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Bosphorus Myeloma Forum 2026

Positioning CAR T in Relapsed Myeloma: Patient Selection, Timing and Toxicity Management in 2026

Istanbul, 06th June 2026

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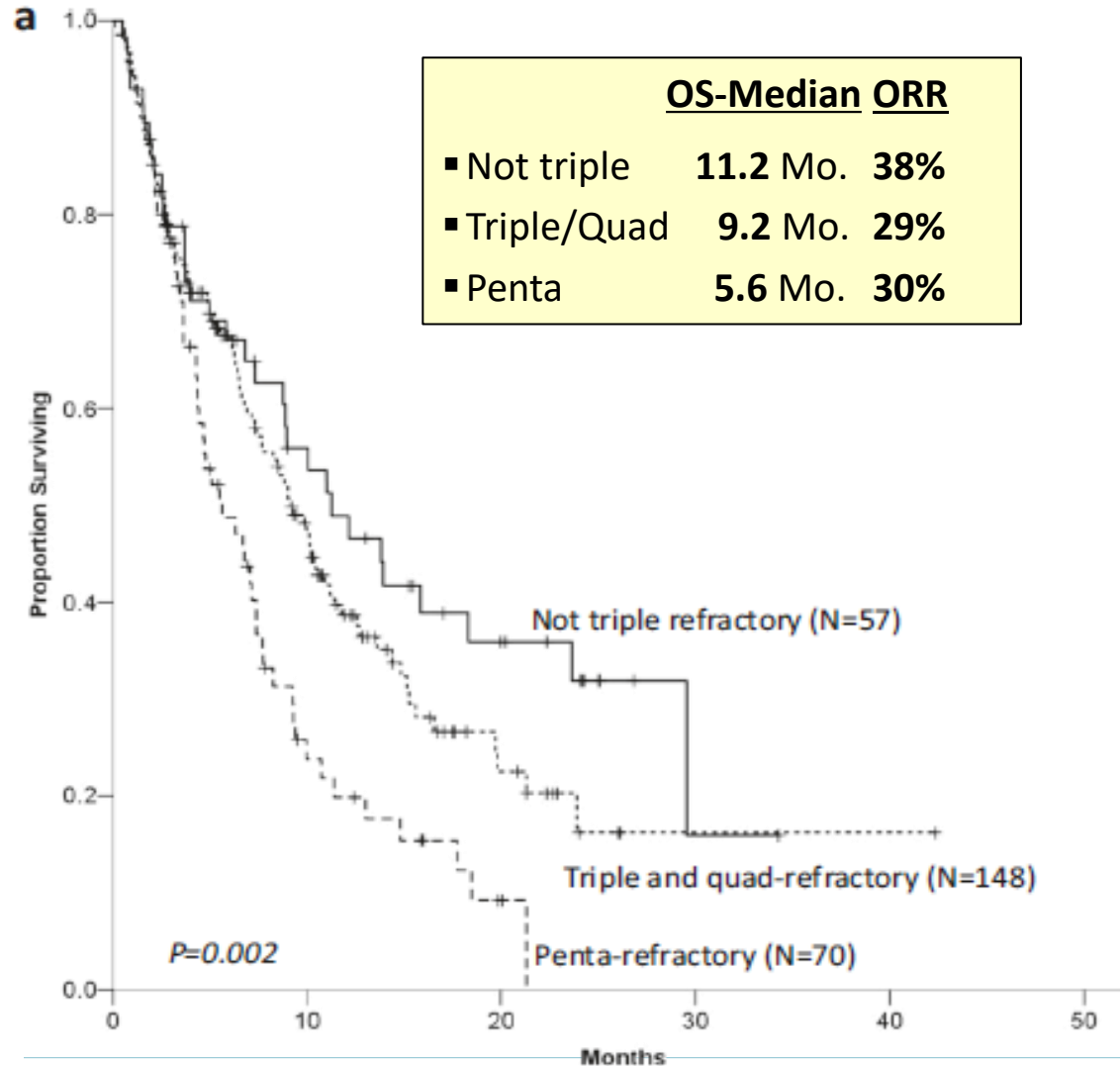
CONFLICTS OF INTEREST

Research grants: Amgen, Gilead/Kite, Stemline/Menarin

Honoraria: Novartis, Gilead/Kite, J&J, BMS/Celgene, Sobi, Astra Zeneca, Caribou, Therakoss/Mallinckrodt, Lilly, Amgen

Travel grants: J&J, Gilead/Kite, Sobi, Amgen, Astra Zeneca, Beigene

OUTCOMES PRIOR TO CAR T / APPROVED CAR T



— *Idecabtagene vicleucel (ide-cel)*

- Adult patients
- relapse or refractory
- ≥ 2 prior lines (incl. PI, IMiD, anti-CD38-AB)

— *Ciltacabtabene autoleucel (cilta-cel)*

- Adult patients
- relapse or refractory
- ≥ 1 treatment line and lenalidomide-refractoriness

PIVOTAL TRIALS - MAIN MESSAGES

IDECABTAGENE VICLEUCEL

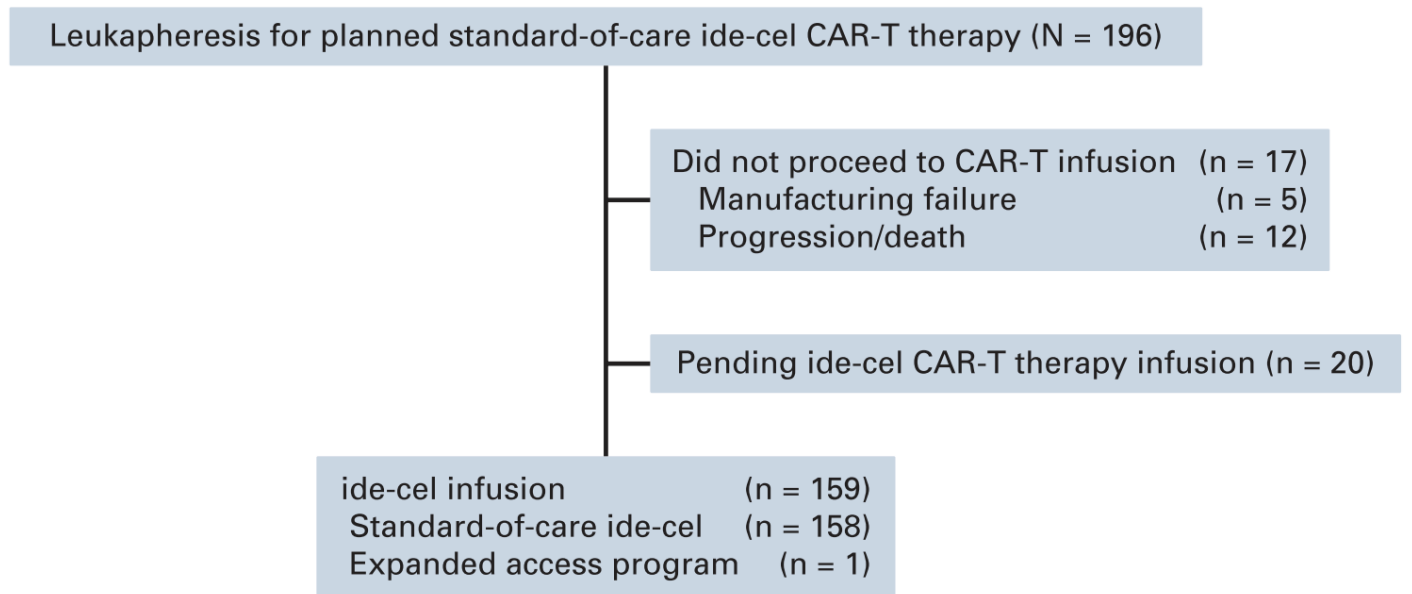
- KarMMA1
 - deep remissions
- KarMMA3
 - dismal outcomes in SOC arm
 - no upper age limit
 - efficacy in earlier treatment lines comparable with later lines

CILTACABTAGENE-AUTOLEUCEL

- CARTITUDE1
 - efficacious treatment with >80% MRD negativity across all groups
- CARTITUDE4
 - better outcomes in earlier treatment lines

REAL WORLD DATA – IDECABTAGENE – VICLEUCEL

- 11 US Institutions
- N=196 underwent apheresis
- N=159 treated
- 134 (84%) tripple-refractory
- 70 (44%) penta-refractory



115 of 129 (89%) patients who were alive had follow-up within a data cutoff of 3 months

DEMOGRAPHY & EXCLUSION CRITERIA

| Characteristic | No. (%) |
|------------------------|------------|
| Patients, No. | 159 |
| Age, years | |
| < 65 | 82 (52) |
| ≥ 65 | 77 (48) |
| Median (range) | 64 (36-83) |
| Sex, male | 91 (57) |
| Extramedullary disease | 76 (48) |
| High marrow burden | 36 (25) |
| Unknown | 13 |
| ECOG PS | |
| 0-1 | 127 (81) |
| 2-4 | 29 (19) |
| Unknown | |
| R-ISS disease stage | |
| I | |
| II | |
| III | |
| Unknown | |

