T-cell engagers (TCE)- not just bispecifics. Everyone needs to be on board. Practical considerations for broad adoption among all hematologists/oncologists.

Jeffrey V. Matous, MD

Colorado Blood Cancer Institute, Sarah Cannon Research Institute
Denver, Colorado

Harvesting Knowledge: A Summit on Multiple Myeloma
Napa April 2026

CBCI COLORADO BLOOD CANCER INSTITUTE

SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center | HealthONE

Choose the best answer

1. Bispecific antibodies in myeloma have similar CRS rates to ciltacel CAR T cell therapy, approximately 90%.
2. ICANS neurotoxicity with BsAb in myeloma occurs in roughly 1/3 of patients
3. BsAb in MM MUST be given inpatient per the FDA labels
4. Prophylactic tocilizumab greatly reduces CRS incidence during step up dosing with teclistamab
5. ICU care is required in roughly 25% of patients with MM who receive a BsAb

Bispecific Antibodies in Multiple Myeloma

Bispecific antibodies simultaneously bind to the tumor cell and an immune effector cell leading to immune cell activation and tumor cell death

Approved BCMA-targeting BsAbs

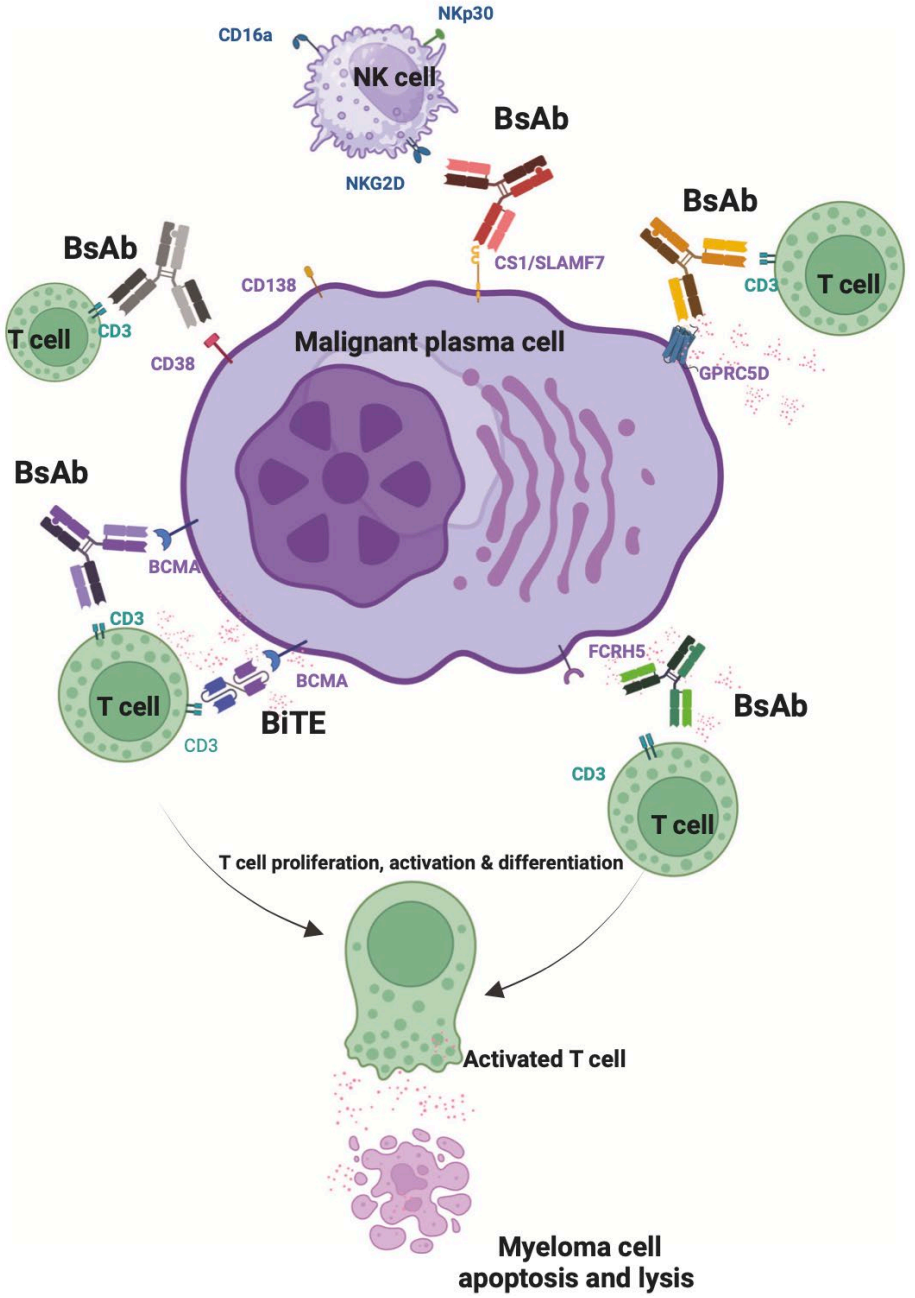
- Teclistamab
- Elranatamab
- Linvoseltamab

Approved GPRC5D-targeting BsAbs

- Talquetamab

Around the corner

- Ententamig (CD3/BCMA)
- Ramantamig (CD3/BCMA/GPRC5D = trispecific)



Devasia AJ et al. *Nature BCJ*. 2024;14:158.

CBCI COLORADO BLOOD CANCER INSTITUTE

SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center

HealthONE

Background Assumptions

Bispecific T-cell engagers represent one of the most (likely THE MOST) transformative therapeutic modality for multiple myeloma developed to date

Community level adoption of bispecifics has been limited due to various resource constraints

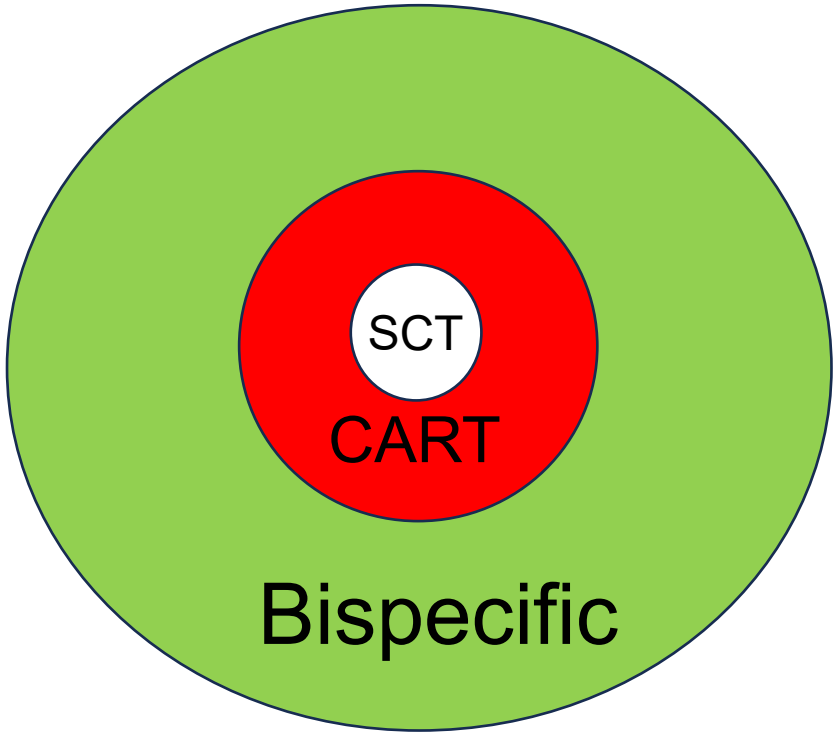
Risk for inequity in bispecific access is very high in the US Health care ecosystem

With our current understanding for risk reduction/toxicity management bispecifics can be safely administered in most oncology clinics

Thesis

- Accelerating community based bispecific adoption and trying to achieve equity in access to bispecifics is THE highest impact goal the myeloma research community can currently undertake

Eligibility



- Eligibility –unlike SCT and CART, no absolute medical contraindication* (age/frailty, cardiac/pulmonary/renal/neurologic dysfunction, bulky disease) to bispecifics

*no active infection

Let’s implement TCE for MM in every practice

Barriers:

- REMS- required for all FDA approved TCE
- Step up dosing and monitoring
- Fear of CRS
- Fear of neurotoxicity
- Cost
- Getting everyone in the group to be on board, as well as ED do
- Difficulties with IvIg- the peer to peer call!

Good News:

- You do not need a neurologist or an ICU doc to do this
- Need to educate hospitalists and ED docs
- CAN be done outpatient- very readily

BCMA x CD3 Monotherapy

Bispecific Antibody	Teclistamab (MajesTEC-1)	Elranatamab (MagnetisMM-3)	Linvoseltamab (LINKER-MM1)
Treatment	Weekly 1.5 mg/kg SC	Weekly SC 76 mg SQ	Weekly IV 200 mg
Patients	n = 165	n = 123	n = 252
Median prior lines	5	5	5
Triple-class refractory	78%	100%	74%
ORR at RP2d	**63%**	**61%**	**71% 200 mg IV (n = 117)**
PFS	**12.5 mos**	**17.2 mos**	**64% @ 18 mos**
DOR	**24 mos**	**69% @ 18 mos**	**29.4 mos**

GPRC5D x CD3 Monotherapy

Bispecific Antibody	Talquetamab Phase 1/2 (MonumenTAL-1)	
Treatment	0.4 mg/kg SQ QW	0.8 mg/kg SC Q2W
Patients	n = 143	n = 154
Median prior lines	5	5
Triple-class refractory	74%	69%
ORR at RP2D	**74%**	**69%**
PFS	**7.5 mos**	**11.2 mos**
DOR	**9.5 mos**	**16.9 mos**

Moreau P et al. *N Engl J Med*. 2022;387(6):495-505. Van de Donk NWCJ et al. IMS 2023. Abstract 2. Lesokhin AM et al. *Nat Med*. 2023;29:2259-2267. Tomasson M et al. ASH 2023. Abstract 3385. Shah MR et al. ASH 2024. Abstract 3369. Chari A et al. *Lancet Heme*. 2025;12(4):e269-e281.

Routes/Doses/Step Ups of Currently Approved BsAbs

Step-Up Dosing Schedule (to minimize CRS)				
Teclistamab SQ (Weight based)	**Day 1**	**Day 4**	**Day 7**	
	Dose 1	Dose 2	First Tx dose	
Elranatamab SQ	**Day 1**	**Day 4**	**Day 8**	
	Dose 1	Dose 2	First Tx dose	
Linvoseltamab IV	**Day 1**	**Day 8**	**Day 15**	
	Dose 1	Dose 2	First Tx dose	
Talquetamab SQ (Weight based)	**Day 1**	**Day 4**	**Day 7**	**Day 10**
	Dose 1	Dose 2	Dose 3	First Tx dose

FDA: Patients "should" be monitored in inpatient setting but increasing data re safety/feasibility outpatient step-ups using

- Prophylactic tociluzumab
- Dexamethasone: prophylactic (day after step up dose) or at home treatment of CRS ("pocket")
- Remote monitoring

Rifkin R et al. ASCO 2024. Abstract 7528. Schinke C et al. IMS 2024. Abstract P401. Varga C et al. ASH 2024. Abstract 4720. Davis JA et al. HOPA 2025. Abstract CR05.

