Study Activities Table

Activity	Screening	Cycle 1 (21-day cycle)				Cycles 2-4 (21-day cycles)			Cycle 5-6 (21-day cycles)	Cycle 7- 8 (21-day cycles)	Unscheduled (as needed per Investigator's discretion)	End of Treatment Week 28 or 6 [+2] week after Cycle 8 Day 1, whichever is later	120 day Safety Follow-up	Post-Treatment Follow-up	Survival Follow-up
	Day -28 to Day -1	Day 1	Day 8	Day 15	Day 16	Day 1 (+ 2 days)	Day 8	Day 15	Day 1 (+ 2 days)	Day 1 (+ 2 days)				± 7 days	± 7 days
INTERVIEWS & QUESTIONNAIRES															
Informed consent	✓														
Eligibility criteria	✓	✓													
Demographics	✓														
Medical/surgical history	✓	✓													
Alcohol and nicotine use	✓														
Adverse event assessment	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Prior/concomitant therapy	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Survival Status															✓
New malignancy and new Anti-Lymphoma therapy														✓	✓
PRO															
EQ-5D-5L		✓				✓			✓	✓		✓		✓	
FACT Lym		✓				✓			✓	✓		✓		✓	
PGIC (Patients' Global Impression of Change)-Lym						✓			✓	✓		✓		✓	

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	Day -28 to Day -1	Day 1	Day 8	Day 15	Day 16	Day 1 (+ 2 days)	Day 8	Day 15	Day 1 (+ 2 days)	Day 1 (+ 2 days)				± 7 days	± 7 days
LOCAL LABS & EXAMS															
Brain MRI or CECT scan (and lumbar puncture for subjects with high-risk for CNS involvement or as clinically indicated)	✓														
Beta2-microglobulin	✓														
Hepatitis B and C screening	✓														
Clinical Tumor Lysis Syndrome chemistry panel		✓	As clinically indicated												
Disease status and subtype	✓	✓													
Molecular (e.g., PCR) test or antigen test for SARS-CoV-2 infection (*only if a subject has signs/symptoms suggestive of SARS-CoV-2 to rule out infection*), details in Protocol Section 5.1	✓														
Quantitative CMV DNA - PCR	✓					C3			C6		✓	✓	✓		
CMV serology (IgM and IgG)	✓														
Echocardiogram or MUGA	✓										As indicated				
12-lead ECG	✓										✓				
Height (screening only) and weight	✓	✓				✓			✓	✓	✓	✓			

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	Day -28 to Day -1	Day 1	Day 8	Day 15	Day 16	Day 1 (+ 2 days)	Day 8	Day 15	Day 1 (+ 2 days)	Day 1 (+ 2 days)				± 7 days	± 7 days
Vital signs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	
ECOG performance status	✓	✓				✓			✓	✓	✓	✓			
Constitutional symptoms (B symptoms)	✓	✓				✓			✓	✓	✓	✓		✓	
Physical examination	✓	✓	Targeted									✓		Targeted	
Lymph node examination	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓		✓	
Neurologic (ICANS) assessment (investigational arm)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Clinical requirements for administration of epcoritamab assessment (if applicable, investigational arm)		✓	✓	✓		✓	✓	✓	✓	✓					
Serum Pregnancy test	✓														
Pregnancy test (urine)		✓				✓			✓	✓	✓	✓	✓	✓	
Urinalysis	✓	✓				✓			✓	✓	✓	✓			
Immunoglobulins (IgA, IgG, and IgM)	✓	✓				✓			✓	✓	✓	✓			
Hematology	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	
Clinical chemistry	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	
Coagulation	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Tuberculosis screening (IGRA) if clinically indicated	✓														

