CANCER RISK OF PEOPLE WITH HIV YOUNGER THAN 50 YEARS: ITALY, 1997-2023

CONTACT INFORMATION:
muccini.camilla@hsr.it

Camilla Muccini[1], Pierluca Piselli[2], Claudia Cimaglia[2], Alessandra Bandera[3], Giulia Carla Marchetti[4], Valentina Mazzotta[2], Luca Pipitò[2], Alessandro Tavelli[6,7], Stefano Rusconi[8], Carlo Federico Perno[9], Enrico Girardi[10], Antonella d'Arminio Monforte[6], Diego Serraino[10], Antonella Cingolani[11] for the Icona Foundation Study Group

1. IRCCS San Raffaele Scientific Institute, Milan, Italy; 2. National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy; 3. Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; 4. ASST Santi Paolo e Carlo, Department of Health Sciences, Milan, Italy; 5. University of Palermo, Palermo, Italy; 6. ICONA Foundation, Milan, Italy; 7. National PhD Programme One Health approaches to infectious diseases and life science research, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, Italy; 8. Ospedale Civile di Legnano, ASST Ovest Milanese, and DIBIC, Milan, Italy; 9. IRCCS Bambino Gesù Pediatric Hospital, Rome, Italy; 10. Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, Aviano, Italy; 11. Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

799

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INTRODUCTION

- HIV infection is associated with an elevated risk of multiple cancer types; these cancers frequently present with an aggressive clinical course and a poor prognosis.
- Recent data concerning the young population are lacking, especially in studies performed in Italy
- The increase in cancer diagnoses in the general population under the age of 50 justified the need to investigate this scenario also in people with HIV (PWH)
- Aim of the study was to assess the cancer risk of PWH aged <50 years in Italy.

MATERIALS AND METHODS

- Observational study in the ICONA cohort enrolling ART-naïve PWH.
- All participants <50 years at HIV-diagnosis (Jan 1997/Dec 2023) were included.
- Follow up was accrued from 30 days after first HIV-diagnosis to the cancer diagnosis, death, reaching 50 years of age, drop out or last follow-up, and person-years (PYs) at risk of cancer was calculated.
- Incident cancers (excluding non-melanoma skin cancers) were reported.
- Standardized incidence ratios (SIRs) were estimated as the ratio between the observed number of cancer cases cohort members and the expected one among the corresponding general population of Italy.
- The expected number of cases was computed by multiplying the person-years at risk among cohort members with sex, age (5-years groups), residence area, and calendar period-specific incidence rates from all Italian cancer registries as published by the International Agency for Cancer (IARC) in Cancer Incidence in Five Continents, vol. VIII (1993–1997), vol. IX (1998-2002), vol. X (2003-2007), vol. XI (2008-2012) and vol. XII (from 2013 thereafter).

RESULTS

- Among 14302 PWH (78.8% males, median age 34 years) during 94055.7 PYs (median follow-up 5.6 years), 406 single new cancers were diagnosed in 400 individuals (2.8%).
- Table 1 reports the main characteristics of the PWH in the study.

Table 1. Baseline Characteristics of 14302 PWH aged <50 years under study

	Total (%)	Males (%)	Females (%)
All	**14302**	**11266**	**3036**
Age at HIV-diagnosis (years), median (IQR)	34 (29-41)	34 (29-41)	33 (27-39)
Age at HIV-diagnosis (years)			
18-24	1762 (12.3)	1303 (11.6)	459 (15.1)
25-34	5909 (41.3)	4558 (40.5)	1351 (44.5)
35-44	5104 (35.7)	4152 (36.9)	952 (31.4)
45-49	1527 (10.7)	1253 (11.1)	274 (9.0)
Mode of HIV acquisition, n (%)			
Men who have sex with men (MSM)	6717 (47.0)	6717 (59.6)	0 (-)
Heterosexual	5517 (38.6)	2942 (26.1)	2575 (84.8)
Intravenous drug users (IDU)	1224 (8.6)	963 (8.6)	261 (8.6)
Other or unknown	844 (5.9)	644 (5.7)	200 (6.6)
First CD4 count cells/mm³ , median (IQR)	390 (198-585)	399 (211-588)	354 (159-565)
First CD4 count cells/mm³			
<200	3574 (25.0)	2687 (23.9)	887 (29.2)
200-349	2681 (18.8)	2075 (18.4)	606 (20.0)
350-499	3038 (21.2)	2477 (22.0)	561 (18.5)
500+	4953 (34.6)	3987 (35.4)	966 (31.8)
missing	56 (0.4)	40 (0.4)	16 (0.5)
First Viral load, log₁₀ copies/mL, median (IQR)	4.7 (4.0-5.3)	4.7 (4.1-5.3)	4.5 (3.7-5.2)
AIDS at time of enrolment event, n (%)			
No	13126 (91.8)	10382 (92.2)	2744 (90.4)
Yes	1176 (8.2)	884 (7.9)	292 (9.6)
Person-years of follow-up:			
Total	94055.7	72093.0	21962.6
Median (IQR)	5.6 (2.3-9.7)	5.5 (2.2-9.4)	6.0 (2.4-10.7)
Patients with one or more cancer# diagnoses at follow-up	400 (2.8)	321 (2.8)	79 (2.6)
Total cancer# diagnoses	406	324	82

