P 307

Blegdamsvej 9, DK-2100
Copenhagen Ø, Denmark
Tel.: 0045 50 17 80 26
alisa.timiryasovao@regionh.dk.

Mortality and Non-fatal Clinical Outcomes After Common Cancers in People With HIV: a Multicohort Collaboration

A. Timiryasova [1], L. Greenberg [1], P. Domingo [2], P.E. Tarr [3], A. Egle [4], C. Martin [5], C. Mussini [6], F. Wit [7], A. Cingolani [8], J.J. Vehreschild [9,10,11], A. Castagna [12], K. Petoumenos [13], C. Sabin [14], W. El-Sadr [15], F. Bonnet [16], M. Botanelli [12], S. Hosein [17], C. Carlander [18], A. Amstutz [3], K. Grabmeier-Pfistershammer [19], H. Garges [20], A. Marongiu[21], L. Young [22], J. Lundgren [1], L. Peters [1], L. Ryom [1,23,24] for the D:A:D and RESPOND Study Groups

[1] CHIP, Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Denmark; [2] EuroSIDA cohort, Hospital de la Santa Creu i Sant Pau, Spain; [3] Swiss HIV Cohort Study (SHCS), University of Basel, Switzerland; [4] 3rd Medical Department, Paracelsus Medical University Salzburg; [5] CHU Saint-Pierre, Centre de Recherche en Maladies Infectieuses a.s.b.l., Belgium; [6] Modena HIV Cohort, Università degli Studi di Modena, Italy; [7] AIDS Therapy Evaluation in the Netherlands (ATHENA) cohort, HIV Monitoring Foundation, the Netherlands; [8] Italian Cohort Naive Antiretrovirals (ICONA), Fondazione Policlinico A. Gemelli, IRCCS, Italy; [9] Department I of Internal Medicine, Faculty of Medicine and University Hospital, Germany; [10] German Centre for Infection Research, Partner Site Bonn-Cologne, Germany; [11] Department II of Internal Medicine, Hematology/Oncology, Goethe University, Germany; [12] San Raffaele Scientific Institute, Università Vita-Salute San Raffaele, Italy; [13] The Australian HIV Observational Database (AHOD), UNSW, Australia; [14] Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, University College London, UK; [15] CPCRA (USA), CAP-Columbia University and Harlem Hospital, USA; [16] CHU de Bordeaux and Bordeaux University, BPH, INSERM U1219,France; [17] European AIDS Treatment Group,Belgium; [18] Karolinska University Hospital, Sweden; [19] Medical University of Vienna, Austria; [20] ViiV Healthcare, Global Medical, Durham, USA; [21] Gilead Sciences, Real World Evidence Virology department, UK; [22] Merck Sharp & Dohme, Global Medical Affair, Rahway, USA; [23] Department of Clinical Medicine, University of Copenhagen, Denmark; [24] Department of Infectious Diseases, Hvidovre University Hospital, Denmark

Background

- Whilst cancer is the leading cause of death among people with HIV in high- and middle- income countries, there is limited data on outcomes after cancer in people with HIV
- This study therefore investigates mortality and clinical outcomes after the most common cancers in people with HIV

Methods

- Participants from the large RESPOND and D:A:D cohort studies, with the five most commonly occurring cancers (Kaposi's sarcoma (KS), Non-Hodgkin lymphoma (NHL), lung, anal and prostate cancers), were included in the analysis
- Participants were followed from the date of cancer diagnosis (after 2006 D:A:D/ 2012 RESPOND) until death, last follow-up, or administrative censoring (1 Feb 2016 D:A:D/ 31 Dec 2021 RESPOND)
- Crude incidence rates (IRs) were assessed for mortality, and for non-fatal individual and composite clinical outcomes (non-fatal CCO; cardiovascular disease (CVD), diabetes, AIDS events, another primary cancer)
- Predictors for mortality and non-fatal CCO after a cancer diagnosis were assessed using generalised estimating equations with Poisson regression (**Figure 2** footnote for considered covariates)

Table 1: Characteristics at time of cancer diagnosis, stratified by type of cancer

