ISSN 1472-4863

hiv treatment bulletin (e)

HTB: 2018 vol 19 no 4

23 February 2018: no.4

CONTENTS

Published by HIV i-Base

EDITORIAL

This short pre-CROI edition of HTB includes likely highlights from the important annual conference – this year being held in Boston.

Rapid reports from CROI will be posted online as they become available, and will also be compiled in the next issues of HTB. Also recommended, the excellent BHIVA feedback meetings that will be held in six cities across the UK a couple of weeks later.

Other news includes several new UK policies:

- Universal ART on diagnosis - approved in the UK
- Gay men to have access to HPV vaccination

Also, importantly for global health, the first FDA tentative approval for a fixed dose combination (FDC) containing dolutegravir, emtricitabine and TAF.

This issue includes several reviews relating to inform the planned large-scale roll-out of generic FDCs based on this integrase inhibitor and new reviews from Richard Jefferys on cure research.

Finally, a review from a recent survey highlighting levels of discrimination and difficulties reported by trans people and links to new resources to mobilise access to PrEP.

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 help is appreciated.

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

CONFERENCE REPORTS

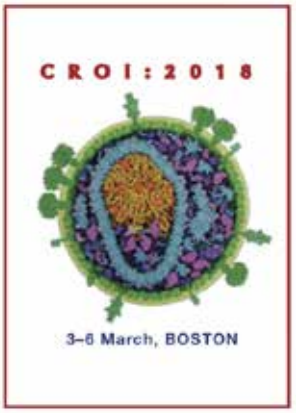
Conference on Retroviruses and Opportunistic Infections (CROI 2018)

4–7 March 2018, Boston

CROI 2018 - highlights from the preliminary programme

Simon Collins, HIV i-Base

Essential for latest HIV treatment advances, the annual Conference on Retroviruses and Opportunistic Infections (CROI) will be held this year from 3-6 March in Boston.



In addition to some of the best scientific research, this meeting has some of the fastest web coverage, so it will be easy to track and view the oral presentations, even if you are unable to attend the meeting.

Based on the preliminary programme only – posted online earlier – the following subjects have been highlighted for overview lectures.

http://www.croiconference.org/preliminary-agenda

We will also review highlights of the full programme after this becomes available a week before the conference starts. This will include the oral presentations and late-breakers together with the approximately 1000 new studies selected for the conference.

http://www.croiconference.org

Plenary lectures and overviews

- Pre-conference workshops for young investigators. A day of overview lectures given by international researchers as grounding for the upcoming meeting. The programme includes the community-led Martin Delaney Memorial lecture that this year will focus on women in research.
- HIV cure research will include results from using various compounds to measure, nudge and manipulate the resting cells that remain out of reach to antiretroviral medicines. It will also include increasingly used strategy of very early HIV treatment, in some cases even before seroconversion. A separate pre-conference workshop will also feature research to be presented at CROI 2018.
- Women's health is the focus of a separate workshop before the main conference that we will report with CROI 2018.
- New drugs - including long-acting antiretrovirals and immune-mediated antibodies - for both treatment and preventions.
- HIV prevention - PrEP and more, including impact on HIV incidence.
- A plenary lecture on growing up HIV positive and adolescent care.
- Breastfeeding - one of the few management situations where international guidelines are different depending on where in the world you live and on your resources in that country. In high-income countries, including the UK, guidelines routinely recommend using formula milk as this has zero risk of transmission to the infant in a setting where the risk of other infections is low. In situations where access to sterile water is difficult and where other background health risks are higher, WHO guidelines recommend exclusive breastfeeding, but only when the mother has an undetectable viral load on ART. A two-hour symposium on Monday will look at latest evidence for all situations.
- Long-term complications: life expectancy and debate over immune activation and ageing.
- TB coinfection: a session looking at TB diagnositcs and management, including multidrug resistance.
- Changing challenges of hepatitis C - including the potential to globally eradicate HCV, other liver complications and transplantation from HIV and/or HCV positive donors.

C O M M E N T

STOP PRESS: The full programme (minus abstracts) went online as this issue of HTB was finalised.

http://www.croiconference.org/sites/default/files/uploads/croi2018-program-conference-information.pdf (PDF)

As with previous years, BHIVA will be organising a series of post CROI feedback meetings (see below).

BHIVA best of CROI feedback workshops

bhiva.org

This year BHIVA will hold six CROI feedback workshops.

These meetings provide a selected review of the key presentations from CROI 2018, with a chance to ask questions.

- Monday 19 March, London
- Tuesday 20 March, Birmingham
- Wednesday 21 March, Haydock
- Tuesday 27 March, Cardiff
- Wednesday 28 March, Wakefield
- Thursday 29 March, Edinburgh

Registration is free – but places are held against a £20 card reservation for no-shows. Please register online.

http://www.bhiva.org/BestofCROI2018.aspx

TREATMENT ACCESS

FDA grants tentative approval to first DTG/FTC/TAF FDC

Polly Clayden, HIV i-Base

On 9 February 2018, the FDA's PEPFAR programme granted Mylan tentative approval for the first fixed-dose combination (FDC) of dolutegravir, emtricitabine, and tenofovir alafenamide (DTG/FTC/TAF). [1]

DTG/FTC/TAF 50/200/25 mg will be the first TAF-based fixed-dose combination available in low- and middle-income countries (LMICs) for first-line ART.

Mylan manufactures this generic product under licenses from the Medicines Patent Pool and Gilead Sciences (for DTG and FTC/TAF, respectively).

According to Mylan's press release, the tablet will be the smallest single-tablet regimen available for people in LMICs. It will be offered in both a 30-day and 90-day package.

C O M M E N T

This FDC has been highlighted as a potential optimised first-line ART regimen for some time – so this is good news. But, although this combination of antiretrovirals is currently recommended in the US and Europe, TAF is not yet recommended (or even mentioned) in WHO guidelines.

Several data gaps remain before it is likely to be recommended, particularly on safety in pregnant women and TB co-treatment.

More data on TAF and rifampicin will be presented at CROI 2018 but data in pregnancy are scant. We look at this in more detail in the March update of the i-Base Fit for Purpose report.

