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hiv treatment bulletin (e)

Ukraine invaded, CROI 2022 (1 March 2022)

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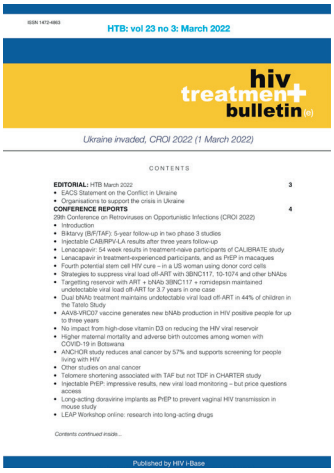
EDITORIAL



We start this issue of HTB by including the EACS statement on the war in Ukraine, now escalated to a full invasion, and causing unimagined distress and loss of life.

i-Base stands with European colleagues to support efforts to relieve this suffering and in our hopes for an early peace.

We also include links for donations to verified organisations that are already responding to this crisis.

Whether you want to support military resistance or families who have fled to nearby countries, a donation is a good place to start.

We include 17 early reports from the recent Conference on Retroviruses and Opportunistic Infections (CROI 2022), held as a virtual meeting over the last two weeks.

As with every year, this meeting included much to report. This included numerous studies on current and pipeline treatments, complications, cure-related research (including a fourth case of remission after stem cell transplant), bNAbs, PrEP, COVID-19 and much more.

We also include a study on HIV and menopause and several reports related to COVID-19, including a small study suggesting that long COVID (PASC) might be more common in people living with HIV.

EACS statement on the war in Ukraine

The following statement was posted by the European AIDS Clinical Society (EACS).

It is with sadness that we have learnt about the war in Ukraine. We would like to extend our support to all our dear friends and colleagues and everyone involved, not least all the people living with HIV and their carers.

At this difficult time, we would urge that all members of EACS, as well as healthcare professionals, healthcare commissioners, the pharmaceutical industry and non-governmental organisations in Ukraine and across Europe to work together to ensure that we can provide all possible support for people living with HIV and their families to ensure:

1. Free and easy access to medical care, psychological support and medicines including antiretrovirals for the treatment initiation, continuation as well as pre-and post-exposure prophylaxis.

2. Free medical insurance for migrant populations from affected areas.

3. Easily available access for infection prophylaxis and vaccines for vaccine-preventable illnesses, including COVID-19 vaccines.

4. Full support for assistance to, and the safety of healthcare professionals providing medical assistance in affected areas.

We would strongly encourage the preparation of national plans to support PLWH migrating from affected areas and emphasise the need for their rapid implementation.

EACS will stand and work together with our members and partners at this difficult time.

Organisations for donations to support the crisis in Ukraine

The following organisations are collecting donations to help people affected by the crisis in Ukraine.

Ukraine's Ministry of Defense designated bank account to accept donations for its troops.

https://ukraine.ua/news/donate-to-the-nbu-fund/

Come Back Alive is a Ukrainian NGO that raises crypto funds for the Ukrainian army

https://savelife.in.ua/en/donate/

Nova Ukraine is a Ukraine-based NGO to support families. It provides citizens with everything from baby food and hygiene products, to clothes and household supplies.

https://novaukraine.org

The **Ukrainian Red Cross** covers many areas of support, from aiding refugees to training doctors.

https://redcross.org.ua/en/donate/

United Help Ukraine receives and distributes donations, food, and medical supplies to displaced Ukrainians, anyone affected by the conflict, and the families of wounded or killed soldiers.

https://www.facebook.com/donate/337101825010055/

Sunflower of Peace is a charity that helps paramedics and doctors with medical tactical backpacks - they have everything to preserve a person's life and get them to proper medical care alive.

https://lnkd.in/eea5g-_E

Online resource map for registering individual and organisational help you can provide:

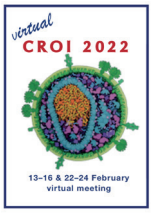
https://mapahelp.me/?fbclid=IwAR1IhRv_Mh_MoxXanX01YTk4d3ckt-n6SyPxwtyiLs4ibQyVogsnvjI_Gic

CONFERENCE REPORTS

29th Conference on Retroviruses and Opportunistic Infections (CROI 2022)

13–16 and 22–24 February 2022

Introduction



The 29th Conference on Retroviruses and Opportunistic Infections (CROI), was held from 13–16 and 22–24 February 2022.

The conference programme is now online as open access.

Although abstracts are online, webcasts will initially only be available to registered delegates for 30 days after the meeting.

https://www.croiconference.org/preliminary-agenda

A PDF file of the full programme is available:

https://www.croiconference.org/wp-content/uploads/sites/2/resources/2022/croi2022-program-abstract-ebook.pdf (PDF)

Other conference material including searchable abstracts, webcasts and posters are expected to become open access four weeks after the meeting ends.

https://croi2022.onlineeventpro.freeman.com

i-Base will post links to early reports from this holding page.

First reports from CROI 2022 are listed below.

ANTIRETROVIRALS

- Biktarvy (B/F/TAF): 5-year follow-up in two phase 3 studies
- Injectable CAB/RPV-LA: phase 3b ATLAS-2M results at three years
- Lenacapavir: 6-monthly dosing in treatment-experienced participants and as PrEP in macaques
- Lenacapavir: 54 week results in treatment-naive participants of CALIBRATE study

CURE-RELATED

- Fourth potential stem cell HIV cure – in a US woman using donor cord cells
- Strategies to suppress viral load off-ART with 3BNC117, 10-1074 and other bNAbs
- Targetting reservoir with ART + bNAb 3BNC117 + romidepsin maintained undetectable viral load off-ART for 3.7 years in one case
- Dual bNAb treatment maintains undetectable viral load off-ART in 44% of children in the Tatelo Study
- No impact of high-dose vitamin D3 on reducing the HIV viral reservoir

COMPLICATIONS, including COVID-19

- Higher maternal mortality and adverse birth outcomes among women with COVID-19 in Botswana
- ANCHOR study reduces anal cancer by 57% and supports screening for people living with HIV
- Other studies on anal cancer
- Telomere shortening associated with TAF but not TDF in CHARTER study

HIV PREVENTION

- CROI 2022: Injectable PrEP: impressive results, new viral load monitoring – but price questions access

L• ong-acting doravirine implants as PrEP to prevent vaginal HIV transmission in mouse study

OTHER NEWS

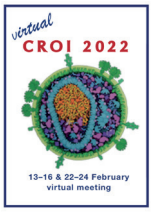
- LEAP Workshop online: research into long-acting drugs

CROI 2022: ANTIRETROVIRALS

Biktarvy (B/F/TAF): 5-year follow-up in two phase 3 studies

Kirk Taylor, HIV i-Base

Single tablet regimen B/F/TAF (bictegravir/emtricitabine/TAF) is one of the leading first line combinations in US guidelines.



CROI 2022 included a poster reporting combined 5-year follow-up in two phase 3 studies in treatment naïve individuals that either excluded HBV positive (GS-US-380-1489) or included those with HBV and/or HCV (GS-US-380-1490). Participants from 1489 and 1490 (n=506) continued onto a 96-week open label extension to evaluate on-treatment 5-year safety and efficacy. [1]

Participants were recruited form multiple centres (USA, UK, Europe, Canada, Australia, Dominican Republic and Puerto Rico) with median age 31 (range: 18 to 71), the proportion of women was low at 9% (1489) and 13% (1490), 33% were Black or African-American, whilst 24% were Hispanic/Latinx. Median body weight was 77 kg (IQR: 68 to 88 kg) and HIV-1 viral load was matched at entry.

Over 97% of participants achieved the primary endpoint of undetectable viral load (<50 copies/mL) by week 48, which was maintained through the 5-year study period. Median CD4 counts increased by 313 cells/mm^3 (IQR: 179 to 475) and 331 cells/mm^3 (IQR: 215 to 467) for participants on 1489 and 1490, respectively. Criteria for resistance testing were met for nine people but neither NRTI nor INSTI resistance were detected.

Low-grade adverse events were commonly reported and included diarrhoea (19% and 24%), headache (16% and 21%) and nasopharyngitis (18% and 19%), all in 1489 and 1490 respectively. Less than 1% of participants (n=5) withdrew from the study due to grade 3-4 adverse events linked to B/F/TAF.

Renal function testing demonstrated an initial decline of eGFR, consistent with previous reports with bictegravir (due to inhibition of tubular secretion of creatinine). No adverse renal events were reported.

Fasting lipid levels were modestly increased over five years with no change in TC:HDL.

Minimal details were included for weight changes although median cummulative weight gain was +6.1 kg. Increases after the first year were reported as comparable to the general population (0.3 to 1.5 kg/year).

Spine and hip bone mineral densities did not decrease beyond 2% across the study period, with a mean decrease of 0.29% at week 240.

These data provide important long-term safety and efficacy data for B/F/TAF.

References

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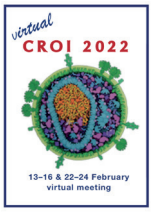
2. Pharmacokinetics and full phase 2 results for bictegravir, a new integrase inhibitor. (HTB 27 February 2017). https://i-base.info/htb/31239

Injectable CAB/RPV-LA results after three years follow-up

Kirk Taylor, HIV i-Base

Long-acting injections of cabotegravir (CAB) plus rilpivirine (RPV) are now a recommended combination in US and EU treatment guidelines based on two-monthly IM dosing.



CAB/RPV-LA is already available in Scotland and will soon be available in the rest of the UK. Long-acting therapies have many potential benefits, but drug resistance has been highlighted by BHIVA and others despite full adherence. [1, 2]

CROI 2022 included a poster of year three results from the ATLAS-2M phase 3b non-inferiority ITT-E study [2]. Participants were randomised to receive injections every four (Q4W, n=523) or eight weeks (Q8W, n=522). Participants on this multicentre study (Argentina, Australia, Canada, Europe, Korea, Mexico, Russia, South Africa and USA) were women (27%, n=280), median age 42 years (range: 19 to 83), white (73%), BMI >30 kg/m^2 (20%); 37% had previous exposure to CAB/RPV.

Non-inferiority of Q4W vs Q8W was reported based on the primary endpoint detectable viral load (>50 copies/mL at week 48) and efficacy remains high at week 152 (86-87%).

