

SUPPLEMENTARY INFORMATION

EXTENDED DETAILS OF THE METHODS

Enrolling Sites for NA-ACCORD cohort

ALIVE: AIDS Link to the IntraVenous Experience
ALLRT: AACTG Longitudinal Linked Randomized Trials
CWRU: Case Western Reserve University Immunology Unit Patient Care and Research Database
DCC: D.C. Cohort Longitudinal HIV Study
EGHCC: Emory-Grady HIV Clinical Cohort
FENWAY: Fenway Community Health Center
HIVRN: HIV Research Network
HOMER: HAART Observational Medical Evaluation and Research
HOPS: HIV Outpatient Study
JHHCC: Johns Hopkins HIV Clinical Cohort
KPMAS: Kaiser Permanente Mid-Atlantic States
KPNC: Kaiser Permanente Northern California
LSOCA: Longitudinal Study of Ocular Complications of AIDS
MWCCS: MACS/WIHS Combined Cohort Study
MHCS-II: Second Multicenter Hemophilia Cohort Study
MLMC: Maple Leaf Medical Clinic
MONT: The McGill University Health Centre, Chronic Viral Illness Service Cohort
OHTN: Ontario HIV Treatment Network Cohort Study
PARKLAND: Parkland/UT Southwestern Cohort
RRC: Retrovirus Research Center
SAC: Southern Alberta Clinic Cohort
SCOPE: Study of the Consequences of the Protease Inhibitor Era
SUN: The Study to Understand the Natural History of HIV/AIDS in the Era of Effective Therapy
UAB: University of Alabama at Birmingham 1917 Clinic Cohort
UCHCC: University of North Carolina, Chapel Hill HIV Clinic
UCSD: University of California at San Diego
UW: University of Washington HIV Cohort
VACS: Veterans Aging Cohort Study and Virtual Cohort
VAND: Vanderbilt Comprehensive Care Clinic HIV Cohort

Enrolling Sites for COMPLETE cohort

Yale University School of Medicine
Memorial Sloan-Kettering Cancer Center
UCLA
Washington University School of Medicine
Seattle Cancer Care Alliance
Stanford University Medical Center
John Theurer Cancer Center at Hackensack University Medical Center
Emory, Winship Cancer Institute
University of Chicago Medical Center
Dartmouth-Hitchcock Medical Center
Medical College of Georgia
USC/Norris Comprehensive Cancer Center
West Virginia University
Vanderbilt University Medical Center
University of Wisconsin Comprehensive Cancer Center

Metro Minnesota Community Clinical Oncology Program
Overlook Hospital and Morristown Memorial Hospital
University of Rochester
UNC - Chapel Hill
Georgetown University Medical Center
Northwestern University Feinberg School of Medicine
Carolinas Medical Center – NorthEast
Arizona Cancer Center
Saint Louis University Cancer Center
University of Miami
St. Francis Medical Group Oncology and Hematology Specialists
Health Cancer Center - Orlando Health (MD Anderson - Orlando)
UT Southwestern
NYU Clinical Cancer Center
Danbury Hospital, Praxair Cancer Center
Research Medical Center
Kootenai Cancer Center
Fox Chase Cancer Center
Washington Cancer Institute at Washington Hospital Center
ProMedica Hematology Oncology Associates
City of Hope National Medical Center
Rush University Medical Center

Moore's UCSD Cancer Center
Simmons Cooper Cancer Institute at SIU School of Medicine
University of Virginia Health System
Northside Hospital (formerly Georgia Cancer Specialists)
Blood and Cancer Center of East Texas
Indiana University Simon Cancer Center
Guthrie Clinic, Ltd.
South Texas Oncology and Hematology, P.A.
Hematology and Oncology Associates of Fayetteville (Carolina Cancer Management, Inc.)
LSU Health Sciences Center
The Cancer Institute of New Jersey
University of Illinois at Chicago
University of Tennessee Cancer Institute
University of Maryland, Greenebaum Cancer Center JPS Center for Cancer Care
Moffit Cancer Center
Olive View UCLA Medical Center
West Michigan Cancer Center

