La personalizzazione del trattamento:

Il caso delle CAR-T

Roberto Ria MD

LE NUOVE FRONTIERE
DELL'IMMUNOTERAPIA
PER LA CURA DEL

MIELOMA MULTIPLO

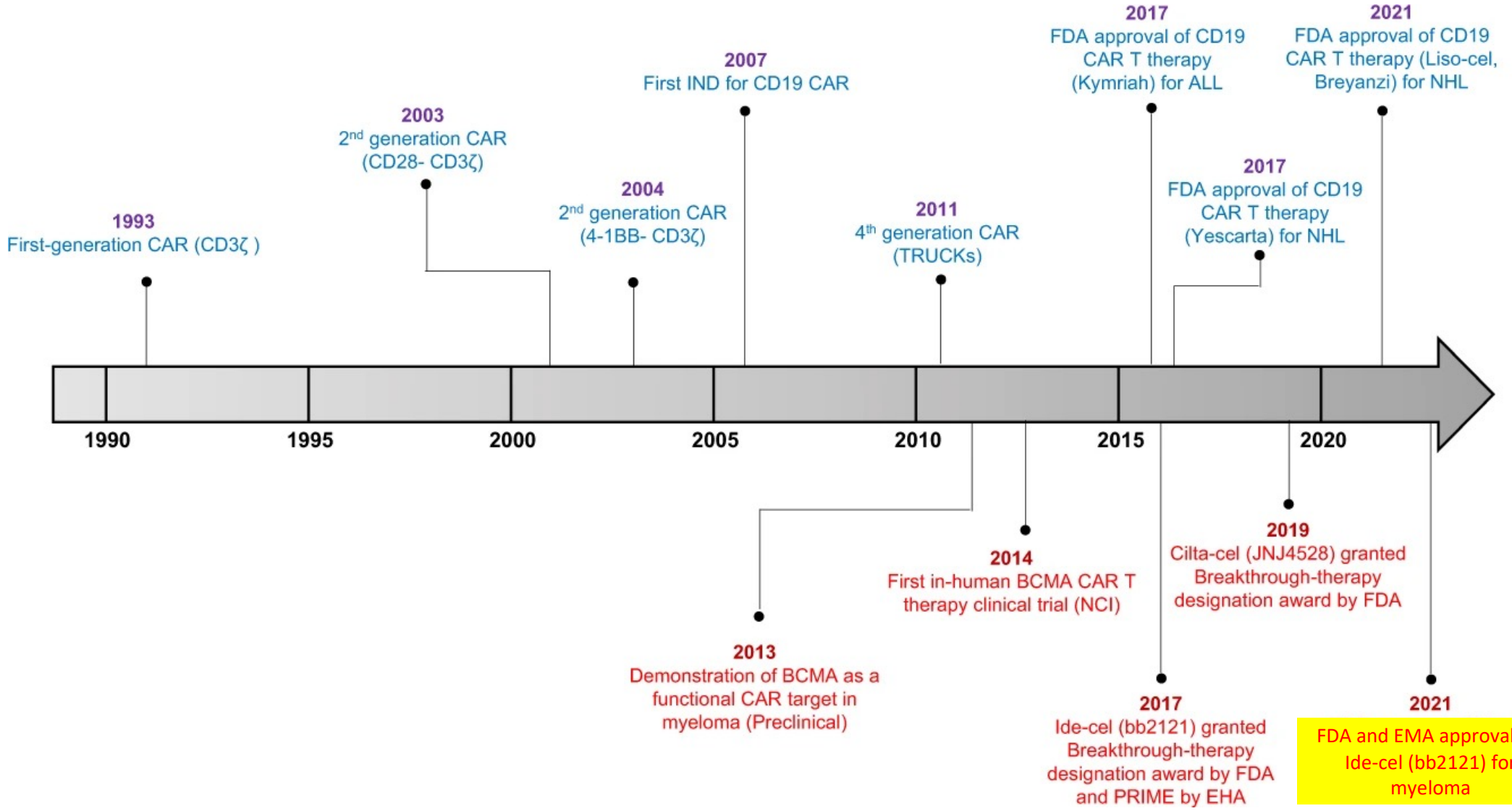
dalla teoria alla pratica

TORINO 3-4 MARZO 2023

Disclosures of NAME SURNAME

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Amgen			x		x	X	
BMS-Celgene			x		x		
CSL Behring	x		x		x	X	
GSK			x		x		
Janssen Cilag			x		x	X	
Octapharma			x				
Takeda			x				
Sanofi-Aventis	x		x				

The time line of CAR T-cell development



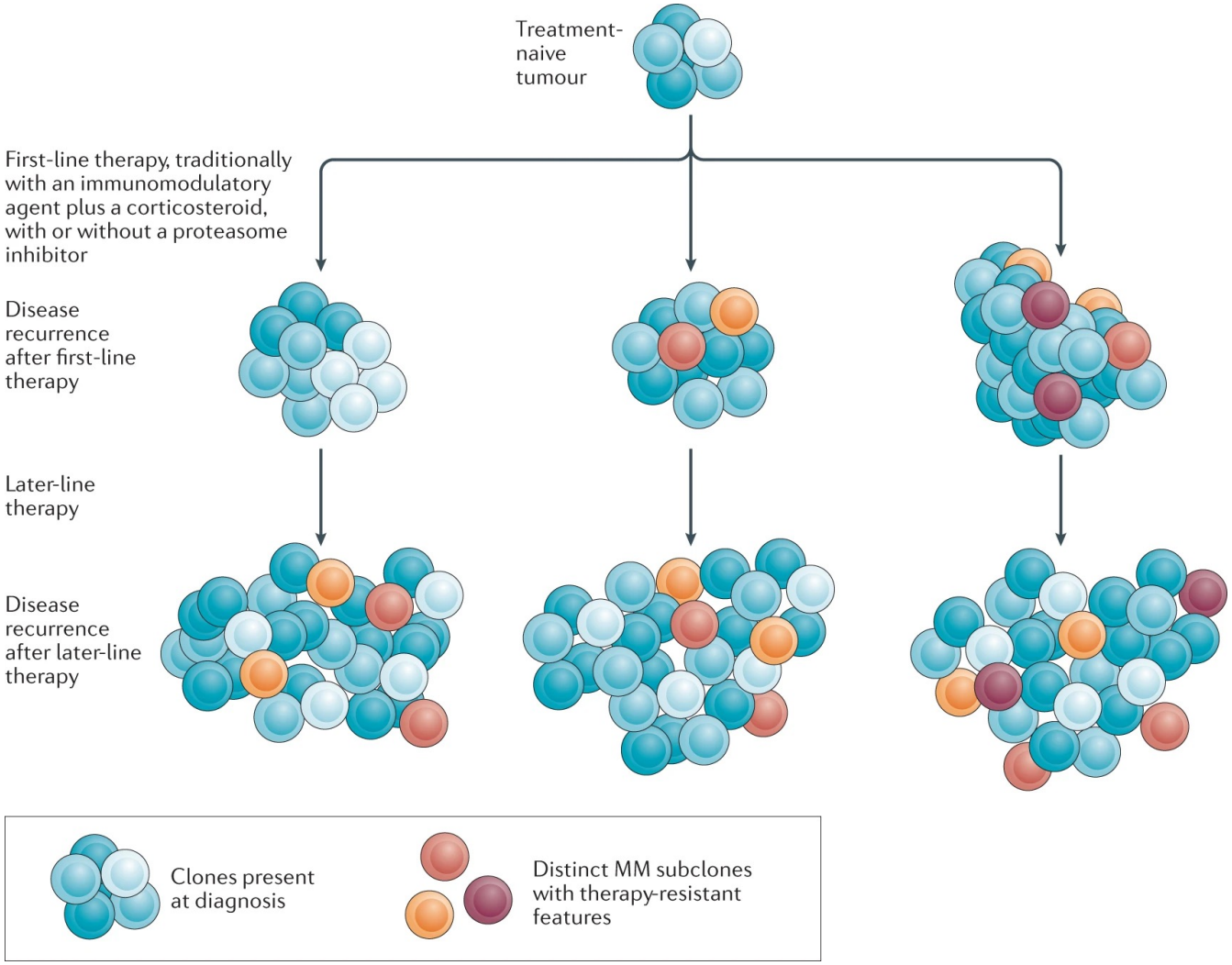
Adapted from Phaik Ju Teoh. Blood Cancer Journal. 2021.

