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Modernizing Clinical Trial Eligibility Criteria: Recommendations of the American Society of Clinical Oncology–Friends of Cancer Research HIV Working Group

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Abstract

Purpose—People with HIV are living longer as a result of effective antiretroviral therapy. Cancer has become a leading cause of morbidity and mortality in this patient population. However, studies of novel cancer therapeutics have historically excluded patients with HIV. Critical review of eligibility criteria related to HIV is required to accelerate development of and access to effective therapeutics for HIV-infected patients with cancer and make studies more generalizable to this patient population.

Methods—From January through April 2016, the HIV Working Group conducted a series of teleconferences; a review of 46 New Drug Applications from registration studies of unique agents studied in adults with cancer that led to the initial US Food and Drug Administration approval of that agent from 2011 to 2015; and a review of HIV-related eligibility criteria from National Cancer Institute–sponsored studies. Results were discussed and refined at a multistakeholder workshop held May 12, 2016. The HIV Working Group developed recommendations for eligibility criteria that focus on pharmacologic and immunologic considerations in this patient population and that balance patient safety, access to appropriate investigational agents, and study integrity.

Results—Exclusion of patients with HIV remains common in most studies of novel cancer agents. Models for HIV-related eligibility criteria in National Cancer Institute–sponsored studies are instructive. HIV infection itself should no longer be an exclusion criterion for most studies. Eligibility criteria related to HIV infection that address concurrent antiretroviral therapy and immune status should be designed in a manner that is appropriate for a given cancer.

Conclusion—Expanding clinical trial eligibility to be more inclusive of patients with HIV is justified in most cases and may accelerate the development of effective therapies in this area of unmet clinical need.

INTRODUCTION

In the modern era of HIV therapeutics, many people infected with HIV are expected to have a normal life expectancy.^{1,2} Despite this dramatic outcome as a result of improvements in the treatment of HIV over the past 20 years, and despite the increasing public health need to treat cancer in people with HIV, most oncology studies exclude all people with HIV. The goal of this working group was to assess the scope of problem and develop recommendations for modernized clinical cancer trial eligibility criteria related to HIV infection to enable appropriate inclusion of people with HIV in cancer clinical trials.

An estimated 1.2 million people in the United States³ and 37 million people globally⁴ are infected with HIV. Since 1996, treatment of HIV has consisted of combination antiretroviral therapy (ART). As of April 2016, ongoing advances in ART drug development have led to 29 agents approved by the US Food and Drug Administration (FDA), which has revolutionized HIV care. Most patients with HIV take once-a-day antiviral medications that have minimal adverse effects.⁵ Treatment of HIV allows for substantial preservation or reconstitution of immune function, and in the era of ART, infectious complications have become increasingly rare. The US Department of Health and Human Services (DHHS) guidelines⁶ and WHO⁷ recommend ART for all people with HIV. Intensive efforts in the United States and globally to increase the proportion of patients with HIV on ART are ongoing.⁸ The life expectancy of people with HIV on ART now approaches that of the general population, especially for those who start therapy with a normal CD4⁺ T-cell count (ie > 350 cells/uL).¹

Cancer in People With HIV

With increased longevity of people with HIV, cancer has become a leading cause of morbidity and mortality.^{9,10} This is largely because HIV increases the risk of some cancers, the prevalence of HIV increases with improved life expectancy, and the population of people

living with HIV is aging. The cancers most closely linked to HIV^{11,12} comprise approximately two thirds of cancers in this population. These cancers include AIDS-defining cancers, such as aggressive B-cell lymphomas (ie, diffuse large B-cell lymphoma, Burkitt's lymphoma, plasmablastic lymphoma, primary effusion lymphoma, primary CNS lymphoma), Kaposi sarcoma, and cervical cancer, and non-AIDS-defining cancers, such as classic Hodgkin lymphoma, lung cancer, anal cancer, liver cancer, and head and neck cancers. Most other cancers occur at the same frequency or slightly increased frequency compared with the general population, and cumulatively, the burden of cancer in people with HIV is expected to increase in the United States and globally for the foreseeable future.

