MM - 770

# Ciltacabtagene Autoleucel in Lenalidomide-Refractory Multiple Myeloma Responding to Bridging Therapy: CARTITUDE-4 Cytogenetic Subgroup Analysis


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## Key Takeaway

Cilta-cel demonstrated a profound benefit in patients with high- and standard-risk cytogenetics when MM is well controlled at time of infusion

## Conclusions

In patients with high- and standard-risk cytogenetics, those with ≥PR to BT had better survival outcomes with cilta-cel compared with those who had <PR to BT

There were no cases of IEC-parkinsonism in patients who had ≥PR to BT

Infections were a key cause of NRM in patients who had <PR to BT


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**Disclosures**

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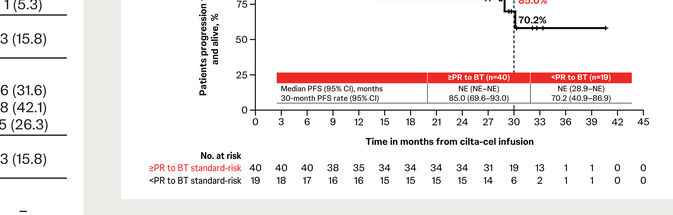
## Introduction

- Previous analyses from the phase 3 CARTITUDE-4 study of patients with lenalidomide-refractory multiple myeloma (MM) after 1–3 prior lines of therapy (pLOT) who were treated with ciltacabtagene autoleucel (cilta-cel) have shown that survival and safety outcomes vary by cytogenetic risk status and response to bridging therapy (BT)[1-3]
  - Patients with high- or standard-risk cytogenetics treated with cilta-cel had improved progression-free survival (PFS) and overall survival (OS) compared with patients treated with standard of care (SOC)[1]
  - Partial response or better (≥PR) during BT was associated with better survival and safety outcomes with cilta-cel[3]
- Emerging real-world data underscore the importance of effective BT before infusion with cilta-cel[4]
- Here, we present efficacy and safety for patients who received cilta-cel as study treatment according to response to BT and cytogenetic risk (median study follow-up, 33.6 months)

## Methods

- CARTITUDE-4 study design is shown in **Figure 1**

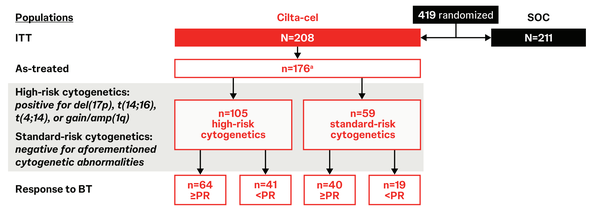
**Figure 1: CARTITUDE-4 study design[2,5]**




[a]Physician's choice. [b]Administered until disease progression. [c]Efficacy data were collected after day 112 every 28 days. [d]Time from randomization to disease progression/death.
AE, adverse event; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; MRD, minimal residual disease; ORR, overall response rate; PD, pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics; PVd, pomalidomide, bortezomib, and dexamethasone.

- Study population is shown in **Figure 2**

**Figure 2: Study population[3,5]**




[a]12 patients did not have cytogenetic risk information available.
ITT, intent-to-treat.

## Results

- 176 patients received cilta-cel as study treatment and were divided into 4 subgroups based on cytogenetics and response to BT:
  - High-risk cytogenetics subgroups (n=105): ≥PR to BT (n=64) and <PR to BT (n=41)
  - Standard-risk cytogenetics subgroups (n=59): ≥PR to BT (n=40) and <PR to BT (n=19)
- Baseline characteristics and response to BT by subgroup are summarized in **Table 1**

**Table 1: Baseline characteristics and response to BT by subgroup**

| Baseline characteristic | High-risk cytogenetics | | Standard-risk cytogenetics | |
|---|---|---|---|---|
| | ≥PR to BT (n=64) | <PR to BT (n=41) | ≥PR to BT (n=40) | <PR to BT (n=19) |
| Median age (range), years | 63.5 (43.0–78.0) | 57.0 (43.0–75.0) | 60.0 (27.0–78.0) | 65.0 (38.0–78.0) |
| ISS stage, n (%) | | | | |
| I | 47 (73.4) | 23 (56.1) | 31 (77.5) | 13 (68.4) |
| II | 16 (25.0) | 13 (31.7) | 7 (17.5) | 5 (26.3) |
| III | 1 (1.6) | 5 (12.2) | 2 (5.0) | 1 (5.3) |
| Higher baseline tumor burden, n (%) | 4 (6.3) | 10 (24.4) | 5 (12.5) | 3 (15.8) |
| pLOT, n (%) | | | | |
| 1 | 26 (40.6) | 9 (22.0) | 14 (35.0) | 6 (31.6) |
| 2 | 24 (37.5) | 17 (41.5) | 14 (35.0) | 8 (42.1) |
| 3 | 14 (21.9) | 15 (36.6) | 12 (30.0) | 5 (26.3) |
| Triple-class[a] refractory, n (%) | 6 (9.4) | 6 (14.6) | 2 (5.0) | 3 (15.8) |
| Response to BT, n (%) | | | | |
| sCR | 1 (1.6) | – | 0 | – |
| CR | 3 (4.7) | – | 1 (2.5) | – |
| VGPR | 17 (26.6) | – | 15 (37.5) | – |
| PR | 43 (67.2) | – | 24 (60.0) | – |
| MR | – | 6 (14.6) | – | 2 (10.5) |
| SD | – | 32 (78.0) | – | 17 (89.5) |
| NE | – | 3 (7.3) | – | 0 |