Per-Label Step-Up Dosing and Monitoring Requirements (BCMA)- Note “should” is just a suggestion

NO ONE DOSES THESE PER THE FDA LABEL

https://www.tecvaylihcp.com/dosing-and-administration/; https://elrexfio.pfizerpro.com/dosing; https://www.lynozyficrems.com/

Long Term Dosing Schedules of Currently Approved BsAbs

	Weekly Dosing	Biweekly Dosing	Every 4 Weeks Dosing
Teclistamab SQ Wt based	One week after first Tx dose and weekly thereafter Subsequent Tx doses 1.5 mg/kg once weekly	Only for patients who have achieved and maintained a CR or better for a minimum of 6 months Dosing frequency may be decreased to 1.5 mg/kg every two weeks	
Elranatamab SQ Flat dose	One week after first Tx dose and weekly thereafter through week 24 Subsequent Tx doses 76 mg	**Week 25 and every 2 weeks thereafter through week 48** Subsequent Tx doses 76 mg	Week 49 and every 4 weeks thereafter Subsequent Tx doses 76 mg
Linvoseltamab IV Flat dose	One week after Day 15 Tx dose and once weekly from Week 4 to 13 for 10 doses Second and subsequent Tx doses 200 mg	**Week 14 and every 2 weeks thereafter** Subsequent Tx doses 200 mg	**At Week 24 or after and every 4 weeks thereafter** Subsequent Tx doses 200 mg
Talquetamab SQ Wt based		Two weeks after first Tx dose and every 2 weeks thereafter	

TCE combinations are (almost always) better

Talquetamab plus daratumumab for the treatment of relapsed or refractory multiple myeloma in the TRIMM-2 study

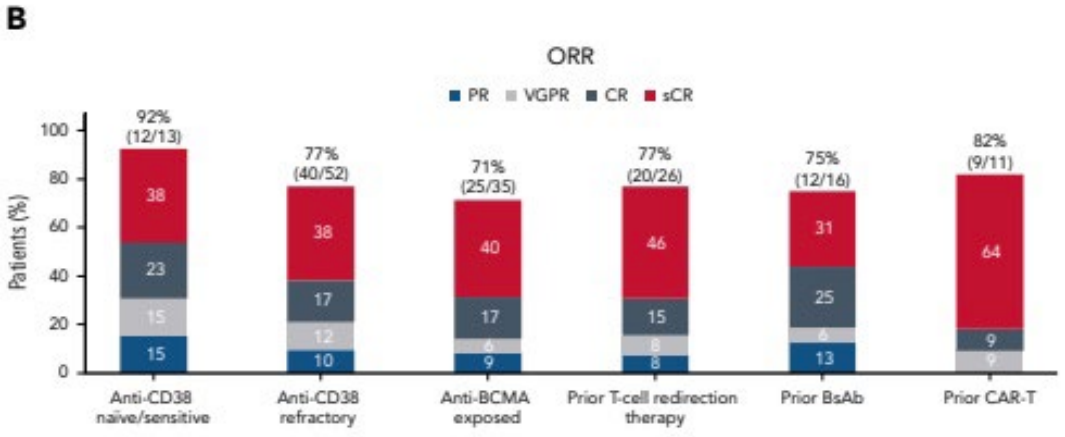
Chari et al Blood. 2025 Dec 11;146(24):2902-2913

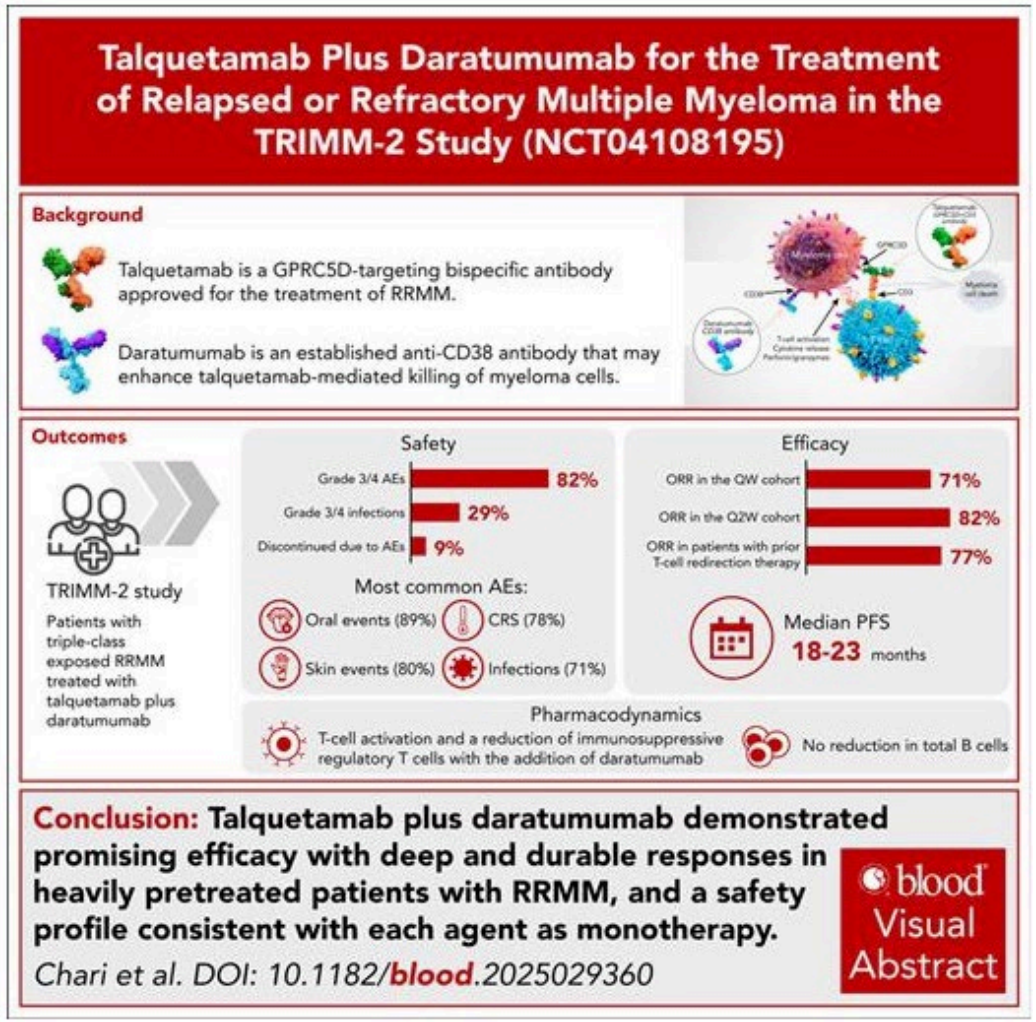
Rationale:

1. Preclinical data showed dara enhanced talq-mediated lysis of MM cells
2. Dara depletes CD38 expressing Treg

Study details:

- ≥ 3 LOT, or double ref. to PI/IMID
- prior TCE/ADC/CAR T/dara permitted (including dara refractory)
- n = 65
- Median prior LOT 5 (2-16)
- 54% prior BCMA





Monumental -2 talq + Pom R/R MM

Methods

MonumenTAL-2[a] phase 1b study design

Eligibility criteria
- Measurable multiple myeloma
- ≥2 prior LOT, including a PI and lenalidomide
- ECOG PS of 0 or 1
- Prior BsAbs, CAR-T, and Pom permitted
- No prior GPRC5D therapy

→

Dosing schedule
Tal[b]
0.4 mg/kg SC QW (n=16) or
0.8 mg/kg SC Q2W (n=19)
+
Pom
Starting at cycle 2, days 1–21 of a 28-day cycle
2.0 mg PO daily with dose escalation to 4.0 mg PO daily permitted[c]

→

Primary endpoint:
Safety[d]

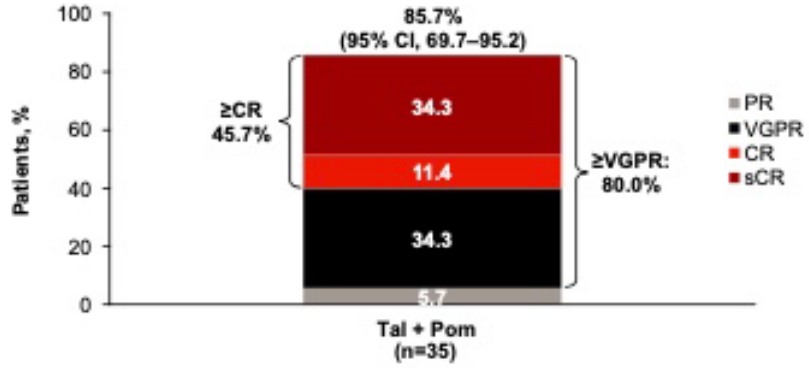
Key secondary endpoints:
Overall response rate (ORR)[e], time to response, duration of response (DOR), progression-free survival (PFS)

[a]NCT05050097. [b]With step-up doses. [c]Based on safety evaluation team recommendation. [d]AEs assessed per CTCAE v5.0, except for CRS and ICANS, which were graded per ASTCT guidelines. [e]Assessed by investigator per IMWG 2016 criteria.
AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMWG, International Myeloma Working Group; PI, proteasome inhibitor; PO, by mouth; Q2W, every other week; QW, weekly; SC, subcutaneous.

Results

Baseline characteristics have been previously presented[6]; median age was 65 years, median prior LOT was 3, 45.0% had high-risk cytogenetics, and 20.0% had extramedullary disease. Prior treatment exposure included Pom, B-cell maturation antigen CAR-T, and BsAbs

Figure 1: Treatment with Tal + Pom elicited a high ORR and deep responses in patients with RRMM with a median follow-up of 20.7 months



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

High ORRs were observed across patient groups, including those with prior exposure to CAR-T (100%, 3/3) or Pom (100.0%, 8/8)

Figure 2: Tal + Pom elicited sustained DOR and PFS outcomes demonstrating long-term efficacy with longer follow-up; median DOR was not reached and nearly half of patients remained progression free at 3 years

