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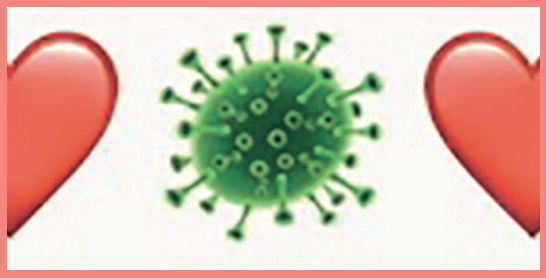
hiv treatment bulletin (e)



First reports from CROI 2021 (12 March 2021)

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Published by HIV i-Base

HTB no.3 (2021): HIV and COVID-19 supplement ISSUE 3

i-Base 2021 appeal

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

This year we are continuing a funding appeal to help i-Base continue to provide free publications and services during 2020.

i-Base now recieve more than 12,000 questions each year and the website has more than 500,000 view each month. We also distribute more than 80,000 booklets and leaflets free to UK clinics every year.

If 1000 people support us with £5 a month we will be on course to meet our funding shortfall. All help is appreciated.

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

Plus a BIG thank you all all supporters over the years including in the recent Solidarity2020 campaign.

More than 70 people bought one or more posters curated by Wolfgang Tillmans and the Between Bridges Foundation, to who we are also really grateful :)

EDITORIAL

This issue of HTB includes news on the unexpected death of the influential HIV scientist and educator Dr Charles Boucher that will have shocked many readers. We include a short tribute in appreciation of his work.

We also include first reports from virtual CROI 2021, which for many people is a marker for the anniversary for COVID-19.

Appropriately, the excellent programme this year included many studies related to COVID-19, perhaps a factor in more that a quarter of presentations. This included the urgency of global access to vaccines, which was the focus of the opening presentation.

Other news in this rapid issue included first reports on pipeline HIV drugs and results from the NADIA study. We also include one of the plenary lectures that changes the consensus understanding of the HIV viral life cycle using electomicroscopy videos to show HIV capsid passing intact into the CD4 nucleus. These fascinating videos should be seen by all.

But this is difficult, because we also report that wider access to studies presented at the conference, including the abstract book, are now freely available online. This was, at least in part, in response to a community letter challenging the proposal for all conference material to remain behind a pay wall for non-delegates.

Until now, CROI has been the best example of ensuring broad access to the latest research, with webcasts of all presentations available on open access as soon as the meeting ends.

The conference should actually be proud of its role in generating community demand for broad access to such important cutting-edge research - including from many who have no formal scientific background.

Hopefully, the decision to block access this year will be reconsidered given the educational aims of this meeting, perhaps in memory of Dr Boucher, who I think would have approved.

IN MEMORY

In Memory: Charles Boucher, leading HIV doctor, researcher and educator

Just as the last HTB was being sent out i-Base learned of the unexpected death of the leading HIV scientist Charles Boucher.

This was especially difficult as Charles was still a young man and although he had been undergoing treatment for cancer, this was not widely known.

Many people, likely tens of thousands, will have known Charles as the driving force and scientific director behind a wide series of specialist workshops developed by Virology Education.

The early workshops focussed on specialised areas of research - notable drug resistance and pharmacology - but actually often the first forum for studies that would later be presented at CROI.

But bringing global experts together in meetings at a scale where everyone could join active discussions developed into such an effective format that this programme expanded over 20 years to cover a much broader range of related issues before these were covered by larger conferences. These included hepatitis, clinical care, HIV transmission, transgender health, integrase inhibitors and also to regional meetings, including in Russia and China.

The focus for these meetings often developed from issues that were increasingly important community issues such as the workshops on HIV and ageing, developed with community activist Jules Levin, that has now been running for ten years.

As a non-technical, far-from-expert community journalist, getting a chance to join scientific meetings was initially daunting. Some drug resistance meetings were just for researchers to present their work. But this just needed to be able to contribute to the discussion. Meeting Charles was actually much more fun: he was incredibly engaging, had a great sense of humour, and just involved wanting to join a discussion and take ideas further. Charles was interested in generating active debates that would underpin better and more relevant science. He supported engagement irrespective of academic background - though this also meant being ready to respond at any time to: “So what does the community think of this?”.

Most people only learnt about Charles’ death by an email announcement from VE that included a link to leave messages of condolence, still open. Within hours, there were hundreds of tributes from colleagues and friends across the world who all spoke of their sadness, but also with gratitude for his work and for knowing such a dynamic, passionate, caring, engaging and inspiring man.

Our thoughts are with Charles family and friends at this difficult time, including his many colleagues at Virology Education.

Simon Collins, HIV i-Base

Reference

In Memoriam and online condolences: Dr. Charles Boucher, Scientific Director at Virology Education and Academic Medical Education.

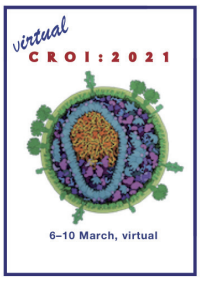
https://academicmedicaleducation.com/in-memoriam-dr-charles-boucher

CONFERENCE REPORTS

28th Conference on Retroviruses on Opportunistic Infections (CROI 2021)

6 – 9 March 2021, virtual

Introduction



For many people, CROI 2021 this anniversary marks the first recognition of the potential global risk from COVID-19: the start of a difficult year, unimaginable before.

A year ago, as delegates were either arriving n Boston or preparing to fly, CROI rapidly adapted a few days before the meeting was due to start, to become the first large virtual conference.

This year CROI was planned as a fully virtual meeting, and included approximately 3500 registered delegates.

The programme was exciting as it always is, with a significant and appropriate focus on COVID-19, including first presentations for new treatments. It also included important presentations on new and pipeline HIV drugs for both prevention and treatment, many using long-acting formulations.

The virtual meeting retained the regular CROI format and included the options to discuss presentations using chat and Q&A options to ask questions about oral presentations in real time.

One advance – a good one – is a new format for the posters. Rather than 1000+ posters, available as PDF files, the virtual meeting has edited posters to around six summary slides with a 4-minute narrative by the presenter (now called a 'science spotlight'). Each virtual poster also allows an online dialogue with the presenter that remains online for general viewing and is a pretty good way to retain something of the direct dialogue that we

Another change though was more difficult was suggesting that a 6-month pay wall before the presentations become open access. CROI has always developed a leading role in democratising access to the latest medical research and at the start of the conference even the abstract book was planned to need a paid subscription. This is disappointing and will hopefully be rethought.

