

How Will We be Treating Multiple Myeloma in 5-10 years

“Everything works better the earlier you try”

Thomas Martin, MD

Helen Diller Family Comprehensive Cancer Center

UCSF Medical Center

San Francisco, California

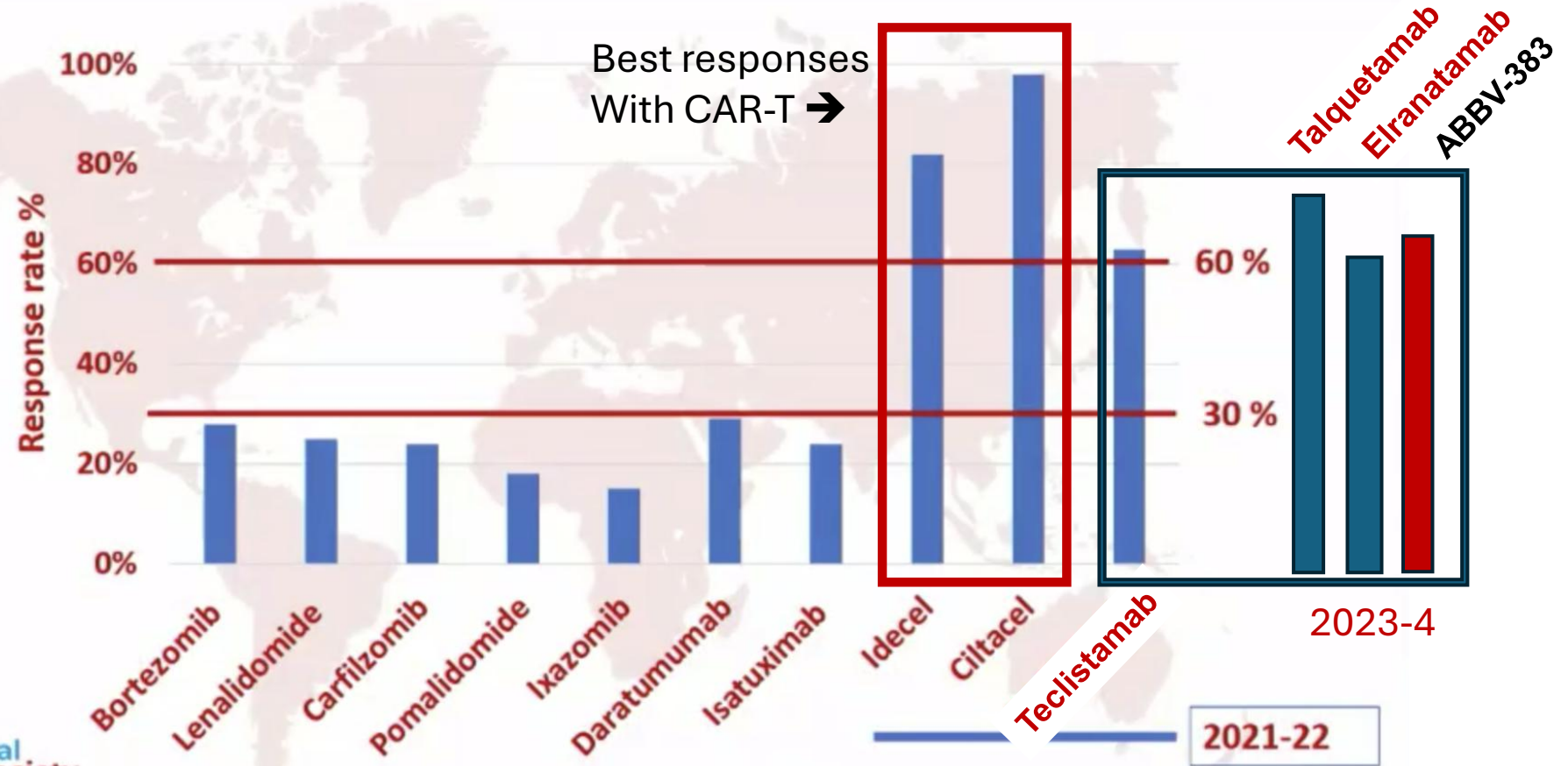


Amazing Success in Immunotherapy for MM

Single Agent Response Rate – Changing Landscape

These agents have Transformative Potential

NOT EVERYONE CHOOSES CART!!



Right patient, right treatment, right time

2030-5: New Diagnostics

- Current Work-up/ Risk Stratification
 - Blood and Urine Tests (SPEP, SIFE, UPEP, UIFE)
 - Blood Tests (B2M, Alb, LDH)
 - BMBx - examination
 - Cytogenetics/fish testing
 - PETCT – standard WB-MRI
- 2030-5 Work-up/ Risk Stratification
 - Blood tests (MASS-FIX, Limited urine testing!!)
 - Blood tests (B2M, soluble BCMA, CTCs)
 - Cell-free-DNA
 - Genomic abnormalities detected in blood
 - Risk status – target identification
 - Infrequent bone marrow biopsy needed
 - CD38-PETCT/ Diffusion weighted MRI
 - T-cell Health Flow Panel (peripheral blood)

- **2025 HR Definition**

- Genomic abnormalities
 - del17p (at least 20%)
 - TP53 mutation
 - Biallelic deletion of 1p32
- Double hit genetic abnormalities
 - T(4;14) or t (14;16) or t(14;20)
 - 1q21 gain
 - Del 1p32
- B2M (normal CrCl)

- **2030 HR Definition**

- Sequencing panel from PB (cfDNA)
- Definition updated to include
 - Myc rearrangements/mutations
 - Ras mutations
 - BCMA/GPRC5D mutations/deletions
 - Circulating myeloma cells

2035: New Response Criteria

- Response Definition 2030-2035
 - ORR – PR, VGPR, CR (No sCR)
 - Measured by MASS- FIX (mass-spectrometry)
 - New definition of CR
 - MRD testing in all when MASS-FIX(-) or below threshold
 - BMBx – examination – rarely needed
 - Blood MRD
 - cfDNA
 - Flow for CD138(+) circulating tumor cells (10^{-6} , 10^{-7})
 - PETCT – Novel isotope with CR/MRD defined by SUV

MASS-FIX = matrix-assisted laser desorption ionization time-of-flight mass-spectrometry

2035: New Definition of Smoldering MM

- IMWG Definition and Pangea Model.

- 20-2-20 + genetics
- Trajectory model
 - Hgb
 - M-prot
 - Cr
 - FLCr

- 2030-2035 New SMM Definition

- MGUS and active MM separated from SMM
- Whole exome/whole genome sequencing
- Tumor microenvironment → help define TMT

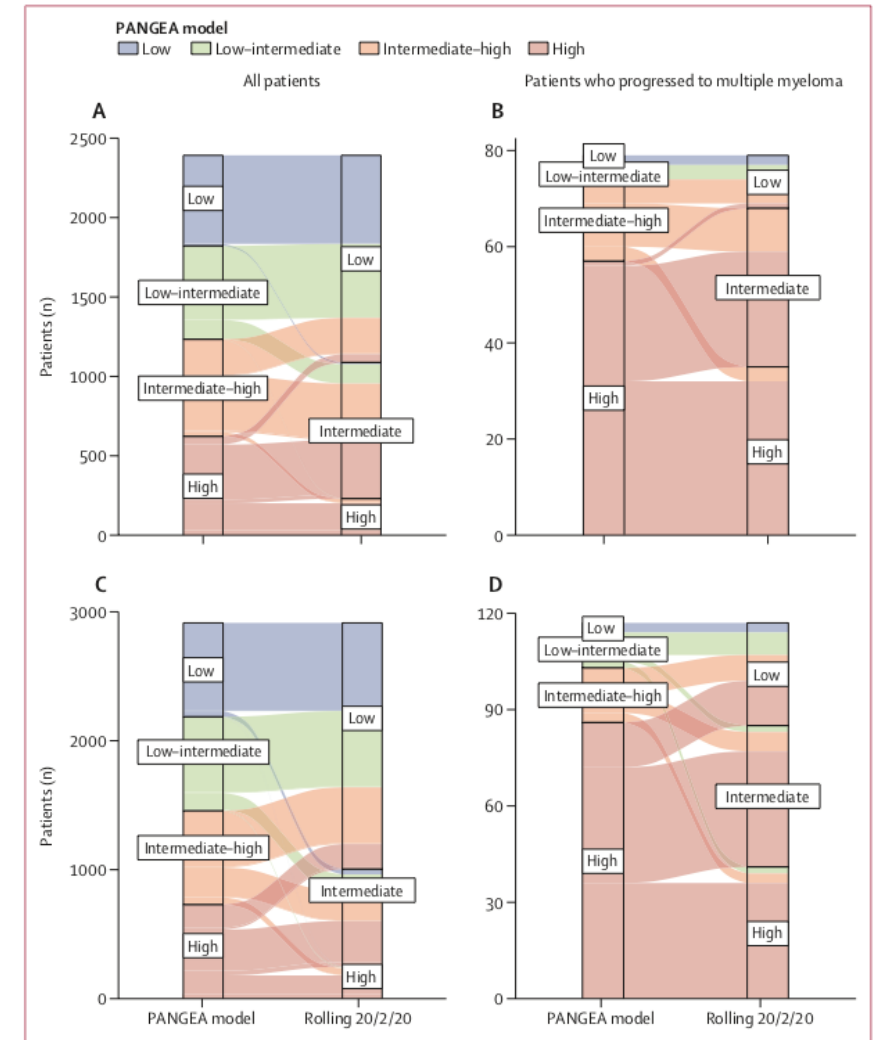
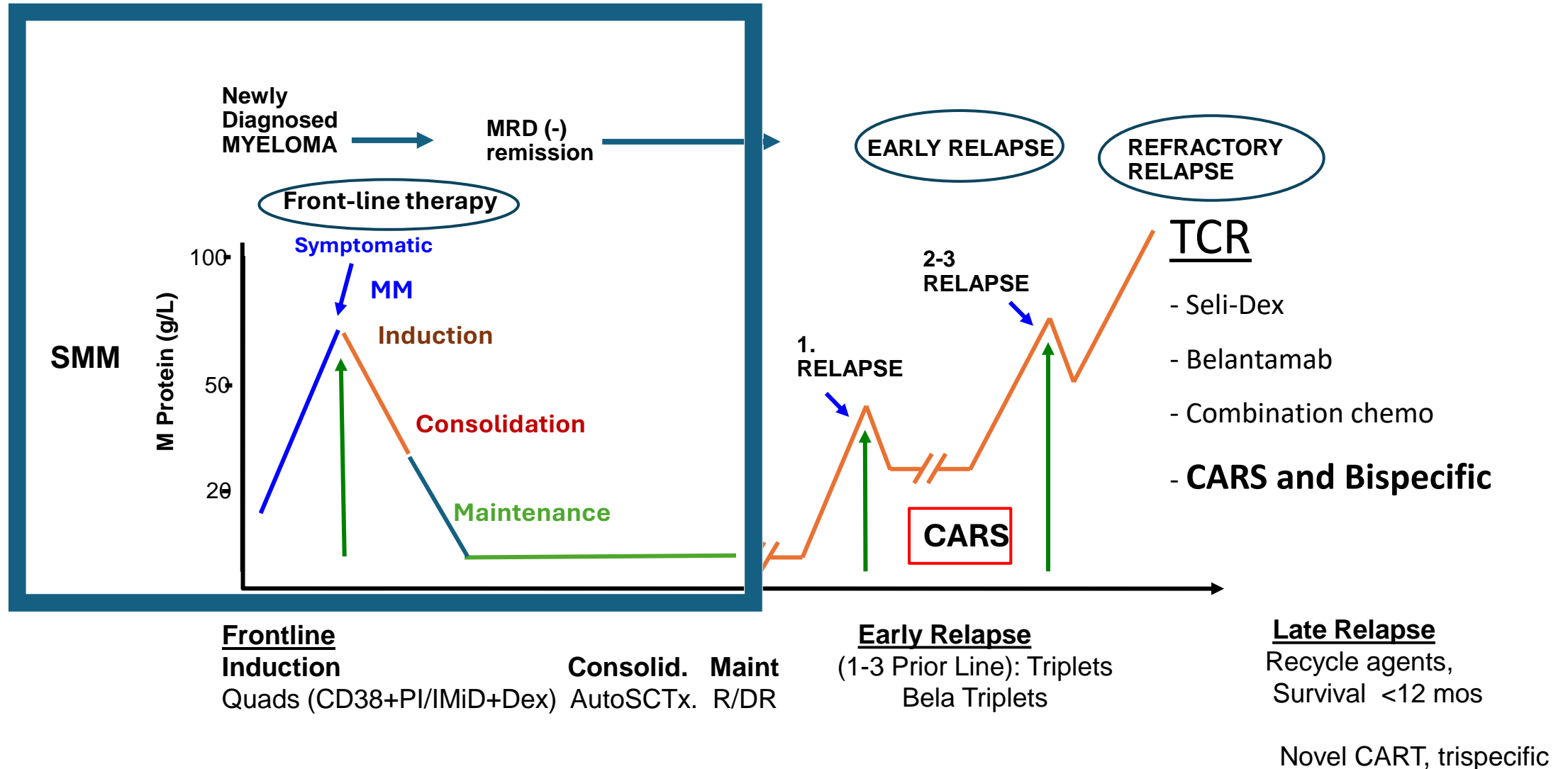


