MM-1081

Absolute Lymphocyte Count as a Key Biomarker for Monitoring Safety After Ciltacabtagene Autoleucel Infusion

Yi Lin[1*], Rocio Montes de Oca[2*], Binod Dhakal[3], Roberto Mina[4], Salomon Manier[5], Paula Rodríguez-Otero[6], Yaël C Cohen[7], Dominik Dytfeld[8], Feng Wang[9], Katharine Henry[10], Ana Caroline Costa Sa[2], Tzu-Min Yeh[11], Ana Slaughter[12], Nikoletta Lendvai[11], Jieqing Zhu[13], Da Xu[13], Mythili Koneru[13], Nitin Patel[13], Vicki Plaks[2*], Adam D Cohen[14*]

[1]Mayo Clinic, Rochester, MN, USA; [2]Johnson & Johnson, Spring House, PA, USA; [3]Medical College of Wisconsin, Milwaukee, WI, USA; [4]University of Torino and Azienda Ospedaliero-Universitaria (A.O.U.) Città della Salute e della Scienza di Torino, Torino, Italy; [5]University of Lille, CHU Lille, Lille, France; [6]Cancer Center Clínica Universidad de Navarra, Cima, Pamplona, Spain; [7]Tel Aviv Sourasky (Ichilov) Medical Center, Tel Aviv, Israel; Faculty of Medical & Health Sciences, Tel Aviv University, Tel Aviv, Israel; [8]Poznan University of Medical Sciences, Poznań, Poland; [9]Johnson & Johnson, Shanghai, China; [10]Johnson & Johnson, Cambridge, MA, USA; [11]Johnson & Johnson, Raritan, NJ, USA; [12]Johnson & Johnson, Zug, Switzerland; [13]Legend Biotech USA Inc., Somerset, NJ, USA; [14]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

*Equally contributing authors.

Key Takeaway

ALC is an early, readily available biomarker for identifying patients at higher risk for MNTs and CNP after cilta-cel infusion. Monitoring ALC in the first 14 days post infusion may help identify patients at higher risk of MNTs or CNP and guide early intervention strategies

Conclusions

ALC and CAR+ T-cell counts are significantly correlated at and around peak expansion and peaked at a median of 14 days post cilta-cel

Heightened CAR+ T-cell levels post infusion may be associated with the development of MNTs and CNP

Multivariate analyses identified elevated ALC, CAR+ T-cell peak expansion, and CD4 T-cell counts in the first 14 days post infusion as factors associated with higher risk of MNTs and CNP; ALC showed the strongest predictive performance

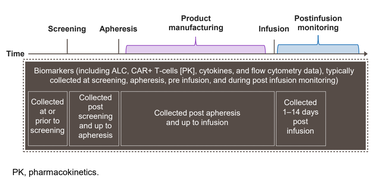
Introduction

- Ciltacabtagene autoleucel (cilta-cel) demonstrated profound efficacy in relapsed/refractory multiple myeloma (RRMM) in CARTITUDE-1[1,2] and CARTITUDE-4[3,4]
- After implementation of mitigation measures, including more effective bridging therapy, the incidence of movement and neurocognitive treatment-emergent adverse events (MNTs) was decreased to 1% in CARTITUDE-4[3,5]
- An association between elevated chimeric antigen receptor (CAR)+ T-cell expansion and MNTs was first observed in CARTITUDE-1[5]
  - In the same study, an association was also observed between MNTs and high absolute lymphocyte counts (ALC) post cilta-cel infusion[5]
- A real-world analysis suggested that elevated ALC at early timepoints post infusion is associated with MNTs and cranial nerve palsy (CNP)[6]
- Emerging data on mitigation of risk of MNTs with prophylactic steroids, such as dexamethasone, show promise[7]
- The objective of this study was to investigate association of biomarkers pre and post cilta-cel with development of MNTs and CNP

Methods

- Longitudinal samples from patients with RRMM who received cilta-cel in CARTITUDE-1 (NCT03548207), CARTITUDE-2 cohorts A/B (NCT04133636), or CARTITUDE-4 (NCT04181827) were analyzed for ALC, CAR+ T-cells, immune cell phenotypes, and serum soluble markers. The timepoints for biomarker collections are shown in **Figure 1**
- Spearman correlations evaluated relationships between 2 continuous variables
- Wilcoxon rank sum test compared continuous variables in patients with MNTs or CNP vs controls (patients without events of CNP, MNTs, or grade ≥2 immune effector cell–associated neurotoxicity syndrome [ICANS])
- Multivariate predictive models were developed to identify risk factors for grade ≥2 neurologic events up to day 14 post infusion using penalized logistic regression. The initial model was developed for grade ≥2 neurologic events given a larger number of cases and subsequently validated in the more limited MNT and CNP cases

Figure 1: Timepoints for biomarker collection



PK, pharmacokinetics.

