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Editor: Simon Collins

Contributing Editor: Polly Clayden

Medical consultants:

Dr Tristan Barber, Royal Free Hospital, London.
Dr Karen Beckerman, Albert Einstein College of Medicine, NY.
Dr Sanjay Bhagani, Royal Free Hospital, London.
Prof. Diana Gibb, Medical Research Council, London.
Dr Gareth Hardy, PhD.
Prof. Saye Khoo, University of Liverpool Hospital.
Prof. Clive Loveday, ILVC, UK.
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Dr Graham P Taylor, Imperial College, London.
Dr Stephen Taylor, Birmingham Heartlands Hospital.
Dr Gareth Tudor-Williams, Imperial College, London.
Dr Edmund Wilkins, Manchester General Hospital..

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HIV i-Base, 107 The Maltings,

169 Tower Bridge Road, London, SE1 3LJ.

T: +44 (0) 20 8616 2210.

http://www.i-Base.info

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EDITORIAL

This edition of HTB has been compiled at the 10th IAS Conference on HIV Science (IAS 2019) in Mexico City to include our first rapid reports from this meeting.

These focus on important treatment news for global health and the latest developments for HIV treatment.

We lead with an optimistic review by Polly Clayden of latest data to inform the earlier signal that linked dolutegravir with a risk of neural tube defects if taken during conception or the first four weeks of pregnancy. Continued surveillance will remain essential. A related report also supports the use of efavirenz 400 mg.

These results led to the latest update of WHO treatment guidelines that recommend dolutegravir as first-line therapy for all. This is a significant achievement for bringing newer, more effective and more tolerable options to people living with HIV globally.

The second set of reports focus on new compounds in development including a new capsid inhibitor GS-6207, phase 2 dose-finding results with the newly-named islatravir (previously MK-9581), and 96-week results on the fostemsavir as an investigational compound for multidrug resistance. Islatravir also has potential for a slow-release long-acting PrEP implant that if shown to be effective would deliver drug levels for more than a year.

Dolutegravir was also widely reported for sustained viral efficacy out to 96-week results in the dual FDC with lamivudine and for the first phase 3 randomised data for this recently FDA and EMA approved combination as a switch option for people currently stable on TAF-containing ART.

We also include as supplements to this issue the i-Base report *Fit for Purpose: antiretroviral treatment optimisation*, and the related HIV Pipeline Report for 2019.

Further reports from IAS 2019 will be posted online as early access reports.

SUPPLEMENTS

Fit for Purpose: antiretroviral treatment optimisation

Updated review of HIV treatment optimisation, including paediatric and adult pipeline compounds.

http://i-base.info/htb/36411

HIV Pipeline Report for 2019

Updated review of new HIV drugs in development.

http://i-base.info/htb/36278

CONFERENCE REPORTS

10th IAS Conference on HIV Science (IAS 2019)

21-24 July 2019

Introduction

The 10th IAS Conference on HIV Science (IAS 2019) in Mexico City was held from 21 – 24 July 2019.

The meeting was attended by more than 5,000 delegates from more than 140 countries.

This year the meeting had a particulaly exciting programme,:

- A strong focus on new antiretroviral drugs, including for PrEP.
- ART strategies with new and existing drugs.
- An important (and optimistic) update on neural tube defects with dolutegravir, with a comprehensive review of the latest data.
- Updates to WHO treatment guidelines

The programme is already posted online, with abstracts and PowerPoint slides available for many of the presentations.

http://www.ias2019.org

Webcasts from oral presentations, including the opening sessions are posted to the conference YouTube channel.
https://www.youtube.com/channel/UC43XbxjX7RZZ_gK9Vt8Z8FA/videos

Early HTB reports in this issue include:

- Dolutegravir neural tube defect risk declines but still slightly higher than with other antiretrovirals
- WHO recommends dolutegravir-based ART regimens for all
- High rates of viral suppression with low dose efavirenz in pregnant Zambian women
- First viral load results for capsid inhibitor GS-6207: mean –2.2 log reduction at day 10.
- Islatravir (MK-8591) in new fixed dose combination (FDC) with doravirine plus lamivudine: 24 week results
- Dual therapy with islatravir (MK-8591) plus doravirine: 24 week results as switch strategy
- Fostemsavir: 96-week follow-up in people with multi-drug resistance
- Dolutegravir/lamivudine dual therapy non-inferior to triple ART at week-96
- Switching to dolutegravir/lamivudine dual therapy is non-inferior to TAF-based triple therapy at week-48 in TANGO study
- Islatravir (MK-8591) implant sustains HIV PrEP protection for more than one year

