P-005

Effectiveness of Bridging Therapy Corresponds to Improved Outcomes After Receiving CAR-T Therapy in the Phase 3 CARTITUDE-4 Study of Patients With Relapsed, Lenalidomide-Refractory Multiple Myeloma

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Key Takeaway

In CARTITUDE-4, an improved response to bridging therapy correlates with longer PFS, highlighting the importance of optimizing bridging therapy for effective disease control prior to administering cilta-cel

Conclusions

In patients who received cilta-cel treatment, a ≥25% tumor burden reduction following bridging therapy correlated with longer PFS

The correlation between tumor burden reduction and PFS may be explained mechanistically by a higher in vivo E:T ratio (calculated by the ratio peak CAR-T expansion and pre-infusion sBCMA) , which was previously shown to be associated with longer PFS with cilta-cel[2]

These findings support the benefits of effective bridging therapy; additional research is needed to further optimize bridging strategies to maximize patient outcomes

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Poster

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Acknowledgments

The authors, Janssen, and Legend Biotech USA Inc. thank the patients who participated in this study, the staff members at the study sites, the data and safety monitoring committee, and the staff members involved in data collection and analyses. This study was funded by Janssen Research & Development, LLC, and Legend Biotech USA, Inc. The authors thank Feng Wang, PhD (of Janssen Research & Development, Shanghai, China) for support with translational correlative analyses, and Nikoletta Lendvai, MD (of Janssen Research & Development, Raritan, NJ, USA) for support with critical review of the poster. Medical writing support was provided by Maggie Hartman, PharmD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Disclosures

SA has no disclosures.

Introduction

- In the phase 3 CARTITUDE-4 trial, patients receiving ciltacabtagene autoleucel (cilta-cel) without pre-infusion disease progression showed high ORR (99.4%), ≥CR (86.4%), and 12-month PFS rate (89.7%[a])[1]
- Bridging therapy helps control disease during manufacturing, potentially reducing the risk of toxicities by debulking
- The impact of disease control prior to CAR-T infusion on post-infusion outcomes is not well established
- Post hoc analyses of cilta-cel efficacy by response to bridging therapy in patients who received cilta-cel as study treatment in CARTITUDE-4 are presented

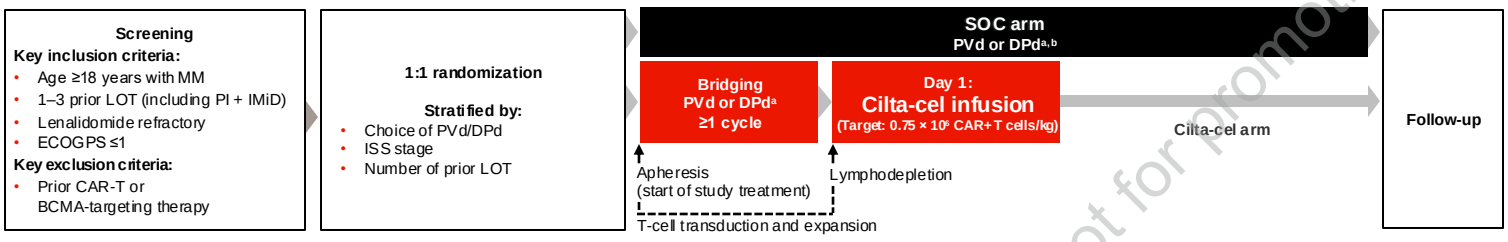
[a]Measured from randomization.

Methods

- Patients in the cilta-cel arm underwent apheresis and bridging therapy followed by a single cilta-cel infusion 5–7 days after the start of lymphodepletion (**Figure 1**)
  - Bridging therapy was physicians' choice of either PVd or DPd
- PFS was measured from randomization and analyzed in patients with a ≥25% tumor burden reduction from baseline to the start of lymphodepletion vs <25% (tumor burden either increased, no change, or <25% reduction)[b]. Tumor burden change was measured by determining the difference between paraprotein at baseline and at lymphodepletion for each patient
- In vivo effector-to-target (E:T) ratio was derived by peak CAR-T cell expansion (assessed by flow cytometry) normalized to pre-infusion serum soluble B-cell maturation antigen (sBCMA) levels

[b]2 patients were not evaluable.

