EDITORIAL

Advances in Treatment and Prevention of HIV

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Advances in antiretroviral therapy (ART) has led to HIV being a manageable and preventable condition and provides the tools that might lead to an end of the HIV pandemic. Despite these advances, in the United States there were approximately 30 000 new infections in 2022, less than 70% of people living with HIV were virologically suppressed, and only 30% of those eligible for preexposure prophylaxis (PrEP) were receiving it. Prioritizing efforts on the significant disparities in access to care and the delivery of equitable health care are essential for future elimination goals.

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Every 2 years, the International Antiviral Society-USA panel for the treatment and prevention of HIV synthesizes the extensive and evolving landscape of HIV management and prevention into a readable and clinically useful guide.[1] Since the 2022 guidelines, notable updates are seen in sections covering ART recommendations for pregnancy, management of virologic failure, switching in virologically suppressed patients, and use of long-acting agents.

A notable theme from the panel focuses on opportunities for simplification of ART regimens. In pregnancy, dolutegravir with tenofovir alafenamide/emtricitabine remains the preferred option based on tolerability and efficacy.[2,3] Although data with bictegravir in pregnancy is limited, the panel now recommends bictegravir/tenofovir alafenamide/emtricitabine as an alternative to dolutegravir-based regimens. This alternative option allows pregnant women to consider a simplified single-tablet regimen, representing a substantial step toward prioritizing patient-centered care.

Since 2022, data from studies such as D2EFT and VISEND have reinforced the safety and efficacy of dolutegravir with 2 nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs) in the setting of resistance to the latter agents, provided there is no integrase strand transfer inhibitor (InSTI) resistance, consistent with prior data from the NADIA study.[4-6] Bictegravir/tenofovir alafenamide/emtricitabine is also recommended in this setting, despite not having been formally studied in this patient population—another effort by the panel toward simplification. Notably, the consideration of combining a second-generation InSTI with a boosted protease inhibitor has been omitted, despite recent evidence of possible superiority to dolutegravir with recycled NRTIs; this combination remains an important option for individuals in whom NRTIs may not be appropriate.[4] In efforts to simplify switch strategies, especially for patients who continue multiclass, complex regimens, the panel added a new box highlighting the potential utility of dolutegravir with tenofovir/emtricitabine or bictegravir/tenofovir alafenamide/emtricitabine, regardless of underlying NRTI resistance, when the InSTI remains fully active.

The panel continues to highlight the role of long-acting cabotegravir/rilpivirine for individuals with virologic suppression, however, emphasizing that access to this novel therapy is limited in resource-constrained settings, including for those who might benefit the most. Additionally, the panel supports the use of long-acting cabotegravir/rilpivirine for select patients with active viremia due to adherence challenges with oral ART. The guidelines make the somewhat unorthodox—but much-needed—recommendation to refer persons with viremia and adherence challenges to available studies of long-acting agents, a throwback to times in which studies were the best option for antiretroviral access. The call for participating in research as standard-of-care rather than direct implementation in new populations has been an important component of ethically advancing new treatments during recent pandemics, and we applaud the endorsement here to ensure equity for marginalized populations with HIV.[7]

A new dedicated section acknowledges the effect cancer has on people living with HIV, with recognition that infection-related cancers disproportionately affect these patients. The ANCHOR trial demonstrated the importance of recognizing and acting on high-grade anal squamous cell atypia to prevent progression to carcinoma, because incidence remains several-fold greater in people living with HIV than in the general population, despite ART.[8] The panel supports anal cancer screening; however, it does so without clear and specific guidance regarding strategies. The guidelines further emphasize that such screening requires access to high-resolution anoscopy, which is limited in many US clinics, and data on recommended timing of screening initiation—and frequency of such assessments when high-resolution anoscopy is available—requires further research.

The cardiovascular section has also been expanded, rightly so due to the practice-changing outcomes of the REPRIEVE trial.[9] This trial demonstrated a roughly one-third risk reduction of major adverse cardiovascular events in people living with HIV who had no other indication for statin therapy at baseline. The panel also addressed a common discussion among patients and clinicians regarding the challenging and conflicting data related to weight gain, diabetes, and hypertension risk associated with ART, especially second-generation InSTIs. While these guidelines have emphasized the importance of cardiovascular health and cancer screening, they no longer include the previously

included section on aging in people living with HIV that had focused on the importance of these comorbid conditions, as well as highlighting other relevant concerns such as polypharmacy and screening for bone health, neurocognitive decline, and frailty; importantly all of these recommendations are incorporated in the updated HIV management guidelines.[10]

New recommendations were put forth on ART management in individuals being treated for latent tuberculosis infection. While current management of latent tuberculosis infection has focused on shorter treatment options, these strategies have been limited in those receiving ART due to drug-drug interactions. Guidelines now summarize new pharmacokinetic data that support the role of simplified dosing for InSTIs when used in combination with rifamycins, including once-daily dolutegravir-based ART in those receiving the often-preferred regimen of weekly isoniazid plus rifapentine for 12 weeks.

Advances in HIV prevention are another area of focus in the guideline. Oral regimens and long-acting cabotegravir remain vital options for PrEP. Excitingly, new data and proposed recommendations are also included for the anticipated approval of lenacapavir PrEP based on recently reported data from PURPOSE 1 and PURPOSE 2.[11] This option, if approved, has the potential to be transformative in supporting the goals of ending the HIV epidemic. However, the guidelines emphasize that despite these advances, new strategies for prevention will only be effective and have an impact on the global pandemic if equitable access is achieved, requiring continued advocacy.[12] There was a notable change in recommendations for people receiving long-acting cabotegravir, no longer endorsing routine HIV RNA testing at every dose as currently recommended by the US Centers for Disease Control[13] and instead recommending rapid antibody with antigen/antibody testing. The panel's deviation from the current recommendation is based on emerging data as well as recognition that requiring RNA testing may be a barrier to PrEP use. Last, the panel strengthened guidance on the use of doxycycline postexposure prophylaxis for men who have sex with men and transgender women. Although a trial in cisgender women did not show efficacy, the panel recommended selected usage in all people with potential exposure, recognizing that the lack of benefit in the trial for cisgender women was likely driven by low adherence.[14] The increasing incidence of syphilis, especially congenital syphilis, in the US makes this recommendation particularly noteworthy.

Two additional sections from the prior guideline were removed in the new version—those dealing with COVID-19 and mpox, both significant infections that disproportionately affect people living with HIV, especially those with advanced disease. While clinicians may welcome a respite from the recent moment-to-moment changes in epidemic updates, mpox has made a resurgence in 2024. Vaccinations for those with exposure potential to mpox should be prioritized, especially persons with advanced or untreated HIV.[15] Similarly, people living with HIV should be encouraged to receive updated COVID vaccinations.

The 2024 International Antiviral Society–USA panel's recommendations for treatment and prevention of HIV provide significant updates and advancements in the field. The focus on pharmacoequity, combined with a push for simplifying treatment regimens and laboratory testing, brings closer a future of comprehensive and equitable care for people living with HIV.

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