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AIDS 2018: first reports



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EDITORIAL

This issue of HTB includes the first reports from the 22nd International AIDS Conference (AIDS 2018) that was held from 23 – 27 July 2018 in Amsterdam.

While HTB featured the likely headline news before the meeting, thanks to the early online conference schedule, the real stories are in the detailed presentations.

So HTB reports include links to the abstract and to the webcasts and the slides are linked to the session section of the programme.

The PARTNER2 study is a highlight worth 10 minutes of everyone's web time. This is as important to see the audience response to the results as for the results themselves. PARTNER2 provides a dataset to support the U=U campaign, that is already widely endorsed by IAS, the US CDC, BHIVA and NHIVNA.

AIDS 2018 also provided the first public forums on the issues of wider access to dolutegravir (DTG) since the recent concern over use during conception. One of the many community demands during AIDS 2018 was from women living with HIV that this potential signal should not be used to delay DTG roll-out. We include several reports on these issues including new WHO recommendations.

Other reports include the GEMINI studies (DTG/3TC dual ART), reduced-dose darunavir/r (400/100 once-daily), DTG use in Brazil, the UK RIVER cure study and PrEP news for transwomen and in use by gay men in Paris.

Further reports will be included in the next issues of HTB, which will also be posted online as early access reports as they become available.

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

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i-Base 2018 appeal

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.

All help is appreciated.

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



CONFERENCE REPORTS

22nd International AIDS Conference (AIDS 2018)

23 – 27 July 2018, Amsterdam

Introduction

The 22nd International AIDS Conference (AIDS 2018) was held this year from 23–27 July in Amsterdam.



Several thousand studies were presented as oral lectures or exhibited as posters over four days - so all reports touch on a minority of the research and activity - but much of the conference is also available online.

- Abstracts are online using a searchable database for the conference programme.

<http://programme.aids2018.org>

Clicking on a search result opens a separate window, either for the abstract or the session in which it was presented.

- Slides are available for most oral presentations and plenary lectures.
- Webcasts are available for many oral presentations (using the “video” link in the session window).
- Posters are available for many abstracts (using a PDF download link at the bottom of the abstract window).
- Oral abstracts are also available online and as a PDF supplement to JIAS.

<https://onlinelibrary.wiley.com/doi/full/10.1002/jia2.25148>

This was an important conference, with UK researchers involved in many interesting studies. These notably included having sites in both the PARTNER and GEMINI studies and for the RIVER study presenting results of the first randomised kick and kill cure-related study.

The meeting attracted high-profile speakers committed to HIV from fields of science, politics, entertainment, global health and human rights. All these talks and interviews are easy to watch on webcasts, especially for the opening and closing ceremonies or by searching the online programme.

This enables mainstream media coverage to highlight for a few days the fact that HIV is still an ongoing global crisis.

So for all the excitement about U=U and PrEP, these advances still only reach a minority of people who need them. Although 22 million people are now on ART, 15 million are not, with many of these people currently untested. Some regions - including Eastern Europe and Central Asia (EECA) still have increasing HIV incidence and mortality. Viral load testing is still not routinely available to millions of people.

A useful discussion in the IAS pre-conference community cure workshop just before AIDS 2018 linked cure research to global HIV care. Both need a new simple home test for viral load, with a sensitivity threshold of perhaps 1000 copies/mL cut-off. This is essential for cure research if larger numbers of people stop ART as part of a cure strategy, as they will be vulnerable to unpredictable viral rebound, perhaps after weeks, months or years. This would also improve effectiveness of ART and give people the certainty to know if ART completely protects their partners.

Access to PrEP is improving in some settings, but globally is still struggling.

Reports included in this issue of HTB.

- Zero HIV transmissions in PARTNER study after gay couples had sex 77,000 times without condoms – an undetectable viral load stops HIV
- DTG/3TC dual therapy is non-inferior to triple-ART in GEMINI study
- Once-daily reduced dose darunavir/ritonavir (400 mg/100 mg) is non-inferior to twice-daily lopinavir/ritonavir in South African switch study
- Superior efficacy with dolutegravir-based ART compared with other regimens at 6 months: real-world data from Brazil
- WHO recommends dolutegravir widely but women’s access will depend on contraception provision
- No additional neural tube defects among a further 170 preconception dolutegravir exposures in Botswana: Tsepamo study (July 2018)
- Swifter viral load suppression with dolutegravir vs efavirenz in late pregnancy: results from DolPHIN 1

- First randomised kick-and-kill cure study fails to reduce HIV reservoir: RIVER study reports vorinostat and vaccines show activity, but not enough
- Using PrEP with feminising hormone therapy supports daily PrEP dosing for transwomen
- Daily and on-demand PrEP both prevent HIV in Prévenir study: high adherence by gay Parisians
- AIDS 2018 online: links to selected webcasts

AIDS 2018: PARTNER2 RESULTS

Zero HIV transmissions in PARTNER study after gay couples had sex 77,000 times without condoms – an undetectable viral load stops HIV

Simon Collins, HIV i-Base

On Tuesday 24 July, the results from the extension to the PARTNER study were presented by Alison Rodger at a press conference at AIDS 2018, ahead of the main conference presentation. In the main presentation the audience response was clear: “the risk is zero, the time for excuses is over”. [1, 2]



After eight years the study was unable to find a single linked HIV transmission when viral load was undetectable, even after 783 couples had sex without condoms 77,000 times.

The results show that ART is as effective for gay men at preventing HIV transmission as it is for heterosexuals. They actually provide an even greater level of evidence for gay men as the first PARTNER results provided for heterosexual couples in 2014.

PARTNER extended to include more gay couples

The second phase of the PARTNER study included some participants from the first phase (which started in 2010) but was expanded from 2014 to 2018 to just enrol gay men.

PARTNER 2 included 972 gay couples where one partner was HIV positive and on effective treatment (ART) and one partner was HIV negative. Before joining the study, couples were already not using condoms. Participants also completed routine confidential questionnaires on their sex life.

To be included in the analysis, only periods when couples had sex without condoms (and without PEP or PrEP) were included, and when the positive partner had undetectable viral load (defined as being less than 200 copies/mL).

Overall, this led to data from 783 couples contributing 1596 couple years of follow up (CYFU). The main reasons for follow-up time not being included in the analysis (477 CYFU), was not having sex without condoms during that period (33%), use of PrEP or PEP (24%) viral load not available (18%) or other missing data. Less than 5% (only ~25 CYFU) were due to viral load being >200 copies/mL.

