Needs Assessment (HIV)

Gap 1: HIV is a complex and rapidly evolving field. There is a need to review key content from the guidelines and to emphasize the importance of a multidisciplinary approach to care.

HIV is a rapidly evolving field.[1] Clinical practice guidelines are continually being updated as new data become available. It can be challenging for providers to keep pace with the latest recommendations. Educational opportunities that emphasize specific guideline recommendations are needed on a continual basis to achieve optimal outcomes.[1]

In September of 2020, the Office of AIDS Research (OAR) restructured its former websites (www.AIDSinfo.nih.gov and www.infoSIDA.nih.gov) which were housed within the National Library of Medicine (NLM).[2] The restructuring resulted in 2 new websites, www.ClinicalInfo.HIV.gov and www.HIVinfo.nih.gov, still sponsored by the OAR, but now housed within the Department of Health and Human Services (HHS) Office of Infectious Diseases and HIV/AIDS Policy (OIDP).[2] This is an important change to highlight because it is where clinicians can find the most recent HIV/AIDS clinical treatment guidelines.[2] Updates to the current version of *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV* (just one of many guideline documents published by the HHS/OAR/OIDP provided for HIV) were released in June 2021, August 2021, and January 2022.[1,3]

Treatment options for HIV have improved substantially over the years.[1] More po and less toxic antiretrovirals (ARV) have become available.[1] The increasing number of ARV drug classes has made viral suppression below detection limits an achievable goal in most troviral therapy (ART) is recommended for all persons with HIV to reduce mo d to reduce transmission of HIV to others.[1] The guidelines recommend initiati r HIV diagnosis for all individuals.[1]

The guidelines emphasize that HIV care requires partne ciplines.[1] Persons living with HIV are often coping with a variety of social, p sues that can be best addressed through a patient-centered, multidis e goal of HIV treatment is to reduce the viral load to an undetectable le bed ART regimen is vital for maintaining durable viral suppression.[1,4] ause an increase in viral load, an associated increased risk of transmi ce of drug-resistant mutations that can compromise future treatment o inical deterioration to AIDS.[1] It therefore behooves providers to enga rs and social workers wherever possible to help patients remain adhere

Gap 2: Although n highly effective and associated with fewer toxicities than older agents, newe t remain completely benign. With the wide array of ART regimens commerci a slightly different safety profile, there is a need to assist providers in under linically important drug-drug and drug-disease interactions, and re to maximize patient safety.

Ther fferent ARV drugs in 8 different mechanistic classes that have been approved by the FDA fo nt of HIV.[1] The 8 classes of HIV drugs currently available include: 1) nucleoside nucleotide reverse transcriptase inhibitors (NRTIs); 2) non-nucleoside reverse transcriptase inhibitors (NNRTIs); 3) protease inhibitors (PIs); 4) integrase strand inhibitors (INSTIs); 5) a fusion

inhibitor; 6) a CCR5 antagonist; 7) a CD4 T lymphocyte post-attachment inhibitor; and 8) a gp120 attachment inhibitor.[1] There are 2 additional drugs that are approved for use as pharmacokinetic (PK) boosters to improve the PK profiles of PIs and the INSTI elvitegravir. They are ritonavir and cobicistat.[1]

With so many effective ART regimen options, there is a need for providers to be aware of the specific risks (including important drug-drug interactions) and potential adverse effects associated with each agent.[1] Reviewing the recommendations contained in the guidelines regarding which agents to select in the presence of other comorbid conditions and coinfections, as well as the recommendations for the type of monitoring required for each agent, can help to maximize patient safety.[1]

There are many factors to consider when selecting an ART regimen. These include resistance test results, toxicity, pill burden, dosing frequency, drug-drug interaction potential, comorbid conditions, access, and cost.[1] Whether or not the ART regimen is commercially available as a single tablet combination product and whether it can be taken without regard to meals are additional factors to consider, all of which can impact patient adherence.[1] While newer ART regimens recommended in the guidelines may have comparable efficacy, they vary with respect to pill burdens, p tial for drug-drug interactions, potential for side effects, and propensity to select out for resista ns if adherence is suboptimal.[1] Predictors of success in achieving maxim al viral an ART regimen include low baseline viremia at time of diagnosis, high poten lerability of the regimen, convenience of the regimen, and excellent adhere

Newer, second-generation ARV drugs have replaced older, fi any of the drug classes because they are more effective, have lower pill l ly less toxic.[1,4] Use of triplet combinations that target different phases of t has become standard practice when initiating therapy.[1,4] The ART regi itial therapy for most patients include a 3-drug combination of 2 NRTIs plu