Personalization of therapy

Process of providing personalized medical care to particular patients based on various features including genetics, inheritance, and lifestyle.

Represent a current strategic goal for improving health care.

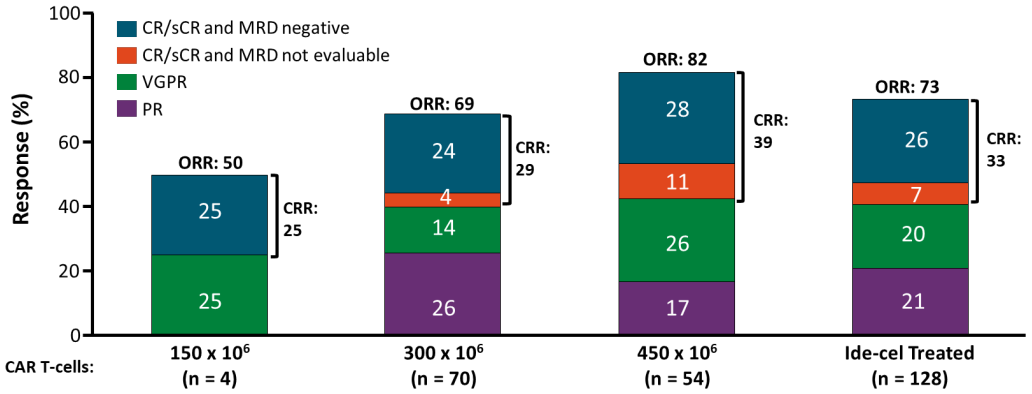
Heterogeneity and resistance of MM subclones



Early intervention with the aim to eradicate highly-resistant subclones

Lekha Mikkilineni. Nature Reviews Clinical Oncology 2020

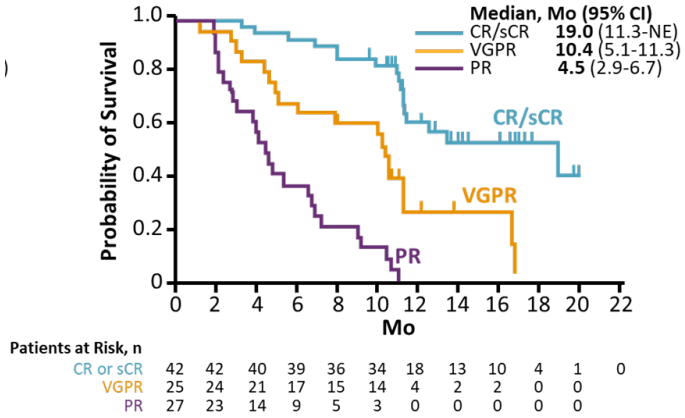
Phase II KarMMa Update



- Median time to first response: 1.0 mo (range: 0.5-8.8); median time to CR: 2.8 mo (range: 1.0-11.8)
- Median follow-up of 13.3 mo across target dose levels
- MRD-negative ($<10^{-5}$) in all treated patients (n = 128) was 26% and 79% in evaluable patients with ≥CR (n = 42)

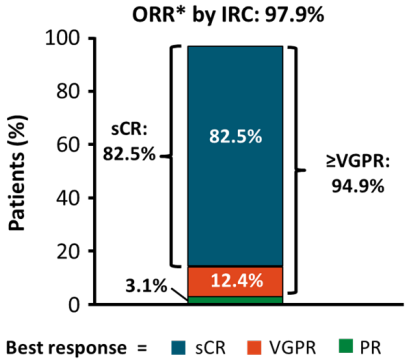
Anderson. ASCO 2021. Abstr 8016. Munshi. NEJM. 2021;384:705.

DoR by Best Response



DoR improves with depth of response
Median DoR: 19.0 mos in patients with CR/sCR

CARTITUDE-1



- No patient had CR or SD as best response

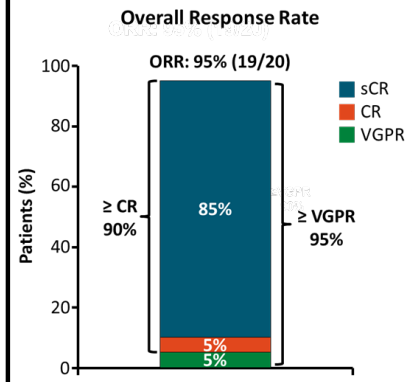
*ORR assessed by independent review committee.

Martin. JCO. 2022;[Epub].

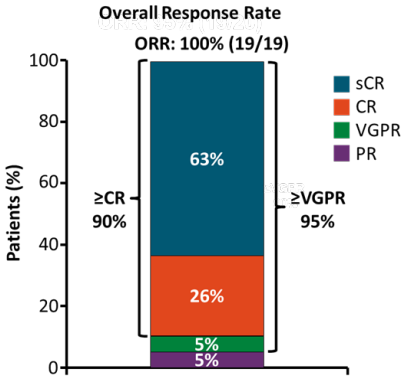
- Median f/u: 17.1 mos
- 15-mo PFS: 70% (95% CI: 45.1-85.3)
- MRD evaluable: n = 16
  - MRD neg at 10^{-5}: 100%
- **At longer follow-up, a single infusion of cilta-cel produced deep, durable responses in lenalidomide-refractory MM with 1-3 prior lines**

CARTITUDE-2

COHORT A



COHORT B

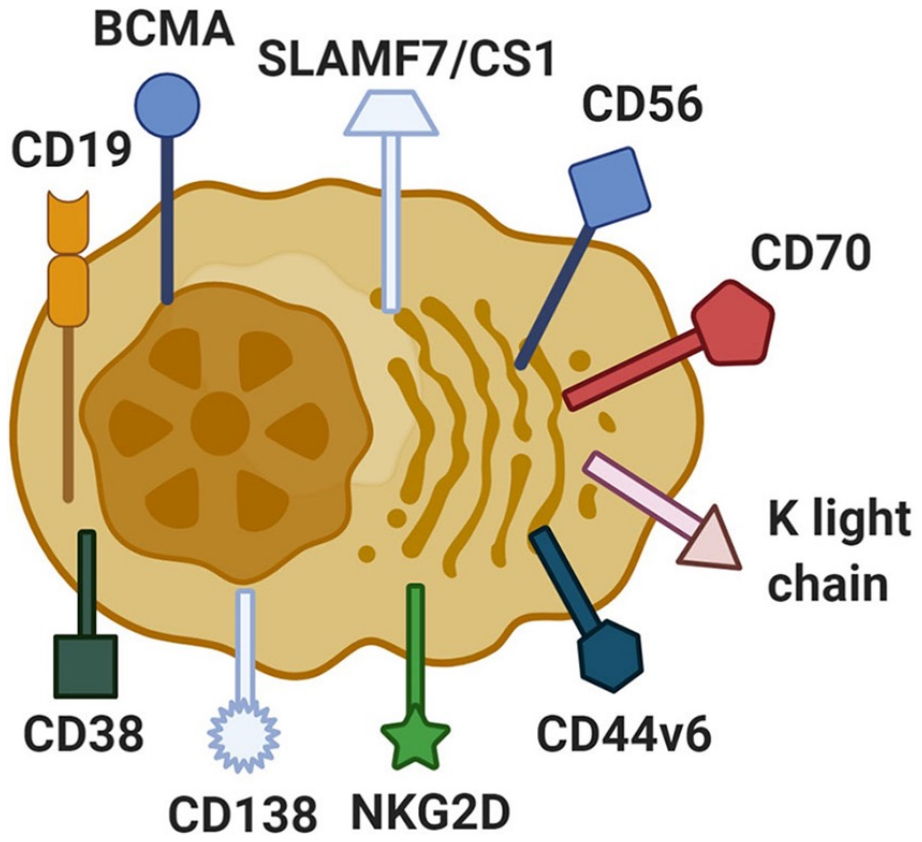


- Median f/u: 13.4 mo
- 12-mo PFS: 89.5% (95% CI: 64.1-97.3)
- MRD evaluable: n = 15
  - MRD neg at 10^{-5}: 14 (93.3%)
- **At longer follow-up, a single infusion of cilta-cel produced meaningful clinical responses in progressive MM with early relapse**

