European Review for Medical and Pharmacological Sciences 2020; 24: 3849-3875

Non-AIDS defining cancers: a comprehensive update on diagnosis and management

M. CECCARELLI[1,2], E. VENANZI RULLO[1,2], M.A. MARINO[3], F. D'ALEO[4], G.F. PELLICANÒ[5], F. D'ANDREA[1], A. MARINO[6], B. CACOPARDO[6], B.M. CELESIA[6], G. LA ROCCA[7], M. DI ROSA[8], F. CONDORELLI[9], M. BERRETTA[10], G. NUNNARI[1]

[1]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[2]Department of Pathology and Laboratory Medicine, School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
[3]Department of Biomedical Sciences and Morphologic and Functional Imaging, University of Messina, Messina, Italy
[4]Unit of Microbiology and Virology, "Bianchi-Melacrino-Morelli" Hospital, Reggio Calabria, Italy
[5]Department of Human Pathology of the Adult and the Developmental Age "G. Barresi", University of Messina, Messina, Italy
[6]Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy
[7]Cancer Biology and Genetics Program, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
[8]Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy
[9]Department of Pharmacological Sciences, University of Oriental Piedmont "A. Avogadro", Novara, Italy
[10]Department of Medical Oncology, Istituto Nazionale Tumori, IRCCS - CRO, Aviano (PN), Italy

Abstract. The increasing incidence of chronic pathologies and especially non-AIDS defining cancers, such as lung cancer, hepatocellular carcinoma, breast cancer, colorectal cancer, prostate cancer, and Hodgkin's lymphoma after the introduction of combined antiretroviral therapy requires the infectious diseases specialist to know how and when to suspect and diagnose cancer in people living with HIV.

The aim of this review is to provide updated studies and information about non-AIDS defining cancers and their management in PLWH sheading a light on possible futures scenarios.

Key Words:
Lung cancer, Hepatocellular carcinoma, HCC, Breast cancer, Colorectal cancer, CRC, Prostate cancer, Hodgkin's lymphoma, HIV, PLWH, People living with HIV.

Introduction

HIV pandemics began during the early 1980s, seemingly appearing from nowhere[1]. At its debut on the world stage, HIV disease was always accompanied by the so-called "AIDS-defining pathologies". These diseases, together with HIV infection, are a certain sign of Acquired Immuno-Deficiency Syndrome (AIDS). Among them, three neoplasms were particularly frequent in People Living with HIV (PLWH). Kaposi's Sarcoma (KS), Non-Hodgkin Lymphoma (NHL) and HPV-related invasive cervical cancer were so frequently diagnosed in PLWH at their terminal stage of the disease, that they deserved the nickname of AIDS-defining cancers (ADCs)[2-13].

After more than ten years of the HIV epidemics, the introduction of the Highly Active Anti-Retroviral Therapy (HAART) led to a real revolution for PLWH[14]. HIV infection was no longer a death sentence, with the possibility of living an almost normal life. However, such good news was soon followed by its downside: the increasing incidence of chronic pathologies and especially non-AIDS defining cancers (NADCs)[5,15-59].

Among NADCs are included lung cancer, hepatocellular carcinoma (HCC), breast cancer, colorectal cancer (CRC), prostate cancer, and Hodgkin's Lymphoma (HL)[60-80].

Increased cancer risk in PLWH is related to different factors. First and foremost, HIV causes a dysregulation of the immune system. This leads to a chronic upregulation of pro-inflammatory cytokines, such as Interleukin (IL)-6, IL-8, IL-12 and Tumor Necrosis Factor (TNF)-, even when the plasmatic viral load (pVL) is undetectable. This chronic inflammatory stimulus has been related to cancer in several studies[81-85]. Moreover, at risk behaviors, such as smoking and alcohol use have been found to be more frequent in PLWH than in the general population[20].

Corresponding Author: Giovanni Francesco Pellicanò, MD; e-mail: gpellicano@unime.it

In addition to its increased frequency, in PLWH cancer is also more aggressive and tends to progress faster. Therefore, for an infectious diseases (ID) specialist, and for every clinician, it is important to know the dangers linked to the infection.

Thus, the aim of this review is to provide updated evidence and information about NADCs and their management in PLWH, also sheading a light on possible futures scenarios.

Lung Cancer

Lung cancer is the most frequent cancer in the world, representing the 11.6% of all cancers newly diagnosed in 2018. This high rate is also found in PLWH, for whom lung cancer is the most common NADC and the most frequent cause of cancer-related death[62,77,86-88].

PLWH are burdened by a risk 3-fold higher of developing lung cancer than the general population, probably because of the higher rate of smoking in this population[61,89,90]. Moreover, PLWH seem to develop lung cancer at a younger age than the general population, with an increased mortality as the cancer exhibits a more aggressive behavior and faster progression[76,91-95]. As a matter of fact, several studies showed that, in the US, the prevalence rate of smoking is 35-70% among PLWH, approximately 20% for the general population[96-98]. Luckily, in the last few years we assisted to a progressive decrease of the smoking habit among PLWH, which was accompanied by a decrease in lung cancer incidence rate[99]. However, lung cancer is still more frequent in PLWH than in the general population and smoking is still a major risk factor[100]. Other risks factors are represented by chronic obstructive pulmonary disease (COPD) and recurrent pneumonitis, which cause an intense and persistent inflammatory stimuli on lung cells and increased levels of $CD8^+$ T-cells activity[101-106].

HIV is an independent risk factor for lung cancer. Hleyhel et al[107] showed that HIV-infected individuals who did not recover a CD4+ T-cell count to at least 500 cells/μL had an increased risk of developing lung cancer. Other studies also highlighted the role of HIV-related chronic inflammation as an independent risk factor for lung cancer. The effects of a persistent increase of plasmatic IL-6, C Reactive Protein, and D-dimer on the incidence of lung cancer, are well described by Borges et al[108]. HIV has been found to infect lung macrophages, a reservoir in which its activity is not suppressed by antiretroviral therapy (ART), even in non-smokers affected by lung cancer[109]. This raised the question on the role of HIV as a direct oncogene[61,62,103,109]. However, there are no conclusive reports about a direct oncogenic activity of HIV on lung, despite some early studies suggestions[62,110-112].

Given its high incidence in PLWH and its burden in mortality, it is important to prevent this cancer or diagnose it at an early stage, when it is still not symptomatic.

Primary prophylaxis is represented by smoking cessation[62]. Several studies[113-116] showed that both behavioral and pharmacologic intervention are effective in reducing lung cancer incidence in PLWH.

A survival rate of 50-80% at 5 years is granted by early diagnosis[93,95,117,118]. Therefore, a once-a-year low-dose (LD) chest computerized tomography (CT) scan is recommended especially for people considered at high-risk of developing lung cancer. Italian guidelines for the diagnosis and management of HIV-1 infection recommend screening to all PLWH who are older than 40 years, with an active smoking history of more than 30 pack/year or who have ceased smoking for less than 15 years[119]. However, Kong et al[120] showed that mortality rate in PLWH with CD4+ T-cell count above 500 cells/μL and an adherence of 100% to ART is not different to the general population by applying the same screening criteria (age > 55 year-old, with an active smoking history of > 30 pack/year or who have ceased smoking for less than 15 years). Moreover, the US Preventive Task Force have already established in 2004 that a screening program for asymptomatic people was not cost-effective, especially in PLWH, who are affected by a high prevalence of non-cancerous pulmonary nodules[120-122]. The same opinion seems to be shared by the European AIDS Clinical Society (EACS) that in 2017 did not include lung cancer screening in their guidelines[123]. Further studies are needed to establish the real risk-benefit ratio for lung cancer screening in PLWH.

Lung cancer is often asymptomatic or accompanied by non-specific symptoms at its onset[61]. When symptomatic, the first step towards a diagnosis is a chest X-ray. However, chest X-ray is burdened by a 90% level of missed diagnosis, mostly because of observer errors, tumor characteristics, and technical issues[124]. Therefore, more often the first examination in the suspect of lung cancer is a chest CT scan, whose level of missed diagnosis is only 5%[61,124]. Missed diagnosis are the most frequent cause for a possible early diagnosed cancer to become an advanced, and unfortunately not curable, one[124]. The most recent positron emission tomog-

raphy (PET) combined with total body CT scan (PET/CT) permits to distinguish a metabolically active pulmonary lesion from a non-active one. Moreover, being a total body scan, it also permits to highlight the presence of metastatic disease[125-128].

There is a need for specific and minimally invasive screening and diagnostic tests. Micro-RNA 411 (miR-411) and long-noncoding RNAs, such as LINC00152, DKFZP434-L187, and LOC285548 have been studied for their correlation with tumor-nodes-metastatic (TNM) stage, differentiation degree, and prognosis[61]. More studies are needed to confirm whether this correlation might be exploited for clinical reasons. In the era of personalized medicine, a chance for early diagnosis is given by the radiomics analysis. Recently, Shi et al[129] analyzed radiologic and radiomic features for identifying opportunistic pulmonary infections misdiagnosed as lung cancers in patients with human immunodeficiency virus in a small group of patients[49]. The authors found that four radiomic parameters of central-type lesions were significantly different between cancer and OPI's patients[129]. However, these data need to be expanded and validated in larger series.

After the diagnosis, it is important to choose the best management. Up-to-date, surgery is still the gold-standard treatment in the case of lung cancer[130,131]. Stage I and II of lung cancers are treated with surgery, mainly lobectomy, and lymph nodes evaluation. For the smallest lesions and only for those types of lung cancer which are at low risk of micro-metastasis, a sub-lobar resection could be the elective surgery[132-135]. More advanced stages (III and IV) require a combined approach with chemotherapy and radiotherapy[136]. Combined therapy can be carried out as a neoadjuvant approach (chemotherapy and/or radiotherapy before surgery) to reduce the local extension of the tumor and possibly destroy micro-metastasis, an adjuvant approach (chemotherapy and/or radiotherapy after surgery) to prevent recurrence, or both[136,137]. Oncology is the most advanced medical discipline in terms of personalized medicine, and classic chemotherapeutic drugs, such as cisplatin and carboplatin are being progressively replaced by monoclonal antibodies, such as erlotinib and afatinib, which are inhibitors of the epithelial growth factor receptor, or crizotinib, an inhibitor of the anaplastic lymphoma kinase and the c-ros oncogene 1[138-141]. However, both erlotinib and afatinib decrease the production of activated and memory CD4+ T-lymphocytes and are therefore not indicated in PLWH. No effect on CD4+ T-lymphocytes is known for crizotinib[138-141]. Erlotinib and afatinib use is affected by a high rate of adverse events, such as diarrhea and low-grade rash, while crizotinib use leads to an increase of transaminases and blood creatinine. Table I shows the adverse effects of the biologic drugs and their drug-to-drug interactions with ART drugs.

Lately, a rising interest has been shown towards a new class of drugs called "inhibitors of the immune-checkpoints". These drugs are directed towards molecules mediating the regulation of the immune system, such as the Programmed cell Death 1 (PD-1) and Programmed cell Death Ligand 1 (PD-L1). Pembrolizumab, nivolumab and atezolizumab are molecules currently under observation for lung cancer[142]. They seem to be effective even against the most difficult type of cancers and have a role in modulating T-cell activation in peripheric tissues[143,144].

Currently, there are no reports showing an increased risk for metastatic cancers or AIDS in PLWH treated with immune-checkpoints inhibitors. On the contrary, Fromentin et al[145] showed that CD4+ T-cells highly expressing PD-1 and TIGIT (T cell immunoglobulin and ITIM domain) have an increased probability to be infected by HIV compared to cells not expressing them (relative ratio 1.18, 95% CI 1.07-1.31, $p = 0.002$). Therefore, the use of immune checkpoints inhibitors directed against PD-1 could also help eradicate the infection by activating latently infected cells and mediating a "shock and kill" approach.

Breast Cancer

Breast cancer represents 11.6% of new cancer diagnosis in the whole world, with a 6.6% mortality. Incidence and mortality are more than double (24.2% and 15.0% respectively) when only considering women[67,87]. Little is known about the epidemiology of breast cancer in PLWH. Different studies had different conclusions, but all of them agree on the fact that breast cancer incidence in PLWH is similar or even slightly lower than in general population[145].

HIV and breast cancer share signaling pathways and receptors, which may explain the complex interactions existing between the virus and this cancer[146,147]. Despite the fact that the incidence of breast cancer is not increased in PLWH, several studies showed how the virus play a role in accelerating the evolution of the cancer, especially acting on immune signaling, angiogenesis upregulation and metastatic spread, leading to a worse prognosis[148-152].

Table I. List of NADCs, biologic and immunotherapeutic drugs used in their treatment with targets, most common adverse effects and possible interactions with antiretroviral drugs.

Cancer	Drug (primarly metabolization)	Target	Common Adverse Events	DDIs with ART drugs
Lung	Erlotinib *(CYP3A4. Lesser extent by CYP1A2 and CYP1A1)*	EGFR	Infections, Anorexia, Loss of weight, dry eye, conjunctivitis, depression, headache, dyspnea, cough, diarrhea, nausea vomiting, abdominal pain, skin rash, itchiness, dry skin, alopecia, asthenia, fever	**Inhibitors of CYP3A4:** Atazanavir Ritonavir Cobicistat Indinavir Lopinavir Saquinavir Tipranavir **Inducers of CYP3A4:** Efavirenz Etravirine Nevirapine Fosamprenavir
	Afatinib *(P-gp and CYP3A5)*	EGFR	Infections, anorexia, epistaxis, diarrhea, nausea, vomiting, stomatitis, skin rash, acneiform dermatitis, itchiness, dry skin	**Inhibitors of P-gp:** Ritonavir Nelfinavir Saquinavir
	Crizotinib *(CYP3A4 Lesser UGTA1A)*	ALK ROS1	Neutropenia, anemia, leukopenia, decreased appetite, neuropathy, dysgeusia, vision disorder, dizziness, bradycardia, vomiting, diarrhea, nausea, constipation, abdominal pain, elevated aminotranspherases, rash, edema, fatigue	**Inhibitors of CYP3A4:** Atazanavir Ritonavir Cobicistat Indinavir Lopinavir Saquinavir Tipranavir **Inducers of CYP3A4:** Efavirenz Etravirine Nevirapine Fosamprenavir Substrates of UGT1A1: Raltegravir **Carried of OCT1 and OCT2:** Dolutegravir Bictegravir
	Pembrolizumab *(plasmatic Esterase)*	PD-L1	Pneumonitis, anemia, thrombocytopenia, lymphopenia, infusion related reactions, hypothyroidism, hyperthyroidism, decreased appetite, hyponatremia, hypokalemia, hypocalcemia, insomnia, headache, dizziness, peripheral neuropathy, lethargy, dysgeusia, dry eye, cardiac arrhytmia, hypertension, dyspnea, cough, diarrhea, abdominal pain, nausea, vomiting, constipation, colitis, dry mouth, rash, itchiness, severe skin reactions, erythema, dry skin, vitiligo, eczema, alopecia, dermatitis acneiform, muscoloskeletal pain, arthralgia, pain in extremities, myositis, arthritis, fatigue, asthenia, edema, fever, influenza-like illness, chills, elevated aminotranspherases, elevated bilirubin, increased blood AlPh, hypercalcemia, increased blood creatinine	**None expected**

Continued

Table I (continued). List of NADCs, biologic and immunotherapeutic drugs used in their treatment with targets, most common adverse effects and possible interactions with antiretroviral drugs.

Cancer	Drug (primarly metabolization)	Target	Common Adverse Events	DDIs with ART drugs
	Nivolumab *(plasmatic Esterase)*	PD-L1	Upper respiratory tract infections, neutropenia, infusion related reactions, hypersensitivity, hypothyroidism, hyperthyroidism, decreased appetite, peripheral neuropathy, headache, dizziness, hypertension, pneumonitis, dyspnea, cough, diarrhea, nausea, colitis, stomatitis, vomiting, constipation, dry mouth, rash, itchiness, vitiligo, dry skin, erythema, alopecia, muscoloskeletal pain, arthralgia, fatigue, fever, edema, elevated aminotranspherases, elevated bilirubin, increased blood AlPh, hypercalcemia, increased blood creatinine	**None expected**
	Atezolizumab *(plasmatic Esterase)*	CTLA-4	Urinary tract infection, thrombocytopenia, infusion related reactions, hypothyroidism, decreased appetite, hypokalemia, hyponatremia, hyperglycemia, hypotension, cough, dyspnea, nausea, vomiting, diarrhea, abdominal pain, colitis, dysphagia, oropharyngeal pain, elevated transaminases, hepatitis, rash, itchiness, arthralgia, back pain, muscoloskeletal pain, fever, fatigue, asthenia, influenza-like illness, chills	**None expected**
Breast	Trastuzumab *(plasmatic Esterase)*	HER-2	Infections, nasopharyngitis, febrile neutropenia, anemia, neutropenia, leukopenia, thrombocytopenia, weight loss, anorexia, insomnia, tremor, dizziness, headache, paresthesia, dysgeusia, conjunctivitis, increased lacrimation, blood pressure disorders, cardiac arrhytmia, decreased ejection fraction, hot flush, wheezing, dyspnea, cough, epistaxis, rhinorrhea, erythema, rash, swelling face, alopecia, nail disorder, palmar-plantar erytrodysesthesia syndrome, arthralgia, muscle tightness, myalgia, asthenia, chest pain, chills, fatigue, influenza-like illness, infusion-related reactions, pain, fever, mucosal inflammation, peripheral edema	**No formal drug interaction study performed**
	Pertuzumab *(plasmatic Esterase)*	HER-2	Nasopharyngitis, febrile neutropenia, neutropenia, leukopenia, anemia, infusion-related reactions, decreased appetite, insomnia, peripheral neuropathy, headache, dysgeusia, peripheral sensory neuropathy, dizziness, paresthesia, increased lacrimation, diarrhea, vomiting, nausea, constipation, dyspepsia, abdominal pain, alopecia, rash, nail disorder, itchiness, dry skin, myalgia, arthralgia, pain in extremities, mucosal inflammation, peripheral edema, fever, fatigue, asthenia, hot flush, cough, epistaxis, dyspnea	**No formal drug interaction study performed, except with other antitumor drugs**
	Lapatinib *(CYP3A4)*	RTK	Anorexia, insomnia, headache, decreased ejection fraction, hot flush, epistaxis, cough, dyspnea, diarrhea, nausea, vomiting, dyspepsia, stomatitis, constipation, abdominal pain, hyperilirubinemia, hepatotoxicity, rash, dry skin, palmar-plantar erythrodysesthesia syndrome, alopecia, itchiness, nail disorder, pain in extremities, back pain, arthralgia, fatigue, mucosal inflammation, asthenia	**Inhibitors of CYP3A4:** Atazanavir Ritonavir Cobicistat Indinavir Lopinavir Saquinavir Tipranavir **Inducers of CYP3A4:** Efavirenz Etravirine Nevirapine Fosamprenavir

Continued

Table I (continued). List of NADCs, biologic and immunotherapeutic drugs used in their treatment with targets, most common adverse effects and possible interactions with antiretroviral drugs.