At least one community sign on letter with more than 200 organisations and individuals has already asked for the whole meeting to have a much shorter window to open access. As a result, the abstract book is now available.

www.croiconference.org/vcroi-2021

Currently, content on the main conference website is only accessible to delegates, although this decision might be reviewed.

www.vcroi2021.org

Even if all links are not yet active to non-delegates, i-Base reports will still include hyperlinks to the abstract, webinars and full presentations. We apologise for this and hope CROI reconsiders this decision after the meeting.

Reports in HTB will also therefore focus on shorter articles to emphasise summary conclusions, with comment, as a way to cover a wider range of presentations.

Report in this issue include:

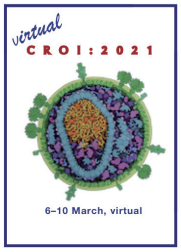
- CROI 2021 opening session: urgency of global access to vaccines, the potential of mAbs and the lessons learned from HIV
- Community call highlights CROI 6-month pay wall rather than usual open access
- Dose ranging results from once-daily GSK254 maturation inhibitor as treatment for HIV multidrug resistance
- Dosing for once-weekly oral ART: islatravir plus MK-8507 studies due to start in 2021
- Islatravir dosing for once-monthly and annual PrEP: if effective this could end HIV
- Dolutegravir with recycled tenofovir and lamivudine performs well second-line: primary results from the NADIA trial
- Dolutegravir with recycled tenofovir and lamivudine performs well second-line: primary results from the NADIA trial
- HIV capsid uncoats in the CD4 nucleus rather than the cytoplasm – viral lifecycle updated…
- CROI 2021: Community HIV cure workshop online

CROI 2021: COVID-19

CROI opening session: urgency of global access to vaccines, the potential of mAbs and the lessons learned from HIV

Simon Collins, HIV i-Base

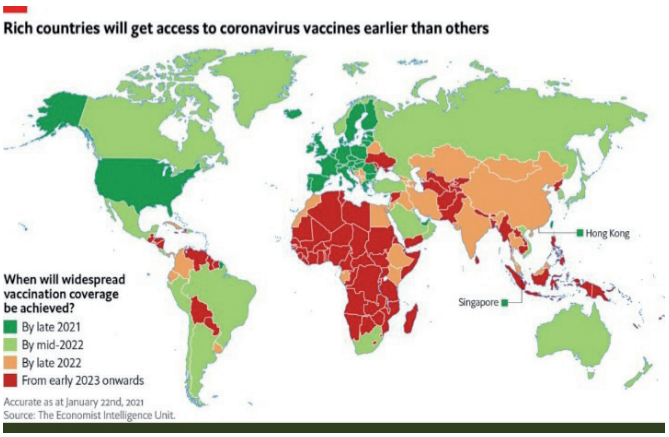
The three opening lectures this year covered both HIV and COVID-19 from community and scientific perspective.



In the first of these, two leading global activists - Gregg Gonsalves and Fatima Hassan - opening CROI on vaccine access, giving the Martin Delaney presentation (which is usually only included in a pre-conference workshop). [1]

The talk drew parallels with the early campaigns to ensure that broadened access to ART beyond high-income countries. Unless access to COVID-19 vaccines globally is developed, as well as within each country, relaxing lockdown will never safely extend to international travel. Current projections do not expect significant vaccine cover in south east Asia until the end of 2022 and in most African countries until 2023.

New variants will continue to develop spontaneously in populations where vaccine cover is limited and those with transmission advantages will spread globally. This included the divisions on equity of access to vaccines by race, where many high income countries (including the US) have lower rates of vaccine uptake by black and ethnic minority citizens and where global access in extremely limited to countries in the global south.



Although some vaccines (including Oxford/AZ) are already being manufactured by generic companies and widely distributed at a not-for-profit cost, the talk called on CROI to endorse the international People's Vaccine campaign and to sign the WHO Vaccine Equity declaration (#VaccinEquity #endvaccineapartheid). [2, 3, 4]

In the two other talks in the opening session were also on COVID-19.

Pamela J Bjorkman from the California Institute of Technology talked about developing neutralising monoclonal antibodies against the spike protein of SARS-CoV-2. This has included using microscopy and X-ray crystallography to map and classify variants as part of a large programme to design a vaccine that would protect against both variants of SARS-CoV-2 and future coronaviruses.

The third talk, given by Anthony Fauci from the US NIAD, reviewed the connections between the HIV and COVID-19 epidemics. [3]

This included lessons that can be learned from responses to both infections that could accelerate new ways to prevent and treat COVID-19, emphasing the considerable role that HIV scientists have played in COVID-19 research.

References

The weblink for all talks in the opening session of CROI 2021, although access is currently restricted to delegates, is:
https://www.vcroi2021.org/live-stream/19762721/OPENING-SESSION

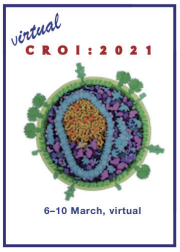
1. Gonsalves G and Hassan F. Vaccine nationalism is killing us: how inequities in research and access to sars-cov-2 vaccines will perpetuate the pandemic. The Martin Delaney Presentation. CROI 2021.6–10 March 2021.
   https://www.vcroi2021.org/sessions/19762721/subsession/25643058
2. The People's Vaccine.
   https://www.oxfam.org/en/tags/peoples-vaccine
3. WHO Vaccine Equity declaration.
   https://www.who.int/campaigns/annual-theme/year-of-health-and-care-workers-2021/vaccine-equity-declaration
4. People's Vaccine Day of Action. An online rally on 10 March at 13:30 Washington / 18:30 London / 19:30 Brussels / 21:30 Nairobi. Free registration:
   https://www.eventbrite.co.uk/e/rally-for-a-peoples-vaccine-tickets-143999701985
5. Bjorkman PJ. Neutralizing antibodies against coronaviruses. The Bernard Fields Lecture. CROI 2021.
   https://ww2.aievolution.com/cro2101/index.cfm?do=abs.viewAbs&abs=2502
6. Fauci A. Lessons from the concurrent HIV/AIDS and covid-19 pandemics: a two-way street.
   https://ww2.aievolution.com/cro2101/index.cfm?do=abs.viewAbs&abs=1006

CROI 2021: ACCESS

CROI 2021: Community challenge 6-month CROI pay wall – rather than usual open access...

Simon Collins, HIV i-Base

This year, CROI has decided to limit access to all conference materials to delegates or new subscribers for up to six month after the conference. This include abstracts, posters and webcasts.



Usually, CROI has made all conference material available as an open access resource as soon as the meeting finishes.

Many people who registered for the virtual conference - and certainly most community delegates - were shocked to learn of this change. A community sign-on letter quickly included more than 200 organisations and individuals calling for the CROI Foundation and the International Antiviral Society–USA (IAS–USA) to reconsider these plans. [1]

Until 2021, CROI had developed an exemplary model for democratising science and medicine - especially as CROI is the most important of the international conferences.