Potential target antigens for CAR-T therapy for mutiple myeloma

Antigen	Expression in MM	Expression in normal hematopoietic cells	Expression in healthy solid organ tissues	Development state
BCMA	60-100%	Late memory B cells, plasma cells	No	Clinical trial
TACI	78%	Naïve and memory B cells, plasma cells, monocytes and dendritic cells	No	Clinical trial
CD19	10-80%	B-cells, plasma cells	No	Clinical trial
SLAMF7 (CD319)	High and uniform expression	NK-cells, monocytes, macrophages, dendritic cells, T cells, B cells, plasma cells	No	Clinical trial
CD38	High and uniform expression	Lymphoid and myeloid cells, hematopoietic precursors, thymocytes	Prostatic epithelium, pancreatic islet cells, cerebellar Purkinje cells	Clinical trial
CD44v6	43% in advanced stage	Activated T cells, monocytes	Keratinocytes	Clinical trial
GPRC5D	≥50% in 65% of patients	B-cells, plasma cells	Hair follicles	Clinical trial
CD138	High expression	Plasma cells	Epithelial cells, gastrointestinal tract and hepatocytes	Clinical trial
NKG2D	Heterogenous	NK, T and γδ T cells	No	Clinical trial
κ light chain	κ-restricted myeloma cells	Mature B cells	No	Clinical trial
CD56	High expression, decreased in extramedullary disease	T and NK cells	Central and peripheral nervous system	Clinical trial
Lewis Y	50%	No	Epithelial cells	Clinical trial
NY-ESO-1	60-100%	No	No	Clinical trial
CD229 (SLAMF3)	High and homogeneous expression, probably in myeloma stem cell	T, NK and B cells	No	Preclinical investigation
Integrin β7	High expression	High expression in B cells and low to moderate expression in $CD34^+$ hematopoietic cells	No	Preclinical investigation
CD70	0.2-42%	Activated T and B cells, dendritic cells and plasma cells	No	Preclinical investigation
CD1d	High expression	Antigen-presenting cells, thymocytes, B cells, and hematopoietic stem cells	Epithelial cells	Preclinical investigation

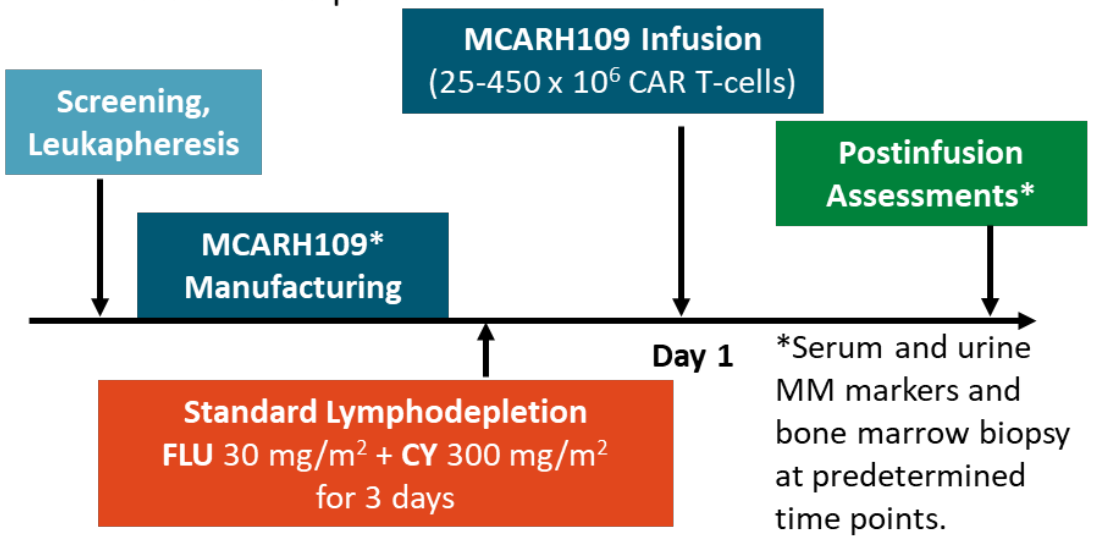
BCMA: B-cell maturation antigen; GPRC5D: G protein-coupled receptor class C group 5 member D; NKG2D: Natural Killer Group 2 member D; NY-ESO-1: New York Esophageal Squamous Cell Carcinoma 1; SLAMF3 and SLAMF7: signaling lymphocytic activation molecules family member 3 and 7; TACI: Transmembrane activator, calcium modulator, and cyclophilin ligand interactor.



Bruno B. Haematologica 2021.

GPRC5D-Targeted CAR T-Cell Therapy MCARH109 in R/R MM

- MCARH109: human-derived scFv targeting $GPRC_5D$ with 4-1BB costimulatory domain and lentiviral vector for transduction; production starts with 1:1 ratio of CD4+ and CD8+ cells
- Open-label, 3 + 3 dose-escalation phase I study enrolling adults with R/R MM after ≥3 lines of tx including PI, IMiD, and CD38 Ab
- 16 evaluable patients



Response, n (%)	25 x 10^6 CAR+ T-Cells (n = 3)	50 x 10^6 CAR+ T-Cells (n = 3)	150 x 10^6 CAR+ T-Cells (n = 5)	450 x 10^6 CAR+ T-Cells (n = 5)	Total (N = 16)
≥ PR	1 (33)	3 (100)	2 (40)	5 (100)	11 (69)
≥ VGPR	1 (33)	2 (67)	0	4 (80)	7 (44)
≥ CR	0	1 (33)	0	3 (60)	4 (25)
BM MRD negativity	2 (67)	2 (67)	2 (40)	2 (50)	8 (50)

Response, n (%)	Prior BCMA-Targeted Tx (n = 10)	Prior CAR T-Cell Tx (n = 8)
≥ PR	8 (80)	6 (75)
≥ CR	3 (30)	3 (38)
BM MRD negativity†	5 (50)	2 (25)

†MRD assessment by flow cytometry, sensitivity: 1 in 10^5.

Dose escalation cohorts: 25 x 10^6 → 50 x 10^6 → 150 x 10^6 → 450 x 10^6 CAR+ T-cells

Mailankody. ASH 2021. Abstr 827.

Dual-Targeted CAR T-Cell Therapy GC012F: Phase I Study in R/R MM

Efficacy Outcome	Total (N = 28)	DL1 (n = 2)	DL2 (n = 10)	DL3 (n = 16)
ORR, %	89.3	100	80.0	94.0
▪ CR/sCR	75.0	100	60.0	81.3
▪ VGPR	10.7	0	20.0	6.3
▪ PR	3.6	0	0	6.3
MRD negative,* n/N (%)	27/27 (100)	2/2 (100)	10/10 (100)	15/15 (100)
MRD negative by EuroFlow at landmark time points, %				
▪ Mo 1 (n = 18)	94.4			
▪ Mo 6 (n = 12)	100			
▪ Mo 12 (n = 8)	87.5			

*Includes 27 total patients; 1 patient who received DL3 was unevaluable. MRD negativity defined as 10^{-4} by flow cytometry (n = 7) or 10^{-6} by EuroFlow (n = 20).

- Time to earliest objective response: 28 days (first assessment timepoint)
- Median DoR not yet reached
- Best response achieved to date:
  - MRD-negative CR/sCR: 75% (21/28)
  - ≥ VGPR: 86% (24/28)
- All patients demonstrated reductions in paraprotein
  - 96% of patients achieved >80% reductions
  - 82% of patients achieved 100% reductions

TEAEs Occurring in ≥25% of Patients (N = 28), n (%)	All Grades	Grade ≥3
Hematologic TEAEs		
Neutropenia	23 (82)	23 (82)
Lymphopenia	18 (64)	18 (64)
Leukopenia	23 (82)	22 (79)
Thrombocytopenia	22 (79)	16 (57)
Anemia	13 (46)	10 (36)
Nonhematologic TEAEs		
LDH increased	17 (61)	0
Hypoalbuminemia	13 (46)	0
AST increased	12 (43)	8 (29)
Hypokalemia	18 (64)	4 (14)
Hypophosphatemia	9 (32)	0
Hypocalcemia	7 (25)	1 (4)

