REAL-WORLD INCIDENCE AND MANAGEMENT OF NON-ICANS NEUROLOGIC EVENTS FOLLOWING CILTACABTAGENE AUTOLEUCEL IN MULTIPLE MYELOMA

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INTRODUCTION

- Ciltacabtagene autoleucel (cilta-cel) was initially approved by the Food and Drug Administration (FDA) for relapsed/refractory multiple myeloma (MM) after ≥4 prior lines of therapy (5L+) and recently approved after ≥1 prior line of therapy[1,2], based on positive results from CARTITUDE-1 and CARTITUDE-4 trials
- Post-infusion non-immune effector cell-associated neurotoxicity syndrome (ICANS) neurologic events (NEs) may occur, including cranial nerve palsy (CNP), parkinsonism, and Guillain-Barré syndrome
- In pivotal CARTITUDE-1 and CARTITUDE-4 trials, the rates of any grade parkinsonism were 6% and 1%, respectively, and rates of CNP were 3% and 9%; no Guillain-Barré syndrome was reported[3]

AIM

- To evaluate the incidence of non-ICANS NEs in patients treated with standard-of-care cilta-cel in second-to-fourth line (2L-4L) and 5L+
- To describe clinical characteristics in patients with non-ICANS NEs
- To assess management strategies of non-ICANS NEs and improvement or resolution of symptoms
- To evaluate clinical outcomes including response and mortality in patients with non-ICANS NEs

METHOD

Study design

- Retrospective cohort study using electronic medical records from Loopback Analytics (02/2017-05/2025) supplemented with physician chart notes from academic and community centers in the United States
- Index date = date of cilta-cel infusion on or after FDA approval; baseline period = 12-months pre-index; follow-up period = index date to earliest of death or end of data availability

Study population

- Adults with MM treated with cilta-cel in 2L-4L and 5L+ with an absolute lymphocyte count (ALC) lab test during the 30-day peri-infusion period and without evidence of baseline NE

Study outcomes and statistical analysis

- Among patients with CNP, parkinsonism and Guillain Barré syndrome, pre-lymphodepletion ALC x 10^3/μL (i.e., closest value pre-index), post-infusion peak ALC x 10^3/μL, non-ICANS NE management strategies, response, and mortality were described

RESULTS

Patient characteristics

- Overall, 171 patients treated with cilta-cel having ≥1 ALC test within 30 days pre- and post-infusion were identified (**Table 1**)
  - 2L-4L: 73; median age was 65 years and 46.6% were female
  - 5L+: 98; median age was 64 years and 37.8% were female
- Among patients with available data, few had high-risk Eastern Cooperative Oncology Group score ≥2 (2L-4L: 6.0%; 5L+: 1.0%) or extramedullary disease (2L-4L: 33.3%; 5L+: 19.4%), while most had high-risk cytogenetic abnormalities (2L-4L: 55.8%; 5L+: 63.3%; **Table 2**)

Table 1. Patient demographic characteristics

	2L-4L N = 73	5L+ N = 98
Age, mean ± SD [median]	64.6 ± 9.0 [65.0]	63.9 ± 8.9 [64.0]
Female, n (%)	34 (46.6)	37 (37.8)
Race, n (%)		
White	49 (67.1)	69 (70.4)
Black	5 (6.8)	5 (5.1)
Asian	4 (5.5)	10 (10.2)
Other	15 (20.5)	14 (14.3)
Payer type, n (%)		
Medicare	34 (46.6)	51 (52.0)
Commercial	30 (41.1)	33 (33.7)
Medicaid	4 (5.5)	9 (9.2)
Other	3 (4.1)	4 (4.1)
Infusion setting available, n (%)	69 (94.5)	98 (100.0)
Inpatient	39 (56.5)	71 (72.4)
Outpatient	30 (43.5)	27 (27.6)

2L-4L: second to fourth line; 5L+: fifth line or later; SD: standard deviation.