IQR: Interquartile Range
de novo malignancies diagnosed at least 30 days after HIV-diagnosis, excluding non-melanoma skin cancers

Table 2. Standardized incidence ratios (SIR) and 95% Confidence Intervals (CI) for selected cancer types.

		No. of cancer cases		
Type/Site [1]	ICD-10 codes [2]	Observed	Expected	SIR (95% CI)
Virus-related				
Anus	C21	25	0.47	53.33 (34.52-78.73)
Liver	C22	6	2.79	2.15 (0.79-4.69)
Kaposi's sarcoma (KS)	C46	138	0.77	180.20 (151.39-212.90)
Cervix uteri (ICC)	C53	13	2.03	6.40 (3.41-10.94)
Hodgkin lymphoma (HL)	C81	39	4.22	9.22 (6.56-12.60)
Non-Hodgkin Lymphoma (All types, NHL)	C82-85, C96	78	8.61	9.06 (7.16-11.31)
Non virus-related				
Oral cavity	C00-10	5	2.68	1.87 (0.61-4.36)
Esophagus	C15	2	0.62	3.23 (0.39-11.65)
Colon-rectum	C18-20	7	9.18	0.76 (0.31-1.57)
Pancreas	C25	4	2.23	1.79 (0.49-4.59)
Larynx	C32	2	1.28	1.56 (0.19-5.63)
Trachea, Bronchus and Lung	C33-34	18	6.02	2.99 (1.77-4.72)
Skin melanoma	C43	10	14.70	0.68 (0.33-1.25)
Other connective and soft tissue	C49	3	1.73	1.73 (0.36-5.06)
Breast, female	C50	11	21.26	0.52 (0.26-0.93)
Corpus uteri	C54	3	1.31	2.30 (0.47-6.71)
Ovary	C56	2	1.62	1.23 (0.15-4.45)
Testis	C62	9	10.52	0.86 (0.39-1.62)
Kidney	C64	8	6.13	1.31 (0.56-2.57)
Bladder	C67	3	6.11	0.49 (0.10-1.43)
Brain	C71	4	4.16	0.96 (0.26-2.46)
thyroid gland	C73	8	13.28	0.60 (0.26-1.19)
Leukaemia	C91-92	2	4.51	0.44 (0.05-1.60)
All, but non-melanoma skin cancers [3]		**406**	**139.96**	**2.90 (2.63-3.20)**

[1] Sites/types with less than 2 observed cases and those not otherwise specified cancers, are not shown in table
[2] ICD-10: International Classification of Diseases, tenth revision. [3] Non-melanoma skin cancers excluded

In **Figure 1** age-specific incidence rates observed in PWH for all cancers and for selected cancer types, are compared with those expected in the corresponding general population of Italy.