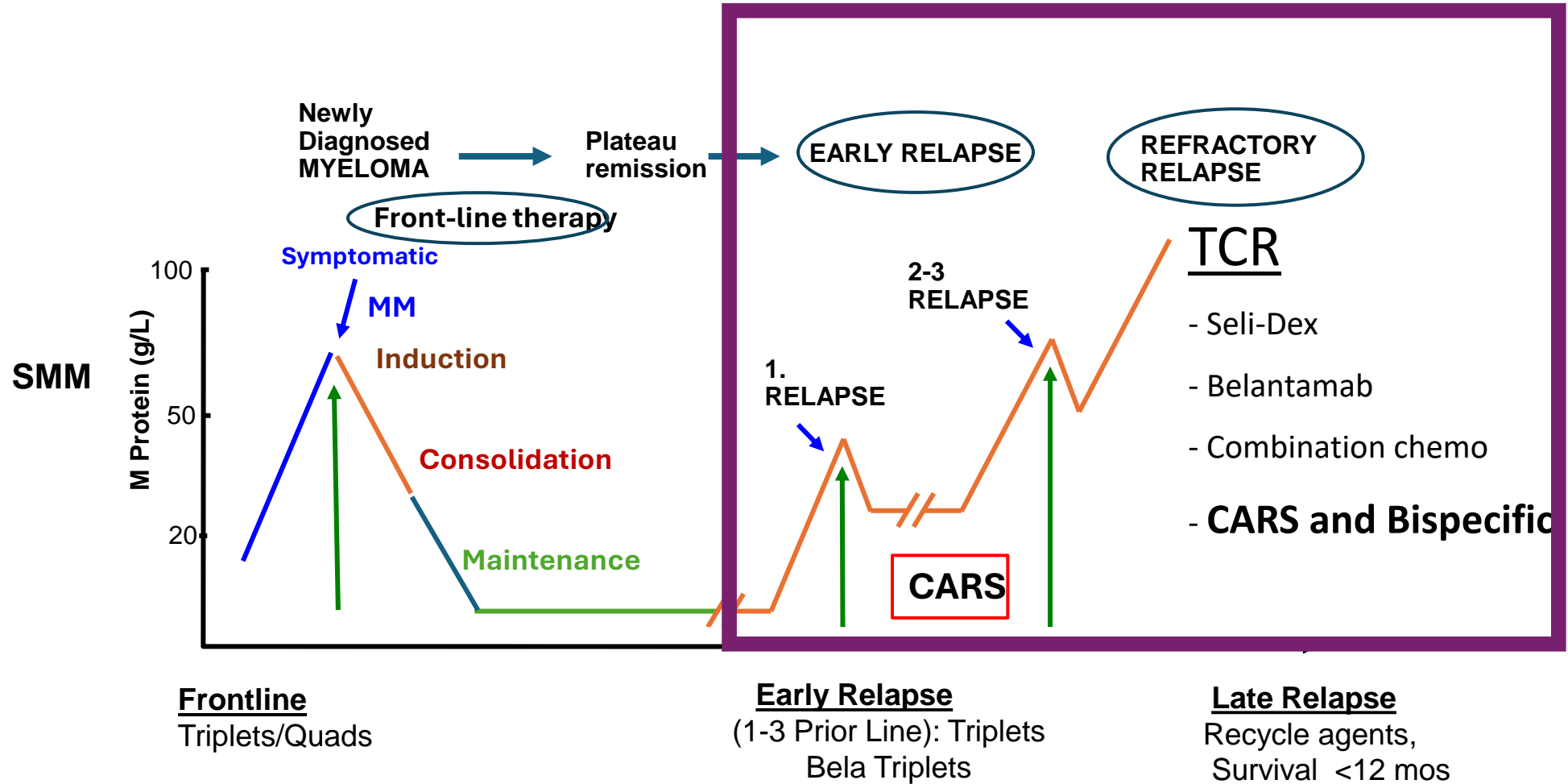
Figure 3: Risk stratification of the PANGEA models compared with the rolling 20/2/20 model in the validation cohorts at visit 1

Therapy for MM: 2030-2035

Where should we deploy all these agents?



Sequencing Therapy in MM: *How should we deploy all these agents?*



Treatment for HR-SMM

1. Ideal Treatment

- Least toxic and most effective
- Minimal acute toxicity
- No long-term toxicity
- Significantly prolongs time to MM
- OR
- Prevents the progression to MM

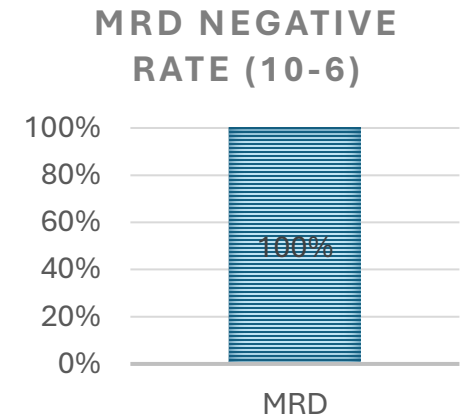
Prediction:

- ALL HR-SMM will be treated
- Bispecifics >> CAR T-cells
- Time limited therapy

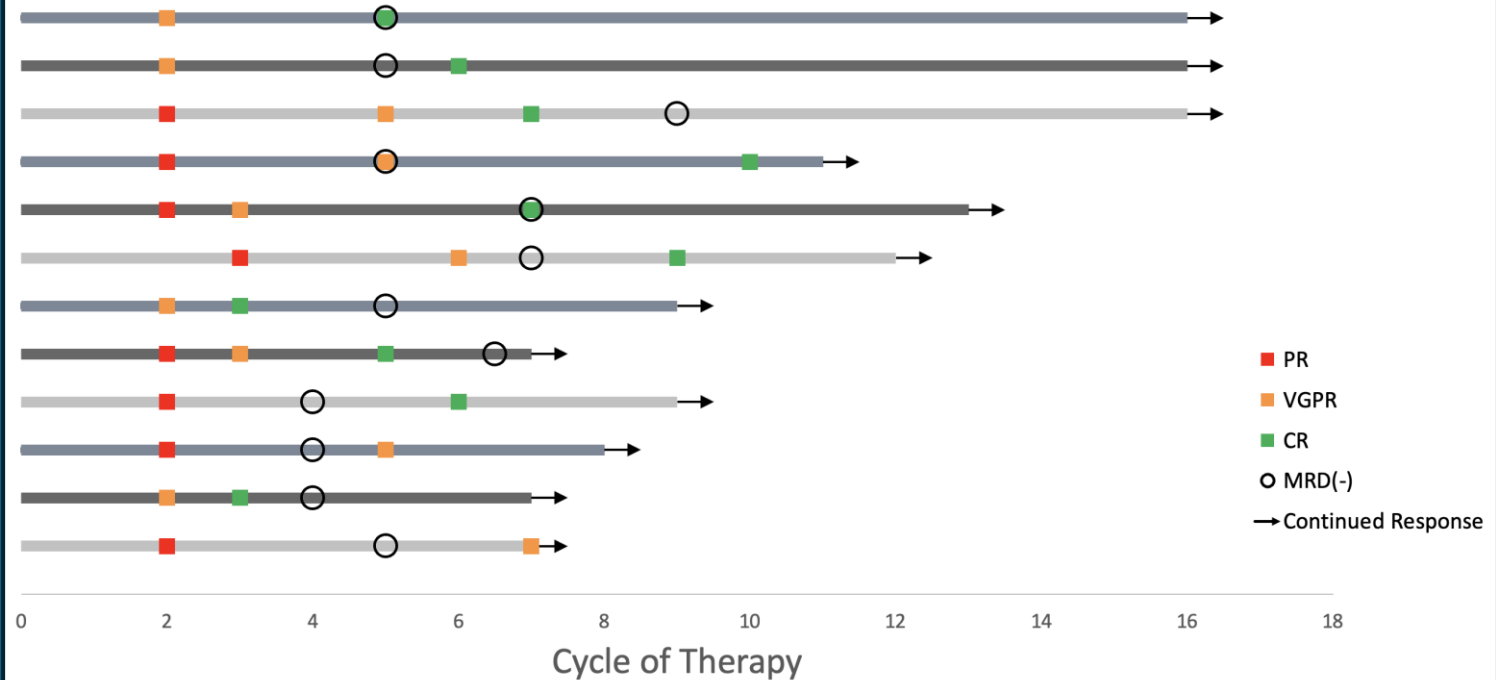
Bispecifics >> CAR T-cells
(toxicity tradeoff)

Teclistamab in HR SMM

Best response	n	%
CR	10	83
VGPR	2	17
ORR	12	100



Swimmer's plot and response to therapy in Teclistamab arm: n = 12

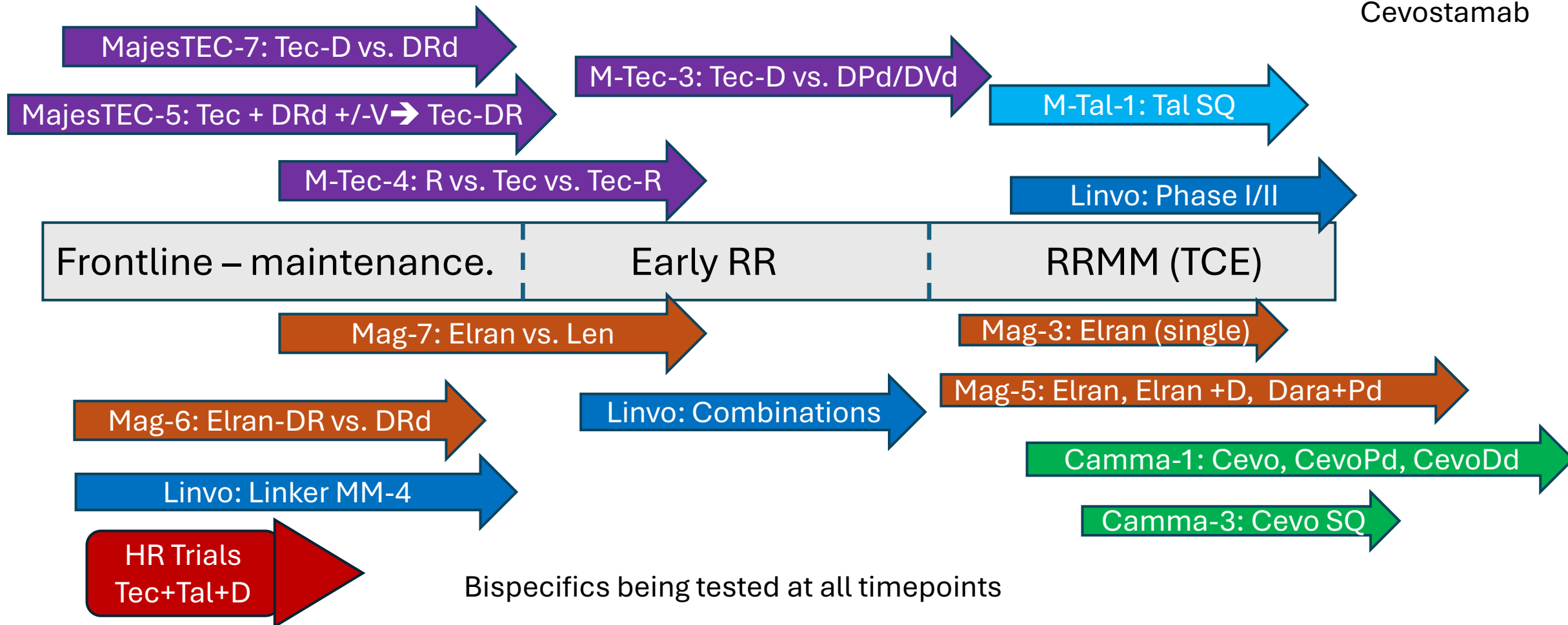


Immunotherapy Bispecific Trials

Current and planned (not inclusive of all trials)

- Future Myeloma Treatment Paradigm

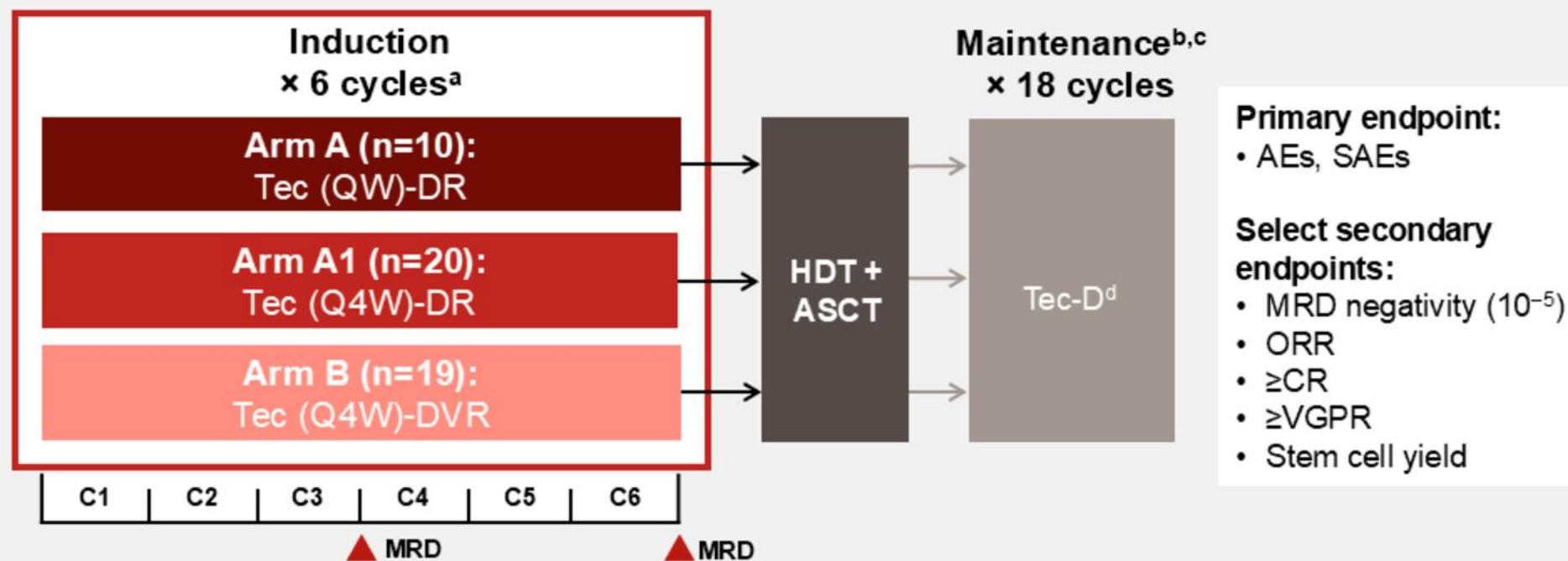
BCMA
Teclistamab
Elranatamab
Linvoseltamab
ABBV-383
Non-BCMA
Talquetamab
Cevostamab



GMMG-HD10/DSMM-XX/MajesTEC-5: Study Design

Key eligibility criteria:

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



- Per protocol, MRD assessments by NGF were planned following completion of C3 and C6 in all patients
- Additional cohorts evaluating Tal and Tec/Tal combinations are also being investigated as part of this study

^aEach cycle is 28 days. Dexamethasone was also administered in C1 and C2. Stem cell collection was planned after 3 cycles of induction. ^bFollowing maintenance therapy, patients could receive additional SoC maintenance treatment per institutional standard and local investigator decision. ^cMaintenance treatment can be discontinued when 12 months of sustained MRD negativity (10^{-5}) have been observed, beginning in induction. ^dPlanned maintenance treatment in Arm A was Tec-DR. A protocol amendment permitted patients initially assigned to Tec-DR maintenance to receive Tec-D maintenance per investigator's choice (patients who started Tec-DR may have discontinued Len to receive Tec-D per investigator's choice). AE, adverse event; ASCT, autologous stem cell transplant; C, Cycle; CR, complete response; D, daratumumab; ECOG PS, Eastern Cooperative Oncology Group performance status; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; HDT, high-dose therapy; Len, lenalidomide; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGF, next-generation flow cytometry; ORR, overall response rate; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; SAE, serious adverse event; SoC, standard-of-care; Tal, talquetamab; TE, transplant-eligible; Tec, teclistamab; V, bortezomib; VGPR, very good partial response.