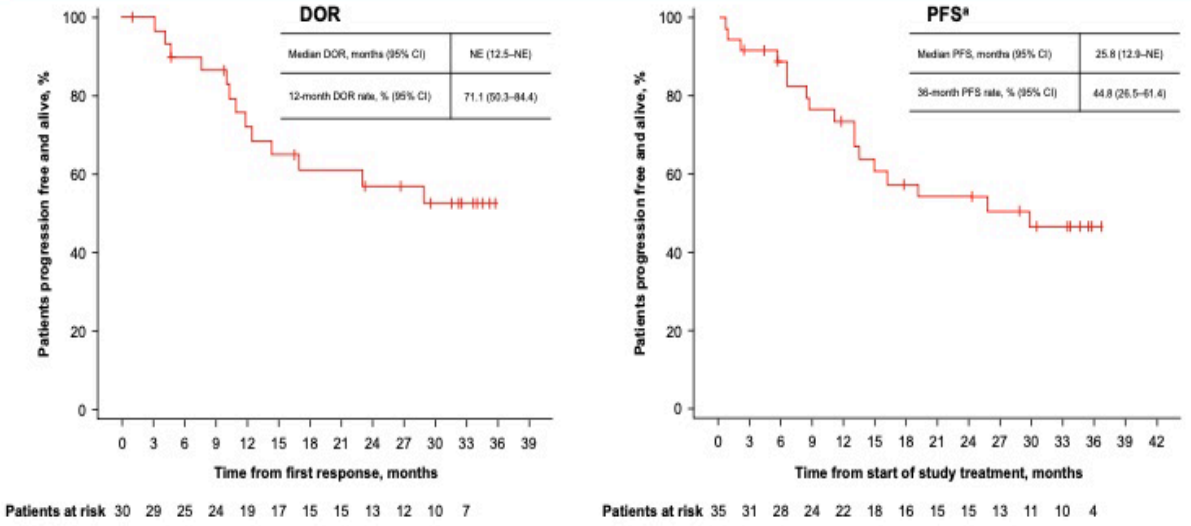
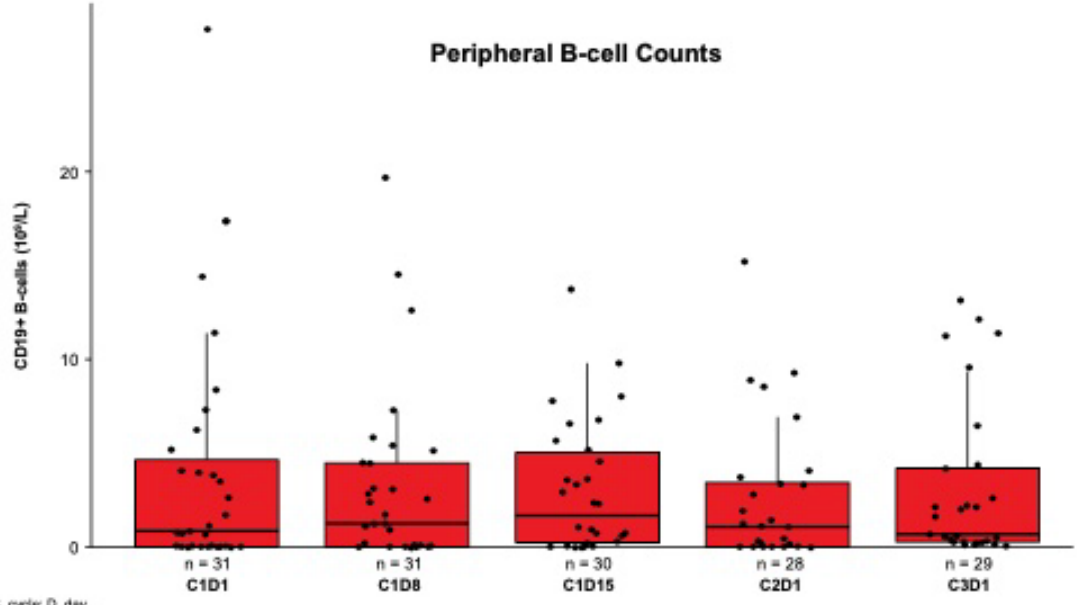


Figure 3: B-cells were retained across the first several cycles of treatment, consistent with prior findings and supporting the B-cell–sparing mechanism of Tal

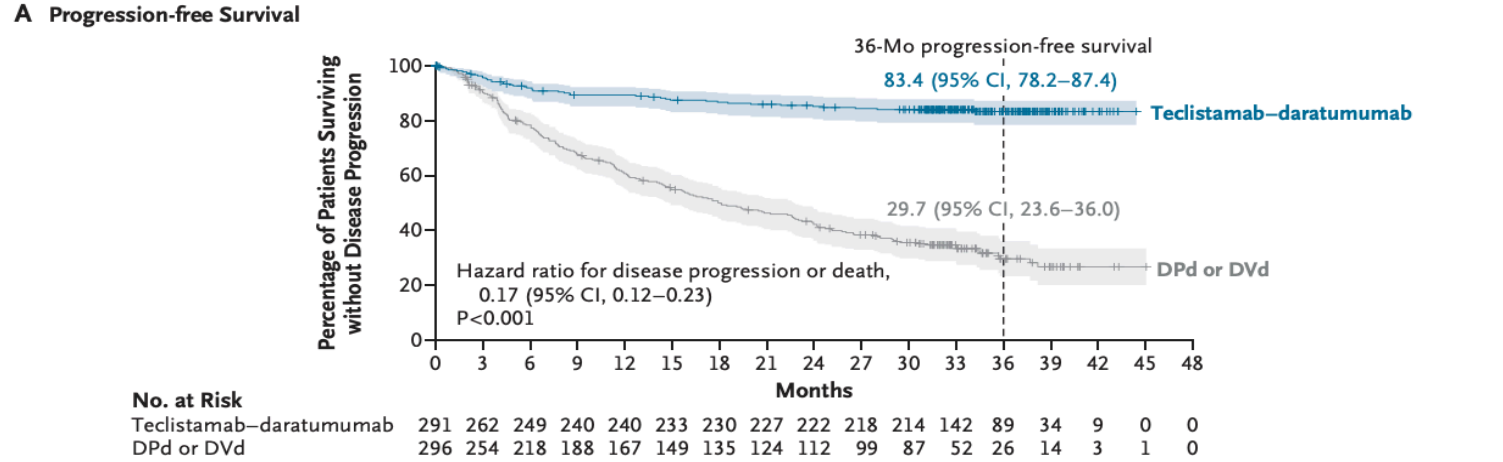


The NEW ENGLAND JOURNAL of MEDICINE

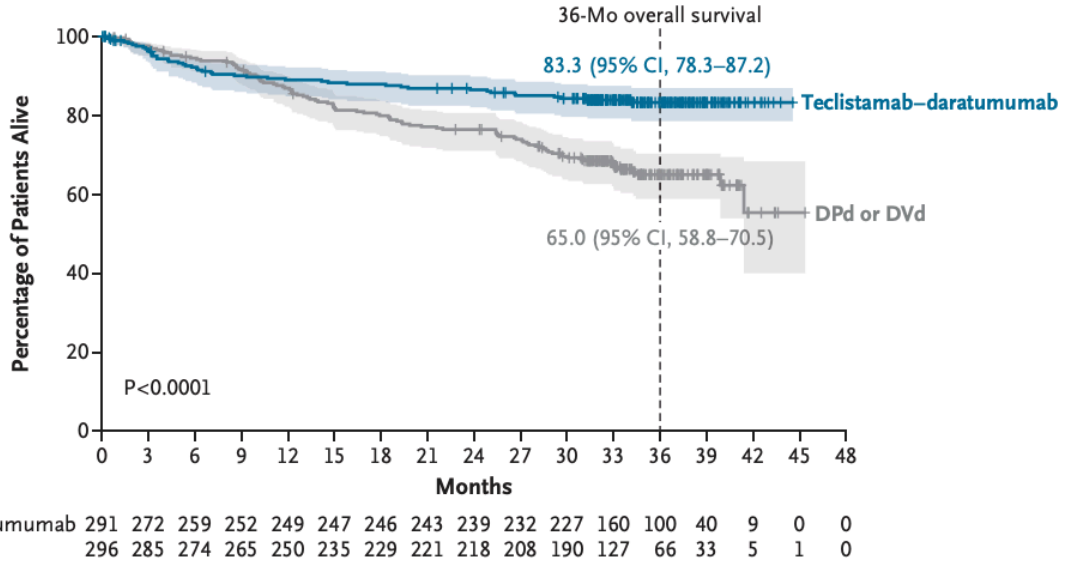
ESTABLISHED IN 1812 FEBRUARY 19, 2026 VOL. 394 NO. 8

Teclistamab plus Daratumumab in Relapsed or Refractory Multiple Myeloma

PFS



OS



1-3 prior LOT

A phase 2 study of teclistamab in combination with daratumumab in elderly patients with newly diagnosed multiple myeloma: the IFM2021-01 TecLille trial, cohort A

S. Manier, J. Lambert, M. Macro, T. Chalopin, M. Dib, A. Rumpler, J. Gay, J.-N. Bastie, C. Jacquet, C. Sonntag, L. Vincent, A. Perrot, C. Mariette, L. Montes, S. Rigaudeau, N. Bigot, M. Doyle, D. Santra, P. Smirnov, C. Albrecht, C. Touzeau, J. Corre, P. Moreau, H. Avet-Loiseau, C. Hulin, X. Leleu, T. Facon

Abstract #367

ASH 2025, Orlando

IFM 2021-01 TecLille – cohort A: Tec-Dara

- n = 3
- Medi
- 1/3 ≥
- Int/fr

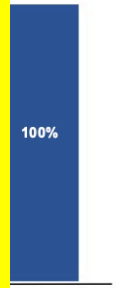
IFM 2021-01 TecLille – cohort A: Tec-Dara Conclusions

- The IFM2021-01 TecLille study demonstrates that an "all-antibody regimen" of teclistamab and daratumumab is highly effective and well-tolerated in TNE patients with NDMM
- With a median follow up of 10.3 months:
  - 100% of patients achieved a VGPR or better
  - All evaluable samples were MRD negative at 10-6 by NGS at 6 months
  - PFS and OS were 100%
  - No grade ≥ 3 CRS and no ICANS occurred
  - The rate of grade ≥ 3 infections was 14% with systematic IVIG prophylaxis

These results support further exploration in phase 3 clinical trial of frontline combination of BCMA/CD3 bispecific with anti-CD38 monoclonal antibodies

IFM 2021-01 TecLille – cohort A: Tec-Dara

S 10^{-6} at 6 months
ble samples



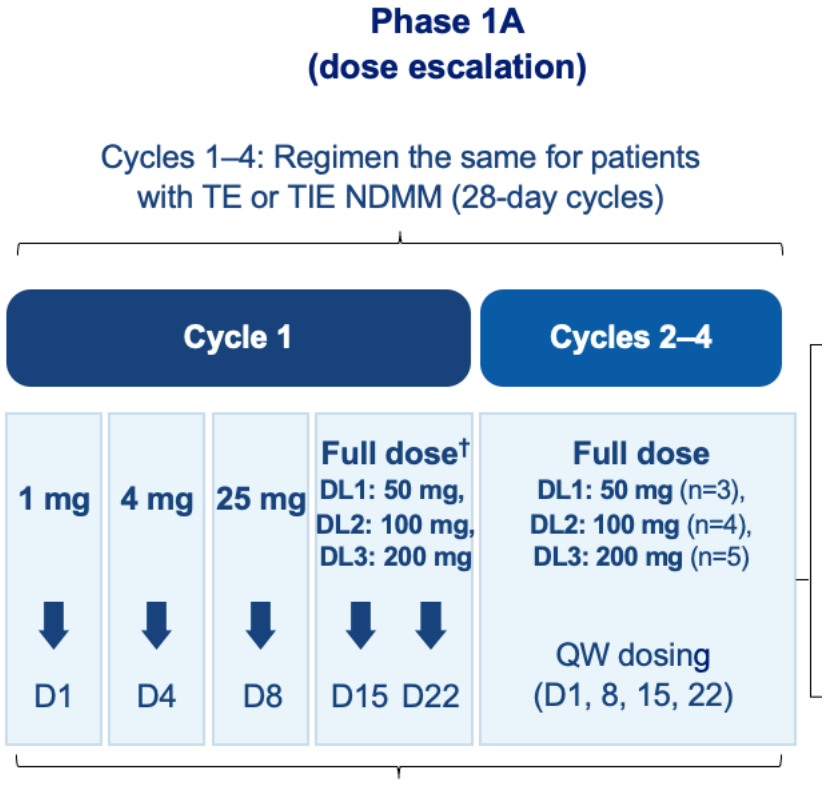
Current amendment:
Teclistamab 3mg/kg Q8W after C13 if CR or better and treatment interruption if 2-years sustained MRD -