Management of cancer for people with HIV should focus on approaches that are appropriate for the malignancy. This generally consists of standard regimens integrated with treatment of HIV and appropriate supportive care when indicated.¹³ In appropriately selected patients treated with this approach, outcomes are comparable to those of the general HIV-uninfected population. This has been demonstrated for diffuse large B-cell lymphoma,¹⁴ Burkitt's lymphoma,¹⁵ classic Hodgkin lymphoma,¹⁶ and lung cancer.¹⁷ Likewise, autologous¹⁸ stem-cell transplantation is feasible in people with HIV, with outcomes comparable to those of the background population. The feasibility and safety of allogeneic transplantation in people with HIV have been evaluated in an 18-person study conducted since September 2011 (Blood and Marrow Transplant Clinical Trials Network 0903/AIDS Malignancy Consortium 080). The trial has recently closed, and results will be reported in the near future. As is true for the general population, there is an ongoing public health need for less toxic and more effective targeted oncology drugs for many cancers in people with HIV. In many instances where standard therapy has failed to control a given cancer, experimental therapy should be the preferred approach.

HIV-specific studies for many types of common cancers that are not associated with HIV are impractical given the diversity of cancers that may occur in this patient population, and therefore, inclusion of appropriately selected patients with HIV in studies of a given disease type or molecular characterization is needed. Lack of prospective data on therapies in people with HIV limits evidence-based treatment decisions and contributes to suboptimal oncology care for people with HIV. Prospective data on novel approaches in this patient population are critical to address unnecessary treatment disparities both within clinical studies and with subsequent use of FDA-approved agents. Routine exclusion to clinical trial participation is not justified, and eligibility criteria related to HIV should be assessed on the basis of current medical knowledge and scientific rationale.¹⁹ Individuals who are healthy from the perspective of their HIV should be eligible for participation in clinical trials provided they meet the other eligibility criteria of a given study. Exclusion based on HIV infection alone is generally not appropriate, and exceptions should be based on sound medical rationale that is clearly articulated in a specific protocol. Recommendations from the HIV Working Group address some of the most common considerations related to modernizing eligibility for this patient population.

PROCESS

HIV Working Group

To address the public health need to update the eligibility criteria related to HIV in oncology studies, the HIV Working Group of the ASCO–Friends of Cancer Research Modernizing Eligibility Criteria Project for Modernizing Eligibility Criteria in Cancer Studies held a series of teleconferences from January through April 2016 to develop an initial draft of recommendations on this topic. The committee consisted of government, academic, and industry investigators with clinical trial and pharmacology expertise, representatives from the FDA, policy experts, and patient and cancer research advocates. The committee reviewed recent clinical oncology studies to evaluate HIV-related eligibility criteria in both industry-sponsored studies and studies sponsored by the National Cancer Institute (NCI). Results were discussed and refined at a multistakeholder workshop held May 12, 2016.

Current HIV-Related Eligibility Criteria

Eligibility criteria for both industry-sponsored and NCI-sponsored cancer studies were reviewed to evaluate current approaches to eligibility and quantify the need for specific recommendations related to HIV. The group reviewed eligibility criteria from studies supporting 46 New Drug Applications (NDAs) of unique agents in patients with cancer that led to initial FDA approval from 2011 to 2015. Eligibility criteria in the relevant clinical studies were evaluated on [ClinicalTrials.gov](https://clinicaltrials.gov) (where available), in the FDA application, and/or in the Methods sections of published results. We evaluated studies for specific HIV-associated inclusion criteria and HIV-associated exclusion criteria. When these were not available as a result of inadequate details about entry criteria, we noted more general exclusion criteria that would likely include HIV (ie, exclusion for active infection or HIV exclusion criteria in studies of the same agent). This review revealed no studies with HIV-specific inclusion criteria, 30 studies with specific HIV exclusion criteria, and an additional nine studies with likely HIV exclusion (Fig 1).

Of the 46 NDA agents examined, as of May 1, 2016, 15 subsequently became available for HIV-infected patients with cancer who met additional eligibility criteria through a variety of studies developed in partnership with NCI (Table 1). This included eight drugs that were subsequently used in one or more studies for HIV-specific populations and/or tumor-specific studies that allowed patients with HIV, as well as seven of the first 12 agents currently used in the NCI Molecular Analysis for Therapy Choice (MATCH) trial. Nonetheless, deferring the undertaking of studies that allowed treatment of patients with HIV until after FDA approval resulted in a delay in availability and specific FDA labeling for these novel agents in patients with HIV. For example, the median delays to availability of novel agents for people with HIV and cancer through either market availability or through HIV-specific studies in the 46 NDAs leading to FDA approval reviewed were 6.8 years (range, 2.3 to 19.7 years) for phase I to approval, 3.9 years (range, 1 to 7.6 years) for NDA study to approval, and 6.3 years (range, 3.5 to 11.7 years) for phase I to HIV-specific study.

