

Cytomegalovirus reactivation after CD19 CAR T-cell therapy is clinically significant

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Supplemental Materials

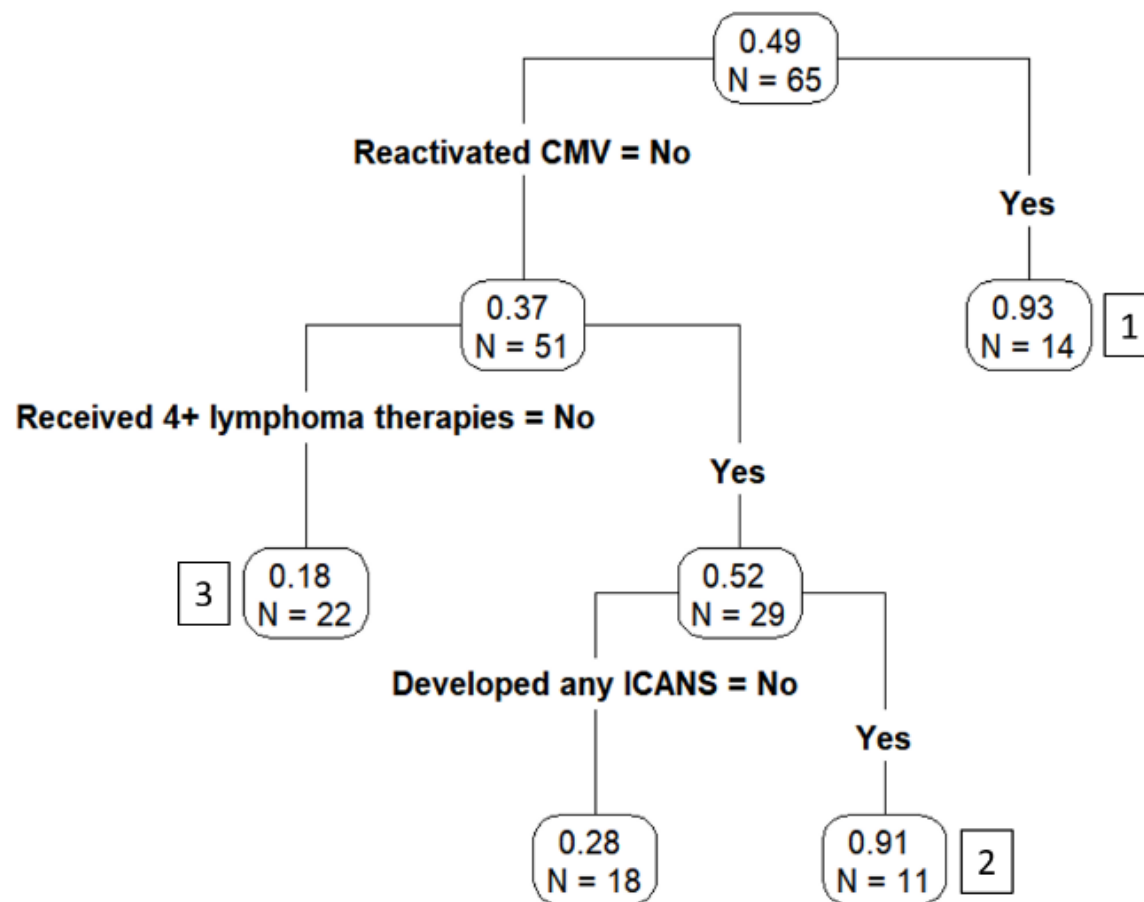
Supplemental Table 1. Clinical Factors Affecting CMV Reactivation		
Clinical Factor	Hazard Ratio (95% CI)	P value
Univariate Analysis		
Age		
≥ 50 versus < 50 years	0.3 (0.1-0.9)	.04
≥ 60 versus < 60 years	0.7 (0.2-2.2)	.57
≥ 70 versus < 70 years	1.3 (0.4-4.1)	.68
CMV serostatus (positive versus negative)	13.8 (2.9-65.3)	<.001
Number of lines of lymphoma therapy		
≥ 3 versus < 3	2.1 (0.3-15.1)	.45
≥ 4 versus < 4	0.4 (0.2-1.3)	.14
≥ 5 versus < 5	0.4 (0.1-3.3)	.42
KPS (< 80 versus 80)	4.3 (0.5-36)	.18
Lymphodepletion regimen (fludarabine/cyclophosphamide versus bendamustine)	1.9 (0.4-8.8)	.40
CAR T cell product (standard of care axicabtagene ciloleucel versus other)	2.1 (0.7-6.4)	.18
Development of ICANS by grade		
≥ 1 versus < 1	1.3 (0.7 – 2.5)	.38
≥ 2 versus < 2	1.4 (0.5-3.7)	.47
≥ 3 versus < 3	1.0 (.3-3.1)	.97
Development of CRS by grade		
≥ 1 versus < 1	1.1 (0.5-2.5)	.84
≥ 2 versus < 2	0.6 (0.2-1.7)	.36
Multivariate analysis		
Age (≥ 50 versus < 50 years)	0.2 (0.1-0.4)	<.001
CMV serostatus (positive versus negative)	18.5 (4.5-76.6)	<.001
Abbreviations: CAR – chimeric antigen receptor, CI – confidence interval, CMV – cytomegalovirus, CRS – cytokine release syndrome, ICANS – immune effector cell associated neurotoxicity syndrome, KPS – Karnofsky performance status		

