

Supplemental Methods

Statistical analyses

Summary statistics were used to describe patient baseline characteristics listed in Table 1.

Comparisons of treatment arms for imbalance with respect to baseline characteristics (demographics, Centers for Disease Control and Prevention risk factors, and cART use) employed Wilcoxon's rank-sum test for age, the standard Fisher's exact test for dichotomous characteristics, and a multinomial extension of Fisher's exact test for polychotomous characteristics such as race, ethnicity, and central-pathology diagnosis. These tests were also used to compare baseline characteristics between subjects who had short DTI (<15 days) versus long DTI (≥ 15 days). Correlation between CR rate and baseline absolute CD4+ count was examined with the Cochran-Armitage trend test. Longitudinal endpoints [HIV VL, immunoglobulin (Ig) levels (IgG, IgM, and IgA) and CD4+ and CD8+ cell counts] were analyzed non-parametrically as follows: (1) Friedman's tests were used to test for the presence of differences across time points, first within each treatment arm, and then with both arms combined. (2) Wilcoxon signed-rank tests (with Baseline values as reference) were used to evaluate the change-from-baseline differences seen at each non-baseline time point, first within each treatment arm, and then with both arms combined. (3) Wilcoxon rank-sum tests were applied at each time point to compare the two treatment arms for their difference at that time point. The 1-, 2-, and 3-year proportions of OS and EFS were determined for each treatment arm using Kaplan-Meier proportions with Greenwood standard errors, and the log-rank test was employed to compare the underlying Kaplan-Meier curves between treatment arms.

Exploratory Analysis of Impact by Pre-Protocol Therapy and Diagnosis to Treatment Interval (DTI)

We also performed exploratory analyses evaluating the clinical characteristics and outcomes for (1) patients who received 1 cycle of pre-protocol therapy compared with those who did not, and (2) those with a short compared with a long DTI (<15 vs. >15 days). The same procedures were also used to compare yearly survival proportions between subjects who had zero versus one cycle of prior

chemotherapy, and between subjects who had short versus long DTI. For subgroup analysis of response to vorinostat, we used Fisher's exact tests to compare treatment arms within clinically relevant subgroups. For further subgroup analysis, we employed the Fisher's Exact test within the same clinically relevant subgroups, first to compare CR rates between subjects with zero versus one cycle of prior chemotherapy, and again to compare CR rates between subjects with short versus long DTI. Except for the planned primary-efficacy comparison of CR rates between treatment arms, all hypothesis tests utilized two-sided $\alpha=0.05$ significance levels. Multiple-testing adjustments were not performed during the subgroup analyses, and type-1 (false-positive) error inflation was accordingly accepted, in order to maintain a low type-2 (false-negative) error rate during this exploratory, hypothesis-generating phase of the analysis.

Supplemental Table S1. Treatment and Supportive Care

Drug or treatment	Dosing and Schedule
Vorinostat (VOR): Arm A only	300 mg PO on Days 1-5 every 3 wks Level -1 (200 mg)
Rituximab (R) if CD20+ (A and B arms)	375 mg/m ² IV on Day 1 every 3 wks
DA-R-EPOCH (A and B arms)	Every 3 weeks x 6 cycles
Etoposide	50 mg/m ² IVCI on Days 1-4 x 96 h
Prednisone	60 mg/m ² PO on Days 1-5
Doxorubicin	10 mg/m ² IVCI on Days 1-4 x 96 h
Vincristine	0.4 mg/m ² IVCI on Days 1-4 x 96 h
Cyclophosphamide (dose-adjusted)	Starting dose: 375 mg/m ² if CD4= 50-200/mm ³ with subsequent dose-adjustment, or maximum dose of 750 mg/m ² if CD4 > 200/mm ³ IVPB on Day 5
Supportive medications and treatment	
G-CSF	Started 24-48 hr after completion of chemotherapy
Pegfilgastrim	6 mg SC once
Or	
Filgastrim	300 mg or 480 mg SC daily for 10 days or longer until ANC ≥ 1,000/mm ³
Infection prophylaxis	Continuous
Trimethoprim-sulfamethoxazole (160-800 mg)	3 times weekly
or dapsone	100 mg PO daily
or atovoquone	1500 mg PO daily
Fluoroquinolone (anti-bacterial agent)	No later than Day 8 of chemotherapy if CD4 count < 100/mm ³ until ANC ≥ 1000/mm ³
Anti-herpetic agent (recommended)	
*CNS prophylaxis: IT methotrexate or Depocyte or cytarabine (per drug package specifications)	For a total of 4-6 doses
ART	Patients not on ART at study entry were required to start AFTER cycle 1 of chemotherapy
Non-zidovudine based regimen required	
ANC= absolute neutrophil count; DA= dose adjusted; IT= intrathecal; IVCI= intravenously (IV) by continuous infusion; IVP= IV push.	
*Central nervous system (CNS) prophylaxis was required in patients who had lymphomatous involvement of bone marrow, testes, sinuses, or epidural regions	

Supplemental Table S2. Dose modifications guidelines for cytopenias.

Event	Action
<p>*ANC nadir on any cycle < 500/mm³ on 2 nonconsecutive days at least 3 days apart and/or platelets < 25,000/mm³ in the previous cycle</p>	<p>1. For subjects on vorinostat:</p> <ul style="list-style-type: none"> • Reduced vorinostat by 100 mg daily (to a minimum of 200 mg daily). Chemotherapy given at dose in previous cycle without escalating cyclophosphamide. • If event recurred after vorinostat dose reduction, reduced vorinostat again by 100 mg daily (to a minimum of 200 mg daily). Chemotherapy given at doses as in previous cycle without escalating cyclophosphamide. • If event recurred at vorinostat dose of 200 mg, vorinostat was discontinued permanently. • If event recurs again after no vorinostat was given, cyclophosphamide was reduced by 187 mg/m². <p>2. If subject has never received, cyclophosphamide was reduced by 187 mg/m².</p>
<p>ANC < 500/mm³ x ≥ 3 days or platelets < 25,000/mm³ x ≥ 3 days, AND subject received no cyclophosphamide or vorinostat in the previous cycle</p>	<p>Doxorubicin and etoposide reduced by 25% of the full doses.</p>
<p>ANC nadir ≥ 500/mm³ AND platelet nadir ≥ 50,000/mm³ in the previous cycle</p>	<p>Cyclophosphamide increased by 187 mg/m² on every cycle to a maximum dose of 750 mg/m².</p>

*ANC= absolute neutrophil count

Supplemental Table S3. EPOCH dose modifications for Day 1 cell counts after a 2-week delay if ANC $\geq 750/\text{mm}^3$ but $< 1,000/\text{mm}^3$, or platelets $\geq 50,000/\text{mm}^3$ but $< 75,000/\text{mm}^3$.

Platelets	Absolute Neutrophil Count (2-week delay)		
	$\geq 1,000/\text{mm}^3$	$750\text{--}999/\text{mm}^3$	$< 750/\text{mm}^3$
$\geq 75,000/\text{mm}^3$	Full-dose	Cyclophosphamide reduced by $187 \text{ mg}/\text{m}^2$. Cyclophosphamide was not administered if previous dose was $187 \text{ mg}/\text{m}^2$. If the participant received no cyclophosphamide in the previous cycle, doxorubicin and etoposide reduced by 25% of previous doses.	Held treatment and removed participant from study
$50,000\text{--}75,000/\text{mm}^3$		Reduced cyclophosphamide by $187 \text{ mg}/\text{m}^2$. Cyclophosphamide was not administered if previous dose was $187 \text{ mg}/\text{m}^2$. If the participant received no cyclophosphamide in the previous cycle, doxorubicin and etoposide by 25% of previous doses.	Held treatment and removed participant from study
$< 50,000/\text{mm}^3$	Held treatment and removed participant from study.		

Supplemental Table S4. All treatment-related adverse events at the patient level.

Event	All Cycles							
	VOR(R)-EPOCH (N= 45)				R-EPOCH (N= 45)			
	AE= n (%)				AE= n (%)			
	Gr ≤2	Gr 3	Gr 4	Gr 5	Gr ≤2	Gr 3	Gr 4	Gr 5
Hematologic								
Anemia	6 (13)	20 (45)	1 (2)	---	11 (24)	14 (31)	0 (0)	---
Febrile neutropenia	---	6 (13)	2 (4)	---	---	4 (9)	3 (7)	---
Lymphopenia	2 (4)	8 (18)	9 (20)	---	6 (13)	9 (20)	3 (7)	---
Neutropenia	2 (4)	4 (9)	21 (47)	---	3 (7)	8 (18)	9 (20)	
Thrombocytopenia	11 (24)	5 (11)	13 (29)	---	16 (33)	2 (4)	1 (2)	---
Non-Hematologic								
Cardiac disorders (systolic dysfunction, sinus arrhythmias, and other)	5 (11)	2 (4)	1 (2)	---	4 (9)	0 (0)	0 (0)	---
Death-NOS	---	---	---	1 (2)	---	---	---	1 (2)
Gastrointestinal								
Abdominal pain	7 (16)	2 (4)	0 (0)	---	3 (7)	2 (4)	0 (0)	---
Constipation	20 (45)	0 (0)	0 (0)	---	18 (40)	0 (0)	0 (0)	---
Diarrhea	15 (33)	2 (4)	0 (0)	---	9 (20)	1 (2)	0 (0)	---
Hemorrhage	0 (0)	0 (0)	0 (0)	---	0 (0)	0 (0)	1 (2)	---
Mucositis Oral	10 (22)	0 (0)	0 (0)	---	9 (20)	0 (0)	0 (0)	---
Nausea	19 (42)	1 (2)	0 (0)	---	22 (49)	1 (2)	0 (0)	---
Vomiting	9 (20)	1 (2)	0 (0)	---	9 (20)	2 (4)	0 (0)	---
General disorders								
Chills	5 (11)	0 (0)	0 (0)	---	0 (0)	0 (0)	0 (0)	---
Edema- Limbs	10 (22)	0 (0)	0 (0)	---	4 (9)	0 (0)	0 (0)	---
Fatigue	18 (40)	0 (0)	0 (0)	---	13 (29)	0 (0)	0 (0)	---
Fever	7 (16)	1 (2)	0 (0)	---	2 (4)	0 (0)	0 (0)	---
Hepatic								
AST increase	13 (29)	2 (4)	0 (0)	---	10 (22)	0 (0)	0 (0)	---
ALT increase	14 (31)	4 (9)	0 (0)	---	7 (16)	2 (4)	0 (0)	---
ALK phos increase	11 (24)	0 (0)	0 (0)	---	9 (20)	0 (0)	0 (0)	---
Infection or infestations								
Sepsis	---	---	0 (0)	---	---	---	1 (2)	---
Other	11 (24)	4 (9)	0 (0)	---	8 (18)	3 (7)	0 (0)	---
Metabolic disorders								
Hyperglycemia	17 (38)	5 (11)	1 (2)	---	12 (27)	4 (9)	0 (0)	---
Hypocalcemia	7 (16)	4 (9)	0 (0)	---	15 (33)	0 (0)	1 (2)	---
Hypoalbuminemia	12 (27)	2 (4)	0 (0)	---	15 (33)	0 (0)	0 (0)	---
Hypokalemia	19 (42)	4 (9)	0 (0)	---	3 (7)	1 (2)	0 (0)	---
Hypomagnesemia	6 (13)	0 (0)	0 (0)	---	7 (16)	0 (0)	0 (0)	---
Hyponatremia	10 (22)	4 (9)	0 (0)	---	10 (22)	2 (4)	0 (0)	---
Hypophosphatemia	1 (2)	6 (13)	0 (0)	---	6 (13)	2 (4)	0 (0)	