We reviewed select NCI-sponsored studies specific to patients with HIV or open to the general population with explicit entry criteria allowing for patients with HIV. These studies

were reviewed for criteria related to CD4⁺ T-cell count, HIV viral load, concomitant HIV medications, and other factors relevant to HIV status. Entry criteria for 13 relevant NCI-sponsored studies, including the NCI-MATCH study, are listed in Table 1 and provide examples that inform future studies. Together, our review emphasized the need for recommendations on HIV entry criteria in oncology studies going forward and provided examples of successful development of studies through partnership between the NCI, academic institutions, and industry.

RISKS AND BENEFITS TO INCLUSION

Inclusion of patients with HIV in clinical studies may provide benefit to patients, physicians, and sponsors and investigators. Importantly, inclusion in studies may accelerate access of appropriate cancer therapeutics to HIV-infected patients, provide increased experience to guide treating physicians, and increase the use of appropriate anticancer agents in patients with HIV. For sponsors, inclusion of patients with HIV may reduce the need for some postmarketing studies, especially in common tumors not strongly associated with HIV, such as breast, colon, and lung cancer. The major risks to be mitigated in developing eligibility criteria in cancer studies in this patient population include avoidance of anticipated drug-drug interactions between cancer therapies and HIV therapies using approaches that are used for patients with other chronic medical conditions, and appropriate consideration of eligibility criteria related to the degree of HIV-associated immunosuppression that may be acceptable for a given study so as to avoid adverse events related to competing infectious morbidity.

RECOMMENDATIONS

The HIV Working Group emphasized that evaluation of the suitability of a patient with HIV for a given study can be accomplished in a straightforward and uniform manner across all studies. Eligibility can be determined through evaluation of present and historic CD4⁺ T-cell counts, review of any history of any potential AIDS complications, and evaluation of use of effective ART. Specific eligibility criteria may vary based on the objectives of the study. It was emphasized that modernized eligibility will improve generalizability of early-phase studies of cancer therapies and improve access to experimental cancer agents to appropriate populations of HIV-infected patients. The committee defined important principles related to entry criteria for patients with HIV, as follows:

1. Criteria to define a population with HIV that is sufficiently healthy from this comorbid perspective to participate in almost any oncology study are recommended.
2. Criteria should select patients with probable long-term survival in the absence of cancer.
3. The later the phase of the trial, the more information is known about a particular therapeutic agent for the treatment of a particular condition. The level of experience with a given agent may inform eligibility criteria.

4. Criteria should not be more stringent than for HIV-uninfected patients with the same disease or treatment history.

The fourth principle above is particularly important in relation to CD4⁺ T-cell criteria. CD4⁺ counts are an essential component of assessing health status in HIV disease. However, it is important to avoid inadvertent exclusion of HIV-infected persons from clinical trials based on CD4⁺ cell depletion mainly as a result of prior cancer therapy, because CD4⁺ cell depletion occurs with certain cancer therapies in the general population. Well-known examples of fludarabine²⁰ or alemtuzumab²¹ serve to illustrate this fact. If only HIV-positive patients are required to have CD4⁺ levels greater than the institutional normal value for a given study, HIV-uninfected patients exposed to either fludarabine or alemtuzumab likely would be more vulnerable than the HIV-infected patients. CD4⁺ counts before cancer therapy can inform the HIV disease status better than the concurrent CD4⁺ level if prior lymphocytotoxic therapy, including radiation therapy, was administered within the past 12 months or perhaps longer in some cases. For these reasons, accurate assessment of HIV disease requires more than one point of assessment. Developing eligibility criteria should take this last principle into consideration, especially in the setting of second-line and later cancer therapy.

The HIV Working Group defined criteria that can be used to define a patient with HIV who is sufficiently healthy from the HIV perspective to participate in almost any oncology study. These criteria are focused on the following two main areas: evaluation of immune function and criteria related to HIV therapy. A discussion, the working group's recommendation, and template protocol language are listed for each main area.