CBCI COLORADO BLOOD CANCER INSTITUTE

Medical Center

Monotherapy first line- Linker MM4

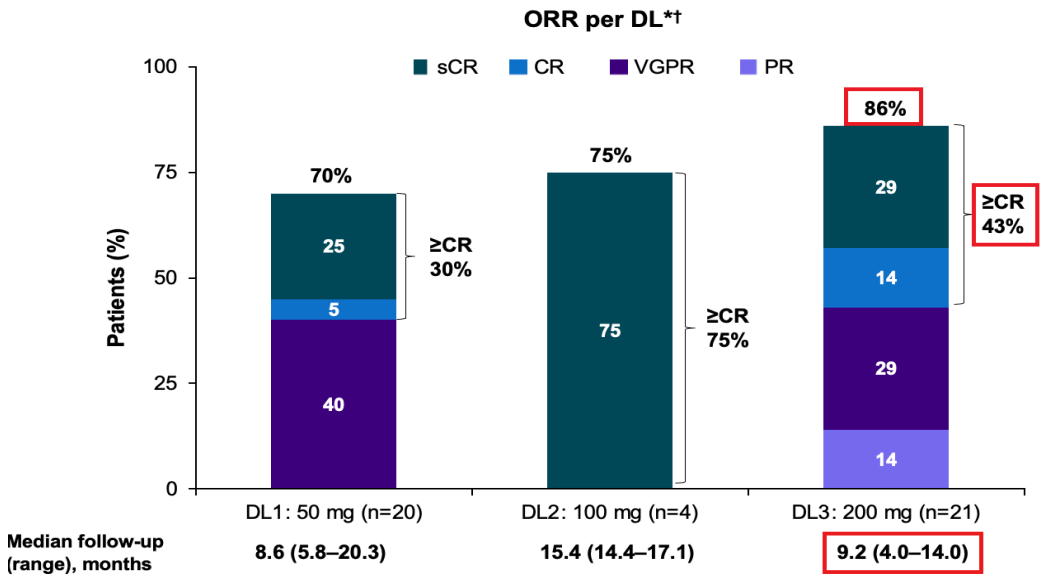
TCE 1L- monotherapy- Linker MM4



Event, n (%)	All doses: Phase 1 total (N=45) Any grade	Grade 3/4
Patients with any TEAE	45 (100)	39 (86.7)
Serious TEAE	30 (66.7)	23 (51.1)
TEAE leading to treatment discontinuation	1 (2.2)*	1 (2.2)*
Treatment-related TEAE	41 (91.1)	30 (66.7)
Infections†	38 (84.4)	15 (33.3)
Most common‡ hematologic TEAE		
Neutropenia§	17 (37.8)	15 (33.3)
Anemia§	12 (26.7)	8 (17.8)
Most common‡ non-hematologic TEAE		
CRS	20 (44.4)	0
Transaminase elevation§	14 (31.1)	6 (13.3)
Hypophosphatemia	14 (31.1)	3 (6.7)
Nausea	14 (31.1)	0
Diarrhea	13 (28.9)	4 (8.9)
Hypogammaglobulinemia	13 (28.9)	0
Infusion-related reactions	12 (26.7)	0

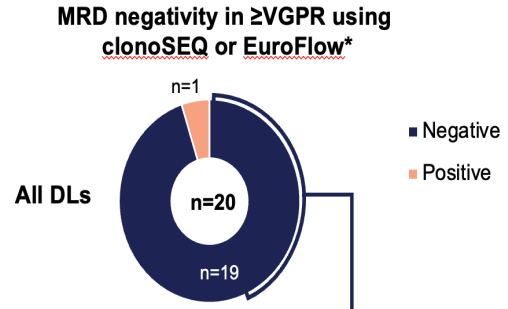
Orlowski et al ASH 2025

Linker MM 4: responses and conclusions



Linvoseltamab induced high rates of MRD negativity in MRD-evaluable patients with ≥VGPR

- MRD was evaluated using clonoSEQ or EuroFlow* in the BMA of 20/32 patients with ≥VGPR
- Across all dose levels, **19/20 MRD-evaluable patients (95%)** were negative at 10^{-5} cell sensitivity
  - 100% of clonoSEQ evaluable patients (12/12) were MRD negative at both 10^{-5} and 10^{-6} sensitivity



200 mg dose level: 100% of patients (9/9) were negative at 10^{-5} sensitivity

- 100% who were MRD-evaluable by clonoSEQ (8/8) were negative at 10^{-6} sensitivity

- Linvoseltamab 200 mg was selected as the RP2D based on the manageable safety profile and promising efficacy
- **No new safety signals** were observed with linvoseltamab in NDMM. Although follow-up was limited, the safety profile appeared more favorable than in RRMM[1]
  - Only Grade 1 CRS (44%) and Grade 1 ICANS (one patient, 2%) occurred; most CRS events occurred during the step-up dosing period
  - **33% Grade 3 infections (no Grade 4 or 5)**; infection rates decreased after the first 3 months of treatment
- At the 200 mg DL, there were **high rates of response** that deepened over time
  - **The ORR was 86% (≥CR rate 43%)**, with a median follow-up of 9.2 months (range 4.0–14.0)
  - All MRD-evaluable patients (9/9) were MRD negative at 10^{-5} sensitivity
- The benefit:risk profile supports exploration of linvoseltamab as a **foundation in frontline therapy in NDMM**

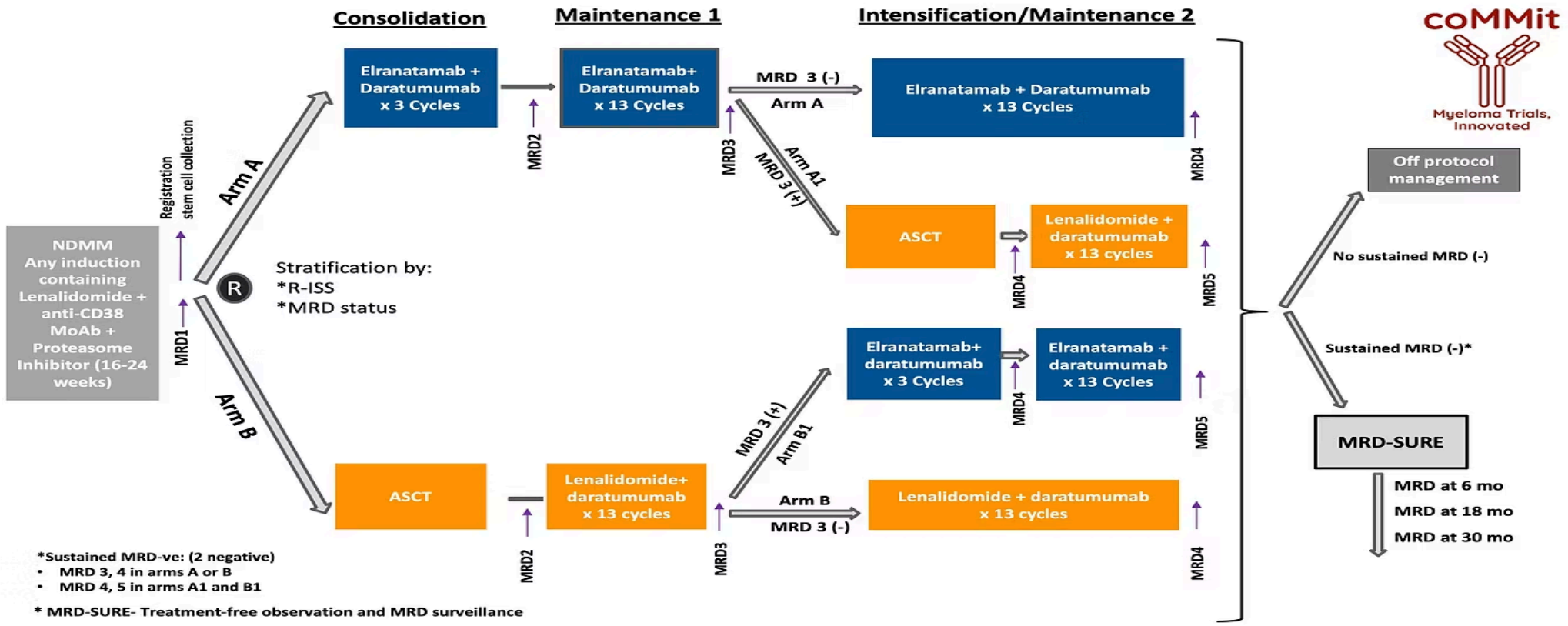
CBC
COLORADO BL
CANCER INSTI

TCE as consolidation front line

Consolidate std induction with TCE- FASTER trial (COMMit)

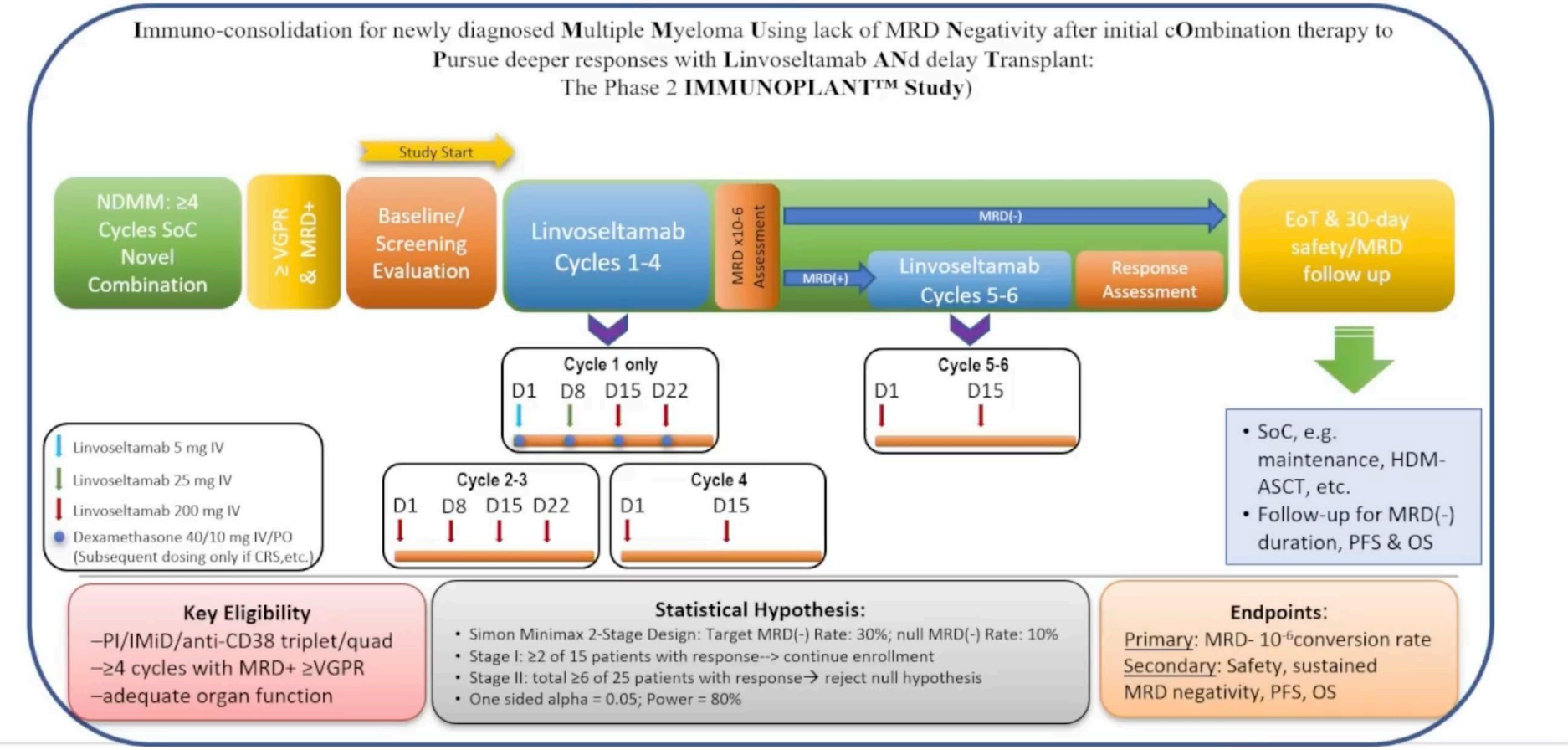
FASTER Trial

The FASTER trial studies whether a combination of anti-CD38 antibody and an BCMA-directed bispecific T-cell engager can outperform autologous stem cell transplantation and anti-CD38 antibody plus lenalidomide maintenance in patients with newly diagnosed multiple myeloma.