Cancer	Drug (primarly metabolization)	Target	Common Adverse Events	DDIs with ART drugs
	Olaparib *(CYP3A4 and CYP3A5)*	PARB	Anemia, neutropenia, thrombocytopenia, leukopenia, lymphopenia, rash, decreased appetite, dizziness, dysgeusia, cough, dyspnea, vomiting, diarrhea, nausea, dyspepsia, upper abdominal pain, stomatitis, fatigue, increased blood creatinine	**Inhibitors of CYP3A4:** Atazanavir Ritonavir Cobicistat Indinavir Lopinavir Saquinavir Tipranavir **Inducers of CYP3A4:** Efavirenz Etravirine Nevirapine Fosamprenavir **Carried of OCT1 and OCT2:** Dolutegravir Bictegravir
	Talazoparib	PARB	Thrombocytopenia, anemia, neutropenia, leukopenia, lymphopenia, decreased appetite, dizziness, headache, dysgeusia, vomiting, diarrhea, nausea, abdominal pain, stomatitis, dyspepsia, alopecia, fatigue	**Inhibitors of P-gp:** Ritonavir Nelfinavir Saquinavir Tipranavir
Prostate	Pembrolizumab	PD-L1	See "lung"	See "lung"
CRC°	Cetuximab *(plasmatic Esterase)*	EGFR	Hypomagnesemia, dehydration, hypocalcemia, anorexia, headache, conjuctivitis, diarrhea, nausea, vomiting, elevated aminotranspherases, skin reactions, infusion related reactions, mucosal inflammation	**No formal drug interaction study performed, except with other antitumor drugs**
	Panitumumab *(plasmatic Esterase)*	EGFR	Conjunctivitis, paronychia, anemia, hypokalemia, hypomagnesemia, decreased appetite, insomnia, dyspnea, cough, diarrhea, nausea, vomiting, abdominal pain, stomatitis, constipation, dermatitis acneiform, rash, erythema, itchiness, dry skin, skin fissures, acne, alopecia, back pain, fatigue, fever, asthenia, mucosal inflammation, peripheral edema, weight loss	**No formal drug interaction study performed, except with other antitumor drugs**
	Bevacizumab *(plasmatic Esterase)*	EGFR	Febrile neutropenia, leukopenia, thrombo-cytopenia, anorexia, hypomagnesemia, hyponatremia, peripheral sensory neuropathy, dysarthria, headache, dysgeusia, eye disorder, increased lacrimation, hypertension, venous thrombo-embolism, dyspnea, epistaxis, rhinitis, cough, rectal hemorrage, stomatitis, constipation, diarrhea, nausea, vomiting, abdominal pain, wound healing complications, exfoliative dermatitis, dry skin, skin discoloration, arthralgia, myalgia, proteinuria, ovarian failure, asthenia, fatigue, fever, pain in extremities, mucosal inflammation, weight loss	**No formal drug interaction study performed, except with other antitumor drugs**
	Atezolizumab *(plasmatic Esterase)*	CTLA-4	See "lung"	See "lung"

Continued

Table 1 (continued). List of NADCs, biologic and immunotherapeutic drugs used in their treatment with targets, most common adverse effects and possible interactions with antiretroviral drugs.

Cancer	Drug (primarly metabolization)	Target	Common Adverse Events	DDIs with ART drugs
	Ipilimumab *(plasmatic Esterase)*	CTLA-4	Tumor pain, anemia, lymphopenia, hypopituitarism, hypothyroidism, decreased appetite, dehydration, hypokalemia, confusional state, peripheral sensory neuropathy, dizziness, headache, lethargy, blurred vision, eye pain, hypotension, flushing, hot flush, dyspnea, cough, diarrhea, vomiting, nausea, gastrointestinal hemorrage, colitis, costipation, gastroesophageal reflux disease, abdominal pain, mucosal inflammation, abnormal hepatic function, rash, itchiness, dermatitis, erythema, vitiligo, urticaria, eczema, alopecia, night sweats, dry skin, arthralgia, myalgia, musculoskeletal pain, muscle spasms, fatigue, injection site reaction, fever, chills, asthenia, edema, pain, influenza-like illness, increased aminotranspherases, increased AlPh, increased blood bilirubin, weight loss	**None expected**
HCC*	Sorafenib *(CYP3A4 and UGTA1A)*	TyK	Infection, lymphopenia, anorexia, hypophosphatemia, hemorrage, hypertension, diarrhea, nausea, vomiting, constipation, dry skin, rash, alopecia, hand foot skin reaction, erythema, itchiness, arthralgia, fatigue, pain, fever, weight loss, increased amylase, increased lipase	**Substrates of UGT1A1:** Raltegravir
	Regorafenib *(CYP3A4 and UGTA1A)*	TyK	Infection, thrombocytopenia, anemia, decreased appetite and food intake, hemorrage, hypertension, dysphonia, diarrhea, stomatitis, vomiting, nausea, hyperbilirubinemia, elevated aminotranspherases, hand-foot-skin reaction, rash, asthenia, fatigue, pain, fever, mucosal inflammation, weight loss	**Inhibitors of CYP3A4:** Atazanavir, Ritonavir, Cobicistat, Indinavir, Lopinavir, Saquinavir, Tipranavir **Inducers of CYP3A4:** Efavirenz, Etravirine, Nevirapine, Fosamprenavir **Substrates of UGT1A1:** Raltegravir
	Lenvatinib	TyK	Urinary tract infection, thrombocytopenia, leukopenia, neutropenia, hypothyroidism, hypocalcemia, hypokalemia, weight loss, decreased appetite, insomnia, dizziness, headache, dysgeusia, hemorrage, hypertension, hypotension, dysphonia, diarrhea, gastrointestinal and abdominal pain, vomiting, nausea, oral inflammation, oral pain, constipation, dyspepsia, dry mouth, increased bilirubin, hypoalbuminemia, elevated aminotranspherases, palmar-plantar erythrodysestesia syndrome, rash, alopecia, back pain, arthralgia, myalgia, pain in extremities, muscolo-skeletal pain, proteinuria, fatigue, asthenia, peripheral edema	**None expected with substrates of CYP3A4 and P-gp. No other studies were conducted**

Continued

Table I (continued). List of NADCs, biologic and immunotherapeutic drugs used in their treatment with targets, most common adverse effects and possible interactions with antiretroviral drugs.

Cancer	Drug (primarly metabolization)	Target	Common Adverse Events	DDIs with ART drugs
HL^	Rituximab	CD20	Bacterial infections, viral infections, bronchitis, neutropenia, leukopenia, febrile neutropenia, thrombocytopenia, infusion-related reactions, angioedema, nausea, itchiness, rash, alopecia, fever, chills, asthenia, headache, decreased IgG levels	**None expected**
	Brentuximab *(plasmatic Esterase)*	CD30	Infection, upper respiratory tract infection, neutropenia, peripheral sensory neuropathy, cough, dyspnea, nausea, diarrhea, vomiting, constipation, abdominal pain, rash, itchiness, arthralgia, myalgia, fatigue, pyrexia, infusion-related reactions, chills, weight loss	**Inhibitors of CYP3A4:** Atazanavir, Ritonavir, Cobicistat, Indinavir, Lopinavir, Saquinavir, Tipranavir **Inducers of CYP3A4:** Efavirenz, Etravirine, Nevirapine, Fosamprenavir **Inhibitors of P-gp:** Ritonavir, Nelfinavir, Saquinavir, Tipranavir
	Pembrolizumab	PD-L1	See "lung"	See "lung"
	Nivolumab	PD-L1	See "lung"	See "lung"
Anal	Cetuximab	EGFR	See "CRC"	See "CRC"
	Panitumumab	EGFR	See "CRC"	See "CRC"

°CRC: Colorectal cancer; *HCC: Hepatocellular Carcinoma; ^HL: Hodgkin Lymphoma
Source: http://www.hiv-druginteractions.org/data/ExtraPrintableCharts/ExtraPrintableChartID7.pdf

Therefore, it is imperative to try and diagnose breast cancer in PLWH as soon as possible[67]. A case-control report by D'Andrea et al[18] showed that PLWH and their doctors are more careful towards periodic screening than the general population, and this is particularly true for breast cancer. Screening tests for breast cancer start with self-breast examination. Every woman should examine her own breast looking for bumps once a month under the shower[67]. In PLWH, breast cancer screening consists in a mammogram performed once a year in women older than 50 years, according to the Italian guidelines[119]. Mammography false negative rate is attested around 20%, meaning that 1 out of 5 cancers are not diagnosed with this method. This happens especially in young women, because of a denser texture of the mammal gland[153]. Therefore, for younger women suspecting breast cancer, it is suggested to use either an ultrasound (US) approach or, if at high risk, a breast MRI[18,19,154,155]. Despite the many downsides of mammography (radiation exposure, uncomfortable examination, false negative rate), it is still the gold standard for breast cancer screening, because of its cost-effectiveness ratio[156,157]. As a matter of fact, mortality by breast cancer is reduced by 19% when a mammography screening is applied[158].

In PLWH, genetic factors (BCRA1 and 2 genes, Li Fraumeni syndrome), familiarity, iatrogenic factors (chest irradiation at a young age, hormonal therapy) and individual factors (atypical hyperplasia, pregnancy in old age, premature menarche and late menopause) contribute to define the level of risk for breast cancer[159].

Both imaging techniques and biochemical markers are important in the diagnosis of breast cancer[158]. We previously highlighted that mam-

mography, US, and MRI are also used in breast cancer screening. Multiparametric MRI with abbreviated protocols, i.e., reduced time of scanning, can be used as screening tool in the high-risk population with excellent results[160,161]. Furthermore, Marino et al[162] have shown the potential benefit of mammography screening in male patients at high-risk for developing breast cancer. PET and single-photon emission computed tomography (SPECT) can be considered second level tests, which are used for confirmation and staging of cancer[163,164].

Several proteins, mRNAs, enzymes and microRNAs (miR) have been highlighted as diagnostic biomarkers by some studies[150-152]. Among them, the Human Epidermal Growth Factor Receptor 2 (HER-2), the Estrogen Receptor (ER), miR-21, miR-10b, miR-155, and miR-145. HER-2 and ER are involved in breast cancer pathogenesis and are also therapy targets[158,165]. miRs are still in a study phase for possible clinical applications, but the interest around them is high, and in the near future we could assist to a miR-targeted drug revolution.

The term "breast cancer" includes different types of cancer. Hormone Receptor (HR) positive breast cancer represent the 85% of the cancers, and they are ER and Progesterone Receptor (PR) positive. This type has the best prognosis. These cancers can be targeted with ER antagonists (tamoxifen), ER expression modulators (fulvestrant) and Aromatase Inhibitors (AIs) (letrozole, anastrozole, exemestane)[165].

A percentage of HR positive breast cancers belongs to a second type: HER-2 positive cancers. This type, which is more aggressive and fast growing, has a worse prognosis than ER-positive cancers. However, HER-2 positive cancers can be targeted with monoclonal antibodies against HER-2 (trastuzumab, pertuzumab) or tyrosine kinase receptor inhibitors (lapatinib), which are well-tolerated[165]. Trastuzumab and pertuzumab increase the number of CD4+, especially those infiltrating the tumor, leading to a better rate of complete response. According to this effect, it is reasonable to think that the use of these molecules is immunologically safe in PLWH with breast cancer.

A third type of breast cancer, called triple-negative (TNBC) because of its lack of expression of ER, PR and HER-2, has a prevalence of 15%. These cancers have the worst prognosis because they lack targeted treatments[165]. Poly-ADP-Ribosyl Polymerase (PARP) inhibitors (olaparib and talazoparib) have been approved for use in BRCA1/2 positive cancers and HER-2 metastatic cancers[166]. More PARP inhibitors are currently under study for the treatment of advanced TNBCs[166]. The interest is also high around the phosphoinositide 3-kinase (PI3K)/AKT pathway, immune checkpoint inhibitors (PD-L1), cyclin-dependent kinase (CDK) 4/6 and topoisomerase-1.

Therapy is not different in PLWH, despite the need to avoid drug-drug interactions. However, Wang et al[167] demonstrated an upregulation of TAR binding protein 2 (TARBP2) in the case of tamoxifen-resistant breast cancers. It is possible to hypothesize that an upregulation of TARBP2 can happen in presence of HIV-1, thus conferring to it tamoxifen resistance[167]. Further studies are needed to confirm this possibility.

Prostate Cancer

Prostate cancer (PC) is the second cancer per incidence in men, with 13.5% new diagnoses per year. It is also the 5th cancer in terms of mortality in men[87]. It is expected that it will become even more frequent in the future[168]. It is more common in Afro-American men; however, it is most frequently diagnosed in Western Europe and North America[87].

Similar to the general population, incidence in PLWH has been progressively increasing[169]. PLWH risk of developing PC seems to be lower than in general population[170]. However, PLWH are burdened by a higher mortality compared to the general population, even though there are discordant evidence[75,95]. The higher mortality rate might be related to a lower screening rate, even though several studies[18,95,171] highlighted that PLWH receive the screening more often than HIV-negative men. However, Coghill et al[172] highlighted that, despite a higher rate of screening, PLWH tend to be diagnosed at a worst tumor-node-metastasis (TNM) stage than the general population.

Age, Afro-American race, positive family history, androgen supplement use and obesity are risk factors for the onset of prostate cancer. In PLWH, there are also HIV-related risk factors[173,174]. In fact, a worse immune status is associated to a more rapid progression of PC. Moreover, HIV seems to be involved in the activation of cellular pathways leading to increased angiogenesis and reduced apoptosis[66,76,175,176].

Screening test for PC consists of prostate-specific antigen (PSA) testing. Italian guidelines for the diagnosis and management of HIV-1 infection suggest that every HIV-positive individual

> 50-year-old should undergo the plasmatic PSA testing at least once a year[119]. Several scholars[177] showed that the screening rate varies with race, ethnicity, income and education. If PSA levels are higher than 4.0 ng/mL, with free-PSA > 25%, digital rectal examination (DRE) and a trans-rectal US with prostate biopsy are performed[178]. However, this approach has a 21% to 28% rate of false negatives[179]. Diagnosis and staging are completed with multiparametric MRI, a technique showing a 89% sensitivity with a 73% specificity[180,181].

The approach to PC depends on the stage of the disease. For localized cancers curative treatment can be delayed, if the patient is willing to undergo watchful waiting and active surveillance[182]. The gold standard for prostate cancer treatment is surgery or radiotherapy. Surgery consists in radical prostatectomy. Radiotherapy can be performed with external beams or brachytherapy. Both surgery and radiotherapy can be associated to androgen deprivation therapy (ADT)[177]. Currently, ADT is the first line treatment in case of metastatic disease[179]. However, some metastatic cancers are ADT-resistant. In these cases, chemotherapy with taxanes (docetaxel, cabazitaxel) or mitoxantrone or estramustine can be applied[183]. The use of the immune checkpoints inhibitors is currently under evaluation in ADT-resistant PC, with disappointing preliminary results[184-186]. However, the use of pembrolizumab in PD-L1 positive metastatic ADT-resistant prostatic cancers has showed promising results in many studies[187-189].

Treatment outcome and adverse effects do not differ in PLWH compared to general population[177]. Further studies are needed to understand the effectiveness of immune checkpoint inhibitors in PC.

Colorectal Cancer

Colorectal Cancer (CRC) is the third cancer per mortality rate in the general population[96]. Reports are discordant about whether PLWH have an increased risk for CRC than HIV-negative individuals[89]. However, most PLWH are diagnosed for CRC in a more advanced stage, at a younger age and with more aggressive forms of cancer, leading to a poorer prognosis[190].

Risk factors for the development of CRC can be divided in modifiable and non-modifiable. Among the modifiable risk factors we have obesity, poor physical activity, alcohol use, smoking, high intake of red meat and decreased intake of vegetable and fruit[64,68,191-198]. Among the non-modifiable risk factors there are a positive personal or familiar history of adenoma, familiar history of CRC, hereditary polyposis, and inflammatory bowel diseases[176,197,199-201].

Several studies have investigated the existence of HIV-related risk factors but have been inconclusive. However, CD4+ T-cell count (current or at nadir), HIV-RNA viral load (current or at nadir), and HPV infection seem to be associated with carcinogenesis[202].

