BITES VS CAR-T

Nisha S. Joseph, MD
Associate Professor
Winship Cancer Institute, Emory University

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DISCLOSURES

Consultant/Advisor/Speaker: BMS, GSK

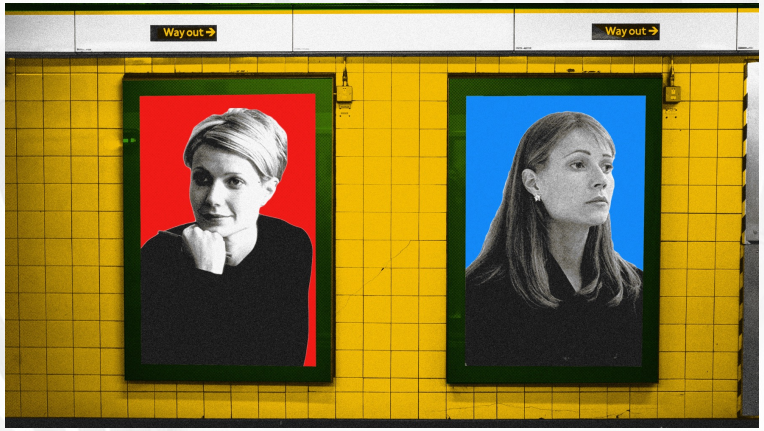
OBJECTIVES

- To crush Dr. Nooka

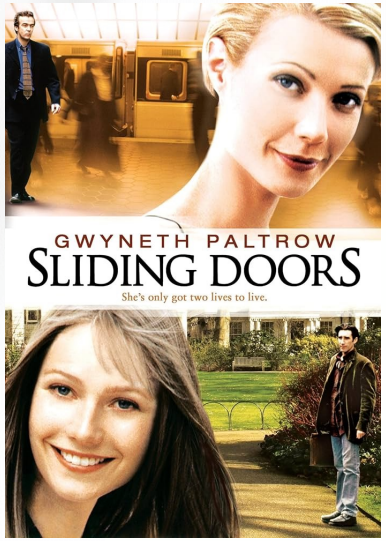
NOOKA-JOSEPH SHOWDOWN: SCOREBOARD			
JOSEPH		NOOKA	
0	1	0	1

LET'S START WITH A PATIENT

55-year-old with a history of RRMM who presents with progressive myeloma. FKLC has risen to 2500 mg/L and M-spike is 3.5 g/dL. Hgb has dropped from 10 g/dL to 8.0 g/dL in the last few weeks and most recent Cr has bumped to 2.1 from a normal baseline. PET-CT shows new lytic disease. Treatment history is summarized below:



1. RVD → ASCT → mLen (relapsed 4 yrs from ASCT)
2. Dara/pom/dex
3. Carfilzomib/Cyclophosphamide/dex
4. Selinexor/bor/dex



CAR-T cell

BsAb

NOOKA-JOSEPH SHOWDOWN: SCOREBOARD

	Bispecific Antibodies		CAR-T Cell Therapy	
	?	?	?	?
Admin			**One and done**	
Approval			**Earlier line**	
Efficacy			**Better efficacy, sequencing**	
Access				
AEs				
Clinical Practice				