Table 2. Patient clinical characteristics

	2L-4L N = 73	5L+ N = 98
Quan-CCI, mean ± SD [median]	2.6 ± 1.3 [2.0]	2.9 ± 1.8 [2.0]
ECOG score available, n (%)	67 (91.8)	97 (99.0)
ECOG score ≥2	4 (6.0)	1 (1.0)
EMD status available, n (%)	48 (65.8)	72 (73.5)
EMD	16 (33.3)	14 (19.4)
Cytogenetic information available, n (%)	43 (58.9)	49 (50.0)
High-risk cytogenetic abnormalities[a], n (%)	24 (55.8)	31 (63.3)
TP53 mutation	3 (7.0)	5 (10.2)
del(17p)	11 (25.6)	14 (28.6)
del(1p32)	5 (11.6)	3 (6.1)
t[14;16]	1 (2.3)	2 (4.1)
t[14;20]	1 (2.3)	0 (0.0)
t[4;14]	10 (23.3)	15 (30.6)
1q (amplification or gain)	31 (44.3)	37 (75.5)
Involved:uninvolved FLC ratio ≥100, n (%)	12 (16.4)	18 (18.4)
Tested for clonal plasma cells in bone marrow, n (%)	54 (74.0)	65 (66.3)
Clonal plasma cells in bone marrow (%), mean ± SD [median]	17.2 ± 21.4 [8.0]	27.4 ± 27.3 [15.0]
Assessment of measurable disease available, n (%)	66 (90.4)	94 (95.9)
Measurable disease	65 (98.5)	93 (98.9)
Received bridging therapy, n (%)	60 (82.2)	80 (81.6)

2L-4L: second to fourth line; 5L+: fifth line or later; CCI: Charlson Comorbidity Index; ECOG: Eastern Cooperative Oncology Group; EMD: extramedullary disease; FLC: free light chain; IMWG: International Myeloma Working Group; SD: standard deviation.
[a]Defined as evidence of del(17p) in sorted plasma cells ≥20%, TP53 mutation, biallelic del(1p32) or any two of the following abnormalities: t(4;14) or t(4;16) or t(14;20), 1q (gain or amplification), monoallelic del(1p32).

Incidence of non-ICANS NEs

- 2L-4L: Over a median follow-up of 6.1 months, CNP - 4 (5.5%); no parkinsonism and no Guillain-Barré syndrome
- 5L+: Over a median follow-up of 17.4 months, CNP - 3 (3.1%), parkinsonism - 1 (1.0%), Guillain-Barré syndrome - 1 (1.0%)

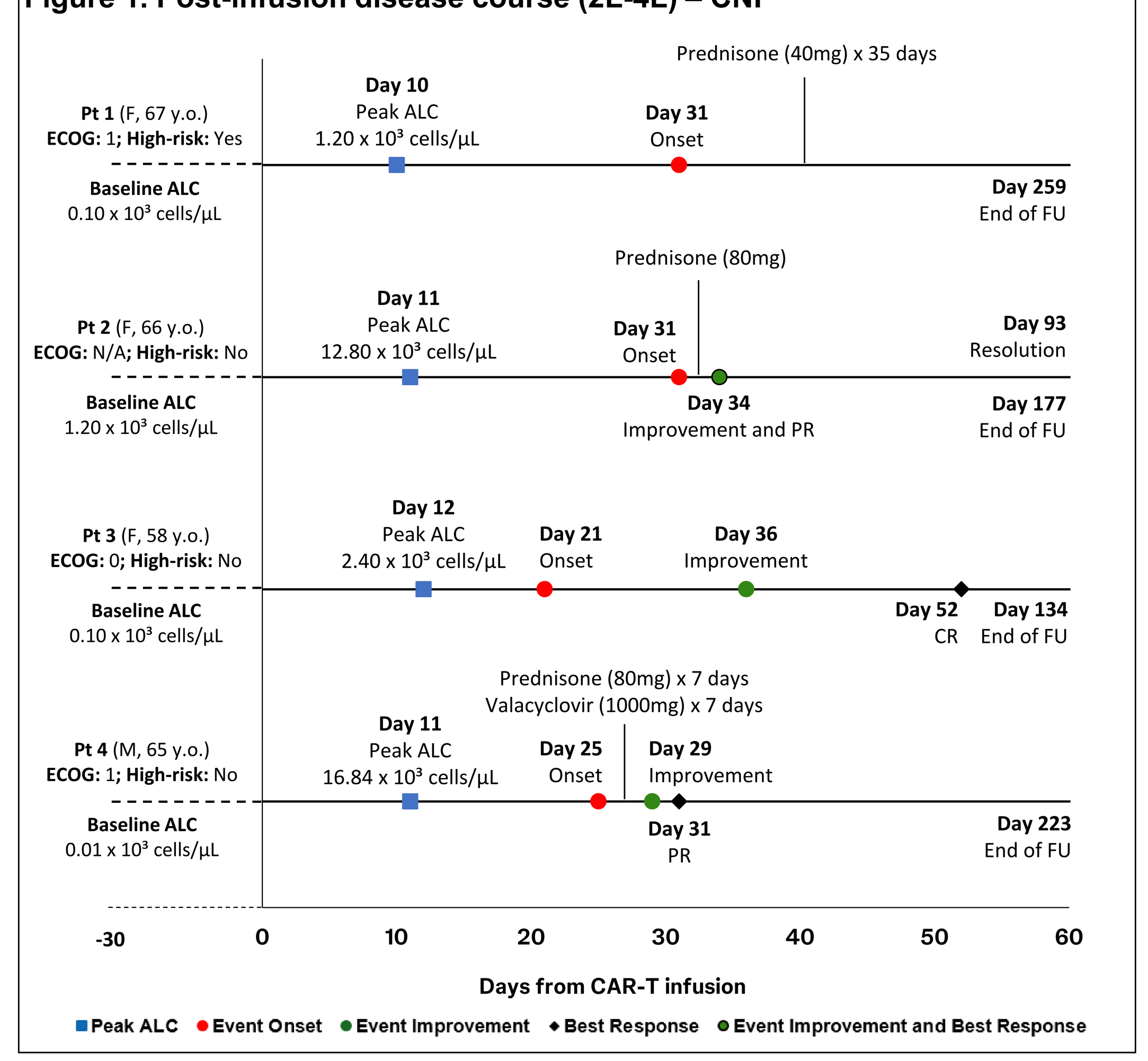
Post-infusion disease course (2L-4L)