Different pathogenetic mechanisms have been identified for CRC. Chromosomal instability is the most frequent cause of cancer onset in individuals not affected by predisposing syndromes[169,203-205]. It accounts for 65-70% of sporadic cancers and it often leads to a dysregulation of mitotic checkpoints, such as *hRod*, *hZwilch*, *hZwl10*[206]. Less frequently, the cause is the mutational activation of the *kRAS*, an oncogene, and the inactivation of *tp53*, a tumor suppressor gene[169,203-205]. Only a minority of the CRCs is linked to hereditary syndromes, such as Lynch syndrome, familiar adenomatous polyposis, APCI 1307K, Peutz-Jehgers syndrome, MYH associated polyposis, juvenile polyposis, and hereditary polyposis. These syndromes cumulatively accounts for 4-6% of all CRCs. Most commonly, cases of CRCs in a syndrome are linked to a mutation in one of the DNA mismatch repair genes (MLH1, MSH2, MSH6, PMS2, EPCAM)[70,207].

A possible downregulation of miRNAs, and especially of miR32, miR34a, miR143, miR153, miR153, miR27a, miR218, miR520, is currently under study for a possible cause-effect with CRC[208-217].

As it happens for other cancers, CRC presents with non-specific symptoms, such as fatigue, anemia and weight loss[70]. The Italian guidelines for the diagnosis and management of HIV-1 infection currently recommend screening PLWH for CRC every year with fecal occult blood test (FOBT). The same criteria apply to the general population[119]. Several studies demonstrate that a periodical screening with FOBT significantly reduce CRC-related mortality rate[191,218,219]. However, Half et al[220] demonstrate that FOBT on three consecutive samples has a rate of false negatives higher than 50%. Therefore, FOBT should be handled carefully, especially in high-risk patients[221].

If positive, FOBT should be followed with rectal sigmoidoscopy and/or colonoscopy. Rectal sigmoidoscopy and colonoscopy should be repeated every five and ten years, respectively[19].

Colonoscopy represent the gold standard for CRC diagnosis, with a high sensitivity which permits to identify cancer, pre-malignant adenomas and differentiate from other symptomatic colon disorders[70,222-224]. In the event that the colonoscopy is incomplete, unfeasible or refused by the patient, computed tomographic colonography (CTC) is a valid option. CTC is a minimally invasive, patient-friendly, safe technique. Different studies have shown similar diagnostic performances for the detection of CRC and large polyps to colonoscopy. However, its role as screening tool is still controversial[225].

The staging of CRC should be performed with thoraco-abdominopelvic CT scan and liver MRI. Moreover, RAS status, BRAF V600E status, micro-satellite instability (MSI), and dihydropyrimidine dehydrogenase (DPD) enzyme activity should be evaluated before starting the treatment[226]. In fact, RAS expression level is a predictor of EGFR inhibitors resistance, both BRAF V600E and MSI are risk factors for a poor prognosis and DPD deficiency can contraindicate the use of fluoropyrimidine[226].

Surgery is the treatment of choice in CRC, and different techniques are applied in different stages of the cancer[70]. Laparoscopic approach is limited to stages with the lowest risk of spreading, while a laparotomic approach is preferred when the disease is more extended[227]. Moreover, a surgical treatment is reserved to those patients whose benefit is higher than the risk, because of anesthesia and resection[226].

There is still no accepted neoadjuvant treatment for CRC, and the debate is still open on the effectiveness of pre-operative radiotherapy, especially in patients with cancers invading the peri-mucosal fat[228]. Adjuvant CT is offered to patients with CRC, to reduce the risk of recurrences[229]. Wang et al[230] evaluated the effectiveness of different combinations of CT and EGFR inhibitors. They demonstrated that CT + cetuximab or panitumumab is effective in increasing the survival of RAS wild-type left-sided tumors, while CT + bevacizumab is more effective in right-sided tumors[230]. Differently from lung, breast, and prostate cancers, anti-PD1 pembrolizumab and nivolumab does not improve the overall survival in patients affected by CRC. However, in cases of MSI-high metastatic CRC refractory to fluoropyrimidine, oxaliplatin, and iridotecan-based chemotherapy, targeting PD-1 seems to have a real clinical benefit[231]. Also, anti-PD-L1 and anti-CTLA4, such as atezolizumab and ipilimumab, have shown clinical benefit in MSI-high metastatic CRC[231]. Further studies are needed to achieve an improvement of the overall survival in CRC, which is currently 20% at 5 years[231].

Most of the drugs used for CRC cause a deep decrease in CD4+ T-cell count. Therefore, particular attention is needed in PLWH[232].

Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and the sixth most common cancer in the world[87]. The majority of the cases are related to Hepatitis C Virus (HCV) or Hepatitis B Virus (HBV) infections. Due to the comparable geographical spread of HCV and HBV infections and HIV infection, HCC has become a burden for PLWH ever since the introduction of cART[233-240]. HCC has a particular geographical distribution. In fact, HCC represent a public health problem especially in Asian countries. The second place for prevalence of HCC is occupied by African countries[241,242].

HCC is the best studied NADC, with its six-fold higher risk of developing the cancer in PLWH than the general population[239]. Risk factors for HCC are represented by chronic HBV- and HCV-related hepatitis, HIV infection, alcohol abuse, smoking, and diabetes. Other, less frequent, risk factors, are high testosterone levels, *Aspergillus spp* aflatoxin, metabolic, and genetic diseases (i.e., hemochromatosis, Wilson's diseases, α-1 antitrypsin deficiency, glycogen storage diseases, porphyria)[242,243].

Italian guidelines for the diagnosis and management of HIV-1 infection suggest to screen PLWH every 6-12 months if co-infected with HCV or HBV and suffering from liver cirrhosis[119]. The same screening is suggested if HBV-DNA is detected in plasma. Screening is performed through a hepatic US and α-fetoprotein (AFP) dosage[19].

Prevention of HBV-related and HCV-related HCC can be achieved by treating the hepatotropic infections. According to the European Association for the Study of the Liver (EASL), PLWH co-infected with HCV and/or HBV should be treated accordingly to their conditions[244,245]. Since 2017, treatment for HCV is available to all the people who are infected, independently from the stage of the disease. Therefore, for HIV/HCV co-infection, similar to general population, the suggestion is to treat the infection as soon as pos-

sible, paying attention to drug-drug interactions with cART[245]. Treating HCV infection with direct acting antiviral (DAA) drugs permits to achieve a cure. Therefore, the infection cannot cause damage to the liver anymore[245].

This is not the reality of HBV. Despite the active research, an eradicating treatment for HBV infection is still missing. EASL guidelines for the treatment of HBV infection suggest that PLWH co-infected with HBV should be treated with a tenofovir disoproxil fumarate (TDF)-based or tenofovir alafenamide fumarate (TAF)-based regimen[244].

However, prevention sometimes fails, or the liver damage is not virus-related, and cancer occurs[64].

Hepatic nodules (HNs) can be detected by US, contrast-enhanced CT scan or MRI[246,247]. US are useful for screening but burdened by several limitations. First of all, with regards to smaller HNs, US cannot differentiate between benign and malign lesions. Moreover, it is an operator-dependent and patient-dependent technique[248,249]. Contrast-enhanced CT scans are usually used to confirm a diagnosis of HCC after a nodule detection by US, because of their high specificity but low sensitivity[243,250,251]. MRI has both high sensitivity and high specificity, but its high costs prevent its application in screening[243,252-254].

Several biomarkers are used for diagnostic and prognostic evaluation. The most useful are AFP, lecithin bound AFP to total AFP ratio (AFP-L3), and des-gamma-carboxy prothrombin (DCP). However, despite their high sensitivity, these markers lack specificity[255]. Therefore, the interest during the last years has been focused on finding a more specific prognostic marker. LncRNA and miRNA related to HCC and its staging were identified. Especially, a cluster of three lncRNAs (LINC00152, RP11-160H22.5 and XLOC014172) and miR-454 raised the interest for being highly predictive for HCC[256-259].

The choice of the best treatment depends on the stage of the disease[64]. Similar to what happens for other cancers, PLWH are often diagnosed with HCC in an advanced stage[243]. Therefore, the therapeutic options are limited. Surgical treatment depends on the stage of the disease. Makuuchi's criteria are the most widespread to determine if the liver functional reserve is sufficient to survive the surgery[260]. Trans-arterial chemoembolization (TACE) is offered to patients with preserved liver functions and absence of metastasis[261]. Portal vein embolization (PE), on the other hand, is the most spread intervention in patients suffering from chronic hepatitis, with a proven efficacy on survival[262]. Surgical resection is the treatment of choice in solitary tumors without vascular invasion or distant metastasis[243]. Liver transplantation offer the best survival rates for HCC. Milan's criteria for eligibility for transplantation in PLWH do not differ from those applied to the general population[263].

Currently, the only medical treatment for advanced HCC with a proven efficacy on survival is sorafenib, a tyrosine-kinase inhibitor[264,265]. The interest about this area is definitely high, with Ras/Raf/MEK/ERK (MAPK), Wnt/catenin and Phospho-inositol-3-kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR) pathways being the most studied targets[261]. Clinical trials led to the approval of regorafenib and lenvatinib in 2017 and 2018, respectively[264]. Both regorafenib and lenvatinib are oral kinase inhibitors. Cabozantinib, another oral kinase inhibitor, and ramucirumab, an intravenous VEGFR-2 inhibitor, are currently under study[264]. Immune checkpoints inhibitor application in HCC has been studied, with contrasting reports. Nivolumab and pembrolizumab showed a 17-20% rate of response in phase I/II studies and are currently in phase III studies[264-266]. However, Wong et al[267] recently showed that immune checkpoint inhibitors can be responsible for hyper progressive disease in HCC.

More studies are thus necessary to establish the efficacy of these drugs in HCC.

Hodgkin's Lymphoma

Hodgkin's Lymphoma (HL) is a lymphoid malignancy. HL has a very low incidence rate in general population (0.01%). However, PLWH have an increased risk for all B-cell lymphoproliferative disorders, and HL in particular[268]. It has been demonstrated that HL has a 13-fold higher incidence in PLWH than in general population[269-272]. Moreover, HL is the most common NADC[273].

Median age at diagnosis is around 30 years, and the highest incidence is around 7 years and a half after the patients are diagnosed with HIV infection[78]. Mortality rate is in steady decrease[78].

HIV infection leads to a chronic activation of B-lymphocytes, due both to a direct activation of cells bearing CD40L and HIV proteins[268]. HL affects PLWH when their CD4+ T-lymphocyte counts are higher[273]. The exact mechanism is not known, but there are different theories. First of all, the increasing number of CD4+ T-lymphocytes stimulates the activation of all B-lympho-

cytes, and tumoral B-lymphocytes (Hodgkin's Reed-Sternberg cells, HRS) in particular[274,275]. A second theory is the exact opposite. The presence of HRS stimulates the activation of CD4+ T-lymphocytes with inflammatory signals. Therefore, the increase in CD4+ T-lymphocytes is caused by the presence of the cancer[273-275]. The third theory suggests that there is a higher risk for other AIDS-related diseases in PLWH with a low CD4+ T-cell count, thus creating a "competition" with HL[273-275].

HL is associated with EBV infection. This association is especially important in PLWH. As a matter of fact, only around 30% of the cases of HL in HIV negative individuals are associated with EBV[276,277]. Chronic B-lymphocytes activation due to HIV infection, together with EBV co-infection, leads to immortalization of the B-cells, especially in presence of an immune system dysregulation[268].

Two histological types of HL are currently known: classic Hodgkin's Lymphoma (CHL) and nodular sclerosis (NSHL). NSHL has a more benign course than CHL. However, despite decreasing mortality, PLWH are affected by less favorable histological types: mixed cellularity (MC) and lymphocyte depleted (LD) HL[78]. Both of them are rich in HRS. Moreover, PLWH are affected by a higher prevalence of B-symptoms, such as fever, night sweats, and/or weight loss > 10% than normal body weight[275], than the general population.

Currently, screening for HL is not possible. Patients presenting with B-symptoms and swollen lymph nodes in the neck, armpits and/or groin should at least undergo a chest and abdomen CT scan if no other diagnosis is possible. CT scan with iodinated contrast is also used for staging[278-282].

Bone marrow (BM) biopsy is also needed to define the stage of the disease. BM invasion, as a matter of fact define stage IV of HL, according to Ann Arbor Classification for HL[283,284].

18-Fluorodeoxyglucose-PET (^{18}FDG-PET) is a nuclear medicine technique that use the accelerated aerobic metabolism of cancer cells to highlight their presence, viability, and spread[285-287]. However, it has been demonstrated that in PLWH the radioactive signal in lymph nodes is higher than in HIV-negative individuals[288]. This increased signal is still lower than that of malignant cells, but the unavailability of quantitative PET methods makes it currently impossible to distinguish metabolically active cells because of infection from those metabolically active because of cancer[288].

Introduction of cART led to an increased survival in PLWH affected by HL[275]. Moreover, the concomitant use of supportive care with granulocyte colony-stimulating factors (G-CSF) and prophylaxis for *Pneumocystis jirovecii* and *Herpes simplex* infections decreased the number and severity of adverse effects[275].

Standard chemotherapy with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) allows complete remission (CR) in 87% of HL in PLWH, with a relapse rate of 11% after 6-8 cycles of therapy[289]. Therefore, the introduction of cART and G-CSF allowed PLWH to reach similar overall survival to the general population.

More intensive chemotherapeutic regimens for HL exist. Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone (BEACOPP), is a regimen well tolerated in HIV-positive individuals with HL, with CR in 100% of the cases and a 2-year overall survival of 83%[290]. Mechlorethamine, doxorubicin, vinblastine, vincristine, bleomycin, etoposide and prednisone (Stanford V) with adjuvant radiotherapy has 81% CR but shows lower 2-year overall survival rates than ABVD and BEACOPP[291].

A regimen with epirubicin, bleomycin, vinorelbine, cyclophosphamide and prednisone (VEBEP), associated with radiotherapy and cART, has a 76% CR rate and 80% overall survival at 30 months[275].

Immunotherapeutic agents have been studied and are currently studied for a possible application in HL. Rituximab, a monoclonal anti-CD20 antibody, was the first agent studied in this setting[292,293]. However, despite the amazing results obtained in other fields, rituximab does not improve the CR or the overall survival in patients affected by CHL[294]. Nonetheless, rituximab is effective in NSHL, although this type of HL is extremely rare in PLWH[295-298].

Brentuximab vedotin, an antibody-drug conjugate, targets CD30. This antigen is specifically expressed by CHL cells[299,300]. Its use has been studied in combination with ABVD, showing pulmonary toxicity. It is currently under study in combination with AVD, a bleomycin-free ABVD[301,302].

Nivolumab and pembrolizumab, immune checkpoint inhibitors targeting PD-1, have been approved for use in CHL. Sintilimab and tislelizumab, other anti-PD1 developed in China, are still under observation, with apparently good results on both CR and overall survival at early timepoints. If the results will be confirmed, these drugs will represent other two weapons against CHL[303].

Immune checkpoint inhibitors have not been studied in PLWH with CHL. Therefore, their use in this setting should be evaluated on a case-by-case basis.

Anal Cancer

Anal cancer (AC) is a squamous epithelium carcinoma, localized in the anus. AC is rare in HIV-negative individuals, with a 2 per 100,000 people prevalence[304]. However, in PLWH, and especially males who have sex with males (MSM), AC has a prevalence of 135 per 100,000 people[72].

AC is related to Human Papilloma Virus (HPV) infection, especially with high-risk (HR) HPV serotypes 16 and 18. HR-HPV infect the squamous epithelium of the anus, leading to a neoplastic transformation when the infection is not cleared[73,96,227,305-311].

PLWH are burdened by a higher incidence of HR-HPV incidence, and the immune dysregulation caused by the HIV infection is correlated to a higher rate of persistence of HPV infection. Moreover, PLWH are more often infected by multiple strains than the general population[309]. Tumorigenesis is often correlated to mutagenesis of tumor suppressor genes, such as p53, deleted in colorectal carcinoma (DCC), and adenomatous polyposis coli (APC) genes[70,312,313].

Given the association with HPV, recent studies have focused on finding a relationship between vaccination against HPV and AC incidence[314].

AC can be diagnosed at different stages, defined similarly to cervical cancer stages. Anal intraepithelial neoplasia (AIN) grade 1 (AIN-1) is a low-grade squamous intraepithelial lesion, while AIN-2/3 are high-grade squamous intraepithelial lesions. AIN-1 can spontaneously regress, while AIN-2/3 are malignant neoplasms[229,315,316].

The Italian Guidelines for the Diagnosis and Management of HIV-1 Infection[119] suggest to screen MSM PLWH once a year with an anal Papanicolau (PAP) smear test and to perform high-resolution anoscopy with acetic acid test if the PAP smear test results abnormal. The same screening should be performed in women with an abnormal cervical PAP test[19]. Screening for AC is not currently recommended in the general population[304,308,317-319].

If both the PAP smear test and the high-resolution anoscopy with acetic acid test result abnormal, a biopsy of the suspected zone should be performed for diagnosis[318,320-323]. MRI is the gold-standard radio-diagnostic test not only to define the metastatic spread of the disease, but also because the intrinsic high contrast and anatomic resolution of pelvic MRI[126,324]. To assess regional or distant metastatic involvement, 18F-FDG PET/CT has been shown to be ideal[325].

Treatment of AC can be divided in topical, systemic and surgical. Topical treatment is performed by direct application of therapeutic agents such as 5-fluorouracil and trichloroacetic acid, or by electrocautery[326,327]. However, topical treatment can be only applied in the case of small lesions. Systemic treatment of AC is needed when the cancer has already spread. Different regimen can be used. Combinations of cisplatin or carboplatin with 5-fluorouracil are associated with CR in 34% of patients with an advanced AC[328]. Paclitaxel, alone or in combination with carboplatin, is a successful alternative[329].

