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Survival outcomes in diffuse large B-cell lymphoma patients with and without HIV in the United States from 2001 to 2016: a population-based analysis

Running title: Outcomes in DLBCL patients with and without HIV

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Data sharing statement
Deidentified data are available at https://seer.cancer.gov/.

Disclosure of conflicts of interest

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BV, SJS, MSS, and LMM do not have any conflict of interest

Authorship contributions

BV, SJS, and LMM conceptualized and designed the study; BV performed the analysis; BV, SJS, and LMM drafted the manuscript; SJS and LMM contributed to data acquisition and acquired funding; LMM supervised and administered the study; SJS, MSS, JJC, and LMM provided valuable edits to the manuscript and approved the final version of the manuscript.

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LETTER TO THE EDITOR

People living with human immunodeficiency virus (HIV) are at an increased risk of developing diffuse large B-cell lymphoma (DLBCL) compared to the general population.[1] Although European-based cohort studies suggest similar outcomes between DLBCL patients with and without HIV after the introduction of antiretroviral therapy (ART),[2-4] United States (US) population-based studies up to 2009 reported that DLBCL patients with HIV still experience inferior survival.[5, 6] Previous studies have not investigated whether survival differences in the US persist within demographic subgroups and for more recent ART regimens, which have fewer toxicities and drug-drug interactions.[7] We compared the overall survival (OS) in a contemporary cohort (2008-2016) and assessed temporal changes, reflecting changes in ART, between DLBCL patients with and without HIV overall and within demographic subgroups.

We conducted a population-based retrospective cohort study using 13 registries with available HIV status from the Surveillance, Epidemiology, and End Results (SEER) database during 2001-2016, with follow-up through 2019. We included patients newly diagnosed with DLBCL at ages 20-79. The following International Classification of Diseases for Oncology, 3rd edition, codes were used: 9680/3, 9684/3 (2001-2009 period), 9688/3, 9712/3, 9735/3 (2010-2016 period), 9737/3, 9738/3. Exclusion criteria were diagnosis through autopsy/death certificate (n=115), no survival time (n=181), unknown race and ethnicity (n=299), and no reported first course of chemotherapy or immunotherapy (n=10,811). This study is not considered human subjects research and did not require the exemption or approval from an Institutional Review Board or Ethics Committee.

The calendar year of DLBCL diagnosis was grouped corresponding to ART approval periods for proxy of ART availability as 2001-2003 (non-nucleoside reverse transcriptase inhibitors era), 2004-2007 (first entry inhibitors), 2008-2012 (1st generation integrase inhibitors), and 2013-2016 (2nd generation integrase inhibitors).[7] We classified patients as young adults (20-39 years) and adults (40-79 years). HIV status was identified at DLBCL diagnosis. Because of the low counts of DLBCL among non-Hispanic Asian/Pacific Islander (n=63) and non-Hispanic American Indian/Alaska Native (n<20) patients with HIV, we grouped these patients as Other.

The primary endpoint was overall survival (OS), defined from diagnosis to death of any cause, end of follow-up, or end of the study. Subgroup analyses involved estimating OS differences within demographic groups (i.e., sex, age, and race and ethnicity).

DLBCL patients with HIV were propensity matched to DLBCL patients without HIV using

the nearest neighborhood method and a 1:3 ratio based on age group, race and ethnicity, cancer registry, sex, year of diagnosis, primary site grouping, and cancer stage. All matching variables were successfully balanced with standard mean differences <0.1. Changes in demographic features across periods were evaluated with a Chi-square for trend or Kruskal-Wallis test, as appropriate. We used the Kaplan-Meier method and Log-rank test to estimate and compare OS. Median follow-up was calculated using the reverse Kaplan-Meier method. Given the matched design, we used univariable Cox regression analysis and reported the findings with hazard ratios (HRs) and 95% confidence intervals (CIs). We fitted interaction models and compared them to models without the interaction terms using a likelihood ratio test to evaluate the impact of ART regimen periods and demographic subgroups on OS. A *P*-value ≤0.05 was considered statistically significant. We used the R software (v4.3.2) for analysis.

We included 8,624 DLBCL patients diagnosed during 2001-2016 after propensity score matching (2,156 with HIV and 6,468 without HIV). The demographic features of DLBCL patients with HIV changed over time (**Supplementary Table 1**). The median age at diagnosis increased from 43 years in 2001-2003 to 48 years in 2013-2016 (*P*<0.001), and the proportion of non-Hispanic Black (NHB) patients rose from 21% in 2001-2003 to 34% in 2013-2016 (*P*<0.001). The male predominance remained consistent across periods, ranging from 83% to 90% (*P*=0.079), as well as the proportion of Hispanic patients (range 21-27%). Advanced stage at diagnosis was consistent across calendar years (range 68-69%; *P*=0.498).