IAS 2019: PREGNANCY:

Dolutegravir neural tube defect risk declines but still slightly higher than with other antiretrovirals

Polly Clayden, HIV i-Base

Data presented at IAS 2019, from the Tsepamo study, showed a declining risk for dolutegravir (DTG)-associated neural tube defects (NTDs), although this remains slightly elevated compared to that with exposure to other antiretrovirals.

Data from Botswana (not covered by Tsepamo), Brazil and the Antiretroviral Pregnancy Registry (APR) were also shown at the conference.

World Health Organization (WHO) now recommends DTG-based ART for all and this recommendation includes women of reproductive potential. [1]

On 18 May 2018, WHO issued a statement following the identification of a potential safety issue with DTG related to NTDs in infants born to women who were taking DTG at the time of conception. [2]

The safety issue was identified at a preliminary unscheduled analysis of the ongoing Tsepamo observational study in Botswana. The analysis revealed 4 cases of NTDs out of 426 women who became pregnant while taking DTG.

July 2018 WHO guidelines recommended that women and adolescent girls of reproductive potential should use DTG with consistent and reliable contraception. And national guidelines also interpreted these results and WHO guidance with varying degrees of caution.

So, the update from Tsepamo, as well as the other studies (these represent the next three largest datasets after Tsepamo), and the revised WHO recommendations are very welcome after what has been a complicated 14 months.

Tsepamo

The most recent update from Tsepamo, reported 5/1683 NTDs among births to women receiving DTG at conception, a rate of 0.3%. [3] As well as the late breaker presentation at IAS 2019, more detail can be found in the simultaneously-published paper in The New England Journal of Medicine. [4]

The Tsepamo birth outcomes surveillance study has been conducted by the Botswana Harvard AIDS Institute Partnership since August 2014.

It was originally designed to evaluate for NTDs with efavirenz (EFV). Secondary analyses include: all major structural malformations and other adverse birth outcomes.

Since 1 May 2018 and as of 31 March 2019 the study accrued data on an additional 29,979 deliveries including: 1,257 to women on DTG at conception; 3,492 to women on non-DTG at conception; 2,172 specifically to women on EFV at conception; 1,028 to women on DTG started during pregnancy; 328 to women on non-DTG started during pregnancy; and 23,315 to HIV negative women.

Of the total study population, there were 98/119,033 NTDs, a rate of 0.08% (95% CI 0.07 to 0.10). For DTG at conception the rate was 5/1683, 0.30% (95% CI 0.13 to 0.69) and for non-DTG at conception 15/14792, 0.10% (95% CI 0.06 to 0.17).

For the other groups the rates were: EFV at conception 3/7959, 0.04% (95% CI 0.01 to 0.11); DTG started during pregnancy 1/3840, 0.03% (95% CI 0.00 to 0.15); non-DTG started in pregnancy 3/5952, 0.05% (95% CI 0.02 to 0.15); and HIV negative 70/89372, 0.08% (95% CI 0.07 to 0.10).

Table 1: Neural tube defect prevalence differences by exposure

DTG at conception vs comparison group	Prevalence difference % (95% CI)
Non DTG at conception	0.20 (0.01 to 0.59)
EFV at conception	0.26 (0.07 to 0.66)
DTG started in pregnancy	0.27 (0.06 to 0.67)
Non-DTG started in pregnancy	0.25 (0.05 to 0.64)
HIV negative	1.22 0.05 to 0.62)

Since May 2018 the overall rate of NTDs has been lower than in previous years: 12/29,979, 0.04% vs 98/119.033, 0.08%. But sensitivity analysis restricted to conceptions during the DTG era was similar. The investigators are looking into environmental factors to try to explain this phenomenon.

