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hiv treatment bulletin (e)

Monkeypox crisis UK (1 July 2022)

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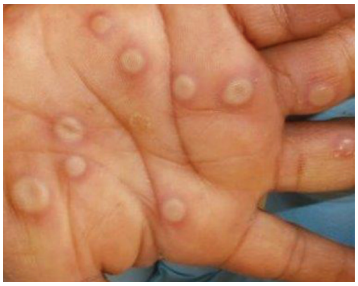
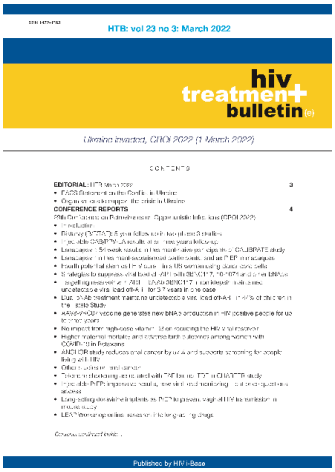
EDITORIAL

This issue of HTB leads with updated information about the monkeypox (MPX) outbreak that has rapidly developed into a health crisis in the UK.



Since 16 May when the initial seven cases had been reported, numbers have approximately doubled every week and by 1 July more than 1075 people have been diagnosed. Globally, there are now more than 4000 cases in 35 countries where MPX is not endemic.

i-Base calls for emergency funding to enable services to adequately respond to the demand for service to cover diagnosis, treatment, management, prevention and information.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hiv treatment bulletin

And we include two recent Q&A to the i-Base information service with information about taking a four-week break from sex. Or at least sex linked to settings where contact with multiple partners is easy and routine.

But the issue includes lots more:

- Reports from the NAMSAL study at CROI 2022
- EU decision to approve lenacapavir to treat MDR HIV – giving priority access to this first in class capsid inhibitor to those with fewest current options.
- Promising results using bNAbs to suppress HIV off-ART in adults.
- Early date supporting the use of dual bNAbs in children.
- Full results from ANCHOR study published in NEJM
- Early news of a potential vaccine against gonorrhoea.
- Review of a study reporting a potential association of cardiovascular events with integrase inhibitors – though based on a single observational study.

We also include several reports on the developments from COVID-19 as the UK enter the early stage of a new wave with BA.4 and BA.5 omicron variants. Two other articles look at vaccine responses in people living with HIV. And reports from the BMJ report on how the government failed to protect doctors from COVID-19.

Plus how tracking PrEP adherence using sensors in the meds and optimistic new that UK funding for UNAIDS has increased this year, though it is still much lower than before last year's cuts.

So, although the July issue of HTB is usually slim in expectation of the upcoming IAS conference and related workshops that are held at the end of this month, we think there is still plenty to read.

Introduction to ART: i-Base guide (June 2022)

The widely used i-Base guide to ART has been updated to include recommendations in the 2022 draft BHIVA guidelines.

Both online and print versions are now updated.

This guide cover information for people newly diagnosed, those about to start ART, and also those who have been living with HIV for many years and who want to learn more about treatment.

https://i-base.info/guides/starting

Changes to this edition include:

- Latest recommendations for ART.
- Information about injectable ART.
- Updates on side effects, including weight changes.
- QR codes linking to additional information online.
- Use of generic meds in the UK.
- Future drugs in development.
- Editing to use fewer words and larger type to make the print booklets easier to read.

As with all i-Base guides, all booklets are free for clinics to order.

https://i-base.info/order

Supporting Ukraine

Simon Collins, HIV i-Base

It is more than three months since Russia invaded Ukraine, displacing more than a third of the population and causing more than 6.8 million people to flee to neighbouring countries.

The significant challenges to support people who remain in Ukraine and those who migrated involves both international and community-based organisations.

HTB includes the following two online resources: one to donate unused medicines and the other to highlight a range of organisations that can benefit from direct financial support.

Sending unused meds to Ukraine: emergency appeal

https://i-base.info/htb/42694

The call for HIV and other meds, and medical supplies is still important. This is even though International agencies and drug manufacturers are also organising to meet this demand.

This project is led by EACS and BHIVA and supported by the UK-CAB.

Medicines need to be in original packaging, ideally in unopened packs. All HIV and related meds are acceptable, *even if they are past the use-by date.*

All donations will be screened beforehand to make sure they are suitable.

The link page includes further details, including postal addresses in the UK, Europe and the US.

Organisations to help support Ukraine

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

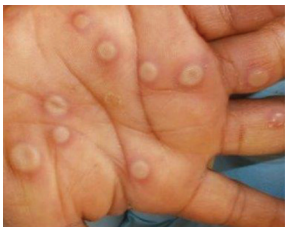
This page including 14 organisations that are helping people affected by the crisis in Ukraine.

This includes organisations that are supporting people living with HIV that are still in Ukraine or who have migrated to other countries.

SPECIAL REPORT

Monkeypox crisis in the UK needs urgent funding: sex, vaccines and Pride

Simon Collins, HIV i-Base



Since 16 May when seven cases of monkeypox (MPX) had been reported, numbers in the UK have approximately doubled every week and by 1 July more than 1075 people had been diagnosed. [1]

MPX is no longer a novel concern that can be absorbed into the work of sexual health clinics and handled by contact tracing.

MPX quickly developed into a health crisis in the UK, that mainly affects networks of gay and bisexual men. Although most cases were initially in London, MPX has now been reported across the UK.

Healthcare responses: the need for rapid emergency funding

The rapid escalation in cases calls for emergency funding to enable services to respond adequately. Emergency funding needs to support diagnosis, treatment, management, prevention and information.

Health policies underestimated the spread of MPX and are now following the crisis rather than leading an adequate response.

- Sexual health clinics, already overstretched, are underfunded to cope with this new outbreak, both for testing or care.
- There is lack of laboratory support to include MPX swabs and samples as part of routine sexual health screen. This could detect asymptomatic infections and current levels of immune responses to plan for vaccine provision.
- Vaccine supplies are so low that the initiative to offer vaccines to people at highest risk, announced last week but without further details, is based on single doses rather than the recommended two dose schedule. See detailed report later in this issue of HTB. [2]

  This will drop expected efficacy to 45% rather than the 85% following two doses. Plans for vaccine roll-out for gay men in New York and Montreal use the two-vaccine schedule. [3]
- Less than 1 in 20 people (5%) are being offered tecovirimat, the likely best treatment. This is being restricted to severe infection, defined as requiring hospitalisation and/or having more than 100 ulcers or blisters. So with only 95 ulcers, advice is to stay home for three weeks and to isolate. Wider access should be offered open-label in addition to any plans for a randomised clinical study. [4]
- The early reliance on contact tracing might help individual cases and is still important. But it is now unable to reduce infections on a population level.
- Unlike COVID-19, so far at least, no support has been announced to help people who are being asked to isolate.

Community responses

MPX is highly infectious in close contact. It is very easily transmitted during close physical contact, whether or not this is sexual. Saliva is a more likely route that sexual fluids making kissing and oral sex possible risks.

So even though MPX is not primarily sexually transmitted, nearly all cases are in men who are gay, bisexual or who otherwise sleep with men. Unfortunately, our communities were unlucky in having some of the early cases.

It is important that many community organisations have been included in helping to shape the response to MPX and this has helped to effectively limit stigma that might otherwise have been linked to the MPX outbreak. Community projects are using their networks to provide information about risk.

But as the UK enter Pride week, the rapid expanded cases probably also need more direct information about risk. This might mean more than advising people to watch out for spots and to wash their hands frequently will have little impact on stopping MPX infections.

Instead, the clearest and most direct advice for an individual to avoid MPX during Pride week is to not have sex in high-risk settings. Or to not have sex with anyone who has had higher-risk sex.

