CD4 Cell Count Trends After Common Cancers in People With HIV: A Multicohort Collaboration

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BACKGROUND

- Whilst opportunistic infection prophylaxis is recommended to all individuals with HIV and CD4 <200 cells/µL, those undergoing chemo- or radiotherapy are advised to commence prophylaxis regardless of the CD4 level according to the EACS guidelines (1)
- These recommendations are based on historical data predating modern antiretroviral therapy (ART). Therefore, there is a pressing need to reevaluate CD4 count trajectories during cancer treatment in the context of contemporary ART

OBJECTIVES

- To assess CD4 trends before and after the most commonly occurring cancers in individuals with HIV and the proportions with CD4 decline to below 200 cells/µL after a cancer
- To assess potential risk factors associated with a decline in CD4 cell count to below 200 cells/µL after a cancer diagnosis

METHODS

- We included participants from the D:A:D and RESPOND cohorts with one of the most commonly occurring cancers (**Kaposi's sarcoma** (KS), **non-Hodgkin lymphoma** (NHL), **lung, anal,** or **prostate cancer**), alive for >6 months after cancer diagnosis, and had a minimum of two CD4 counts within 6-12 months after cancer diagnosis
- Participants were followed from the latest of cohort enrolment and 1 Jan 2006 (D:A:D)/2012 (RESPOND) until death, last follow-up (FU), or cohort censoring (D:A:D 1 Feb 2016; RESPOND 31 Dec 2021)
- Median CD4 count at the time of cancer diagnosis and the proportion of participants with a CD4 count decline below 200 cells/µL (up to three years after cancer diagnosis) was calculated, and mixed effects logistic regression models assessed predictors of the decline
- Sensitivity analysis evaluated death as a competing risk of CD4 decline <200 cells/µL after cancer diagnosis

Table 1. Characteristics at time of cancer diagnosis

	Kaposi's sarcoma (n=504)		Non-Hodgkin lymphoma (n=390)		Lung cancer (n=206)		Anal cancer (n=333)		Prostate cancer (n=237)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	%
Sex/Gender										
Male	470	(93.3)	326	(83.6)	152	(73.8)	296	(88.9)	237	(100.0)
Ethnicity/Race										
White	214	(42.5)	213	(54.6)	137	(66.5)	215	(64.6)	171	(72.2)
Black	25	(5.0)	27	(6.9)	2	(1.0)	6	(1.8)	8	(3.4)
Cancer stage										
Localised	75	(15)	43	(11.0)	78	(37.9)	218	(65.5)	143	(60.3)
Disseminated	41	(8)	63	(16.1)	85	(41.3)	44	(13.2)	30	(12.7)
Unknown	388	(76.9*)	284	(72.8*)	43	(20.9)	71	(21.3)	64	(27)
ART experienced	320	(63.5)	325	(83.3)	194	(94.2)	319	(95.8)	229	(96.6)
	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**
Age, years	43	(36, 51)	48	(40, 55)	57	(50, 63)	52	(46, 58)	63	(59, 69)
CD4 nadir, cells/mm³	170	(48, 300)	160	(68, 272)	141	(43, 252)	113	(26, 225)	178	(80,276)
Baseline CD4, cells/mm³	300	(106, 469)	328	(190, 499)	460	(310, 701)	484	(299, 682)	559	(410, 725)