Although this might have been suggested as a cautious approach when planning the virtual conference - when there might have been a worry that delegates might not register if the content was available free within a few days?

Actually, more than 3500 delegates registered for the virtual 2021 conference, only slightly down from last year.

Also, researchers who present their work at the conference might also want this wider access.

C O M M E N T

Hopefully this retrograde decision to restrict access might be reconsidered by the meeting organisers. CROI this year had an extremely dynamic and important programme, also covering COVID-19.

The quality of the scientific and medical research presented at CROI is actually the reason why broader access is essential. CROI should be proud that they have contribute to this level of interest in science and medicine from the community. Researchers, often supported by public funding, might also was their work to be more widely accessible.

https://www.croiconference.org/contact-us

STOP PRESS: The abstract book has now been posted online as PDF and flipbook:

https://www.croiconference.org/vcroi-2021

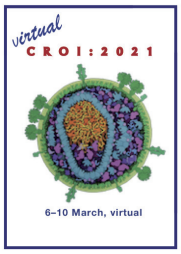
Reference

1. Community letter to the Conference on Retroviruses and Opportunistic Infections (CROI) regarding access to presentations and abstracts. (10 March 2021).
https://docs.google.com/forms/d/e/1FAIpQLSfbTuIS2D8KbD71MPLX4AV0BuM9n7gbWnURKrDlcwkepkql9w/viewform

CROI 2021: ANTIRETROVIRALS

CROI 2021: Once-daily GSK254 maturation inhibitor as treatment for HIV multidrug resistance

Simon Collins, HIV i-Base



CROI 2021 included several studies on an investigational second-generation maturation inhibitor GSK3640254 (GSK254) that is active against natural polymorphisms that limited efficacy of the first compounds in this class.

Maturation inhibitors work at a late stage of the viral life cycle blocking the final protease cleaving and assembly and resulting in immature and noninfectious virions

Christoph Spinner presented results from a phase 2a two-stage dose-finding study in 34 treatment-naïve participants (n=6 per dose and n=2 placebo in each stage). Oral dosing was once-daily and given with a moderate fat meal.

Mean age was 31, 94% were men and mean baseline viral load range from about 15,000 to 65,000.

In stage 1, participants were randomised to either 10 mg of 200 mg for ten days. In part two, doses were 40 mg, 80 mg or 140 mg for seven days. Follow-up in stage 1 continued without treatment from days 11 to 17, with ART started on day 18. In stage 2, ART was started on day 8.

Changes in viral load were roughly proportional to dose, with mean changes in plasma viral load ranging from –2.0 to 0.2 log copies/mL. The greatest mean reductions of –2.0 and –1.5 log were greatest in the 200 mg and 140 mg groups, respectively.

However, 4/6 participants in the 200 mg arm in stage 1 developed drug resistance at day 11 with A364A/V partial mixed variant which by day 21 had developed into the full mutation in 1/4 with 132-fold phonotypic resistance. No resistance was seen in the 10 mg arm. but these results promped the reduction to 7 days monotherapy in stage 2 (and where no drug resistance was reported).

Tolerability was good with all adverse events at grade 1 or 2 and no dose signal. The only two serious events (anal abscess and congestive cardiomyopathy) were not judged related to the study drug.

A second study, GSK254 retained activity against a panel of clade B and C viruses with site directed mutations in gag (including V362I, V370A, Γ370, or R286K/V370A) that had limited activity of earlier maturation compounds, but showed a significant loss of sensitivity to A364V.

Median EC50 values were 1.4 nM (range: 0.48 to 6.9 nM) and 1.4 nM (range: 0.85 to 1.9 nM) for Subtype B and C respectively and the study also reported in vitro studies clarifying the mechanism of action.

The phase 2b study, also in treatment naïve, is planned to use 100 mg, 150 mg and 200 mg with 2 NRTIs.

C O M M E N T

As with all drugs in new classes, maturation inhibitors would be active against resistance to other drug classes. GSK254 shows good antiviral activity.

The early cases of drug resistance though show a lower genetic barrier to drug resistance than PIs and NSTRIs and this will make it essential to be used in combination with other active drugs.

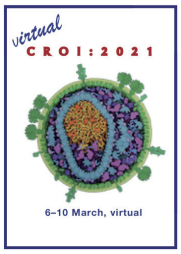
References

1. Spinner C et al. Phase IIa proof-of-concept trial of next-generation maturation inhibitor GSK3640254. CROI 2021.6–10 March 2021. Oral abstract 126.
https://ww2.aievolution.com/cro2101/index.cfm?do=abs.viewAbs&abs=1928 (abstract)
https://www.vcroi2021.org/live-stream/19762744/NEW-WEAPONS-AGAINST-SARS-CoV-2-AND-HIV (webcast)
https://natap.org/2021/CROI/croi_51.htm
2. Jeffrey JL et al. GSK3640254 is a novel maturation inhibitor with an optimized virology profile. CROI 2021.6–10 March 2021. Poster 421.
https://ww2.aievolution.com/cro2101/index.cfm?do=abs.viewAbs&abs=1783 (abstract)
https://www.vcroi2021.org/sessions/19764929/subsession/25642415/GSK3640254-IS-A-NOVEL-MATURATION-INHIBITOR-WITH-AN-OPTIMIZED-VIROLOGY-PROFILE (webcast)

Dosing for once-weekly oral ART: islatravir plus MK-8507 studies due to start in 2021

Simon Collins, HIV i-Base

CROI 2021 included several studies on a once-weekly oral combinations using islatravir and a new NNRTI MK-8501. [1]



A single 20 mg once-weekly dose of islatravir was shown to produce intracellular concentrations that is similar to steady-state using the 0.75 mg daily dose. After 14 days, islatravir levels were still five-fold above the inhibitory quotient for lamivudine resistant HIV, showing this would also have some flexibility it a single dose was later or missed. [1]

The study modelling for dosing MK-8507 was based on real world simulations in combination with islatravir and assuming 80% adherence. The study reported that the three doses studies - 100 mg, 200 mg and 400 mg - should all provide >90% efficacy against common NNRTI mutations including K103N and Y181C.

MK-8507 has a half-life of ~70 hours and mean viral load reductions of –1.5 log once week after a single dose were reported at Glasgow 2020. [2]

An oral presentation at CROI 2021 also presented additional new information about MK-8507, including activity against early NNRTIs (K103N, Y181C and G190A) – with a resistance profile similar to doravirine. [3]

Studies using islatravir plus MK-8507 in a dual once-weekly combination are planned to start later in 2021.

