

CROI 2022 Overview

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Treatment Action Group

CROI 2022: Global Advocates Offer Insights and Directions on the Science and Next Steps Needed, April 27, 2022

Margarita Breakfast Clubs

- [How New ARVs are Rewriting the Script for HIV Prevention and Treatment](#) - Dr. Chloe Orkin, February 14, 2022
- [River Deep, Mountain High: Pathways Toward a Cure for HIV](#) - Dr. Katharine Bar and Moses Supercharger, February 16
- [Aging with HIV: Frailty, Comorbidities and a Call to Action](#) - Dr. Kristine Erlandson and Jules Levin, February 22
- [Rings and Injectable Things: Moving from options to choices for HIV prevention in cisgender women](#) - Drs. Sinead Delany-Moretlwe and Kenneth Ngunjiri, February 23
- [Long COVID: What We Know, What We Need to Know, and What We Need to Do](#) - Dr. Steve Deeks and JD Davids, February 24

Long-acting therapies: Cabenuva

Treatment : LA CAB+ RPV

↻
SUPPRESSED SWITCH



CAB +RPV LA :
Non-inferior to daily oral ART
Q2M non-inferior to Q1M dosing

Efficacy:

Non inferior to oral therapy at 48, 96 and 124 weeks

Adverse events (AE's):

2% AE-related withdrawal rate
Mild/moderate in severity
Injection Site Reactions (ISR's) reduced over time

Virological failure rate:

1-15%

Resistance:

Usually to two classes and mostly in first year

Oral Lead in:

Can be used with or without without oral lead in

Preference :

9 out of 10 patients preferred it to oral therapy

Swindells S, et al. N Eng J Med 2020;382:1112-232.

Orkin C, et al. N Eng J Med 2020;382:1124-353.

Overton ET, et al. CROI 2020. Oral 3334.

Overton et al abstract 479 CROI 2022.

Long-acting therapies: Cabenuva

- Virologic failure more common with bimonthly vs. monthly dosing
- After three years, 11 cases in bimonthly vs. 2 in monthly
- Equates to a 1/40 chance of failure after three years for bimonthly vs. 1/100 for monthly
- About half the cases in Russia, risk increased by local HIV variant (A6)
- Most cases required switch to protease inhibitor regimens

Long-acting therapies: Lenacapavir

- ~1 year of follow up reported from CAPELLA trial (extensive treatment experience) and CALIBRATE trial (first-line treatment)
 - CAPELLA: 83% of recipients maintained undetectable viral loads, average CD4 T cell count increase 83 cells, no serious adverse events (SAEs); the most common side effect was injection site reactions
 - CALIBRATE: High rates of viral load suppression (>85%), average CD4 T cell count increase 219 cells. No SAEs, most common side effects injection site reactions (3 discontinuations), headache & nausea (both 13% of participants reporting)
- Resistance documented in 2/157 recipients, both re-suppressed with integrase inhibitor regimens

NADIA trial

Efficacy and safety of dolutegravir or darunavir in combination with lamivudine plus either zidovudine or tenofovir for second-line treatment of HIV infection (NADIA): week 96 results from a prospective, multicentre, open-label, factorial, randomised, non-inferiority trial

Nicholas I Paton, Joseph Musaazi, Cissy Kityo, Stephen Walimbwa, Anne Hoppe, Apolo Balyegisawa, Jesca Asienzo, Arvind Kaimal, Grace Mirembe, Abbas Lugemwa, Gilbert Ategeka, Margaret Borok, Henry Mugerwa, Abraham Siika, Eva Laker A Odongpiny, Barbara Castelnuovo, Agnes Kiragga, Andrew Kambugu for the NADIA Trial Team

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[https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018\(22\)00092-3/fulltext](https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00092-3/fulltext)

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NADIA trial

Week 96 conclusions

- **DTG + 2NRTIs gives durable suppression second line, even if no 'active' NRTIs**
 - Supports WHO recommendation for DTG use in second-line
 - Supports safety of programmatic switch to DTG if no pre-switch VL/resistance testing
- **DTG resistance is a concern**
 - Impact on individual and programme outcomes uncertain
 - Low threshold for additional counselling/adherence support may help to mitigate
 - Using TDF/3TC (not AZT/3TC) may decrease risk
- **DRV/r + 2NRTIs has equivalent efficacy to DTG + 2NRTIs, without resistance**
 - Preferred alternative to DTG in second-line
- **TDF/3TC vs ZDV/3TC**
 - Maintaining TDF/3TC **superior** to switching to ZDV/3TC: VL suppression, rebound (& resistance?)
 - Guidelines recommending switch from TDF/3TC to ZDV/3TC in the Public Health Approach should be reconsidered

Scientists have possibly cured HIV in a woman for the first time

Following a cutting-edge treatment four years ago, the “New York patient” is now off of HIV medication and remains “asymptomatic and healthy,” researchers say.

Patient Possibly Cured of HIV Infection by Special Stem-Cell Transplant

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Stem cell transplant specialists Dr. Koen Van Besien, left, and Dr. Jingmei Hsu, center, and infectious disease specialist Dr. Marshall Glesby, right, led a clinical trial at Weill Cornell Medicine that has possibly cured a patient of HIV. Credit: Benjamin Ryan/NBC News @benryanphotos

A Woman Is Cured of H.I.V. Using a Novel Treatment

She's the third person ever to be cured. Researchers announced that the new approach holds the potential for curing more people of racially diverse backgrounds.