Non-inferiority was confirmed between Q4W and Q8W regimens within 4% and 10% margins for detectable and undetectable viral load, respectively. This was 3% (n=14, Q8W) vs 1% (n=5, Q4W) in the ITT-E analysis. Withdrawal rates were higher in Q4W (18%) vs Q4W (14%) with participants citing frequency of visits and intolerability of injections.

Total confirmed virologic failure (CVF) occurred in 11 and 2 for Q8W and Q4W, respectively, with two new CVF between weeks 96 to 152 on Q8W.

Both participants developed resistance associated mutations to both CAB and RPV, despite perfect protocol adherence. Viral suppression with alternative ART was achieved. Of concern, viral load at failure was approximately 24,000 and 59,000, sufficiently high to risk HIV transmission to partners who are relying on U=U for prevention.

Adverse events were similar to week 96 results.

Two new low-grade drug-related (non-ISR) adverse events were reported (lipoatrophy and pyrexia).

Treatment satisfaction scores were higher for Q8W than Q4W regimens (p=0.004).

C O M M E N T

This study confirms previous safety and efficacy data supporting a Q8W strategy, which is also much preferred by people using this option.

However, the mechanism to explain drug resistance in some participants, despite perfect adherence, has not been explained.

In a predictive model, viral failure has been associated with having two or more of the following four factors: (i) BMI >30; (ii) low RPV levels at week 8; (iii) baseline mutations to RPV; and (iv) the A1 or A6 HIV subtype (common in Russia). Of these, low RPV levels and baseline mutations are easiest to monitor and explain, as they would results in periods of effective cabotegravir monotherapy.

But the unpredictability of rebound, and the related implications for HIV transmission for people relying on U=U will involve new discussion on acceptability of risk.

Potential differences in interpatient PK related to injection technique might also be related. [4]

Other posters at CROI 2022 include early results from a phase 1/2 PK study in 23 adolescents adding either cabotegravir or rilpivirine to current active ART. Both involved oral formulations before the IM injections and reported comparable drug levels to adults. [5]

There were 2/23 discontinuations, both in the rilpivirine group. One was due to a hypersensitivity reaction to the first oral dose and one due to pain from the needle, before the full injection.

Another poster used physiologically-based pharmacokinetic (PBPK) modelling to predict that dose adjustment should not be needed during pregnancy. [6]

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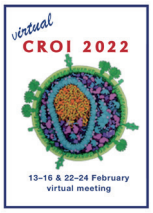
Lenacapavir: 54 week results in treatment-naive participants of CALIBRATE study

Simon Collins, HIV i-Base

Samir Gupta from Indiana University presented 54-week results on the capsid inhibitor lenacapavir in 182 treatment-naive individuals in the randomised phase 2 CALIBRATE study. [1]



The study design included randomisation to one of four open-label once-daily group (2:2:2:1), with differences in the three maintenance combinations at week 28 (Q6M LEN injections +TAF, Q6M LEN injections + bictegravir or oral LEN+F/TAF) compared to a control group of bictegravir/F/TAF (n=25); groups 1, 2, 3, and 4 respectively). [2]

Interim results were reported at IAS last year [3] and 92% subsequently achieved viral suppression at week 28.

Baseline characteristics previously reported included median age 29 years (range: 19 to 72), 93% men (7% women), 52% black, 45% Hispanic/Latinx. Median viral load and CD4 count at baseline were 4.3 log copies/mL (IQR: 3.8 to 4.7) with 15% >100,000 c/mL and 437 cells/mm^3 (IQR: 332 to 599), with only two participants <200 cells/mm^3.

The primary endpoint of viral efficacy (<50 copies/mL) was reported for 90%, 85%, 85% and 92% for groups 1, 2, 3, and 4 respectively. Viral failure was reported for 4%, 4%, 6% and 0 of the same groups, with remaining participants having missing data.

Six participants met criteria for resistance testing (1, 1, 3 and 1 in groups 1 to 4 respectively), two with resistance to lenacapavir. One participant in group 2 developed Q57H + K70R in capsid at week 10 (20-fold resistance) and one in group 3 developed Q57H alone at week 54 (7-fold). Both were reported in the context of likely low adherence to oral ART and both resuppressed using combinations of an INSTI and two NRTIs.

Lenacapavir generated similar early rapid viral suppression as the integrase inhib0otor-based control group. Minimal data was provided on CD4 count other than similar average increases of about 200 cells/mm^3 in each arm.

Tolerability was generally good and similar to oral control with headache 13% vs 12%, nausea 13% vs 4% and COVID-19 10% vs 12%, all in combined LEN vs control, respectively. There were no serious AE's related to lenacapavir, or discontinuations, other than to injection site reactions (ISRs).

ISRs were common (approximately 15% after injection 1 and 12% after injection 2, but were mainly grade 1 or 2 and caused only three participants to discontinue (all grade 1). However, nodules or hard skin persisted for over six months (median 195 and 202 days for nodules and induration respectively).

There were no clinically relevant or grade 3/4 lab abnormalities.

Other studies on lenacapavir including Week 48 results in treatment experienced participants in the CAPELLA study and use as PrEP are reported is a separate i-Base report. [4]

C O M M E N T

Lenacapavir is currently on clinical hold related to a technical concern about glass vials used in these studies. A press statement from Gilead outlines further details to resolve this. [5]

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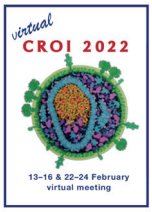
Lenacapavir in treatment-experienced participants, and as PrEP in macaques

Simon Collins, HIV i-Base

Lenacapavir is a capsid inhibitor given by 6-monthly subcutaneous injections that is currently in phase 2/3 studies for HIV treatment and prevention.



CROI 2022 includes six studies that focus on this long-acting compound. These include results in treatment-experienced participants with multi-drug resistance (CAPELLA study, reported below) and people who are treatment-naive (CALIBRATE study, reported separately – both with results out to one year. [1, 4]

CAPELLA included both a randomised (Cohort 1, n=36, randomised 2:1) and open label cohort (Cohort 2, n=36), with 24-week results, including drug resistance reported at IAS 2021 and EACS 2021 meetings (including 4 cases of breakthough with lenacapavir drug resistance, linked to either resistance or low adherence to the optimised background regimen (OBR). [2, 3]

Baseline demographics based on earlier reports include: 25% women, 38% Black, median age 52 years. Median baseline viral load was 4.5 log copies/mL (range: 1.3 to 5.7), with 28/72 >75,000 copies/mL. Median baseline CD4 count was 150 cells/mm^3 (range: 3 to 1296) with 64/72 <200 cells/mm^3. Approximately 46% had resistance to all four major classes (NRTI, NNRTI, PI, INSTI), and 17% had no fully active agents in the OBR.

At week-52, viral load was undetectable in 83% (30/36) although most of Cohort 2 have not yet reached this endpoint. Median overall follow-up was 376 days (IQR: 306 to 501).

CD4 count increased by a median 83 cells/mm^3 (IQR: +21 to +142, n=41). In addition to the four participants from Cohort 1 with breakthrough drug resistance reported at EACS 2022 [3] another four new cases were reported from Cohort 2, also related to limited support from the OBR.

All eight continue on lenacapavir, with 3/8 re-suppressing (2/3 after a change in OBR).

There were no discontinuations due to serious adverse events, but one participant stopped due grade 1 injection site nodules. ISRs occurred in 63% (45/72) and were mostly mild or moderate (43/45). Diarrhoea, nausea and COVID-19 were all reported at <10%.

Results from the CALIBRATE study in treatment-naive participants will be reported separately after the oral presentation on the third day of CROI 2022. [4]

Other studies include posters related to drug interactions and drug resistance, and a late-breaking macaque study supporting use as PrEP.

A phase 1 study in 54 HIV negative individuals reported no significant drug interactions between lenacapavir and the investigational long-acting compound islatravir. This promising compound with ideal PK to support use with lenacapavir now appears uncertain since the US FDA suspended islatravir studies due to unexpected side effects that reduced total and CD4 lymphocytes. [5, 6]

Even though lenacapavir is not excreted renally, a poster from a phase 1 study reported slightly increased lenacapavir PK in ten people with severe renal impairment (CrCl 15 to ≤ 29 mL/min) compared to ten unimpaired HIV negative controls. The increases however, due to a minor p-gp pathway, were not judged clinically significant. [7]

The poster on drug resistance reported the activity of lenacapavir was similar to wild-type (mean susceptibility 1.0; range 0.3 to 1.7) in HIV-1 isolates from 72 people regardeless of their phenotypic resistance to entry inhibitors (maraviroc, fostemsavir, ibalizumab, and enfuvirtide (T20). [8]

Efficacy and PK as PrEP

The macaque PrEP study included efficacy and PK results. [9]

Protection again infection occurred in all animals (n=4 dosed at 25 mg/kg with lenacapavir 30 days before a high-dose IV challenge and, interestingly, three animals given an active PrEP control of daily sc TDF/FTC/dolutegravir for 3 days before), followed for 8 months. This compared to early infection in all four placebo animals within 10 days.

In the PK study, plasma concentrations in six animals given two injections six weeks apart using either 15 mg/kg and 50 mg/kg dosing. Drug levels peaked 3-4 weeks after the second dose with mean levels maintained above the paEC95 (1.46 nM) for approximately 4.8 and 6.6 months (>145 and >200 days) after the second 15 mg/kg and 50 mg/kg doses, respectively. [10]

C O M M E N T S

These results support potent viral efficacy and broad safety of lenacapavir for HIV treatment and prevention.

Longer follow up is needed from CAPELLA to confirm rates of viral suppression in Cohort 1 of 67%, 79% and 94% with 0, 1 and 2 active drugs in the OBR, especially in those with no active drugs.

Phase 3 PrEP studies are already ongoing, although lenacapavir is currently on clinical hold related to a technical concern about glass vials used in these studies. A press statement from Gilead outlines further details to resolve this. [11]

References

Unless stated otherwise, references are to the 29th Conference on Retroviruses and Opportunistic Infections, 12–16 and 22–24 February 2022, virtual meeting. Depending on CROI policy, links might require conference registration and might only be active for a limited time on this platform after the meeting.

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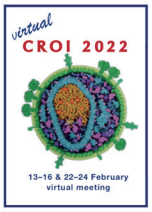
CROI 2022: Fourth potential stem cell HIV cure – in a US woman using donor cord cells

Richard Jefferys, TAG



In a session today on HIV cure research, Yvonne Bryson and colleagues from the IMPAACT research network presented important news about another potential example of an HIV cure achieved by stem cell transplantation. [1]

The case involves a woman living with HIV who was diagnosed with acute myelogenous leukemia (AML), a life-threatening cancer, in 2017. The researchers sourced cord blood stem cells from a donor homozygous for the CCR5 delta-32 mutation that prevents expression of the CCR5 co-receptor that most HIV strains use as an entryway into cells.

