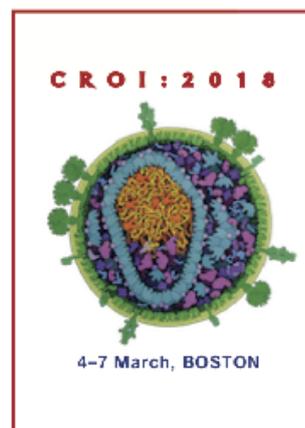


30 March 2018: no.6

*Further reports from CROI 2018*

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## 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 online:

<http://www.i-Base.info>

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**HIV i-Base is a registered charity no 1081905 and company reg no 3962064. HTB was formerly known as DrFax.**

## EDITORIAL

**This is the second issue of HTB to lead with reports from CROI 2018, the main annual HIV scientific conference that was held this year in Boston.**

We lead with results from the phase 3 ibalizumab study - the monoclonal antibody that was approved in the US during CROI, with an indication for multidrug resistant HIV.

Other positive news included that statins might reduce risk of some cancers and that reductions in bone mineral density on ART (irrespective of drug choice), seems to stabilise after the first year.

One study, a retrospective analysis from data that is at least ten years old, quantified just how women were much more likely to become HIV positive during at the end of pregnancy or post partum, than at other times. A small pharmacology study provided reassuring results on dolutegravir levels during pregnancy.

Plus an overview of cure studies that includes new studies about treatment interruptions as part of cure research. See also the reviews by Richard Jefferys later in this issue for more discussion.

If you missed the previous HTB issue, those first reports are still online. And stay tuned for further news in April. CROI is a conference that keeps on giving...

### Subscriptions

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

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

### **i-Base 2018 appeal: we still need your help...**

Last year we launched a funding appeal to help i-Base continue to provide free publications and services.

Your help has been inspiring – and we hope this support will continue during 2018. If 1000 people support us with £5 a month we will be on course to meet our shortfall.

HTB is the UK's longest running activist HIV treatment publication - starting as DrFax from 1996-2000 and relaunched as HTB from 2000-2018.

We are the only HIV organisation to provide free booklets to NHS clinics on HIV treatment. All support is appreciated.

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



## CONFERENCE REPORTS

### Conference on Retroviruses and Opportunistic Infections (CROI 2018)

4–7 March 2018, Boston

#### Introduction

**We continue our reports from CROI 2018, which was held this year from 4 - 7 March in Boston.**

CROI is one of the most important HIV conferences, and comprehensive conference material is available free online.

This includes the full programme and abstracts with webcasts from oral presentations. Approximately 1100 new studies were selected for the conference this year.

<http://www.croiconference.org>

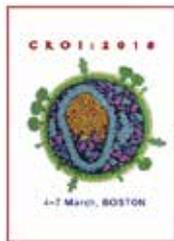
<http://www.croiconference.org/abstracts/search-abstracts> (abstracts and posters)

<http://www.croiwebcasts.org> (webcasts)

Reports from CROI 2018 in this issue include:

- Ibalizumab phase 3 results and susceptibility to drug-resistant HIV
- Statin use might reduce risk of cancer in HIV positive people
- Rate of bone loss on ART slows after the first year
- Standard dose of dolutegravir sufficient in late pregnancy: interim results from DolPHIN1 study
- Women's risk of becoming HIV positive increases three-fold in late pregnancy and four-fold postpartum
- Cure research at CROI 2018: defining and reducing the reservoir and the risks from interrupting treatment

i-Base reports signpost to key studies, and hyperlinks take you to the full results.

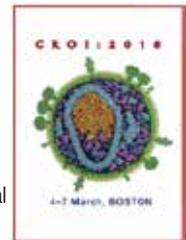


#### CROI 2018: ANTIRETROVIRALS

### Ibalizumab phase 3 results and susceptibility to drug-resistant HIV

Simon Collins, HIV i-Base

**CROI 2018 included a poster on the most recent HIV drug, ibalizumab, which was given FDA approval in the US during the conference week.**



Ibalizumab is a monoclonal antibody that post-attachment, blocks HIV entry into cells while preserving normal CD4 functions. After an initial loading dose, it is given by infusion every two weeks.

Baseline susceptibility data was presented for 38/40 highly treatment-experienced participants in the 24-week, single arm, phase 3 TBM-301 study. At baseline, 50% of participants had resistance to at least three classes, with major mutations to NRTIs, NNRTIs, PIs and INIs on 93%, 85%, 83% and 61%, respectively.

Results from the main study were previously reported in HTB last year, but in summary, include 83% of participants meeting the primary endpoint of >0.5 log reduction in viral load seven days after adding a single dose as virtual monotherapy to the background failing combination and mean viral load reduction of 1.1 log copies/mL. Background ART was then optimised with 24-week follow-up. [3]

At week 24, viral load was <50 copies/mL in 43% (50% < 200 c/mL) with median viral load reductions of 1.6 log at week 24.

The poster at CROI presented results of in vitro analysis showing that ibalizumab retained sensitivity irrespective of baseline resistance to NRTIs, NNRTIs, PIs and INSTIs.

#### C O M M E N T

**Although ibalizumab is not currently approved in the EU, the company are actively pursuing the regulatory pathway in Europe.**

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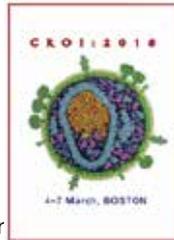
1. Weinheimer S et al. Ibalizumab susceptibility in patient HIV isolates resistant to antiretrovirals. 25th CROI, 4 – 7 March 2018, Boston. Poster abstract 561.  
[www.croiconference.org/sessions/ibalizumab-susceptibility-patient-hiv-isolates-resistant-antiretrovirals](http://www.croiconference.org/sessions/ibalizumab-susceptibility-patient-hiv-isolates-resistant-antiretrovirals) (abstract and poster)
2. HTB. FDA approves ibalizumab in the US to treat multidrug HIV resistance. (06 March 2018).  
<http://i-base.info/htb/33659>
3. HTB. Ibalizumab infusion reduces viral load in people with HIV multi-drug resistance. HTB (29 November 2017).  
<http://i-base.info/htb/30877>

CROI 2018: SIDE EFFECTS &amp; COMPLICATIONS

## Statin use might reduce risk of cancer in HIV positive people

Simon Collins, HIV i-Base

**A large case-control analysis from the Veteran's Ageing Cohort Study (VACS) reported an overall association between statin use and a reduced risk of virus-mediated cancers in HIV positive people.**



Although mechanisms for statins to positively impact on the immune responses against tumor cells have been proposed, individual studies are often small. Several large meta-analyses conducted in the general population over the last five years, produced conflicting results, with only one study reporting a protective benefit against liver cancer.