Covariates

Covariates were measured as close to cancer diagnosis as possible, within the window of 6 months before through 3 months after cancer diagnosis. In the NA-ACCORD, the patient's age was denoted by the year of birth. Sex was noted as male or female based on the patient's birth sex. Self-reported race was divided into 7 categories including: Asian, Black, indigenous, multiracial, white, missing, or other (this included Asian/indigenous/multiracial or Hispanic depending on the cohort). Comorbid conditions included chronic kidney disease (CKD) defined as glomerular filtration rate (eGFR) <60 mL/min/1.73m² for at least 3 months; Diabetes was defined by use of insulin, oral hypoglycemic drug or diagnostic code or a glycated hemoglobin ≥6.5%; Hepatitis B infection defined as evidence of HBV infection while under observation with positive HBV surface antigen, HBV e antigen or HBV DNA test. Hepatitis C infection as evidence of HCV infection while under study observation with positive HCV antibody test, detectable HCV RNA, or the presence of HCV genotype. Hypertension was defined as prescription of antihypertensive medication with a hypertension diagnosis. AIDS-defining illness was defined according to the 1993 CDC revised classification system. ART therapy was defined as use of at least one class of antiretroviral medications during the NA-ACCORD enrollment period.

For the analysis comparing PWH in NA-ACCORD to PWoH in COMPLETE, age, sex, race, evidence of HIV, HBV and HCV infections were assessed at study entry. In COMPLETE, self-reported race was categorized as black vs. nonblack. Definitions for HIV, HBV and HCV infections were like those utilized by the NA-ACCORD cohort. Data on variables such as CKD, diabetes, hypertension, dyslipidemia, substance use, smoking or alcohol use were collected whenever possible for COMPLETE participants.

Statistical Analysis

People in the COMPLETE study were followed from the date of their cancer diagnosis (occurring between February 5, 2010, and February 5, 2014) to date of death, date of loss to follow-up (defined as no proactive communication by the patient or next of kin back to the site, that the patient was

proactively withdrawing from the study, and that after multiple attempts to communicate, the patient or next of kin could not be contacted, in the absence of any confirmation of death), 5 years after cancer diagnosis or administratively censored on December 17, 2018, whichever came first.

PWH entered observation into our nested study on the date of cancer diagnosis. To ensure incident diagnoses while under observation in the NA-ACCORD, only those with cancer diagnoses occurring after the later of the following were included: enrollment date into the NA-ACCORD, the date that marks the start of the period when cancers diagnoses were investigated using the validation protocol (i.e., the cancer observation window start date), or January 1, 1996. PWH were followed from diagnosis to the first of the following: date of death, December 31, 2016, 5 years after cancer diagnosis or the cohort-specific end of the observation window of validated cancer diagnosis (if it was before December 31, 2016) whichever came first. To account for effect on any uncaptured mortality due to loss to follow up, we performed sensitivity analysis where date of loss to follow up was defined as 18 months after the date of last HIV RNA or CD4 cell count measurement. To compare the survival of PWH and PWoH with T and NK/TCL over the same study periods, we performed additional sensitivity analysis whereby only those patients whose lymphomas were diagnosed between 2010-2014, the overlapping years of diagnosis were included.

Categorical and ordinal variables were summarized by frequencies and percentages and comparisons between groups were performed using Pearson's Chi-squared test and Fisher's exact test. Continuous variables were summarized by mean, median, standard deviation and interquartile range and comparison between groups were performed using t-test, Wilcoxon rank-sum test, and Kruskal-Wallis test. Kaplan-Meier method was used to estimate the survivor function and 95% confidence interval (95% CI). Comparison between survival curves among TCL and ALCL patients with and without HIV, between the TCL and BCL among PWH and over calendar periods from 1996-2016 was performed using log-rank test. A continuous time-to-event approach was used, and Cox proportional model estimated crude (HR) and stepwise adjusted (aHR) hazard ratios of mortality and 95% CI. Analyses were performed using R version 4.1.0 or greater (The R Foundation for Statistical Computing-<http://www.r-project.org/>) and a p-value <0.05 determined statistical significance.