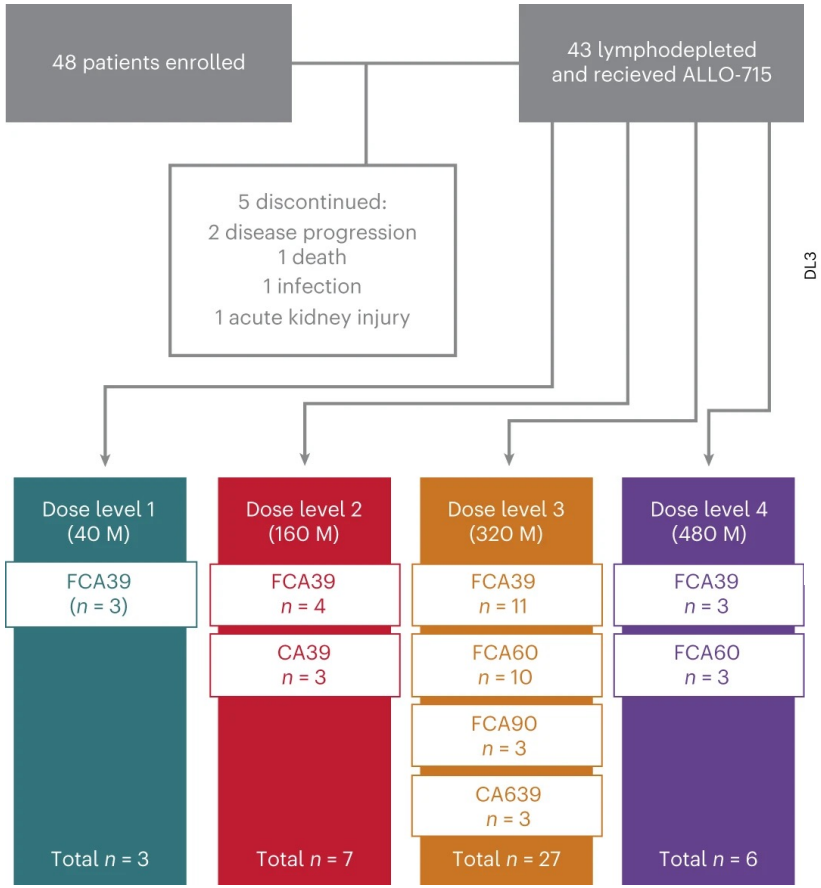
AEs of Special Interest (N = 28), n (%)	CRS	ICANS
Grade 0	3 (11)	0
Grade 1/2	23 (82)	0
Grade 3	2 (7)	0
Grade 4/5	0	0

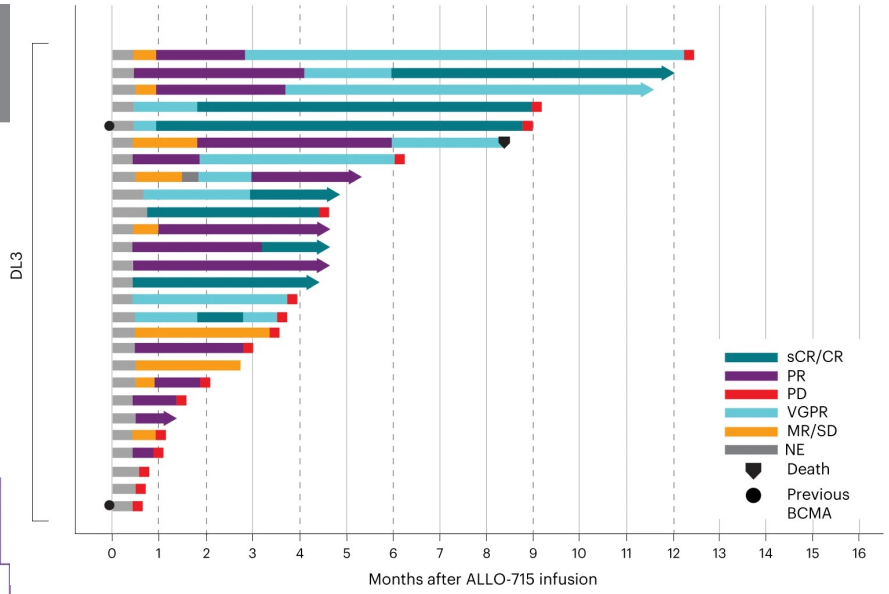
Cytokine-release syndrome

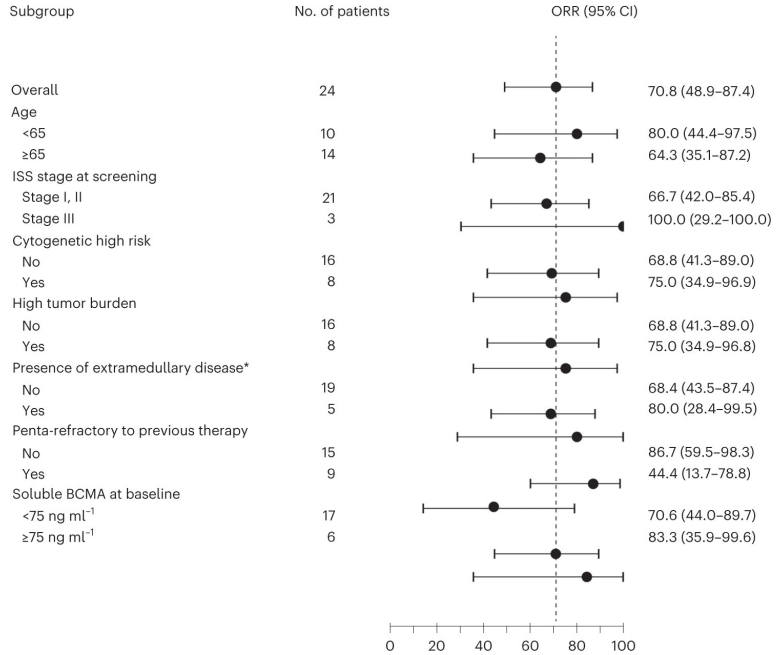
- Managed with tocilizumab, vasopressors, and dexamethasone
- Median time to CRS onset: 6 days (range: 2-10)
- Median CRS duration: 3 days (range: 1-8)

Boucher. Clin Cancer Res. 2012;18:6155. Nerreter. Nat Commun. 2019;10:3137. Munshi. NEJM. 2021;384:705. Du. ASCO 2022. Abstr 8005.

Allogeneic BCMA-targeting CAR T cells in relapsed/refractory multiple myeloma: phase 1 UNIVERSAL







At a median follow-up of 10.2 months, 24 of 43 patients (55.8%) had a response, with 15 patients (34.9%) experiencing a very good partial response or better (VGPR+). Responses were observed in 0 of 3 patients receiving DL1, 2 of 7 patients receiving DL2 (28.6%), 19 of 27 patients receiving DL3 (70%) and 3 of 6 patients receiving DL4 (50%). Based on clinical responses and cellular kinetics, DL3 (320 × 106 CAR+ cells) FCA39, FCA60 or FCA90 LD was expanded to treat additional patients (n = 24; 11 with FCA39 LD, 10 with FCA60 and 3 with FCA90). Among these patients, 17 (70.8%) achieved a partial response or better whereas 11 (46%) were VGPR+ and 6 (25%) were in complete remission/stringent complete remission (CR/sCR). The median time to response for this cohort was 16 days (range 15–57 days) and the mDOR was 8.3 months (95%).

ALLO-715 is the first allogeneic CAR T cell therapy for myeloma and these initial results from the UNIVERSAL trial provide evidence of feasibility, safety and efficacy for this off-the-shelf cellular therapy as a potential treatment for patients with MM.

Sham Mailankody. Nature Medicine 2023

CAR T-Cell toxicity

Cytokine-Release Syndrome

- Systemic inflammatory response that occurs as CAR T-cells activate and expand
- High levels of CRP, ferritin, IL-6, IL-10
- Flu-like symptoms with fever
- Can progress to life-threatening hypotension, hypoxia, and death
- High disease burden associated with more severe CRS

Neurotoxicity Syndrome

- Symptoms
  - Delirium
  - Encephalopathy
  - Aphasia
  - Lethargy
  - Difficulty concentrating
  - Agitation
  - Tremor
  - Seizures
  - Cerebral edema
  - (Headache)

"…an awake patient who is mute and does not respond verbally or physically to an examiner"

Product	Construct	CRS, %	Grade ≥3 CRS, %	Median Time to Onset, Days (Range)	Median Duration, Days (Range)
Cilta-cel	BCMA-41BB	95	5*	7 (1-12)	4 (1-40)
Ide-cel	BCMA-41BB	85	9*	1 (1-23)	7 (1-63)

Malig.	Product	Construct	NT, %	Grade ≥3 NT, %	Median Time to Onset, Days (Range)	Median Duration, Days (Range)
MM	Cilta-cel	BCMA-41BB	26	11	8 (1-28)‖	8 (2-927)‖
	Ide-cel	BCMA-41BB	23	4	2 (1-42)	6 (1-578)

KarMMa Update: AEs of Interest

AEs of Interest, n (%)	Ide-cel Treated (n = 128)	
	Any Grade	Grade 3/4
Hematologic (>25%)		
▪ Neutropenia	117 (91)	114 (89)
▪ Anemia	90 (70)	78 (61)
▪ Thrombocytopenia	82 (64)	67 (52)
▪ Leukopenia	54 (42)	50 (39)
▪ Lymphopenia	36 (28)	35 (27)
Gastrointestinal		
▪ Diarrhea	45 (35)	2 (2)
▪ Nausea	37 (29)	0

CRS	Ide-cel Treated (n = 128)
Any grade, n (%)	107 (84)
Grade ≥3, n (%)	7 (5)
Median onset, days	1
Tocilizumab use, %	52
Steroid use, %	15

Neurotoxicity	Ide-cel Treated (n = 128)
Any grade, n (%)	23 (18)
Grade 3, n (%)	5 (4)
Median onset, days	2
Median duration, days	3

Munshi. NEJM. 2021;384:705. Anderson. ASCO 2021. Abstr 8016.

