Impact of Cancer Treatment on Immune Status in People Living with HIV

#636

Lily M Waddell BA[1], Geliang Gan PhD MPH[2], Yanhong Deng MPH[2], Jessica B Lewis PhD[1], Brinda Emu MD[1]

[1]Yale School of Medicine, New Haven, CT, USA, [2]Yale School of Public Health, New Haven, CT, USA

Background

- As people with HIV (PWH) live longer, cancer has become the leading non-AIDS defining cause of death among PWH.[1]
- PWH experience worse cancer outcomes compared to people without HIV.[2-4]
- Low CD4 count is associated with increased cancer incidence, and low CD4 count at time of diagnosis is a predictor of poorer outcome.[5]
- However, limited research also suggests that cancer treatment itself may depress CD4 count, potentially contributing to loss of viral control, increased risk of infection, and/or increased mortality.[6,7]
- **Objective: to characterize the associations between cancer type, cancer treatments (chemotherapy, radiation therapy [RT], and surgery), and CD4 count/HIV viral load (VL) trajectories in PWH**

Methods

Study Population

- Retrospective chart review of all PWH treated for cancer at Yale New Haven Hospital (YNHH) between 2016-2022

Data Collection

- From YNHH HIV registry, collected age, sex, race/ethnicity, insurance status, and all absolute CD4, CD4/CD8 ratio, CD4%, and VL measurements
- From CT Tumor Registry, collected age at cancer diagnosis, primary tumor site, stage, year of diagnosis, and first line treatment regimen

Analysis

- Defined baseline absolute CD4 and VL as the most recent value in the six months leading up to treatment initiation
- Defined loss of viral control as sustained VL <200 copies/mL two years before cancer diagnosis followed by any VL >200 copies/mL within two years of treatment initiation
- Unadjusted analysis was used to compare slopes of mean CD4 decline from 0-1 year post-treatment initiation between groups
- Kaplan-Meier survival curves were used to estimate time to 80% recovery of baseline CD4 count after treatment initiation

Cancer treatment in PWH is associated with a steep, sustained decline in CD4 count, particularly with radiation therapy and in head & neck cancer.

Results

- Lung, prostate, head & neck, anal, and breast cancers were the most prevalent non-AIDS-defining cancers in the cohort.
- At cancer diagnosis, 89% of patients were virally suppressed.
- Baseline CD4 was 501 cells/μL among all cancers; breast cancer had the highest baseline (787 cells/μL) while anal cancer had the lowest baseline (395 cells/μL).
- From baseline to 1 year after treatment initiation, mean change in CD4 count was -88 cells/μL. Head & neck cancer exhibited the steepest CD4 decline in the first year after treatment initiation (-223 cells/μL), followed by breast (-189 cells/μL) and prostate (-159 cells/μL).
- Patients treated with RT had greater CD4 decline from baseline to 1 year than patients not treated with RT [-167 vs. +6 cells/μL, p<0.0001]. The differences in CD4 decline for chemotherapy vs. no chemotherapy or surgery vs. no surgery were not statistically significant.
- Recovery to 80% of baseline CD4 took a median of 184 days after treatment initiation (95% CI 134, 230 days). At two years, a quarter of patients still had not recovered to 80% of baseline CD4.
- Head & neck cancer had the longest estimated time to reach 80% CD4 recovery (median 1532 days), followed by breast (783 days) and prostate (634 days). Patients treated with RT took longer to reach 80% CD4 recovery than patients not treated with RT (median 634 days vs. 89 days).
- No patients that were initially virally suppressed lost viral control within two years after cancer diagnosis.

Table 1. Descriptive characteristics of the cohort.

