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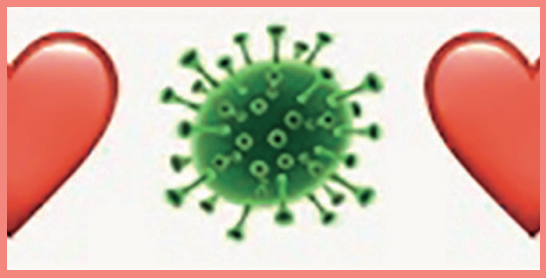
hiv treatment bulletin (e)



EACS, injectable RT and cure (30 November 2021)

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Published by HIV i-Base

EDITORIAL

This issue contains more coverage from the EACS 2021 conference held as a hybrid meeting in London last month.

We include the important news that long-acting cabotegravir/rilpivirine (CAB/RPV-LA) injectable ART has just been approved by NICE for use in England and Wales. This follows approval in Scotland last month.

This is an important signal that new drugs will still be made available, even if they are more expensive that other current ART. Although actual drug prices are not public – only list prices are published in the BNF – CAB/RPV-LA is likely to be close to higher priced non-generic combinations, such as Biktarvy (bictegravir/F/TAF). It will certainly be higher than combinations using generic ARVs.

Unfortunately, we also include the disappointing news about the stopped development of the NNRTI MK-8507. This is due to unexpected reductions in total lymphocyte and CD4 counts. The press release also refers to a signal that something similar might be linked to islatravir. Other islatravir studies are all continuing – both for treatment and prevention – but with closer monitoring.

Good news about a new oral history project from CHIVA for young people to record their experiences of living with HIV from birth.

And just in time for World AIDS Day, news of the third IAS report of a Global Scientific Strategy to develop an HIV cure. Published with open access in Nature Medicine, this comprehensive review covers more than 170 recent studies and is recommended reading.

i-Base have posted an easy-to-read Q&A version online that is less technical. This will hopefully be a way for most people living with HIV to learn about exciting developments for a cure.

i-Base 2021 appeal

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

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

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

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CONFERENCE REPORTS

18th International European AIDS Conference (EACS 2021)

27–30 October 2021, hybrid, London

Introduction

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

EACS are to be congratulated for taking this decision.

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

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

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

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

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

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

https://eposters-eacs2021.medicalcongress.online (ePosters)

https://europeanaidsconference.eacs.cyim.com (webcasts – needs EACS membership)

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

Reports in this issue of HTB are below.

- Lenacapavir: drug resistance in treatment experienced participants
- Implications of historical M184V on use of dual dolutegravir/lamivudine ART
- Stopping long-acting cabotegravir/rilpivirine: 1 in 5 trial participants don't restart oral ART within eight weeks
- Islatravir plus doravirine dual ART: 144-week follow-up from phase 2 study
- Access to HIV-specific mental health services across the EU

Lenacapavir: drug resistance in treatment experienced participants

Simon Collins, HIV i-Base

An oral presentation at EACS 2021 included an analysis of drug resistance from the 26-week CAPELLA study of the capsid inhibitor lenacapavir in people with extensive drug resistance to other classes.

In vitro, key mutations to lenacapavir occur at L68I, M66I, Q67H, K70N, N74S/D and T107M in the binding site, all with reduced fitness (other than Q67H) and none of which are found in people naive to this capsid inhibitor, including at baseline in this study. Mean susceptibility at baseline was 1.0 (0.3 to 1.7).

This study reported results from Cohort 1 in the important CAPELLA study where 36 participants were randomised to 14-day monotherapy or placebo, followed by optimised background regimen (OBR).

Overall, approximately half the participants had four-class resistance and half had resistance to three classes at baseline, limiting active drugs in the OBR.

By week 26, 11/36 participants qualified for resistance testing, with 4/11 (11%) showing capsid resistance. All four had M66I, with single or dual additional mutations from the in vitro list above in 3/4. Follow-up out to week 40 was presented for each of these four cases, which are worth reporting in detail.

Case 1 included suboptimal adherence to OBR suggesting an extended period of lenacapavir monotherapy. Viral rebound at week 28 with M66I (136-fold loss of sensitivity). This person resuppressed by week 40 following adherence support and a second dose of lenacapavir. As the OBR of darunavir/r + dolutegravir BID + rilpivirine was sensitive at baseline, this does not mean that lenacapavir remained active.

Case 2 had resistance to all five drugs in background OBR drugs at baseline, saw a 3-log drop in viral load following the first lenacapavir dose, but with viral load rebound from weeks 12 - 20 with M66I and multiple secondary capsid mutations (>1400-fold loss of sensitivity). Viral load subsequently returned to <50 copies/mL by week 28 (after switching 3TC to F/TAF) and remained this low following the second lenacapavir dose at week 30.