With a median follow-up of 59 months (95% CI=58-61 months) in the latest period (2013-2016), DLBCL patients with HIV had consistently worse 5-year OS rates and an increased risk of all-cause mortality (HRs 1.47-1.86) compared to DLBCL patients without HIV across all ART periods (**Figure 1** and **Supplementary Table 2)**. This mortality risk was attenuated in 2013-2016 (from $HR_{2001\text{-}2003}$=1.85, 95% CI=1.58-2.16 to $HR_{2013\text{-}2016}$=1.47, 95% CI=1.26-1.73; P_{trend}=0.021). Subgroup analyses revealed that this overall attenuation in the HRs across calendar periods was limited to males (from $HR_{2001\text{-}2003}$=1.85, 95% CI=1.57-2.18 to $HR_{2013\text{-}2016}$=1.43, 95% CI=1.21-1.69; P_{trend}=0.011) and non-Hispanic White (NHW) patients (from $HR_{2001\text{-}2003}$=2.04, 95% CI=1.63-2.55 to $HR_{2013\text{-}2016}$=1.38, 95% CI=1.05-1.80; P_{trend}=0.010). HRs remained elevated and constant over time for females (P_{trend}=0.900), young adults (P_{trend}=0.572), older adults (P_{trend}=0.107), Hispanic patients (P_{trend}=0.216), and NHB patients (P_{trend}=0.938).

In the contemporary cohort (2008-2016) (**Supplementary Table 3**), the median age among patients with HIV was 47 years at diagnosis. Most patients were male (85%), were diagnosed at advanced stages (65%), and most had primary nodal disease at

presentation (62%). With a median follow-up of 88 months (95% CI=86-89 months) during 2008-2016, the overall 5-year OS rate for DLBCL patients with HIV was 53% (95% CI=50-56%) and 65% for DLBCL patients without known HIV (95% CI=63-67%; *P*<0.0001; HR=1.56, 95% CI=1.41-1.73) (**Figure 2** and **Table 1**). The 5-year OS rates for DLBCL young adults with HIV were notably lower than patients without known HIV (56% vs. 81%; HR=2.84, 95% CI=2.24-3.59). Similarly, the 5-year OS rates for older, male, female, NHB, NHW, and Hispanic patients were lower among patients with HIV (**Table 1**).

This population-based study identified persistent survival differences overall and within demographic subgroups for DLBCL patients with HIV compared to those without HIV in the US. Our study expands the observation period of previous US studies (up to 2009)[5, 6, 8] and indicates that mortality remains higher among DLBCL patients with HIV.

Our findings contrast with European studies in academic centers suggesting that HIV status is not associated with poor outcomes among those treated with immunochemotherapy while on ART.[2-4] However, our report aligns with previous US population-based studies reporting inferior 5-year OS ranging from 41-44% among DLBCL patients with HIV compared to 54-61% among the general DLBCL population in the ART era.[5, 6, 8] The worse OS among patients with HIV in the US may be associated with several factors, including differences in management between academic versus community centers, healthcare access, challenges of managing HIV while receiving cancer-directed therapy, and differences in treatment approaches.[5, 9-11]

Notable results were identified within demographic groups. Only males and NHW patients with HIV appeared to have a reduction in the survival gap, indicating that further efforts to improve access to care and disease control should reach all demographic subgroups. Historically, underrepresented racial and ethnic groups have been excluded from pivotal clinical trials, and HIV status has been suggested as an unnecessary exclusion criterion.[12] Our findings may indicate persistent challenges in providing cancer care for DLBCL patients with HIV, even in the era after the Affordable Care Act was implemented in 2010,[13] suggesting remaining barriers to receiving optimal care. Additionally, the recent approval of chimeric antigen receptors T-cell therapy for relapsed/refractory disease based on trials excluding patients with HIV could potentially exacerbate the observed survival difference. Future analyses should evaluate whether the receipt of novel therapies and standard of care for DLBCL is similar across demographic subgroups in the HIV setting.

Remarkably, young adult patients with HIV had the most significant survival difference (HR=2.84), and OS was similar to their older counterparts with HIV, contrasting the

typical higher survival outcomes among DLBCL young adults without HIV. Although our results are exploratory, this similar OS across age groups may align with previous descriptions of less heterogeneous disease biology arising in the HIV setting, irrespective of age.[11, 14] Additionally, young adults have been recognized as an underserved group whom little dedicated trials have been conducted.[15] It is likely that the described difficulties in accessing timely cancer care and lack of supportive networks for this population may explain the observed poor survival. Identifying factors associated with this higher mortality risk is warranted.

The findings of this study should be interpreted within the limitations of its retrospective design. We did not have detailed information on cancer-directed therapy, ART regimens, HIV-related factors (e.g., CD4 count, HIV viremia, HIV transmission groups), treatment-related adverse events, type of center (academic versus community), or social determinants of health. The small sample size for certain race and ethnicity subgroups precluded meaningful comparisons.