BISPECIFIC ANTIBODIES IN LATE RELAPSE: CLINICAL TRIALS & EFFICACY SUMMARY

Bispecific Antibody	Teclistamab[1-3]	Elranatamab[4]	Talquetamab			Linvoseltamab
Pivotal Study	**MajesTEC-1**	**MagnetisMM-3 (BCMA-naïve cohort)**	**MonumenTAL-1**			**LINKERMM-1**
Target	BCMA	BCMA	GPRC5D			BCMA
Dosing & Frequency	Step-up dosing D 1 and 4 (0.06 mg/kg and 0.3 mg/kg SC)→1.5 mg/kg SC QW	Step-up dosing D 1 and 4 (12 mg and 32 mg SC→ 76 mg SC QW	Step-up dosing on D 1 and 4 (0.01 mg/kg and 0.06 mg/kg)→ 0.4 mg/kg SC QW	Step-up dosing on Ds 1, 4, and 7 (0.01 mg/kg, 0.06 mg/kg and 0.04 mg/kg)→ 0.8 mg/kg SC Q2W	Prior TCR	Step up dosing day 1, 8
Patients, n	165	123	143	154	78	252
Prior therapy	BCMA-therapy naive	BCMA-therapy naive	TCR naïve or pretreated cohorts			BCMA naive
Prior LOT, n	5 (2-14)	5 (2-22)	6 (2-17)			5 (1-16)
High-risk cytogenetics, %	26	25	29-31			12
Median f/u, mo	30.4	28.4	18.8	12.7	14.8	11.3
Median time to 1st response	1.2 months	1.22 months	1.9 months			0.95 months
mDOR, mo	24	NR	9.5	17.5	N/A	12m – 72%
PFS, mo	11	17	7.5	11.2	7.7	
OS	Median: 22 mo 30-mo: 42%	Median: 25 mo 15-mo: 56%	Median: NR 24-mo: 61%	Median: NR 24-mo: 67%	24-mo: 57%	

1. Schlinke CD, et al. ASCO 2023. Abstract 8030. 2. von de Donk N, et al. ASCO 2023. Abstract 8011. 3. Ohol, et al. EHA 2024. Abstract P 542. 4. Monty M, et al. EHA 2024. Abstract P 952. 5. Rasche L, et al. EHA 2024.

PATIENT CASE CONTINUED..

- Patient is started on Teclistamab
- She achieved PR after C1

- Patient decides to move forward with CAR-T cell therapy. Restaging and apheresis are scheduled. Bridging therapy with Talq is started.

SEQUENCING – TALQ BRIDGING DATA

blood®

Volume 144, Supplement 1, 5 November 2024, Page 931

Oral Abstracts

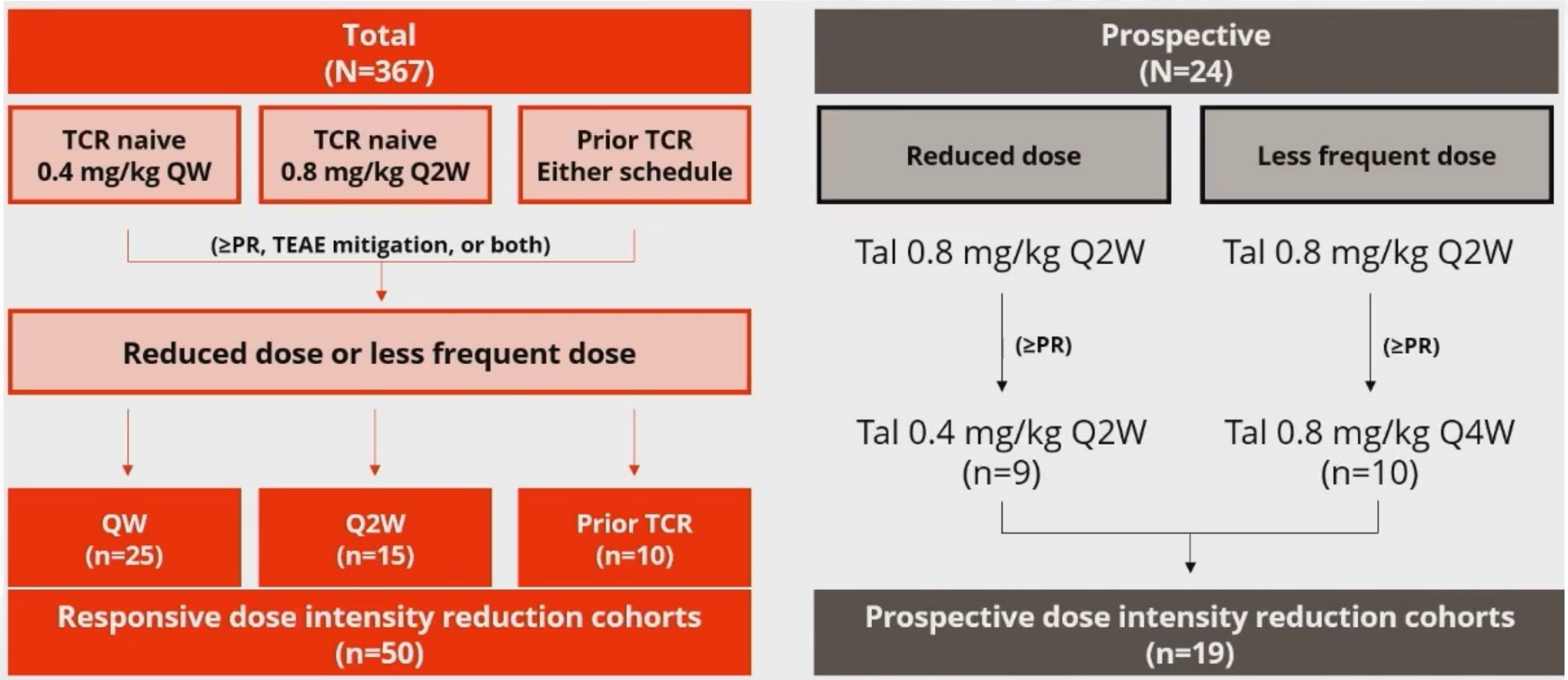
907.Outcomes Research: Plasma Cell Disorders