Even when studies in HIV positive people have reported a benefit, these have also sometimes included small numbers with limited follow-up, or with limited cancer-specific information.

The study presented at CROI 2018 by Roger Bedimo and colleagues, was a case-control analysis from 150,000 patients (97% male, one-third are HIV positive) in VACS. From this cohort, approximately 25,000 participants who used a statin were identified from 2001 to 2012 and matched 1:2 to 50,000 non-statin users.

A smaller propensity score model involving 24,000 participants (half using a statin and half not) included approximately 5,000 HIV positive people vs 19,000 who were HIV negative, with follow-up continuing until first cancer diagnosis. This was to match for factors that were more likely to be associated with prescribing a statin, including age, calendar year, chronic infections and laboratory markers (LDL, albumin, Fib-4 index).

Cancer incidence was higher in the positive group (9.0% vs 7.1%). Cancers also occurred earlier in the HIV positive group (after 3.6 vs 4.5 years) and later in people using a statin (4.9 vs 3.7 years).

Overall, the use of a statin was associated with a lower risk of all cancers, irrespective of HIV status, but with borderline significance of a greater impact for the HIV positive group. See Table 1.

Virally mediated cancers (anal, oropharynx, liver and NHL, but not Hodgkin's lymphoma) were all significantly reduced in the overall cohort, with larger reductions in anal and liver cancer reductions in the HIV negative group (both HR: 0.28; 95%CI: 0.10 to 0.82). Overall, non-virus cancers were also reduced (HR: 0.63; 95%CI: 0.57 to 0.70,  $p < 0.0001$ )

Both overall and in subgroups, there were no cancers where statin use was associated with an increased risk.

Out of 4,431 incident deaths in the main cohort, statin use was also associated with a significantly reduced risk of death (HR: 0.55; 95%CI: 0.50 to 0.61).

In questions after the presentation, confounding by better socioeconomic states (in people receiving statins) was ruled out as the VACS is largely a low-income health provider. Further analyses are planned to look for whether individual statins have different effects.

### COMMENT

**Even though statins are safe, effective and widely used, several studies have reported suboptimal management of cardiovascular risks in HIV positive cohorts, perhaps linked to a reluctance to use statins.**

**These data might provide an additional reason to encourage their use.**

Reference

Bedimo R et al. Statin exposure is associated with decreased risk of cancer. 25th CROI 2018, Boston. Oral abstract 132.

<http://www.croiconference.org/sessions/statin-exposure-associated-decreased-risk-cancer> (abstract)

<http://www.croiwebcasts.org/console/player/37301> (webcast)

**Table 1: Statin exposure and risk of Cancer: By HIV Status and Cancer Type**

| Cancer type                      | All participants<br>HR (95% CI) | p       | HIV negative<br>HR (95% CI) | HIV positive<br>HR (95% CI) | p for interaction |
|----------------------------------|---------------------------------|---------|-----------------------------|-----------------------------|-------------------|
| <b>Any cancer</b>                |                                 |         |                             |                             |                   |
| n=1799                           | 0.61<br>(0.56 to 0.67)          | <0.0001 | 0.65<br>(0.59 to 0.72)      | 0.51<br>(0.40 to 0.64)      | 0.051             |
| <b>AIDS-defining cancers</b>     |                                 |         |                             |                             |                   |
| n=64                             | 0.61<br>(0.56 to 0.67)          | <0.0001 | 0.65<br>(0.59 to 0.72)      | 0.51<br>(0.40 to 0.64)      | 0.8               |
| <b>Non-AIDS defining cancers</b> |                                 |         |                             |                             |                   |
| n=1712                           | 0.63<br>(0.58 to 0.69)          | <0.0001 | 0.67<br>(0.60 to 0.74)      | 0.53<br>(0.41 to 0.67)      | 0.1               |

## Rate of bone loss on ART slows after the first year

Simon Collins, HIV i-Base

**A sub-study from the international START study provided reassuring data that the initial loss in bone mineral density (BMD) during the first year of ART, slowed during subsequent years,**

The START study randomised more than 4600 participants to either starting ART immediately while the CD4 count was still about 500 or wait until it reached 350. The sub-study involving just over 200 people in each arm were presented by Andrew Carr from St Vincent's Hospital, Sydney and colleagues from the INSIGHT research network.

Bone mineral density (BMD) was measured at the spine, hip and femoral head at baseline and annually. Mean percentage changes in BMD were calculated using both ITT and observed analyses (ie censoring data from the deferred ART group when treatment was started. The percentage of people on ART in the deferred arm was 18%, 28%, 58% and 85% after 1, 2, 3 and 4 years respectively.

In the ITT analysis which compared all participants by the initial randomisation, the initial 2% drop at both sites over the first year for the group on immediate ART converged over subsequent years, to show non-significant differences at the spine by year 3 (diff = -0.5%, p=0.26) and at the hip by year 4 (diff = -0.2%, p=0.68).

In the observed analysis, significant differences at all three sites continued between groups at all time points, although a slower age-related reduction was seen over time.

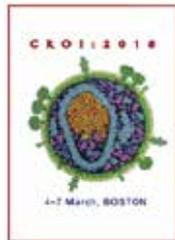
Predictors of greater BMD decline in the deferred group included lower baseline CD4 count (-at the spine and neck) and in the immediate group this was higher baseline viral load (in the hip and neck).

No differences were reported by choice of ART, although tenofovir DF was used by 83% of participants, efavirenz by 89% and PI by 13%.

### Reference

Carr A et al. Rates of bone loss slow after the first year of ART: START BMD substudy final results. 25th CROI 2018, Boston. Poster abstract 722.

<http://www.croiconference.org/sessions/rates-bone-loss-slow-after-first-year-art-start-bmd-substudy-final-results-0> (abstract and poster)

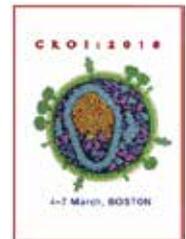


CROI 2018: PREGNANCY

## Standard dose of dolutegravir sufficient in late pregnancy: interim results from DoIPHIN1 study

Polly Clayden, HIV i-Base

**As with other published studies, DoIPHIN1 shows standard dose of dolutegravir should be used in the third trimester. But HIV positive women who start ART in late pregnancy are a vulnerable group with a higher risk of adverse outcomes and vertical transmission of HIV.**



DoIPHIN1 is a randomised study looking at dolutegravir (DTG) 50 mg + 2NRTIs vs efavirenz (EFV) 600 mg + 2NRTIs (standard of care) in 60 ART-naive pregnant women presenting at 28 to 36 weeks of gestation to routine ante natal clinics in Kampala, Uganda and Cape Town, South Africa. The preliminary findings were shown at CROI 2018. These are from a scheduled interim analysis after the first 16 women delivered, conducted to evaluate safety and ensure that DTG exposure in the third trimester is sufficient.