- Among 2L-4L patients without non-ICANS NEs, median (interquartile range [IQR]) post-infusion peak ALC was 2.12 (1.10-4.62) x 10^3 cells/μL
- Among 2L-4L patients with CNP, median (IQR) post-infusion peak ALC was 7.60 (1.80 - 14.82) x 10^3 cells/μL (median day 11 post-infusion); 75% of patients had an improvement in symptoms
- No parkinsonism or Guillain-Barré syndrome was observed

Post-infusion disease course (5L+)

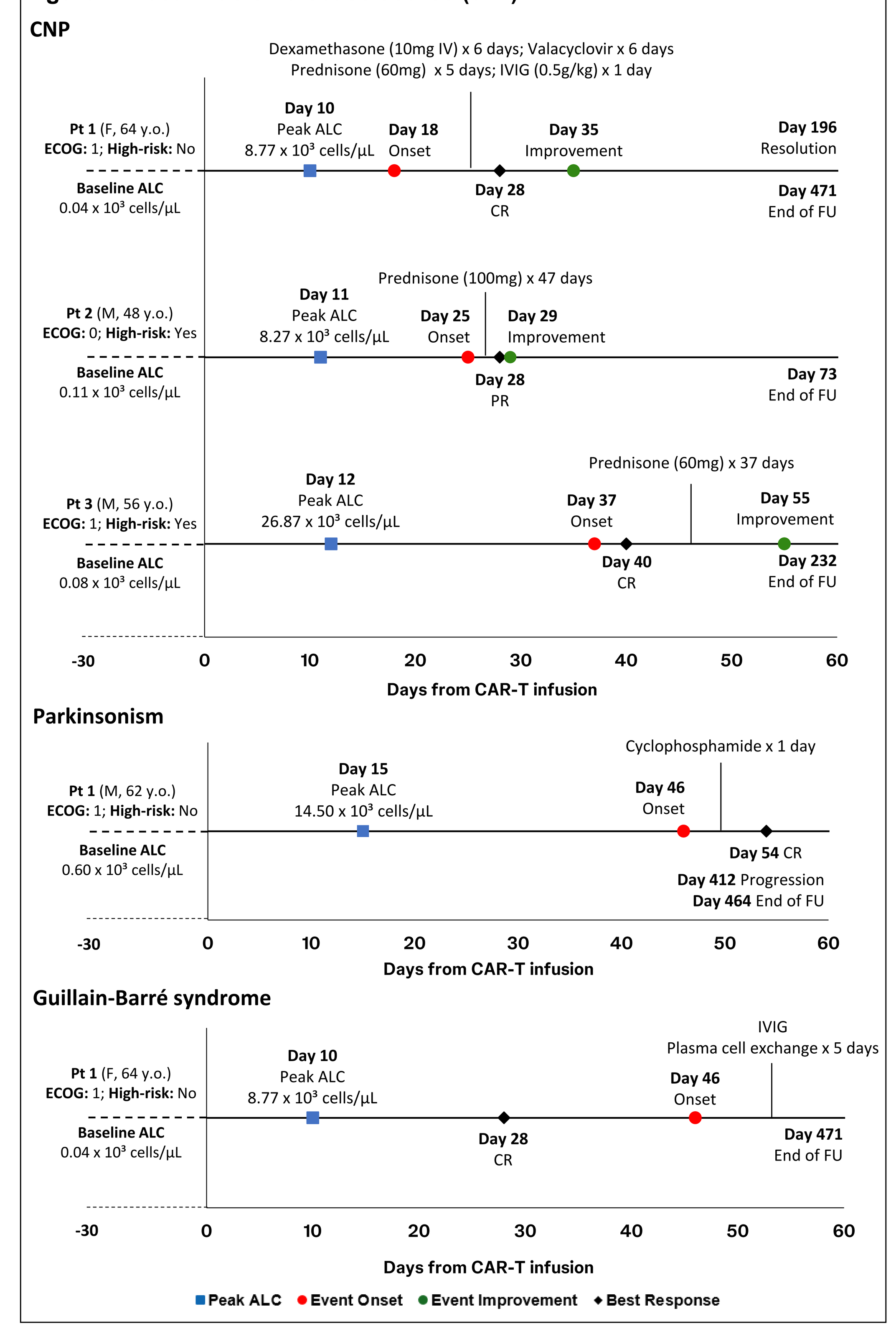
- Among 5L+ patients without non-ICANS NEs, median [IQR] post-infusion peak ALC was 1.96 (1.24-3.56) x 10^3 cells/μL
- Among 5L+ patients with CNP, median [IQR] post-infusion peak ALC was 8.77 (8.27-26.87) x 10^3 cells/μL (median day 11 post-infusion); all patients had an improvement in symptoms

Figure 1. Post-infusion disease course (2L-4L) – CNP



2L-4L: second to fourth line; ALC: absolute lymphocyte count; CNP: cranial nerve palsy; CR: complete response; ECOG: Eastern Cooperative Oncology Group; F: female; FU: follow-up; M: male; N/A: not available; PR: partial response; Pt: patient; y.o.: years old.

Figure 2. Post-infusion disease course (5L+)



5L+: fifth line or later; ALC: absolute lymphocyte count; CNP: cranial nerve palsy; CR: complete response; ECOG: Eastern Cooperative Oncology Group; F: female; FU: follow-up; IVIG: intravenous immunoglobulin; M: male; PR: partial response; Pt: patient; y.o.: years old.

LIMITATIONS