The aim was to treat the cancer while also generating a new immune system made up of HIV-resistant cells, following the model that has produced three other known cases of likely HIV cures in men (Timothy Ray Brown, Adam Castillejo and the Düsseldorf patient).

A difference with prior cases is that stem cells from umbilical cord blood are less efficient at generating a new immune system after transplantation, so the woman also received stem cells from the peripheral blood of an adult relative who lacked the CCR5 delta-32 mutation. Shortly after the transplant, most of the immune cells that could be detected were derived from the adult blood stem cells, but over time the proportion of cells derived from the cord blood transplant increased.

From day 100 of follow-up, all T cells and myeloid cells (monocyte/macrophages) were progeny of the cord blood transplant and therefore possessed the CCR5-delta32 mutation. As reported at the Annual Meeting of the American Society for Hematology in 2018, remission of AML was achieved and the woman initially continued on antiretroviral therapy (ART) with HIV viral load remaining suppressed. [2]

At CROI today, Yvonne Bryson reported that ART was interrupted three years after the transplant with no HIV viral load rebound. The woman, who's described as middle aged and of mixed race, has now been off ART for more than 14 months with persistently undetectable HIV viral load (during this time they've received COVID-19 vaccination without any untoward effect).

Tests for HIV DNA, a surrogate measure of the HIV reservoir, have also been negative except one detection of trace amounts at an early timepoint after ART cessation. Antibody and T cell responses against HIV are no longer detectable. The absence of ART has been confirmed by measuring drug levels in blood. The researchers have tested the woman's cells in the laboratory and found them to be resistant to HIV.

The case bolsters the evidence that an HIV cure is achievable and demonstrates that, for people with HIV and certain life-threatening cancers, stem cell transplantation from donors homozygous for the CCR5 delta-32 mutation can work in women as well as men.

Bryson pointed out that cord blood stem cell banks can be tested for the presence of the CCR5Δ32 mutation, and the approach used in this case could increase the chances of identifying CCR5-negative donors for people with HIV who require stem cell transplants for cancers (cord blood stem cells have less stringent requirements for matching the genetics of recipients).

Background on the use of cord blood stem cell transplants in HIV cure research and the possibilities of identifying matches for people of different races can be found in an overview article published in 2015 by Lawrence Petz and colleagues. For both adults and children, the chance of successful matches are significantly reduced for African, Hispanic and Chinese Americans. [3]

COMMENT

Although this woman also had to undergo chemotherapy and whole body irradiation, this new case has significant differences to some of the stem cell procedures used by the Berlin, London and Dusseldorf cure cases.

This included a suggestion that the use of cord cells could have been the reason that graft-vs-host disease was not experienced in this case.

However, an earlier paediatric case using cord blood cells was unfortunately not successful when the 12 year old boy died from graft-vs-host disease. The cases are not easy to compare though because of both age and more advanced ill health. [4]

It is significant that this case was a women, and also from a mixed race background where matching donors becomes significantly more difficult.

The use of cord stem cells was also reported to reduce the stringency needed with adult donors, although fewer cells available needed to an adult relative donor to contribute to the overall transplant.

The caution in referring to this case as remission is because the previous three cases needed longer follow-up before researchers felt confident to refer to a cure.

For some reason, many media reports, including the New York Times and Washington Post, seem to have forgotten the Düsseldorf patient, reported along with the London patient at CROI 2019. [5]

Source

Jefferys R. CROI 2022 Update: A New Potential HIV Cure Case; Broadly Neutralizing Antibody Enhances Post-Treatment Control. TAG basic Science Blog. (15 February 2022)
https://tagbasicscienceproject.typepad.com/tags_basic_science_vaccin/2022/02/croi-2022-update-a-new-potential-hiv-cure-case-broadly-neutralizing-antibody-enhances-post-treatment.html

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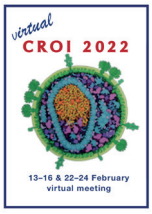
https://i-base.info/htb/35767

Strategies to suppress viral load off-ART with 3BNC117, 10-1074 and other bNAbs

Simon Collins, HIV i-Base



Some of the most intriguing results presented at CROI 2022 included several studies using two broadly neutralising antibodies (bNAbs) – 3BNC117 and 10-1074 – both developed at the Rockefeller University and have since been bought by Gilead.

This combination has shown the potential to be able to maintain viral suppression for six months after ART has been discontinued, including two cases where this continued for over a year. [1]

Together, they have 96% coverage in vitro in neutralising of a wide panel of pseudoviruses and clades and 83% coverage when tested against non-B primary isolates.

Research studies are looking at a potential role in reducing the viral reservoir and in whether bNAbs can generate a vaccine-like immune response in addition to their direct antiviral action as treatment and PrEP.

CROI included at least a dozen studies using these immune-based treatments in different clinical settings. Important differences between the studies include whether long-acting (LS) rather than original formulations were used, timing of antibody treatment and whether viral load was undetectable, and whether baseline screening for sensitivity to these compounds was included.

The oral presentations included a phase 1 study using both long-acting formulations, a paediatric study using monthly bNAbs instead of daily ART and two presentations from using bNAbs in early ART (with or without romepdepsin) that reported a vaccine-like effect with one participant remaining off-ART out to 3.7 years.

Marina Caskey, from Rockefeller University, presented results from a phase 1 study of long-acting versions of 3BNC117 and 10-1074 (with half-lives of approximately 62 and 80 days respectively) given by infusion to six HIV positive men with CD4 counts >300 cells/mm^3 and detectable viral load, having been off ART for at least four weeks for personal reasons, often for several years. One participant was ART-naive. [2]

Previous modelling predicted that dosing at 30 mg/kg and 10 mg/kg would produce therapeutic levels for a year.

Baseline characteristics included median age 34 (range: 24 to 56) with median CD4 count 523 cells/mm^3 (range: 360 to 891) and viral load of 48,000 copies/mL (range: 1,050 to 257,000).

Viral load declined in all participants with a median maximum decline of –1.86 log (range: 1.1 to 2.49; SD: 0.48) reached at a median of 1.5 weeks after dosing. This was not significantly different to the original formulations (p=0.81).

Reductions were transient in 4/6 men (~4 weeks) who had higher viral load at baseline despite good plasmas concentrations. In contrast, 2/6 with baseline viral load <4 log copies/mL achieved durable viral suppression.

Restarting ART was recommended at week 8 but this was only followed by the 4/6 participants with viral rebound.

Viral load remained undetectable in 2/6 without ART for the 24 weeks of follow up. One participant was reported to still be on study as viral load stayed undetectable for a further 12 weeks.

It is unfortunate that bNAb sensitivity was only reported afterwards and as a post hoc analysis. The four people whose treatment failed showed reduced sensitivity at baseline to either bNAb, and would therefore have been treated with effective monotherapy. The two viral responders were sensitive to both compounds at baseline (and achieved viral load reductions of 3.0 and 3.5 logs).

The PK analysis showed 10-1074-LS to have a slower clearance than 3BNC117-LS and but that levels of both were lower than historical controls that were HIV negative or on ART.

There were no infusion reactions or grade 3/4 side effects and no grade 2 or higher lab abnormalities.

The Tatelo study reported the potential for monthly infusions of dual bNAb treatment to maintain viral suppression in young children as an alternative to daily oral ART. [3]

In this case, the bNAbs were VRC01-LS and 10-1074 and participants were 28 children >2 years old who started ART after birth and who had undetectable viral load for at least the previous 6 months.

This proof-of-concept study included at least eight weeks overlap of ART with bNAbs before interrupting HIV treatment. Median age was 3.6 years (range 2.4, 5.6) and all children were taking lopinavir/r-based ART.

Viral load remained <40 copies/mL through to week-24 in 11/28 children (44%, 95%CI: 24 to 65%). Viral load rebounded >400 copies/mL in 14/28 at a median of 4 weeks (range: 1 to 20) and immediately re-started on ART. Median viral load rebounded to 4.42 log copies/mL (range: 2.87 to 6.42) with resuppression achieved in all children after a median of 4.1 weeks (range: 0.9 to 20.3).

The bNAbs were generally well-tolerated with five grade 3 events (one neutropenia considered possibly study drug-related). This alternative was reported to be highly acceptable by parents of the children, reducing the difficulties associated with daily oral ART.

This study is also reported in detail in a separate i-Base report. [4]

A study from the IMPAACT network presented new results in a poster by Coleen Cunningham and colleagues on the safety and PK from using long-acting VRC07-523-LS as PrEP in 22 HIV-exposed but uninfected infants in the US and South Africa, supporting 3-monthly dosing. [5]

Other oral presentations, reported the durable impact of two infusions of 3BNB117 in early ART, also with romedepsin in a randomised study that included an analytic treatment interruption (ATI) after a year.

The remarkable aspect of this study was this long delay between the immune-mediated treatment and the ATI, that still showed clinical benefits in the 3BNC117 plus romidepsin arm that included one participant sustaining viral suppression for over 3.7 years. [6]

This study is also reported in more detail in a separate i-Base report. [7]

In a second oral presentation from the same romedepsin study Míriam Rosás-Umbert from Aarhus University Hospital in Denmark reported the vaccine-like effect from giving 3BNC117 with ART. [8]

Although all four randomised groups had similar levels of HIV-specific CD4 and CD8 T cells responses at baseline, the frequency of Gag-specific CD8 T cells was significantly higher in participants who received 3BNC117 both at 3 months

(median 0.69% vs 0.29%, p=0.04) and at 12 months (median 0.91% vs 0.31%, p=0.03). This was together with ART but irrespective of romidepsin.

Other selected posters included a phase 1b study adding bNAbs to people already on effective ART, another study using pegylated interferon and three studies looking at testing for bNAb sensitivity.

In the first poster, Christian Gaebler and colleagues reported a phase 1b, open label study of 3BNC117 and 10-1074, in 26 participants (23 men, 3 women) who had been on stable ART for at least a year. This study did not include baseline screening for bNAb susceptibility. [9]

Participants were randomised to discontinue ART two days before the bNAb infusions (Group 1, n=18) or to remain on ART throughout (Group 2, n=6). All participants received up to seven infusions of 30 mg/kg of each antibody over 20 weeks (at weeks 0, 2, 4, 8, 12, 16 and 20), with follow-up out to a year.