The study is a collaboration between University of Liverpool, Infectious Disease Institute, Kampala, Uganda, Desmond Tutu HIV Foundation, Cape Town and University of Cape Town.

As women diagnosed with HIV in late pregnancy need to start ART immediately (before laboratory results to determine study eligibility are available), all participants began treatment with standard of care EFV-based ART and were randomised to continue or switch to DTG + 2NRTI at a median of 3 days (range 1 to 8) later.

The primary endpoint was AUC<sub>0-24</sub> of DTG in the third trimester and at two weeks postpartum. Secondary endpoints included viral load <50 copies/mL at delivery and safety and tolerability of DTG in the women and infants.

After two weeks on DTG, samples were collected pre-dose and at 0.5, 1, 2, 3, 4, 6, 8 and 24-hours post-dose with the same sampling schedule postpartum.

Of the 16 women who delivered, eight each received DTG and EFV. Median baseline viral load was 4.15 log copies/mL (range 2.43 to 6.07) and this was similar between arms. By days 14 and 28, viral load was undetectable in 5/8 and 4/8 participants receiving DTG, and 1/5 and 2/7 receiving EFV, respectively. At 2-weeks postpartum, viral load was undetectable in 5/6 and 4/7 participants in the respective treatment arms.

There were two virological failures among participants receiving DTG and none EFV. One had no detectable drug in plasma and was non-adherent (17815 copies/mL at day 28), the second had evidence of three class drug resistance (NNRTI, NRTI and protease mutations; 145 copies/mL at day 28). The investigators noted adherence was a problem across both arms.

There was a modest reduction in DTG exposure in the third trimester but the standard 50 mg dose did not need adjustment. The study used data from non-pregnant population in SPRING 1 and SPRING 2 as reference. See Table 1.

**Table 1: Dolutegravir PK parameters**

|                    | Third trimester<br>n=7<br>GM (95% CI) | Postpartum<br>n=2<br>(Both values) | Reference<br>(SPRING 1&2) |
|--------------------|---------------------------------------|------------------------------------|---------------------------|
| Cmax (ng/<br>mL)   | 2645<br>(1965 to 3325)                | 4224, 4055                         | 3670                      |
| C24 (ng/<br>mL)    | 778<br>(447 to 1108)                  | 1211, 603                          | 1110                      |
| AUC24<br>(ng.h/mL) | 39415<br>(28296 to 50534)             | 59633, 44305                       | 53600                     |

Key: AUC: Area under the curve; C: concentration, CI: confidence interval; GM: Geometric mean.

Both regimens were well-tolerated. Four SAEs were reported, two in one participant in the DTG arm and two in the EFV arm. DTG arm: grade 3 elevation in liver function tests (possibly drug related, concomitant herbal medicine); stillbirth (asphyxia from tight cord around the neck, deemed unrelated to study drug). EFV arm: one grade 3 hypertension; one infant with polydactyly.

DoIPHIN1 confirms that women who start ART in late pregnancy are a vulnerable group who might have a higher rate of treatment failure.

## C O M M E N T

**Women who present late are a very difficult population to reach and recruit into studies – including DoIPHIN1 – and usually have poorer outcomes than those who start ART earlier in pregnancy. These women need extra support and careful management.**

**DoIPHIN1 completed recruitment in January 2018 and follow up is ongoing.**

**DoIPHIN2 – which has just begun – will randomise 250 late presenting women 1:1 to either DTG- or EFV-containing ART. The mothers and infants will be followed up from initiation until weaning of the infant or 18-months postpartum (whichever is earlier).**

**DoIPHIN2 is designed to generate high-quality evidence on the efficacy and safety of DTG to help inform recommendations, and operational guidance on use of DTG in this high-risk scenario.**

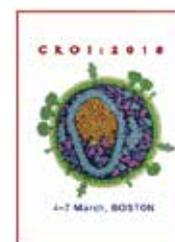
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1. Waitt C et al. DoIPHIN-1: dolutegravir vs efavirenz when initiating treatment in late pregnancy. 25th CROI. Boston. 4–7 March 2018. Poster abstract 807.  
<http://www.croiconference.org/sessions/dolphin-1-dolutegravir-vs-efavirenz-when-initiating-treatment-late-pregnancy> (abstract and poster)
2. DoIPHIN2 website.  
<https://www.dolphin2.org>

## Women's risk of becoming HIV positive increases three-fold in late pregnancy and four-fold postpartum

Polly Clayden, HIV i-Base

**The probability of HIV acquisition per condomless sex act rose steadily throughout pregnancy and was highest during the postpartum period in an analysis of two HIV prevention studies. This suggests that biological changes occurring during pregnancy and postpartum increase women's HIV risk.**



These findings were presented at CROI 2018 and also published online in *The Journal of Infectious Diseases* 5 March 2018. [1, 2]

Previous studies have found pregnancy to be a risk factor for HIV acquisition – a 2014 meta-analysis of five studies reported an increased risk of 30% overall with two showing double the risk and two other studies no increase.

For this analysis, investigators from Partners in Prevention HSV/HIV Transmission Study and Partners PrEP Study estimated the probability of HIV acquisition per sex act during pregnancy and postpartum and compared these probabilities to non-pregnant time periods.

The primary outcome was first evidence of HIV infection in HIV negative women linked to HIV positive male study partner.

Frequency of sex within partnership and condom use was reported monthly. HIV and pregnancy testing was monthly or quarterly depending on the original study. Time periods were categorised by reproductive stage: early pregnancy (0–13 weeks gestation), late pregnancy (14 weeks to delivery/loss), postpartum (delivery to 6 months; less for losses), or not pregnant/postpartum.

The investigators used a complementary log-log model adjusted for male partner viral load, active PrEP use, condom use and age. Reference case was a non-pregnant 25-year old woman, not using PrEP with male partner viral load 10,000 copies/mL.

Participants were 2,751 African HIV negative women with HIV positive male partners (not receiving ART) followed prospectively for up to 48 months in the two prevention studies. Data were censored from study visits after male partner started ART and seroconversions from unlinked HIV infections (from non-study partners).

At enrollment women were a median of 32.0 years of age (IQR 27.0–37.7); number of sex acts with study partner in the last month was 4.0 (IQR 2.0–8.0); and 670 (24%) had condomless sex with study partner in the past month.

Results accounted for decrease in sexual frequency and condom use as pregnancy progressed.

There were 686 pregnancies during follow up: 426 (62.1%) live births; 169 (24.6%) loss; and 91 (13.3%) ongoing at study exit.