References
1. FDA tentative approval letter dolutegravir, emtricitabine, and tenofovir alafenamide. 9 February 2018. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/210237Orig1s000TAltr.pdf
2. Mylan press release. Mylan receives tentative approval for combination HIV treatment DTG/FTC/TAF under FDA's PEPFAR program. 20 February 2018. http://investor.mylan.com/news-releases/news-release-details/mylan-receives-tentative-approval-combination-hiv-treatment

Universal ART on diagnosis: approved by NHS England

Simon Collins, HIV i-Base

After several years of consultation, and two years after WHO guidelines recommended universal ART, NHS England will commission immediate ART for anyone who is diagnosed HIV positive. [1]

The announcement was made at the end of 2017, to take effect from 1 April 2018.

The press release notes that an estimated 3000 people are expected to directly benefit from this updated policy in the first year.

Officially, commissioning still remained at only providing ART once the CD4 count approached 350 cells/mm^3.

C O M M E N T

The clinical evidence supporting the benefit of early ART was sufficiently strong in July 2015 (following the results of the START study) that WHO guidelines indicated an immediate notice to change with a rapid updates later in 2015. [2, 3]

The process for NHS England was considerably slower.

Luckily, most doctors were able to ignore the official commissioning policy by prescribing early ART to prevent HIV transmission.

References
1. NHS news. NHS England announces new specialised treatments for patients. (18 December 2017) https://www.england.nhs.uk/2017/12/nhs-england-announces-new-specialised-treatments-for-patients/?mc_cid=411c600fa4&mc_eid=316679c113
2. Collins S. Starting HIV treatment at high CD4 counts protects against both AIDS and non-AIDS events: overall and in subgroup analyses of START study. HTB 01 August 2015. http://i-base.info/htb/28606
3, Clayden P. New directions in the 2015 WHO ART guidelines. HTB, July 2015. http://i-base.info/htb/28597

PREGNANCY

Standard once-daily dolutegravir dosing achieves target levels during pregnancy

Polly Clayden, HIV i-Base

Dolutegravir exposure is lower in pregnancy compared to postpartum in the same women receiving once-daily dosing. Trough concentrations were lower than those in non-pregnant adults but above dolutegravir EC90.

IMPAACT 1026s is an ongoing non-randomised, open label, parallel-group, multicentre, phase 4 prospective pharmacokinetic (PK) study. It recruits HIV positive women receiving newly approved antiretrovirals in routine clinical care at IMPAACT sites in the US. [1]

Interim data from 15 women pregnant women in the dolutegravir arm of the study were first presented at CROI 2016. [2, 3] The full data set including 29 women receiving dolutegravir in pregnancy was published ahead of print on 23 January in AIDS. [4]

The 29 women had a median age of 32 years (range 21 to 42). Paired post-partum data were available for 12 of 15 women with second trimester visits and 22 with third trimester visits.

Median (IQR) dolutegravir AUC0-24 in the second, third trimester and postpartum were respectively: 47.6 mcg*hr/mL (33.4 to 63.7), 49.2 mcg*hr/mL (36.4 to 62.0) and 65mcg*hr/mL (47.8 to 88.4). Dolutegravir AUC0-24 was 29% lower in the third trimester compared to postpartum p=0.0003; and 37% lower in the second trimester, p=0.002.

Dolutegravir Cmax was 26% lower in the second trimester and 25% lower in the third trimester compared to paired postpartum data, respectively p=0.0098 and p=0.0025. And dolutegravir C24 was 51% lower in the second trimester and 34% lower in the third trimester compared to paired postpartum data, respectively p=0.0039 and p=0.0062.

Two women had pre-dose concentrations below the limit of quantification at the postpartum visit, which the authors suggested might be linked to recent non-adherence.

Median (IQR) concentrations of dolutegravir in cord blood and maternal plasma at delivery were respectively: 1.67 mcg/mL (1.17 to 2.00) and 1.24 mcg/mL (0.57 to 1.68). The ratio of cord blood to maternal plasma was 1.25 (1.07 to 1.40).

Infant median dolutegravir Cmax (washout data) was 1.85 mcg/mL (1.42–2.48) at a median 6.9 hours (3.5 to 9.2) after birth. At the final infant washout PK evaluation (between 5–9 days of life), all samples still had measurable dolutegravir (>0.005 mcg/mL).

One of 16 infants with washout PK data was breast fed but the study did not evaluate dolutegravir concentrations in breast milk. Plasma dolutegravir concentrations in this infant were 4.57 mcg/mL, 1.94 mcg/mL, 1.66 mcg/mL, and 0.44 mcg/mL at 7, 25, 46, and 150 hours after delivery. Excluding this breast fed infant – for whom the authors noted half-life could not be reliably calculated – median (IQR) dolutegravir half-life was 32.8 hours (25.9–35.9).

Grade 3 adverse events were reported in eight women: low haemoglobin (n=3), pre-eclampsia (n=2), and pre-term delivery, nausea/vomiting, cesarean wound infection/fever, blurry vision/headache, low albumin, and proteinuria (each n=1).

In the third trimester, 28/28 (100%) of women had viral load <50 copies/mL; and 27/29 (93%) at delivery (one >400 copies/mL). At postpartum PK visit, 14/19 (74%) women had viral load <50 copies/mL.Infants were born at a median of 38.9 weeks of gestation (range: 34.9–42.3). Four were pre-term, five small for gestational age, and four were low birth weight (one very low birth weight). All infants were HIV negative (based on best available data): 24 confirmed uninfected and five indeterminate (due to incomplete testing).

The authors reported clinical abnormalities at or shortly after birth in seven infants. Three were considered to be normal variants: one each with congenital filum terminale fibrolipoma, two vessel umbilical cord without other abnormalities, and post-axial polydactyly. The authors judged these unrelated to dolutegravir exposure.

Total anomalous pulmonary venous return was diagnosed in one infant – also considered unrelated to dolutegravir. One infant had increased jitteriness and chin tremors that resolved over the first months of life, these were also judged unrelated to dolutegravir exposure.