Rates of any other adverse birth outcomes since October 2016 between EFV and DTG at conception were similar: adjusted RR 0.94 (95% CI 0.86 to 1.02).

The prevalence of NTDs with DTG at conception remains higher than all other exposure groups but the estimated difference is small (0.2–0.27%). Compared with all other ART at conception, the 95% confidence interval indicates that this difference is as low as 0.01% and as high as 0.67%.

Tsepamo surveillance continues and DTG at conception exposures also continue to accrue: 240 since 31 March 2019.

Tsepamo remains the most informative dataset on which to base guidance and policy.

Botswana

One NTD was reported among 152 DTG at conception exposures at non-Tsepamo sites in Botswana. [5]

The Botswana Ministry of Health and Wellness expanded NTD surveillance to sites not covered by Tsepamo.

Data on all deliveries (live births and stillbirths) at 22 facilities added coverage for a further 19% of Botswana's births (currently Tsepamo covers 72%).

Midwives identified potential NTDs before infants were discharged. A clinical geneticist (blinded to HIV status and ART exposure) reviewed suspected NTDs.

There were 3076 pregnancies: 76% among HIV negative women; 24% HIV positive women; and <1% among women with unknown HIV status.

Seventy-three per cent (n=544) of HIV positive women were on ART at conception; of these 28% (n=152) were on DTG.

This process identified 6 suspected NTDs: 1 confirmed; 2 classified as not NTDs; 2 probably NTDs; and 1 possible NTD.

Three NTDs were included in the final analysis (1 confirmed and 2 probable). One NTD was in the 152 DTG at conception pregnancies, giving a prevalence of 0.66% (95% CI 0.02 to 3.69). The other 2 were in infants born to the 2328 HIV negative mothers, giving a prevalence of 0.09% (95% CI 0.01 to 0.31).

There were none among the 381 no-DTG ART and 261 EFV ART exposures.

Although these findings suggest an increased prevalence of NTDs among infants who were DTG-exposed at conception compared to those born to HIV negative mothers, consistent with previous findings from Tsepamo, the study was only conducted for 6 months, so the numbers of pregnancies to date are small.

Brazil

No neural tube defects were reported among 382 women on DTG at conception in Brazil. [6]

DTG was available in the public sector for first-line ART from 2017. Although the drug was restricted in pregnancy, as of May 2018 over 22,624 women between 15–49 years were on DTG in Brazil. And the NTD signal led to a national investigation.

Women who became pregnant on ART containing either DTG, EFV, or raltegravir (RAL) during the periconception period (within 8 weeks before or after the estimated date of conception) between January 2015 and May 2018 were identified retrospectively using the Brazilian ART database.

There were 1468 women included in the evaluation: 382 DTG exposures; 1115 EFV exposures; and 125 RAL exposures.

There were 2 NTDs, 1 exposed to EFV and 1 to RAL at conception and there were none among the DTG exposures.

This study was retrospective, had a large amount of missing data and was probably underpowered to detect a difference in exposure groups.

Antiretroviral Pregnancy Registry

One NTD was reported with 248 periconception DTG exposures in the APR through January 2019. [7]

Since 1989, the APR has collected prospective, voluntary, anonymised reports of women on ART during pregnancy.

For overall birth defects (prevalence 3%) 200 exposures can rule-out a 2-fold increase. But, to rule-out a 3-fold increase in a rare event like NTD (prevalence 0.1%), approximately 2,000 exposures are needed.

For the analyses, earliest timing of exposure was assigned to each drug: periconception (exposure from 2 weeks before conception through 28 days after conception ie 6 weeks estimated gestational age); later 1st trimester (after 6 weeks estimated gestational age) and 2nd/3rd trimester.

There was a total of 20,372 reports (20,727 pregnancy outcomes) of which 8546 (78%) were periconception exposures.

The overall prevalence of NTDs in 8546 periconception exposures was 0.03%. Notably, most of the reports in the APR come from North America, where there is national food folic acid fortification, which has been shown to reduce NTD risk by 36–68% in the general population.

So, this rate is consistent with the observed low NTD prevalence (0.01–0.08%) in most high-income countries with food folic acid fortification.