Analysis of 78 new HIV infections revealed overall incidence per 100 person years of 1.62 (95% CI 1.29 to 2.01). Incidence varied considerably during the respective time periods: 1.25 (95% CI

0.95 to 1.62) during non-pregnant/-postpartum time; 5.37 (95% CI 3.44 to 7.99) during early pregnancy through postpartum; 3.75 (95% CI 1.22 to 8.75) during early pregnancy; 7.02 (95% CI 3.74 to 12.01) during late pregnancy; and 4.68 (95% CI 1.72 to 10.18) during postpartum.

HIV infectivity per 1000 sex acts (calculated using reference case) was: 1.05 during non-pregnant/-postpartum time; 2.19 during early pregnancy; 2.97 during late pregnancy; and 4.18 during postpartum.

Adjusted relative risk (RR) with non-pregnant/-postpartum as reference, early pregnancy through postpartum was 2.76 (95% CI 1.58 to 4.81),  $p < 0.001$ . RR was 2.07 (95% CI 0.78 to 5.49),  $p = 0.14$  and 2.82 (95% CI .29 to 6.15),  $p = 0.01$ , in early and late pregnancy respectively.

Sensitivity analyses using estimated data of HIV infection, excluding women randomised to active PrEP arms, excluding women who were never pregnant during follow up and including a longer postpartum period gave similar results.

In summary, there was a 3-fold increased risk of HIV per sex act in late pregnancy and 4-fold increase postpartum. The investigators noted that these results suggest that biological changes associated with pregnancy and postpartum, contribute to increased risk of HIV acquisition. But they did not directly assess any biological mechanisms for this phenomenon.

## C O M M E N T

**As the investigators stressed, antenatal care presents tremendous opportunities to promote HIV prevention and care.**

**These data highlight the importance of four key points.**

- **Making sure women are counseling on this increased risk.**
- **Repeat HIV testing during maternal health visits, including closer to delivery and postpartum.**
- **Identifying HIV positive male partners and linking them to ART programmes.**
- **Promoting HIV prevention strategies during these periods of elevated risk, including oral PrEP.**

## References

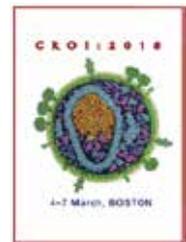
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## CROI 2018: CURE RESEARCH

### Cure research at CROI 2018: defining and reducing the reservoir and the risks from interrupting treatment

Simon Collins, HIV i-Base

**Although most news from CROI covered clinical research, hundreds of studies at the conference were on basic science, many of which were linked to cure research.**



This year this included several themes that are important to report.

- Studies defining, measuring and identifying the viral reservoir.
- Research in people who started ART in very early acute infection.
- The risks and safety of treatment interruptions in cure research.
- Whether current ART needs to be more active.
- Optimistic results regarding monkeys enabled to stop ART without viral load rebounding.

## Introduction

A good update on progress in cure research that also highlighted studies at CROI 2018 was given by Huldrych Günthard as part of the pre-CROI workshop for young investigators, and is now online as a webcast. [1]

As an introduction, much cure research is focussed on the latently infected reservoir of resting CD4 T-cells that is established in early infection. These cells predominate in lymph tissue throughout the body but the reservoir also includes other body sites and possibly other immune cells. This pool is established within three weeks of infection (by Fiebig stage 1), persists during untreated infection, and only gradually declines over decades on ART.

Many presentations focused on defining and measuring this reservoir, an essential research goal to judge whether interventions are having any impact. Outgrowth tests are a specialist research tool and underestimate replication-competent virus while PCR tests (generally for integrated HIV DNA in PBMCs or tissue as a surrogate but other methods are also used) also measure defective virus. More than 90% of HIV-identified particles picked up by PCR tests are sufficiently defective as to no longer be infectious. (As reference, several years ago, Eriksson et al published a nice review paper, online as open access, that compares ways to measure the reservoir. [2])

By definition, these HIV-containing resting cells are not affected ART which targets active stages of the HIV lifecycle. Although the resting cells periodically and unpredictably wake, slowly reducing the pool, they are so long-lived that it would take many decades for the body to completely clear them on ART alone. In

someone with a small reservoir (ie from starting ART within weeks of infection) this would take 60 years and considerably longer for someone who started ART in chronic infection.

So other studies reported on ways to activate these resting cells. Even if HIV is not eradicated, significantly reducing the pool might allow for a shorter period during which ART alone might provide a cure.

Although many existing drugs are, and have been, studied for the potential to activate resting cells, at least in vitro, Deborah McMahon from the University of Pittsburgh presented results from a placebo controlled ACTG study showing that none of the three single infusion doses of the approved HDAC inhibitor romidepsin were successful at inducing HIV in adults on ART, despite potent results *ex vivo*. [3]

Also, as any intervention needs to selectively activate only cells that contain HIV, another research goal is to find a way to identify latently infected cells in vivo. Two studies at CROI 2018, showed that the initial hope that CD32+ cells might be a biomarker for latently infected cells was not supported in practice. [4, 5]

### Studies in acute infection

As a smaller reservoir might be easier to cure, many researcher groups are looking to study people who started ART during acute infection.

An overview of such interventions was presented by Eugène Kroon from the Thai RV-254/SEARCH 010 study, now also webcast. This ongoing cohort includes 527 participants who were diagnosed as part of an intensive HIV testing programme and who started ART during acute HIV infection, many while still HIV antigen negative. [6]

This study has already reported results from three small single-intervention cure studies – using early ART, the HDAC inhibitor vorinostat and the bNAb VRC01, respectively. Unfortunately, after treatment was interrupted, all 40 participants had rapid viral rebound (at median 22 days, range 9 to 296). The treatment interruption protocol in these studies was to closely monitor viral load (every 3-7 days) and to restart ART after rebound is confirmed >1000 copies/mL. A fourth study going is using an Ad28/MVA therapeutic vaccine.

Although none of these interventions were effective – VRC01 having the most promising results in terms of delayed viral rebound – safety results for participants included no CD4 decline, no drug resistance or acute HIV symptoms, and that all participants resuppressed HIV after restarting with the same ART regimen. However, the interruption did cause HIV seroconversions in 70% of the participants who until the study had remained HIV antibody negative on 4th generation HIV tests. [7] These participants had the negative outcome of now testing HIV antibody positive in Thailand where this outcome has social consequences related to employment and insurance. Also, despite the early restart protocol, viral load had rebounded to more than 10,000 copies/mL for some participants before ART was resumed, and two had CD4 declines of more than 20%.