Two infants with renal abnormalities were deemed possibly related to dolutegravir exposure: one whose mother began dolutegravir treatment during week 12 of gestation, had an isolated renal cyst in the left kidney; the other whose mother began dolutegravir treatment during week 11 of gestation, had a multicystic dysplastic right kidney.

Other adverse events were reported in five infants. Two had transient low blood glucose shortly after birth. The infant with the multicystic dysplastic right kidney was also diagnosed with cystic fibrosis and experienced numerous adverse events over the first months of life. One infant had neonatal abstinence syndrome following maternal opiate use during pregnancy and respiratory failure. The fifth was diagnosed with sickle cell trait.

The authors summarised the PK, “dolutegravir exposure is decreased in pregnancy compared to postpartum, but remains at therapeutic concentrations during pregnancy with standard once daily dosing” and noted that further data are needed to assess infant safety.

References

1. US National Institutes of Health. Pharmacokinetic study of antiretroviral drugs and related drugs during and after pregnancy. https://clinicaltrials.gov/ct2/show/NCT00042289
2. Mulligan N et al. Dolutegravir pharmacokinetics in HIV-infected pregnant and postpartum women. Conference on Retroviruses and Opportunistic Infections (CROI) 2016. 22–25 February 2016. Boston, Massachusetts. Poster abstract 438.
www.croiconference.org/sessions/dolutegravir-pharmacokinetics-hiv-infected-pregnant-and-postpartum-women-0 (Abstract)
http://www.croiwebcasts.org/console/player/29497 (Webcast)
3. Clayden P. Early data from dolutegravir use during pregnancy. HTB. 22 March 2016. http://i-base.info/htb/29856
4. Mulligan N et al. Dolutegravir pharmacokinetics in pregnant and postpartum women living with HIV. AIDS. 23 January 2018. Publish ahead of print doi: 10.1097/QAD.0000000000001755.
https://journals.lww.com/aidsonline/Abstract/publishahead/Dolutegravir_pharmacokinetics_in_pregnant_and.97307.aspx

SIDE EFFECTS

Meta-analysis reports no significant risk of cardiac, IRIS or suicide with dolutegravir

Polly Clayden, HIV i-Base

Meta-analysis shows no significant effect of dolutegravir on the risk of cardiac, IRIS or suicide-related serious adverse events. There was a higher risk of insomnia with dolutegravir-based ART.

The results were first presented at EACS 2017 and published in the March 2018 edition of Current Opinion in HIV and AIDS. [1, 2, 3]

Although slightly expanded in the recent article the safety findings have remained consistent.

In this meta-analysis of 6647 patient-years follow up, the authors found a higher risk of Grade 1–4 insomnia adverse events for dolutegravir compared to other antiretrovirals: 6.1 vs 4.5% respectively, p=0.02.

But they found no significant difference between dolutegravir and other antiretrovirals in the risk of cardiovascular serious adverse events.

The authors note that as there are plans to switch millions of people onto dolutegravir-based treatment in sub-Saharan Africa within the next 18 months, this transition needs to be supported by continued pharmacovigilance with meta-analysis to monitor safety.

As other randomised trials looking at dolutegravir are completed these should be included in further safety evaluations: DAWNING (n=627), SWORD 1 and 2 (n=1024), Gilead trial 1489 (n=629) and Gilead trial 1490 (n=645).

The authors also highlight a recent analysis of the psychiatric disorders reported to the WHO pharmacovigilance database suggesting a higher risk of depression, suicide and self-injury for dolutegravir and raltegravir, compared with elvitegravir. [4] “Analyses of this type need to be repeated regularly and checked for potential confounding factors” they add.

C O M M E N T

Many other studies at EACS 2017 found few differences between dolutegravir and other integrase inhibitors. [5-8]

Also, an intensive six-month dolutegravir sleep study in older participants (>60 years), was presented at the PK workshop last year by Marta Boffito and colleagues. This study reported that higher dolutegravir Cmax and AUC were associated with reduced sleep time, but there were no significant changes in sleep scores over the first 28 days after switching to dolutegravir/abacavir/3TC. [9]

Unlike with sleep disturbance with efavirenz, dolutegravir can be taken in the morning and anecdotally this overcomes difficulties with insomnia in most cases, without causing additional problems during the day.

References

1. Hill A and Mitchell N. Meta-analysis of safety for DTG versus other ARVs in randomised trials: analysis of cardiovascular, CNS and IRIS endpoints. 16th EACS, 2017, Milan. Poster abstract PE12/17.
2. Clayden P. Studies on dolutegravir and sleep, cardiovascular and CNS side effects, and risk of IRIS. HTB. 28 November 2017. http://i-base.info/htb/32830
3. Hill AM et al. Risks of cardiovascular or central nervous system adverse events and immune reconstitution inflammatory syndrome, for dolutegravir versus other antiretrovirals: meta-analysis of randomised trials. Curr Opin HIV AIDS. 13 (2) March 2018. https://journals.lww.com/co-hivandaids/Abstract/2018/03000/Risks_of_cardiovascular_or_central_nervous_system.3.aspx
4. Kheloufi F et al. Neuropsychiatric events and dolutegravir in HIV patients: a worldwide issue involving a class effect. AIDS 2017; 31:1775 –1777.
5. Bollen P et al. Discontinuation of dolutegravir- and elvitegravir-containing cART in the Netherlands: incidence rates and risk factors. 16th EACS, 2017, Milan. Poster abstract PE12/10.
6. Mondi A et al. Effectiveness and discontinuation rate of dolutegravir (DTG)-based regimens as either first line or switch antiretroviral therapy (ART): data from the Icona Cohort. 16th EACS, 2017, Milan. Poster abstract PE9/83.
7. Migliorini D et al. Experience in using dolutegravir in experienced and treatment naïve patients attending two HIV clinics in Northamptonshire UK. 16th EACS, 2017, Milan. Poster abstract PE12/3.
8. Lüftenegger D et al. Tolerability and persistence of dolutegravir-based regimens: second interim analysis of the prospective multicenter DOL-ART cohort. 16th EACS, 2017, Milan. Poster abstract PE9/52.
9. Elliot E et al. Relationship between dolutegravir plasma exposure, quality of sleep and its functional outcome in patients living with HIV over the age of 60 years. 18th International Workshop on Clinical Pharmacology of Antiviral Therapy, 14- 16 June 2017, Chicago. Oral abstract O8. http://regist2.virology-education.com/2017/18AntiviralPK/11_Boffito.pdf (PDF)

DRUG INTERACTIONS

Significant drug-drug interaction between dolutegravir and isoniazid-rifapentine

Polly Clayden, HIV i-Base

Dolutegravir given with once-weekly isoniazid-rifapentine led to marked cytokine release and serious adverse events in a drug-drug interaction study conducted by the US NIH. Symptoms included flu-like syndrome and elevated transaminase levels in two participants.