AC is characterized by a high expression of EGFR, therefore it has always been considered an ideal target for EGFR-inhibitors, such as cetuximab and panitumumab. However, the knowledge on EGFR-inhibitors in advanced AC is episodical and limited to case reports or small case series. Therefore, it is difficult to determine their real effectiveness in the setting of advanced AC[328].

Recently, the effectiveness of pembrolizumab and nivolumab, anti-PD-1, was assessed also in AC[330]. These two drugs showed good results as monotherapy in a phase Ib and phase II study, respectively, raising hopes for their possible future use[330].

Surgery is effective as local therapy, when the lesion is small, and the cancer has not spread. However, in some cases, a surgical approach can be used in cancers that have spread above the anus reaching the rectum. Surgery is associated with significant morbidity and a high rate of recurrence[74,331-334].

Further studies are needed to find if an alternative medical approach is possible for PLWH, since this is the population most burdened by AC.

Conclusions

Cancer has always been an important cause of death in PLWH, becoming the first one after the introduction of cART. Furthermore, after the introduction of cART we assisted to a decrease in frequency of ADCs and an increase in frequency of NADCs.

NADCs are especially frequent in PLWH in a good immune-virologic status, with high CD4+ T-lymphocytes and undetectable viremia. Therefore, it is particularly important for cancer screening

schedules to be followed attentively. The knowledge of the right schedule for each patient and of their risk is essential to promptly diagnose cancer in an early stage, as cancer onset happens around 10 years earlier in PLWH compared to general population. As a matter of fact, too often PLWH are still diagnosed to be affected by late-stage cancers, leading to a worse prognosis even in patients who are well controlled for the HIV infection.

Moreover, too often PLWH are still kept out of clinical trials and use of new molecules, which have less adverse effects and are safer for immunocompromised patients than the molecules used in the past. In conclusion, due to the fact that NADCs represent the most frequent cause of death in PLWH, that their onset is in younger patients who are in a good viro-immunologic status, and that the prognosis in these patients is worse than that of the general population, we think that clinical trials should include PLWH and that new schedules for cancer screening should be proposed.

Conflict of Interests

The authors declare they do not have any conflict of interest.

References

1) Barré-Sinoussi F, Ross AL, Delfraissy J-F. Past, present and future: 30 years of HIV research. Nat Rev Clin Oncol 2013; 11: 877-883.
2) 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: 5868-5879.
3) D'Andrea F, Pellicanò GF, Venanzi Rullo E, D'Aleo F, Facciolà A, Micali C, Coco M, Visalli G, Picerno I, Condorelli F, Pinzone MR, Cacopardo B, Nunnari G, Ceccarelli M. Cervical cancer in women living with HIV: a review of the literature. World Cancer Res J 2019; 6: e1224.
4) La Ferla L, Pinzone MR, Nunnari G, Martellotta F, Lleshi A, Tirelli U, De Paoli P, Berretta M, Cacopardo B. Kaposi' s sarcoma in HIV-positive patients: the state of art in the HAART-era. Eur Rev Med Pharmacol Sci 2013; 17: 2354-2365.
5) Simonelli C, Tedeschi R, Gloghini A, Talamini R, Bortolin MT, Berretta M, Spina M, Morassut S, Vaccher E, De Paoli P, Carbone A, Tirelli U. Plasma HHV-8 viral load in HHV-8-related lymphoproliferative disorders associated with HIV infection. J Med Virol 2009; 81: 888-896.
6) Colafigli M, Bonadies A, Ferraresi V, Tonachella R, Cristaudo A, Latini A. Kaposi Sarcoma in HIV-infected patients: an infectious-dermatological outpatient service experience. Infect Dis Trop Med 2017; 3: e410.
7) Franceschi S, Maso LD, Rickenbach M, Polesel J, Hirschel B, Cavassini M, Bordoni A, Elzi L, Ess S, Jundt G, Mueller N, Clifford GM. Kaposi sarcoma incidence in the Swiss HIV Cohort Study before and after highly active antiretroviral therapy. Br J Cancer 2008; 99: 800-804.
8) Sung JCY, Louie SG, Park SY. Kaposi's sarcoma: advances in tumor biology and pharmacotherapy. Pharmacotherapy 1997; 17: 670-683.
9) De Paoli P, Carbone A. Kaposi's Sarcoma Herpesvirus: twenty years after its discovery. Eur Rev Med Pharmacol Sci 2016; 20: 1288-1294.
10) Dittmer DP, Damania B. Kaposi sarcoma associated herpesvirus pathogenesis (KSHV)--an update. Curr Opin Virol 2013; 3: 238-244.
11) Robbins HA, Strickler HD, Massad LS, Pierce CB, Darragh TM, Minkoff H, Keller MJ, Fischl M, Palefsky J, Flowers L, Rahangdale L, Milam J, Shrestha S, Colie C, DĐSouza G. Cervical cancer screening intervals and management for women living with HIV: a risk benchmarking approach. AIDS 2017; 31: 1035-1044.
12) Madeddu G, Mameli G, Capobianco G, Babudieri S, Maida I, Bagella P, Rocca G, Cherchi PL, Sechi LA, Zanetti S, Nunnari G, Dessole S, Mura MS. HPV infection in HIV-positive females: the need for cervical cancer screening including HPV-DNA detection despite successful HAART. Eur Rev Med Pharmacol Sci 2014; 18: 1277-1285.
13) Heard I. Prevention of cervical cancer in women with HIV. Curr Opin HIV AIDS 2009; 4: 68-73.
14) Arts EJ, Hazuda DJ. HIV-1 antiretroviral drug therapy. Cold Spring Harb Perspect Med 2012; 2: a007161
15) Pinzone MR, Ceccarelli M, Venanzi Rullo E, Maresca M, Bruno R, Condorelli F, Di Rosa M, Madeddu G, Focà E, Calcagno A, Celesia BM, Cacopardo B, Nunnari G, Pellicanò GF. (2019) Circulating angiopoietin-like protein 2 levels are associated with decreased renal function in HIV+ subjects on cART: a potential marker of kidney disease. Biomed Rep 2019; 10: 140-144.
16) Ceccarelli M, Venanzi Rullo E, Vaccaro M, Facciolà A, D'Aleo F, Paolucci IA, Cannavò SP, Cacopardo B, Pinzone MR, Pellicanò GF, Condorelli F, Nunnari G, Guarneri C. HIV-associated psoriasis: epidemiology, pathogenesis, and management. Dermatol Ther 2019; 75: e12806
17) Venanzi Rullo E, Ceccarelli M, Condorelli F, Facciolà A, Visalli G, D'Aleo F, Paolucci I, Cacopardo B, Pinzone MR, Di Rosa M, Nunnari G, Pellicanò GF. Investigational drugs in HIV: Pros and cons of entry and fusion inhibitors (review). Mol Med Rep 2019; 19: 1987-1995.
18) D'Andrea F, Ceccarelli M, Venanzi Rullo E, Facciolà A, D'Aleo F, Cacopardo B, Iacobello C, Costa A, Altavilla G, Pellicanò GF, Nunnari G. Cancer screening in HIV-infected patients: early diagnosis in a high-risk population. World Cancer Res J 2018; 5: e1130.
19) Ceccarelli M, Condorelli F, Venanzi Rullo E, Pellicanò GF. Editorial - Improving access and adherence to screening tests for cancers: a new, though old, challenge in the HIV epidemics. World Cancer Res J 2018; 5: e1030.

20) Ceccarelli M, Venanzi Rullo E, Facciolà A, Madeddu G, Cacopardo B, Taibi R, D'Aleo F, Pinzone MR, Picerno I, Di Rosa M, Visalli G, Condorelli F, Nunnari G, Pellicanò GF. Head and neck squamous cell carcinoma and its correlation with human papillomavirus in people living with HIV: a systematic review. Oncotarget 2018; 9: 17171-17180.
21) Visalli G, Facciolà A, D'Aleo F, Pinzone MR, Condorelli F, Picerno I, Nunnari G, Pellicanò GF, Ceccarelli M, Venanzi Rullo E. HPV and urinary bladder carcinoma: a review of the literature. World Cancer Res J 2018; 5: e1038.
22) Pinzone MR, Cacopardo B, Condorelli F, Rosa MD, Nunnari G. Sirtuin-1 and HIV-1: an overview. Curr Drug Targets 2013; 14: 648-652.
23) Celesia BM, Nigro L, Pinzone MR, Coco C, La Rosa R, Bisicchia F, Mavilla S, Gussio M, Pellicanò G, Milioni V, Palermo F, Russo R, Mughini MT, Martellotta F, Taibi R, Cacopardo B, Nunnari G. High prevalence of undiagnosed anxiety symptoms among HIV-positive individuals on cART: a cross-sectional study. Eur Rev Med Pharmacol Sci 2013; 17: 2040-2046.
24) Celesia BM, Castronuovo D, Pinzone MR, Bellissimo F, Mughini MT, Lupo G, Scarpino MR, Gussio M, Palermo F, Cosentino S, Cacopardo B, Nunnari G. Late presentation of HIV infection: predictors of delayed diagnosis and survival in Eastern Sicily. Eur Rev Med Pharmacol Sci 2013; 17: 2218-2224.
25) Motta D, Bonito A, Casari S, Brianese N, Hamad El I, Pezzoli MC, Forleo MA, Ferraresi A, Scalzini A, Roldan EQ, Torti C, Castelli F, Focà E. Effectiveness of routine lumbar puncture in patients with HIV-associated dementia (HAD) receiving suppressive antiretroviral treatment. Infect Dis Trop Med 2015; 1: e41.
26) Fontana del Vecchio R, Pinzone MR, Celesia BM, Palermo F, Cacopardo B, Nunnari G. ZDV/3TC to ABC/3TC switch and bone marrow toxicity in the post-HAART era. Infect Dis Trop Med 2015; 1: e39.
27) Bagella P, Madeddu G, Are R, Peruzzu F, Bagella G, Calia GM, Mura MS. Drug-resistant disseminated polyclonal Mycobacterium avium complex in a patient with AIDS: a case report and review of the literature. Infect Dis Trop Med 2015; 1: e37.
28) Zanet E, Berretta M, Martellotta F, Cacopardo B, Fisichella R, Tavio M, Berretta S, Tirelli U. Anal cancer: focus on HIV-positive patients in the HAART era. Curr HIV Res 2011; 9: 70-81
29) Nunnari G, Malaguarnera L, Lazzara F, Cambria D, Distefano G, Longo A, Palumbo M, Fagone P, Di Rosa M. Th17 common genes in CD4 T-cells of HIV-1-infected naïve patients and elite controllers. Infect Dis Trop Med 2015; 1: e121.
30) 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.
31) Pinzone MR, Gussio M, Bellissimo F, Coco C, Bisicchia F, Pellicanò GF, Palermo F, Mughini MT, Cacopardo B, Nunnari G, Celesia BM. Self-reported sexual dysfunction in HIV-positive subjects: a cross-sectional study. Infect Dis Trop Med 2015; 1: e104.
32) Scibilia E, Maresca M, Cacopardo B, Pinzone MR. Acute transverse myelitis in a patient with AIDS. Infect Dis Trop Med 2015; 1: e94.
33) Calcagno A, Rostagno R, Arnaudo I, Zanusso G, Bonora S, Lucchini A, Maiello A, Dal Conte I, Meoli I, Ferrari S, Monaco S, Rizzuto N, Di Perri G. CSF 14-3-3 protein and its ζ isoform are prognostic markers in HIV positive patients with CNS disease. Infect Dis Trop Med 2015; 1: e92.
34) Tavio M, Grossi P, Baccarani U, Scudeller L, Pea F, Berretta M, Adani G, Vivarelli M, Riva A, Tirelli U, Bresadola V, Viale P, Risaliti A. HIV-infected patients and liver transplantation: who, when and why. Curr HIV Res 2011; 9: 120-127.
35) Pinzone MR, Nunnari G. Prevalence of comorbidities in a cohort of women living with HIV. Infect Dis Trop Med 2015; 1: e165.
36) Di Benedetto F, De Ruvo N, Berretta M, Masetti M, Montalti R, Di Sandro S, Quintini C, Codeluppi M, Tirelli U, Gerunda GE. Don't deny liver transplantation to HIV patients with hepatocellular carcinoma in the highly active antiretroviral therapy era. J Clin Oncol 2006; 24: e26-e27
37) Pinzone MR, Berretta M, Cacopardo B, Nunnari G. Epstein-Barr virus- and Kaposi sarcoma-associated herpesvirus-related malignancies in the setting of human immunodeficiency virus infection. Semin Oncol 2015; 42: 258-271
38) Lai V, Zizi B, Vadini F, Calia GM, Bagella P, Fiore V, Peruzzu F, Caruana G, Babudieri S, Mura MS, Madeddu G. Fib-4 values and neurocognitive function in hiv-infected patients without hepatic coinfections. Infect Dis Trop Med 2016; 2: e293.
39) Di Rosa M, Fagone P, Pinzone MR, Nunnari G. Cathepsin A levels in CD4+ T cells from HIV-positive patients. Infect Dis Trop Med 2016; 2: e245.
40) Nozza S, Ripa M, Chiappetta S, Tambussi G. Primary HIV infection: are current data definitive to treat all patients? Infect Dis Trop Med 2016; 2: e243.
41) Pinzone MR, VanBelzen J, Weissman S, Bertuccio MP, Cannon L, Venanzi Rullo E, Migueles S, Jones RB, Mota T, Joseph SB, Groen K, Pasternak A, Hwang WT, Sherman B, Vourekas A, Nunnari G, O'Doherty U. Longitudinal HIV sequencing reveals reservoir expression leading to decay, which is obscured by clonal expansion. Nat Commun 2019; 10: 728.
42) Di Biagio A, De Hoffer L, Prinapori R, Cheli M, Bonora S, Taramasso L, Balbi M, D'Avolio A, Viscoli C. Bosentan and Fosamprenavir: an effective and safe combination in an HIV-infected patient with pulmonary arterial hypertension. Infect Dis Trop Med 2016; 2: e231.
43) Postorino MC, Luciani F, Pellicanò GF, Mangano C, Carpentieri MS, Scerbo P, Priamo A, Berardelli G, Marino R, Vallone A, Carioti J, Serrao N, Pisani A, Costa C, Cesario F, Terremoto A, Foti G, Cosco L, Corigliano D, Mazzitelli M, Strazzulla A, Nunnari G, Torti C. Number and characteristics of new HIV diagnoses in the Calabria Region and in one nearby centre in Messina: a resurgent or still hidden epidemic in Southern Italy? Infect Dis Trop Med 2016; 2: e297.