SUPPLEMENTARY TABLES

Table S1: Extended clinical characteristics for people without HIV (PWoH) with T-cell and NK/T-cell lymphoma in COMPLETE (N=450)

Characteristic	PWoH with T-cell and NK/T-cell lymphoma (N=450)
ECOG Perf. Status, No. (%)	
0-1	421 (93.3)
2	26 (5.8)
≥ 3	4 (0.9)
Any B Symptoms % (CI)	48.6 (44.0, 53.2)
LDH Elevated % (CI)	46.1 (41.5, 50.8)
IPI at diagnosis, Median (IQR)	2.0 (1.0, 3.0)

ECOG-Eastern Co-operative Oncology Group, values for ECOG performance status range from 0 to 5, with higher scores indicating greater disability

B symptoms defined as presence of fever or drenching night sweats or loss of more than 10 percent of body weight over 6 months

LDH-lactate dehydrogenase level

The standard Internal Prognostic Index (IPI) score is calculated based on risk factors such as age ≥ 60 years, LDH above baseline, Ann Arbor stage III or IV disease, ECOG performance status ≥2 and more than one extranodal site to determine prognosis

Abbreviations: ATLL-Adult T-cell Leukemia/Lymphoma, AITL-Angioimmunoblastic T-cell Lymphoma, ALCL-Anaplastic Large-Cell Lymphoma, CTCL-Cutaneous T-cell Lymphoma, PTCL-NOS-Peripheral T-cell Lymphoma not otherwise specified, NK/TCL-Natural Killer-T-cell lymphoma, T-LGL-T-cell large granular lymphocytic leukemia, LDH-lactate dehydrogenase, IPI- International prognostic Index, the IPI score is determined based on a subject's disease characteristics and represents increasing degrees of risk), IQR-Inter-Quartile Range, (CI)-95% Confidence Intervals, y-year(s), NA-not available

Table S2. Survival probability since lymphoma diagnosis

Time since lymphoma diagnosis (y)	S(t) (95% CI)	
	NA-ACCORD (PWH with T-cell and NK/T-cell lymphoma) (n = 52)	COMPLETE (PWoH with T-cell and NK/T-cell lymphoma) (n = 450)
1	0.52 (0.40, 0.67)	0.75 (0.71, 0.80)
2	0.44 (0.32, 0.60)	0.62 (0.58, 0.67)
3	0.37 (0.26, 0.53)	0.56 (0.52, 0.61)
4	0.35 (0.23, 0.51)	0.48 (0.44, 0.54)
5	0.32 (0.21, 0.49)	0.45 (0.41, 0.51)
Median (mo)	12.9 [6.6-51.8]	46.2 [36.7-NA]

Abbreviations: (CI)-95% Confidence Intervals, S(t)-survival probability, PWH-patients with HIV, PWoH-patients without HIV, mo-months, NA-not reached, y-year(s)

Table S3. Survival probability since lymphoma diagnosis

Time since lymphoma diagnosis (y)	S(t) (95% CI)	
	NA-ACCORD (PWH with ALCL) (n = 26)	COMPLETE (PWoH with ALCL) (n = 79)
1	0.42 (0.27, 0.66)	0.88 (0.81, 0.96)
2	0.31 (0.17, 0.55)	0.84 (0.76, 0.93)
3	0.23 (0.11, 0.47)	0.82 (0.73, 0.91)
4	0.23 (0.11, 0.47)	0.76 (0.66, 0.87)
5	0.23 (0.11, 0.47)	0.76 (0.66, 0.87)
Median (mo)	10.6 [2.1-33.4]	NA [NA-NA]

Abbreviations: (CI)-95% Confidence Intervals, S(t)-survival probability, ALCL-anaplastic large cell lymphoma, PWH-patients with HIV, PWoH- patients without HIV, mo-months, NA-not reached, y-year(s)

Table S4: Survival probability of PWH and T-cell lymphoma based on immunological cell count and HIV viremia in NA-ACCORD