Among 248 DTG at conception periconception exposures there was 1NTD giving a prevalence of 0.40%, and 0.14% for the integrase inhibitor class (there were no NTDs among 268 RAL and 217 elvitegravir exposures). But this estimate is based on a single NTD in relatively small number of exposures.

C O M M E N T

It is most fortunate that Tsepamo was ongoing during the roll-out of DTG in Botswana and was able to capture this elevated rate of a rare event in a systematic way. A denominator of 1663 DTG at conception exposures is still greater than the next three largest data sources above: 382 Brazil, 248 APR, and 152 Botswana MoH. Other publically-presented datasets range from 1 to 69 exposures. [8, 9,10]

It is critically important that sustainable birth outcomes surveillance continues in low- and middle-income countries, including Tsepamo, the newer surveillance set up by PEPFAR in Uganda and Malawi and those under consideration for Eswatini and South Africa.

Critical too is that more ART-exposed pregnancies are reported to the APR so it can increase its numbers more swiftly and include a broader geographical scope than mostly North America.

The momentum that was gained after the first report of a potential DTG at conception safety signal must continue. And surveillance must be in place as other new antiretrovirals are rolled out. Women make up over half the HIV positive population and lack of safety data in pregnancy affects all of their access to newer drugs.

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High rates of viral suppression with low dose efavirenz in pregnant Zambian women

Polly Clayden, HIV i-Base

The 400 mg dose of efavirenz (EFV) was associated with high levels of maternal viral suppression during pregnancy, according to data presented at IAS 2019. [1]

EFV 400 mg was introduced in Zambia in 2017 as part of the alternative first-line regimen. It is co-formulated with tenofovir disoproxil fumarate and lamivudine and known as TLE400.

It was further recommended as the preferred regimen in pregnancy after the dolutegravir (DTG) at conception safety concerns from the Botswana Tsepamo study and the favorable tolerability, efficacy and CYP2B6 pharmacogenetics of EFV 400 mg in pregnant women living with HIV in a small study conducted in Uganda and UK. [2, 3]

The investigators evaluated maternal viral suppression (<1000 copies/mL) among women receiving EFV 400 mg based ART with documented maternal viral load at/near time of delivery. They also looked at infant HIV status (HIV DNA PCR).

Two hundred and eighty-seven (287) mother-infant pairs were evaluated. Of these 271 (94%) women started or were switched to EFV 400 mg during pregnancy and the remaining 16 (6%) were on EFV 600 mg.

Women were a mean age of 30 years (SD 6.56) with median ART duration of 19.43 months (IQR 5.26 to 55.69). Over half, 202 (58.72%) started ART in pregnancy and the remaining 142 (41.28%) were receiving it at conception.

Maternal viral suppression at delivery was 92.68% among those receiving EFV 400 mg and 88% among those receiving EFV 600 mg.

Two infants were HIV DNA PCR positive (0.7%). There were 2 with 3 (0.75%) non-viable outcomes and 8 (2.97%) foetal abnormalities.

EFV 400 mg was associated with high levels of maternal viral suppression during pregnancy and delivery. The investigators noted that this rate was higher than the previously reported suppression rates of 75% with EFV 600 mg in the same Zambian population. They suggested that this could be due to the improved tolerability of the lower EFV dose.

COMMENT

These findings support the use of EFV 400 mg as an alternative option to DTG in pregnancy.

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IAS 2019: GUIDELINES

WHO recommends dolutegravir-based ART regimens for all

Polly Clayden, HIV i-Base

New World Health Organization (WHO) recommendations, released on 22 July 2019 at IAS 2019, include dolutegravir (DTG) as the preferred antiretroviral drug in first- and second-line regimens.

This recommendation recognises the declining estimate DTG-associated neural tube defect risk and observed efficacy.

The new policy brief is entitled: Update of recommendations on first- and second-line antiretroviral regimens July 2019. It is a forerunner to the revised 2019 WHO consolidated antiretroviral guidelines to be released later this year.

WHO now recommends tenofovir disoproxil fumarate (TDF)/ lamivudine (3TC) or emtricitabine (FTC) (XTC)/DTG as the preferred first- and second-line ART regimen for adults, adolescents and children (with approved DTG dosing). Low dose efavirenz (EFV 400 mg) is now recommended for adults and adolescents as the alternative first-line ART.