This study was in healthy volunteers and was stopped early due to the toxicities. Results were first presented at CROI 2017. [1, 2]

In a paper published in Clinical Infectious Diseases, 3 February 2018, the authors provide additional insights into potential mechanisms resulting in elevated adverse events – although they note this was "not the original intent" of the study. [3]

Treating latent TB infection (LTBI) is critical in preventing its progression to active TB. Three months of once-weekly isoniazid-rifapentine (3HP) is a good potential LTBI treatment option for HIV positive people. This regimen has similar efficacy to nine months of daily isoniazid, but with shorter duration and higher rates of adherence and treatment completion. Drug-drug interaction studies currently only support the use of 3HP in people receiving efavirenz- or raltegravir-based ART.

The study was a single-centre, open-label, fixed-sequence, drug-drug interaction study. Participants received once-daily dolutegravir 50 mg alone (days 1 to 4) and with once-weekly isoniazid 900 mg, rifapentine 900 mg, and pyridoxine 50 mg (days 5 to 19).

Dolutegravir concentrations were measured on days 4, 14, and 19. Rifapentine, 25-desacetyl-rifapentine, and isoniazid concentrations were measured on day 19. The investigators examined cytokines and anti-drug antibodies to isoniazid and rifapentine at select time points during and after drug completions.

Two of four participants developed serious toxicities after the third isoniazid-rifapentine dose – causing the study to be terminated.

The investigators found highly elevated levels of interferon-γ, CXCL10, CRP and other cytokines to be temporally associated with symptoms. They rarely detected anti-drug antibodies.

Dolutegravir AUC was decreased by 46% on day 14, 48 to 72 hours after the second isoniazid-rifapentine dose. Rifapentine and 25-desacetyl rifapentine levels were comparable to reference data, but isoniazid AUCs were 67 to 92% higher in the participants who developed toxicities.

In the discussion, the authors note that drug-drug interaction studies between rifamycins and antiretrovirals – in particular boosted protease inhibitors – in healthy volunteers have previously been associated with unexpected toxicities including elevated transaminases and hypersensitivity reactions.

These interactions were thought to be linked to either higher than FDA-approved antiretroviral doses or increased levels of rifamycins and their metabolites due to cytochrome CYP3A4 inhibition by ritonavir.

But when the same regimens were studied in people with HIV/TB-coinfection, the toxicities were not replicated. So, unidentified mechanisms for differences in immune response or tolerability of these drugs might also exist between people with/without HIV/TB.

"Further studies are needed to carefully evaluate the safety and efficacy of dolutegravir-based regimens when coadministered with isoniazid-rifapentine, especially given the recent availability of generic dolutegravir in countries with high TB burden, and the desire to use this once-weekly regimen in patients living with HIV" the authors wrote.

COMMENT

Data on safe and effective administration with active TB or LTBI treatment are essential for any new antiretroviral recommended for use in low- and middle-income countries.

Because of this unexpected finding with dolutegravir and isoniazid-rifapentine, the IMPAACT-4TB programme [4] – conducted in South Africa led by the Aurum Institute – includes a single-arm phase 1/2 PK and safety study of dolutegravir-based ART and once-weekly 3HP in 60 HIV positive adults with HIV (receiving ART with suppressed viral load) with LTBI. This PK study has just started and country implementation of the programme and starting 3HP will not start in HIV positive people or child contacts until the results of the study are analysed (expected in early 2019).

24-week data from the INSPIRING study looking at dolutegravir-based ART with rifampicin-based TB treatment will be presented at CROI 2018. [5]

References
1. Brooks KM et al. Early termination of a PK study between dolutegravir and weekly isoniazid/rifapentine. CROI 2017. 13–16 February 2017, Seattle. Poster abstract 409a.
   http://www.croiconference.org/sessions/early-termination-pk-study-between-dolutegravir-and-weekly-isoniazidrifapentine (abstract and poster).
2. Clayden P. Significant interaction between once-weekly isoniazid/rifapentine and daily dolutegravir: study stopped due to toxicity. HTB. 24 April 2017.
   http://i-base.info/htb/31476
3. Brooks KM et al. Cytokine-mediated systemic adverse drug reactions in a drug-drug interaction study of dolutegravir with once-weekly isoniazid and rifapentine. Clin Inf Dis Feb 3 2018.
   https://academic.oup.com/cid/advance-article-abstract/doi/10.1093/cid/ciy082/4836314
4. Unitaid. Tuberculosis prevention for high-risk groups (IMPAACT4TB).
   https://unitaid.eu/project/tuberculosis-prevention-high-risk-groups-impaact4tb/#en
5. US National Institutes of Health. Open-label study of dolutegravir (DTG) or efavirenz (EFV) for HIV/TB co-infection.
   https://clinicaltrials.gov/ct2/show/NCT02178592

CURE RESEARCH

New data on identifying and targeting the latent HIV reservoir

Richard Jefferys, TAG

Several recently presented and published studies offer potentially important new data relevant to efforts to identify cells containing latent HIV and target them for elimination.

