

# EDITORIAL – IMPROVING ACCESS AND ADHERENCE TO SCREENING TESTS FOR CANCERS: A NEW, THOUGH OLD, CHALLENGE IN THE HIV EPIDEMICS

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## Editorial

Since the introduction of Highly Active Anti-Retroviral Therapy (HAART) in 1996, life quality and life expectancy of People Living with HIV (PLWH) dramatically improved. An infection leading to death in just after a few months after the first appearance of its symptoms became a chronic infection, which allowed to lead an almost normal life to people who acquired it. Consequently, we assisted to an increase of chronic pathologies, associated to ageing, to the natural history of the HIV infection and to adverse effects of the drugs<sup>1-6</sup>.

Among the chronic disorders, which prevalence has increased in PLWH, we find neoplasms<sup>7-11</sup>. In the last twenty years, the so-called post-HAART era, the incidence of AIDS-defining cancers, such as Kaposi's Sarcoma (KS), Non-Hodgkin Lymphoma (NHL) and HPV-related cervical cancer, has reduced, even though it is still higher than the general population. On the other hand, the incidence of non-AIDS-defining cancers (NADCs), e.g. lung cancer, skin cancer, prostate cancer, breast cancer, anal cancer, colon cancer, and hepatocellular carcinoma (HCC), increased<sup>12,13</sup>.

The HIV infection alone is a risk factor for cancers, being them related to persistent inflammation and immune dysregulation. As a matter of fact, HIV protein *tat* action leads to an increase of pro-inflammatory cytokines such as IL-6, IL-8, IL-12 and TNF- $\alpha$ . A high concentration of this cytokines is often found associated to pre-malignant mucosal lesions.

Moreover, PLWH are more often smokers and alcohol consumers than the general population, adding other risk factors to an already unbalanced scale. It is then easy to see how PLWH are in constant need of being screened for cancers. A need that is recognized by the scientific community, which clearly regulated times and ways to perform said screening tests including them in international and national guidelines<sup>14-16</sup>.

Screening tests used to early detect neoplasms in PLWH are the same tests applied to the general population: mammography for breast cancer in women aged 50-70 in Europe or more than 40-year-old in the United States; digital rectum examination (DRE) and prostate specific antigen (PSA) to detect prostate cancer in men aged > 50 years; fecal occult blood, flexible recto-sigmoidoscopy and colonoscopy for colorectal cancer in people aged 50-75 years in Europe or > 50 years in the US; low-dose CT chest scan for lung cancer in people smoking more than 30 pack/years or ex-smokers who quit less than 15 years before the examination; Papanicolau (PAP) test and colposcopy to identify cervical squamous cell cancer; PAP test and high resolution anoscopy to detect anal cancer, especially in men who have sex with men (MSM) and women with a positive cervical PAP test. The timings are slightly different, though: it is recommended for PLWH to undergo screening tests more often than the general population, once a year for most of them<sup>14, 16</sup> (Table 1). However, access and adherence to screening tests



**TABLE 1.** Screening tests differences between general population and PLWH.

Cancer	Screening Test	General Population	PLWH
<b>Anal</b>	Anal PAP test Anoscopy	Not recommended	MSM, once a year Women with abnormal cervical PAP smear, once a year MSM, if abnormal PAP smear
<b>Breast</b>	Mammography Breast MRI	Women > 50-year-old, every two years high-risk < 40-year-old	Women > 50-year old, once a year
<b>Cervical</b>	PAP test Colposcopy	Women > 25-year-old, every two years If abnormal PAP test	Once a year after HIV infection diagnosis
<b>Colorectal</b>	FOB Rectal sigmoidoscopy Colonoscopy	Every year Every five years Every ten years	Same as general population
<b>Hepatocellular</b>	Hepatic ultrasounds $\alpha$ -fetoprotein	If liver cirrhosis for every cause If HBV or HCV infection If Asian, men > 40-year-old or women > 50-year-old Every 6 months	If HIV/HCV or HIV/HBV coinfection, with cirrhosis If HIV/HBV coinfection, when HBV-DNA is detectable Every 6-12 months
<b>Lung</b>	Low-dose CT chest scan	> 55-year-old with > 30 pack/year smoking history Active or cessation < 15 year	> 40-year-old with > 30 pack/year smoking history Active or cessation < 15 year Once a year
<b>Prostate</b>	DRE PSA	Population-based screening is not recommended (IC)*	Men > 50-year-old Once a year

