# Anti BCMA CART post BITE’s or Belantamab treatment

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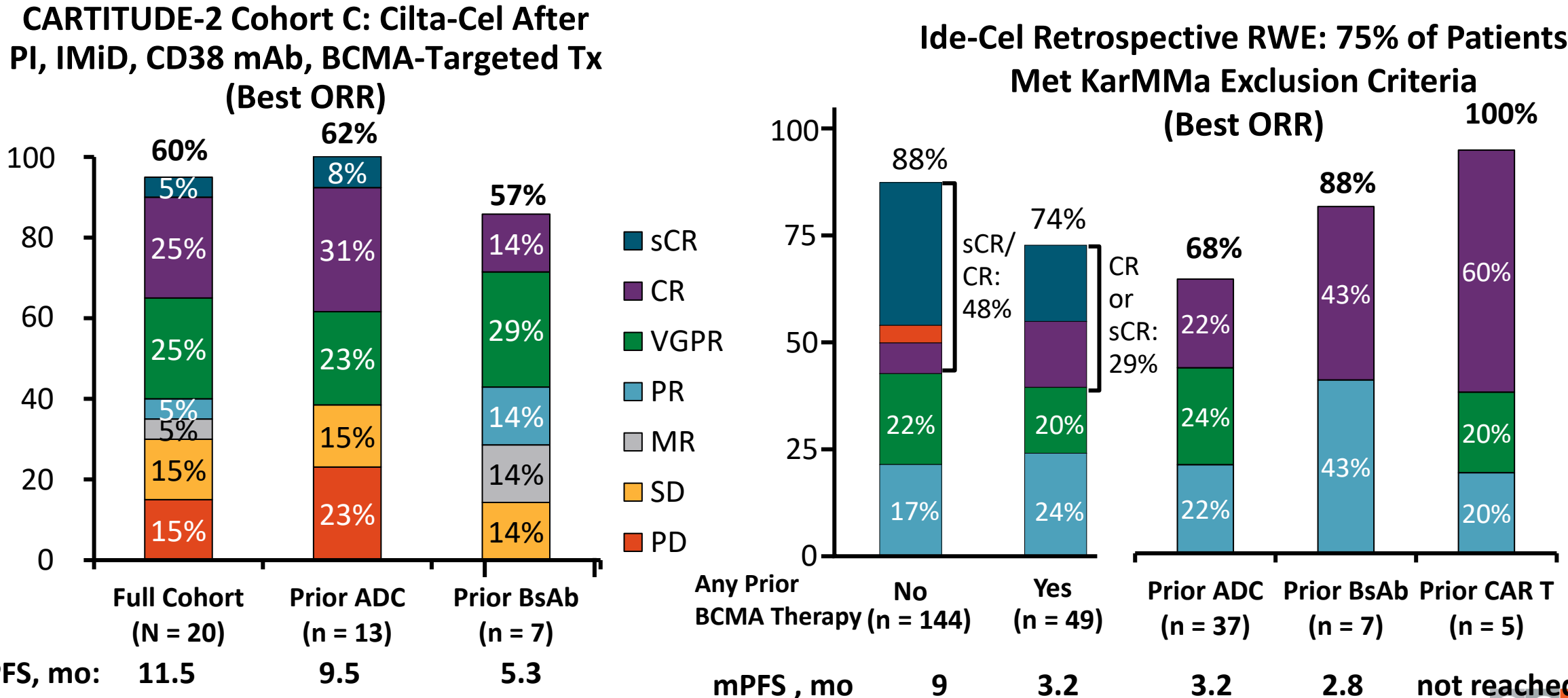
5/2025

# Role of Prior BCMA-Targeted Therapies on CAR T-Cell Therapy Outcomes




Cohen. Blood. 2023;141:219. Ferreri. Blood Cancer J. 2023;13:117.