Musculoskeletal	7 (16)	1 (2)	0 (0)	---	4 (9)	0 (0)	0 (0)	---
Neurologic								
Dizziness	6 (13)	0 (0)	0 (0)	---	5 (11)	0 (0)	0 (0)	---
Headache	9 (20)	1 (2)	0 (0)	---	16 (35)	1 (2)	0 (0)	---
Other (dysgeusia, concentration problem, lethargy, unspecified)	5 (11)	1 (0)	0 (0)	---	3 (7)	0 (0)	0 (0)	---
Peripheral motor neuropathy	3 (7)	1 (2)	(0)	---	2 (4)	0 (0)	(0)	---
Peripheral sensory neuropathy or paresthesia	13 (29)	0 (0)	0 (0)	---	20 (44)	2 (4)	0 (0)	---
Psychiatric disorders	6 (11)	2 (4)	0 (0)	---	10 (22)	0 (0)	0 (0)	---
Renal and Urinary disorders								
Creatinine increase	5 (11)	0 (0)	0 (0)	---	5 (11)	0 (0)	0 (0)	---
Other	2 (4)	0 (0)	0 (0)	---	4 (9)	0 (0)	1 (2)	---
Respiratory disorders								
Respiratory failure	---	---	1 (2)	---	---	---	0 (0)	---
Other	18 (40)	0 (0)	---	---	10 (22)	0 (0)	---	---
Skin disorders								
Alopecia	4 (8)	0 (0)	0 (0)	---	6 (13)	0 (0)	0 (0)	---
Rash and others	4 (8)	0 (0)	0 (0)	---	6	1 (2)	0 (0)	---
Vascular disorders								
Hypertension	3 (7)	0 (0)	0 (0)		1 (2)	0 (0)	0 (0)	---
Hypotension	0 (0)	0 (0)			4 (9)	0 (0)		
Thromboembolic events	---	1 (2)	1 (2)	---	0 (0)	0 (0)	0 (0)	---

Supplemental Table S5. Bcl-2, Bcl-6, Myc protein and corresponding BCL2, BCL6, and MYC gene rearrangements (-R) according to study arm and Non-Hodgkin lymphoma (NHL) subtype.

PIDN	Study arm	NHL subtype	Bcl-2 protein	Bcl-6 protein	Myc protein	BCL2-R	BCL6-R	MYC-R
17	EPOCH	DLBCL Non-GCB	Positive	Positive	Negative	NR or NP	NR or NP	NR or NP
18	EPOCH	PBL	NR or ND	NR or NP	NR or NP	NR or NP	NR or NP	NR or NP
19	EPOCH	DLBCL Non-GCB	Positive	Positive	NR or NP	NR or NP	NR or NP	NR or NP
20	EPOCH	DLBCL-GCB	Negative	Positive	NR or NP	NR or NP	NR or NP	Negative
21	VOR-EPOCH	DLBCL Non-GCB	Positive	Positive	Negative	Negative	Negative	Negative
22	VOR-EPOCH	DLBCL Non-GCB	Positive	Negative	Positive	Negative	Negative	Negative
23	EPOCH	DLBCL-GCB	Negative	Positive	NR or NP	Negative	Positive	Positive
24	VOR-EPOCH	DLBCL Non-GCB	Positive	Positive	Negative	Negative	NR or ND	Negative
25	EPOCH	DLBCL-GCB	Positive	Positive	Negative	Negative	NR or ND	Negative
26	VOR-EPOCH	DLBCL Non-GCB	Positive	Negative	NR or ND	NR or ND	NR or ND	NR or ND
27	EPOCH	BL	Negative	Positive	Positive	Negative	Negative	Positive
28	EPOCH	BCL-U	Positive	Positive	Positive	NR or ND	NR or ND	Positive
29	VOR-EPOCH	DLBCL-GCB	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
30	EPOCH	DLBCL Non-GCB	Positive	Negative	Positive	NR or ND	NR or ND	NR or ND
31	VOR-EPOCH	PEL	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	Negative
32	VOR-EPOCH	BCL-U	Positive	NR or ND	Positive	NR or ND	NR or ND	Positive
34	VOR-EPOCH	DLBCL Non-GCB	Positive	Positive	NR or ND	NR or ND	NR or ND	NR or ND
35	VOR-EPOCH	PBL	NR or ND	Positive	NR or ND	NR or ND	NR or ND	NR or ND
36	EPOCH	PBL	Positive	Negative	Positive	NR or ND	NR or ND	NR or ND
37	EPOCH	DLBCL-GCB	Positive	Positive	NR or ND	Negative	Positive	Negative
38	EPOCH	DLBCL Non-GCB	Positive	Negative	NR or ND	Negative	Positive	Negative
39	VOR-EPOCH	DLBCL Non-GCB	Positive	Positive	Positive	NR or ND	NR or ND	NR or ND
40	VOR-EPOCH	DLBCL Non-GCB	Negative	Positive	Positive	NR or ND	Positive	NR or ND
42	EPOCH	PEL	NR or ND	Negative	NR or ND	NR or ND	NR or ND	NR or ND
43	VOR-EPOCH	PBL	Positive	Negative	Positive	NR or ND	NR or ND	Positive
44	VOR-EPOCH	DLBCL Non-GCB	Negative	Positive	Positive	NR or ND	NR or ND	NR or ND
45	VOR-EPOCH	PBL	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
46	VOR-EPOCH	PEL	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
47	EPOCH	DLBCL Non-GCB	Positive	Positive	NR or ND	NR or ND	NR or ND	NR or ND
48	VOR-EPOCH	DLBCL-GCB	Positive	Negative	NR or ND	NR or ND	NR or ND	NR or ND
51	VOR-EPOCH	DLBCL-GCB	Negative	Positive	NR or ND	Negative	NR or ND	Negative
52	EPOCH	DLBCL-GCB	Positive	Positive	Negative	Negative	Positive	Negative
53	VOR-EPOCH	DLBCL-GCB/FL	NR or ND	Positive	NR or ND	NR or ND	NR or ND	NR or ND
54	VOR-EPOCH	PBL	NR or ND	NR or ND	Positive	NR or ND	NR or ND	Positive
55	EPOCH	DLBCL Non-GCB	Negative	Positive	Negative	NR or ND	NR or ND	NR or ND