At the 8th International Workshop on HIV Persistence held in Miami last December, [multiple research groups reported on their attempts to confirm a newly published – and widely publicised – claim that the cell surface molecule CD32a is preferentially expressed on latently infected cells. [1, 2]

The results indicate that the picture is considerably more complicated: the original findings could not be verified and instead it appears that expression of CD32a may be driven by other factors, including cell activation and active HIV transcription. Summaries of these studies can be found in the published abstracts from the workshop (see abstract numbers OP 1.5, OP 2.4, OP 2.6 and OP 4.2). [3]

While disappointing, this work does not end hopes that markers of latently infected cells can be identified – other candidates that are being examined are CCR5, when expressed by resting memory CD4 T cells (see the study from the laboratory of Robert Siliciano published late last year [4]), and CD30, a cell surface molecule better known for its association with lymphoma that is being investigated by Tim Henrich and colleagues. [5]

One of the reasons why markers of latently infected cells would be a boon to the cure research field is that they might facilitate elimination strategies akin to those now being used successfully against cancers. A number of effective cancer immunotherapies involve equipping T cells with receptors that target cell surface molecules on malignant cells, such as CD19, CD22, and CD30. It is conceivable that this “chimeric antigen receptor” (CAR) T cell approach could be adapted to target latently infected cells if appropriate markers could be identified.

CAR T cells are also being developed that target HIV antigens, with a recent paper in PLoS Pathogens from Scott Kitchen colleagues reporting some encouraging results obtained with stem cell-derived CAR T cells in macaques. [6] However, in order for the approach to work against latently infected cells, it would be necessary to activate the latent HIV first to trigger production of viral antigens.

An article in STAT News by Sharon Begley provides an accurate and nuanced perspective on Kitchen’s paper, offering the appropriately cautious headline: “Preliminary study hints that genetically modified T cells might fight HIV.” [7] In contrast, coverage in The Daily Beast unfortunately opts for misleading hype, with their piece titled: “This doctor’s revolutionary stem cell treatments could eradicate HIV.” [8]

The research group of Jonathan Angel in Canada is pursuing a novel method for targeting latently infected cells: an oncolytic rhabdovirus named MG1, which is primarily being developed for its ability to preferentially infect and destroy cancer cells. Angel and colleagues have published a study in the Journal of Infectious Diseases demonstrating that MG1 also appears capable of targeting cells latently infected with HIV, while sparing uninfected cells (the paper is open access). [9]

In an analysis of the effects of MG1 on memory CD4 T cells isolated from 14 HIV positive individuals on ART, both total and integrated HIV DNA levels declined in 12 out of the 14 samples. The mechanism for MG1’s preferential targeting

is unclear, but may relate to changes in latently infected cells that affect their response to the cytokine interferon. The authors note that clinical trials are already underway in cancer [10], which should help discern if the approach can be safely studied in HIV infection. In an interview with MD Magazine, Angel notes MG1 that can cause fever and malaise, and adverse events may be dose-dependent. [11]

Another paper in PLoS Pathogens comes from Christina Gavegnano and colleagues, who show that a class of drugs called Jak inhibitors can inhibit the maintenance of latently infected cells, and prevent them spreading infection when latent HIV is reactivated. [12] Jak inhibitors target a pathway involved in the survival and proliferation of memory CD4 T cells, and have been found safe in the treatment of certain inflammatory diseases and myelofibrosis. The authors note that an ongoing clinical trial is evaluating the effects of the Jak inhibitor ruxolitinib in HIV positive people on ART. [13]

Source

Jefferys R. TAG Basic Science Blog (17 January 2018)

http://tagbasicscienceproject.typepad.com

References

1. 8th International Workshop on HIV Persistence
http://www.hiv-persistence.com
2. Jefferys R. Flagging the HIV reservoir. TAG basic science blog. (16 March 2017).
http://tagbasicscienceproject.typepad.com/tags_basic_science_vaccin/2017/03/flagging-the-hiv-reservoir.html
3. Abstracts from the 8th International Workshop on HIV Persistence.
http://viruseradication.com/supplement-details/Abstracts_of_the_Eighth_International_Workshop_on_HIV_Persistence_during_Therapy
4. Jefferys R. HIV latency: tapped in transition, lurking in Treg. TAG basic science blog. (16 November 2017).
http://tagbasicscienceproject.typepad.com/tags_basic_science_vaccin/2017/11/hiv-latency-trapped-in-transition-lurking-in-treg.html
5. NIH grant listings. Henrich TJ et al. Targeting latent HIV-1 reservoirs with the antibody-drug conjugate, brentuximab vedotin
http://grantome.com/grant/NIH/R33-AI116205-04
6. Zhen A et al. Long-term persistence and function of hematopoietic stem cell-derived chimeric antigen receptor T cells in a nonhuman primate model of HIV/AIDS. PLoS Pathogens (28 December 2017).
https://doi.org/10.1371/journal.ppat.1006753
7. Begley S. Preliminary study hints that genetically modified T cells might fight HIV. (02 January 2018).
www.statnews.com/2018/01/02/car-t-cells-hiv-treatment
8. Schultz KJ. This Doctor's Revolutionary Stem Cell Treatments Could Eradicate HIV. Daily Beast, (15 January 2018).
www.thedailybeast.com/this-doctors-revolutionary-stem-cell-treatments-could-eradicate-hiv
9. Ranganath N et al. The oncolytic virus MG1 targets and eliminates cells latently infected with HIV-1: implications for an HIV cure. JID, 217(5);721–730. https://doi.org/10.1093/infdis/jix639. (14 February 2018)
https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jix639/4706282
10. Ottawa hospital news release. Cancer patients treated in world-first clinical trial of Canadian viral therapy. (10 July 2015)
http://www.ohri.ca/newsroom/newsstory.asp?ID=649
11. Kaltwasser J. Virus seems able to destroy latent HIV-infected cells. MD mag. (04 January 2018).
www.mdmag.com/medical-news/virus-seems-able-to-destroy-latent-hivinfected-cells
12. Gavegnano C et al. Novel mechanisms to inhibit HIV reservoir seeding using Jak inhibitors. PLoS Pathogens. https://doi.org/10.1371/journal.ppat.1006740. (21 December 2017).
http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1006740
13. Clinicaltrials.gov. Evaluating the safety and tolerability of ruxolitinib in antiretroviral-treated HIV-infected adults.
https://clinicaltrials.gov/ct2/show/NCT02475655

Recruiting natural killer cells to target HIV persistence

Richard Jefferys, TAG

An important goal in HIV cure research is the identification of immune responses that might be induced or enhanced to promote clearance of virus-infected cells. The main focus of this work has been on adaptive immunity – components of the immune system that can specifically recognise HIV, which include CD4 T cells, CD8 T cells, B cells and antibodies.