Viral suppression in Group 1 was maintained for a median of 28 weeks that continued out to week-48 in two participants. This was longer than previous historical controls using either bNAb monotherapy or using six-weekly dosing (p=0.0224).

Viral rebound generally coincided with drug levels of one of the antibodies dropped below the target therapeutic threshold of 10 ug/mL.

In a second poster, Pablo Tebas and colleagues presented results from the open label BEAT2 study in 14 participants on stable ART (12 men, 2 women; 11 African-American) who were given 'combination immunotherapy' using weeklypegylated interferon-alpha2b (peg-IFN) and seven cycles of both bNAbs (also at weeks 0, 2, 4, 8, 12 ,16 and 20), during an HIV treatment interruption of up to 26 weeks. [10]

Median age was 50 years (range: 31 to 60) and baseline CD4 count was 869 cells/mm^3 (IQR: 739 to 1079).

Entry criteria included CD4 count >450 cells/mm^3 and sensitivity to both 3BNC117 and 10-1074 at baseline. ART was restarted in viral load rebounded to >1000 copies/mm^3 for six consecutive weeks or if CD4 count dropped below 300 cells/mm^3.

Two participants had viral rebound during immunotherapy (at week 8 and week 14) with 10/14 maintaining undetectable viral load for 26 weeks. Three participants experienced chills during the 3BNC117 infusion, and 2/3 discontinued (at week 5 and week 10), both while viral load was undetectable. Further analyses will report on the impact of treatment on the viral reservoir.

It will also be important to distinguish the role played by weekly peg-IFN, which as a treatment for HCV has usually been reported to have a difficult side effect profile.

The three other posters reported on baseline sensitivity to these bNAbs. Although not always carried out in earlier research, screening for sensitivity at baseline is now essential and comes with the challenge that testing itself is not always successful.

Luis Montaner and colleagues used the PhenoSense mAb Assay to evaluate susceptibility to 3BNC117 and 10-1074 in 61 participants on ART with undetectable viral load (<20 copies/mL), CD4 counts >450 cells/mm^3 and nadir >200. Baseline demographics included 9 female, 1 transgender, 53 African American and 8 Caucasian (3/8 Hispanic). [11]

A total of 54 samples were amplified (two after repeat testing) and seven were not able to be tested.

Of these, 41/54 (76%) were susceptible to 3BNC117, 37/54 (69%) to 10-1074 and 30/54 (56%, 95% CI: 41 to 69) were susceptible to both bNAbs.

Importantly, age, gender and race were not associated with susceptibility.

A second sensitivity poster was presented by Penny Zacharopoulou and colleagues from the UK RIO and RIVER studies. RIO is currently enrolling participants to use both bNAbs for a new ATI study, with many potential participants coming from the earlier RIVER study. [12]

This study analysed samples from 173 people who started ART within six months of seoconversion and who had been undetectable on ART for at least one year.

Of these 147/173 (85%) produced amplifiable proviral env samples and an average of 20 sequences per sample led to 3138 proviral env sequences being tested (70% were clade B).

Resistance to one or both bNAbs was detected in 48% of participants, with 29% (43/147) including any mutations associated with resistance to 10-1074, 13% (19/147) to 3BMC117 and 3.4% (5/147) to both. Phylogenetic analysis suggested evidence for both transmitted resistance and in-host evolution.

The led researchers to report that overall "approximately 40% of individuals treated during PHI in this cohort had potential pre-existing resistance to 10-1074 and 3BNC117 based on current in silico approaches" and that "screening may be key to guide effective treatment".

A third poster compared three different bNAb sensitivity tests (on 59 treatment naive participants): a phenotypic test from Monogram and two genotypic algorithms developed by Rockefeller and the US NIH. Sensitivity was defined if >90% of env samples for an individual were sensitive to the bNAbs tested (10-1074 and 3BNC117). [13]

Sensitivity was concordant using all three methods for 79% and 52% of participants for 10-1074 and 3BNC117, respectively. Compared to the phenotypic test, the algorithms had 87% and 83% sensitivity to 10-1074, with 60 and 75% agreement for 3BNC117.

Finally, an oral presentation by Boris Julg from Massachusetts General Hospital reported a phase 1 study using triple bNAb combination of PGDM1400, PGT121 and VRC07-523LS (which target V2, V3 and CD4 binding sites, respectively). [14]

This included randomising small groups of HIV negative people (n=3) to different doses of PGF121 with PDDM1400; and an open label study adding VRC017-523LS in four HIV positive people who were treatment-naive.

In people receiving the triple therapy, viral load reduced by –1.7 log at day 7 (with nadir of –2.0 log at day 10) but rebounded a median of 20 days post nadir (range: 13 to 70 days). Although 1/4 participants was lost to follow-up, baseline and rebound resistance is reported below for the 3/4 remaining participants.

1. Baseline: partial resistance to PGT121: rebound fully resistant to PGT121 and PGDM1400.

2. Full resistance to both PGT121 and PGDM1400 at baseline and rebound, also with partial resistance to VRC017-523LS at rebound.

3. Baseline: full sensitivity to all three bNAbs. Rebound partially resistant to PGT121 and PGDM1400.

This third case suggests different barriers to resistance for different bNAbs, even with triple therapy. Good plasma concentrations were reported VRC017-523LS at rebound (93 ug/mL; target 10 ug/mL).

Tolerability was good with the single grade 3 event was elevated CK, unrelated to the study drugs.

The half-life of PGDM1400 was about 20 days alone and when given with PGT121 in HIV negative people but dropped to about 11 days in HIV positive people with viraemia.

C O M M E N T

Although these studies report early stage research, the results hint at alternative approaches to managing HIV that might not just depend on antiretroviral treatment.

However, pre-existing resistance at baseline is common and vulnerability to developing new resistance on suboptimal treatment, shows that combination therapy with potent bNAbs should follow the same cautions as other antiretroviral drugs. This challenge is highlighted by limited agreement between the current available sensitivity tests.

The UK RIO study includes long-acting formulations of both 3BNC117 and 10-1074 to look at viral suppression during an ATI off-ART. It is currently enrolling participants on stable ART who started treatment in primary infection (within six months of becoming HIV positive) and includes baseline screening for bNAb sensitivity. [15]

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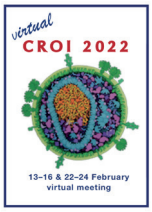
Targetting reservoir with ART + bNAb 3BNC117 + romidepsin maintained undetectable viral load off-ART for 3.7 years in one case

Richard Jefferys, TAG



During the CROI session on HIV cure research, Ole Søgaard presented results from the "eClear" trial, which investigated the broadly neutralising antibody (bNAb) 3BNC117 and a candidate latency-reversing agent, romidepsin. [1]

The study enrolled 60 participants, approximately half with recent HIV infection (less than 6 months), and randomly assigned them to one of four groups:

1. ART alone
2. ART plus 3BNC117 at day 7 and 21 after ART initiation
3. ART plus romidepsin at day 10, 17 and 24
4. ART plus 3BNC117 and romidepsin (administered at the same times listed above)

The primary aim was to assess if administering these interventions around the time of ART initiation could accelerate clearance of the HIV reservoir and promote control of HIV viral load after an analytical treatment interruption (ATI) a year later.

The rationale derived from a study demonstrating that the persistent HIV reservoir is formed close to the time of ART initiation in a substantial proportion of people with HIV. [2]

Participants were followed for a year and then given the option of undergoing a 12-week analytical treatment interruption (ATI) at day 400 of follow up. The majority of participants were white men; a total of five women were enrolled but none were randomized to receive 3BNC117.

Receipt of 3BNC117 was associated with greater declines in levels of cells expressing HIV RNA and the HIV p24 protein, as well as increases in HIV-specific CD8 T cell responses. Furthermore, four out of the five participants whose pre-ART HIV samples were fully sensitive to 3BNC117 (i.e. no evidence of resistance to the anti-HIV effects of the antibody) maintained HIV viral load below 5,000 copies/mL throughout the 12-week ATI, compared to three of 15 participants who had pre-ART evidence of HIV resistance to 3BNC117 or did not receive the antibody. These effects appeared independent of receipt of romidepsin.

One participant from the 3BNC117 and romidepsin group still remains off ART and has maintained undetectable HIV viral load for 3.7 years and counting. In the Q&A session after his talk, Søgaard noted that the HIV reservoir in this individual (as measured by an intact proviral DNA assay) is continuing to shrink in size over time.

Additional information on the association between 3BNC117 and improved CD8 T cell responses will be presented at CROI tomorrow by Míriam Rosás-Umbert (embargoed when this report was posted). [3]

The results indicate that bNAbs like 3BNC117 may have the potential to enhance clearance of the HIV reservoir and promote containment of viral load after treatment interruption. Additional ongoing studies involving combinations of bNAbs and ATIs, such as the RIO trial, should shed further light on the efficacy of the approach. [4]

Combinations of bNAbs may be necessary to circumvent the problem of baseline HIV resistance to individual antibodies.

Links to the relevant CROI abstract pages are below – the abstract text and presentation webcasts will become available on these pages in around 30 days (at the current time access is restricted to conference registrants).

C O M M E N T

The full paper from this study has just been published open access in Lancet Microbe. [5]

Source

Jefferys R. CROI 2022 Update: A New Potential HIV Cure Case; Broadly Neutralizing Antibody Enhances Post-Treatment Control. TAG basic Science Blog. (15 February 2022)

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Dual bNAb treatment maintains undetectable viral load off-ART in 44% of children in the Tatelo Study

Polly Clayden, HIV i-Base

Data from a proof-of-concept study, conducted in Botswana and presented at virtual CROI 2022, showed treatment with broadly neutralising antibodies (bNAbs) maintained viral suppression for 24 weeks without ART in early-treated children with HIV.

Tatelo Study evaluated monthly combination intravenous VRC01LS and 10-1074 as an alternative to ART in a cohort of very early treated children.

Children were recruited from the Early Infant Treatment (EIT) cohort, who had received continuous ART, starting at 7 days old or less (and 1 child with intra-partum infection started at 31 days). Eligible children were at least 96 weeks old and had viral load <40 copies/mL for 24 weeks before entry.

Following 8 weeks of overlap with ART (the first 6 participants had 32 weeks while awaiting PK assessment of dual bNAb dosing), ART was stopped and bNAb treatment was continued.