HIV cure case

- A middle-aged woman of mixed race living with HIV was diagnosed acute myelogenous leukemia (AML)
- Required a stem cell transplant, which aim to generate a new, cancer-free immune system from donor stem cells
- Doctors used a combined stem cell transplant approach:
 - Adult stem cells from a relative
 - Stored umbilical cord blood units from a donor with a rare mutation that makes cells resistant to most HIV strains (CCR5 Δ 32 mutation)

HIV cure case

- Donor stem cells generated a new immune system, and after 55 days 100% of cells were derived from the cord blood donor with the CCR5 Δ 32 mutation
- Cancer successfully treated and in remission
- ART was interrupted three years after the stem cell transplant with no HIV viral load rebound for >14 months
- HIV genetic material (DNA) not detectable by ultra-sensitive tests (apart from trace amounts at one early timepoint)
- Antibodies against HIV are no longer detectable
- Immune system cells resistant to HIV infection in lab studies

Broadly neutralizing antibodies (bNAbs)

- Two studies reported that dual bNAb administration associated in small but significant declines in the intact HIV reservoir measurable in blood
- Three examples of long-term control of HIV viral load for an extended period after receipt of dual bNAbs
- Dual bNAbs in infants kept viral load undetectable for 12 weeks in 11 of 15 (44%) of cases after ART interruption
- Baseline HIV resistance to bNAbs a key issue, may require resistance testing prior to administration
- One abstract reporting bNAb VRC07-523LS can safely be given to newborns, unclear if issue of resistance could limit use for prevention of breastfeeding HIV transmission

Pediatric: IMPAACT P1115

- Ongoing study evaluating potential for HIV remission in early-treated infants
- 33% met criteria for potentially undergoing an ART interruption after two years (undetectable viral load, negative HIV-1 antibody tests, and undetectable HIV DNA)

HIV & aging

- Marc Thompson's Martin Delaney Presentation: [We're Still Here: HIV, Aging, and the Invisible Generation](#) cited eight key concerns:
 - The impact of HIV on aging and vice versa
 - Threats to the continuity of care e.g. less specialist care, not equipped to manage HIV/aging issues
 - Experiencing comorbidities and non-HIV conditions e.g. CVD, diabetes, leading to diverse medical care needs
 - Polypharmacy, including interactions between HIV and other meds
 - Increased need for community-based support services: physical, emotional, social, including housing, transportation
 - Persistent loneliness and isolation
 - Heightened concerns about stigma and discrimination, including when dealing with inexperienced providers (race, gender, sexuality, age)
 - Quality of life and aging well: **"after decades of surviving we want to continue to survive, but we also want to thrive"**

HIV & aging

- A study reported that people with HIV in the San Francisco and Boston areas had a 60% greater risk of a heart attack over five years of follow up compared to HIV-negative people in the period 2010-2017 (1.2% vs 0.9%) compared to 2005-2009 (1.1% in both groups)
- Receipt of anticholinergic drugs, including codeine, citalopram, loperamide and amitriptyline, was associated with frailty and recurrent falls in the UK POPPY study of PWHIV >50 years of age
- A poster presentation described positive effects of a class of drugs called senolytics on parameters related to cellular senescence in lab studies, “suggesting that these drugs could be useful to reverse cellular senescence in PLWH”
- NATAP Webinar: Aging, Comorbidities, & HIV: CROI Update:
https://event.webcasts.com/starthere.jsp?ei=1518394&tp_key=231458b0f5

The ANCHOR study

- 10,723 people with HIV aged ≥ 35 in US screened for high-grade squamous intraepithelial lesions (HSIL) using anal Pap smears (cytology) and high-resolution anoscopy
- 4446 people with HSIL identified, randomized to receive either immediate treatment or active monitoring
- Median age 51, 80% men, 16% women, 3% transgender, 33% White, 42% Black, 16% Latino
- Nine people in the immediate treatment arm and 21 in the active monitoring arm were diagnosed with invasive anal cancer (a 57% reduction in risk)
- Study lead Professor Joel Palefsky: “I think the data support inclusion [of screening and treatment] in the standard of care for people with HIV over 35”

The REACH study

- Assessed the safety and acceptability of the monthly dapivirine vaginal ring and Truvada PrEP in adolescent girls and young women
- Study gave the ring and Truvada PrEP, each for six months, and then for the final six months participants could decide which one to use or to use neither
- Nearly all (98%) of the 227 participants who took part in the choice period opted to use one of the two HIV prevention products being offered
- Of these, 67% chose to use the ring and 31% chose to use PrEP – only 2% didn't want to use either.
- Most participants used their product of choice some or most of the time

Tuberculosis

- TB-PRACTECAL: “24 week all oral regimens containing a backbone of bedaquiline, pretomanid and tapered dose linezolid are both safe and efficacious in the treatment of rifampicin-resistant tuberculosis”
- ACTG A5375: Dose adjustment of levonorgestrel for emergency contraception (1.5 to 3mg) required in women receiving rifampicin for TB
- Long-acting TB drugs in development

COVID-19

- Long COVID may be more common in unvaccinated people with HIV, associated with inflammatory biomarkers
- Vaccine boosters efficacious in preventing death among immunocompromised populations
- In an Italian study, an additional dose of mRNA vaccine boosted antibody responses in people with HIV, although the risk of lower antibody titers was somewhat greater in people with CD4 T cell counts <200