Case 3 only had partial sensitivity to TAF in the OBR. Viral load reduced by 2-log but remained detectable, with M66I detected at week 8, though to the second lenacapavir dose at week 32, which had no further impact on reducing viral load, but allowed further capsid mutations to develop.

Case 4 included active darunavir/r + dolutegravir (both BID) in the OBR but also started with higher baseline viral load. Lenacapavir produced a 1-log drop in viral load, before rebounding with M66I and other mutations from week 6. However, drug levels of OBR drugs were not present at early failure and viral load largely became undetectable from week 18 without changing OBR.

C O M M E N T

These four cases, all with emerging capsid resistance during periods of effective lenacapavir monotherapy highlight the importance of active drugs in OBR. They also highlight the importance of good adherence to the OBR.

The cases reporting subsequent viral suppression after development of resistance are likely due to improved adherence to the background OBR, rather than residual capsid activity, although this wasn't supported by further drug levels monitoring in this presentation.

The level of background antiretroviral activity needed to support lenacapavir is not currently known.

Reference

Margot N et al. Resistance analysis of long-acting lenacapavir in highly treatment-experienced people with HIV after 26 weeks of treatment. EACS 2021, Oral abstract session, 28 October 2021, 3-4 pm. Oral abstract OS1/1.
https://eacs2021.abstractserver.com/program/#/details/presentations/308

Implications of historical M184V on use of dual dolutegravir/lamivudine ART

Simon Collins, HIV i-Base

Whether or not historically recorded lamivudine-resistant M184V jeopardises dual ART that includes lamivudine is a controversial issue.

Some doctors point to data suggesting that only a recent history of M184V within the previous five years has been linked to viral failure. Others question the ethics of studying suboptimal ART with potential dolutegravir monotherapy, despite the potential reduced fitness associated with M184.

This retrospective French study looked at risk of low level viral failure (2 x >50 copies/nmL or 1 x >200 copies/mL) in 695 people switched to dual dolutegravir/lamivudine with resistance results. Of these, M184V was documented in 105 (15%) and no M184V was in 590 (85%). Median time from resistance to the switch was 10 years (IQR: 3 to 14).

Participants were highly treatment experienced, but significantly more so if M184V was present. Median duration of ART was 21.3 years (IQR: 17.6 to 23.1) vs 8.8 years (IQR: 5.3 to 15.5) in the M184V vs no-mutation group respectively ($p<0.0001$). They had used significantly more median lines of ART (11 vs 4) and had been undetectable for longer (median 10.7 vs 6.7), both $p<0.0001$.

Overall, 9/695 participants reported viral failure, with similar rates in the two groups: 2/105 vs 7/590. Viral rebound was also only to <250 copies/mL in 4/9, including the 2 participants with historical M184V. This meant genotype results were only available for 4/9, none showing M184I/V on failure, with 4/9 also remaining on dual ART.

There were no differences in the rates of viral rebound by presence of recorded M184V (p=0.81) or within the M184V group when stratified by recency of the mutation (more than vs > less than five years ago), (p=0.94). However, follow-up on dual ART was also fairly short: median 1.2 years (IQR: 0.7 to 2.1) and similar in both groups (p<0.56).

Although the study concluded that viral failure was low in all participants, with no impact of previously recorded M184V, even if this was relatively recent, it rightly noted that longer follow-up was needed.

This is essential because of both the extensive duration of viral suppression and the long time since M184V had been recorded.

C O M M E N T

Although these results question whether M184V remains archived after 5, 10 or 15 years on suppressive ART, modelling might suggest that low or extremely limited viral turnover might just need longer follow-up. For context, viral breakthrough to dolutegravir monotherapy only occurs in a minority of people over a year (though with such significant resistance that this should never be used).

The need for longer follow-up was also raised in the panel discussion after the session, suggesting that 2-3 years follow-up might be a more appropriate minimum time in this long-suppressed cohort. Also, that the results are not appropriate for people with more recently document resistance to lamivudine.

Reference

Hocqueloux L et al. Archived mutation M184V does not increase virologic failure during maintenance therapy with dolutegravir + lamivudine in the French DAT'AIDS cohort. EACS 2021, EACS 2021, oral abstract session, 28 October 2021, 3-4 pm. Oral abstract OS1/2.

https://eacs2021.abstractserver.com/program/#/details/presentations/382 (abstract)

Stopping long-acting cabotegravir/rilpivirine: 1 in 5 trial participants don't restart oral ART within eight weeks

Simon Collins, HIV i-Base

With long-acting cabotegravir/rilpivirine injections are now approved in the US and EU, and by NHS Scotland (with NHS England about to decide), other aspects from these formulations are also important to follow.