56	VOR-EPOCH	PBL	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	Negative
57	EPOCH	PBL	NR or ND	NR or ND	Positive	NR or ND	NR or ND	NR or ND	Negative
58	VOR-EPOCH	DLBCL Non-GCB	NR or ND	Negative	Negative	NR or ND	NR or ND	NR or ND	NR or ND
59	EPOCH	DLBCL-GCB	Negative	Positive	Negative	NR or ND	NR or ND	NR or ND	NR or ND
60	VOR-EPOCH	DLBCL-GCB	Positive	NR or ND	Positive	Negative	Negative	Positive	Positive
61	EPOCH	DLBCL-GCB	NR or ND	Positive	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
62	VOR-EPOCH	DLBCL Non-GCB	Positive	Negative	Negative	NR or ND	NR or ND	NR or ND	NR or ND
63	EPOCH	DLBCL-GCB	Positive	Positive	NR or ND	Negative	Negative	Negative	Negative
64	EPOCH	PBL	NR or ND	NR or ND	Positive	NR or ND	NR or ND	NR or ND	Positive
65	EPOCH	DLBCL-GCB	Positive	Negative	NR or ND	Negative	Negative	Positive	Positive
66	EPOCH	DLBCL-GCB	Negative	Positive	Positive	NR or ND	NR or ND	NR or ND	NR or ND
67	EPOCH	DLBCL-GCB	Negative	Positive	Positive	Negative	Negative	Positive	Positive
68	VOR-EPOCH	DLBCL-GCB	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
69	EPOCH	DLBCL-GCB	Negative	Positive	NR or ND	Negative	NR or ND	NR or ND	NR or ND
70	VOR-EPOCH	DLBCL-U/FL	Positive	Positive	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
71	EPOCH	DLBCL Non-GCB	Negative	Negative	Positive	Negative	Negative	Positive	Positive
72	EPOCH	PBL	Positive	Negative	NR or ND	NR or ND	NR or ND	NR or ND	Positive
73	EPOCH	PBL	Negative	Negative	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
74	EPOCH	DLBCL Non-GCB	Positive	Positive	Positive	Negative	Positive	Negative	Negative
75	VOR-EPOCH	DLBCL Non-GCB	Positive	Positive	Negative	NR or ND	NR or ND	NR or ND	NR or ND
76	EPOCH	DLBCL-GCB	Positive	Positive	Positive	NR or ND	NR or ND	NR or ND	NR or ND
77	EPOCH	PEL	NR or ND	NR or ND	Negative	NR or ND	NR or ND	NR or ND	NR or ND
78	VOR-EPOCH	DLBCL-GCB	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
79	EPOCH	DLBCL-GCB	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
80	VOR-EPOCH	DLBCL Non-GCB	NR or ND	NR or ND	Positive	Negative	Negative	Negative	Negative
81	VOR-EPOCH	DLBCL-GCB	Negative	Negative	Positive	Negative	Negative	Negative	Negative
82	VOR-EPOCH	DLBCL Non-GCB	Positive	Positive	Positive	Negative	Positive	Negative	Negative
83	EPOCH	DLBCL-GCB	Negative	Positive	Positive	NR or ND	NR or ND	NR or ND	NR or ND
84	VOR-EPOCH	PBL	Positive	Negative	Positive	NR or ND	NR or ND	NR or ND	NR or ND
85	VOR-EPOCH	PEL	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
86	EPOCH	DLBCL-GCB	Negative	Positive	Positive	Equivocal	Negative	Negative	Negative
87	EPOCH	PBL	Positive	Negative	Positive	Negative	Negative	Positive	Positive
88	VOR-EPOCH	PBL	Negative	NR or ND	Positive	NR or ND	NR or ND	NR or ND	NR or ND
89	VOR-EPOCH	PBL	Negative	NR or ND	Positive	NR or ND	NR or ND	NR or ND	Positive
90	EPOCH	DLBCL-GCB	Negative	Positive	NR or ND	Negative	Negative	Positive	Positive
91	VOR-EPOCH	DLBCL-GCB	Negative	Positive	Negative	Negative	Equivocal	Positive	Positive
92	VOR-EPOCH	DLBCL Non-GCB	NR or ND	Positive	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND
94	VOR-EPOCH	PEL	Negative	NR or ND	Negative	NR or ND	NR or ND	NR or ND	NR or ND
95	VOR-EPOCH	DLBCL-GCB	Positive	Positive	Negative	NR or ND	NR or ND	NR or ND	NR or ND
96	EPOCH	DLBCL Non-GCB	Positive	Positive	NR or ND	NR or ND	NR or ND	NR or ND	NR or ND

97	VOR-EPOCH	DLBCL-GCB	Positive	Positive	Negative	Negative	Positive	Negative
99	EPOCH	DLBCL Non-GCB	Positive	Positive	Positive	Negative	Positive	Negative
100	VOR-EPOCH	PEL	Negative	Negative	Negative	NR or ND	NR or ND	NR or ND
101	VOR-EPOCH	DLBCL-GCB	Negative	Positive	Negative	Negative	Negative	Positive
102	VOR-EPOCH	DLBCL-GCB	NR or ND	NR or ND	Negative	NR or ND	NR or ND	Negative
103	VOR-EPOCH	DLBCL-GCB	Positive	Positive	Negative	NR or ND	NR or ND	NR or ND
104	VOR-EPOCH	DLBCL-GCB	Negative	Positive	NR or ND	NR or ND	NR or ND	NR or ND
105	EPOCH	DLBCL Non-GCB	Positive	Positive	Negative	Negative	Negative	Negative
106	EPOCH	DLBCL Non-GCB	Positive	Negative	Positive	Negative	Negative	Negative
107	EPOCH	DLBCL-GCB	Positive	Positive	Negative	NR or ND	NR or ND	NR or ND

BL= Burkitt lymphoma. **BCL-U**= B-cell lymphoma, unclassifiable, with features between DLBCL and BL. **DLBCL**= Diffuse large B-cell lymphoma. **DLBCL-U**= Diffuse large B-cell lymphoma, unclassified. **GCB**= germinal center, **FL**= follicular lymphoma. **ND**= not done. **NR**= No report. **PBL**= Plasmablastic lymphoma. **PEL**= Primary effusion lymphoma. **PIDN**= patient identification number.

Supplemental Table S6. Baseline demographics and characteristics of evaluable patients, divided by diagnosis-to-treatment interval (DTI) of <15 versus ≥15 days.

Patient Subgroups	DTI of less than 15 days (N=44)			DTI of 15 or more days (N=42)			P†
	N	Median (range)	%	N	Median (range)	%	
Characteristic							
Gender							1.00
Female	3		7%	2		5%	
Male	41		93%	40		95%	
Race/Ethnicity							0.37
White/non-Hispanic	21		48%	15		36%	
White/Hispanic	9		20%	6		14%	
Other Hispanic	5		11%	5		12%	
African American	7		16%	13		31%	
Asian	0		0%	2		5%	
Unknown	2		5%	1		2%	
Age, years		48 (24–67)			48 (28–70)		0.83
<u>CDC risk factor</u>							
Homosexual/bisexual contact	21		48%	23		55%	0.39
Heterosexual contact	18		41%	14		33%	0.65
IV drug use	2		5%	4		10%	0.43
Transfusion recipient	3		7%	0		0%	0.24
Other CDC risk factor	2		5%	3		7%	0.67
Multiple risk factors	4		9%	4		10%	1.00
ART use at baseline							0.48
Yes	41		93%	37		88%	
No	3		7%	5		12%	
Absolute CD4 count at baseline (cells/mm³)							
Numeric values		180.5 (50–1137)			230.5 (50–1061)		0.34
50-100	6		14%	5		12%	0.34
100-200	21		48%	14		33%	
>200	17		39%	23		55%	
HIV viral load at baseline (copies/ml)							
Positive and >limit	25		57%	27		64%	0.51
Undetectable or <limit	19		43%	15		36%	
Positive Values >limit		24,700 (25–1,712,000)			211 (2–901,000)		0.079
Ann Arbor stage							0.16
I-II	5		11%	10		24%	
III-IV	39		89%	32		76%	
aa-IPI risk							0.82
0-1	14		32%	15		36%	

2-3	30	68%	27	64%	
LDH elevation					0.63
Yes	31	70%	32	76%	
No	13	30%	10	24%	
Pathologic diagnosis					0.74
DLBCL	30	68%	31	74%	0.80
<i>GCB</i>	17/30	57%	17/31	55%	
<i>Non-GCB</i>	12/30	40%	14/31	45%	
<i>Unclassified</i>	1/30	3%	0/31	0%	
PBL	8	18%	7	17%	
PEL	3	7%	4	10%	
BCL-U	2	5%	0	0%	
BL	1	2%	0	0%	
Ki-67 expression					0.12
< 80%	8	18%	2	5%	
≥ 80%	31	70%	37	88%	
Inconclusive /ND	5	11%	3	7%	
EBV status					
<i>DLBCL</i>					0.58
EBER-Positive	9	30%	7	23%	
EBER-Negative	14	47%	19	61%	
Inconclusive /ND	7	23%	5	16%	
<i>PBL</i>					1.00
EBER-Positive	7	88%	6	86%	
EBER-Negative	1	12%	1	14%	
<i>PEL</i>					1.00
EBER-Positive	2	67%	3	75%	
EBER-Negative	1	33%	1	25%	
<i>BCL-U</i>					----
EBER-Negative	2	100%	0	0%	
<i>BL</i>					----
EBER-Negative	1	100%	0	0%	
Bcl-2 protein					
<i>DLBCL</i>					0.65
Positive	14	47%	18	58%	
Negative	10	33%	9	29%	
Inconclusive /ND	6	20%	4	33%	
<i>PBL</i>					1.00
Positive	2	25%	3	43%	
Negative	2	25%	1	14%	
Inconclusive /ND	4	50%	3	43%	
<i>PEL</i>					1.00
Negative	1	33%	1	25%	
Inconclusive /ND	2	67%	3	75%	
<i>BCL-U</i>					----
Positive	2	100%	0	0%	
<i>BL</i>					----

Negative	1	100%	0	0%	
Myc protein					
<i>DLBCL</i>					0.85
Positive	10	33%	8	26%	
Negative	8	27%	10	32%	
Inconclusive /ND	12	40%	13	42%	
<i>PBL</i>					1.00
Positive	5	63%	4	57%	
Inconclusive /ND	3	37%	3	43%	
<i>PEL</i>					0.49
Negative	2	67%	1	25%	
Inconclusive /ND	1	33%	3	75%	
<i>BCL-U</i>					----
Positive	2	100%	0	0%	
<i>BL</i>					----
Positive	1	100%	0	0%	
Concurrent vorinostat					0.39
Yes	25	57%	19	45%	
No	19	43%	23	55%	
One cycle of prior chemo					0.083
Yes	22	50%	13	31%	
No	22	50%	29	69%	
<p>aa-IPI= age-adjusted International Prognostic Index. BL= Burkitt lymphoma. DLBCL= Diffuse Large B-cell lymphoma. DTI= Diagnosis to treatment interval. ND= not done. PBL= Plasmablastic lymphoma. PEL= Primary effusion lymphoma. BCL-U= B-cell lymphoma, unclassifiable, with features between DLBCL and BL. †P-values are from Wilcoxon rank-sum tests on Age, Absolute CD4 counts, and HIV viral load, and from Fisher exact tests on all other patient characteristics.</p>					

Supplemental Table S7. Clinical Outcomes According to Pre-protocol Therapy. Shows complete response (CR) rates, yearly event-free survival (EFS) and overall survival (OS), all versus pre-protocol therapy.