IMMUNOPLANT: Linvoseltamab consolidation after induction therapy for NDMM

Study Design: Schema

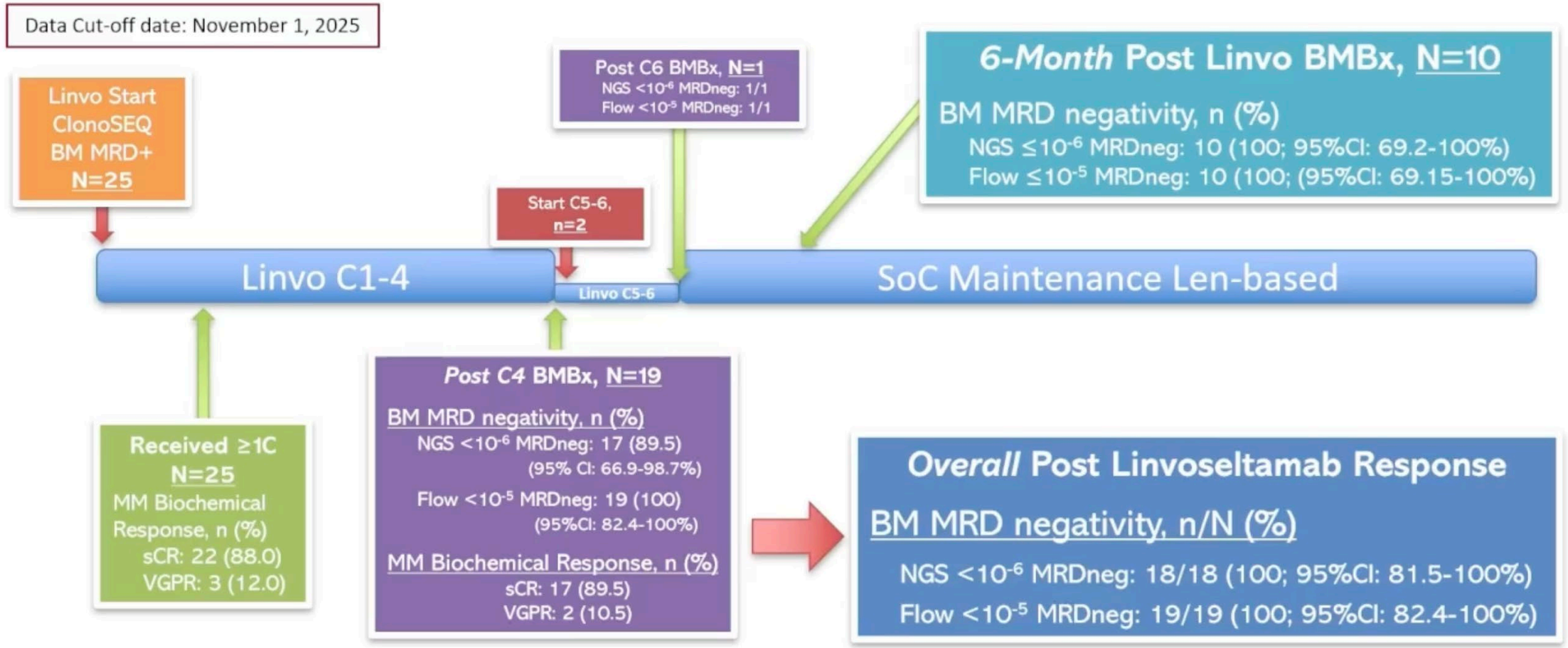


CBCI COLORADO BLOOD CANCER INSTITUTE

SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center | Health ONE

Kazandjian et al, *Blood* 2025; 146 (Supplement 1): 94.

IMMUNOPLANT: Linvoseltamab Consolidation Efficacy



CBCI COLORADO BLOOD CANCER INSTITUTE

SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center | HealthONE

Kazandjian et al, *Blood* 2025; 146 (Supplement 1): 94.

IMMUNOPLANT: Linvoseltamab Consolidation Safety

- No patients had CRS/ICANS
- No patient deaths
- One patient had a Grade 3 SAE (peritonsillar abscess)
- No Grade 4 TRAEs
- Temporary dose delays occurred in 6 patients due to infection-related symptoms or neutropenia

Tocilizumab prophylaxis given prior to first step-up dose of linvoseltamab

Kazandjian et al, *Blood* 2025; 146 (Supplement 1): 94.

CRS

CRS Rates with FDA-Approved Bispecific T Cell Engagers (Plus Etentamig)

Drug (Brand)	Targets	Indication	N	Any Grade CRS	Grade ≥2 CRS	Key Trial
Etentamig (ABBV-383)*	BCMA × CD3	R/R MM (≥3L; investigational)	23¶	30%	4%	Ph1b 2-mg SUD + Dex† (Voorhees et al., ASCO 2025)
Mosunetuzumab	CD20 × CD3	R/R Follicular Lymphoma (≥2L)	90	44%	NR†	GO29781 (Budde et al., Lancet Oncol 2022)
Epcoritamab	CD20 × CD3	R/R DLBCL (≥2L); R/R FL (≥2L)	157†	51%	~18%	EPCORE NHL-1 (Thieblemont et al., JCO 2023)
Glofitamab	CD20 × CD3	R/R DLBCL (≥2L)	154	64%	~17%	NP30179 (Dickinson et al., NEJM 2022)
Teclistamab	BCMA × CD3	R/R MM (≥4L)	165	72%	~22%	MajesTEC-1 (Moreau et al., NEJM 2022)
Elranatamab	BCMA × CD3	R/R MM (≥4L)	123	58%	~14%	MagnetisMM-3 (Lesokhin et al., Nat Med 2023)
Talquetamab	GPRC5D × CD3	R/R MM (≥4L)	339‡	77%	~19%	MonumenTAL-1 (Chari et al., NEJM 2022)
Linvoseltamab	BCMA × CD3	R/R MM (≥4L)	117	46%	~11%	LINKER-MM1 (FDA Approval, July 2025)
Tarlatamab	DLL3 × CD3	ES-SCLC (post-platinum)	100§	57%*	~21%	DeLLphi-301 (Ahn et al., NEJM 2023)

Abbreviations: BCMA = B-cell maturation antigen; DLBCL = diffuse large B-cell lymphoma; DLL3 = delta-like ligand 3; ES-SCLC = extensive-stage small cell lung cancer; FL = follicular lymphoma; GPRC5D = G protein-coupled receptor class C group 5 member D; L = prior lines of therapy; MM = multiple myeloma; R/R = relapsed/refractory; SUD = step-up dose.

* Etentamig (ABBV-383) is investigational; not FDA approved. Data from ASCO 2025 Abstract #7527 (NCT05650632). Phase 3 CERVINO trial (NCT06158841) ongoing. ¶ N=23 is the 2-mg SUD expansion cohort; all-cohort step-up pooled N=70 had 40% any-grade CRS, 0% grade ≥2. † Dexamethasone 36 mg premedication. ‡ N=157 reflects DLBCL cohort (approval basis). § N=339 reflects pooled MonumenTAL-1 recommended-dose cohorts (405 mg QW + 800 mg Q2W). ‖ N=100 reflects 10 mg approved dose arm (DeLLphi-301). NR = grade ≥2 not separately reported from grade 1 in published trial data (GO29781 reports G1–2 combined; grade ≥2 rate is not disaggregated). Grade ≥2 values are derived from published grade-level CRS breakdowns from pivotal trial publications and prescribing information.

Prophylactic Tociluzumab with bsab

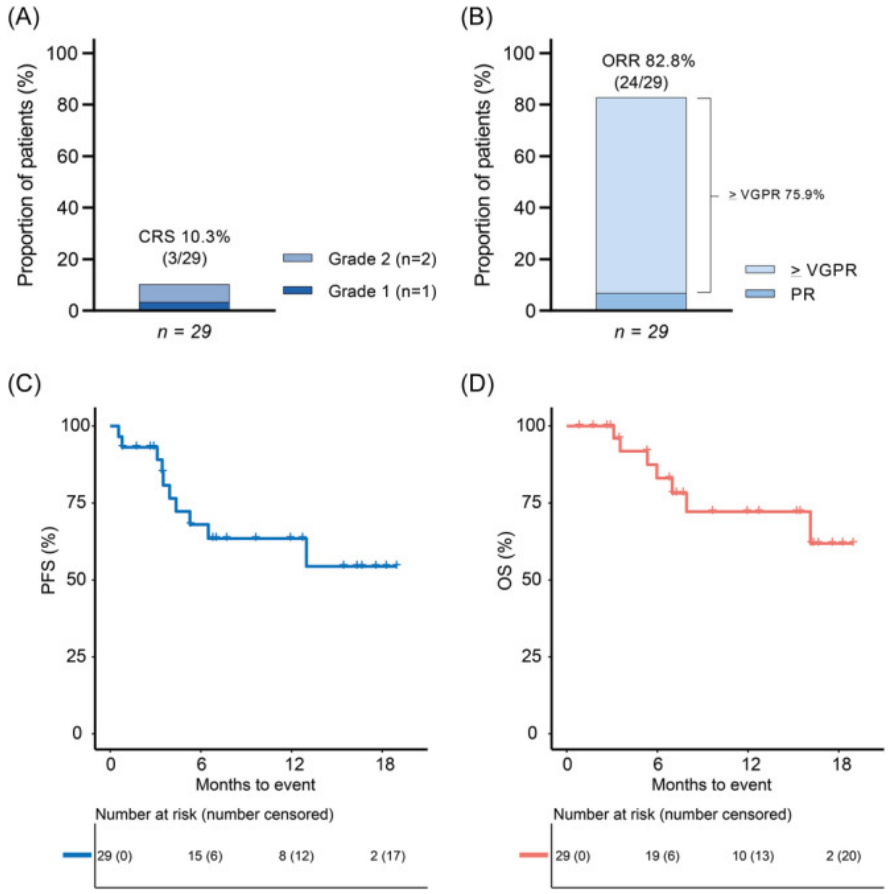
		No toci prophylaxis					+ Toci prophylaxis		
	n	All	G 1/2/3/4	ICANS	n		All	Gr 1/2/3/4	ICANS
Teclistamab	165	72%	50/21/0.6/0	3%	24[2]	≤4h pre SU1	25%	8/17/0/0%	NR
Cevostomab	160	81%	43/37/1.2/0%	14%					
	44	91%	55/34/2.3/0%	14%	31	pre SU1	39%	19/16/3.2/0%	6.5%
Talquetamab	297	75-79%	75/2/0/0%	3-11%	27	Pre SU1 + Dex 8 mg qd * 2d after each SU	19%	19/ 0 / 0 / 0	7.4%

- Prophylactic toci reduce all grade CRS from 70-90% to 20-40%
- but grade 2 still occurs with prophylactic toci - * BM PC > 60%, circulating PC
- ? trend towards lower rate of ICANS , increased neutropenia in some studies