Intravenous infusion doses were: VRC01LS 30 mg IV load, 15 mk/kg IV every 4 weeks; 10-1074 30 mg/kg IV every 4 weeks.

Viral load was tested every 1–2 weeks and ART was restarted (and bNAbs discontinued) if >400 copies/mL, or at 24 weeks. Viral load was checked weekly until <40 copies/mL after re-starting ART.

Twenty-eight children entered Tatelo Study. Median age was 3.6 years (range: 2.4 to 5.6) and median CD4 count 1198 cells/mm^3. All were receiving lopinavir/ritonavir-based ART.

Three had viral rebound (all in 8 week overlap group). In two participants this was before starting bNAbs and one child rebounded at 4 weeks of ART + bNAbs.

Twenty-five continued bNAbs alone. Of these 11 (44%) maintained viral load <40 copies/mL through 24 weeks. These children were categorised as successes with 95% CI 24 to 65%. One participant had a single viral load result of 234 copies/mL at week 16 but re-suppressed to <40 copies/mL.

Fourteen (56%) had viral rebound to >400 copies/mL during 24 weeks of bNAb only treatment. Median time to failure for these participants was 4 weeks (range 1 to 20).

These results exceeded the study's pre-defined threshold for success of 30%.

When the investigators looked at characteristics of children categorised as successes, those with longer ART + bNAb overlap were more likely to succeed: 5 of 6 (83%) with 32 week overlap. Children enrolled earlier in the study were also more likely to succeed (those with longest continuous viral suppression were enrolled first). As well as those with favourable clinical and reservoir characteristics.

By response group, sustained viral suppression on ART before receiving bNAbs, which occurred in 9 of 11 successes (82%) vs 4 of 14 (29%) failures; and median DNA from PBMCs at birth, 155 copies/10^6 successes vs 784 copies/10^6were significant predictors of success (both p>0.02).

For the 14 children who failed on bNAbs alone, ART was re-started at a median of 4 days from rebound. Median viral load on the day of re-start was 4.42 $\log_{10}$ copies/mL. Re-suppression to <40 copies/mL was achieved in all children, at a median of 4.1 weeks (range 1 to 20) from ART re-start.

The investigators noted that no child in either group had a concerning pattern of CD4 decline.

No infusion reactions were reported and bNAbs were well-tolerated with only 5 grade 3 events – 1 neutropenia was judged possibly related to study drugs. There were no grade 4 events.

bNAb concentrations were considred adequate. During the bNAb only period, overall mean pre-dose troughs were in the expected range: VRC01LS, 281 mcg/mL and 10-1074, 256 mcg/mL.

Ongoing analyses include: PBMC HIV DNA change over time, baseline viral sequencing to look for pre-existing resistance and neutralisation assay data for bNAbs at failure.

C O M M E N T

In this impressive proof-of-concept study, dual bNAb treatment with VRC01LS and 10-1074 maintained viral suppression for 24 weeks in the absence of ART.

Presenting author Roger Shapiro added: "Newer bNAb combinations with greater breadth and potency, used in children with favorable pre-treatment characteristics and possibly with longer bNAb/ART overlap, may improve treatment success for this novel ART-sparing strategy."

For example, long-acting LS formulations, including 10-1074-LS, enable 3 to 6-monthly dosing that would making this a much easier intervention.

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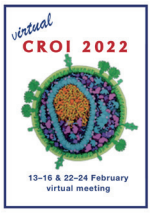
AAV8-VRC07 vaccine generates new bNAb production in HIV positive people for up to three years

Kirk Taylor, HIV i-base



CROI 2022 included updated results from using an AAV8 vector virus to deliver HIV neutralising antibodies and that participants not only produced and sustained new antibodies but that these neutralised HIV in vitro. [1]

Broadly neutralising antibody (bNAb) therapies have been studied for a potential role in HIV cure-related research for over a decade. One challenge is whether treatment can lead to a recipients immune system producing the new antibody, limiting the need for repeated infusions. A second related challenge is the risk that the immune system can develop anti-bNAb antibodies (anti-drug antibodies; ADA) that reverse any potential benefit.

Initial results from the AAV8-VRC07 bNAb trial in eight HIV positive participants (six men and two women, with five African American and three Caucasian) were first presented two years ago at CROI 2020. This reported that de novo VRC07 was produce by participants in vivo. [1]

The researchers, led by Joseph J Casazza from the US NIAID and colleagues, now report VRC07 antibody levels and their ability to neutralise HIV-1 in the lab.

Participants on the AAV8-VRC07 trial had median baseline CD4 counts of 528 cells/mm^3 (range: 351 to 950) at entry, no new participants have been included. [2]

Additional data were presented for participants that received low (n=3), intermediate (n=2) and high (n=3) vaccine doses. Five out of eight participants did not produce ADA and their VRC07 antibody levels have remained stable up to week 80 (intermediate and high dose) and week 130 (low dose).

However, bNAbs were maintained at lower levels for up to three years in participants with ADAs.

Antibodies collected from participants were capable of neutralising HIV in a similar manner to synthetic VRC07 (n=5). These experiments indicate that concentrations of VRC07 >1 ug/mL are required for 100% inhibition. Plasma concentrations of VRC07 were approximately ten-fold lower and maximal inhibition ranged from 60 to 90%.

This study therefore reported sustained long-term stability of AAV8-mediated VRC07 bNAb production in 5/8 participants and that these antibodies were active in vitro.

C O M M E N T

Early bNAb studies (e.g. the Miami macaque) gave hope of a functional cure after sustainable production of two bNAbs (3BNC117 and 10-1074) led to undetectable viral loads over 2 years and a reduced viral reservoir. [3]

In response to a question from Dr Joseph Eron, the lead author confirmed that treatment interruptions are not currently planned in order to assess bNAb efficacy in vivo.

Instead, the team plan to use ultrasensitive testing to determine whether VRC07 can further reduce viral load.

Another study at CROI 2022 using romidepsin with 3BNC117 and ART reported a positive effect on reducing the reservoir and maintaining undetectable viral loads in some participants following treatment interruption a year later. [4]

A recent study in Nature employed an mRNA vaccine approach (technology used for Pfizer-BioNTech COVID-19 vaccine) to induce production of bNAbs against HIV-1 envelope proteins in macaques. Whilst the authors described a 79% reduction in the chance of macaques becoming SIV positive, there was no effect of vaccination on viral load for SIV positive macaques (n=7). [5]

It will be interesting to see whether this approach can be developed for HIV treatment and prevention.

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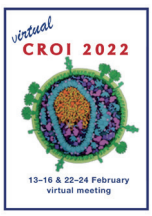
No impact from high-dose vitamin D3 on reducing the HIV viral reservoir

Simon Collins, HIV i-Base

A poster from HIV researchers in Australia looked at whether vitamin D3 supplements might reduce the reservoir of sleeping cells by reducing CD4 cell proliferation.



This pilot study randomised 30 people on effective ART to either high-dose oral vitamin D3 (10,000 international units daily) for 24 weeks or a matching placebo.

There were no differences in the primary endpoint of changes in HIV DNA in cells over the 24 weeks (p=0.19) - a marker for waking cells in the reservoir,

However, there was a 1.24 (95% CIL 1.01 to 1.51) fold increase (p = 0.039) from week 0 to week 12 and a 0.76 (95% CI: 0.62 to 0.94) fold decrease (p = 0.009) from week 0 to week 36 in frequency of total HIV DNA relative to placebo.

Vitamin D3 levels remained high at week 36 due to long half-life but there were no safety issues from the study.

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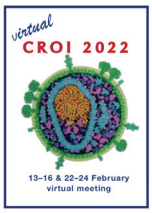
CROI 2022: COMPLICATIONS

Higher maternal mortality and adverse birth outcomes among women with COVID-19 in Botswana

Polly Clayden, HIV i-Base



Maternal mortality was higher among women with COVID-19 compared to those without in the Tsepamo Study, and infants born to women with COVID-19 had increased risk of adverse birth outcomes. Maternal deaths did not differ by HIV status but infants exposed to both COVID-19 and HIV were at the highest risk for most adverse outcomes.

These data from Botswana were presented at virtual CROI 2022.

Botswana has a high prevalence of women living with HIV and, like most countries, experienced a COVID-19 epidemic in 2021. The Tsepamo Study performs birth outcomes surveillance at government hospitals countrywide.

Both COVID-19 and HIV can lead to adverse birth outcomes. But there are limited data describing the combined effect. This study looked at adverse birth outcomes among women routinely tested for COVID-19 by HIV status. Notably it was conducted during a period when few women had access to COVID-19 vaccination in Botswana.

The investigators analysed data from 13 Tsepamo sites that performed routine COVID-19 screening at delivery with rapid antigen or PCR testing between 1 September 2020 and 15 November 2021. This period included Beta and Delta variants but not Omicron.

Singleton deliveries with known HIV status and a COVID-19 screening test 14 days before and three days after delivery were evaluated.

Adverse outcomes included maternal death, preterm delivery, very preterm delivery, small for gestational age, very small for gestational age, stillbirth, and neonatal death.

There were 20,410 deliveries during the study period (44% without a COVID-19 test); 11,483 were screened for COVID-19 and 539 (4.7%) were positive. Of these, 144 (5.6%) were among women living with HIV and 392 (4.3%) among HIV negative women. Women with HIV were more likely to be COVID-19 positive at delivery (p<0.01).

Maternal deaths were high with COVID-19, particularly during Delta, but did not differ by HIV status.

Overall, there were 19 (4%) vs 12 (0.1%) deaths among women with and without COVID-19, respectively. Age adjusted risk ratio (aRR) 31.6 (95% CI 15.4 to 64.7).

Among women living with HIV, for those with and without COVID-19, there were: 4 (3%) vs 3 (0.1%) deaths respectively; aRR 23.3 (95% CI 5.3 to 102.8). The respective values for HIV negative women were: 15 (5%) vs 5 (0.1%); aRR 35.6 (95% CI 15.7 to 81.0). Of note ART use is very high in this cohort: 97% of women with HIV receiving ART of which over 75% started before conception.

By variant, pre-Delta and during Delta with and without COVID-19, maternal deaths were respectively: 3 (2%) vs 5 (0.1%); aRR 13.9 (95% CI 3.4 to 57.2) and 15 (5%) vs 5 (0.1%); aRR 56.3 (95% CI 20.5 to 154.7).

