ISSN 1472-4863

HTB: vol 24 no 7/8: July/August 2023

hiv treatment bulletin (e)

IAS 2023: first reports (1 August 2023)

CONTENTS

EDITORIAL: HTB July/August 2023 3
- New i-Base pocket leaflets 2

CONFERENCE REPORTS

12th IAS Conference on HIV Science (IAS 2023)
23 – 26 July 2023, Brisbane, Australia
- Introduction
- Navigating the programme online
- WHO endorses "zero" transmission risk for people with HIV with an undetectable viral load
- Viral load level when suppressed <1000 predicts future rebound: 3-monthly monitoring required
- ART-associated hypertension can be successfully treated in African settings
- REPRIEVE study: statin benefits people living with HIV at low to mederate CVD risk
- Early press conference: cure, gay circumcision, PrEP choices, mpox, and COVID-19
- Rapporteur summaries: track B clinical science
- Geneva patient and other HIV cure-related research
- Other HIV cure-research in the IAS 2023 programme
- Anal cancer: 1 in 5 risk of missing precancerous lesions if only HSIL are biopsied
- High rates of occult HBV in Botswana: risks from relying on HBsAg screening

CONFERENCE REPORTS **24**

BHIVA Spring Conference 2023 (BHIVA 2023)
24–26 April 2023, Gateshead
- Introduction
- No vertical HIV transmissions from women eligible for supported breastfeeding in the UK

Contents continued inside...

Published by HIV i-Base

Contents cont...

- Adverse birth outcomes with diabetes and hypertensive disorders in pregnancy

ANTIRETROVIRALS **27**
- CAB-LA receives positive opinion for EU approval as PrEP

SIDE EFFECTS **28**
- Help needed: UK surveys on access to New-Fill for facial lipoatrophy

TREATMENT & VACCINE GUIDELINES **29**
- New UK vaccine schedule for HPV depends on HIV status
- UK shingles vaccine: changes from 1 September 2023 on HIV status
- New guidelines on cognitive impairment in people living with HIV

HIV PREVENTION & TRANSMISSION **31**
- Breakthrough HIV infections on CAB-LA PrEP

FUTURE MEETINGS 2023/24 **33**
- Meetings and workshops in 2023/24

PUBLICATIONS & SERVICES FROM i-BASE **34**
HTB ADVISORY BOARD **35**
ORDER FORM **36**

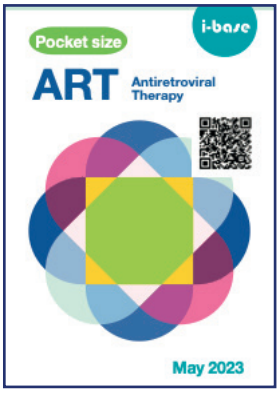
New i-Base pocket leaflets

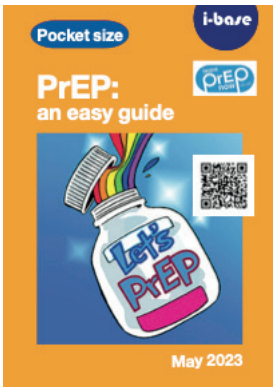
Four new pocket leaflets were recently updated and reprinted.

Each leaflet is 10 x 7 cms and they use minimal text and QR codes to summarise and link to more detailed A5 booklets.

All leaflets are free - please order online:

https://i-base.info/forms/order.php





EDITORIAL

This issue of HTB leads with early reports from the 12th IAS conference held in Brisbane from 23 to 26 July 2023.

This was a major conference and our early reports fill most of this issue - and more will continue to be posted online as they are written.

The meeting included important news related to WHO endorsement of U=U, but this also stresses the need for more frequent viral load monitoring when low level viral load remains detectable but less than 1000 copies/mL.

We link this report to data from three posters that clearly show why the WHO called for this additional monitoring. This low level viraemia is a temporary not a stable state. Closer monitoring is needed to know whether viral load becomes undetectable with adherence support, or whether drug resistance develops.

Many studies also focused on side effects and complications from ART or HIV including hypertension, weight changes, diabetes, cure research, statin use and much more.

It is still a shame that the first press conference three days before the meeting started broke the headline news, before the data was even presented. This makes reporting more difficult and is not a good way to release scientific news about research that has taken years of work.

Also in this issue, the last two reports from the UK BHIVA conference on the efficacy of ART in preventing vertical transmission and looking at the complications of diabetes in pregnancy.

This HTB issue also includes other important news including on further steps to make long-acting cabotegravir (CAB-LA) as PrEP available in Europe and the UK.

The UK-CAB is also partnering with BHIVA to look at current access to New-Fill to treat facial lipoatrophy caused by early HIV drugs. These NHS services were established many years ago but many of the specialist New-Fill clinics are no longer running and pathways for referral to these services are no longer equitable across the UK. Your help with these surveys would be appreciated.

New UK guidelines cover both the HPV and shingles vaccines and cognitive impairment in people living with HIV.

Finally, we report a case of breakthrough HIV infection on CAB-LA PrEP, which we noticed at CROI 2023 and that has now been published.

Lots to read, if you get a break to enjoy a little August sunshine.

CONFERENCE REPORTS

12th IAS Conference on HIV Science (IAS 2023)

23 – 26 July 2023, Brisbane, Australia

Introduction

IAS 2023 was held this year in Brisbane, Australia, and as a hybrid conferences with a strong programme that included latest scientific progress in HIV treatment.

For those able to attend in person, there is no substitute for discussions that give broader perspectives to the presentations and that often lead to new collaborations with colleagues, researchers and activists in other countries.

But meetings will always be difficult to attend for those living furthest away. Funding and sponsorship to attend is becoming more difficult and visa applications from many countries can be difficult and easy travel is still not assured.

Recognising this, and building on the experience from COVID, it is notable that IAS 2023 was a hybrid meeting that enabled access to live presentations, next-day webcasts and online digital resources.

Australia has a long history of producing leading HIV research and is an example of one of the few countries where healthcare, including for HIV, is relatively unpoliticised – with a shared commitment to public health by all major political parties. In addition to HIV care, examples of leading public health initiatives include comprehensive early access to HCV drugs, HPV vaccines and HIV PrEP. Several sessions focused on the Australian progress to 95:95:95 targets for 2030.

It was good to see the conference remembering the late Professor David Cooper.

For all the focus on science, progress towards better health is dependent on people. David was one of the doctors who led many of the early responses to HIV in Australia and who collaborated internationally to make sure this response was also global.

Originally this two-yearly meeting was planned to focus on the treatment and pathogenesis of HIV, alternating with the IAS World AIDS Conferences which had a broader community scope.

This focus expanded over the years to five tracks: basic science, clinical science, HIV prevention, social science and implementation. There were also three pre-meetings – on cure-related research, HIV-related migration and HPV-related research.

We include key highlights from the excellent rapporteur summaries to give a snapshot of the whole conference.

Much of the conference focused on global health goals for both treatment and prevention. Differences between regions include Eastern and southern Africa producing some of the highest rates of viral suppression on ART. The detail in calculations of targets though needs to include many populations where data is currently limited, including awareness of people who become disconnected from care and who then drop out of data.

Globally, the goal of 10 million people accessing PrEP by 2025 is unlikely to be met - although this might increase with access to new PrEP formulations.

We include separate reports on the launch of new WHO policies that emphasise that an undetectable viral load has a zero risk of transmission and an important clarification that with a detectable but highly suppressed low-level viral load (less than 1000 copies/mL) this risk remains very low and effectively zero, based on a new data review simultaneously published in the Lancet.

The meeting also focused on complications associated with ART, notably the problem of weight gain, hypertension, diabetes mellitus and metabolic changes.

The conference also included a symposium on the large international REPRIEVE study that could lead to earlier use of statins.

ART news included studies with long-acting injections, islatravir, lenacapavir, bNAbs and ways to deliver new formulations of these and other long-acting drugs. ART strategy studies included dual DTG/3TC ART, rapid ART and management of low-level viremia on DTG-based ART.

Cure-related research included a potential cure case from a donor without the CCR5-delta-32 deletion and five children who had significant periods of viral load suppression off-ART. Mainstream new coverage of these studies were complicated by a media press conference held several days before the actual conference. This is a really unhelpful way to release important new study results and remains perhaps the most significant criticism for what looks like an otherwise exciting and impressive conference.

Rapid i-Base reports will be published online during the meeting and in the weeks after the conference.

Reports have been compiled by accessing the hybrid meeting as this year it was difficult to attend in person.

As in each of the conference sessions, i-Base also gives thanks and pays respect to the elders – past, present and future – who are custodians of the lands on which the conference took place.

Reports in this issue of HTB are linked below.

- Navigating the programme and online access
- WHO endorses “zero” transmission risk for people with HIV with an undetectable viral load
- Viral load level when suppressed <1000 predicts future rebound: 3-monthly monitoring required
- ART-associated hypertension can be successfully treated in African settings
- REPRIEVE study: statin benefits people living with HIV at low CVD risk
- Early press conference: cure, gay circumcision, PrEP choices, mpox, and COVID-19
- Rapporteur summaries: track B clinical science
- Geneva patient and other HIV cure-related research
- Other HIV cure-research in the IAS 2023 programme
- Anal cancer: 1 in 5 risk of missing precancerous lesions if only HSIL are biopsied
- High rates of occult HBV in Botswana: risks from relying on HBsAg screening

Navigating the programme and online access

Simon Collins, HIV i-Base

The abstract database should be open access to non-delegates shortly after the conference finishes, and the full programme, including webcasts, will be available roughly four weeks after the conference.

The open access programme links to abstracts online and includes rapporteur summaries. It doesn’t currently link to any webcasts, and satellite and plenary sessions don’t include abstracts for these talks.

https://programme.ias2023.org

Abstracts are also available from a separate URL:

https://programme.ias2023.org/Abstract/Index

Abstract book (PDF)

https://www.iasociety.org/sites/default/files/IAS2023/abstract-book/IAS_2023__Abstracts.pdf

More than 30 very short rapporteur summaries are collected under a separate URL.

https://www.iasociety.org/conferences/ias2023/programme/rapporteurs

For registered delegates, access to webcasts seem to be linked using this URL.

https://conference.ias2023.org/programme-live-1

This brings another version of the programme, selected by each day, with the window opened for each session, includes a ‘watch now’ link.

Open access to all conference material, including webcasts and posters is usually made available within four weeks to all IAS members and within eight weeks for everyone else.

These IAS meetings alternate with the larger IAS World AIDS Conferences and have a stronger focus on clinical science.

IAS 2023: GLOBAL HEALTH PREVENTION

WHO endorses "zero" transmission risk for people with HIV with an undetectable viral load

Polly Clayden, HIV i-Base

World Health Organisation (WHO) states that people living with HIV who have an undetectable viral load, using any WHO-prequalified test and sample, who are taking ART as prescribed, have zero risk of transmitting HIV to their sexual partner(s). And, people with a viral load that is suppressed to less than 1000 copies/mL, but that is still detectable, have almost zero or negligible risk of transmitting HIV to their partner(s), so long as they are still taking ART as prescribed.

These announcements were made at the launch of a new WHO policy brief at a satellite symposium in the run up to IAS 2023. [1, 2]

The policy brief is supported by a systematic review published simultaneously in The Lancet, 23 July 2023. [3]

WHO policy brief: key messages

The brief is intended for a wide audience and is written in simple language.

It stresses that viral suppression is critical to improve health, prevent sexual transmission and reduce vertical transmission.

Viral load measurements are divided into three categories: (i) undetectable, (ii) suppressed, and (iii) unsuppressed.