In another presentation from the same cohort, Timothy Schacker from the University of Minnesota presented results on how very early ART can reduce the reservoir (and can reduce lymph node fibrosis), but that this needs to be during Fiebig stages 1 and 2. There was little difference to starting in chronic infection

for people starting in Fiebig stage 3 or later (approximately 4-5 weeks post infection). [8]

### Treatment interruptions in cure studies

The inclusion of treatment interruptions in research is complicated by safety concerns given that continuous ART is recommended in all guidelines. These include:

- Reseeding or expanding the latent reservoir.
- Clinical outcomes from increased immune activation and inflammation.
- Impact in compartment sites, especially the brain/CSF.
- The risk of seroconversion symptoms after a long period on ART.
- CD4 declines that might not fully recover.

Two posters at CROI 2018 also reported reassuring data that concerns about reseeding the reservoir after a short treatment interruption might only have limited short-term risks.

Katherine Clarridge and colleagues from NIAID, reported on the impact of short treatment interruptions (maximum 16 weeks with protocol to restart with rebound >1,000 copies/mL) in ten people who started ART in chronic infection. [9]

These participants in bNAb VRC01 study had a median CD4 nadir of 345 cells/mm<sup>3</sup> (but this ranged from 16 to 900) and had been suppressed on ART for a median of 8 years (range: 3 to 17). The poster reported that the size of the HIV reservoir and immune parameters returned within 6-12 months of restarting ART. However, despite a protocol with a low threshold to restart ART, median levels reached 30,000 copies/mL (mean 50,000; range 340–273,000) when ART was restarted. Details are available in the open access paper published earlier this year in PLoS Pathogens. [10]

Also related, a recently published paper from a small vaccine study using a 16-week treatment interruption (where viral load rebounding to >50,000 copies/mL). Although the vaccine was unsuccessful, the longer time taken to restart ART revealed higher than expected rates of spontaneous viral control without ART in four participants. That these participants were all in the placebo arm, shows the uncertainties linked to small numbers of people in this research. This level of rebound is higher than many participants, researchers and advocates would support, but also shows the lack of consensus for the time that might be needed to observe an active result. [11]

A related poster from Zachary Strongin and colleagues reported an analysis of a 12-week treatment interruption on the viral reservoir in 12 participants in ACTG studies. Although the poster included limited details about the interruption (no viral rebound or CD4 results), the results on HIV DNA showed a return to pre-interruption levels six months after restarting ART. [12]

Although these results from short treatment interruptions are encouraging, they only include small numbers of participants. Serious seroconversion symptoms have previously been reported from stopping ART, and the concern that renewed inflammation in other sites, principally CSF, was referred to in several presentations. Neurological complications are always a focus at CROI and this year an oral presentation by Serena Spudich from

Yale University reported that HIV is detectable in CSF cells in up to half of participants on long-term suppressive ART. [13]

The median age of the 69 participants (97% male) was 50 years, with current and nadir CD4 counts of approximately 700 and 300 cells/mm<sup>3</sup> respectively. Median duration on ART was 8.6 years (range 5.4-16.4).

Persistence of HIV-containing cells in CSF was not associated with higher levels of HIV DNA in blood or with levels of inflammation in blood or CSF. However, plasma viral load was associated with both cell-free HIV RNA and myeloid cell activation in CSF.

A timely oral presentation by Joseph Mankowski from Johns Hopkins included results that could inform the risk of treatment interruptions in this site. This macaque study looked at the CSF reservoir, comparing four animals euthanised on ART with six animal who first interrupted treatment for four months. [14]

As well as showing that SIV RNA rebounded in CSF during the treatment interruption, they found high SIV DNA in spinal cord even on ART, and that rebound was high in the newly reported site during the treatment interruptions. Viral rebound in CSF during the treatment interruptions came from SIV that was already in these compartments rather than being reseeded. These researchers concluded that their result showed that HIV drugs should be developed to better target this site.

One limitation of this study is that it involved a model of dual SIV infection in which one of the viruses is known to be very virulent in the brain. Macaques infected with these viruses all develop central nervous system disease and progress to AIDS within three months. The model was designed to facilitate studies of AIDS-related dementia rather than answer questions related to curing HIV, so the relevance of the results to the human situation will need to be confirmed.

### Does HIV continue to replicate on ART?

The underlying question of whether the reservoir is relatively fixed (archived from when ART is started, and maintained by clonal proliferation) or whether it is continuously repopulated and evolving (reseeded by ongoing replication from body sites not reached by ART) has important implications for cure strategies. Two studies at CROI 2018, both reported in detail in an earlier HTB report, failed to find evidence of ongoing replication on ART. [15]

Mary Kearney and colleagues used phylogenetic analysis to show identical HIV retained viral sequences from plasma and lymph tissue, even after many years on ART, including using the same integration sites, including in longitudinal lymph samples. [16]

Thomas Rasmussen and colleagues showed no impact from ART intensification in a randomised placebo-controlled study from adding dolutegravir in 40 participants who had been suppressed on standard ART for more than three years. [17]

Both studies concluded that from a virological perspective, current ART doesn't need to be more potent or effective.

Results from a large observational study were important for showing the range of individual responses. An oral presentation from Nadine Bachmann and colleagues from the Swiss HIV Cohort reported that 25% of people on long-term suppressive continuous ART (defined as >5 years without two having

consecutive viral load results >200 copies/mL) did not have reductions in their reservoir size. In these participants, total HIV DNA remained either stable over time or increased. Although early viral blips were associated with a lower rate of reservoir decay, the observational nature of the study means that cause and effect can't be shown (or even inferred). [18]

This was a large study in 1078 HIV positive participants with three or more PBMC samples from the first 5 years on ART and 429 people with an additional late sample > 8 years (median 10.5 years).

The mean reservoir size declined very slowly and steadily (by 0.05 log/year) over five years and more slowly still over subsequent years. However, there were very wide differences in reservoir size between individuals. In multivariate analysis, having an early viral load blip over the first 18 months of ART, was associated with a higher reservoir, with earlier ART, faster time to suppression, higher CD4 count and non-B sub-type associated with a lower reservoir. Blips were significantly associated with a slower decay of the reservoir.

### Successful results with bNAbs PGT-121 and a TLR-7 agonist

And then dozens of other studies were presented as posters, and highlighted in six poster discussion sessions on defining the reservoirs, insights from viral rebound, the reservoir in acute infection and the impact of ART in both human and animal studies.

In addition to ART, the range of therapeutic interventions includes 'shock and kill' approaches with various latency inducing drugs, vaccines, bNAbs with effector functions, immune modulation and direct targeting of infected cells, many of which were reported at CROI, or more likely, combination approaches.