* Cancer stage for KS and NHL was not collected in D:A:D

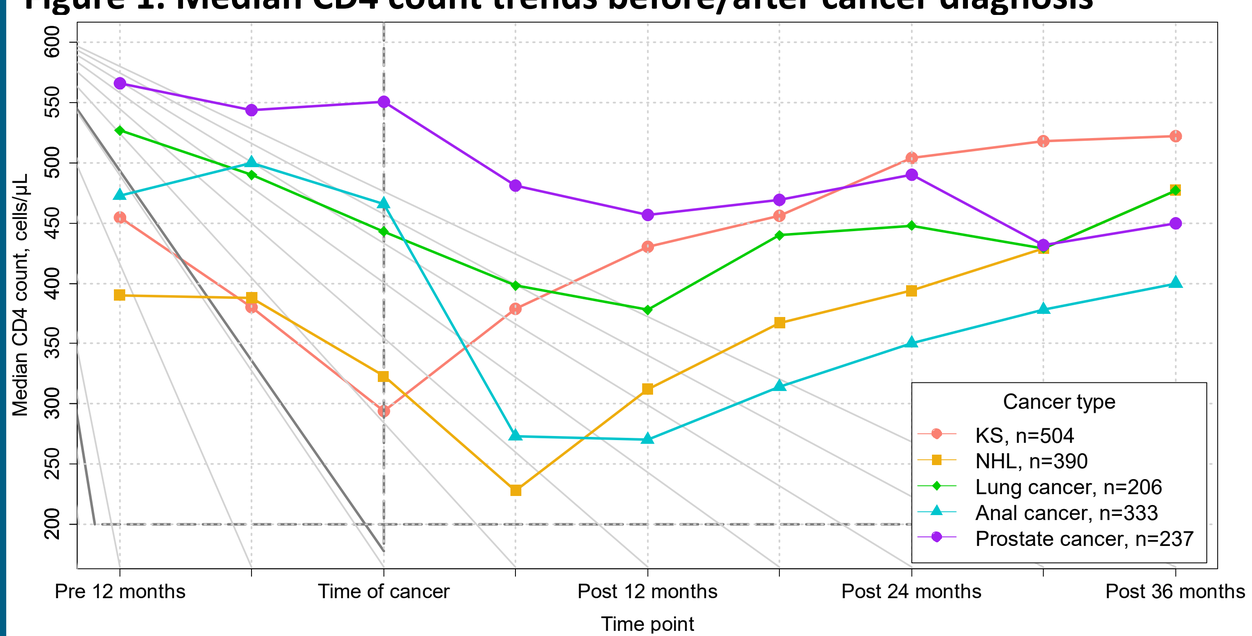
RESULTS

- In all, 1,670 persons (KS: 504, NHL: 390, lung: 206, anal: 333, prostate cancer: 237) with 9,597 person-years of follow-up (FU) after cancer diagnosis were included, baseline characteristics are shown in **Table 1**
- Median FU time was 5.3 years, [Interquartile Range (IQR) 2.3-8.4] (KS: 7.0 [4.0-9.3], NHL: 5.5 [2.2-8.8], anal: 5.1 [2.6-8.0], prostate: 4.9 [2.8-7.7], lung: 1.7 [0.9-3.9])
- We excluded 815 participants due to the lack of two CD4 counts within 6-12 months after cancer diagnosis; 50% died within 12 months after diagnosis, and 50% had no CD4 measurements in their HIV clinics

MEDIAN CD4 COUNT AFTER CANCER DIAGNOSIS

The median CD4 count at cancer diagnosis varied depending on the type of cancer: lowest for KS, highest for prostate cancer (KS: 294 cells/µL [IQR 105-474], NHL: 323 [163-495], lung: 443 [290-664], anal: 466 [270-680], prostate: 551 [407-696]) **(Figure 1)**