Time since cancer diagnosis (y)	S(t) (95% CI)	
	CD4 \geq 200 and/or HIV RNA <500 (n = 12)	CD4 <200 and HIV RNA \geq 500 (n = 10)
1	0.82 (0.63, 1)	0.50 (0.27, 0.93)
2	0.73 (0.52, 1)	0.50 (0.27, 0.93)
3	0.73 (0.52, 1)	0.50 (0.27, 0.93)
4	0.73 (0.52, 1)	0.33 (0.12, 0.92)
5	0.73 (0.52, 1)	0.17 (0.03, 0.93)
Median (mo)	NA [NA-NA]	26.1 [1.3-NA]

Abbreviation: PWH-patients with HIV, CD4 count is quantified in cells/ μ L before initiation of antiretroviral drugs, HIV RNA level is quantified in copies/ml before initiation of antiretroviral drugs, (CI)-95% Confidence Intervals, S(t)-survival probability, mo-months, NA-not reached, y-year(s)

Table S5. Bonferroni adjusted p values for baseline demographic and clinical characteristics in NA-ACCORD

Patient Features	PWH with T-cell and NK/T-cell lymphoma	PWH with Burkitt's lymphoma	PWH with Primary CNS lymphoma	PWH with DLBCL	P value^a	Pairwise comparisons – Bonferroni adjusted p values
	(n = 52)	(n = 101)	(n = 64)	(n = 500)		
Age at diagnosis of lymphoma (years), Median (IQR)	49 (43-55)	47 (39-51)	41 (37-49)	47 (40-55)	<0.001	0.045 (Burkitt's vs. Primary CNS) <0.001 (Primary CNS vs. TCL) <0.001 (Primary CNS vs. DLBCL)
Race, No. (%)					0.04 ^b	0.03 (Burkitt's vs. Primary CNS)
White	30/47 (64)	58/94 (62)	21/58 (37)	255/461 (55)		
Black	16/47 (34)	31/94 (33)	34/58 (59)	189/461 (41)		
Other	1/47 (2)	5/94 (5)	3/58 (5)	17/461 (4)		
Co-morbid conditions, No. (%)						
Chronic kidney disease	10 (19)	7 (7)	2 (3)	62 (12)	0.02 ^b	0.03 (Primary CNS vs. TCL)
No of cases diagnosed per calendar period, No. (%)						
1996-1999	10 (19)	13 (13)	27 (42)	67 (13)	<0.001	<0.001 (Primary CNS vs. Burkitt's)
2000-2009	29 (56)	54 (53)	31 (48)	292 (58)		<0.001 (Primary CNS vs. DLBCL)
2010-2016	13 (25)	34 (34)	6 (9)	141 (28)		
Alive, No. (%)	18 (35)	53 (52)	11 (17)	200 (40)	<0.001	<0.001 (Primary CNS vs. Burkitt's) <0.001 (Primary CNS vs. DLBCL)
Age at NA-ACCORD Enrollment (years), Median (IQR)	44 (41-50)	43 (35-47)	39 (34-45)	43 (36-50)	0.01	0.01 (DLBCL vs. Primary CNS) 0.01 (TCL vs. Primary CNS)

^aP values for the comparison between patients in different lymphoma groups (T-cell and NK/T-cell lymphomas, Burkitt's, PCNSL, DLBCL) were calculated using ANOVA and chi-square test for continuous and categorical variables, respectively

^bP-values based on Fisher's exact test due to some small cell counts

Patient with chronic kidney disease (CKD) were defined as those who ever had an eGFR consistently <60 mL/min/1.73m² for at least 3 months

Abbreviations: PWH-people with HIV, IQR-Inter-Quartile Range, PCNSL-primary central nervous system lymphoma, DLBCL-diffuse large B-cell lymphoma

Table S6: Extended clinical characteristics for patients with HIV with non-Hodgkin lymphomas