INSTIs are a relatively new class of ARV n high efficacy, rapid virologic suppression, and a favorable side e some emerging data has suggested that INSTIs may cause weight gain i ssible mechanisms for this may be their potential to induce adipogenesis, lip s, fibrosis, and insulin resistance.[4] Factors that predispose a person to include lower CD4+ count and/or higher viral load at initiation, female s thnicity, and older age.[4,6,7] If weight gain is a concern due to the presence o metabolic risk factors, then a non INSTI-containing regimen may be preferr 2 NRTIs + an NNRTI; or 2 NRTIs + a PI with booster).[1]

Rec at persons with HIV have a higher comorbidity burden and greater like acy than their matched counterparts without HIV.[8] These findings suggest that comor medications are important factors for providers to consider when choosing an ART regimen drug-disease and drug-drug interactions can be minimized, thus maximizing potential for adherence to the ART regimen.[8]

Since most ARVs undergo hepatic metabolism, monitoring for treatment-emergent hepatoxicity and potential drug-drug interactions with other hepatically eliminated drugs is a clinically important issue.[1,9] Most ARVs are substrates in the cytochrome P450 enzyme system; however, not all are inducers or inhibitors. The guidelines outline in great detail each of these potential interactions.[1] Clinicians should always consult a pharmacist or the package insert for potential drug-drug interactions.

A drug-drug or drug-food interaction commonly encountered with ARV therapy is chelation (and subsequent reduction in absorption and efficacy) with INSTIs and polyvalent cations (e.g., calcium, magnesium, aluminum, or iron found in antacids, supplements, laxatives, or dairy).[6] Each INSTI is slightly different regarding when and how to separate co-administration of polyvalent-containing products, and providers should be aware of this potential interaction so that they can appropriately counsel their patients.[6] If this is a concern or would overly complicate adherence for a particular patient, a non-INSTI-based regimen should be selected. [6]

Another key consideration for providers is whether the patient has coinfection with hepatitis C virus (HCV) and is taking anti-HCV therapy. There is potential for clinically significant drug-drug interactions with anti-HCV therapy, and the ART regimen may need to be modified. Some ARVs are not recommended to be used with certain anti-HCV drugs, while others can be used safely.[1] Providers can consult the tables in the guidelines to get an idea of these interactions, but should always consult the prescribing information and/or a pharmacist for complete information and recommendations.

One of the commonly used NRTIs, tenofovir, comes in two forms: tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF), both of which are approved by the FDA for use in treatment of HIV.[1] However, there are key differences between the two that are worth highlighting viders. TAF is associated with fewer bone and kidney toxicities compared to TDF and shou over TDF in the presence of kidney disease and / or osteoporosis.[1] However, TDF ha e a lipid-lowering effect and may be preferred over TAF in when there is con risk factors.[1,10]

As ART drugs are not benign, there are important monitori ders musr consider to ensure patient safety during ARV treatment. Liver fun cose tolerance, and lipids should all be monitored on a routine basis.[1]

Gap 3: The number of persons living with HI aximally suppressed viral loads is less than ideal and stems mainly from u g or retaining patients into adequate care, and lack of adherence to ART r d. There is a need to review screening recommendations and potential adherence. There is also a need to increase awareness of considerations , and those who identify as transgender who are living with HIV.

According to a 201 ople with HIV in the U.S. had maximally suppressed viral loads. [1] This is far fr ation of ART to achieve and maintain viral suppression is key to preventin to others, lowering the risk of AIDS-defining illnesses, decreasing the costs r f AIDS and its comorbidities, improving quality of life, and allowing pe at approaches that of persons without HIV.[1]

Reas nal viral suppression among those with HIV in the U.S. is multifactorial. Lack of screeni k of adherence to ART once HIV has been identified are contributors. The guidelines recommen HIV testing for all persons aged 15-65 and for all pregnant individuals.[1] However, one study found that less than 40% of American adults have ever been tested for HIV. Improvements in HIV screening to allow for early diagnosis are greatly needed. Risk factors associated with a delayed HIV diagnosis include nonwhite race, use of IV drugs, living in a rural community, and advanced age.[1] Sadly, due to diagnostic delays, many individuals in these groups develop AIDS-defining illnesses within 1 year

of diagnosis.[1] HIV screening is crucial to catching HIV early enough, preventing transmission to others, and ultimately, ending the epidemic.[1] Beginning ART immediately and then achieving and maintaining an undetectable viral load reduces the risk of transmission (either sexually or via birth).[1] Having a high plasma HIV RNA level is a known risk factor for transmission.[1]

The guidelines recommend baseline evaluation of factors that may impede a patient's ability to remai adherent to ART.[1] These include lack of social support, comorbidities such as mental illness, homelessness or unstable housing, inadequate medical insurance, complex medication regimens, side effects, and/or inadequate treatment education and support.[1] Once identified, the provider team should act to address these barriers.

