ISSN 1472-4863

HTB: vol 23 no 4: April 2022

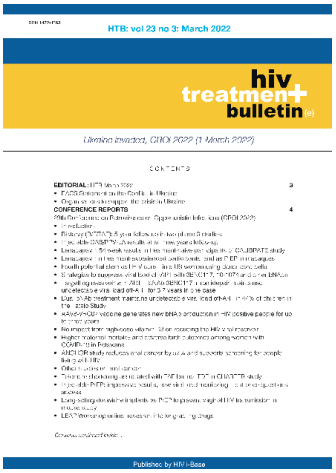
hiv treatment bulletin (e)

Ukraine support, CROI 2022 (1 April 2022)

CONTENTS

Published by HIV i-Base

EDITORIAL



The ongoing war in Ukraine has dominated the news and continues to deeply affect our lives, even when we are lucky enough to not be directly involved and are mainly watching from a distance.

The impact on the people of Ukraine has been terrible and, as with the last issue, we include organisations that are accepting financial support.

https://i-base.info/htb/42633

This includes the EACS collaboration which includes donation of drugs and other medical supplies from doctors and other health professionals.

https://awarehiv.com/en/Dare-to-Share-Care/Ukraine

The rest of this issue continues our reports from CROI 2022, which has now enabled open-access to all conference materials, including webcasts.

https://i-base.info/htb/42605

Reports focus on complications including diabetes, mental health, NAFLD, long COVID and liver disease. We also include a review of islatravir studies, PEP starter packs in the UK and a report on cure-related research from Richard Jefferys.

Other news include the FDA expanded indication to adolescents for cabotegravir/rilpivirine-LA and making the oral lead-in dose now being optional.

COVID-19 news includes the support from BHIVA for a fourth vaccine dose for all people living with HIV in the UK.

Organisations to support the war 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 US-based NGO that works with oganisations in Ukraine 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

The Young Investigators (YING) network in EACS is working to support HIV care in the Ukraine and other countries most directly affected. They have appealed for medical supplies and HIV treatments and financial support.

https://awarehiv.com/en/Dare-to-Share-Care/Ukraine

Frontline AIDS Ukraine Appeal (previously the International HIV/AIDS Alliance) are appealing for support for their partner HIV organisation in Ukraine, Alliance for Public Health (APH)

https://frontlineaids.org/donate/

United Help Ukraine is another US-based non-profit that 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.

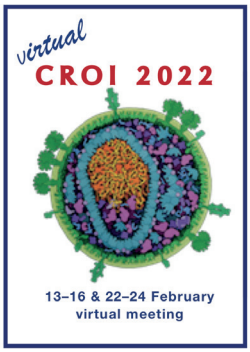
https://mapahelp.me/?fbclid=IwAR1IhRv_Mh_MoxXanX01YTk4d3ckt-n6SyPxwtyiLs4ibQyVogsnvjI_Gic

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.

https://www.croiconference.org

A PDF file of the full programme is available:

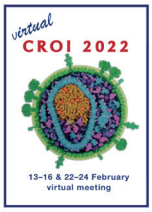
https://www.croiconference.org/wp-content/uploads/sites/2/resources/2022/croi2022-program-abstract-ebook.pdf (PDF)

Our second set of reports are linked below.

- Webcasts now online and open access
- Islatravir studies for treatment and PrEP
- UK study reports diabetes mellitus in 9% of HIV positive Africans in the UK on stable ART
- Life expectancy reduced by eight years following hospitalisation for a mental health condition in South Africa
- Long COVID persists for over a year: evidence for divergent immune responses
- Risk factors for NAFLD and proteinuria in HIV positive people on ART in REPRIEVE study
- UK study shows PEP is started earlier using home starter packs
- Summary of 14 key studies on HIV and liver disease
- Genomic Entrapment of HIV in People on Long-Term ART, chimeric antigen receptor T cells and more on bNAbs

CROI 2022: Webcasts now online and open access

Simon Collins, HIV i-Base



The decision to hold CROI as a virtual meeting this year limited access to the conference webcasts to registered delegates for the first month.

This included 3414 attendees from 86 countries, with about 40% coming from outside the US.

After this, the website platform used for the 2022 meeting has been closed, with the content moving the main CROI website that hosts archived contents from previous conferences.

https://www.croiconference.org/croi-2022

There is a separate link for webcasts:

http://www.croiwebcasts.org

Abstracts from CROI 2022 are also now released as PDF abstract book and as a supplement to Topics in Antiviral Medicine (TAM).

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

https://www.iasusa.org/tam/march-2022

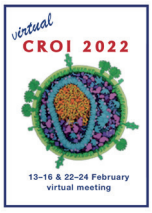
From 1580 abstracts submitted, 898 were accepted (with 214 linked to COVID-19).

Those with a focus on special populations included: adolescents (48), 48 MSM (94), People Who Inject Drugs(39), Transgender (37) and Women (130).

CROI 2022: ANTIRETROVIRALS

CROI 2022: Islatravir studies for treatment and PrEP

Kirk Taylor, HIV i-Base



CROI 2022 included several studies showing the strengths of islatravir for both treatment and prevention, even though this pipeline compound is currently on hold (see comments below). [1]

Results from a phase 2 pharmacokinetic (PK) study reported stable plasma and tissue concentrations of islatravir at week 24 on a monthly dosing regimen, that was similar in plasma, vaginal and rectal tissue. [2]

And a separate poster on penile tissue (often not studied) also supported monthly oral dosing. [3]

Two safety studies reported no significant effects of islatravir upon bone mineral density, renal function, weight gain or QTc. [4-5]

Stable PK for monthly dosing of islatravir at 6 months

A phase 2a placebo-controlled sub-study in HIV negative adults tracked the PK profile of oral islatravir. [3] PK data were calculated for mucosal tissues (cervical, vaginal and rectal), rectal cells and PBMCs.

Participants were female (39%), predominantly Black or African American (70%), median age was 34 years (SD: 11), and were randomised to islatravir (60 mg QM or 120 mg QM) or matching placebo.

Islatravir concentrations peaked at week 1 before dropping to a steady state by week 4 that was then maintained through week 24. Comparable PK profiles were reported for all tissues and cell types tested. The peak and steady state values were higher for the 120 mg group but followed the same trend as the 60 mg group.

Islatravir levels remained above the PBMC PK threshold at each timepoint.

Similar tissue distribution profiles were observed in males and females and islatravir was detected in rectal and vaginal tissues.

Islatravir protects against penile HIV transmission in mice

A mouse study reports tissue distribution and efficacy of daily islatravir (1.8 mg/mL) as PrEP in a penile HIV challenge model. [3]

HIV positive humanised mice responded to islatravir with rapidly declining viral RNA in peripheral blood and penile tissues.

The islatravir group had higher CD4 counts than control animals in peripheral blood and penile tissues.

Islatravir was administered as PrEP and penile HIV challenge performed on three occasions. Whilst 6/11 untreated mice had detectable viremia, all mice in the islatravir group were protected from HIV transmission up to four weeks post-challenge (p=0.0238).

Islatravir does not affect BMD, renal function or QTc interval

The metabolic and renal profile of islatravir was assessed in a phase 2a placebo-controlled trial. [4] Participants were recruited from USA, Israel and South Africa, female (67%), Black (42%), white (53%), Hispanic/Latinx (15%) and median age was 31 (IQR: 18 to 58). Participants received once-monthly islatravir (either 60 mg, n=97 or 120 mg, n=97) or placebo (n=48).

Baseline renal function and median weights were comparable across groups. No significant changes were observed at week 24.

Median weight gain at week 24 was 1.8% for the 120 mg QM islatravir group, which translated to small rises in peripheral (2.5%) and trunk (3.4%) fat. No differences were observed between placebo and the 60mg QM islatravir groups.

A further study evaluated QTc following single dose of islatravir (0.75 mg or 240 mg) or moxifloxacin. [5]

Participants were randomised to islatravir (n=28), moxifloxacin (n=7) or placebo (n=7). Participant characteristics were female (76%), white (89%), Hispanic/Latinx (78%) and median age was 41 (IQR: 19-64).

A transient QTc rise was observed for the 240 mg islatravir group. This effect started after one hour and returned to baseline by hour 4. The rise did not exceed 10 ms and was smaller than the effect of moxifloxacin, which is known to prolong QTc.

C O M M E N T

These studies highlight the stable PK profile of islatravir, consistency in different tissue types (allowing similar dosing irrespective of gender and biological risk) and promising evidence for its efficacy as PrEP.

It shows good renal, metabolic and cardiac safety profiles in HIV negative people.

However, the underlying mechanism of lowered CD4 counts in HIV positive people enrolled on islatravir trials has yet to be explained and is sufficiently serious for most studies to be on clinical hold.

Long-term safety data, including the potential for reversibility, are likely to be and FDA requirement to restart studies, which could easily take longer than a year to establish.

The high demand for the range of long-acting formulations means that the development of islatravir is not likely to be easily dropped.

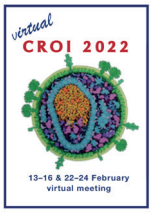
References

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.

1. Collins S. FDA further limit use of islatravir in ongoing studies. HTB (17 December 2022). https://i-base.info/htb/41866
2. Hendrix CW et al. Islatravir distribution in mucosal tissues, PBMC & plasma after monthly oral dosing. CROI 2022. 12-16 February 2022, virtual. Oral presentation 83. https://www.croiconference.org/abstract/islatravir-distribution-in-mucosal-tissues-pbmc-plasma-after-monthly-oral-dosing/
3. Kovarova M et al. EFda Offers complete protection from repeated penile HIV challenges. CROI 2022. 12-16 February 2022, virtual. Poster 210 https://www.croiconference.org/abstract/efda-offers-complete-protection-from-repeated-penile-hiv-challenges/
4. Macdonald P et al. Phase 2a trial of islatravir once monthly for HIV PrEP: Week 24 metabolic and renal outcomes. CROI 2022. 12-16 February 2022, virtual. Oral presentation 85. https://www.croiconference.org/abstract/phase-iia-trial-of-islatravir-qm-for-hiv-prep-week-24-metabolic-and-renal-outcomes/
5. Matthews RP et al. Islatravir does not prolong QTc in a thorough QT study in healthy participants. CROI 2022. 12-16 February 2022, virtual. Poster 432. https://www.croiconference.org/abstract/islatravir-does-not-prolong-qtc-in-a-thorough-qt-study-in-healthy-participants/

CROI 2022: Risk factors for NAFLD and proteinuria in HIV positive people on ART in REPRIEVE study

Kirk Taylor, HIV i-Base



REPRIEVE is a large international clinical study of cardiovascular disease (CVD) risk factors in people with HIV (PWH). Participants were randomised to daily statins or placebo. A sub-study recently reported increased ECG abnormalities for 44% of participants. [1]

Two further REPRIEVE sub-studies that assessed non-alcoholic fatty liver disease (NAFLD) and proteinuria were presented at CROI 2022.

NAFLD was identified in 20% of sub-study participants. Risk factors for NAFLD were BMI >30 kg/m^2, metabolic syndrome and being male. [2]

Relative risk of kidney disease was elevated in women, living in lower income countries, hypertension and TDF use. [3]

The double-blind REPRIEVE trial (NCT02344290) enrolled 7,770 people living with HIV on ART, aged between 40 to 75 years. Participants were randomised to daily pitavastatin (4 mg QD) or placebo.

Several sub-studies are embedded within the trial to evaluate CVD risk.

NAFLD reported for 1 in 5 participants in sub-study

NAFLD is common in people living with HIV and associated with increased CVD risk. Data from the mechanistic sub-study reported risk factors for NAFLD and inflammatory markers. [2]

Participants undergoing non-contrast CT scans were included in the study (n=655).

Clinical criteria for NAFLD were hepatic steatosis <40 HU or liver to spleen ratio <1.0. Steatosis was recorded in 21% of participants (139/655). Exclusion of participants that reported drinking >1 to 2 units per day, led to NAFLD diagnosis for 1 in 5 participants (97/477).

Participants in the NAFLD group were male (82%) and aged >40. Ethnicity was White (63%), Black or African American (20%), Hispanic or Latinx (34%).

BMI was 25 to 29.9 kg/m^2 in 42% of participants and >30 kg/m^2 in 45%; 51% had elevated waist circumference.

Average ASCVD risk scores in the NAFLD group were 5.8 (95% CI: 3.3 to 7.7, p=0.002). Scores indicated borderline or intermediate risk of atherosclerotic disease in 60% of participants.

The NAFLD group also had elevated liver enzymes (ALT; 45% vs 25%, p=0.001) and were more likely to have history of an AIDS-defining event.

NAFLD risk factors were BMI >30 kg/m^2 (RR: 1.76; 95% CI: 1.21 to 2.57) and metabolic syndrome (RR: 1.56, 95% CI: 1.06 to 2.30), whilst females had reduced risk (RR: 0.47, 95% CI: 0.26 to 0.86).

Time since HIV diagnosis, CD4 count, CD4 nadir and viral load were not predictors of NAFLD risk.

Markers of arterial disease (LpPLA-2) and general inflammation (CRP) were modestly elevated in the NAFLD group but remained within the normal range.

NAFLD was not associated with ART or HIV-specific measures.

NAFLD or MAFLD?

Guaraldi and colleagues presented data from two cross-sectional studies showing a significant overlap of NAFLD and MAFLD (metabolic dysfunction-associated fatty liver disease) in HIV positive participants. [4] MAFLD is emerging as a more sensitive criteria for liver disease than NAFLD. [5] Uptake of MAFLD criteria may therefore lead to earlier detection of liver disease in the HIV population.

Women over 50 with previous TDF use have increased chance of proteinuria

People living with HIV have a greater chance of chronic kidney disease, compared to HIV negative people.

Risk factors for kidney disease (proteinuria and albuminuria) are being evaluated in the REPRIEVE kidney ancillary sub-study are assessing risk factors for kidney disease. [3]

Participants were split into three groups by proteinuria: normal to mildly increased (n=1963), moderately increased (n=655) or severely increased (n=74).

Participants were women (38%) and median age was 49 years (IQR: 44 to 54). Ethnicity was Black (48%), White (31%) and Asian (17%). Viral load was <400 copies/mL (98%) and CD4 counts ranged from 443 to 629 cells/mm^3.

Risk factors for kidney disease were being female (RR: 1.71, 95%CI: 1.42 to 2.05), aged over 50 (RR: 1.28, 95% CI: 1.06 to 1.78), current smoker (RR: 1.34, 95% CI: 1.12 to 1.61) and history of TDF use (RR: 1.90, 95% CI: 1.43 to 2.67).

Reduced risk of proteinuria was noted in Black participants and those with BMI <25 kg/m^2.

Albuminuria was less common (9% of participants) and was associated with hypertension (RR: 1.56, 95% CI: 1.20 to 2.04). Participants on thymidine analogues had reduced risk (RR: 0.42, 95% CI: 0.19 to 0.97).

Kidney disease was more common in participants recruited from lower income regions (e.g., sub-Saharan Africa and East Asia). This difference may be due to reduced access to prevention services and other factors not covered by this study.

In summary, REPRIEVE sub-study data indicate associations between NAFLD and increased BMI, metabolic dysfunction, and male sex. Kidney disease was more common in women aged over 50 with history of TDF use.

C O M M E N T

These data highlight CVD risk factors but have not been adjusted for statin use. It will be important to determine whether these associations persist in the unblinded datasets.

Dr Overton answered questions from Drs Hunt, Mallon and Kallianpur during the poster discussion. Their exchanges highlighted that higher, but non-significant, rates of kidney disease reported from lower income countries may be related to reduced access to treatment and prevention services.

Associations between women and kidney disease may partly be explained by higher numbers of female participants from lower income countries.

Finally, reduced risk of albuminuria with thymidine analogues may be related to PWH that did not experience side effects and were not switched onto alternatives, such as TDF.

A patient leaflet on NAFLD and HIV is available from i-Base. [6]

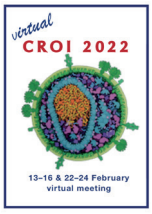
References

1. Collins S. ECG abnormalities reported by 44% of people older than 40 on ART: results from REPRIEVE study. (HTB 20 December 2021). https://i-base.info/htb/41907
2. Fichtenbaum CJ. NAFLD is common and associated with cardiovascular risk in REPRIEVE participants. CROI 2022. 12-16 February 2022, virtual. Poster 520. https://www.croiconference.org/abstract/nafld-is-common-and-associated-with-cardiovascular-risk-in-reprieve-participants/
3. Overton ET. Proteinuria is common among people with HIV with controlled viremia. CROI 2022. 12-16 February 2022, virtual. Poster 607. https://www.croiconference.org/abstract/proteinuria-is-common-among-people-with-hiv-with-controlled-hiv-viremia/
4. Guaraldi G. From NAFLD to MAFLD: implications of change in terminology for people with HIV. CROI 2022. 12-16 February 2022, virtual. Poster 521 https://www.croiconference.org/abstract/from-nafld-to-mafld-implications-of-change-in-terminology-in-pwh/
5. Yamamura S. MAFLD identifies patients with significant hepatic fibrosis better than NAFLD. Liver International, Vol 40 (12) (3018-3030). DOI:10.1111/liv.14675 (30 September 2020). https://onlinelibrary.wiley.com/doi/epdf/10.1111/liv.14675
6. i-Base. NAFLD: HIV and fatty liver disease. (September 2019). https://i-base.info/guides/side/hiv-and-fatty-liver-disease.

CROI 2022: UK study reports diabetes mellitus in 9% of HIV positive Africans in the UK on stable ART

Kirk Taylor, HIV i-Base

CROI 2022 included a UK study looking at the prevalence of diabetes mellitus (DM) in HIV positive Africans on ART. [1]



The GEN-AFRICA cross-sectional cohort study enrolled HIV positive participants that attended 15 UK clinics between 2018 to 2020 and evaluated risk factors for DM.

Participants (n=2,308) were from West (36%), East (33%), South (24%) or Central Africa (7%), were female (62%) and heterosexual (87%). HIV was well managed with 99% on ART, viral load of <200 copies/mL (94%) and median CD4 count of 556 cells/mm^3 (IQR 409 to 721). Mean age was 48.0 years [SD 9.9].

Common comorbidities were obesity (44%), hypertension (31%), and proteinuria (22%), whilst only 4% had cardiovascular disease. Type 2 diabetes was reported for 9% (n=216) and was most common in participants over 50 (72%).

DM and obesity increased with age but the association between DM and obesity was lost after multivariate analysis. Female participants were more likely to be obese (52% vs 31%, p<0.001), but males were more likely to have DM (12.8% vs 7.4%, p<0.001).

The authors emphasise the importance of routinely screening HIV positive Africans for DM, especially if they are older than 40.

C O M M E N T

These data highlight associations between HIV, age and obesity and diabetic risk. Approximate prevalence of DM is currently about 6% in the UK general population, which will be older than an HIV cohort.

However, this was a small cross-sectional sample and longitudinal data are needed to further understand diabetic risk in HIV positive African populations.

Associations between DM and obesity in this study are limited by use of BMI measurements rather than measures of central obesity.

Earlier studies have reported that HIV is associated with higher rates of DM than the general population, and that this also increases with age. [2]

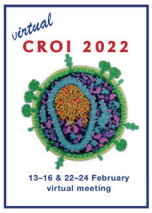
These results highlight the importance of the BHIVA recommendation for baseline assessment for diabetes and annual metabolic assessment including HbA1c and lipid profile if aged >40 years. [3]

References
1. Hardy G. Increased prevalence of diabetes in HIV positive people. HTB (26 June 2017). https://i-base.info/htb/31692
2. Hamzah et al. Age and obesity as risk factors for diabetes in Africans with HIV. CROI 2022, 12–16 February 2022, virtual. Poster 604 https://www.croiconference.org/abstract/age-and-obesity-as-risk-factors-for-diabetes-in-africans-with-hiv/
3. BHIVA. BHIVA guidelines for the routine investigation and monitoring of adult HIV-1-positive individuals 2016 (2019 interim update). https://www.bhiva.org/monitoring-guidelines

CROI 2022: Life expectancy reduced by eight years following hospitalisation for a mental health condition in South Africa

Kirk Taylor, HIV i-Base

CROI 2022 included a study from South Africa that predicted loss of eight years life for HIV positive people who had been hospitalised for a mental health disorder. [1]



Links between mental health and mortality were studied using records from a private HIV management programme in South Africa. Data from 122,853 HIV positive people that had median age of 39 (IQR: 33 to 46) at first hospital admission were analysed.

Hospitalisation for mental health disorders accounted for 8,505 cases and classified as depression (84%), substance abuse (12%), bipolar (10%), organic (6%) or psychotic disorders (3%).

Life years lost (LYL) were a prediction of reduction in life expectancy due to hospitalisation for a mental health condition. LYL was mostly accounted for by natural deaths. These data show that LYL was greater for men (9.2 years, 95% CI: 7.9 to 10.4) than women (6.6 years, 95% CI: 5.0 to 8.3). Furthermore, LYL were three times greater for organic vs non-organic causes at 16.6 years (95% CI 15.3 to 17.7).

C O M M E N T

This study reports significant increase in mortality for HIV positive people that have been hospitalised for a mental health condition. However, this is a single-centre study with small sample size.

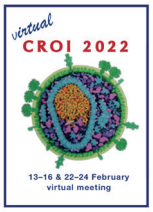
More data are required to determine whether this is a regional effect or more widely observed trend.

References
1. Ruffieux et al. Excess life-years lost associated with hospitalization for mental illness. CROI 2022, 12–16 February 2022, virtual. Poster 766. https://www.croiconference.org/abstract/excess-life-years-lost-associated-with-hospitalization-for-mental-illness/

CROI 2022: Long COVID persists for over a year: evidence for divergent immune responses

Kirk Taylor, HIV i-Base

Approximately 20% of the studies at CROI 2022 had a link to COVID-19, included several focused on long COVID (PASC).



A French cohort study reported persistence of COVID symptoms a year after hospital admission that was was more common in women than men with 25% of people not returning to work after a year. [1]

Another study differentiated people with ong COVID by antibody responses, although the clinical impact this has on disease progression was unclear. [2]

Persistent COVID symptoms 12 months post-hospital admission

A prospective cohort study followed people hospitalised with COVID (n=737) for a year after admission.

Participants were male (64%) with median age of 61 years (IQR: 51 to 70), 37% had been admitted to ICU and 27% had ≥3 symptoms at 12 months.

Follow-up visits were conducted at 3, 6 and 12 months post-admission. Participant interviews assessed quality of life, COVID symptoms and psychological distress. The most reported symptoms were fatigue (46%), shortness of breath (33%) and joint pain (21%).

Overall, 25% of participants had not returned to work after a year. This was more common for women (34%) than men (24%). Women also reported more COVID symptoms, depression, and anxiety.

Differential antibody responses of people with long COVID

Antibody responses were evaluated from people with long COVID who had persistent or resurgent symptoms three months post-infection. [2]

Participants either had long COVID (n=44), had recovered from COVID (n=25) or were uninfected (n=14).

Anti-COVID spike IgG and IgA antibody titres were measured and 48% of long COVID patients were seropositive. Seropositive patients had increased T Cell responses to inflammatory stimuli and COVID proteins in vitro. The seronegative group responses were not statistically different to people who had recovered.

These data show differences in the adaptive immune responses of people with long COVID that might help to understand reasons for disease persistence and potential therapies.

C O M M E N T

Long COVID is now a well-established complication that is complicated by very diverse symptoms and the lack of a single mechanism or simple diagnostic test,

These studies highlight the persistence of COVID symptoms and associated quality of life implications.

Kervevan and colleagues report divergent antibody responses that map to altered T cell responses but their study does not describe how these findings relate to disease progression or severity.

Further studies are required to understand the aetiology of long COVID and identify potential risk factors to facilitate clinical management.

The UK 100-page guidelines on late COVID were recently updated by NICE, the Scottish Intercollegiate Guidelines Network (SIGN) and the Royal College of General Practitioners (RCGP). [3]

These guidelines were also previously criticised for a limited focus on potential causes and the range of symptoms and for minimal involvement of people living with long COVID. [4]

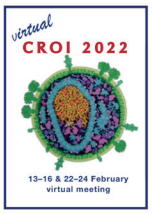
References

1. Chirouze et al., PersistentCOVID-19 symptoms are highly prevalent 12 months after hospitalisation. CROI 2022, 12–16 February 2022, virtual. Poster 628.
https://www.croiconference.org/abstract/persistent-covid-19-symptoms-are-highly-prevalent-12-months-after-hospitalization/
2. Kervevan et al. Divergent adaptive immune responses define two types of long COVID. CROI 2022, 12–16 February 2022, virtual. Poster 322.
https://www.croiconference.org/abstract/divergent-adaptive-immune-responses-define-2-types-of-long-covid/
3. NICE et al. COVID-19 rapid guideline: managing the long- term effects of COVID-19. (3 March 2022).
https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-51035515742
4. Gorna R et al. Long COVID-19 guidelines need to reflect lived experience. Lancet. 2021; 397: 455-457.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32705-7/fulltext

CROI 2022: HIV PREVENTION

CROI 2022: UK study shows PEP is started earlier using home starter packs

Simon Collins, HIV i-Base



A UK study reported benefits from having 5-day starter packs of PEP at home for people at risk of HIV that included a significantly shorter time to starting PEP – the most important factor for PEP efficacy.

During 2018/19, the phase 4 HOME PEP study randomised 139 gay men (1:1) to either immediate access to starter packs (once-daily maraviroc plus TDF/FTC) for 48 weeks or to current standard of care, with access to starter packs for six months after week 48.

The study enrolled mainly youngish gay men who were sexually active, at risk of HIV and engaged in care.

Baseline characteristics included median age 30 (IQR: 26 to 30); 70% White, 9% Black/African; 72% University education; 72% full-time work, 7% part-time, 15% college; 55% born in the UK and 65% currently single.

More than half (56%) had an STI diagnosis in the previous 12 months, with one-third rectal. Most people had several HIV tests in the previous year (median 3; IDR 2 to 4) and 39% had previously used PEP.

If PEP was started, based on a self-completed risk questionnaire, the decision to continue was decided by a doctor. The most common use (81% cases) was due to receptive anal sex with a man of unknown HIV status. Risk and quality of life questionnaires were completed by all participants every three months.

Based on results for the first 48 weeks, access to starter packs meant that PEP was used more often: in 22 vs 13 cases). This didn't lead to inappropriate use which was judged appropriate in 29/33 cases (88%, 95% CI: 73 to 95%).

The home packs significantly reduced the median time to first dose: 7.6 hours (IQR: 3.0 to 20.9; n=22) vs 28.5 hours (IQR: 17.3 to 34; n=13), p<0.01. PEP was used more than once by 6 vs 2 people in the immediate vs deferred arm, respectively.

Most participants using PEP in the immediate arm started PEP straight after sex (n=10), with 4 and 6 cases starting before 10 and 20 hours respectively. One person in each arm didn't start PEP until after 48 hours (perhaps because risks don't always occur at home).

Access to the packs did not change risk behaviour during the study, with risks remaining similar in each arm to the three months before the study (512 vs 911 in the immediate vs deferred groups respectively, p = 0.215).

Although the immediate group had almost half the number of missed chances to use PEP (268 vs 474,) 9/12 (75%) of participants reporting >10 missed chances were in the deferred arm, making the difference non-significant (p = 0.62).

One person became HIV positive in the deferred arm during 231 person years of follow-up. The participant had document high risk and had been encouraged to use PrEP.

A similar number of bacterial STIs were reported in each arm (27 vs 31, p=0.70).

C O M M E N T

The only evidence for PEP efficacy from a randomised study used a similar design involving starter pack, r strategy of having starter supplies of PEP has

Time to starting PEP is also directly related to efficacy with advice to begin asap. This is important as recent animal studies using 3D imaging have detected infections in macaques occuring within two hours of exposure and by contrast, access to PEP from travelling to an A&E service commonly delays practical access to 24 to 48 hours.

Study limitations included significant loss to follow-up, affected by limited clinic access during COVID-19.

Reference

Fox J et al. Self-start home PEPSE to reduce uptake time and increase PEPSE efficacy: RCT. CROI 2022. 12-16 February 2022, virtual. Poster abstract 849.

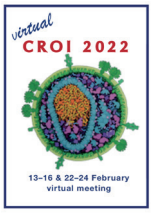
https://www.croiconference.org/abstract/self-start-home-pepse-to-reduce-uptake-time-and-increase-pepse-efficacy-rct

CROI 2022: HEPATITIS COINFECTION

CROI 2022: Summary of 14 key studies on HIV and liver disease

Jurgen K Rockstroh for NATAP.org

Unfortunately, 2022 has now become the third year in row where CROI had to take place as a virtual conference meeting.



This however, has not strongly impacted interest or participation in the CROI meeting but has been accompanied by a significantly lower number of abstract submissions in the liver disease field. As a consequence of shifted interests but also rechanneled research money and working capacity, new results around COVID-19 vaccines and antivirals have dominated the scientific submissions to CROI with many subsequent oral abstract sessions covering various new aspects of COVID-19 research.

The oral abstract session for hepatitis research was integrated into the session on tuberculosis, opportunistic infections, and hepatitis. Indeed, there was only one oral abstract on translational HBV research, two on HCV, one on talaromycosis and five on various aspects around tuberculosis in that particular session. Nevertheless, there were still numerous interesting abstract submissions which could be found in the poster sessions focusing on various aspects of liver disease in HIV**.**

The main topic in the oral abstract session was HCV elimination targets in light of the COVID-19 pandemic but also availability of easy to administer all oral HCV DAA-based therapies. [1, 2]

Whereas, the US appears to struggle even more under the impact of COVID-19 on hepatitis services to stay on target for reaching the HCV elimination goals, Western Europe and Australia are well on track in their HIV/HCV coinfected population to reach HCV elimination by 2030.

Another important HCV presentation highlighted the advantages of universal HCV screening among pregnant people attending care in Western Pennsylvania versus risk-based HCV screening. [3]

Other important topics discussed at this year CROI included results of a randomized HBV vaccination trial, new HBV infections in an HIV cohort in Texas, new long-acting tenofovir formulation for HBV therapy, HCV elimination in MSM, DAA salvage therapy, clinical outcomes after SVR and various aspects around fatty liver disease. [4-14]

The following summary aims at highlighting some of the exciting new data reported at CROI 2022 and to initiate a discussion about their usefulness and relevance for clinical management of liver disease in HIV-coinfected individuals.

Summary points

- HBV revaccination with three double doses of HBV vaccine achieves higher serological responses than with three standard-doses of HBV vaccine among MSM who were born in the era of universal neonatal HBV vaccination. Reassuringly, virologically suppressed people living with HIV with CD4 counts >500 cells/mm^3 show similar responses after revaccination as HIV negative MSM.
- People living with HIV who are unvaccinated for hepatitis B are at higher risk for new hepatitis B infections. A particular high risk was found among those individuals with hepatitis C. In conclusion, this study strongly recommends HBV vaccination in HBV seronegative people living with HIV even if they are on dual active HIV/HBV antiviral therapy.
- A nanoformulated TFV prodrug suppresses HBV DNA in humanised and transgenic mice for three months. These data suggest that a long-acting tenofovir formulation for treatment of HBV infection can be developed.
- The US is currently not on track to achieve the WHO elimination targets pre-pandemic and has fallen further behind during the COVID-19 pandemic. Increased efforts including scale-up of HCV diagnosis, treatment, and prevention are needed to overcome this unfavorable development.
- Pooled analysis from Australia and selected Western European countries demonstrates that following broad access to DAA therapy these countries are on track to meet the WHO elimination incidence target for people living with HIV in care by 2030.
- The German NoCo cohort demonstrates stable HCV incidence rates despite a broad use of DAAs up to 2019. In 2021, however, micro-elimination goals are met due to a drop in HCV incidence, possibly due to behavior changes related to the SARS-CoV-2 pandemic and associated containment measures or because of a declining HCV reservoir over time with many MSM successfully treated with DAAs. These results emphasise that HCV elimination in MSM is achievable.

- With regular HCV testing and improved access to antiviral treatments, particularly highly effective direct-acting antivirals (DAAs) in Taiwan, the incidence rate and prevalence of HCV viremia have declined by 80% among people living with HIV between 2011 and 2021.
- Risk-based HCV screening is insensitive for HCV detection within the general obstetric population. In contrast universal HCV screening of pregnant people does not only ensure that the pregnant person is linked to treatment, but also enables detection of all cases of perinatal HCV transmission.
- SOF/VEL/VOX is highly effective for HCV treatment in people living with HIV previously failing to DAA regimens. Effectiveness was confirmed across all genotypes and in the presence of cirrhosis.
- Ravidasvir + sofosbuvir was well tolerated with excellent safety and efficacy in chronic HCV infection, including in difficult-to-treat populations (GT3, cirrhosis, prior HCV treatment, HIV co-infection).
- The risk of clinical progression to liver disease associated events following DAA-induced SVR in people with HIV/HCV coinfection with advanced fibrosis is independently associated with age, sex, liver disease severity, and changes in liver stiffness one year after finalization of HCV therapy.
- Within the MACS Coronary Atherosclerosis Progression Study the incidence rate of CT-measured NAFLD was high at 2.5/100 PYs. Higher BMI and visceral adiposity, but not HIV, were associated with incident NAFLD.
- A high prevalence of liver steatosis can be found among people living with HIV on ART in Switzerland. In addition to well-established risk factors such as age, ethnicity and obesity, the use of TAF was significantly associated with hepatic steatosis.
- Among people living with HIV without concomitant causes of liver disease other than NAFLD, liver stiffness as well as FAST score predict overall survival.
- Cannabis use may reduce the risk of hepatic steatosis in HIV/HCV-negative and those with HIV monoinfection, but not in HCV-positive individuals. Further studies are needed to help better understand the biological mechanisms for the beneficial effect of cannabis use observed in this study.

This article only includes the introduction, summary points and references from a longer detailed report of these studies. For the full article, please see NATAP.org.

Source

Rockstroh JK. Summary from virtual CROI 2022 for HIV and liver disease Hepatitis elimination for 2030 on track? Is fatty liver disease a growing concern? New insights from CROI 2022.

https://natap.org/2022/CROI/croi_182.htm

References

These references are for the full online report at natap.org.

https://natap.org/2022/CROI/croi_182.htm

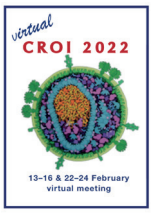
1. Ortega REF et al. Modelling impact of COVID-19 pandemic on hepatitis C virus elimination in the US. CROI 2022, 12–16 February 2022, virtual. Oral abstract 72.
   https://www.croiconference.org/abstract/modeling-impact-of-the-covid-19-pandemic-on-hepatitis-c-virus-elimination-in-the-us/
2. Van Santen DK et al. Effect of direct-acting antivirals on HCV incidence among people living with HIV. CROI 2022, 12–16 February 2022, virtual. Oral abstract 73.
   https://www.croiconference.org/abstract/effect-of-direct-acting-antivirals-on-hcv-incidence-among-people-living-with-hiv/
3. Chappell C et al. Uprising circulation of HBV-complex profiles with HBsAG vaccine-escape mutations. CROI 2022, 12–16 February 2022, virtual. Oral abstract 27.
4. Huang C et al. Randomized Trial of HBV Revaccination in MSM Born in the Neonatal Vaccination Era. CROI 2022, 12–16 February 2022, virtual. Poster abstract 544.
   https://www.croiconference.org/abstract/a-randomized-trial-of-hbv-revaccination-in-msm-born-in-the-neonatal-vaccination-era/
5. Jain MK et al. New Hepatitis B infection among HIV patients: Who is at risk? CROI 2022, 12–16 February 2022, virtual. Poster abstract 548.
   https://www.croiconference.org/abstract/new-hepatitis-b-infection-among-hiv-patients-who-is-at-risk
6. Das S et al. A nanoformulated TFV prodrug suppresses HBV DNA in humanized and transgenic mice for three months. CROI 2022, 12–16 February 2022, virtual. Poster abstract 545.
   https://www.croiconference.org/abstract/a-long-acting-tenofovir-prodrug-suppresses-hbv-replication-for-over-3-months
7. Ingiliz P et al. The impact of COVID-19 on HCV microelimination in MSM in Germany. CROI 2022, 12–16 February 2022, virtual. Poster abstract 539.
   https://www.croiconference.org/abstract/the-impact-of-covid-19-on-hcv-micro-elimination-in-msm-in-germany
8. Ho SY et al. Progress towards HCV microelimination among HIV-positive patients in Taiwan. CROI 2022, 12–16 February 2022, virtual. Poster abstract 538.
   https://www.croiconference.org/abstract/progress-toward-hcv-microelimination-among-hiv-positive-patients-in-taiwan
9. Carbonero LM et al. Treatment with SOF/VEL/VOX in HIV-HCV coinfected patients previously exposed to DAAs. CROI 2022, 12–16 February 2022, virtual. Poster abstract 529.
   https://www.croiconference.org/abstract/treatment-with-sof-vel-vox-in-hiv-hcv-coinfected-patients-previously-exposed-to-daas/
10. Berenguer J et al. Impact of SVR with DAAs in coinfected patients with advanced fibrosis/cirrhosis. CROI 2022, 12–16 February 2022, virtual. Poster abstract 531.
    https://www.croiconference.org/abstract/impact-of-svr-with-daas-in-coinfected-patients-with-advanced-fibrosis-cirrhosis
11. Price J et al. High incidence of CT-measured NAFLD in men with and without HIV infection. CROI 2022, 12–16 February 2022, virtual. Poster abstract 523.

https://www.croiconference.org/abstract/high-incidence-rate-of-ct-measured-nafld-in-men-with-and-without-hiv-infection
12. Riebensahm C et al. Determinants of liver steatosis in people living with HIV on antiretroviral therapy. CROI 2022, 12–16 February 2022, virtual. Poster abstract 524.
https://www.croiconference.org/abstract/determinants-of-liver-steatosis-in-people-living-with-hiv-on-antiretroviral-therapy
13. Macias J et al. Impact of NASH on the survival of people living with HIV. CROI 2022, 12–16 February 2022, virtual. Poster abstract 518.
https://www.croiconference.org/abstract/impact-of-nash-on-the-survival-of-people-living-with-hiv/
14. Diaz-Martinez J et al. Cannabis use and hepatic steatosis by MRI-PDFF. CROI 2022, 12–16 February 2022, virtual. Poster abstract 525.
https://www.croiconference.org/abstract/cannabis-use-and-hepatic-steatosis-by-mri-pdff
15. Jain MK et al. Low rates of hepatitis B vaccination among people with HIV. CROI 2022, 12–16 February 2022, virtual. Poster abstract 546.
https://www.croiconference.org/abstract/low-rates-of-hepatitis-b-vaccination-among-hiv-patients
16. Heuft MM, et al. Protective effect of hepatitis B virus-active antiretroviral therapy against primary hepatitis B virus infection. AIDS. 2014;28:999-1005.
https://pubmed.ncbi.nlm.nih.gov/24685742
17. Kusejko K et al. A systematic re-screening for hepatitis C RNA among men who have sex with men living with HIV in the Swiss HIV Cohort Study two years following a nation-wide elimination program reveals a sustainable effect towards hepatitis C elimination. EACS 2021; OS2/3.
18. Tan SS et al. Efficacy & safety of ravidasvir + sofosbuvir in hepatitis C: STORM-C-1 final results. 29th Virtual Conference on Retroviruses and Opportunistic Infections, February 12-16, 2022, abstract 528.
https://www.croiconference.org/abstract/efficacy-safety-of-ravidasvir-sofosbuvir-in-hepatitis-c-storm-c-1-final-results/
19. Bischoff J et al. Stratifying the risk of NAFLD in patients with HIV under combination antiretroviral therapy (cART). EClinicalMedicine. 2021 Sep 5;40:101116.
https://pubmed.ncbi.nlm.nih.gov/34522873/
20. Eslam M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol 2020; 73(1):202-209.
https://pubmed.ncbi.nlm.nih.gov/32278004

CROI 2022: Genomic entrapment of HIV in people on long-term ART, chimeric antigen receptor T cells and more on bNAbs

Richard Jefferys, TAG

Genomic entrapment of HIV in people on Long-Term ART



Kyra Seiger from the Ragon Institute of MGH, MIT and Harvard described results demonstrating that the makeup of the HIV reservoir shifts over time in people on long-term antiretroviral therapy (ART). [1]

The key finding is that a substantial proportion of the intact HIV that persists after long-term ART appears to be entrapped in the genetic code of remaining infected cells, and likely unable to emerge and replicate.

The finding relates to how HIV integrates its genetic code—in the form of HIV DNA—into the human DNA (known as the genome) of the cells that it infects.

As a loose analogy, if you think of a cell's genome as a factory for producing all the proteins the cell needs to go about its daily business, HIV DNA tends to integrate in machinery that gets switched on regularly. This gives the virus opportunities to hijack that machinery to make more HIV proteins (and potentially more copies of infectious HIV).

But HIV DNA can also land in the genomic equivalent of a darkened factory storage room nobody goes into (sometimes referred to as a "gene desert")—in that case, the virus can become trapped and unable to reactivate.

The importance of where HIV DNA integrates into a cell's genome was first highlighted by studies of elite controllers, which provided evidence that their immune responses can clear cells containing more active HIV, leaving behind only those cells containing HIV integrated in places in the genome from which it can't reactivate. Essentially, the intact HIV that remains in their bodies appears entrapped, and unable to replicate or cause harm. [2]

In two widely publicised cases involving elite controllers – Loreen Willenberg and the Esperanza Patient – this phenomenon may have resulted in a natural cure of HIV.

More recently, a small study published by the laboratory of Xu Yu at the Ragon Institute has offered a hint that something similar may be occurring in people on long-term ART. [5]

Seiger's CROI presentation built on this work, analyzing the location of integrated HIV in eight people who've been on ART for an average of around 20 years (the range was 17-23 years). In this group, approximately 84% of the intact HIV that could be detected was in locations in the genome that are unfavorable to reactivation. In contrast, only 31% of intact HIV in a cohort of 43 people on ART for a shorter duration (1-13 years) was in similar locations.

Seiger noted that this offers evidence that cells containing HIV capable of reactivating are preferentially eliminated over time in people on long-term ART—likely because the activity of HIV can generate viral proteins that flag the cells for destruction by the immune system.

Additional evidence supporting this scenario is that non-intact, defective integrated HIV DNA doesn't show a similar pattern. When Seiger analyzed defective integrated HIV DNA in the group on long-term ART, there was no evidence for preferential elimination of defective HIV DNA located in more active regions of the genome.

The results are encouraging because they suggest that, over time, HIV-specific immune responses in people on ART can contribute to reducing the reservoir of intact HIV.

As reported by Jon Cohen for Science Magazine in January, the next step for this research is to conduct careful analytical treatment interruptions (ATIs) in people who've been on long-term ART and whose remaining intact HIV DNA is integrated into apparent gene deserts. [6]

The hope is that the only intact HIV left in their bodies may be inert and incapable of causing viral load rebound. The researchers stress, however, that only individuals with a particular HIV reservoir profile will be eligible for these studies, and people on long-term ART shouldn't attempt ATIs on their own.

The evidence that HIV-specific immune responses can reduce the intact viral reservoir in people on ART also provides a fillip for efforts to bolster these responses with immune-based therapies, such as CAR T cells, broadly neutralising antibodies and therapeutic vaccines.

Chimeric antigen receptor (CAR) T cells

During an interactive session on chimeric antigen receptor (CAR) T cells, Jim Riley from the University of Pennsylvania revealed preliminary results from an ongoing clinical trial in people with HIV. [7, 8]

The CAR approach involves genetic modification of T cells to equip them with receptors that enable better recognition and killing of specific targets. CAR T cell candidates designed to recognize and kill cancerous cells have shown efficacy in clinical trials and several are now licensed as cancer treatments.

Riley's study administered CAR T cells designed to target HIV-infected cells, in combination with CD4 T cells that have been genetically modified to block expression of the CCR5 receptor (which HIV uses to enter cells). The latter strategy was developed by Sangamo Therapeutics. Each study participant had their cells sampled, expanded and modified in the laboratory, and then reinfused.

Riley was able to share data from eight participants. Four started an ATI the day after receiving the cell infusions and four waited eight weeks after the infusion before undergoing ATI. All participants in the first group experienced viral load rebounds over 100,000 copies/ml, which necessitated restarting ART before the end of the planned 16-week ATI. In contrast, the second group were able to complete the ATI with viral loads mostly in the low thousands.

One participant maintained a very low viral load and didn't restart ART after 16 weeks. This individual has now been followed for around 16 months off ART and the most recent viral load was 37 copies/ml.

Riley noted that this person had participated in previous Sangamo trials and had received two infusions of CD4 T cells genetically modified to block expression of the CCR5 receptor. While this single case of extended viral load control off ART is an outlier in the context of the trial, the outcome suggests that strategies aiming to bolster the number of gene-modified cells are worth pursuing.

Riley's research group already has a potentially enhanced CAR T cell design that they intend to move into trials. This newer CAR T cell includes the co-stimulatory molecules 4-1BB and CD28 and, in animal models, showed increased proliferative potential and activity.

More on broadly neutralising antibodies (bNAbs)

The day after Ole Søgaard debuted the primary results from the eCLEAR study (see prior blog post [9]), Míriam Rosás-Umbert from Aarhus University provided additional details on the immune-enhancing effects of the bNAb 3BNC117. [10]

Rosás-Umbert explained that bNAbs can bind to HIV and chaperone the virus into cell pathways that promote antigen presentation (in other words, help make HIV visible to other components of the immune system, including T cells). Evidence for bNAbs boosting virus-specific CD8 T cell responses has been previously reported in both macaque and human studies. [11, 12]

Among eCLEAR study participants with HIV that was sensitive to 3BNC117, Rosás-Umbert found that CD8 T cell responses targeting HIV Gag and Pol proteins were significantly higher at months three and 12 of follow up compared to other participants.

The ability of T cells to produce the cytokine interferon gamma in response to HIV Gag was also significantly greater in participants with HIV that was sensitive to 3BNC117, and this capacity was associated with maintenance of viral load below 5,000 copies/mL during an ATI (in one case, HIV viral load has remained undetectable for 3.7 years off ART). [13]

A poster presentation by Christian Gaebler from Rockefeller University debuted results from a trial combining two bNAbs, 3BNC117 and 10-1074, in people with HIV on ART. [14]

As in previously published studies from the same group, the bNAbs showed strong anti-HIV activity. [15]

The most intriguing finding was that two participants were able to maintain HIV viral load suppression without ART for an extended period after bNAb administration. One of the individuals has since been lost to follow up, but the other is approaching three years off ART with no viral load rebound. Similarly prolonged post-treatment control of viral load was observed for two participants in a prior trial of this bNAb combination. [16]

Taken together, these results strongly support the idea that bNAbs can have a vaccine-like effect that improves the immune response to HIV. The challenge now is to increase the proportion of people able to control viral load after an ATI. Multiple trials of bNAb combinations are ongoing (see TAG's Research Toward a Cure Trials listing) and many more are planned. [17]

Source

Jefferys R. Genomic entrapment of HIV in people on long-term antiretroviral therapy, chimeric antigen receptor T cells and more on bNAbs. TAG Basics Science Blog. (21 March 2022).

https://tagbasicscienceproject.typepad.com/tags_basic_science_vaccin/2022/03/croi-2022-genomic-entrapment-of-hiv-in-people-on-long-term-antiretroviral-therapy-chimeric-antigen-r.html

References

1. Seiger K et al. Selection of intact HIV-1 proviruses in deep latency during long-term ART. CROI 2022, oral abstract 05.
https://www.croiconference.org/abstract/selection-of-intact-hiv-1-proviruses-in-deep-latency-during-long-term-art
2. Jiang C et al. Distinct viral reservoirs in individuals with spontaneous control of HIV-1. ***Nature***. 2020;585(7824):261-267. doi:10.1038/s41586-020-2651-8.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7837306
3. Cohen J. How 'elite controllers' tame HIV without drugs. Science. (26 August 2020.
https://www.science.org/content/article/how-elite-controllers-tame-hiv-without-drugs
4. TAG. Story: The Esperanza Patient – Argentinian woman's immune system may have cleared all intact HIV .(November 2021).
https://www.treatmentactiongroup.org/cure/media-monitor/story-the-esperanza-patient-argentinian-womans-immune-system-may-have-cleared-all-intact-hiv
5. Einkauf et al. Parallel analysis of transcription, integration, and sequence of single HIV-1 proviruses. Cell, doi: 10.1016/j.cell.2021.12.011. (12 January 2022).
https://www.cell.com/cell/fulltext/S0092-8674(21)01449-5
6. Cohen J. Mapping where HIV hides its genes suggests cure strategy. 12 January 2022).
https://www.science.org/content/article/mapping-where-hiv-hides-its-genes-suggests-cure-strategy
7. ClinicalTrials.gov. CD4 CAR+ ZFN-modified T cells in HIV therapy.
https://clinicaltrials.gov/ct2/show/NCT03617198
8. CROI 2022. Chimeric antigen receptors (CARs): what's next? Webcasts.
http://www.croiwebcasts.org/s/2022croi/Interactive-6
9. TAG, CROI 2022: CROI 2022 Update: a new potential HIV cure case; broadly neutralizing antibody enhances post-treatment control.
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
10. Rosás-Umbert M et al. Administration of 3BNC117 at ART initiation induces long-term HIV CD8 T-cell immunity. CROI 2022, 12–16 and 22–24 February, virtual meeting. Oral abstract 62.
https://www.croiconference.org/abstract/administration-of-3bnc117-at-art-initiation-induces-long-term-hiv-cd8-t-cell-immunity (abstract)
11. Nishimura Y et al. Early antibody therapy can induce long lasting immunity to SHIV. Nature. 2017 Mar 23; 543(7646): 559–563.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5458531
12. Neissl J et al. Combination anti-HIV-1 antibody therapy is associated with increased virus-specific T cell immunity. Nat Med. 2020; 26(2): 222–227.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7018622
13. https://en.wikipedia.org/wiki/Interferon_gamma
14. Gaebler C et al. Prolonged viral suppression by immunotherapy with anti-HIV antibodies 3BNC117/10-1074. CROI 2022. 12-16 February 2022, virtual. Poster abstract 686.
https://ww2.aievolution.com/cro2201/index.cfm?do=abs.viewAbs&abs=2950 (abstract)
15. Bar-On Y et al. Safety and anti-viral activity of combination HIV-1 broadly neutralizing antibodies in viremic individuals. Nat Med. 2018 Nov; 24(11): 1701–1707.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6221973
16. Mendoza P et al. Combination therapy with anti-HIV-1 antibodies maintains viral suppression. Nature. 2018 Sep; 561(7724): 479–484.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6166473
17. TAG. Research toward a cure trials.
https://www.treatmentactiongroup.org/cure/trials

ANTIRETROVIRALS

US FDA removes need for oral lead-in with long-acting cabotegravir/rilpivirine injections: indication extended to adolescents

Simon Collins, HIV i-Base

On 24 March 2022, the US FDA announced that the need to use one month on oral formulations of cabotegravir and rilpivirine before using the long-acting injectable formulations, is now optional. [1]

Until now, the oral lead-in has been a safety requirement to reduce the risk of a hypersensitivity reaction or other side effects from drugs that have an extremely long half-life and that are not otherwise removeable.

Oral formulations will still be available for people who want to use this additional safety option.

A few days later, the FDA also extended the indication from adults to also include adolescents who are 12 years or older and weighing at least 35 kg. [2]

For more details please refer to the full prescribing information.

References

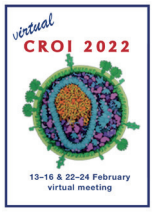
1. ViiV Healthcare. ViiV Healthcare announces label update for its long-acting HIV treatment, Cabenuva (cabotegravir, rilpivirine), to be initiated with or without an oral lead-in period. (24 March 2022).
https://viivhealthcare.com/hiv-news-and-media/news/press-releases/2022/march/viiv-healthcare-announces-label-update-for-its-long-acting-hiv
2. ViiV Healthcare. ViiV Healthcare announces US FDA approval of Cabenuva (cabotegravir, rilpivirine) for virologically suppressed adolescents living with HIV who are 12 years of age or older and weigh at least 35 kg. (29 March 2022).
https://viivhealthcare.com/en-us/media-center

COMPLICATIONS: COVID-19

BHIVA statement on 4th vaccine dose for people living with HIV in the UK

BHIVA.org

The Joint Committee on Vaccination and Immunisation (JCVI) recommends that this Spring booster vaccines should be given to all people who are immunosuppressed, including everyone with HIV.



The vaccine should be given about six months after their last vaccine dose.

The JCVI has made this recommendation to keep things simple, and to ensure that all people at higher risk are protected from COVID.

BHIVA strongly encourages all people living with HIV to have the recommended COVID vaccines. Responses to first and second vaccine doses can be lower in some people with HIV, particularly those with a damaged immune system (a CD4 count less that 350 or with a detectable HIV viral load). The extra vaccine doses should boost immune responses.

The full statement linked below includes more information.

Reference

BHIVA. Community version: BHIVA Statement on JCVI recommendations for COVID vaccine Spring 2022 booster dose. (29 March 2022).
https://www.bhiva.org/BHIVA-community-statement-on-JCVI-recommendations-for-COVID-vaccine-spring-2022-booster-dose

Temporary protection against omicron needs mRNA booster: limited data for those at highest risk

Simon Collins, HIV i-Base

A UK study published in the NEJM reports waning protection from using two primary doses of the Oxford and Pfizer vaccines, but that booster with mRNA vaccines six months later can increase protection for a limited time.

The study used a case-control design including more than 880,000 people with omicron, 200,000 with delta and 1,500,000 negatively tested individuals (from November 2021 to January 2022).

At all timepoints, and for all vaccine combinations, vaccine efficacy was higher against delta than omicron.

By 20 weeks. primary doses of the Oxford vaccine was estimated to no longer provide protection against symptomatic disease from Omicron, but this increased to 62% 2-4 weeks after a booster with Pfizer. This protection waned to 39% after ten or more weeks. Responses to a Moderna booster were higher at 70% and 60% for the same timepoints, respectively.

The efficacy of primary doses of the Pfizer vaccine dropped to 8% by week 25, increasing to 67% after a Pfizer booster, and dropping to 45% ten or more weeks later. Responses to a Moderna booster were similarly higher than a Pfizer boost, at 74% and 64% for the same timepoints, respectively.

However, as with phase 3 studies, the majority of participants were not at high risk: only 7% were older than 65 and only 12% were from Black or south Asian populations, By vaccine priority group, roughly 6% were health workers, 5% were extremely clinically vulnerable, 18% were at risk and less than 1% were severely immunocompromised.

C O M M E N T

These data support the importance of using mRNA vaccines as booster doses in the UK and show the need for a similar response globally to protect against the omicron variant.

Longer follow-up and is needed to understand the duration of protection from the booster dose and future strategies.

As with most studies, this paper included very limited data on people who are severely immunocompromised.

Reference

Andrews N et al. Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant. NEJM. DOI: 10.1056/NEJMoa2119451. (2 March 2022).

https://www.nejm.org/doi/full/10.1056/NEJMoa2119451

HIV PREVENTION

HIV vaccine study using mRNA technology starts in the US

Simon Collins, HIV i-Base

The rapid development of vaccines against COVID-19 led many people to question whether similar investment could have achieved an effective HIV vaccine.

One response emphasised that decades of HIV research were actually enabling faster treatments for COVID-19. Another reported that mRNA technology behind the Pfizer and Moderna vaccines might now be transferrable back to efforts against HIV.

On 14 March 2022, the US NIH issued a press statement about the launch of a phase 1 study of three experimental HIV vaccine based on mRNA technology. [1]

The HVTN 302 study will look at safety and immune responses in up to 108 adult participants in ten US cities. The three candidate vaccines are: (i) BG505 MD39.3 mRNA, (ii) BG505 MD39.3 gp151 mRNA, and (iii) BG505 MD39.3 gp151 CD4KO mRNA.

This research programme was first announced by Moderna in January 2021. [2]

Reference
1. NIH launches clinical trial of three mRNA HIV vaccines: phase 1 study is among first to examine mRNA technology for HIV. (14 March 2022). https://www.nih.gov/news-events/news-releases/nih-launches-clinical-trial-three-mrna-hiv-vaccines
2. Moderna PR. Moderna provides business update and announces three new development programs in infectious disease vaccines. (11 January 2021). https://investors.modernatx.com/news/news-details/2021/Moderna-Provides-Business-Update-and-Announces-Three-New-Development-Programs-in-Infectious-Disease-Vaccines-01-11-2021/default.aspx

South Africa approves dapivirine vaginal ring for HIV prevention

Simon Collins, HIV i-Base

On 11 March 2022, the South African regulatory authority (SAHPRA) approved a monthly vaginal ring for use by adult women to protect against sexual transmission of HIV.

This is approximately 18 months after the EMA issued a positive opinion supportive approval in countries with high HIV incidence. [2]

The press release from the International Partnership for Microbicides (IPM) emphasises the high need for better options for women and the advantages of the formulation that is easy to self-administer.

But it also notes that efficacy is significantly lower that other methods of PrEP.

The two phase 3 studies supporting approval reported overall efficacy rates of only 31% and 27% in the Ring and ASPIRE studies respectively. Subgroup and post-hoc analyses showed higher efficacy with greater adherence, as with other PrEP studies, and that this was higher in older women. [3, 4, 5]

References
1. IMP press statement. South Africa approves dapivirine vaginal ring for use by women. (11 March 2022). https://www.ipmglobal.org/content/south-africa-approves-dapivirine-vaginal-ring-use-women
2. EMA supports use of dapivirine vaginal ring to prevent HIV in high-incidence countries. HTB (August 2020). https://i-base.info/htb/38818
3. IMP press statement. Two large studies show IPM's monthly vaginal ring helps protect women against HIV. (22 February 2016). https://www.ipmglobal.org/publications/two-large-studies-show-ipm's-monthly-vaginal-ring-helps-protect-women-against-hiv
4. Baeten JM et al. Use of a vaginal ring containing dapivirine for HIV-1 prevention in women. N Engl J Med 2016;375:2121-2132. https://www.nejm.org/doi/full/10.1056/NEJMoa1506110
5. Nel A et al. Safety and efficacy of a dapivirine vaginal ring for HIV prevention in women. N Engl J Med 2016;375:2133-2143. https://www.nejm.org/doi/full/10.1056/NEJMoa1602046

Future meetings and webinars 2022/23

The following listing covers selected upcoming HIV-related meetings and workshops. Registration details, including for community and community press are included on the relevant websites.

Due to the new coronavirus health crisis, most meetings will now be virtual, including those that were rescheduled in the hope that COVID-19 restrictions would be relaxed.

Academic Medical Education (AME) meetings and workshops

Several AME workshops (previously Virology Education) are highlighted below but 35 meetings are planned each year. Many virtual meetings include free registrations for health workers, researchers and community.

https://academicmedicaleducation.com (meetings listings)

Webcasts from meetings (YouTube listing)

2022

HIV Prevention Review Meeting 2022

30-31 March, virtual

https://academicmedicaleducation.com

BHIVA Spring Conference 2022

20–22 April 2022, Manchester

https://www.bhiva.org/AnnualConference2022

24th International AIDS Conference (AIDS 2022)

29 July – 2 August 2022, Montreal, Canada, and virtually

https://www.aids2022.org

13 International Workshop on HIV & Aging

13 – 14 October 2022, USA (tbc)

https://academicmedicaleducation.com

2023

19th European AIDS Conference (EACS 2023)

18-21 October 2023, Warsaw, Poland

https://www.eacsociety.org

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

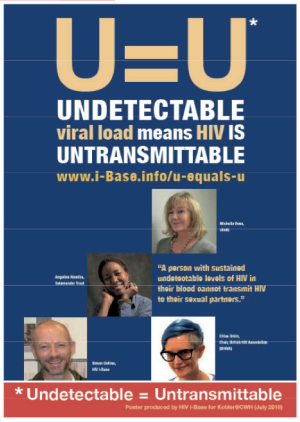
i-Base have produced a new series of posters, postcards and leaflets to help raise awareness about U=U in clincs.

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.

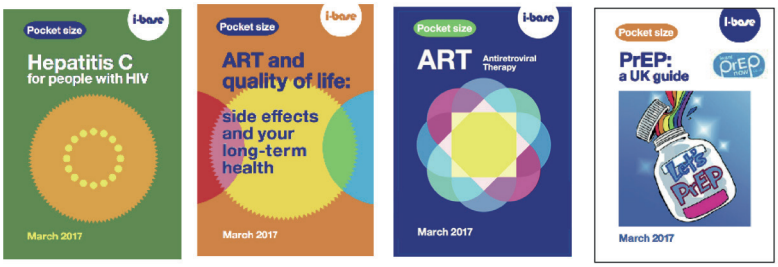
Personalising these for your clinic is cheap and easy and might be an especially nice way to highlight the good news.

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

roy.trevelion@i-Base.org.uk

Order publications and subscribe online

All publications can be ordered online for individual or bulk copies. All publications are free. Unfortunately bulk orders are only available free in the UK. http://i-base.info/order



h-tb

HIV TREATMENT BULLETIN

HTB is published in electronic format by HIV i-Base. As with all i-Base publications, subscriptions are free and can be ordered using the form on the back page or directly from the i-Base website:

http://www.i-Base.info

by sending an email to: subscriptions@i-Base.org.uk

Editor: Simon Collins

Contributing Editor: Polly Clayden

HTB is a not-for-profit community publication that aims to provide a review of the most important medical advances related to clinical management of HIV and its related conditions as well as access to treatments. Comments to articles are compiled from consultant, author and editorial responses.

Some articles are reproduced from other respected sources. Copyright for these articles remains with the original credited authors and sources. We thank those organisations for recognising the importance of providing widely distributed free access to information both to people living with HIV and to the healthcare professionals involved in their care. We thank them for permission to distribute their work and encourage HTB readers to visit the source websites for further access to their coverage of HIV treatment.

HIV i-Base receives unconditional educational grants from charitable trusts, individual donors and pharmaceutical companies. All editorial policies are strictly independent of funding sources.

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

http://www.i-Base.info

HIV i-Base is a registered charity no 1081905 and company reg no 3962064. HTB was formerly known as DrFax.

107 Maltings Place,169 Tower Bridge Road, London, SE1 3LJ
T: +44 (0) 20 7407 8488

Orders and subscriptions

Please use this form to amend subscription details for HIV Treatment Bulletin and to order single or bulk copies of publications. All publications are free, but donations are always appreciated - please see the form on the previous page.

Name _____ **Position** _____

Organisation _____

Address _____

_____

Telephone _____ **Fax** _____

e-mail _____

☐ I would like to make a donation to i-Base - *Please see inside back page*

- **HIV Treatment Bulletin (HTB) every two months** ☐ **by e-mail**
- **Pocket leaflets** - *A7 small concertina-folded leaflets (2017)*

Pocket HCV coinfection	**quantity** _____	**Pocket PrEP**	**quantity** _____
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** _____

Phoneline *posters (A4)* **quantity** _____

Please post to the above address, or email a request to HIV i-Base:

subscriptions@i-Base.org.uk