Recent cases reported from Portugal included two important observations. Firstly, that some MPX spots can be difficult to differentiate from an insect bite. Secondly, that one case included a single internal ulcer in the rectum (that was only identified by proctoscopy due to local pain). This case should inform the discussion about the potential for MPX as an STI. [2]

And this strategy will probably work on a population level too. This information is provided knowing that any message to reduce sex will have limited acceptability. It is also possible that the suggestion will produce some less than supportive community responses. This is also an important part of the community response.

This is a short-term suggestion - maybe for four weeks. This covers roughly once cycle (allowing one week from infection to symptoms and three weeks for recovery. Four weeks is long enough to limit the current spread and limit further overloading sexual health services. It is short enough to be socially acceptable as an emergency response.

This strategy includes not having sex in settings where connecting with multiple partners is easy, whether at private parties, saunas, darkrooms or cruising grounds. These settings generally have low light and limited other contact. Plus MPX can remain infectious on hard surfaces for weeks, and on soft materials, likely longer. [5]

Even with careful cleaning, sex-on-premises venues are likely to only be able to reduce risk. In situations where higher risk sex occurs, swapping contact details in case one of you later tests positive for MPX, might be an appreciative acknowledgment of respect.

An otherwise excellent webinar organised by the WHO last week on the implications of MPX for large festivals and other social and community gatherings planned for the summer, did not differentiate events like Glastonbury from Pride. [6]

As part of the wider information on MPX provided by community organisations, i-Base has posted two recent Q&A resources that include information about reducing risk in sexual settings for the upcoming Pride events. [7, 8]

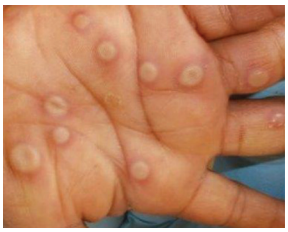
One suggests that the safest way to avoid MPX is to limit sex for four weeks. The second explains why we are not saying to not have sex.

References

1. International Monkeypox case tracker. [Kraemer MUG et al. Lancet Inf Dis, DOI: 10.1016/S1473-3099(22)00359-0] https://monkeypox.healthmap.org
2. EACS/YING. EACS Live! Journal Club webinar. (23 June 2022). https://www.eacsociety.org/activities/eacs-live
3. Collins S. UK offers limited vaccine to gay and bisexual men at risk of monkeypox: full dose offered in NYC. HTB (21 June 2022). https://i-base.info/ht2b/43164
4. NIHR. Efficacy of Tecovirimat for the treatment of non-hospitalised patients with confirmed monkeypox - research brief. (30 May 2022). https://www.nihr.ac.uk/documents/efficacy-of-tecovirimat-for-the-treatment-of-non-hospitalised-patients-with-confirmed-monkeypox-research-brief/30705
5. US CDC. Disinfection of the Home and Non- Healthcare Settings. (6 June 2022). https://www.cdc.gov/poxvirus/monkeypox/pdf/Monkeypox-Interim-Guidance-for-Household-Disinfection-508.pdf (PDF)
6. WHO webinar. Monkeypox and mass gatherings. (24 June 2022). https://www.youtube.com/channel/UC-t0AL4GoNJYJOOtt2UhvMg
7. i-Base Q&A. How can I avoid monkeypox during Pride week? (24 June 2022). https://i-base.info/qa/20053
8. i-Base Q&A. Why is i-Base saying to not have sex during Pride? (24 June 2022). https://i-base.info/qa/20063

Why is i-Base saying to not have sex during Pride?

https://i-base.info/qa/20063



Q: Hi i-Base, why are you telling gay men to not have sex during Pride. Is the risk of MPX really this bad?

A: Hi there

Thanks - great to have this discussion.

First though, i-Base isn't telling anyone to not have sex. But we are providing info for people can make their own choice, and this is one option.

One recent Q&A post asked about how to not catch monkeypox (MPX) during Pride.

The most direct answer is to only have sex with someone who hasn't been at risk of MPX over the last two weeks. It is also accurate to say that the highest risks are likely to be linked to group sex, whether private parties, saunas or outdoor parks - even if you only connect with one person.

This isn't to stop having sex with new partners. Just to say that this is likely to come with a risk of MPX. This is especially true in London, but MPX cases have now been reported across the UK.

The Q&A only suggested stopping anonymous sex for the next few weeks.

This is because risks will either become much higher or much lower over the next month. It might also be possible to have a vaccine by then.

This is the recent Q&A you referred to - which includes more details about MPX and how it is transmitted.

How can I avoid monkeypox during Pride week?

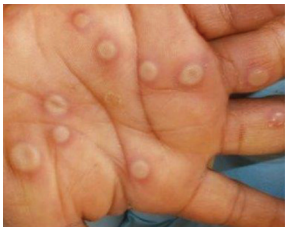
https://i-base.info/qa/20053

More detailed information on MPX:

https://i-base.info/monkeypox

How can gay men avoid monkeypox during Pride?

https://i-base.info/qa/20053



Q: Hi, I am a gay man in London and I am worried about monkeypox. What can I do to stay safe during Pride this week? Will being undetectable on ART help?

Answer:

Thanks for your question.

The easiest way to avoid monkeypox (MPX) is to not have sex for the next few weeks. Or at least, not with anyone who has been at recent risk of catching MPX.

That is the easiest and most direct suggestion.

This will also protect sexual health services who are already are overwhelmed with the current outbreak. These services urgently need rapid and adequate funding to respond to this new outbreak in our communities.

Being on HIV meds is great for HIV but won't protect against MPX. A high proportion of current cases are in men living with HIV. But based on limited data, HIV doesn't make the risk of catching MPX any higher, or make the symptoms any worse.

You can do everything else at Pride that you love doing. March, celebrate, dance – and in any state you like. Just limit physical contact, even though is normally why Pride is so important.

The info below explains why i-Base is giving this information so directly.

The highest risks of catching MPX come from situations when it is easy to have several partners, especially anonymously. This includes in private parties, sauna's, darkrooms, sex-clubs and outdoor cruising spaces.

In some situations MPX is not a rare infection. It is highly infectious. It is very easy to catch and very easy to transmit.

- Skin contact is the highest risk even if you don't have sex with many people.
- Saliva is likely to be infectious, whether kissing or during oral sex.
- Lighting is usually very low so any small rash will not be easy to see.
- In some cases, early spots can look as harmless as as mosquito bite.
- In some cases spots have been reported where they are difficult to see.
- MPX stays active on hard surfaces that are difficult to clean throughout the night.
- MPX can stay active for longer on soft materials like cloths, towels and bedding.

Over the last six weeks, MPX in the UK went from a handful of cases in mid-May to over 800 cases in late June. Although nearly all the early cases were in London, MPX is already reported now across the UK.

Nearly all the cases are in gay and bisexual men, with most occurring when people were likely unaware that anything was wrong. Without careful cleaning, MPX remains infectious on hard surfaces for 2-3 weeks and possibly longer on clothes and towels.

Almost half the cases in one UK study had more than ten partners over the previous few months.

Although MPX is usually a mild infection, it can still be difficult and unpleasant. It also involves self isolation at home, usually for at least three weeks.

Within the next month, there will be much more information about MPX. A vaccine might also become more widely available.

As a caution, one vaccine shot might give 45% protection. This only reduces the risk of catching MPX by about half, but it might also reduce symptoms.

Two shots of the vaccine, given 28 days apart, gives up to 85% protection. However, limited vaccine supplies might mean one shot is initially planned for most people in the UK.

This link is to more detailed information on MPX.