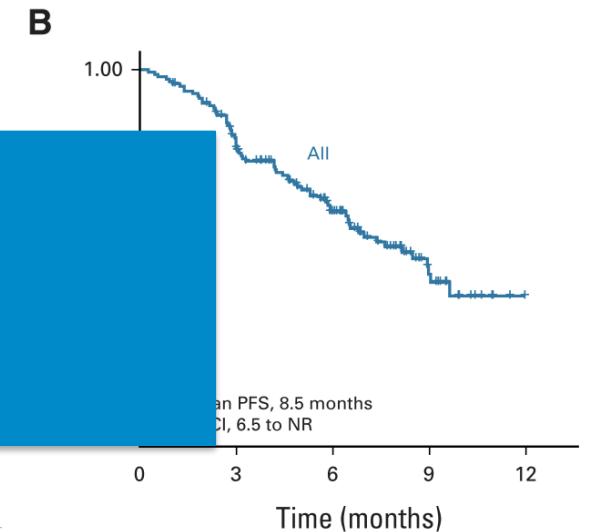
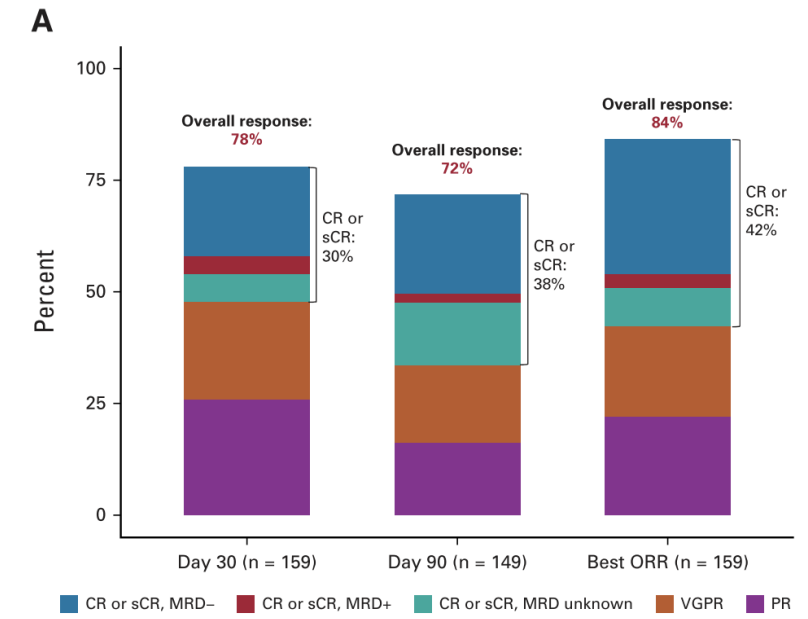
| | |
|--|----------|
| Prior therapies | |
| Prior antimyeloma therapies, No., median (range) | 7 (4-18) |
| Refractory disease | 107 (67) |
| Relapsed disease | 45 (28) |
| Prior autologous SCT | 134 (84) |
| Prior allogeneic SCT | 9 (6) |
| Prior anti-BCMA therapy | 33 (21) |
| Refractory status | |
| IMiD | 148 (93) |
| PI | 148 (93) |
| Anti-CD38 antibody | 148 (93) |

120 patients not meeting inclusion criteria for KARMMA trial!

SAFETY AND OUTCOMES

| Event and Grade | No. (%) |
|--|----------|
| CRS | |
| Any | 131 (82) |
| 0 | 28 (18) |
| 1 | 99 (62) |
| 2 | 27 (17) |
| 3 | 2 (1) |
| 4 | 1 (1) |
| 5 | 2 (1) |
| Time to maximum severity, days, median | 1 |
| Range | 0-14 |
| IQR | 1-2 |

| Event and Grade | No. (%) |
|--|----------|
| NT | |
| Any | 29 (18) |
| 0 | 130 (82) |
| 1 | 12 (8) |
| 2 | 8 (5) |
| 3 | 4 (3) |
| 4 | 5 (3) |
| Time to maximum severity, days, median | 3 |
| Range | 0-15 |
| IQR | 1-4 |



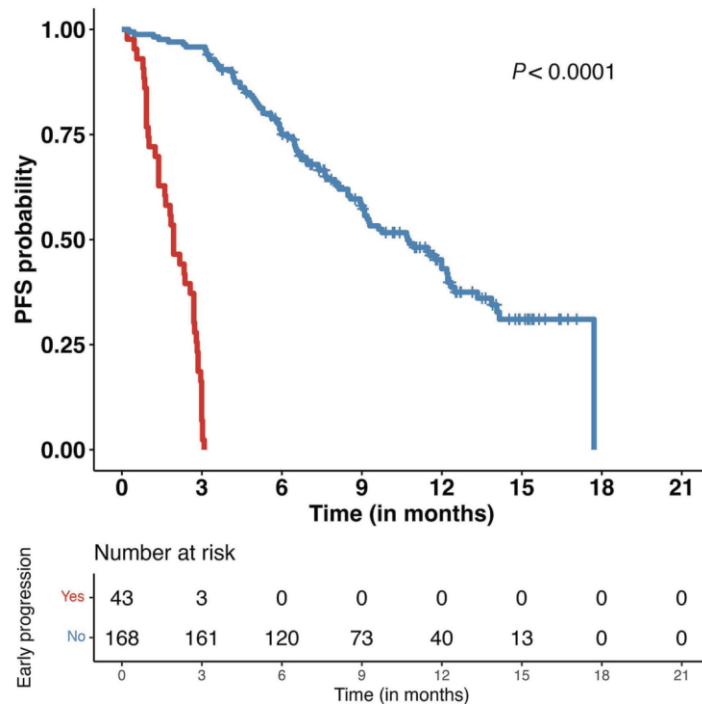
Efficacy and safety comparable to KarMMA trial!

IDECABTAGENE VICLEUCEL – PROGNOSTICATION

- Adverse prognosis for:
 - prior exposition to BCMA targeted therapies
 - high-risk cytogenetics
 - ECOG ≥ 2
 - younger age

| Characteristic | N (event N) | PFS | |
|------------------------|-------------|---------------------|-------------|
| | | HR (95% CI) | P |
| Prior BCMA-TT | | | .003 |
| No | 104 (42) | 1.00 (referent) | |
| Yes | 31 (18) | 2.81 (1.44 to 5.51) | |
| High-risk cytogenetics | | | .003 |
| No | 86 (33) | 1.00 (referent) | |
| Yes | 49 (27) | 2.31 (1.34 to 3.97) | |
| Extramedullary disease | | | .06 |
| No | 70 (25) | 1.00 (referent) | |
| Yes | 65 (35) | 1.68 (0.97 to 2.90) | |
| CAR T-cell dose | | | .6 |
| < 400 $\times 10^6$ | 57 (26) | 1.00 (referent) | |
| $\geq 400 \times 10^6$ | 78 (34) | 0.86 (0.50 to 1.47) | |
| ECOG PS at LD | | | .02 |
| 0-1 | 108 (42) | 1.00 (referent) | |
| 2-4 | 27 (18) | 2.19 (1.16 to 4.14) | |
| Penta-refractory | | | .8 |
| No | 76 (33) | 1.00 (referent) | |
| Yes | 59 (27) | 0.92 (0.53 to 1.58) | |
| Patient age | 135 (60) | 0.97 (0.95 to 1.00) | .04 |
| Prior lines of therapy | 135 (60) | 0.97 (0.88 to 1.07) | .5 |