Characteristic	N = 283
Age at time of cancer diagnosis, years [mean (SD)]	58 (11)
Sex [n (%)]	
Female	91 (32%)
Male	192 (68%)
Race/Ethnicity [n (%)]	
Black, non-Hispanic	121 (43%)
White, non-Hispanic	85 (30%)
Hispanic	68 (24%)
Other/Unknown	9 (3%)
Baseline HIV Viral Load, copies/mL [n (%)] (N = 132)	
<400	117 (89%)
>400	15 (11%)
Baseline CD4 Count, cells/μL [mean (SD)] (N = 134)	501 (355)
Primary Tumor Site [n (%)]	
Lung	41 (14%)
Prostate	30 (11%)
Head & Neck	27 (10%)
Anal	22 (8%)
Breast	15 (5%)
Other	148 (52%)
Modality Included in First Line Regimen* [n (%)]	
Chemotherapy	144 (51%)
Radiation Therapy	112 (40%)
Surgery	88 (31%)
None	44 (16%)

*modalities not mutually exclusive, patients may have received >1 in first line regimen

Table 2. Baseline CD4 and Change after Treatment Initiation

		Baseline CD4, cells/μL [mean (SD)]	Change from Baseline-1 year**, cells/μL [mean (SE)]	Median time to reach 80% CD4 recovery, days (95% CI)
Overall Cohort		521 (371)	-88 (23), **p<0.0001**	184 (134, 230)
Primary Tumor Site				
Lung		467 (319)	-43 (56), p=0.44	141 (59, 188)
Prostate		561 (310)	-159 (49), **p=0.001**	634 (26, 2132)
Head & Neck		546 (357)	-223 (56), **p<0.0001**	1532 (171, ∞)
Anal		395 (296)	-98 (58), p=0.09	277 (6, ∞)
Breast		787 (310)	-189 (77), **p=0.01**	783 (32, ∞)
Other		463 (376)	-16 (32), p=0.61	90 (46, 160)
Modality in First Line Regimen?				
Chemotherapy	Yes	449 (349)	-66 (30), **p=0.03**	153 (86, 214)
	No	564 (354)	-112 (29), **p=0.0001**	212 (128, 391)
Radiation	Yes	523 (316)	-167 (29), **p<0.0001**	634 (230, 788)
	No	483 (385)	+6 (30), p=.83	89 (48, 141)
Surgery	Yes	605 (358)	-124 (31), **p<0.0001**	208 (110, 323)
	No	438 (340)	-60 (28), **p=0.03**	160 (86, 256)

**Unadjusted analysis

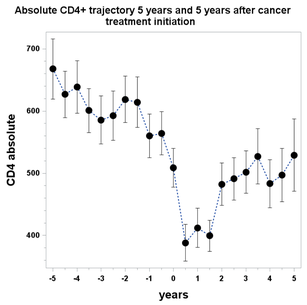

Figure 1. PWH and cancer exhibit a steep, sustained decline in CD4 count after initiation of cancer treatment.

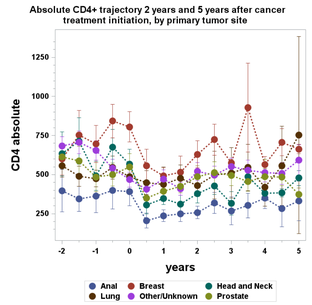

Figure 2. Head & neck, breast, and prostate cancer exhibit the sharpest declines in CD4 and take the longest to recover.

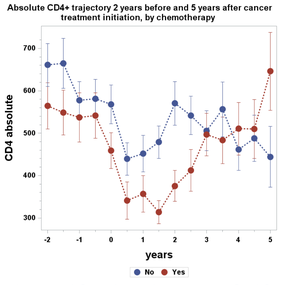

Figure 3 (above). Patients treated with chemotherapy had a lower baseline CD4 (p=0.06), but comparable decline to patients who did not receive chemo (p=0.23).

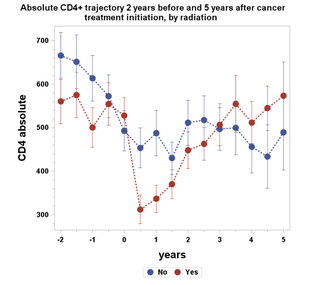

Figure 4 (top right). Patients treated with RT vs. without RT had comparable baseline CD4, but patients treated with RT had significantly greater (difference -174 cells/μL, p<.0001) CD4 decline and delayed recovery than without RT.