Patient Subgroups	CR rates			P†
	EPOCH with 1 cycle of Prior Chemo, #CR/N (%)†	EPOCH Without Prior Chemo, #CR/N (%)†	Both Groups, #CR/N (%)†	
All patients [95% CI]§	22/35 (63) [47–79]	39/51 (76) [65–88]	61/86 (71) [61–81]	0.23
Pathologic Diagnosis				
DLBCL	15/25 (60)	30/36 (83)	45/61 (74)	0.074
• GCB type	10/16 (62)	15/18 (83)	25/34 (74)	0.25
• Non-GCB type	5/8 (62)	15/18 (83)	20/26 (77)	0.33
• Unclassified DLBCL	0/1 (0)	0/0 (–)	0/1 (0)	----
PBL	3/5 (60)	7/10 (70)	10/15 (67)	1.00
PEL	3/3 (100)	2/4 (50)	5/7 (71)	0.43
BCL-U	1/2 (50)	0/2 (0)	1/2 (50)	----
BL	0/0 (–)	0/1 (0)	0/1 (0)	----
EBV status				
Positive	13/18 (72)	12/16 (75)	25/34 (74)	1.00
Negative	6/12 (50)	22/28 (79)	28/40 (70)	0.13
Not Performed	3/5 (60)	5/7 (71)	8/12 (67)	1.00
Absolute CD4 count				
<100 cells/mm ³	1/4 (25)	4/7 (57)	5/11 (45)	0.55
100-200 cells/mm ³	9/16 (56)	13/19 (68)	22/35 (63)	0.50
>200 cells/mm ³	12/15 (80)	22/25 (88)	34/40 (85)	0.65
#Cycles of Protocol Therapy				
1-4 Cycles	1/9 (11)	0/5 (0)	1/13 (8)	1.00
5-6 Cycles	21/26 (81)	39/46 (85)	60/72 (83)	0.75
Diagnosis-to-Treatment Interval (DTI)				
Less than 15 days	10/22 (45)	15/22 (68)	25/44 (57)	0.22
15 days or more	12/13 (92)	24/29 (83)	36/42 (86)	0.65
Kaplan-Meier Survivals	Proportion (SE)€	Proportion (SE)€	Proportion (SE)€	P‡
Event-Free Survival after:				
12 months	74% (7.4%)	71% (6.4)	72% (4.8%)	0.85
24 months	71% (7.7%)	64% (6.8)	67% (5.1%)	
36 months	68% (8.1%)	64% (6.8)	69% (5.2%)	
Overall Survival after:				
12 months	77% (7.1%)	84% (5.2%)	81% (4.3%)	0.50
24 months	71% (7.7%)	79% (5.8%)	76% (4.7%)	
36 months	67% (8.2%)	77% (6.1%)	73% (5.0%)	

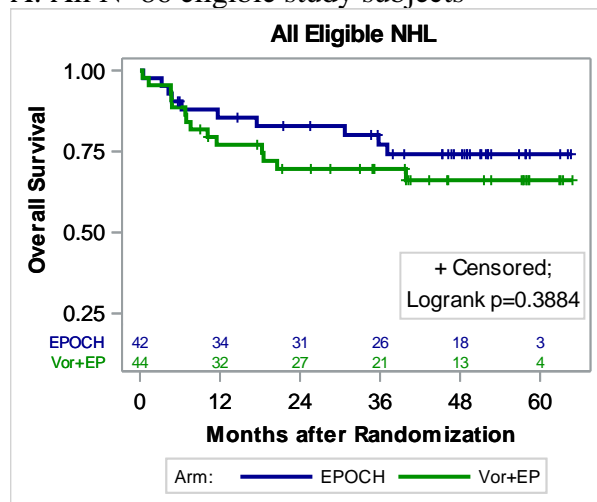
† Number of Complete Responses / Number of subjects (CR rate in percent units)
Two-sided P-values are from ‡ Fisher Exact tests and †† log-rank tests.
§ 95% confidence interval on CR rate. Numbers are in percent units.
€ Proportion Surviving (standard error of proportion)

Supplemental Table S8: Shows complete response (CR) rates versus diagnosis-to-treatment Interval (DTI) dichotomized as $</\geq 15$ days.

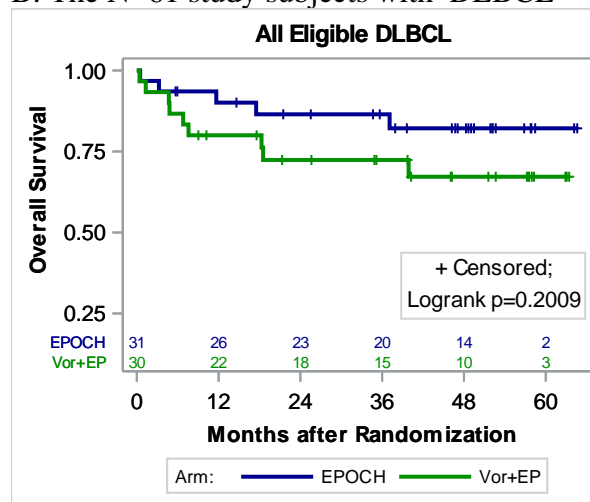
Patient Subgroups	CR rates			P [†]
	DTI <15 days, #CR/N (%) [†]	DTI ≥ 15 days, #CR/N (%) [†]	Both Groups, #CR/N (%) [†]	
Pathologic Diagnosis				
DLBCL	17/30 (57)	28/31 (90)	45/61 (74)	0.0036
• GCB type	9/17 (53)	16/17 (94)	25/34 (74)	0.0065
• Non-GCB	8/12 (67)	12/14 (86)	20/26 (77)	0.37
• Unclassified DLBCL	0/1 (0)	---	0/1 (0)	-----
Kaplan-Meier Survivals	Proportion (SE)[€]	Proportion (SE)[€]	Proportion (SE)[€]	P[‡]
Event-Free Survival after:				
12 months	61% (7.3%)	83% (5.8%)	72% (4.8%)	0.032
24 months	57% (7.5%)	78% (6.4%)	67% (5.1%)	
36 months	57% (7.5%)	76% (6.8%)	66% (5.2%)	
Overall Survival after:				
12 months	72% (6.8%)	90 (4.6%)	81% (4.3%)	0.052
24 months	62% (7.5%)	90 (4.6%)	76% (4.7%)	
36 months	62% (7.5%)	85 (5.9%)	73% (5.0%)	
† Number of Complete Responses / Number of subjects (CR rate in percent units) Two-sided P-values are from ‡ Fisher Exact tests and ‡‡ log-rank tests. € Proportion Surviving (standard error of proportion)				

Supplemental Figure S1. Kaplan-Meier curves of overall survival after vorinostat-R-EPOCH and R-EPOCH for all study eligible patients with aggressive HIV-NHL (A), (B) all DLBCL, (C) Non-GCB DLBCL (C), (D) GGB-type DLBCL, (E) Plasmablastic lymphoma, and (F) Primary effusion lymphoma.

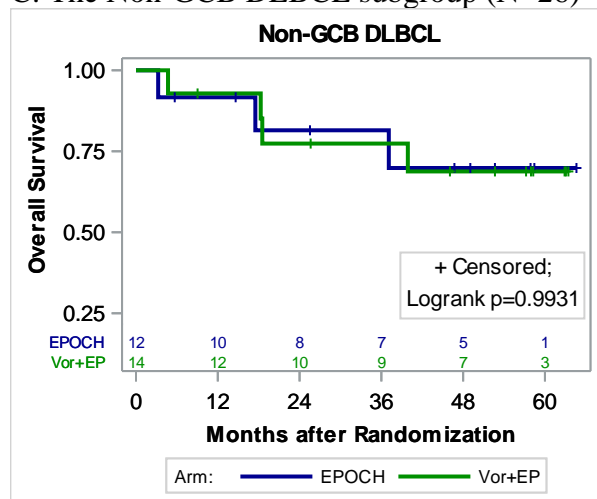
A: All N=86 eligible study subjects



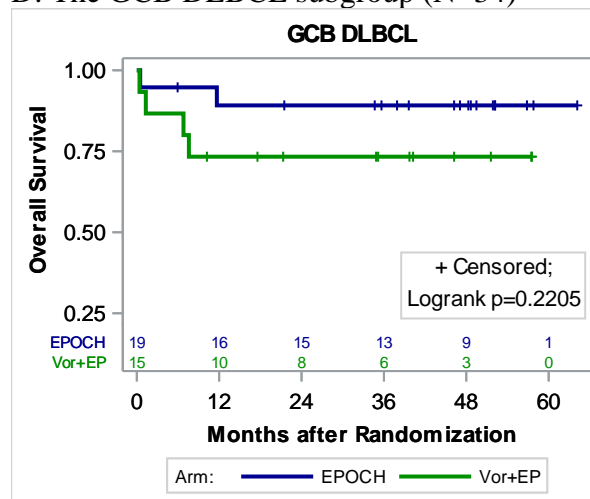
B: The N=61 study subjects with DLBCL



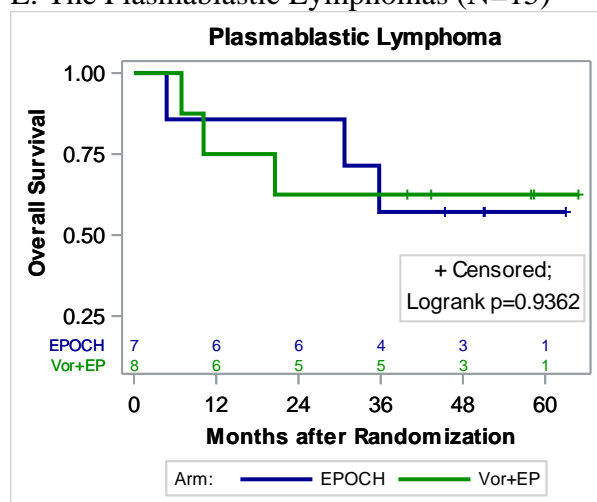
C: The Non-GCB DLBCL subgroup (N=26)