\*Parker C, Gillissen S, Heidenreich A, Horwich A. Cancer of the Prostate: ESMO Clinical Practice Guidelines. *Ann Oncol* 2015; 26: v69-v77.

are often suboptimal and PLWH still come to a doctor attention when they are symptomatic, complaining of loss of weight, asthenia and fever despite their adherence to the combined Anti-Retroviral Therapy (cART). Sadly, their complaints often come from an advanced stage neoplasm. Moreover, PLWH are ever more frequently affected than the general population by rare and more aggressive forms of tumors, such as HPV-related head and neck squamous cell carcinoma (HNSCC) and bladder carcinoma, for which screening tests are not yet available<sup>17</sup>. It is clear how, in this age full of technological revolutions, with new drugs and new methods of administration, we should try to achieve the highest screening coverage for the wellbeing of our patients. It is not admissible anymore to lose a battle without even trying to fight it.

#### CONFLICT OF INTERESTS

The authors declared no conflict of interests.

#### REFERENCES

1. CALCAGNO A, SIMIELE M, ALBERIONE MC, BRACCHI M, MARINARO L, ECCLESIA S, DI PERRI G, D'AVOLIO A, BONORA S. Cerebrospinal fluid inhibitory quotients of antiretroviral drugs in HIV-infected patients are associated with compartmental viral control. *Clin Infect Dis* 2015; 60: 311-317. doi: 10.1093/cid/ciu773
2. TROVATO M, RUGGERI RM, SCIACCHITANO S, VICCHIO TM, PICERNO I, PELLICANÒ G, VALENTI A, VISALLI G. Serum interleukin-6 levels are increased in HIV-infected patients that develop autoimmune disease during long-term follow-up. *Immunobiology* 2018; 223: 264-268. doi: 10.1016/j.imbio.2017.10.039. Epub 2017 Oct 16.
3. PINZONE MR, NUNNARI G. Prevalence of comorbidities in a cohort of women living with HIV. *Infect Dis Trop Med* 2015; 1:e165.
4. CASTRONUOVO D, PINZONE MR, MORENO S, CACOPARDO B, NUNNARI G. HIV infection and bone disease: a review of the literature. *Infect Dis Trop Med* 2015; 1: e116.
5. VISALLI G, BERTUCCIO MP, CURRÒ M, PELLICANÒ G, STURNIOLO G, CARNEVALI A, SPATARO P, IENTILE R, PICERNO I, CAVALLARI V, PIEDIMONTE G. Bioenergetics of T cell activation and death in HIV type 1 infection. *AIDS Res Hum Retroviruses* 2012; 28: 1110-1118. doi: 10.1089/AID.2011.0197
6. BRUNO R, SCUDERI D, LOCATELLI ME, PAMPALONI A, PINZONE MR. Prevalence of micronutrients deficiencies in a cohort of HIV-positive individuals on ART. *Infect Dis Trop Med* 2017; 3: e431.
7. D'ALEO F, CECCARELLI M, VENANZI RULLO E, FACCIOLÀ A, DI ROSA M, PINZONE MR, CONDORELLI F, VISALLI G, PICERNO I, BERRETTA M, PELLICANÒ GF, NUNNARI G. Hepatitis C-related hepatocellular carcinoma: diagnostic and therapeutic management in HIV-patients. *Eur Rev Med Pharmacol Sci* 2017; 21: 5859-5867. doi: 10.26355/eurrev\_201712\_14035
8. FACCIOLÀ A, VENANZI RULLO E, CECCARELLI M, D'ALEO F, DI ROSA M, PINZONE MR, CONDORELLI F, VISALLI G, PICERNO I, FISICHELLA R, NUNNARI G, PELLICANÒ GF. Kaposi's sarcoma in HIV-infected patients in the era of new antiretrovirals. *Eur Rev Med Pharmacol Sci* 2017; 21: 5868-5869. doi: 10.26355/eurrev\_201712\_14036
9. FONTANA DEL VECCHIO R, PINZONE MR, CACOPARDO B, NUNNARI G. Anal cancer in HIV-positive patients. *WCRJ* 2014; 1: e405.