Tenofovir alafenamide (TAF) is recommended in special circumstances for adults with established osteoporosis and/ or impaired kidney function. It is recommended as part of an alternative first-line regimen for children of age and weight groups with approved dosing.

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

Since then, rapidly evolving evidence of safety and efficacy as well as programmatic data has accumulated on the use of DTG and efavirenz (EFV) 400 mg in pregnant women and people coinfected with TB.

Although risk of neural tube defects, associated with DTG, has declined since May 2018 it still remains slightly higher than with other ART exposure groups.

The new recommendations lift any previous restrictions on DTG for women of child-bearing potential. And WHO continues to emphasise the importance of a women-centred approach, providing women with up-to-date information on risks and benefits to make an informed choice.

The recommendations also highlight potential DTG-associated weight gain and the importance of a healthy diet and regular exercise to help manage weight.

See WHO ART recommendations Tables 1, 2 and 3.

Table 1: WHO recommendations July 2019

First-line ART
1. DTG in combination with a nucleoside reverse-transcriptase inhibitor (NRTI) backbone may be recommended as the preferred first-line regimen for people living with HIV starting ART • Adults and adolescents (strong recommendation, moderate-certainty evidence) • Infants and children with approved DTG dosing (conditional recommendation, low-certainty evidence) 2. Efavirenz at low dose (EFV 400 mg) in combination with an NRTI backbone is recommended as the alternative first-line regimen for adults and adolescents living with HIV initiating ART (strong recommendation, moderate-certainty of evidence) 3. A raltegravir (RAL)-based regimen may be recommended as alternative first-line regimen for infants and children for whom approved DTG dosing is not available (conditional recommendation, low-certainty evidence) 4. A RAL-based regimen may be recommended as the preferred first-line regimen for neonates (conditional recommendation, very-low-certainty evidence)
Second-line ART
1. DTG in combination with an optimised NRTI backbone may be recommended as a preferred second-line regimen for people living with HIV for whom non-DTG- based regimens are failing. • Adults and adolescents (conditional recommendation, moderate certainty evidence) • Children with approved DTG dosing (conditional recommendation, low-certainty evidence) 2. Boosted protease inhibitors in combination with an optimised NRTI backbone may be recommended as a preferred second-line regimen for people living with HIV for whom DTG-based regimens are failing (strong recommendation, moderate-certainty evidence)

Table 2: Preferred and alternative first-line ART regimens

Population	Preferred first-line regimen	Alternative first-line regimen	Special circumstances
Adults and adolescents	TDF + 3TC (or FTC) + DTG	TDF + 3TC (or FTC) + EFV 400 mg	TDF + 3TC (or FTC) + EFV 600 mg AZT + 3TC + EFV 600 mg TDF + 3TC (or FTC) + PI/r TDF + 3TC (or FTC) + RAL TAF + 3TC (or FTC) + DTG ABC + 3TC + DTG
Children	ABC + 3TC + DTG	ABC + 3TC + LPV/r TDF + 3TC + RAL TAF + 3TC (or FTC) + DTG	ABC + 3TC + EFV (or NVP) AZT + 3TC + EFV (or NVP) AZT + 3TC + LPV/r (or RAL)
Neonates	AZT + 3TC + RAL	ABC + 3TC + NVP	AZT + 3TC + LPV/r

Key: AZT, zidovudine; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; LPV/r, ritonavir-boosted lopinavir; NVP, nevirapine; PI/r, ritonavir-boosted protease inhibitor; RAL, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; 3TC, lamivudine