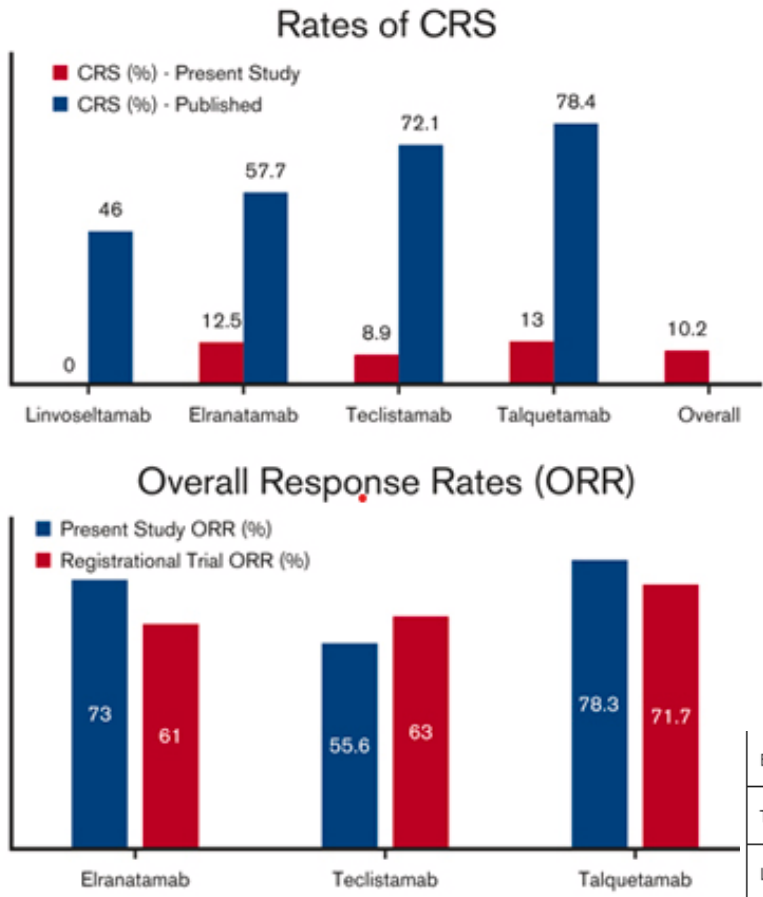
Martin et al Cancer 2023. Van de donk ASCO 2024.
Trudel S et al, ASH 2021. Trudel et al ASH 2022
Chari et al Lancet Heme 2025. Dyfeld et al EHA 2025

Reducing CRS: Prophylactic Toci

Amsterdam data: MajesTEC-1 + Compassionate use Tec



U Miami, Real World Data



Elra	40 (33.6)
Tec	45 (37.8)
Linvo	10 (8.4)
Tal	23 (19.3)
Tec/Tal	1 (0.8)

CBCI COLORADO BLOOD CANCER INSTITUTE

SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center

Health ONE

Korst et al. Hemasphere 2024, Jul 2024; 8(7):e132
Kowalski et al. Blood Adv (2025) 9 (19): 4979-4986

OpTEC

- Trial performed across Sarah Cannon Network
- Multicenter, community based
- Many centers without prior bispecific startup experience

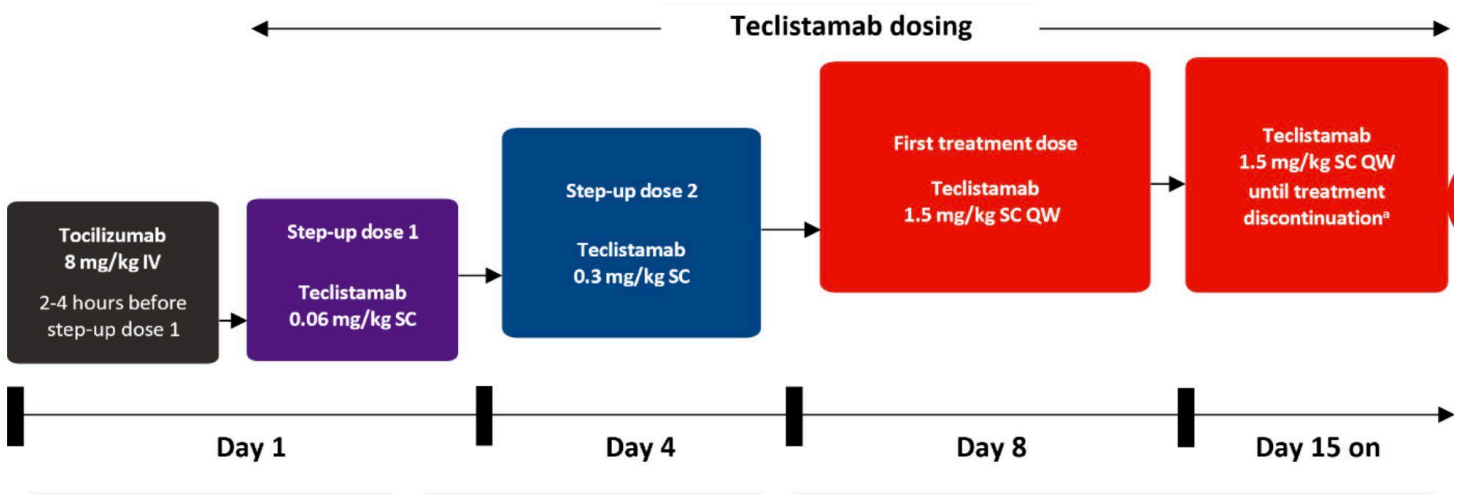
CBCI COLORADO BLOOD CANCER INSTITUTE

SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center | HealthONE

Outpatient Teclistamab (OpTEC) Trial

- Prospective phase 2 trial
- Arm A:

OPTec Study Design[1-3,5]



- Protocol-defined patient safety measures[5]:
  - Premedication: administer corticosteroids, H_1 receptor antagonists, or antipyretics 1-3 hours prior to each SUD of teclistamab
  - Investigator observation: monitor patients for 2 days after each teclistamab SUD and first full treatment dose; remote follow-up (eg, phone) permitted on weekends.
  - Home monitoring: instruct patients to record temperature and oxygen saturation twice daily (≥8 hours apart); report fever ≥38 °C (≥100.4 °F) immediately and hospitalization for CRS as determined by investigator.
  - IVIG support: recommend intravenous immunoglobulin (IVIG) if IgG <400 mg/dL.
  - Companion requirement: ensure the presence of a trained adult for 48 hours after each SUD and first full treatment dose.
  - Travel restriction: limit patient travel within 30 minutes of study site.

OpTEC Interim results

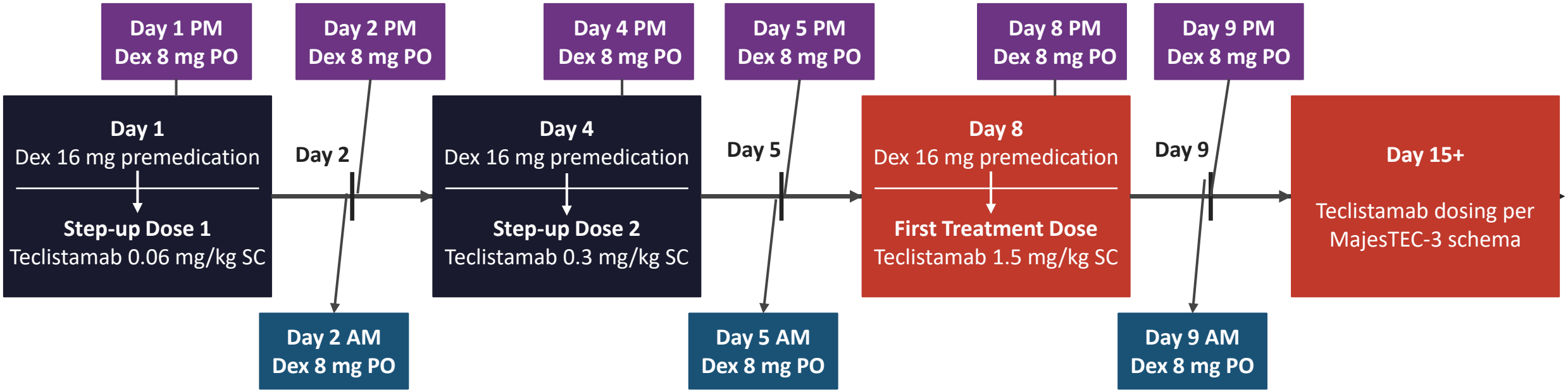
- Finishing prophylactic toci cohort enrollment (planned 50 patients), 43 evaluable
- 2 patient with Grade 1 CRS (5%), no ICANs
- ORR 82%
- 47% overall infection rate, 17% Gr 3+
- At 11.8 months median F/U 74.4% progression free
- No concerning safety signals with outpatient community-based dosing

Is prophylactic tocilizumab a viable path?

- Despite clear data regarding CRS reduction and NCCN inclusion community based toci premedication adoption appears limited
- Cost + difficulty in assuring authorization prior to administration with gov't payors tough combination

Product	Acquisition cost per vial size	Acquisition cost 800 mg dose
Tofidence™ (tocilizumab-bavi)	80 mg/4 mL = $319.30 200 mg/10 mL = $798.25 400 mg/20 mL = $1596.49 *Rebate: 30% off invoice discount 2Q2026 if meet market share (>20%)	$3192.98 *without rebate*
Tyenne™ (tocilizumab-aazg)	80 mg/4 mL = $368.05 200 mg/10 mL = $920.14 400 mg/20 mL = $1840.26	$3680.52
Actemra™ (tocilizumab) brand	80 mg/4 mL = $511.96 200 mg/10 mL = $1279.90 400 mg/20 mL = $2559.81	$5119.62
Avtozma™ (tocilizumab-anoh)	80 mg/4 mL = $297.94 200 mg/10 mL = $744.48 400 mg/20 mL = $1489.72	$2979.44

OpTEC Arm C: Prophylactic Dex



CBCI COLORADO BLOOD CANCER INSTITUTE

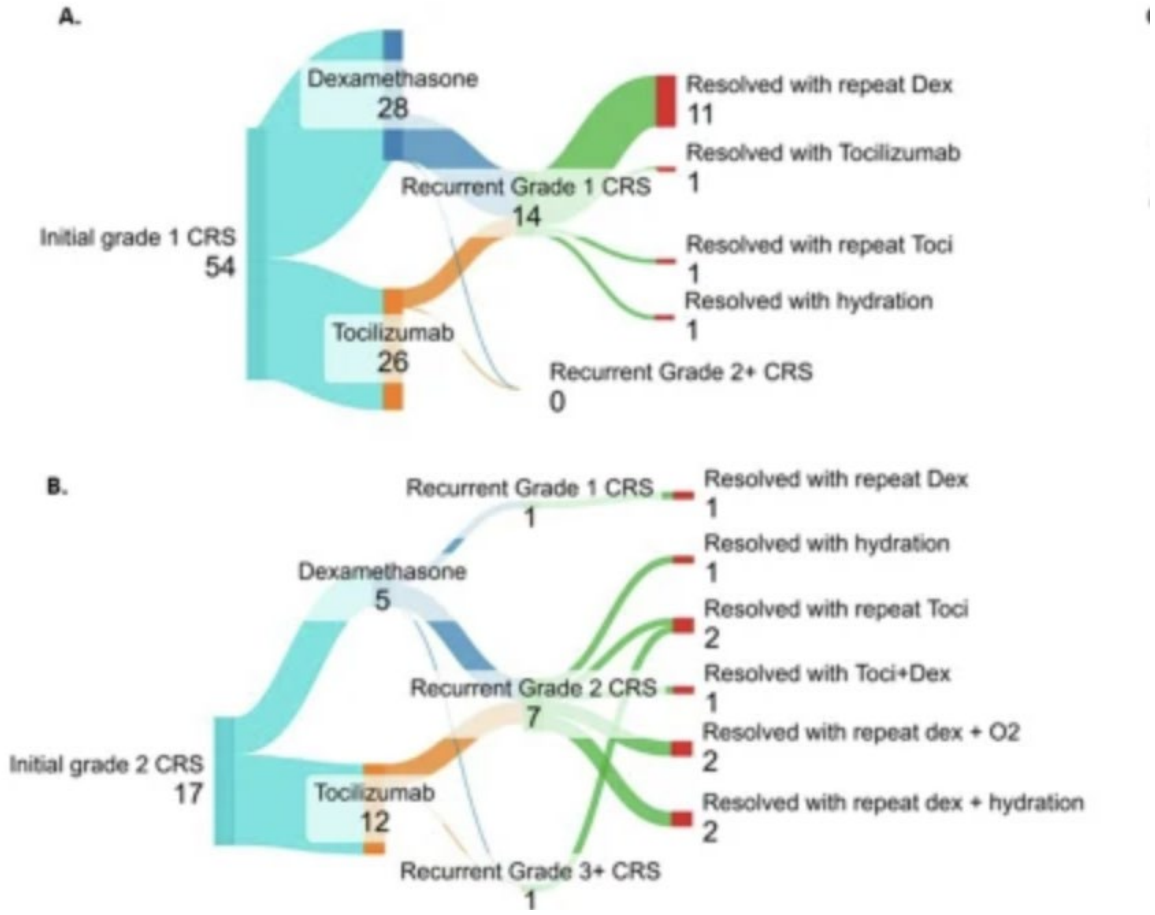
SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center | HealthONE