GMMG-HD10/DSMM-XX/MajesTEC-5: Dosing Schedule

	C1 ^a	C2-C6 ^a
Arm A (n=10)	Tec + Dara	Tec 1.5 mg/kg QW + Dara + Len
Arm A1 (n=20)	Tec + Dara	Tec 3.0 mg/kg Q4W + Dara + Len
Arm B (n=19)	Tec + Dara + Btz	Tec 3.0 mg/kg Q4W + Dara + Len + Btz

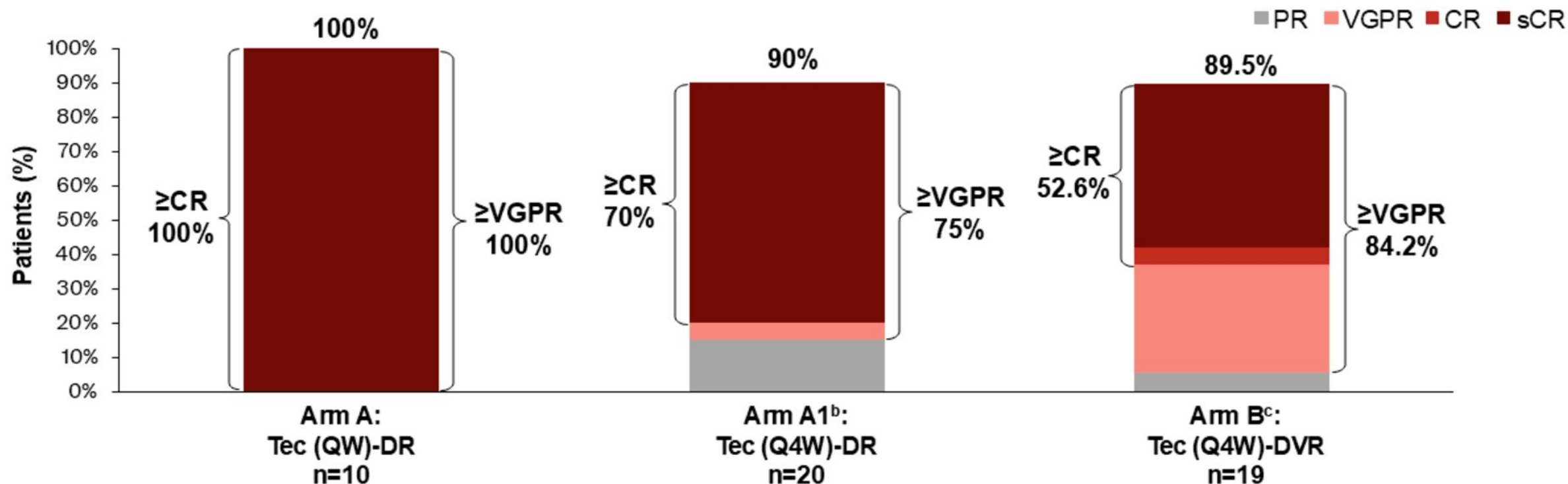
▲ Initiate Len in C2

- **Tec in C1:** Tec step up^a + 1.5 mg/kg on Days 8 and 15^b
- **Dara:** 1800 mg SC per label (QW for C1 and C2; Q2W for C3-C6)
- **Btz:** 1.3 mg/m² SC QW
- **Len:** 25 mg PO daily starting in C2 (Days 1-21)
- **Dex:** 20 mg (PO or IV) in C1 and C2^c

^aPatients received step-up doses of 0.06 and 0.3 mg/kg on Day 2 and 4. ^bPatients in Arm A received an additional dose of Tec 1.5 mg/kg on Day 22: Days 1-2, 8-9, 15-16, and 22-23. Btz, bortezomib; C, Cycle; Dara, daratumumab; Dex, dexamethasone; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; IV, intravenously; Len, lenalidomide; PO, orally; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneously; Tec, tedistamab.



GMMG-HD10/DSMM-XX/MajesTEC-5: Response Rates^a



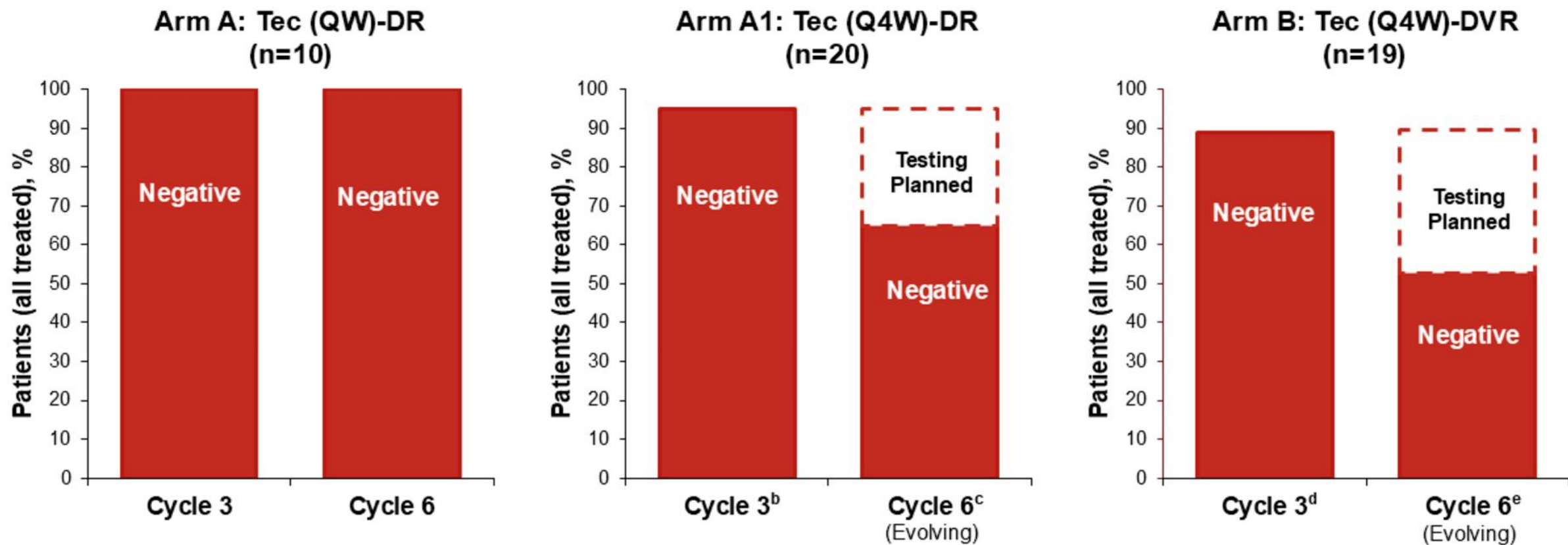
Induction complete, n	10	5 ^d	8 ^e
Induction ongoing, n	0	14	10

100% sCR observed in Arm A, with deepening responses in maturing cohorts

Data cutoff: September 30, 2024. ^aResponse was assessed by investigators based on IMWG criteria. Confirmed response required ≥ 2 consecutive identical response assessments. Response rates are presented during induction only. ^b2 (10.0%) patients had stable disease. ^c2 (10.5%) patients had stable disease. ^d1 patient discontinued due to refusal of further treatment. ^e1 patient discontinued due to refusal of further treatment. CR, complete response; D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; IMWG, International Myeloma Working Group; PR, partial response; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; sCR, stringent complete response; Tec, tedistamab; V, bortezomib; VGPR, very good partial response.



GMMG-HD10/DSMM-XX/MajesTEC-5: MRD Negativity (10^{-5})^a



100% of evaluable patients achieved MRD negativity by C3; no patients were MRD positive

Data cutoff: September 30, 2024. ^aMRD-negativity rate was defined as the proportion of patients who achieved MRD negativity (10^{-5}), regardless of response. MRD was determined by NGF testing. ^bIn Arm A1, 1 patient did not have bone marrow collected after C3. ^cIn Arm A1, 1 patient did not have MRD testing (10^{-5}) after C6. ^dIn Arm B, 1 patient was not tested at C3, but was MRD-negative at C6; 1 patient discontinued before C3 and had no on-study MRD testing. ^eIn Arm B, 1 patient was MRD negative at 10^{-4} after C6 and was considered indeterminate and without available MRD testing (10^{-5}); 1 patient discontinued before C3 and had no on-study MRD testing.
C, Cycle; D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; MRD, minimal residual disease; NGF, next-generation flow cytometry; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; Tec, teclistamab; V, bortezomib.



GMMG-HD10/DSMM-XX/MajesTEC-5: Infections

TEAE, n (%) ^a	Arm A: Tec (QW)-DR (n=10)		Arm A1: Tec (Q4W)-DR (n=20)		Arm B: Tec (Q4W)-DVR (n=19)		Total (N=49)	
	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4
Any infection	10 (100)	4 (40)	18 (90)	9 (45)	11 (57.9)	4 (21.1)	39 (79.6)	17 (34.7)
Infections^b								
URTI	6 (60)	0	8 (40)	1 (5)	6 (31.6)	0	20 (40.8)	1 (2)
COVID-19	2 (20)	0	4 (20)	1 (5)	3 (15.8)	3 (15.8)	9 (18.4)	4 (8.2)
Nasopharyngitis	3 (30)	0	2 (10)	0	2 (10.5)	0	7 (14.3)	0
Bronchitis	2 (20)	0	0	0	0	0	2 (4.1)	0
Infection (NOS)	0	0	1 (5)	1 (5)	2 (10.5)	1 (5.3)	3 (6.1)	2 (4.1)
Pneumonia	1 (10)	1 (10)	1 (5)	0	2 (10.5)	2 (10.5)	4 (8.2)	3 (6.1)

- 17 (34.7%) patients had grade 3/4 infections
 - URTI and COVID-19 were the most common all grade
 - No discontinuations due to infection
 - No grade 5 infections
- Hypogammaglobulinemia^c was reported in 45 (91.8%) patients
 - 44 (89.8%) received ≥1 dose of IVIg^d
- Infection prophylaxis, including Ig replacement, was strongly recommended^e

Data cutoff: September 30, 2024. ^aAEs are graded according to the NCI-CTCAE Version 5.0. ^bInfections reported in >10% of patients in any arm. ^cIncludes patients with ≥1 TEAE of hypogammaglobulinemia or post-baseline IgG value <400 mg/dL. ^dIncludes patients who started IVIg prior to Tec. ^eProphylaxis for *Pneumocystis jirovecii* pneumonia and herpes zoster reactivation was also recommended, as well as routine antibiotic prophylaxis. D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; Ig, immunoglobulin; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NOS, not otherwise specified; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; TEAE, treatment-emergent adverse event; Tec, tecetamab; URTI, upper respiratory tract infection; V, bortezomib.

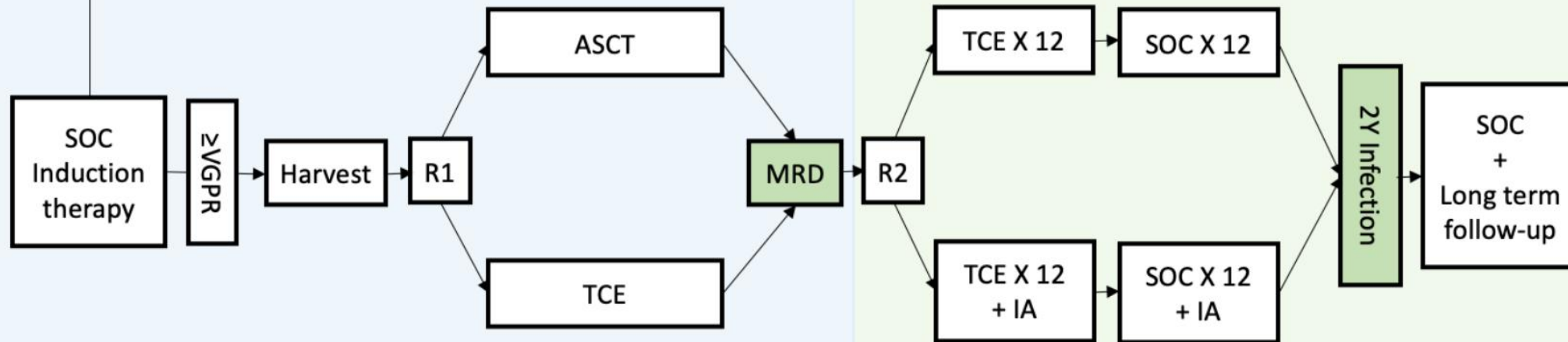
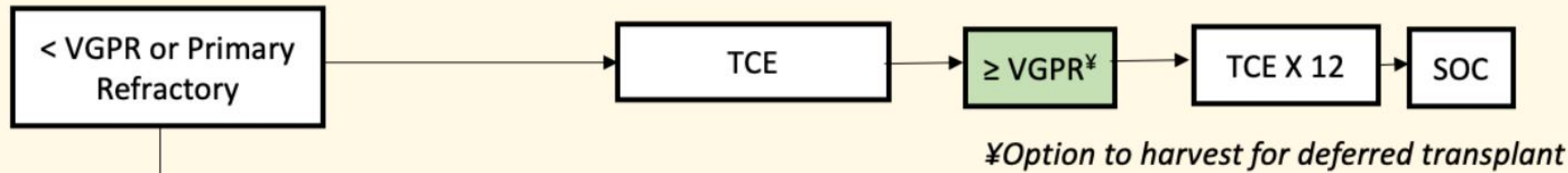


UKMRA OPTIMMUNE/Myeloma XVII

National phase 3 trial for TE NDMM patients

CIs: Matthew Jenner, Martin Kaiser

Efficacy question: Response to BCMAxCD3 TCE in Primary Refractory MM



Efficacy question: BCMAxCD3 TCE vs ASCT

Safety question:

Infection rate with immune augmentation (IA) vs SOC alone



IFM 2022-01 phase 2 trial



Induction and PBSC harvest

MRD-adapted strategy

- NDMM <66
- TE patients
- ECOG 0-2

Dara -VRd x 6
(28-day cycle)

PBSC Harvest after cycle 3
(G-CSF+- plerixafor)

MRD

MRD standard-risk
($<10^{-5}$)

MRD High-risk
($>10^{-5}$)

Cohort A

Tec – Len
2 years

Cohort B

Tec- Tal
2 years

Primary objective :
Arm A : sustained MRD (-) at 1 yr
Arm B : MRD conversion at 1 yr

Secondary objectives :
- ORR, CR
- DOR, PFS, OS
- Safety
- Biomarkers

EMN30: randomized phase 3 trial of Teclistamab in NDMM

N van de Donk and E Zamagni

MajesTEC-4



Screening
(max 28d before randomization;
36 mo accrual period)

Study Enrollment

Treatment (28d cycle; 26 cycles)*
(for 2 years or until PD, death, intolerable toxicity, consent withdrawal, EOS)

Follow-up
(until death, consent withdrawal,
loss of follow up, EOS)

Participants with NDMM who have received 4-6 cycles of a 3 or 4 drug-induction that includes a PI and/or an IMiD and a single or tandem ASCT with or without consolidation

1:1 Randomization

Arm A (N=500)
Tec – Len

Arm B (N=500)
Len

Arm C (N=500)
Tec

Study will continue until approximately 380 deaths have been observed in the pooled Tec-Len (Arm A) and Len (Arm B) arms and approximately 380 deaths have also been observed in the pooled Tec (Arm C) and Len (Arm B) arms.