The most encouraging of these was included in the first press conference at CROI 2018, before the results were shown at the main conference. The results in a macaque study showed significantly delayed time to viral load rebound off ART following dual treatment with the bNAbs PGT-121 and a TLR-7 agonist. The full results were presented as a late breaker oral abstract by Dan Barouch from Beth Israel Deaconess Medical Centre, Boston, and are reported in detail in an earlier HTB report. In the group receiving dual therapy, 5/11 animals maintained undetectable viral load for six months without restarting ART. [19, 20]

However, even these most promising results were presented as very preliminary stages for an HIV cure.

*Thanks to Richard Jefferys for editorial comments to this article.*

### C O M M E N T

**Please see later in this issue of HTB for an excellent article by Ricahrd Jefferys on assessing treatment interruptions in cure research studies. [21]**

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## IMMUNOLOGY

### Elite controllers: sex differences and factors associated with loss of immune control

Richard Jefferys, TAG

**Over the past few months, several interesting papers addressing elite control of HIV infection have seen publication.**

The ability of elite controllers to maintain undetectable viral loads and relatively preserved CD4 T cell counts in the absence of ART has led them to be proposed as a model for a functional cure of HIV infection. But there is also evidence that many elite controllers exhibit elevated levels of inflammation compared to HIV negative counterparts, and eventually experience disease progression, leading some researchers to call this proposition into question. [1]

The uncertain relevance of elite control to HIV cure research is prompting studies that attempt to parse the factors distinguishing individuals who preserve elite controller status from those who ultimately progress.

In the journal *eBioMedicine*, Wang Zhang and colleagues explore the expression of a variety of genes and proteins in a cohort of 19 elite controllers, compared to 32 individuals with progressive HIV infection and 23 healthy HIV negative controls. [2]

Of particular note, nearly half the elite controllers (9) were women, allowing the researchers to compare results based on sex. The authors point out that several previous studies have reported that women tend to be overrepresented among elite controllers (e.g. see Crowell et al [3] and de Azevedo et al [4]).

A potentially important finding is that the gene expression profiles of female elite controllers were similar to HIV negative women, but there were significant differences between male elite controllers and HIV negative male controls. A potential implication is that women will be more likely to maintain elite controller status over time compared to men – this possibility will need to be investigated further.

Among the differences observed in elite controllers compared to individuals with progressive HIV infection were downregulation of the genes for CXCR6 and SIGLEC1. The authors explain that these differences could be associated with decreased susceptibility of CD4 T cells for HIV entry and reduced cell-to-cell virus transmission mediated by myeloid cells.

Levels of the chemokine CCL4 (MIP-1 $\beta$ ) were found to be higher among elite controllers versus progressors, consistent with a previous study. [5] Conversely, levels of the inhibitory immune cell receptor PD-1 (and its ligand PD1-L2) were significantly lower, echoing another recent paper reporting lower levels of multiple inhibitory receptors in elite controllers. [6]

*BMC Medicine* has published an analysis by José Benito and colleagues that looks at possible contributors to loss of elite control. [7]

The researchers evaluated 36 elite controllers followed for approximately a decade on average, comparing multiple immunological parameters between those with stable CD4 T cell counts (n=22) and those exhibiting significant CD4 T cell decline during the follow up period (n=14). Interestingly, women made up 67% of the former group but only 31% of the latter, a statistically significant difference (p=0.04). The authors don't offer any comment on this apparent overrepresentation of women in the group of elite controllers with stable CD4 T counts.

Many immunological variables were found to differ between elite controllers and HIV-negative healthy controls, as well as between stable elite controllers and those experiencing CD4 T cell declines. Distinctions between elite controllers and HIV negative healthy controls included lower levels of several T cell subsets: naïve, recent thymic emigrant, stem cell memory, and regulatory. Expression of the T cell costimulatory receptor CD28 was lower, whereas CD95 – involved in apoptotic cell death – was increased.

Comparisons between the stable elite controllers and progressors revealed that the latter group had lower levels of naïve and recent thymic emigrant CD8 T cells, as well as higher levels of CD8 T cells with effector memory and senescent phenotypes. The finding suggests that CD8 T cells may have been differentiating at a higher rate in this group – in other words, naïve CD8 T cells were more frequently becoming activated and transitioning into memory cells (perhaps reflective of a more strenuous battle to keep HIV contained). The progressor group also showed increased expression levels of PD-1 in both total CD4 T cells and the central memory CD4 T cell subset.

In a separate study published in the *Journal of Virology* earlier this month, María Pernas and colleagues conducted a retrospective, longitudinal analysis of factors contributing to loss of viral load suppression in a cohort of elite controllers. [8]

A total of 31 elite controllers were included, defined based on having viral load below detectable levels (50 copies/mL) on three consecutive measures over a year of follow up.

Fourteen of these individuals subsequently experienced increases in viral load (two consecutive measures above the detection limit within a year), and were classified as transient controllers. The remaining 17 maintained undetectable viral loads and were classified as persistent controllers. Sex differences were not apparent in this study, with women making up 43% of the former group and 41% of the latter. The only significant differences were for time since diagnosis (averaging 8 years and 18 years, respectively) and sexual transmission as mode of HIV acquisition (71% vs. 35%).

The availability of samples prior to the viral load increases in the transient controller group allowed several factors associated with the loss of HIV suppression to be identified. CD8 T cells targeting the HIV Gag protein were found to be significantly less polyfunctional (assessed based on production of the cytokines IFN- $\gamma$ , TNF- $\alpha$  and IL-2) and displayed a more activated phenotype a year prior to viral load becoming detectable. HIV genetic diversity within the *env* gene was also significantly higher, with a similar trend observed for the *gag* gene. In contrast, persistent controllers showed little or no evidence of ongoing viral evolution.

Inflammatory biomarkers were elevated in the transient controllers, and an analysis of 70 different cytokines and chemokines in plasma samples revealed that increased levels of RANTES and Platelet Derived Growth Factor (PDGF) AA were the best predictors of subsequent loss of elite controller status. RANTES in particular showed a strong association, being an average of four-fold higher in transient controllers.

In discussing their results, the authors emphasise the importance of focusing on examples of strict, persistent control of HIV if the goal is to identify “the right model of functional remission.” They also suggest that factors strongly predictive of future viral load rebound—such as RANTES levels—might have the potential to help discriminate elite controllers likely to benefit from ART from those who may not require it.