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	Day -28 to Day -1	Day 1	Day 8	Day 15	Day 16	Day 1 (+ 2 days)	Day 8	Day 15	Day 1 (+ 2 days)	Day 1 (+ 2 days)				± 7 days	± 7 days
TUMOR ASSESSMENTS															
Fresh/archival tumor biopsy sample	✓		After screening, fresh tumor biopsy sample to be collected at C2D15 (optional sample) and at time of tumor progression (optional).												
PET/CT scan with contrast enhancement (CT must be of diagnostic quality), CECT or MRI (if CT component of PET/CT is not of diagnostic quality) details in Operations Manual Section 3.24)	✓							End of C4			✓	✓		✓	
PET/CT scan with contrast enhancement (CT must be of diagnostic quality), CECT or MRI (if CT component of PET/CT is not of diagnostic quality) for exploratory biomarkers **(select sites only)**								End of C2							
CECT or MRI (details in Operations manual Section 3.24)														✓	
Bone marrow biopsy and/or aspirate for local analysis of lymphoma involvement	✓	Bone marrow exam is needed to confirm CR in subjects who had bone marrow involvement at screening. Sample to be collected upon detection of CR by PET-CT scan.													
CENTRAL LABS															
Pharmacokinetic samples (investigational arm)		✓	✓	✓	✓	✓	✓	✓	✓	✓					

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CSF sample (only for subjects who require Lumbar Puncture)	✓								Prior to any intrathecal MTX (on or after C5D1)		✓				
ADA/nAb		✓		✓		✓			✓	✓					
Cytokine (soluble factors) (control arm)		✓				C2, C3									
Cytokine (soluble factors) (investigational arm)		✓	✓	✓	✓	C2, C3	C2D 8	C2D15							
TBNK (by flow cytometry) (control arm)		✓				✓			✓	✓		✓		✓	
TBNK (by flow cytometry) (investigational arm)		✓	✓	✓		✓			✓	✓		✓		✓	
Immuno-phenotyping (by flow cytometry (control arm)		✓				✓			✓	✓		✓		✓	
Immuno-phenotyping (by flow cytometry) (investigational arm)		✓	✓	✓		✓			✓	✓		✓		✓	
Immuno-phenotyping (exploratory) (control arm)		✓				✓			✓	✓		✓		✓	
Immuno-phenotyping (exploratory) (investigational arm)		✓	✓	✓		✓			✓	✓		✓		✓	
T-cell receptor clonality		✓				C2, C3						✓			
Whole blood PG DNA Sample		✓													
Whole blood MRD (details in Operations Manual Section 3.9)		✓				C2, C3			C5	✓		✓		✓	

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	Day -28 to Day -1	Day 1	Day 8	Day 15	Day 16	Day 1 (+ 2 days)	Day 8	Day 15	Day 1 (+ 2 days)	Day 1 (+ 2 days)				± 7 days	± 7 days
Whole blood ctDNA (details in Operations Manual Section 3.9)		✓				C2, C3			C5	✓		✓		✓	
Whole blood for exploratory biomarkers (cfDNA and EV-miRNA, etc, details in Operations Manual Section 3.9)		✓				C2, C3			C5	✓		✓		✓	
Bone marrow aspirate MRD						• For subjects with confirmed bone marrow involvement at screening, if a subject is in CR by FDG-PET a portion of the aspirate collected to confirm CR will be used to assess MRD. • For subjects with no bone marrow involvement at baseline, no bone marrow examination for MRD is required.										
℞ TREATMENT															
Randomization/drug assignment		✓													
Hospitalization (at investigator's discretion or if clinically indicated)				✓											
CRS prophylaxis and temperature monitoring (investigational arm)		✓	✓	✓	✓	✓	✓	✓	✓	✓					
Epcoritamab		✓	✓	✓		✓	✓	✓	✓	✓					
Vincristine		✓				✓			✓						
Rituximab		✓				✓			✓	✓					
Cyclophosphamide		✓				✓			✓						
Doxorubicin HCL		✓				✓			✓						
Prednisone		D1-D5				D1-D5			D1-D5						

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Dispense Subject Diary		✓				✓			✓	✓					
Collect and Review Subject Diary						✓			✓	✓		✓			