- Physician notes often capture care received outside of the facilities; however, some services received outside network may not be fully captured thus underestimation of risk was possible
- Misclassification was possible due to coding inaccuracies and variations in recording of events
- Daily ALC was not available for all patients, therefore, imprecision in peak ALC was possible

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CONCLUSIONS

- In this real-world cohort, CNP, parkinsonism, and Guillain-Barré syndrome cases were infrequent following cilta-cel infusion with distinct management strategies, both in 2L-4L and 5L+
- Patients with non-ICANS NEs had higher post-infusion peak ALCs suggesting that ALC may serve as a potential biomarker for identifying patients at risk for NEs and guiding management strategies
- Despite experiencing non-ICANS NEs, most patients showed an improvement in symptoms, all with available response assessments responded to cilta-cel, and no deaths were reported

Rates of CNP, parkinsonism, and Guillain-Barré syndrome were low after cilta-cel infusion, with ALC serving as a potential biomarker for the identification of high-risk patients

ACKNOWLEDGEMENTS

This study was funded by Janssen Scientific Affairs, a Johnson & Johnson Company, and Legend Biotech USA Inc. Analytical support was provided by Alvi Rahman, Vicky Wei, and Alessio Palladino at Analysis Group, Inc., under the direction of the authors in accordance with this project.

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