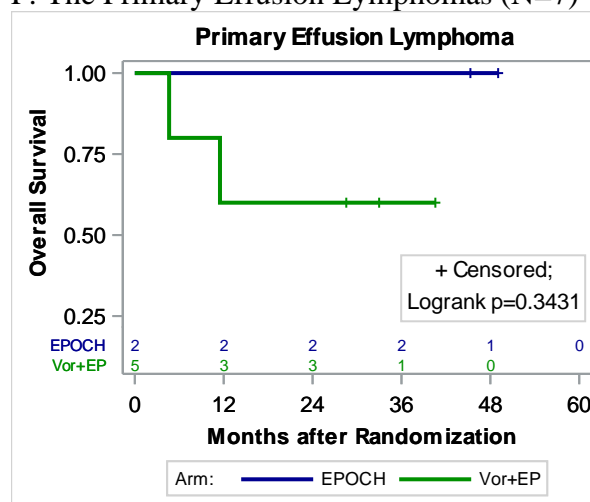
D: The GCB DLBCL subgroup (N=34)



E: The Plasmablastic Lymphomas (N=15)

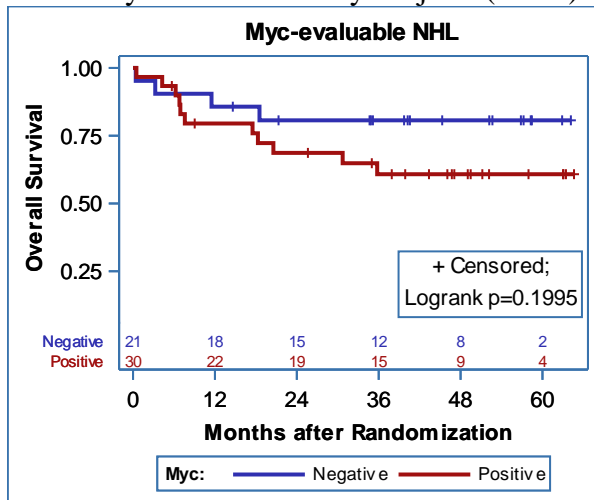


F: The Primary Effusion Lymphomas (N=7)

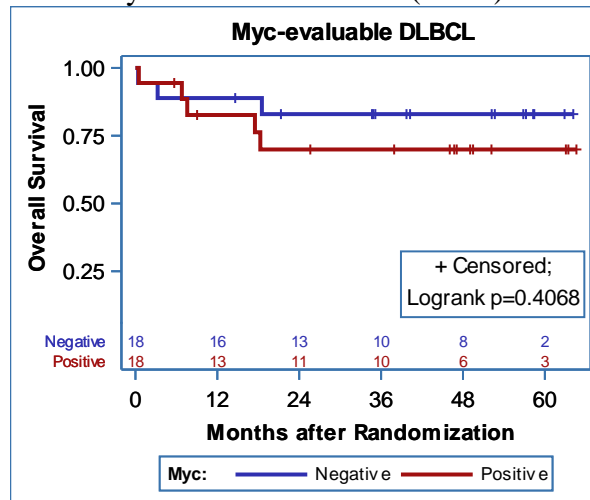


Supplemental Figure S2. Overall Survival (OS) According to Myc Protein Expression. Shows Kaplan-Meier curves of OS in evaluable Myc+ versus Myc negative cases in all NHL subtypes.

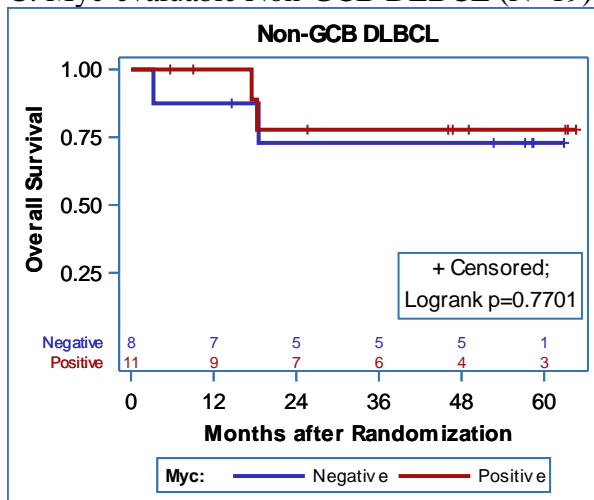
A: All Myc-evaluable study subjects (N=51)



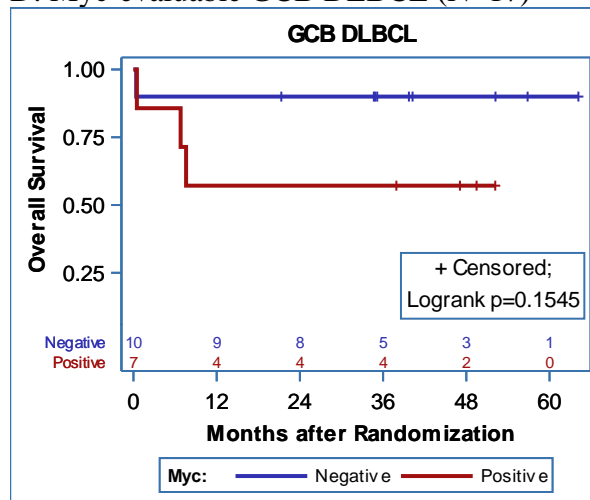
B: All Myc-evaluable DLBCL (N=36)



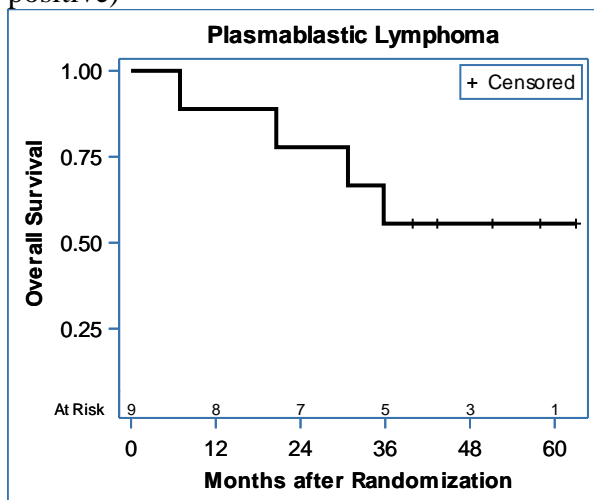
C: Myc-evaluable Non-GCB DLBCL (N=19)



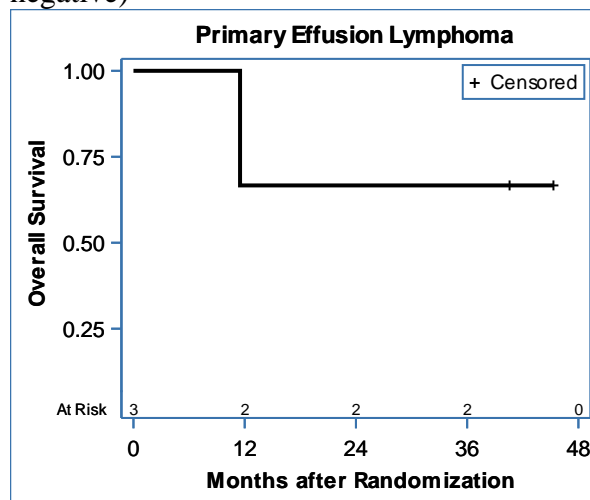
D: Myc-evaluable GCB DLBCL (N=17)



E: Myc-evaluable PBL (9/9 were Myc-positive)