These are illustrated by a traffic light system and defined as:

- Undetectable (not detected): no measurable virus. Zero risk of transmission to sexual partner(s); minimal risk of vertical transmission. Coded as green (for go).
- Suppressed (detected but less than 1000 copies/mL): some virus replicating and present. This could be due to recently starting treatment, intermittent adherence, or drug resistance. Almost zero or negligible risk of transmission to sexual partner(s). This situation requires three-monthly viral load monitoring. Coded as amber (for caution or get ready).
- Unsuppressed (greater than 1000 copies/mL): significant virus replicating and present. This could be due to missing doses, recently starting treatment or drug resistance. Increased risk of falling ill and/ or passing virus on to sexual partner(s) or children. Coded as red (for stop).

Any current WHO-prequalified tests and samples – including point-of-care tests and dried blood spot (DBS) samples – can be used to measure and define viral load results in the three categories. The sensitivity threshold for DBS is usually 300 - 400 copies/mL.

The brief also states that anyone with a detectable viral load – including suppressed to less than 1000 copies/mL should be supported with adherence counselling and a follow up viral load test.

And, "The ultimate goal for all people living with HIV is to reach and sustain undetectable viral loads. Taking ART as prescribed will support this goal, prevent transmission to their sexual partner(s) and/or children, and improve their own clinical well-being."

Systematic review

WHO conducted a systematic review to understand the clinical impact of being suppressed but detectable (less than 1000 copies/mL) and inform these new recommendations. This has important implications, particularly in low- and middle-income countries that use alternatives to plasma-based viral load testing.

The authors noted: "Although it is generally accepted that HIV viral loads of less than 200 copies/mL are associated with zero risk of sexual transmission and this threshold is used for U=U messaging in many high-income settings, the risk at virus levels higher than 200 copies per mL has been controversial."

Studies included in the review looked at sexual transmission between serodifferent couples at various levels of viraemia (ie the evidence behind U=U), and the public health impact of low-level viraemia.

The authors identified 244 studies that might be relevant but only eight were included eight in the analysis, with 7762 serodifferent couples across 25 countries.

Three studies showed no HIV transmission when the partner living with HIV had a viral load less than 200 copies/mL. In the remaining four prospective studies, there were 323 transmissions – none were in participants considered suppressed on ART. There were two cases of transmission when the partner with HIV's most recent viral load was less than 1000 copies per mL. But the authors noted that the interpretation of both cases was complicated by long intervals (50 days and 53 days) between the transmission date and the most recent viral load result.

The systematic review found no evidence of HIV transmission to sexual partners when viral loads were less than 600 copies/mL and an incredibly rare occurrence of possible transmissions with viral loads between 600 and 1000 copies/mL.

Importantly, the prevalence of low-level viraemia remains relatively low: one study found that among people with a suppressed viral load (less than1000 copies/mL), the majority (95%) had an undetectable viral load.

This suggests that the U=U message also applies to people living with HIV experiencing low-level viraemia.

The authors emphasised two important caveats to the results and in turn messages informed by the review.

First, that they do not apply to vertical transmission that can happen during pregnancy (ie in utero), at delivery or through breastfeeding, so the length and strength of exposure to viraemia is considerably more than that of sexual transmission.

Second that there are no data on risk of transmission through sharing of injection drug use equipment at varying levels of viraemia.

And, the authors noted that these outcomes have not been thoroughly studied in the context of current, optimal integrase inhibitor-based ART.

They also note that people with suppressed viral load need more frequent viral load monitoring – ideally every three months – to determine whether viral load is likely to be a temporary blip or genuine rebound.

They concluded: "An undetectable viral load should be the ultimate goal for clinical management of all people living with HIV on ART. However, the evidence showing almost zero risk of sexual transmission when HIV viral loads are less than 1000 copies/mL provides a powerful opportunity to destigmatise people who are living with HIV and promote adherence to ART through dissemination of this positive public health message."

Testing and sampling

The policy brief also summarises the various WHO-prequalified viral load testing options available for national programmes to consider. [1]

These range from high-throughput laboratory-based technologies to simpler point of care tests that can be decentralised.

Although considered to be the gold standard, collecting and processing plasma samples is too complex (storage, transport, laboratory equipment etc) in many settings and using alternatives, such as dried blood spots, can massively expand access to viral load testing.

Lower limits of detection of some tests and sample types tend to be higher than plasma (due to the smaller volume of samples) but this does not stop the technologies from correctly classifying people living with HIV as unsuppressed, suppressed or undetectable.

The brief includes a useful summary for programmes and healthworkers, describing typical viral load technology reporting outputs.

And it emphasises that all HIV viral load tests and sample types available and with WHO prequalification can accurately identify people living with HIV in the three viral load categories.

C O M M E N T

That the generally measured-in-its-language WHO describes people living with HIV with an undetectable viral load by any WHO-prequalified test and take their ART as prescribed having "zero risk" of transmitting HIV to their sexual partner(s) is a big step forward.

It is also extremely useful to have clarification on the "almost zero or negligible risk" for people in the grey area below 1000 copies/mL. And notable that only 5% of these people are not also likely to be undetectable too.

The brief explains that suppressed below 1000 copies/mL is a transitory state – either in people who have just recently started ART or those whose viral load might be increasing. It is important that people in this situation are supported with adherence counselling and more frequent follow up viral load tests, ideally every three months.

The IAS listed this as one of its "Eight takeaways from IAS 2023" [4] And wrote: "This is a massive boost to the undetectable equals untransmittable (U=U) messaging."

Overall, this message is hugely important for people living with HIV in low- and middle-income countries who can now have the peace of mind about onward transmission in the same way that people in high-income countries do.

For national programmes and healthworkers it is also a critical message that all WHO prequalified viral load technologies can identify people living with HIV as unsuppressed, suppressed and undetectable. Dried blood spots particularly will help national programmes to ensure more widespread and equitable access to viral load for all people living with HIV

References
1. World Health Organization. The role of HIV viral suppression in improving individual health and reducing transmission. Policy brief. 22 July 2023.
   https://www.who.int/publications/i/item/9789240055179
2. What's new in WHO guidelines: innovations, treatment, integration and monitoring. IAS 2023. Brisbane, Australia. 23–26 July 2023. Satellite session SAT026.
   https://conference.ias2023.org/programme-live-1?coday=2023-07-23&embed=
   https://conference.ias2023.org/media-1149-what39s-new-in-who-guidelines-innovations-treatment-integration-and-monitoring
3. Broyles LN et al. The risk of sexual transmission of HIV in individuals with low-level HIV viraemia: a systematic review. The Lancet. 23 July 2023.
   https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00877-2/fulltext
4. Eight takeaways from IAS 2023.
   https://www.iasociety.org/conferences/ias2023/takeaways-from-ias-2023

Viral load level when suppressed <1000 predicts future rebound: 3-monthly monitoring required

Simon Collins, HIV i-Base

Several studies at IAS 2023 in different populations and settings reported on the risk of viral failure when HIV viral load is suppressed to less than 1000 but not to less than 50 copies/mL.

This has implications for both clinical care and the new WHO guidelines on treatment as prevention.

Although similar results were reported more than 20 years ago in the early ART era, it is important to show that this principle of drug resistance is just as relevant with modern HIV combinations.

The first study is a poster from the Gaitonde Center for AIDS Research and Education, Infectious Diseases, Chennai, India.

This was a longitudinal retrospective analysis of viral load results from 3498 people living with HIV and treated at this centre between 2013-2018. Of these, 2965 (84.8%) were fully suppressed (<40 copies/mL) and 533 (15.2%) had low level viraemia (LLV) but less than 1000 copies/mL.

During follow-up, 126/2965 people with full suppression had viral load rebound to >1000 copies/mL. This was 3.6% of the overall cohort and 4.3% of people who were fully suppressed. By comparison, 217/533 people with LLV rebounded to >1000 copies/mL. This was significantly higher, accounting for 6.2% of the overall cohort and 31% of those with LLV.

There was a clear link between the higher bands of low-level viraemia and a higher subsequent risk of treatment failure. See Table 1.

People on first-line ART had a higher incidence of VF (HR 15.8, 95% CI: 11.4 to 21.9) than second-line (HR 5.6, 95% CI 4.1 to 7.7), perhaps because of the urgency of better adherence.

Table 1: Risk of viral rebound >1000 c/mL by viral load and treatment line

		Risk of rebound >1000 copies/mL	
LLV category	n	First-line ART HR (95%CI)	Second-line ART HR (95%CI)
LLV-I: 40 to 199 c/mL	225	12.9 (7.9 to 21.1)	4.1 (2.8 to 6.1)
LLV-II: 200 to 399 c/mL	130	13.3 (8.3 to 21.4)	6.2 (4.0 to 9.6)
LLV-III: 400 to 999 c/mL	178	22.8 (15.2 to 34.3)	8.1 (5.5 to 12.0)

Other similar studies reported similar outcomes in different populations.

This included a retrospective analysis of 670 children and adolescents living with HIV in Tanzania, which reported the same association between levels of LLV and future risk of viral failure. [2]

Another poster reported a retrospective analysis of 8610 adults in Zambia with a viral load result >1000 copies/mL between April 2018 and January 2022. This study reported that people who had a previous low-level viral load result (60 to 1000 c/mL) were 3.4-fold more likely to have viral failure compared to those with a previous undetectable viral load <60 copies/mL. [3]

C O M M E N T

These posters are important to report because of the new WHO policy brief that defines three key categories for HIV viral load results: unsuppressed (>1000 copies/mL), suppressed (detected but ≤1000 copies/mL) and undetectable (viral load not detected by test used). [4, 5]

Undetectable includes results from both PCR tests sensitive to 20, 40 or 50 copies/mL and dried blot spot (DBS) tests where the cut-off is slightly higher at 300 or 400 copies/mL.

It also states that having suppressed viral load between 200 to <1000 copies/mL means having such a negligible risk for sexual transmission without a condom that the risk of transmission is close to zero.

This policy brief was based on a review published in the Lancet and released at the same time. [6]

This important document resolves the grey area between having an undetectable viral load <50 copies/mL using PCR tests, and settings where the threshold of 1000 copies/mL is used to manage care.

Having a zero risk of sexual transmission is based on results from the PARTNER and other studies but WHO guidelines use the threshold of 1000 copies/mL to define viral failure in low- and middle-income countries (LMICs).

The new WHO policy now enables people globally to benefit from lifting the fear associated with a risk of transmitting HIV. This is significant for connecting people to the global U=U campaign. [7]

However, it is essential to also remember that for most people, viral load suppression to between 200 and 1000 is not a stable state but a temporary situation.

It requires more frequent viral load monitoring – every three months – with more careful adherence, to determine whether viral load will either become undetectable or continue to rebound to >1000 copies/mL.

Thinking of 'suppression' as a stable state misses that viral load can rebound in some cases within a few months to levels that could enable sexual transmission.

References

1. Dinesha TR et al. HIV-1 Low level viremia predicts virological failure in first-line and second-line ART experienced individuals in India. IAS 2023, poster abstract EPB0115.
   https://programme.ias2023.org/Abstract/Abstract/?abstractid=2841
2. McKenzie KP et al. Low-level viremia as a risk factor for virologic failure in children and adolescents living with HIV. IAS 2023, poster abstract EPB0117.
   https://programme.ias2023.org/Abstract/Abstract/?abstractid=3599
3. Mwamba D et al. Can HIV low level viremia predict future anti-retroviral treatment failure? A retrospective cohort analysis from Zambia. IAS 2023, poster abstract EPB0120.
   https://programme.ias2023.org/Abstract/Abstract/?abstractid=4020
4. WHO policy brief. The role of HIV viral suppression in improving the individual health and reducing transmission. 22 July 2023.
   https://www.who.int/publications/i/item/9789240055179
5. Clayden P. WHO endorses "zero" transmission risk for people with HIV with an undetectable viral load. HTB, 26 July 2023.
   https://i-base.info/htb/45887
6. Broyles LN et al. The risk of sexual transmission of HIV in individuals with low-level HIV viraemia: a systematic review. Lancet 2023; 21 July 2023.
   https://doi.org/10.1016/S0140-6736(23)00877-2.
7. U=U and Prevention Access Campaign.
   https://preventionaccess.org

IAS 2023: SIDE EFFECTS & COMPLICATIONS

ART-associated hypertension can be successfully treated in African settings

Polly Clayden, HIV i-Base

Hypertension, after starting HIV treatment, was common in an analysis of two African trials comparing first-line ART regimens – according to data presented at IAS 2023. [1]

In NAMSAL, in which hypertension was not routinely treated, this was more frequent among people receiving dolutegravir (DTG)-based than efavirenz (EFV)-based ART (plus tenofovir disoproxil fumarate [TDF] and 3TC), at 192 weeks.