Table 3: Preferred and alternative second-line ART regimens

Population	Failing first-line regimen	Preferred second-line regimen	Alternative second-line regimen
Adults and adolescents	TDF + 3TC (or FTC) + DTG	TDF + 3TC + ATV/r (or LPV/r)	ABC + 3TC + DRV/r
	TDF + 3TC (or FTC) + EFV (or NVP)	AZT + 3TC + DTG	AZT + 3TC + ATV/r (or LPV/r or DRV/r)
	AZT + 3TC (or FTC) + EFV (or NVP)	TDF + 3TC (or FTC) + DTG	TDF + 3TC (or FTC) + ATV/r (or LPV/r or DRV/r)
Children and infants	ABC + 3TC + DTG	ABC (or AZT) + 3TC + LPV/r (or ATV/r)	ABC + 3TC + DRV/r
	ABC (or AZT) + 3TC + LPV/r	ABC (or AZT) + 3TC + DTG	ABC (or AZT) + 3TC + RAL
	ABC (or AZT) + 3TC + EFV	ABC (or AZT) + 3TC + DTG	ABC (or AZT) + 3TC + LPV/r (or ATV/r)
	ABC + 3TC + NVP	ABC + 3TC + DTG	ABC (or AZT) + 3TC + LPV/r (or ATV/r or DRV/r)

Key: ATV/r, ritonavir-boosted atazanavir; AZT, zidovudine; DTG, dolutegravir; DRV/r, ritonavir-boosted darunavir; EFV, efavirenz; FTC, emtricitabine; LPV/r, ritonavir-boosted lopinavir; NVP, nevirapine; PI/r, ritonavir-boosted protease inhibitor; RAL, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; 3TC, lamivudine

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IAS 2019: ARVs

First viral load results for capsid inhibitor GS-6207: mean –2.2 log reduction at day 10

Simon Collins, HIV i-Base

The IAS 2019 conference includes several presentations with new results on pipeline compounds, including the first viral efficacy results in HIV positive people with the capsid inhibitor GS-6207. [1]

Until now, the only in vivo data with this new compound were single-dose safety and tolerability results presented at CROI 2019 earlier this year. Of note, this study reported possible multiple mechanisms of action and the feasibility for this molecule to have an extended release formulation, given the compound is detectable six months after a single dose. [2]

The new results are from an ongoing double-blind placebo-controlled dose-finding phase 1b study in 24 HIV positive participants (22 men, 2 women) who were either treatment-naive or who had used ART for <12 weeks.

Participants were randomised 3:1 (n=8 per group) to a single sub-cutaneous dose of GS-6207 (20, 50, 150, 450, or 750 mg) or placebo. The primary endpoint was viral load reduction at day 10, when all participants started triple-ART with bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF).

Other baseline characteristics included median (range) CD4 and viral load of 442 cells/mm^3(340 to 661) and 4.48 log copies/mL (4.3 to 4.6), respectively. Ethnicity included 58% white, 33% black and 4% Asian. Median BMI was 25 kg/m^2 (range: 20 to 34).

Viral load results included mean reductions in viral load for the 50 mg, 150 mg and 450 mg doses of –1.8, –1,8 and –2.2 log copies/mL respectively, with maximum viral load reductions of –2.4, –2.1 and –2.9 respectively. See Table 1.

No serious adverse events were reported, including no grade 3 or 4 side effects or laboratory abnormalities.

Plasma levels of GS-6207 at day 10 remained above the protein adjusted IC95 for all doses.

A second poster at IAS 2019 confirmed the susceptibility to drug resistance from in vitro passaging studies, which occurred more slowly than efavirenz or elvitegravir but which still generated high level resistance. Early mutations at N74D in capsid led to 5.3 fold reduced sensitivity but this increased to >100-fold with later development of N74D + Q57H. These are apparently highly conserved regions of capsid and have an impact on viral fitness. [3]

Both studies concluded that these early data support further evaluation of GS-6207 as a long-acting antiretroviral for treatment of HIV.

C O M M E N T

These are impressive early results, especially given the potential for a new long-acting formulation.

Details of other pipeline HIV drugs in development, including studies to watch for at IAS 2019, are included in the i-Base 2019 pipeline report, now online. [4]

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Table 1: Viral load responses at day 10 following single dose of GS-6207

VL reduction, log copies/mL	50 mg, n=6	150 mg, n=6	450 mg, n=6	Placebo, n=6
Mean	–1.8	–1.8	–2.2	–0.2
95% CI	(–2.3, –1.3)	(–2.0, –1.6)	(–2.7, –1.7)	(–0.4, –0.1)
Median (Q1, Q3)	–1.7 (–1.2, –1.6)	–1.8 (–1.9, –1.6)	–2.2 (–2.5, –1.8)	–0.2 (–0.3, –0.1)
Min, max	–2.4, –1.2	–2.1, –1.5	–2.9, –1.6	–0.4, –0.1

Islatravir (MK-8591) in new fixed dose combination (FDC) with doravirine plus lamivudine: 24 week results

Simon Collins, HIV i-Base

New results using the investigational nucleoside reverse transcriptase translocation inhibitor (NRTTI) MK-8591 – newly named islatravir – was the focus of several presentations at IAS 2019.