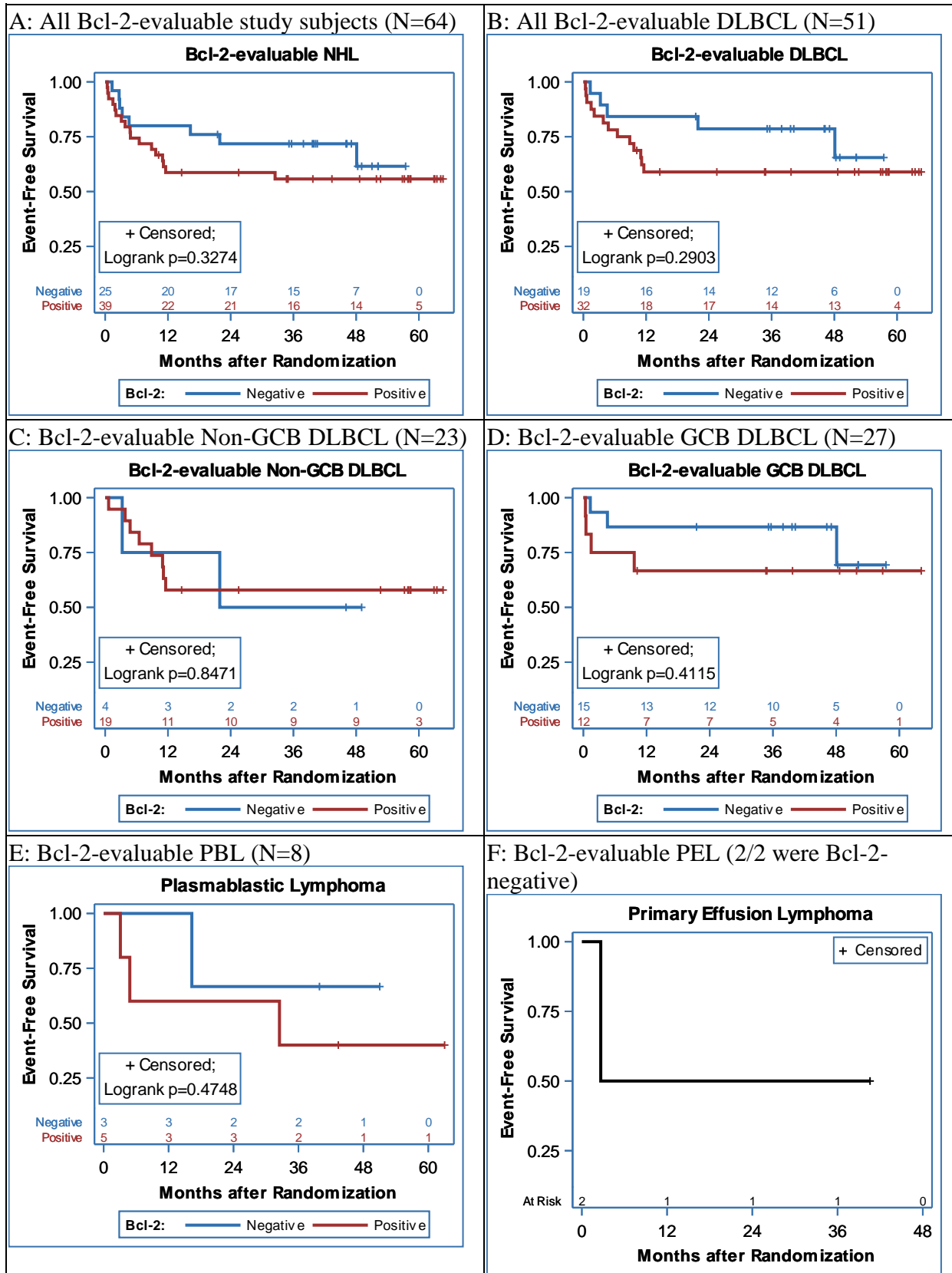


F: Myc-evaluable PEL (3/3 were Myc-negative)

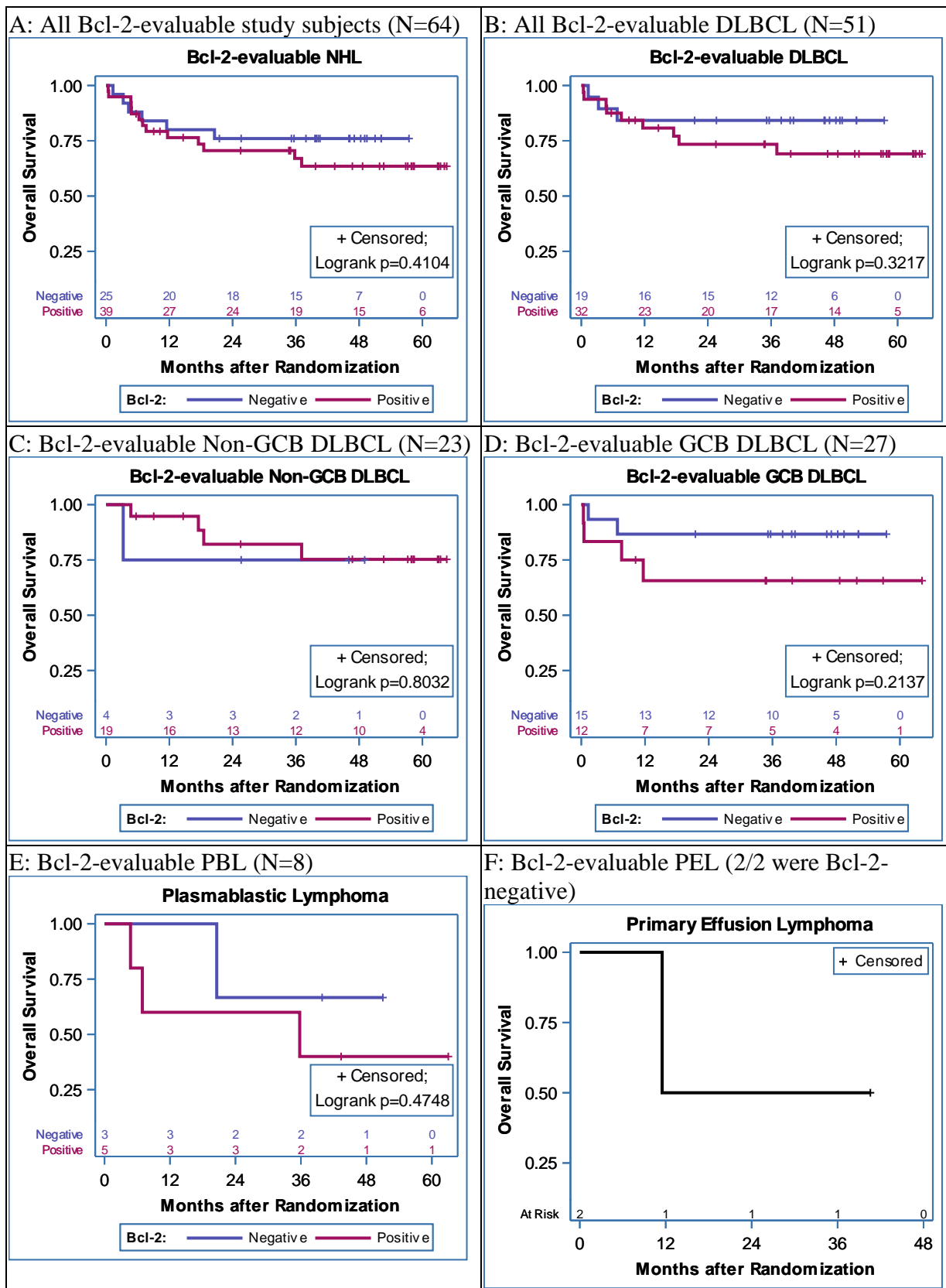


Supplemental Figure S3. Event-Free Survival (EFS) According to Bcl-2 Protein Expression.

Shows Kaplan-Meier curves of EFS in evaluable Bcl-2+ versus Bcl-2 negative cases in all NHL subtypes.

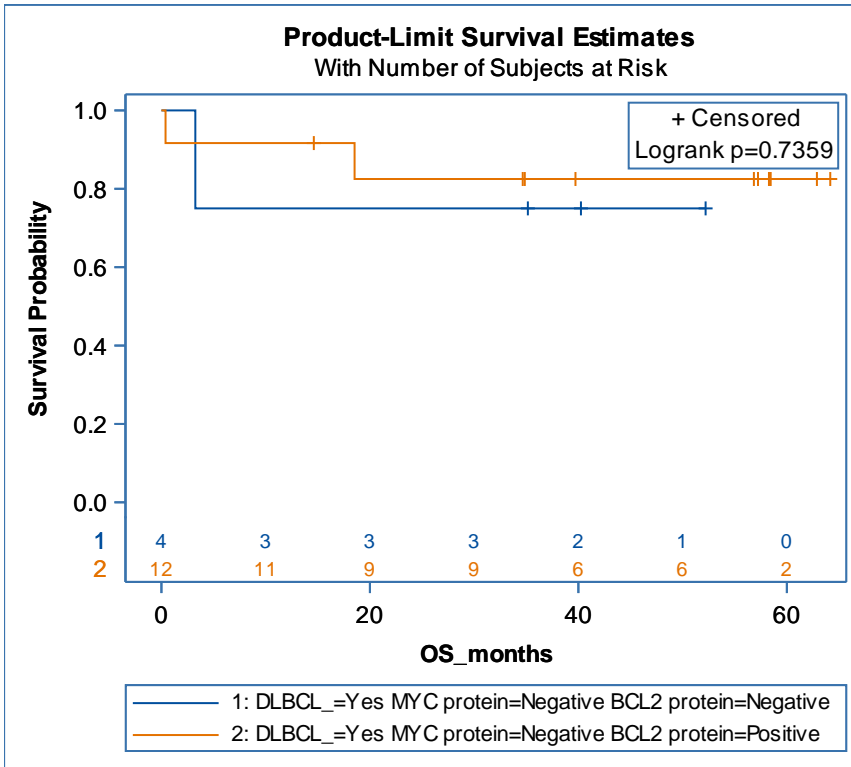


Supplemental Figure S4. Overall Survival (OS) According to Bcl-2 Protein Expression. Shows Kaplan-Meier curves of OS in evaluable Bcl-2+ versus Bcl-2 negative cases in all NHL subtypes.

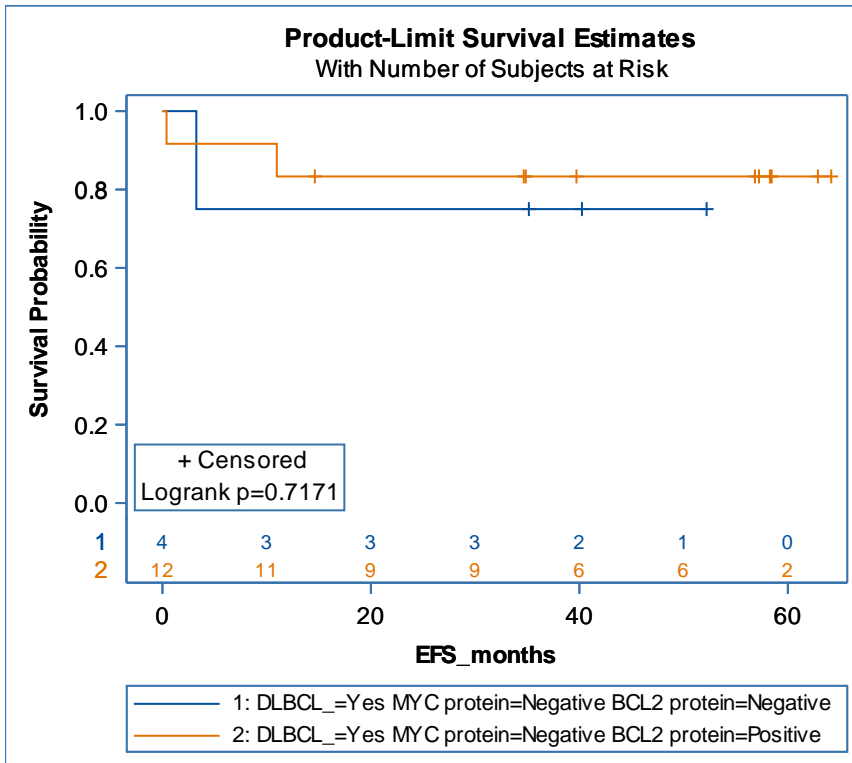


Supplemental Figure S5. Survival According to Myc and Bcl-2 protein co-expression. Shows Kaplan-Meier curves of event-free survival (EFS) and overall survival (OS) rates in evaluable Myc+/Bcl-2 negative versus Myc+/ Bcl-2+ cases.