In ADVANCE, where most cases of hypertension were successfully treated, there was no difference between DTG and EFV arms, including in ART that included DTG and tenofovir alafenamide (TAF), at 192 weeks.

Presenting author Francois Venter made the case for diagnosing and treating hypertension, which can be done successfully with inexpensive generic drugs.

Hypertension is a leading cause of death in sub-Saharan Africa, with a high background prevalence in the general population. TAF and DTG have been associated with higher risks of obesity than tenofovir disoproxil fumarate (TDF) or efavirenz (EFV). Clinical obesity increases the risks of hypertension and other non-communicable diseases.

The study was a secondary analysis of NAMSAL and ADVANCE, looking at ART and hypertension and whether this was associated with particular antiretrovirals.

NAMSAL

In the NAMSAL trial, 613 participants in Cameroon were randomised to TDF/3TC/DTG or TDF/3TC/EFV (EFV 400 mg). Blood pressure was measured at every study visit.

In Cameroon, like many African countries, free routine hypertension treatment is not offered in primary healthcare. About 1% of participants in NAMSAL had hypertension at entry and very few were treated over the course of the study.

Median BMI was 23 kg/m^2 in this study and CD4 was about 280 cells/mm^3.

As the participants' BMI increased, so did the prevalence of hypertension. Over a third (37%, 17/46) of

participants with BMI over 30 developed grade 1 hypertension compared to less than 10% of those with normal BMI.

NAMSAL previously demonstrated a rise in weight over 192 weeks, which was more significant on the DTG arm and among women.

Blood pressure increased in both study arms. Between week 60 and 72 mean SBP became significantly greater in the DTG arm, p=0.02. By week 192 this difference was 6.5 mm/Hg, p<0.01.

At baseline 12% and 10% of participants in the DTG and EFV arms had high blood pressure (SBP>140 or DBP>90). This difference became significant at by week 144, when these proportions were 25% and 12%, p=0.001. At week 192, 31% of participants had developed hypertension in the DTG arm, vs 19% in the EFV arm, p=0.002. There were also corresponding significant differences across DAIDS hypertension grades 1 to 3. Very few participants in NAMSAL had their blood pressure treated over this course of events.

ADVANCE

In the ADVANCE trial, 1053 participants in South Africa were randomised to TAF/FTC/DTG, TDF/FTC/DTG or TDF/FTC/EFV (standard dose EFV, 600 mg).

In South Africa, people are routinely treated for hypertension.

BMI at baseline was slightly higher in ADVANCE than NAMSAL, median 24 kg/m^2, as was CD4 count at about 340 cells/mm^3.

Weight also increased over time in this study and this was more pronounced among black women and in the TAF arm and both DTG arms. Francois Venter noted that this is likely to be due to EFV and TDF mitigation of weight gain.

About 10% of participants entered the study already being treated for hypertension. This increased by about 11% during the study and almost all (95%) the participants with hypertension were treated.

The risk of treatment-emergent grade 1 hypertension was significantly higher in the TAF/FTC/DTG arm vs TDF/FTC/EFV, p=0.038.

By 192 weeks there was just over 2 mm/Hg difference between the TAF and DTG arm and the EFV arm.

The difference in blood pressure between the merged DTG arms and the EFV arm only became significant at week 192: respectively 54% vs 45%, p=0.047.

There was almost no difference between the combined DTG arms and the EFV arms in DAIDS graded hypertension at week 192, except for 43% vs 35% with high normal blood pressure, p=0.047.

C O M M E N T

The authors pointed out that an important limitation to this analysis is that blood pressure measurement is not standardised – and not just across HIV studies. One of the confounders was standardised cuff size (bigger sizes are recommended for people with BMI of 35 and above).

The analysis is ongoing and the group are looking at weight and renal markers. Of note, when people on hypertensive drugs in ADVANCE were removed from the analysis, initial data suggests that blood pressure is mediated by weight gain not drug choice. They also noted that higher risks of hypertension are at least partly due to rising body weight on ART and ageing. And they asked the question if this is a "return to health" effect?

When the authors looked at the risk of hypertension in over 20 randomised first- and second-line studies the results were inconsistent. And some studies did not measure blood pressure at all. But seven observational studies in various populations and settings showed higher risk of hypertension with DTG vs EFV.

The authors cautioned that mistakes were made with attribution to specific antiretrovirals with weight gain and the need to take care with these analyses.

The key message that hypertension "can be very successfully treated, if you diagnose it" deserves repeating here.

Reference

Venter F et al. Risks of hypertension with first-line dolutegravir (DTG) and tenofovir alafenamide (TAF) in the NAMSAL and ADVANCE trials. IAS 2023. Brisbane. Australia. 23–26 July 2023. Oral abstract 5640.

https://ias.reg.key4events.com/key4register/AbstractList.aspx?e=96&preview=1&aig=-1&ai=52401 (abstract)

https://conference.ias2023.org/media-1110-track-b-late-breaker (late breaker webcast)

REPRIEVE study: statin benefits people living with HIV at low to moderate CVD risk

Simon Collins, HIV i-Base

Introduction

One of the most prominent studies at IAS 2023 was the NIH-funded international phase 3 Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE), which was given a symposium in the programme and was simultaneous published in the NEJM. [1, 2]

The top-line results of a reduction by the statin in reducing cardiovascular events by 35% were reported in HTB in April 2023 when the study was stopped early following a recommendation by the DSMB for efficacy. This is the first time the full results were presented. [3]

The main results were presented by lead investigator Steven Grinspoon from Harvard Medical School. [4]

Related talks covered the implications for the results globally and in women, followed by a panel discussion and open Q&A. [5, 6]

Study design and demographics

From March 2015 to July 2019, REPRIEVE randomised 7769 people living with HIV to either pitavastatin (4 mg day) or matching placebo. Entry criteria included being 40 to 75 years old and having mild to moderate risk of cardiovascular disease (CVD), based on LDL levels in US guidelines. The median screening LDL was 108 mg/dL (IQR: 87 to 128) or 2.79 mmol/L (IQR: 2.25 to 3.31 mmol/L).

The study included 145 sites in 12 countries and was stopped early following a recommendation from the independent Data and Safety Monitoring Board (DSMB) based on early efficacy.

The study was designed to have 85% power to detect a 30% reduction in the risk of a major CVD event (HR: 0.70) in the pitavastatin group on the basis of a maximum of 288 events. The DSMB recommended ending the randomisation after 225 events.

The primary outcome of serious CVD, included CVD death; myocardial infarction; hospitalisation for unstable angina; stroke; transient ischemic attack (TIA); peripheral arterial ischemia, revascularisation of a coronary, carotid, or peripheral artery, or death from other causes.

Baseline characteristics included: 31% women, median age 50 (IQR: 45 to 55), median CD4 count 621 cells/mm^3(IQR: 448 to 827) and viral load <50 copies/mL in 5250/5997 participants (87.5%) with data. Of note, and not mentioned in the presentation, almost half the participants (48%), had a nadir CD4 count <200 cells/mm^3. This history is perhaps important for higher CVD risk.

Overall, 41% were Black, 15% Asian and 35% white. In North America, 18% were Hispanic or Latinx.

The majority of participants were cisgender (95%) with 1.6% transgender and data was not reported for the remaining participants.

Participant breakdown by country was: Botswana (n=281), Brazil (n=1099), Canada (n=131), Haiti (n=140), India (n=504), Peru (n=148), South Africa (n=570), Spain (n=213), Thailand (n=590), Uganda (n=181) and the US (n=3787).

Study results

In March 2023, the trial was stopped early for efficacy after a median follow-up of 5.1 years (IQR: 4.3 to 5.9). Overall, 83% (6452/7769) of participants remained in the study, with 74% vs 71% still on their randomised treatment in the active vs placebo arms.

Treatment-related discontinuations occurred in 82 (2.1%) vs 46 (1.2%) and open label statin was started in 223 (5.7%) vs 373 (9.6%), in the active vs placebo groups respectively. Self-reported adherence was >80% each year.

The incidence of primary endpoint of serious CVD events was lower in the statin group with 4.81 vs 7.32 per 1000 person-years (HR 0.65; 95% CI, 0.48 to 0.90; p=0.002). This translated to a number needed to treat (NNTT) of 106 in the study overall. Sensitivity analyses also favoured the statin group and the results were not apparently related to COVID-19.

The reduction was balanced by more cases of diabetes mellitus in the statin group: 206 (5.3%) vs 155 (4.0%) participants (IRR: 1.35; 95% CI: 1.09 to 1.66).

Muscle-related symptoms were also higher, reported in 91 (2.3%) vs 53 (1.4%) in the active vs placebo groups, respectively. Grade 3 or higher were also more frequent (IRR 1.74; 95% CI, 1.24 to 2.45) as were related withdrawals: 44 (1.1%) vs 21 (0.5%).

LDL dropped from a median of 107 to 74 mg/dL (2.77 to 1.91 mmol/L) in the statin group and were unchanged in the placebo arm. This was roughly double the expected drop for reasons that are not yet understood.

For full details please see the open access NEJM paper, together with supplementary material. [2]

COMMENT

These results showed benefits in reducing serious CVD events with a generally good safety profile.

Statins are low-cost drugs (the pitavastatin patent ends later in 2023) and so long as statin choice avoids drug interactions with ART, the same results would be expected with other statins, which have a similar lipid and anti-inflammatory effect.

In the panel discussion following the presentations, many members noted the importance of REPRIEVE as being likely to change treatment guidelines and clinical practice.

The panel also discussed the implications for implementation, focusing on the NNTT supporting wider access.

As with other large randomised studies, REPRIEVE supported a wealth of substudies and future analyses will continue.

References

Unless stated otherwise, references are to the programme and abstracts for the IAS 2023 conference, 23-26 July, Brisbane, Australia.

1. The REPRIEVE trial: Developing a cardiovascular disease prevention strategy for people living with HIV. Symposium, IAS 2023 https://programme.ias2023.org/Programme/Session/4435 (symposium) https://conference.ias2023.org/media-1185-the-reprieve-trial-developing-a-cardiovascular-disease-prevention-strategy-for-people-livi (webcast)
2. Grinspoon SK et al. Pitavastatin to Prevent Cardiovascular Disease in HIV Infection. NEJM, DOI: 10.1056/NEJMoa2304146. (23 July 2023). https://www.nejm.org/doi/10.1056/NEJMoa2304146
3. Statins reduce heart disease by 35% in the international HIV REPRIEVE study. HTB (6 April 2023). https://i-base.info/htb/45288
4. Grinspoon SK et al. Key REPRIEVE results and the utility of statins among people living with HIV: What have we learned? IAS 2023.
5. Bloomfield G et al. Cardiovascular disease among people living with HIV in high- and low-income countries: Can one strategy fit all?
6. Zanni M et al. Unique aspects of cardiovascular disease among women with HIV: Lessons from REPRIEVE.

IAS 2023: MIXED REPORTS AND OVERVIEWS

Early press conference: cure, gay circumcision, PrEP choices, mpox, and COVID-19

Simon Collins, HIV i-Base

IAS 2023 will be one of the most important HIV conferences this year and an early press conference several days before the meeting included a handful of studies selected by the organisers.