In conclusion, US DLBCL patients with HIV continue to experience a higher mortality risk compared to those without HIV. This increased mortality risk suggests that changes and improvements in DLBCL management, HIV control, and supportive care have not fully reached this vulnerable population in the US. Although we observed an overall decrease in mortality risk over time, stratified analyses revealed that this mortality gap reduction was restricted to males and NHW patients, suggesting the need to improve care delivery with particular attention to other demographic subgroups. Notably, young adults aged 20-39 experienced the most significant survival difference. Identifying social determinants of health, age-related demographic, biological, or healthcare system factors mediating survival outcomes and receipt of treatment is warranted to further design interventions and mitigate differences in mortality risk.

REFERENCES

1. Hernández-Ramírez RU, Shiels MS, Dubrow R, Engels EA. Cancer risk in HIV-infected people in the USA from 1996 to 2012: a population-based, registry-linkage study. Lancet HIV. 2017;4(11):e495-e504.
2. Conconi A, Zucca E, Margiotta-Casaluci G, et al. Population-based outcome analysis of diffuse large B-cell lymphoma in people living with HIV infection and competent individuals. Hematol Oncol. 2018;36(5):757-764.
3. Coutinho R, Pria AD, Gandhi S, et al. HIV status does not impair the outcome of patients diagnosed with diffuse large B-cell lymphoma treated with R-CHOP in the cART era. AIDS. 2014;28(5):689-697.
4. Besson C, Lancar R, Prevot S, et al. Outcomes for HIV-associated diffuse large B-cell lymphoma in the modern combined antiretroviral therapy era. AIDS. 2017;31(18):2493-2501.
5. Olszewski AJ, Fallah J, Castillo JJ. Human immunodeficiency virus-associated lymphomas in the antiretroviral therapy era: Analysis of the National Cancer Data Base. Cancer. 2016;122(17):2689-2697.
6. Han X, Jemal A, Hulland E, et al. HIV Infection and Survival of Lymphoma Patients in the Era of Highly Active Antiretroviral Therapy. Cancer Epidemiol Biomarkers Prev. 2017;26(3):303-311.
7. Tseng A, Seet J, Phillips EJ. The evolution of three decades of antiretroviral therapy: challenges, triumphs and the promise of the future. Br J Clin Pharmacol. 2015;79(2):182-194.
8. Gopal S, Patel MR, Yanik EL, et al. Temporal trends in presentation and survival for HIV-associated lymphoma in the antiretroviral therapy era. J Natl Cancer Instit. 2013;105(16):1221-1229.
9. Pellowski JA, Kalichman SC, Matthews KA, Adler N. A pandemic of the poor: social disadvantage and the U.S. HIV epidemic. Am Psychol. 2013;68(4):197-209.
10. Sullivan PS, Satcher Johnson A, Pembleton ES, et al. Epidemiology of HIV in the USA: epidemic burden, inequities, contexts, and responses. Lancet. 2021;397(10279):1095-1106.
11. Carbone A, Vaccher E, Gloghini A. Hematologic cancers in individuals infected by HIV. Blood. 2022;139(7):995-1012.
12. Harkins RA, Patel SP, Lee MJ, et al. Improving eligibility criteria for first-line trials for patients with DLBCL using a US-based Delphi-method survey. Blood Adv. 2022;6(9):2745-2756.
13. Patient Protection and Affordable Care Act HRPL, 111th Congress. 2010.
14. Carbone A, Cesarman E, Spina M, Gloghini A, Schulz TF. HIV-associated lymphomas and gamma-herpesviruses. Blood. 2009;113(6):1213-1224.
15. Dunleavy K, Gross TG. Management of aggressive B-cell NHLs in the AYA population: an adult vs pediatric perspective. Blood. 2018;132(4):369-375.

Table 1. Kaplan-Meier and Cox regression analyses evaluating the effect of human immunodeficiency virus status on overall survival among patients with diffuse large B-cell lymphoma in the contemporary matched cohort (2008-2016) derived from 13 Surveillance, Epidemiology, and End Results registries.

