



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALY AVAILABLE THERAPIES

Bendamustine Versus Fludarabine and Cyclophosphamide for Lymphodepletion Prior to CAR-T Therapy

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Background

As CAR-T treatment volumes and approved indications rapidly expand, identifying optimal lymphodepleting chemotherapy (LDC) regimens is an urgent and unmet need. A combination of fludarabine and cyclophosphamide (flu/cy) is most commonly performed. However, an ongoing international fludarabine shortage¹ has led to the use of bendamustine (benda), a potent lymphotoxin, as LDC, with initial reports suggesting similar efficacy with less toxicity^{2, 3}. We performed a multi-center retrospective analysis of patients with non-Hodgkin lymphoma (NHL) who have received benda or flu/Cy LDC prior to infusion of FDA-approved CAR-T products across the Sarah Cannon Transplant and Cellular Therapy Network (SCTCTN). We hypothesized that, compared with flu/cy, benda is noninferior in terms of lymphodepletion, hematologic recovery, CAR-T response and toxicities, as well as resource utilization.

Methods

We retrospectively analyzed 215 NHL patients receiving benda (46) or flu/cy (169) LDC prior to commercial CAR-T from 2018-2023 in the SCTCTN CAR-T registry. Patients on clinical trials, who received CAR-T for other malignancies than NHL, or were within 30 days of CAR-T infusion were excluded. Absolute lymphocyte count (ALC), neutrophil, and platelet kinetics were measured. Cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS) were graded according to consensus criteria of the American Society of Transplant and Cellular Therapy (ASTCT), and the occurrence, maximum grade, days to onset/resolution, and tocilizumab dosing were recorded.

Overall survival (OS), progression free survival (PFS), and resource utilization (length of stay in hospital and ICU requirement) were recorded.

Results

Characteristics of patients receiving benda and flu/cy were matched in terms of age, gender, race, ethnicity, NHL subtype, performance status. Flu/cy and benda produced deep absolute lymphocyte count (ALC) nadirs by the date of CAR-T infusion (day 0) with subsequent partial recovery by day 30. Lymphodepletion nadir at day 0 was deeper [$P < 0.001$] with flu/cy (ALC 0.03 K/uL, IQR range 0.01-0.05) than benda (ALC 0.21 K/uL, IQR range 0.1-0.3) but not at other time points. The kinetics of neutrophil and platelet recovery were similar between groups suggesting an equivalent extent of marrow suppression. Parameters of resource utilization such as inpatient hospitalization, length of stay, ICU utilization, and the use of tocilizumab were similar between flu/cy and benda recipients.

Conclusion

In a large cohort of real-world CAR-T recipients, benda produced efficient lymphodepletion and equivalent outcomes compared to traditional flu/cy. While flu/cy produces a deeper nadir than benda at day 0, this difference did not exert clinical relevance.

Disclosures Rao: Janssen: Honoraria. **Flinn:** TG Therapeutics: Consultancy; Myeloid Therapeutics: Consultancy; Vincerx Pharma: Consultancy; Innocare Pharma: Consultancy; Kite: Consultancy; Novartis: Consultancy; Secura Bio: Consultancy; Servier Pharma: Consultancy; Hutchinson MediPharma: Consultancy; Genmab: Consultancy; Genentech: Consultancy; Century Therapeutics: Consultancy; BeiGene: Consultancy; AbbVie: Consultancy. **Pantin:** Omeros, Sanofi: Speakers Bureau; Orca Bio: Research Funding; Omeros: Honoraria. **Shaughnessy:** Sanofi: Speakers Bureau; BMS: Speakers Bureau. **Battiwalla:** Novartis: Research Funding; Fate Therapeutics: Research Funding.

	FLU CY n=169	BENDAMUSTINE n=46
Median age (range)	63 (16-84)	68 (32-79)
Male sex	63%	65%
Race		
White	75%	76%
Black	4%	7%
Asian	3%	0%
Other	18%	17%
Ethnicity		
Non-hispanic	73%	71%
Hispanic	27%	29%
NHL subtype		
DLBCL	72%	67%
Follicular	12%	13%
Mantle cell	9%	13%
Other	7%	7%
Median KPS (range)	90% (70-100%)	90% (80-100%)
Median HCT-CI (range)	4 (0-7)	4 (0-4)
Year		
2019-2021	47%	52%
2022	32%	48%
2023	21%	
Inpatient CAR-T administration	54%	26%
Dexamethasone premed (day 0-2)	25%	48%
CAR-T product		
Axi-cel (Yescarta)	51%	70%
Tisa-cel (Kymriah)	19%	2%
Liso-cel (Breyanzi)	19%	15%
Brexu-cel (Tecartus)	10%	13%
Any inpatient hospitalization	93%	80%
Median inpatient LOS in days (range)	10 (0-85)	7 (0-49)
Any ICU stay	30%	26%
Median ICU LOS in days (range)	0 (0-25)	0 (0-19)
Tocilizumab use	38%	43%
Median tocilizumab doses (range)	1 (0-5)	1 (0-4)
ANC ≥ 0.5 at day 30	80%	80%
Platelets <20K at day 30	17%	11%

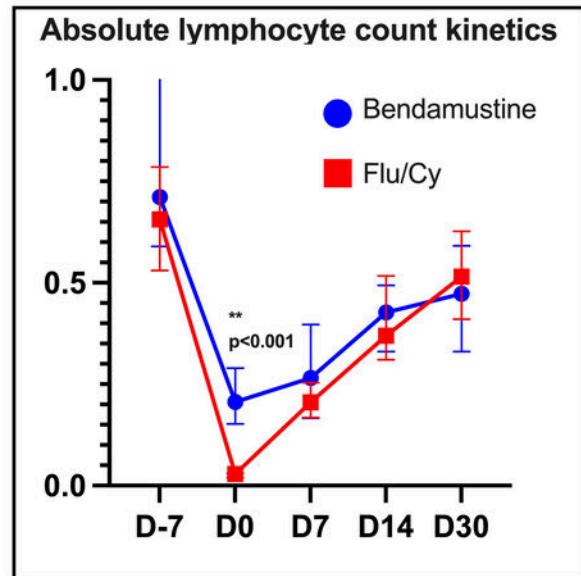


Figure 1

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