	Kaposi's sarcoma (n=604)		Non-Hodgkin lymphoma (n=597)		Lung cancer (n=518)		Anal cancer (n=442)		Prostate cancer (n=324)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	%
Sex/Gender										
Male	557	(92.5)	505	(84.3)	414	(79.9)	390	(88.2)	324	(100.0)
Ethnicity /Race										
White	247	(41.0)	320	(53.4)	321	(62.0)	278	(62.9)	214	(66.6)
Black	31	(5.1)	43	(7.2)	5	(1.0)	9	(2.0)	13	(4.0)
HIV risk										
MSM	447	(74.3)	286	(47.7)	213	(41.1)	306	(69.2)	202	(62.3)
IDU	11	(1.8)	79	(13.2)	124	(23.9)	45	(10.2)	12	(3.7)
Heterosexual	109	(18.1)	178	(29.7)	152	(29.3)	67	(15.2)	91	(28.1)
ARV history										
Naive	207	(34.4)	95	(15.9)	18	(3.5)	13	(2.9)	11	(3.4)
ART experienced	**392**	(65.2)	**502**	(83.8)	**493**	(95.2)	**427**	(96.6)	**312**	**(96.3)**
Cancer stage										
Localised	97	(16.1)	64	(10.7)	124	(23.9)	290	(65.6)	201	(62.0)
Disseminated	52	(8.6)	105	(17.5)	298	(57.5)	64	(14.5)	48	(14.8)
Unknown*	453	(75.2)	430	(71.8)	96	(18.5)	88	(19.9)	75	(23.1)
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Age, years	43	(36, 51)	48	(41, 56)	57	(51, 63)	52	(46, 58)	64	(59, 69)
CD4 cell nadir, cells/mm³	160	(42, 290)	137	(49, 250)	150	(60, 247)	108	(26, 220)	180	(80, 285)
Baseline CD4, cells/mm³	280	(90, 469)	300	(141, 465)	441	(281, 684)	502	(299, 718)	562	(430, 729)
Viral Load copies/mL	18410	(54, 152600)	70	(50, 27274)	50	(29, 50)	50	(39, 50)	40	(19, 50)

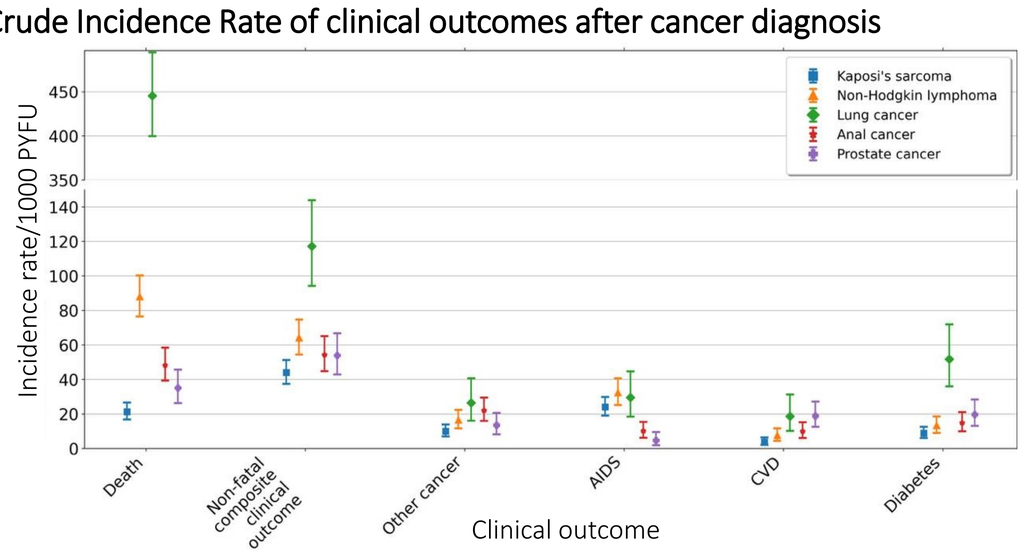
Abbreviations: MSM- men having sex with men, IDU- intravenous drug use, ARV-antiretroviral; IQR- interquartile range

