

NMAC @ CROI 2026: Staff Takeaways

Clinical Highlights

by Moisés Agosto

Aging and HIV related comorbidities

As the global HIV population ages, concerns about brain health, dementia, and neurodegenerative disorders persist. While life expectancy has improved, cognitive decline risks remain, and more research is needed on how aging and HIV affect brain health, considering multiple factors.

Presentations reviewed current knowledge of brain health and dementia risk in aging individuals with HIV, addressed misconceptions, and highlighted new insights for those on antiretroviral therapy (ART).

An integrated approach is needed for brain health in older individuals with HIV. Clinical teams must distinguish between HIV-related and age-related causes when cognitive symptoms arise. Comprehensive assessments should cover physical, mental, and social well-being. Screening tools like the Montreal Cognitive Assessment (MoCA, a test that evaluates different types of thinking abilities) and Mini-Mental State Examination (MMSE, a brief questionnaire used to screen for cognitive impairment) help identify impairment. The 'treatable traits' model targets modifiable risks, while individualized care and support for independent living remain priorities.

Comorbidities, Aging, and Multimorbidity

Presentations showed that aging and multiple health conditions significantly affect people with HIV. As life expectancy increases, clinical focus is shifting to managing long-term comorbidities.

Many aging individuals with HIV have at least two chronic conditions. These include cardiovascular disease, diabetes, kidney disease, osteoporosis, frailty, or cognitive impairment. Evidence shows that multimorbidity appears earlier in people with HIV than in those without.

Immune Activation

Despite effective antiretroviral therapy (ART), ongoing immune activation continues to cause health complications. CROI 2026 reported higher levels of inflammatory markers,

including IL-6 and CRP, linked to increased risk of cardiovascular disease, frailty, and functional decline.

Persistent immune activation due to cytomegalovirus (CMV), a common virus that causes lifelong infection after initial exposure, could worsen multimorbidity in individuals with HIV. The association between CMV Immunoglobulin G (IgG, a type of antibody indicating prior CMV exposure) levels and the presence of multiple health conditions was examined using data from the POPPY study (a study of older people with HIV).

People with HIV and high CMV IgG levels are at greater risk for neuropsychiatric, musculoskeletal, and cancer-related comorbidities. Assessing CMV IgG levels can help identify patients who need closer monitoring and older adults with HIV or those with multiple comorbidities.

Cardiovascular disease (CVD)

As the HIV-positive population ages, heart disease becomes more common. Presentations noted higher rates of atherosclerosis and heart failure. They stressed the need to manage blood pressure, cholesterol, and tobacco use. Preventive approaches, such as statin therapy, were discussed.

Major Adverse Cardiovascular Events (MACE)

Major adverse cardiovascular events (MACE, serious heart-related events such as heart attack, stroke, or cardiovascular death) are more prevalent among individuals with HIV. The REPRIEVE trial (a large study looking at heart disease prevention in people with HIV) demonstrated a 36% reduction in such events with pitavastatin therapy. Associations between biomarkers and cardiovascular events in asymptomatic individuals remain unclear. Inflammatory and cardiac biomarkers were associated with these events, even among statin-treated patients, supporting the utility of risk assessment tools.

Hypertension and Statins

Hypertension is a major risk for cardiovascular disease. Statins lower blood pressure in the general population, but limited data exist for people with HIV. The REPRIEVE trial found that pitavastatin reduced hypertension risk. However, new hypertension still raises cardiovascular risk even on statins. Continued blood pressure monitoring is required.

CROI 2026 presentations addressed polypharmacy (the use of multiple medications by a patient) and management strategies. Older adults with HIV often need multiple medications, raising the risk of drug interactions. The complexity of HIV management

increases with additional chronic conditions. Experts agreed that HIV care for older adults must be customized to these problems. To manage polypharmacy effectively, regular medication assessments should be conducted to evaluate the necessity, safety, and potential interactions of each drug. Additionally, involving a multidisciplinary healthcare team, including pharmacists, in routine care can optimize medication regimens, reduce unnecessary medications, and support individualized care plans for older adults with HIV.

Research highlighted how frailty and aging affect physical function and quality of life in people with HIV. Early screening for cardiovascular and metabolic conditions, careful review of drug interactions, and age-appropriate assessments are recommended. Comprehensive care should prioritize inflammation, modifiable lifestyle risks, and overall quality of life.

CROI 2026 emphasized moving HIV care beyond viral suppression to address aging and chronic comorbidities. Long-term survivors need comprehensive care focused on overall health, daily functioning, and equal access to services.

HIV Therapies

Long-acting antiretroviral treatments with reduced dosing frequency, including once-monthly dosing, are increasingly used. Recent data show HIV therapies with extended dosing intervals. Investigational very long-acting treatments are under evaluation. Antibody-based therapies are also being studied. These new therapies yield promising results.