References

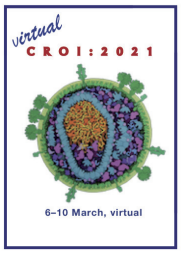
1. Kandala B et al. Model-informed dose selection for islatravir/MK-8507 oral once-weekly phase 2b study. CROI 2021, 6–10 March 2021. Poster 376.
2. Single doses of MK-8507 reduce viral load by mean –1.5 log and support once-weekly dosing above 80 mg. HTB (14 October 2020). https://i-base.info/htb/39085
3. Diamond T et al. Resistance profile of MK-8507, a novel NNRTI suitable for weekly oral HIV treatment. CROI 2021, 6–10 March 2021. Oral abstract 129.
https://ww2.aievolution.com/cro2101/index.cfm?do=ev.viewEv&src=ext&ev=2914 (abstract)
https://www.vcroi2021.org/live-stream/19762744/NEW-WEAPONS-AGAINST-SARS-CoV-2-AND-HIV (webcast)

CROI 2021: PREVENTION

Islatravir dosing for once-monthly and annual PrEP: if effective, this will end HIV transmission

Simon Collins, HIV i-Base

Two of the first oral abstracts at CROI reported on the next stages of one of the most important pipeline compounds for HIV prevention.



Munjal Patel from Merck/MSD presented results of PK/PD analyses that defined the islatravir exposure threshold for PrEP and the 60 mg oral once monthly dose that will be used in the upcoming phase 3 studies. [1]

This was based on intracellular triphosphate (TP) levels derived from macaque studies and phase 1 studies. In a phase 2 study, the 60 mg dose resulted in observed mean islatravir-TP that was still 26-fold higher than the minimum target PK threshold of 0.05 pmol/million cells and that levels will be reached from the first dose.

A second oral presentation is the same session, presented similar results for an islatravir implant that will provide PrEP cover for a year. [2]

The technical name for this device – in case it catches on – is a “radiopaque next-generation islatravir-eluting implant”. This was a double-blind phase 1 study and 36 participants (8 active, 4 placebo per dose) at low risk of HIV either had one of three doses of an islatravir implant (48 mg, 52 mg or 56 mg) for 12 weeks or a matched placebo. This is a new formulation of islatravir implant that has a different PK and dose compared to the first dosing studies. This includes barium as a safeguard to be able to track the implant if it migrates within the body.

Islatravir-TP remained above target levels throughout and PK modelling predicted and at doses of 52 mg and above would maintain target levels for at least 52 weeks.

Tolerability was generally good. Common adverse events included haematoma, red skin, tenderness, itching and induration, with little difference between the active and placebo groups and no dose-related adverse events.

Larger phase 2 studies are now planned.

C O M M E N T

Although research into islatravir for HIV prevention is still in early stages, this compound has the potential to effectively end HIV transmission.

If efficacy matches other formulations of PrEP, and there is no concern about drug resistance, these long-acting formulations need to become as accessible as aspirin including as single-dose over-the-counter. A single pill could possibly provide both PEP and PrEP cover for a month.

Islatravir PrEP could have a larger market than statins and Viagra, probably combined.

Development and regulatory decisions should understand this urgency and pricing should match affordability for global demand.

References

The weblink for this oral abstract session, currently restricted to delegates, is:

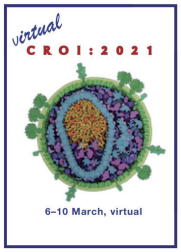
https://www.vcroi2021.org/live-stream/19762731/HIV-TREATMENT-AND-PREVENTION-NEW-OPPORTUNITIES-TO-OPTIMIZE-DRUG-DOSING-ADHERENCE-AND-ANTIRETROVIRAL-THERAPY

1. Patel M et al. islatravir PK threshold & dose selection for monthly oral HIV-1 PrEP. CROI 2021, 6 – 10 March 2021. Oral abstract 87. https://ww2.aievolution.com/cro2101/index.cfm?do=abs.viewAbs&abs=1159
2. Matthews RP et al. Next-generation islatravir implants projected to provide yearly HIV prophylaxis. CROI 2021, 6 – 10 March 2021. Oral abstract 88. https://ww2.aievolution.com/cro2101/index.cfm?do=abs.viewAbs&abs=2598

CROI 2021: TREATMENT STRATEGIES

Dolutegravir with recycled tenofovir and lamivudine performs well second-line: primary results from the NADIA trial

Polly Clayden, HIV i-Base



Second-line treatment with dolutegravir (DTG) plus two NRTI led to good viral suppression at week 48 in the Nucleosides and Darunavir/Dolutegravir in Africa (NADIA) Trial – according to data shown at CROI 2021. [1]

NADIA included many participants with substantial resistance and no predicted NRTI activity. The results suggest that tenofovir (TDF) can be maintained in second-line therapy instead of switching to zidovudine (AZT).

After first-line NNRTI-based ART failure, WHO currently recommends switching to DTG plus two NRTI. People with HIV who previously received TDF/lamivudine (3TC) are recommended to change to AZT/3TC. As well as standardised first- and second-line regimens, the public health approach includes simplified monitoring: sparse viral load and safety checks and no resistance testing.

These WHO recommendations were based on one randomised controlled trial that used resistance testing to select NRTI, excluded people with no predicted active NRTIs and had frequent viral load monitoring.[2] How generalisable these findings are to public health approach was uncertain, particularly the performance of DTG when it was not protected by NRTIs with predicted activity.

The aim of NADIA was to investigate whether second-line ART with DTG is non-inferior to ritonavir-boosted darunavir (DRV/r) and TDF/3TC non-inferior to AZT/3TC, in people with considerable baseline NRTI resistance with a public health approach (including no resistance tests and sparse viral load monitoring).

NADIA is a two-by-two factorial, open-label, non-inferiority trial. Participants failing an NNRTI/TDF/3TC first-line regimen with confirmed viral load of above 1000 copies/mL received DTG vs DRV/r with a second randomisation of AZT/3TC vs TDF/3TC. The primary endpoint is viral load less than 400 copies/mL at week 48 using FDA snapshot algorithm (non-inferiority margin 12%).

Participants had viral load testing at 24 and 48 weeks, in accordance with WHO guidelines. Real-time resistance testing was performed for participants with confirmed viral load 1000 copies/mL and above. Batched resistance testing was on stored samples (results blinded).

There were 464 participants enrolled at seven sites in Kenya, Uganda and Zimbabwe. Five died before week 48 and one was lost to follow up. They attended 99% of scheduled visits and remained on their assigned regimen for 96% of follow up.

Baseline characteristics overall included: 61% women; 51% with CD4 of 200 cells/mm^3 or less and 28% viral load above 100,000 copies/mL. There was extensive baseline resistance: 50% had K65R/N and 87% M184V/I. Participants were similar across all treatment groups.