Features	T-cell and NK/T-cell lymphoma (n = 52)	Burkitt's lymphoma (n = 101)	Primary CNS lymphoma (n = 64)	DLBCL (n = 500)	^a P
HIV transmission group, No. (%)					
IV drug use	12 (23)	23 (23)	15 (23)	108 (22)	0.98
MSM	9 (17)	44 (44)	9 (14)	154 (31)	<0.001
Heterosexual transmission	5 (10)	10 (10)	9 (14)	73 (15)	0.51
Other ^b	0	1 (1)	3 (5)	14 (3)	0.34 ^c
Unknown	28 (54)	29 (29)	28 (44)	171 (34)	0.008
AIDS-defining illnesses infections, No. (%)					
Candidiasis	4 (8)	5 (5)	15 (23)	63 (13)	0.003
CMV	4 (8)	7 (7)	9 (14)	47 (9)	0.50 ^c
Coccidiomycosis	0	1 (1)	0	1 (<1)	0.51 ^c
Cryptococcus	1 (2)	1 (1)	5 (8)	24 (5)	0.12 ^c
Cryptosporidiosis	1 (2)	0	3 (5)	5 (1)	0.06 ^c
HSV	1 (2)	1 (1)	2 (3)	10 (2)	0.74 ^c
Histoplasmosis	0	2 (2)	1 (2)	13 (3)	0.87 ^c
Isosporiasis	0	0	0	2 (<1)	>0.99 ^c
MAC	1 (2)	2 (2)	7 (11)	18 (4)	0.04 ^c
Mycobacterium	1 (2)	1 (1)	6 (9)	14 (3)	0.03 ^c
TB	0	3 (3)	10 (16)	17 (3)	<0.001 ^c
PCP	6 (12)	5 (5)	14 (22)	76 (15)	0.01
Toxoplasmosis	0	0	4 (6)	10 (2)	0.047 ^c
Co-morbid conditions, No. (%)					
Diabetes	6 (12)	15 (15)	8 (13)	73 (15)	0.91
Hypertension	15 (29)	32 (32)	10 (16)	168/494 (34)	0.03

^aP-values for the comparison between patients in different lymphoma groups (T-cell lymphomas, Burkitt's, PCNSL, DLBCL) were calculated using chi-square test for categorical variables

^bReceipt of blood transfusion, blood components, or tissue, or other risk factor

^cP-values based on Fisher's exact test due to some small cell counts

Abbreviations: Burkitt's- Burkitt's lymphoma, TCL-T-cell lymphoma, PCNSL-primary central nervous system lymphoma, DLBCL-diffuse large B-cell lymphoma, IV-intravenous, MSM-men having sex with men, CMV-cytomegalovirus, HSV-herpes simplex virus, MAC-mycobacterium avium intracellulare, TB-tuberculosis, PCP-pneumocystis carinii pneumoniae

Table S7. Survival probability since lymphoma diagnosis in NA-ACCORD

Time since cancer diagnosis (y)	S(t) (95% CI)				
	T-cell and NK/T-cell lymphoma		Burkitt's lymphoma (n=101)	Primary CNS lymphoma (n = 64)	DLBCL (n = 500)
	ALCL (n = 26)	Non-ALCL (n = 26)			
1	0.42 (0.27, 0.66)	0.62 (0.45, 0.83)	0.59 (0.50, 0.70)	0.27 (0.18, 0.41)	0.55 (0.51, 0.60)
2	0.31 (0.17, 0.55)	0.57 (0.41, 0.80)	0.54 (0.45, 0.65)	0.21 (0.13, 0.34)	0.44 (0.40, 0.49)
3	0.23 (0.11, 0.47)	0.53 (0.36, 0.77)	0.53 (0.44, 0.64)	0.18 (0.10, 0.30)	0.42 (0.38, 0.46)
4	0.23 (0.11, 0.47)	0.46 (0.29, 0.73)	0.52 (0.43, 0.63)	0.16 (0.09, 0.28)	0.40 (0.36, 0.45)
5	0.23 (0.11, 0.47)	0.40 (0.23, 0.68)	0.52 (0.43, 0.63)	0.16 (0.09, 0.28)	0.38 (0.34, 0.43)
Median (mo)	10.6 [2.1-33.4]	45.6 [2.8-NA]	NA [13.1-NA]	3.8 [2.0-7.2]	15.6 [12.7-22.2]