The EMBRACE study found that intravenous CAB LA every four months maintained viral suppression in 94% of participants at 12 months. These long-acting regimens are not yet routine. However, they suggest a future with fewer dosing visits and more options beyond daily pills.

Studies evaluated long-acting HIV integrase inhibitors, which are a class of drugs that prevent HIV from integrating its genetic material into the host cell's DNA. These agents may be less prone to resistance and provide durable treatment options. Long-acting CAB/RPV (a combination of cabotegravir and rilpivirine) has shown usefulness in people with adherence challenges.

The LATITUDE Phase 3 trial (a late-stage study testing long-acting injectable HIV therapies) found long-acting (LA) CAB/RPV injections noninferior to daily oral ART in

people with adherence challenges. Regimen failure at 48 weeks was 22.8% for LA and 41.2% for oral therapy; virologic failure was 6.8% for LA and 28.2% for oral. Adverse events were similar, mostly injection-site reactions, leading to two discontinuations. For patients with adherence barriers, LA CAB/RPV reduces risk with support. In adolescents (IMPAACT 2017/MOCHA, a clinical study in young people), every-8-week CAB/RPV was effective, with 94.4% maintaining viral suppression at week 96, and over 97% preferring injections. Expanded LA ART use in pediatric and adolescent populations will require adjustments to clinic workflows.

In addition to long-acting therapies, treatment simplification with single-tablet regimens (combining all necessary HIV medications into one pill) was also a focus at CROI 2026.

Bictegravir/Lenacapavir (BIC/LEN, an integrase inhibitor and a capsid inhibitor, administered as a single tablet) demonstrated efficacy comparable to that of existing regimens. In a switch study, week 48 HIV-1 RNA ≥ 50 copies/mL was observed in approximately 1% of patients in both groups, indicating equivalent virologic suppression.

If approved, this could simplify treatment, especially for people on complex regimens, including many older adults who take multiple medicines.

Doravirine/Islatravir (DOR/ISL, a two-drug daily regimen combining doravirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI), and islatravir, a nucleoside reverse transcriptase translocation inhibitor (NRTTI)), was found to be noninferior to the current standard at 48 weeks in a Phase 3 study: 91.8% (DOR/ISL) versus 90.6% (BIC/FTC/TAF, a single-tablet regimen with bictegravir, emtricitabine, and tenofovir alafenamide). Merck, the producer of doravirine and islatravir, a two-drug daily regimen, has announced an anticipated FDA decision on the New Drug Application (NDA) for adults with suppressed HIV on stable ART by April 28, 2026.

If approved, DOR/ISL would expand single-tablet regimen options, with standard considerations for resistance, drug interactions, and patient preferences.

HIV Cure Research Progress

Updates from the first clinical HIV cure program in South Africa included genetic data and long-term viral control results from the FRESH group, demonstrating ongoing progress toward scalable cure strategies. Continued HIV cure research, including new interventions and genetic studies, was reported, along with progress toward realistic applications of early cure research programs.

GLP-1 and HIV

A major session led by Todd Brown (Johns Hopkins) examined the expanding use of GLP-1 receptor agonists (such as semaglutide and tirzepatide) beyond diabetes and obesity. GLP-1 agents are increasingly recognized for their effects on multiple physiological systems, including HIV-related comorbidities, inflammation, aging, and cardiovascular disease. The session explored whether these drugs are becoming comprehensive 'whole-body therapies' rather than being limited to weight management.

Evidence confirms the health benefits of GLP-1 receptor agonists in people with HIV, including weight loss and improved glycemic control. Tirzepatide and semaglutide have shown efficacy in clinical trials and real-life settings for type 2 diabetes and obesity. These agents may reduce weight gain from antiretroviral therapy and are especially helpful for older adults with HIV, who are at higher risk for diabetes.

GLP-1 drugs may also lower inflammatory markers before significant weight loss, which is notable given the role of chronic inflammation in cardiovascular disease, frailty, and other HIV-related complications. Persistent inflammation in people with HIV is driven by latent viral reservoirs and prolonged ART exposure, making GLP-1s potential therapies for both immune modulation and metabolic health. GLP-1 receptors are found on immune cells, and early evidence suggests possible immunological effects in the gut, a key site of HIV persistence. These findings suggest GLP-1s may benefit HIV management, immune function, and gut health, though these uses are still under investigation.

GLP-1 receptor agonists are established for reducing cardiovascular risk and improving metabolic health in the general population, and are increasingly considered for aging-related complications in HIV. GLP-1 receptor agonists may have potential in treating substance use disorders. They appear to affect neural pathways involved in craving and reward, which may help with weight management and with alcohol use, drug dependence, and smoking cessation.