Talquetamab Bridging: Paving the Way to B-Cell Maturation Antigen (BCMA) CAR-T Cell Therapy in Relapsed/Refractory Multiple Myeloma (RRMM)

Binod Dhakal MBBS [1], Othman S. Akhtar MD [2], Andrew J. Cowan MD [3], Shambavi Richard MD [4], Reed Friend [5], Matthew J Rees MD [6], Patrick Costello MS [7], Mariola Vazquez Martinez [8], Oren Pasvolsky MD [9], Charlotte B Wagner PharmD [10], Alexandria Jensen [11], James A Davis PharmD [12], Ran Reshef MDMSc [13], Danai Dima [14],

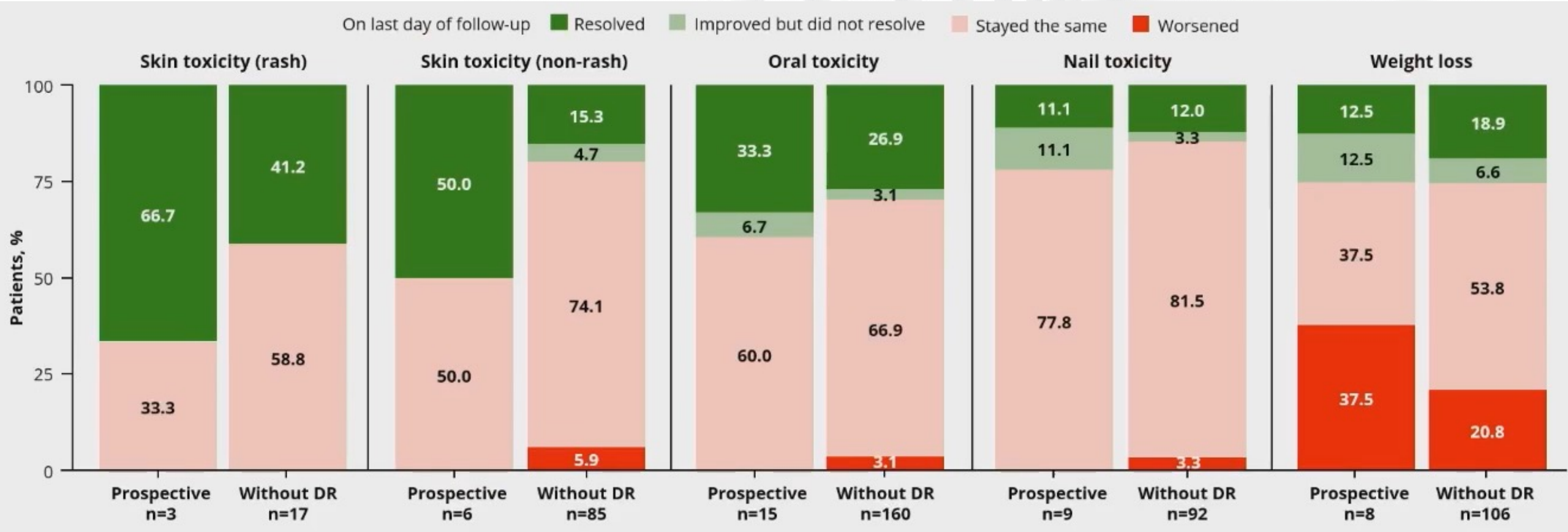
- Often used as bridging therapy to Cilta-cel → have to use a BsAb either way!
- 45% HR (CTG, EMD) and; 73% TCR (13% BCMA exposed)
- ORR in 45/72 = 62% (10 VGPR, 14 CR
  - Median time on Talq 22 days
  - 58/61 pts were successfully infused, no increased Aes
    - 5 PD, 6 manufacturing failures