Retrospective Study: Dexamethasone vs Toci for CRS w/Teclistamab

- 133/243 (55%) experienced CRS
  - 31 (23%) dexamethasone monotherapy
  - 38 (29%) tocilizumab monotherapy
  - 30 (23%) both
  - 34 (25%) received supportive care only

	dex	toci	
CRS, any grade	33 (100)	38 (100)	
Grade 1	28 (85)	26 (68)	0.16
Grade 2	5 (15)	12 (32)	0.16
Grade 3+	0	0	
Repeat CRS after subsequent dose	14 (42)	6 (16)	**0.018**
Subsequent dose delay	9 (27)	8 (21)	0.59
Subsequent dose delay for grade 1 CRS only	6 (18)	5 (13)	0.74
Duration of CRS, days	1 (1–4)	1 (1–4)	0.19

- Dex 10 mg used for 73% of CRS events (range 4 mg to 20 mg)
- median number of dex doses 1 (range 1–5) with
  - 10 (30%) requiring a 2nd dose for recurrent CRS
  - 5 (15%) > 2 doses, dex 10 mg q6 h until CRS resolution.



Davies et al Blood Ca J 2025

Infection Mitigation Strategies for BCMA BsAb-TCEs

Prophylactic Measures

Prophylactic Anti-Microbials

- ✓ Antiviral prophylaxis for HSV and VZV
- ✓ **Anti-PJP prophylaxis**
- ✓ Anti-bacterial/anti-fungal for:
  - – Prolonged or G-CSF-resistant neutropenia
  - – High-risk/history of recurrent infection
  - – History of prolonged high-dose steroid use (anti-fungal)
  - – NOT recommended for aspergillosis

Vaccinations

- ✓ VZV
- ✓ Influenza
- ✓ SARS-COV-2/COVID-19 (per CDC/local guidelines)

Screenings

- ✓ HBV

Management of AEs

HGG

- ✓ Monitor Ig levels
- ✓ **Monthly IVIG after period of CRS complete**
  - – **Continue even 6 -12 mos+ after stopping sAb**

Neutropenia

- ✓ Monitor neutrophil levels
- ✓ G-CSF for patients with ≥ Grade 3 neutropenia
- ✓ Avoid G-CSF during periods of CRS risk

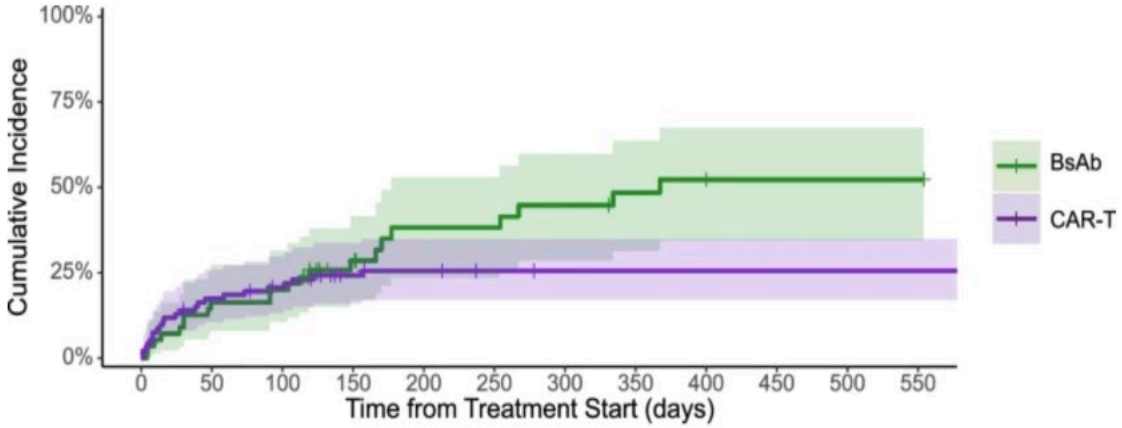
BsAb Dose Management

BsAb Dosing Adjustments

- ✓ **Withhold** dosing temporarily for:
  - – ANC < 0.5 x 10^9/L or febrile neutropenia
  - – Active infection
    - ▪ eg, COVID-19, CMV infection (or high titer viremia), HBV reactivation
- ✓ **Decrease** dosing frequency once MM maximally debulked
- ✓ **Discontinue** if recurrent infections despite best supportive care and MM well controlled (i.e., fixed duration)

ANC, absolute neutrophil count; BsAb, bispecific antibody; CDC, Centers for Disease Control and Prevention; CRS, cytokine release syndrome; G-CSF, granulocyte-colony stimulating factor; HBV, Hepatitis B; HGG, hypogammaglobulinemia; HSV, herpes simplex virus; IgG, immunoglobulin G; IVIG, intravenous immunoglobulin; PJP, pneumocystis jirovecii pneumonia; SARS-COV-2, severe acute respiratory syndrome coronavirus 2; VZV, varicella zoster virus. 1. Raje N et al. *Lancet Haematol*. 2022;9(2):e143-e161. 2. Rodriguez-Otero P et al. *Lancet Oncol*. 2024;25(5):e205-e216. 3. Mohan M et al. *J Haematol*. 2023;203(5):736-746.

Infections are an issue with CD3/BCMA TCE

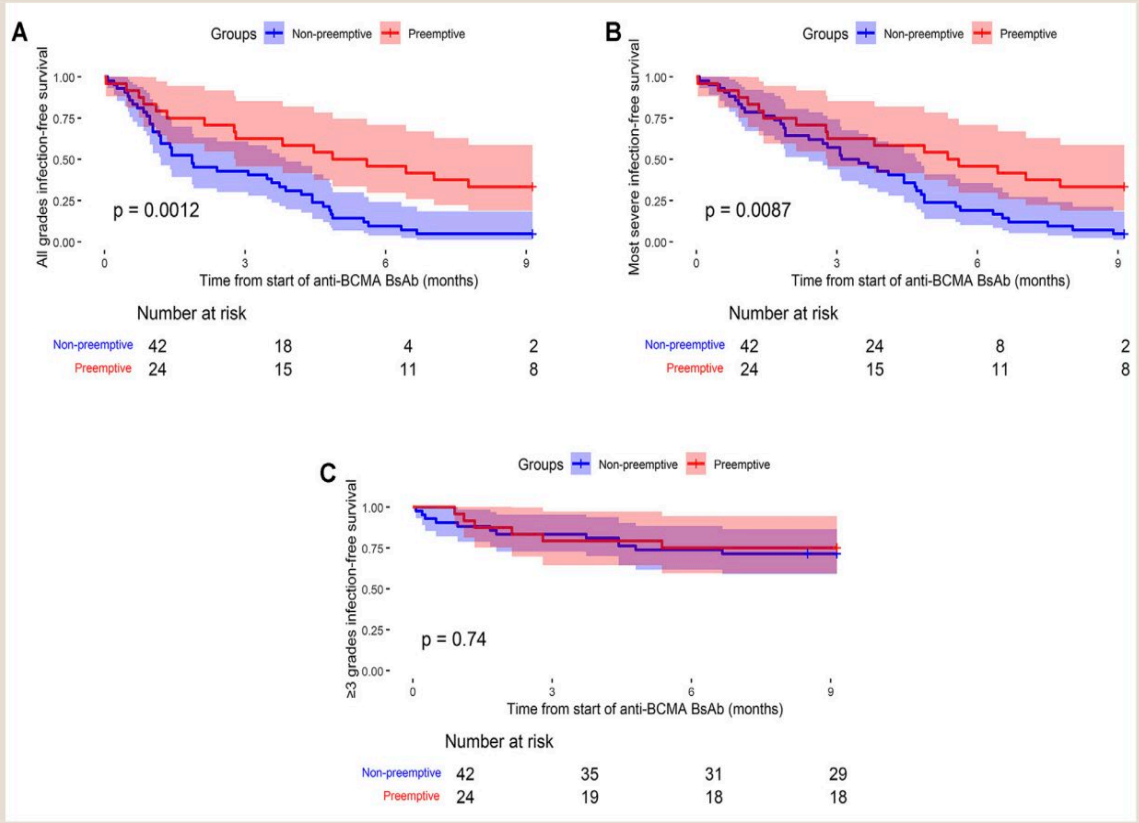


Estimated cumulative incidence of grade ≥3 infections over time.

Nath K et al, BCJ 2024. PMID: 38821925.
Jelinek T et al. Blood. 2025. PMID: 41405507.

Bénédicte Piron et al

Figure 1 Time to first onset infection per patient supplemented with non-preemptive IG and preemptive IG. (A) Time to first onset all-grade infection. (B) Time to first onset most severe all-grade 1-5 (CTCAE) infectious event. (C) Time to first onset ≥ 3 grades (CTCAE) infectious event.

