HIV Treatment at IDWeek 2024

Author:	Maurice Policar[1] 1. New York City Health and Hospitals/Elmhurst, New York, USA

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AT IDWeek 2024, held in Los Angeles, California, researchers converged from across the world to discuss the latest research surrounding HIV prevention and the most effective treatment for people with HIV (PWH).

LONG-ACTING INJECTABLE MEDICATION

The use of long-acting injectable medication (LAI) for the treatment of HIV infection was featured in many abstracts and presentation discussions at the event. Some addressed the (off label) use of bimonthly injectable cabotegravir/rilpivirine (CAB/RPV) for patients who were not virally suppressed. Although these agents have proven to be effective, original studies and FDA approval support their use only in people who have achieved viral suppression with oral agents.

Tara Vijayan, UCLA Health, Los Angeles, California, suggested the use of LAI as a possible intervention to help re-engage struggling patients, while at the same time emphasizing that this should ideally be coupled with intensive case management and addressing mental health, substance use, and other social issues.[1]

Elizabeth Hastie, University of California, San Diego, reviewed the interim results of the ongoing LATITUDE study, which showed that LAI in patients with adherence issues achieved a 14% lower failure rate compared with oral regimens. She also presented the results of a study from her clinic (Abstract 157), which showed a >80% suppression rate at 24 and 48 weeks for viremic patients with adherence issues who were treated with CAB/RPV.[2]

These and other recent series suggest that CAB/RPV may be used for select people who are not virally suppressed, as a means of overcoming adherence issues seen with daily oral treatments. This has helped to balance some of the concerns about possible resistance that can occur with missed doses of long-acting agents. It is extremely important to note that positive outcomes have been demonstrated only in settings which provide intensive medical case management and extensive support for social issues. It is also unclear if similar outcomes can be achieved with patients who have higher baseline viral loads. In Hastie's cohort, patients with viral loads over 10,000 were also treated with additional agents at the time of CAB/RPV initiation, some with lenacapavir (LEN). In the LATITUDE study, participants were offered financial incentives as motivation to complete an oral induction phase leading to viral suppression, before starting CAB/RPV.

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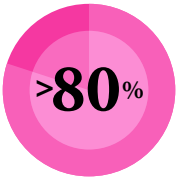

Poster 558, presented by James Brock, University of Mississippi Medical Center, Jackson, described nine patients with viremia, and with resistance-associated mutations to CAB or RPV, who were treated with LEN injection every 6 months along with bimonthly CAB/RPV. From a mean baseline viral load of >36,000, all patients maintained a viral load <200 for at least 26 weeks.[3]

Susan Koletar, Ohio State University, Columbus, reviewed results of a trial by Eron et al. evaluating the efficacy of LEN plus two different broadly neutralizing antibody preparations, all administered parenterally twice yearly. At least 90% maintained viral suppression at 6 months.[4]

Since many patients we treat today are older and have one or more comorbidities, reducing the pill burden by one tablet may not be much incentive to take bimonthly injections. Extending the interval to every 6 months may sway some patients to opt for LAI administered at the time of routine clinic visits.

HIV PREVENTION (PrEP)

Colleen Kelley, Emory University, Atlanta, Georgia, presented an updated analysis of studies examining the use of twice-yearly LEN injections as pre-exposure prophylaxis (PrEP), in cisgender women (PURPOSE 1) and in men who have sex with men, transgender individuals, and non-binary individuals (PURPOSE 2). Impressive results suggested 100% and 96% efficacy, respectively.[5]

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Koletar reported on the pharmacokinetics of a new formulation of ultra long-acting cabotegravir/rilpivirine, which suggests effectiveness with extended dosing intervals of every 4 months.[4]

Raphael J. Landovitz, University of California, Los Angeles, warned of the rare Long-acting Early Viral Inhibition (LEVI) Syndrome; a masking of the symptoms of acute HIV infection and possible suppression of HIV RNA and HIV Ab in persons with undiagnosed HIV infection using CAB for PrEP. Appearance of HIV Ab may be delayed up to 24 months.[6]

LAI PrEP is an incredibly effective tool for HIV prevention, but one that is costly and requires additional staff resources. It will be challenging to overcome disparities in access to LAI PrEP that exist in the US and globally.