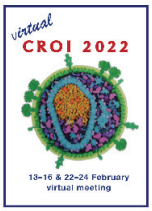
https://i-base.info/monkeypox

CONFERENCE REPORTS

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

13–16 and 22–24 February 2022

Introduction



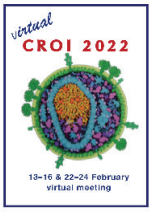
The 29th Conference on Retroviruses and Opportunistic Infections (CROI), was held from 13–16 and 22–24 February 2022.

Further reports from CROI 2022 are listed below.

- NAMSAL study comparing DTG to EFV400 in Cameroon: week 192 results

NAMSAL study comparing DTG to EFV400 in Cameroon: week 192 results

Polly Clayden, HIV i-Base



Four-year follow-up of ART-naive adults living with HIV in Cameroon, who were randomised to either dolutegravir (DTG)-based or low-dose efavirenz (EFV 400)-based treatment, suggests durability of both regimens long-term.

These findings from the NAMSAL study were presented at CROI 2022.

Drug resistance was reported at low rates in the EFV arm and in none of the DTG participants. Weight gain continued to be notable among women receiving DTG.

NAMSAL was an open-label, multicenter, randomised, phase 3 non inferiority trial, conducted over 96 weeks. This was extended as a prospective cohort until week 192.

Adults with viral load >1000 copies/mL were randomised (1:1) to receive DTG or EFV 400 – both combined with tenofovir-disoproxil-fumarate (TDF)/lamivudine (3TC).

The primary end point was the proportion of participants with viral load of <50 copies/mL at week 48.

Week 48 and 96 data showed DTG to be non-inferior to EFV. [2, 3] But DTG was associated with substantial and continuing weight gain, particularly among women.

At week 192, a slightly higher proportion of participants (ITT population) in the DTG arm, achieved viral load <50 copies/mL vs the EFV arm 214/310 (69%) vs 187/303 (62%): difference 7.3% (CI 95% 0.20 to 15.45), p=0.057.

In the fourth-year of follow-up there were five (2 in DTG and 3 in EFV 400 arms) new virological failures without related resistance mutations (NNRTI+/-NRTI).

At week 192, the mean weight gain was greater in women compared to men: women, DTG +8.0 kg and EFV 400 +5.0 kg (p=0.010); men, DTG +6.0 kg, EFV400 +4.0 kg (p=0.024). Incidence of obesity in the respective arms was: women, 17% and 11% (p=0.140) and men 26% and 3% (p<0.001).

The investigators noted that close cardiovascular and metabolic monitoring should be recommended to take into account risks related to weight-gain.

References

1. Mpoudi Ngole-Etame M et al. Long-term outcomes of dolutegravir and efavirenz-400 as first-line ART in Cameroon. CROI 2022.12–16 February. Virtual. Poster abstract 493.
https://www.croiconference.org/abstract/long-term-outcomes-of-dolutegravir-and-efavirenz-400-as-first-line-art-in-cameroon/ (abstract and poster)
2. Clayden P. Dolutegravir non-inferior to low dose efavirenz in real-life African study conducted in Cameroon. HTB. 13 November 2018.
https://i-base.info/htb/35235
3. Clayden P. Dolutegravir non-inferior to efavirenz at week 96 in the NAMSAL study but associated with substantial weight gain. HTB. 28 August 2020.
https://i-base.info/htb/38778

ANTIRETROVIRALS

Lenacapavir gets positive opinion for approval in the EU to treat MDR HIV

Simon Collins, HIV i-Base

On 24 June 2022, the CHMP recommended EU approval for lenacapavir as a treatment for people with multiple drug resistance to other HIV drugs. [1]

This is based on 26-week results from the CAPELLA study that were recently published in the NEJM (and presented at CROI 2022 and EACS 2021). [2]

Lenacapavir is a capsid inhibitor given by subcutaneous injection every six months.

Positive opinions from the CHMP are routinely given full approval in the EU within three months.

C O M M E N T

This is good news - and the first example of an ARV first being approved with an MDR indication.

Lenacapavir needs to be used in combination with other HIV drugs that are active. As monotherapy, it has a low genetic barrier to drug resistance which will quickly lead to loss of this new class.

Cases of viral failure in the CAPELLA study resulted from low adherence to oral ART in the optimised background regimen.

A decision from the US FDA is also expected shortly as Gilead also announced that an issue relating to manufacturing and storage has also been resolved. [3, 4]

References

1. Gilead press release. Investigational lenacapavir receives positive CHMP opinion for people with multi-drug resistant HIV. (24 June 2022).
   https://www.gilead.com/news-and-press/press-room/press-releases/2022/6/investigational-lenacapavir-receives-positive-chmp-opinion-for-people-with-multi-drug-resistant-hiv
2. Lenacapavir in MDR HIV: phase 3 results of CAPELLA study published. HTB (! June 2022).
   https://i-base.info/htb/42883
3. Lenacapavir submitted to EMA for MDR HIV. HTB (17 September 2021).
   https://i-base.info/htb/41294
4. Gilead resubmits new drug application to US Food and Drug Administration for lenacapavir, an investigational, long-acting HIV-1 capsid inhibitor. (27 June 2022).
   https://www.gilead.com/news-and-press/press-room/press-releases/2022/6/gilead-resubmits-new-drug-application-to-us-food-and-drug-administration-for-lenacapavir-an-investigational-longacting-hiv1-capsid-inhibitor

Combination bNAb's sustain viral suppression for 40 weeks: phase 1 results

Kirk Taylor, HIV i-Base

A combination of two broadly-neutralising antibodies (bNAbs) – 3BNC117 and 10-1074 – maintainedundetectable viral load after interrupting ART for over 40 weeks. [1]

This paper was published in 1 June 2022 edition of Nature reported on two studies run from September 2018 to January 2021. The first was a randomised placebo-controlled study in 14 participants already suppressed on ART that had been started during acute infection. A second open-label study was in five treatment naive participants. Neither study screened participants for sensitivity to the bNAbs.

Participants were randomised 1:1 to bNAb's or placebo (Group 1); or enrolled in the open label study (Groups 2). All participants were male, 12/19 were white and median age was 39 (range: 27 to 57).

Median baseline CD4 counts were 799 cells/mm^3 (range: 543 to 1,177) vs 612 cells/mm^3 (426 to 832) in the active vs placebo arms; and 640 cells/mm^3 (540 to 1,1011) in Group 2 where viral load ranged from 200 to 5,000 copies/mL

Participants received bNAbs across 8 infusions: twice in month 1 and then monthly for 6 months, ART was stopped three days after the first infusion.

Those receiving bNAbs in group 1 were off ART for a median of 39.6 weeks (range 9.9 to 49.6). Median viral suppression for 40% of group 2 participants was 41.7 weeks. In Group 1, ART was restarted for 6 out of 7 participants in the placebo group before week 28 (median 9.4 weeks; range 5.3 to 26).

Longitudinal measurements did not indicate a reduction HIV reservoir in participants that received bNAbs. Participant CD4 counts did however remain stable across the study period.

C O M M E N T

Although ART is highly effective, stopping treatment usually leads to rapid viral rebound often within two weeks. Early results using bNAbs have included the potential to maintain viral suppression off-ART.

3BNC117 and 10-1074 are promising bNAb therapies that target the CD4 binding site and V3 loop of the HIV, respectively. Previous studies have also reported sustained suppression off ART. [2, 3]

Of note, both antibodies are older formulations, with more recent LC variants now providing significantly longer half-lives, with a single infusion expected to last more than 16 weeks.