Week 48 viral load was less than 400 copies/mL in 90.2% in the DTG group and 91.7% in the DRV/r group: difference –1.49%; (95% CI –6.7 to 3.7%), p=0.576. This indicated non-inferiority of DTG (but not superiority).

The proportion with confirmed viral rebound above 1000 copies/mL was around 6% in each group with no difference between groups (p=0.897). Four participants with viral rebound in the DTG group had major DTG resistance mutations associated with intermediate or high-level resistance, but none of the participants who rebounded in the DRV/r group had DRV mutations.

When the investigators looked at responses in pre-specified subgroups, those with baseline viral load above 100,000 copies/mL had similar suppression rates to the overall population: 89.4% DTG and 90.3% DRV/r.

Importantly in the subgroup with no predicted NRTIs activity these proportions were: 92.4% DTG and 93.7% DRV/r.

In the TDF vs AZT comparison, the results were: 92.3% TDF and 89.6% AZT; difference 2.7% (95% CI –2.6 to 7.9), p=0.317. Also indicating non-inferiority but not superiority of TDF.

In the subgroup with the K65R/N mutation, suppression rates were: 94% TDF and 96% DRV/r. And for those with the M184V/I mutation: 94% DTG and 92% DRV/r.

Grade 3/4 adverse events were uncommon and similar in frequency DTG vs DRV/r and TDF vs AZT.

Presenting author Nick Paton remarked: “This finding is at variance with the traditional approach to infectious disease treatment where there is a long-standing aversion to switching just one drug in a failing regimen.”

“It also suggests we may need to revise the nucleoside prediction algorithm” he added.

COMMENT

These findings fill the evidence gap for use of DTG with compromised NRTIs (no predicted active NRTIs), which was the high-risk evidence-free group left behind by DAWNING.

They are important for people switching from NNRTI to DTG second-line, after known treatment failure, as well as programmes switching stable people routinely from NNRTI to DTG-based regimens in settings without pre-switch viral load and resistance testing.

WHO guidelines currently recommend switching NRTIs based on rather sketchy evidence. Here is an opportunity to change this recommendation based on good quality evidence that will make things easier – people can just use the TDF/3TC/TLD fixed dose combination (TLD) rather than twice-daily NRTIs.

The findings also make the argument to reposition DRV/r in the hierarchy of PIs.

NADIA is continuing to 96 weeks which, among other things, will mean the study can monitor further for major resistance among participants with viral rebound in the DTG group.

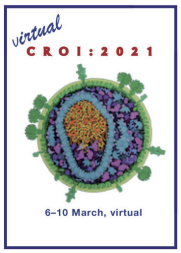
Reference

1. Paton N et al. Nucleosides and darunavir/dolutegravir in Africa (NADIA) trial: 48 wks primary outcome. CROI 2021 (virtual). 6–10 March 2021. Oral abstract 94.
   https://ww2.aievolution.com/cro2101/index.cfm?do=abs.viewAbs&abs=2609 (abstract)
   https://www.vcroi2021.org/live-stream/19762731/HIV-TREATMENT-AND-PREVENTION-NEW-OPPORTUNITIES-TO-OPTIMIZE-DRUG-DOSING-ADHERENCE-AND-ANTIRETROVIRAL-THERAPY (webcast session oral O2)
2. Clayden P. Dolutegravir outperforms lopinavir/ritonavir second-line: interim results from the DAWNING study. HTB. 10 August 2017.
   https://i-base.info/htb/32241

CROI 2021: VIROLOGY

CROI 2021: HIV capsid uncoats in the CD4 nucleus rather than the cytoplasm - viral lifecycle updated…

Simon Collins, HIV i-Base



In the first plenary lecture at CROI 2021, Hans-Georg Kräusslich prevented evidence showing that HIV capsid remains intact until entering the CD4 cell nucleus. [1]

This has been an ongoing debate for many years that i-Base has reported before, including at previous CROI. [2, 3]

The talk included incredible animations using electromicrosopy for both SARS-CoV-2 and HIV.

In the HIV studies, radio-labelled proteins showed the capsid journey in real-time, to slip through pores in the nuclear core complex, narrow end first, with nanometres to spare. These images are able to show the empty capsid still intact within the nucleus (from 24.30 in the webcast).

C O M M E N T

The accumulating studies showing capsid uncoating as a late-stage event seem to be convincing a wider consensus among researchers.

This seemed a good time to update community diagrams on the viral lifecycle – and the most used versions are now updated on the i-Base website. [4–7]

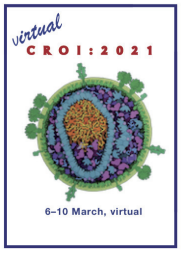
References

1. Kräusslich H-G. Imaging viral lifecycles. Plenary talk. CROI 2021.
   https://ww2.aievolution.com/cro2101/index.cfm?do=abs.viewAbs&abs=2498 (abstract)
   https://www.vcroi2021.org/live-stream/19762730/MONDAY-PLENARY-SESSION (webcast)
2. New online animation of HIV lifecycle. HTB (May 2018)
   https://i-base.info/htb/34110
3. Iwasa J. Seeing HIV: animating the HIV lifecycle. Program committee workshop for new investigators and trainees. CROI 2018 Abstract 14.
   http://www.croiwebcasts.org/console/player/37002 (webcast)
4. HIV i-Base. The viral lifecycle - updated diagram.
   https://i-base.info/guides/wp-content/uploads/2021/03/simple-HIV-lifecycle-2021.png
5. HIV i-Base. The viral lifecycle. ART in Pictures (2019)
   https://i-base.info/guides/art-in-pictures/the-hiv-lifecycle
6. HIV i-Base. The viral lifecycle in detail. ART in Pictures (2019)
   https://i-base.info/guides/art-in-pictures/the-hiv-lifecycle-in-detail
7. HIV i-Base. HIV life cycle – how drugs work in different ways. Introduction to ART.
   https://i-base.info/guides/starting/hiv-life-cycle

CROI 2021: CURE RESEARCH

CROI 2021: Community HIV cure workshops online

Simon Collins, HIV i-Base



For many years, a group of HIV community activists in the US have organised a two-day workshop linked to CROI.

These excellent meeting feature key research that will be presented at the main conference.

They also do this in an informal setting that is ideal to both meet the researchers and other community activists interested in cure research.

This year the programme included several shorter virtual workshops (one to be after CROI on 16 March). Free registration is still available for the post-CROI workshop.

https://www.treatmentactiongroup.org/webinar/pre-and-post-croi-community-hiv-cure-research-workshop/

The webcasts from the first two workshops are now available online (open access).