EOT Visit

Follow Up

Study End

FU for response until PD or next line.
FU post-PD for survival, SST, 2nd primary malignancy Q16W until EOS

stratified by:

- consolidation use: yes/no
- ≥CR vs <CR
- anti-CD38 vs non-anti-CD38 antibody-based induction/consolidation

* Participants in Arm A (Tec-Len) who achieve a CR or better after 1 year of treatment (13 cycles) will discontinue teclistamab but continue lenalidomide for the second year (cycles 14-26)

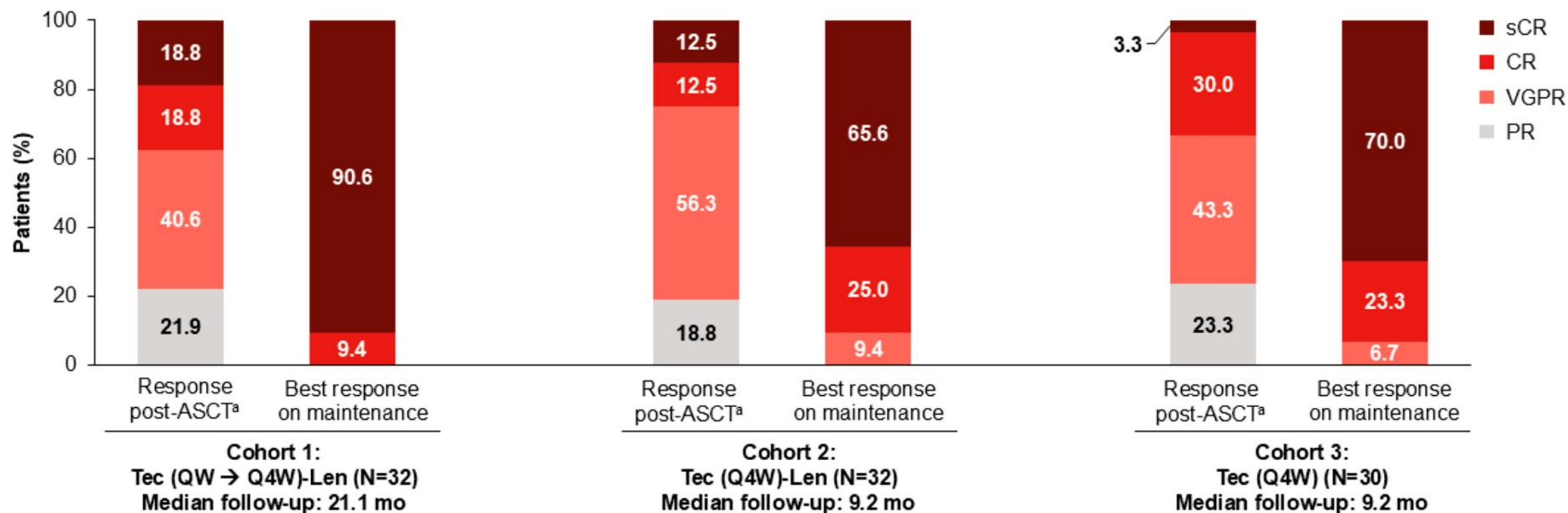
MRD assessment

- ✓ At study entry and at 6 & 24 months after C1D1
- ✓ Time of suspected CR or sCR
 - For participants with suspected CR or sCR, additional samples at 12,18,30,36,48, & 60 months post C1D1

ASCT, autologous stem cell transplant; EOT, end of treatment; IMiD, immunomodulatory agent; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; PI, proteasome inhibitor; flow cytometry; CR, complete response; PD, progression disease; EOS, end of study; Tec, teclistamab

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

≥CR rate 37.6% → 100% 25.0% → 90.6% 33.3% → 93.3%



Responses deepened during maintenance in all treatment cohorts

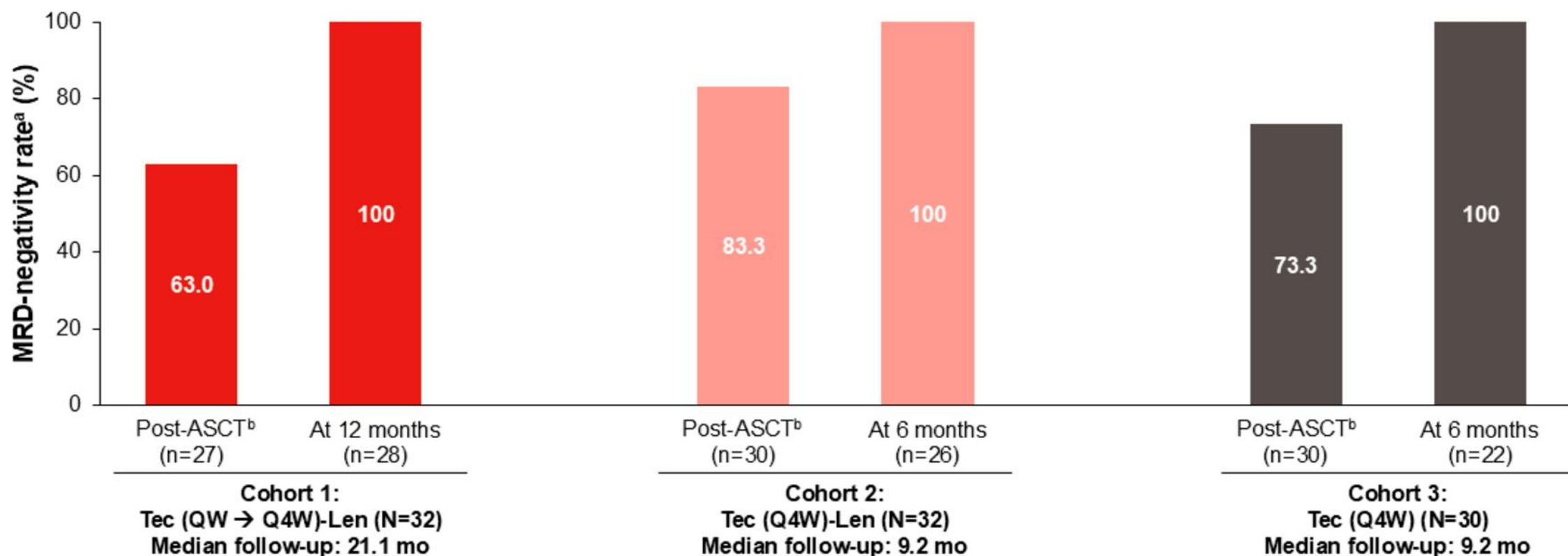
Data cutoff date: September 9, 2024.

^aPost-ASCT ± consolidation.

ASCT, autologous stem cell transplantation; CR, complete response; EMN, Stichting European Myeloma Network; Len, lenalidomide; PR, partial response; QW, weekly; Q4W, every 4 weeks; sCR, stringent complete response; SRI, safety run-in; Tec, teclistamab; VGPR, very good partial response.



EMN30/MajesTEC-4 SRI: MRD Negativity (10^{-5}) in Evaluable Patients Post-ASCT and During Maintenance



100% of evaluable patients were MRD negative during maintenance

Data cutoff date: September 9, 2024.

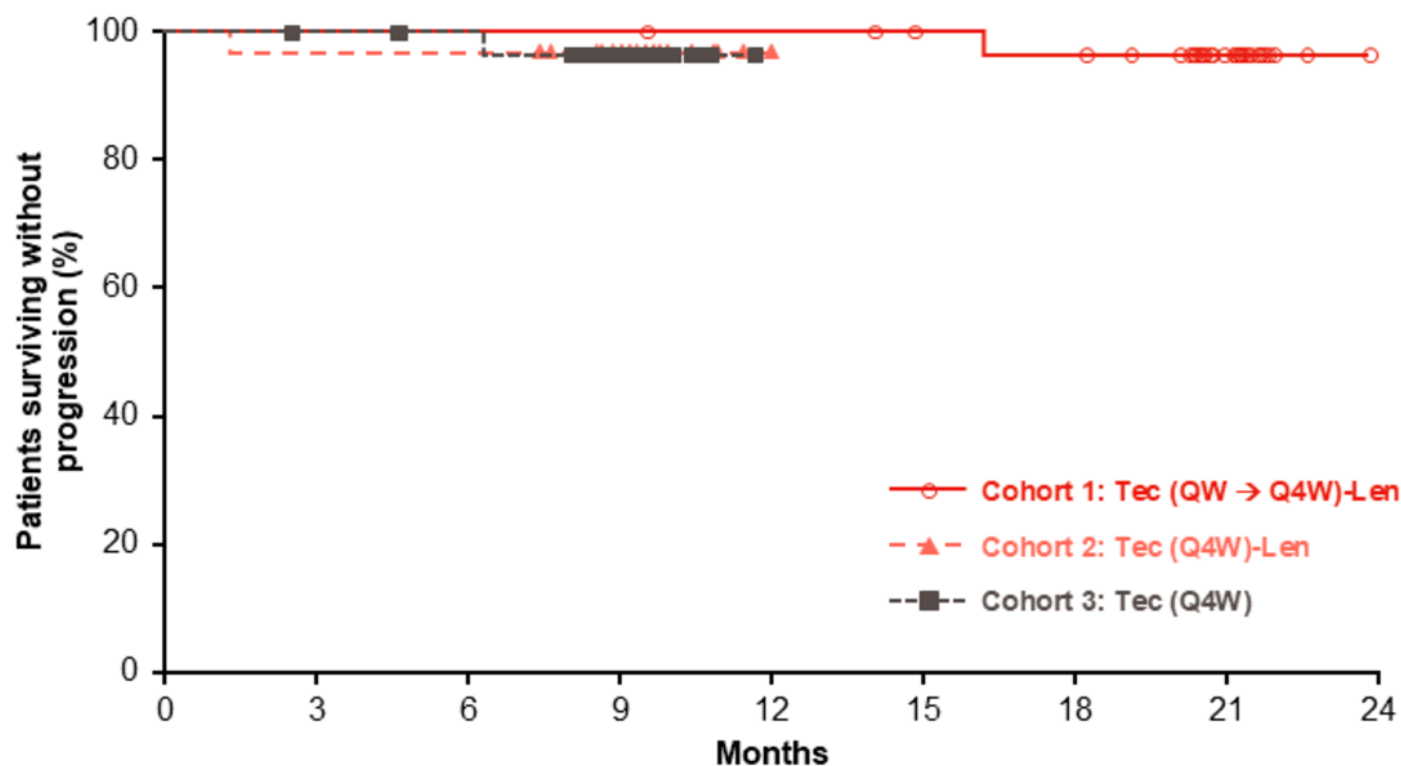
^aMRD-negativity rate was defined as the proportion of patients who achieved MRD negativity (10^{-5}), regardless of response. Percentages are out of evaluable patients. Among 87 evaluable patients, 23 patients were MRD positive at screening (Cohort 1, n=10; Cohort 2, n=5; Cohort 3, n=8). All patients who were MRD positive at study entry and had an assessment during treatment were MRD negative during treatment. One patient in Cohort 1 was MRD positive at 18 months. ^bPost-ASCT ± consolidation.

ASCT, autologous stem cell transplantation; EMN, Stichting European Myeloma Network; Len, lenalidomide; MRD, minimal residual disease; QW, weekly; Q4W, every 4 weeks; SRI, safety run-in; Tec, teclistamab.