But there is growing interest in cells considered part of the innate immune system, particularly natural killer (NK) cells. [1]

NK cells have the potential to destroy virus-infected cells by several mechanisms, including the identification of generic signs of cellular distress or infection, or via antibody-mediated recruitment to a target cell (known as antibody-dependent cellular cytotoxicity/ADCC).

Over the past few months a number of studies have been published that support the idea that NK cells can play an important role in controlling virus replication. In the journal Nature Medicine, Nicolas Huot and colleagues describe evidence that NK cells contribute to suppression of SIV replication in the lymph nodes of African Green Monkeys (AGMs), a host species that does not experience pathogenic consequences from the infection. [2]

In experiments comparing nonpathogenic SIV infection of AGMs to pathogenic infection in macaques, NK cells were found to localise within and around lymph node B cell follicles – the major site of virus replication and persistence – in AGMs, but were scattered randomly in macaques, with no accumulation in follicles. NK cell numbers in lymph nodes also progressively declined in macaques, while being maintained at pre-infection levels in AGMs.

Additional analyses found that these differences were associated with an increased frequency of NK cells expressing CXCR5 (a receptor governing homing into follicles) and localised production of the cytokine IL-15 in the follicles of AGMs. The role of IL-15 was further confirmed by administration of an anti-IL-15 antibody, which depleted NK cells from the lymph nodes of the AGMs and led to a significant increase in SIV replication.

The authors write in their conclusion: "On the basis of our results, we anticipate that better comprehension of NK cell biology in lymphoid tissues, as provided here, will endorse the search for new NK cell-based immunotherapies for HIV infection."

A review published in the journal AIDS in November covers some of the potential NK cell–based immunotherapies that are under investigation. [3] A panoply of clinical trials are testing broadly neutralising antibodies (bNAbs), which may have the ability to promote NK cell-mediated ADCC. In some cases bNAbs are being evaluated in tandem with latency-reversing agents, with the aim of depleting the HIV reservoir. [4]

Also cited is the toll-like receptor 9 (TLR9) agonist MGN1703, which researchers at the University of Aarhus have shown can promote NK cell activation in HIV positive people on ART. [5] The same research group has also reported that NK cell responses may have been linked to an HIV DNA decline in some participants in a trial of the latency-reversing agent panobinostat. [6]

Other NK cell–based immunotherapies in clinical trials include ALT-803, a modified version of the cytokine IL-15. The research group of Timothy Schacker at the University of Minnesota is conducting a small study involving ALT-803 administration to HIV-positive individuals on ART. [7]

A paper published in the Journal of Virology late last year describes a transient anti-SIV effect of the compound in macaques that were not receiving ART. [8] Schacker and colleagues have also recently launched a trial in which individuals will receive infusions of NK cells from matched donors in combination with the cytokine IL-2. [9]

The effects of the cytokine alpha interferon on HIV persistence are a major topic of interest at the newly-funded BEAT-HIV Collaboratory led by Luis Montaner at the Wistar Institute in Philadelphia. [10]

Last month in *Clinical Infectious Diseases*, Stéphane Hua and colleagues presented evidence that NK cell activation associates with a decline in HIV DNA levels in HIV positive individuals receiving alpha interferon for the treatment of hepatitis C. [11]

In sum, after a long period in the shadow of the better-known components of the adaptive immune system, NK cells are now emerging as potentially important players in HIV cure research. Results from the ongoing trials should soon shed additional light on how they might be able to contribute.

Source

Jefferys R. TAG Basic Science Blog (18 January 2018)
http://tagbasicscienceproject.typepad.com

References

1. Scully E et al. NK cells in HIV disease. Curr HIV/AIDS Rep. 2016; 13: 85–94. doi: 10.1007/s11904-016-0310-3. (21 March 2016).
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4821863
2. Huot N et al. Natural killer cells migrate into and control simian immunodeficiency virus replication in lymph node follicles in African green monkeys. Nature Medicine (2017). 23: 1277–1286. doi:10.1038/nm.4421.
https://www.nature.com/articles/nm.4421
3. Mikulak J et al. Natural killer cells in HIV-1 infection and therapy. AIDS: 31(17);2317–2330. doi: 10.1097/QAD.0000000000001645. (13 November 2017).
https://journals.lww.com/aidsonline/Abstract/2017/11130/Natural_killer_cells_in_HIV_1_infection_and.1.aspx
4. TAG cure trial listing.
http://www.treatmentactiongroup.org/cure/trials
5. Vibholm L et al. Short-course toll-like receptor 9 agonist treatment impacts innate Immunity and plasma viremia in individuals with HIV Infection. CID: 64(12); 1686–1695, https://doi.org/10.1093/cid/cix201. (15 June 2017).
https://academic.oup.com/cid/article-abstract/64/12/1686/3064483?redirectedFrom=fulltext
6. Olesen R et al. Innate immune activity correlates with CD4 T cell-associated HIV-1 DNA decline during latency-reversing treatment with panobinostat. J Virol. 2015 Jul 29. pii: JVI.01484-15.
http://jvi.asm.org/content/early/2015/07/24/JVI.01484-15.abstract
7. Clincaltrials.gov. Proof of principle study of pulse dosing of IL-15 to deplete the reservoir in HIV infected people (ALT-803).
https://clinicaltrials.gov/ct2/show/NCT02191098
8. Ellis-Connell AL et al. ALT-803 transiently reduces SIV replication in the absence of antiretroviral treatment. J Virol. J92(5), March 2018. VI.01748-17.
http://jvi.asm.org/content/early/2017/11/02/JVI.01748-17.abstract
9. Clincaltrials.gov. Adoptive transfer of haploidentical natural killer cells and IL-2.
https://clinicaltrials.gov/ct2/show/NCT03346499