44) Nicolè S, Lanzafame M, Lattuada E, Mazzi R, Rigo F, Cucchetto G, Gibellini D, Concia E, Vento S. Dolutegravir montherapy in HIV-infected naïve patients with <100,000 copies/ML HIV RNA load, an update of a little cohort in Verona. Infect Dis Trop Med 2016; 2: e295.
45) Lai V, Fiore V, Calia GM, Lovigu C, Zizzi B, Budroni C, Peruzzu F, Bagella P, Mura MS. Relationship between neurocognitive impairment and cardiovascular risk in an HIV-infected patient: a case report. Infect Dis Trop Med 2015; 1: e182.
46) Spina M, Berretta M, Tirelli U. Hodgkin's disease in HIV. Hematol Oncol Clin N Am 2003; 17: 843-858
47) Taramasso L, Del Puente F, Riccardi N, Di Biagio A. PrEP in Europe--two different studies, one incontrovertible result. Infect Dis Trop Med 2016; 2: e339.
48) Montrucchio C, Biagini R, Alcantarini C, Calcagno A, Barco A, Ferrara M, Milesi M, Costa C, Trentalange A, Trunfio M, Tettoni MC, Grosso Marra W, D'Ascenzo F, Ballocca F, Lonni E, Gili S, Vai D, Imperiale D, Gaita F, Bonora S, Di Perri G. Cardiovascular risk and neurocognitive deficits in HIV-positive individuals. Infect Dis Trop Med 2017; 3: e370.
49) Celesia BM, Sofia SA, Rapisarda L, Maresca M, Vinci L. Anxiety, depression and sleep disturbances in HIV+ patients chronically treated with an efavirenz-based regimen. Infect Dis Trop Med 2017; 3: e394.
50) Ceccarelli G, Vassalini P, Corano Scheri G, Cavallari EN, Bianchi L, Di Girolamo G, Fratino M, Vullo V, D'Ettorre G. Improvement of neuropsychological performances and reduction of immune-activation markers after probiotic supplementation and change of life-style in an HIV positive male: targeting the microbiota to act on gut-brain axis. Infect Dis Trop Med 2017; 3: e404.
51) Nunnari G, Coco C, Pinzone MR, Pavone P, Berretta M, Di Rosa M, Schnell M, Calabrese G, Cacopardo B. The role of micronutrients in the diet of HIV-1-infected individuals. Front Biosci E 2012; 4: 2442-2456
52) Zanet E, Berretta M, Benedetto FD, Talamini R, Ballarin R, Nunnari G, Berretta S, Ridolfo A, Lleshi A, Zanghì A, Cappellani A, Tirelli U. Pancreatic cancer in HIV-positive patients. A case-control study. Pancreas 2012; 41: 1331-1335.
53) Milesi M, Murgia S, Rollino C, Calcagno A, Sciascia S, Alcantarini C, Bonora S, Roccatello D. Acute rhabdomyolisis following a single dose of methylprednisolone in an HIV-positive subject receiving ritonavir-boosted antiretroviral therapy. Infect Dis Trop Med 2017; 3: e423.
54) Caruana G, Bagella P, Larivière E, De Vito A, Fiore V, Madeddu G. Dolutegravir-based combination antiretroviral therapy and central nervous system tolerability: a review of the literature. Infect Dis Trop Med 2018; 4: e447.
55) Ronzoni N, Bagella P, Atzeni F, Borghero G, Porcu F, Sannia A, Fiore V, Babudieri S. Rapid development of unmasking disseminated tuberculosis-related immune reconstitution inflammatory syndrome in a young HIV-infected patient after starting combination antiretroviral therapy. Infect Dis Trop Med 2018; 4: e445.
56) Doglietto F, Castelli F. AIDS-associated central nervous system lymphoma: the great mime. A case report and literature review. Infect Dis Trop Med 2018; 4: e472.
57) Taramasso L, Ricci E, De Socio GV, Madeddu G, Menzaghi B, Orofino G, Carenzi L, Parruti G, Bonfanti P, Di Biagio A, on behalf of CISAI Study Group. Aspartate-to-platelet ratio index evaluation in a cohort of HIV/HCV infected patients treated with raltegravir. Infect Dis Trop Med 2018; 4: e490.
58) Ceratti U, Valobra T, Gandino A. An unusual case of distributive shock. Infect Dis Trop Med 2019; 5: e527.
59) Atteritano M, Mirarchi L, Venanzi Rullo E, Santoro D, Iaria C, Catalano A, Lasco A, Arcoraci V, Lo Gullo A, Bitto A, Squadrito F, Cascio A. Vitamin D status and the relationship with bone fragility fractures in HIV-infected patients: a case control study. Int J Mol Sci 2018; 19: 119. doi:10.3390/ijms19010119.
60) Bearz A, Vaccher E, Martellotta F, Spina M, Talamini R, Lleshi A, Cacopardo B, Nunnari G, Berretta M, Tirelli U. Lung cancer in HIV positive patients: the GICAT experience. Eur Rev Med Pharmacol Sci 2014; 18: 500-508.
61) D'Aleo F, Cama BAV, Paolucci IA, Venanzi Rullo E, Condorelli F, Facciolà A, Di Francia R, Savasta A, Pinzone MR, Picerno I, Visalli G, Nunnari G, Pellicanò GF, Ceccarelli M. New and old assumptions on lung cancer in people living with HIV. World Cancer Res J 2018; 5: e1036.
62) Sigel K, Makinson A, Thaler J. Lung cancer in persons with HIV. Curr Opin HIV AIDS 2017; 12: 31-38.
63) Berretta M, Garlassi E, Cacopardo B, Cappellani A, Guaraldi G, Cocchi S, de Paoli P, Lleshi A, Izzi I, Torresin A, Di Gangi P, Pietrangelo A, Ferrari M, Bearz A, Berretta S, Nasti G, Di Benedetto F, Balestreri L, Tirelli U, Ventura P. Hepatocellular carcinoma in HIV-infected patients: check early, treat hard. Oncologist 2011; 16: 1258-1269.
64) 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.
65) Dika IE, Harding JJ, Abou-Alfa GK. Hepatocellular carcinoma in patients with HIV. Curr Opin HIV AIDS 2017; 12: 20-25.
66) Coghill AE, Engels EA, Schymura MJ, Mahale P, Shiels MS. Risk of breast, prostate, and colorectal cancer diagnoses among HIV-infected individuals in the United States. J Natl Cancer Inst 2018; 52: 203.
67) D'Andrea F, Ceccarelli M, Facciolà A, Nunnari G, Pellicanò GF, Venanzi Rullo E. Breast cancer in women living with HIV. Eur Rev Med Pharmacol Sci 2019; 23: 1158-1164.
68) Mitsuyasu RT. Non-AIDS-defining cancers. Top Antivir Med 2014; 22: 660-665.
69) Wasserberg N, Nunoo-Mensah JW, Gonzalez-Ruiz C, Beart RW, Kaiser AM. Colorectal cancer in HIV-infected patients: a case control study. Int J Colorectal Dis 2007; 22: 1217-1221.

70) D'Aleo F, Venanzi Rullo E, Ceccarelli M, Facciolà A, Condorelli F, Pinzone MR, Cacopardo B, Di Rosa M, Nunnari G, Pellicanò GF. HIV and colorectal cancer. New insights and review of the literature. World Cancer Res J 2018; 5: e1122.
71) Kan M, Wong PHP, Press N, Wiseman SM. Colorectal and anal cancer in HIV/AIDS patients: a comprehensive review. Expert Rev Anticancer Ther 2014; 14: 395-405.
72) D'Aleo F, Ceccarelli M, Venanzi Rullo E, Facciolà A, D'Andrea F, Micali C, Coco M, Pinzone MR, Focà E, Condorelli F, Picerno I, Visalli G, Cacopardo B, Nunnari G, Pellicanò GF. Anal cancer in people living with HIV: the importance of the screening and of early diagnosis. World Cancer Res J 2019; 6: e1319.
73) Gandra S, Azar A, Wessolossky M (2015) Anal high-risk human papillomavirus infection and high-grade anal intraepithelial neoplasia detected in women and heterosexual men infected with human immunodeficiency virus. HIV AIDS (Auckl) 2015; 7: 29-34.
74) Kreuter A, Brockmeyer NH, Altmeyer P, Wieland U. Anal intraepithelial neoplasia in HIV infection. J Dtsch Dermatol Ges 2008; 6: 925-934.
75) Facciolà A, Ceccarelli M, Venanzi Rullo E, D'Aleo F, Condorelli F, Visalli G, Cacopardo B, Pinzone MR, Di Rosa M, Nunnari G, Pellicanò GF. Prostate cancer in HIV-positive patients--a review of the literature. World Cancer Res J 2018; 5: e1136.
76) Mahale P, Engels EA, Coghill AE, Kahn AR, Shiels MS. Cancer risk in older people living with human immunodeficiency virus infection in the United States. Clin Infect Dis 2018; 67: 50-57.
77) Shiels MS, Pfeiffer RM, Gail MH, Hall HI, Li J, Chaturvedi AK, Bhatia K, Uldrick TS, Yarchoan R, Goedert JJ, Engels EA. Cancer burden in the HIV-infected population in the United States. J Natl Cancer Inst 2011; 103: 753-762.
78) Facciolà A, Venanzi Rullo E, Ceccarelli M, D'Aleo F, D'Andrea F, Visalli G, Pinzone MR, Picerno I, Cacopardo B, Condorelli F, Madeddu G, Nunnari G, Pellicanò GF. Hodgkin's lymphoma in people living with HIV: epidemiology and clinical management. World Cancer Res J 2019; 6: e1295.
79) Spina M, Carbone A, Gloghini A, Serraino D, Berretta M, Tirelli U. Hodgkin's disease in patients with HIV infection. Adv Hematol 2011; 2011: 402682.
80) Hessol NA, Katz MH, Liu JY, Buchbinder SP, Rubino CJ, Holmberg SD. Increased incidence of Hodgkin disease in homosexual men with HIV-infection. Ann Intern Med 1992; 117: 309-311.
81) Deeks SG. HIV infection, inflammation, immunosenescence, and aging. Annu Rev Med 2011; 62: 141-155.
82) Wada NI, Jacobson LP, Margolick JB, Breen EC, Macatangay B, Penugonda S, Martinez-Maza O, Bream JH. The effect of HAART-induced HIV suppression on circulating markers of inflammation and immune activation. AIDS 2015; 29: 463-471.
83) Angelidou K, Hunt PW, Landay AL, Wilson CC, Rodriguez B, Deeks SG, Bosch RJ, Lederman MM. Changes in inflammation but not in T cell activation precede non-AIDS-defining events in a case-control study of patients on long-term antiretroviral therapy. J Infect Dis 2018; 218: 239-248.
84) Richert Q, Trajtman A, Arroyave L, Toews J, Becker M, Kasper K, McLaren P, Rueda Z, Keynan Y. Systemic inflammation before and after antiretroviral therapy initiation as a predictor of immune response among HIV-infected individuals in Manitoba. Cytokine 2017; 91: 74-81.
85) Tenorio AR, Zheng Y, Bosch RJ, Krishnan S, Rodriguez B, Hunt PW, Plants J, Seth A, Wilson CC, Deeks SG, Lederman MM, Landay AL. Soluble markers of inflammation and coagulation but not T-cell activation predict non-AIDS-defining morbid events during suppressive antiretroviral treatment. J Infect Dis 2014; 210: 1248-1259.
86) Morlat P, Roussillon C, Henard S, Salmon D, Bonnet F, Cacoub P, Georget A, Aouba A, Rosenthal E, May T, Chauveau M, Diallo B, Costagliola D, Chene G, Grp AEM2S. Causes of death among HIV-infected patients in France in 2010 (national survey): trends since 2000. AIDS 2014; 28: 1181-1191.
87) Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68: 394-424.
88) Winstone TA, Man SFP, Hull M, Montaner JS, Sin DD. Epidemic of lung cancer in patients with HIV infection. Chest 2013; 143: 305-314.
89) Engels EA, Yanik EL, Wheeler W, Gill MJ, Shiels MS, Dubrow R, Althoff KN, Silverberg MJ, Brooks JT, Kitahata MM, Goedert JJ, Grover S, Mayor AM, Moore RD, Park LS, Rachlis A, Sigel K, Sterling TR, Thorne JE, Pfeiffer RM; North American AIDS Cohort Collaboration on Research and Design of the International Epidemiologic Databases to Evaluate AIDS. cancer-attributable mortality among people with treated human immunodeficiency virus infection in North America. Clin Infect Dis 2017; 65: 636-643.
90) Engels EA, Biggar RJ, Hall HI, Cross H, Crutchfield A, Finch JL, Grigg R, Hylton T, Pawlish KS, McNeel TS, Goedert JJ. Cancer risk in people infected with human immunodeficiency virus in the United States. Int J Cancer 2008; 123: 187-194.
91) Chaturvedi AK, Pfeiffer RM, Chang L, Goedert JJ, Biggar RJ, Engels EA. Elevated risk of lung cancer among people with AIDS. AIDS 2007; 21: 207-213.
92) Vaccher E, Serraino D, Carbone A, de Paoli P. The evolving scenario of non-AIDS-defining cancers: challenges and opportunities of care. Oncologist 2014; 19: 860-867.
93) Shiels MS, Engels EA (2017) Evolving epidemiology of HIV-associated malignancies. Curr Opin HIV AIDS 2017; 12: 6-11.
94) Hall EC, Pfeiffer RM, Segev DL, Engels EA. Cumulative incidence of cancer after solid organ transplantation. Cancer 2013; 119: 2300-2308.
95) Coghill AE, Shiels MS, Suneja G, Engels EA. Elevated cancer-specific mortality among HIV-infected patients in the United States. J Clin Oncol 2015; 33: 2376-2383.
96) Pinzone MR, Fiorica F, Di Rosa M, Malaguarnera G, Malaguarnera L, Cacopardo B, Zanghi G, Nunnari G. Non-AIDS-defining cancers among HIV-infected people. Eur Rev Med Pharmacol Sci 2012; 16: 1377-1388.

97) Burkhalter JE, Springer CM, Chhabra R, Ostroff JS, Rapkin BD (2005) Tobacco use and readiness to quit smoking in low-income HIV-infected persons. Nicotine Tob Res 2005; 7: 511-522.
98) Centers for Disease Control and Prevention (CDC). Vital signs: current cigarette smoking among adults aged >or=18 years --- United States, 2009. MMWR Morb Mortal Wkly Rep 2010; 59: 1135-1140.
99) Silverberg MJ, Lau B, Achenbach CJ, Jing Y, Althoff KN, D'Souza G, Engels EA, Hessol NA, Brooks JT, Burchell AN, Gill MJ, Goedert JJ, Hogg R, Horberg MA, Kirk GD, Kitahata MM, Korthuis PT, Mathews WC, Mayor A, Modur SP, Napravnik S, Novak RM, Patel P, Rachlis AR, Sterling TR, Willig JH, Justice AC, Moore RD, Dubrow R; North American AIDS Cohort Collaboration on Research and Design of the International Epidemiologic Databases to Evaluate AIDS. cumulative incidence of cancer among persons with HIV in North America: a cohort study. Ann Intern Med 2015; 163: 507-518.
100) Park LS, Hernandez-Ramirez RU, Silverberg MJ, Crothers K, Dubrow R. Prevalence of non-HIV cancer risk factors in persons living with HIV/AIDS: a meta-analysis. AIDS 2016; 30: 273-291.
101) Crothers K, Goulet JL, Rodriguez-Barradas MC, Gibert CL, Oursler KAK, Goetz MB, Crystal S, Leaf DA, Butt AA, Braithwaite RS, Peck R, Justice AC. Impact of cigarette smoking on mortality in HIV-positive and HIV-negative veterans. AIDS Educ Prev 2009; 21: 40-53.
102) Diaz PT, King MA, Pacht ER, Wewers MD, Gadek JE, Nagaraja HN, Drake J, Clanton TL. Increased susceptibility to pulmonary emphysema among HIV-seropositive smokers. Ann Intern Med 2000; 132: 369-372.
103) Twigg HL, Soliman DM, Day RB, Knox KS, Anderson RJ, Wilkes DS, Schnizlein-Bick CT. Lymphocytic alveolitis, bronchoalveolar lavage viral load, and outcome in human immunodeficiency virus infection. Am J Respir Crit Care Med 1999; 159: 1439-1444.
104) Morris AM, Huang L, Bacchetti P, Turner J, Hopewell PC, Wallace JM, Kvale PA, Rosen MJ, Glassroth J, Reichman LB, Stansell JD. Permanent declines in pulmonary function following pneumonia in human immunodeficiency virus-infected persons. The pulmonary complications of HIV Infection Study Group. Am J Respir Crit Care Med 2000; 162: 612-616.
105) Morris A, Alexander T, Radhi S, Lucht L, Sciurba FC, Kolls JK, Srivastava R, Steele C, Norris KA. Airway obstruction is increased in pneumocystis-colonized human immunodeficiency virus-infected outpatients. J Clin Microbiol 2009; 47: 3773-3776.
106) Christensen PJ, Preston AM, Ling T, Du M, Fields WB, Curtis JL, Beck JM. Pneumocystis murina infection and cigarette smoke exposure interact to cause increased organism burden, development of airspace enlargement, and pulmonary inflammation in mice. Infect Immun 2008; 76: 3481-3490.
107) Hleyhel M, Bouvier AM, Belot A, Tattevin P, Pacanowski J, Genet P, De Castro N, Berger J-L, Dupont C, Lavole A, Pradier C, Salmon D, Simon A, Martinez V, Spano J-P, Costagliola D, Grabar S, Cancer Risk Group of the French Hospital Database on HIV (FHDH-ANRS CO4). Risk of non-AIDS-defining cancers among HIV-1-infected individuals in France between 1997 and 2009: results from a French cohort. AIDS 2014; 28: 2109-2118.
108) Borges AH, Silverberg MJ, Wentworth D, Grulich AE, Fätkenheuer G, Mitsuyasu R, Tambussi G, Sabin CA, Neaton JD, Lundgren JD, INSIGHT SMART, ESPRIT, SILCAAT Study Groups. Predicting risk of cancer during HIV infection: the role of inflammatory and coagulation biomarkers. AIDS 2013; 27: 1433-1441.
109) Cribbs SK, Lennox J, Caliendo AM, Brown LA, Guidot DM. Healthy HIV-1-infected individuals on highly active antiretroviral therapy harbor HIV-1 in their alveolar macrophages. AIDS Res Hum Retroviruses 2015; 31: 64-70.
110) Sigel K, Wisnivesky J, Gordon K, Dubrow R, Justice A, Brown ST, Goulet J, Butt AA, Crystal S, Rimland D, Rodriguez-Barradas M, Gibert C, Park LS, Crothers K. HIV as an independent risk factor for incident lung cancer. AIDS 2012; 26: 1017-1025.
111) Altavilla G, Caputo A, Lanfredi M, Piola C, Barbanti-Brodano G, Corallini A. Enhancement of chemical hepatocarcinogenesis by the HIV-1 tat gene. Am J Pathol 2000; 157: 1081-1089.
112) Giagulli C, Marsico S, Magiera AK, Bruno R, Caccuri F, Barone I, Fiorentini S, Andò S, Caruso A. Opposite effects of HIV-1 p17 variants on PTEN activation and cell growth in B cells. PLoS One 2011; 6: e17831.
113) Makinson A, Tenon J-C, Eymard-Duvernay S, Pujol J-L, Allavena C, Cuzin L, Poizot-Martin I, la Tribonnière de X, Cabié A, Pugliese P, Reynes J, Le Moing V. Human immunodeficiency virus infection and non-small cell lung cancer: survival and toxicity of antineoplastic chemotherapy in a cohort study. JTO Acquisition 2011; 6: 1022-1029.
114) Hoffmann C, Kohrs F, Sabranski M, Wolf E, Jaeger H, Wyen C, Siehl J, Baumgarten A, Hensel M, Jessen A, Schaaf B, Vogel M, Bogner J, Horst H-A, Stephan C. HIV-associated lung cancer: Survival in an unselected cohort. Scand J Infect Dis 2013; 45: 766-772.
115) Pakkala S, Chen Z, Rimland D, Owonikoko TK, Gunthel C, Brandes JR, Saba NR, Shin DM, Curran WJ Jr., Khuri FR, Ramalingam SS. Human immunodeficiency virus-associated lung cancer in the era of highly active antiretroviral therapy. Cancer 2011; 118: 164-172.
116) Lavolé A, Wislez M, Antoine M, Mayaud C, Milleron B, Cadranel J. Lung cancer, a new challenge in the HIV-infected population. Lung Cancer 2006; 51: 1-11.
117) Matsumoto Y, Ohara S, Furukawa R, Usui K. The prognosis of small cell lung cancer in patients with pulmonary fibrosis. Anticancer Res 2017; 37: 5791-5795.
118) Leduc C, Antoni D, Charloux A, Falcoz P-E, Quoix E. Comorbidities in the management of patients with lung cancer. Eur Respir J 2017; 49: 1601721.
119) Società Italiana di Malattie Infettive e Tropicali. Linee Guida Italiane sull'utilizzo della Terapia Antiretrovirale e la gestione diagnostico-clinica delle persone con infezione da HIV-1. http://www.salute.gov.it/imgs/C_17_pubblicazioni_2696_allegato.pdf Accessed 14 July 2019