The long-acting formulations of these bNAbs are included in the UK RIO study that is currently recruiting in London and Brighton and shortly begin in Manchester. [4]

References

1. Sneller MC et al. Combination anti-HIV antibodies provide sustained virological suppression. Nature. Doi: 10.1038/s41586-022-04797-9 (01 Jun 2022).
   https://www.nature.com/articles/s41586-022-04797-9
2. Mendoza P et al. Combination therapy with anti HIV-1 antibodies maintains viral suppression. Nature. DOI: 10.1038/s41586-018-0531-2 (26 Sep 2018)
   https://www.nature.com/articles/s41586-018-0531-2
3. Jefferys R. CROI 2022: targeting reservoir with ART + bNAb 3BNC117 + romidepsin maintained undetectable viral load off-ART for 3.7 years in one case. (HTB 01 Mar 2022).
   https://i-base.info/HTB/42209
4. The RIO study.
   https://riotrial.org

PAEDIATRIC CARE

Dual bNAbs in children: dose-finding and safety data using VRC01LS and 10-1074 in the Tatelo study

Polly Clayden, HIV i-Base

Treatment with dual broadly neutralising monoclonal antibodies (bNAbs) was safe and well-tolerated in children receiving ART. [1]

Initial dose-finding and safety data from the Tatelo study was published ahead of print in JAIDS, 9 June 2022.

Trough levels exceeded minimal targets with four-weekly administration of 10-1074 dosed at 30 mg/kg and VRC01LS at 15 mg/kg.

The Tatelo study (A clinical trial to evaluate the impact of broadly neutralising antibodies VRC01LS and 10-1074 on maintenance of HIV-1 suppression in a cohort of early-treated children in Botswana) is an ongoing phase 1/2, multi-site clinical trial in virally suppressed children with HIV.

The overall aim is to evaluate dual bNAb treatment as an alternative to ART for up to 24 weeks.

The JAIDS manuscript covered the first two phases of the study (phases A and B) for dose-finding and safety. Data recently presented at virtual CROI 2022, showed treatment with dual bNAbs maintained viral suppression in 44% of children (n=25) for 24 weeks without ART. [2]

In the first pharmacokinetic (PK) and safety phase (phase A), 6 children on suppressive ART were given 3 intravenous (IV) doses (every 4 weeks) of 10-1074, and 6 received 3 (IV) doses (every 4 weeks) of VRC01LS and received safety and PK testing for 12 weeks.

These data were reviewed by a Safety Monitoring Committee before continuing the second phase of the study (phase B). In phase B, the children continued ART and 6 received both bNAbs every 4 weeks, with PK evaluation of dual bNAb dosing for 8 weeks, and safety evaluations for 32 weeks.

Eligible children had started ART before they were 7 days old and continued for at least 96 weeks, with viral load <40 copies/mL for at least 24 weeks before enrollment.

In phase A, 6 children received 10-1074 (30 mg/kg on day 0, 28, and 56) and 6 VRC01LS (30mg/kg on day 0, 10mg/kg on days 28 and 56).

Their median age at baseline was 3.1 years (range 2.1 to 4.1). Nine of 12 (75%) were girls.

All children were treated with lopinavir/ritonavir (LPVr) plus zidovudine (AZT) and lamivudine (3TC); one child also received abacavir. All started phase A on the LPVr liquid formulation; 7 switched to solid formulations (granules and/or tablets) during the study.

In phase B, 6 children received dual bNAb treatment (with higher VRC01LS maintenance dose, 15 mg/kg) every 4 weeks for 32 weeks with PK evaluations over 8 weeks.

At the start of phase B, median age was 4.5 years (range 3.4 to 4.9). All children sustained an undetectable viral load, while continuing LPVr/AZT/3TC.

The investigators developed population PK models to predict steady-state concentrations.

The study found the bNAbs to be well-tolerated in both phases. There were no infusion reactions or any bNAb-related grade 3⁄4 adverse events.

The first dose median Cmax and trough (day 28) for 10-1074 were: 1,405 mcg/mL (range 876 to1,999) and 133 mcg/mL (84 to 319). These values for VRC01LS were: 776 mcg/mL (range 559 to 846) and 230 mcg/mL (range 158 to 294).

The investigators noted that these concentrations were similar with single or dual bNAbs. They also reported little accumulation of 10-1074 Cmax with repeated doses of 30 mg/kg in both phases. Cmax after the second dose (10–15 mg/kg) of VRC01LS was lower than the Cmax after the first dose of 30 mg/kg.

10-1074 trough concentrations increased with each 30 mg/kg dose and the median 10-1074 day 84 concentration in phase B was 258 mcg/mL (range 122 to 467).

Based on adult data, the steady-state VRC01LS concentrations were expected to be 200 mcg/mL or more with 10 mg/kg IV every 4 weeks. But the median VRC01LS day 84 concentration in phase A was 156.9 mcg/mL (range 125.8 to 201.4). So the investigators increased the VRC01LS maintenance dose to 15 mg/kg for phase B.

The median first dose Cmax and trough combined from both phases were: 1,405 (range 876 to 1,999) mcg/mL and 133 (range 84 to 319) mcg/mL for 10-1074 and 776 (range 559 to 846) mcg/mL and 230 (158 to 294) mcg/mL for VRC01LS.

The investigators reported less Cmax/trough fluctuation and higher steady-state troughs with VRC01LS than 10-1074, despite the lower maintenance dose of VRC01LS. They noted this was to be expected because of slower elimination associated with the LS modification.

The predicted median steady-state troughs with phase B dosing for 10-1074 and VRC01LS were 261 mcg/mL and 266 mcg/mL, respectively. Both met the pre-specified targets for phase B and this dosing was approved for the final phase of the Tatelo Study, using dual bNAbs without ART.

COMMENT

These initial PK and safety data from the Tatelo Study provide the first information to guide IV use of dual bNAbs in children, and the first data on 10-1074 use in this population. The findings support further evaluation of these two agents as paediatric treatment strategy.

Further proof-of-concept data from Tatelo, presented at CROI [2], went on to show dual bNAb treatment with VRC01LS and 10-1074 maintained viral suppression for 24 weeks in the absence of ART.

Four-weekly IV dosing is not without complications and longer acting LS formulations (including 10-1074-LS) might enable less frequent dosing intervals (3 to 6 montly) that could potentially make bNAb use easier for both adults and children.

References

1. Capparelli EV et al. Safety and pharmacokinetics of intravenous 10-1074 and VRC01LS in young children. JAIDS Journal of Acquired Immune Deficiency Syndromes. Volume 10. Issue 1097. 9 June 2022. https://journals.lww.com/jaids/pages/articleviewer.aspx?year=9900&issue=00000&article=00064&type=Abstract
2. Clayden P. Dual bNAb treatment maintains undetectable viral load off-ART in 44% of children in the Tatelo Study. HTB. 1 March 2022. https://i-base.info/htb/42175

COMPLICATIONS

UK offers limited vaccine to gay and bisexual men at risk of monkeypox: full dose offered in NYC

Simon Collins, HIV i-Base

On 21 June 2022, the UKHSA announced plans to offer a vaccine against monkeypox (MPX) to (some) gay and bisexual men. [1]

Although this strategy has been wanted by many people at highest risk, vaccines until now have been mainly given to heatlh workers or houseold contacts of people with confirmed MPX.

The Imvanex vaccine is non-replicating and can be given in people with reduced immune systems, including in people living with HIV. Although it is only approved in Europe to protect against smallpox, it is also approved in the US as a vaccine against monkeypox. [2, 3]

The announcement include few details on access to the vaccine but more details are expected shortly.

Criteria for access are suggested as similar to PrEP (but irrespective of HIV status). This will likely include people who "have multiple partners, group sex or who attend sex-on-premises venues".

Current stocks cover about 20,000 people with additional order expected next month and in September. In people not already vaccinated against smallpox, the vaccine is usually given in two injections, 28 days apart.

However, limited vaccine stocks mean that men in the UK will initially only be given one vaccine shot. This is expected to provide up to 45% protection. The time needed for protection to develop is not currently clear.