Session 1 - Introduction to cure and community perspectives

YouTube - via defeathiv

https://youtube.com/playlist?list=PLpzfC_l8Lo1ebdnnXp4an1pjIzAe1UpXJ

Session 2 - Focus on gene therapy

YouTube - via defeathiv

https://youtube.com/playlist?list=PLpzfC_l8Lo1dQemy8yG3XgQljOAFcFfKx

HIV SIDE EFFECTS AND COMPLICATIONS

Chronic kidney disease (CKD) in HIV positive people linked to time with low CD4 count: partly reversible after effective ART

Simon Collins, HIV i-Base

The large prospective D:A:D cohort, with approximately 49,000 participants, looked at a range of markers of HIV-related immunosuppression, including baseline, nadir and recovery CD4 counts and time spent <200 cells/mm^3.

This analysis included 33,791 participants followed from 2004 to 2016. During a median of 8 years follow-up, 2226 participants (6.6%) developed CKD, defined as eGFR <60 mL/min/1.73. The majority (6.3%) developed grade 3 (eGFR <60 to >30).

However, 0.3% developed grade 4 and 0.3% grade 5, with 0.1% needing chronic dialysis and 0.01% a kidney transplant.

In univariate analysis, all measures of immunosuppression measures predicted CKD.

In mutivariate analysis, including all factors in the D:A:D 5-year CKD calculator, the strongest predictor was the percentage of time spent with a CD4 ≤200 cells/mm^3: 0 vs >25%; IRR: 0.77 (95%CI: 0.68 to 0.88).

The highest effect was in people at low D:A:D CKD risk: IRR 0.45 (95% CI: 0.24 to 0.80) vs 0.80 (95% CI: 0.70 to 0.93).

Of the 4328 with baseline CD4 <200 cells/mm^3, 309 developed CKD.

The results also suggested that the increased risk from severe immunosuppression may be at least partially reversible after immune recovery to >500 cells/mm^3 on ART when CKD was rare.

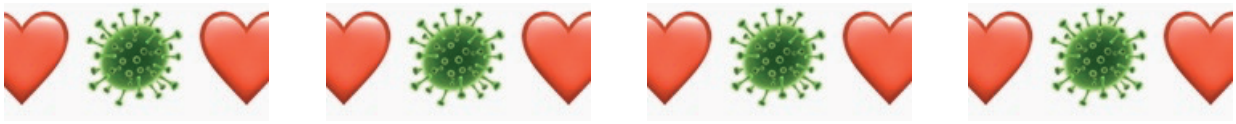
C O M M E N T

Although this study was presented in part at CROI 2016, the publication of the full dataset is important to report.

Reference

Ryom L et al. The Impact of Immunosuppression on Chronic Kidney Disease in People Living With Human Immunodeficiency Virus: The D:A:D Study. JID 223(4):632–637. DOI:10.1093/infdis/jiaa396. (5 February 2021).
https://academic.oup.com/jid/article/223/4/632/5868947

HTB SUPPLEMENT ON COVID-19: Issue 9



COVID-19: VACCINE RESEARCH

Janssen/J&J vaccine against COVID-19 is approved in the EU

Simon Collins, HIV i-Base

On 11 March 2021, the European Union authorised the COVID-19 vaccine developed by Janssen/J&J. [1]

Approval is based on results that include an international phase 3 study (ENSEMBE 1).

The was a double-blind that equally randomised 44,000 adults (age 18 years and older) in the United States, South Africa and Latin American countries to either a single dose of the Janssen vaccine or placebo.

Results included a 67% reduced risk of symptomatic COVID-19 two weeks: 116 vs 348, in active vs placebo groups respectively.

Side effects were usually mild or moderate and cleared within a couple of days after vaccination. The most common were pain at the injection site, headache, tiredness, muscle pain and nausea.

comment

A date for approval in the UK is not yet available, but news on EU approval was also with notice that access in Europe was not expected until April.

The US FDA approved this vaccine a couple of weeks earlier, on 27 February 2021.

The ENSEMBLE 2 study using a double dose vaccine schedule that includes UK sites is still ongoing. [3]

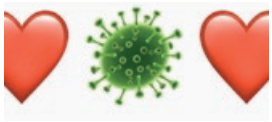
References

1. EMA recommends COVID-19 Vaccine Janssen for authorisation in the EU. (11 March 2021). https://www.ema.europa.eu/en/news/ema-recommends-covid-19-vaccine-janssen-authorisation-eu
2. FDA. Janssen COVID vaccine. https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine
3. ClinicalTrials.gov. A Study of Ad26.COV2.S for the Prevention of SARS-CoV-2-mediated COVID-19 in Adults (ENSEMBLE 2). https://clinicaltrials.gov/ct2/show/NCT04614948

COVID-19: INVESTIGATIONAL TREATMENTS

Baricitinib improves recovery in sub-group of adults hospitalised COVID-19: results from ACTT-2 study

Simon Collins, HIV i-Base



On 4 March 2021, results from a large randomised controlled study reported faster recovery overall from using the oral anti-inflammatory drug baricitinib in adults hospitalised with COVID-19. However, when categorised by baseline clinical score, only a subgroup of participants had a benefit and no effect was reported for those who were either least sick or most sick (based on a clinical ordinal score). [1]

Baricitinib is a JAK inhibitor that inhibits the signaling pathway of cytokines elevated in severe Covid-19, including IL-2, IL-6, IL-10, IFN-gamma and gmCSF and improves lymphocyte counts in patients with Covid-19. Several early studies reported potential benefits. [2, 3, 4]

This large international study included 1033 participants who were randomised to add either baricitinib (oral 4 mg/day or by nasal drip for 14 days) or placebo to current standard of care that included remdesivir (10 days) for all participants. Results have just been published in the NEJM. Although most sites were in the US (55/67) other sites were in Singapore (4), South Korea (2), Mexico (2), Japan (1), Spain (1), the UK (1), and Denmark (1). Enrollment was during May and June 2020.

The primary outcome was median time to recovery with secondary endpoints that included clinical recovery at day 15 measured on an eight point ordinal scale.

Baseline characteristics included mean age 55 years, 63% male, race: 48% white, 15% Black, 10% Asian; 51% were Hispanic/Latino. Mean BMI was 32 and median time from symptom to randomization was 8 days (IQR: 5 to 10). Roughly two-thirds had moderate COVID-19 and one-third severe. Half were receiving supplementary oxygen score 5) with another 20% high flow (score 6) and 10% invasive (score 7).

In the study overall, median recovery with baricitinib vs placebo was 7 day (95%CI: 6 to 8) vs 8 days (95% CI: 7 to 9) with rate ratio: 1.16 (95% CI: 1.01 to 1.32), p=0.03). Baricitinib also improved clinical improvement by 30% at day 15 (OR: 1.3 (95%CI: 1.0 to 1.6).