Similar points are made in a commentary in *EBioMedicine* by Laura Tarancon-Diez and colleagues. [9] The commentary accompanies a paper describing an elite controller who has maintained extremely low levels of HIV RNA and HIV DNA for a decade, without fully seroconverting on the Western Blot antibody assay. [10] Evidence of polyfunctional HIV-specific CD8 T cell responses and strong antibody-mediated cellular cytotoxicity (ADCC) by natural killer cells is reported. The individual acquired HIV from a partner who was not able to control the same CRF02\_AG virus variant. Neither partner possesses known favorable HLA alleles although both are heterozygous for the CCR5Δ32 mutation. [10]

The commentary also cites work published last year from the French CODEX cohort, which described a subset of HIV controllers in whom viral load had never been detectable using routine assays during an average of 18 years of follow up. In a comparison with controllers who had experienced viral load blips, T cell counts were reported to be stable (as opposed to progressively declining), and this was accompanied by lower T cell activation and HIV DNA measurements. This study also showed a trend toward an overrepresentation of women in the persistently undetectable group (34 out of 52, 65%) versus the viral load blips group (90 out of 178, 51%,  $p=0.06$ ).

Tarancon-Diez and colleagues advocate concentrating on “this very scarce proportion of individuals that are able to persistently control the virus” in order to inform the design of cure strategies aiming to induce long-term remission in the absence of ongoing ART.

Whether there might be particular features of the immune response (or other factors) in women that increase the likelihood of persistent elite control needs to be elucidated. Ongoing work is investigating possible differences related to HIV persistence in women receiving ART, with Eileen Scully presenting the latest findings from her research as a poster at the CROI 2018 conference. [11]

Scully has uncovered a number of significant sex-based associations, including higher expression of several antiviral genes.

As Zhang and colleagues argue in the closing section of their *EBioMedicine* paper: “Despite extensive data on the male and female difference on disease outcome, research does not

sufficiently take gender into account. Altogether, our study showed that it would be important to carefully consider gender in cohort design for future transcriptomic and intervention studies on HIV-1 patients.”

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## BASIC SCIENCE & CURE RESEARCH

### Assessing antiretroviral therapy interruptions in HIV cure research

Richard Jefferys, TAG

**Last month, researchers from the Laboratory of Immunoregulation at the National Institute of Allergy and Infectious Diseases (NIAID) [1] published a paper in PLoS Pathogens addressing the use of antiretroviral therapy (ART) interruptions in HIV cure research [2].**

The joint lead authors were Katherine E. Clarridge and Jana Blazkova, and the focus of the study was on the effects of an analytical treatment interruption (ATI) performed during a clinical trial of the broadly neutralizing antibody VRC01. The main results offer reassurance that the ATI had no long-term negative effects for participants – as articulated in an accompanying NIAID press release titled NIH Study Supports Use of Short-Term HIV Treatment Interruption in Clinical Trials – but there are some possible safety concerns that the data does not address. [3]

Results of the VRC01 trial were published in 2016 in the New England Journal of Medicine. [4]

The protocol design involved an initial VRC01 infusion upon entering the study, followed by an ATI three days later. VRC01 infusions were subsequently administered every four weeks until week 24. Criteria for restarting ART included:

- A confirmed >30% decline in baseline CD4 cell count or an absolute CD4 cell count <350 cells/mm<sup>3</sup>
- A sustained (≥4 weeks) HIV RNA level of >5,000 copies/mL
- Any HIV-related symptoms

Ten participants were enrolled. VRC01 only led to a slight delay in viral load rebound, so ART was restarted in all cases with the duration of the ATI ranging from 22 to 115 days (median 57 days). Nine of the individuals restarted ART due to meeting the criteria for a sustained viral load increase to over 5,000 copies/mL, while the remaining participant experienced a confirmed >30% decline in baseline CD4 cell count. No participant had a CD4 T cell drop to less than 350 cells/mm<sup>3</sup>.

The researchers evaluated multiple HIV reservoir measures as well as biomarkers of immune activation and inflammation, comparing results obtained prior to the ATI with those observed after viral load was re-suppressed by ART. In almost all cases, there were no significant differences pre- and post-ATI. The lone exception was the chemokine RANTES, a potential inflammatory biomarker, which remained significantly elevated after ART resumption (at least at the time point measured, which was a median of 363 days after restarting).

Several parameters were evaluated *during* the ATI, revealing that there were increases in measures of the HIV reservoir and immune activation that subsequently declined to baseline levels after ART was resumed. However, data on inflammatory biomarkers during the ATI are not reported, making it unclear to what extent inflammation may have been temporarily elevated

– it seems likely that it was, given the transient spike in markers of immune activation. The relationship between short-term inflammation and risk of clinical events is uncertain but potentially of concern, so this is an aspect of ATIs that deserves additional study. Among the steps taken to maximise safety in the trial, the exclusion criteria included evidence of heart disease, which might render an individual particularly susceptible to inflammation-related risks.

Another question that has been raised regarded the safety of ATIs – particularly by longtime treatment activist Jules Levin of the National AIDS Treatment Advocacy Project (NATAP.org) – is whether HIV levels in the central nervous system (CNS) might increase and have the potential to cause harm. CNS samples were not taken in this NIAID study.

Overall, the trial results are consistent with the idea that short-term ATIs can be performed safely in the context of HIV cure research, but they do not necessarily represent the last word on the topic. There was a robust dialogue regarding the use of ATIs at the recent Regulation of Clinical Research Related to HIV Cure meeting that took place in Bethesda on January 25, and a webcast of the session should soon be available on the Forum for Collaborative Research website ([www.forumresearch.org](http://www.forumresearch.org)). [5] TAG has also received support from the Elizabeth Taylor AIDS Foundation to survey community-based treatment activists regarding their views on ATIs, and a report will be published in the fall of 2018.

The Laboratory of Immunoregulation at NIAID has recently published a different study involving an ATI that highlights another important consideration in this type of HIV cure research: the inclusion of a placebo arm. [5]

The researchers conducted a clinical trial of a combination therapeutic HIV vaccine approach (DNA primes followed by a vesicular stomatitis virus vector boost) administered to individuals who initiated ART soon after infection. The vaccines were found to induce HIV-specific T cell responses, but this did not lead to superior control of viral load rebound during an ATI compared to placebo immunisation.

The researchers noted that, perhaps surprisingly, there were four cases of post-ATI control of viral load to low levels that occurred in the placebo arm of the trial. The finding emphasises that a subset of early-treated individuals can exhibit prolonged viral load suppression after an ATI, and that this needs to be considered when designing trials of therapeutic interventions. In the absence of a placebo arm, spontaneous control of HIV replication could be misinterpreted as evidence of a therapeutic effect. The authors specifically cite the open-label trial of therapeutic vaccination plus romidepsin that was presented by Beatriz Mothe at CROI 2017, pointing out that a similar proportion of participants in the placebo arm of their study maintained viral loads below 2000 copies/ml for at least 16 weeks.

The inclusion of placebo control arms in trials is not necessarily as simple as it might sound, because there are cost and logistical issues that are prohibitive for some research groups. However, it is clearly a necessary step for establishing that a candidate intervention has had a genuine effect, and results from open-label trials should be interpreted with caution until confirmed in a randomised controlled context.