Slide credit: clinicaloptions.com

# CARTITUDE-2 Cohort C

**Timing of B-cell maturation antigen (BCMA)-targeting treatment**

| Treatments | Total cilta-cel N = 18* | |
|---|---|---|
| | Responders n = 12 | Nonresponders n = 6 |
| Duration of last anti-BCMA treatment, days | | |
| Median | 29.5 | 63.5 |
| Range | 1-277 | 22-527 |
| Time from last anti-BCMA treatment to apheresis, days | | |
| Median | 161.0 | 56.5 |
| Range | 26-695 | 40-895 |
| Time from last anti-BCMA treatment and cilta-cel infusion, days | | |
| Median | 235.0 | 117.5 |
| Range | 62-749 | 95-944 |

# Ide-Cel Retrospective RWE

## Table 3 Selected variables for ide-cel responders compared to non-responders in the prior BCMA-TT cohort.

From: Real-world experience of patients with multiple myeloma receiving ide-cel after a prior BCMA-targeted therapy

| Variable | Responders (*N* = 36) | Non-responders (*N* = 13) | *P* |
|---|---|---|---|
| Duration of therapy with prior BCMA-TT in days, median (range)[a] | 23 (1–208) | 63 (1–370) | 0.025 |
| Time from last BCMA-TT to apheresis in days, median (range) | 169.5 (30–1066) | 84 (1–286) | 0.017 |
| Time from last BCMA-TT to ide-cel infusion in days, median (range) | 209 (16–1118) | 128 (32–362) | 0.052 |
| Ide-cel cell dose ($\times 10^6$), mean (SD) | 392.3 (58.9) | 397.7 (43.7) | 0.95 |
| Received systemic therapy between last BCMA-TT and apheresis, *n* (%) | 28 (78%) | 9 (69%) | 0.539 |

## Supplemental Table 1. Responses by treatment history with BCMA-targeting agent

| Patient | Best response to anti-BCMA agent | Duration of last anti-BCMA agent (days) | Time from last anti-BCMA agent to apheresis (days) | Time from last anti-BCMA agent to cilta-cel infusion (days) | Received anti-BCMA as last line (Y/N) | Responder to cilta-cel (Y/N) | Best confirmed response to cilta-cel[a] | Cause of death (if applicable) |
|---|---|---|---|---|---|---|---|---|
| ADC-1 | sCR | 527 | 895 | 944 | N | N | SD | |
| ADC-2[b] | PD | 1 | 594 | 679 | N | Y | sCR | |
| ADC-3 | SD | 21 | 695 | 749 | N | Y | VGPR | PD |
| ADC-4 | VGPR | 277 | 182 | 271 | N | Y | CR | AE: Covid-19 pneumonia |
| ADC-5[c] | PD | 63 | 57 | 99 | Y | N | PD | |
| ADC-6 | PD | 23 | 161 | 243 | N | Y | CR | |
| ADC-7[d] | NE | 1 | 85 | 147 | N | Y | CR | |
| ADC-8[b] | PD | 64 | 26 | 62 | Y | Y | CR | |
| ADC-9 | SD | 22 | 139 | 180 | N | Y | VGPR | |
| ADC-10 | PD | 22 | 49 | 177 | Y | N | SD | |
| ADC-11 | PD | 44 | 128 | 210 | N | Y | VGPR | |
| ADC-12 | SD | 64 | 56 | 116 | Y | N | PD | PD |
| ADC-13 | VGPR | 54 | 40 | 95 | N | N | PD | PD |
| BsAb-1 | SD | 127 | 280 | 329 | N | Y | CR | |
| BsAb-2 | SD | 36 | 281 | 325 | N | Y | VGPR | |
| BsAb-3 | VGPR | 71 | 161 | 227 | Y | Y | PR | AE: Covid-19 pneumonia |
| BsAb-4 | CR | 260 | 77 | 119 | N | N | SD | |
| BsAb-5 | PD | 15 | 251 | 307 | N | N | MR | AE: Subarachnoid hemorrhage |
| BsAb-6[b] | PD | 23 | 28 | 84 | Y | Y | VGPR | |
| BsAb-7 | SD | 130 | 84 | 124 | N | N | NE | AE: *C difficile* colitis |