Presented by E. Zamagni at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA



EMN30/MajesTEC-4 SRI: PFS



- Median PFS was not reached in all cohorts

Patients at risk:	0	3	6	9	12	15	18	21	24
Cohort 1: Tec (QW → Q4W)-Len	32	32	32	32	31	29	28	14	0
Cohort 2: Tec (Q4W)-Len	32	31	31	17	0	0	0	0	0
Cohort 3: Tec (Q4W)	30	29	28	14	0	0	0	0	0

Responses were maintained in all cohorts

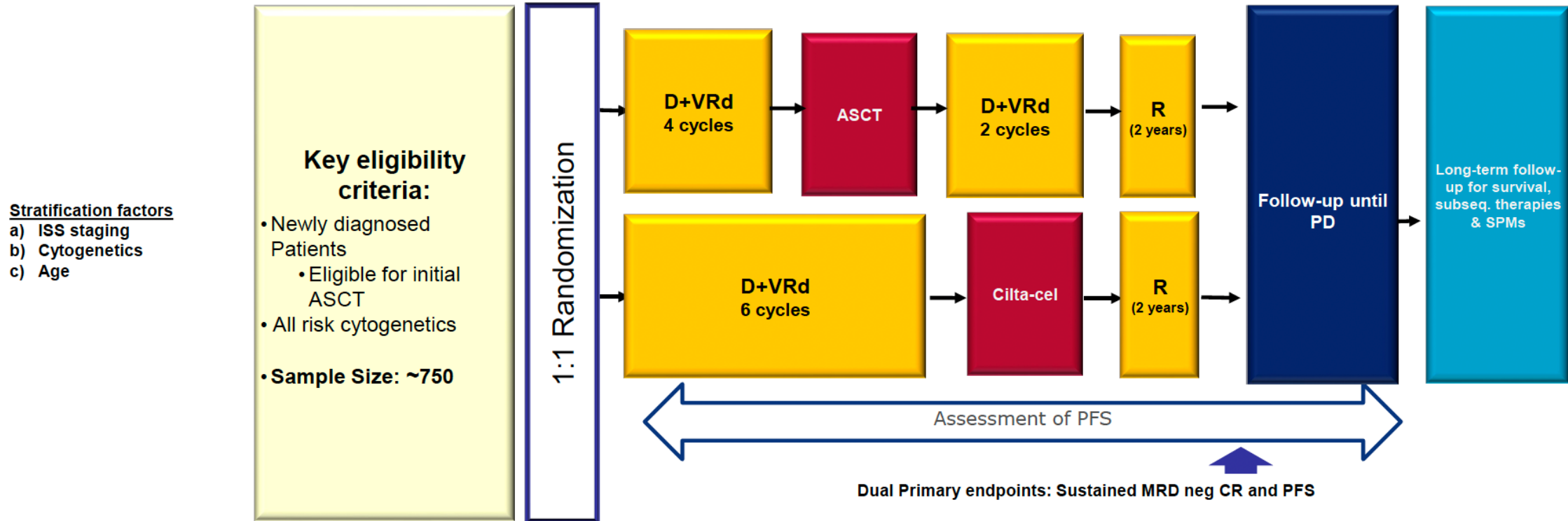


EMN28 – Cartitude-6 / Emagine study

P. Sonneveld/M. Boccadoro

Dual primary endpoints:

Sustained MRD-neg CR and PFS



MRD (BM aspirate) time-points:

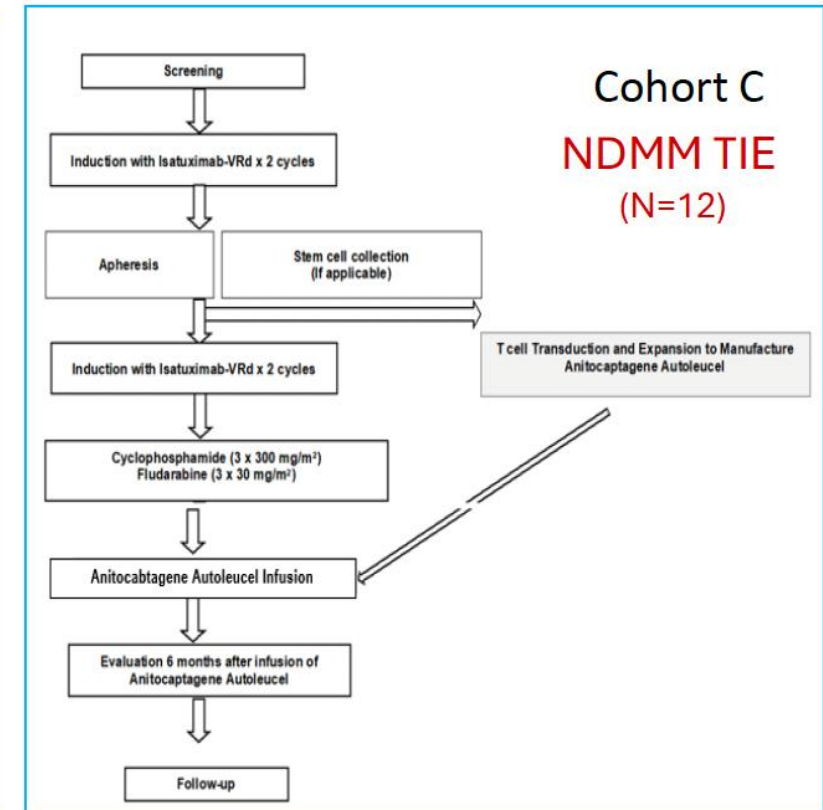
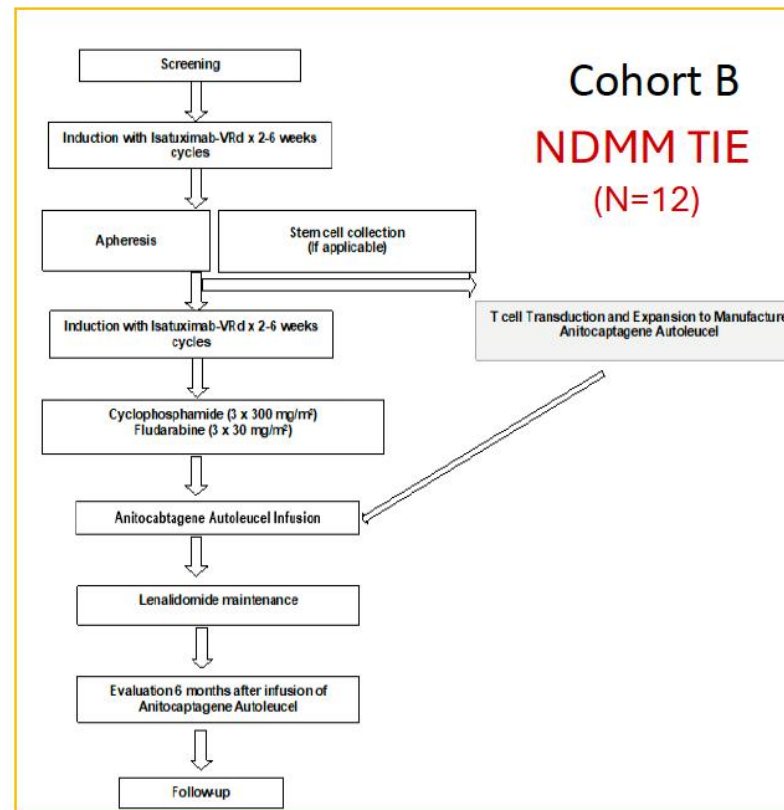
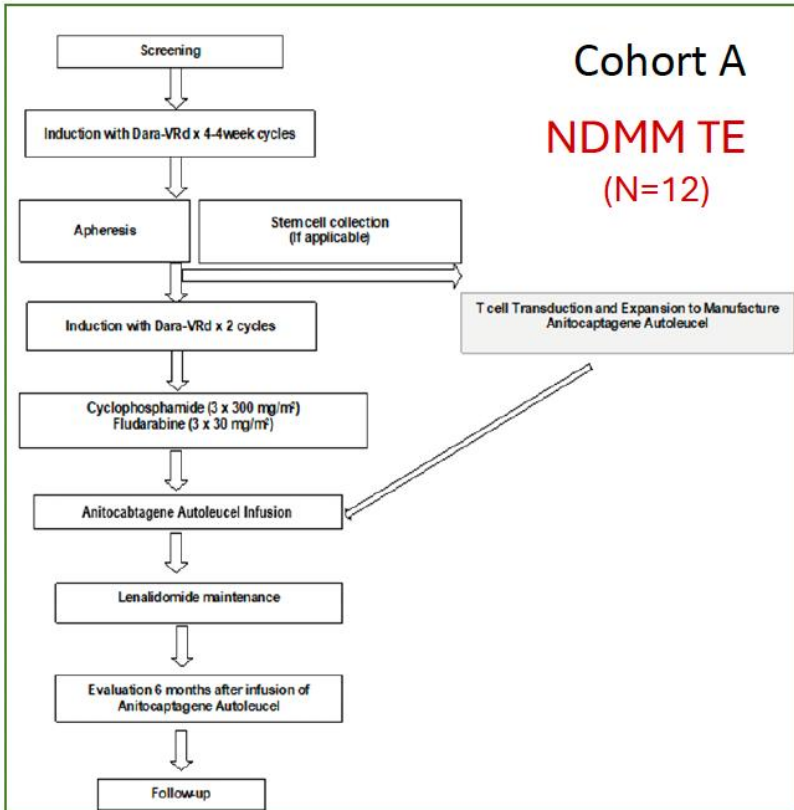
- Within 7 days prior to melphalan conditioning.
- After D+VRd consolidation, prior to initiating lenalidomide maintenance therapy.
- At time of suspected CR or sCR.
- After initial CR or sCR is confirmed, then once 3 months after, then every 6 months (+1 month) for 5y, then yearly until PD for participants that are in CR or sCR.

MRD by PET/CT (optional, if locally available): At time of BM MRD-negative CR and every 12 months in BM MRD-negative participants.

Dara, daratumumab; V, bortezomib; R, lenalidomide; d, dexamethasone; ASCT, autologous stem-cell transplantation; PFS, progression-free survival; MRD, minimal residual disease; CR, complete response; sCR, stringent complete response; ISS, International Staging System; SPM, second primary malignancy; PD, progressive disease; BM, bone marrow.

450/750 patients recruited; MRD Read-out 2027/2028

GEM-ANITOFIRST: “A Phase 2, open-label, multicenter multi-cohort study to evaluate the efficacy and safety of anitocabtagene autoleucel in participants with newly diagnosed multiple mieloma”

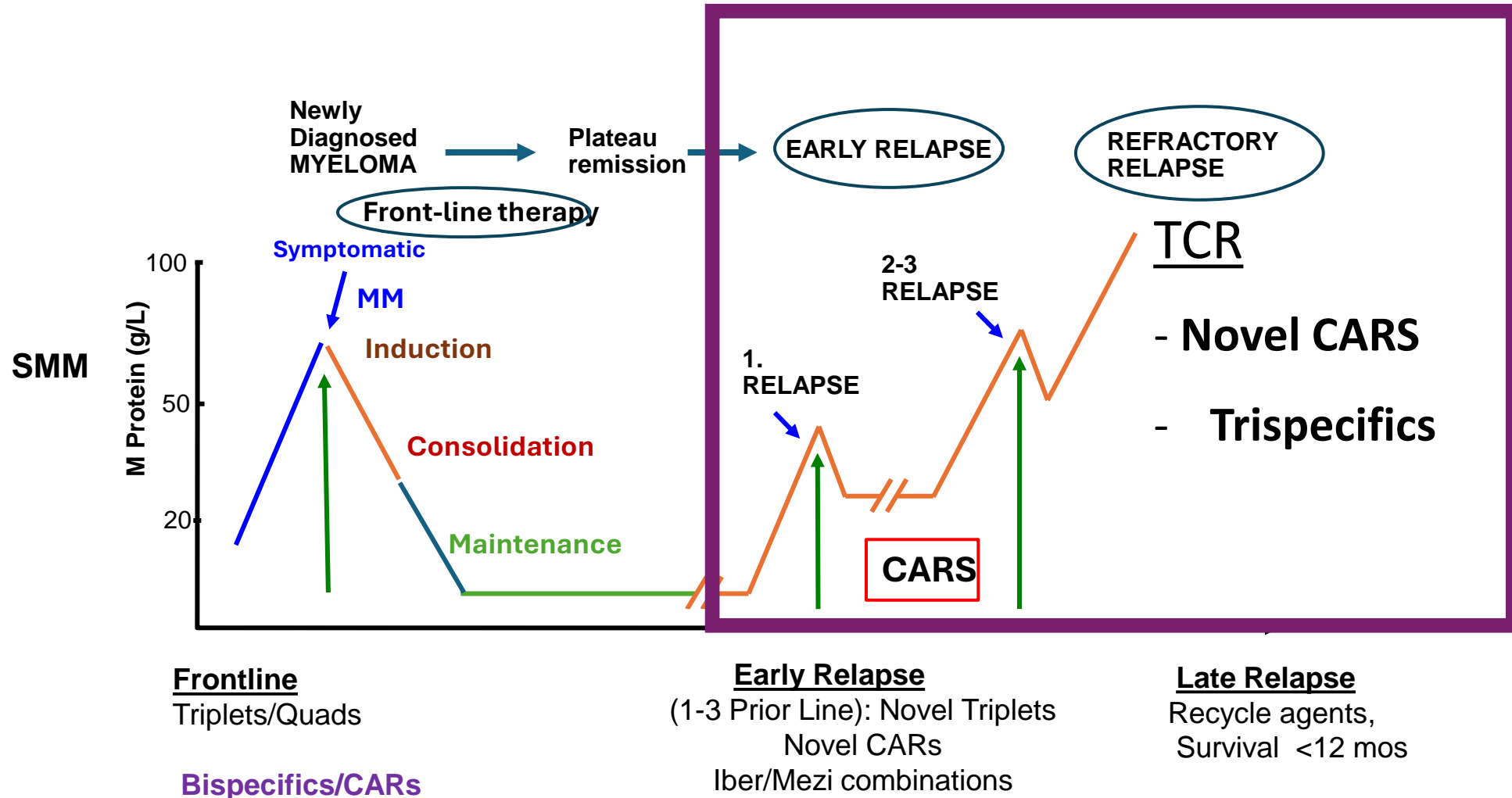


Summary: Frontline Therapy in 2030-35

- Randomized Data forthcoming (2028-2035)
 - TE -
 - MRD(-) after induction – SCTx vs No
 - SCTx vs. bispecific (MASTER2/UK)
 - SCTx vs Cilta-cel (CART6)
 - Maintenance: Len Vs TEC (Majestic5)
 - Maintenance: Iber vs. Len (EXCALIBER)
 - TI
 - Bela- VRd vs. VRd (DreaMM-9)
 - Elra-Dara-R vs. DRd
 - Tec- Dara-R vs. DRd
- Predictions – QUAD induction will prevail
 - SCT will have limited use in frontline therapy
 - CART will be used as consolidation (HR, MRD(+))
 - Bispecifics will be used as maintenance
- Overall
 - Transplant Ineligible
 - Frail – Bispecific + CD38 – x 1-2 years
 - Beware of Belantamab-VRd
 - Non-Frail – Bispecific + Dara-Len → MRD (-) 2yr

 - Transplant Eligible:
 - SR – QUAD x4 – MRD(-) → QUAD → CD38+Len
 - SR- QUAD x4 – MRD(+) → CART → Len x1-2yr
 - HR- QUAD – AutoSCTx → Bispecific → CeLMOD
 - HR- QUAD – CART → Bispecific → CeLMOD