Acknowledgments

We thank the patients who participated in the study and their families and caregivers, the physicians and nurses who cared for patients and supported this clinical trial, staff members at the study sites, and staff members involved in data collection and analyses. This study was funded by Johnson & Johnson and Legend Biotech USA Inc. Medical writing support was provided by Smitha Reddy, PhD, of Eloquent Scientific Solutions, and funded by Johnson & Johnson and Legend Biotech USA Inc.

Disclosures

YL is a consultant for and has received research funding from Bluebird Bio, Celgene/BMS, Kite/Gilead, Legend Biotech, and Takeda; is a consultant for Caribou, Fosun Kite, Gamida Cells, Juno/BM, Merck, Novartis, and Sorrento; and has received research funding from Boston Scientific, Johnson & Johnson, and Merck.

This poster was previously presented at **the European Hematology Association (EHA) 2025 Hybrid Congress; June 12-15, 2025; Milan, Italy**

Results

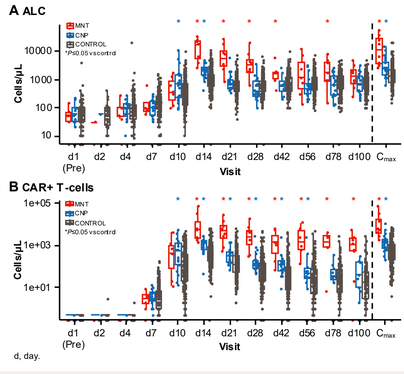
Analysis set

- A total of 355 patients with RRMM received cilta-cel in CARTITUDE-1 (n=97), CARTITUDE-2 cohorts A/B (n=62), and CARTITUDE-4 (n=196)
- 9 (2.5%) patients developed MNTs, 21 (5.9%) developed CNP, and 288 served as controls (39 patients did not meet criteria for any of the 3 groups, 1 patient with MNT had unusually late onset [914 days], and 1 patient had polyradiculoneuritis in addition to CNP, none of whom were included in this analysis)
- Median time to onset of CNP and MNT was 22 days (range, 17–101) and 41 days (range, 19–108), respectively

ALC and CAR+ T-cells post cilta-cel

- ALC and CAR+ T-cell counts peaked at a median of 14 days post cilta-cel (**Figure 2A** and **2B**), after median onset of cytokine release syndrome (CRS; 7 days) and ICANS (8 days)
- On day 14 post cilta-cel, and at CAR+ T-cell peak expansion (C_{max}):
  - Patients with MNTs had significantly higher ALC (day 14: median 17,600 vs 970 cells/μL; P<0.0001) and CAR+ T-cell counts (day14: median 5520 vs 384 cells/μL; P<0.0001) vs controls
  - Patients with CNP had significantly higher ALC (day 14: median 2180 vs 970 cells/μL; P<0.0001) and CAR+ T-cell counts (day 14: median 1230 vs 384 cells/μL; P<0.001) vs controls
- Compared with CNP and controls, patients with MNTs showed elevated CAR+ T-cell levels up to day 100 post infusion (longer persistence) (**Figure 2B**)

Figure 2: (A) ALC and (B) CAR+ T-cell counts pre (d1) and post cilta-cel infusion in patients with MNTs or CNP vs controls

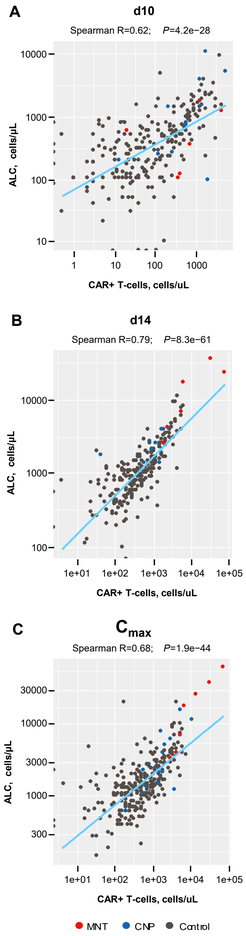


d, day.

Correlation of ALC and CAR+ T-cell counts

- Following cilta-cel infusion, CAR+ T-cell counts significantly correlated with ALC on day 10, day 14 (**Figure 3A** and **3B**), day 21, and day 28 post infusion and at the time of peak levels (C_{max}) of both covariates (**Figure 3C**)