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

Results

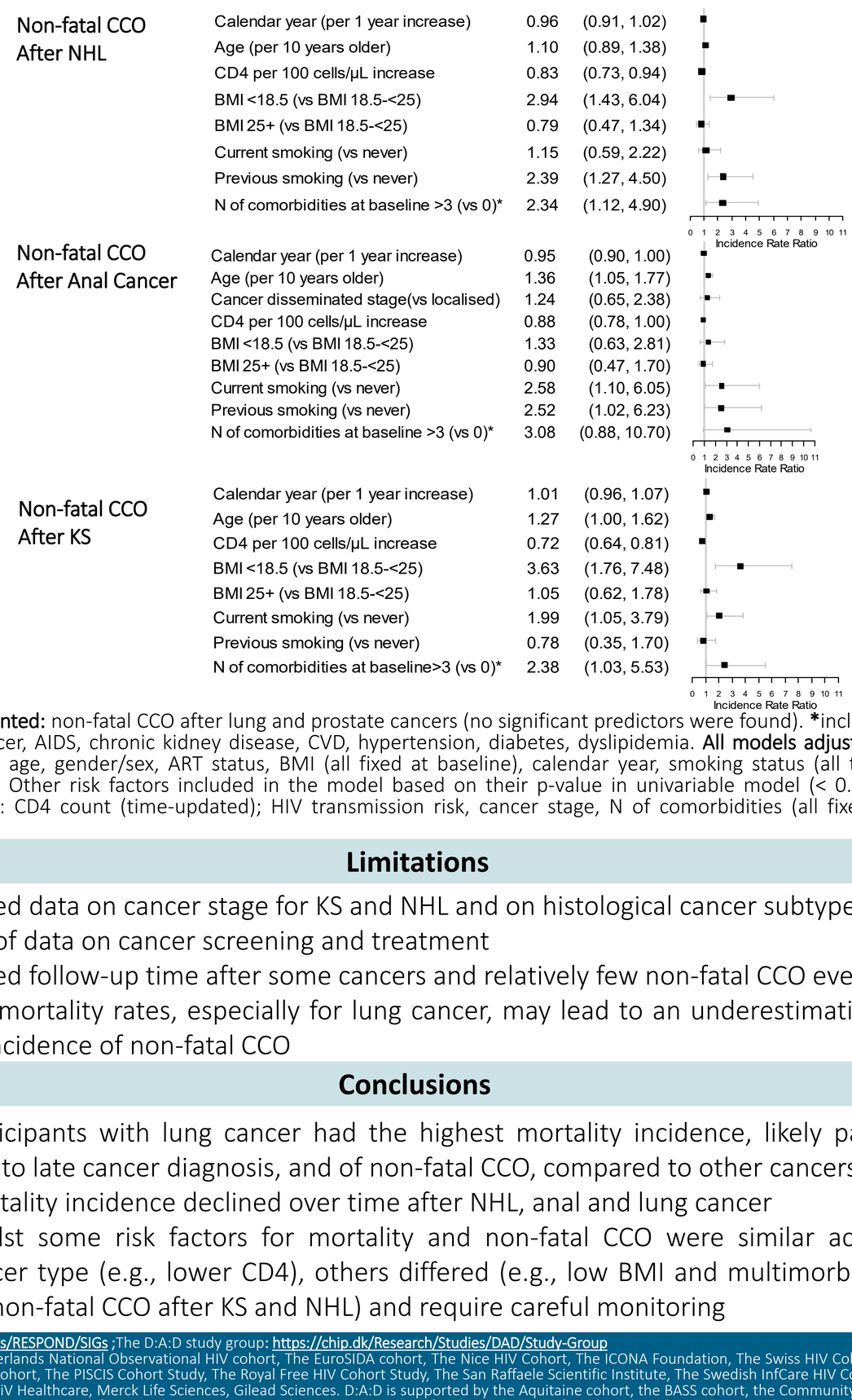
- In all, 2,485 participants with 10,630 person years of follow-up were included; baseline characteristics in **Table 1**
- Median follow-up time varied by cancer: lung cancer 0.7 years (IQR 0.3-1.7); NHL 2.5 (0.5-6.8); anal cancer 4.0 (1.7-7.4); prostate cancer 4.0 (1.7-6.8); KS 6.4 (2.9-8.8)
- **Mortality after cancer:**
  - Mortality incidence was highest after lung cancer (IR/1000 person-years 445.4 [95% CI 399.7, 494.9]) and lowest after KS (21.3 [16.9, 26.6]), compared to other cancers **(Figure 1)**
  - Disseminated cancer stage (vs localised) was associated with increased mortality after lung (adjusted IR ratio (aIRR) 4.69 [95% CI 3.27, 6.72]) and anal (2.05 [1.24, 3.40]) cancer
  - Calendar year was associated with 7-10% decreased mortality risk per later year after NHL and anal cancer (aIRR 0.90 [0.86, 0.94], 0.93 [0.89, 0.98] respectively)
  - Older age (/10 years) was associated with 24-45% higher mortality in those with NHL or anal cancer (1.24 [1.03, 1.48], 1.45 [1.13, 1.85] respectively)
  - Persons with injecting drug use (IDU) as mode of HIV acquisition had 3 times higher risk of death after anal cancer vs men who have sex with men (MSM; aIRR 3.06 [1.78, 5.26]). However, this was based on low numbers (20 persons with IDU, 61 MSM)
  - A higher CD4 count (time-updated) was associated with reduced mortality after NHL, anal and lung cancers (aIRR 0.60 [95% CI 0.53, 0.68], 0.83 [0.73, 0.94], 0.85 [0.80, 0.90] respectively)
- **Non-fatal clinical outcomes after cancer**
  - The most common non-fatal clinical outcome after cancer: AIDS after NHL and KS (51%, 61%), diabetes after lung and prostate cancers (47%, 35%), another primary cancer after anal cancer (36%)
  - Non-fatal CCO incidence was highest after lung cancer (IR/1000 person-years 117.1 [94.3-143.8]) and lowest after KS (43.9 [37.5-51.3], **(Figure 1)**
  - Predictors of non-fatal CCO after cancer shown **in Figure 2**
  - A higher CD4 count (time-updated) was associated with a reduced non-fatal CCO incidence after NHL, KS and anal cancer. However, when AIDS-related events were excluded the CD4 association only remained after KS