Median age was 43 (IQR: 31-46) and couples had already been having sex without condoms for a median of 1.0 years (IQR: 0.4 to 2.9). The positive partners had been on ART for a median of 4.0 years (IQR: 2.0 to 9.0), with high adherence (98% participants took >90% of meds), and 93% self-reported having an undetectable viral load.

Result: zero linked HIV transmissions after having sex 77,000 times without condoms

During median 1.6 years of follow-up (IQR: 0.9 to 2.9), couples had sex without condoms about once a week. The average (median) was 43 times a year (IQR: 19 to 74). And during the study this added up to almost 77,000 times.

Many of these couples were in open relationships and 37% of the HIV negative partners reported having other sexual partners. During follow-up, 24% of the negative partners and 27% of the positive partners reported at least one STI.

Over eight years, 15 HIV negative partners did become HIV positive. Importantly, all the new infections were with HIV that was structurally too different to be linked to their main partner. Phylogenetic analysis compared was the pol region of HIV in 15/15 paired cases and for env region in 13/15, with differences that were sufficiently distinct to rule out linked transmissions.

Range of theoretical risk - allowing for chance

An important aspect of the PARTNER study was to quantify risk. So even when no transmissions occurred, the study also reported an upper range of risk that might be possible, given that data is always limited. This is the 95% confidence interval (95%CI).

The initial PARTNER study produced an upper 95%CI of 0.46/100 CYFU overall, which is equivalent to a worst case of a couple needing to have sex for about 200 years for a transmission to occur. This is the highest level - in reality, this would be more likely to take thousands of years. Because two-thirds of participants were heterosexual, this figure was higher for gay men at 0.84/100 CYFU.

The new results from PARTNER2 are able to reduce the upper 95%CI to 0.23/100 CYFU for overall risk in gay couples: equivalent to a worst case when a couple would need to have sex for 400 years - if the true risk is at the upper 95%CI level.

The 95%CI was calculated using the 77,000 times that couples had sex without condoms. As this is a factor of number of CYFU, by definition, this figure becomes higher for sub-groups of risk. For example, the upper 95%CI for insertive anal sex was 0.27 (based on more than 52,000 times), 0.43 for receptive anal sex without ejaculation (>23,000 times), and 0.57 for receptive anal sex with ejaculation (based on 20,000 times). In the subgroup that included sex with a recent STI, the upper 95%CI was 2.9/100.

Note that these events add up to more than 77,000, as individuals could report more than one type of activity when they had sex.

Conclusion: PARTNER2 supports U=U

The PARTNER study was designed to provide a careful dataset that individuals could use as a basis for their own personal decisions. In doing this, even with extensive follow-up over eight years, the study has not been able to find a single case where HIV transmission occurred when viral load was undetectable (defined as less than 200 copies/mL).

The results provide the largest dataset to show how effectively HIV treatment prevents sexual HIV transmission. They support the U=U campaign that an undetectable viral load makes HIV untransmittable.

The research group have also produced a non-technical Q&A resource to cover additional questions. [3]

Simon Collins is a community representative on the PARTNER study.

C O M M E N T

After eight years of trying to find a case of transmission with undetectable viral load, we have a dataset that covers both gay and straight sex - without a single linked transmission.

The PARTNER researchers should be acknowledged for extending the initial PARTNER study for another four years to produce an equitable level of confidence for gay men as for heterosexual couples.

Enrolling, following and retaining couples over eight years has been a considerable achievement. The complexity and the rigour of the phylogenetic analysis prove that none of the transmissions were linked.

As receptive anal sex carries a higher HIV risk than vaginal sex, these data can also reasonably be used to inform the risk from heterosexual anal sex.

This shows the risk of HIV transmission with an undetectable viral load to be effectively zero.

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AIDS 2018: ANTIRETROVIRALS

DTG/3TC dual therapy is non-inferior to triple-ART in GEMINI study

Simon Collins, HIV i-Base

Summary results from using a two-drug combination of dolutegravir (DTG) plus lamivudine (3TC) were presented by Pedro Cahn from Fundación Huésped, Buenos Aires, in a press conference at the AIDS 2018 conference in Amsterdam. [1]



Full results were presented later that morning in an oral presentation. Unlike many other studies that had embargos lifted at the press conference, advance slides of this study was not available beforehand, limiting the details in any early reports. [2]

As background, several years ago, the high genetic barrier to drug resistance reported for dolutegravir, prompted a small single-arm pilot study to report use of this two-drug maintenance therapy in 20 treatment-naive participants. [3]

The results were sufficiently encouraging for the manufacturer (ViiV Healthcare) to launch several large randomised studies dropping one of its own drugs (abacavir) from an already approved fixed dose combination (FDC) and using dolutegravir plus TDF/FTC as the standard-of-care control arm. [4, 5]

The top-line results of these strategy trials were released several weeks before AIDS 2018: reporting that 2-drug ART was non-inferior to 3-drug standard of care. [6]

GEMINI 1 and 2 are identically designed studies. Both are large, international phase 3 studies, and each randomised just over 700 treatment-naive participants to either DTG+3TC or DTG+TDF/FTC. The primary endpoint was the proportion of participants with plasma viral load <50 copies/mL at week-48 (using ITT snapshot analysis).

GEMINI 1 and 2 randomised 714 and 719 treatment-naive participants respectively with screening viral load <500,00 copies/mL. Baseline characteristics included median CD4 and viral load of 432 cells/mm³ (range: 19 to 1497), with 10% <200 cells/mm³, and 4.4 log copies/mL (range: 1.6 to 6.4) respectively, with 20% >100,000 copies/mL.

Approximately 2% of participants in each arm were later reported as having viral load above entry criteria threshold of 500,000 copies/mL (explained by fluctuations between screening and baseline).

Other baseline characteristics included median age 32 years (range 18 to 72); 85% were men and 15% women; 70% were white, 12% African-American, 10% Asian and 10% other ethnicity.

At week-48, viral load was <50 copies/mL in the 2- vs 3-drug arms in 90% (320/356) vs 93% (332/358) in GEMINI 1 and 93% (335/360) vs 94% (337/359) in GEMINI 2. This resulted in adjusted between-arm differences that were slightly lower in the two-drug arm, though with a 95%CI that was well within the predefined margin of -10%: -2.6 (95%CI: -6.7 to +1.5) and -0.7 (-4.3 to +2.9), in GEMINI 1 and 2 respectively. Although the adjusted treatment differences favoured the triple therapy arm, non-inferiority was also easily met in the combined analysis: -1.7 (-4.4 to +1.1).