120) Kong CY, Sigel K, Criss SD, Sheehan DF, Triplette M, Silverberg MJ, Henschke CI, Justice A, Braithwaite RS, Wisnivesky J, Crothers K. Benefits and harms of lung cancer screening in HIV-infected individuals with CD4+ cell count at least 500 cells/µl. AIDS 2018; 32: 1333-1342.
121) Aboulafia DM. Cancer screening in women living with HIV infection. Womens Health (Lond) 2017; 13: 68-79.
122) Mena A, Meijide H, Marcos PJ. Lung cancer in HIV-infected patients. AIDS Rev 2016; 18: 138-144.
123) Collini P, Morris A. Maintaining lung health with longstanding HIV. Curr Opin Infect Dis 2016; 29: 31-38.
124) European AIDS Clinical Society. EACS GUIDELINES - Version 9.0 October 2017. http://www.eacsociety.org/files/guidelines_9.0-english.pdf Accessed 14 July 2019
125) Ciello AD, Franchi P, Contegiacomo A, Cicchetti G, Bonomo L, Larici AR. Missed lung cancer: when, where, and why? Diagn Interv Radiol 2017; 23: 118-126.
126) Wang S, Li M, Chen H, Li J, Zeng Q. FDG PET/CT in hepatoid adenocarcinoma of the lung. Clin Nucl Med 2016; 41: e340-e341.
127) Counts SJ, Kim AW. Diagnostic imaging and newer modalities for thoracic diseases PET/computed tomographic imaging and endobronchial ultrasound for staging and its implication for lung cancer. PET Clin 2018; 13: 113-126.
128) Delbeke D, Martin WH, Sandler MP, Chapman WC, Wright JK, Pinson CW. Evaluation of benign vs malignant hepatic lesions with positron emission tomography. Arch Surg 1998; 133: 510-515.
129) Shi W, Zhou L, Peng X, Ren H, Wang Q, Shan F, Zhang Z, Liu L, Shi Y. HIV-infected patients with opportunistic pulmonary infections misdiagnosed as lung cancers: the clinicoradiologic features and initial application of CT radiomics. J Thorac Dis 2019; 11: 2274-2286. doi:10.21037/jtd.2019.06.22.
130) Dennie C, Thornhill R, Souza CA, Odonkor C, Pantarotto JR, MacRae R, Cook G. Quantitative texture analysis on pre-treatment computed tomography predicts local recurrence in stage I non-small cell lung cancer following stereotactic radiation therapy. Quant Imaging Med Surg 2017; 7: 614-622.
131) Lackey A, Donington JS. Surgical management of lung cancer. Semin Intervent Radiol 2013; 30: 133-140.
132) Passlick B. Initial surgical staging of lung cancer. Lung Cancer 2003; 42: S21-S25.
133) Viti A, Terzi A, Bogina G, Bertolaccini L. Lymph-nodal micrometastases in NSCLC: where do we stand? Lung Cancer Manag 2016; 5: 53-55.
134) Carretta A. Clinical value of nodal micrometastases in patients with non-small cell lung cancer: time for reconsideration? J Thorac Dis 2016; 8: E1755-E1758.
135) Coello MC, Luketich JD, Litle VR, Godfrey TE. Prognostic significance of micrometastasis in non-small-cell lung cancer. Clin Lung Cancer 2011; 5:214-225.
136) Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg 1995; 60: 615-623.
137) Tieu BH, Sanborn RE, Thomas CR. Neoadjuvant therapy for resectable non-small cell lung cancer with mediastinal lymph node involvement. Thorac Surg Clin 2008; 18: 403-415.
138) Tazza M, Metro G. Adjuvant treatment of non-small cell lung cancer: focus on targeted therapy. J Thorac Dis 2017; 9: 4064-4069.
139) Kazaz SN, Oztop I. Treatment after first-generation epidermal growth factor receptor tyrosine kinase inhibitor resistance in non-small-cell lung cancer. Turk Thorac J 2017; 18: 66-71.
140) Ghafoor Q, Baijal S, Taniere P, O'Sullivan B, Evans M, Middleton G. Epidermal Growth Factor Receptor (EGFR) kinase inhibitors and non-small cell lung cancer (NSCLC) - Advances in Molecular diagnostic techniques to facilitate targeted therapy. Pathol Oncol Res 2017; 24: 1-9.
141) Vavala T. Role of afatinib in the treatment of advanced lung squamous cell carcinoma. Clin Pharmacol 2017; 9: 147-157.
142) Mezouita L, Planchard D. The role of brigatinib in crizotinib-resistant non-small cell lung cancer. Cancer Manag Res 2018; 10: 123-130.
143) Bunn PA, Schenk E, Pacheco J, Dimou A. New developments in neoadjuvant therapy for lung cancer. Oncology 2019; 33: 101-106, 109.
144) Obeid JM, Erdag G, Smolkin ME, Deacon DH, Patterson JW, Chen L, Bullock TN, Slingluff CL. PD-L1, PD-L2 and PD-1 expression in metastatic melanoma: correlation with tumor-infiltrating immune cells and clinical outcome. Oncoimmunology 2016; 5: e1235107.
145) Fromentin R, Bakeman W, Lawani MB, Khoury G, Hartogensis W, DaFonseca S, Killian M, Epling L, Hoh R, Sinclair E, Hecht FM, Bacchetti P, Deeks SG, Lewin SR, Sékaly R-P, Chomont N. CD4+ T cells expressing PD-1, TIGIT and LAG-3 contribute to HIV persistence during ART. PLoS Pathog 2016; 12: e1005761.
146) Ben-Baruch A. Host microenvironment in breast cancer development. Inflammatory cells, cytokines and chemokines in breast cancer progression: reciprocal tumor-microenvironment interactions. Breast Cancer Res 2003; 5: 31-36.
147) Mañes S, Mira E, Colomer R, Montero S, Real LM, Gómez-Moutón C, Jiménez-Baranda S, Garzón A, Lacalle RA, Harshman K, Ruíz A, Martinéz-A C. CCR5 expression influences the progression of human breast cancer in a p53-dependent manner. J Exp Med 2003; 198: 1381-1389.
148) Endo M, Inatsu A, Hashimoto K, Takamune N, Shoji S, Misumi S. Human immunodeficiency virus-induced apoptosis of human breast cancer cells via CXCR4 is mediated by the viral envelope protein but does not require CD4. Curr HIV Res 2008; 6: 34-42.
149) Nix LM, Tien PC. Metabolic syndrome, diabetes, and cardiovascular risk in HIV. Curr HIV/AIDS Rep 2014; 11: 271-278.
150) Cançado Porto-Mascarenhas E, Assad DX, Chardin H, Gozal D, De Luca Canto G, Acevedo AC, da Silva Guerra EN. Salivary biomarkers in the diagnosis of breast cancer: A review. Crit Rev Oncol Hematol 2017; 110: 62-73.
151) Metcalfe S, Wheeler TK, Picken S, Negus S, Milner AJ. P53 autoantibodies in 1006 patients followed up for breast cancer. Breast Cancer Res 2000; 2: 438-443.

152) Jung JH, Park HY, Lee YH. Clinical value of CEA, CA15-3 and TPS in breast cancer. J Korean Breast Cancer Soc 2001; 4: 136-143.
153) Nelson HD, O'Meara ES, Kerlikowske K, Balch S, Miglioretti D. Factors associated with rates of false-positive and false-negative results from digital mammography screening: an analysis of registry data. Ann Intern Med 2016; 164: 226-223.
154) Elmore JG, Jackson SL, Abraham L, Miglioretti DL, Carney PA, Geller BM, Yankaskas BC, Kerlikowske K, Onega T, Rosenberg RD, Sickles EA, Buist DSM. Variability in interpretive performance at screening mammography and radiologists' characteristics associated with accuracy. Radiology 2009; 253: 641-651.
155) Marino MA, Riedl CC, Bernathova M, Bernhart C, Baltzer PAT, Helbich TH, Pinker K. Imaging phenotypes in women at high risk for breast cancer on mammography, ultrasound, and magnetic resonance imaging using the fifth edition of the breast imaging reporting and data system. Eur J Radiol 2018; 106: 150-159.
156) Hooley RJ, Scoutt LM, Philpotts LE. Breast ultrasonography: state of the art. Radiology 2013; 268: 642-659.
157) Schenberg T, Mitchell G, Taylor D, Saunders C. MRI screening for breast cancer in women at high risk; is the Australian breast MRI screening access program addressing the needs of women at high risk of breast cancer? J Med Radiat Sci 2015; 62: 212-225.
158) Jafari SH, Saadatpour Z, Salmaninejad A, Momeni F, Mokhtari M, Nahand JS, Rahmati M, Mirzaei H, Kianmehr M. Breast cancer diagnosis: imaging techniques and biochemical markers. J Cell Physiol 2018; 233: 5200-5213.
159) Wellings E, Vassiliades L, Abdalla R. Breast cancer screening for high-risk patients of different ages and risk--Which modality is most effective? Cureus 2016; 8: e945.
160) Leithner D, Moy L, Morris EA, Marino MA, Helbich TH, Pinker K. Abbreviated MRI of the breast: does it provide value? J Magn Reson Imaging 2019; 49: e85-e100.
161) Marino MA, Helbich T, Baltzer P, Pinker-Domenig K. Multiparametric MRI of the breast: a review. J Magn Reson Imaging 2018; 47: 301-315.
162) Marino MA, Gucalp A, Leithner D, Keating D, Avendano D, Bernard-Davila B, Morris EA, Pinker K, Jochelson MS. Mammographic screening in male patients at high risk for breast cancer: is it worth it? Breast Cancer Res Treat 2019; 18: e997.
163) Bénard F, Turcotte E. Imaging in breast cancer: single-photon computed tomography and positron-emission tomography. Breast Cancer Res 2005; 7: 153-162.
164) Marino MA, Helbich TH, Blandino A, Pinker K. The role of positron emission tomography in breast cancer: a short review. Memo 2015; 8: 130-135.
165) Tang Y, Wang Y, Kiani MF, Wang B. Classification, treatment strategy, and associated drug resistance in breast cancer. Clin Breast Cancer 2016; 16: 335-343.
166) McCann KE, Hurvitz SA, McAndrew N. advances in targeted therapies for triple-negative breast cancer. Drugs 2019; 79: 1217-1230.
167) Wang MY, Huang HY, Kuo YL, Lo C, Sun HY, Lyu YJ, Cheng BR, Li JN, Chen PS. TARBP2-enhanced resistance during tamoxifen treatment in breast cancer. Cancers 2019; 11: 210-218.
168) Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2014; 136: E359-E386.
169) Robbins HA, Shiels MS, Pfeiffer RM, Engels EA. Epidemiologic contributions to recent cancer trends among HIV-infected people in the United States. AIDS 2014; 28: 881-890.
170) Shiels MS, Pfeiffer RM, Engels EA. Age at cancer diagnosis among persons with AIDS in the United States. Ann Intern Med 2010; 153: 452-460.
171) Marcus JL, Chao CR, Leyden WA, Xu L, Klein DB, Horberg MA, Towner WJ, Quesenberry CP, Abrams DI, Van Den Eeden SK, Silverberg MJ. Prostate cancer incidence and prostate-specific antigen testing among HIV-positive and HIV-negative men. J Acquir Immune Defic Syndr 2014; 66: 495-502.
172) Coghill AE, Han X, Suneja G, Lin CC, Jemal A, Shiels MS. Advanced stage at diagnosis and elevated mortality among US patients with cancer infected with HIV in the National Cancer Data Base. Cancer 2019; 285: 1736-1739.
173) Silberstein J, Downs T, Lakin C, Kane CJ. HIV and prostate cancer: a systematic review of the literature. Prostate Cancer Prostatic Dis 2009; 12: 6-12.
174) Crum-Cianflone N, Hullsiek KH, Satter E, Marconi V, Weintrob A, Ganesan A, Barthel RV, Fraser S, Agan BK. Cutaneous malignancies among HIV-infected persons. Arch Intern Med 2009; 169: 1130-1138.
175) Godbole SV, Nandy K, Gauniyal M, Nalawade P, Sane S, Koyande S, Toyama J, Hegde A, Virgo P, Bhatia K, Paranjape RS, Risbud AR, Mbulaiteye SM, Mitsuyasu RT. HIV and cancer registry linkage identifies a substantial burden of cancers in persons with HIV in India. Medicine 2016; 95: e4850.
176) Yanik EL, Katki HA, Engels EA. Cancer risk among the HIV-infected elderly in the United States. AIDS 2016; 30: 1663-1668.
177) Amarasekera C, Wong V, Yura E, Manjunath A, Schaeffer E, Kundu S. Prostate cancer in sexual minorities and the influence of HIV status. Nat Rev Urol 2019; 16: 404-421.
178) Faraji SN, Nejatollahi F, Tamaddon AM, Mohammadi M, Aminsharifi AR. Generation and characterization of a specific single-chain antibody against DSPP as a prostate cancer biomarker involvement of bioinformatics-based design of novel epitopes. Int Immunopharmacol 2019; 69: 217-224.
179) Litwin MS, Tan H-J. The diagnosis and treatment of prostate cancer: a review. JAMA 2017; 317: 2532-2542.
180) Woo S, Suh CH, Kim SY, Cho JY, Kim SH. Diagnostic performance of prostate imaging reporting and data system version 2 for detection of prostate cancer: a systematic review and diagnostic meta-analysis. Eur Urol 2017; 72: 177-188.
181) Polanec SH, Pinker-Domenig K, Brader P, Georg D, Shariat S, Spick C, Susani M, Helbich TH, Baltzer PA. Multiparametric MRI of the prostate at 3 T: limited value of 3D 1H-MR spectroscopy as a fourth parameter. World J Urol 2016; 34: 649-656.

182) Filson CP, Marks LS, Litwin MS. Expectant management for men with early stage prostate cancer. CA Cancer J Clin 2015; 65: 265-282.
183) Fujiwara M, Akamatsu S, Sumiyoshi T, Segawa T, Mizuno K, Yoshino T, Goto T, Sawada A, Saito R, Kobayashi T, Yamasaki T, Inoue T, Ogawa O. Efficacy and safety of carboplatin plus paclitaxel as the first-, second-, and third-line chemotherapy in men with castration-resistant prostate cancer. Clin Genitourin Cancer 2019. In press. doi:10.1016/j.clgc.2019.04.017.
184) Topalian SL, Hodi FS, Brahmer JR, Gettinger SN, Smith DC, McDermott DF, Powderly JD, Carvajal RD, Sosman JA, Atkins MB, Leming PD, Spigel DR, Antonia SJ, Horn L, Drake CG, Pardoll DM, Chen L, Sharfman WH, Anders RA, Taube JM, McMiller TL, Xu H, Korman AJ, Jure-Kunkel M, Agrawal S, McDonald D, Kollia GD, Gupta A, Wigginton JM, Sznol M. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. N Engl J Med 2012; 366: 2443-2454.
185) Brahmer JR, Drake CG, Wollner I, Powderly JD, Picus J, Sharfman WH, Stankevich E, Pons A, Salay TM, McMiller TL, Gilson MM, Wang C, Selby M, Taube JM, Anders R, Chen L, Korman AJ, Pardoll DM, Lowy I, Topalian SL. Phase I study of single-agent anti-programmed death-1 (MDX-1106) in refractory solid tumors: safety, clinical activity, pharmacodynamics, and immunologic correlates. J Clin Oncol 2010; 28: 3167- 3175.
186) Taube JM, Klein A, Brahmer JR, Xu H, Pan X, Kim JH, Chen L, Pardoll DM, Topalian SL, Anders RA. Association of PD-1, PD-1 ligands, and other features of the tumor immune microenvironment with response to anti-PD-1 therapy. Clin Cancer Res 2014; 20: 5064-5074.
187) Hansen AR, Massard C, Ott PA, Haas NB, Lopez JS, Ejadi S, Wallmark JM, Keam B, Delord JP, Aggarwal R, Gould M, Yang P, Keefe SM, Piha-Paul SA. Pembrolizumab for advanced prostate adenocarcinoma: findings of the KEYNOTE-028 study. Ann Oncol 2018; 29: 1807-1813.
188) Lu X, Horner JW, Paul E, Shang X, Troncoso P, Deng P, Jiang S, Chang Q, Spring DJ, Sharma P, Zebala JA, Maeda DY, Wang YA, DePinho RA. Effective combinatorial immunotherapy for castration-resistant prostate cancer. Nature 2017; 543: 728-732.
189) Isaacsson Velho P, Antonarakis ES. PD-1/PD-L1 pathway inhibitors in advanced prostate cancer. Expert Rev Clin Pharmacol 2018; 11: 475-486.
190) Berretta M, Cappellani A, Di Benedetto F, Lleshi A, Talamini R, Canzonieri V, Zanet E, Bearz A, Nasti G, Lacchin T, Berretta S, Fisichella R, Balestreri L, Torresin A, Izzi I, Ortolani P, Tirelli U. Clinical presentation and outcome of colorectal cancer in HIV-positive patients: a clinical case-control study. Onkologie 2009; 32: 319-324.
191) Kumar A, Shah N, Modi Y, Shaaban HS, DePasquale J, DeBari VA, Yerrabothala S, Maroules M, Guron GK. Characteristics of colorectal cancer in the human immunodeficiency virus-infected African American population. Med Oncol 2012; 29: 1773-1779.
192) Patel P, Hanson DL, Sullivan PS, Novak RM, Moorman AC, Tong TC, Holmberg SD, Brooks JT. Incidence of types of cancer among HIV-infected persons compared with the general population in the United States, 1992-2003. Ann Intern Med 2008; 148: 728-73.
193) Patel N, Naidoo P, Mosiane P, Jann-Kruger C. HIV/AIDS-associated Kaposi's sarcoma of the gastrointestinal tract: A pictorial spectrum. S Afr Med J 2016; 106: 986-987.
194) Rahmanian S, Wewers ME, Koletar S, Reynolds N, Ferketich A, Diaz P. Cigarette smoking in the HIV-infected population. Proc Am Thor Soc 2011; 8: 313-319.
195) Botteri E, Iodice S, Bagnardi V, Raimondi S, Lowenfels AB, Maisonneuve P. Smoking and colorectal cancer: a meta-analysis. JAMA 2008; 300: 2765-2778.
196) Berretta M, Lleshi A, Cappellani A, Bearz A, Spina M, Talamini R, Cacopardo B, Nunnari G, Montesarchio V, Izzi I, Lanzafame M, Nasti G, Basile F, Berretta S, Fisichella R, Schiantarelli CC, Garlassi E, Ridolfo A, Guella L, Tirelli U. Oxaliplatin based chemotherapy and concomitant highly active antiretroviral therapy in the treatment of 24 patients with colorectal cancer and HIV infection. Curr HIV Res 2010; 8: 218-222
197) Vazquez-Castellanos JF, Serrano-Villar S, Latorre A, Artacho A, Ferrus ML, Madrid N, Vallejo A, Sainz T, Martinez-Botas J, Ferrando-Martinez S, Vera M, Dronda F, Leal M, Del Romero J, Moreno S, Estrada V, Gosalbes MJ, Moya A. Altered metabolism of gut microbiota contributes to chronic immune activation in HIV-infected individuals. Mucosal Immunol 2015; 8: 760-772.
198) Chander G, Josephs J, Fleishman JA, Korthuis PT, Gaist P, Hellinger J, Gebo K, HIV Research Network. Alcohol use among HIV-infected persons in care: results of a multi-site survey. HIV Med 2008; 9: 196-202.
199) Iqbal S, Browne-McDonald V, Cerulli MA. Recent trends for colorectal cancer screening in HIV-infected patients. Dig Dis Sci 2010; 55: 761-766.
200) Chang VW, Asch DA, Werner RM. Quality of care among obese patients. JAMA 2010; 303: 1274-1281.
201) Bommart S, Cournil A, Eymard-Duvernay S, Raffi F, Bouassida I, Le Moing V, Reynes J, Makinson A, Agence Nationale de Recherche sur le Sida et les Hépatites Virales (ANRS) HIV CHEST Study Team. Smoking-associated morbidities on computed tomography lung cancer screens in HIV-infected smokers. HIV Med 2017; 18: 787-789.
202) 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.
203) Romassi M, Nagle D. Images in HIV/AIDS. The changing face of anal cancer. AIDS Read 2008; 18: 185-187.
204) Bhalla A, Zulfiqar M, Bluth MH. Molecular diagnostics in colorectal carcinoma: advances and applications for 2018. Clin Lab Med 2018; 38: 311-342.