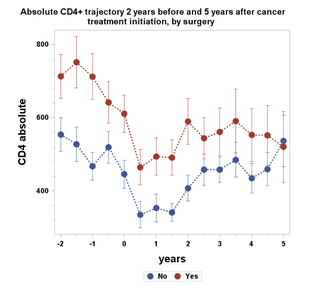

Figure 5 (right). Patients treated with surgery had higher baseline CD4 than those who did not receive surgery (p=0.008), but both groups had comparable CD4 decline (difference -63 cells/μL, p=0.10).

Conclusions

- The vast majority of patients were virally suppressed at cancer diagnosis with a median CD4 count of approx. 500 cells/μL.
- PWH exhibit significant decreases in CD4 count upon cancer treatment initiation. Though 50% of patients achieved CD4 recovery at 6 months, 25% of patients still had not achieved CD4 recovery at two years after cancer treatment initiation.
- CD4 decline is associated with both cancer type and treatment type. Treatment with RT showed a sharp decline and delayed recovery of CD4. Head/neck, breast, and prostate cancer exhibited the steepest declines in CD4 and longest time to CD4 recovery.
- CD4 decline after treatment initiation does not appear to be associated with loss of HIV viral control.
- This study had a relatively small sample size. Future research with a larger dataset will allow for multivariate analysis to determine impact of individual cancer types and treatment combinations as predictors of CD4 decline and recovery.
- This study highlights the importance of close monitoring of CD4 count in patients with HIV who are undergoing treatment for cancer, particularly in the first 6-9 months after cancer treatment initiation.

Acknowledgements

This research was supported by the Yale School of Medicine Fellowship for Medical Student Research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Yale School of Medicine Fellowship for Medical Student Research. This work was also supported by NIH P30 Cancer Center Support Grant and Yale Cancer Center Pilot Grant in Cancer Disparities.

References

1. Smith CJ, Ryom L, Weber R, et al. Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration. Lancet. 2014;384(9939):241-248. doi:10.1016/S0140-6736(14)60604-8
2. Reid E, Suneja G, Ambinder RF, et al. Cancer in People Living With HIV, Version 1.2018, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2018;16(8):986-1017. doi:10.6004/jnccn.2018.0066
3. Salahuddin S, Cohen O, Wu M, Perez Irizarry J, Vega T, Gan G, Deng Y, Isaeva N, Prasad M, Schalper KA, Mehra S, Yarbrough WG, Emu B. Human Immunodeficiency Virus Is Associated With Poor Overall Survival Among Patients With Head and Neck Cancer. Clin Infect Dis. 2023 Apr 17;76(8):1449-1458. doi: 10.1093/cid/ciac924. PMID: 36520995; PMCID: PMC10319962.
4. Hysell K, Yusuf R, Barakat L, Virata M, Gan G, Deng Y, Perez-Irizarry J, Vega T, Goldberg SB, Emu B. Decreased Overall Survival in HIV-associated Non-small-cell Lung Cancer. Clin Lung Cancer. 2021 Jul;22(4):e498-e505. doi: 10.1016/j.cllc.2020.11.006. Epub 2020 Dec 2. PMID: 33468393; PMCID: PMC8169710.
5. Helleberg M, Kronborg G, Larsen CS, et al. CD4 decline is associated with increased risk of cardiovascular disease, cancer, and death in virally suppressed patients with HIV. Clin Infect Dis. 2013;57(2):314-321. doi:10.1093/cid/cit232
6. Calkins KL, Chander G, Joshu CE, et al. Immune Status and Associated Mortality After Cancer Treatment Among Individuals With HIV in the Antiretroviral Therapy Era. JAMA Oncol. 2020;6(2):227-235. doi:10.1001/jamaoncol.2019.4648
7. Zhou Y, Lau B, Rudolph JE, Zhang X, Xu X, Yenokyan K, Wentz EL, Calkins KL, Joshu CE. Incidence of AIDS-defining Illness by Cancer Status in an Observational Study among Medicaid Beneficiaries Living with HIV in the United States, 2001 - 2015. J Acquir Immune Defic Syndr. 2025 Dec 18:10.1097/QAI.0000000000003820. doi: 10.1097/QAI.0000000000003820. Epub ahead of print. PMID: 41410240; PMCID: PMC12805858.