A.

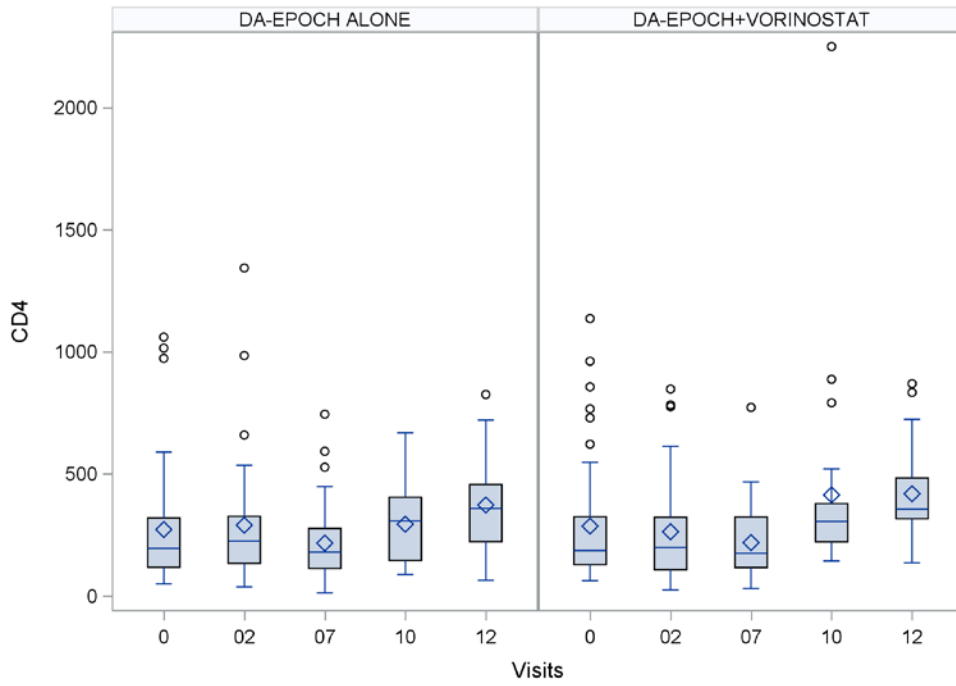


B.

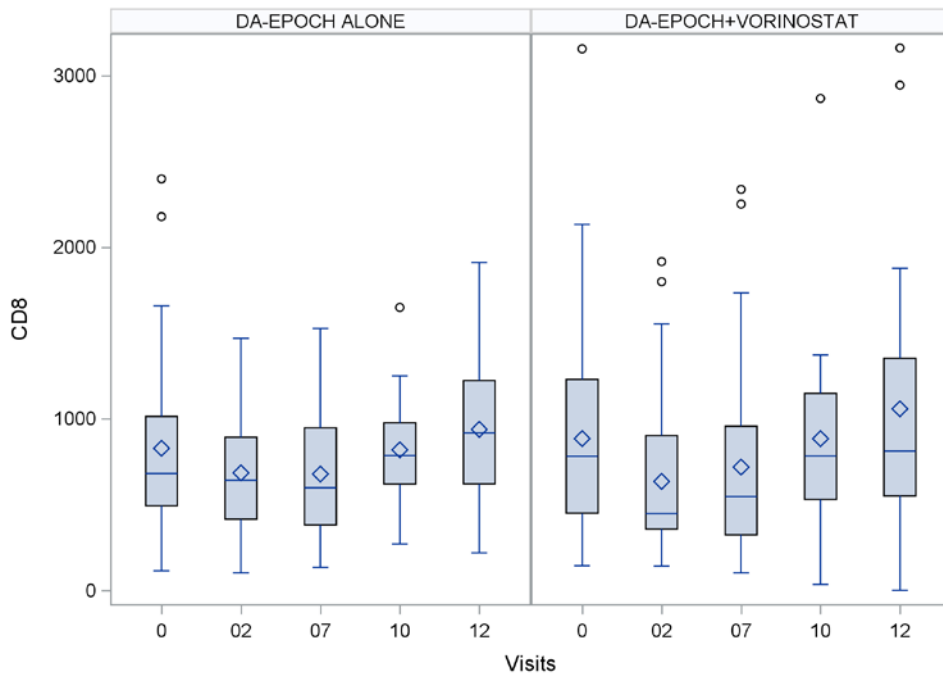


Supplemental Figure S6. CD4 counts (**A**) and CD8 counts (**B**) across visits (0= baseline; 02= after cycle 2; 07= after cycle 6; 10= month 10; 12= 12 months from treatment start).

A.

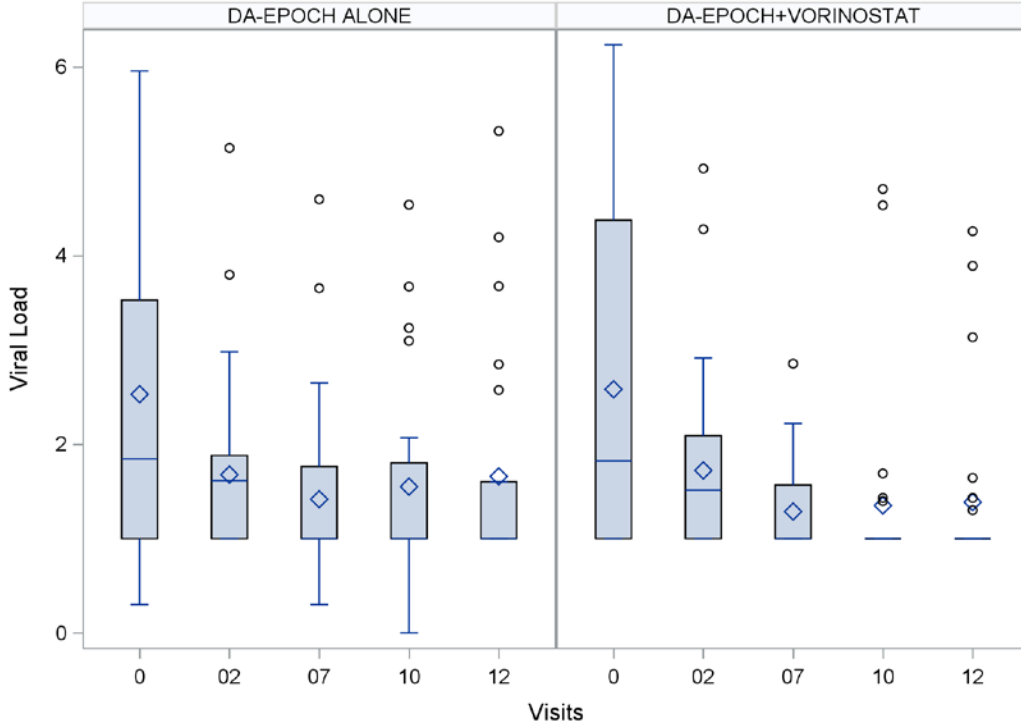


B.

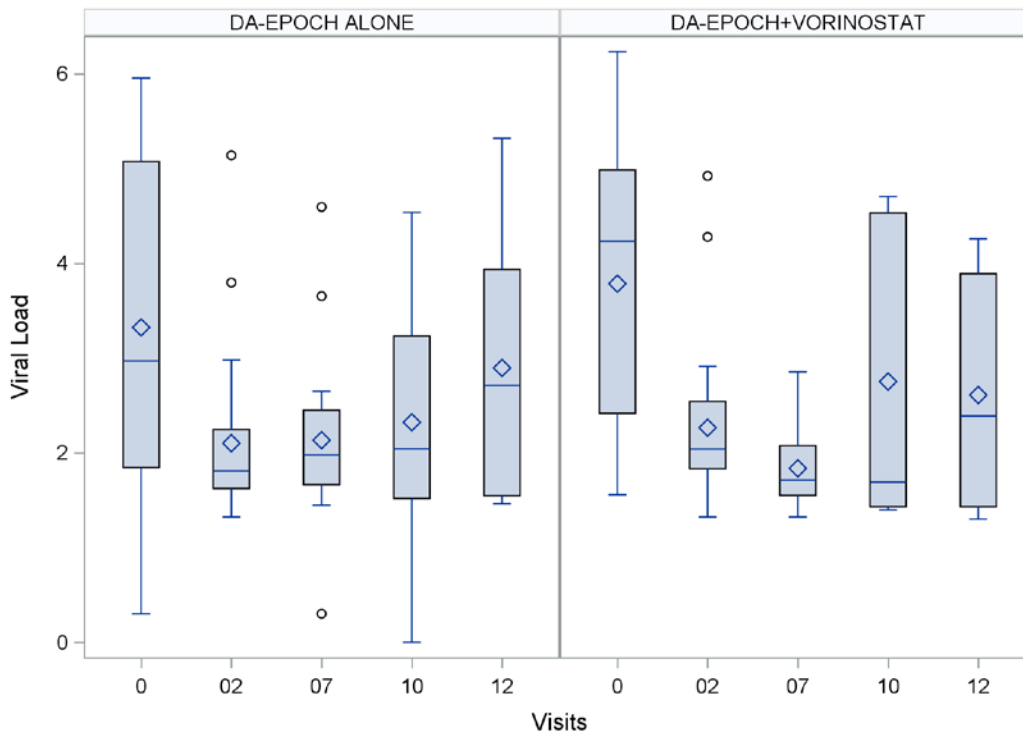


Supplemental Figure S7. Log 10 transformed HIV viral loads (RNA copies/ml) across visits (0= baseline; 02= after cycle 2; 07= after cycle 6; 010= month 10; 012= 12 months from treatment start) for all patients (**A**), and those with detectable viral load only (**B**).