[a]PI + immunomodulatory agent + CD38 antibodies.
MR, minimal response; NE, not evaluable; PD, progressive disease; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

### High-risk cytogenetics subgroups by response to BT

- In patients with ≥PR to BT, median PFS and OS were not reached; 30-month PFS and OS rates were 65.1% (95% CI, 51.4–75.8) and 87.2% (95% CI, 76.1–93.4), respectively
- Patients with <PR to BT had median PFS of 35.2 months and median OS was not reached; 30-month PFS and OS rates were 51.2% (95% CI, 35.1–65.2) and 75.6% (95% CI, 59.4–86.1), respectively

### Standard-risk cytogenetics subgroups by response to BT

- In patients with ≥PR to BT, median PFS and OS were not reached; 30-month PFS and OS rates were 85.0% (95% CI, 69.6–93.0) and 92.5% (95% CI, 78.5–97.5), respectively
- For patients with <PR to BT, median PFS and OS were not reached; 30-month PFS and OS rates were 70.2% (95% CI, 40.9–86.9) and 76.6% (48.0–90.7)

### Kaplan-Meier estimated PFS and OS by cytogenetic risk status and response to BT

- Deeper responses to BT were associated with improved PFS and OS outcomes in the high- and standard-risk cytogenetics subgroups (**Figures 3 and 4**)

**Figure 3A: PFS from cilta-cel infusion in the high-risk cytogenetics subgroup by response to BT**

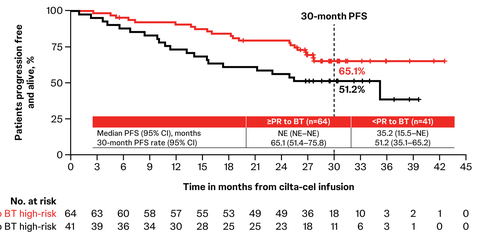



**Figure 3B: OS from cilta-cel infusion in the high-risk cytogenetics subgroup by response to BT**

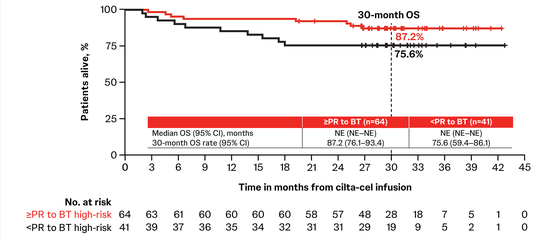
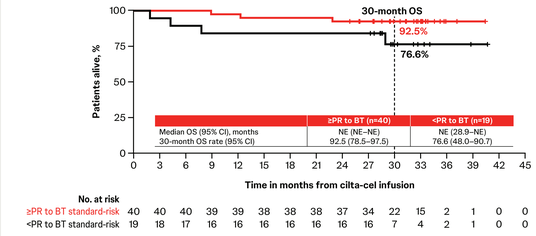



**Figure 4A: PFS from cilta-cel infusion in the standard-risk cytogenetics subgroup by response to BT**




**Figure 4B: OS from cilta-cel infusion in the standard-risk cytogenetics subgroup by response to BT**




### Safety (Table 2)

- Grade 3/4 infections were numerically higher in patients with high-risk cytogenetics (≥PR to BT, 43.8%; <PR to BT, 48.8%) vs standard-risk cytogenetics (≥PR to BT, 30.0%; <PR to BT, 26.3%) subgroups
- Patients with ≥PR to BT experienced fewer fatal infections, irrespective of cytogenetic risk
- There were no cases of immune effector cell (IEC)-parkinsonism in patients who achieved ≥PR to BT
- Nonrelapse mortality (NRM) rates were higher in patients who had <PR to BT, regardless of cytogenetic risk

**Table 2: AEs in patients with high- and standard-risk cytogenetics**

| AE, n (%) | High-risk cytogenetics | | Standard-risk cytogenetics | |
|---|---|---|---|---|
| | ≥PR to BT (n=64) | <PR to BT (n=41) | ≥PR to BT (n=40) | <PR to BT (n=19) |
| CRS | 47 (73.4) | 34 (82.9) | 28 (70.0) | 16 (84.2) |
| ICANS | 5 (7.8) | 2 (4.9) | 0 | 1 (5.3) |
| CNP | 7 (10.9) | 4 (9.8) | 2 (5.0) | 2 (10.5) |
| IEC-parkinsonism | 0 | 1 (2.4)[b] | 0 | 0 |
| Grade 3/4 infections | 28 (43.8) | 20 (48.8) | 12 (30.0) | 5 (26.3) |
| NRM | 7 (10.9) | 6 (14.6) | 2 (5.0) | 4 (21.1) |
| Infections[a] | 4 (6.2) | 5 (12.2) | 0 | 2 (10.5) |

[a]≥PR to BT: COVID-19 infection (n=2), cytomegalovirus colitis (n=1), fungal pneumonia (n=1); <PR to BT: COVID-19 infection (n=5), pneumonia (n=1), *Pneumocystis jirovecii* pneumonia (n=1).
[b]Occurred in a patient with unconfirmed PD at cilta-cel infusion.
CNP, cranial nerve palsy; ICANS, immune effector cell-associated neurotoxicity syndrome.


**References**

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Multiple Myeloma