However, recovery varied considerable depending on ordinal score and use of oxygen at baseline. Baricitinib made no difference for people not using oxygen (score 4), supplemental oxygen (score 5) or who were most ill (mechanical oxygen, score 7) - only showing a significant impact for the 20% of participants with score 6. In this group (with baseline use of high-flow oxygen or noninvasive ventilation) recovery was 10 vs 18 days, with RR: 1.51 (95% CI: 1.10 to 2.08).

Overall mortality at 28-days was 5.1% vs 7.8% which was not statistically significant (HR: 0.65; 95% CI: 0.39 to 1.09).

Serious adverse events were significantly less frequent with baricitinib (16% vs 21%; diff –5.0 percentage points; 95% CI, –9.8 to –0.3) p=0.03. New infections were also significantly reduced (5.9% vs 11.2%; diff –5.3 percentage points; 95% CI, –8.7 to –1.9) p=0.003.

C O M M E N T

UK studies currently using include baricitinib include the TACTIC study and, more recently, the RECOVERY study. [5, 6]

References

1. Kalil AC et al. Baricitinib plus remdesivir for hospitalized adults with covid-19. N Engl J Med 2021; 384:795-807 DOI: 10.1056/NEJMoa2031994. (4 March 2021).
   https://www.nejm.org/doi/full/10.1056/NEJMoa2031994
2. Cantini et al. Retrospective, multicenter study on the impact of baricitinib in COVID-19 moderate pneumonia. J Infect. 2020 doi: 10.1016/j.jinf.2020.04.017. (24 June 2020).
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7313480
3. Titanji BK et al. Use of baricitinib in patients with moderate and severe COVID-19. Clinical Infectious Diseases, ciaa879, DOI: 10.1093/cid/ciaa879. (29 June 2020).
   https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa879/5864596
4. Stebbing J et al. Mechanism of baricitinib supports artificial intelligence-predicted testing in COVID -19 patients. Embo Mol Med (2020), e12697. DOI: 10.15252/emmm.202012697. (24 June 2020).
   https://www.embopress.org/doi/full/10.15252/emmm.202012697
5. ClinicalTrials.gov. Multi-arm therapeutic study in pre-ICU patients admitted with COVID-19 - repurposed drugs (TACTIC-R) (TACTIC-R).
   https://clinicaltrials.gov/ct2/show/NCT04390464
   https://cctu.org.uk/portfolio/COVID-19/TACTIC/TACTIC-R
6. RECOVERY study. Baricitinib to be investigated as a possible treatment for COVID-19 in the RECOVERY trial. (2 February 2021).
   https://www.recoverytrial.net/news/baricitinib-to-be-investigated-as-a-possible-treatment-for-covid-19-in-the-recovery-trial

Ivermectin shows no impact in treating mild COVID-19 in randomised

Simon Collins, HIV i-Base

Results from a randomised placebo controlled study published in JAMA, report no benefit from using the antiparasitic drug ivermectin to treat mild COVID-19. This follows months of speculation that ivermectin might provide a low cost oral treatment that could be used globally.

Between July and November 2020, this study randomised 476 adults with PCR-confirmed mild COVID-19 disease to either combinectin (300 µg/kg) or placebo for five days, given as an oral solution. Mild disease was defined by having had symptoms for less than seven days and not requiring oxygen and participants could be treated at home or in hospital. The study was run at a single site in Columbia.

The original primary endpoint, expected in 18% of participants was worsening symptom by two points in an eight point ordinal scale. This included participants who progressed to hospitalisation of oxygen were combined as an esclation endpoint.

However, fewer progression endpoints during the study and the primary endpoint was changed to time to symptoms recovery, during 21-days follow-up, using the same eight-point scale.

Also, for 17 days at the beginning of October, labelling error meant that all participants received ivermectin. Where these had been new participants, they were excluded from the primary analysis and new patients were recruited, but retained for sensitivity analyses. This meant that overall there were 275 participants in the ivermectin arm and 200 in the placebo group, although the primary analyses included 200 and 198 participants, respectively.

Consent and follow-up was conducted by phone for participants at home.

Baseline characteristics included median age 37 (IQR: 29 to 48), 58% were women, and 79% had no recorded comorbidities. Just over 58% were still at home. Median time from symptoms to randomisation was 5 days (IQR: 4 to 6) in each arm. Most were 1 on the ordinal scale (59% vs 55%) or 2 (39% vs 43%), in the active vs placebo arms respectively.

There were no significant differences in the time to resolving symptoms between the two groups: 10 vs 12 days; HR: 1.07 (95CI: 0.87 to 1.32), p=0.53, with symptoms resolving in 82% and 79% in the active vs placebo groups respectively. Similar results were reported in sensitivity analyses,

Few participants progressed by two points, again with no significant difference between groups: 2 % vs 3.5%, difference –1.53 (95%CI: –4.75 to 1.69).There was also no difference in participants whose care escalated to hospitalisation or oxygen: absolute difference –3.05 (95% CI: –6.67 to 0.56); OR, 0.38 (95% CI: 0.12 to 1.24). Although these numerical results favour ivermectin, this was not statistically significant and results were further attenuated when four participants with very early hospitalisation (median of 3.5 hours after randomisation) were excluded.

The discussion did note the low age and risk of participants and that measuring impact on more serious progressions would need larger studies. However, it also noted that pharmacokinetic models don't support ivermectin reaching effective plasma and total concentrations to be active, even using a dose ten times higher than currently approved.

Adverse events were also similar between the two arms.

C O M M E N T

Although this study had many problems the lack of any significant benefit is disappointing - and also sobering. Several community medical organisations have been lobbying for compassionate access to ivermectin in the US and South Africa. [2, 3, 4]

Several meta-analysis have reported a potential benefit from ivermectin, including well-publicised presentation on YouTube by Andrew Hill, also reported in a pre-review paper. Most of the included studies were small, unpublished and with very different designs and doses. The presentation notes that another 45 studies with >7000 participants are ongoing. [5, 6]

Given the history of negative results from other repurposed medicines without clear PK support for the mechanism of action finding out efficacy will depend on results from randomised controlled studies. In addition to the study here from Columbia, two similar sized studies in Brazil and Argentina are due to report this month. [7, 8]

Their results should decide whether or not other ongoing studies should continue, including the large international ANTICOV study proposing to use ivermectin in 13 African countries.