Figure 1: Crude Incidence Rate of clinical outcomes after cancer diagnosis



	Death (n)	Non-fatal composite clinical outcome(n)	Another primary cancer (n)	AIDS (n)	CVD (n)	Diabetes (n)
KS	79	163	36	81	14	32
NHL	218	159	39	71	18	31
Lung cancer	346	91	20	22	14	35
Anal cancer	103	116	44	21	21	30
Prostate cancer	54	83	20	7	28	28

Figure 2: Adjusted Incidence Rate ratios (IRR) for non-fatal CCO after NHL, anal cancer and KS



Not presented: non-fatal CCO after lung and prostate cancers (no significant predictors were found). *included prior cancer, AIDS, chronic kidney disease, CVD, hypertension, diabetes, dyslipidemia. **All models adjusted a priori for:** age, gender/sex, ART status, BMI (all fixed at baseline), calendar year, smoking status (all time-updated). Other risk factors included in the model based on their p-value in univariable model (< 0.1 for inclusion): CD4 count (time-updated); HIV transmission risk, cancer stage, N of comorbidities (all fixed at baseline)

Limitations

- Limited data on cancer stage for KS and NHL and on histological cancer subtypes
- Lack of data on cancer screening and treatment
- Limited follow-up time after some cancers and relatively few non-fatal CCO events
- High mortality rates, especially for lung cancer, may lead to an underestimation of the incidence of non-fatal CCO

Conclusions

- Participants with lung cancer had the highest mortality incidence, likely partly due to late cancer diagnosis, and of non-fatal CCO, compared to other cancers
- Mortality incidence declined over time after NHL, anal and lung cancer
- Whilst some risk factors for mortality and non-fatal CCO were similar across cancer type (e.g., lower CD4), others differed (e.g., low BMI and multimorbidity for non-fatal CCO after KS and NHL) and require careful monitoring

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.