Adverse birth outcomes were higher among infants born to women with COVID-19 (n=539) compared with those without (n=10,944): 185 (34.5%) vs 2899 (26.6%); aRR 1.31 (95% CI 1.16 to 1.48).

These were elevated across all adverse outcomes among infants born to women with COVID-19 and most notable for still birth: 30 (5.6%) vs 297 (2.7%); aRR 1.97 (95% CI 1.37 to 2.84).

Adverse birth outcomes were highest among infants born to women with COVID-19 and HIV (n=144) compared to HIV only (n=2277): 62 (43.1%) vs 692 (30.4%); aRR 1.78 (95% CI 1.47 to 2.16).

The investigators concluded that maternal mortality was higher in women who were COVID-19 positive – with nearly 4% maternal mortality, giving a 30-fold increase compared with those women without COVID-19 at delivery.

Infants born to COVID-19 positive women had more adverse birth outcomes, including a 5.5% risk of still birth – a 2-fold increase.

Infants born to women with COVID-19 and HIV had the highest risk for adverse birth outcomes.

C O M M E N T

Presenting author, Maya Jackson-Gibson, highlighted three limitations to this study:

1. **It was not possible to evaluate the effect of vaccination as this was not documented in maternal obstetric cards, but vaccination was limited in Botswana during the study period (only less than 15% fully vaccinated by late 2021).**
2. **If the availability of test kits was limited, symptomatic women might have been preferably screened.**
3. **Omicron variant only became dominant in Botswana in December 2021 – after the study period.**

Numbers in the maternal mortality subgroup analyses were also notably small with wide confidence intervals, but the overall effect is concerning and hopefully will improve as the vaccination programme matures in Botswana.

Tsepamo is continuing to look at the effect of COVID-19 on maternal mortality and infant outcomes and this next period of surveillance includes the Omicron variant.

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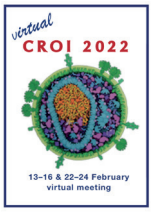
Jackson-Gibson M et al. The impact of COVID-19 on adverse birth outcomes in Botswana by HIV status. CROI 2022, 12–16 and 22–24 February, virtual meeting. Oral abstract 29.

https://www.croiconference.org/abstract/the-impact-of-covid-19-on-adverse-birth-outcomes-in-botswana-by-hiv-status/ (abstract)

ANCHOR study reduces anal cancer by 57% and supports screening for people living with HIV

Kirk Taylor and Simon Collins, HIV i-Base

Anal cancer is an AIDS defining cancer and the fourth most common cancer in people living with HIV in the US. Incidence rates of 160/100,000 person-years are significantly higher than the general population and are highest in gay men older than 45. HIV also increases the risk for other groups, including heterosexual men and women, also linked to duration for being HIV positive.



Although successfully treatable, especially if diagnosed early, late diagnosis is largely due to a lack of screening programmes, even though the causative link to HPV is the same as for cervical cancer.

The phase 3 ANCHOR study was launched in 2014 to see whether treating HIV positive people with anal high grade squamous intraepithelial lesions (HSIL) could reduce incidence of anal cancer. Secondary outcomes included the efficacy and safety of treatment, including quality of life. [2, 3]

In October 2021, the Data Safety Monitoring Board recommended stopping further randomisation and for all participants to be offered active treatment. [4]

The first trial results the ANCHOR study were presented by lead investigator Dr Joel Palefsky at a special session of CROI 2022. [5].

Participants were recruited onto the randomised controlled trial from 15 US sites and either received immediate treatment for HSIL or six-monthly active monitoring (AM) with annual biopsy. Both arms could have more frequent monitoring and biopsy if cancer was suspected. Over 10,700 HIV positive people were screened with high resolution anoscopy, with over half (52%) having biopsy-proven HSIL. Rates were similarly high in all groups (53% in men, 45% in women and 62% in trans people).

Nearly all those screened (99.7%) were then randomised (stratified by nadir CD4 count (above/below 200 cells/mm^3, lesion size and study site) to either treatment (n=2,227) or AM (n=2,219).

The 17 individuals who were diagnosed with anal cancer at screening (0.16%, 160/100,000) were all referred for immediate treatment, outside the study. This is about 20-fold higher than current rates of cervical cancer in th largely screened US general population.

Baseline demographics included median age 51 (IQR: 44 to 57) and people had been living with HIV for a median of 17 years (IQR: 10 to 25). Approximately 80% were male, 16% female and 3% transgender. Ethnicity included 42% African-American, 23% white, 16% Hispanic.

Approximately 32% were current smokers, with CDC likely risk group including 78% gay men, 23% heterosexual, 7% drug users and 3% blood products or other.

HIV characteristics included mainly controlled viral load was (80% <50, 7% 50 to 200 and ~5% >1000 copies/mL), median CD4 count approximately 600 cells/mm^3 (IQR: 400 to 850) and roughly half had a nadir CD4 <200. Participants had been diagnosed with HIV for a median 17 years (IQR: 10 to 24).

Participant characteristics were similar between groups.

Treatment was primarily by office-based electrocautery (93%), with smaller numbers using infrared or topical treatments.

DSMB were informed when 32 cancers were diagnosed, of which 30 were included in the final analysis. Invasive cancers were more common in the AM arm (21 vs 9). Median follow-up time was 25.8 months and a 57% reduction in anal cancer was observed (95% CI: 6% to 80%; p=0.029). The annual incidence rate of anal cancer was 173 vs 402/100,000 in the treatment vs monitoring arm respectively.

The randomised arm of the study was stopped early and treatment recommended for all participants, with follow-up continuing for another two years.

Overall, there were 54 vs 48 deaths in the treatment vs AM arms, none related to the study; similar adverse events (683 vs 635) and serious events (586 vs 658).

There were seven study-related serious adverse events were in the treatment arm, of which five related to the treatment procedure and two were infection or abscess due to anal biopsy. There was a single biopsy related serious adverse event in the AM arm.

The authors concluded that this is the first study to prove that treatment of anal HSIL is effective in preventing anal cancer and that these data should be used to support screening and treatment as a new standard of care.

They also commented that training programmes are required to improve detection of anal cancers and support roll-out of screening programmes for high-risk individuals, and also to further improve treatment.

It also sets a significant challenge for how these results can be immediately used, given the high prevalance of HSIL and the current lack of resources to screen and treat (see comments below).

C O M M E N T S

The ANCHOR study is a significant achievement for producing a dataset that will now support a new services and a new standard of care for people living with HIV.

It is also significant for supporting so many people to consent to monitoring after being diagnosed with HSIL. Although immediate treatment of HSIL seems intuitive, it does carry uncertain risks due to greater size of anal lesions (compared to cervical screening) and that lesions can be missed, badly treated or can recur.

However, the very high prevalence of HSIL means that screening algorithms should certainly prioritise HIV positive people with symptoms, that following digital exam, HRA should be prioritise for those with bumps. and then older men with longer duration of infection and lowest CD4 nadir.

The ANCHOR study is also working to identify biomarkers that will predict risk of progression.

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Other studies at CROI 2022 on anal cancer

Kirk Talyor, HIV i-Base

In addition to the ANCHOR study reported above [1], CROI 2022 included two other posters that are worth reporting.

Risk factors associated with anal cancer

The first was a retrospective chart review of young MSM (n=100) and transgender women (n=3) that attended a youth clinic in Atlanta, GA. [2].

HIV positive subjects were aged 19 (SD± 2) at presentation, 91% were Black.

Anal warts were reported by 83% and 65% had received surgical treatment; 12% of subjects had received full course of HPV vaccination.

High grade anal intraepithelial neoplasia (AIN) was detected in 63% of participants.

Adjusted odds ratios indicated that incomplete HPV vaccination (5.34; 90% CI: 1.30 to 21.93; p=0.05) and previous surgical treatment (2.59; 90% CI: 1.18 to 5.66; p=0.05) were associated with increased chance of anal cancer.

Although this study identifies potential risk factors for anal cancers, it is limited to a single youth clinic in Atlanta and the low number of trans women included (n=3) limit the conclusions that can be drawn for this population.

HPV risk correlates with anal cancer risk

A second larger study reported that screening for pre-cancerous anal dysplasia was conducted between 2014 to 2020 in 1397 HIV positive people aged under 35. [3]

Participants in this group were 93% male and 28% had received HPV vaccination prior to screening.

Prevalence of high grade anal HSIL was 44% across the cohort. Age at time of diagnosis did not correlate with risk of anal cancer.

HPV vaccination was associated with lower rates of HPV infection, suggesting a need to increase rates of vaccination in high-risk populations.

Taken together, these studies indicate the need to increase screening programmes for HSIL to prevent and treat anal cancers in high-risk individuals. Further data is required to stratify relative risk for different populations (e.g. trans women).

HPV vaccines may provide protection against HSIL and anal cancers in MSM and HIV positive populations.

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Telomere shortening associated with TAF but not TDF in CHARTER study

Simon Collins, HIV i-Base

A poster at CROI 2022 from the CHARTER study reported that TAF was associated with telomere shortening, but not tenofovir disoproxil. [1]

This was in 121 HIV positive people first assessed from 2003–7 and again a median of 12 years later – but this had the significant limitation that baseline samples were not available for TAF because it had not yet been developed.

Last month, a prospective 17-year study from the Swiss HIV Cohort reported that untreated HIV was associated with significant reductions in telomere length (TL) but that effective ART stopped further damage. This study did not find any association with individual HIV drugs. [2, 3]

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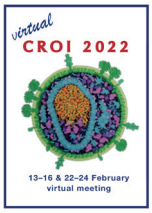
CROI 2022: HIV PREVENTION

CROI 2022: Injectable PrEP: impressive results, new viral load monitoring – but price questions access

Simon Collins, HIV i-Base

Two oral presentations at CROI 2022 provided follow-up data on injectable PrEP using long-acting cabotegravir. [1, 2]



One study reported that CAB-LA continued to be highly effective at preventing HIV transmission in the HPTN 083 study, including in full data from the planned three year study as well as from the open-label roll-over from the subsequent unblinded year.

The other study recommended routine monitoring with viral load testing to limit drug resistance in the few breakthrough infections that were either missed at baseline or had delayed diagnoses during the study.

The large international randomised phase 3 HPTN 083 study was previously reported in detail after the IAS 2000 conference. It is a notable success that due to prespecified enrolment criteria, the study included people at high risk of HIV: 12% of participants were transgender and 67% were younger than 30, and 50% of US participants were Black.