Sequencing Therapy in MM: *How should we deploy all these agents?*



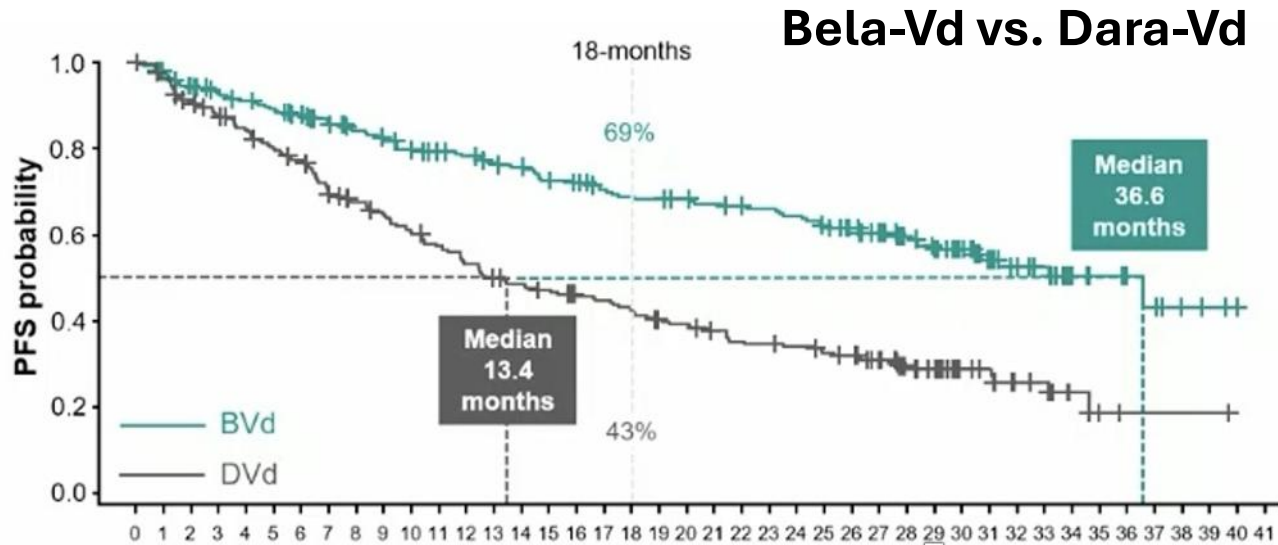
Trials:

Both DreaMM-7 and -8 Show Significant PFS Benefit – No Blurriness Here

DREAMM

7

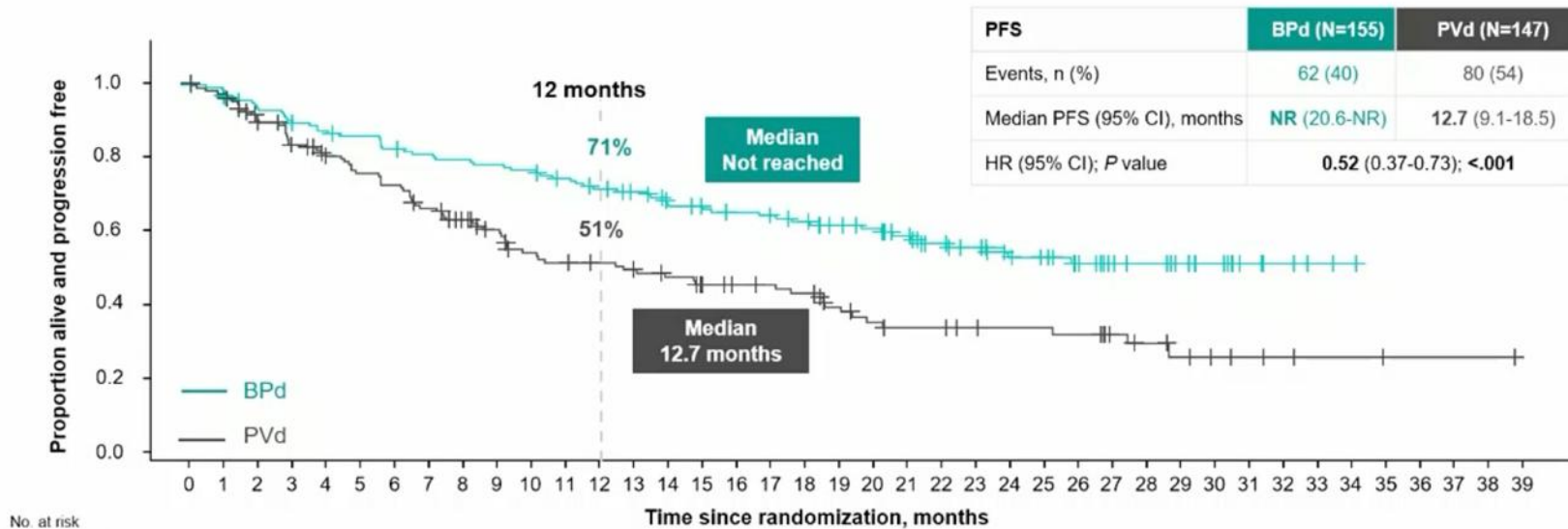
Mateous et al.
EHA2024



Significant PFS Benefit with BPd vs PVd

8

Dimopoulos et al.
EHA2024



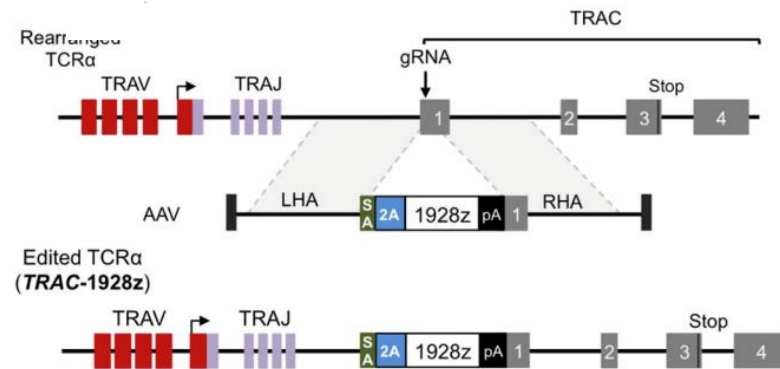
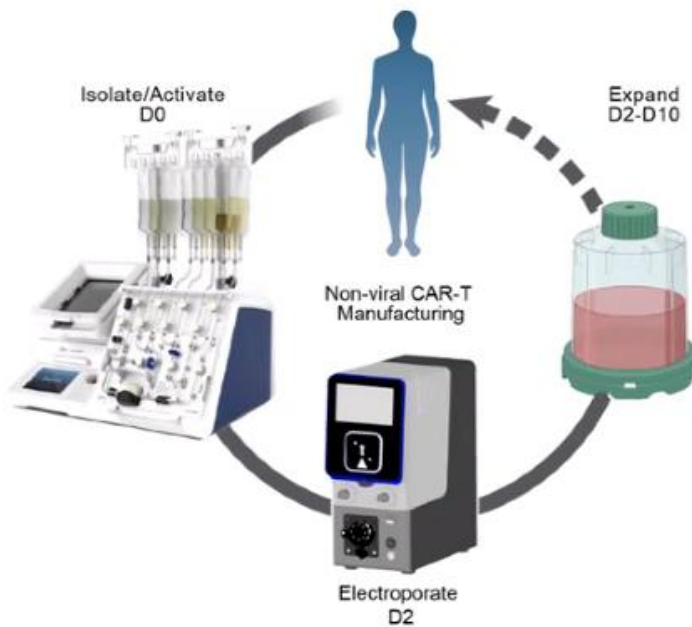
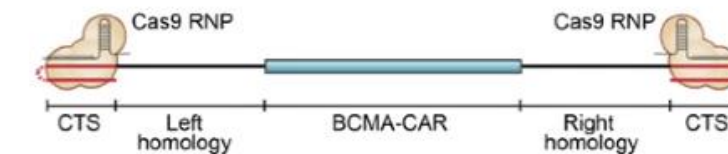
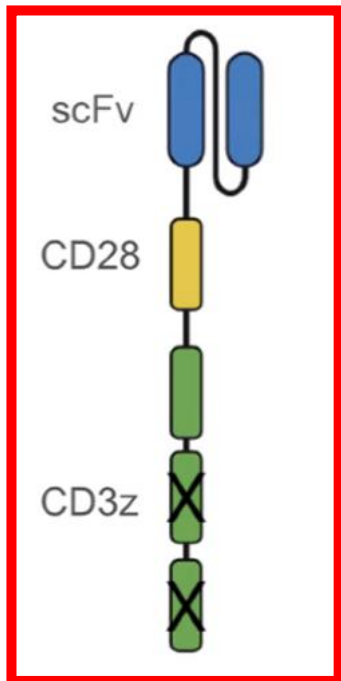
P3-RRMM – Possible salvage options in 2030-5

- Randomized P3 trials (1-3 PLT)
 - Iber Dd vs. Dara Rd (EXCALIBER)
 - Mezi KD vs. Kd (SUCCESSOR-2)
 - Mezi Vd vs. PVd (SUCCESSOR-1)
 - Many Bispecific trials
 - Tal-Pom, Tec-Tal vs. E-Pd, PVd (Monumental-6)
- CART
 - Anito-cel Vs triplets/doublet
 - Awaiting AZD0120 (Dual) Vs. SOC
 - Arlo-cel (QUINTESSENTIAL-3)

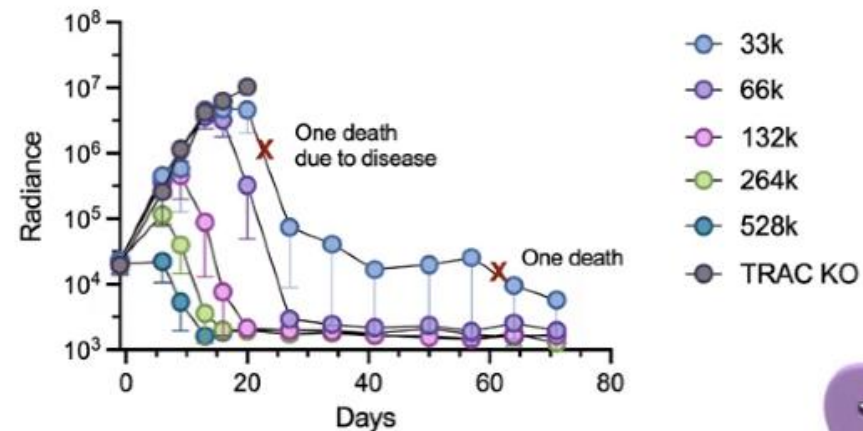
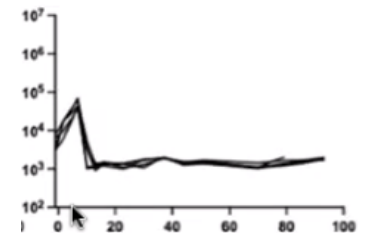
UCSF Homegrown CART 2.0

1XX-Enhanced and Fully Non-viral BCMA CAR for RRMM

BCMA



TRAC-1XX

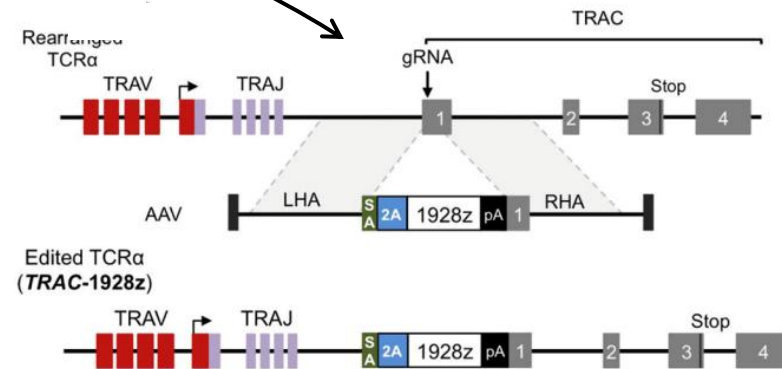
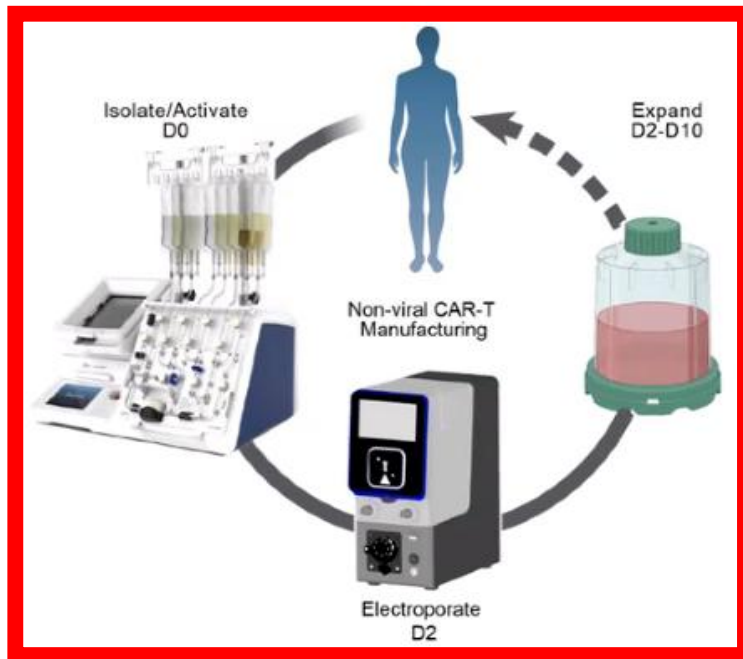
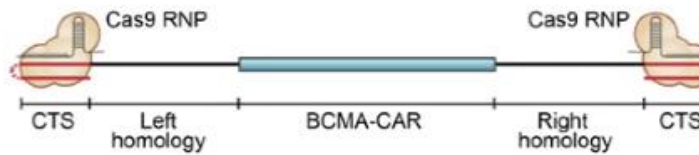
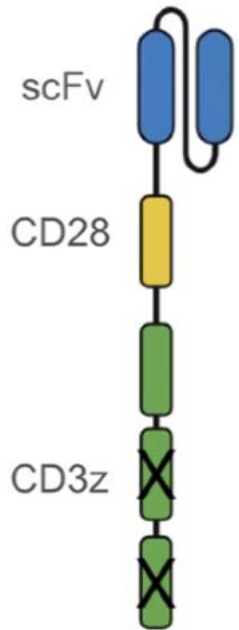


UCSF Homegrown CART 2.0

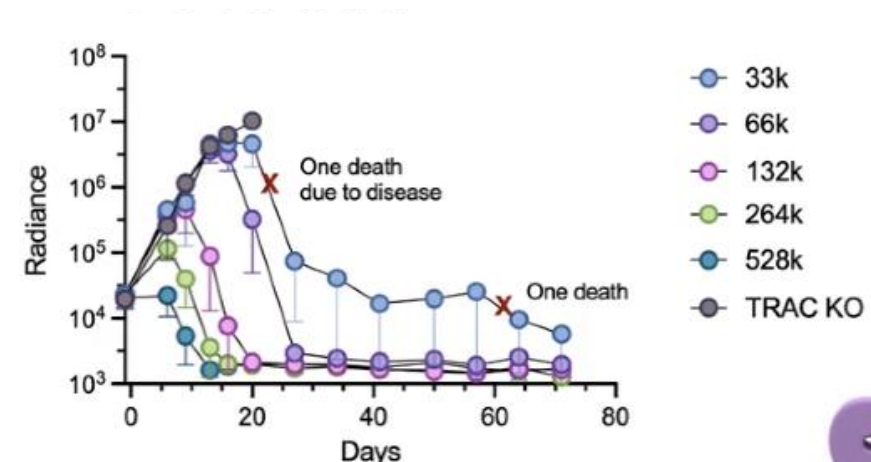
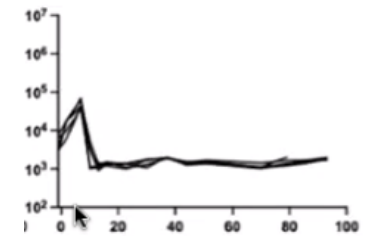
IND SUBMITTED THIS WEEK!!