205) Feodorova Y, Tashkova D, Koev I, Todorov A, Kostov G, Simitchiev K, Belovejdov V, Dimov R, Sarafian V. Novel insights into transcriptional dysregulation in colorectal cancer. Neoplasma 2018; 65: 415-424.
206) Gil-Raga M, Jantus-Lewintre E, Gallach S, Giner-Bosch V, Frangi-Caregnato A, Safont-Aguilera MJ, Garde-Noguera J, Zorraquino-Pina E, García-Martínez M, Camps-Herrero C. Molecular subtypes in early colorectal cancer associated with clinical features and patient prognosis. Clin Translat Oncol 2018; 20: 1422-1429.
207) Strafford JC. Genetic testing for lynch syndrome, an inherited cancer of the bowel, endometrium, and ovary. Rev Obstet Gynecol 2012; 5: 42-49.
208) Wang Z, Cummins JM, Shen D, Cahill DP, Jallepalli PV, Wang T-L, Parsons DW, Traverso G, Awad M, Silliman N, Ptak J, Szabo S, Willson JKV, Markowitz SD, Goldberg ML, Karess R, Kinzler KW, Vogelstein B, Velculescu VE, Lengauer C. Three classes of genes mutated in colorectal cancers with chromosomal instability. Cancer Res 2004; 64: 2998-3001.
209) Bedi GC, Westra WH, Farzadegan H, Pitha PM, Sidransky D. Microsatellite instability in primary neoplasms from HIV + patients. Nat Med 1995; 1: 65-68.
210) Feng H, Xu M, Zhang Y, Han B, Wang J, Sun P. Identification of differentially expressed microRNAs involved in the pathogenesis of colorectal cancer. Clin Lab 2018; 64: 797-804.
211) Gao S, Zhao Z-Y, Wu R, Zhang Y, Zhang Z-Y. Prognostic value of microRNAs in colorectal cancer: a meta-analysis. Cancer Manag Res 2018; 10: 907-929.
212) Falzone L, Scola L, Zanghì A, Biondi A, Di Cataldo A, Libra M, Candido S. Integrated analysis of colorectal cancer microRNA datasets: identification of microRNAs associated with tumor development. Aging (Albany NY) 2018; 10: 1000-1014.
213) Chorti A, Bangeas P, Papavramidis TS, Tsoulfas G. Role of microRNA in the diagnosis and therapy of hepatic metastases from colorectal cancer. Microrna 2018; 07: 1-11.
214) Liu T, Yin L, Yan G, Li C, Wang L. A meta-analysis of microRNA-17 as a potential biomarker in diagnosis of colorectal cancer. Cell Mol Biol 2018; 64: 86-93.
215) Chi Y, Zhou D. MicroRNAs in colorectal carcinoma--from pathogenesis to therapy. J Exp Clin Cancer Res 2016; 35: 43.
216) Jin Y, Cheng H, Cao J, Shen W. MicroRNA 32 promotes cell proliferation, migration, and suppresses apoptosis in colon cancer cells by targeting OTU domain containing 3. J Cell Biochem 2019; 7: 339.
217) Moradi Marjaneh R, Khazaei M, Ferns GA, Avan A, Aghaee-Bakhtiari SH. MicroRNAs as potential therapeutic targets to predict responses to oxaliplatin in colorectal cancer: from basic evidence to therapeutic implication. IUBMB Life 2019. In press. doi:10.1002/iub.2108.
218) Surmann E-M, Voigt AY, Michel S, Bauer K, Reuschenbach M, Ferrone S, Knebel Doeberitz von M, Kloor M. Association of high CD4-positive T cell infiltration with mutations in HLA class II-regulatory genes in microsatellite-unstable colorectal cancer. Cancer Immunol Immunother 2015; 64: 357-366.
219) Goedert JJ, Hosgood HD, Biggar RJ, Strickler HD, Rabkin CS. Screening for cancer in persons living with HIV infection. Trends Cancer 2016; 2: 416-428.
220) Half EE, Mlynarsky L, Naftali T, Benjaminov F, Konikoff FM. False negative fecal occult blood test may be associated with increased mortality from colorectal cancer. Dig Dis Sci 2013; 58: 2639-2645.
221) Kawada T. Fecal occult blood test and colorectal cancer: Validation study with special reference to false-negative patients. Dig Dis Sci 2013; 58: 3057-3058.
222) Bini EJ, Green B, Poles MA. Screening colonoscopy for the detection of neoplastic lesions in asymptomatic HIV-infected subjects. Gut 2009; 58: 1129-1134.
223) Campbell J, Young B. Use of screening colonoscopy in ambulatory HIV-infected patients. J Int Assoc Physicians AIDS Care (Chic) 2008; 7: 286-288.
224) Claridge LC. Barium enema and diagnosis of colorectal cancer. Br Med J 2011; 343: d7704-d7704.
225) Laghi A. CT Colonography: an update on current and future indications. Expert Rev Gastroenterol Hepatol 2016; 10: 785-794.
226) Phelip JM, Tougeron D, Léonard D, Benhaim L, Desolneux G, Dupré A, Michel P, Penna C, Tournigand C, Louvet C, Christou N, Chevallier P, Dohan A, Rousseaux B, Bouché O. Metastatic colorectal cancer (mCRC): French intergroup clinical practice guidelines for diagnosis, treatments and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, SFR). Dig Liver Dis 2019; 51: 1357-1363.
227) Shebl FM, Engels EA, Goedert JJ. Opportunistic intestinal infections and risk of colorectal cancer among people with AIDS. AIDS Res Hum Retroviruses 2012; 28: 994-999.
228) Bujko K, Michalski W. Does Adjuvant chemotherapy after preoperative chemoradiation improve overall survival in patients with rectal cancer? Dis Colon Rectum 2018; 61: e36.
229) Shah N, Schechter S, Garcia-Henriquez N. Adjuvant chemotherapy after preoperative chemoradiation improves survival in patients with locally advanced rectal cancer. Dis Colon Rectum 2018; 61: e35.
230) Wang Z-X, Wu H-X, He M-M, Wang Y-N, Luo H-Y, Ding P-R, Xie D, Chen G, Li Y-H, Wang F, Xu R-H. Chemotherapy with or without anti-EGFR agents in left- and right-sided metastatic colorectal cancer: an updated meta-analysis. J Natl Compr Canc Netw 2019; 17: 805-811.
231) Franke AJ, Skelton WP IV, Starr JS, Parekh H, Lee JJ, Overman MJ, Allegra C, George TJ. Immunotherapy for colorectal cancer: a review of current and novel therapeutic approaches. J Natl Cancer Inst 2019; 111: djz093.
232) Oliver NT, Chiao EY. Malignancies in women with HIV infection. Curr Opin HIV AIDS 2017; 12: 69-76.
233) 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.

234) Berretta M, Zanet E, Di Benedetto F, Simonelli C, Bearz A, Morra A, Bonanno S, Berretta S, Tirelli U. Unusual presentation of metastatic hepatocellular carcinoma in an HIV/HCV coinfected patient: case report and review of the literature. Tumori 2008; 94: 589-591.
235) 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.
236) Berretta S, Fisichella R, Spartà D, Lleshi A, Nasti G. Primary liver cancer: clinical aspects, prognostic factors and predictive response to therapy. World Cancer Res J 2015; 2: e561.
237) Di Benedetto F, Di Sandro S, De Ruvo N, Berretta M, Montalti R, Guerrini GP, Ballarin R, De Blasiis MG, Spiaggiari M, Smerieri N, Iemmolo RM, Guaraldi G, Gerunda GE. Human immunodeficiency virus and liver transplantation: our point of view. Transplant Proc 2008; 40: 1965-1971
238) Fiore V, Vidili G, Bagella P, Lobrano G, Muredda AA, Caruana G, Babudieri S, Madeddu G. Hepatocellular carcinoma development in a patient with HCV infection after eradication with direct-acting antiviral agents. World Cancer Res J 2017; 4: e833.
239) Nunnari G, Berretta M, Pinzone MR, Di Rosa M, Berretta S, Cunsolo G, Malaguarnera M, Cosentino S, De Paoli P, Schnell JM, Cacopardo B. Hepatocellular carcinoma in HIV positive patients. Eur Rev Med Pharmacol Sci 2012; 16: 1257-1270.
240) Canzonieri V, Alessandrini L, Caggiari L, Perin T, Berretta M, Cannizzaro R, De Re V. Hepatocellular carcinoma: an overview of clinico-pathological and molecular perspectives. World Cancer Res J 2015; 2: e485
241) Crissien AM, Frenette C. Current management of hepatocellular carcinoma. Gastroenterol Hepatol 2014; 10: 153-161.
242) Balogh J, Victor D, Asham EH, Burroughs SG, Boktour M, Saharia A, Li X, Ghobrial RM, Monsour HP. Hepatocellular carcinoma: a review. J Hepatocell Carcinoma 2016; 3: 41-53.
243) Bellissimo F, Pinzone MR, Cacopardo B, Nunnari G. Diagnostic and therapeutic management of hepatocellular carcinoma. World J Gastroenterol 2015; 21: 12003-12021.
244) European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol 2017; 67: 370-398.
245) European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C 2018. J Hepatol 2018; 69: 461-511.
246) Marrero JA, Hussain HK, Nghiem HV, Umar R, Fontana RJ, Lok AS. Improving the prediction of hepatocellular carcinoma in cirrhotic patients with an arterially-enhancing liver mass. Liver Transpl 2005; 11: 281-289.
247) Willatt JM, Hussain HK, Adusumilli S, Marrero JA. MR Imaging of hepatocellular carcinoma in the cirrhotic liver: challenges and controversies. Radiology 2008; 247: 311-330.
248) Wu W, Chen M-H, Sun M, Yan K, Yang W, Li J-Y. Contrast-enhanced ultrasound of hepatocarcinogenesis in liver cirrhosis. Chin Med J 2012; 125: 3104-3109.
249) Matsui O, Kadoya M, Kameyama T, Yoshikawa J, Takashima T, Nakanuma Y, Unoura M, Kobayashi K, Izumi R, Ida M. Benign and malignant nodules in cirrhotic livers: distinction based on blood supply. Radiology 1991; 178: 493-497.
250) Kim SH, Choi BI, Lee JY, Kim SJ, So YH, Eun HW, Lee JM, Han JK. Diagnostic accuracy of multi-/single-detector row CT and contrast-enhanced MRI in the detection of hepatocellular carcinomas meeting the milan criteria before liver transplantation. Intervirology 2008; 51: 52-60.
251) Hayashi M, Matsui O, Ueda K, Kawamori Y, Gabata T, Kadoya M. Progression to hypervascular hepatocellular carcinoma: correlation with intranodular blood supply evaluated with CT during intraarterial injection of contrast material. Radiology 2002; 225: 143-149.
252) Ito K. Hepatocellular carcinoma: conventional MRI findings including gadolinium-enhanced dynamic imaging. Eur J Radiol 2006; 58: 186-199.
253) Cadier B, Bulsei J, Nahon P, Seror O, Laurent A, Rosa I, Layese R, Costentin C, Cagnot C, Durand-Zaleski I, Chevreul K. Early detection and curative treatment of hepatocellular carcinoma: A cost-effectiveness analysis in France and in the United States. Hepatology 2017; 65: 1237-1248.
254) Elsayes KM, Narra VR, Yin Y, Mukundan G, Lammle M, Brown JJ. Focal hepatic lesions: diagnostic value of enhancement pattern approach with contrast-enhanced 3D gradient-echo MR imaging. Radiographics 2005; 25: 1299-1320.
255) Hann H-W, Wan S, Myers RE, Hann RS, Xing J, Chen B, Yang H. Comprehensive analysis of common serum liver enzymes as prospective predictors of hepatocellular carcinoma in HBV patients. PLoS One 2012; 7: e47687.
256) Yuan W, Sun Y, Liu L, Zhou B, Wang S, Gu D. Circulating LncRNAs serve as diagnostic markers for hepatocellular carcinoma. Cell Physiol Biochem 2017; 44: 125-132.
257) Schütte K. Current biomarkers for hepatocellular carcinoma: Surveillance, diagnosis and prediction of prognosis. World J Hepatol 2014; 7: 139.
258) Tan Y, Ge G, Pan T, Wen D, Gan J. A pilot study of serum microRNAs panel as potential biomarkers for diagnosis of nonalcoholic fatty liver disease. PLoS One 2014; 9: e105192.
259) Giordano S, Columbano A. MicroRNAs: new tools for diagnosis, prognosis, and therapy in hepatocellular carcinoma? Hepatology 2013; 57: 840-847.
260) Makuuchi M, Kosuge T, Takayama T, Yamazaki S, Kakazu T, Miyagawa S, Kawasaki S. Surgery for small liver cancers. Semin Surg Oncol 1993; 9: 298-304.
261) Rinninella E, Cerrito L, Spinelli I, Cintoni M, Mele MC, Pompili M, Gasbarrini A. Chemotherapy for hepatocellular carcinoma: current evidence and future perspectives. J Clin Transl Hepatol 2017; 5: 235-248.
262) Armengol C, Sarrias MR, Sala M. Hepatocellular carcinoma: present and future. Med Clin 2018; 150: 390-397.