IDECABTAGENE VICLEUCEL – EARLY PROGRESSION

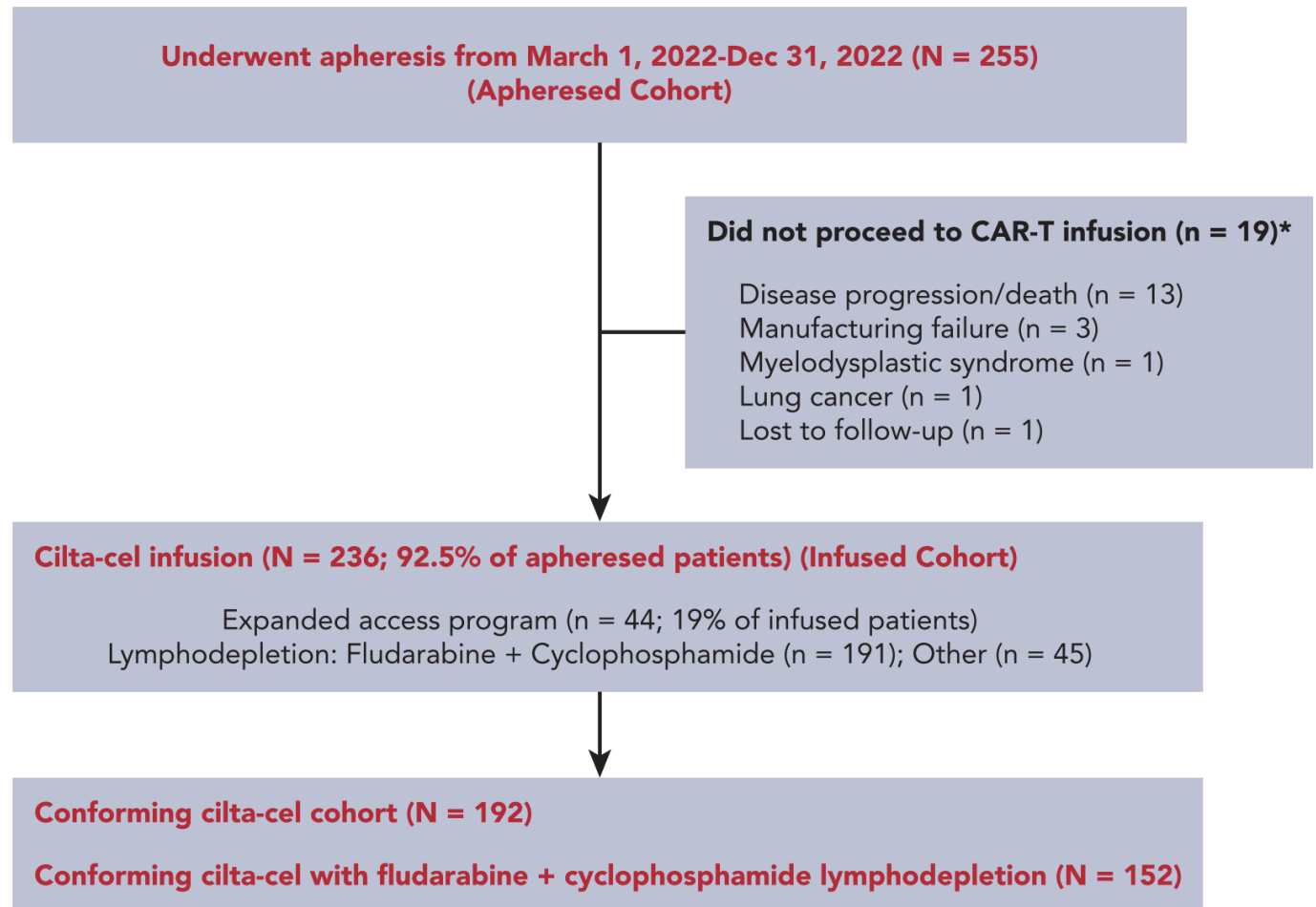


| Early progression risk factors | PFS | | | OS | | |
|--------------------------------|-------------|------------------|--------|-------------|------------------|--------|
| | N (N event) | HR (95% CI) | P | N (N event) | HR (95% CI) | P |
| Prior BCMA therapy | | | | | | |
| No | 135 (79) | 1.00 Ref. | | 134 (42) | 1.00 Ref. | |
| Yes | 49 (38) | 1.64 (1.08-2.50) | 0.02 | 49 (23) | 1.56 (0.90-2.71) | 0.1 |
| Extramedullary disease | | | | | | |
| No | 100 (53) | 1.00 Ref. | | 99 (28) | 1.00 Ref. | |
| Yes | 84 (64) | 1.71 (1.16-2.51) | 0.006 | 84 (37) | 1.69 (1.00-2.86) | 0.048 |
| Baseline ferritin at LD | | | | | | |
| Normal | 100 (53) | 1.00 Ref. | | 100 (22) | 1.00 Ref. | |
| ≥ULN | 84 (64) | 1.95 (1.33-2.88) | <0.001 | 83 (43) | 2.56 (1.51-4.35) | <0.001 |
| Bridging therapy | | | | | | |
| No | 40 (19) | 1.00 Ref. | | 40 (6) | 1.00 Ref. | |
| Yes | 144 (98) | 1.42 (0.84-2.38) | 0.2 | 143 (59) | 2.23 (0.94-5.26) | 0.07 |
| Race and ethnicity | | | | | | |
| Non-Hispanic White | 126 (81) | 1.00 Ref. | | 126 (45) | 1.00 Ref. | |
| Non-Hispanic Black | 33 (21) | 1.48 (0.90-2.46) | 0.1 | 32 (12) | 1.45 (0.75-2.79) | 0.3 |
| Hispanic | 19 (12) | 1.15 (0.60-2.17) | 0.7 | 19 (7) | 1.45 (0.61-3.25) | 0.4 |
| Other | 6 (3) | 0.56 (0.18-1.81) | 0.3 | 6 (1) | 0.27 (0.04-2.04) | 0.2 |
| Plasma cell leukemia | | | | | | |
| No | 175 (108) | 1.00 Ref. | | 174 (58) | 1.00 Ref. | |
| Yes | 9 (9) | 4.27 (2.06-8.87) | <0.001 | 9 (7) | 3.97 (1.66-9.46) | 0.002 |
| t(4;14) at infusion | | | | | | |
| No | 163 (98) | 1.00 Ref. | | 162 (52) | 1.00 Ref. | |
| Yes | 21 (19) | 1.82 (1.07-3.09) | 0.03 | 21 (13) | 1.58 (0.80-3.11) | 0.2 |

dismal prognosis associated with: prior BCMA treatment, EMD, increased ferritin, PCL, t(4;14)

CILTACABTAGENE-AUTOLEUCEL – REAL WORLD DATA

- 16 US Institutions
- N=255 underwent apheresis
- N=236 (92.5%) treated



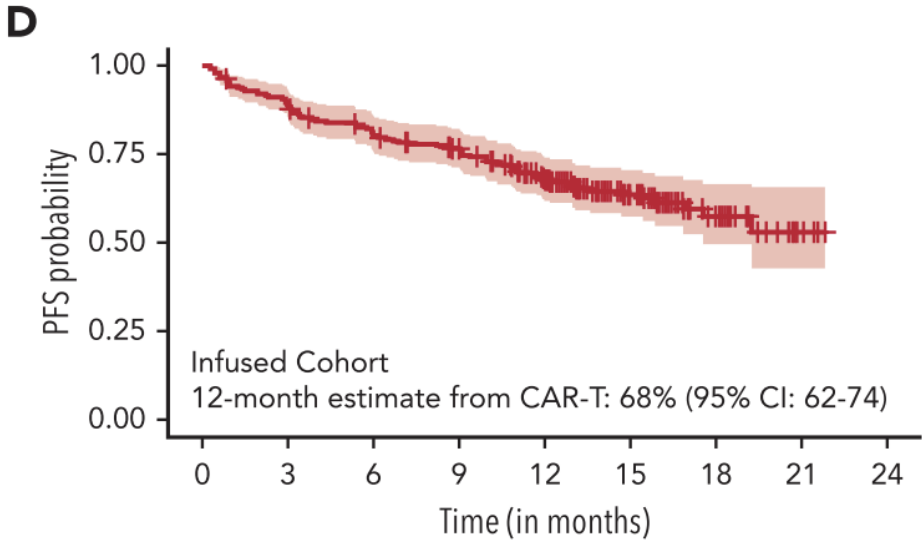
CILTACABTAGENE AUTOLEUCEL; DEMOGRAPHY & EXCLUSION CRITERIA

| Characteristic | N = 255 (apheresis) | N = 236 (infused) |
|--------------------------------|--------------------------|-------------------------|
| | n (%) or median (range) | n (%) or median (range) |
| Age, y | 64 (30-84) | 64 (30-84) |
| Age ≥70 y | 65 (25%) | 62 (26%) |
| Male sex | 145 (57%) | 134 (57%) |
| Race and ethnicity | | |
| Non-Hispanic White | 190 (75%) | 177 (76%) |
| Hispanic (any race) | 20 (8%) | 19 (8%) |
| Black | 30 (12%) | 26 (11%) |
| Asian/Pacific Islander | 8 (3%) | 7 (3%) |
| American Indian/Alaskan Native | 1 (0.4%) | 1 (0.4%) |
| Other | 4 (1.6%) | 4 (1.7%) |
| Unknown | 2 | 2 |
| ECOG PS | At CAR T-cell evaluation | At lymphodepletion |
| 0-1 | 215 (92%) | 183 (89%) |
| 2-4 | 19 (8%) | 23 (11%) |
| Unknown | 21 | 30 |
| Myeloma subtype | | |
| Intact immunoglobulin | 184 (72%) | 170 (72%) |
| Light chain | 40 (16%) | 39 (17%) |
| Oligo/nonsecretory | 31 (12%) | 27 (11%) |
| R-ISS disease stage | | |
| I | 44 (27%) | 43 (28%) |
| II | 87 (53%) | 81 (53%) |
| III | 34 (21%) | 30 (19%) |
| Unknown | 90 | 82 |
| EMD | 66 (26%) | 60 (26%) |
| Unknown | 2 | 1 |
| Refractory status | | |
| Immunomodulatory agent | 201 (79%) | 188 (80%) |
| Proteasome inhibitor | 197 (77%) | 184 (78%) |
| Anti-CD38 antibody | 209 (82%) | 196 (83%) |
| Triple-refractory | 176 (69%) | 163 (69%) |
| Penta-refractory | 75 (29%) | 70 (30%) |

| | N = 255 (apheresis) | N = 236 (infused) |
|---|-------------------------|-------------------------|
| | n (%) or median (range) | n (%) or median (range) |
| Was patient ineligible for the CARTITUDE-1 trial criteria at the time of leukapheresis | 144 (56%) | 128 (54%) |
| Ineligible for 1 criterion | 61 (24%) | 58 (25%) |
| Ineligible for ≥2 criteria | 83 (33%) | 70 (30%) |
| Organ dysfunction* (renal, cardiac, and hepatic) | 31 (13%) | 27 (12%) |
| Unknown | 9 | 8 |
| Creatinine clearance <40 mL/minute | 22 (9%) | 18 (8%) |
| Unknown | 1 | 0 |
| Prior anti-BCMA therapy | 38 (15%) | 33 (14%) |
| Cytopenias | 45 (18%) | 37 (16%) |
| Unknown | 1 | 1 |
| ECOG PS ≥2 | 28 (11%) | 25 (11%) |
| Unknown | 7 | 7 |
| History or presence of PCL, amyloidosis or POEMS | 28 (11%) | 24 (10%) |
| History of CNS myeloma and other CNS pathology | 12 (5%) | 12 (5%) |

CILTACABTAGENE AUTOLEUCEL; SAFETY & EFFICACY

| Event* | n (%) or median (range) |
|--|-------------------------|
| CRS | |
| Any grade | 177 (75%) |
| Unknown | 1 |
| Grade ≥3 | 12 (5%) |
| Grade 1 | 115 (49%) |
| Grade 2 | 49 (21%) |
| Grade 3 | 6 (3%) |
| Grade 4 | 3 (1%) |
| Grade 5 | 3 (1%) |
| Grade unknown | 1 |
| Median time to onset from CAR T-cell therapy | 7 days (0-14; IQR, 6-8) |
| ICANS | |
| Any grade | 32 (14%) |
| Unknown | 6 |
| Grade ≥3 | 9 (4%) |
| Grade 1 | 14 (6%) |
| Grade 2 | 8 (3.5%) |
| Grade 3 | 4 (2%) |
| Grade 4 | 4 (2%) |
| Grade 5 | |
| Grade unknown | |
| Median time to onset from CAR T-cell therapy | |