Although these early reports in mainstream media might help the profile of the conference, they will usually be based on limited data from abstract summaries and a short informal talk from the lead author.

This is not a good way to present the results from years or research and it undermines the importance of full access to the study details before these have been presented in a peer-reviewed context.

With this caveat, please read these early reports cautiously - including from i-Base.

Our later coverage however will benefit from access to the full data.

A potential HIV cure from a stem cell donor susceptible to HIV

The press conference led with a new potential case of HIV cure presented by Asier Sáez-Cirión from the Pasteur Institute, Paris and Alexandra Calmy from the Institute of Hospitals, Sion, Switzerland, on behalf of the ICISTEM study group.

As with the five previous cases - this will be the sixth - this involved undergoing a complicated and risky allogeneic hematopoietic stem cell transplant (aHSCT) that was needed to treat refractory cancer. This case is notable however for not using a donor with the CCR5 delta-32 deletion which produces a genetic barrier against the most common strain of HIV.

Although the exact mechanism for earlier cure cases is not fully understood, having a donor with the CCR5 delta-32 deletion has up until now been thought to be essential.

In 2018, this person received chemotherapy to treat a biphenotypic sarcoma followed by aHSCT from an unrelated HLA-matched (9/10) wild-type CCR5 donor.

He stopped ART in November 2019 and has now been off-ART for 20 months without detection of rebound viremia or replication-competent HIV. HIV DNA has not been detected in blood or tissue samples, and testing for HIV-specific T-cell responses are also negative. Nevertheless, this is still a relatively short time and further follow-up is needed.

The individual concerned is a man in his fifties who was diagnosed HIV positive in 1990 and he has been on continuous effective ART since 2005. He has chosen to remain anonymous at the moment and is being referred to as the Geneva patient.

He is also case number 34 in the Icistem database. [2]

Further information about the treatment procedures and subsequent follow-up will become available after the case is presented in the main conference.

Early cases of viral suppression off-ART in five infants

Another cure-related study in the press conference included early cases of viral control presented by Gabriela Cromhout from the University of KwaZulu-Natal. The five infants, all male, were part of a longitudinal study from 2015 to 2023 involving 281 mother-child pairs monitored from delivery following in utero HIV transmission.

Intermittent adherence identified by ART drug levels showed periods for viral control off-ART from 3 to 10 months. One child never used ART and has remained undetectable for 19 months. Most of the others are now back on ART. [3]

The results included differences in viral sensitivity to type I interferon (IFN-I) by sex and viral replicative capacity, which was significantly lower in the five cases reported.

As with other studies in the report, further details will be reported during the actual conference presentation.

Targeting the viral reservoir with anticancer drug delays viral rebound in mice

Also cautiously, the press conference reported that the anticancer drug venetoclax has activity in human cells ex vivo and target the viral reservoir in a study in humanised mice.

The impact of daily dosing for six weeks was to significantly delay the time to viral rebound in the treated mice especially when used with a second protein inhibitor S63845. [4]

The investigators, including IAS president Professor Sharon Lewin who chaired the press conference, noted that extensive experience of venetoclax as an approved drug warrants further research in human studies.

Circumcising gay men as HIV prevention

Both observational and interventional studies have reported that circumcision approximately halves the chance that heterosexual men become HIV positive. [5]

The context is that men are having insertive sex with the likely mechanism being due to the inner foreskin being a mucous membrane with a high concentration of HIV target CD4 cells. [6]

As an HIV prevention strategy, the benefits have been seen in settings where HIV prevalence is high. It is also essential that the intervention is voluntary medical circumcision (VMMC) in adult men rather than just circumcision. Although VMMC is still used in some countries as an HIV prevention strategy it is notable that these studies pre-dated PrEP.

Up until now, circumcision has not been reported as effective for gay and bisexual men, largely because of the higher remaining risk from receptive sex and that few men are exclusively active. A positive benefit was reported in an Indian study of MSM at least ten years ago, which was also before PrEP.

Yanxiao Gao from Sun Vat-sen University, Shenzhen, presented results of a very small randomised study of immediate vs delayed circumcision in 247 gay men enrolled in eight Chinese cities who mainly had insertive sex. [7]

After approximately 116 person-years of follow-up in each arm, there were zero vs five HIV seroconversion in the immediate vs deferred groups respectively. This was reported as an HIV incidence rate (IR), per 100 person-years of 0.00 (95% CI: 0.00 to 3.18) vs 4.27 (95% CI: 1.38 to 9.97) arms.

Adverse events related to VMMC were mild and resolved quickly. The abstract notes that final results are expected by July 2023 and so are likely to be presented at the actual conference.

The short presentation of this study noted that the intervention was designed in China due to the very limited access to PrEP. Also, that although results would need to be confirmed in larger studies, these are unlikely to be run in countries where PrEP is available.

Choice of injectable vs oral PrEP in extension to HPTN-084 study

The HPTN 084 study showed that injectable cabotegravir (CAB) was superior to oral PrEP at preventing HIV infections on cisgender African women due to more difficult adherence associated with daily oral pills.

All participants then had the option to choose PrEP formulations in the open label extension (OLE) to this phase 3 study and results of this choice were presented in the press conference before IAS 2023. Results were presented by lead Delany-Moretlwe from the University of the Witwatersrand, South Africa. [8]

The abstract reports that 2472/3028 women from HPTN-084 enrolled in the OLE study. Of these, 1931/2472 (78%) chose injections and 536 (22%) chose oral PrEP.

Previous experience affected the choice to change formulations. Of those originally using oral PrEP, approximately 67% chose injections and 33% continued on oral treatment. Of those originally using injections, approximately 89% continued injections and 11% switched to oral treatment.

Reasons for choosing injections included preferred injections (77%), being more convenient (11%) and effectiveness (8%).

Choosing oral PrEP was linked to preferring pills (81%), fear of injections (5%), wanted to become pregnant (1%) or efficient benefit of clinic visits (1%).

Most participants (66%) reported their choice was their own, discussions with study staff (20%) or family and friends (11%) were also influential.

Although the majority of participants chose injectable PrEP, a significant majority continued or switched to oral PrEP, showing the importance of choice.

HIV and mpox: WHO review

Ana Hoxha from WHO presented a review of date on mpox collected from January to December 2022 as part of the WHO international case-based surveillance programme. This reported that immunosuppression rather than HIV increases the risk associated with mpox. [9]

In some countries up to 50% of cases were in men living with HIV and this study reported on whether HIV status was related to serious mpox outcomes including hospitalisation, admission to ICU or death.

Of the 80,843 cases reported, HIV status was available for 44%. Of these, approximately half (16,788) were living with HIV.

Although the data was limited, immunosuppression was reported in 5,023 of the cases in people living with HIV, 735 were hospitalised, 20 admitted to ICU, and 23 died. Immunosuppression increased the risk of hospitalisation in cases that were HIV positive (OR: 2.00 (95% CI: 1.64 to 2.43, $p \leq 0.001$) and HIV negative (OR: 3.56 (95%CI: 1.80 to 7.01, $p \leq 0.001$).

Due to the small sample size, no risk factors for ICU admission and death were found.

This study rightly emphasised the need for increased HIV testing in people at higher risk for mpox.

HIV and COVID-19

While the mpox epidemic dramatically declined in most countries by the end of 2022, COVID-19 is still ongoing, albeit with reduced numbers.

A second study from the WHO surveillance team reported on the impact of COVID-19 on the risk of mortality in people living with HIV during the pre-Delta, Delta and Omicron variant waves.

Silvia Bertagnoli from WHO summarised this study at the press conference referring to data from the abstract. [10]

Compared to people without HIV, people living with HIV had a 54% (aHR 1.54, 95%CI: 1.42 to 1.68), 56% (aHR 1.56, 95%CI: 1.4 to -1.74) and 142% (aHR 2.42, 95%CI: 2.11 to 2.78) increased risk of mortality in adjusted analyses, during the pre-Delta, Delta and Omicron variant waves, respectively.

Having a low CD4 count less than 200 cells/mm^3 was consistently linked to poorer outcomes and vaccination was consistently linked with lowering this risk.

References

Unless stated otherwise, all references are to the programme and abstracts of the 12th IAS conference 23 to 26 July 2023, Brisbane, Australia. Abstract URLs are initially restricted to delegates and might also change later.

1. Sáez-Cirión A et al. Absence of viral rebound for 20 months without antiretrovirals after allogeneic hematopoietic stem cell transplantation with wild-type CCR5 donor cells to treat a biphenotypic sarcoma. IAS 2023, Brisbane. Oral abstract OALBA0504.
   https://programme.ias2023.org/Abstract/Abstract/?abstractid=5819
2. International Collaboration to guide and investigate the potential for HIV cure by Stem Cell Transplantation (Icistem).
   https://www.icistem.org
3. Cromhout G et al. Sustained aviraemia in the absence of anti-retroviral therapy in male children following in utero vertical HIV transmission. IAS 2023, Brisbane. Oral abstract OALBX0104.
   https://programme.ias2023.org/Abstract/Abstract/?abstractid=5727
4. Arandjelovic P et al. Venetoclax, alone and in combination with the BH3-mimetic S63845, depletes HIV-1 latently infected cells and delays rebound in humanized mice. IAS 2023, Brisbane. Oral abstract OALBA0503.
   https://programme.ias2023.org/Abstract/Abstract/?abstractid=5735
5. Gray RH et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet 2007; 369:657-666.
   https://pubmed.ncbi.nlm.nih.gov/17321311/
6. Collins S. Male circumcision: new data supporting protective mechanism. HTB (February 2010).
   https://i-base.info/htb/7782
7. Gai Y et al. Voluntary medical male circumcision and incident HIV acquisition among men who have sex with men: a randomized controlled trial. IAS 2023, Brisbane. Oral abstract MOPEC16.
   https://programme.ias2023.org/Abstract/Abstract/?abstractid=1002
8. Delany-Moretlwe S et al. Initial PrEP product choice: results from the HPTN 084 open-label extension. IAS 2023, Brisbane. Oral abstract OALBX0203.
   https://programme.ias2023.org/Abstract/Abstract/?abstractid=5998

9. Hoxha A et al. HIV among mpox cases: clinical characteristics and outcomes in the WHO global surveillance 2022. IAS 2023, Brisbane. Oral abstract OAB0302.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=3953
10. Bertagnolio S et al. High in-hospital mortality in SARS-CoV-2 infected patients living with HIV during pre-Delta, Delta and Omicron variant waves: finding from the WHO Global Clinical Platform for COVID-19. IAS 2023, Brisbane. Oral abstract OALBC0604.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=5988

Rapporteur summaries: track B clinical science

Simon Collins, HIV i-Base

The webcast of the rapporteur summaries at the end of the conference is a good way to appreciate the breadth of research presented.

These talks are thanks to small groups of people who spend their conference chasing and reporting in real time on presentations and compressing the most important studies into a short 10-minute summary.

The work involved is often under-appreciated and the conference hall is under-attended as delegates often need to leave early. These summaries deserve a higher profile and should be included in the material made available to non-delegates immediately when the conference ends.

The following report is based on the Track B talk and credit should go to the rapporteurs. Other tracks will be posted shortly online for the next issue of HTB.

https://conference.ias2023.org/media-1123-rapporteur-report-back-session

Rapporteur summary: Track B clinical science

The track B summary was given by Vidya Mave, co-director of the Johns Hopkins Centre for Infectious Diseases in India, who included 20 oral presentations in seven key themes. [1]

Long-acting formulations

Long-acting drugs were noted as a game-changing development. Although the current focus is on injectables (cabotegravir-LA, rilpivirine-LA and lenacapavir), other technologies include implants, rings and other formulations.