Recommendations for Eligibility Criteria

Immune criteria recommendations

1. Patients with CD4⁺ T-cell counts ≥ 350 cells/ μ L should generally be eligible for any study if otherwise eligible.
2. Lower CD4⁺ count eligibility is often appropriate (Table 1).
3. Patients with no history of AIDS-defining opportunistic infections (or only remote AIDS-defining opportunistic infections; ie, none in the past year) should generally be eligible for any study if otherwise eligible.
4. Recommend time frame for exclusion of AIDS-defining opportunistic infections. For cancers common in people with HIV, a shorter time frame is appropriate (Table 1).
 - For many studies, recommend no opportunistic infections within past 12 months.
 - For studies of AIDS-defining cancers with curative potential, exclusion limited to uncontrolled opportunistic infections may be appropriate (ie, for studies evaluating therapy for lymphoma or Kaposi sarcoma that may commonly include patients with newly diagnosed HIV).

- Patients on prophylactic antimicrobials need not be excluded, although specific agents may be excluded for drug-drug interactions or overlapping toxicities.

HIV therapy criteria recommendations

1. Generally, recommend concurrent treatment with effective ART according to DHHS treatment guidelines (Table 2).
2. Recommend criteria specifying timing of ART initiation that are appropriate for study goals and take into consideration patients recently diagnosed with HIV or patients not on effective ART. Examples include the following:
 - Patients agree to ART if not currently on ART (timing at investigator discretion, often appropriate, and is important for first-line studies of curable malignancies such as aggressive lymphomas, where cancer therapy requires prioritization).
 - ART > 4 weeks (to ensure ART is tolerated and that toxicities are not confused with study drug toxicities)
 - ART > 4 weeks plus HIV viral load < 400 copies/mL (to ensure ART is tolerated and HIV controlled)
3. Recommend exclusion of specific ART agents, when indicated, based on predicted drug-drug interactions from absorption, distribution, metabolism, and excretion data or potential overlapping toxicities.
 - Although many drug-drug interactions occur with CYP3A4, other metabolic routes and drug transporters may be involved. Recommend assessment of the absorption, distribution, metabolism, and excretion data known to date for the anticancer agent. Contraindicated agents are then rationally selected based on drug-drug interaction potential using known sources (Table 2). Recommend providing tables of contraindicated agents that include ART and other drugs. For sensitive CYP3A4 substrates, concurrent strong CYP3A4 inhibitors (ritonavir and cobicistat) or inducers (efavirenz) should be contraindicated.
 - Consider exclusion of ART agents based on toxicity (eg, zidovudine [neutropenia], stavudine [neuropathy], didanosine [neuropathy], atazanavir [QT prolongation], ritonavir boosted lopinavir [QT prolongation], and saquinavir [QT prolongation]).
4. Although effective ART is generally recommended, exceptions to concurrent ART should be considered in both development of eligibility criteria and conduct of studies.¹³
 - Treatment interruption or deferred initiation is appropriate in curable malignancies when ART may compromise intended full-dose oncology therapy with investigational agent(s).
 - Treatment interruptions for toxicity management

- Treatment interruptions to meet scientific objective of study

Studies of Cancers Common in People With HIV, Including Studies Specific to People With HIV

Although this template provides recommendations for development of eligibility criteria to allow for selection of appropriate HIV-infected patients with preserved immune function across a broad range of studies, particular emphasis should be placed on design of studies that disproportionately affect people with HIV. For all phases of studies, the HIV Working Group encourages commitment to eligibility criteria that allow for inclusion of a broader population of HIV patients for the most common malignancies associated with HIV (ie, lung cancer, lymphoma, anal cancer, head and neck cancer, cervical cancer, hepatocellular carcinoma, Kaposi sarcoma).

In addition, HIV-specific studies for malignancies remain critical, especially for cancers most strongly associated with HIV (Kaposi sarcoma, aggressive B-cell lymphomas, classic Hodgkin lymphoma). Long-term survival is feasible in most patients with these malignancies, and therefore, substantially different entry criteria are appropriate (Table 1). Furthermore, HIV-specific studies allow for analysis of the safety and efficacy of a given agent across a broader range of patients with HIV and allow for specific evaluation of the effects of an agent on immune parameters in this patient population. Partnership with the NCI or academic centers with expertise in HIV and cancer is encouraged for HIV-specific studies.