CARTITUDE-1: Safety

AE in ≥20%, n (%)	N = 97	
	Any Grade	Grade 3/4
Hematologic AE		
▪ Neutropenia	93 (95.9)	92 (94.8)
▪ Anemia	79 (81.4)	66 (68.0)
▪ Thrombocytopenia	77 (79.4)	58 (59.8)
▪ Leukopenia	60 (61.9)	59 (60.8)
▪ Lymphopenia	52 (53.6)	49 (50.5)
Gastrointestinal		
▪ Diarrhea	29 (29.9)	1 (1.0)
▪ Nausea	27 (27.8)	1 (1.0)
Others		
▪ AST increased	28 (28.9)	5 (5.2)
▪ ALT increased	24 (24.7)	3 (3.1)

Toxicity	N = 97
CRS	
Any grade, n (%)	92 (95)
▪ Grade ≥3	5 (5)
▪ Median time to onset, days (IQR)	7 (5-8)
Neurotoxicity	
Any grade neurotoxicity, n (%)	20 (21)
▪ Grade ≥3	9 (9)
ICANS (any grade), n (%)	16 (17)
▪ Grade ≥3	2 (2)
▪ Median time to onset, days (range)	8 (6-8)
Other neurotoxicity (any grade), n (%)	12 (12)
▪ Grade ≥3	9 (9)
▪ Median time to onset, days (range)	27 (16-73)

Martin. JCO. 2022;June 4:[Epub]. Berdeja. Lancet. 2021;398:314.

CARTITUDE-2: Multicohort Phase II Study of Cilta-cel in Earlier Lines of Myeloma Treatment

COHORT A

AE, %	N = 20	
	Any Grade	Grade ≥3
Neutropenia	95	95
Thrombocytopenia	80	35
CRS	95	10
▪ Median time to onset, days (range)	7 (5-9)	
Neurotoxicity	30	3.5
Median time to onset, days (range)*	8 (7-10)	

*No cases of movement or neurocognitive AEs

Cohen. ASH 2021. Abstract 3866.
Einsele. ASCO 2022. Abstract 8020.
Agha. ASCO 2021. Abstr 8013.

COHORT B

AE, %	N = 19	
	Any Grade	Gr ≥3
Neutropenia	95	90
Thrombocytopenia	58	26
CRS	84	5*
▪ Median time to onset, days (range)	8 (5-11)	
Neurotoxicity	26	5*
Median time to onset, days†	11	

*n = 1 with CRS or neurotoxicity.
†1 case movement, neurocognitive AE.

van de Donk. ASCO 2022. Abstract 8029.

Future Directions for Ide-cel and Cilta-cel in Myeloma

Key Trials in Earlier Stage of Disease			
Trial	**Agent**	**Phase**	**Patient Population/Design**
KarMMa-2 (NCT03601078)	Ide-cel	II	Multiple cohorts, including early relapse
CARTITUDE-2 (NCT04133636)	Cilta-cel	II	Multiple cohorts, including early relapse
KarMMa-3 (NCT03651128):	Ide-cel	III	Ide-cel vs SoC in patients with 2-4 prior lines
CARTITUDE-4 (NCT04181827)	Cilta-cel	III	Cilta-cel vs SoC in patients with 1-3 prior lines
Key Trials in Frontline			
Trial	**Agent**	**Phase**	**Patient Population/Design**
KarMMa-4 (NCT04196491):	Ide-cel	I	High-risk, newly diagnosed MM
CARTITUDE-5 (NCT04923893)	Cilta-cel	III	VRd → cilta-cel vs VRd → Rd in newly diagnosed, transplant-ineligible patients
CARTITUDE-6 (NCT05257083)	Cilta-cel	III	Trial of DVRd → cilta-cel vs DVRd → ASCT in newly diagnosed MM

Ongoing studiesof BCMA-Targeted CAR T-Cell Therapies for RRMM

Study	CAR T-Cell Therapy	Phase	Key Findings
KarMMa-3 (NCT03651128)	Idecabtagene vicleucel	III	▪ Ongoing; **RCT vs standard triplet therapy**
KarMMa-2 (NCT03601078)	Idecabtagene vicleucel	II	▪ Ongoing
CARTITUDE-6 (NCT05257083)	Ciltacabtagene autoleucel	III	▪ Ongoing
CARTITUDE-5 (NCT04923893)	Ciltacabtagene autoleucel	III	▪ Ongoing
CARTITUDE-4 (NCT04181827)	Ciltacabtagene autoleucel	III	▪ Ongoing; **RCT vs standard triplet therapy**
CARTITUDE-2 (NCT04133636)	Ciltacabtagene autoleucel	II	▪ Active
CARTIFAN-1 (NCT03758417)	Ciltacabtagene autoleucel	I/II	▪ Ongoing
LUMMICAR-2 (NCT03915184)	CT053 (Zevor-cel)	I/II	▪ Ongoing; ORR 100% (n = 10)[1]
NCT04155749	CART-ddBCMA	I	▪ Ongoing; ORR 100% (n = 16)[2]

- Additional products (trial): bb21217 (CRB-402), P-BCMA-101 (PRIME)