CLINICAL TRIALS AND OBSERVATIONS | JANUARY 2, 2025

# Safety and efficacy of standard-of-care ciltacabtagene autoleucel for relapsed/refractory multiple myeloma

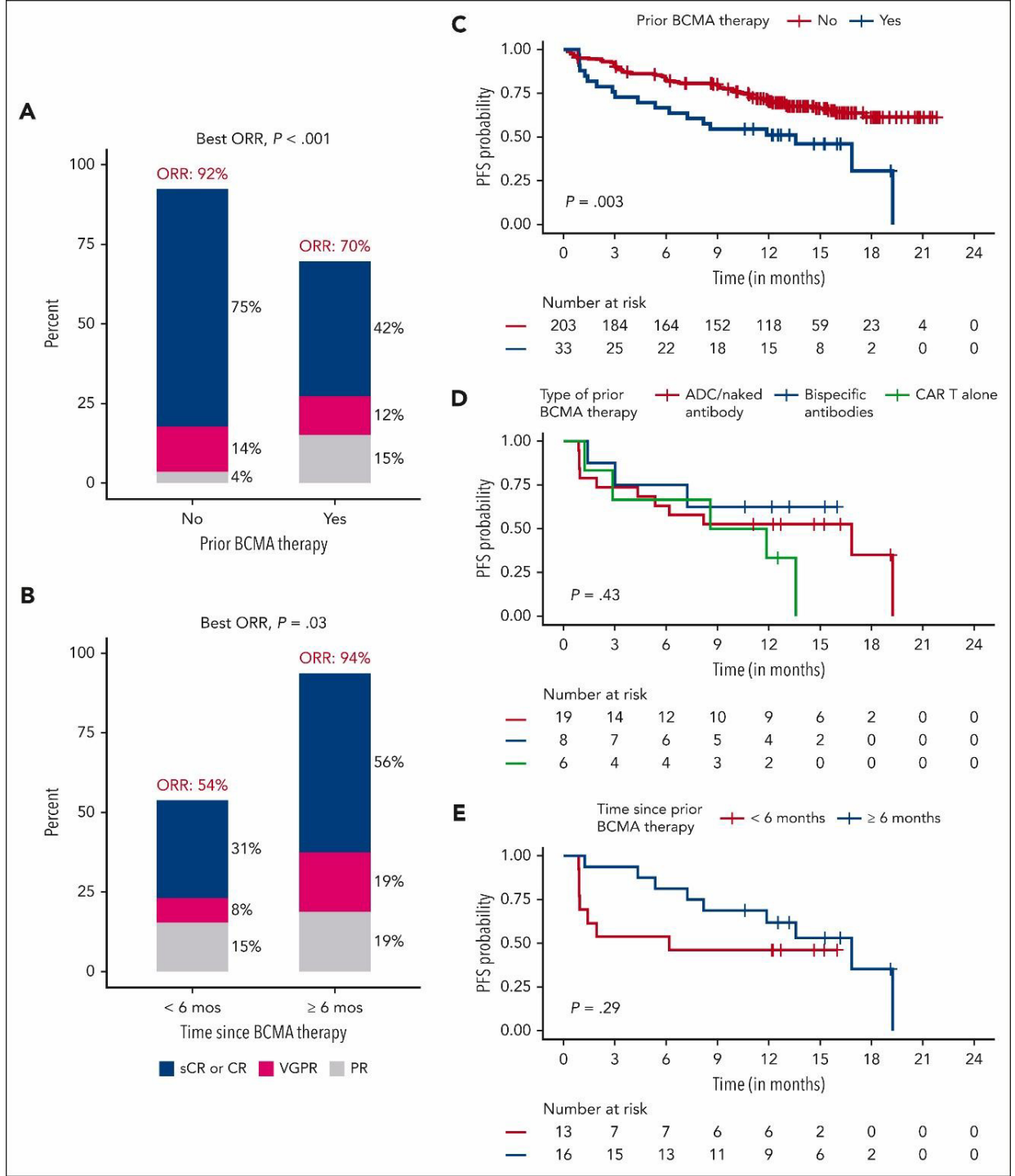
Clinical Trials & Observations

Surbhi Sidana, Krina K. Patel, Lauren C. Peres, Radhika Bansal, Mehmet H. Kocoglu, Leyla Shune, Shebli Atrash, Kinaya Smith, Shonali Midha, Christopher Ferreri, Binod Dhakal, Danai Dima, Patrick Costello, Charlotte Wagner, Ran Reshef, Hitomi Hosoya, Lekha Mikkilineni, Djordje Atanackovic, Saurabh Chhabra, Ricardo Parrondo, Omar Nadeem, Hashim Mann, Nilesh Kalariya, Vanna Hovanky, Gabriel De Avila, Ciara L. Freeman, Frederick L. Locke, Melissa Alsina, Sandy Wong, Megan Herr, Myo Htut, Joseph McGuirk, Douglas W. Sborov, Jack Khouri, Thomas Martin, Murali Janakiram, Yi Lin, Doris K. Hansen

16 US centers
236 received cilta-cel, of which 54% would not have met CARTITUDE-1 eligibility criteria.

| | |
|---|---|
| Prior anti-BCMA therapy | 33 (14%) |
| Prior bispecific antibody (any target) | 10 (4%) |

ADC 16
CART 6
ADC_CART 2
BCMA BITE 8
ADC+BITE 1


A
Best ORR, P < .001
ORR: 92%
ORR: 70%
75%
14%
4%
42%
12%
15%
Percent
No
Yes
Prior BCMA therapy
B
Best ORR, P = .03
ORR: 54%
ORR: 94%
31%
8%
15%
56%
19%
19%
Percent
< 6 mos
≥ 6 mos
Time since BCMA therapy
sCR or CR
VGPR
PR
C
Prior BCMA therapy
No
Yes
PFS probability
P = .003
Time (in months)
Number at risk
203 184 164 152 118 59 23 4 0
33 25 22 18 15 8 2 0 0
D