Figure 1. Median CD4 count trends before/after cancer diagnosis

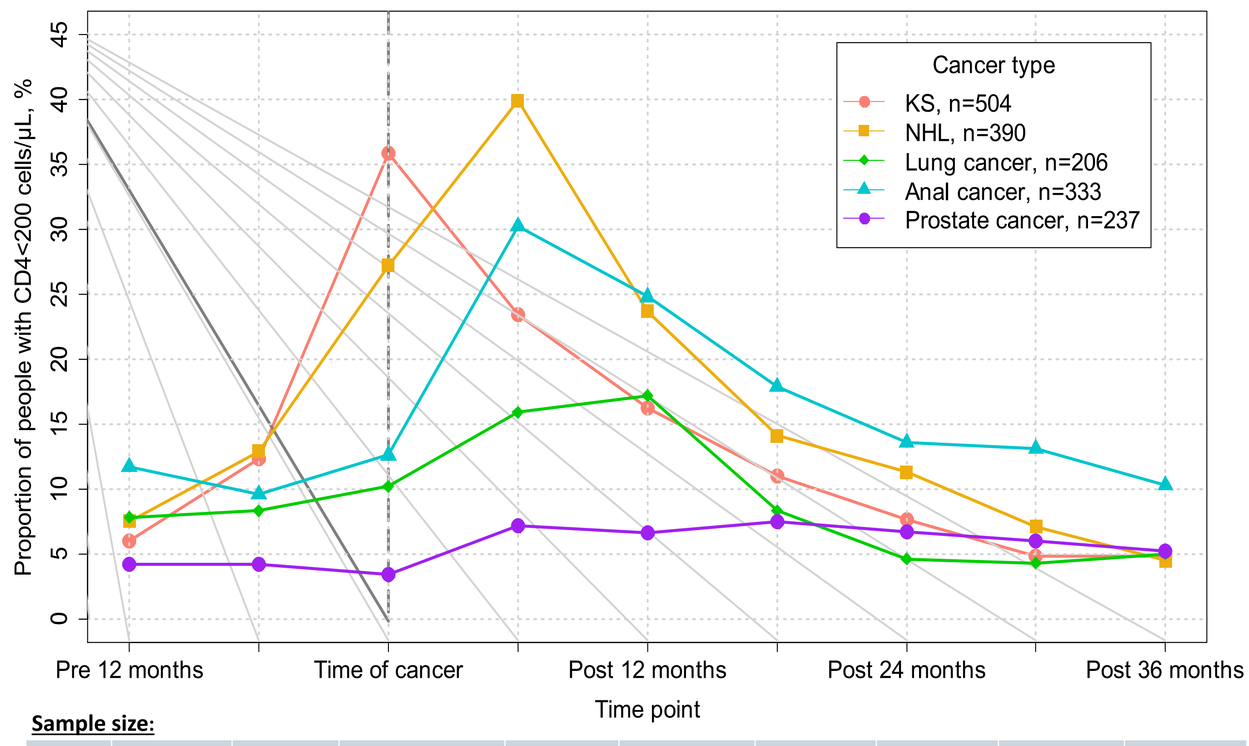


	Pre 12m (n)	Pre 6m (n)	Time of cancer (n)	Post 6m (n)	Post 12m (n)	Post 18m (n)	Post 24m (n)	Post 30m (n)	Post 36m (n)
KS	234	279	482	481	437	416	400	374	343
NHL	262	281	362	371	319	291	270	255	225
Lung	172	173	188	198	138	91	77	64	51
Anal	282	281	297	312	283	246	235	213	182
Prostate	208	214	210	222	205	187	174	155	146

PROPORTION OF PARTICIPANTS WITH A CD4 COUNT BELOW 200 CELLS/µL

The highest proportion of individuals with a CD4 count below 200 cells/µL was at time of cancer diagnosis for KS (36%) and at 6 months after cancer diagnosis in those with NHL (40%) and anal cancer (30%) (**Figure 2**)

Figure 2. Proportion of people with CD4<200 cells/µL after cancer



Sample size:

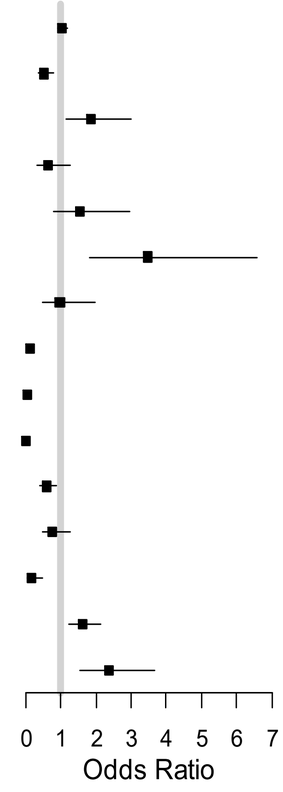
	Pre 12m (n)	Pre 6m (n)	Time of cancer (n)	Post 6m (n)	Post 12m (n)	Post 18m (n)	Post 24m (n)	Post 30m (n)	Post 36m (n)
KS	504	504	504	496	481	462	448	433	416
NHL	389	389	389	381	342	319	301	281	268
Lung	206	206	206	201	151	109	87	70	60
Anal	333	333	333	331	318	296	273	252	232
Prostate	236	236	236	235	229	213	195	182	174

RISK FACTORS FOR CD4 COUNT BELOW 200 CELLS/µL AFTER CANCER

- In adjusted models, higher CD4 counts at the time of cancer diagnosis were associated with lower odds of CD4 decline to below 200 cells/µL after cancer
- Participants with anal cancer had 3,5 times higher odds of having a CD4 decline below 200 cells/µL compared to those with lung cancer
- Other predictors of having CD4 decline below 200 cells/µL included disseminated cancer stage, male gender and injection drug use as HIV transmission risk **(Figure 3)**
- Results of sensitivity analysis were consistent with the results of the primary regression model

Figure 3. Adjusted Odds Ratios (aOR) (95% Confidence Interval) for CD4 decline <200 cells/µL after cancer