New York City recently announced a vaccine programme that will be given as two injections. This is being made available to "all gay, bisexual, and other men who have sex with men (cisgender or transgender) ages 18 and older who have had multiple or anonymous sex partners in the last 14 days". [4]

Uptake is extremely high, with stocks being used almost as soon as they have been delivered. [5]

On 28 June 2022 the US Department of Health (HSS) announced a national vaccine programme using 290,000 doses of the Jynneos vaccine (56,000 available immediately and the rest within a few weeks). This decisions was made after only 300 cases had been diagnosed in the US. [6]

C O M M E N T

Although this is initially good news, but current stocks will need to be made available quickly if they are to make much impact on the current outbreak.

Demand for the vaccine is likely to be high. Even though most MPX cases are mild, few people want to limit social interactions or spend weeks in self isolation, just as summer approaches.

However, the proposal to use single doses with much lower rates of protection might have much lower impact on future cases. Many people might not want to rely on 45% protection and instead continue just avoiding higher risk situations. This would effectively waste the currently limited vaccine supplies.

The increase in MPX cases over the last four weeks has been exponential in the UK, with more than 900 people diagnosed by the end of June. As many of the new cases have also not been connected to known transmission networks, MPX has already spread much more widely than initially thought.

Vaccine demand will also quickly become limited on an international level.

In Canada, Montreal planned to widely vaccinate gay and bisexual men at highest risk, at a time when only 136 cases had been reported. [7]

References
1, UKHSA press release. Monkeypox vaccine to be offered more widely to help control outbreak. (21 June 2022). https://www.gov.uk/government/news/monkeypox-vaccine-to-be-offered-more-widely-to-help-control-outbreak
2. EMEA. Imvanex. Summary of product characteristics (SPC). https://www.ema.europa.eu/en/medicines/human/EPAR/imvanex
3. FDA. Jynneos. Summary of product characteristics (SPC). https://www.fda.gov/vaccines-blood-biologics/jynneos

4. NYC Health Department. Health Department Launches Monkeypox Vaccine Clinic for People Who May Have Been Exposed to Monkeypox. (23 June 2023).
https://www1.nyc.gov/site/doh/about/press/pr2022/monkeypox-vaccine-clinic.page
5. NBC New York. NYC monkeypox cases rise again as Feds tap stockpile for emergency vaccines. (28 June 2022).
https://www.nbcnewyork.com/news/local/nyc-monkeypox-cases-rise-again-as-feds-tap-stockpile-for-emergency-vaccines/3755312/
6. HHS press release. HHS Announces Enhanced Strategy to Vaccinate and Protect At-Risk Individuals from the Current Monkeypox Outbreak. (28 June 2022).
https://www.hiv.gov/blog/hhs-announces-enhanced-strategy-vaccinate-and-protect-risk-individuals-current-monkeypox
7. CBC news. Quebec expands monkeypox vaccination efforts as virus continues to spread. (14 June 2022).
https://www.cbc.ca/news/canada/montreal/monkeypox-quebec-montreal-vaccine-expansion-1.6488551

Full results from ANCHOR study published in NEJM

Simon Collins, HIV i-Base

Results from the large US ANCHOR study showing the importance of actively treating high grade interepithelial lesions (HSIL) to prevent anal cancer have now been published in the NEJM. [1]

Even though cases of anal cancer are rare, the incidence among HIV positive gay men is 89 per 100,000 person-years. The rate in women living with HIV is from 18.6 to 35.6.

In the general population, this compares to rates of 1.6 for anal cancer and 7.5 for cervical cancer among women in the US.

Screening approximately 10,000 people living with HIV who were older than 35 led to roughly half being diagnosed with HSIL. Of these, ANCHOR randomised 4446 participants to either treatment (mainly with clinic-based electrocautery) or to active monitoring.

Over median follow-up of 26 months, participants in the active arm were 57% less likely to progress to anal cancer (95%CI: 6 to 80; p=0.03). Overall, 30 participants were diagnosed with invasive anal cancer (9 active, 21 monitoring only). Benefits were also reported for the 25 people who were non-adherent to active treatment.

The NEJM paper includes more details about progressions rates. For example, progression rates per 100,000 person-years were 173 (95%CI: 90 to 332) vs 402 (95%CI: 262 to 616) in the active vs monitoring groups respectively. This was higher than expected in the control arm, perhaps due to earlier diagnosis of HSIL. It also shows that treatment was not always successful.

Time to progression (hazard ratio) was also significantly associated with lesion size (HR 5.26; 95% CI: 2.54 to 10.87) but not with nadir CD4 count (HR: 1.93; 95% CI: 0.88 to 4.23).

However, nadir CD4 count was <200 cells/mm3 in 70% (21/30) in the group with progression vs 50% (2230/4416) in those without.

The rate of progression was also significantly higher in participants with a lesion size of more than 50% of the anal canal or perianal region.

This was one of the headline studies from CROI 2022 that we reported in details in HTB in March. [2]

References

1. Palefsky J et al. Treatment of anal high-grade squamous intraepithelial lesions to prevent anal cancer. N Engl J Med 2022; 386:2273-2282 DOI: 10.1056/NEJMoa2201048. (16 June 2022).
https://www.nejm.org/doi/full/10.1056/NEJMoa2201048 (main article)
https://www.nejm.org/doi/suppl/10.1056/NEJMoa2201048/suppl_file/nejmoa2201048_appendix.pdf (supplementary material)
2. ANCHOR study reduces anal cancer by 57% and supports screening for people living with HIV. HTB (1 March 2022).
https://i-base.info/htb/42226

Gonorrhoea vaccine might halve infections and help combat drug resistance

Kirk Taylor, HIV i-Base

New research indicates that a meningitis vaccine might reduce gonorrhoea transmission by 46%. [1]

This is important given how common gonorrhoea remains in the UK and the concerns over antibiotic-resistant strains which call for new treatment, even currently treated with ceftriaxone.

Gonorrhoea and meningitis are genetically similar and both express outer membrane vesicles (OMV). The two major meningitis vaccines: MenACWY and 4CMenB target surface sugars and OMV, respectively. MenACWY

is widely used with 2CMenB used for meningitis B outbreaks.

Observational studies noted lower gonorrhoea case rates in young adults that had received 4CMenB vaccination. [2]

Researchers conducted a retrospective cohort study of young adults registered at Kaiser Permanente Southern California (KPSC) to evaluate links between gonorrhoea transmission and meningitis vaccines. Participants that had received at least one 4CMenB dose were matched 1:4 with people that received MenACWY only.

The 4CMenB group (n= 6,641) were female (55.1%), White (37.4%), Hispanic (32.2%), Black (9%), Asian (15.3%) and median age at first vaccination was 18 (IQR: 17 to 20). The MenACWY only group (n= 26,471) were female (54.9%), White (38%), Hispanic (47.7%), Black (8.5%), Asian (10.8%) and median age at first vaccination was 18 (IQR: 17 to 19).

Gonorrhoea rates per 1,000 person years were 2.0 (95% CI: 1.3 to 2.8) vs 5.2 (95% CI: 4.6 to 5.8) for the 4CMenB and MenACWY only groups, respectively. 4CMenB was associated with 46% lower chance of gonorrhoea transmission.

Gonorrhoea rates were higher amongst HIV positive people and those using PrEP. Adjusted hazard ratios for 4CMenB vs MenACWY only groups were 6.99 (95% CI: 3.79 to 12.89) and 9.10 (95% CI: 5.07 to 16.33) for HIV positive people and PrEP users, respectively.

These findings suggest that re-purposing meningitis vaccines could be a valuable tool in the fight against antibiotic-resistant gonorrhoea. It will therefore be important to follow the outcomes of an interventional trial in this area. [3]

C O M M E N T

This is an interesting study that provides hope for a gonorrhoea vaccination by repurposing an existing and well-tolerated meningitis vaccine.