1. Kumar. ASH 2020. Abstr 28. 2. Frigault. ASCO 2022. Abstr 8003.

Key Factors in Determining Candidacy for CAR T-Cell Therapy

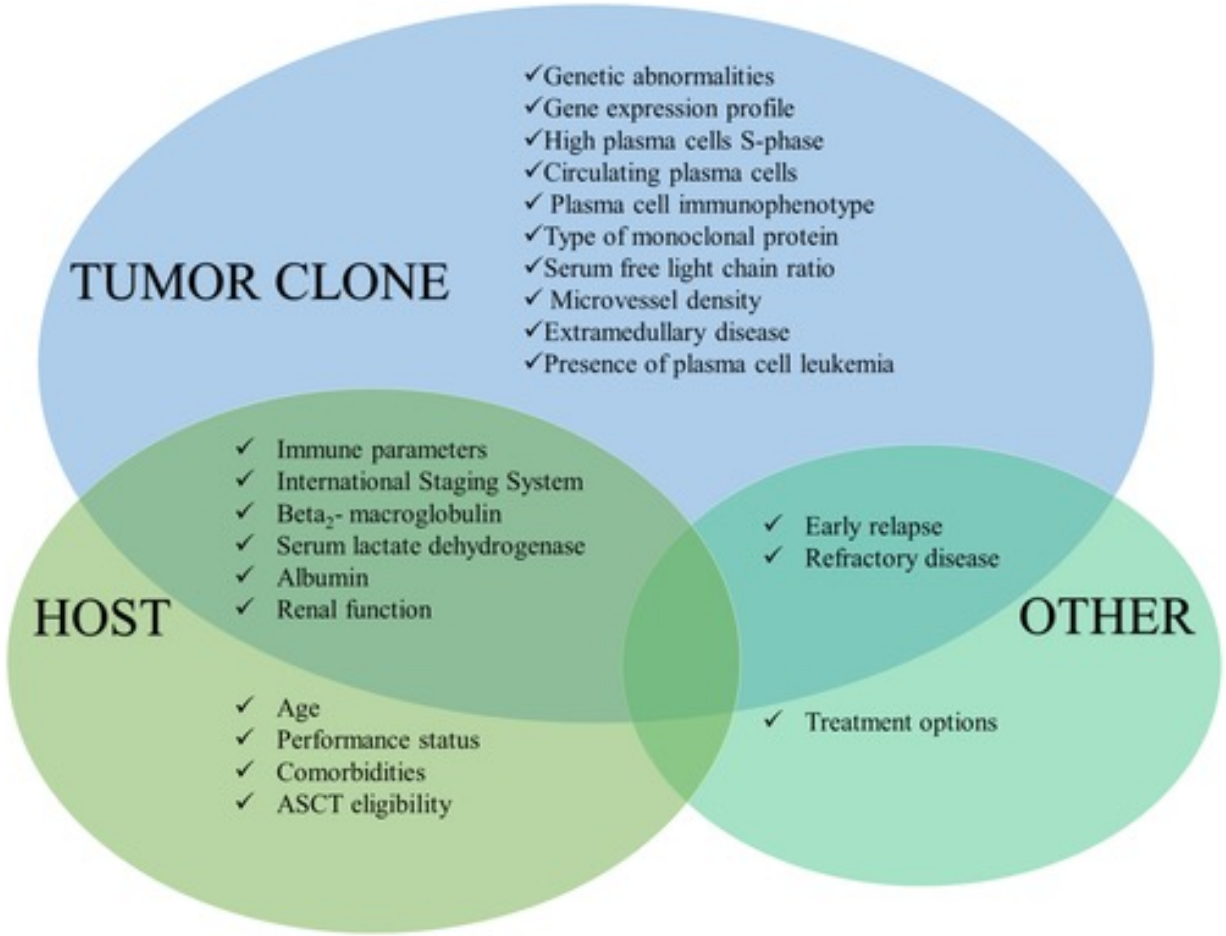
Indications

- History of disease and therapy that meets inclusion criteria.
- The patient must meet the criteria for a clinical trial.

Kinetics of disease progression

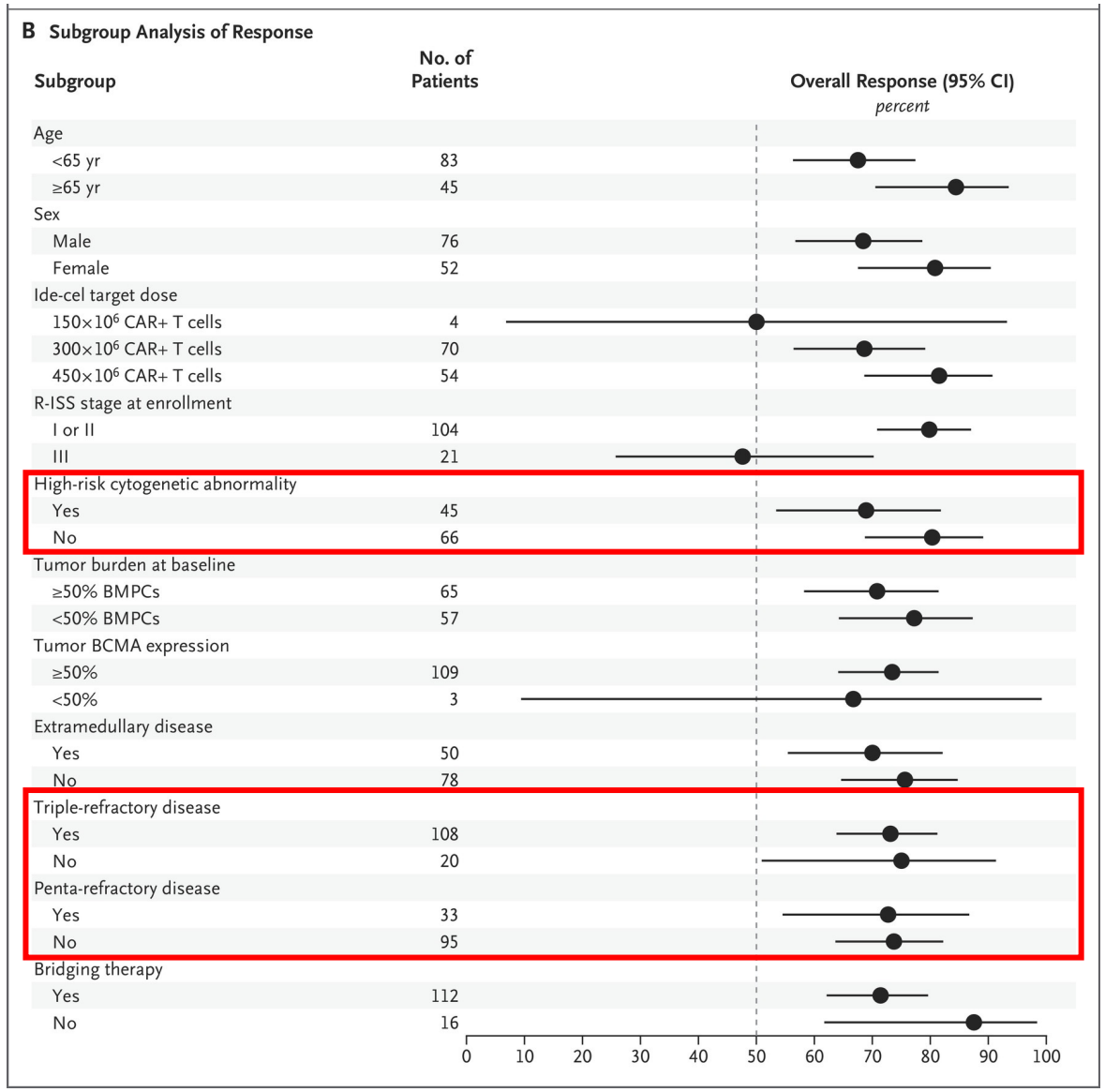
- The patient must be able to go through leukapheresis (without immediate use of steroids/chemotherapy) and remain stable until the T-cell infusion (3-4 wk).
- The patient must not need alternative therapy prior to CAR T-cell therapy.

High-risk myeloma



- ✓ International staging system (ISS)
- ✓ Revised international staging System (R-ISS)
- ✓ International myeloma working group (IMWG) Staging
- ✓ Mayo clinic risk stratification for multiple myeloma (mSMART)
- ✓ Gene-expression-based signatures
- ✓ Cytogenetic prognostic index (PI) by the Intergroupe Francophone du Myélome

Ide-cel Subgroup Analysis of Response.



High incidences of response (overall response in ≥50% of patients and complete or stringent complete response in ≥10% of patients) were consistently observed in most subgroups examined, including older patients, those who received bridging therapy, and those with more aggressive disease features, including high-risk cytogenetic abnormalities, triple- or penta-refractory disease, a high tumor burden, and extramedullary disease

Nikhil C. Munshi. N Engl J Med 2021

CAR-T in High-risk myeloma

Title	Interventions	Primary end point	Phase
Exploratory study to evaluate efficacy and safety of GC012F injection in chromosomal abnormalities high-risk BCMA+ multiple myeloma	Single dose of GC012F cells (an autologous dual CAR-T targeted BCMA and CD19)	Incidence and severity of adverse events after GC012F injection	Early 1
Descartes-11 consolidation treatment in patients with high-risk multiple myeloma who have residual disease after induction therapy	Descartes 11 (an autologous CD8+ anti-BCMA CAR-T cell therapy) after completing pre-transplant induction treatment	Rate of stringent complete response	2
A phase 1, open-label, multicenter study to evaluate the safety of bb2121 in subjects with high risk, newly diagnosed multiple myeloma (KarMMa-4)	1. Lymphodepleting chemotherapy (fludarabine and cyclophosphamide) 2. bb2121 autologous CAR-T (anti-BMCA) 3. Lenalidomide maintenance	Dose-limiting toxicity rates Adverse Events	1
Phase 1 study of CART-BCMA with or without huCART19 as consolidation of standard first or second-line therapy for high-risk multiple myeloma	CAR-T-BCMA: 1. As consolidation of early therapy for MM 2. With addition of fludarabine to the lymphodepleting chemotherapy regimen 3. In combination with huCART19, and 4. As a single rather than split-dose infusion	Adverse event reporting	1
Study of T cells targeting CD19/BCMA (CART-19/BCMA) for high risk multiple myeloma followed with auto-HSCT	CAR-T-anti-CD19/BCMA infused 14 and 20 days after ASCT	Number of patients with grade 1 through grade 4 cytokine release syndrome and other toxicities	1/2