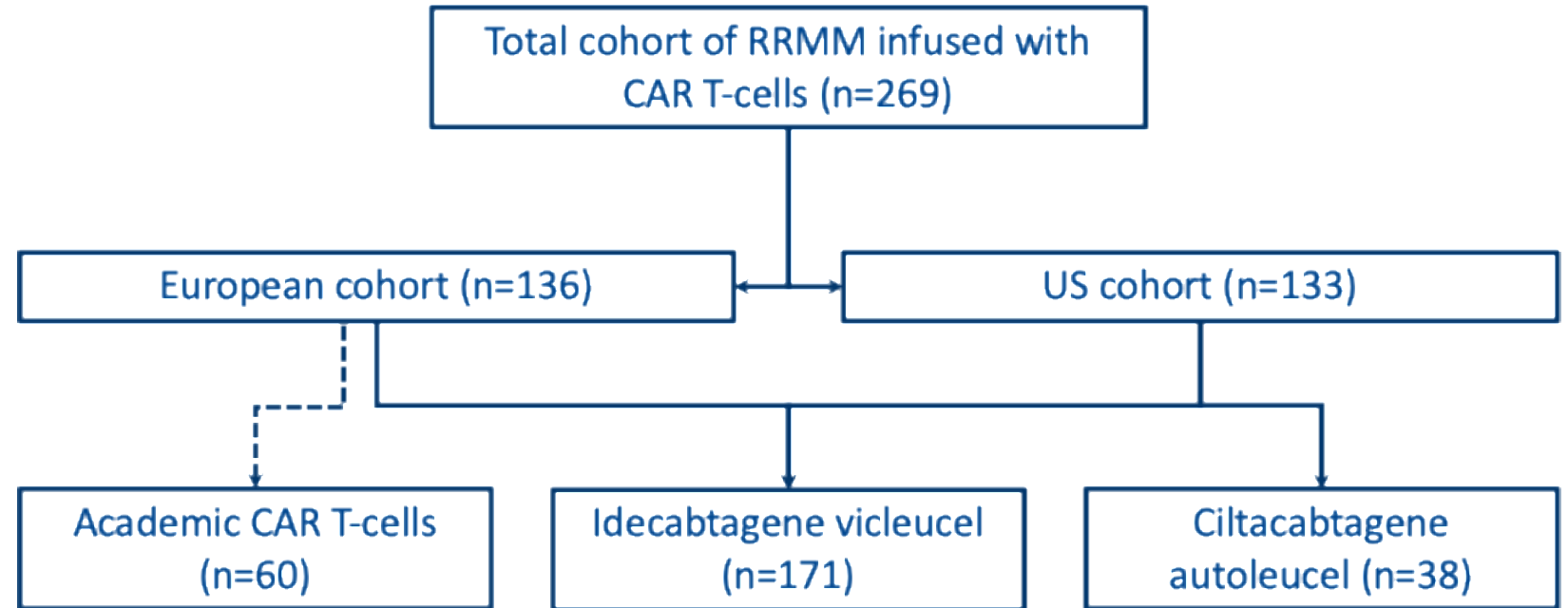


| | HR (95% CI) | P value |
|---|------------------|---------|
| PFS | | |
| Prior BCMA-TT, yes vs no | 1.65 (0.94-2.89) | .08 |
| Ferritin, ≥400 vs <400 ng/mL | 2.99 (1.86-4.80) | <.001 |
| High-risk cytogenetics, yes vs no | 1.90 (1.20-3.02) | .006 |
| | | .009 |
| comparable efficacy to CARTITUDE1 trial | | <.001 |
| 10% Non relapse mortality | | .005 |
| dismal outcomes for: high ferritin level, high risk cytogenetics, EMD | | .04 |

What did we learn?

PROGNOSTIC MARKERS – CLINICAL PARAMETERS

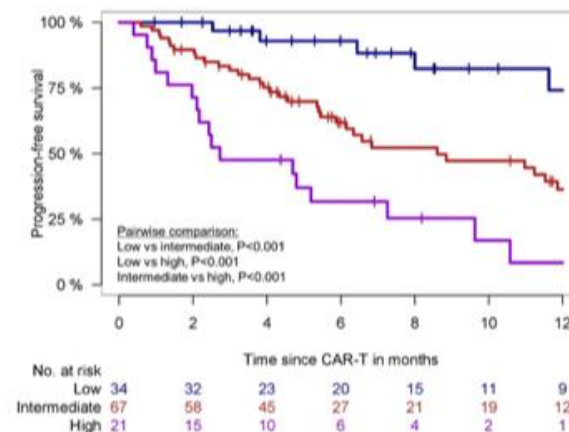
- international cohort
 - Europe N=136
 - USA N=133
- ide-cel, cilta-cel and academic CAR T



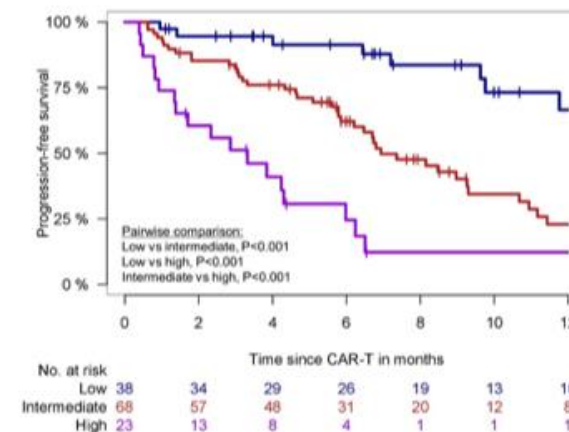
MYCARE SCORE

| Factor | HR | 95% CI | P | Score |
|-------------------------------------|------|------------|--------|-------|
| EMD or PCL present | 1.92 | 1.30-2.82 | <0.001 | 1 |
| High risk cytogenetics | 1.95 | 1.31-2.92 | 0.001 | 1 |
| Ferritin >NL (sex-/age-adjusted) | 1.59 | 1.07-2.37 | 0.02 | 1 |
| Lenalidomide refractoriness | 1.69 | 1.02-2.82 | 0.04 | 1 |
| MyCARE | | | | |
| Low (score 0-1) | Ref | | | |
| Intermediate (score 2-3) | 3.27 | 1.87-5.72 | <0.001 | |
| High (score 4) | 7.89 | 4.21-14.79 | <0.001 | |

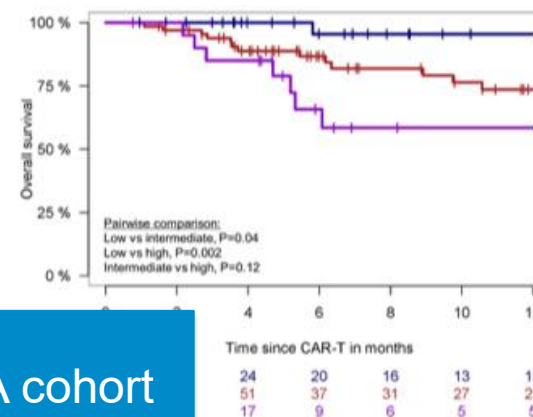
Europe



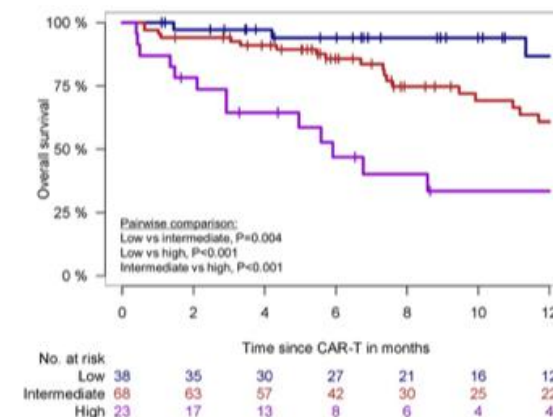
US



Europe



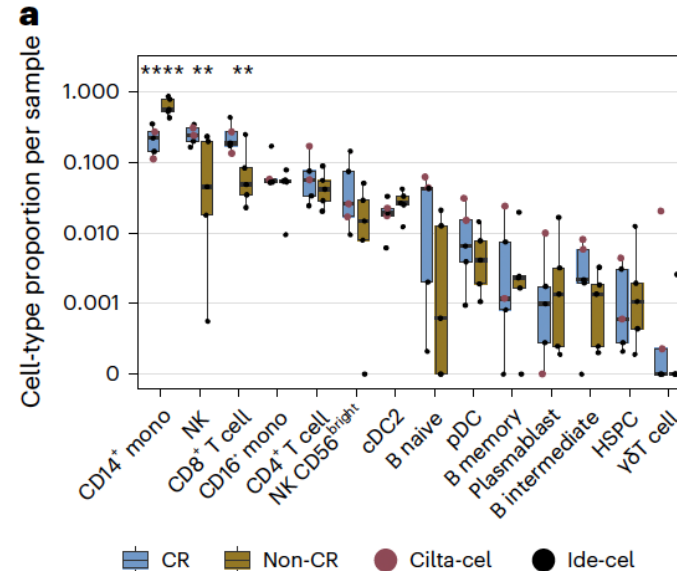
US



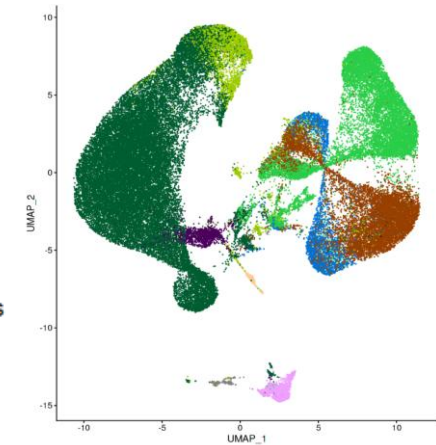
MyCARE Score validated in both European and USA cohort
Not a randomized trial!!!