Characteristics		Events	Total	5-year OS % (95% CI)	Log-rank P-value	HR (95% CI)	P-value for interaction
All patients	HIV-/unknown	1165	3429	65 (63-67)	<0.0001	Ref	
	HIV+	526	1143	53 (50-56)		1.56 (1.41-1.73)	-
Sex	Female						
	HIV-/unknown	159	486	66 (62-71)	<0.0001	Ref	
	HIV+	84	174	51 (44-59)		1.79 (1.37-2.35)	0.259
	Male						
	HIV-/unknown	1006	2943	65 (63-67)	<0.0001	Ref	
	HIV+	442	969	53 (50-57)		1.52 (1.36-1.71)	
Age at diagnosis, in years (yrs)	20-39 yrs						
	HIV-/unknown	162	864	81 (78-83)	<0.0001	Ref	
	HIV+	124	288	56 (50-62)		2.84 (2.24-3.59)	< 0.0001[a]
	40-79 yrs						
	HIV-/unknown	1003	2565	60 (58-62)	<0.0001	Ref	
	HIV+	402	855	52 (49-56)		1.35 (1.2-1.52)	
Race and ethnicity	Non-Hispanic White						
	HIV-/unknown	451	1341	66 (63-68)	<0.0001	Ref	
	HIV+	185	422	56 (51-60)		1.46 (1.22-1.73)	
	Non-Hispanic Black						
	HIV-/unknown	370	1077	65 (62-68)	<0.0001	Ref	
	HIV+	199	381	47 (42-52)		1.86 (1.56-2.21)	0.092
	Hispanic						
	HIV-/unknown	300	887	64 (61-68)	0.001	Ref	
	HIV+	126	297	56 (51-62)		1.42 (1.15-1.75)	
	Others[b]						
	HIV-/unknown	44	124	63 (55-72)	0.666	Ref	
	HIV+	<20	43	62 (49-78)		1.14 (0.64-2.03)	

Counts <20 were suppressed

a Likelihood ratio test suggests a statistically significant interaction between HIV status and age based on comparing model fit with and without the interaction term.

b Others race and ethnicity includes non-Hispanic Asian/Pacific Islander and non-Hispanic American Indian/Alaska Native

Abbreviations: CI, confidence interval; HR, Hazard ratio; HIV, human immunodeficiency virus; OS, overall surviva