Strategies that can help improve adherence to ART include simplifying the ART regimen commercially-available single tablet regimens (STR) to decrease pill burden and sele at can be taken without regard to meals due to a food agnostic oral bioavailability.[1,11] T specific recommendations for each of these scenarios. Regimens that can b meals include bictegravir-, doravirine-, dolutegravir-, and raltegravir-bas boxes and test-message reminders also have a proven track record of imp Use of a multidisciplinary team is often required to address more comple stance use disorders, comorbid mental illness, access to food, homeles ty, and economic hardships.[11]

The guidelines offer specific recommendations to patients with HIV who are part of specific populations, including older adults identify as transgender.[1] Co-infection with hepatitis B (HBV) also has s s. HIV/HBV co-infection should utilize an ART regimen that includes tenofov ine or emtricitabine, as these agents also have activity against HBV.[1]Care fo pecified in the guidelines can be particularly complex and is why multidisci mended.

As nearly 50% of person e aged 50 years or older and is projected to account for nearly 70% of peopl e is a growing population of patients in this age bracket whose care will at of aging individuals.[12] Concerns for this population include noninfectio heart disease, malignancy, cognitive decline, mood disorders, and osteoporos ese conditions and management of the conditions themselves in the aging HIV popu s suboptimal.[12] Polypharmacy is of general concern among all older adults, but can be espec portant to monitor among those with HIV who are aging.[12] As potential for comorbidities increases, management of older individuals with HIV often results in a prescribing cascade where side effects of one medication are misdiagnosed as a new condition, resulting in additional drugs being prescribed.[12] There is a need for providers to be aware of this potential clinical pitfall in the aging population.[12] Multidisciplinary teams can be particularly helpful in this regard. [12]

Care of the transgender patient with HIV should be provided with a gender-affirmative care model to increase the likelihood of adherence.[1] Potential drug-drug interactions exist between some ART regimens and gender-affirming hormone therapies (GAHT).[1] If a patient is on GAHT, selection of ARV agents that have lower potential for interactions should be selected.[1] In addition, as GAHT can cause hyperlipidemia, elevated cardiovascular risks, and osteopenia, these affects may be additive with certain ART regimens that cause similar affects and thus, ART regimens should be chosen carefully in these patients.[1] Barriers to adherence may also exist in this patient population. Such barriers known to be

present for transgender people living with HIV include unstable housing, poverty, and trauma from discrimination or violence.[1]

Providers caring for women with HIV should consider the potential drug-drug interactions that exist between some ARV drugs and hormonal contraceptives and hormone replacement therapy.[1] In addition, women have higher risk for weight gain with selected ARVs compared to men.[1] If this is a concern due to other risk factors, ARVs that are weight-neutral and have less potential for drug-drug interactions should be selected.[1]

References

1. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guideli… Antiretroviral Agents in Adults and Adolescents with HIV. Departm… Services. Updated January 30, 2022. Accessed August 31, 202… https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adoles…
2. National Institutes of Health (NIH), Office of AIDS Rese… of Health and Human Services (HHS), Office of Infectious Disease… IDP). About Clinical Info. Accessed August 31, 2022. https://clinicali… nical-info
3. National Institutes of Health (NIH), Office o… epartment of Health and Human Services (HHS) Office of Infectio… Policy (OIDP). Archived Guidelines. Updated January 21, 20… 2022. https://clinicalinfo.hiv.gov/en/gu… nes/all-archived-guidelines
4. Menéndez-Arias L, Delgado R… ances in antiretroviral therapy. *Trends Pharmacol Sci.* 2022;43(1…
5. Riddell J 4th. 2018 IAS… for the use of antiretroviral therapy for HIV: building on decad… 018;320(4):347-349.
6. Scarsi KK, Hav… ssian SN, Fletcher CV. HIV-1 Integrase Inhibitors: A Comparati… d Safety. *Drugs*. 2020;80(16):1649-1676.
7. Buzón… HIV-infected individuals using distinct antiretroviral drugs. *AIDS Re…*
8. Pauc… Buysman EK, et al. Comorbidity and comedication burden among people living w… e United States. *Current Medical Research and Opinion*. 2022;38(8):1443-1450.
9. Rivera CG, Otto AO, Zeuli JD, Temesgen Z. Hepatotoxicity of contemporary antiretroviral drugs. *Curr Opin HIV AIDS*. 2021;16(6):279-285.
10. Lee D. HIV: How to manage dyslipidaemia in HIV. *Drugs Context*. 2022;11:2021-8-7.
11. McCluskey SM, Siedner MJ, Marconi VC. Management of Virologic Failure and HIV Drug Resistance. *Infect Dis Clin North Am*. 2019;33(3):707-742.
12. Erlandson KM, Karris MY. HIV and Aging: Reconsidering the Approach to Management of Comorbidities. *Infect Dis Clin North Am*. 2019;33(3):769-786.