PROGNOSTIC MARKERS – CELLULAR COMPOSITION AT APHERESIS

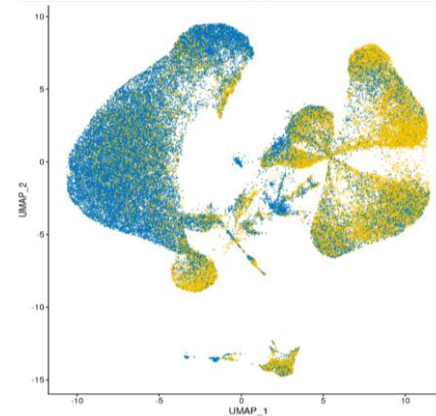
- longitudinal cell-samplings starting from apheresis
- flow cytometry
- single-cell sequencing



● B cells
● CD4 T cells
● CD8 T cells
● cDC
● gdT
● Monocytes
● NK
● pDC
● Plasma cells
● Treg
● dnT
● Others



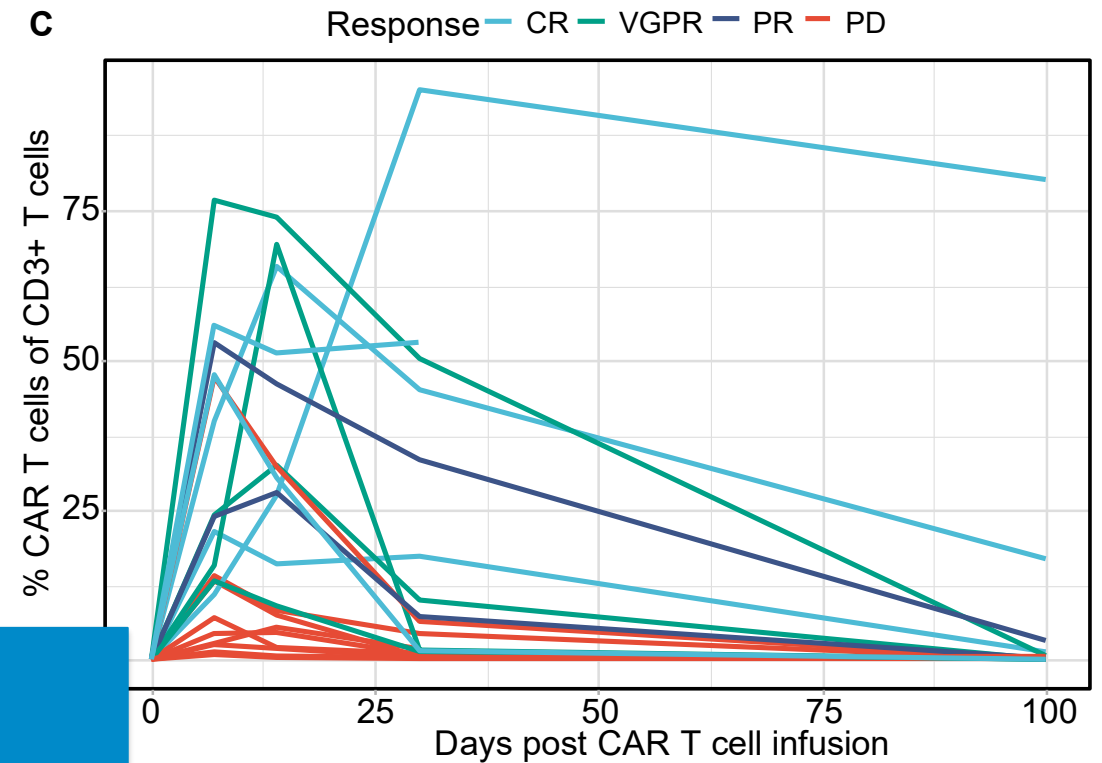
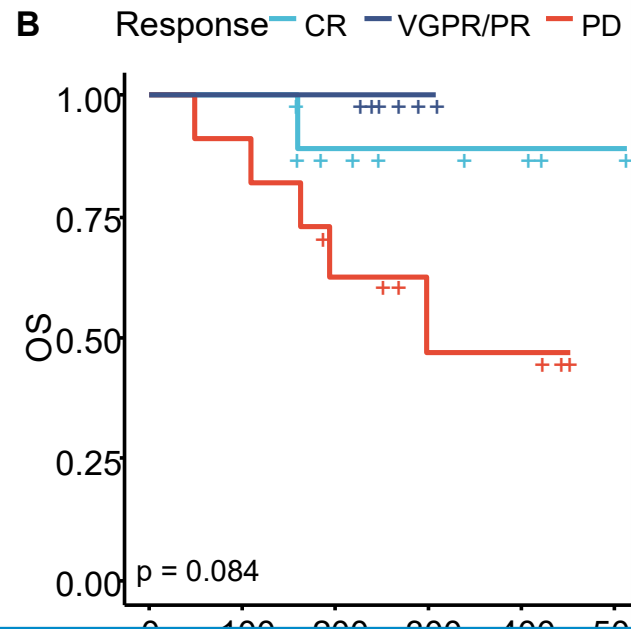
● CR
● nonCR



Immunocompetence at apheresis is predictive for outcomes

PROGNOSTIC MARKERS – CELLULAR DYNAMICS

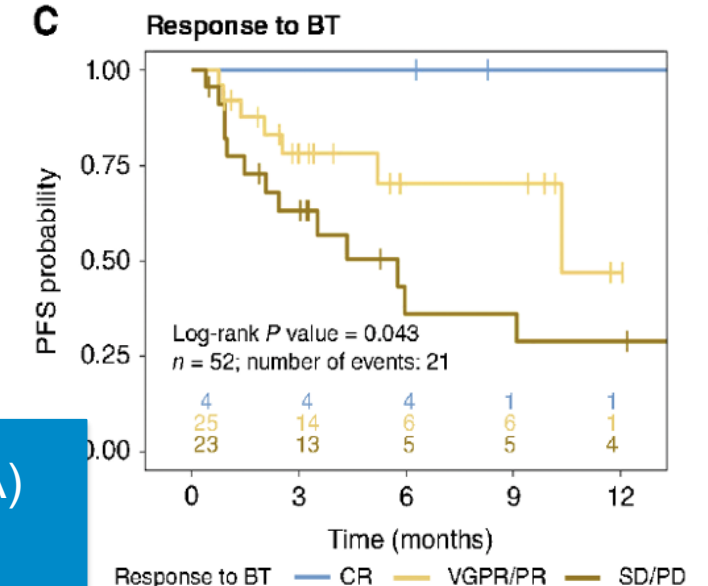
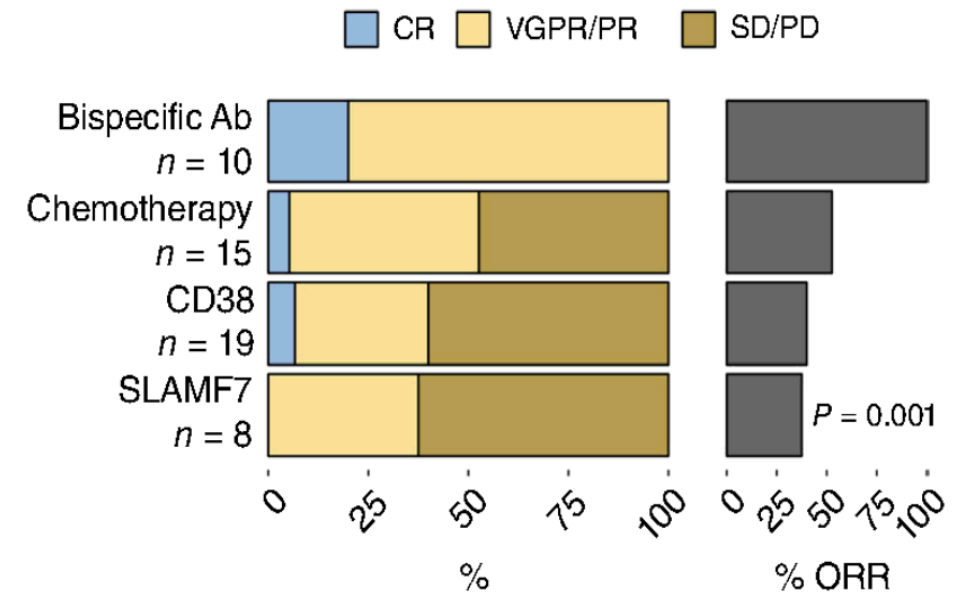
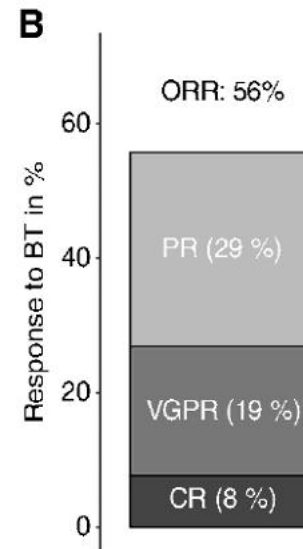
- N=27 patients treated with idecabtagene vicleucel
- single-center experience



High CAR T expansion is positive prognostic factor
(harmonization, quantification?)

BRIDGING STRATEGIES – RETROSPECTIVE ANALYSIS

- 52 patients (ide-cel N=34; ciltacel N=18) – all receiving bridging:
- N=10 (19%) bispec AB
- N=15 (29%) chemotherapy
- N=19 (37%) anti CD38 antibody
- N=8 (15%) SLAMF7 antibody



bridging with bispecific antibodies – (in some cases) YES (but not anti-BCMA)
Increased rate of OOS!!!