Figure 1. Age-specific incidence rates (IR) for all cancers and selected cancer types in ICONA cohort and in the general population
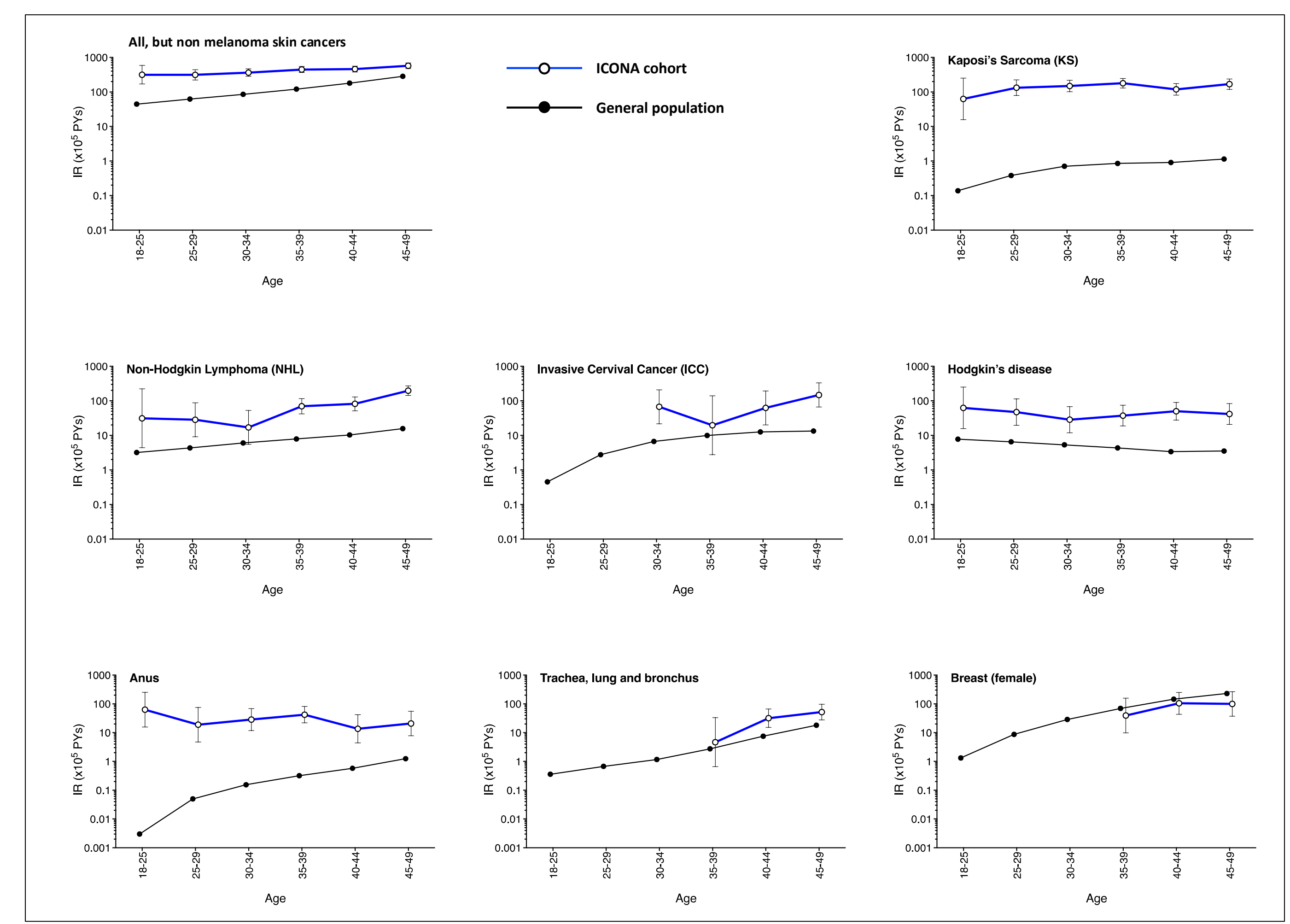