Virologic non-response in dual vs triple arm were 4% vs 2% in GEMINI 1 and 2% vs 2% in GEMINI 2. The percentage of participants with missing data was 6% vs 6% and 5% vs 4% in GEMINI 1 and 2 respectively.

Virologic responses by prespecified criteria of viral load above vs below 100,000 copies/mL were broadly similar, at 90-94% with no suggestion that dual therapy was less effective.

However, there was a significant difference when results were stratified by baseline CD4 count above vs below 200 cells/mm³. While each arm reported 93% (51/55) viral suppression to <50 copies/mL at week-48 when CD4 count was >200 cells/mm³, this dropped to only 79% (50/63) of the participants who started with CD4 counts <200 cells/mm³.

Only 1/13 had confirmed viral failure, with 2/3 participants with viral load >50 copies/mL resuppressing without changing treatment. Two participants discontinued due to adverse events (TB, Chagas disease), two were protocol violations, two were lost to follow-up, one withdrew consent, one withdrew to start HCV treatment and one changed in ART (due to incarceration).

Across both studies, six participants on DTG+3TC vs four on DTG+TDF/FTC met protocol-defined virologic failure. Of these, none developed new primary mutations associated with INSTI or NRTI drug resistance.

Overall rates of side effects were similar between arms, with 2% of participants in each group discontinuing for this reason. More drug related side-effects were reported with DTG+TDF/FTC.

Although the presentation emphasised that each side effect was only reported by one or two people, this was largely linked to separating similar or related side effects. For example, single reports of anxiety, depression, suicide attempt, suicide ideation, insomnia and sleep disorder, would more commonly be combined as under neuropsychological events.

The fewer side effects reported overall for the dual therapy arm, were not statistically different to the triple-ART arm.

Differences in renal and bone biomarkers significantly favoured the dual-therapy group at week-24, similar to other TDF vs non-TDF comparing studies.

Lipid differences were not presented but a back-up slide of a pooled analysis showed that changes in lipid parameters, all significantly favoured the triple-ART arm, including the difference in TC:HDL ratio ($p < 0.05$), but these changes were generally small with limited clinical significance.

C O M M E N T

The GEMINI studies show that dual therapy with DTG/3TC was non-inferior to the triple ART, with these particular drugs.

On the basis of these results, the fixed dose formulation of dolutegravir/3TC is expected to soon be submitted to the FDA and EMA for regulatory approval.

Viral load changes between screening and baseline led to some participants having baseline viral load $>1,000,000$ copies/mL when entry criteria included an upper threshold of 500,000 copies/mL. Just under 10% of participants in each arm had baseline CD4 counts <200 copies/mL with some CD4 counts in both arms as low as 19 cells/mm³. These details were not included in ViiV's press release. [7]

In response to a question by Andrew Hill after the presentation, Dr Cahn confirmed that the results could only be interpreted for settings in a high-income country and were not applicable in other settings. An editorial review in AIDS, co-authored by Dr Hill and colleagues suggested that the disadvantages of dual therapy (for example, when HBV is a concern) are currently likely to outweigh advantages in low- and middle-income settings. [8]

In high-income settings, with easier access to monitoring, the use for DTG/3TC is likely to be very different. The results are also encouraging for people who have complication related to use of current NRTIs.

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Once-daily reduced dose darunavir/ritonavir (400 mg/100 mg) is non-inferior to twice-daily lopinavir/ritonavir in South African switch study

Polly Clayden, HIV i-Base

Stable patients on a twice-daily lopinavir/ritonavir (LPV/r)-based second-line regimen who switched to a once-daily 400/100 mg darunavir/ritonavir (DRV/r) one maintained similar virological suppression to those who remained on LPV/r at 48 weeks. [1] These data from Johannesburg were presented at AIDS 2018.



The approved dose of DRV/r is 800/100 mg once daily for people with no PI resistance. [2] DRV/r is rarely used in sub-Saharan Africa because of its high cost. DRV/r is considered to be a good candidate for dose optimisation. [2]

In this study, 300 participants, stable on 2 NRTI + LPV/r with viral load < 50 copies/mL, were randomised to 2 NRTI + DRV/r 400/100 mg once daily (n=148) or to continue on their LPV/r-based regimen (n=152).

The study defined treatment success as viral load <50 copies/mL at week 48 (FDA snapshot). Treatment arms were compared using the new FDA non-inferiority margin for switch studies of -4%, using the Intent to Treat (ITT) population.

At baseline participants were 68% female and 99.7% black, with median of age 42 years, and CD4 count >600 cells/mm³.

In the primary efficacy analysis, viral load < 50 copies/mL by week 48 was 95.3% in the DRV/r arm versus 93.4% in the LPV/r arm. Difference +1.9% (95% CI: -3.7% to +6.5).

DRV/r at the lower dose of 400/100 mg once daily showed non-inferior efficacy to LPV/r in this switch study.

C O M M E N T

These results support further studies with low dose DRV/r, including in PI-naive second-line patients.

Optimised DRV/r 400/100 mg could be cheaper to produce than LPV/r and atazanavir/r.

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Superior efficacy with dolutegravir-based ART compared with other regimens at 6 months: real-world data from Brazil

Polly Clayden, HIV i-Base

A dolutegravir (DTG)-based regimen showed greater efficacy after controlling for possible confounders compared with all other ART regimens. These data from the Brazilian Ministry of Health were shown at AIDS 2018.



There were 42–162% higher odds of not achieving virological suppression at 6 months with non DTG-based ART.

The Ministry of Health of Brazil introduced tenofovir/lamivudine/DTG (TDF/3TC/DTG; TLD) as the preferred first-line regimen in early 2017.

Mariana Veloso Meireles presented programmatic data from the Brazilian national database – June 2014 to June 2017 – conducted to describe the effectiveness of different regimens in initial response to ART.

Of 103,240 participants included in the analysis: 67.6% were men; median age, CD4, viral load and adherence at baseline were 34 years old, 394 cells/mm³, 38,057 copies/mL and 96.2%, respectively.

Overall, 76.9% of participants achieved viral load <50 copies/mL.

Almost three quarters of participants received an efavirenz (EFV)-based regimen; 7.2% received TLD.

Viral suppression ranged from 63.7% with lopinavir/ritonavir-based ART to 85.2% with TLD.

In multivariate analysis, with TLD as reference, aOR of failing to achieve virological suppression was: 1.42 (95% CI: 1.32 to 1.52) for TDF/3TC/EFV.

C O M M E N T

These results support the decision made by Brazil, many other countries and the WHO to recommend TLD for preferred first-line ART.