A. All patients

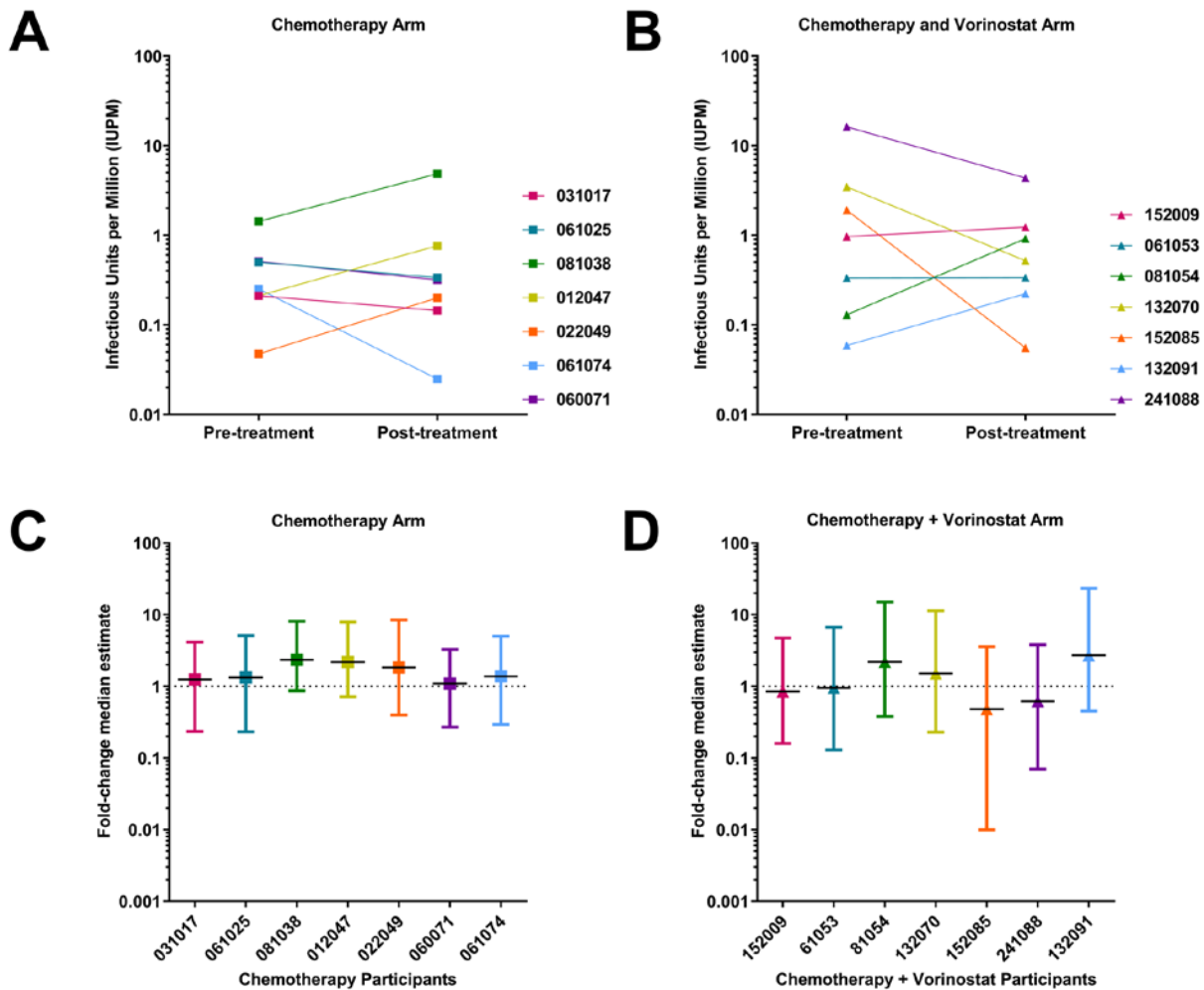


B. Patients with detectable viral load only



Supplemental Figure S8. Impact of treatment (chemotherapy alone vs. chemotherapy and vorinostat) on HIV reservoirs measured longitudinally by quantitative viral outgrowth assay.

Panels A and B show the frequency of HIV-infected CD4 T cells per million (IUPM) capable of viral outgrowth over time. Panels C and D demonstrate the fold change in the IUPM pre- and post-treatment using a mixed-effects Bayesian model with an unconstrained treatment and temporal effect. Symbols (95% confidence intervals) represent fold-changes, each reported as 50 percentile (or median estimate) in the size of the latent HIV-reservoir, at any point post treatment compared to its pre-treatment value within each patient.



Appendix: AIDS Malignancy Consortium

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Chuang, David Chumba, Christine Chung, David Chung, Jennifer Chuy, Aubrey Ciatto, Deborah Citron, Laura Clark, Melissa Cloete, Joan Coetzee, Anna Coghill, Janet Cogswell, Abigail Cohen, Justine Cohen, Seth Cohen, Donald Colbourn, Cynthia Coles, Vivian Colon-Lopez, James Colyar, Kathleen Comerford, Mercedes Condry, Adriana Corera, Patricia Cornejo-Juarez, Lynne Cornelissen, Melissa Cortes, Bukre Coskun, Patricia Costantini, Mark Cotton, Paul Couey, Dorothy Coyle, Shammaia Crisler, Stephanie Cruz, Ramon Cruz, Maria Cugliari, Judith Currier, Peter Curtin, Christina Curtiss, Nichole Czajkowski, Sandra D'Angelo, Cecilia Ferreira da Silva, Maria DaCosta, Joseph Monko Dafrosa, Parastoo Dahi, Lucrecia Dalmasso, Usha Dalvi, Lloyd Damon, Lina Damrah, Daniel Danila, Teresa Darragh, Theresa Davey, Keith Davidson, Lamesha Davis, Alexandre Dayrell, Mildred De Jager, Ina de Jongh, Mariano De Stefano, Emanel Dell'Isola, Camille DeMarco, Jeremy Deni, Husam Dennaoui, Nadia DePaola, Gabriela Deronato, Avni Desai, Gisela Di Stefano, Mark Dickson, Martine Diez, Paige DiMambro, Noel DIP, Asekanadziwa DIP, Mena DIP, Dirk Dittmer, Christopher Dittus, Tara Doga, Martin Donach, Mary Downey, Rachel Dowty, Jamie Doyle, Vance Doyle, Pamela Drullinsky, Viktoriya Duda, Tara Duggan, Agustina Dupont, Elisabeth Dwyer, Christina Dyer, Anthony Eason, Allison Easterbrook, Ximena Echeverria, Pamela Eckardt, Edith Matsikidze, Nader El-Mallawany, Pavana Elavalakanar, Theresa Elko, Annare Ellmann, Grant Ellsworth, Juliana Eng, Yoko Eng, Fabiana Enjamio, Marta Epeldegui, Narendranath Epperla, Joseph Erinjeri, Roxana Escalante, Tatiana Estrada, Simone Maia Evaristo, Geriga Fadhil, Lorenzo Falchi, Karen Fehn, Celia Fenceroy, Desire Fenderson, Salli Fennessey, Paulo Fernandes, Judy Ferreira, James Fetten, Maria Figueroa, Silvina Figurelli, Valeria Fink, Carter Finneran, John Fiore, Anne Fischer, Richard Fisher, Khaliah Fleming, Misty Fleming, Sofie Fliss-Zadra, John Paul Flores, Lisa Flowers, Keli Ford, Lauren Foster, Matthew Foster, Done Fourie, Claudia Francis, Irma Franco-Gonzalez, Jennifer Frederick, Audrey French, Claudia Frenzel, Natalie Frey, Henry Fung, Edward Furlani, Neo Gaaje, Leigh Gaffney, Lindee Ganger, Jennifer Garbarino, April Garbuz, Cristal Garcia, Patricia Garcia, Madhur Garg, Odette Garland, Amanda Garner, Samantha Garst, Benjamin Gartrell, Dieter Geiger, Laura Geran, Caroline Gettens, Arnab Ghosh, Raof Giali, Nancy Giallombardo, LeAnne Gildehaus, Sergio Giralt, Marcelo Gismondi, Anna Giullano, Douglas Gladstone, Marshall Glesby, Bridgette Goeieman, Sanjay Goel, Kathryn Gold, Zoe Goldberg, Stephen Goldstone, Lucero Gonzalez, Aaron Goodman, Satish Gopal, Pamela Gorejena Chidawanyika, Mila Gorsky, Noah Goss, Mrinal Gounder, Gail Graham, Claudia Grandas, Elana Grandberg, Lissa Gray, Rhamoana Green, Gregory Gressel, Candace Griffin, Catherine Griffin, Ashley Griffin-Ellison, Juneko Grilley-Olson, Michelle Grindley, Natalie Grover, Jennifer Gruhn, Ping Gu, Rasim Gucalp, Elizabeth Gudesblat, Ivy Gudza, Jenny Guerra, El Hadji Gueye, Humberto Guiot, Clifford Gunthel, Wilfred Gurupira, Boglarka Gyurkocza, Zainab Hadithi, Michael Hagensee, Renee Hall, Mark Hallman, Balazs Halmos, Audrey Hamilton, Paul Hamlin, Alan Hanash, Helen Hancock, Ashley Harley, Thomas Harrington, Lee Hartner, Kevan Hartshorn, Hani Hassoun, Kaitlyn Haughey, Ericka Hayes, Bing He, Nicole Heinz, Avelina Hemingway, Zurayda Hendricks, David Henry, Alexandra

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