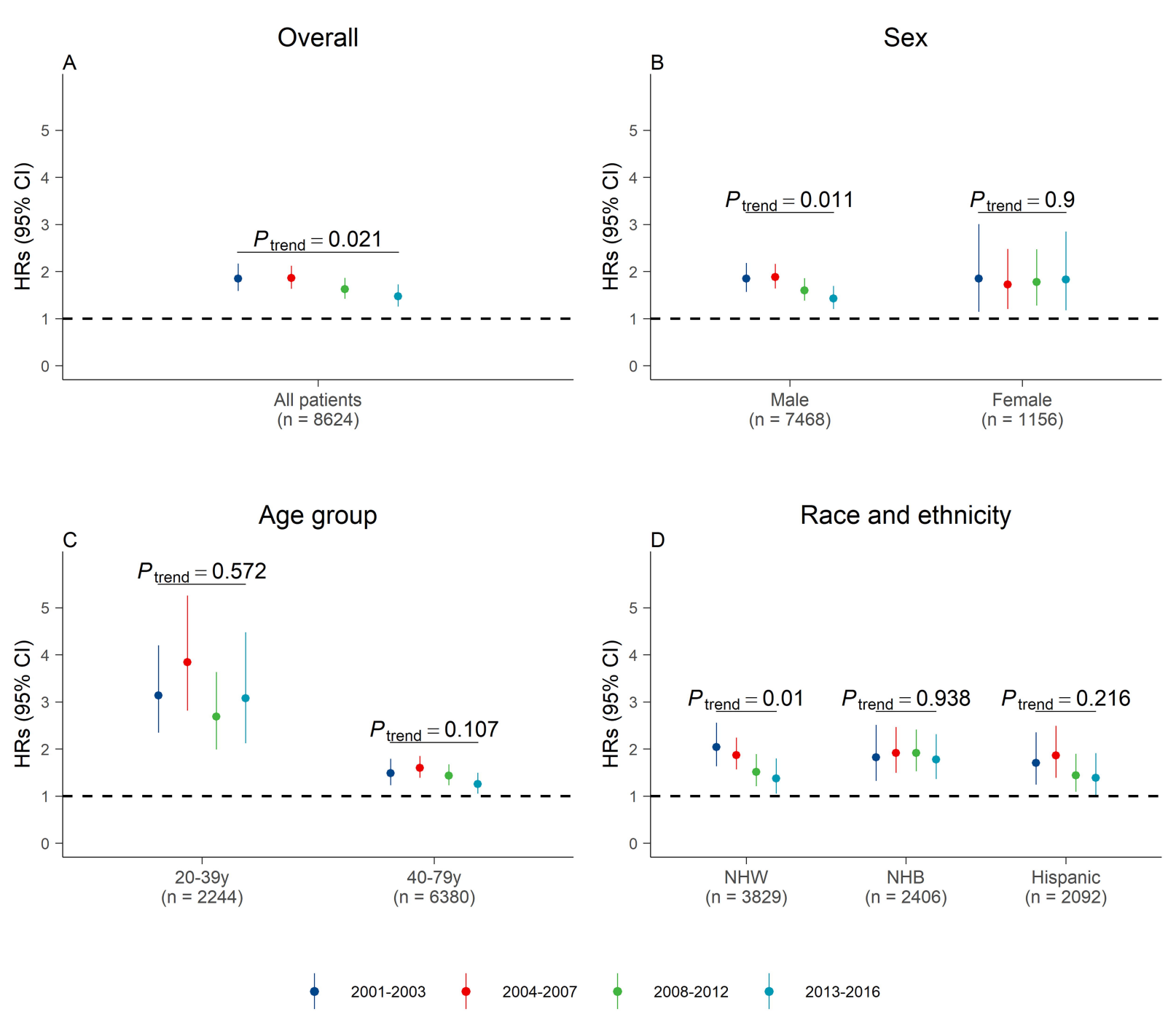
FIGURE LEGENDS

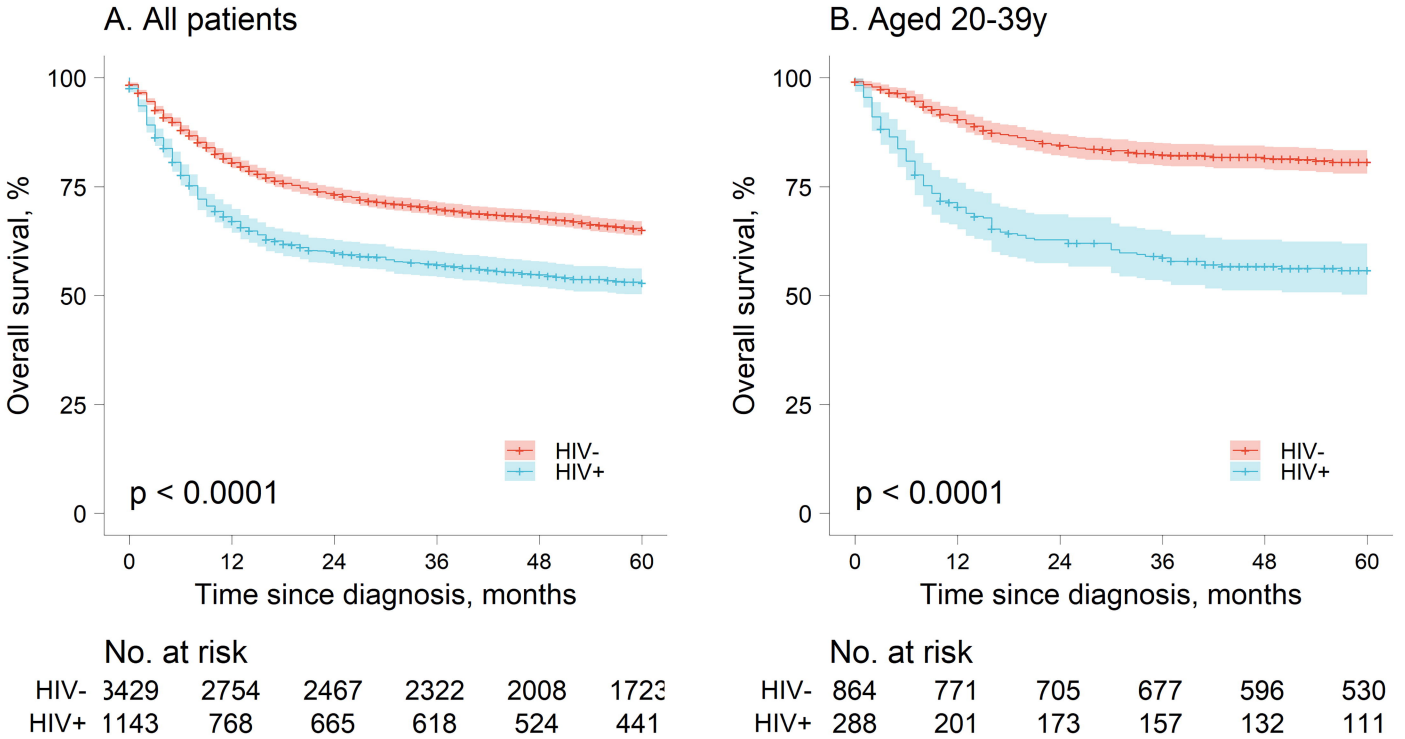
Figure 1. Hazard ratios for overall survival across antiretroviral therapy periods (2001-2016) in a matched cohort derived from 13 Surveillance, Epidemiology, and End Results registries.

Estimates for Other race and ethnicity includes are not shown. P-values reflect the likelihood ratio test comparing model fit with and without the interaction term of HIV and calendar year.
Abbreviations: CI, confidence interval; HR, Hazard ratio; NHB, Non-Hispanic Black; NHW, Non-Hispanic White

Figure 2. Kaplan-Meier curves evaluating the effect of human immunodeficiency virus status on overall survival among all included patients and selected demographic groups with remarkable survival differences, with diffuse large B-cell lymphoma in the contemporary matched cohort (2008-2016), derived from 13 Surveillance, Epidemiology, and End Results registries.