BRIDGING THERAPY – CONSENSUS OPINION (EU EXPERTS)

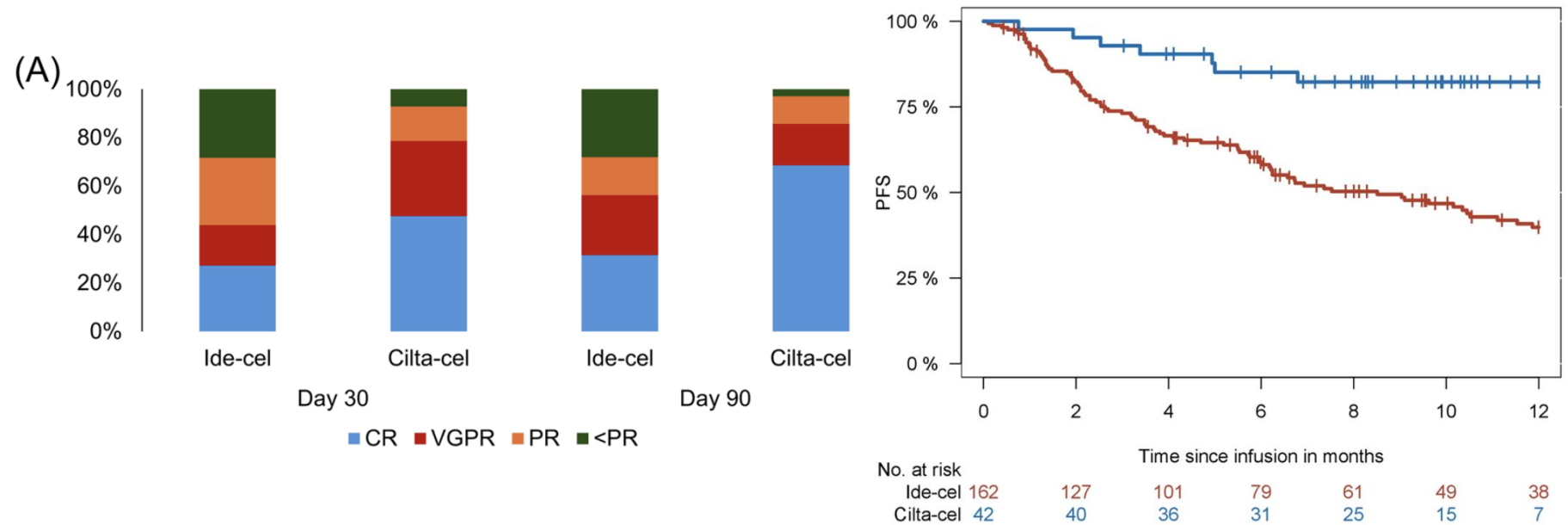
Balance between
safety, efficacy
and timing

Aim: deepest
possible
remission, but

no delay (or
risking not to
perform) CAR
infusion

CILTACABTAGENE AUTOLEUCEL VS IDECABTAGENE VICLEUCEL

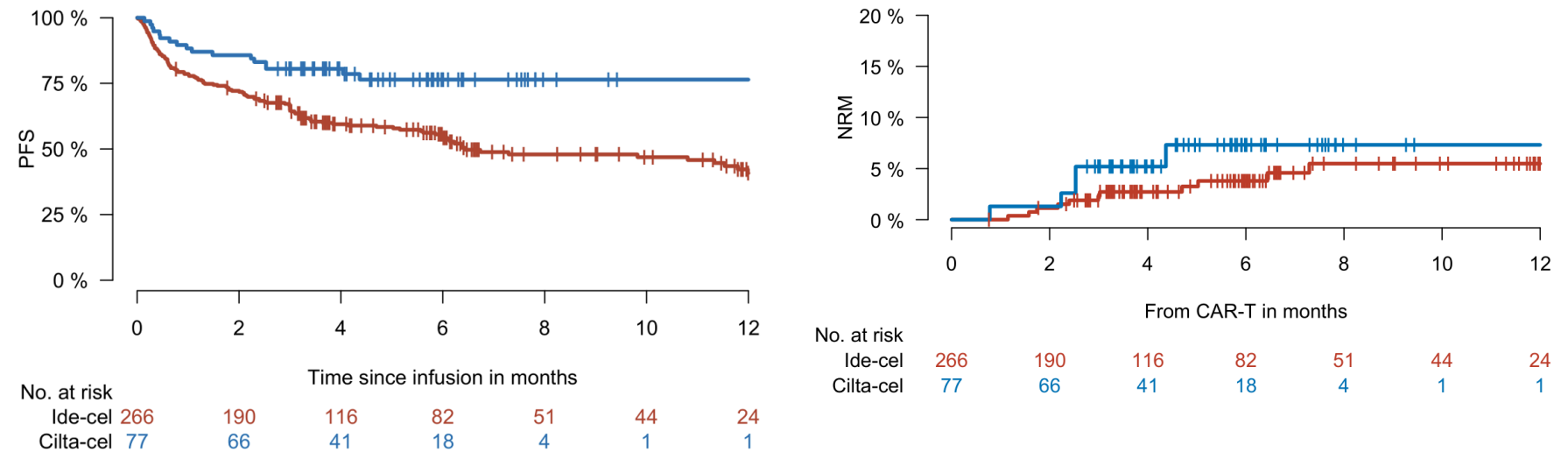
- retrospective analysis from USA and EU
- total N=204
- N=162 ide-cel
- N=42 cilta-cel



cilta-cel showed significantly better efficacy to ide-cel
but no randomized trial!!!!

CILTACABTAGENE AUTOLEUCEL VS IDECABTAGENE VICLEUCEL GERMANY (DRST ANALYSIS)

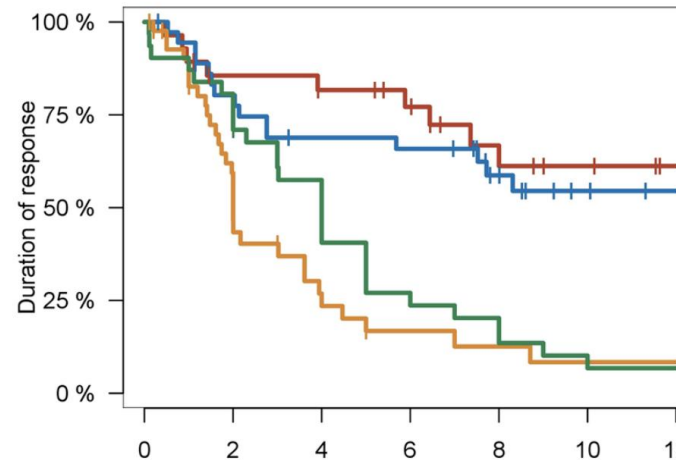
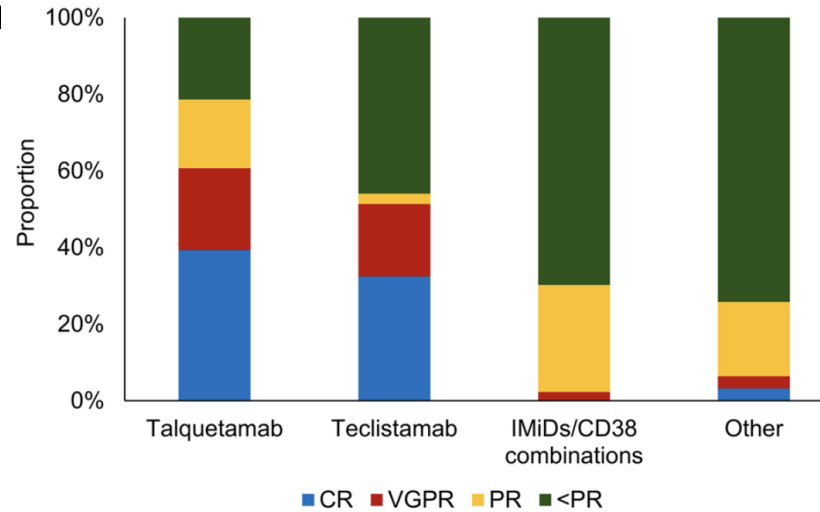
- retrospective analysis from 18 German centers
- N=266 ide-cel
- N=77 cilta-cel



better efficacy of cilta-cel confirmed
no randomized trial!!!

SALVAGE STRATEGIES

- international cohort of N=139 patients with MM relapsing after CAR T
- salvage strategies:
 - talquetamab N=28
 - teclistamab N=37
 - comb. of IMiDs, PI& CD38 N=43
 - others N=31