Reference

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AIDS 2018: TREATMENT ACCESS

WHO recommends dolutegravir widely but women's access will depend on contraception provision

Polly Clayden, HIV i-Base

WHO launched new interim guidance on HIV treatment at AIDS 2018 recommending dolutegravir (DTG) for everyone aged six years and above. [1, 2]



But access to DTG for women and adolescent girls of child bearing potential will depend on the availability of consistent and reliable contraception and how countries decide to interpret this.

The 2016 WHO consolidated guidelines recommended tenofovir/lamivudine or emtricitabine/efavirenz 600 mg (TDF/3TC or FTC [XTC] EFV 600 mg) as preferred adult and adolescent first-line ART regimen. [3]

Dolutegravir (DTG)-based first-line ART was recommended as an alternative regimen due to evidence gaps for its use in pregnancy, preconception and with rifampicin (RIF)-based tuberculosis (TB) treatment and lack of generic formulations at that time.

Use of dolutegravir

WHO has recently updated its ART systematic review and meta-analysis (not yet published in full). This review confirmed the 2016 review findings, showing a regimen with two nucleoside reverse-transcriptase inhibitors (NRTIs) plus DTG to be more effective, with better viral suppression, CD4 count recovery and lower risk of treatment discontinuation compared with EFV-based ART in treatment-naive adults.

DTG has other advantages compared with EFV, including fewer drug-drug interactions, faster viral suppression and a higher genetic barrier to developing resistance. Unlike EFV, DTG is also effective against HIV-2.

But, there are safety concerns with women and adolescent girls using DTG at conception. Although starting DTG in pregnancy appears to be safe. For women and adolescent girls of childbearing potential who do not wish to become pregnant, and are fully informed of the benefits and risks, DTG is recommended with consistent contraception. DTG and hormonal contraception do not have documented or expected drug-drug interactions. This is based on limited data but is not at all likely.

WHO recommends women and adolescent girls of child-bearing potential receive EFV or protease inhibitor (PI)-based regimens if consistent and reliable contraception cannot be assured or if a woman wishes to become pregnant.

WHO also recommends DTG for children six years and above and notes that raltegravir (RAL) could be an effective integrase inhibitor for younger children for whom dosing information is not yet available.

WHO also recommends that countries with pre-treatment resistance to EFV or nevirapine (NVP) at 10% or above should urgently consider using an alternative regimen that does not contain non-nucleoside reverse-transcriptase inhibitors (NNRTIs). DTG with consistent and reliable contraception for women and adolescent girls or atazanavir/ritonavir (ATV/r) are suitable options.

Second-line

WHO recommends DTG for people who have failed an NNRTI or protease inhibitor (PI)-based first-line, with the same preconception safety caveats for women. PI-based treatment with an ATV/r or lopinavir/ritonavir (LPV/r)-based regimen is recommended for people who receive DTG first-line.

An optimised NRTI backbone should be used for second-line, such as zidovudine (AZT) following TDF or abacavir (ABC) failure and vice versa.

Table 1. Summary of options for first-, second- and third-line ART regimens for adults (including pregnant women and adolescents) and children

Population	First-line	Second-line	Third-line
Adults and adolescents (including women and adolescent girls of child bearing potential or pregnant)	2 NRTIs + DTG	2 NRTIs + ATV/r or LPV/r	DRV/r + DTG + 1–2 NRTIs (consider genotyping if possible)
	2 NRTIs + EFV	2 NRTIs + DTG	
Children	2 NRTIs + DTG	2 NRTIs + ATV/r or LPV/r	
	2 NRTIs + LPV/r	2 NRTIs + DTG	
	2 NRTIs + NNRTIs	2 NRTIs + DTG	

Key: ATV/r, atazanavir/ritonavir; DTG, dolutegravir; DRV/r, darunavir/ritonavir; EFV, efavirenz; LPV/r, lopinavir/r; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleos(t)ide reverse transcriptase inhibitor.

C O M M E N T

Women with HIV attending AIDS 2018 quite rightly made it abundantly clear that they must: have access to DTG, be consulted as policies and guidelines are developed, be given information and be provided with contraception and choice.

If the DTG signal can lead to improvement of sexual and reproductive health services for HIV positive women, in settings where this is shockingly inadequate, that would be something good to have come out of this unfortunate situation.

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2. WHO policy brief. Antiretroviral regimens for treating and preventing HIV infection and update on early infant diagnosis of HIV. July 2018.
<http://apps.who.int/iris/bitstream/handle/10665/273129/WHO-CDS-HIV-18.19-eng.pdf> (PDF)
3. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - Second edition. June 2016.
<http://www.who.int/hiv/pub/arv/arv-2016/en/>

AIDS 2018: PREGNANCY

No additional neural tube defects among a further 170 preconception dolutegravir exposures in Botswana: Tsepamo study (July 2018)

Polly Clayden, HIV i-Base

From 1 May to 15 July 2018 there were no more neural tube defects reported among infants born to women taking dolutegravir (DTG) at conception in the Tsepamo study – according to late breaking findings presented at AIDS 2018. [1]



Rebecca Zash showed this update on behalf of the study group which reported 4/426 neural tube defects in infants born to women taking DTG at conception in May: 0.94% (95% CI: 0.37 to 2.4). i-Base has previously commented extensively on this unexpected safety signal from Botswana and the resulting statements from WHO and other agencies. [2–4]

Since May, there have been two more neural tube defects among this cohort: one in an infant exposed to DTG started during pregnancy at eight weeks' gestation and one birth to an HIV negative woman. Prevalence of neural tube defects started in pregnancy: 1/3104, 0.03% (95% CI: 0.01 to 0.18).

The updated prevalence with DTG exposure at conception is: 4/596, 0.67% (95% CI: 0.26 to 1.7). Dr Zash noted that the 95% CI still does not overlap with any other exposure group (including other ART at conception and HIV negative).

The next formal analysis will occur after 31 March 2019 and will include women already exposed to DTG from conception before the recent change in guidance. Tsepamo has plans in place to expand the study from 8 to 18 sites, increasing from 45% to 72% of births in the Botswana.

The next analysis will include: neural tube defects; all major malformations; all major malformations; and other adverse birth outcomes (stillbirth, preterm, small for gestational age and neonatal death).

With the expanded surveillance to 18 sites the investigators anticipate approximately 1226 births with exposure to DTG from conception by the time of analysis.

It is uncertain what will happen with this signal between now and March 2019. Dr Zash explained that with no more neural tube defects, the total prevalence will be 0.33% and the lower CI of 0.13% will overlap with the upper CI for other ART at conception (0.21%), EFV at conception (0.15%) and with HIV negative (0.13%).