Further studies are required to evaluate efficacy in HIV positive people due to low sample sizes; n= 6 and 294 for 4CMenB and MenACWY only, respectively.

References

1. Bruxvoort KJ et al. prevention of Neisseria gonorrhoeae with meningococcal B vaccine: a matched cohort study in Southern California. Clinical Infectious Diseases. https://doi.org/10.1093/cid/ciac436 (01 Jun 2022).
https://academic.oup.com/cid/advance-article-abstract/doi/10.1093/cid/ciac436/6596517?redirectedFrom=fulltext
2. Paynter J et al. Effectiveness of a group B outer membrane vesicle meningococcal vaccine in preventing hospitalisation from gonorrhoeae in New Zealand: A retrospective cohort study. Vaccines. DOI: 10.3390/vaccines7010005 (05 Jan 2019).
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6466174/#!po=65.3846
3. Safety and efficacy study of meningococcal group B vaccine rMenB+OMV (Bexsero) to prevent gonococcal infection. https://clinicaltrials.gov/ct2/show/NCT04350138

INSTIs and cardiovascular events in the RESPOND cohort: early increase at six months normalises after two years

Kirk Taylor, HIV i-Base

New data from the international multi-cohort RESPOND study published in The Lancet HIV reports a link between cardiovascular disease (CVD) and integrase inhibitors (INSTIs). [1]

Over a median follow-up of six years, the incidence of CVD for people on INSTI-containing regimens was approximately twice as high as for people not using INSTIs: at 8 vs 4 events per 1,000 person years. This association was greatest at six months but normalised after two years.

The RESPOND consortium collected data from on CVD events from 17 Australian and European cohorts. Baseline demographics of the INSTI-naive participants (n=29,340) included male (74%). female (25%). transgender (<1%); White (70%), Black (10%). The median age was 44 (IQR: 36 to 51) and recent CD4 counts were 524 (IQR: 357 to 715) cells/mm^3. [1]

Retrospective data was included for 5 years prior to enrolment and prospectively updated annually thereafter. CVD events were centrally validated for those that occurred in the year prior to enrolment and thereafter. This included fatal and non-fatal myocardial infarction, strokes, and invasive coronary procedures (coronary angioplasty or stenting, bypass surgery and carotid endarterectomy).

Participants on INSTI-based regimens were taking dolutegravir (62%), elvitegravir (24%), raltegravir (24%) or

bictegravir (6%). The study was not powered to detect associations for specific INSTIs.

Over a median follow-up was 6.16 years (IQR: 3.87 to 7.52) there were 748 events giving an incidence of CVD of 2.5%. Myocardial infarction was most common (40%), followed by stroke (30%) and invasive procedures (30%). The incidence rate across the cohort was 4.67 events (95% CI: 4.34 to 5.01) per 1,000 person years.

CVD incidence was reported at baseline 6, 12, 24, 36 and ≥36 months. At 6 months, CVD incidence increased from 4.19 (95%CI: 3.83 to 4.57) to 8.46 (95% CI: 6.58 to 10.71) events per 1000 person years for people on INSTI-based regimens.

However, there was no cumulative link to use of INSTI-based ART. Instead, CVD risk decreased after six months and was no longer significant at two years.

Baseline risk factors (smoking, hypertension, diabetes, kidney disease, smoking status, dyslipidaemia and age) were good predictors of CVD events during follow-up. However, the higher early association with INSTI-based ART remained after adjustment for traditional CVD risks above and HIV history including CD4 counts and HIV treatment.

The INSTI signal remained in several sensitivity analysis except when the model only included centrally adjudicated CVD events (n=145). In this case the adjusted incidence rate ratio dropped to 1.37 (95%CI: 0.89 to 2.12) and was no longer significant (p=0.22).

Mechanism for CVD risk

As an observational study, RESPOND is unable to identify causal links for CVD risk.

The early increase of risk means that slower progressing conditions (e.g. atherosclerosis) are unlikely to be at play. The authors also ruled out dyslipidaemia, hypertension, and immune reconstitution syndrome.

The accompanying editorial further reflects on the mechanism. It notably rules out INSTI-associated weight gain, as adjustment for BMI did not explain the increased CVD risk. [2]

Insomnia is linked to both INSTI use and CVD risk and warrants further investigation. Biomarker and switch studies have also noted complex changes of inflammatory profiles for INSTIs that may explain transient rises of CVD risk.

If these changes are short-lived, it is possible that modification of traditional CVD risk factors could reduce the signal at 6 months.

C O M M E N T

This INSTI-naive cohort was largely treatment experienced. Traditional risk factors for CVD were also significantly associated with risk of CVD events.

The results therefore describe an increased initial risk of CVD of the first six months that then steadily normalises over the next 18 months. The early risk though remained after adjusting for baseline CVD risk, including use of PIs and abacavir.

Established links between CVD and other HIV drugs include a cumulative association with indinavir, lopinavir, and darunavir and an association with recent use of abacavir in people at higher baseline CVD risk.

The discussion is not able to explained the observed short-term increase in CVD including a platelet mechanism (similar to abacavir). It also notes the lask of association between INSTIs and early CVD in regulatory phase 3 studies and calls for further research in larger studies.

INSTIs are recommended as first-line therapy in BHIVA guidelines as they have a high barrier to genetic resistance, rapidly lower viremia and restore CD4 counts. [3]

The RESPOND consortium was formed in 2017 with the earliest data from 2012 before INSTIs were recommended as first-line ARVs. Dolutegravir received FDA approval in 2013 and was the most frequently used INSTI in the current study. Bictegravir was approved 5 years later, and less data is available for this structurally similar INSTI. More data points are required to evaluate signals for specific INSTIs.

A meta-analysis of eight randomised trials investigated links between DTG and CVD. [4]

Serious adverse cardiovascular events were 0.7% for DTG and 0.4% for other ARVs (raltegravir or efavirenz). The increased relative risk of 1.6 was not significant and only one event was considered DTG-related. The majority of serious adverse events (19/23) were in people with underlying CVD risk factors.

The authors suggest that studies of platelet function for people on INSTIs should be investigated to evaluate this as a

potential mechanism. A poster from CROI 2019 reported a modest reduction of platelet function for HIV negative volunteers that received DTG for one week. [5] Further studies of platelet function in HIV positive people on INSTI-based regimens are required to explore this mechanism.

There are similarities to the abacavir and CVD risk reported by the D:A:D study. The risk for people on abacavir regimens was only in people that already had elevated CVD risk, largely driven by age. This is a major reason why the RCTs by GSK did not find a link. [6]

The earliest reports from D:A:D initially reported a signal for ART and then later by ARV class. Both these initial signals were misleading though because longer follow-up was needed to show associations to individual drugs rather than drug classes. RESPOND is not currently able to report on individual drugs.