After a median of only 1.4 years, significantly fewer infections were reported among the 4700 gay men and transgender women by those in the CAB-LA vs oral TD/FTC arms: 13 vs 39 respectively [HR: 0.34 (95% CI: 0.18 to 0.62), p=0.0005]. [3]

Similar results were reported in the slightly smaller HPTN-084 study in African women, with 4 vs 34 new infections in the injectable vs oral arms respectively. [4]

The updated results, presented by Raphael Landovitz from UCLA, now includes four new infections from the initial blinded period (two in each arm) plus 48 new infections from the unblinded year (11 with CAB-LA and 37 in TDF/FTC). This maintains almost identical results as the initial report [HR: 0.33 (95% CI: 0.17 to 0.56).

However, overall incidence in both arms was approximately 1.5-fold higher than during the blinded period, lined to lower adherence in both arms, including CAB-LA coverage dropping from 91% to 79%: accounting for 40% of the increased cases. Most of the additional 60% was explained by higher HIV background incidence in Latin American study sites who made up a greater proportion and the follow-up data (from 32% to 54%).

Both incident infections on CAB-LA during the final blinded period and four during the unblinded period were classified as D. The remaining 7/11 infections occurred more than 6 months since last prescription.

There were no new safety concerns.

Open-label extensions continue but now with optional oral lead-in dosing and viral load monintoring for HIV detection.

This last point was the focus of the second oral presentation from HPTN 083 by Susan Eshleman from Johns Hopkins University. [2]

Although breakthrough HIV infections while using injectable PrEP were uncommon in HPTN 083/084, some HIV diagnoses were delayed (median time: 60 days; range 35 to 117). The longer time is associated with a higher risk of resistance developing to cabotegravir and cross-resistance to other integrase inhibitors.

The seven acute infections reported from HPTN 083 included INSTI resistance in 6/7 and modelling the outcomes from using viral load (sensitive to <30 copies/mL) would have detected HIV before INSTI resistance in 4/6 cases and before accumulted INSTI resistance in the remaining 2/6.

This led researchers to recommend routine HIV monitoring using viral load rather than antibody testing, in settings where this is an option.

However, the study also concluded that access to CAB-LA PrEP should not be restricted in settings where viral load testing is not easily available.

COMMENT

As with oral PrEP, HTB has reported the remarkable scientific development of long-acting injectable PrEP over nine years – from initial animal studies through to US approval two months ago in December 2021. [5, 6]

Additional regulatory submissions have been submitted to Australia, Brazil and six countries in southern Africa – but, at least in the CROI 2022 talk, the EU was noticeably missing. [1, 8]

Global access will need CAB-LA to be affordable in settings where oral PrEP uses generic TDF/FTC, recognising that injectable formulations are likely to always be more expensive to manufacture than tablets. If ViiV/GSK supports generic licenses for CAB-LA (similar to the way it supported this for dolutegravir) it might still delay access for many years. Pricing for these settings has not yet been disclosed.

The suggested US list price of $22,000 is a difficult signal to community organisations in other countries who otherwise support the importance of PrEP and new formulations.

Even allowed for discounts, the US list price is significantly higher than for the CAB-LA when used as treatment, when the expectation that greater demand for PrEP should make this much less expensive. It is also considerably higher than the price for TAF/FTC (Descovy), the newer version of Gilead's oral PrEP that was withdrawn from EU regulatory approval due to lack of a financial market, even though the registrational studies included European study sites.

EU countries use social health care systems and even the wiliest health economist hasn't been able to support list price TAF/FTC over generic TDF/FTC.

ViiV provided the following response when asked about registration in the EU, including a weblink for future updates: "ViiV Healthcare remains committed to working collaboratively and transparently to develop new approaches that are sustainable, relevant, address public health needs, and deliver for the people that need them. We are on track with our submissions to other Global regulatory authorities outside of the US." [7]

References

1. Landovitz RJ et al. Updated efficacy, safety, and case studies IN HPTN 083: CAB-LA vs TDF/FTC for PrEP, CROI 2022, 12–16 and 22–24 February, virtual meeting. Oral abstract 96.
   https://ww2.aievolution.com/cro2201/index.cfm?do=abs.viewAbs&abs=3241 (abstract)
   https://croi2022.onlineeventpro.freeman.com/live-stream/23875374/GLOBAL-PERSPECTIVES-ON-HIV-TESTING-TREATMENT-AND-PREVENTION (webcast)
2. Eshleman S et al. CAB-LA PrEP: early detection of HIV infection may reduce INSTI resistance risk. CROI 2022, 12–16 and 22–24 February, virtual meeting. Oral abstract 95.
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4. Two-monthly cabotegravir injections prevent HIV infection in African women: HPTN 084 study recommends early unblinding. HTB (11 November 2020).
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   https://viivhealthcare.com/content/dam/cf- (link page)
   viiv/viivhealthcare/master/files/cab-prep-wwrs-10-jan-2022-for-external-use.pdf (PDF)

CROI 2022: Long-acting doravirine implants as PrEP to prevent vaginal HIV transmission in mouse study

Kirk Taylor, HIV i-Base

A poster at CROI 2022 reported results from a mouse study using a long-acting formulation of the NNRTI doravirine (LA-DOR) as a PrEP that could be used in a removable implant. [1]

Long-acting (LA) HIV therapies have potential to increase adherence and reduce risk of drug-resistant mutations. Doravirine is an NNRTI that has an IC_{95} of 8.1 ng/mL against HIV-1 and has efficacy against NNRTI-resistant strains.

Doravirine was stably released into the plasma of mice across the five-month study period consistently exceeded IC_{95} values.

LA-DOR achieved good tissue distribution with plasma:tissue ratios >1.0. Doravirine concentrations were highest in GI tissues. Concentrations of doravirine (in three animals) in vaginal (mean: 206 ng/g, range: 38.2 to 229), cervical (mean: 271.2 ng/g, range: 42.5 to 336) and uterine (mean: 122.3 ng/ml, range: 51.6 to 157) tissues should a wide range but that were all consistently above IC_{95} levels at week 5.

The animals were challenged by vaginal transmission. LA-DOR reduced viral load in plasma and cervical tissue sections of mice who became HIV positive by 2 and 3-5 log copies/mL, respectively.

Efficacy of LA-DOR as PrEP was assessed following repeated exposure to HIV. HIV infection occurred after the first exposure in 80% of mice that received placebo (n=5). LA-DOR effectively reduced vaginal HIV transmission with a single mouse testing positive after the third exposure (n=8).

This preclinical study indicates that LA-DOR implants stably release drug for >5 months. Plasma (week 20) and tissue concentrations (week 5) exceeded the IC_{95} and implant removal rapidly lowered plasma DOR.

Further studies will evaluate the tissue distribution of DOR at later timepoints. Vaginal transmission data raise the prospect that LA-DOR implants could contribute to PrEP strategies for high-risk women.

C O M M E N T

NNRTIs are not generally a good class for PrEP due to the class potential for hypersensitivity reactions and low threshold to drug resistance.

The clinical implications of drug resistance are also more serious when the same drugs are commonly used for both PrEP and treatment.

Whilst the data presented are promising, the barrier for PrEP efficacy also needs to be closer to 100%, although sample sizes in this study are very small and longer-term efficacy data are required.

References

Kovarova et al. Long acting doravirine for treatment and prevention of vaginal HIV transmission. CROI 2022. 12-16 February 2022, virtual. Poster abstract 446.

https://ww2.aievolution.com/cro2201/index.cfm?do=abs.viewAbs&abs=2750 (abstract)

CROI 2022: OTHER NEWS

LEAP Workshop online: research into long-acting drugs

Simon Collins, HIV i-Base

Presentations from this annual workshop held just before CROI are now available online for open access.

The Long-Acting Extended Release Antiretroviral Research Resource Program (LEAP) coordinates and collaborates with research groups looking into developing long-acting formulations.

It includes doctors, investigators, developers, community advocacy groups, not-for-profit institutions and regulatory authorities.

The workshop consisted of two plenary sessions and four focus groups. Video recordings and text summaries of these are now online.

Reference

Long-Acting/Extended Release (LA/ER) Antiretroviral Research Resource Program (LEAP) Investigator Meeting and Annual Workshop 2022. (12 February 2022).

https://longactinghiv.org/content/LEAP-WORKSHOP-2022

HIV: COMPLICATIONS

Timing of menopause: experiences of women in Swiss HIV Cohort

Simon Collins, HIV i-Base

This important European cohort reported the median age at menopause was 50 (range: 32 to 55 years), with 115 women (10%) having an early menopause (defined by occurring under 45), and 23 (2%) with premature ovarian insufficiency (when under 40).

The analysis included 1,130 women who reported menopause (defined as being without menstrual bleeding for at least 12 months). Approximately 67% were Caucasian and 25% were African.

Several issues related to management were reported.

Firstly, that although menopause occurred approximatly two years earlier than HIV negative women, this was largely linked to African women.

Secondly, that rates of documented depression were high (at 27%), which in multivariate analyses was linked to African race (adj OR: 4.2; 95% CI: 2.5 to 7.2), but not HIV-related factors.

Thirdly, that within three years after documentation of menopause, only 11% of women received hormone replacement therapy, and only 27% had a bone mineral density measurement to evaluate the risk for osteoporosis.

The study concluded that awareness and management of menopause should be improved as an important part of HIV care. As the average age of HIV positive people in this cohort increases the proportion of women in menopause rose from 11.5% in 2010 to 36% in 2018.

Reference

Hachfeld A et al. Women with HIV transitioning through menopause: Insights from the Swiss HIV Cohort Study (SHCS) HIV Medicine 2022 Feb 22. doi: 10.1111/hiv.13255.

https://pubmed.ncbi.nlm.nih.gov/35194949

HIV: OTHER NEWS

Robert Carr Research Award: call for nominations

ICASO

The Robert Carr Research Award celebrates Robert's vision of collaboration between community organizations, academic researchers, and advocates to advance human rights-based policies and practices in the AIDS response.

The Award aims to highlight a research project conducted by a community-academia partnership in which all partners were equally involved in designing the study, collecting and analyzing the data and disseminating the results. To be eligible, the nomination must demonstrate how the project has led to evidence-based programs and/or influenced policies in the field of HIV.

Robert's commitment to translating findings from research collaborations between community and academic partners into tangible policy development and advocacy efforts is the driving force behind this prize.