Abbreviations: HIV, human immunodeficiency virus


Overall
A
HRs (95% CI)
$P_{trend} = 0.021$
All patients
(n = 8624)
Sex
B
$P_{trend} = 0.011$
$P_{trend} = 0.9$
Male
(n = 7468)
Female
(n = 1156)
Age group
C
$P_{trend} = 0.572$
$P_{trend} = 0.107$
20-39y
(n = 2244)
40-79y
(n = 6380)
Race and ethnicity
D
$P_{trend} = 0.01$
$P_{trend} = 0.938$
$P_{trend} = 0.216$
NHW
(n = 3829)
NHB
(n = 2406)
Hispanic
(n = 2092)
2001-2003
2004-2007
2008-2012
2013-2016

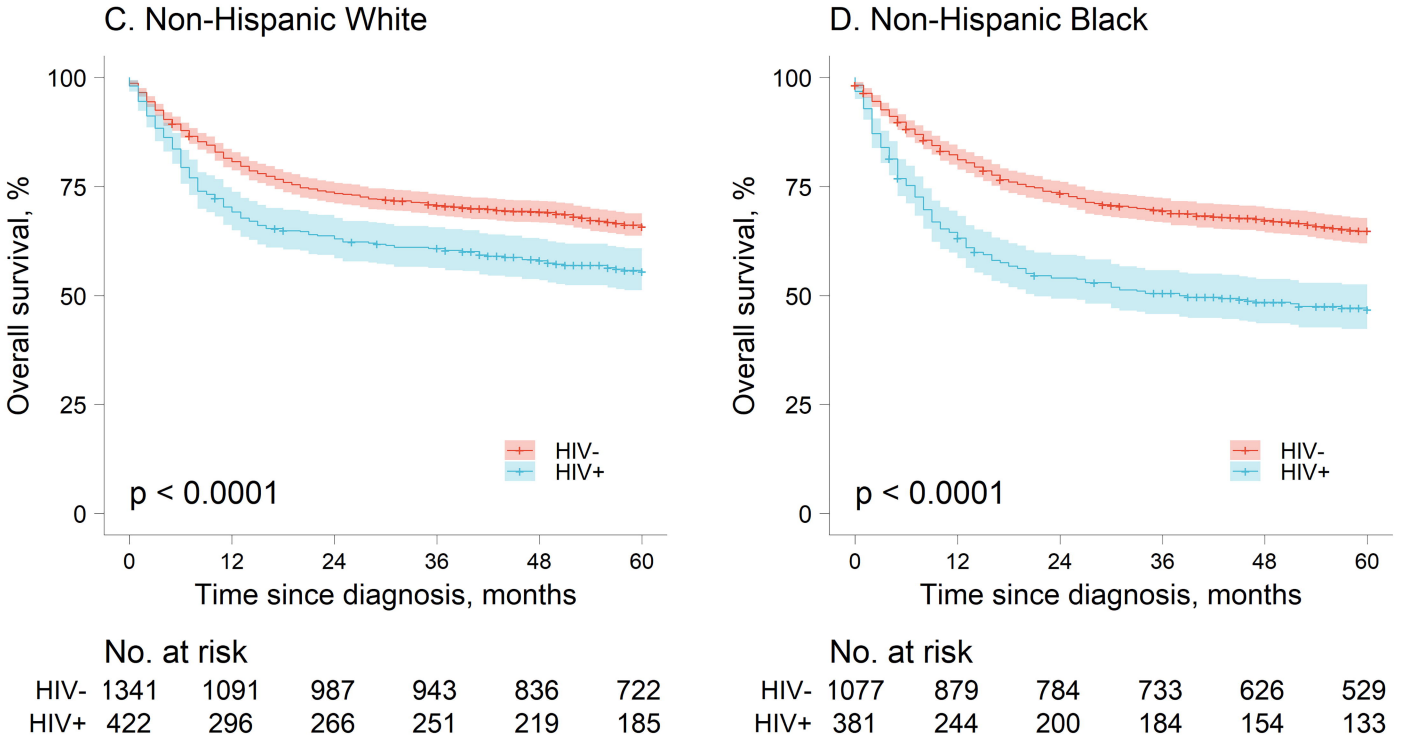


No. at risk

HIV-	3429	2754	2467	2322	2008	1723
HIV+	1143	768	665	618	524	441

No. at risk

HIV-	864	771	705	677	596	530
HIV+	288	201	173	157	132	111



No. at risk

HIV-	1341	1091	987	943	836	722
HIV+	422	296	266	251	219	185

No. at risk

HIV-	1077	879	784	733	626	529
HIV+	381	244	200	184	154	133

Supplementary Table 1. Demographic and clinical characteristics of diffuse large B-cell patients with human immunodeficiency virus over combined antiretroviral therapy approval periods in the 2001-2016 period from 13 Surveillance, Epidemiology, and End Results registries.