Supplemental Table 2. Mortality after CD19 CAR T Cell Therapy in Relation to CMV Reactivation			
Status / Cause of Death	All Subjects N=65 N (%)	No CMV Reactivation* N=51 N (%)	CMV Reactivation* N=14 N (%)
Alive	33 (51)	32 (63)	1 (7)]
Dead	32 (49)	19 (37)	13 (93)
Relapsed / refractory NHL	20 (63)	11 (58)	9 (69)
Infection	4 (13)	2 (11)	2 (15)
ICANS	3 (9)	3 (16)	0 (0)
Second cancer	2 (6)	1 (5)	1 (8)
Hemorrhage	1 (3)	0 (0)	1 (8)
Infection / hemorrhage	1 (3)	1 (5)	0 (0)
Unknown	1 (3)	1 (5)	0 (0)

Notes: Percentage of causes of death is of total dead subjects. Percentage of dead and alive subjects is of all subjects studied. **Abbreviations:** CAR – chimeric antigen receptor, CMV – cytomegalovirus, ICANS – immune effector cell associated neurotoxicity syndrome, NHL – non-Hodgkin lymphoma, * CMV reactivation defined as CMV DNA qPCR >400 IU/mL

Supplemental Figure 1. Classification tree for survival outcomes. The entire dataset (N=65) was repeatedly split according to pre and post CAR T cell therapy factors to determine the best combination for classifying patients into groups that correlated with survival. The tree is composed of multiple splits which classify the patients into distinct groups (nodes, rounded boxes). Each node shows the number of patients in the node (2nd row) and the proportion of patients in the node that died (1st row). Each split shows the pre- or post-infusion factor used to dichotomize patients. Patients meeting the criteria flow to the left and patients not meeting the criteria flow to the right. Patients who reactivated CMV (node 1) had the highest probability of death (0.93). The causes of death were disease (N=9), hemorrhage (N=1), infection (N=2), second cancer (N=1). Patients who did not reactivate CMV but received ≥ 4 prior lymphoma therapies and developed ICANS (node 2) also had a high probability of death (0.91). The causes of death were ICANS (N=3), disease (N=3), unknown (N=1), infection (N=2), and infection / hemorrhage (N=1). Patients who did not reactivate CMV and received < 4 prior lymphoma therapies (node 3) had the lowest probability of death (0.18).

Abbreviations: CAR – chimeric antigen receptor, CMV – cytomegalovirus, ICANS – immune effector cell associated neurotoxicity syndrome.



Supplemental Figure 1.