#CT-009: Prognostic Role of Lymphocyte to Monocyte Ratio in Patients Treated with CAR-T for Aggressive Lymphoma

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Background

- Rate of complete remission (CR) in patients with B cell malignancies with chimeric antigen receptor T cell (CAR-T) therapy is 30-40%.[1,2,3]
- Low absolute lymphocyte to monocyte ratio (ALC/AMC) predicts decreased survival in aggressive lymphoma (NHL) patients (pts) receiving chemotherapy and autologous stem cell transplant (ASCT).[4, 5]
- We report the clinical significance of ALC/AMC at lymphodepletion chemotherapy (LD) on day -5 and associated cellular phenotype changes in pts receiving CAR-T.

Results

- Retrospective review of medical records from 6/2016 to 12/2020 identified 81 pts with aggressive NHL who were treated with axicabtagene ciloleucel.

Figure 1: ALC/AMC correlates with CR (A). Using logistic regression, ROC curve for best cut-off point for ALC/AMC to predict CR was 0.8 (B)

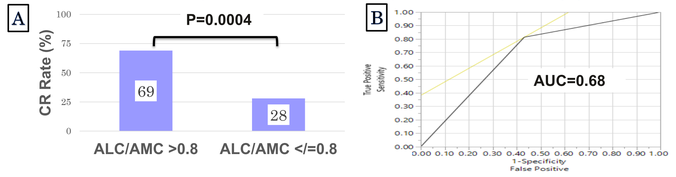


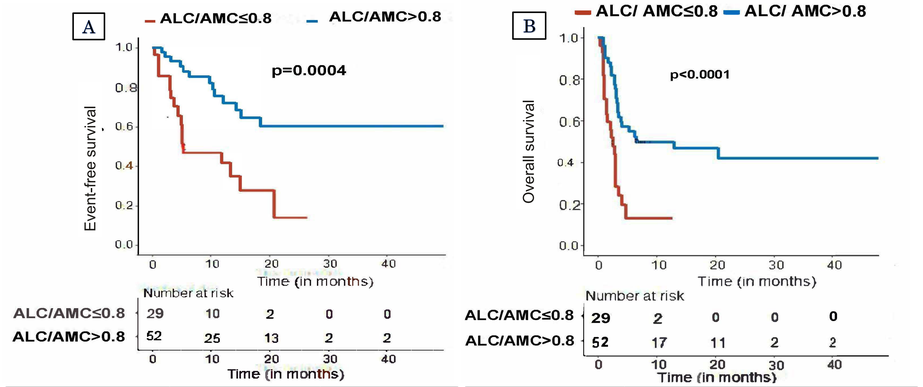
Table 1: Patient demographics

Variable	All patients (N=81)	ALC/AMC >0.8 (N=52)	ALC/AMC ≤0.8 (N=29)
Age (years), median (range)	58 (26-76)	57 (26-75)	59 (29-76)
Male, n (%)	53 (65)	37 (71)	16 (55)
Lymphoma stage III/IV, n (%)	78 (94)	49 (95)	27 (93)
ECOG ≥2, n (%)	4 (5)	2 (4)	2 (7)
International prognostic index ≥3, n (%)	42 (52)	25 (48)	17 (58)
Previous ASCT, n (%)*	38 (47)	30 (58)	8 (28)
Bridging therapy, n (%)*	50 (61)	28 (54)	22 (76)
C-reactive protein (CRP) at day of CAR-T infusion (mg/l), median (range)*	17.2 (2.9-251.7)	11.65 (3-251.7)	32.3 (2.9-191.7)
Ferritin at day of CAR-T infusion (mcg/l), median (range)	528 (72-12980)	487 (72-12980)	648 (72- 6058)

*P<0.05 between high and low ALC/AMC groups

Results

Figure 2: Low ALC/AMC group predicts shorter (A) Event-free survival, EFS and (B) Overall survival, OS