1XX-Enhanced and Fully Non-viral BCMA CAR for RRMM

BCMA



TRAC-1XX



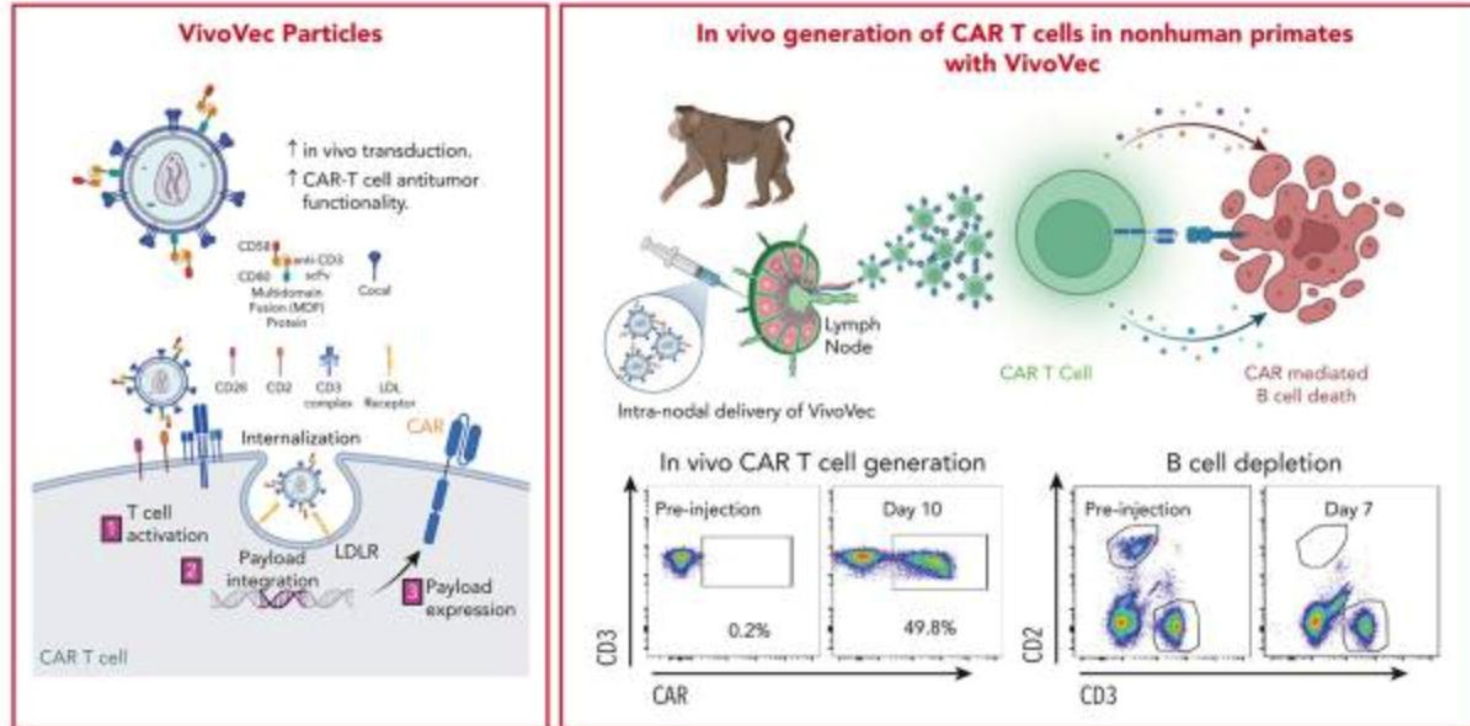
1. Expansion
2. Persistence
3. Decrease tonic sign



Novel CART Cell Designs

- In Vivo CAR T-cell
 - Apheresis-NO
 - Ex-vivo manufacturing-NO
 - Quality control testing – NO
 - LD Chemotherapy – NO
 - Reinfusion of CART-NO
- Off-the shelf- YES
- Inject virus/particles
- Targeted to T-cells – Yes
- In vivo T-Cell Expansion YES

In Vivo CAR T-Cell Generation in Nonhuman Primates Using Lentiviral Vectors Displaying a Multidomain Fusion Ligand

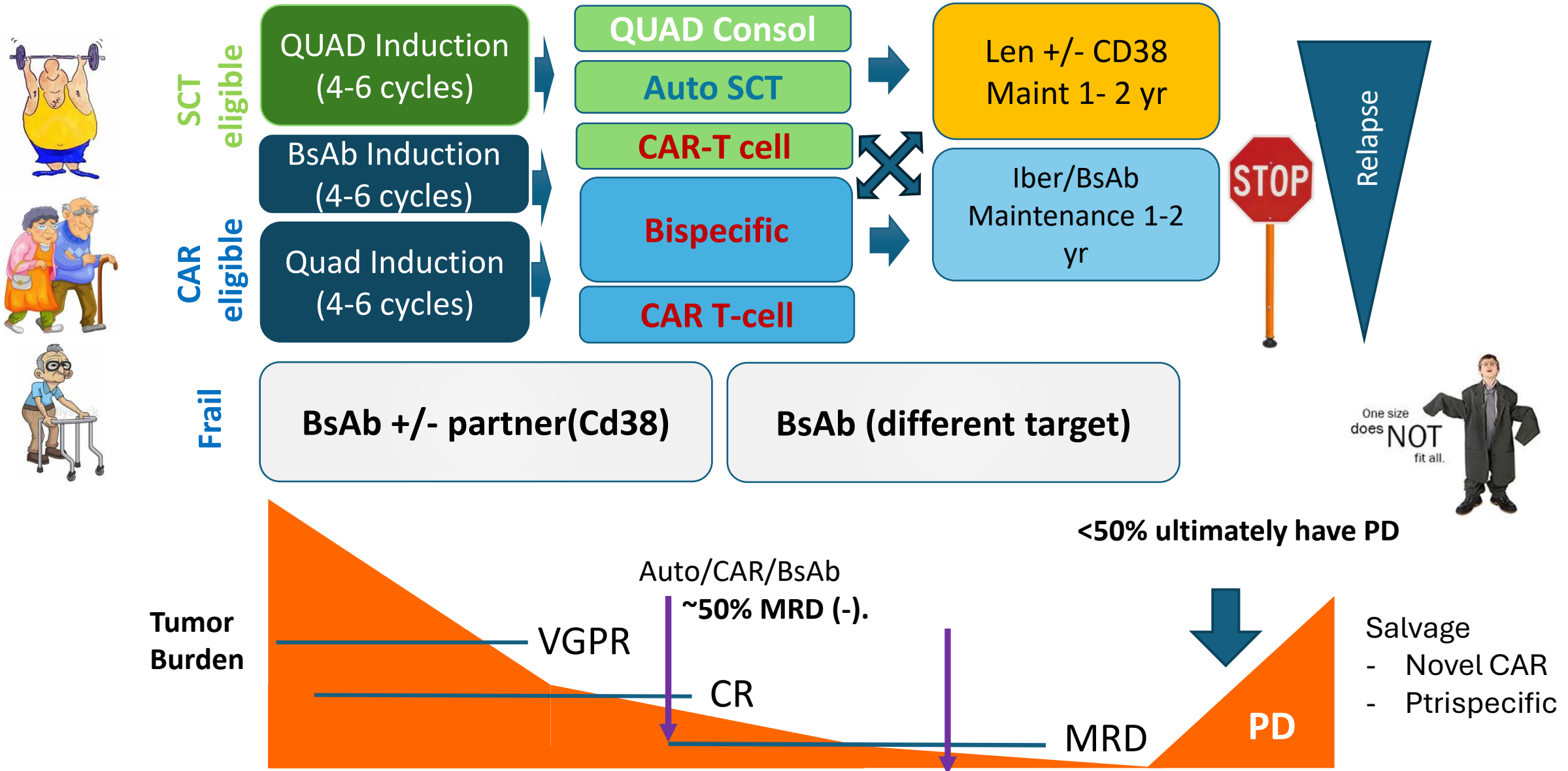


Conclusion: Administration of VivoVec particles into nonhuman primates in the absence of lymphodepleting chemotherapy resulted in a robust generation of anti-CD20 CAR T cells and complete depletion of B cells.

Nicolai et al. DOI: 10.1182/*blood*.2024024523

Conclusions: MM can be CURED? CARs and BsAbs → are the way !!!

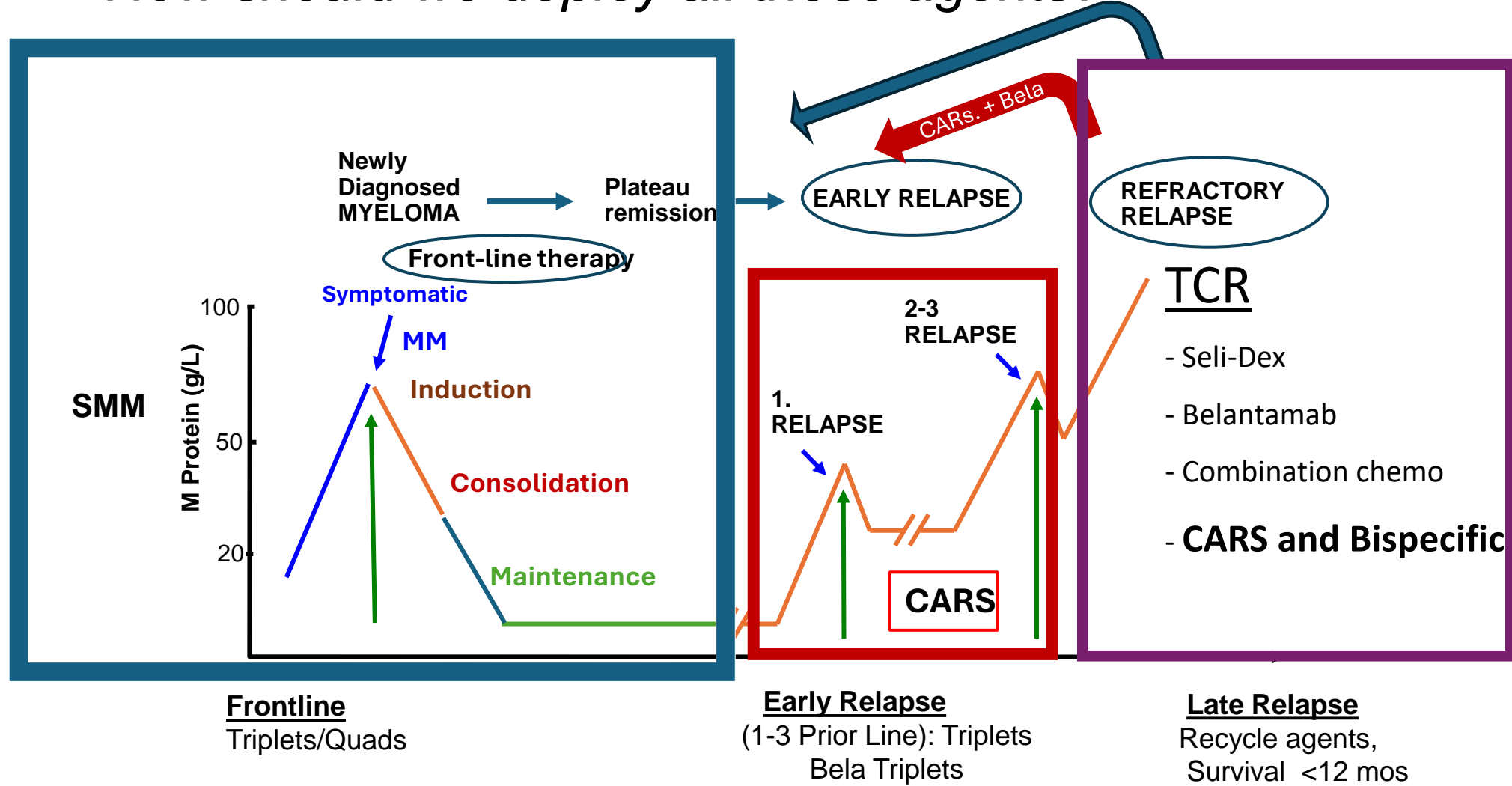
Future treatment paradigms.....



Predictions in RRMM

- Prediction 1-3 PLT
 - Non-CART
 - Iber-Dara-Dex will win for non-IT
 - Tal combo's will follow BCMA exposed
 - CART
 - Dual targeted for BCMA exposed
 - CARs with least toxicity/best manufacturing success/fastest delivery will win!!
 - Salvage Therapy
 - Trispecific (GPRC5D-BCMA; BCMA-CD38)
 - *In vivo* CARs – They ARE THE FUTURE in MM.

Sequencing Therapy in MM: How should we deploy all these agents?