Additional Trial Design Practical Considerations

Once eligibility is established, HIV infection should be managed as part of standard of care and should not be dictated by the protocol, unless the protocol has specific objectives regarding HIV outcomes. ART should be considered concomitant medications, with avoidance of contraindicated ART agents and other concomitant medications during the duration of treatment with the study agent. This is consistent with the management of other chronic diseases such as hypertension and diabetes, which are generally not dictated in an oncology protocol. Management of HIV can be performed in collaboration with a study participant's primary care provider or HIV specialist. The physicians managing HIV for patients on cancer studies should be aware of DHHS guidelines (Table 2) regarding management of HIV and prevention of opportunistic infections.

For studies that include people with HIV, HIV-specific treatment-related considerations are not required in the informed consent. However, delineating who is responsible for treating and monitoring HIV is appropriate. For studies with eligibility criteria that require exclusion of specific ART agents, consider providing patient educational material with a list of acceptable and unacceptable ART agents.

CONCLUSION

Cancer is a leading cause of morbidity and mortality in the estimated 37 million people living with HIV globally. Modernization of eligibility criteria to include appropriate HIV-infected patients in cancer clinical studies is important for decreasing the burden of cancer in

this patient population. A variety of NCI-sponsored studies have demonstrated that inclusion of patients with HIV on cancer clinical trials is feasible. HIV infection alone should no longer be an exclusion criterion in any study. Straightforward eligibility criteria related to HIV should take into consideration an approach to concurrent ART and criteria related to immune status appropriate for a given study.

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Fig 1.
HIV-related eligibility in New Drug Applications from 2011 to 2015.

Table 1

HIV Eligibility Criteria in Select NCI-Supported Studies From 2011 to 2015

Disease, Lead Organization, and ClinicalTrials.gov Identifier	Study Drug(s)	Study Phase	CD4 ⁺ Count (cells/ μ L)	ART	HIV Viral Load	Other
Open to HIV						
Advanced Kaposi sarcoma, CCR, NCT02659930	Pomalidomide + liposomal doxorubicin	I	None	Effective ART required	None	Allows for treatment-naïve or uncontrolled HIV in patients with progressive or life-threatening disease
Myeloid malignancies, Princess Margaret Cancer Center, NCT02381548	Belinostat + AZD1775	I	Preleukemia 250	Willing to adhere to ART with minimal overlapping toxicity and PK interactions; AZT, ritonavir, and cobicistat contraindicated		No history of AIDS-defining condition other than CD4 ⁺ count < 200 cells/ μ L
Burkitt lymphoma, Intergrup CTSU 9117/AMC-086, NCT01092182	EPOCH-R	II	None	Suspend ART (with exceptions)	None	Exclude patients with advanced immune suppression and evidence of HIV resistant to all ART considered at high risk of non-lymphoma-related death within 12 months as a result of AIDS
Relapsed anal cancer, The University of Texas MD Anderson Cancer Center-P2C, NCT02314169	Nivolumab	II	300	Required	Undetectable	HIV care by infectious disease specialist required; HIV-related laboratory studies sent to study team
Relapsed refractory cancer, ECOG-ACRIN, NCT02465060	Genetic testing-directed therapy (12 agents [*] , some FDA approved)	II	250	Not required; if used, minimal interactions or overlapping toxicities	None	Exclude history of AIDS-defining conditions other than low CD4 ⁺ counts; probably long-term survival if cancer not present
Operable hormone receptor-positive HER2-positive breast cancer, NSABP-B-52, NCT02003209	Docetaxel, carboplatin, trastuzumab, and pertuzumab with or without estrogen deprivation	III	250	ART with potential overlapping toxicities excluded	None	No prior AIDS-defining conditions
Previously untreated CLL in patients 65 years old, Alliance 041202, NCT01886872	Rituximab and bendamustine v rituximab and ibrutinib v ibrutinib	III	350	ART with cytochrome P-interacting medications prohibited	None	NA
Ibrutinib v placebo before and after stem-cell transplantation in DLBCL, Alliance 051301, NCT02443077	Ibrutinib, autologous stem-cell transplantation	III	None	AZT, protease inhibitors, and cobicistat prohibited	Patients with multidrug-resistant HIV excluded	No history of AIDS-defining conditions other than low CD4 count; HIV expert opinion of long-term survival from HIV perspective