MONUMENTAL-1: PROSPECTIVE AND RESPONSIVE DOSE REDUCTION COHORTS



MONUMENTAL-1: TEAES IMPROVE WITH DOSE REDUCTION

Trend toward improved resolution of GPRC5D-related AEs, except weight loss



PATIENT CASE CONTINUED..

- Patient is started on Teclistimab the next week
- She achieved PR after C1
- **VGPR after C2, q2w dosing. Mild cytopenias but doing well**
- **At 6 months, CR – monthly dosing**

- Patient decides to move forward with CAR-T cell therapy. Restaging and apheresis are scheduled. Starts bridging.
- **Infused. 15 day hospital stay, experienced persistent G2 CRS s/p Toci x 4 and started on dex that was tapered over several weeks. Took 4-6 weeks to start to recover.**
- **Multiple appts in two months. Coming monthly for IVIG until month 6**

BISPECIFIC AB IN COMBINATION

Trial	Treatment Arms	ORR	PFS/OS
MajesTEC-2 [a]	Tec/Dara/Len	ORR 93.5%, ≥ VGPR 90.3%	
TRIMM-2[b]	Tec/Dara/Pom	ORR 78%	12 months PFS 76%
MonumenTAL-2[c]	Talq/pom	ORR 93.8%/84.2%	12 month PFS 72.6%
RedirecTT-1[d]	Tec/Tal	ORR 78% (EMD)/80%	18 month PFS 77%/ 86%
ONGOING			
MagnetisMM-20	Elra/Car		
MagnetisMM-30	Elra/Iber		
REGN2012	Linvo + Car/Isa/Dara/Niro/ Len/Pom		
Talq+ Mezi			
Tec + Iber			

a. Searle et al 2022; b. Dholaria et al ASCO 2023; c. Matous et al ASH 2023 d. Cohen et al NEJM 2025

ADVERSE EVENTS

MajesTEC-1

AEs of Interest[a], N (%)	N = 165 Any Grade	N = 165 Grade ≥ 3
Hematologic		
Neutropenia	118 (71.5)	108 (65.5)
Anemia	90 (54.5)	62 (37.6)
Thrombocytopenia	70 (42.4)	37 (22.4)
Lymphopenia	60 (36.4)	57 (34.5)
Leukopenia	33 (20.0)	15 (9.1)
Non-Hematologic		
Infection	132 (80.0)	91 (55.2)
COVID-19	48 (29.1)	35 (21.2)
Hypogammaglobulinemia	34 (20.6)	3 (1.8)