One study using long-acting cabotegravir/rilpivirine (CAB-LA/RPV-LA) reported high efficacy in adolescents. [2]

Another included off-label use in San Francisco in people with detectable viral load who didn't want to use oral meds or when daily adherence was complicated by living on the street or injecting drug use. Currently, CAB-LA/RPV-LA is only indicated as a switch option for people who have had a sustained undetectable viral load for six months on oral ART. [3]

Although lenacapavir is being developed as a six-monthly injection, the potential for oral weekly dosing was shown after study participants needed to switch to oral meds for six months due to supply difficulties. All participants maintained undetectable viral load using the weekly oral version. [4]

ADVANCE study and DTG rebound

An oral presentation from the ADVANCE study reported that providing additional adherence support was able to bring viral load to undetectable in 95% of participants who remained detectable on first-line dolutegravir-based ART. Drug resistance did not develop during this period. [5]

Delayed switching was less successful with efavirenz-based ART with only 66% of participants becoming undetectable after adherence support. Drug resistance was also likely to be higher.

REPRIEVE study and statin use

This large international RCT in people at low-moderate risk of major adverse cardiovascular events (MACE) showed significant benefits from using a daily statin. The study was important enough for the conference to devote a symposium to cover the findings. The discussion noted that the results could chance management guidelines but that there might be regional differences in the results. [6, 7, 8, 9]

ART and hypertension, diabetes and weight changes

Several studies, including NAMSAL and ADVANCE provided data on risks of hypertension and diabetes with ART. [10]

Weight gain on INSTI-containing ART was not reversed after switching to doravirine/islatravir. [11]

Although not highlighted by the rapporteurs, a similar study switching to boosted darunavir was also unsuccessful, but the design of these studies was also not ideal. [12]

Coinfections

High completion rates (>90%) of short-course rifapentine-based TB preventative treatment were reported in a retrospective analysis from Taiwan. This study reported on one-monthly use of daily rifapentine/isoniazid or three-monthly use of weekly rifapentine/isoniazid in people on dolutegravir or bictegravir-based ART. The daily regimen had slightly higher rates of skin and liver side effects. [13]

Although high rates of HCV reinfection were reported in HIV positive gay men in Thailand, sustained virological response rates (SVR) to subsequent retreatment with DAAs was also high (>95%). [14]

Women and children

Two studies reported the benefits of integrase-based ART, including as second-line therapy and another study reported lower drug levels of bictegravir during the third trimester of pregnancy, but that viral suppression was still maintained. [15, 16, 17]

COVID-19 and mpox

Finally, the review recommended two studies in the importance of COVID-19, including research into Long COVID, which more frequently occurs in people living with HIV. [18, 19]

Also, the higher risk of severe mpox in people living with HIV who have severe immunosuppression and that although now greatly reduced, mpox infections are still being reported in some countries. [20, 21]

C O M M E N T

Some of the studies highlighted in the excellent rapporteur summary, including REPRIEVE, are already reported by i-Base in detail and others will be reported shortly. [22]

It is also important to hear the results from CAB-LA/RPV-LA being used as first-line ART - and that it is also being used off-label with lenacapavir. [23]

References

1. Mave V. Track B Rapporteur summary. IAS 2023, plenary session PL08.
https://programme.ias2023.org/Programme/Session/4398
2. Moore C et al Implementation of LA-ART in low-middle-income countries in adults and adolescents: Possibilities and expectations of populations. IAS 2023 Symposium SY19.
https://programme.ias2023.org/Programme/Session/4363
3. Ghandi M et al. Injectable therapies for treatment and prevention. IAS 2023, symposium SY08.
https://programme.ias2023.org/Programme/Session/4424
4. Ogbugo O et al. Lenacapavir oral bridging maintains efficacy with a similar safety profile when SC LEN cannot be administered. IAS 2023, oral abstract OAB0205.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=5297
5. Hill A et al. High rates of long-term HIV RNA re-suppression after virological failure on dolutegravir in the ADVANCE trial. IAS 2023, oral abstract OAB0204.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=3810

6. The REPRIEVE trial: Developing a cardiovascular disease prevention strategy for people living with HIV. IAS 2023, symposium SY06.
https://programme.ias2023.org/Programme/Session/4435 (symposium)
https://conference.ias2023.org/media-1185-the-reprieve-trial-developing-a-cardiovascular-disease-prevention-strategy-for-people-livi (webcast)
7. Grinspoon SK et al. Key REPRIEVE results and the utility of statins among people living with HIV: What have we learned? IAS 2023, symposium SY06, see reference 6.
8. Bloomfield G et al. Cardiovascular disease among people living with HIV in high- and low-income countries: Can one strategy fit all? IAS 2023, symposium SY06, see reference 6.
9. Zanni M et al. Unique aspects of cardiovascular disease among women with HIV: Lessons from REPRIEVE. IAS 2023, symposium SY06, see reference 6.
10. Venter F et al. Risks of hypertension with first-line dolutegravir (DTG) and tenofovir alafenamide (TAF) in the NAMSAL and ADVANCE trials. IAS 2023, oral abstract OALBB0504.
https://programme.ias2023.org/Programme/Session/4569
11. McComsey G et al. Weight and body composition after switch to doravirine/islatravir (DOR/ISL) 100/0.75mg once daily: week 48 results from 2 randomized active-controlled phase 3 trials, MK8591A-017 (P017) and MK8591A-018 (P018). IAS 2023, oral abstract OAB0203.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=883
12. Blick G et al. Prior M184V/I and multiple prior virological failures have no impact on the efficacy of switching HIV+ adults to DTG/3TC through 96Wks in SOLAR-3D. IAS 2023, oral abstract OAB0202.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=496
13. Lin K.-Y. et al. Short-course rifapentine-based regimens for latent tuberculosis infection among people living with HIV who received integrase inhibitor-based antiretroviral therapy. IAS 2023, oral abstract OAB0304.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=3454
14. Promsena P et al. High rate of hepatitis C and reinfection after direct-acting antiviral treatment among men-who-have-sex-with-men living with HIV in Bangkok, Thailand. IAS 2023, oral abstract OAB0303.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=2072
15. Musiime V et al. Increasing second-line antiretroviral therapy options for children with HIV in Africa: week-96 efficacy and safety results of the CHAPAS-4 randomised trial. IAS 2023, oral abstract OALBB0503.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=5764
16. Ani I et al. Virological dynamics among children living with HIV transitioned to a dolutegravir-based regimen in Nigeria. IAS 2023, oral abstract OAB0105.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=5091
17. Zhang H et al. Pharmacokinetics, safety, and efficacy of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in virologically suppressed pregnant women with HIV. IAS 2023, oral abstract OAB0104.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=681
18. Matthews G. Lessons from COVID and mpox: Preparing for future pandemics and improving outcomes for people living with and affected by HIV. IAS 2023, symposium SY10.
https://programme.ias2023.org/Programme/Session/4432
19. Corral Herrera E.A. et al. Post-acute sequelae of COVID-19 (PASC) and Quality of Life in people with HIV. IAS 2023, E-poster EPB0282.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=3138
20. Orkin C et al. Lessons from COVID and mpox: Preparing for future pandemics and improving outcomes for people living with and affected by HIV. IAS 2023, symposium SY10.
https://programme.ias2023.org/Programme/Session/4432
21. Hoxha A et al. HIV among mpox cases: clinical characteristics and outcomes in the WHO global surveillance 2022. IAS 2023, oral abstract OAB0302.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=3953
22. Collins S. REPRIEVE study: statin benefits people living with HIV at low CVD risk. HTB 26 July 2023.
https://i-base.info/htb/45808
23. HIV, New Drugs & Restoring Trust. Interview with Monica Gandhi.
https://www.youtube.com/watch?v=Q60x76-3GQE

IAS 2023: CURE-RELATED RESEARCH

Geneva patient and HIV cure research at IAS 2023

Richard Jefferys, TAG

The first press conference of IAS 2023 meeting was held three days beforehand and featured several cure-related presentations. [1]

Most notably, Asier Sáez-Cirión and Alexandra Calmy described a possible case of an HIV cure (or at least extended remission) in an individual in Geneva who received a stem cell transplant to treat cancer. There are previously reported cases of HIV cures (or likely cures) in people who received stem cell transplants for cancer diagnoses, but all have involved stem cell donors homozygous for the CCR5Δ32 mutation, which makes immune cells resistant to infection by most HIV strains. [2]

In this new case report, the donated stem cells were "wild type," meaning they lacked this mutation.

A full description of the case won't occur until the conference track A late breaker session on Monday 24 July. [3]

The study abstract has been shared with journalists and is no longer under embargo, but it's still unavailable and listed as embargoed for the public on the IAS 2023 website. [4]

The individual is in his early 50s and received the stem cell transplant to treat a biphenotypic sarcoma. Afterward, HIV became undetectable by multiple tests and antiretroviral therapy (ART) was stopped in 2021. After 20 months of subsequent follow up, no viral load rebound has occurred, no HIV-specific T cell responses can be detected, and antibodies against HIV are waning. Sáez-Cirión noted that traces of HIV DNA have been detected at some timepoints, but it didn't appear to comprise intact, replication-competent virus.

There are similarities to two people with HIV known as the Boston patients who also received wild type stem cell transplants to treat cancers and subsequently stopped ART without a viral load rebound. But in those prior cases, HIV viral load did return after three months and eight months, respectively. [5]

The reasons for the far more extended absence of HIV viral load rebound in the Geneva case are uncertain at this juncture. Speculative possibilities include:

- The effects of graft-versus-host disease (GVHD), which involves the newly transplanted immune cells attacking and clearing the original host immune cells (potentially including CD4 T cells harbouring HIV). GVHD was also reported in the Boston patients.
- The use of the drug ruxolitinib to facilitate the transplant, which wasn't reported in the Boston patients. Ruxolitinib belongs to a class of compounds called Janus kinase (JAK) inhibitors that have been shown to inhibit HIV infection and the seeding of the reservoir in laboratory studies. [6, 7, 8]
- Ruxolitinib and other JAK inhibitors are being investigated in people with HIV on ART, and on Saturday in Brisbane at the HIV Cure and Immunotherapy pre-meeting Monica Reece is giving a presentation on the effects of ruxolitinib on the HIV reservoir in an AIDS Clinical Trials Group (ACTG) study. [9, 10, 11]
- The occasional use of pre-exposure prophylaxis (PrEP) after stopping his therapeutic ART regimen. This wasn't discussed during the press conference but is mentioned by Tim Henrich in an excellent, detailed article for POZ Magazine by Liz Highleyman. Henrich suggests that PrEP use might have suppressed any lingering embers of HIV infection and prevented transfer of the virus to the transplanted immune cells. [12]

The hope is that the individual may be cured of HIV infection, but — as has been emphasised in some of the media coverage of the case — this cannot be considered proven. Mathematical modeling work by Alison Hill and colleagues indicates that if HIV has infected a tiny number of the new immune system cells generated by the transplant, viral load rebound could potentially occur after a delay of several years. [13]

The risk is considered higher in this case because the stem cell donor lacked the CCR5Δ32 mutation and hence the newly generated immune system remains vulnerable to HIV infection. Ongoing monitoring will be important and the potential for rebound needs to be borne in mind because, as Gary Steinkohl explained after disclosing his identity as one of the Boston patients, the re-emergence of virus after a long delay can be very traumatic (in his words: "emotionally devastating"). [14]

Another cure-related presentation at the press conference was given by Gabriela Cromhout from the University of KwaZulu-Natal. Cromhout reported the identification five male infants with HIV who experienced apparent control of viral load in the absence of ongoing ART. The cases were identified during a project assessing ART blood levels among infants who acquired HIV via vertical transmission. The testing revealed an absence of sustained ART levels suggestive of non-adherence, but without HIV viral load rebound. Time off-ART was estimated to range from 3-10 months.

One of the infants has never been restarted on ART and has maintained an undetectable viral load after around 19 months of ongoing follow up. The four others have had ART restarted, with three enrolled in a study that plans to eventually undertake an analytical treatment interruption (ATI) to assess if control of viral load will recur.