Key Factors in Determining Candidacy for CAR T-Cell Therapy

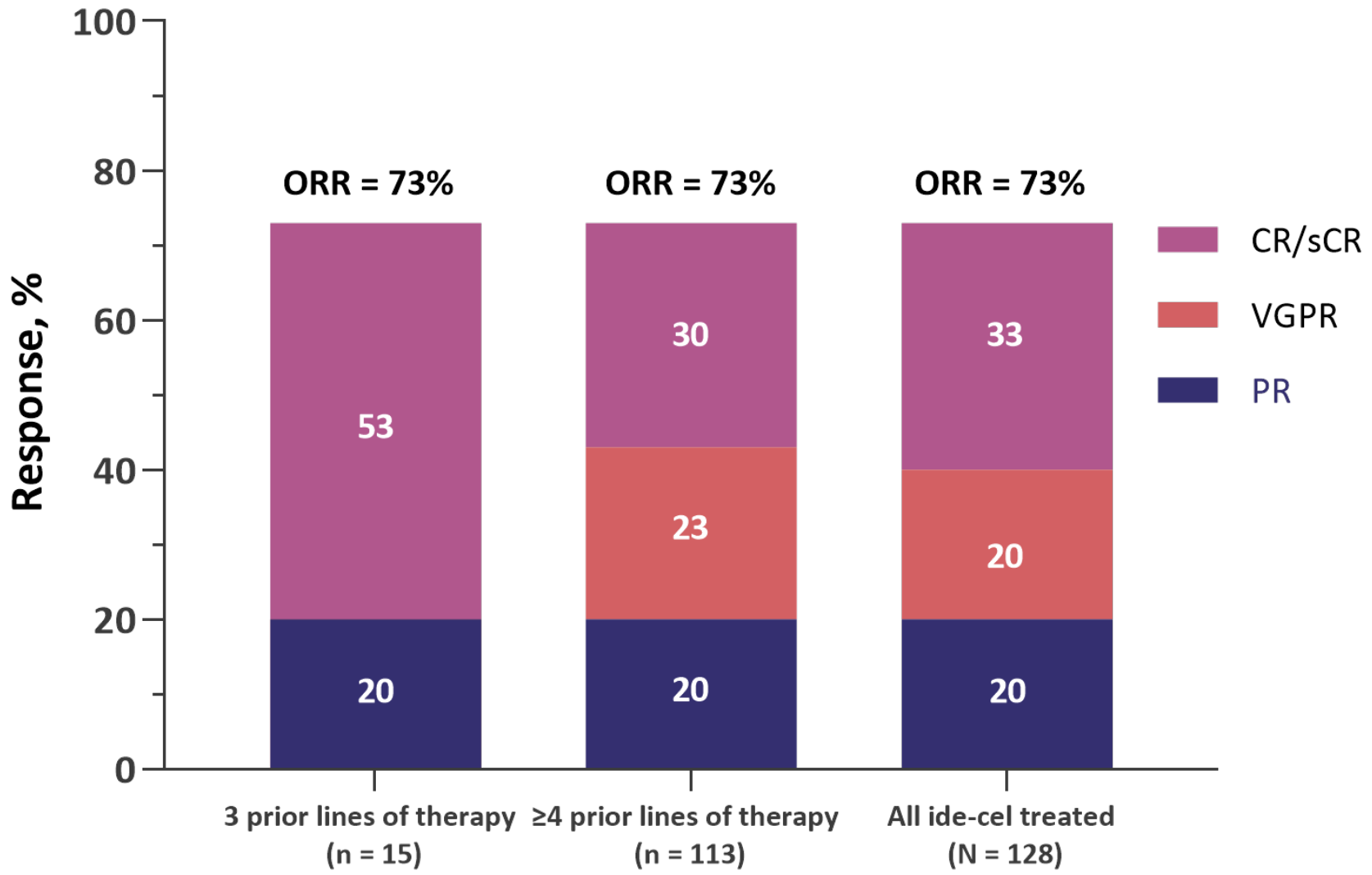
Immediate prior therapy

- Previous therapy must not affect successfully manufacture CAR T-cells (ie, obtain sufficient numbers of T-cells and expand).

Concomitant immunosuppressive therapy

- Must be safely stopped prior to collection.

ORRs to ide-cel by number of prior lines of therapy



Key Factors in Determining Candidacy for CAR T-Cell Therapy

Active infections

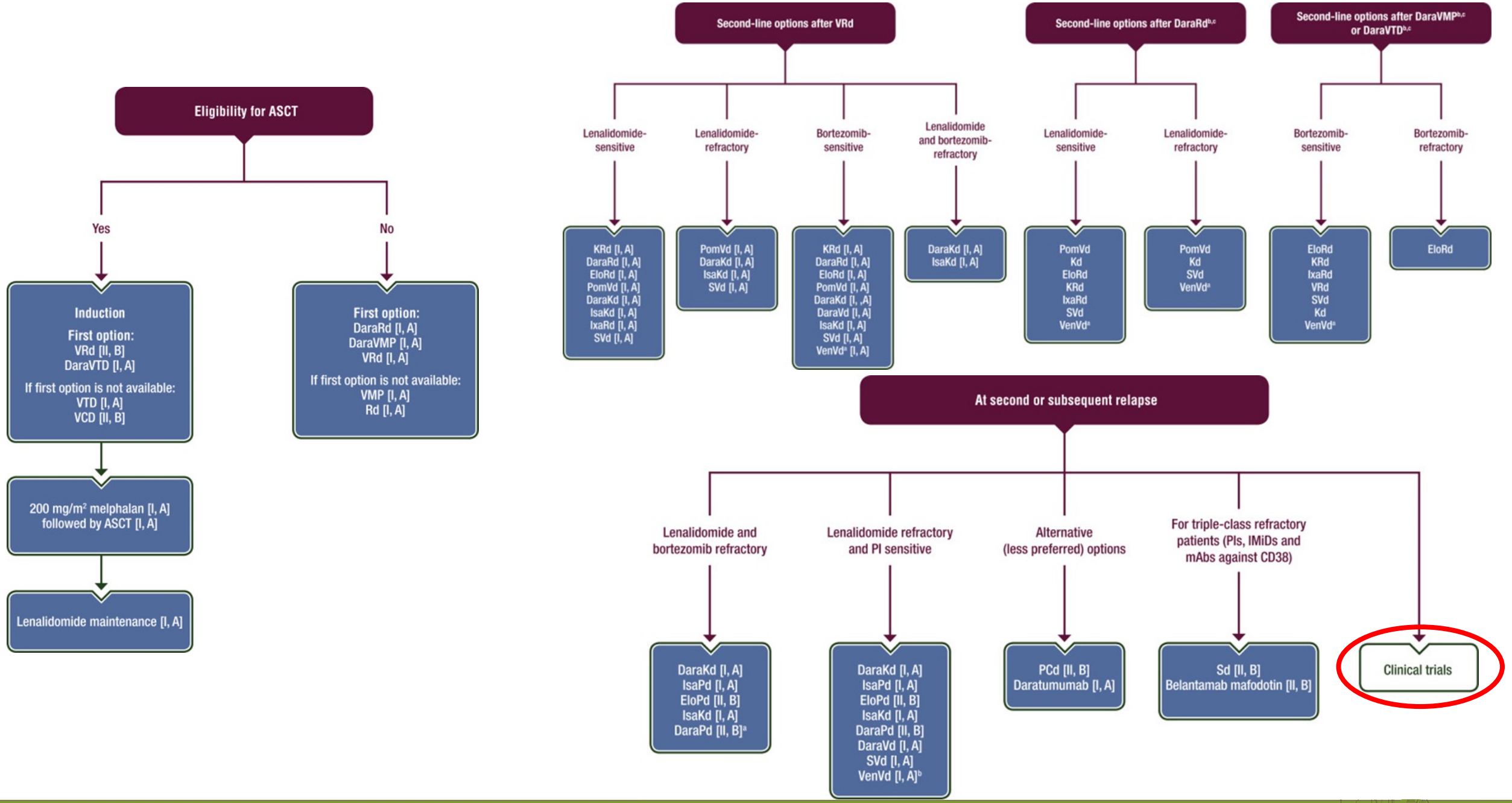
- Causes higher risk of complications, particularly if patient experiences CRS.

Comorbidities

- The organ function reserve (cardiac, pulmonary, renal, bone marrow, CNS) need to be sufficient to tolerate toxicities of CAR T-cell therapy, namely CRS and ICANS.