Figure 3: Correlation of ALC and CAR+ T-cell counts at d10, d14, and C_{max}

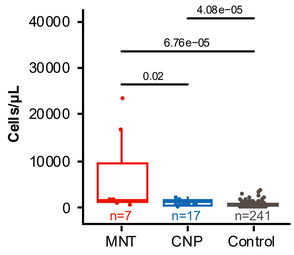


Association of ALC, CAR+ T-cells, and CD4+ T-cells with MNTs and CNP

- CD4+ T-cells were also significantly elevated at and around C_{max} in patients with RRMM who experienced MNTs or CNP post cilta-cel infusion (**Figure 4A**). CD4 T-cell counts remained elevated up to day 100 in MNT cases
- In multivariate analyses, elevated ALC, CAR+ T-cell peak expansion, and CD4+ T-cell counts in the first 14 days post infusion were among the top covariates associated with grade ≥2 neurologic events (**Figure 4B**), and were subsequently validated in CNP and MNTs, despite limited numbers of MNT/CNP events
  - ALC showed the strongest predictive performance

Figure 4: Association of ALC, CAR+ T and CD4+ T-cells with neurological events

A CD4+ T-cells on d14



B 3-fold cross-validation performance at 14 days post infusion for grade ≥2 neurologic events

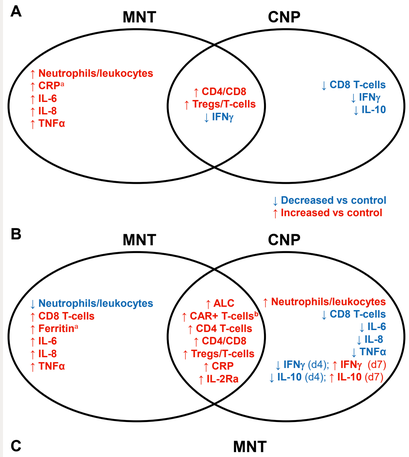
Features	AUROC	AUPRC
ALC	0.76	0.36
CD4	0.72	0.33
CAR+ T (C_{max})	0.72	0.30
ALC + CD4	0.77	0.37
ALC + CD4 + C_{max}	0.75	0.33
All features considered	0.80	0.35

AUROC is the tradeoff between sensitivity and false positive rate at different prediction thresholds. AUPRC is the trade-off between sensitivity and precision at different prediction thresholds. Both metrics range between 0 and 1 with higher value indicating better performance. AUROC=0.5 indicates random chance performance. AUPRC, area under the precision-recall curve; AUROC, area under the receiver operator curve.

Additional biomarkers associated with MNTs and CNP

- Additional inflammatory biomarkers, including interleukin (IL)-6, IL-8, and C-reactive protein (CRP), alongside regulatory T-cells (Tregs), and neutrophil/leukocyte ratio pre and post cilta-cel infusion, were also associated with MNTs and CNP (**Figure 5**). Notably, some biomarkers were common and some distinct between MNT and CNP cases
- Better understanding of these biomarkers may help identify the mechanistic underpinnings of neurologic events and potentially their early detection and monitoring, as well as support tailoring of targeted interventions to MNTs vs CNP

Figure 5: Biomarkers common and distinct between MNTs and CNP (A) pre infusion (aph, LD, d1) and (B) post infusion (≤d14). Association of selected biomarkers longitudinally with (C) MNTs and (D) CNP



C MNT

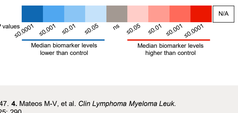
Timepoint

Biomarker	Pre infusion: Aph	Pre infusion: LD	Pre infusion: d1	Post infusion: d4	Post infusion: d7	Post infusion: d10	Post infusion: d14
ALC							
CAR+ T-cells							
CD4 T-cells							
Tregs/T-cells							
N/L							
CRP (abs)							
Ferritin (abs)							
IL-6							
IL-8							
IFNγ							
TNFα							

D CNP

Timepoint

Biomarker	Pre infusion: Aph	Pre infusion: LD	Pre infusion: d1	Post infusion: d4	Post infusion: d7	Post infusion: d10	Post infusion: d14
ALC							
CAR+ T-cells							
CD4 T-cells							
Tregs/T-cells							
N/L							
CRP (abs)							
Ferritin (abs)							
IL-6							
IL-8							
IFNγ							
TNFα							



[a]Both as absolute counts and fold/ULN. [b]High CAR+ T-cells were observed in MNTs up to d100. Abs, absolute; aph, apheresis; LD, lymphodepletion; N/A, not available; N/L, neutrophil/leukocyte ratio; ns, not significant; ULN, upper limit of normal.

References

1. Berdeja JG, et al. *Lancet.* 2021;398:314-24. **2.** Martin T, et al. *J Clin Oncol.* 2023;41:1265-74. **3.** San-Miguel J, et al. *N Engl J Med.* 2023;389:339-47. **4.** Mateos M-V, et al. *Clin Lymphoma Myeloma Leuk.* 2024;24:S290. **5.** Cohen AD, et al. *Blood Cancer J.* 2022;12:32. **6.** Lim KJC, et al. *Transplant Cell Ther.* 2025;31:S202. **7.** Turner et al. *TANDEM.* 2025; 290.