Results were presented at EACS on 150/1651 participants (9%) in the phase 2/3 studies (TANGO, ATLAS and ATLAS-2M) who discontinued long-acting injections. Of these 92/150 completed 12 months follow-up, 4 had withdrawn and 54 were still being followed. [1]

Median duration on CAB-LA/RPV-LA was 36 weeks (range: 1 to 144), with about one-third lasting more than a year. Most (76%) were on monthly rather than two-monthly injections.

The most common reasons for discontinuations were side effects (40%), participant choice (23%) or lack of efficacy (18%). Although most people (82%) switched to oral ART within 8 weeks (median 4 weeks; IQR: 4 to 6), reasons were not given for the 18% that did not restart HIV treatment..

Of those that restarted oral ART, 60% used INSTI-based ART, with roughly 20% using PI-based and 20% using NNRTI-based treatment. Tolerability of oral ART was reported as good with no further discontinuations due to side effects.

Virologic outcomes for the 92/150 people who completed 12 month follow-up, 84/92 (91%) achieved viral suppression on oral ART, although this included several people with missing data. No results were presented by dosing regimen (4- or 8-week) or time taken to restart.

C O M M E N T

Although it is good that most participants achieved undetectable viral load on subsequent oral ART, it is concerning that this dataset did not include information on why almost one in five trial participants who consented to follow-up, hadn't restarted oral ART.

The detailed prescribing information for these long-acting treatments state: *"it is essential to adopt an alternative, fully suppressive antiretroviral regimen no later than two months after the last two-monthly injection".[2, 3]*

CAB-LA/RPV-LA was approved by NHS Scotland on 11 October and by NHS England on 18 November 2021.

Reference
1. Teichner P et al. Outcomes for participants during long-term follow-up after discontinuation of cabotegravir + rilpivirine long-acting in the phase III/IIIb clinical trials. EACS 2021, oral abstract session, 28 October 2021, 3-4 pm. Oral abstract OS1/2.
https://eacs2021.abstractserver.com/program/#/details/presentations/255 (abstract)
2. EMA. Cabotegravir-LA, Summary of Product Characteristics (SPC).
https://www.ema.europa.eu/en/documents/product-information/vocabria-epar-product-information_en.pdf (PDF)
3. EMA. Rilpivirine-LA, Summary of Product Characteristics (SPC).
https://www.ema.europa.eu/en/documents/product-information/rekambys-epar-product-information_en.pdf (PDF)

Islatravir plus doravirine dual ART: 144-week follow-up from phase 2 study

Simon Collins, HIV i-Base

Extended results from the early phase 2 study daily oral islatravir plus doravirine were presented at EACS 2021 in an oral presentation. This dual combination is already in phase 3 development. [1]

This was initially a randomised dose-finding study in 120 treatment naive participants with 30 people in each of the 0.25, 0.75, and 2.25 mg groups (used with 3TC/TDF) and a control arm of doravirine/3TC/TDF.

Several efficacy and safety results at 96-week were presented at Glasgow 2020, CROI 2021 and IAS 2021 and generally were similar at 144 weeks (when participants had received 60-84 weeks on dual islatravir + doravirine).

By snapshot analysis, 72% (65/90) of the combined islatravir participants had viral suppression <50 copies/mL, with 83% (25/30) in the original dose-selected 75 mg islatravir arm, compared to 77% (24/30) in the control arm.

Viral failure was rare, with viral load >50 copies/mL in 7 vs 1 participants in the combined vs control arms. Approximately 20% in each group (18/90 vs 6/30) had missing data at week 144, with most of those in the islatravir arms not related to study drug.

Of the 7 who discontinued with protocol defined viral failure (confirmed VL >50 copies/mL), all had viral load < 80 copies/mL. Of these 5/7 had baseline viral load >100,000 copies/mL. There was only one non-responder (in the higher dose islatravir arm).

C O M M E N T

A recent safety analysis of ongoing islatravir studies has reported reductions in mean total lymphocyte counts (and sometimes CD4 counts), although these are still within normal ranges.