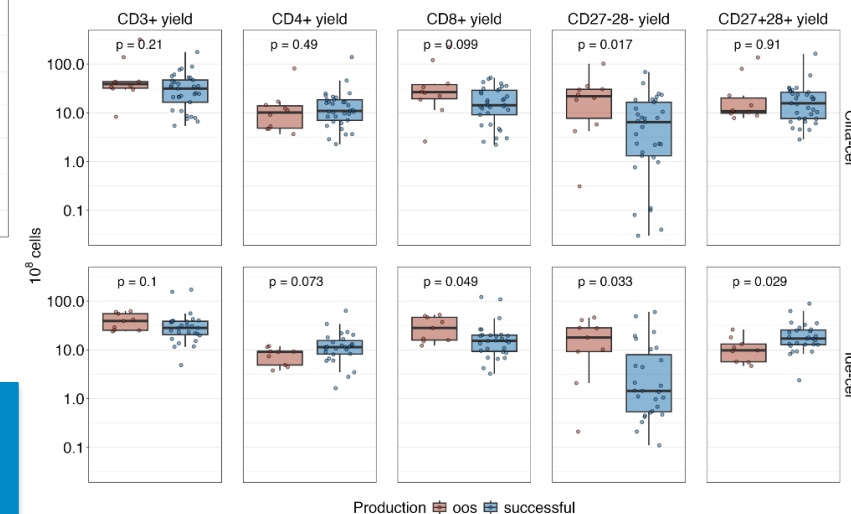
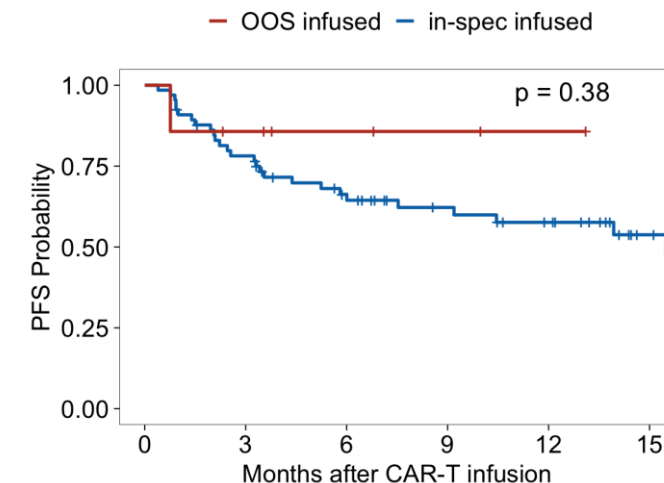
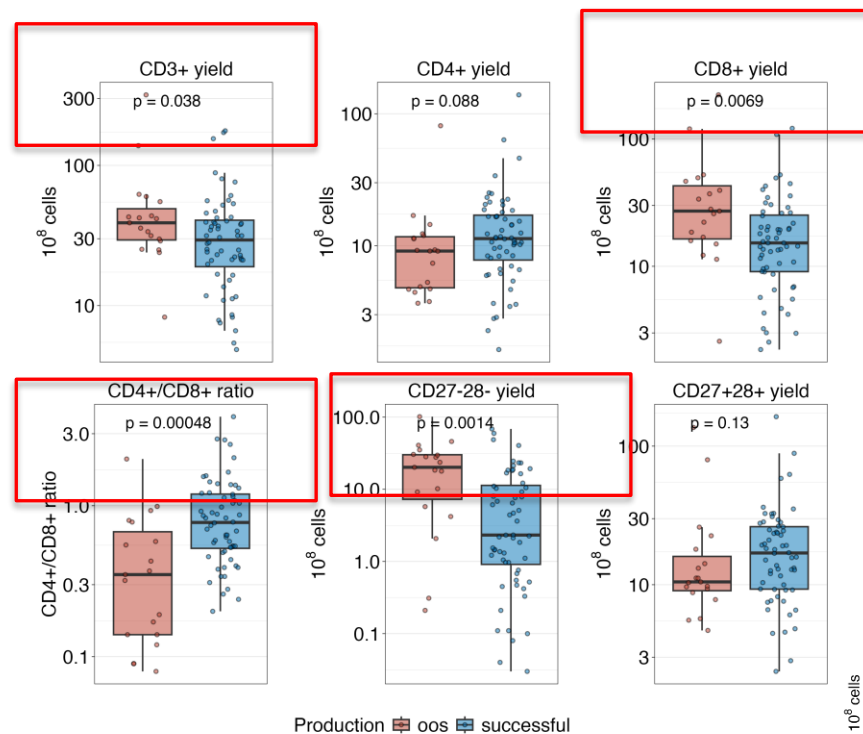
| Factor | Hazard ratio | 95% confidence interval | P |
|---|--------------|-------------------------|--------|
| Model 1 Concordance = 0.74 | | | |
| Treatment group | | | |
| Talquetamab | Reference | | |
| teclistamab | 2.43 | 0.66–9.05 | 0.18 |
| IMiDs/PIs/CD38 | 6.05 | 1.79–20.39 | 0.004 |
| Other | 9.34 | 2.76–31.59 | <0.001 |
| Relapse type | | | |
| No EMD | Reference | | |
| EMD | 2.53 | 1.45–4.43 | 0.001 |
| Time of relapse | | | |
| Early, <3 months | Reference | | |
| Late, >3 months | 0.46 | 0.27–0.80 | 0.006 |
| Penta-refractoriness | 0.89 | 0.52–1.50 | 0.65 |
| ECOG | | | |
| 0 | Reference | | 0.73 |
| 1 | 1.46 | 0.52–2.51 | 0.05 |
| 2 | 2.76 | 1.02–7.05 | |
| Response to 1st salvage | | | |
| CR/VGPR | Reference | | |
| PR or less | 2.54 | 1.45–3.73 | 0.001 |

salvage with bispecific antibodies is associated with better outcomes
no randomized trial!!!!

What should we understand better?

OUT OF SPECIFICATIONS – CLINICAL PARAMETER?

- Unicentric analysis of 84 collections (74 patients)
- focus on clinical data and cellular composition of lymphocyte concentrates
- successful production N=62 (74%)
- terminations N=3 (3%), OOS N=19 (23%)
- No influence of age, gender, product, R-ISS, cytogenetics, remission, prior treatment lines, but...



prior exposition to bispecific antibodies associated with higher rates of OOS

SECONDARY MALIGNANCIES

PERSPECTIVE f X in

Secondary Cancers after Chimeric Antigen Receptor T-Cell Therapy

Authors: Nicole Verdun, M.D., and Peter Marks, M.D., Ph.D. 👤 [Author Info & Affiliations](#)

Published January 24, 2024 | N Engl J Med 2024;390:584-586 | DOI: 10.1056/NEJMp2400209 | [VOL. 390 NO. 7](#)

ORIGINAL ARTICLE | BRIEF REPORT f X in

Indolent CD4+ CAR T-Cell Lymphoma after Cilta-cel CAR T-Cell Therapy

Authors: Metin Ozdemirli, M.D., Ph.D., Thomas M. Loughney, M.D., Emre Deniz, Ph.D., Joefrey J. Chahine, Ph.D., Maher Albitar, M.D., Stefania Pittaluga, M.D., Sam Sadigh, M.D., Philippe Armand, M.D., Ph.D., Aykut Uren, M.D., and Kenneth C. Anderson, M.D. [Author Info & Affiliations](#)

ORIGINAL ARTICLE f X in

Risk of Second Tumors and T-Cell Lymphoma after CAR T-Cell Therapy

Authors: Mark P. Hamilton, M.D., Ph.D., Takeshi Sugio, M.D., Ph.D. 👤, Troy Noordenbos, M.D., Ph.D., Shuyu Shi, B.Med., Philip L. Bulterys, M.D., Ph.D., Chih Long Liu, Ph.D., Xiaoman Kang, B.S., 👤, and David B. Miklos, M.D., Ph.D. [Author Info & Affiliations](#)

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Aggressive Lymphoma after CD19 CAR T-Cell Therapy

Authors: Guido Kobbe, M.D., Monika Brüggemann, M.D., Ben-Niklas Baermann, M.D., Laura Wiegand, Heiko Trautmann, Ph.D., Schayan Yousefian, M.Sc. 👤, Silvana Libertini, Ph.D., +31, and Sascha Dietrich, M.D. [Author Info & Affiliations](#)

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T cell malignancies after CART cell therapy in the DESCART registry

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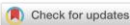
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705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES | NOVEMBER 2, 2023

CAR+ T-Cell Lymphoma Post Ciltacabtagene Autoleucl Therapy for Relapsed Refractory Multiple Myeloma

Simon J. Harrison, Tamia Nguyen, Marzia Rahman, Jeremy Er, Jessica Li, Katherine Li, Nikoletta Lendvai, Jordan M. Schecter, Arnob Banerjee, Tito Roccia, Brad Foulk, Junchen Gu, Hao Zhao, Denis Smirnov, Ana Slaughter, Carolina Lonardi, Erin Lee, Loreta Marquez, Shirin Jadidi, Octavio Costa Filho, Nitin Patel, Dong Geng, Nicole M Haynes, Hannah Kelly, Stephen Lade, Sean Grimmond, Piers Blombery

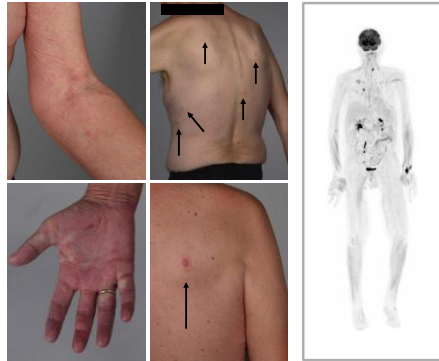


Blood (2023) 142 (Supplement 1): 6939.

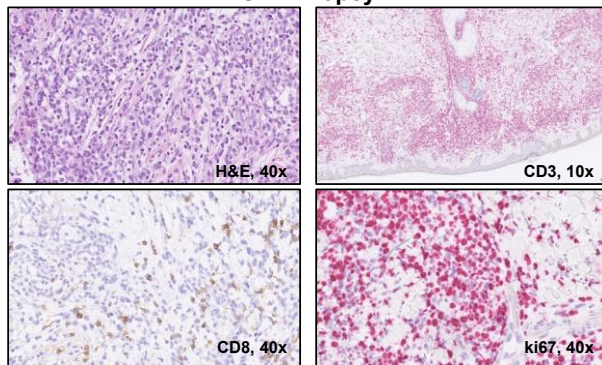
<https://doi.org/10.1182/blood-2023-178806>

SECONDARY MALIGNANCIES - EXAMPLE

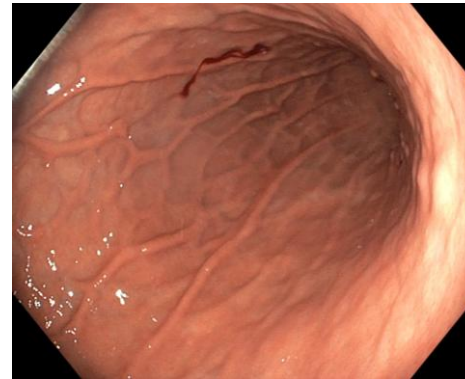
(Sub-)cutaneous T-cell infiltration
[9 months post CAR-T infusion]



