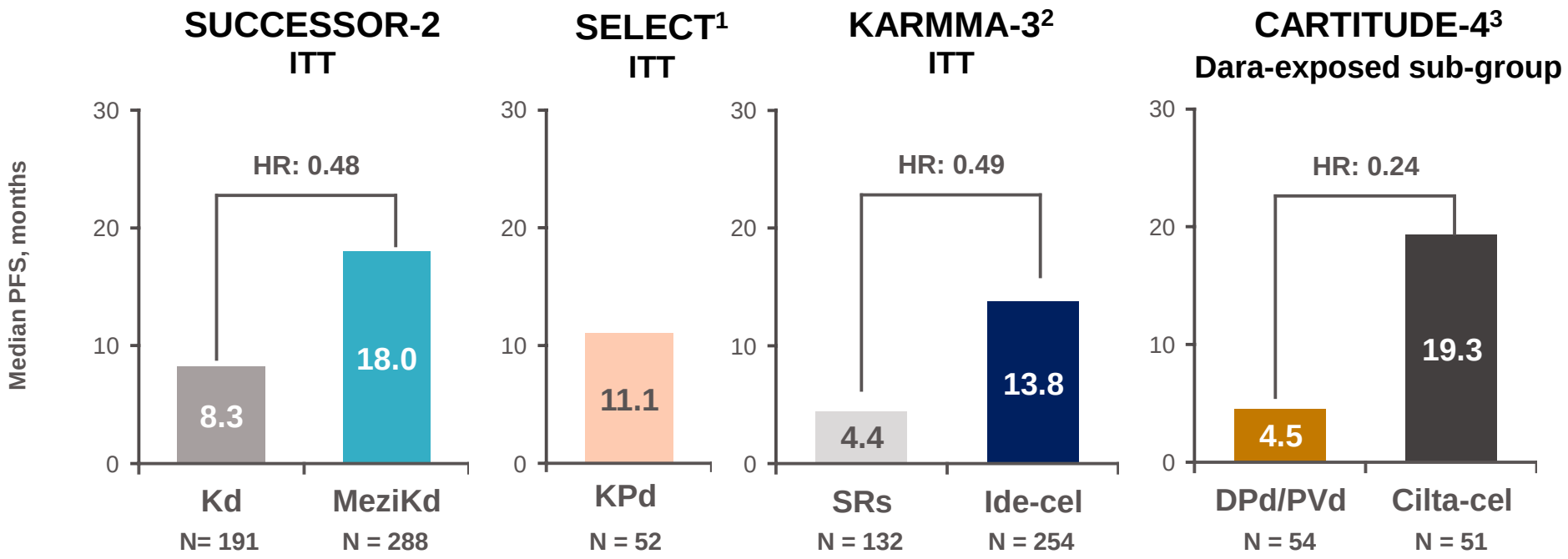
PFS and OS Rates Estimated by Kaplan-Meier

N=117	PFS Rate (%) (95% CI)	OS Rate (%) (95% CI)
6-Month	91.9% (85.0%, 95.7%)	96.6% (91.1%, 98.7%)
12-Month	79.3% (68.6%, 86.7%)	95.2% (88.7%, 98.0%)

Median follow-up of 12.6 months (range: 5 to 29 months)

1. Kaur et al. Updated Results from iMMagine-1. European Hematology Association (EHA) 2025, Abstract S201

MeziKd; Contextualization of Clinical Benefit seen in SUCCESSOR 2 for Anti-CD38 mAb- and LEN-exposed RRMM Patients across multiple settings



All patients[a] were anti-CD38 mAb- and LEN-exposed

Median pLoT, n (range)	2 (1–9)	2 (1–9)	2 (1–2)	3 (2-4)	3 (2-4)	NR	NR
LEN ref., %	76.9	74.4	100	73	79	100	100
aCD38 ref., %	85.3	86.1	75	95	94	83.3	90.5

Trials are not intended for direct comparison. Side-by-side data are presented solely to summarize information.
[A] 77% of patients received prior anti-CD38 mAb in the SELECT trial. pLoT, prior lines of therapy; SRs, standard of care regimens; NR, not reported

1. Perrot A, et al. *Leuk Lymphoma* 2024;65(6):833-842; 2. Ailawadhi S, et al. *Blood* 2024;144(23):2389-2401; 3. Einsele H, et al. *Lancet Oncol* 2026;27(2):254-268.