Limited details are available, but this also included PrEP studies using islatravir monotherapy in HIV negative people. [2]

References
1. Molina J-M et al. Efficacy and safety of islatravir in combination with doravirine through 144 weeks for treatment-naïve adults with HIV-1 infection in a phase 2b trial. EACS 2021, oral abstract session, 28 October 2021, 3-4 pm. Oral abstract OS1/5.
https://eacs2021.abstractserver.com/program/#/details/presentations/410 (abstract)
2. MSD/Merck stop once-weekly NNRTI MK-8507: islatravir studies continue with closer monitoring. HTB (19 November 2021).
https://i-base.info/htb/41647

Access to HIV-specific mental health services across the EU

Simon Collins, HIV i-Base.

One of the community sessions at EACS 2021 included a panel discussion on HIV and mental health issues – perhaps better referred to as mental quality of life – including services provided by HIV clinics and organisations in the WHO European Union.

This was informed by results of a cross-sectional survey run by the European AIDS Treatment Group (EATG) during October-November 2020 that was distributed online in seven languages.

There were 646 individual responses (389 from inside the EU/EEA) and 241 organisation responses (187 from the EU/EEA) and results were presented for the individual responses. Respondents were educated (85% with high school education), urban (56%), employed (57%) - who would generally be able to negotiate health services. Median age was around 45 years and roughly 52% were heterosexual.

Roughly half reported symptoms linked to depression, (increasing from 40% before diagnosis to 58% after) and half had never been assessed for mental health. Most people reported that HIV negatively affected their mental health, including during COVID-19. Most reported support from family and friends rather than an HIV organisation (13%) or HIV clinic (11%).

Although the presentation didn't report the degree to which needs were matched by services, the full results are available in a 60-page report. [2]

Community workshops organised to develop issues raised in the survey focussed on the importance of developing HIV-specific non-judgemental mental health services with clear and easy referral pathways, and these recommendations have been summarised in a short online report. [3]

This included the need to develop different services for different risk groups, including sex workers, gay men, injecting drugs users and older people, as models developed for one group often were less relevant to others.

The following panel discussion, including clinical responses from western and eastern EU countries was important, for an easy to engage dialogue about how unrealistic it is for such services to be easily developed for 50% of HIV positive people with background symptoms of depression, not least because most doctors are neither confident or trained in this area. Mental health are not always obvious and when identified usually involve intensive interventions over time.

Services vary between countries but many HIV services do not include psychological support and appointments for screening also need to cover the whole range of ongoing clinical assessments. Plus HIV positive people are getting older, often are becoming isolated and lonely.

EACS guidelines recommended simple psychological screening (historical, baseline and then annually) based on two questions: (i) Have you often felt depressed, sad or without hope in the last few months? and (ii) Have you lost interest in activities that you usually enjoy?

Diagnosis involves regular assessment of 7 key symptoms, including weight loss, fatigue, insomnia and aspects of self-worth. Management interventions require at least 4/7 symptoms when antidepressants can be considered, but expert referral is only recommended with >6 symptoms.

The discussion also used the example of chemsex-related mental health issues where specialised professional services

are not commonly available in most countries – and where cases of such extreme psychosis are beyond most doctors experiences. Often the most successful responses can be linked to community developed services with peer support. Similarly, migrant women have a very different pattern of mental health services that demand similarly culturally appropriate services. This involves developing new services at a time when current budgets are being cut.

Criminalisation of key populations, or activities that are common in key populations means that people are lost to mental health care - and make it essential that people living with HIV are involved in developing appropriate services.

A recent UK report included that nearly 40 per cent of HIV clinics do not have access to a psychological or mental health professional even though people living with HIV are twice as likely to have mental health issues compared to the general population. [5]

In practice, the demand for services often means that people in the UK in critical need of support often face delays of weeks, or more likely months, before a specialised referral. GPs likely to prescribe antidepressants which may or may not be appropriate.

References

1. EATG community session. Mental health and access to mental health services for people living with HIV in the WHO European Region – Recommendations for the healthcare sector.
https://eacs2021.abstractserver.com/program/#/details/sessions/109
2. Survey Report: Mental Health of People Living with HIV and Staff of Organisations Working in the Field of HIV in the WHO European Region. (June 2021).
https://www.eatg.org/wp-content/uploads/2021/06/eatg-hiv-and-mental-heatlh-survey-report-english.pdf (60-page PDF report).
3. Briefing Paper: Mental Health of People Living with HIV. (21 October 2021)
https://www.eatg.org/publications/briefing-paper-mental-health-of-people-living-with-hiv/
https://www.eatg.org/wp-content/uploads/2021/10/eatg-hiv-and-mental-heatlh-briefing-paper-english.pdf (3-page PDF report)
4. EACS guidelines, versions 11, pages 96-104. (October 2021).
https://www.eacsociety.org/guidelines/eacs-guidelines (download page)
https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf (PDF)
5. APPG HIV. The Missing Link: HIV and Mental Health. (March 2020).
https://www.appghivaids.org.uk/news/2020/3/4/press-release-mental-health-services-failing-patients-with-hiv
https://static1.squarespace.com/static/5b7d333855b02cc3853805ce/t/5e60ec83633a0705fb4d4a32/1583410309413/The+Missing+Link+Web+version.pdf (60-page PDF report).