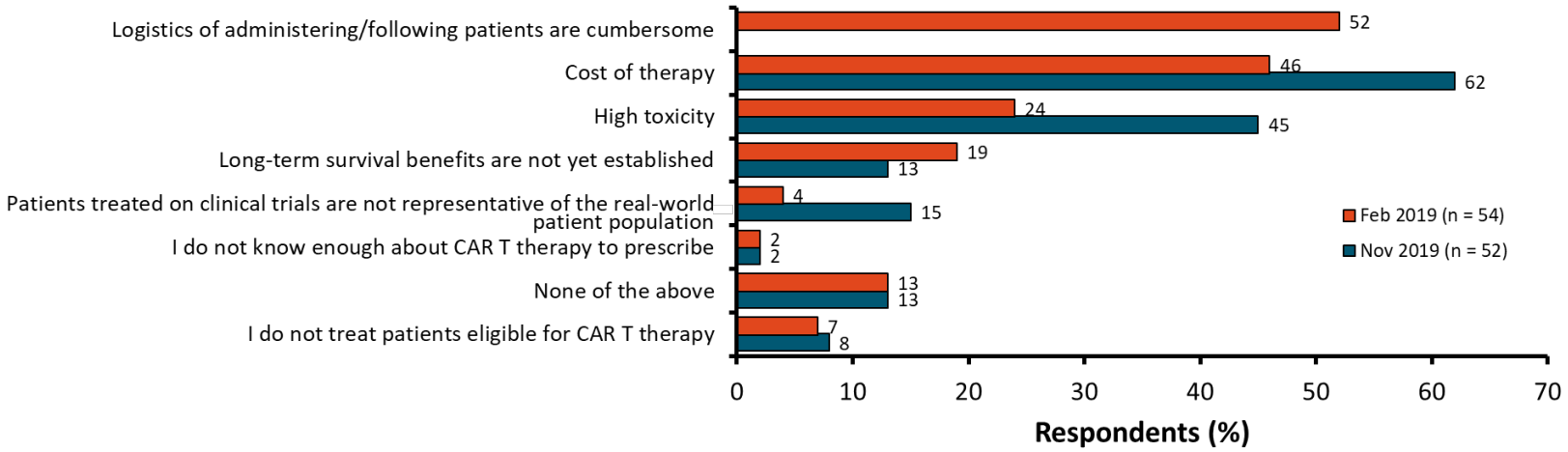
CAR-T: EMA indications

- Adult patients with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.
- Patients with active central nervous system (CNS) disorder or inadequate renal, hepatic, pulmonary or cardiac function are likely to be more vulnerable to the consequences of the adverse reactions described below and require special attention.
- It is not recommended that patients receive CAR-T cell within 4 months after an allogeneic stem cell transplant (SCT) because of the potential risk of CAR-T worsening GVHD. Leukapheresis for CAR-T manufacturing should be performed at least 12 weeks after allogeneic SCT.
- The efficacy/safety of BCMA-CAR-T in patients previously exposed to other anti-BCMA treatments is unknown.
- There is limited evidence available on efficacy/safety of CAR-T in re-treated patients. Some fatal events have been noticed.

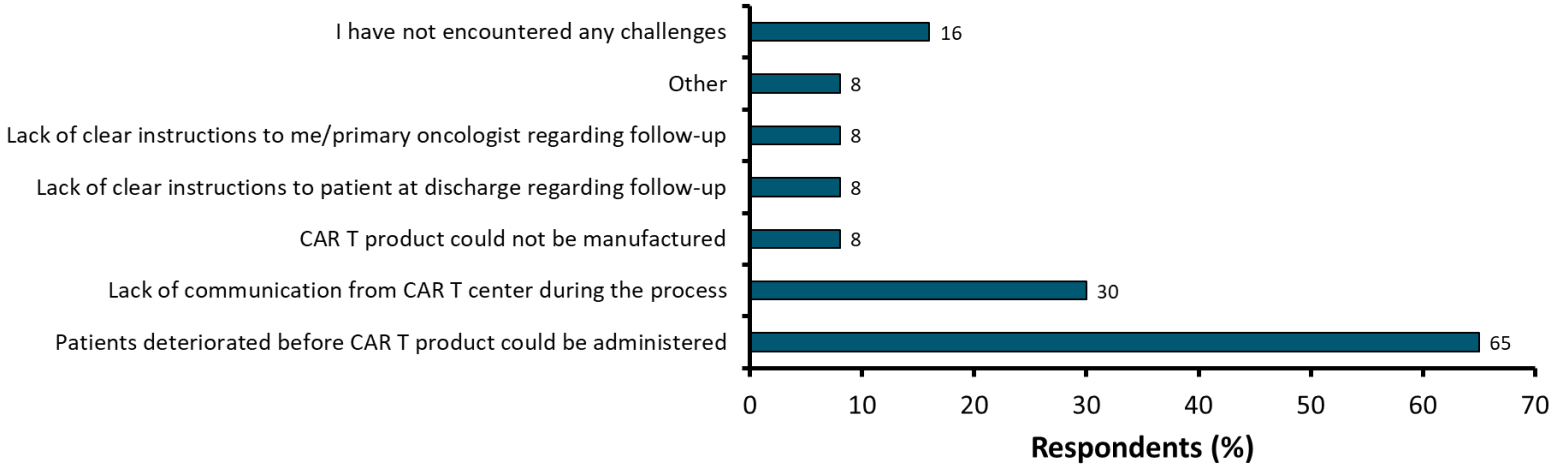

Eligibility for ASCT
Yes
No
Induction
First option:
VRd [II, B]
DaraVTD [I, A]
If first option is not available:
VTD [I, A]
VCD [II, B]
200 mg/m² melphalan [I, A] followed by ASCT [I, A]
Lenalidomide maintenance [I, A]
First option:
DaraRd [I, A]
DaraVMP [I, A]
VRd [I, A]
If first option is not available:
VMP [I, A]
Rd [I, A]
Second-line options after VRd
Lenalidomide-sensitive
KRd [I, A]
DaraRd [I, A]
EloRd [I, A]
PomVd [I, A]
DaraKd [I, A]
IsaKd [I, A]
IxaRd [I, A]
SVd [I, A]
Lenalidomide-refractory
PomVd [I, A]
DaraKd [I, A]
IsaKd [I, A]
SVd [I, A]
Bortezomib-sensitive
KRd [I, A]
DaraRd [I, A]
EloRd [I, A]
PomVd [I, A]
DaraKd [I, ,A]
DaraVd [I, A]
IsaKd [I, A]
SVd [I, A]
VenVd[a] [I, A]
Lenalidomide and bortezomib-refractory
DaraKd [I, A]
IsaKd [I, A]
Second-line options after DaraRd[b,c]
Lenalidomide-sensitive
PomVd
Kd
EloRd
KRd
IxaRd
SVd
VenVd[a]
Lenalidomide-refractory
PomVd
Kd
SVd
VenVd[a]
Second-line options after DaraVMP[b,c] or DaraVTD[b,c]
Bortezomib-sensitive
EloRd
KRd
IxaRd
VRd
SVd
Kd
VenVd[a]
Bortezomib-refractory
EloRd
At second or subsequent relapse
Lenalidomide and bortezomib refractory
DaraKd [I, A]
IsaPd [I, A]
EloPd [II, B]
IsaKd [I, A]
DaraPd [II, B][a]
Lenalidomide refractory and PI sensitive
DaraKd [I, A]
IsaPd [I, A]
EloPd [II, B]
IsaKd [I, A]
DaraPd [II, B]
DaraVd [I, A]
SVd [I, A]
VenVd [I, A][b]
Alternative (less preferred) options
PCd [II, B]
Daratumumab [I, A]
For triple-class refractory patients (PIs, IMiDs and mAbs against CD38)
Sd [II, B]
Belantamab mafodotin [II, B]
Clinical trials

Perceptions of Community Hematologists/Oncologists on Barriers to CAR T-Cell Therapy for DLBCL

In your opinion, which of the following are top barriers to prescribing/recommending CAR T-cell therapy?



What additional challenges have you encountered in your patient's CAR T-cell journey? (n = 37)



Gajra. Immunotherapy. 2020;12:725.

Advantages and disadvantages of CAR-T Cells therapy in Multiple Myeloma

Advantages	Disadvantages
Novel therapy for refractory/relapsed patients	Potentially can cause life-threatening complications
Recognize cells without HLA expression	Relapses after treatment (antigen escape)
Eliminates only cells with targeted antigen	Immunogenicity of CARs
One-time treatment with long therapy-free intervals providing patients with a high quality of life	High costs of the therapy


Thanks for your attention