Until then, the most optimistic outcome, as suggested in the accompanying editorial comment, is that a class effect is not confirmed in future studies. [2]

References

1. Neesgaard B et al., Associations between integrase strand-transfer inhibitors and cardiovascular disease in people living with HIV: a multicentre prospective study from the RESPOND cohort consortium. The Lancet HIV. DOI:10.1016/S2352-3018(22)00094-7. (07 June 2022). https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00094-7/fulltext
2. Venter WDF et al., Integrase inhibitors hand us a new HIV clinical puzzle. The Lancet HIV. DOI:10.1016/S2352-3018(22)00122-9. (07 June 2022). https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00122-9/fulltext
3. BHIVA guidelines on antiretroviral treatment for adults living with HIV-1 2022 – consultation version. (09 June 2022). https://www.bhiva.org/guidelines
4. Hill AM et al., Risks of cardiovascular or central nervous system adverse events and immune reconstitution inflammatory syndrome, for dolutegravir versus other antiretrovirals: meta-analysis of randomized trials. Current opinion in HIV and AIDS. DOI:10.1097/COH.0000000000000445. (March 2018) https://journals.lww.com/co-hivandaids/Abstract/2018/03000/Risks_of_cardiovascular_or_central_nervous_system.3.aspx
5. Taylor KA et al., Platelet function after dolutegravir and/or darunavir/cobicistat in healthy subjects. CROI 2019. 4-7 March 2019, Seattle. Poster 640. https://www.croiconference.org/abstract/platelet-function-after-dolutegravir-andor-darunavircobicistat-healthy-subjects/
6. Increased risk of myocardial infarction associated with abacavir and ddI. HTB (1 February 2008). https://i-base.info/htb/1792

COMPLICATIONS: COVID-19

New wave of COVID-19 in the UK with BA.4 and BA.5: all omicron variants linked to reduced antibody responses to vaccines

Simon Collins, HIV i-Base

The last two webinars from the excellent weekly webinars from the Independent Sage group continues to report on COVID-19 in the UK. Over the last three weeks positive diagnoses are increasing in all countries in the UK, with highest rates in Scotland and Northern Ireland. This is now driven by BA4 and BA.5 omicron variants. [1]

Hospital admissions are still increasing, especially in those older than 65, although rates are still relatively low compared to earlier peaks (especially January 2021).

Approximately 20-25% of the UK population is still unvaccinated and only 10-20% of children age 5 to 11 have so far received a first vaccine.

The latest webinar also covered COVID treatment, including antiviral treatments and mAbs (important for the roughly 500,000 people in the UK who do not respond to vaccines).

There are currently 5008 people hospitalised with COVID-19 which is still much lower than the 16,000 in April. Numbers in intensive care are also still low.

Correspondence in the latest issue of the NEJM also reports the importance of booster doses of COVID vaccines, as antibody titres are reduced against all omicron variants, and especially against BA.4 and BA.5.

Researchers from the Beth Israel Deaconess Medical Center, Boston reported antibody titres against omicron variants in 27 participants receiving a booster dose of the Pfizer mRNA vaccine.

Two weeks after the booster, median neutralising antibody titres significantly increased to 5783 against the

WA1/2020 reference isolate, and to 900, 829, 410 and 275 against the BA.1, BA.2, BA.2.12.1 and BA.4/5 subvariants, respectively. Compared to the reference isolate, titres were reduced by factors of 6.4, 7.0, 14.1 and 21.0 against the same subvariants, respectively.

Similar results were reported for people who had been recently infected with BA.1 or BA.2, despite vaccination.

C O M M E N T

Together, the results show that the latest subvariants substantially escape neutralising antibodies induced by both vaccination and infection and that the virus has continue to evolve in the BA.4 and BA.5 strains.

They also explain the increased cases that are now being reported again,

References
1. Independent SAGE.
https://www.youtube.com/watch?v=g8pC_bOu4fA (24 June 2022)
https://www.youtube.com/watch?v=g60waH14oZg (17 June 2022).
2. Hachmann NP et al. Neutralization escape by SARS-CoV-2 omicron subvariants BA.2.12.1, BA.4, and BA.5. NEJM. DOI: 10.1056/NEJMc2206576 |. (22 June 2022).
https://www.nejm.org/doi/full/10.1056/NEJMc2206576

Importance of booster vaccines to protect against emergent COVID-19 strains

Kirk Taylor, HIV i-Base

A small study showing the importance of booster vaccination to protect against COVID-19 variants by researchers from Ohio University was published as a letter in the 15 June edition of the NEJM. [1]

Neutralising antibody (nAb) titres against different COVID-19 strains were analysed from stored serum samples. Participants were healthcare workers that had been triple vaccinated with Moderna (n=4) or Pfizer (n=11) mRNA vaccines. Additional samples from people admitted to ICU during the delta wave (n=18) or hospitalised during omicron wave (n=30) were also studied.

Compared to the D416G COVID-19 strain, nAb titres were 4.1-fold and 3.2-fold lower against BA.4/5 and BA.2.12.1 variants, respectively ($p<0.001$).

Overall, nAb titres against emergent strains were lowest in twice vaccinated participants. Boosting or previous COVID-19 disease generated greater levels of nAbs compared to unboosted individuals.

C O M M E N T

This is a short letter to NEJM that concerns an important topic, but it is important to note that the sample sizes are low.

Boosting of immune responses following COVID-19, is strain-dependent. A study of 700 triple vaccinated healthcare workers in the UK reports that immune boosting is lower for omicron than compared to other variants. [2]

These data highlight the importance of receiving COVID-19 boosters as required by local vaccination programmes.

References
1. Qu P et al. Neutralization of the SARS-CoV-2 omicron BA.4/5 and BA.2.12.1 subvariants. NEJM. DOI: 10.1056/NEJMc2206725 (15 Jun 2022). https://www.nejm.org/doi/full/10.1056/NEJMc2206725
2. Reynolds CJ et al. Immune boosting by B.1.1.529 (Omicron) depends on previous SARS-CoV-2 exposure. Science. DOI: 10.1126/science/abq1841 (14 Jun 2022).
https://www.science.org/doi/10.1126/science.abq1841

Similar COVID-19 vaccination responses in HIV positive people on ART and with good CD4 counts compared to HIV negative controls

Kirk Taylor, HIV i-Base

A small Canadian cohort reported similar vaccine responses irrespective of HIV status although people living with HIV in the study were on ART with CD4 counts generally above 200 cells/mm^3. [1]

The participants living with HIV (n=99) were aged 54 (IQR: 40 to 61), male (88%) and ethnicity was White (69%), Black (5%) or Asian (10%). Recent CD4 counts were 715 cells/mm^3 (IQR: 545 to 943) at entry, whilst CD4 nadir was 280 cells/mm^3 (IQR: 123 to 490). Viral load was <50 copies/mL on ART.

Control participants (n=152) were aged 47 (IQR: 35 to 70), male (33%) and ethnicity was White (51%), Black (0.7%) or Asian (38%).

Antibody responses were comparable and booster vaccines equally effective for both groups. Although protection against the omicron variant was reduced compared to wild-type virus. Greatest antibody responses were in people that received mRNA boosters.

Lower antibody responses were associated with being older, having co-morbidities and receiving two doses of adenoviral-based vaccines.

However, CD4 counts correlate with vaccine response and nearly all participants were >200 cells/mm^3 which generates greater antibody responses.

The present study did not detect differences in post-vaccination antibody levels between groups, but it is unclear whether people with HIV that received mRNA vaccines received higher doses, as recommended.

C O M M E N T

As with many other similar studies, only one or two of the people living with HIV had CD4 counts <200 cells/mm^3 which has been linked to reduced antibody responses but neither the paper nor the editorial commented on this.

The authors did not discuss this limitation of the study although an commentary questioned whether immune responses would be lower with unsuppressed viral load and CD4 counts <200 cells/mm^3. [2]

Although most people on ART have CD4 counts >200 cells/mm^3, late diagnoses is still common, often at CD4 counts where vaccine protection should not be assumed.