10. BEAT collaboratory.
http://beat-hiv.org
11. Hua S et al. Pegylated interferon-α–induced natural killer cell activation Is associated with HIV-1 DNA decline in ART-treated HIV-1/hepatitis C virus-coinfected patients. CID, cix1111, https://doi.org/10.1093/cid/cix111. (20 December 2017).
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/cix1111/4767848

OTHER NEWS

Discrimination against gay men overturned with new UK HPV vaccine programme

Simon Collins, HIV i-Base

After many years of criticism for a discriminatory public health programme and a protracted pilot scheme, gay men in the UK are finally to start to benefit from access to the HPV vaccine. [1]

The announcement was made on 5 February 2018, noting that access would still only be available in phases, following successful results from the pilot programme. [2, 3]

Less than 4% of men eligible for the vaccine declined participation, although recorded first-dose uptake is so far only 45%.

Support from NHS clinics was very high for the programme, with reimbursement of only £10 per injection.

A previous criticism from the pilot programme is that no baseline data were collected on prevalence of HPV genotypes, and no efficacy data was collected on immune response post vaccination. [4]

C O M M E N T

This announcement is good news, however late, although no details were provided about the proposals to phase in access, other than this would start from April 2018.

Although the programme was welcomed by the British Association for Sexual Health and HIV (BASHH) the organisation also noted that "we ultimately believe that HPV vaccination should be made available to all adolescents regardless of gender, and across the entirety of the UK". [5]

References

1. Dept of Health and Social Care. HPV vaccination programme for men who have sex with men. (05 February 2018).
https://www.gov.uk/government/news/hpv-vaccination-programme-for-men-who-have-sex-with-men?mc_cid=411c600fa4&mc_eid=316679c113
2. Dept of Health and Social Care. HPV vaccination for men who have sex with men: year 1 pilot. (05 February 2018).
https://www.gov.uk/government/publications/hpv-vaccination-for-men-who-have-sex-with-men-year-1-pilot
3. Public Health England (PHE). Human papillomavirus (HPV) vaccination for Men who have sex with Men (MSM) 2016/17 pilot evaluation. (February 2018)
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/678987/HPV_msm_year1_evaluation_report.pdf (PDF)
4. Collins S. AT LAST: Gay men and transgender people in England get vaccine to prevent genital warts and anal cancer – impressive pilot results. HTB, 27 February 2017.
http://i-base.info/htb/31151
5. BASHH statement. BASHH welcomes decision to extend HPV vaccination programme for men who have sex with men in England. (06 February 2018).
https://www.bashh.org/news/news/bashh-welcomes-decision-to-extend-hpv-vaccination-programme-for-men-who-have-sex-with-men-in-england/?mc_cid=411c600fa4&mc_eid=316679c113

UK study highlights discrimination against trans people living with HIV

Roy Trevelion, HIV i-Base

The first study to measure stigma and discrimination in health and social care towards trans people in the UK was published this month. [1] This is much needed, it reports on stigma generally for trans people, and on increased risk factors for HIV.

The community-led HIV StigmaSurvey UK 2015 investigated experiences of people living with HIV in the past 12 months. The anonymous online survey went out to over 120 community organisations and 46 HIV clinics to people aged over 18.

Trans participants self-identified via questions on gender identity and gender at birth. The term cisgender referred to people who identified with the gender they were assigned at birth.

31 out of 1576 participants identified as trans. There were 19 trans women, 5 trans men, 2 gender queer/non binary, and 5 other. Multivariate analysis was used to identify social and demographic predictors of being treated differently to non-HIV patients. High levels of social stigma were reported for trans compared to cisgender. Respectively, there were 39% vs 23% worrying about verbal harassment, and 23% vs 9% with exclusion from family gatherings. 10% of trans participants reported physical assault within the last 12 months, compared to 4% of cisgender participants.

High levels of stigma and discrimination were reported in healthcare settings. Trans people reported being treated differently to non-HIV patients with 48% vs 30% (aOR 2,61, CI 1.06, 6.42) respectively, and 41% vs 16% (aOR 4.58, CI 1.83, 11.44) being delayed or refused healthcare.

Findings highlighted several notable factors for increased risk of HIV for trans people. In the past 12 months 29% vs 13% reported ever injected drug use for trans vs cisgender respectively. In the same period 39% vs 12% (trans vs cisgender) reported ever been paid for sex.

The findings call for increased awareness and training of healthcare staff around trans/non binary issues. Health services need to address multiple and complex needs of trans people living with HIV. This includes additional increased risk of HIV from injecting drug use and experiences of transactional sex.

Further research is needed to explore stigma and discrimination for trans people. This research should be inclusive of trans not only because of increased risk of HIV, but also for trans rights, understanding and representation in the wider community. Trans people should be included in all areas of research where gender information is collected.

C O M M E N T

In the UK, trans women are 49 times more likely to have HIV. This study confirms that clinical training programmes within the NHS must include trans/non binary issues. This awareness is important for HIV treatment and care, and also for PrEP and HIV prevention for all trans people.