Characteristics	All patients, N (%)	Antiretroviral therapy periods, N (%)				P-value for trend
		2001-2003	2004-2007	2008-2012	2013-2016	
No. of patients	2156	390	623	649	494	
Age at diagnosis						< 0.001
Median	45	43	44	46	48	
Range	21 - 79	21 - 79	21 - 79	21 - 78	21 - 79	
Age at diagnosis, in years (yrs)						0.006
20-39 yrs	561 (26)	133 (34)	140 (22)	176 (27)	112 (23)	
40-79 yrs	1595 (74)	257 (66)	483 (78)	473 (73)	382 (77)	
Sex						0.079
Female	291 (13)	38 (10)	79 (13)	113 (17)	61 (12)	
Male	1865 (87)	352 (90)	544 (87)	536 (83)	433 (88)	
Race and ethnicity						< 0.001
Non-Hispanic White	942 (44)	200 (51)	320 (51)	244 (38)	178 (36)	
Non-Hispanic Black	621 (29)	83 (21)	157 (25)	213 (33)	168 (34)	
Hispanic	520 (24)	95 (24)	128 (21)	175 (27)	122 (25)	
Others[a]	73 (3)	12 (3)	18 (3)	17 (3)	26 (5)	
Primary site						0.04
Lymph nodes	1358 (63)	265 (68)	390 (63)	403 (62)	300 (61)	
Gastrointestinal	342 (16)	48 (12)	107 (17)	114 (18)	73 (15)	
Central nervous system	115 (5)	15 (4)	24 (4)	33 (5)	43 (9)	
Other/Unspecified	341 (16)	62 (16)	102 (16)	99 (15)	78 (16)	
Cancer stage[b]						0.498
Early-stage disease	718 (34)	121 (32)	224 (37)	225 (35)	148 (31)	
Advanced-stage disease	1397 (66)	263 (68)	387 (63)	415 (65)	332 (69)	
Missing[c]	41	6	12	9	14	

a Others race and ethnicity includes non-Hispanic Asian/Pacific Islander and non-Hispanic American Indian/Alaska Native

b Cancer stage was identified using the Ann Arbor and SEER Summary Stage classification variables in the SEER database and was defined as early- (Ann Arbor stage I or II, or SEER localized or regional stage) and advanced-stage disease (Ann Arbor stage III or IV or SEER distant stage)

c Missing values in the cancer stage were added in the propensity matching using a “Missing category.”

Supplementary Table 2. Five-year overall survival rates and Hazard ratios over combined antiretroviral therapy approval periods in the matched cohort in the 2001-2016 period from 13 Surveillance, Epidemiology, and End Results registries.