HIV-specific studies

Disease, Lead Organization, and ClinicalTrials.gov Identifier	Study Drug(s)	Study Phase	CD4 ⁺ Count (cells/ μ L)	ART	HIV Viral Load	Other
Relapsed refractory cancer, CITN12-CCR, NCT02595866	Pembrolizumab	I	Stratified: 100–199, 200–350, and > 350	ART 4 weeks	< 400 copies/mL	If CD4 ⁺ < 200 cells/ μ L; CD4/CD8 ratio > 0.4
Relapsed refractory solid tumors, AMC-095, NCT02408861	Ipilimumab + nivolumab	I	Stratified: 100–200 and > 200	ART > 4 weeks	Undetectable (< 75 copies/mL)	Opportunistic infection in past 3 months
Relapsed refractory solid tumors, AMC-087, NCT01822522	Cabozantinib	I	> 50	ART if clinically indicated	None	ART strata for PK studies; under care of physician with experience in HIV management; exclude patients with active infections requiring systemic therapy in past 28 days
HIV-associated advanced Hodgkin lymphoma, AMC-085, NCT01771107	AVD + brentuximab	I/II	50	Required ART according to guidelines; prohibited AZT, ddI, ritonavir, cobicistat	None	Uncontrolled opportunistic infection
HIV-associated aggressive B-cell lymphomas, AMC-078, NCT01193842	Vorinostat + EPOCH-R	II	50	Concurrent ART; if not on ART, start after first cycle; AZT excluded	None	Excluded if serious ongoing infection

Abbreviations: AMC, AIDS Malignancy Consortium; ART, antiretroviral therapy; AVD, doxorubicin, vinblastine, and dacarbazine; AZT, zidovudine; CCR, Center for Cancer Research, National Cancer Institute; CITN, Cancer Immunotherapy Trials Network; CLL, chronic lymphocytic leukemia; CTSU, Clinical Trials Support Unit; ddI, didanosine; DLBCL, diffuse large B-cell lymphoma; ECOG-ACRIN, Eastern Cooperative Oncology Group–American College of Radiology Imaging Network; EPOCH-R, etoposide, prednisone, vincristine, cyclophosphamide, and rituximab; FDA, US Food and Drug Administration; HER2, human epidermal growth factor receptor 2; NA, not applicable; NSABP, National Cancer Institute; NSABP, National Cancer Institute; Phase II Consortium; PK, pharmacokinetics.

* Number of agents listed on [ClinicalTrials.gov](https://clinicaltrials.gov) as of May 1, 2016.

Table 2**Sources for Management of Concurrent HIV and Prevention of Drug-Drug Interactions**

<p>Management of concurrent HIV</p> <p>DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents⁶: Includes up-to-date recommendations for preferred ART regimens. Physicians should be familiar with broad guidelines of HIV care, which include DHHS recommendations for laboratory monitoring, including CD4⁺ monitoring at baseline and every 3 months and HIV viral load monitoring at baseline and every 3 months, or 2 months of follow-up after initiation or change of ART</p> <p>Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents²²: Physicians who treat HIV-infected patients on clinical studies should also be aware of guidelines for administration of concomitant antimicrobial prophylaxis in this patient population, including prophylaxis against HSV/VZV for patients with recurrent HSV infections or in studies of agents with immunosuppressive effects; prophylaxis against atypical mycobacterial infection with azithromycin 1,200 mg weekly if CD4⁺ count < 50 cells/μL; and prophylaxis against <i>Pneumocystis pneumonia</i> with trimethoprim/sulfamethoxazole or alternative agent if CD4⁺ count < 200 cells/μL, or at any CD4⁺ count if study drug(s) has potential immunosuppressive effects</p>
<p>Available antiretroviral agents and relevant pharmacology to avoid drug-drug interactions</p> <p>Rudek et al²³: Review of antineoplastic agents in patients with cancer who have HIV/AIDS: Includes tables on drug interaction potential of antiretroviral agents</p> <p>UpToDate Systemic Therapy for Malignancies in Patients on Antiretroviral Therapy: Includes table of relevant drug-drug interactions</p> <p>University of Liverpool HIV Drug Interaction Web site (http://www.hiv-druginteractions.org): Searchable database</p> <p>POZ List of HIV Medications (https://www.poz.com/drug_charts/hiv-medications): Comprehensive list of ART with dosing information and photos of medications</p>

Abbreviations: ART, antiretroviral therapy; DHHS, Department of Health and Human Services; HSV, herpes simplex virus; VZV, varicella-zoster virus.