Abbreviation: ALCL-anaplastic large cell lymphoma, PCNSL- primary central nervous system lymphoma, DLBCL-diffuse large B-cell lymphoma, (CI)-95% Confidence Intervals, S(t)-survival probability, mo-months, NA-not reached

Table S8: Sensitivity analysis for patients lost to follow up in NA-ACCORD

Time of follow-up (y)	Min	1 st Quarter	Median	Mean	3 rd Quarter	Max
Main analysis	0.0	0.22	1.07	2.09	5.0	5.0
Sensitivity analysis	0.0	0.14	0.55	1.34	1.66	5.0

Abbreviation: y-year(s)

Table S9. Baseline demographic and clinical characteristics for PWH with T-cell and NK/T-cell lymphoma vs. PWH with Hodgkin's lymphoma within NA-ACCORD (N=298)

Characteristic	PWH with T-cell and NK/T-cell lymphoma (n = 52)	PWH with Hodgkin's lymphoma (n = 246)	P ^a
Age at diagnosis of lymphoma (years), Median (IQR)	49 (43-55)	48 (43-56)	0.63
Biological Sex, No. (%)			
Male	50 (96)	233 (95)	>0.99 ^b
Race, No. (%)			
White	30/47 (64)	99/218 (45)	0.04
Black	16/47 (34)	115/218 (53)	
Other	1/47 (2)	4/218 (2)	
Co-morbid conditions, No. (%)			
Chronic kidney disease ^c	10 (19)	47 (19)	>0.99
Co-infections, No. (%) [#]			
HBV	7 (13)	28 (11)	0.86
HCV	10 (19)	36 (15)	0.53
No of cases per calendar period, No. (%)			
1996-1999	10 (19)	31 (13)	0.28
2000-2009	29 (56)	131 (53)	
2010-2016	13 (25)	84 (34)	
Alive at study exit, No. (%)	18 (35)	160 (65)	<0.001
Age at NA-ACCORD Enrollment (years), Median (IQR)	44 (41-50)	43 (36-50)	0.16
Time to diagnosis of lymphoma from time of NA-ACCORD Enrollment (years), Median (IQR)	2.3 (0.3-5.9)	3.9 (1.9-7.5)	0.004

^aP values for the comparison between patients with TCL and NK/TCL versus with Hodgkin's lymphoma were calculated using t-test, Wilcoxon rank sum test, and chi-square test for normally distributed continuous, non-normally distributed continuous, and categorical variables, respectively

^bP-values based on Fisher's exact test due to some small cell counts

^cPatient with chronic kidney disease (CKD) were defined as those who ever had an eGFR consistently < 60 mL/min/1.73m² for at least 3 months

[#]HBV: hepatitis B virus, as determined by detection of surface antigen, e antigen or DNA quantification; HCV: hepatitis C virus as determined by detection of antibody, RNA quantification or genotype

Abbreviations: PWH-people with HIV, IQR-Inter-Quartile Range

Table S10. Survival probability since lymphoma diagnosis within NA-ACCORD

Time since lymphoma diagnosis (y)	S(t) (95% CI)	
	PWH with T-cell and NK/T-cell lymphoma (n = 52)	PWH with Hodgkin's lymphoma (n = 246)
1	0.52 (0.40, 0.67)	0.76 (0.71, 0.81)
2	0.44 (0.32, 0.60)	0.69 (0.63, 0.75)
3	0.37 (0.26, 0.53)	0.67 (0.61, 0.73)
4	0.35 (0.23, 0.51)	0.64 (0.58, 0.70)
5	0.32 (0.21, 0.49)	0.63 (0.57, 0.69)