Characteristics		2001-2003				2004-2007				2008-2012				2013-2016				P-value for trend of HRs
		Events	Total	5-year OS % (95% CI)	HR (95% CI)	Events	Total	5-year OS % (95% CI)	HR (95% CI)	Events	Total	5-year OS % (95% CI)	HR (95% CI)	Events	Total	5-year OS % (95% CI)	HR (95% CI)	
All patients	HIV-/unknown	483	1170	58 (56-61)	Ref	681	1869	63 (61-66)	Ref	659	1947	66 (64-68)	Ref	506	1482	64 (62-67)	Ref	
	HIV+	235	390	39 (35-45)	1.85 (1.58-2.16)	347	623	44 (40-48)	1.86 (1.63-2.12)	306	649	52 (49-56)	1.63 (1.42-1.86)	220	494	54 (49-58)	1.47 (1.26-1.73)	0.021
Sex	Female																	
	HIV-/unknown	58	139	58 (50-67)	Ref	93	240	61 (55-68)	Ref	101	304	66 (61-72)	Ref	58	182	67 (60-74)	Ref	
	HIV+	23	38	40 (27-58)	1.85 (1.14-3.01)	43	79	46 (36-58)	1.73 (1.20-2.48)	54	113	52 (43-62)	1.77 (1.27-2.47)	30	61	49 (38-64)	1.83 (1.18-2.85)	0.900
	Male																	
	HIV-/unknown	425	1031	58 (55-62)	Ref	588	1629	64 (61-66)	Ref	558	1643	66 (63-68)	Ref	448	1300	64 (61-66)	Ref	
	HIV+	212	352	39 (35-45)	1.85 (1.57-2.18)	304	544	44 (40-48)	1.88 (1.64-2.16)	252	536	52 (48-57)	1.60 (1.38-1.86)	190	433	54 (50-59)	1.43 (1.21-1.69)	0.011
Age at diagnosis, in years (yrs)	20-39 yrs																	
	HIV-/unknown	107	399	73 (69-77)	Ref	82	420	80 (76-84)	Ref	101	528	80 (77-84)	Ref	61	336	81 (77-86)	Ref	
	HIV+	80	133	40 (32-49)	3.14 (2.35-4.20)	77	140	44 (36-53)	3.84 (2.81-5.25)	74	176	57 (50-65)	2.69 (1.99-3.63)	50	112	54 (45-64)	3.08 (2.12-4.48)	0.572
	40-79 yrs																	
	HIV-/unknown	376	771	51 (47-55)	Ref	599	1449	58 (56-61)	Ref	558	1419	60 (58-63)	Ref	445	1146	59 (56-62)	Ref	
	HIV+	155	257	39 (34-46)	1.48 (1.23-1.79)	270	483	44 (39-48)	1.60 (1.39-1.85)	232	473	51 (46-55)	1.43 (1.23-1.67)	170	382	54 (49-59)	1.25 (1.05-1.50)	0.107
Race and ethnicity	Non-Hispanic White																	
	HIV-/unknown	219	587	63 (59-67)	Ref	350	959	64 (60-67)	Ref	262	778	66 (63-70)	Ref	189	563	65 (61-70)	Ref	
	HIV+	120	200	40 (34-47)	2.04 (1.63-2.55)	179	320	44 (39-50)	1.87 (1.56-2.24)	110	244	55 (49-62)	1.51 (1.21-1.89)	75	178	57 (50-65)	1.38 (1.05-1.80)	0.010
	Non-Hispanic Black																	
	HIV-/unknown	123	258	52 (46-59)	Ref	174	450	61 (57-66)	Ref	207	593	65 (61-69)	Ref	163	484	65 (60-69)	Ref	
	HIV+	54	83	35 (26-47)	1.82 (1.32-2.51)	94	157	40 (33-48)	1.92 (1.49-2.47)	116	213	45 (39-52)	1.92 (1.53-2.41)	83	168	49 (42-57)	1.77 (1.36-2.31)	0.938
	Hispanic																	
	HIV-/unknown	119	284	57 (51-63)	Ref	138	401	65 (60-70)	Ref	173	526	66 (62-70)	Ref	127	361	62 (56-67)	Ref	
	HIV+	55	95	41 (32-52)	1.71 (1.24-2.35)	68	128	46 (38-55)	1.86 (1.39-2.49)	72	175	58 (51-66)	1.44 (1.09-1.89)	54	122	53 (44-63)	1.39 (1.01-1.91)	0.216
	Others[a]																	
	HIV-/unknown	22	41	45 (32-64)	Ref	19	59	68 (57-81)	Ref	17	50	66 (54-80)	Ref	27	74	60 (49-74)	Ref	
	HIV+	6	12	50 (28-88)	1.05 (0.43-2.59)	6	18	65 (46-92)	1.11 (0.44-2.77)	8	17	53 (34-83)	1.65 (0.71-3.82)	8	26	68 (52-89)	0.86 (0.39-1.90)	0.853

a Others race and ethnicity includes non-Hispanic Asian/Pacific Islander and non-Hispanic American Indian/Alaska Native

Abbreviations: CI, confidence interval; HR, Hazard ratio; HIV, human immunodeficiency virus; OS, overall survival

Supplementary Table 3. Characteristics of patients with diffuse large B-cell lymphoma according to human immunodeficiency virus status in the contemporary matched cohort (2008-2016) derived from 13 Surveillance, Epidemiology, and End Results registries.

Characteristics	All patients, N (%)	HIV status, N (%)		P-value
		HIV-/ unknown	HIV+	
No. of patients	4572	3429	1143	
Age group at diagnosis, in years (yrs)				1.000
20-39 yrs	1152 (25)	864 (25)	288 (25)	
40-79 yrs	3420 (75)	2565 (75)	855 (75)	
Sex				0.382
Female	660 (14)	486 (14)	174 (15)	
Male	3912 (86)	2943 (86)	969 (85)	
Race and ethnicity				0.549
Non-Hispanic White	1763 (39)	1341 (39)	422 (37)	
Hispanic	1184 (26)	887 (26)	297 (26)	
Non-Hispanic Black	1458 (32)	1077 (31)	381 (33)	
Others[a]	167 (4)	124 (4)	43 (4)	
Cancer stage[b]				0.997
Early-stage disease	1490 (33)	1117 (33)	373 (33)	
Advanced-stage disease	2991 (65)	2244 (65)	747 (65)	
Missing[c]	91 (2)	68 (2)	23 (2)	
Primary site				0.007
Lymph nodes	2939 (64)	2236 (65)	703 (62)	
Gastrointestinal	658 (14)	471 (14)	187 (16)	
Central nervous system	239 (5)	163 (5)	76 (7)	
Other/Unspecified	736 (16)	559 (16)	177 (15)	

a Others race and ethnicity includes non-Hispanic Asian/Pacific Islander and non-Hispanic American Indian/Alaska Native

b Cancer stage was identified using the Ann Arbor and SEER Summary Stage classification variables in the SEER database and was defined as early- (Ann Arbor stage I or II, or SEER localized or regional stage) and advanced-stage disease (Ann Arbor stage III or IV or SEER distant stage)

c Missing values in the cancer stage were added in the propensity matching using a “Missing category.”

Abbreviations: HIV, human immunodeficiency virus