With one more neural tube defect, the prevalence will be 0.41% and the lower CI of 0.18% will overlap with the upper CI for other ART at conception.

C O M M E N T

Once again, this is an excellent observational study and the results from the expanded surveillance, in March 2019, will be critical to better understanding the safety signal.

Meanwhile other cohorts of women who conceived while taking DTG are also being scrutinised and should be able to contribute data to a pooled analysis.

References

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<http://programme.aids2018.org/Programme/Session/1589>
2. Clayden P. Preconception safety signal with dolutegravir: data from the Tsepamo study. HTB. 21 July 2018.
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3. Clayden P. Dolutegravir preconception signal: time is up for shoddy surveillance. HTB. 11 July 2018.
<http://i-base.info/htb/34459>
4. Clayden P. Potential safety signal for dolutegravir from the time of conception. HTB. 21 May 2018.
<http://i-base.info/htb/34133>

Swifter viral load suppression with dolutegravir vs efavirenz in late pregnancy: results from DoIPHIN 1

Polly Clayden, HIV i-Base

A significantly greater proportion of women achieved undetectable viral load starting a dolutegravir (DTG)-based regimen late in pregnancy, compared with an efavirenz (EFV)-based one. [1] Median time to undetectable viral load with DTG was approximately half of that with EFV.



These findings from the DoIPHIN1 study, conducted in South Africa and Uganda, were shown at AIDS 2018.

Presenting author, Saye Khoo, from the University of Liverpool, explained that in South Africa around a fifth of HIV positive women start ART late in the third trimester. Late initiation is associated with a 7-fold increase in risk of vertical transmission and doubling of infant mortality in the first year of life.

DoIPHIN 1 was a pilot study designed to look at whether DTG reduces vertical transmission at delivery and during breast feeding among women starting ART in the third trimester.

The study randomised 60 treatment naive pregnant women at 28–36 weeks' gestation 1:1 to receive EFV (n=31) or DTG (n=29) plus tenofovir disoproxil fumarate (TDF) and either lamivudine (3TC; Uganda) or emtricitabine (FTC; South Africa) until two weeks postpartum. The primary endpoint was pharmacokinetics (PK) of DTG in women and breastfed infants; secondary endpoints included viral suppression.

In line with national guidelines, which state that women diagnosed in pregnancy start ART immediately, participants started EFV plus TDF/3TC or FTC while waiting for randomisation. All participants randomised to DTG switched within 7 days.

At baseline participants were a median age of 26 years, with CD4 count of 394 cells/mm³ and viral load of 4.0 log copies/mL, across the two arms. Median gestation was 31 weeks, weight 66 kg and BMI 26. A high proportion (approximately 22%) of participants used traditional medicines.

Rich PK sampling was performed in the third trimester and postpartum. Third trimester DTG exposures were low with C_{trough} at or below target (MEC 324 ng/mL) in 9/28 (32%) participants. All but one was above DTG protein adjusted IC₉₀ (64 ng/mL). Postpartum exposures were not significantly different to third trimester but Professor Khoo noted that the time of sampling (median 8 days) did not reflect return to normal physiology.

Maternal:cord blood ratio was 1.21 and breast milk:maternal plasma 0.03. After cessation, DTG was rapidly eliminated from breast milk; but infant washout was prolonged.

By ITT, a significantly greater proportion of participants in the DTG vs EFV arm achieved viral load <50 copies/mL at 2 weeks postpartum: 20 (69%) vs 12 (38.7%), $p=0.02$. Median time to < 50 copies/mL was approximately halved with DTG compared to EFV.

Safety of DTG and EFV was comparable but this evaluation is limited by the small sample size, short follow up and initial use of EFV in participants randomised to DTG-based ART.

C O M M E N T

An earlier report from a scheduled interim analysis of DoIPHIN 1, after the first 16 women delivered, emphasised that 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 than those who start ART earlier. [2, 3]

DoIPHIN 2 is ongoing and randomising 250 late presenting women 1:1 to either DTG- or EFV-based ART. The mothers and infants will be followed up from start of treatment 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.

It is important not to conflate the recent findings with preconception DTG exposure with starting it in pregnancy, particularly among late presenters, where the rapid viral suppression associated with DTG appears to have an advantage over current EFV-based standard of care.

Polly Clayden is on the trial steering committees of DoIPHIN 1 and 2.

References

1. Orrell C et al. DoIPHIN-1: randomised controlled trial of dolutegravir (DTG)- versus efavirenz (EFV)-based therapy in mothers initiating antiretroviral treatment in late pregnancy. AIDS 2018. Amsterdam. 23–27 July 2018. Oral abstract THAB0307LB.
<http://programme.aids2018.org/Abstract/Abstract/13144> (abstract)
https://www.youtube.com/watch?v=djY2rjG_F-c (webcast)
2. 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)
3. DoIPHIN2 website.
<https://www.dolphin2.org>

AIDS 2018: CURE RESEARCH

First randomised kick-and-kill cure study fails to reduce HIV reservoir: RIVER study reports vorinostat and vaccines show activity, but not enough

Simon Collins, HIV i-Base

The first randomised human study using a kick-and-kill strategy to reduce the viral reservoir has unfortunately not been successful, even though the individual components were active.

Results from the UK phase 2 open-label RIVER study were presented on 24 July at a press conference at the international AIDS 2018 conference. The kick-and-kill strategy involves using one drug to reactivate sleeping HIV-infected CD4 cells (the kick) and then effectively target these cells with a second intervention of immune-boosting vaccines (the kill). [1]

Several compounds have shown promising results in test-tube and animal studies but RIVER is the first human study that also included a control arm. It used the HDAC inhibitor vorinostat as the kick and a combination of two vaccines (ChAdV63.HIVconsv to prime immune responses and MVA.HIVconsv to boost them) as the follow-up kill, with ART-only as the control arm.



The study enrolled 60 HIV positive men diagnosed during primary HIV infection (PHI) who started effective ART within four weeks.

The first vaccine was given in the first week, with the second eight weeks later. Vorinostat was then given every three days for ten doses. This involved an intensive level of involvement and control participants had a similar number of matched clinic visits.

Baseline characteristics were balanced between the active and control arms. Overall, median age was 32 years (IQR: 29 to 40). Median CD4 count was 708 (IQR: 568 to 788). At baseline, viral load was <200 copies/mL in all participants with 98% <50 copies/mL. Median time on ART from primary HIV infection (PHI) to randomisation was 28 months (IQR: 27 to 36).