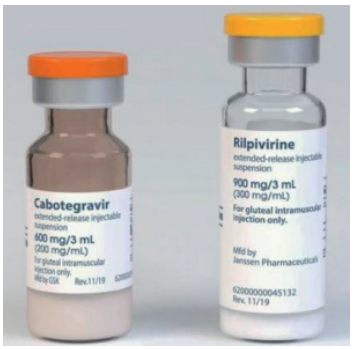
ANTIRETROVIRALS

NICE approves long-acting cabotegravir and rilpivirine injections in England and Wales

Simon Collins, HIV i-Base

On 18 November 2021, after several delays, NICE announced the long-awaited decision to approve an injectable HIV combination that is given every two months.

Access is expected by April 2022, and estimated for expected use by up to 13% of people living with HIV. [1]



Long-acting cabotegravir plus rilpivirine (CAB/RPV-LA) currently involves oral tablets for the first month, higher dose first injections, and then two separate intramuscular injections every two months. Injections need to be given by a health professional.

Approval is as a switch option for people who already have an undetectable viral load on their current oral combination, and who do not have drug resistance or a history of previous treatment failure with similar drugs.

Importantly, the statement from NICE does not expect to make injectable ART an option for everyone. It modelled that up to 13,000 people might want to use CAB/RPV-LA. This is approximately 1 in 6 (~15%) of people currently living with HIV in the UK. Criteria for deciding access if demand proves to be much higher are not included in the announcement.

Approval is based on results from the large international FLAIR, ATLAS and ATLAS-2M phase 3 studies. CAB/RPV-LA originally involved monthly injected but the ATLAS-2M study showed similar efficacy from two-monthly dosing. ATLAS-2M also included a sub-study looking at whether the monthly oral dosing might be able to be dropped in the future. This option is already referred to in the European prescribing information.

The combination is marketed by ViiV Healthcare with separate trade names for cabotegravir-LA (Vocabria) and rilpivirine-LA (Rekambys, developed by Janssen). In the US, both drugs are packaged together, with a single trade name Cabenuva.

CAB/RPV-LA was approved in the EU on 21 December 2020. Approval by NHS Scotland was announced on 11 October 2021. [3]

The expected timeline for first access is April 2022, meeting the requirement for access to be within three months of final published advice (expected January 2022). Access in Wales should be within two months.

Please see full details on both drugs for further information. The i-Base "Know your meds" resource includes summary information with links to the full prescribing information on the EMA website. [4, 5, 6]

C O M M E N T

Approval and significant access is strongly welcomed, and is likely to have reflected strong and consistent community support for the importance of alternative treatments to oral tablets. This included examples of how long-acting treatment could improve quality of life for a wide range of people living with HIV, by helping to overcome continued high levels of stigma and discrimination. [7]

News of the decision was handled less well by NICE however. Many clinics spent the day explaining that access was not going to be for several months: not until April in England but possibly a month earlier in Wales

The development of new and improved treatments are significant scientific advances, and this can only be justified if they then become widely available for people living with HIV. The announcement from NICE means that the NHS is also prepared to pay higher prices compared to standard HIV treatments.

Approval is also an important signal for other long-acting HIV drugs in development. If results from ongoing studies with other compounds are similarly effective, future options might include once-weekly oral ART and six-monthly injectable ART.

The NICE review documents are important for including personal preference as being an acceptable reason to access injectable ART, but they don't include guidance for criteria for how this would be managed if demand turns out to be high, especially as injectable ART is likely to be priced higher than most current combinations that include generic drugs.

The list price for the two-monthly doses of CAB-LA (Vocabria) and RPV-LA (Rekambys) is approximately £1200 and £440 respectively: just short of £10,000 for a year. VAT will increase this further when medicines are dispensed at a clinic. The discounted NHS price has not been published, but unless the discount is considerable, this is likely to be significantly higher and perhaps double the price of many oral combinations. This might therefore also be the first example for many years where premium pricing has been allowed for a new combination.

The cost-effectiveness analysis included that CAB/RPV-LA was within the higher range of £20,000 to £30,000 per quality adjusted life year (QALY), considered acceptable by NHS England. This was even if injectable ART has no impact on improving adherence - a contested issue in the submission.