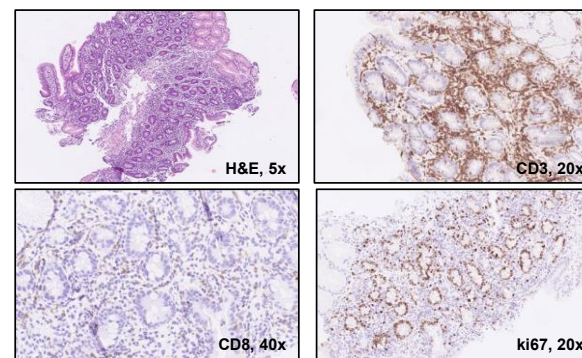
Skin Biopsy



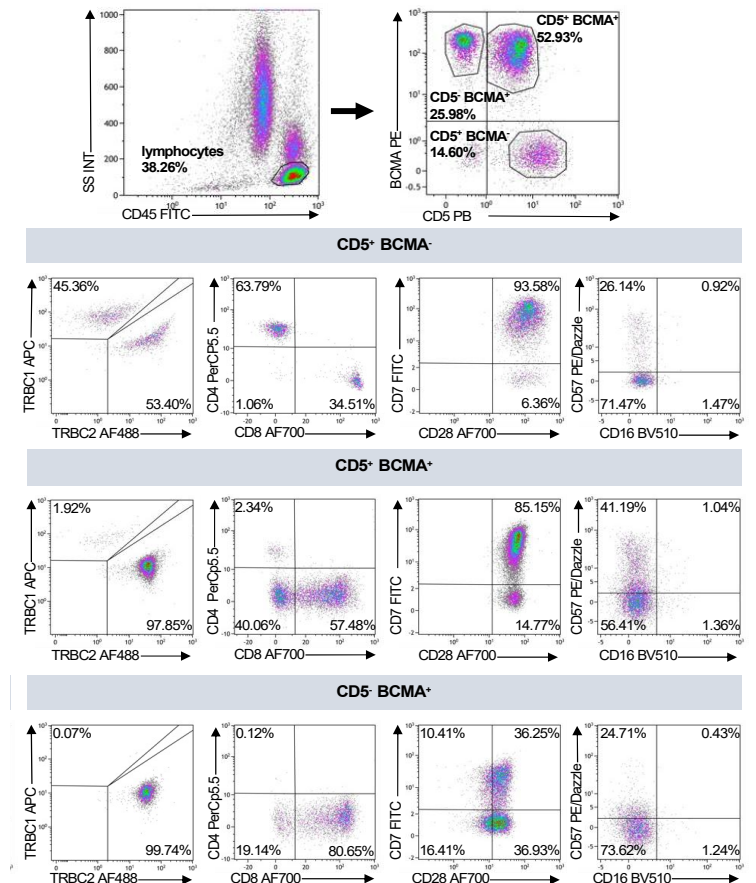
Duodenal T-cell infiltration
[12 months post CAR-T infusion]



Duodenal Biopsy

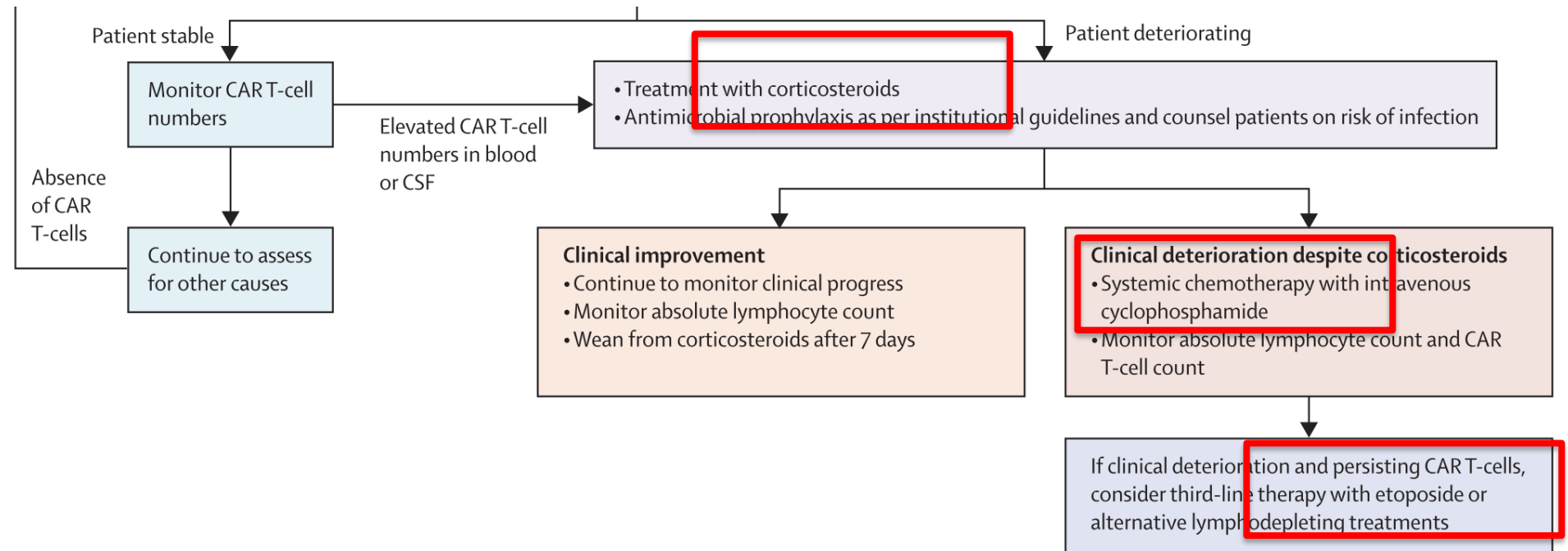


Biclonal CAR+ T-cell proliferation in pB



NON-ICANS NEUROTOXICITIES (EXAMPLE MOTONEURON DISEASE)

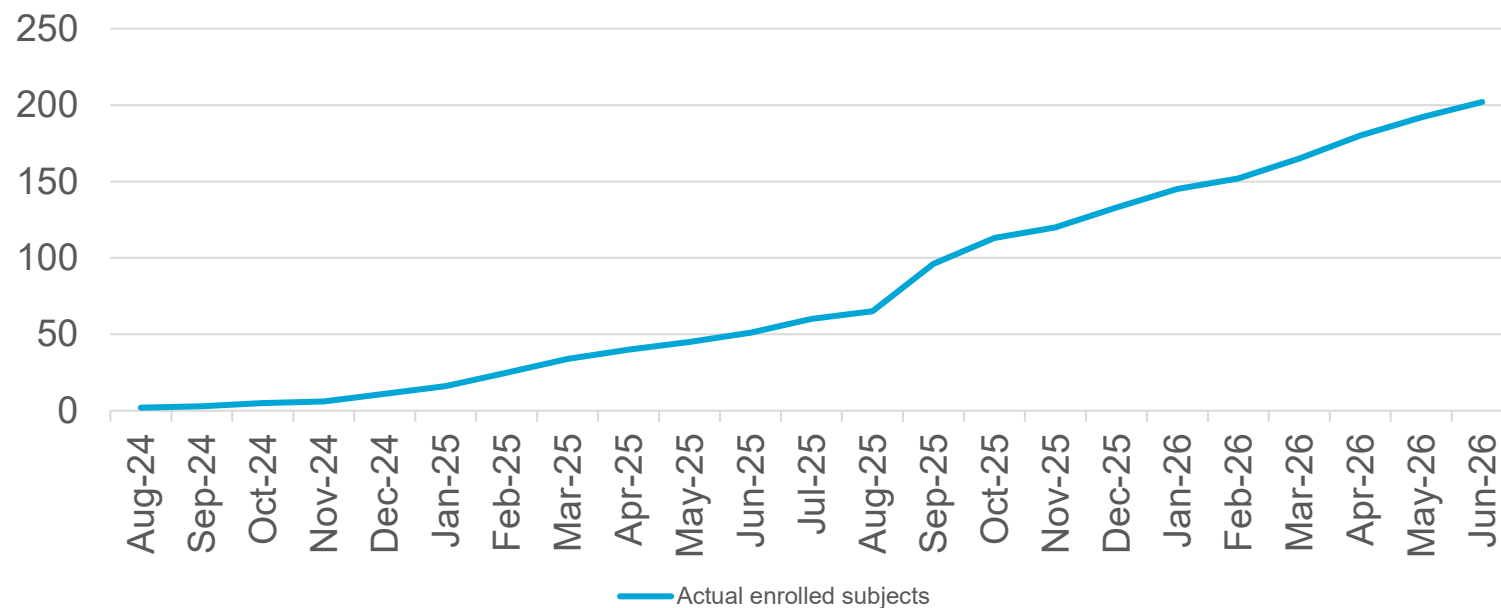
- complication associated with BCMA CAR T
- on-target toxicity (BCMA expression in basal ganglia)



HOW CAN WE LEARN MORE?

Enrollment Status 05Jun2026
202 patients enrolled/ 2 in screening

- CARTITUDE-P9
- Assessment of real-world issues regarding cilta-cel



the way to try to understand the efficacy and management of late events

What will we learn soon?

CAR T vs high-
dose therapy?

new BCMA
targeted
products

dual targeting
CAR T
(BCMA/GPRC5D
or
BCMA/CD19)

CAR T from
stemness like T-
cells
(optimization of
starting material)

CONCLUSION

- CAR T treatment is standard for patients with relapsed multiple myeloma, and the landscape of therapies is changing (rapidly)
- Factors like EMD, high-risk cytogenetics or pre-treatment ferritine can influence outcomes
- in-vivo expansion of CAR T cells seems to be associated with better outcomes (and side-effects)
- late complications like motoneuron-disease or IEC-induced enterocolitis are associated with extensive CAR T expansion
- cilta-cel is associated with better outcomes, BUT

CLINICAL TRIALS ARE NECESSARY TO VALIDATE THE REAL-WORLD RESULTS

THANK YOU FOR YOUR ATTENTION!



Fraunhofer-Institut für Zelltherapie und Immunologie IZI



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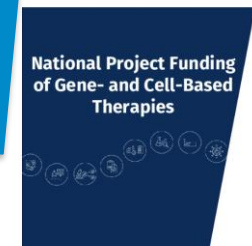
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2025



Patients and their families