10. MARTELLOTTA F, SCHIOPPA O, CACOPARDO B, FISICHELLA R, TIRELLI U. Current status and perspectives of AIDS-related Kaposi's Sarcoma in the c-ART era. *WCRJ* 2014; 1: e393.
11. GLOGHINI A, VOLPI CC, GUALENI AV, CORTELLAZZI B, PERONE F, PILOTTI S (2015) Defining the better algorithm for the accurate identification of HPV status among oropharyngeal squamous-cell carcinoma. Results from a pilot study. *WCRJ* 2015; 2: e497.
12. BERRETTA M, MARTELLOTTA F, DI FRANCIA R, SPINA M, VACCHER E, BALESTRERI L, BORSATTI E, BEARZ A, DE PAOLI P, TIRELLI U. Clinical presentation and outcome of non-AIDS defining cancers, in HIV-infected patients in the ART-era: the Italian Cooperative Group on AIDS and tumors activity. *Eur Rev Med Pharmacol Sci* 2015; 19: 3619-3634.
13. DI BENEDETTO F, TARANTINO G, ERCOLANI G, BACCARANI U, MONTALTI R, DE RUVO N, BERRETTA M, ADANI GL, ZANELLO M, TAVIO M, CAUTERO N, TIRELLI U, PINNA AD, GERUNDA GE, GUARALDI G. Multicenter Italian experience in liver transplantation for hepatocellular carcinoma in HIV-infected patients. *Oncologist* 2013; 18: 592-599. doi: 10.1634/theoncologist.2012-0255
14. SMITH RA, ANDREWS K, BROOKS D, DeSANTIS CE, FEDEWA SA, LORTET-TIEULENT J, MANASSARAM-BAPTISTE D, BRAWLEY OW, WENDER RC. Cancer screening in the United States, 2016: a review of current American Cancer Society guidelines and current issues in cancer screening. *CA Cancer J Clin* 2016; 66: 96-114. doi: 10.3322/caac.21336
15. EUROPEAN COMMISSION: council recommendation on cancer screening. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:327:0034:0038:EN:PDF> Accessed on 4 February 2018.
16. ANDREONI M, MARCOTULLIO S, CHIRIANNI A, ANTINORI A, GALLI M, LAZZARIN A, D'ARMINIO MONFORTE A, DI PERRI G, PERNO CF, PUOTI M, VELLA S, DI BIAGIO A, AMMASARI A, ANGARANO G, ARMIGNACCO O, BABUDIERI S, BINI T, BONFANTI P, BONORA S, BORDERI M, BREVEGLIERI M, BRUNO R, CALZA L. Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1. <http://www.simit.org/medias/1047-lg-hiv-2016-c17pubblicazioni2545allegato.pdf> Accessed on 4 February 2018.
17. WALLINE HM, CAREY TE, GOUDSMIT CM, BELLILE EL, D'SOUZA G, PETERSON LA, McHUGH JB, PAI SI, LEE JJ, SHIN DM, FERRIS RL. High-risk HPV, biomarkers, and outcome in matched cohorts of head and neck cancer patients positive and negative for HIV. *Mol Cancer Res* 2016; 15: 179-188. doi: 10.1158/1541-7786.MCR-16-0255