Figure 1: CARTITUDE-4 study design



[a]Physicians' choice. [b]Administered until disease progression. BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; LOT, line of therapy; PI, proteasome inhibitor; PVd pomalidomide, bortezomib, and dexamethasone; SOC, standard of care.

Results

Patients

- A total of 176 patients received cilta-cel as study treatment, and among these, 158 received DPd bridging therapy and 18 received PVd
- During the bridging period, 148 (84%) had a ≥25% tumor burden reduction, while 28 (16%) had <25% decrease
- The group with ≥25% decrease had a higher proportion of patients with International Staging System (ISS) Stage I disease (70.9% vs 57.1%) and fewer patients with ≥60% plasma cells (15.6% vs 35.7%) compared with the <25% decrease group, respectively (**Table**)

Table: Baseline disease characteristics of patients who received cilta-cel as study treatment (N=176; ≥25% decrease N=148, <25% decrease, N=28)

Baseline characteristic	Tumor burden decrease ≥25% (N=148)	Tumor burden decrease <25% (N=28)
ISS stage, n (%)		
I	105 (70.9)	16 (57.1)
II	37 (25.0)	8 (28.6)
III	6 (4.1)	4 (14.3)
Years since diagnosis, median (range)	3.4 (0.3-18.1)	3.2 (0.3-12.1)
Presence of soft tissue plasmacytomas, n (%)	25 (16.9)	5 (17.9)
≥60% plasma cells[a], bone marrow aspirate, n (%)	23 (15.6)	10 (35.7)
Cytogenetic risk,[a] n (%)		
Standard risk	50 (34.0)	9 (32.1)
High risk	88 (59.9)	17 (60.7)

[a]Percentages were based out of n=147 for the ≥25% tumor burden reduction subgroup based on sample availability.

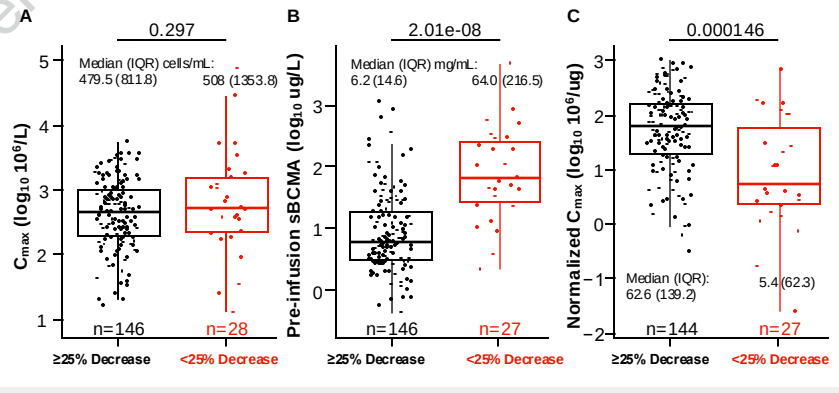
Cilta-cel efficacy by response to bridging therapy

- At 15.9-month median follow-up, median PFS was not reached (95% CI, not estimable [NE]–NE) in patients with ≥25% decrease vs 19.2 months (95% CI,15.8–NE) in the <25% decrease group (HR, 0.32; 95% CI, 0.16–0.66) (**Figure 2**)
  - Estimated 15-month PFS rates were 87.5% and 74.0%, respectively

Biomarker correlates of response to bridging therapy and post cilta-cel outcomes

- In patients with available biomarker data, those with a ≥25% decrease in tumor burden had a comparable CAR-T peak expansion in the blood (C_{max}), lower sBCMA levels pre-infusion, and hence a significantly higher in vivo E:T ratio vs the <25% decrease group (**Figure 3**)
  - Lower pre-infusion sBCMA levels were observed in patients with greater tumor burden reduction, but no difference in C_{max} was observed
  - The in vivo E:T ratio, adjusted for baseline tumor burden variations, was higher in patients with effective bridging therapy

Figure 3: C_{max} (A), sBCMA (B), and E:T ratio (C) by response to bridging therapy in patients with ≥25% tumor reduction