This year's winners will be announced at the 24th International AIDS Conference in Montreal, Canada (AIDS2022) in July 2022 during the biannual Robert Carr Memorial Lecture.

The deadline for nominations is 31 March 2022.

Nomination form:

https://docs.google.com/forms/d/e/1FAIpQLSetvhBL5StP3q5ii7rmUEk394R5apvuRkIlhN4xPm0BYfJiew/viewform

For more information:

https://icaso.org/robert-carr-research-award

COVID-19: HIV and COVID-19

Long COVID may be more common in people living with HIV

Simon Collins, HIV i-Base

A US paper published ahead of peer-review reported broadly similar SARS-CoV-2 specific humoral and cellular immune responses in 39 people living with and 43 closely-matched HIV negative people recovering from COVID-19, but significantly higher rates of long COVID (OR: 4.01, 95% CI: 1.45 to 11.1), p=0.008.

Participants were enrolled in the Long-term Impact of Infection with Novel Coronavirus (LIINC) COVID-19 recovery cohort at UCSF (NCT 04362150). Long COVID was defined by any symptoms present more than six weeks after diagnosis of COVID-19. Median time to assessment and severity of symptoms were similar between groups.

HIV positive participants were on effective ART with undetectable viral load. Median (IQR) CD4 count and CD4:CD8 ratios were 596 cells/mm^3 (IQR: 404 to 740) vs 670 cells/mm^3 (IQR: 594 to 918) and 0.94 (IQR: 0.51 to 1.10) vs 2.00 (IQR: 1.52 to 2.32), in the HIV+ vs HIV– groups, respectively.

Higher proportions of PD-1 CD4 T cells and significantly higher levels of some inflammatory markers (IL-6, TNF-alpha, and IP-10) were associated with persistent symptoms.

Detailed immunological responses are also reported.

C O M M E N T

This study reported early four-fold higher risks of long COVID compared to well-matched HIV negative controls.

However, the small size makes the study unlikely to be powered to look at the HIV effect and also cautioned that the results need to be supported by larger studies.

Reference

Peluso MJ. Post-acute sequelae and adaptive immune responses in people living with HIV recovering from SARS-COV-2 infection. (14 February 2022).

https://www.medrxiv.org/content/10.1101/2022.02.10.22270471v1.full

COVID-19: TREATMENT

Major review finds little benefit of remdesivir in people hospitalised with COVID-19

Simon Collins, HIV i-Base

A final update to this ongoing review of randomised controlled trials using remdesivir concludes that In hospitalised adults with COVID-19, remdesivir probably results in little to no difference in mortality.

Although remdesivir may reduce time to clinical improvement and may lead to small reductions in serious adverse events it may also results in a small increase in any adverse event.

Reference

Kaka AS et al. Major update 2: remdesivir for adults with COVID-19: A living systematic review and meta-analysis for the American College of Physicians. Ann Intern Med. [Epub ahead of print 1 March 2022]. doi:10.7326/M21-4784.

https://doi.org/10.7326/M21-4784

https://www.acpjournals.org/doi/10.7326/M21-4784

COVID-19: PREVENTION

Melatonin does not protect against SARS-CoV-2

Simon Collins, HIV i-Base

Results from a randomised study reported no benefit of daily oral melatonin (2 mg QD) for 12 weeks compared to placebo as prophylaxis against SARS-CoV-2 in 314 Spanish health workers.

More infections occurred in the active arm (5.5% vs 2.6%, p-0.2) together with more treatment-related side effects (n=67 vs 43, p=0.04), mainly poor sleep.

It is important that the thousands of research studies hoping to find benefits in preventing or treating COVID-19 with repurposed drugs publish their results, even when no effect is found.

Participants would have brought their own hopes to these studies.

Reference

Garcia-Garcia et al. Melatonin in the prophylaxis of SARS-CoV-2 infection in healthcare workers (MeCOVID): A randomised clinical trial. J. Clin. Med. 2022, 11(4), 1139. (21 February 2022).

https://doi.org/10.3390/jcm11041139.

COVID-19: ON THE WEB

Resources on long COVID

Simon Collins, HIV i-Base

Recent links added to this page on long COVID.

Upcoming virtual workshop:

Long-Term Health Effects from COVID-19 and Implications

Monday, March 21, 2022 - 10:30am - 4:00pm US Eastern time

Tuesday, March 22, 2022 - 10:30am - 3:30pm US Eastern tim

The National Academies will hold a public workshop to explore the long-term and potentially disabling health effects stemming from COVID-19 infection and how they might impact survivors' ability to work.
Free registration.

https://www.eventbrite.com/e/long-term-health-effects-from-covid-19-and-implications-for-the-ssa-registration-267022701087

Long COVID may be more common in people living with HIV

HTB review of small US study (Peluso et al, see below).

https://i-base.info/htb/42389

Post-acute sequelae and adaptive immune responses in people living with HIV recovering from SARS-COV-2 infection. Peluso MJ et al. Preprint. medRxIV. (14 February 2022).

https://www.medrxiv.org/content/10.1101/2022.02.10.22270471v1.full

WHO webinars: COVID-19 Global Research and Innovation Forum

WHO webinars

The third WHO webinar in this series was held on 24 – 25 February 2022 and can now be viewed online.

It had two main aims.

1. To continue to accelerate research that can contribute end the current pandemic and facilitate that those affected receive optimal care; while integrating innovation fully within each research area.
2. To support research priorities in a way that contributes to the development of global research platforms and research priorities and leads to better preparation for future pandemics.

Over 100 research scientists, experts, policy makers and donors worldwide contributed.

Reference

WHO. COVID-19 Global Research and Innovation Forum: An invitation to the research community. (22-23 February 2022).

https://www.who.int/news-room/events/detail/2022/02/24/default-calendar/covid-19-global-research-and-innovation-forum-an-invitation-to-the-research-community

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

All i-Base publications are available online, including editions of the treatment guides.

http://www.i-Base.info

The site gives details about services including the UK Community Advisory Board (UK-CAB), our phone service and Q&A service, access to our archives and an extensive range of translated resources and links.

Publications and regular subscriptions can be ordered online.

The Q&A web pages enable people to ask questions about their own treatment:

http://www.i-base.info/qa

i-Base treatment guides

i-Base produces six booklets that comprehensively cover important aspects of treatment. Each guide is written in clear non-technical language. All guides are free to order individually or in bulk for use in clinics and are available online in web-page and PDF format.

http://www.i-base.info/guides

- Introduction to ART (May 2018)
- HIV & quality of life: side effects & long-term health (Sept 2016)
- Guide to PrEP in the UK (March 2019)
- HIV testing and risks of sexual transmission (June 2016)
- Guide to changing treatment and drug resistance (Jan 2018)
- Guide to HIV, pregnancy & women's health (April 2019)

Pocket guides

A series of pocket-size concertina folding leaflets that is designed to be a very simple and direct introduction to HIV treatment.

The five pocket leaflets are: Introduction to ART, HIV and pregnancy, ART and quality of life, UK guide to PrEP and HCV/HIV coinfection.

The leaflets use simple statements and quotes about ART, with short URL links to web pages that have additional information in a similar easy format.

U=U resources for UK clinics: free posters, postcards and factsheets

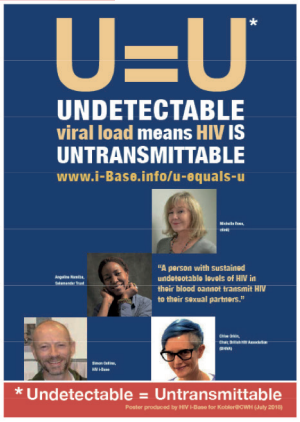
i-Base have produced a new series of posters, postcards and leaflets to help raise awareness about U=U in clincs.

This project was developed with the Kobler Centre in London.

As with all i-Base material, these resources are all free to UK clinics.

Until our online order form is updated to include the U=U resources, more copies can be orded by email or fax.

email: subscriptions@i-base.org.uk



Customise U=U posters for your clinic

i-Base can customise U=U posters to include pictures of doctors. nurses, pharmacists, peer advocates or any other staff that would like to help publicise U=U.

Personalising these for your clinic is cheap and easy and might be an especially nice way to highlight the good news.

For further information please contact Roy Trevelion at i-Base:

roy.trevelion@i-Base.org.uk

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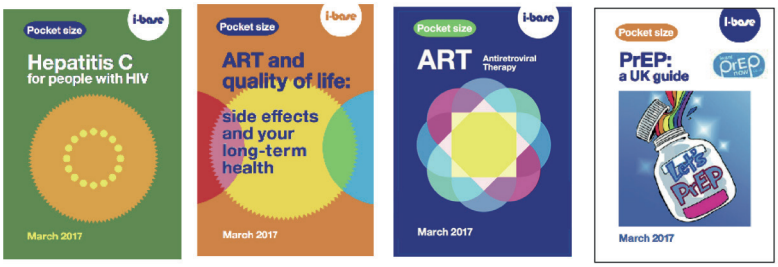

h-tb

HIV TREATMENT BULLETIN

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Editor: Simon Collins

Contributing Editor: Polly Clayden

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HIV i-Base, 107 The Maltings,169 Tower Bridge Road, London, SE1 3LJ. T: +44 (0) 20 8616 2210. F: +44 (0) 20 8616 1250

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- **HIV Treatment Bulletin (HTB) every two months** ☐ **by e-mail**
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Pocket ART	**quantity** _____	**Pocket pregnancy**	**quantity** _____
Pocket side effects	**quantity** _____	**PrEP for women**	**quantity** _____

- **Booklets about HIV treatment**

Introduction to ART *(March 2022): 48-page A5 booklet* **quantity** _____

UK Guide To PrEP *(February 2022): 24-page A5 booklet* **quantity** _____

ART in pictures: HIV treatment explained *(June 2019): 32-page A4 booklet* **quantity** _____

Guide to HIV, pregnancy and women's health *(April 2019): 36-page A5 booklet* **quantity** _____

Guide to changing treatment: what if viral load rebounds *(Aug 2021): 24-page A5 booklet* **quantity** _____

HIV and quality of life: side effects and long-term health *(Sept 2016): 96-page A5* **quantity** _____

Guide to HIV testing and risks of sexual transmission *(June 2021): 52-page A5 booklet* **quantity** _____

- **Other resources**

U=U resources:

A3 posters quantity _____ **A5 leaflets quantity** _____ **A6 postcards quantity** _____

HIV Treatment 'Passports' - Booklets for patients to record their own medical history **quantity** _____

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