CROI 2026 underscored the dedication and resilience of HIV clinicians and researchers in confronting challenges posed by political and ideological opposition to scientific progress. Activist Peter Staley's opening plenary was a prominent highlight, delivering a persuasive call to action for the scientific community. He reflected on ACT UP's historical activism and addressed contemporary threats to scientific integrity, eliciting a standing ovation from leading HIV clinicians and scientists.

HIV Prevention Takeaways

by Damián Cabrera

PREVENIR Study

The PREVENIR study followed over 3,000 participants in Paris, primarily gay men and transgender women. Participants could use PrEP either daily or on demand before potential HIV exposure. Many transitioned between these regimens based on their needs, demonstrating the strategy's flexibility.

The study identified a low incidence of new HIV cases (approximately 0.1% per year), demonstrating that both daily and event-driven PrEP are effective when adhered to as prescribed. HIV infection typically occurs when PrEP use is discontinued, emphasizing the importance of maintaining adherence. Switching between PrEP methods highlights the value of offering flexible prevention options.

The study identified divergent trends: a reduction in HIV cases among individuals born in France and an increase among migrant populations. These findings reveal inequitable access and highlight the necessity for tailored prevention strategies. Advocacy efforts may include supporting multilingual outreach, engaging migrant organizations to disseminate targeted information, and ensuring culturally responsive healthcare delivery. Addressing systemic barriers such as language and transportation and integrating prevention services within migrant communities can enhance equitable benefits from new interventions.

PURPOSE 1 & PURPOSE 2 Trials

These studies compared lenacapavir injections every six months to daily oral PrEP (F/TDF). PURPOSE 1 looked at cisgender women, while PURPOSE 2 included men who have sex with men, as well as trans and nonbinary people. In PURPOSE 1, it showed a 96% reduction in HIV risk vs daily PrEP, while in PURPOSE 2, it showed an 88% reduction.

There were five new HIV cases. In some of these, researchers identified mutations in the virus (e.g., N74D and Q67H+K70R) that reduced the drug's effectiveness. This is called drug resistance, which happens when the virus changes so the medicine no longer works as well, often when drug levels drop or after long breaks without medication.

Both trials included diverse participants, making the research more useful for all affected by HIV and supporting more equitable prevention strategies. Inclusive research helps identify unique challenges and supports fairer approaches.

PURPOSE 365 Trial (Once-Yearly Lenacapavir for PrEP)

PURPOSE 365 is a forthcoming trial designed to evaluate lenacapavir as a once-yearly PrEP intervention. The study will enroll approximately 300 participants, all of whom will receive the investigational regimen.

The dosing plan is based on studies of how the drug distributes in the body (called pharmacokinetics) to determine the optimal protective dose. Participants will get a 3000mg injection once a year, plus 600mg pills on the first two days to reach protective levels.

This builds on PURPOSE 1 and 2, where long-acting doses offered strong protection, particularly for people struggling with routine use.

MK-8527 Monthly Oral PrEP

MK-8527, a once-monthly oral PrEP agent, is advancing to large-scale Phase 3 testing. (EXPrESSIVE study).

A monthly 11mg dose maintained protective plasma concentrations in at least 95% of participants, including pregnant individuals and adolescents. "Protective drug level" means the amount of medicine in the body needed to prevent HIV infection.

The study found that MK-8527 maintained protective levels even with delayed dosing, demonstrating flexibility.

Dose determination was informed by prior safety and pharmacokinetic studies, supporting continued evaluation of efficacy in further research.

Once-a-year HIV prevention & contraception implant

In addition to oral and injectable regimens, a novel implant capable of concurrent HIV and pregnancy prevention was discussed as a potential innovation.

At present, this implant has only been evaluated in animal models. Preclinical results indicate sustained drug levels and a favorable safety profile, with only mild adverse events reported.

For women, teenagers, and those with complex needs, a one-time implant could offer year-long protection.

SEARCH Study

This study in rural Kenya and Uganda combined home HIV testing, treatment, PrEP, and digital tools (including mobile apps for tracking, scheduling, and info sharing), which reduced care delays and increased prevention uptake.

After a two-year follow-up period, communities receiving the intervention experienced an approximately 70% reduction in HIV incidence. Increased utilization of prevention tools significantly impacted outcomes. The uptake of PrEP and PEP was approximately 4 times higher in communities that received the intervention.

In conclusion, these studies, taken together, demonstrate progress, but access and choice remain at the heart of real change. Moving forward, advocates should share these results, work with local partners, and encourage policies that make prevention widely available. By putting these insights into action, we can help ensure no one is left out and move closer to ending HIV.