Trials:

Bispecifics/CARs

Bispecifics/trispecifics

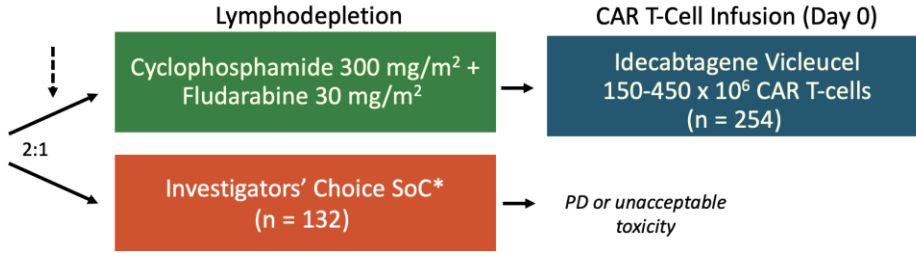
CART in Earlier Lines

KarMMa-3: Phase III Trial of Ide-Cel vs SoC in R/R MM

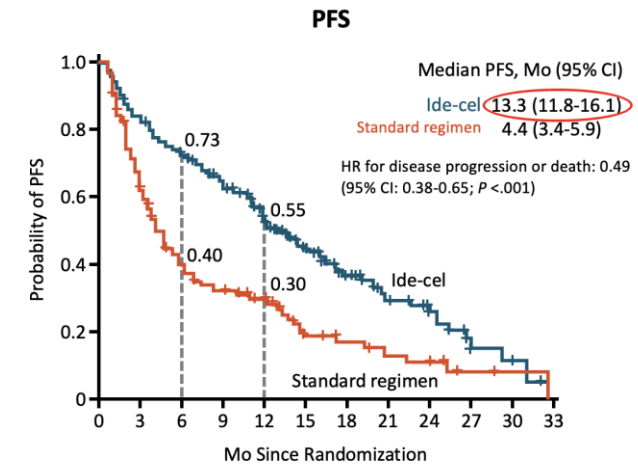
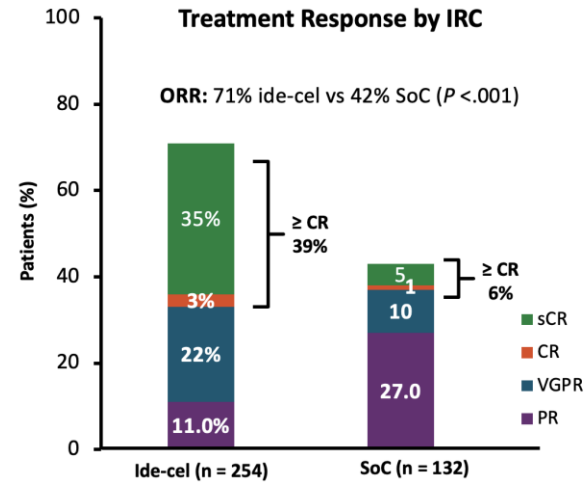
- International, open-label, randomized phase III trial

Stratified by age (<65 vs ≥65), prior therapies (2 lines vs 3-4 lines), and high-risk cytogenetics (present or absent)

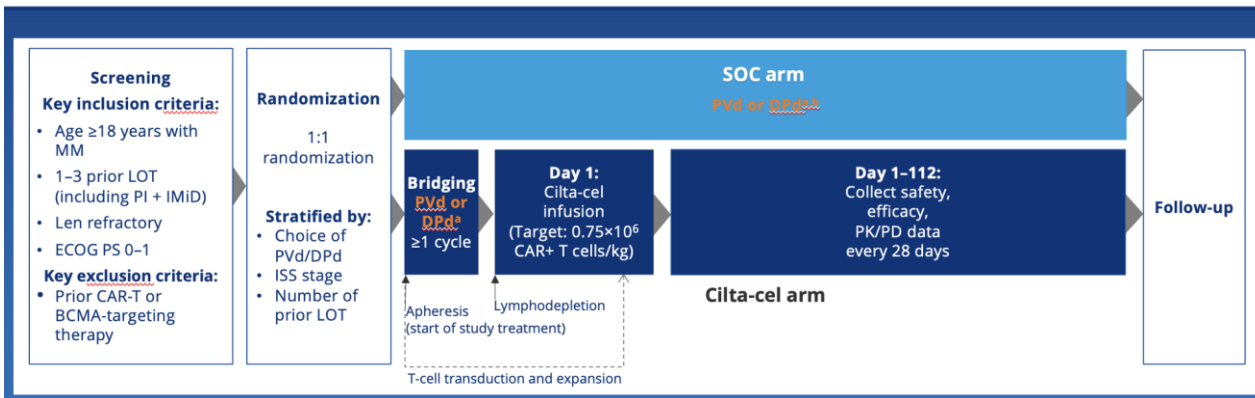
Patients with R/R MM after 2-4 prior lines of therapy; including a PI, an IMiD, and daratumumab; disease progression in ≤60 days after last therapy
ECOG PS ≤1
(N = 386)



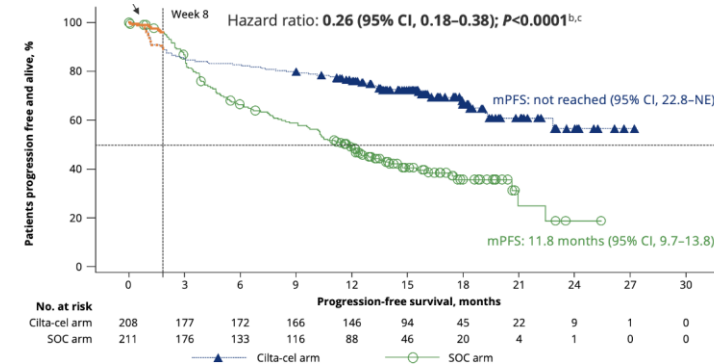
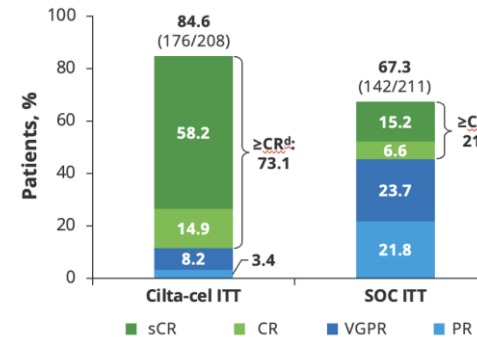
Median 3 PLT (TCR 65%): ORR 71%, PFS 13.3m



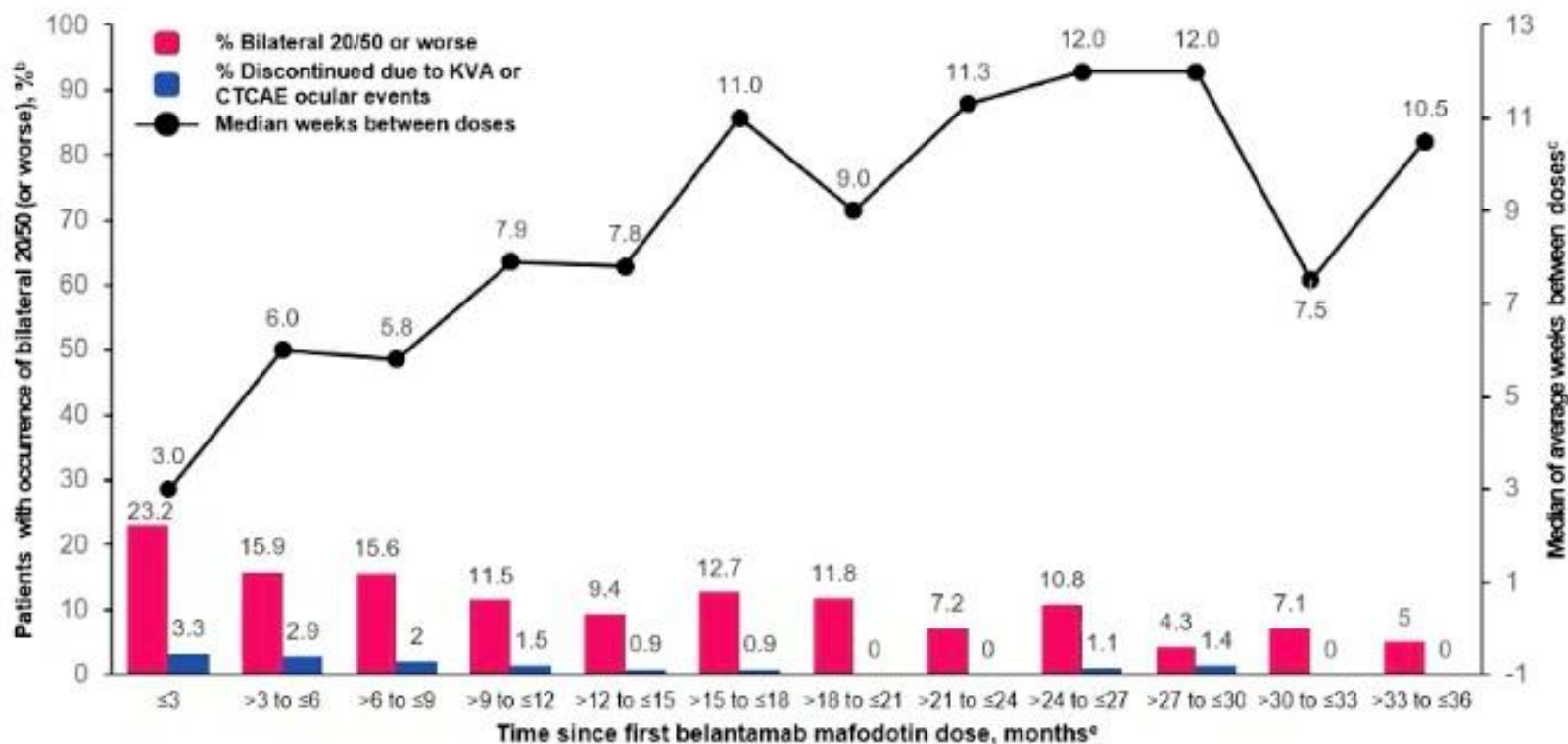
CARTITUDE-4: Study Design and Endpoints



Median 2 PLT (TCR 15%): ORR 99%, PFS NR



DREAMM-7: impact of dose modifications on PFS and ocular management^a



- Median time between doses increased with treatment duration
- Dose delays did not have a negative impact on PFS^d
 - BVd patients with ≥1 dose delay of ≥12 weeks (N=126), mPFS 36.6 months
- 23% of patients experienced 20/50 or worse events in first 3 months; prevalence decreased thereafter
- Rate of treatment discontinuation due to ocular events were low

	≤3	>3 to ≤6	>6 to ≤9	>9 to ≤12	>12 to ≤15	>15 to ≤18	>18 to ≤21	>21 to ≤24	>24 to ≤27	>27 to ≤30	>30 to ≤33	>33 to ≤36
No. of patients on treatment ^b	211	170	147	131	117	110	102	97	93	69	42	20
No. of patients with bilateral 20/50 or worse	49	27	23	15	11	14	12	7	10	3	3	1
Median days between doses	21	42	41	55	54	77	63	79	84	84	53	74
No. of patients who discontinued due to KVA or ocular CTCAE event	7	5	3	2	1	1	0	0	1	1	0	0

CTCAE, Common Terminology Criteria for Adverse Events; KVA, Keratopathy and Visual Acuity scale; mPFS, median progression-free survival; PFS, progression-free survival; PD, progressive disease.
^a Only belantamab mafodotin treatment period considered in these post hoc analyses. ^b Only patients with 20/25 or better in either or both eyes at baseline are considered. ^c Mean of days between doses, for each patient, per interval is used. ^d Only patients receiving ≥6 months of treatment included in analysis to exclude early discontinuations (eg, rapid PDs). ^e Graph is truncated at 36 months because the data beyond 36 months represented a low number of patients on treatment (>36 to ≤39 months, n=8 and >39 to ≤42 months, n=3).

Other belantamab mafodotin combinations in RRMM

Study	Phase	ClinicalTrials.gov	Combination	N	Setting	Primary endpoint	Initial completion
DREAMM-5 ¹	1/2	NCT04126200	<ul style="list-style-type: none"> Platform study, multiple combinations Belamaf + GSK3174998 / feladilimab / nirogacestat / dostarlimab / isatuximab / nirogacestat-Rd / nirogacestat-Pom-dex 	~464	• ≥3 prior lines	DLTs, AEs ORR	February 2026
DREAMM-6 ²	1/2	NCT03544281	<ul style="list-style-type: none"> Belamaf + Rd or Vd 	152	• ≥1 prior line	Safety ORR	February 2023
GEM-BELMA	1/2	NCT05060627	<ul style="list-style-type: none"> Belamaf + Kd 	~60	• 1–3 prior lines, Len-refractory	Toxicity ORR	May 2024
ALGONQUIN ³	1/2	NCT03715478	<ul style="list-style-type: none"> Belamaf + Pom-dex 	~120	• ≥1 prior line, RRMM	RP2D ORR	June 2024
LCI-HEM-NDMYE-KRDB-001	1/2	NCT04822337	<ul style="list-style-type: none"> Belamaf + KRd 	~70	• ≥1 prior line	MTD CR rate	October 2024
University of Chicago	2	NCT05789303	<ul style="list-style-type: none"> Belamaf + K-Pom-dex 	~83	• ≥2 prior lines	≥VGPR in CAR T-naive	July 2028
EAE127	1/2	NCT05581875	<ul style="list-style-type: none"> Belamaf + Dara-Pom-dex 	~48	• 1 prior line, Len-refractory	DLTs, AEs, ORR	October 2026
ISABELA	2	NCT05922501	<ul style="list-style-type: none"> Belamaf + Isa-Pom-dex 	~50	• ≥1 prior line	ORR	December 2025
University of Maryland ⁴	1/2	NCT04896658	<ul style="list-style-type: none"> Belamaf + Cd 	10	• ≥3 prior lines, including an CD38 mAb; PI/IMiD-refractory	AEs ORR	June 2023
Yale	1/2	NCT05002816	<ul style="list-style-type: none"> Belamaf + elotuzumab 	~24	• ≥3 prior lines	MTD, DLTs	January 2025
BELI(E)VE	1/2	NCT05853965	<ul style="list-style-type: none"> Belamaf + venetoclax 	~45	• ≥1 prior line, t(11;14) MM	RP2D	November 2026
DREAMM-4 ⁵	1/2	NCT03848845	<ul style="list-style-type: none"> Belamaf + pembrolizumab 	41	• ≥3 prior lines, including an CD38 mAb, an IMiD, and a PI	DLTs, AEs ORR	June 2023
MSKCC	1	NCT05556798	<ul style="list-style-type: none"> Belamaf + nirogacestat 	~30	• ≥3 prior lines	DLTs	October 2026
DREAMM-20	1/2	NCT05714839	<ul style="list-style-type: none"> Bela or Belamaf + xRd 	~124	• ≥3 prior lines, including an CD38 mAb, an IMiD, and a PI	Safety	September 2027

ClinicalTrials.gov, April 30, 2024

1. Lonial S, Richardson PG, Callander N et al. J Clin Oncol 2022;40(16_suppl):abstract 8019. 2. Quach H, et al. J Clin Oncol 2022;40(16_suppl):abstract 8017. 3. Trudel S, et al. Blood 2022;140(suppl 1):abstract 3248. 4. Badros A, et al. Blood 2023;142(suppl 1):abstract 6723. 5. Suvannasankha A, et al. J Clin Oncol 2022;40(16_suppl):abstract 8018.