- Patients with higher E:T ratios demonstrated improved PFS (**Figure 4**)
  - In vivo E:T ratio has previously been shown to have a strong correlation with PFS in cilta-cel–treated patients.[2] In vivo E:T ratio is defined by the ratio of C_{max} to tumor burden (pre-infusion sBCMA)
  - Our data show that C_{max} is similar in both higher and lower tumor burden subgroups, hence the key driver of association to higher PFS probability is reduced tumor burden at baseline, estimated by pre-infusion sBCMA

Figure 4: PFS by E:T ratio (C_{max}/sBCMA after bridging therapy and prior to cilta-cel infusion)

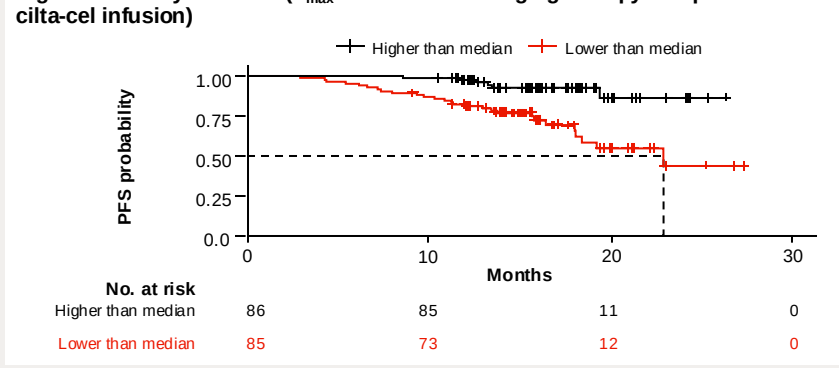
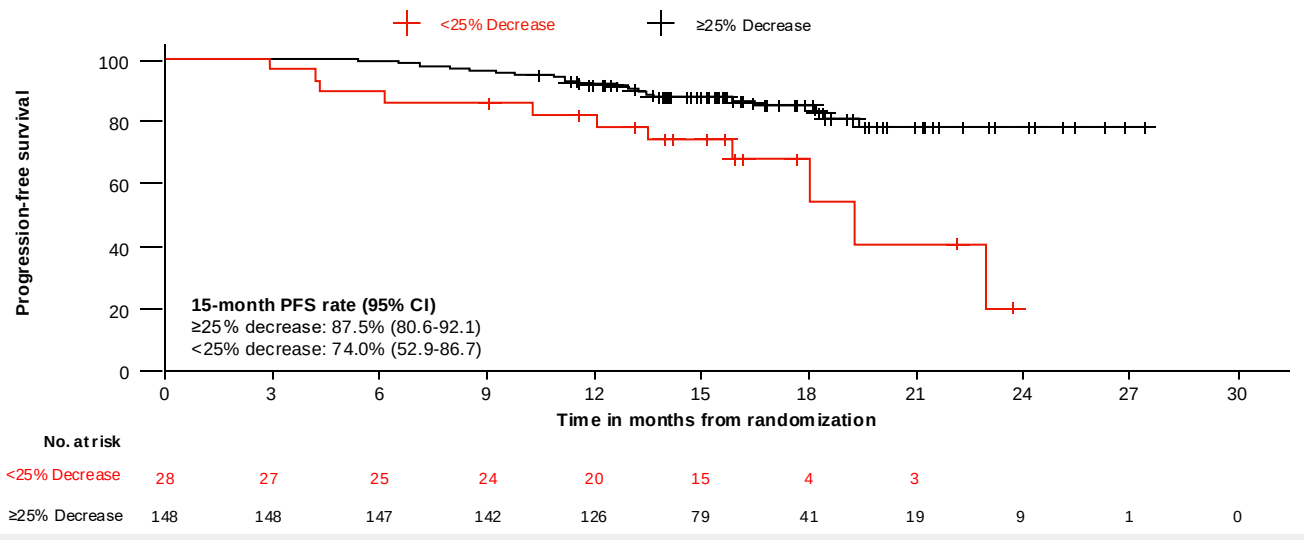


Figure 2: PFS by Tumor burden change of ≥25% between baseline and start of lymphodepletion



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Multiple Myeloma

Presented by S Anguille at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil