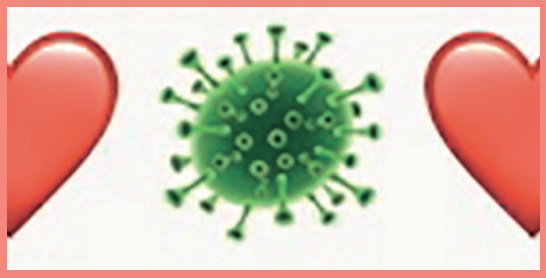
ISSN 1472-4863

HTB: vol 22 no 10: plus COVID-19 supplement

hiv treatment bulletin (e)



EACS 2021 conference (31 October 2021)

CONTENTS

Contents continued inside...

Published by HIV i-Base

HTB no.10 (2021): HIV and COVID-19 supplement ISSUE 10

Contents continued ...

i-Base 2021 appeal

Please support i-Base with £5 or £10 a month...

Our appeal to help i-Base continue to provide free publications and services continues through 2021.

i-Base now recieve more than 12,000 questions each year and the website has more than 500,000 view each month. We also distribute more than 80,000 booklets and leaflets free to UK clinics every year. If 1000 people support us with £5 a month we will be on course to meet our funding shortfall. All help is appreciated.

http://i-base.info/i-base-appeal-we-need-your-help

Subscriptions

To join the email list for HTB please register free online:

http://i-base.info/htb/about/subscribe

EDITORIAL

Although this issue is published slightly later in the month than is usual, it allows us to lead with first reports from the 18th EACS hybrid conference hosted in London.

The conference was a great success, and EACS deserve support for developing a hybrid conference that included the option of attending either virtually or face-to-face.

Those able to attend appreciated the first chance to connect at a large international meeting with friends and colleagues since COVID-19.

Other news includes:

- The approval in Scotland of the first injectable ART.
- The decision not to seek approval of F/TAF as PrEP in the EU.
- BHIVA guidelines for HIV-2,
- Continued use in some settings of cotrimoxazole at high CD4 counts and
- The long awaited results on the clinical benefits of screening for anal cancer in people living with HIV.

Plus much more, including updates on HIV and COVID-19 and related vaccine news.

CONFERENCE REPORTS

18th International European AIDS Conference (EACS 2021)

27–30 October 2021, hybrid, London

Introduction

The 18th International European AIDS Conference (EACS 2021) ran from 27-30 October 2021 as a hybrid conference.

EACS are to be congratulated for taking this decision.

Approximately a quarter of the more than 3000 delegates attended the ExCel Centre in London, reconnecting for the first time since COVID-19 with interactions that can only come from face-to-face meetings - many commenting on how important this felt.

Other delegates were able to watch all the same sessions simultaneously as a live virtual meeting - with instant access to all content. Many of the sessions were also simultaneously translated into Russian.

This means that the conference immediately became available online for delegates.

The programme and abstract book from the meeting are available as open access,

https://eacs2021.abstractserver.com/program (programme)

https://onlinelibrary.wiley.com/toc/14681293/2021/22/S3 (PDF abstract book)

https://eacs2021.opade.events/en/event (conference platform - needs registration)

Abstracts can also be accessed through the online programme (first link above). For oral sessions this involves click on the day of the presentation and for posters this is through clicking the two elibrary listing in the programme (for Thursday and Friday).

First reports in this issue of HTB are below.

- EACS 2021 opening: a call for collaboration for both HIV and COVID-19
- Reduced responses to COVID-19 vaccines at low CD4 counts
- EACS guidelines: 11th edition launched (October 2021)
- Community "Respect my HIV" march: 30 October 2021 in London

EACS 2021: a call for collaboration for both HIV and COVID-19

Simon Collins, HIV i-Base

On Wednesday 27 October, the 18th International European AIDS Conference was opened by conference co-chair Dr Sanjay Baghani with an appropriately-focused reflection on the parallels between HIV and COVID-19 and a call to improve future care.

This recognised that the COVID pandemic has changed the world for us all, and more directly than we ever would have wanted. And how both pandemics should focus on inequalities in care, as these are areas we can hope to improve.

For all the remarkable achievements in HIV – and there are many – it still remains a global health crisis, even with achieving 90-90-90 targets. And the map for better access to HIV care mirrors that showing the biggest inequities in global access to COVID-19 vaccines.

The theme of this year's conference is "crossing borders". This includes the importance of learning from each other to share ideas – whether these are geographical, clinical, or across multi-disciplines. The importance of collaboration ran through all the other opening talks.

Conference co-chair Dr Annemarie Wensing started with a tribute to Charles Boucher, who died earlier this year, and who used his brilliance as a scientist to also bring people together as an educator, inspiring people to collaborate.

Dr Wensing then talked about some of EACS current projects. The organisation currently has more than 2600 members, approximately divided equally between each of the four main regions of Europe and the rest of the world. One project is to focus on the standard of care in Europe, closely linked to the EACS clinical guidelines, with the 11th edition due to be launched on the last day of the conference. EACS also support the training of new investigators and doctors and are due to expand the long-running training schools and other educational training.

Community involvement in EACS 2021 was covered by Matthew Hodson, the community co-chair for the conference, who emphasised the importance of the diversity of people living with HIV and of including local HIV organisations like Positive East and the UK AIDS Memorial Project. He spoke of his personal experiences of living with HIV, and thanked everyone attending for their role in developing the medical advances in treatment. And, moving forward, he spoke of the importance of U=U to actively challenging the stigma associated with HIV that continues, at least in part, as a legacy of fear from the UK government's tombstone campaign.

The keynote lecture from Professor Kevin Fenton reported on the progress in reducing HIV transmission in London, acknowledging so many people who contributed to the reductions over the last five years. Approximately half of the 105,000 people living with HIV in the UK, where testing, monitoring and treatment are all free, live in London. Based on 2019 data, this has helped the city reach an impressive 95-93-89 cascade passing the UNAIDS 90-90-90 target. This is also based on combination prevention that include more frequent testing, early ART on diagnosis and HIV prevention programmes. HIV prevention in London also included broad and expanded use of PrEP by gay men, despite long delays from the NHS. Although this was not mentioned specifically, it was the reduction in this population that drove the overall drop in HIV diagnoses.

As in nearly all settings, late diagnosis is still a significant concern in the UK. In this London is doing well, reporting that 7% of people are still diagnosed with a CD4 count that is less than 350 cells/mm^3 - but this compares to the national average of 40%. Rates are still significantly higher for those of black African ethnicities.

Fast Track Cities in London is another ambitious collaboration coordinated across the city to achieve zero new infections, zero HIV preventable deaths and zero stigma by 2030. And for all the challenges, it is also okay to hope that some of these goals might happen earlier.

The opening ceremony included two awards from EACS in recognition of sustained contributions of excellence to HIV care. The first was awarded to Professor Andrzej Horban who developed and led HIV services in Poland, from treating the first cases to establishing and running the largest national clinic for over 25 years. Professor Horban also cochaired the EACS conference when it was held in Warsaw in 2003 and brought a long-needed focus on the importance of the HIV epidemic in eastern Europe.

Also, strange to report, but very gratefully appreciated, the second award went to me, in part to recognise the importance of community advocacy in HIV care. This is indeed an honour, and it was certainly accepted in this spirit, especially thinking of the many thousands of other community advocates who work tirelessly and often in much more difficult conditions.

In summary, EACS are to be congratulated for holding this year's conference at such a difficult time and for leading with the first international fully hybrid meeting. It will be viewed simultaneously by more than 3000 delegates, a quarter of whom are attending in person, and 146 participants have been supported with scholarships.

The upcoming meeting has an exciting programme of over 90 oral and poster sessions over 120 hours that will cover everything including advances in ART, COVID-19, cure research and women's health – with the active involvement of people living with HIV. Abstracts for the meeting are already online as open access as a supplement to HIV Medicine:

https://onlinelibrary.wiley.com/toc/14681293/2021/22/S3

Several community related projects at EACS include a display of the UK AIDS Memorial Quilts at the conference and exhibitions from HIV organisations. Also, a charity walk where anyone can take part to contribute to the 6864 kilometres between London and Lake Issyk Kul in Kyrgyzstan, where a summer camp for HIV positive children will be held next summer. The time taken to run, walk or travel by wheelchair is not important, but there are only 36 days to help as the run needs to be completed by 1 December 2021. [2]

The end of the conference will be marked by a 700 metre march on Saturday 30 October. This is open for everyone, whether attending the main conference or not. It is to support a campaign for respect for HIV and for the People First Charter on using person-centred language for people living with HIV. [3, 4, 5]

Please meet at Westminster Hall (off Parliament Square) by 2.15 pm to walk to Trafalgar Square at 2.30 for events and speeches. This will be a wonderful event and a chance to meet friend and colleagues. All are welcome.

Conference delegates could even enter their walk for the Saturday march as part of the charity walk.

References

1. Opening ceremony and talks. 18th International AIDS Conference (EACS 2021), 27-30 October 2021. https://eacs-conference2021.com
2. HIV run website. https://life4me.plus/campaigns/hivrun
3. Campaign and march website. https://respectmyhiv.com
4. People First Charter. https://peoplefirstcharter.org
5. Community "Respect my HIV" march: 30 October 2021 in London https://i-base.info/htb/41417

Reduced responses to COVID-19 vaccines at low CD4 counts

Simon Collins, HIV i-Base

New data were presented at EACS 2021 on immune responses to COVID-19 vaccines in people with lower CD4 counts. Until now, nearly all results have been in people with median CD4 counts >500 cells/mm^3, reporting similar responses to HIV negative people.

This study, by Andrea Antinori from the National Institute for Infectious Diseases in Rome and colleagues, included 166 people living with HIV (16% women; median age 56 (49 to 60). Of these, 32 had CD4 counts < 200, 56 were between 200 to 500 and 78 were >500 cells/mm^3.

This prospective study at a single centre compared both neutralising antibody titres and cell-mediated immune responses in whole blood samples taken a month after the second of two doses of mRNA vaccines. Results were compared to 169 unmatched HIV negative health workers (72% women; median age 42 years (IQR 32 to 53).

At baseline, median (IQR) counts in the HIV groups were 140 (100 to 163), 335 (245 to 441) and 727 (585 to 856) cells/mm3 respectively. The low CD4 group had a significantly lower median CD4:CD8 ratio (0.16 vs 0.44 vs 0.90) and was less likely to have undetectable viral load (68% vs 92% vs 100%); both p<0.001.

Median (IQR) RBD binding response levels were 20 (5 to 40), 40 (10 to 150), 80 (40 to 160) and 80 (40 to 160) across the four groups respectively. The percentage of neutralising antibody levels >10 were 70%, 88%, 93% and 98% respectively.

All immune responses were significantly lower in the CD4 <200 group compared to both the high CD4 and HIV negative controls (all p<0.001). By comparison, responses in the high CD4 group were all roughly comparable to HIV negative controls.

The magnitude of overall humoral and cellular antibody responses strongly correlated with higher CD4 counts. Differences between the <200 and 200 to 500 CD4 groups were significant for humoral (anti-RBD, p<0.05) and cellular (IFN-gamma, p<0.01) responses.

Table 1: Humoral responses by study group (from the abstract, n=127)

	CD4 <200	CD4 200-500	HIV negative
Neutralisation activity	69% (p <0.001)*	87% (p<0.007)*	(99 to 100%)
Detectable anti-RBD response	87% (p <0.001)*	99% (p=0.177)*	(99 to 100%)

* p-values compared to control group

In multivariate analysis, having a CD4 count <200 was significantly associated with anti-RBD (Beta –0.64 [95%CI: –0.94 to –0.34], p<0.001), neutralising (Beta –0.41 [95%CI –0.70 to –0.12], p<0.006) and cell-mediated (Beta –.74 [95%CI: –1.13 to –0.34], p<0.001) responses.

Longer follow-up is needed to be able to comment on durability of immune responses.

In questions after the presentation it was noted that no breakthrough infections have been reported. However, the data suggest a role for earlier use of a third dose in those with low CD4 counts.

Reference

Antinori A et al. Immunogenicity of mRNA vaccination against SARS-CoV-2 in persons living with HIV (PLWHs) with low CD4 count or previous AIDS. Oral abstract OS4/3.

https://eacs2021.opade.events/en/event/2044?ref=program (webcast for registered delegates).

EACS Guidelines: 11th edition (October 2021)

Simon Collins, HIV i-Base

The 11th update of the EACS guidelines were launched in a special session on the last day of the conference, to discuss the major updates. [1]

These guidelines are primarily as an easy reference guide for doctors that covers the minimum standards of care for the management of HIV. They are designed as a handbook based on look-up tables and algorithms for all aspect of care, and are available in two electronic formats. [2]

- An 150-page PDF file.
- A free App for IOS and Android devices.

The printed booklet version was not produced this year.

Introduction

The guidelines are organised into seven main sections.

1. Assessment of and monitoring from first diagnosis
2. ART (including first and subsequent treatment, pregnancy, PEP and PrEP)
3. Drug interactions and prescribing issues, including for different demographic groups
4. Prevention and management of comorbidities. This cover 50 different complications of care including a wide range of side effects and lifestyle, quality of life and age-related issues.
5. Management of coinfection with viral hepatitis
6. Opportunistic infections, including COVID-19
7. Paediatric HIV care

Each section has a separate writing group, and an overall editorial group means that more than 100 leading experts from across Europe are involved in each edition.

Main changes to this edition

The guidelines have been updated throughout, with two new sections added on COVID-19 and paediatric care. Key updates are highlighted below but please refer to the comprehensive summary of all changes on page 4 of the PDF file.

ART section

- Recommended drugs have been updated to add doravirine and long-acting cabotegravir plus rilpivirine. Dropped drugs include elvitegravir, atazanavir/b, darunavir/b plus raltagravir, and abacavir combinations with efavirenz, darunavir/b and raltegravir. The dual ART of atazanaivr/b plus 3TC is also dropped.
- In pregnancy, criteria for using dolutegravir and TAF are updated and atazanavir/b, AZT and lopinavir/r have been removed.
- Timing for ART in TB coinfection.
- A fully updated section on all aspects of PrEP.

Drug interactions

- Interactions for latest drugs: cabotegravir oral, CAB/RPV LA and fostemsavir.
- New interaction tables for TB drugs, anxiolytics, COVID-19 treatments and hormone replacement therapy.
- All recent updates to Liverpool Drug Interaction website are added. This include new drugs added to antidepressants, hypertensives, analgesics, anticoagulants, bronchodilators and malarial drugs.

Comorbidities

- This section has the most updates including side effects with latest ARVs and new management guidelines for cancer screening, cardiovascular disease, hypertension, diabetes, renal and hepatic toxicity (including NAFLD) and organ transplant.
- Major revisions on weight gain and obesity.
- A new section on anxiety and major update on frailty.
- Significant updates to the section on sexual health, including new sections on managing the menopause, transgender sexual health and improving sexual health for women.

- U=U and PrEP are now prioritised for HIV prevention.

OIs

- Minor changes overall, mainly on ART timing.
- New section added on management of COVID-19

Paediatric care

- This is a new section adding the PENTA-ID guidelines for the first time, including coordinating with some recommendations for adult care.

Translations

The current edition is in English with translated updates planned shortly.

The previous edition is still online in Chinese, French, German, Dutch, Japanese, Portuguese, Russian, Spanish and Turkish.

Feedback

Comments and feedback is welcomed by emailing:

guidelines@eacsociety.org

References

1. EACS guidelines special session. EACS 2021. Saturday 30 October, 11.30 - 12.45. https://eacs2021.opade.events/en/event/2053 (webcast for delegates only).
2. EACS. EACS Guidelines, 11th edition (October 2021). https://www.eacsociety.org/guidelines/eacs-guidelines https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf (PDF)

Community "Respect my HIV" march: 30 October 2021 in London

Simon Collins, HIV i-Base

On Saturday 30 October 2021 a community march was organised in central London with the theme of 'respect my HIV' for the diverse range of people living with HIV. [1]

It celebrated advances in HIV care focused on goals to reduce HIV transmission and also the stigma and discrimination against people living with HIV. It also emphasised the importance of using person-first language when talking about health care. [2]

It also marked the 18th European AIDS Conference that was held from 27 – 30 October at the ExCel Centre in London. [3]

This was be a lively event, supported by many local and international HIV community organisations, and it was one of the few times that HIV has been celebrated publicly in this way.

The march started in Parliament Square and walked to Trafalgar Square to hear distinguished panel of community speakers.

Webcasts are available thanks to Andrew London. [4]

References

1. Campaign and march website. https://respectmyhiv.com
2. People First Charter. https://peoplefirstcharter.org
3. EACS conference, 27-30 October 2021. https://eacs-conference2021.com
4. Andrew London. Photographs and video clips from the speeches at Trafalgar Square. https://www.instagram.com/mrandrewlondon

ANTIRETROVIRALS

NHS Scotland approves long-acting cabotegravir and rilpivirine injections

Simon Collins, HIV i-Base

On 11 October 2021, the Scottish Medicines Agency (SMA) approved the first long-acting injectable HIV combination of cabotegravir (CAB-LA) and rilpirivine (RPV-LA) as a new treatment for HIV. [1]

The indication is as a switch option for people already on stable ART with undetectable viral load, without previous resistance or viral failure with combinations that include an NNRTI or integrase inhibitor.

Each injection is packaged separately and is given as an intramuscular injection every two months. Use first involves a four-week oral lead-in period and a higher dose initial injection.

Potential benefits compared to oral treatment linked to improved quality of life includes easier adherence although the indication for people to already have sustained viral suppression limits use by people who are currently less adherent and who might benefit most.

Other advantages include no longer needing to hide medicines, being easier for those with swallowing difficulties, or for people without stable housing, although more clinic visits will be needed.

The list price for the two-monthly doses of CAB-LA (Vocabria) and RPV-LA (Rekambys) is approximately £1200 and £440 respectively: just short of £10,000 for a year.

The reduced negotiated price as part of a Patient Access Scheme (PAS) have not been released, but ICER/QALY models and base-case scenarios are references in the detailed SMA advice. [2]

The SMA document doesn't include either national targets or caps on the number of people who could access this injectable combination, but numbers submitted by ViiV Healthcare estimated a hoped for 700 people in year one and 800 in year two.

For clinical details, please see full prescribing details for each drug. [3, 4]

C O M M E N T

This news is welcomed, after such a long development programme for such an innovative new treatment.

CAB-LA plus RPV-LA were approved in the EU on 21 December 2020. [4]

The outcome of the review by NHS England previously is expected by 20 October 2021.

References
1. Scottish Medicines Consortium. Cabotegravir (Vocabria) is accepted for use within NHS Scotland.
https://www.scottishmedicines.org.uk/medicines-advice/cabotegravir-vocabria-full-smc2376/
2. Scottish Medicines Consortium. Detailed advice.
https://www.scottishmedicines.org.uk/media/6331/cabotegravir-vocabria-final-sept-2021-for-website.pdf
3. EMA. CAB-LA.
https://www.ema.europa.eu/en/medicines/human/EPAR/vocabria
4. EMA. RPV-LA.
https://www.ema.europa.eu/en/medicines/human/EPAR/rekambys
5. Long-acting injectable HIV treatment approved in the EU: includes two-monthly dosing. HTB (January 2020).
https://i-base.info/htb/39602

HIV COMPLICATIONS

Early treatment prevents anal cancer in people living with HIV: ANCHOR study stops early

Simon Collins, HIV i-Base

For many years, the lack of randomised data has limited screening programmes for anal cancer, even though rates are significantly higher in people living with HIV than in the general population.

A large phase 3 US study has now reported significant benefits from active treatment. Although detailed results have not been published, based on a report from the Data and Safety Monitoring Board (DSMB) all participants will now be offered treatment. [1]

This is years earlier than expected, so although the actual results are not reported, the difference between arms must be significant for the primary endpoint.

The Anal Cancer/HSIL Outcomes Research (ANCHOR) study has so far enrolled almost 4500 HIV positive adults (out of a target of more than 5000). Participants need to have precursor lesions for anal cancer and randomisation is to either removal (usually with electrocautery) or to monitoring. [2, 3]

Similar to studies in cervical cancer, the results show that screening and removing high-grade squamous intraepithelial lesions (HSIL), significantly reduce the risk of progression to anal cancer.

C O M M E N T

The ANCHOR study is an amazing achievement - not least for the participants who volunteered and were in the control arm. It took many years to plan and enrol and results will change guidelines.

However, the press release should include top-line results for such an important study, and these will hopefully be released shortly.

References
1. University of California at San Francisco (UCSF) press release. Treating anal cancer precursor lesions reduces cancer risk for people with HIV. (7 October 2021).
2. ClinicalTrials.gov. Topical or ablative treatment in preventing anal cancer in patients with HIV and anal high-grade squamous intraepithelial lesions (ANCHOR).
   https://clinicaltrials.gov/ct2/show/NCT02135419
3. ANCHOR Study website.
   https://anchorstudy.org

Benefits reported for continued use of cotrimoxazole prophylaxis at high CD4 counts in Malawi

Simon Collins, HIV i-Base

Although cotrimoxazole prophylaxis is discontinued in high-income countries following CD4 recovery on ART to >200 cells/mm^3, guidelines in many low-income countries recommend continued use even at much higher CD4 counts.

Researchers who ran a randomised controlled study in Malawi support this continued use, even though the primary endpoint results were not significant.

The study randomised almost 1500 participants with CD4 counts >250 cells/mm^3 to either continue or discontinue daily cotrimoxazole, or switch to daily hydroxychloroquine. Mean CD4 count was actually much higher (568 cells/mm^3, SD+/–236).

Neither active arm produced significant benefits based on preventing death or WHO stage 3-4 events (approximate 20% reductions were p=0.20 and p=0.14, respectively). The was linked to the lower event rate than predicted (3.9 vs per 100 patient years of follow-up), reducing the power of the study.

However, when stage 2 secondary endpoints were included, the preventive effect increased to 31% (95%CI: 3 to 51%; p=0.032) and 32% (95%CI: 4 to 51%; p=0.026), for cotrimoxazole and hydroxychloroquine respectively. Both drugs significantly reduced the risk of malaria (p<0.001).

Although co-trimoxazole prophylaxis can cause hematologic toxicity, including neutropenia, which was higher in this arm, it didn't cause higher rates of bacterial infections.

However the low event rate also means that the number needed to treat (NNT) to prevent and even also becomes much higher, and these data were not presented.

These results were first published online in March 2021.

C O M M E N T

The benefits in this study are likely relevant in high malaria settings and where rates of bacterial pneumonia much greater.

Although the confidence intervals are still wide, cotrimoxazole is so safe that this makes sense, especially if vaccination is not available.

Reference

Laurens MB et al. Revisiting co-trimoxazole prophylaxis for African adults in the era of antiretroviral therapy: a randomized controlled clinical trial. Clinical Infectious Diseases, 73 (6): 1058–1065. doi: 10.1093/cid/ciab252. (15 September 2021).

https://academic.oup.com/cid/article-abstract/73/6/1058/6179299

HIV: PREVENTION

Gilead withdraws EU application for F/TAF as PrEP

Simon Collins, HIV i-Base

On 20 October 2021, Gilead Sciences announced that the company will no longer look to market F/TAF (Descovy) as PrEP in the EU.

This is a significant policy change given the years of investment and positive results from phase 3 studies showing that F/TAF had potential advantages compared to F/TDF. However, these were generally slight: statistically significant reductions in bone and kidney toxicity were unlikely to be clinically significant for most people and numerically fewer HIV infections were not statistically significant.

The reason for the withdrawal is likely be linked to the large price difference charged for F/TAF compared to F/TDF would not be acceptable to European health systems.

EU countries have wider access to generic versions of F/TDF which is at least 90% cheaper than the hoped for marketing price for F/TAF.

The press release states that Gilead will continue to provide F/TAF to study participants in the EU who were enrolled in the phase 3 DISCOVER study.

This may be to cover the ethical and regulatory requirements (including in the Helsinki declaration) that pharmaceutical companies need to provide post-trial access to treatment for patients participating in clinical trials. [2]

This decision is a shame. If both options were the same price, F/TAF would be widely used.

It is a smaller tablet and it has better pharmacokinetics that likely make is more protective if doses are missed.

UK residents are able to buy and important generic versions of F/TAF online for personal use, although this is only allowed in a few other EU countries.

References

1. Gilead press statement. Gilead announces decision not to pursue marketing authorization for Descovy for pre-exposure prophylaxis in the European Union. (20 October 2021).
   https://www.gilead.com/news-and-press/company-statements/gilead-announces-decision-not-to-pursue-marketing-authorization-for-descovy-for-pre-exposure-prophylaxis-in-the-european-union
2. World Medical Association. Declaration of Helsinki: Ethical principles for medical research involving human subjects.
   http://www.wma.net/en/30publications/10policies/b3/.pdf .(PDF)

HIV: GUIDELINES

BHIVA guidelines for the management of HIV-2 (2021)

Simon Collins, HIV i-Base

The British HIV Association (BHIVA) has produced new guidelines for best clinical practice in the treatment and management of HIV-2 infection.

The guidelines are similar to the approach to treatment HIV-1, although diagnosis, monitoring and management of HIV-2 remain challenging. Treatment is also more limited as some HIV drugs are only active against HIV-1.

With no published randomised controlled trials of ART for HIV-2,most evidence is based on cohort studies and observational data.

This document updates the previous edition from 2010.

Reference
BHIVA. British HIV Association guidelines for the management of HIV-2. (October 2021).
https://www.bhiva.org/HIV-2-guidelines

HIV: CURE-RELATED RESEARCH

Explaining rare cases of HIV remission - and risk of viral rebound after many years off-ART

Simon Collins, HIV i-Base

On 28 October 2021, a press release from the US National Institute of Health (NIH) reported on a recent publication of two cases of continued HIV suppression with ART. [1]

Such cases are extremely rare, but are sometimes observed in studies looking at strategies to cure HIV.

In this case, the main research paper, published in Nature Medicine, reports at least two different mechanisms. [2]

The first case, where HIV was controlled for more than 3.5 years after stopping ART as part of a research study, was explained by high levels of HIV-specific CD8 T cells. This person restarted suboptimal ART without telling the HIV team.

The second person, also from the same research study, remained off-ART for nearly four years, has lower CD8 cells, but had very strong neutralising antibody responses. In this case, ART needed to be restarted after reinfection with another strain of HIV.

Both cases show the challenges of long-term monitoring after short-term examples of HIV remission, and the vulnerability to viral rebound, even after many years of what appears to be HIV remission.

References
1. US NIH press statement. NIH researchers identify how two people controlled HIV after stopping treatment: different mechanisms suppressed the virus in each person. (28 October 2021).
   https://www.niaid.nih.gov/news-events/nih-researchers-identify-how-two-people-controlled-hiv-after-stopping-treatment
2. Blazkova J et al. Distinct mechanisms of long-term virologic control in two HIV-infected individuals after treatment interruption of antiretroviral therapy. Nature Medicine DOI: 10.1038/s41591-021-01503-6 (2021).
   https://www.nature.com/articles/s41591-021-01503-6

HIV: UK CLINICAL TRIALS

Switch study for people with insomnia using dolutegravir

St Mary's London and Sussex Brighton

A new study being run in London and Brighton is looking to recruit 46 adults who are experiencing sleep problems using dolutegravir-based ART. [1]

The study will look at whether switching ART from Triumeq (abacavir/lamivudine/dolutegravir) to Biktarvy (tenofovir-AF/emtricitabine/bictegravir) is associated with improved sleep.

Half the participants will switch and half will continue on their current treatment.

The study will look at brain function using two functional MRI brain imaging scans. It will also include participant questionnaires, including on sleep quality. The study involves six routine clinic visits over five months and two scanning visits. It is running at St. Mary's Hospital in London and Brighton and Royal Sussex County Hospital in Brighton. It is funded by Gilead Sciences.

HIV positive people are able to self-refer if interested.

Please email the study team if you would like more information or if you are interested in joining.

rebecca.hall30@nhs.net

Further details are also on the online. [1]

Reference

Bictegravir central nervous system (CNS) study. ICRCTN register 17508886.

https://www.isrctn.com/ISRCTN17508886

HIV: ON THE WEB

CHAI 2021 HIV market report: the state of the HIV market in low- and middle-income countries

Clinton Health Access Initiative (CHAI)

On 12 October 2021, CHAI release the 12th issue of their annual HIV market report.

The report reviews a global perspective on the complex, changing markets for HIV medicines in low- and middle-income countries.

All aspects of the global HIV response have had important updates over the past year.

These include:

- The rollout of a generic, affordable paediatric formulation of dolutegravir.
- Exciting clinical trial results set to change how cryptococcal meningitis is treated.
- Further advances in long-acting drugs for HIV prevention.
- Pricing deals that continue to make HIV self-testing more affordable.

An excellent 60-minute webinar review of the many changes to global HIV health is also available online:

https://www.clintonhealthaccess.org/webinar-highlighting-the-latest-updates-in-hiv-treatment-prevention-and-diagnostics

Reference

CHAI. 2021 HIV market report (12th edition).

https://www.clintonhealthaccess.org/2021-hiv-market-report-the-state-of-the-hiv-market-in-low-and-middle-income-countries

HIV and COVID-19 - bulletin

COVID-19: HIV and COVID-19 coinfection

Continued evidence for poorer COVID-19 outcomes in people with HIV

Simon Collins, HIV i-Base

Several studies in Lancet HIV have added to evidence supporting an independent association between HIV and worse outcomes from COVID-19. [1, 2]

Editorial commentary in the same issue by Marta Boffito and Laura Waters nicely summarise both studies and discusses potential explanations for these results. [3]

About a month ago, HTB reported the US study by Yang et al when still a pre-press article. It is perhaps the most thorough and convincing dataset of people living with HIV so far. [4]

References

1. Nomah DK et al. Sociodemographic, clinical, and immunological factors associated with SARS-CoV-2 diagnosis and severe COVID-19 outcomes in people living with HIV: a retrospective cohort study. Lancet HIV. 2021. DOI: 10.1016/S2352-3018(21)00240-X. (13 October 2021).
2. Yang X et al. Associations between HIV infection and clinical spectrum of COVID-19: a population level analysis based on US National COVID Cohort Collaborative (N3C) data. Lancet HIV. 2021. DOI: 10.1016/S2352-3018(21)00239-3. (13 October 2021).
3. Boffito M and Waters L. More evidence for worse COVID-19 outcomes in people with HIV. Lancet HIV. DOI: 10.1016/S2352-3018(21)00272-1. (13 October 2021).
   https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(21)00272-1/fulltext
4. HIV increases risk of severe COVID-19 in largest US study. HTB (17 September 2021).
   https://i-base.info/htb/41117

Immune responses to natural COVID-19 infection in HIV positive people

Simon Collins, HIV i-Base

This review in Nature Communications earlier this month is important for reporting that both magnitude and duration of vaccine responses in HIV positive people are related to both CD4 counts and CD4:CD8 ratio in people living with HIV.

The implications of a reduced immune response to ART is therefore related to the individual management of vaccines against COVID-19.

This study was based on cross-sectional data collected between July and November 2020 comparing different branches of adaptive immunity in 47 HIV positive (24 confirmed SARS and 23 likely) compared to 35 HIV negative health workers.

The results report that despite effective ART, incomplete immune reconstitution can reduce T-cell responses to SARS-CoV-2, especially with a low/inverted CD4:CD8 ratio.

The researchers suggest that “CD4:CD8 ratio should be considered as a readily accessible biomarker for assessing individual risks in people living with HIV, a proportion of whom may require tailored vaccine strategies to achieve long-term protective immunity”.