Cromhout explained that the results may provide evidence of a sex difference in the capacity to control HIV replication among infants, because the cohort comprises 60% females but all the cases were males. In beginning to look for contributing factors, the researchers have noted that when male infants acquire HIV, the virus typically displays sensitivity to the inhibitory effects of the cytokine alpha interferon but a high replication capacity. In females, this is reversed with viruses showing reduced sensitivity to alpha interferon and lower replication capacity.

In the five cases reported by Cromhout, this pattern wasn't observed – the viruses detectable in the male infants at acquisition were sensitive to alpha interferon and hada low replication capacity.

The detailed presentation of the study will occur on Monday July 24 during a session that starts at 10:30am local time. [15]

As is the case with Sáez-Cirión's report, the abstract remains embargoed to the public on the IAS Programme website even though the media embargo has been lifted and the abstract shared with journalists. [16, 17]

TAG and many other advocates are calling for a revision of this policy of publicising results ahead of their actual presentation at the conference.

Source:

Richard Jefferys, TAG Basic Science Blog (20 July 2023).
https://tagbasicscienceproject.typepad.com/tags_basic_science_vaccin/2023/07/hiv-cure-research-news-from-the-opening-ias-2023-press-conference.html

References

1. IAS 2023. Official Press Conference. Scientific Highlights. (20 July 2023).
https://www.iasociety.org/conferences/ias2023/media/press-conference-programme
2. Jefferys R. HIV Cure Research Information Sheet. Treatment Action Group. (March 2023).
https://www.treatmentactiongroup.org/publication/hiv-cure-research-information-sheet/
3. Caskey, M et al. Track A Rapporteur Summary, IAS 2023. (24 July 2023).
https://programme.ias2023.org/Programme/Session/4568
4. Sáez-Cirión A et al. Absence of viral rebound for 18 months without antiretrovirals after allogeneic hematopoietic stem cell transplantation with wild-type CCR5 donor cells to treat a biphenotypic sarcoma. IAS 2023, oral abstract OALBA0504.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=5819
5. Henrich T. J. et al. Antiretroviral-Free HIV-1 Remission and Viral Rebound Following Allogeneic Stem Cell Transplantation: A Report of Two Cases. Ann Intern Med; 161(5): 319–327, DOI: 10.7326/M14-1027 (2 September 2014).
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4236912/
6. Reece M. D. et al. Repurposing BCL-2 and Jak 1/2 inhibitors: Cure and treatment of HIV-1 and other viral infections. Frontiers in Immunology, Viral Immunology, volume 13, DOI: 10.3389/fimmu.2022.1033672 (9 December 2022).
https://www.frontiersin.org/articles/10.3389/fimmu.2022.1033672/full
7. Gavegnano C et al. Ruxolitinib and Tofacitinib Are Potent and Selective Inhibitors of HIV-1 Replication and Virus Reactivation In Vitro. Antimicrobial Agents and Chemotherapy, volume 58, number 4, DOI: 10.1128/aac.02496-13 (18 March 2014).
https://journals.asm.org/doi/10.1128/AAC.02496-13#
8. Gavegnano C et al. Novel mechanisms to inhibit HIV reservoir seeding using Jak inhibitors. PLOS Pathogens, 13(12): e1006740, DOI: 10.1371/journal.ppat.1006740 (21 December 2017).
https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1006740
9. ClinicalTrial.gov. STUDY00004498 (U.S. NIH Grant/Contract 1R01MH128158-01A1). Phase II Study to Evaluate the Efficacy and Safety of Baricitinib for Reduction of HIV in the Central Nervous System.
https://clinicaltrials.gov/study/NCT05452564
10. IAS 2023. HIV Cure & Immunotherapy Forum (22 July 2023).
ttps://www.iasociety.org/conferences/ias2023/programme/pre-meetings/hiv-cure-immunotherapy-forum
11. Marconi V. C. et al. Randomized Trial of Ruxolitinib in Antiretroviral-Treated Adults With Human Immunodeficiency Virus. Clinical Infectious Diseases, volume 74, issue 1, DOI: 10.1093/cid/ciab212 (6 March 2021).
https://academic.oup.com/cid/article/74/1/95/6159796

12. Highleyman L. Geneva Man May Be Cured of HIV After Wild-Type Stem Cell Transplant. Poz Magazine (19 July 2023). https://www.poz.com/article/geneva-man-may-cured-hiv-wildtype-stem-cell-transplant
13. Hill A. L. et al. Predicting the outcomes of treatment to eradicate the latent reservoir for HIV-1. PNAS, volume 111, number 37, DOI: 10.1073/pnas.140666311 (5 August 2014). https://www.pnas.org/doi/10.1073/pnas.1406663111
14. Halter C. A Tale of Two Diagnoses. Poz Magazine (3 November 2015). https://www.poz.com/article/boston-patient-q-a-27970-4298
15. Gilks C et al. Co-Chairs' Choice. IAS 2023, oral abstract session OALBX01 (24 July 2023). https://programme.ias2023.org/Programme/Session/4566
16. Cromhout G et al. Sustained aviraemia in the absence of anti-retroviral therapy in male children following in utero vertical HIV transmission. IAS 2023, oral abstract OALBX0104. https://programme.ias2023.org/Abstract/Abstract/?abstractid=5727
17. IAS 2023. Conference Programme (23–26 July 2023). https://programme.ias2023.org/

Other HIV cure-research in the IAS 2023 programme

Richard Jefferys, TAG

The links below are to events and sessions related to HIV cure research at the IAS 2023 conference.

Abstracts should become publicly available starting on Monday July 24, but access to session recordings will be delayed until sometime after the conference has ended.

Saturday July 22

HIV Cure & Immunotherapy Forum

Not broadcast live, but according to IAS a recording will be made available afterwards.

Sunday July 23

Target setting and leadership for Cure - Insights that show the way to HIV and Sick Cell Disease Cures for Africa

SAT003 - Satellite. Plaza Auditorium/Channel 4. 7:30-9am local time

Monday July 24

Vaccines and cure: Spotlight on antibodies

PL01 - Plenary session, Great Hall/Channel 1. 9-10am local time..

HIV cure research: Why are single cells harbouring HIV latent?

SY07 - Symposium. Track A: Basic science
M4/Channel 6, 2:45-3:45pm local time.

Track A late-breaker OALBA05 - Oral abstract session
Plaza Terrace Room/Channel 2. 4-5pm local time.

Viral replication and reservoirs beyond the periphery: A deeper look at tissues
OAA01 - Oral abstract session. Track A: Basic science. Boulevard Auditorium/Channel 7. 4-5pm local time.

Tuesday July 25

Advances in gene delivery and engineering of T and B cells: Implications for prevention, therapy and cure
SY12 - Symposium. Track A: Basic science. Boulevard Auditorium/Channel 7. 10:30-11:30am local time (US Eastern time: July 24, 8:30-9:30pm)

Immune-based interventions towards an HIV cure
OAA02 - Oral abstract session. Track A: Basic science. Boulevard Auditorium/Channel 7. 2:45 - 3:45pm local.

Novel insights into viral persistence
OAA03 - Oral abstract session. Track A: Basic science. M3/Channel 5. 4-5pm local time.

bnAbs: From prevention to cure
SAT054 - Satellite. Boulevard Auditorium/Channel 7. 6:30-8pm local time.

Wednesday July 26

Understanding the HIV reservoir: New technologies and specific populations
PL07 - Plenary session
Great Hall/Channel 1
July 26, 9-10am local time (US Eastern time: July 25, 7-8pm)

Immune responses critical for viral control and approaches to harness them in vivo
SY20 - Symposium. Track A: Basic science. Boulevard Auditorium/Channel 7. 10:30-11:30am local time.

IAS 2023: HIV AND CANCER

Anal cancer: 1 in 5 risk of missing precancerous lesions if only HSIL are biopsied

Simon Collins, HIV i-Base

A poster from researchers at the AIDS Clinical Center in Shinjuku-ku, Japan identifies a high risk of missing precancerous lesions due to the current approach to only biopsy lesions that are judged as HSIL after high-resolution anoscopy (HRA). [1]

From June 2021 to September 2022, the group reanalysed samples from 673 lesions from 122 individuals using sextant biopsies.

This collected at least six lesion samples in all directions regardless of abnormal findings from HRA.

The prevalence of HSIL was 81.3% (91/112) for individuals and 43.5% (293/673) for lesions.

The rate of the biopsy-proven HSIL that was predicted as LSIL was 36.5%(107/293) for each lesion and 19.8% (18/73) for each individual.

The authors concluded that approximately 1 in 5 HSIL cases were considered low-risk lesions based on their appearance and that these results might explain cases of recurrence after treatment.

A prospective, longitudinal Spanish study in 493 gay men living with HIV reported an approximate 5% annual risk of progression from low- to high-grade lesions over a median of 43 months (IQR: 12 to 76) follow-up between May 2010 and December 2021. [2]

Risk factors for progression included acquiring high-risk HPV genotypes (HR: 4.15; IC 95%: 1.14 to 15.03), low-risk HPV genotypes (HR: 3.68 IC95%: 1.04 to 12.94), in particular genotype 6 (HR:4.47, IC95%: 1.34 to 14.91)] and history of AIDS (HR: 5.81, 95%CI: 1.78 to 18.92).

C O M M E N T

This study shows the importance of biopsy for any suspected lesion – and that it is essential even when a lesion might look harmless.

Some services might have even higher rates of false negative results depending on the experience of the anoscopist.

One of the official pre-meetings before IAS 2023, was the first international workshop on HIV and HPV infection. One of the outcomes was a call for global targets for the elimination of HPV-related cancers, not just cervical cancer. [3]

Reference

1. Ando N et al. Standard biopsy with high-resolution anoscopy could miss potentially precancerous lesions. IAS 2023, poster abstract EPB0135.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=1427
2. Tenorio CH et al. Role of low-risk HPV PCR in screening for HSIL lesions and anal cancer in men who have sex with men (MSM) living with HIV (MSM-LWHIV). IAS 2023, poster abstract EPB0129.
https://programme.ias2023.org/Abstract/Abstract/?abstractid=276

3. IAS 2023 premeeting. Putting people first in the prevention, treatment and care of HPV-related cancers among people living with HIV. (22 July 2023).
https://www.iasociety.org/conferences/ias2023/programme/pre-meetings/putting-people-first-prevention-treatment-and-care-hpv-related-cancers-people

IAS 2023: VIRAL HEPATITIS

High rates of occult HBV in Botswana: risks from relying on HBsAg screening

Simon Collins, HIV i-Base

Although screening for hepatitis B often relies on testing for HBsAg, a poster at IAS 2023 with data from two longitudinal HIV studies in Botswana reported high rates of occult HBV infection (OBI) that can still cause liver disease and be transmissible.

This highlights an advantage from using triple therapy ART that is active against both HIV and HBV.

The study tested for HBsAg using ELISA and negative samples were screened for OBI using an in-house real-time PCR.

Baseline prevalence of HBsAg and OBI was 2.1% (8/382) and 14.7% (11/75), respectively.

During a median of 1.02 years follow-up (IQR: 1.00 to 2.00) in 90 participants, there were 34 incident OBI cases, with an IR of 26.4/100 person-years (95% CI: 18.9 to 36.9). The median time to incident OBI was 372 days (IQR: 365 to 730).

Reference

Anderson M et al. Incidence of occult hepatitis B virus among people living with HIV in Botswana, IAS 2023. poster abstract EPB0158.

https://programme.ias2023.org/Abstract/Abstract/?abstractid=4926 (abstract)

https://conference.ias2023.org/media-1007-incidence-of-occult-hepatitis-b-virus-among-people-living-with-hiv-in-botswana (poster)

CONFERENCE REPORTS

BHIVA Annual Conference 2023

24 – 26 April 2023, Gateshead, UK

Introduction

Simon Collins, HIV i-Base

This year the BHIVA conference was held in Newcastle at the Gateshead conference centre over three sunny spring days.