MonumenTAL-1

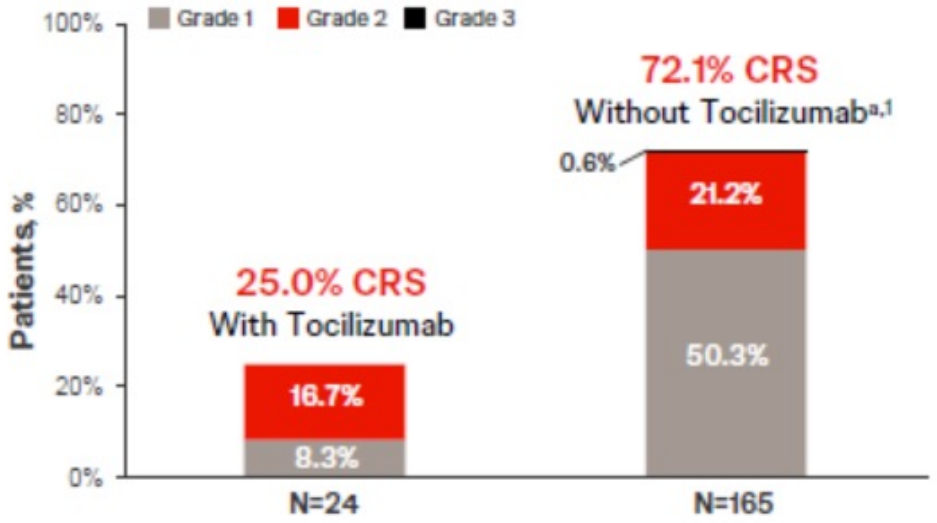
G3-4 infections: 16.8% and 11.7% (0.4 mg/kg qw; 0.8 mg/kg q2w)

AEs (≥20% of any RP2D cohort), n (%)	0.4 mg/kg SC QW[a] (n=143) mFU, 11.0 months[b]		0.8 mg/kg SC Q2W[a] (n=145) mFU, 5.1 months[c]	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
CRS	113 (79.0)	3 (2.1)	105 (72.4)	1 (0.7)
Skin-related AEs[d]	80 (55.9)	0	98 (67.6)	1 (0.7)
Nail-related AEs[e]	74 (51.7)	0	63 (43.4)	0
Dysgeusia[f]	69 (48.3)	NA	67 (46.2)	NA
Rash-related AEs[g]	56 (39.2)	2 (1.4)	39 (26.9)	8 (5.5)
Weight decreased	57 (39.9)	3 (2.1)	47 (32.4)	2 (1.4)
Diarrhea	34 (23.8)	3 (2.1)	32 (22.1)	0
Dysphagia	34 (23.8)	0	33 (22.8)	3 (2.1)
Fatigue	32 (22.4)	5 (3.5)	29 (20.0)	1 (0.7)
Decreased appetite	25 (17.5)	2 (1.4)	29 (20.0)	2 (1.4)

- **Low rates of discontinuation due to Aes** were observed with QW (4.9%) and Q2W (6.2%) schedules

MajesTEC-1 Prophylactic Tocilizumab Cohort: CRS Incidence and Severity

Van de Donk N WCJ et al. ASCO 2024 07517



Prophylactic tocilizumab cohort (N=24)			
Characteristic	No CRS (n=18)	CRS Grade 1 (n=2)	CRS Grade 2 (n=4)
BMPCs, % median (range)	8.0 (0–80)	19 (8–30)	62.5 (30–80)
ISS stage[b], %			
I	72.2	50	50
II	22.2	50	50
III	5.6	0	0
No. of EMPs, median (range)	0 (0–4)	0 (0)	0 (0–2)

- **25% CRS with prophylactic tocilizumab**
  - Grade I (n=2), grade 2 (n=4); no grade 3 events
  - All initial events occurred during SUD; 3 recurrent events
  - Median time to onset: 2 days (range, 1–3)
  - Median duration: 2 days (range, 2–4)
  - All events resolved

- **No disease characteristic associated with CRS, consistent with pivotal cohort**
  - Small sample size precludes clinically meaningful conclusions

[a]Pivotal MajesTEC-1 population. [b]Derived based on the combination of serum β2-microglobulin and albumin.
BMPC, bone marrow plasma cell; CRS, cytokine release syndrome; EMP, extramedullary plasmacytoma; ISS, International Staging System; SUD, step-up dosing.
1. Martin TG, et al. *Cancer* 2023;129(13):2035-2046.