Reference

Alrubayyi A et al. Characterization of humoral and SARS-CoV-2 specific T cell responses in people living with HIV. Nature Communications, vol 12: article 5839. DOI:10.1038/s41467-021-26137-7. (05 October 2021).

https://www.nature.com/articles/s41467-021-26137-7

COVID-19: vaccine research

Durability of immune responses to COVID-19 vaccines in HIV positive people

Simon Collins, HIV i-Base

Extended follow-up from the HIV positive substudy in 54 HIV positive men reports that six months after vaccination with Oxford/AstraZeneca ChAdOx1 vaccine, both humoral and cell mediated immunity decline. [1]

Similar declines were reported for HIV negative controls. Importantly, participants were all on suppressed ART with very high CD4 counts (median ~700 cells/mm^3 (IQR: 573 to 859). Levels generally remained higher than before vaccination.

Responses to the variants of concern were detectable, but lower than wild type.

Two additional studies recently also reported on vaccines responses in people living with HIV. As with the Oxford above, both were in people with high median CD4 counts. [2, 3]

These included n=143 and n=121 HIV positive people, respectively.

The first included just three people with CD4s <200 cells/mm^3 who responded comparably to people with higher counts (but no overall correlation with CD4 counts is reported for the entire study population).

The second study included six people with CD4 counts <250 cells/mm^3 and reported significantly lower immunogenicity compared to other groups.

References

1. Ogbe A el al. Durability of ChAdOx1 nCov-19 (AZD1222) vaccination in people living with HIV - responses to SARS-CoV-2, variants of concern and circulating coronaviruses. Preprint. medRxiv 2021.09.28.21264207. doi: 10.1101/2021.09.28.21264207. https://www.medrxiv.org/content/10.1101/2021.09.28.21264207v1
2. Levy I et al. Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in people living with HIV-1. Clinical microbiology and infection. DOI: 10.1016/j.cmi.2021.07.031. (23 August 2021). https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00423-7/fulltext
3. Nault L et al. Covid-19 vaccine immunogenicity in people living with HIV-1. Preprint article. (13 August 2021). https://www.biorxiv.org/content/10.1101/2021.08.13.456258v1

Sputnik V vaccine not approved in South Africa due to potential increased risk of HIV

Simon Collins, HIV i-Base

On 18 October 2021, after an eight-month review, the South African Health Products Regulatory Authority (SAPHRA) decided not to grant emergency use approval to the Sputnik V vaccine. [1]

This was due to lack of data proving safety in a population with high background of HIV infection.

The concerns came from previous Ad-5 vector HIV vaccine studies (STEP and PHAMBILI) , that reported increased risk of HIV acquisition in uncircumcised heterosexual men. This issue was raised by other researchers in a letter to the Lancet in October 2020. [2]

The Sputnik V vaccine was developed by the Gamaleya Research Institute of Epidemiology and Microbiology in the Russian Federation. It has also not received emergency use listing by the WHO.

Namibia has also followed the South African decision by suspending use of the Sputnik V vaccine.

References

1. SAHPRA press release. Update on the SAHPRA review of the Sputnik V vaccine. (18 October 2021). https://www.sahpra.org.za/wp-content/uploads/2021/10/MEDIA-RELEASE-Sputnik-Vaccine_18Oct-2021.pdf (PDF)
2. HIV risk from some COVID-19 vaccines might be unlikely due to rarity of vector viruses involved. HTB (December 2020). https://i-base.info/htb/39455
3. Reuters. Namibia suspends use of Russian COVID vaccine after South Africa flags HIV concerns. (23 October 2021). https://www.reuters.com/world/africa/namibia-suspends-use-russian-covid-vaccine-after-safrica-flags-hiv-concerns-2021-10-23

Sanofi reports phase 1/2 mRNA results but withdraws from further COVID19 vaccines

Positive interim results generated significant antibody responses at all studied doses, as proof of concept.

However, clinical efficacy results would require phase 3 studies over the next two years. Instead the company plan to withdraw from further COVID vaccine development and use mRNA technology for vaccines against influenza.

Reference

Sanofi press statement. Sanofi announces positive phase 1/2 study interim results for its first mRNA-based vaccine candidate. (28 September 2021).

https://www.sanofi.com/en/media-room/press-releases/2021/2021-09-28-08-00-00-2304069

COVID-19: TREATMENT

Early efficacy results with oral molnupiravir focuses attention on price and access

Simon Collins, HIV i-Base

On 1 October 2021, early results reported that a five-day course of treatment with the oral antiviral drug molnupiravir significantly halved the risk of hospitalisation or dying from COVID-19 from 14% to 7% (p=0.0012). [1]

These were planned interim results in approximately 750 non-hospitalised participants with mild to moderate COVID-19 enrolled in an ongoing phase 3 study.

The results were sufficient for the study data safety monitoring board (DSMB) to recommend stopping further recruitment - with approximately 1500 participants now in the study.

Molnupiravir is being developed by Merck/MSD who announced plans to file an emergency application with the US FDA.