The conference included a strong programme of presentations about HIV care in the UK and included more that 150 posters.

BHIVA should be recognised (and thanked) for making webcasts online so promptly. This is a really important responsibility that comes with running and arranging medical conferences, especially given the financial challenges of organising face-to-face meetings.

Wider access to the data presented, should also be appreciated by sponsors who support these meetings. Community reports, including from i-Base, can only cover a fraction of the information that is presented, even from a single study. Our reports are primarily to flag research and to signpost to the presentations that include the full data.

Please use the links in our reports to see the webcasts and see the full posters. There is no substitute for going to the original presentations.

Conference programme and abstract book

https://www.bhiva.org/SpringConference2023

Conference presentations

https://www.bhiva.org/SpringConference2023Presentations

https://vimeo.com/britishhivassoc/videos

The following reports from BHIVA 2023 are included in this issue of HTB.

- No vertical HIV transmissions from women eligible for supported breastfeeding in the UK
- Adverse birth outcomes with diabetes and hypertensive disorders in pregnancy

No vertical HIV transmissions from women eligible for supported breastfeeding in the UK

Polly Clayden, HIV i-Base

There were no vertical transmissions in the UK among women living with HIV supported to breastfeed from 2012 to 2021 – according to data presented at the BHIVA spring conference 2023. [1]

These cases are small but increasing. Although the results to date are very reassuring, some infants were lost to follow up or still in follow-up during the monitoring period.

The current rate of vertical transmission from women in the UK diagnosed with HIV is less than 0.3%. BHIVA recommends formula-feeding to eliminate the risk of post-natal transmission.

But the guidelines also say that women who are virologically suppressed on ART with good adherence may be supported to breastfeed (supported breastfeeding).

Since 2018, BHIVA guidelines for supported breastfeeding have included:

- Monthly review in clinic and viral load testing for mother and baby during the breastfeeding period and for two months after cessation
- Maternal ART rather than infant pre-exposure prophylaxis.
- Breastfeeding for as short a time as possible, exclusively for the first six months, and recommendation to stop if: signs of breast infection/mastitis, gastrointestinal symptoms in mother or infant, or blip in maternal viral load.
- Infant HIV antibody testing for seroconversion at 22 to 24 months of age, or at a minimum of eight weeks after cessation of breastfeeding if this is later.

The study objective was to describe the characteristics and clinical monitoring of BHIVA supported breastfeeding among women living with HIV in the UK in the period 2012 to 2021.

The Integrated Screening Outcomes Surveillance Service (ISOSS) conducts surveillance of all pregnancies to diagnosed women living with HIV in the UK.

There were 267 reports of intention to breastfeed and/or supported breastfeeding. Commonly reported reasons were: bonding (69%), health benefits (60%), disclosure concerns (26%), previous breastfeeding since diagnosis (26%) and family or friends' expectations or pressure (22%).

Among 8,513 live birth deliveries, 203 (2.4%) women were confirmed supported to breastfeed, with some breastfeeding more than one infant.

There was a four-fold increase in cases from less than 10 per year from 2012 to 2014 to 40–50 during 2019 to 2021. The majority (95%, 190/201) were in women diagnosed before pregnancy and 84.0% (170/201) were in women born abroad, with 79% (154/197) from sub-Saharan Africa.

Median maternal age was 35 years (IQR: 31 to 40). Breastfeeding duration ranged from one day to two years: median 56 days (IQR: 23 to 140).

In 46 cases, monthly testing was known not to be applicable due to breastfeeding duration. Where applicable, 80.2% (77/96) of mother-infant pairs had monthly testing according to BHIVA guidelines. In 11 cases, reasons for not having monthly testing included: scheduling miscommunications, parental requests, and long-term maternal virological suppression. Attendance issues were reported in 32.5% (25/77) of cases with monthly testing.

For most women, cessation of breastfeeding was part of a plan to stop. But in 10 cases, breastfeeding was stopped due to maternal viral load rebound.

Of 150 infants, 106 had a negative antibody result at 18 months of age or older, five were discharged based on negative antibody result dated less than 18 months, 34 were awaiting confirmatory testing and five were lost to follow-up.

Presenting author Rebecca Sconza noted that supported breastfeeding is varied in both duration of breastfeeding and attendance for monthly testing.

COMMENT

There is a lack of evidence to recommend breastfeeding among women with HIV in high-income countries, so these data are welcome. Although BHIVA primarily recommends formula feeding, there has been guidance for supported breastfeeding since 2018 in the UK.

In January 2023, US guidance was updated to include breastfeeding for the first time. [2]

Similar to BHIVA, the panel recommends: "Individuals with HIV who are on ART with a sustained undetectable viral load and who choose to breastfeed should be supported in this decision".

The extremely small numbers of documented cases from high-income countries is notable in the panel's data summary. Case series cited from Germany, Italy, US and Canada include as few as three breastfed, HIV-free infants and only as many as 30.

Continual monitoring and documentation of supported breastfeeding management and vertical transmission outcomes is essential – both in this country and other high-income settings – to support future guidelines and safe infant feeding for women living with HIV who choose to do so.

References

1. Francis K et al. Monitoring clinical practice of BHIVA-supported breastfeeding guidelines for women living with HIV in the UK. BHIVA 2023 spring conference. Gateshead, UK. 24–26 April 2023. Oral abstract O12. https://www.bhiva.org/file/645ba42b0e61f/O12.pdf (pdf)
2. US National Institutes of Health. Infant feeding for individuals with HIV in the United States. 31 January 2023. https://clinicalinfo.hiv.gov/en/guidelines/perinatal/infant-feeding-individuals-hiv-united-states

Adverse birth outcomes with diabetes and hypertensive disorders in pregnancy

Polly Clayden, HIV i-Base

Women living with HIV with diabetes or hypertensive disorders in pregnancy are more likely to have adverse birth outcomes than women without these complications.

These data from the Integrated Screening Outcomes Surveillance Service (ISOSS) were presented at the BHIVA spring conference 2023. [1, 2]

Diabetes and hypertensive disorders in pregnancy are associated with adverse birth outcomes. Adults with HIV are more likely to have diabetes then those without (there is conflicting evidence with hypertension).

The study aim was to estimate the prevalence and to compare maternal characteristics and birth outcomes in pregnant women living with HIV with and without these comorbidities.

ISOSS collects population level data on all pregnant women living with HIV in the UK (England only from 2020).

The evaluation included pregnancies with deliveries between 2010 to 2020 at 24 gestational weeks or more. Diabetes was defined as pre-existing or gestational diabetes and hypertensive disorders were: pre-eclampsia, hypertension, or pregnancy-induced hypertension. The comparator group were pregnancies in women living with HIV without these complications.

The study compared the following outcomes: preterm birth (<37 weeks), low birthweight (<2.5 kg), small for gestational age (<10th percentile, INTERGROWTH-21) and birthweight z-scores (INTERGROWTH-21).

During the study period, there were 10401 pregnancies reported in 9016 women. Diabetes was reported in 554 pregnancies to 503 women and 92% of these cases were gestational diabetes. Hypertensive disorders were reported in 511 pregnancies to 458 women and 75% of these were pre-eclampsia. A small proportion had both complications: 46 pregnancies to 43 women. There were 8232 pregnancies among 5937 women in the comparator group.

Prevalence of diabetes increased over time. Between 2010 and 2020 this changed from 2.7% to 10.3% ($p<0.001$). There was a notably steeper incline from 2015 onward. Hypertensive disorder prevalence remained similar over the 10 year period: 3.9% to 5.8% ($p=0.07$).

Risk factors for diabetes, hypertensive disorders or both were: aged 35 years and above, black African or Caribbean, first pregnancy and ART at conception.

Women aged 35 and above were 32.4% of the pregnant population in 2010 vs 52.8% in 2020 ($p<0.0001$).

Emergency Caesarean section occurred in 1 in 3 pregnancies among women with diabetes, 1 in 2 in those with hypertensive disorders compared to 1 in 5 in the comparator group.

Stillbirth was 4.8 and 12 times more prevalent than the comparator in the diabetes and hypertensive disorders groups respectively: 1.3% and 3.1% vs 0.26% (comparator).

Preterm birth occurred in 1 in 5 pregnancies among women with diabetes and 2 in 5 in those with hypertensive disorders compared to less than 1 in 10 (7.7%) in the comparator group.

Almost half (46%) of infants born to women with hypertensive disorders were low birth weight. This proportion was 13.4% among the infants born to women with diabetes and 8.8% in the comparator group.

One in 5 (21.1%) of infants born to women with hypertensive disorders were small for gestational age. This compares with 6% in the diabetes and 8.2% in the comparator groups.

The prevalence of comorbidities has changed significantly over time with implications for birth outcomes. Further research is required to understand possible mechanisms and optimise pregnancy outcomes for women.

COMMENT

Maternal age may account for the increase in diabetes in this cohort, although weight might also be a driver and these data were not previously routinely collected. ISOSS are now collecting BMI and other weight indices.

The study was not able to assess the contribution of ART to the prevalence of these comorbidities. A number of evaluations are currently looking at hypertensive disorders in adults on ART in large studies, including comparisons of different antiretrovirals – notably in African populations and in pregnancy. Some of these data will be presented at the upcoming IAS conference.

Apart from ART at conception the risk factors are similar to those in the general population.

References
1. Bukasa L et al. Diabetes and hypertensive disorders in pregnant women living with HIV in the UK and Ireland. BHIVA 2023 spring conference. Gateshead, UK. 24–26 April 2023. Oral abstract O11. https://www.bhiva.org/file/645ba42b19006/O11.pdf
2. Integrated Screening Outcomes Surveillance Service (ISOSS) https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/integrated-screening-outcomes-surveillance-service-isoss

ANTIRETROVIRALS

CAB-LA receives positive opinion for EU approval as PrEP

Simon Collins, HIV i-Base

On 24 July 2023, the European Medicine Agency (EMA) issued a positive opinion on approving long-acting cabotegravir injections (CAB-LA) and related oral tablets for HIV PreExposure Prophylaxis (PrEP). [1]

This is based on results from two large phase 3 international studies: HPTN 083 and 084 studies.

The indication will be to reduce the risk of sexually acquired HIV in adults and adolescents at high risk of infection, weighing at least 35 kg.

The US FDA approved CAB-LA PrEP in December 2021. As we noted then, price will determine the degree to which injectable PrEP will be accessed in Europe. [2]

In the UK, NICE are currently leading a scoping consultation for CAB-LA for PrEP, although it has not yet been approved by the MHRA. [3]

Source
1. ViiV press statement. ViiV Healthcare's cabotegravir for HIV prevention receives positive CHMP opinion from European Medicines Agency. (24 July 2023). https://www.gsk.com/en-gb/media/press-releases/viiv-healthcare-s-cabotegravir-for-hiv-prevention-receives-positive-chmp-opinion-from-european-medicines-agency/
2. US FDA approves long-acting cabotegravir injections for PrEP: price set at $22,000 a year. HTB December 2021. https://i-base.info/htb/41890
3. Cabotegravir injections for preventing HIV-1 in adults and young people ID6255. https://www.nice.org.uk/guidance/indevelopment/gid-ta11304

SIDE EFFECTS

Help needed: UK surveys on access to New-Fill for facial lipoatrophy

Simon Collins, HIV i-Base

New-Fill has been available and commissioned from the NHS for over 15 years as a way to correct for facial fat loss caused by early HIV drugs, principally stavudine (d4T) and zidovudine (AZT).

It is an injectable non-permanent filler that works by generating new collagen growth rather than being used as a traditional filler. The higher volumes used to correct HIV-related lipoatrophy require specialist services.

Some clinics already have either have an in-house service or a commissioned referral route to a local clinic. However, access to New-Fill still seems to vary by hospital and region. These services were put on-hold during COVID-19 which also reduced the number of people who can be treated.