Type of prior BCMA therapy
ADC/naked antibody
Bispecific antibodies
CAR T alone
PFS probability
P = .43
Time (in months)
Number at risk
19 14 12 10 9 6 2 0 0
8 7 6 5 4 2 0 0 0
6 4 4 3 2 0 0 0 0
E
Time since prior BCMA therapy
< 6 months
≥ 6 months
PFS probability
P = .29
Time (in months)
Number at risk
13 7 7 6 6 2 0 0 0
16 15 13 11 9 6 2 0 0

# Role of Talquetmab prior anti BCMA CART

| | Previous TCR | Subsequent TCR | ORR, % | Median DOR, mos | Median PFS, mos | Median OS, mos |
|---|---|---|---|---|---|---|
| **MonumenTAL-1 (123)** | talquetamab | CAR-T | 67 | NA | NA | NA |

| Therapy | Line of Therapy (n) | ORR on Subsequent Therapy, % (n) | Median Interval From TALVEY to Subsequent Therapy (Range), Months |
|---|---|---|---|
| CAR-T | First (17) | 64.7 (11/17) | 0.9 (0.1-7.4) |
| | Second (12) | 53.8 (7/13) | 5.6 (1.7-14.8) |
| | Third (1) | 0 (0/1) | 8.0 (8.0-8.0) |
| | Fourth (2) | 50.0 (1/2) | 5.3 (5.2-5.5) |

Sanchez et al. Clinical Outcomes of Subsequent Therapies in patients with relapsed/refractory multiple myeloma following talquetamab treatment: analyses from the phase 1/2 MonumenTAL-1 Study. Blood. 2023

P-036

# BCMA after GPRC5D: Efficacy of BCMA-Directed Therapy on Patients with Relapsed/Refractory Multiple Myeloma (RRMM) Progressing After GPRC5D-Directed Therapy

*Laura Joiner[1], Luciano Costa[1], Smith Giri[2], Gayathri Ravi[1], Kelly Godby[2], Caitlin Hagedorn[1], Susan Bal[2]*

77 patient received GPRC5D

30 had progression (39%)