## Source

Jefferys R. Assessing Antiretroviral Therapy Interruptions in HIV Cure Research. (22 February 2018).

[http://tagbasicscienceproject.typepad.com/tags\\_basic\\_science\\_vaccin/2018/02/assessing-antiretroviral-therapy-interruptions-in-hiv-cure-research.html](http://tagbasicscienceproject.typepad.com/tags_basic_science_vaccin/2018/02/assessing-antiretroviral-therapy-interruptions-in-hiv-cure-research.html)

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## TRANSMISSION &amp; PREVENTION

## Update on PrEP IMPACT study

## Simon Collins, HIV i-Base

**The latest update from the UK PrEP IMPACT trial has reported that more than 5,000 people have already been recruited over the first five months and are now receiving PrEP.**

This means half the original 10,000 places are now recruited, from more than 100 clinics.

The update details new proposal to reallocate half of the approximately 2,000 trial places that were initially for women and people from other high-risk groups.

This change was due to much lower recruitment from these populations, linked to lower current awareness of PrEP. These places will now become available to gay and bisexual men, where demand meant many clinics quickly filled their initial allocations.

The oversight board from the study also plans to set up a new planning group to plan the process commissioning PrEP by NHS England and local authorities.

The next update will be in April 2018.

For further information on the trial please visit the trial website.

<http://www.prepimpacttrial.org.uk>

## C O M M E N T

**In is important that this study has quickly passed the halfway mark for enrolment, but this target has only been met for gay and bisexual men.**

**An important focus remains to make this study widely available to everyone.**

## References

NHS England HIV CRG. Update on the PrEP trial following the Oversight Board meeting in March 2017.

<https://www.england.nhs.uk/commissioning/spec-services/npc-crg/blood-and-infection-group-f/f03/prep-trial-updates>

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## OTHER NEWS

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### US Congress rejects Trump's proposed cuts to research budget for 2018

Simon Collins, HIV i-Base

**As the largest single funder of HIV research, the proposed cuts to the US research budget threatened to undermine recent advances in global health, especially in relation to HIV/AIDS.**

It is therefore reassuring that a recent press statement from the US-based Treatment Action Group (TAG) outlined that the US congress would continue to support the research agenda for the 2018 financial year.

Instead, Congress approved a budget that increased the National Institutes of Health (NIH) budget by \$3.0 billion, rejecting the proposed \$5.8 billion cut for 2018 that would have halted many ongoing programmes. This included a \$353 million increase the National Institute of Allergy and Infectious Diseases (NIAID) that leads the country's largest HIV research programme.

However, the Ryan White programme which affects treatment and care for more than half of all people living with HIV in the United States was flat-funded.

Although the CDC hepatitis programme received a small additional \$5 million, this increase is still far short of the \$100 million in funding needed to expand viral hepatitis screening and surveillance efforts.

The Division of TB Elimination at CDC (DTBE) was also flat-funded at \$142.2 million for yet another year. Despite its continued success, DTBE has not seen a significant increase since 1994.

Source:

TAG press release. TAG statement on final appropriations for fiscal year 2018. (23 March 2018)

<http://www.treatmentactiongroup.org/content/tag-statement-final-appropriations-fiscal-year-2018>

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## ON THE WEB

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### HCV advocacy training manual

**Hepatitis C virus & coinfection with HIV: training manual for treatment advocates (2018)**

An excellent updated resource from US activist organisation TAG.

<http://www.treatmentactiongroup.org/content/updated-training-manual-hcv-coinfection-hiv>

[http://www.treatmentactiongroup.org/sites/default/files/HCV\\_Curriculum\\_english\\_2\\_20\\_18.pdf](http://www.treatmentactiongroup.org/sites/default/files/HCV_Curriculum_english_2_20_18.pdf) (PDF)

## FUTURE MEETINGS

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### Conference listing 2018

The following listing covers some of the most important upcoming HIV-related meetings and workshops.

#### 4th Joint BHIVA/BASHH Spring Conference

17 – 20 April 2018, Edinburgh

[www.bhiva.org](http://www.bhiva.org)

#### International Workshop on Clinical Pharmacology of Antiviral Therapy 2018

22 – 24 May 2018, Washington

[www.virology-education.com](http://www.virology-education.com)

#### 12th INTEREST

29 May – 1 June 2018, Kigali

[interestworkshop.org](http://interestworkshop.org)

#### 22nd International AIDS Conference (AIDS 2018)

23 – 27 July 2018, Amsterdam

[www.aids2018.org](http://www.aids2018.org)

#### International Workshop on HIV & Aging

13 – 14 September 2018, New York, USA.

[www.virology-education.com](http://www.virology-education.com)

#### Australasian HIV&AIDS Conference 2018

24 – 26 September 2018, Sydney

[www.hivaidsconference.com.au](http://www.hivaidsconference.com.au)

#### HIV Glasgow 2018

28 – 31 October 2018, Glasgow

[www.hivglasgow.org](http://www.hivglasgow.org)

## PUBLICATIONS & SERVICES FROM i-BASE

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### 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 (September 2016)
- HIV & quality of life: side effects & long-term health (Sept 2016)
- Guide to PrEP in the UK (November 2016)
- HIV testing and risks of sexual transmission (June 2016)
- Guide to changing treatment and drug resistance (February 2015)
- Guide to HIV, pregnancy & women's health (December 2015)

### New pocket guides

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

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

We hope these are especially useful as low literacy resources.

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.

### Order publications and subscribe online

All publications can be ordered online for individual or bulk copies. All publications are free. Unfortunately bulk orders are only available free in the UK.

<http://i-base.info/order>



## HIV i-Base

All publications are free, including bulk orders, because any charge would limit access to this information to some of the people who most need it.

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• **Booklets about HIV treatment****ART in pictures: HIV treatment explained** (*June 2017*): 32-page A4 booklet      quantity \_\_\_\_\_**Guide to hepatitis C coinfection** (*April 2017*): 52-page A5 booklet      quantity \_\_\_\_\_**UK Guide To PrEP** (*November 2016*): 24-page A5 booklet      quantity \_\_\_\_\_**Introduction to ART** (*September 2016*): 48-page A5 booklet      quantity \_\_\_\_\_**HIV and quality of life: guide to 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 HIV, pregnancy and women's health** (*November 2015*): 52-page A5 booklet      quantity \_\_\_\_\_**Guide to changing treatment: what if viral load rebounds** (*Jan 2018*): 24-page A5 booklet      quantity \_\_\_\_\_• **Other resources****HIV Treatment 'Passports'** - Booklets for patients to record their own medical history      quantity \_\_\_\_\_**Phoneline posters (A4)**      quantity \_\_\_\_\_

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