So this is an exciting time for HIV treatment. While many new issues relating to injectable ART are still being explored, these are likely to become much more clear with wider use.

New practical issues include:

- **The need for more frequent clinic visits each year: 6 vs 1 for oral ART.**
- **Delayed/missed dosing (detailed in the SPCs with oral tablets a back-up for short delays).**
- **Potential use as first-line therapy.**
- **Future use by people whose adherence to oral ART is too difficult to become undetectable (the obvious group who are currently not covered).**

It also includes results from a recent report that 1 in 5 participants who discontinued injectable ART in phase 3 studies did not return to oral ART. [8]

The extremely long half-lives for these drugs would make development of drug resistance highly likely to one or both drug classes in this combination. Detectable drug levels are still common more than a year after the last injection and in some cases have still been reported after several years.

References
1. NICE. NICE approves first long-acting injectable HIV-1 treatment. (18 November 2021). https://www.nice.org.uk/news/article/nice-approves-first-long-acting-injectable-hiv-1-treatment
2. NICE. Draft guidance. Cabotegravir and rilpivirine for treating HIV-1 [ID3766] In development [GID-TA10658] Expected publication date: 05 January 2022. (18 November 2021). https://www.nice.org.uk/guidance/indevelopment/gid-ta10658/documents
3. NHS Scotland approves long-acting cabotegravir and rilpivirine injections. HTB (October 2021). https://i-base.info/htb/41408
4. i-Base. Check Your Meds. Cabotegravir LA + rilpivirine LA (Vocabria+Rekambys; Cabenuva). https://i-base.info/guides/15361
5. EMA. Cabotegravir-LA SPC. https://www.ema.europa.eu/en/documents/product-information/vocabria-epar-product-information_en.pdf (PDF)
6. EMA. Rilpivirine-LA SPC. https://www.ema.europa.eu/en/documents/product-information/rekambys-epar-product-information_en.pdf (PDF)
7. UK-CAB press statement. NICE decision on cabotegravir with rilpivirine (Long-Acting Injectables) – Community Statement from UK-CAB (UK Community Advisory Board) and National AIDS Trust. (18 November 2021). https://ukcab.net/2021/11/nice-approves-first-long-acting-injectable-treatment-for-people-living-with-hiv
8. Stopping long-acting cabotegravir/rilpivirine: 1 in 5 trial participants don't restart oral ART within eight weeks. HTB (14 November 2021). https://i-base.info/htb/41601

MSD/Merck stop once-weekly NNRTI MK-8507: islatravir studies continue with closer monitoring

Simon Collins, HIV i-Base

On 18 November 2021, a press release from MSD/Merck included top line concerns about an investigational NNRTI currently being studied with islatravir as a component of once-weekly oral ART.

The statement reports decreases in total lymphocyte and CD4 counts in participants receiving MK-8507 + islatravir that were dose-related to the NNRTI and were sufficient for dosing to be stopped.

The press release notes that the company are confident in the profile of islatravir and that both treatment and prevention studies with this compound are continuing.

However it also reports that a review of other ongoing studies reported small and non-significant mean changes in total lymphocyte counts. This included a decrease in HIV negative people using once-monthly islatravir as PrEP at 60 mg and 120 mg that was dose-dependent, but that remained within the normal range.

It also included small mean CD4 decreases in two phase 3 switch studies (ILLUMINATE A nd B) - using daily dual ART with doravirine and islatravir (0.75 mg) - both of which are continuing.

The development of MK-8507 is now on hold.

C O M M E N T

This is very disappointing news.

It shows the difficulties in drug development even after promising compounds have cleared in vitro, animal studies and phase 1 studies.

A conference call with community advocates shortly after the press release included additional details on these early findings. This included the significance of the mean dose-related reductions in both total lymphocytes and CD4 T cells in the highest dose (400 mg) MK-8507 group.

It also included details of reductions in total lymphocyte counts in ongoing islatravir studies.

For example, similar mean dose-related reductions in total lymphocytes have been seen in ongoing PrEP studies in HIV negative people (compared to a small increase in the placebo group). While mean reductions are still within the normal range, and no individuals went below this range, this might require new entry criteria for these studies.

Although the mean CD4 reductions at week-48 in ongoing treatment experienced phase 3 studies using daily islatravir with doravirine are small, by definition, this makes it likely that larger CD4 reductions will have been experienced by a minority of participants.

The company emphasised that these signals are being taken seriously and that participant safety remains central to continued research with all investigational compounds.

No increase in side effects have been reported. Increasing monitoring will be added to all studies in discussion with investigators.