Presented by NWCJ van de Donk at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA & Virtual

LET'S TALK ABOUT THE THOSE SIDE EFFECTS

	Cilta-cel (CART-1 and -4)	Teclistimab
CRS	84% (4%)	72% (0.6%)
ICANS	24% (7%)	6%
Cytopenias	A LOT	A LOT
Non-ICANS neurotox **Parkinsonism** **Peripheral neuropathy** **CN palsies** **Guillain-Barre Syndrome** **Myelitis (G3)**	 **3% (2%)** **7% (1%)** **7% (1%)** **1**	 1
HLH/MAS	**1%**	
Secondary hem malignancies(AML, MDS)	**5%**	
IEC-Enterocolitis	**~2-3%**	
Infections URI Viral PNA Sepsis	CART-4 only 28% (3%) 23% (7%) 14% (13%) 10% (7%)	 26% (2.4%) 24% (15%)

Presentation of IE-enterocolitis

Severe

Grade ≥3 in all cases[1]
92% grade ≥ 3[2]

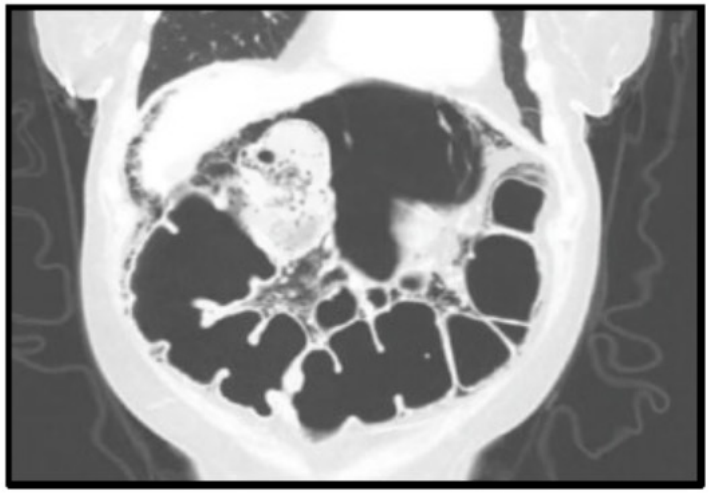
Delayed onset

Median time post CART
92.5 days[1] / 98 days[2]

Upper and lower GI involvement

83% by endoscopy or imaging[2]

Pneumatosis Intestinalis was seen in 5/23 (22%)

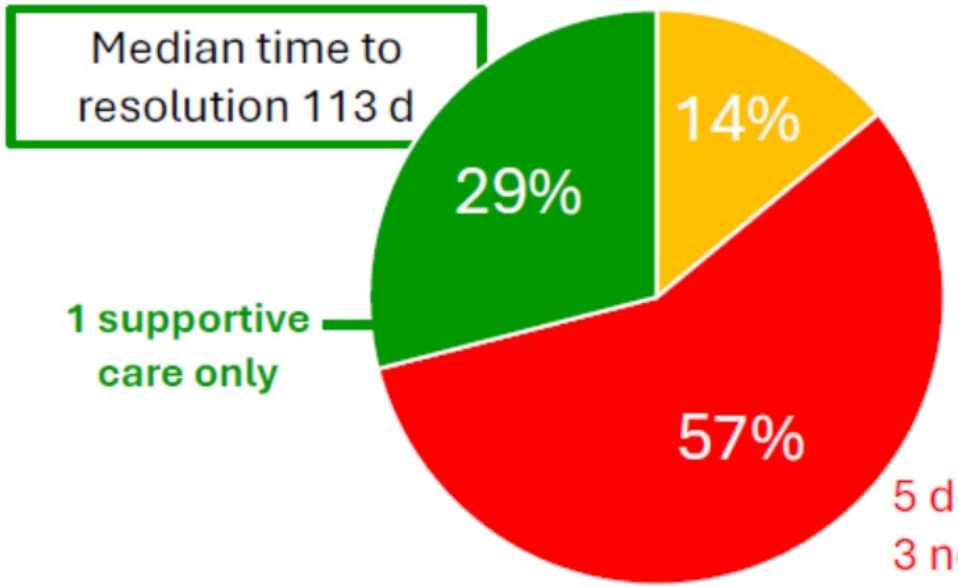


1. Fortuna et al. Blood Cancer Journal. 2024; 2. Susanibar-Adaniya et al. Clinical Lymphoma myeloma and Leukemia. 2024 (IMS 21st Annual Meeting)