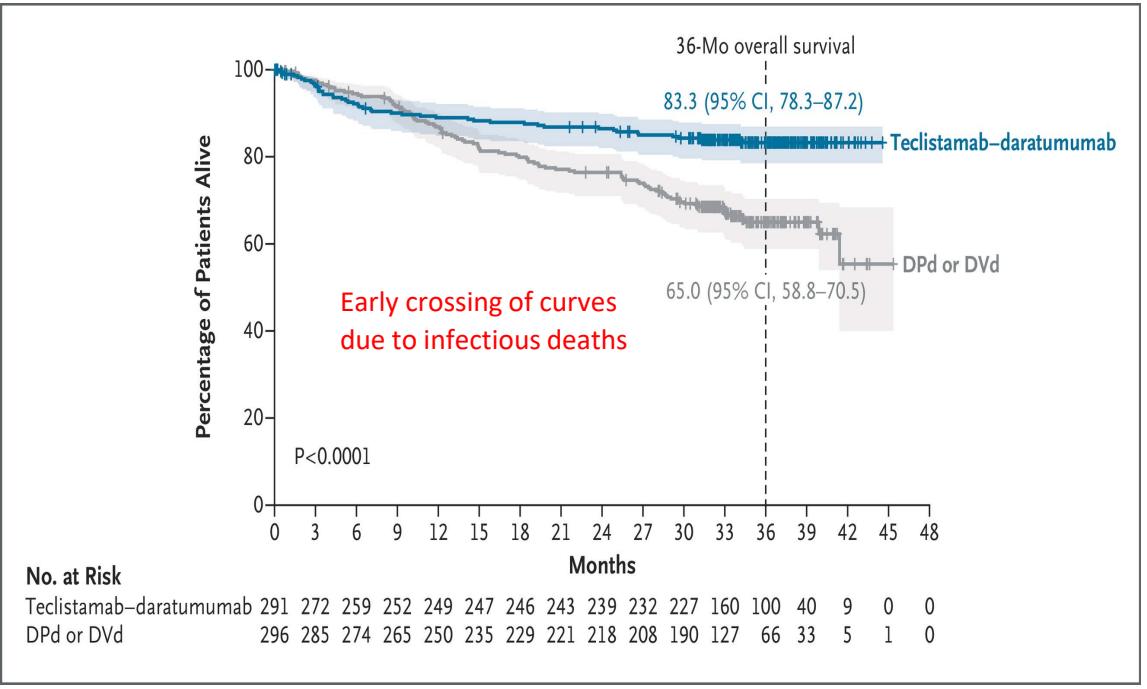


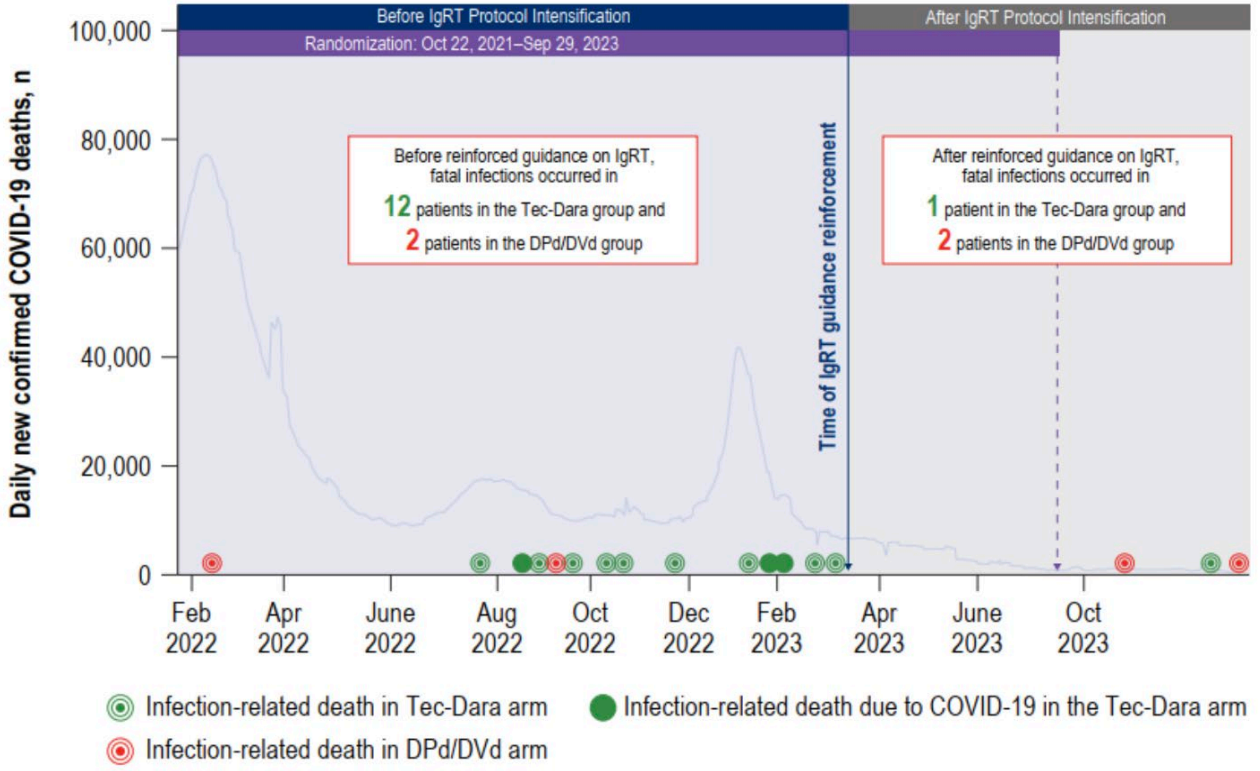
Clinical Lymphoma, Myeloma and Leukemia, 2025; 26, 115-122.e6

CBCI COLORADO BLOOD CANCER INSTITUTE
SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center
HealthONE

Two recent examples from ASH 2025

- Example #1: Tec-dara (teclistamab + daratumumab) in RRMM, as now famously published in MajesTEC-3
- Example #2: Tec-Lille IFM study we already reviewed





Courtesy Rahul Banarjee

Costa LJ et al, NEJM 2025. PMID 41363801.

Abbreviations: ASH, American Society of Hematology; RRMM, relapsed/refractory multiple myeloma; tec/dara, teclistamab / daratumumab.

ADVANCES VIEWPOINT

blood advances

Immunoglobulin prophylaxis should be initiated after bispecific antibody therapy in multiple myeloma, regardless of IgG levels

Rahul Banerjee,[1] Meera Mohan,[2] Kai Rejeski,[3,4] Benjamin R. Puliafito,[5] Diana D. Cirstea,[5] Gurbakhash Kaur,[6] Shonali Midha,[7] Georgia J. McCaughan,[8] Nikhil M. Kumar,[9] Nikita Mehra,[10] Bhausaheb Bagal,[11,12] and Noopur S. Raje[5]

[1]Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA; [2]Department of Medicine, Medical College of Wisconsin, Milwaukee, WI; [3]Department of Medicine III, Hematology/Oncology, LMU University Hospital, LMU Munich, Munich, Germany; [4]Adult Bone Marrow Transplantation Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY; [5]Department of Medicine, Massachusetts General Hospital, Boston, MA; [6]Department of Medicine, The Mount Sinai Hospital, New Nork, NY; [7]Department of Medicine, Dana-Farber Cancer Institute, Boston, MA; [8]Department of Haematology, St Vincent's Hospital, Sydney, Australia; [9]Department of Medicine, Fortis Memorial Research Institute, Gurugram, India; [10]Department of Medicine, Cachar Cancer Hospital & Research Centre, Silchar, India; [11]Department of Medicine, Tata Memorial Centre, Mumbai, India; and [12]Department of Medicine, Homi Bhabha National Institute, Mumbai, India

Table 1. Rationales for primary immunoglobulin RT prophylaxis with bsAb therapy in MM

Rationale	Summary	Relevance to decision-making
The risk of infections with bsAb therapy is concerningly high.	With every continued month on BCMA bsAb therapy, 3% of patients develop de novo high-grade infections.[11]	High-grade infections can cause morbidity and treatment delays for patients; these infections are also very expensive for payers.
Primary IgRT prophylaxis almost certainly lowers this risk of infections.	Primary prophylaxis has been associated with a 90% reduction in grade ≥3 infection rates.[28]	Given its safety and tolerability in this setting, the benefit-risk ratio of IgRT supports its use as primary prophylaxis to prevent infections.
An IgG threshold of 400 mg/dL does not adequately risk-stratify infections.	IgG ≥400 mg/dL does not guarantee protection against circulating pathogens and may be inaccurately normal.*	Restricting IgRT until IgG falls below 400 mg/dL is not evidence-based and may put patients at risk of high-grade infections.

*In the setting of an IgG κ or λ paraprotein, which is present in approximately half of patients with MM.[29-31]

Banerjee R et al, Blood Adv 2025. PMID: 40690761.

CRS & Neurotox/ICANS summary

- CRS with RARE exception is just a drug fever, rarely causes significant morbidity (high tumor burden and proliferation patients)
- Can be largely mitigated by prophylactic toci and even dex

- Neurotox is REALLY RARE, mostly headache if there is a fever
- VERY RARELY can see if high tumor burden and proliferation

Patient Selection for Bispecific Antibodies

Key Considerations: Age, frailty, ECOG status, and **caregiver availability- we believe that just about anybody can tolerated a TCE**

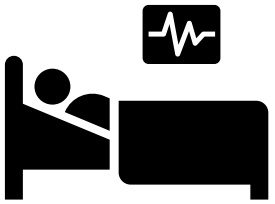
Requirements for Caregivers

Education:

- Attend all consenting and education visits with the patient
- Demonstrate ability to recognize signs/symptoms of toxicity
- Understand when and who to call for signs and symptoms of toxicity

Direct Care:

- Able to provide direct, in-home care for at least 48 hours
- Ability to provide transportation to any health-care visits for at least 72 hours



Monitoring:

- Ability to assist patient in utilizing monitoring equipment (BP, thermometers, pulse ox)
- Vitals should be taken Q4H
- Ability to administer ICE score assessment BID
- Ability to record and report all monitoring

CBCI COLORADO BLOOD CANCER INSTITUTE

SARAH CANNON Cancer Institute at Presbyterian/St. Luke's Medical Center | HealthONE

Zahra Mahmoudjafari et al. JADPRO. https://doi.org/10.6004/jadpro.2024.15.8.15

Moving Towards Outpatient Administration of Bispecifics

Many centers have implemented step-up dosing protocols to **optimize site feasibility and improve patient access**. Outpatient administration of bispecifics continues to become safer and more effective as we apply **proactive AE mitigation strategies** and **robust MDT protocols** for monitoring and symptom triage.

Clinical Pearls:

- **Treat your first bispecific patients in an inpatient setting** until you become comfortable with managing adverse effects
- **Select a fit patient with low disease burden for your first bispecifics case** to maximize your chance of successful implementation
- **Consider administering SUD 1 on Mondays** to limit CRS events occurring overnight or on the weekend

Co-Managing Bispecifics with Academic Centers

Many community sites will rely on **academic centers for initiation** and then assume **maintenance dosing**. A smooth transition of care requires communication and coordination between both care teams.

Essential elements of transition include:

- Patient hand-off with step-up completion date, last dose, and CRS/ICANS history
- REMS certification and authorization for drug access at the referring institution
- Direct contact channels between both centers in case of AEs

Garfall et al. *Front Oncol*. 2025;15:1630146.

Treatment of Off-Tumor On-Target GPRC5d Toxicities

- Educate pt/caregiver what to expect PRIOR to start of therapy
- Engage interdisciplinary team at your facility at onset of therapy

Oral Toxicities	
Dysgeusia	• Reducing dose intensity at time of response
Xerostomia	• Hydration (saliva substitutes), or sugar-free chewing gum to stimulate saliva flow. • Sodium lauryl sulfate (SLS) free toothpastes • Regular dental review
Weight loss	• Nutritional supplements
Treatment of oral comorbidities	• e.g., thrush or nutritional deficiencies leading to glossitis

Skin Toxicities	
Prevention	• Emollients (e.g., urea 10%/ammonium lactate 12% cream) • Sunscreen
Low grade rash	• Low potency topical corticosteroids (e.g., hydrocor, triamcinolone) & escalation to medium potency prn
Grade ≥ 3 rashes or refractory to topical therapies	• Short courses of oral steroids (e.g., prednisone)
Rashes C2+ or refractory to above	• Dermatology consultation

Nail Fragility	• **Nail hardener solution** • **Vitamin E oil/emollients**

Contains information on unapproved drugs in Japan.

Chari A et al. ASH 2023. Abstract 1010. Rodriguez-Otero P et al. *Lancet Oncol*. 202425(5):e205-e216.

Thank you