TWO DRUG ANTIRETROVIRAL REGIMENS

The longstanding dogma of needing at least three drugs to effectively treat HIV infection is slowly giving way to a new paradigm. The inclusion of more potent integrase inhibitors has permitted the successful use of two-drug regimens to achieve viral suppression in many PWH.

In an interesting session formatted as a debate, speakers defended their position for or against switching virally suppressed PWH to two-drug regimens. Amesika Nyaku, Rutgers New Jersey Medical School, Newark, argued that we should routinely consider switching to two drugs in selected patients (who are not infected with the hepatitis B virus and who have no viral resistance to these agents), recounting a great many studies that revealed non-inferiority of dolutegravir + lamivudine, dolutegravir + rilpivirine, and CAB/RPV when compared with three-drug regimens.[7] Arguing against this approach was Darcy Wooten, Washington University in St. Louis, Missouri, maintaining that you don't want to "rock the boat"; and by doing so, you run the risk that something could go wrong: adverse events, insurance issues, new drug-drug interactions. She suggested that real-world results may not have the same outcomes seen in these clinical trials and that we have decades of experience with three-drug regimens.[8]

When switching from three to two drug regimens, we are usually removing tenofovir, which has been associated with renal and bone toxicity. Some would argue that using tenofovir alafenamide is safe and results in less tenofovir exposure than tenofovir dipivoxil fumarate. For PWH treated with abacavir + dolutegravir + lamivudine, a decision to change to a two-drug regimen may be a less complicated choice given that abacavir has at times been associated with an increased risk of cardiac events.

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CARDIOVASCULAR DISEASE RISK CALCULATORS FOR PEOPLE WITH HIV

Poster 434 was presented by Caitlin Bettger, Brooke Army Medical Center, Fort Sam Houston, Texas, whose team compared several atherosclerotic cardiovascular disease (ASCVD) risk calculators in a population of 134 PWH seen between 2006–2019 who had known ASCVD events. They applied four risk calculators, including a newly published HIV-CARDIO-PREDICT, at 10, 5, and 2 years prior to the ASCVD event. HIV-CARDIO-PREDICT had the highest percentage of high-risk participants at any given time interval (>90%), performing significantly better than the other 3 more commonly used risk calculators.[9]

> **The REPRIEVE trial suggested benefits from statin use in lowering the risk of major cardiovascular events in PWH between ages 40–75 years**

Evidence from the REPRIEVE trial suggested benefits from statin use in lowering the risk of major cardiovascular events in PWH between ages 40–75 years, and resulted in updated recommendations for statin use in this group. The treatment group had a 35% lower rate of events over 5 years in comparison with placebo, despite a median 10-year ASCVD risk score of only 4.5%. The availability of a more accurate risk calculator for PWH might allow us to better stratify risk for individuals within this group. More evaluation is needed to clarify the predictive ability of these calculators.

TREATMENT OF *PNEUMOCYSTIS JIROVECII* PNEUMONIA

Amy Bethel Peralta-Prado, Research Centre of Infectious Diseases, Instituto Nacional de Enfermedades Respiratorias, Mexico City, Mexico, described a randomized open-label trial in PWH and *Pneumocystis jirovecii* pneumonia (PCP). This compared the conventional 21-day steroid regimen with a shortened steroid regimen of 8 days for moderate and 14 days for severe PCP. There was no difference between the two groups in the incidence of immune reconstitution inflammatory syndrome, mechanical ventilation, mortality, respiratory function testing, baseline and 90-day viral load, and CD4. The shortened steroid regimen group had a shorter hospital stay (12 versus 18 days).[10]

Although this was a small study of only 44 participants, it suggested non-inferiority for a shorter regimen of steroids, a meaningful change in the approach to PCP treatment for the first time since the early HIV epidemic. Given the advances made in the treatment of HIV since that time, using shorter courses of steroids is logical.

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