Retention during follow-up was high, with no discontinuations, and all participants providing data for the primary endpoint. Participants in the active arm included nearly 100% of visit attendance, with slightly more missed clinic visits in the control arm.

There were no significant differences between groups for the primary endpoint of change in the viral reservoir between weeks 16 and 18 post-randomisation, measured by total DNA/million CD4 cells (difference: 0.04 log/million cells [95%CI: -0.03 to + 0.11], $p=0.26$). By this primary endpoint, the combined interventions were no different to the control arm on ART. There was also no difference in a secondary endpoint of the proportion with undetectable viral outgrowth measuring replication competence (0.42 [95%CI: 0.13 to 1.37], $p=0.151$).

However, the intervention arm showed significantly higher HIV-specific CD4 responses post vaccination (including IFN-gamma, IL-2, TNF-alpha and CD154 and higher functional CD8 responses (IFN-gamma and TNF-alpha) compared to the control group. In samples from 22/30 participants in the active arm, histone acetylation increased by 3.2 (95%CI: 2.4 to 4.2), two hours post-vorinostat, $p < 0.001$, with no differences between study visits.

Simon Collins is a community representative on the RIVER study.

C O M M E N T

These results raise many questions about the lack of effect on the viral reservoir. Was this related to needing more potent compounds; whether the primary endpoint was measured too early; whether this was the best cure outcome to measure; or whether alternative kick-and-kill strategies would be more effective?

The conclusion also emphasised that the results showed the importance of always including a control arm in cure intervention studies.

References

1. Press conference. RIVER study results. Tuesday 24 July 2018. 10.00 am.
<http://www.aids2018.org/Media-Centre/Resources/Press-programme>
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[http://programme.aids2018.org/Abstract/Abstract/12977\(abstract\)](http://programme.aids2018.org/Abstract/Abstract/12977(abstract))

AIDS 2018: HIV PREVENTION

Using PrEP with feminising hormone therapy supports daily PrEP dosing for transwomen

Simon Collins, HIV i-Base

Two studies were publicised by AIDS 2018 several weeks before the conference with a suggestion that there might be a safety concern linked to interactions between PrEP and feminising hormone therapy (FHT).



In practice, now the studies have been presented, the results do not seem an important concern. PrEP drugs do not affect the levels of FHT and the possible interactions to reduce tenofovir in PrEP does not seem clinically significant.

Both studies involved very small numbers of participants and reported observations that are not directly related to PrEP efficacy. The results should not limit effectiveness for transgender women of each treatment, though the results emphasise the importance of using daily-dosing for PrEP.

The first study, presented in a later breaker poster discussion by Akarin Hiransuthikul from the Thai Red Cross AIDS Centre in Bangkok, was included in the official AIDS2018 press conference. [1]

Between January to March 2018, the study enrolled 20 transwomen who had not underwent orchiectomy and had not used injectable FHT in the previous six months. This single arm study included five weeks of FSH (estradiol valerate 2 mg and cyproterone acetate 25 mg), with PrEP added at week 3 and continued to week 15. FHT was started again from weeks 8 to 15, enabling each participant to be their own control for all drug and hormone levels measured at weeks 3, 5, 8.

There were no significant changes in PK parameters for FHT levels with and without PrEP.

Although the reduced levels of tenofovir exposure in plasma when taken with FST were statistically significant, the 13% reduction in AUC and 17% reduction in C24 are unlikely to have clinical significance with daily dosing.

The second study was presented by Mackenzie Cottrell and colleagues from University of North Carolina and used a different approach. This group compared intracellular drug levels in rectal tissue in four transgender women compared to four cis-gendered women who were already on TDF/FTC-containing ART. FHT included oral or injectable E2, medroxyprogesterone, and spironolactone. In addition to the drug levels, the group reported levels increased levels of endogenous triphosphate levels (dATP/dCTP) that if increased by FHT might reduce levels of PrEP drugs.

Although the TDF-dp:dATP ratio was 7-fold lower in trans compared to cis woman, the clinical implications of the results are not clear. Target levels have not been defined and daily PrEP might still achieve protective levels. Also, one comment in questions after the presentation suggested that drug levels in rectal tissue might not be the most important tissue to measure. The results were also compared with a very small group of cisgendered men (n=2).

C O M M E N T

In addition to this study having small participant numbers, the absolute TFV-dp levels were still similar. The lower ratio highlights transgender TGW for having slightly lower TFV-dp, and slightly higher dATP.

If the FHT is really having a negative effect then the results in ciswomen and the cismen ought to have been different and this wasn't seen.

Clinical results from the iPrEX study showed the benefits of PrEP in more than 300 transgender women, although only 20% of these women (67/339) were using FHT. [3, 4]

As with most questions about trans health, this shows the importance of earlier prospective studies continued collection of data from ongoing PrEP studies.

References

1. Cottrell ML et al. Altered TDF/FTC pharmacology in a transgender female cohort: Implications for PrEP. TUPDX0106. <http://programme.aids2018.org/Abstract/Abstract/11225>
2. Hiransuthikul A et al. Drug-drug interactions between the use of feminizing hormone therapy and pre-exposure prophylaxis among transgender women: The iFACT study. TUPDX0107LB. <http://programme.aids2018.org/Abstract/Abstract/13177>
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Daily and on-demand PrEP both prevent HIV in Prévenir study: high adherence by gay Parisians

Simon Collins, HIV i-Base

Interim results from the PREVENIR (“prevent”) study, presented by Jean-Michel Molina in a press conference and as a late-breaker oral abstract at the AIDS 2018 conference in Amsterdam, continue to show the high efficacy of PrEP. [1, 2]



No new HIV infections were reported when oral TDF/FTC was taken in either daily or on-demand dosing (only using PrEP when needed).

The study, predominantly in gay men, reported very high levels of adherence. This is an ongoing open label study that provided PrEP to all participants and also allowed participants to choose their dosing strategy when appropriate. Women and transgender people are only recommended to use daily dosing in order to achieve protective drug levels. Men in the study were able to use less frequent dosing and were also able to switch between dosing strategies during the study.

The three-year Prévenir study was designed to find out how PrEP was used outside of a randomised study and to look at whether PrEP would reduce new infections in a real-world setting.

Prévenir started in May 2017 and has already enrolled more than 1600 of the planned 3000 adults at 22 HIV centres in Paris. The study hypothesis is that this level of PrEP use should show a 15% reduction in new infections among gay men in the city. HIV, creatinine and STI testing is recommended every three months, but is flexible based on the decision of the treating doctor. Participants also provide anonymised confidential information including about their sexual activity, partner numbers and pattern of PrEP use.