A pilot project is looking to map current access to services to help understand the demand for New-Fill in order to support more stable and equitable access.

Hopefully showing a continued unmet need, we can keep proper funding and commissioning support to make sure services are stable for the future.

There are two short surveys - one for community and one for health professionals.

Community survey via the UK-CAB:

https://www.surveymonkey.co.uk/r/LWVRK35

BHIVA use a similar short survey for doctors and HIV clinics.

https://www.surveymonkey.co.uk/r/YXBF9YD

Thank you for your help.

TREATMENT & VACCINE GUIDELINES

New UK vaccine schedule for HPV depends on HIV status

Simon Collins, HIV i-Base

On 29 June 2023, UKHSA announced new guidelines on the HPV vaccine schedule.

From 1 September 2023, the HPV vaccine programme will change from a two dose to a one dose HPV vaccine schedule for adolescents and men who have sex with men (MSM) aged less than 25 years.

However, the schedule will continue to use three doses for people living with HIV.

The vaccine is also available for all gay and bisexual men up to the age of 45, 'regardless of risk, behaviour or [HIV] status'.

This raises the important practical issue of routinely including HIV testing before giving the HPV vaccine., though this is not included in the related papers or recommendations.

The change in policy is based on a recommendation from the Joint Committee on Vaccination and Immunisation (JCVI) nearly a year ago. [3]

C O M M E N T

The simplified vaccine schedule for many people is welcomed and should improve vaccine coverage.

However, people need to know their HIV status in order to access the appropriate HPV vaccine schedule.

Although the HPV vaccine for gay and bisexual men is only available from specialist sexual health services (SHSs) and HIV clinics, it might be good for the guidelines to include that HIV testing would be good practice, without making this a barrier to the HPV vaccine. Some people attending these clinics will not have had an HIV test and the default assumption might be that they are negative.

Without HIV testing, people who are not yet diagnosed will not receive the three-dose schedule. Based on the latest statistics from England, people aged 16 to 25 still account for nearly a third (230/794) of new HIV diagnoses. [4]

As mentioned earlier in reports from IAS 2023, one of the three official pre-meetings was an international workshop on HPV infection, which included a call for global health targets for all HPV-related cancers, not just cervical cancer. [5]

References

1. UKHSA. HPV vaccination programme: changes from September 2023 letter. (29 June 2023). https://www.gov.uk/government/publications/hpv-vaccination-programme-changes-from-september-2023-letter
2. UKHSA. Change in schedule for the routine adolescent HPV programme and eligible men who have sex with men (MSM) under age 25 years 29 June 2023).

https://www.gov.uk/government/publications/hpv-vaccination-programme-changes-from-september-2023-letter/hpv-vaccination-programme-changes-from-september-2023-letter
3. JCVI. JCVI statement on a one-dose schedule for the routine HPV immunisation programme (05 August 2022). https://www.gov.uk/government/publications/single-dose-of-hpv-vaccine-jcvi-concluding-advice/jcvi-statement-on-a-one-dose-schedule-for-the-routine-hpv-immunisation-programme
4. UKHSA. UK surveillance statistics (2022). National HIV surveillance data tables. Table 1a. https://www.gov.uk/government/statistics/hiv-annual-data-tables
5. IAS 2023 premeeting. Putting people first in the prevention, treatment and care of HPV-related cancers among people living with HIV. (22 July 2023). https://www.iasociety.org/conferences/ias2023/programme/pre-meetings/putting-people-first-prevention-treatment-and-care-hpv-related-cancers-people

UK shingles vaccine: changes from 1 September 2023

Simon Collins, HIV i-Base

On 4 July 2023, UKHSA published a letter outlining upcoming changes to the UK shingles vaccine programme.

These include expanding access to the vaccine at an earlier age for people with a weakened immune system.

The changes are based on recommendations from the Joint Committee on Vaccination and Immunisation (JCVI). Hundreds of thousands more people will then be able to get protected against shingles each year.

The vaccine that is used in the programme is also changing. All newly eligible individuals will be offered two doses of the non-live vaccine Shingrix instead of the live vaccine Zostavax.

- Those aged 70-79 will still be able to get the shingles vaccine from their GP. They will either be offered one dose of Zostavax or two doses of Shingrix (6 to 12 months apart).
- All those aged 50 and over with a weakened immune system will be offered two doses of the Shingrix vaccine by their GP practice (8 weeks to 6 months apart).
- Those turning 65 and 70 will be offered two doses of the Shingrix vaccine (6 to 12 months apart) by their GP practice as they become eligible (eligibility will go down to 60 years old in September 2028).

Source

UKHSA. Shingles vaccination programme: changes from September 2023 letter. (4 July 2023).

https://www.gov.uk/government/publications/shingles-vaccination-programme-changes-from-september-2023-letter

New guidelines on cognitive impairment in people living with HIV

Simon Collins, HIV i-Base

New international consensus guidelines have been published that update earlier documents related to the diagnosis and management of neurocognitive impairment in people living with HIV.

They aim to correct the earlier potential for overdiagnosis linked to HIV Associated Neurocognitive Disease (HAND) criteria and focus on differentiating between HIV and numerous other causes.

The new guidelines propose using HIV-associated brain injury (HABI) as a new term for cases where HIV directly causes complications and highlight that low performance of neurocognitive testing can result from social, educational and language skills rather than any active injury.

The document also emphasises the importance of differentiating between historical archive or legacy damage and ongoing active neurological problems.

These guidelines differ from earlier criteria used in the HAND criteria by identifying HIV as the direct cause of symptoms and in requiring a clinical assessment to interpret results from neurocognitive testing.

The writing panel – the International HIV-Cognition Working Group) – included doctors, researchers and community advocates from South Africa, India, Uganda, Kenya, Zambia, Europe, the US and the UK.

The six main recommendations are included below.

1. HIV-associated brain injury (HABI) should be considered as one cause of cognitive impairment alongside

other potential causes of brain injury occurring in people living with HIV.

2. HABI should be differentiated on the basis of HIV RNA suppression and the activity of pathology.
3. Low performance on cognitive tests should not be labelled as cognitive impairment without clinical context.
4. When interpreting cognitive data, the false-classification rate should be considered.
5. A research classification of cognitive impairment in people living with HIV should consider a combination of cognitive symptoms, low performance on cognitive testing, and abnormality on neurological investigations.
6. Cognitive symptoms should refer to any change in cognition that has been noticed by the individual or an observer, whether or not this change has an impact on daily functioning.

Reference

Nightingale S et al. Cognitive impairment in people living with HIV: consensus recommendations for a new approach. Nat Rev Neurol (2023). https://doi.org/10.1038/s41582-023-00813-2.
https://www.nature.com/articles/s41582-023-00813-2

HIV PREVENTION & TRANSMISSION

Breakthrough HIV infection on PrEP with injectable cabotegravir

Kirk Taylor, HIV i-Base

Although rare, HIV infections can occur with all formulations of PrEP - whether oral TDF/FTC or TAF/FTC - or the more recently FDA-approved long-acting cabotegravir (CAB-LA) injections.

The few cases that have been reported in research studies vary depending on the PrEP formulation. Cases from use of oral PrEP have been generally linked to either low adherence or contact with drug-resistant HIV. Those with injectable CAB-LA however have been linked to missed infections that occurred during the window period for seroconversion.

A case report of breakthrough HIV on injectable PrEP was published as an early access concise communication in the journal AIDS. [1]

A 28-year-old gender diverse person switched from daily oral PrEP (TAF/FTC) to CAB-LA PrEP due to regularly missing doses. Their primary partner is living with HIV and carries resistance mutations for NRTIs (65R and 118I) and INSTIs (92G). HIV antigen tests were negative before CAB-LA doses on D0, D27 and D91. However, a positive HIV RNA test was reported on D91 with a. viral load of 1.48 log copies/mL. Subsequent antigen testing at D100 was positive.

ART was initiated with TAF/FTC in addition to CAB-LA. This was later switched to DRV/c plus DTG to match their primary partners regimen. HIV antigen and viral load testing at D191 were both negative.

Plasma CAB levels at D128 (37 days post injection) were 1.18 µg/mL (7x greater than the PA-IC90). This case presentation is consistent with long-acting early viral inhibition (LEVI) syndrome and highlights the need to conduct viral load testing alongside antigen testing to reduce the risk of INSTI resistance.

C O M M E N T

Considering the many millions of people now using PrEP globally, PrEP is actually significantly more effective than rates of protection reported in clinical studies. But even if real-world experience suggests.

The small chance of breakthrough infections should be included when first discussing PrEP.

Currently, only TDF/FTC is approved as PrEP in the EU and UK.

The lead author commented that the underlying cause of the breakthrough infection are unclear but may be linked to the number of unique sexual partners (20 to 30 per month) or periods of vulnerability during transition between oral and long-acting PrEP, without overlap.

This case was also presented as a poster at CROI 2023. [2]

References

1. Hazra A et al. Breakthrough HIV-1 infection in setting of cabotegravir for HIV pre-exposure prophylaxis. AIDS. DOI: 10.1097/QAD.0000000000003644. (04 July 2023).
   https://pubmed.ncbi.nlm.nih.gov/37418423
2. Hazra A et al. Breakthrough HIV-1 infection in setting of long-acting cabotegravir for PrEP. CROI 2023 19 – 22 February, Seattle and Hybrid. Poster abstract 981.
   https://www.croiconference.org/abstract/breakthrough-hiv-1-infection-in-setting-of-long-acting-cabotegravir-for-prep/ (abstract)

MEETINGS & WORKSHOPS 2023/4

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.

Some meetings are in person, some are virtual and others offer both options.

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)

2023

30th Intl Workshop on HIV Drug Resistance and Treatment Strategies

20–22 September 2023, Cape Town, South Africa

www.hivresistance.co.za

19th European AIDS Conference (EACS 2023)

18 – 21 October 2023, Warsaw, Poland

www.eacsociety.org

14th International Workshop on HIV & Aging HIV & Aging 2023

26-27 October 2023, Washington DC, USA and hybrid

https://academicmedicaleducation.com/

6th Southern African HIV Clinicians Society Conference (SAHCS 2023)

8 – 10 November 2023, Cape Town, South Africa

www.sahcsconference.co.za

2024

CROI 2024

3 – 6 Mach 2024, Denver, Colorado

https://www.croiconference.org

5th HIV Research for Prevention Conference (R4P 2023)

6 – 10 October 2023, Lima, Peru, and virtual.

www.iasociety.org/conferences/HIVR4P2023

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.

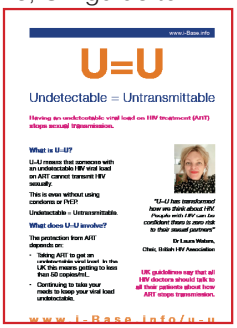
http://www.i-base.info/guides

- Introduction to ART (May 2022)
- HIV & quality of life: side effects & long-term health (Sept 2016)
- Guide to PrEP in the UK (February 2022)
- HIV testing and risks of sexual transmission (June 2021)
- Guide to changing treatment and drug resistance (August 2021)
- Guide to HIV, pregnancy & women's health (April 2019)

Pocket guides

A series of pocket-size concertina folding leaflets that are 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 has 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 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 email: subscriptions@i-Base.org.uk

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.

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: *44-page A5 booklet* **quantity** _____

UK Guide To PrEP: *24-page A5 booklet* **quantity** _____

ART in pictures: HIV treatment explained: *32-page A4 booklet* **quantity** _____

Guide to changing treatment: *8-page A5 leaflet* **quantity** _____

Guide to side effects and quality of life: *8-page A5 leaflet* **quantity** _____

Guide to HIV testing and risks of sexual transmission *52-page A5 booklet* **quantity** _____

- **Other resources**

U=U resources:

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

HIV treatment passports - Booklets to record your HIV 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