21 started subsequent therapy

12 received subsequent BCMA TCRT ( 5 post GPRC5D TCE; 7 post CART)

5 were BCMA naïve. For the 7 BCMA exposed patients ,the BCMA TCRT used prior to GPRC5D TCRT was CART in 6 patients and TCE in 1

9 of the 12 received BCMA TCRT directly following GPRC5D (5 BCMA TCE, 4 BCMA CART)
and 3 received BCMA targeted therapy in subsequent line of treatment (all BCMA TCE)

**1.Response to BCMA therapy *after* GPRC5D failure:**

- **ORR overall: 50%**
  - **80% in BCMA-naïve**
  - **29% in BCMA-exposed**
- **Median follow-up:** 12.23 months (range 0–37.6)

**2.PFS (Progression-Free Survival) after BCMA re-treatment:**

- Overall: **7.06 months**
  - **8.2 months in BCMA-naïve** (95% CI: 2.34–NR)
  - **1.38 months in BCMA-exposed** (95% CI: 0.36–NR)

**3.Efficacy by type of BCMA TCRT:**

- **ORR:**
  - **75% for CAR-T**
  - **38% for TCE**
- **Median PFS:**
  - **7.07 months** for CAR-T (95% CI: 1.25–NR)
  - **2.39 months** for TCE (95% CI: 0.26–NR)
  - .

**Efficacy of Anti-BCMA CAR-T Cell Therapies in Multiple Myeloma Patients with Prior Exposure to Bispecific Antibodies- Results from a Retrospective Multi-Center Registry Analysis**

*Johannes Waldschmidt, MD[1], David Fandrei, MSc[2], Vladan Vucinic, MD[3], Ralph Wäsch[4], Axel Nogai, MD[5], Winfried Alsdorf[6], Annamaria Brioli, MDPhD[7,8], Evgenii Shumilov[9], Fabian Mueller, MD[10], Raphael Teipel, MD[11], Nico Gagelmann, MD[12], Monika Engelhardt, MD[13], Jan Krönke, MD[14], Julia Mersi, MD[1], Michael Hudecek, MD PhD[1], Martin K. Kortüm[15], Uwe Platzbecker, MD[2], Hermann Einsele, MD[16], Max S. Topp[1], Leo Rasche, MD[17,1], Maximilian Merz, MD[2]*

- Retrospective, 9 centers in Germany
- n=39 bsAb-exposed MM pts treated
- Idecel 16 (ORR 62.5%, ≥ VGPR 41.2%), Ciltacel 20 (ORR 85%, ≥ VGPR 70%),
- Med. follow-up of 5.1 months after CAR-T infusion, PFS across the entire cohort was 9.6 months (0.7-NR) with no significant difference between ide-cel and cilta-cel (p=0.63).
- Disease stabilization at the time of lymphodepletion, but not at apheresis showed a relevant trend for longer duration of response to CAR-T (P=0.091)

| | without bsAb exposure prior to apheresis (9) | teclistamab (7) | Talquetamab (15) | both teclistamab and talquetamab before apheresis (5) |
|---|---|---|---|---|
| **PFS m** | Not reached | 9.1 | 16.3 | 4.4 |
| | | | | |

Long-term exposure and refractoriness to teclistamab were specically linked with primary refractoriness to anti-BCMA CAR-Ts. This was illustrated by 2 pts who had been treated with teclistamab for ≥3.0 months and were retrospectively confirmed to have carried a biallelic TNFRSF17 loss by whole-genome sequencing before CAR-T

# Mechanisms to resistance

- **Antigen Escape and Loss of BCMA Expression-** **antigen modulation or downregulation- biallelic BCMA losses or monoallelic losses plus an extracellular mutation) in approximately 40% of patients**
- **T-cell exhaustion**
- **Cytokine Environment**
- **Immune Suppression**
- **Immune Evasion** residual **immune checkpoint signaling** or altered antigen-presenting cells that reduce the CAR T-cell's ability to activate and proliferate effectively.
- **Immunomodulatory Effects of BiTEs:** immune checkpoint upregulation