Figure 2. Standardized incidence ratios (SIR) and 95% Confidence Intervals (CI) for selected cancer types.
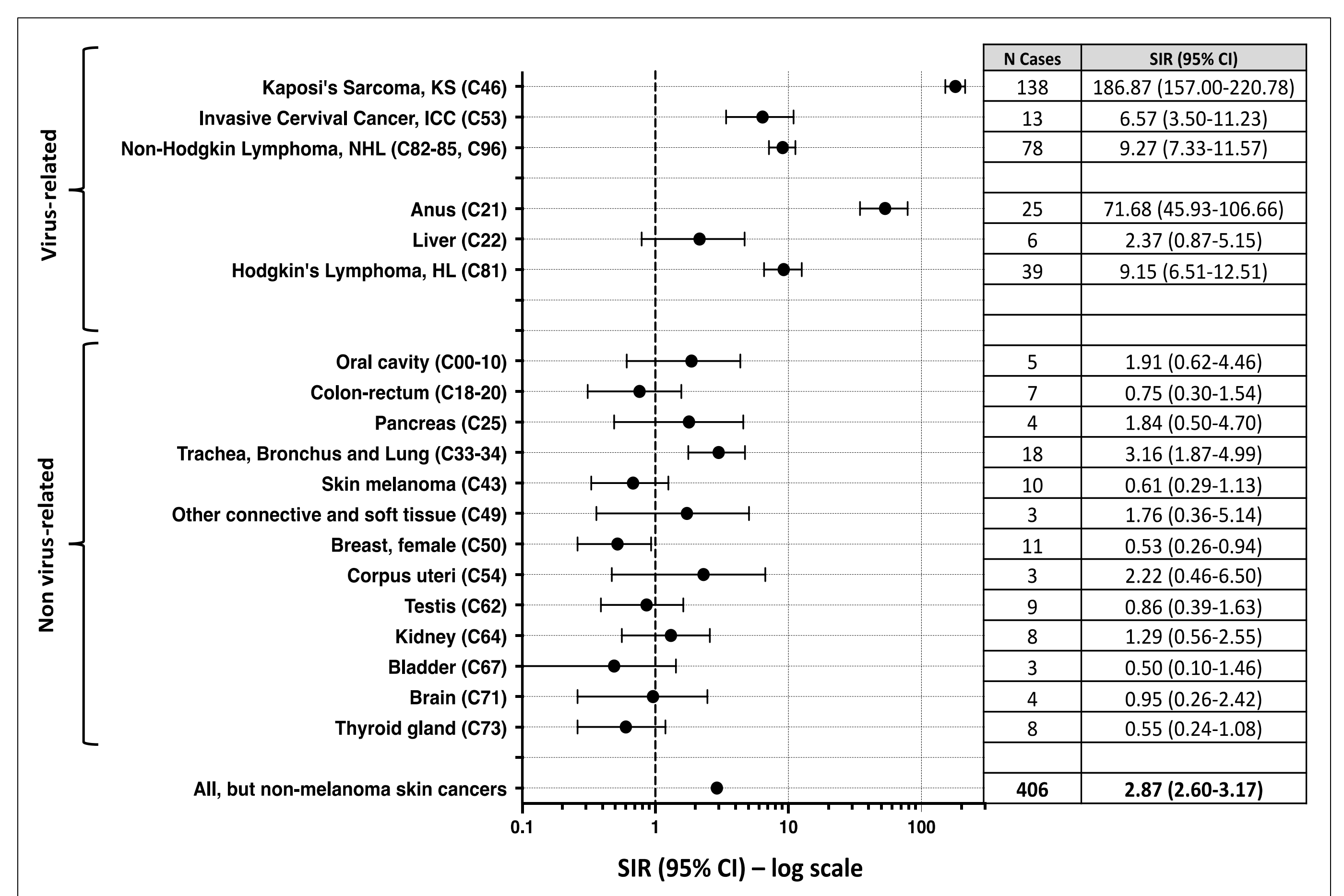

Table 2 and Figure 2 show standardized incidence ratios (SIRs) for all cancers overall and for main cancer groups and types.

- PWH had a 2.9-fold increased risk for all cancers compared with the general population (95% CI: 2.6-3.2; SIR=3.5 in males and 1.7 in females).
- Significantly elevated SIRs were observed for individual cancers: Kaposi sarcoma (SIR=180.2), non-Hodgkin lymphoma (SIR=9.1), invasive cervical cancer (SIR=6.), anal cancer (SIR=53.3) and Hodgkin lymphoma (SIR=9.2).
- No evidence for a difference in risk was observed for non virus-related cancers overall, with decreased risks for leukaemia, bladder, skin melanoma, and thyroid cancer; a significant risk reduction was reported only for breast cancer (SIR=0.5).
- Conversely, a significant increased risk was observed for trachea/bronchus/lung cancer (SIR=3.0).

CONCLUSIONS

- In PWH <50 years old, cancer risk is almost 3-times higher than in the comparable general population.
- Higher frequencies of coinfections, smoking and HIV-related chronic inflammation might explain these findings.
- A patient-centered approach that considers cancer risk factor common in PWH should guide the age cut-off when to start cancer screening, in order to reduce risk gap between young people with and without HIV.