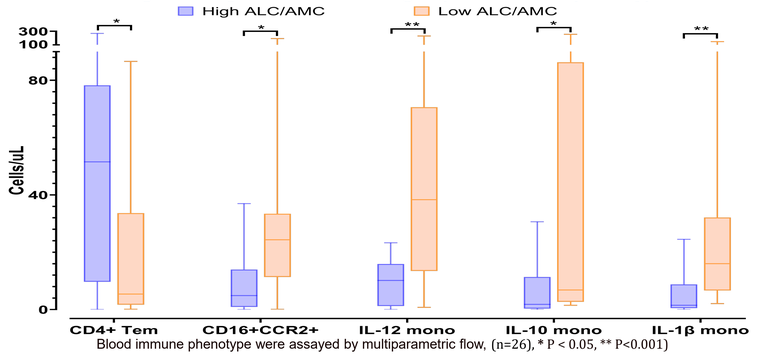
	Univariate analysis HR (95% CI), P-Value	Multivariate analysis HR (95% CI), P-Value
ALC/AMC >0.8 at LD	**0.31 (0.17-0.56), 0.0001**	**0.37 (0.18-0.74), 0.005**
Prior ASCT	0.95 (0.54-1.67), 0.86	
Bridging therapy	1.45 (0.79-2.68), 0.22	
CRP >10 (mg/l) at CAR-T infusion	2.16 (1.1-4.2), 0.024	1.8 (0.88-3.73), 0.1

EFS: Time from CAR-T infusion to PD/next therapy/death.

	Univariate analysis HR (95% CI), P-Value	Multivariate analysis HR (95% CI), P-Value
ALC/AMC >0.8 at LD	**0.36 (0.14-0.64), 0.002**	**0.26 (0.12-0.57), 0.0007**
Prior ASCT	0.96 (0.46-1.98), 0.92	
Bridging therapy	2.7 (1.12-6.85), 0.03	1.85 (0.72-4.76), 0.2
CRP >10 (mg/l) at CAR-T infusion	1.54 (0.65-3.58), 0.32	

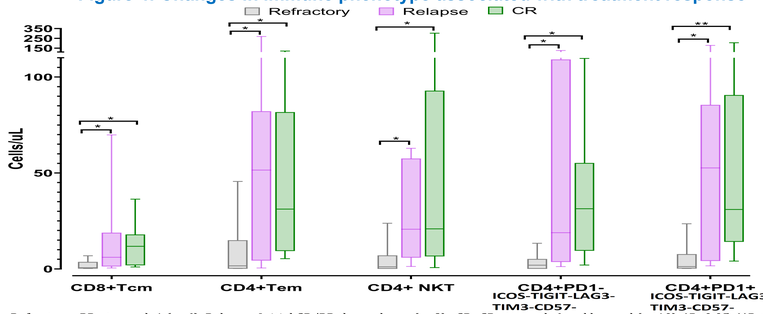
OS: Time from CAR-T infusion to death of any cause.

Figure 3: High vs low ALC/AMC group has different phenotype



Blood immune phenotype were assayed by multiparametric flow, (n=26), * P < 0.05, ** P<0.001)

Figure 4: Changes in immune phenotype associated with treatment response



Refractory- PD at month 1 (n=6), Relapse- Initial CR/PR then relapse (n=9) , CR- CR at month 6 and beyond (n=10), *P<0.05, **P<0.01

Discussion

- ALC/AMC at LD is a clinically accessible test that is strongly associated with CAR-T response and survival.
- Increased inflammation has been found to negatively impact CAR-T response, with some cytokines known to be from the myeloid lineage. We show low ALC/AMC group had increased CRP on day of CAR-T infusion and was associated with increased monocytes cytokine production.
- Examination of additional immune phenotype identified changes associated with primary refractory disease versus responders. These data could inform future therapeutic strategies to improve clinical outcome with CAR-T.

Presenter- Radhika Bansal, MBBS

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