Reference

Merck press release. Merck provides update on phase 2 clinical trial of once-weekly investigational combination of MK-8507 and islatravir for the treatment of people living with HIV-1. (18 November 2021).

https://finance.yahoo.com/finance/news/merck-provides-phase-2-clinical-225700816.html

HIV: CURE RESEARCH

IAS review on HIV cure research: A global scientific strategy to cure HIV (2021)

Simon Collins, HIV i-Base

World AIDS Day 2021 includes a new focus on finding a cure for HIV.

This is helped by a new review on cure research published by the International AIDS Society. [1]


nature medicine
REVIEW ARTICLE
Research priorities for an HIV cure: International AIDS Society Global Scientific Strategy 2021

The report, published in the medical journal Nature Medicine summarises scientific advances from 170 new studies over the past five years. And it also sets a Global Scientific Strategy for the next five years.

As the report is quite technical, i-Base produced a Q&A summary in everyday language for general readers. This will be easier for most people living with HIV. [2]

A lay summary for journalist was also produced by IAS. [3]

References

1. Global Scientific Strategy (2021). Nature Medicine (1 December 2021). DOI: 10.1038/s41591-021-01590-5. https://www.nature.com/articles/s41591-021-01590-5
2. IAS strategy for an HIV cure (2021): an easy-to-read Q&A https://i-base.info/ias-towards-an-hiv-cure-2021
3. Summary for medical journalists. Also in French, Portuguese and Spanish. https://www.iasociety.org/wad2021

HIV: OTHER NEWS

UK oral history project for young people who were born with HIV

Simon Collins, HIV i-Base

Some of the most important and moving HIV history projects include those that support people to record their experiences of living with HIV.

On 1 December 2021, the Children's HIV Association (CHIVA) are launching a new project called Positively Spoken. This will offer this opportunity to young people who were born with HIV.

The project is being led by young adults living with HIV and will run for two years. It will also involve trained interviewers to help record these stories.

Participants need to be aged 16 or over. They can choose to keep some parts or the whole of their story hidden for up to 100 years. This lets people decide which parts of their story can be shared at different times, when they are ready.

The project is part of the British Library Sound Archive which has recorded stories of adults living with HIV since the late 1980's.

For more information see the CHIVA website or contact Sam Williams.

www.chiva.org.uk/positivelyspoken (website)

sam.williams@chiva.org.uk (email)

Tel: +44 (0)117 905 5149

HIV and COVID-19 - bulletin

COVID-19: TREATMENT

Colchicine: no clinical benefits against COVID-19 in pooled analysis of RCTs

Simon Collins, HIV i-Base

Results from a pooled analysis of available studies reports from using the anti-inflammatory gout medication colchicine against clinical risks from COVID-19, including hospitalisation or mortality. [1]

It also reported an increased risk of side effects, including diarrhoea.

The analysis included results from six randomised controlled trials involving more than 16,000 participants. Level of evidence for the GRADE analysis was generally moderate.

However, the six studies used different designs and doses and 5/6 studies were in more advanced infection when participants were already hospitalised. This is not discussed in the paper.

The single study in early COVID-19 was a Canadian study that in January 2021, reported benefits at reducing hospitalisation (Tardif et al). However, this study discontinued recruiting before full enrolment (at approximately 75%) after a positive signal of benefit. At this stage, by ITT analysis, the benefit was not statistically significant. [2]

References

1. Mehta KG et al. Efficacy and safety of colchicine in COVID-19: a meta-analysis of randomised controlled trials. doi: 10.1136/rmdopen-2021-001746. https://rmdopen.bmj.com/lookup/doi/10.1136/rmdopen-2021-001746
2. Oral colchicine reduces hospitalisation in international randomised phase 3 outpatient study. HTB (January 2021). https://i-base.info/htb/39776

Eli Lilly withdraw EU application for bNAbs etesevimab and bamlanivimab

Simon Collins, HIV i-Base

On 29 October 2021, Eli Lilly announced that the current EU application for dual bNAbs etesevimab and bamlanivimab against COVID-19 would be withdrawn. [1]

This was based on low level demand for these compounds, which would also limit to collect further data that was requested as part of the application.

In response, the EMA have stopped the rolling review of these bNAbs. [2]

The US Government has invested more than $1.3 billion in acquiring stocks of etesevimab and bamlanivimab for treatment and prophylaxis of COVID-19. [3]

This is covered in the US by emergency use authorisation in people 12 years and above with mild-to-moderate COVID-19 at high risk for progression.