Recent studies report lower incidence of breakthrough COVID cases for people with higher CD4 counts, and a greater chance of severe symptoms for those with CD4 counts <350. [3, 4]

References

1. Lapointe HR et al. People with HIV receiving suppressive antiretroviral therapy show typical antibody therapy durability after dual COVID-19 vaccination, and strong third dose responses. J. Inf. Dis. DOI:10.1093/infdis/jiac229 (07 June 2022).
https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiac229/6603521
2. Jacobsen JM. Immune responses to SARS-CoV-2 vaccination in people with HIV: A tale of two pandemics. J. Inf. Dis. DOI: 10.1093/infdis/jiac231 (07 June 2022).
https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiac231/6603522
3. Coburn SB et al. Analysis of postvaccination breakthrough COVID-19 infections among adults with HIV in the United States. JAMA. DOI:10.1001/jamanetworkopen.2022.15934 (07 June 2022).
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793102
4. Lang R et al. Analysis of severe illness after post-vaccination COVID-19 breakthroguh among adults with and without HIV in the United States. medRxiv. DOI: 10.1101/2022.04.15.22273913. (16 April 2022).
https://www.medrxiv.org/content/10.1101/2022.04.15.22273913v1

US study reports higher rates of breakthrough COVID in HIV positive vs negative controls

Kirk Taylor, HIV i-Base

A large US cohort study reported that although rate of breakthrough infections were generally low, this was 28% higher in people living with HIV.

The study, published in JAMA matched controls (n=80,965) 3:1 to HIV positive people (n=33,029) and compared incidence of COVID-19 following vaccination.

The incident rate for breakthrough cases (per 1,000 person years) was 55 (95% CI: 52 to 58) vs 43 (95% CI;

42 to 45) in HIV positive vs negative controls.

Participants were well matched between groups and were male (92%), White (38%), Black (41%), Hispanic (13%) and Asian (3.4%), 70% were aged ≥55 (range: 18 to ≥75) and 98% received mRNA vaccines.

HIV was well controlled with 91% <50 copies/mL and CD4 counts of 636 cells/mm^3 (95% CI: 449 to 858) after full vaccination. Nadir CD4 counts were 636 cells/mm^3 (95% CI: 202 to 584).

Breakthrough cases were lower for people with HIV aged ≥55 who received mRNA vaccines and for those with CD4 counts ≥500 cells/mm^3. There were no differences is risk of severe illness between the two groups.

Cases were more common for people that received adenoviral vaccine this only represented 2% of participants.

C O M M E N T

Breakthrough COVID-19 cases following vaccination account for a small percentage of all cases in the USA. Many studies have now reported comparable immune responses for people with HIV with good CD4 counts on ART.

The authors report associations between CD4 counts below 200 cells/mm^3 and greater incidence of breakthrough COVID-19. However, it is unlikely the present study was sufficiently powered to detect associations between CD4 counts and COVID-19 cases.

References

Coburn SB et al. Analysis of postvaccination breakthrough COVID-19 infections among adults with HIV in the United States. JAMA. DOI:10.1001/jamanetworkopen.2022.15934 (07 June 2022).
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793102

BMJ reports UK government failed to protect doctors during COVID-19

Simon Collins, HIV I-Base

Two BMJ reports on risks to doctors during the COVID-19 conclude that the UK government failed in its duty of care. [1, 2]

These are the first of five reports as part of a wider BMJ inquiry.

It uses the experiences of doctors to cover the critical shortages of PPE that led to hundreds of health workers losing their lives due to COVID-19. Nearly all the cases in the early epidemic were from an ethnic minoritised background.

The reports conclude that the evidence in the reports demonstrates that the UK government failed in its duty of care to the medical profession.[3]

References

1. BMA. Covid review 1: How well protected was the medical profession from covid-19? (19 May 2022). https://www.bma.org.uk/advice-and-support/covid-19/what-the-bma-is-doing/covid-19-how-well-protected-was-the-medical-profession
2. BMA. Covid review 2: The impact of the pandemic on the medical profession. (19 May 2022). https://www.bma.org.uk/advice-and-support/covid-19/what-the-bma-is-doing/covid-19-the-impact-of-the-pandemic-on-the-medical-profession
3. BMJ press release. Covid-19: Government failed to protect doctors during pandemic, BMA inquiry finds. BMJ 2022; 377 doi: https://doi.org/10.1136/bmj.o1235 (19 May 2022).
https://www.bmj.com/content/377/bmj.o1235

HIV PREVENTION

Fantastic voyage: tracking adherence sensors in PrEP meds

Simon Collins, HIV i-Base

A recent study reported patterns in PrEP adherence by using meds that were made with tiny sensors inside. The sensors are harmless but provided a direct record of when people took PrEP.

Apart from the novelty of bringing Fantastic Voyage to HIV prevention, the study reported two important patterns.

One was that the days when PrEP was not taken were often clustered together, rather than just appearing to be random single days ($p<0.003$).

The second was that adherence and the clusters of missed days was associated with self-reported use of crystal meth [OR 5.0; CI 95: 2.2 to 11.5), $p<0.001$].

The study included 71 HIV negative people using PrEP, with 63/71 continuing for at least 28 days. Mean age was 37 years (range: 18 to 69), 90% male, 77% white, 34% Hispanic. Most had stable housing (96%) housed and 75% were in paid work.

The 63 remaining participants provided just under 5000 observation days: average of 79 days (range: 29 to 105). Overall adherence was 86% but this steading declined over time (by about 90% each week, $p<0.001$).

An important caution that was not included discussing whether the missing days were part of a structured decision related to meth use. For example that adherence might have been good during the times when meth use increased risk of HIV – and conversely, when not using meth, PrEP might also not be needed.

Reference

Browne SH et al. Medication adherence patterns in persons prescribed ingestible sensor-enabled oral pre-exposure prophylaxis to prevent HIV infection. Clinical Infectious Diseases, ciac280, doi: 10.1093/cid/ciac280. (23 May 2022).

https://academic.oup.com/cid/advance-article-abstract/doi/10.1093/cid/ciac280/6588129

OTHER NEWS

UK increases funding to UNAIDS: still dramatically lower than before last years' 80% cut

Simon Collins, HIV i-Base

On 22 June 2022, UNAIDS announced recent pledges to support the work of UNAIDS, the United Nations Joint Programme on HIV/AIDS.

This includes noting that the UK government increasing funding to £8 million per year, up from £2.5 million in 2021.

Last year however, the UK cut support by more than 80%. Previously the UK contributed £15 million for each of the previous five years. [2, 3]

References

1. UNAIDS press release. Governments announce increased financial support to the global AIDS response. (22 June 2022). https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2022/june/20220622_financial_support_AIDS
2. UNAIDS statement on UK's proposed reduction in financial support GENEVA. (29 April 2021). https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2021/april/20210429_uk_funding
3. STOP AIDS. UK to slash funding for the global HIV response, including cutting UNAIDS' funding by more than 80%. (29 April 2021). https://stopaids.org.uk/2021/04/29/uk-to-slash-funding-for-the-global-hiv-response-including-cutting-unaids-funding-by-more-than-80

Future meetings and webinars 2022

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

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

Academic Medical Education (AME) meetings and workshops

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

https://academicmedicaleducation.com (meetings listings)

Webcasts from meetings (YouTube listing)

2022

HIV Paediatrics 2022

27 – 28 July 2022, Montreal, Canada, and virtual

https://academicmedicaleducation.com

24th International AIDS Conference (AIDS 2022)

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

https://www.aids2022.org

13th International Workshop on HIV & Aging

13 – 14 October 2022, USA (tbc)

https://academicmedicaleducation.com

HIV Glasgow 2022

23 – 26 October 2022, Glasgow and hybrid

https://www.hivglasgow.org

BHIVA Autumn Conference 2022

Friday 25 November 2022, London

https://www.bhiva.org/HIVEventDiary

2023

19th European AIDS Conference (EACS 2023)

18-21 October 2023, Warsaw, Poland

https://www.eacsociety.org

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

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

http://www.i-Base.info

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

Publications and regular subscriptions can be ordered online.

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

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

i-Base treatment guides

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

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

- Introduction to ART (May 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 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 v
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

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.

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- **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 HIV, pregnancy and women's health: *36-page A5 booklet* **quantity** _____

Guide to changing treatment: *16-p A5 booklet* **quantity** _____

HIV and quality of life: side effects and long-term health: *96-page A5* **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