References

1. López-Medina E et al. Effect of ivermectin on time to resolution of symptoms among adults with mild COVID-19: a randomized clinical trial. JAMA. doi:10.1001/jama.2021.3071. (4 March 2021).
https://jamanetwork.com/journals/jama/fullarticle/2777389

2. Marik P, Kory P. Front line covid-19 critical care alliance (FLCCC). FLCCC alliance response to the NIH Guideline Committee recommendation on ivermectin use in COVID-19. (14 January 2021).
https://covid19criticalcare.com
https://covid19criticalcare.com/wp-content/uploads/2021/01/FLCCC-Alliance-Response-to-the-NIH-Guideline-Committee-Recommendation-on-Ivermectin-use-in-COVID19-2021-01-18.pdf (PDF)
3. Heywood M. South Africa's medicines regulator finds middle ground to authorise 'compassionate use' of ivermectin, whilst still stating that there is not yet sufficient evidence for full registration. Daily Maverick. (27 January 2021).
https://www.dailymaverick.co.za/article/2021-01-27-ivermectin-and-covid-19-sa-drug-regulator-allows-controlled-compassionate-access
4. Sax P. Ivermectin for COVID-19 — breakthrough treatment or hydroxychloroquine redux? MEJM Blog post. (4 January 2021).
https://blogs.jwatch.org/hiv-id-observations/index.php/ivermectin-for-covid-19-breakthrough-treatment-or-hydroxychloroquine-redux/2021/01/04
5. Hill A. Ivermectin meta analysis. Presentation to UNITAIDS. YouTube.
https://www.youtube.com/watch?v=yOAh7GtvcOs (since removed)
https://www.youtube.com/watch?v=FyuIDxn9_IQ (similar lecture reposted)
6. Hill A. Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection. (19 January 2021).
https://www.researchsquare.com/article/rs-148845/v1
7. Comparative study of hydroxychloroquine and ivermectin in COVID-19 prophylaxis.
https://www.clinicaltrials.gov/ct2/show/NCT04447235
8. Ivermectin to prevent hospitalizations in COVID-19 (IVERCORCOVID19)
https://www.clinicaltrials.gov/ct2/show/NCT04529525
9. ANTICOV study.
https://dndi.org/research-development/portfolio/anticov

No benefit from BRII and GSK monoclonal antibodies against COVID-19 in ACTIV-3 study

Simon Collins, HIV i-Base

On 1 March 2021, two sub-studies of the ACTIV-3 trial using monoclonal antibodies (mAbs) to treatment COVID-19 were closed to further enrolment, both due to futility.

This was based on planned early interim reviews and recommendations from the independent Data and Safety Monitoring Board (DSMB).

Each review was based on approximately 340 participants and was designed to detect any signal of early benefit. [1]

The investigational mAbs were VIR-7831 (developed by GSK and Vir Biotechnology) and a dual combination of BRII-196 and BRI-198 (developed by Brii Biosciences).

The ACTIV-3 study is one of five studies looking to rapidly evaluate potential treatments for COVID-19, with each study able to look at multiple different treatments. [2]

An earlier sub-study using bamlanivimab (LY-CoV555 from Eli Lilley) also closed early after finding no benefit in hospitalised participants. However, bamlanivimab has been shown to be effective (in the BLAZE-2 study) when used as prophylaxis against COVID-19. [3, 4]

As with the BRII combination, LY-CoV555 continues to be studies in earlier infection as part of the six-arm ACTIV-2 study.

A fourth study arm using AZD7442 (a mAb developed by AstraZeneca) is still ongoing and further compounds with also be added to ACTIV-3.

References

1. NIH press release. NIH-sponsored ACTIV-3 clinical trial closes enrollment into two sub-studies. (4 March 2021).
https://www.nih.gov/news-events/news-releases/nih-sponsored-activ-3-clinical-trial-closes-enrollment-into-two-sub-studies
2. NIH. COVID-19 therapeutics prioritized for testing in clinical trials.
https://www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials
3. Monoclonal antibody bamlanivimab is not effective in advanced COVID-19: lack of early signal stops study early. HTB (22 January 2021).
https://i-base.info/htb/39663
4. Bamlanivimab (LY-CoV555) prophylaxis prevents COVID-19 in care homes: results of BLAZE-2 study. HTB (24 February 2021).
https://i-base.info/htb/39886

FUTURE MEETINGS

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

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

Virology Education meeting and workshops

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

https://www.virology-education.com

Community HIV Cure Research Workshop 2021

Virtual - just before and after CROI

16 March 2021 (after).

COVID-19 Clinical Forum (one of a series)

Virtual (to cover research presented at CROI)

23 March 2021 at 20:00 CET / 15:00 EDT

11th International Workshop on HIV & Women

26 – 28 April 2021, virtual

https://www.virology-education.com

International Workshop on HIV and Transgender People 2021

17 July 2021. virtual.

https://www.virology-education.com

11th IAS Conference on HIV Science (IAS 2021)

18 – 21 July 2021, Hybrid - virtual and in Berlin

https://www.ias2021.org

12th International Workshop on HIV & Aging

23 – 24 September 2021, virtuaal

https://www.virology-education.com

18th European AIDS Conference (EACS 2021)

27 – 30 October 2021, Hybrid - virtual and in London
https://eacs-conference2021.com

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

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

http://www.i-Base.info

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

Publications and regular subscriptions can be ordered online.

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

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

i-Base treatment guides

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

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

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

Pocket guides

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

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

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

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

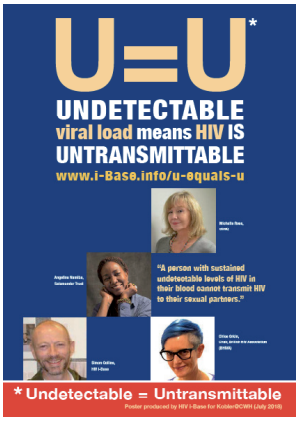
i-Base have produced a new series of posters, postcards and leaflets to help raise awareness about U=U in clincs.

This project was developed with the Kobler Centre in London.

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

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

email: subscriptions@i-base.org.uk



Customise U=U posters for your clinic

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

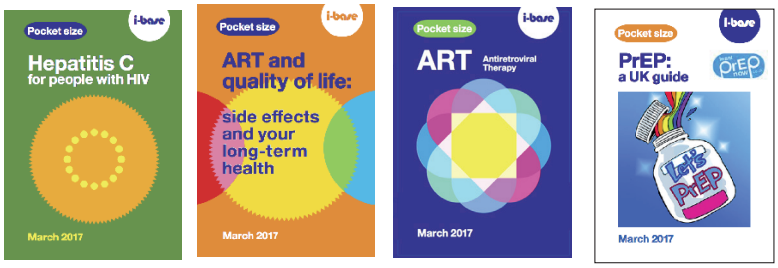
Personalising these for your clinic is cheap and easy and might be an especially nice way to highlight the good news.

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

roy.trevelion@i-Base.org.uk

Order publications and subscribe online

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



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HIV TREATMENT BULLETIN

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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.

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

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U=U resources:

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