The EMA are currently reviewing an application for the dual bNAbs casirivimab and imdevimab developed by Regeneron. [4]

COMMENT

Part of the limited demand for bamlanivimab might likely be due to lack of activity against the Delta variant, when used as a single bNAb. [5]

The Regeneron bNAbs are now routinely available in the UK in selected cases in the UK based on risk of COVID-19 progression. [6]

References

1. Eli Lilly. Bamlanivimab(EMEA/H/C/005836/0000) and Etesevimab (EMEA/H/C/005837/0000). Letter. (29 October 2021). https://www.ema.europa.eu/en/documents/withdrawal-letter/withdrawal-letter-bamlanivimab-etesevimab_.pdf (PDF)
2. EMA. EMA ends rolling review of the antibodies bamlanivimab and etesevimab for COVID-19 following withdrawal by Lilly. (2 November 2021). https://www.ema.europa.eu/en/news/ema-ends-rolling-review-antibodies-bamlanivimab-etesevimab-covid-19-following-withdrawal-lilly
3. Eli Lilly. Lilly to supply 614,000 additional doses of bamlanivimab and etesevimab to the U.S. Government for the treatment or post-exposure prevention of COVID-19. (2 November 2021). https://investor.lilly.com/news-releases/news-release-details/lilly-supply-614000-additional-doses-bamlanivimab-and-etesevimab
4. EMA. EMA receives application for marketing authorisation for Ronapreve (casirivimab / imdevimab) for treatment and prevention of COVID-19. (11 October 2021).
h ttps://www.ema.europa.eu/en/news/ema-receives-application-marketing-authorisation-ronapreve-casirivimab-imdevimab-treatment
5. Coronavirus (COVID-19) update: FDA revokes emergency use authorization for monoclonal antibody bamlanivimab. (16 April 2021). https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab
6. MHRA. Casirivimab and imdevimab for patients hospitalised due to COVID-19. (17 September 2021). https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103175

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

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

6 – 9 December 2021, virtual.

https://www.intmedpress.com/comorbidities

Conference on Retroviruses and OIs (CROI 2022)

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

https://www.croiconference.org

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

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

http://www.i-Base.info

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

Publications and regular subscriptions can be ordered online.

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

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

i-Base treatment guides

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

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

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

Pocket guides

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

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

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

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

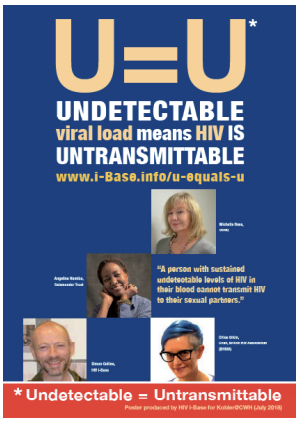
i-Base have produced a new series of posters, postcards and leaflets to help raise awareness about U=U in clincs.

This project was developed with the Kobler Centre in London.

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

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

email: subscriptions@i-base.org.uk



Customise U=U posters for your clinic

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

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

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

roy.trevelion@i-Base.org.uk

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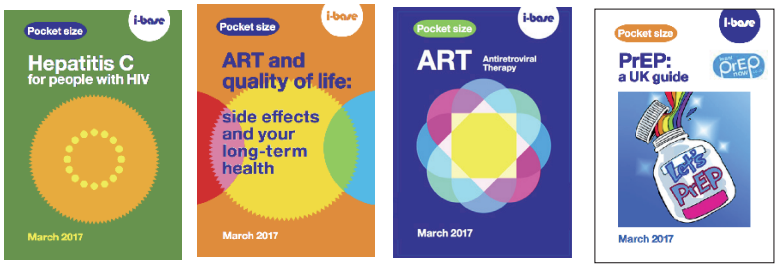

h-tb

HIV TREATMENT BULLETIN

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http://www.i-Base.info

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Editor: Simon Collins

Contributing Editor: Polly Clayden

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

  UK Guide To PrEP *(June 2021): 24-page A5 booklet* **quantity** _____

  ART in pictures: HIV treatment explained *(June 2019): 32-page A4 booklet* **quantity** _____

  Guide to HIV, pregnancy and women's health *(April 2019): 36-page A5 booklet* **quantity** _____

  Guide to changing treatment: what if viral load rebounds *(August 2021): 8-page A5 leaflet* **quantity** _____

  HIV and quality of life: side effects and long-term health *(Sept 2016): 96-page A5* **quantity** _____

  Guide to HIV testing and risks of sexual transmission *(July 2016): 52-page A5 booklet* **quantity** _____

  Guide to hepatitis C coinfection *(April 2017): 52-page A5 booklet* **quantity** _____

- **Other resources**

  U=U resources:

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

  HIV Treatment 'Passports' - Booklets for patients to record their own medical history **quantity** _____

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

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subscriptions@i-Base.org.uk