As potentially the first oral medication in earlier infection, there was an almost immediate focus on access, after a 5-day course was priced at $700 for a pre-approval order for the US market, despite costing less than $20 to manufacture. [2]

Several plans were also quickly announced, including by the Gates Foundation and the Medicines Patent Pool for access in low- and middle-income countries. [3, 4, 5]

The EMA has already started a rolling review for a regulatory decision in Europe. [6]

S T O P P R E S S

Shortly after this issue of HTB was distributed, the UK became the first country to conditionally approve molnupiravir. [7, 8]

References

1. Merck press statement. Merck and Ridgeback's investigational oral antiviral molnupiravir reduced the risk of hospitalization or death by approximately 50 percent compared to placebo for patients with mild or moderate COVID-19 in positive interim analysis of phase 3 study
   https://www.merck.com/news/merck-and-ridgebacks-investigational-oral-antiviral-molnupiravir-reduced-the-risk-of-hospitalization-or-death-by-approximately-50-percent-compared-to-placebo-for-patients-with-mild-or-moderat
2. CommonDreams.org. 'Entirely unsurprising': Merck slammed for 4,000% markup of taxpayer-funded COVID-19 drug. (6 October 2021).
   https://www.commondreams.org/news/2021/10/06/entirely-unsurprising-merck-slammed-4000-markup-taxpayer-funded-covid-drug
3. Gates provides US$120 million to support generic production of molnupiravir
   https://www.statnews.com/pharmalot/2021/10/20/covid19-merck-gates-pill-patents-who
4. Merck press statement. The Medicines Patent Pool (MPP) and Merck Enter Into License Agreement for Molnupiravir, an Investigational Oral Antiviral COVID-19 Medicine, to Increase Broad Access in Low- and Middle-Income Countries. (27 October 2021).
   https://www.merck.com/news/the-medicines-patent-pool-mpp-and-merck-enter-into-license-agreement-for-molnupiravir-an-investigational-oral-antiviral-covid-19-medicine-to-increase-broad-access-in-low-and-middle-income-countri
5. WHO-Unitaid statement on the MPP licensing agreement for molnupiravir. (27 October 2021),
   https://www.who.int/news/item/27-10-2021-who-unitaid-statement-on-the-mpp-licensing-agreement-for-molnupiravir
6. EMA. COVID-19: EMA starts rolling review of molnupiravir. (25 October 2021).
   https://www.ema.europa.eu/en/news/covid-19-ema-starts-rolling-review-molnupiravir
7. MHRA press release. First oral antiviral for COVID-19, Lagevrio (molnupiravir), approved by MHRA. *4 November 2021).
   https://www.gov.uk/government/news/first-oral-antiviral-for-covid-19-lagevrio-molnupiravir-approved-by-mhra
8. MHRA. Regulatory approval of Lagevrio (molnupiravir). (4 November 2021).
   https://www.gov.uk/government/publications/regulatory-approval-of-lagevrio-molnupiravir

FUTURE MEETINGS

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.

Virology Education meeting and workshops

Several VE workshops are highlighted below but 35 meetings are planned for 2021:

https://www.virology-education.com

Liverpool Masterclass in Antiviral Pharmacology (LMAP) 2021

10 November 2021, virtual workshop, 3.00 - 5.30 pm (UK)

https://www.livmap.org

International Workshop on HIV Transmission 2021

10 – 11 November 2021, virtual workshop

https://academicmedicaleducation.com/hiv-transmission-2021

Workshop On Long-Term Complications Of HIV And SARS-CoV-2

6 – 9 December 2021, virtual.

https://www.intmedpress.com/comorbidities

Conference on Retroviruses and OIs (CROI 2022)

13 – 16 February 2022, hybrid (Denver and virtual).

https://www.croiconference.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.

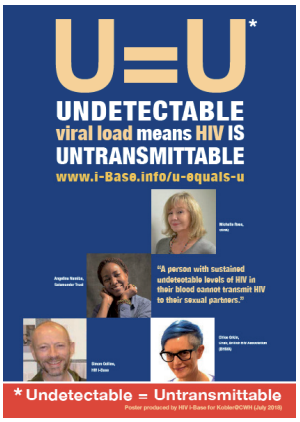
This project was developed with the Kobler Centre in London.

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.

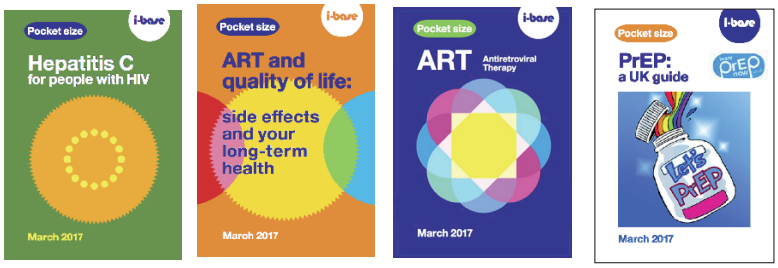
Personalising these for your clinic is cheap and easy and might be an especially nice way to highlight the good news.

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

Medical consultants:
Dr Tristan Barber, Royal Free Hospital, London.
Dr Karen Beckerman, Albert Einstein College of Medicine, NYC.
Dr Sanjay Bhagani, Royal Free Hospital, London.
Prof. Diana Gibb, Medical Research Council, London.
Dr Gareth Hardy, PhD.
Prof. Saye Khoo, University of Liverpool Hospital.
Prof. Clive Loveday, International Laboratory Virology Centre.
Prof. James McIntyre, Chris Hani Baragwanath Hosp. South Africa
Dr Graeme Moyle, Chelsea & Westminster Hosp, London.
Dr Stefan Mauss, Düsseldorf.
Prof. Caroline Sabin, UCL Medical School, London.
Dr Graham P Taylor, Imperial College, London.
Dr Stephen Taylor, Birmingham Heartlands Hospital.
Dr Gareth Tudor-Williams, Imperial College, London.
Dr Edmund Wilkins, Manchester General Hospital, Manchester.

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 *(October 2019): 48-page A5 booklet* **quantity** _____

UK Guide To PrEP *(June 2021): 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 *(Jan 2018): 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 *(July 2016): 52-page A5 booklet* **quantity** _____

Guide to hepatitis C coinfection *(April 2017): 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