A new report from Stonewall also highlights transgender experiences in the UK. [2]

References

1. Hibbert M et al. Experiences of stigma and discrimination in social and healthcare settings among trans people living with HIV in the UK. AIDS Care 2018 Feb 6:1-8. doi:10.1080/09540121.2018.1436687. (February 2018).
http://www.tandfonline.com/doi/full/10.1080/09540121.2018.1436687
2. LGBT in Britain: Trans report (2018)
http://www.stonewall.org.uk/lgbt-britain-trans-report?mc_cid=411c600fa4&mc_eid=316679c113

ON THE WEB

Online resources

PrEP resources for access

The following PDF resources were developed by the International Treatment Preparedness Coalition (ITPC) after a community-led consultative meeting on access to and use of PrEP in low - and middle-income countries.

http://itpcglobal.org/resources

- **What's out there on PrEP: a literature review.**

http://itpcglobal.org/wp-content/uploads/2018/02/ITPC-PrEP-Literature-Review-2017.pdf (PDF)

- **Meeting Report from ITPC meeting on access to PrEP.**

http://itpcglobal.org/wp-content/uploads/2018/02/ITPC-PrEP-Meeting-Report-2017.pdf (PDF)

- **Position Statement on community-led demand creation for PrEP among key populations**.

http://itpcglobal.org/wp-content/uploads/2018/02/PrEP-Position-Statement-2017.pdf (PDF)

- **Key population activist toolkit on PrEP.**

http://itpcglobal.org/resources/key-population-activist-toolkit-prep

http://itpcglobal.org/wp-content/uploads/2018/02/ITPC-PrEP-Toolkit-English.pdf (PDF)

FUTURE MEETINGS

Conference listing 2018

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

Conference on Retroviruses and Opportunistic Infections (CROI 2018)

4 – 7 March 2018, Boston

www.croiconference.org

BHIVA 'Best of CROI' Feedback Meetings 2018

Monday 19 March, London

Tuesday 20 March, Birmingham

Wednesday 21 March, Haydock

Tuesday 27 March, Cardiff

Wednesday 28 March, Wakefield

Thursday 29 March, Edinburgh

www.bhiva.org/BestofCROI2018.aspx

4th Joint BHIVA/BASHH Spring Conference

17 – 20 April 2018, Edinburgh

www.bhiva.org

12th INTEREST

29 May – 1 June 2018, Kigali

interestworkshop.org

International Workshop on Clinical Pharmacology of Antiviral Therapy 2018

Tbc May 2018, Washington

www.virology-education.com

22nd International AIDS Conference (AIDS 2018)

23 – 27 July 2018, Amsterdam

www.aids2018.org

International Workshop on HIV & Aging

13 –14 September 2018, New York, USA.

www.virology-education.com

Australasian HIV&AIDS Conference 2018

24 – 26 September 2018, Sidney

www.hivaidsconference.com.au

HIV Glasgow 2018

28 – 31 October 2018, Glasgow

www.hivglasgow.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 (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 by post, fax or 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

h-tb

HIV TREATMENT BULLETIN

HTB is published in electronic format by HIV i-Base. As with all i-Base publications, subscriptions are free and can be ordered using the form on the back page or directly from the i-Base website:
http://www.i-Base.info
by sending an email to: subscriptions@i-Base.org.uk
Editor: Simon Collins
Contributing Editor: Polly Clayden

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

HIV i-Base, 107 The Maltings,169 Tower Bridge Road, London, SE1 3LJ. T: +44 (0) 20 8616 2210. F: +44 (0) 20 8616 1250

http://www.i-Base.info

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

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.

However, any donation that your organisation can make towards our costs is greatly appreciated.

STANDING ORDER DONATION **THANK YOU FOR YOUR SUPPORT**

Title: _____ First Name _____ Surname _____

Address _____

_____

_____ Postcode _____

Email _____ @ _____

Telephone (s) _____ _____ _____

Please pay HIV I-Base £ _____ each month until further notice

Please debit my account number _____

Name of account (holder) _____ Bank sort code _____/_____/_____

Starting on _____/_____/_____ (DD/MM/YY)

Signature _____ Date _____/_____/_____ (DD/MM/YY)

To: Manager: (Bank name, branch and address)

_____

_____

Please complete the above and return to: HIV i-Base, 107 Maltings Place,169 Tower Bridge Road, London, SE1 3LJ

(Our bank details for donations: NatWest, Kings Cross Branch, 266 Pentonville Road, London N1 9NA.
Sort Code: 60-12-14. Account Number: 28007042)

ONE-OFF DONATION

I do not wish to make a regular donation at this time but enclose a one-off cheque in the sum of £ _____ .

GIVE AS YOU EARN

If your employer operates a Give-As-You-Earn scheme please consider giving to i-Base under this scheme. Our Give-As-You-Earn registration number is **000455013**. Our Charity registration number is 1081905

Since many employers match their employees donations a donation through Give-As-You-Earn could double your contribution. For more information on Give-As-You-Earn visit www.giveasyouearn.org

REFUNDS FROM THE TAX MAN

From April 2005 the Inland Revenue is operating a system whereby you can request that any refunds from them should be paid to a charity of your choice from the list on their website. If you feel like giving up that tax refund we are part of this scheme and you will find us on the Inland Revenue list with the code: **JAM40VG** (We rather like this code!) Any amount is extremely helpful.

However you chose to donate to i-Base,
we would like to thank you very much for your support.

REG IN ENGLAND WALES WITH LIMITED LIABILITY REG NO 3962064 CHARITY REG 1081905

107 Maltings Place,169 Tower Bridge Road, London, SE1 3LJ
T: +44 (0) 20 7407 8488 F: +44 (0) 20 7407 8489

Fax-back orders and subscriptions

Please use this form to amend subscription details for HIV Treatment Bulletin and to order single or bulk copies of publications. All publications are free, but donations are always appreciated - please see the form on the previous page.

Name _____ **Position** _____

Organisation _____

Address _____

_____

Telephone _____ **Fax** _____

e-mail _____

☐ I would like to make a donation to i-Base - *Please see inside back page*

- **HIV Treatment Bulletin (HTB) every two months** ☐ **by e-mail**

- **Pocket leaflets** - *A7 small concertina-folded leaflets (2017)*

Pocket HCV coinfection	**quantity** _____	**Pocket PrEP**	**quantity** _____
Pocket ART	**quantity** _____	**Pocket pregnancy**	**quantity** _____
Pocket side effects	**quantity** _____	**PrEP for women**	**quantity** _____

- **Booklets about HIV treatment**

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*

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 HIV, pregnancy and women's health *(November 2015): 52-page A5 booklet* **quantity** _____

Guide to changing treatment: what if viral load rebounds *(Nov 2017): 24-page A5* **quantity** _____

- **Other resources**

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

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

Please fax this form back, post to the above address, or email a request to HIV i-Base:

020 8616 1250 (fax) subscriptions@i-Base.org.uk