Risk factors	aOR (95% CI)
Age (per 10 years increase)	1.04 (0.93 - 1.17)
Female gender (ref. male)	0.53 (0.35 - 0.78)
IDU as HIV transmission risk (ref. MSM)	1.87 (1.16 - 3.01)
KS (ref. lung cancer)	0.64 (0.32 - 1.27)
NHL (ref. lung cancer)	1.53 (0.79 - 2.98)
Anal cancer (ref. lung cancer)	3.46 (1.82 - 6.60)
Prostate cancer (ref. lung cancer)	0.97 (0.48 - 1.98)
CD4 at time of cancer 200-350 cells/µL (ref. <200)	0.12 (0.08 - 0.16)
CD4 at time of cancer 350-500 cells/µL (ref. <200)	0.05 (0.03 - 0.07)
CD4 at time of cancer >500 cells/µL (ref. <200)	0.02 (0.02 - 0.04)
Pre-cancer CD4 nadir 200-350 (ref. <200)	0.59 (0.39 - 0.89)
Pre-cancer CD4 nadir 350-500 (ref. <200)	0.76 (0.46 - 1.27)
Pre-cancer CD4 nadir >500 (ref. <200)	0.15 (0.05 - 0.46)
ART experience at time of cancer (ref. ART-naive)	1.61 (1.21 - 2.13)
Disseminated cancer stage (ref. localised)*	2.38 (1.54 - 3.67)



Model was additionally adjusted for ethnicity, time-updated smoking (with non-significant results)
*Cancer stage was available only for lung, anal and prostate cancer

LIMITATIONS

- Limited data about the type of cancer treatment (unavailable for 60% of participants) and lack of data about using of opportunistic infections prophylaxis
- As participants without two CD4 measurements within 6-12 months post-cancer diagnosis were excluded, we have introduced some selection bias, and our findings may, therefore predominantly represent outcomes in participants who survived >6 months after cancer and had available data on CD4 counts

CONCLUSIONS

1) Dynamics and severity of immunosuppression after cancer varied across cancer type
2) In people who survived >6 months after cancer and had longitudinal data of CD4 after cancer diagnosis, rates of CD4 below 200 cells/µL after cancer were high for NHL and anal cancer, and low for KS and prostate cancers
3) Higher CD4 count at cancer diagnosis was associated with lower odds of CD4 decline below 200 cells/µL after cancer
4) A significant proportion of people with HIV and cancer did not have CD4 count measurements in HIV clinics after cancer diagnosis
5) Considering use of opportunistic infection prophylaxis in people with HIV after cancer diagnosis could be more individualised in settings where regular CD4 monitoring is available

References: 1) EACS 2024 guidelines

Acknowledgements: The RESPOND Study Group: https://www.chip.dk/Studies/RESPOND/Study-Group ; RESPOND Scientific Interest Groups: https://chip.dk/Research/Studies/RESPOND/SIGs ;The D:A:D study group: https://chip.dk/Research/Studies/DAD/Study-Group
RESPOND and D:A:D are both supported by The CHU St Pierre Brussels HIV Cohort, The Australian HIV Observational Database, The AIDS Therapy Evaluation in the Netherlands National Observational HIV cohort, The EuroSIDA cohort, The Nice HIV Cohort, The ICONA Foundation, The Swiss HIV Cohort Study. RESPOND is also supported by The Austrian HIV Cohort Study, The Frankfurt HIV Cohort Study, The Georgian National AIDS Health Information System, The Modena HIV Cohort, The PISCIS Cohort Study, The Royal Free HIV Cohort Study, The San Raffaele Scientific Institute, The Swedish InfCare HIV Cohort , The University Hospital Bonn HIV Cohort, The University of Cologne HIV Cohort, The Brighton HIV Cohort and The National Croatian HIV cohort and financially supported by ViiV Healthcare, Merck Life Sciences, Gilead Sciences. D:A:D is supported by the Aquitaine cohort, the BASS cohort, the Community Programs for Clinical Research on AIDS, and the HIV-BIVUS and financially funded by the Highly Active Antiretroviral Therapy Oversight Committee, a collaborative committee with representation from academic institutions, the European Agency for the Evaluation of Medicinal Products, the United States Food and Drug Administration, the patient community, and pharmaceutical companies with licensed anti-HIV drugs in the European Union: AbbVie, Bristol-Myers Squibb, Gilead Sciences Inc., ViiVHealthcare, Merck & Co Inc., Janssen Pharmaceuticals.