263) Guerrini GP, Berretta M, Tarantino G, Magistri P, Pecchi A, Ballarin R, Di Benedetto F. Multimodal oncological approach in patients affected by recurrent hepatocellular carcinoma after liver transplantation. Eur Rev Med Pharmacol Sci 2017; 21: 3421-3435.
264) Kudo M. Targeted and immune therapies for hepatocellular carcinoma: predictions for 2019 and beyond. World J Gastroenterol 2019; 25: 789-807.
265) Berretta M, Di Benedetto F, Dal Maso L, Cacopardo B, Nasti G, Facchini G, Bearz A, Spina M, Garlassi E, De Re V, Fiorica F, Lleshi A, Tirelli U. Sorafenib for the treatment of unresectable hepatocellular carcinoma in HIV-positive patients. Anti-Cancer Drugs 2013; 24: 212-218.
266) Okusaka T, Ikeda M. Immunotherapy for hepatocellular carcinoma: current status and future perspectives. ESMO Open 2018; 3: e000455.
267) Wong DJ, Lee J, Choo SP, Thng CH, Hennedige T. Hyperprogressive disease in hepatocellular carcinoma with immune checkpoint inhibitor use: a case series. Immunotherapy 2019; 11: 167-175.
268) Lilly AJ, Fedoriw Y. Human immunodeficiency virus-associated lymphoproliferative disorders. Surg Pathol Clin 2019; 12: 771-782.
269) Castel AD, Young H, Akiwumi A-M, Vargas A, Rogers K, West T, Levine PH. Trends in cancer diagnoses and survival among persons with AIDS in a high HIV prevalence urban area. AIDS Care 2015; 27: 860-869.
270) Hernandez-Ramirez RU, Shiels MS, Dubrow R, Engels EA. Cancer risk in HIV-infected people in the USA from 1996 to 2012: a population-based, registry-linkage study. Lancet HIV 2017; 4: e495-e504.
271) Hleyhel M, Belot A, Bouvier AM, Tattevin P, Pacanowski J, Genet P, De Castro N, Berger J-L, Dupont C, Lavole A, Pradier C, Salmon D, Simon A, Martinez V, Spano J-P, Costagliola D, Grabar S, FHDH-ANRS CO4. Trends in survival after cancer diagnosis among HIV-infected individuals between 1992 and 2009. Results from the FHDH-ANRS CO4 cohort. Int J Cancer 2015; 137: 2443-2453.
272) Hodgkin lymphoma in the elderly, pregnant, and HIV-infected. Semin Hematol 2016; 53: 203-208.
273) Naidoo N, Abayomi A, Locketz C, Musaigwa F, Grewal R. Incidence of hodgkin lymphoma in HIV-positive and HIV-negative patients at a tertiary hospital in South Africa (2005-2016) and comparison with other African countries. S Afr Med J 2018; 108: 563-567.
274) Levine AM. Hodgkin lymphoma: to the HAART of the matter. Blood 2006; 108: 3630.
275) Martis N, Mounier N. Hodgkin lymphoma in patients with HIV infection: a review. Curr Hematol Malig Rep 2012; 7: 228-234.
276) Rezk SA, Weiss LM. Epstein-Barr virus-associated lymphoproliferative disorders. Hum Pathol 2007; 38: 1293-1304.
277) Errante D, Gabarre J, Ridolfo AL, Rossi G, Nosari AM, Gisselbrecht C, Kerneis Y, Mazzetti F, Vaccher E, Talamini R, Carbone A, Tirelli U. Hodgkin's disease in 35 patients with HIV infection: an experience with epirubicin, bleomycin, vinblastine and prednisone chemotherapy in combination with antiretroviral therapy and primary use of G-CSF. Ann Oncol 1999; 10: 189-195.
278) Ricke J, Wust P, Wieners G, Beck A, Cho CH, Seidensticker M, Pech M, Werk M, Rosner C, Hanninen EL, Freund T, Felix R. Liver malignancies: CT-guided interstitial brachytherapy in patients with unfavorable lesions for thermal ablation. J Vasc Interv Radiol 2004; 15: 1279-1286.
279) Numata K, Luo W, Morimoto M, Kondo M, Kunishi Y, Sasaki T, Nozaki A, Tanaka K. Contrast enhanced ultrasound of hepatocellular carcinoma. World J Radiol 2010; 2: 68-82.
280) Hutchings M. FDG-PET after two cycles of chemotherapy predicts treatment failure and progression-free survival in Hodgkin lymphoma. Blood 2006; 107: 52-59.
281) Jerusalem G, Beguin Y, Fassotte MF, Najjar F, Paulus P, Rigo P, Fillet G. Whole-body positron emission tomography using 18F-fluorodeoxyglucose for posttreatment evaluation in Hodgkin"s disease and non-Hodgkin"s lymphoma has higher diagnostic and prognostic value than classical computed tomography scan imaging. Blood 1999; 94: 429-433.
282) Tirelli U, Errante D, Dolcetti R, Gloghini A, Serraino D, Vaccher E, Franceschi S, Boiocchi M, Carbone A. Hodgkin's disease and human immunodeficiency virus infection: clinicopathologic and virologic features of 114 patients from the Italian Cooperative Group on AIDS and Tumors. J Clin Oncol 1995; 13: 1758-1767.
283) Carbone A, Gloghini A, Dotti G. EBV-associated lymphoproliferative disorders: classification and treatment. Oncologist 2008; 13: 577-585.
284) Setoguchi S, Solomon DH, Glynn RJ, Cook EF, Levin R, Schneeweiss S. Agreement of diagnosis and its date for hematologic malignancies and solid tumors between medicare claims and cancer registry data. Cancer Causes Control 2007; 18: 561-569.
285) Park J-W, Kim JH, Kim SK, Kang KW, Park KW, Choi J-I, Lee WJ, Kim C-M, Nam BH. A prospective evaluation of 18F-FDG and 11C-acetate PET/CT for detection of primary and metastatic hepatocellular carcinoma. J Nucl Med 2008; 49: 1912-1921.
286) Pakos EE, Fotopoulos AD, Ioannidis JPA. 18F-FDG PET for evaluation of bone marrow infiltration in staging of lymphoma: a meta-analysis. J Nucl Med 2005; 46: 958-963.
287) Giraudo C, Karanikas G, Weber M, Raderer M, Jaeger U, Simonitsch-Klupp I, Mayerhoefer ME. Correlation between glycolytic activity on [18F]-FDG-PET and cell density on diffusion-weighted MRI in lymphoma at staging. J Magn Reson Imaging 2018; 47: 1217-1226.
288) Mhlanga JC, Durand D, Tsai H-L, Durand CM, Leal JP, Wang H, Moore R, Wahl RL. Differentiation of HIV-associated lymphoma from HIV-associated reactive adenopathy using quantitative FDG PET and symmetry. Eur J Nucl Med Mol Imaging 2014; 41: 596-604.
289) Xicoy B, Ribera J-M, Miralles P, Berenguer J, Rubio R, Mahillo B, Valencia ME, Abella E, López-Guillermo A, Sureda A, Morgades M, Navarro J-T, Esteban H. Results of treatment with doxorubicin, bleomycin, vinblastine and dacarbazine and highly active antiretroviral therapy in advanced stage, human immunodeficiency virus-related Hodgkin's lymphoma. Haematologica 2007; 92: 191-198.

290) Hartmann P, Rehwald U, Salzberger B, Franzen C, Sieber M, Wöhrmann A, Diehl V. BEACOPP therapeutic regimen for patients with Hodgkin's disease and HIV infection. Ann Oncol 2003; 14: 1562-1569.
291) Spina M, Gabarre J, Rossi G, Fasan M, Schiantarelli C, Nigra E, Mena M, Antinori A, Ammassari A, Talamini R, Vaccher E, di Gennaro G, Tirelli U. Stanford V regimen and concomitant HAART in 59 patients with Hodgkin disease and HIV infection. Blood 2002; 100: 1984-1988.
292) Younes A, Oki Y, McLaughlin P, Copeland AR, Goy A, Pro B, Feng L, Yuan Y, Chuang HH, Macapinlac HA, Hagemeister F, Romaguera J, Samaniego F, Fanale MA, Dabaja BS, Rodriguez MA, Dang N, Kwak LW, Neelapu SS, Fayad LE. Phase 2 study of rituximab plus ABVD in patients with newly diagnosed classical Hodgkin lymphoma. Blood 2012; 119: 4123-4128.
293) Kasamon YL, Jacene HA, Gocke CD, Swinnen LJ, Gladstone DE, Perkins B, Link BK, Popplewell LL, Habermann TM, Herman JM, Matsui WH, Jones RJ, Ambinder RF. Phase 2 study of rituximab-ABVD in classical Hodgkin lymphoma. Blood 2012; 119: 4129-4132.
294) Strati P, Fanale MA, Oki Y, Turturro F, Fayad LE, Bartlett NL, Gladstone DE, Kasamon YL, Portlock CS, Wilson WH, Goy A, Younes A, Lee HJ. ABVD plus rituximab versus ABVD alone for advanced stage, high-risk classical Hodgkin lymphoma: a randomized phase 2 study. Haematologica 2019; 104: e65-e67.
295) Advani RH, Horning SJ, Hoppe RT, Daadi S, Allen J, Natkunam Y, Bartlett NL. Mature results of a phase II study of rituximab therapy for nodular lymphocyte-predominant Hodgkin lymphoma. J Clin Oncol 2014; 32: 912-918.
296) Schulz H, Rehwald U, Morschhauser F, Elter T, Driessen C, Rüdiger T, Borchmann P, Schnell R, Diehl V, Engert A, Reiser M. Rituximab in relapsed lymphocyte-predominant Hodgkin lymphoma: long-term results of a phase 2 trial by the German Hodgkin Lymphoma Study Group (GHSG). Blood 2008; 111: 109-111.
297) Ekstrand BC, Lucas JB, Horwitz SM, Fan Z, Breslin S, Hoppe RT, Natkunam Y, Bartlett NL, Horning SJ. Rituximab in lymphocyte-predominant Hodgkin disease: results of a phase 2 trial. Blood 2003; 101: 4285-4289.
298) Vassilakopoulos TP, Chatzidimitriou C, Asimakopoulos JV, Arapaki M, Tzoras E, Angelopoulou MK, Konstantopoulos K. Immunotherapy in Hodgkin lymphoma: present status and future strategies. Cancers 2019; 11: 1071.
299) Younes A, Bartlett NL, Leonard JP, Kennedy DA, Lynch CM, Sievers EL, Forero-Torres A. Brentuximab vedotin (SGN-35) for relapsed CD30-positive lymphomas. N Engl J Med 2010; 363: 1812-1821.
300) Vassilakopoulos TP, Angelopoulou MK. Advanced and relapsed/refractory Hodgkin lymphoma: what has been achieved during the last 50 years. Semin Hematol 2013; 50: 4-14.
301) Younes A, Connors JM, Park SI, Fanale M, O'Meara MM, Hunder NN, Huebner D, Ansell SM. Brentuximab vedotin combined with ABVD or AVD for patients with newly diagnosed Hodgkin's lymphoma: a phase 1, open-label, dose-escalation study. Lancet Oncol 2013; 14: 1348-1356.
302) Connors JM, Ansell SM, Fanale M, Park SI, Younes A. Five-year follow-up of brentuximab vedotin combined with ABVD or AVD for advanced-stage classical Hodgkin lymphoma. Blood 2017; 130: 1375-1377.
303) Diefenbach C, Hong F, Ambinder RF, Cohen JB, Robertson M, David KA, Advani RH, Fenske TS, Barta SK, Palmisano N, Svoboda J, Morgan D, Karmali R, Kahl BS, Ansell SM. A Phase I study with an expansion cohort of the combinations of ipilimumab, nivolumab and brentuximab vedotin in patients with relapsed/refractory Hodgkin lymphoma: a trial of the ECOG-ACRIN Research Group (E4412: Arms G-I). Blood 2018; 132: 679.
304) Sigel K, Dubrow R, Silverberg M, Crothers K, Braithwaite S, Justice A. Cancer screening in patients infected with HIV. Curr HIV/AIDS Rep 2011; 8: 142-152.
305) Casper C, Crane H, Menon M, Money D. HIV/AIDS Comorbidities: Impact on Cancer, Noncommunicable Diseases, and Reproductive Health. In: Holmes KK, Bertozzi S, Bloom BR, Jha P, eds. Disease Control Priorities: Volume 6. Major Infectious Diseases. Vol 41. The World Bank; 2017: 45-66.
306) Lin C-C, Hsieh M-C, Hung H-C, Tsao S-M, Chen S-C, Yang H-J, Lee Y-T. Human papillomavirus prevalence and behavioral risk factors among HIV-infected and HIV-uninfected men who have sex with men in Taiwan. Medicine 2018; 97: e13201.
307) Taylor S, Bunge E, Bakker M, Castellsagué X. The incidence, clearance and persistence of non-cervical human papillomavirus infections: a systematic review of the literature. BMC Infect Dis 2016; 16: 293.
308) Palefsky J. Human papillomavirus infection in HIV-infected persons. Top HIV Med 2007; 15: 130-133.
309) Roberts JR, Siekas LL, Kaz AM. Anal intraepithelial neoplasia: a review of diagnosis and management. WJGO 2017; 9: 50-53.
310) Gautier M, Brochard C, Lion A, Henno S, Mallet AL, Bodere A, Bouguen G, Lièvre A, Siproudhis L. High-grade anal intraepithelial neoplasia: progression to invasive cancer is not a certainty. Dig Liver Dis 2018; 48: 806-811.
311) SLAMA J, SEHNAL B, DUSEK L, ZIMA T, Cibula D. Impact of risk factors on prevalence of anal HPV infection in women with simultaneous cervical lesion. Neoplasma 2015; 62: 308-314.
312) Brickman C, Palefsky JM. Cancer in the HIV-infected host: epidemiology and pathogenesis in the antiretroviral era. Curr HIV/AIDS Rep 2015; 12: 388-396.
313) Riedel DJ, Tang LS, Rositch AF. The role of viral co-infection in HIV-associated non-AIDS-related cancers. Curr HIV/AIDS Rep 2015; 12: 362-372.
314) D'Andrea F, Ceccarelli M, Venanzi Rullo E, Facciolà A, Marino A, Cacopardo B, Pellicanò GF, Nunnari G. Vaccines against HPV in people living with HIV: a review. World Cancer Res J 2019; 6: e1348.
315) Müller MF, Ibrahim AEK, Arends MJ. Molecular pathological classification of colorectal cancer. Virchows Arch 2016; 469: 125-134.

316) Hoots BE, Palefsky JM, Pimenta JM, Smith JS. Human papillomavirus type distribution in anal cancer and anal intraepithelial lesions. Int J Cancer 2009; 124: 2375-2383.
317) Long KC, Menon R, Bastawrous A, Billingham R. Screening, surveillance, and treatment of anal intraepithelial neoplasia. Clin Colon Rectal Surg 2016; 29: 57-64.
318) Goncalves PH, Montezuma-Rusca JM, Yarchoan R, Uldrick TS. Cancer prevention in HIV-infected populations. Semin Oncol 2016; 43: 173-188.
319) Robison K, Cronin B, Bregar A, Luis C, DiSilvestro P, Schechter S, Pisharodi L, Raker C, Clark M. Anal cytology and human papillomavirus genotyping in women with a history of lower genital tract neoplasia compared with low-risk women. Obstet Gynecol 2015; 126: 1294-1300.
320) Tong WWY, Jin F, McHugh LC, Maher T, Sinclair B, Grulich AE, Hillman RJ, Carr A. Progression to and spontaneous regression of high-grade anal squamous intraepithelial lesions in HIV-infected and uninfected men. AIDS 2013; 27: 2233-2243.
321) Palefsky JM, Holly EA, Ralston ML, Jay N, Berry JM, Darragh TM. High incidence of anal high-grade squamous intra-epithelial lesions among HIV-positive and HIV-negative homosexual and bisexual men. AIDS 1998; 12: 495-503.
322) Palefsky JM, Holly EA, Hogeboom CJ, Berry JM, Jay N, Darragh TM. Anal cytology as a screening tool for anal squamous intraepithelial lesions. J Acquir Immune Defic Syndr Hum Retrovirol 1997; 14: 415-422.
323) Sendagorta E, Herranz P, Guadalajara H, Bernardino JI, Viguer JM, Beato MJ, Garcia-Olmo D, Pena JM. Prevalence of abnormal anal cytology and high-grade squamous intraepithelial lesions among a cohort of HIV-infected men who have sex with men. Dis Colon Rectum 2014; 57: 475-481.
324) Torkzad MR, Kamel I, Halappa VG, Beets-Tan RGH. Magnetic resonance imaging of rectal and anal cancer. Magn Reson Imaging Clin N Am 2014; 22: 85-112.
325) Kochhar R, Plumb AA, Carrington BM, Saunders M. Imaging of anal carcinoma. AJR Am J Roentgenol 2012; 199: W335-W344.
326) Cranston RD, Baker JR, Liu Y, Wang L, Elishaev E, Ho KS. Topical application of trichloroacetic acid is efficacious for the treatment of internal anal high-grade squamous intraepithelial lesions in HIV-positive men. Sex Transm Dis 2014; 41: 420-426.
327) Singh JC, Kuohung V, Palefsky JM. Efficacy of trichloroacetic acid in the treatment of anal intraepithelial neoplasia in HIV-positive and HIV-negative men who have sex with men. J Acquir Immune Defic Syndr 2009; 52: 474-479.
328) Sclafani F, Rao S. Systemic therapies for advanced squamous cell anal cancer. Curr Oncol Rep 2018: 20: 53.
329) Kim R, Byer J, Fulp WJ, Mahipal A, Dinwoodie W, Shibata D. Carboplatin and paclitaxel treatment is effective in advanced anal cancer. Oncology 2014; 87: 125-132.
330) Morris VK, Eng C. Role of immunotherapy in the treatment of squamous cell carcinoma of the anal canal. J Natl Compr Canc Netw 2018; 16: 903-908.
331) Chang GJ, Berry JM, Jay N, Palefsky JM, Welton ML. Surgical treatment of high-grade anal squamous intraepithelial lesions: a prospective study. Dis Colon Rectum 2002; 45: 453-458.
332) Panther LA, Wagner K, Proper J, Fugelso DK, Chatis PA, Weeden W, Nasser IA, Doweiko JP, Dezube BJ. High resolution anoscopy findings for men who have sex with men: inaccuracy of anal cytology as a predictor of histologic high-grade anal intraepithelial neoplasia and the impact of HIV serostatus. Clin Infect Dis 2004; 38: 1490-1492.
333) Siekas LL, Aboulafia DM. Establishing an anal dysplasia clinic for HIV-infected men: initial experience. AIDS Read 2009; 19: 178-186.
334) Marchesa P, Fazio VW, Oliart S, Goldblum JR, Lavery IC. Perianal Bowen's disease: a clinicopathologic study of 47 patients. Dis Colon Rectum 1997; 40: 1286-1293.