Variable Outcomes of Enterocolitis

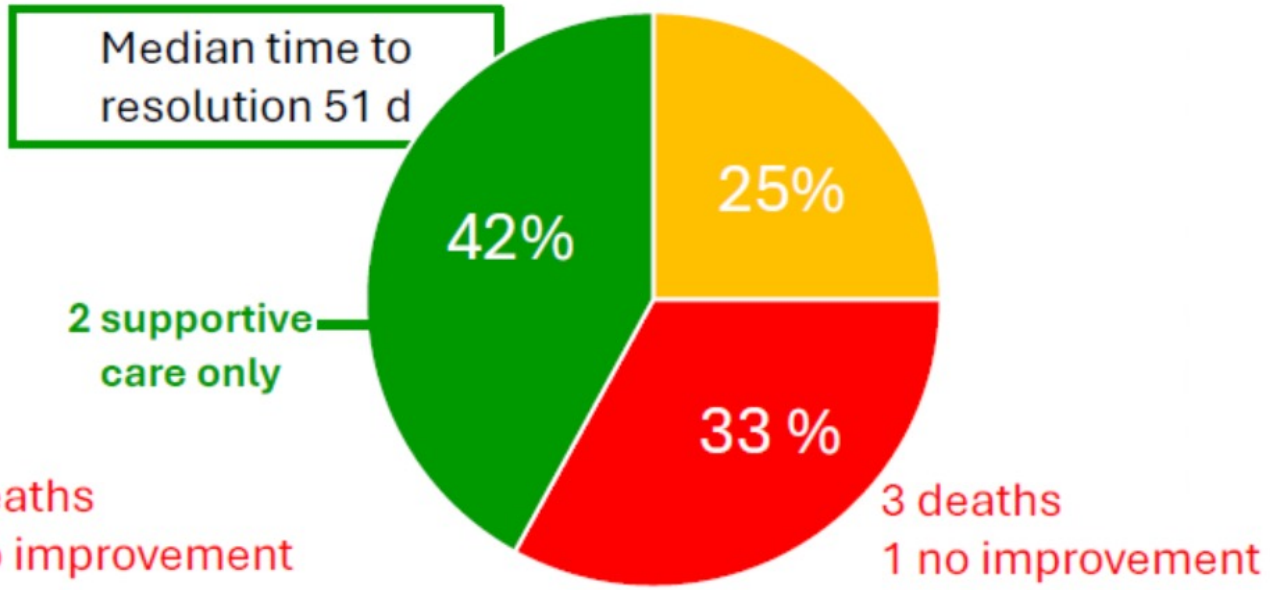
Fortuna *et al* N=14

Median f/u from diarrhea 187 d [44- 538]



Our study N=12

Median f/u from diarrhea 412 d [84-713]



Resolution Improvement No improvement/death

26% Overall death rate related to EC (N=23)

1. Fortuna et al. Blood Cancer Journal. 2024; 2. Susanibar-Adaniya et al. Clinical Lymphoma myeloma and Leukemia. 2024 (IMS 21st Annual Meeting)

PATIENT CASE CONTINUED..

- Continues on monthly dosing with monthly IVIG in CR

- 90 Day restaging shows sCR, MRD-
- Around 100 days post CAR-T, develops profound watery diarrhea 6-8 times per day and is readmitted for work up. Started on steroids for presumed IEC

NOOKA-JOSEPH SHOWDOWN: SCOREBOARD

Bispecific Antibodies		CAR-T Cell Therapy	
?	?	?	?

Admin	**Continuous – monthly, fixed duration**	**One and done**
Approval	**Earlier line is coming, trials ongoing**	**Earlier line**
Efficacy	**Efficacy will improve in combination**	**Better efficacy, sequencing**
Access	**Off the shelf, work quickly**	**6-8 weeks**
AEs	**Decreased CRS with ppx Toci No MNT, IEC risk**	**Small but non-zero: HLH, MNTs, IEC, secondary ca**
Clinical Practice	**Often used as bridging, 4 options (++) More than one antigenic target, no manufacturing failures/OOS**	