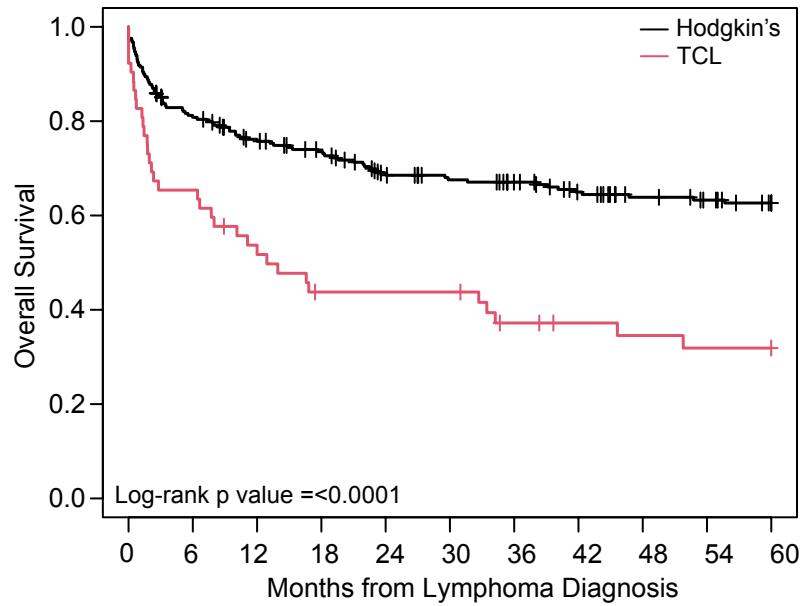
Median (mo)	12.9 [6.6-51.8]	NA [NA-NA]
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Abbreviations: (CI)-95% Confidence Intervals, S(t)-survival probability, PWH-patients with HIV, mo-months, NA-not reached, y-year(s)

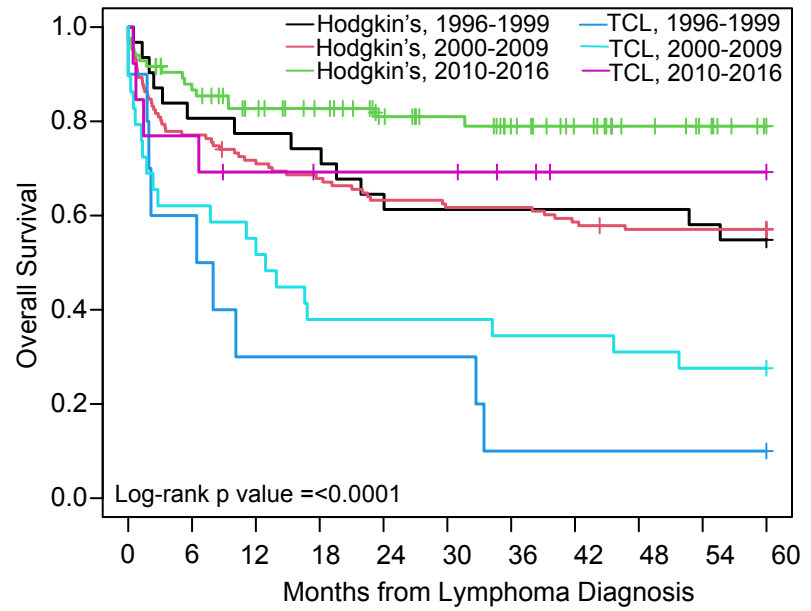
FIGURE LEGEND

Supplementary Figure 1. Overall survival (OS) at 5 years for PWH with T-cell and NK/T-cell lymphoma (TCL and NK/TCL) relative to PWH with Hodgkin's lymphoma enrolled in NA-ACCORD between 1996-2016. Kaplan-Meier analysis of (A) OS for all mature TCL and NK/TCL patients in contrast with Hodgkin's lymphoma, and (B) OS for all mature TCL and NK/TCL patients in contrast with Hodgkin's lymphoma stratified by period of diagnosis.

Abbreviations: Hodgkin's-Hodgkin's lymphoma

A

N = 246	195	177	165	147	139	132	121	110	105	1
N = 52	34	27	21	21	21	16	14	13	12	

B

N = 31	25	24	23	20	19	19	19	19	18	
N = 131	101	93	88	82	80	80	76	73	73	1
N = 84	69	60	54	45	40	33	26	18	14	
N = 10	6	3	3	3	3	1	1	1	1	
N = 29	18	16	11	11	11	10	10	9	8	
N = 13	10	8	7	7	7	5	3	3	3	