Baseline characteristics so far include median age 36 years (IQR: 30 to 44), with approximately 8% aged between 18 to 25. Although the study aimed for 85% gay men, so far very few participants are either heterosexual (0.8%) or transgender (0.5%). Roughly half the participants are single, roughly half have previously used PrEP, and chemsex was also common (used by 40% within the previous year).

Roughly half the participants chose on-demand dosing, with the only significant baseline differences being that these people were having sex slightly more often and with a higher median number of partners (15 vs 10 in the previous 3 months, $p < 0.001$).

So far, 1102 participants have reported having sex 2279 times (1088 vs 1191 times in daily vs on demand groups), with PrEP covering >95% vs 81% of these times, respectively. Adherence was defined as taking at least one dose before sex and one after, with a 24-hour window period allowed for each dose. Condom use was also reported for about 20% of times people had sex in both groups. This might show that when PrEP was missed in the on demand group, participants compensated by using condoms.

Mean follow-up time is 7 (SD +/- 4) months, with 443 vs 506 participant years of follow up (PYFU) in the daily vs on demand groups respectively.

The principal efficacy results are that there have been no new HIV diagnoses in either group, with HIV incidence at 0 and upper 95%CI of 0.8 vs 0.7 in daily vs on demand groups. Based on historical incidence of 9.1/100 PY in the IPERGAY study, Prévenir has already prevented 85 HIV infections.

Approximately 3% of participants have discontinued the study, but none were due to side effects. Acute viral hepatitis was reported in 11 people, with 7/11 cases of hepatitis C, with no difference between groups.

Over time there were few behaviour differences reported between arms, but a possible trend for participants in both groups to have slightly more sex, interestingly, with fewer partners.

C O M M E N T

As well as adding to efficacy and safety data on PrEP, these early results show that gay men in Paris have high adherence levels and high retention in the study.

Similar to the UK IMPACT study, uptake by heterosexual and transgender communities is much less than for gay men whose PrEP awareness is already high.

Results on the impact of PrEP on HIV incidence in the Paris region are still pending.

References

1. AIDS 2018 press conference. Prévenir study results. Tuesday 24 July 2018. 9.00 am.
<http://www.aids2018.org/Media-Centre/Resources/Press-programme>
2. Molina J-M et al. Incidence of HIV-infection in the ANRS Prévenir study in Paris region with daily or on-demand PrEP with TDF/FTC. AIDS 2018, 23-27 July 2018, Amsterdam. Late breaker oral abstract WEA0406LB.
<http://programme.aids2018.org/Abstract/Abstract/13278>

AIDS 2018 online: links to selected webcasts

The following selected webcasts can be accessed in various ways.

AIDS 2018 also has several YouTube channels and the conference programme includes a video link for most sessions. This links to the whole session, rather than to individual presentations.



AIDS 2018 live

<http://www.aids2018.org/Live>

This link included the opening and closing ceremonies, press conferences and informal interviews are also webcast on YouTube from a variety of links.

President Clinton Keynote Address

<https://www.youtube.com/watch?v=jhZy2IPV3lc>

Bill Clinton drew huge crowds for his hour-long address during closing ceremony, at least some of which was given over to several extended community protests. A leading statesman who has had a huge impact on global access to ART through strategically supporting initiatives to lower prices for better drugs.

Putting HIV science into the criminal justice system: Impacting lives - Allan Maleche, KELIN, Kenya

<https://youtu.be/l-5FgDcllRQ?t=4785>

Talk by social and civil rights lawyer on successfully fighting criminalisation laws in Africa by the recipient of the Elizabeth Taylor Human Rights Award at AIDS 2018.

Partner study results

<https://youtu.be/jEiUTU7wqbA?t=2952>

As important to see the audience response to this dataset that supports the understanding that U=U.

Robert Suttle

<https://youtu.be/l-5FgDcllRQ?t=5889>

US activist with SERO project and victim of US HIV criminalisation laws.

iFara interviews from AIDS 2018

<http://accessshiv.org/ias-2018>

Several dozen interviews by US iFara activist web coverage.

CONFERENCE REPORTS

10th International Workshop on HIV Paediatrics

20–21 July 2018, Amsterdam

The 10th International Workshop on HIV Paediatrics was held 20–21 July 2018 in Amsterdam, just before the AIDS 2018 conference.

The paediatrics workshop is the only HIV meeting devoted to research in prevention and treatment for infants, children and adolescents. Since 2009, this workshop has preceded the IAS conference and dual submissions to both meetings are permitted.

This year's meeting included: pharmacokinetic and early safety and efficacy data for dolutegravir in children aged four weeks to six years; the first public presentation from the Tsepamo study of a potential safety signal with dolutegravir from conception; first data from the ODYSSEY trial; data on tenofovir alafenamide in the bicitegravir-based fixed dose combination for six to twelve year olds; and much more.

The abstracts as well as slides of the presentations and webcasts will be posted online when consent has been provided.

<http://www.infectiousdiseasesonline.com>

Conference website:

<http://www.virology-education.com/event/upcoming/10th-workshop-hiv-pediatrics>

HTB reports from this workshop are:

- Preconception safety signal with dolutegravir: data from the Tsepamo study

Preconception safety signal with dolutegravir: data from the Tsepamo study

Polly Clayden, HIV i-Base

More details from the Tsepamo study, Botswana, which identified a potential safety signal with preconception dolutegravir (DTG) exposure, were shown at the 10th International Workshop on HIV Paediatrics. [1]

We have described this study previously in HTB, as well as the statements following the safety signal, since these were released in May 2018. [2,3,4]

Rebecca Zash presented data on behalf of the study group. She explained that Tsepamo started in August 2014 to look at birth outcomes by HIV status and ART regimen and to see if there is an increased risk of neural tube defects (NTDs) in infants exposed to efavirenz (EFV) from conception.

The original plan was a four-year analysis (to August 2018) to compare the prevalence of NTDs in infants born to women on EFV at conception vs other ART regimens. The sample size of 94,000 births was based on ability to detect a 2-fold increase in NTDs with the assumption of 0.1% prevalence.

Mid-2016 Botswana changed first-line ART from an EFV-based to a DTG-based regimen. Recently published data from women who started DTG during pregnancy showed no difference in adverse birth outcomes compared with those who started EFV. [5] There was no increased risk of birth defects among 280 women who started DTG in the first trimester.

The Tsepamo group were asked to provide any preliminary data on outcomes for women who started DTG before conception for WHO guidelines committee in May 2018.

At the time of analysis there had been 89,064 births at eight surveillance hospitals: 21,955 among HIV positive mothers; 11,726 of these who received ART from conception; and 426 (3.3%) of these were on a DTG-based regimen. Of the remaining 11,300 mothers on ART from conception, 5,787 received EFV.

Overall, 86 NTDs were identified among 88,755 births: 0.1% (95% CI: 0.08 to 0.12).

There were 4/426 NTDs in infants born to women receiving DTG at conception: 0.94% (95% CI: 0.37 to 2.4). This compared with 14/11,300 among non-DTG at conception exposures: 0.12% (95% CI: 0.07 to 0.21). And 3/5787 EFV at conception exposures: 0.05% (95% CI: 0.02 to 0.15).

There were 0/2812 NTDs in infants born to mothers who started DTG during pregnancy: 0% (95% CI: 0 to 0.13). And 61/66, 057 among those born to HIV negative mothers: 0.09% (95% CI: 0.07 to 0.12).

The lower bound of the DTG-exposures' confidence interval did not overlap with any of the other exposure groups.

The four defects were: encephalocele, anencephaly, myelomeningocele, and iniencephaly.

None of the women were reported to be on folate supplementation before pregnancy – this was similar across exposure groups.

Review of maternal data found no other risk factor for NTDs and there was no clustering by site. A sensitivity analysis, restricted to births occurring after the rollout of DTG, showed there was no increase in NTDs overall.

To check for differences in assessment the investigators looked at prevalence of post-axial polydactyly and found no differences across exposure groups compared with an expected rate of about 1%.

This preliminary signal for NTDs needs further data to confirm or refute.

Dr Zash emphasised that, although statistically significant, the signal is based on only four cases and the absolute prevalence difference of about 0.8% is small. She also noted that the different defects among the DTG-exposed at conception infants is unusual.

Tsepamo continues to collect data and the investigators hope to have over 1200 births with DTG exposure to report by end of March 2019. In this analysis, they will also evaluate all major abnormalities and adverse birth outcomes.

She concluded that, in the meantime, we need to:

Improve pregnancy outcomes

- Improve access to contraception, comprehensive sexual and reproductive health services for HIV positive (and all) women.
- More countries can implement folate supplementation of grain and ensure that women of reproductive age are folate replete before pregnancy.
- Improve infrastructure for viral load monitoring and resistance testing for people who may remain on EFV.

Implement more/better surveillance for ART safety in pregnancy

- Is the DTG signal real? If so, is it a class effect? If so, in all settings?
- Will tenofovir alafenamide (TAF) be safe (and in which regimens)?
- Which PI is safest?
- What is the plan to work out whether BNABs, vaccines, long-acting ART, etc are safe in pregnancy?

C O M M E N T

This was the first public presentation of the Botswana DTG preconception data.

Updates to these data, as well as findings from elsewhere, interpretations and implications will be shown and discussed at AIDS 2018. [6]

References

1. Zash R. Special session: Birth defect surveillance – Tsepamo Study. 10th International Workshop on HIV Paediatrics. 20–21 July 2018.
2. Clayden P. Efavirenz, tenofovir and emtricitabine associated with fewest adverse birth outcomes in Botswana. HTB. 27 February 2017. <http://i-base.info/htb/31313>
3. Clayden P. Potential safety signal for dolutegravir from the time of conception. HTB. 21 May 2018. <http://i-base.info/htb/34133>
4. Clayden P. Dolutegravir preconception signal: time is up for shoddy surveillance. HTB. 11 July 2018. <http://i-base.info/htb/34459>
5. Zash R et al. Comparative safety of dolutegravir-based or efavirenz-based antiretroviral treatment started during pregnancy in Botswana: an observational study. *Lancet Glob Health*. Published online 4 June 2018. [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(18\)30218-3/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30218-3/fulltext)
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FUTURE MEETINGS

Conference listing 2018/19

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

International Workshop on HIV & Ageing

13 –14 September 2018, New York, USA.
www.virology-education.com

Australasian HIV&AIDS Conference 2018

24 – 26 September 2018, Sidney
www.hivaidconference.com.au

BHIVA Autumn Conference

4 – 5 October 2018
www.bhiva.org

20th International Workshop on Comorbidities and Adverse Drug Reactions in HIV

13–14 October 2018, New York
www.intmedpress.com/comorbidities

HIV Research for Prevention (HIVR4P 2018)

21 – 25 October 2018
www.hivr4p.org

HIV Glasgow 2018

28 – 31 October 2018, Glasgow
www.hivglasgow.org

26th Conference on Retroviruses and Opportunistic Infections (CROI 2019)

4 – 7 March 2018, Seattle
www.croiconference.org

25th Annual BHIVA Conference

2 – 5 April 2019, Bournemouth
www.bhiva.org

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

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

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

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

Publications and regular subscriptions can be ordered online.

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

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

i-Base treatment guides

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

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

- Introduction to ART (May 2018)
- HIV & quality of life: side effects & long-term health (Sept 2016)
- Guide to PrEP in the UK (November 2016)
- HIV testing and risks of sexual transmission (June 2016)
- Guide to changing treatment and drug resistance (December 2017)
- 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.

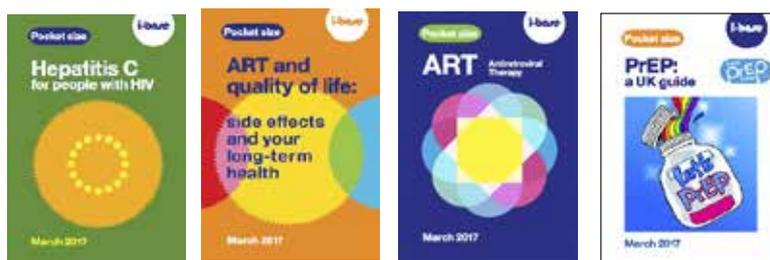
We hope these are especially useful as low literacy resources.

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

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HTB is a not-for-profit community publication that aims to provide a review of the most important medical advances related to clinical management of HIV and its related conditions as well as access to treatments. Comments to articles are compiled from consultant, author and editorial responses.

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HIV i-Base

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

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Pocket ART	quantity _____	Pocket pregnancy	quantity _____
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• **Booklets about HIV treatment**

ART in pictures: HIV treatment explained (*June 2017*): 32-page A4 booklet **quantity** _____

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UK Guide To PrEP (*November 2016*): 24-page A5 booklet **quantity** _____

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• **Other resources**

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