One of these included 24-week results in a new FDC coformulated with doravirine and lamivudine (3TC). It is notable that this study also includes a switch to islatravir/doravirine dual therapy (at week 24). [1]

This is a phase 2b, randomised, double-blind, placebo-controlled, dose-ranging study in treatment-naïve participants with an active control arm using an FDC of doravrine/3TC/TDF.

The study randomised 121 treatment-naïve participants (1:1:1:1) to one of three doses for islatravir (0.25, 0.75, or 2.25 mg) plus doravirine (100 mg) and 3TC (300 mg) for at least the first 24 weeks, or to doravirine/3TC/TDF, with appropriate placebo.

Entry criteria included baseline CD4 count >200 cells/mm^3 and viral load ≥1,000 copies/mL. The primary efficacy endpoint is viral reductions at week 24. Participants with viral load <50 copies/mL at week-24 can discontinue 3TC and remain on dual therapy with islatravir plus doravirine.

Baseline characteristics included mean age 31 years, 93% male. Mean CD4 count was 492 cells/mm^3 (SD: 188) and 22% had viral load >100.000 copies/mL.

Race included 76% white and 20% black but the study also referred to approximately half the participants being Hispanic or Latin American. Approximately 40% were treated in sites in North America, 30% in South American and 25% in Europe.

Mean viral load reductions at week-24 in the pooled islatravir arms was –2.9 log copies/mL (with no differences between doses) compared to –2.8 with doravirine/3TC/TDF. All groups also reported mean viral load reductions of –2 log copies/mL by week 2.

Viral load <50 copies/mL at week 24 were reported in 89%, 100%, 87% an 87% in the 0.25, 0.75, 2.25 mg and control arm respectively. See Table 1.

Eleven participants did not achieve <50 copies/mL at week 24, mainly due to either low level viral load <200 copies/mL (n=5), missing data but previously < 50 copies/mL (n=2), or early study discontinuation (n=4). There were no cases of protocol defined failure (ie confirmed viral load > 200 copies/mL etc).

Tolerability was good with no serious drug-related AEs or discontinuations due to AEs. Common low grade side effects included diarrhoea, bronchitis and headache. One participants in the 0.7 mg arm reported abnormal dreams, fatigue, fever, abdominal distention and anxiety through to week 24 and one reported initial insomnia. One participant in the 2.25 mg arm reported insomnia through to week 24 and one reported rash. Two serious events were not judged treatment related: one facial paralysis and moderate dysentery (for 3 days at day 56).

Table 1: Viral load responses and side effects at week 24

	0.25mg	0.75 mg	2.25 mg	doravirine/3TC/TDF
n	29	30	31	31
<50 c/mL	89% (26/29)	100% (30/30)	87% (27/31)	87% (27/31)
BL <100K	90% (20/22)	100% (24/24)	90% (20/22)	88% (23/26)
BL >100K	85% (6/7)	100% (6/6)	77% (7/9)	80% (4/5)
Drug-related AEs	0% (0/29)	7% (2/30)	7% (2/31)	19% (6/31)
Serious AE	0%	3% (1)	0%	1% (1)

Nearly all participants switched to two-drug islatravir plus doravirine at week-24 and these results will be added to this report after they are presented at IAS 2019 in two days time. [2]

Another late-breaker abstract reported on a long-acting slow-release implant formulation of islatravir that produced sustained drug levels for more than one year. This will be reported in a separate article. [3]

Islatravir is in development at Merck (MSD), who also developed doravirine. Generic lamivudine is used in these FDCs.

References

1. Molina J-M et al. Tolerability, safety and efficacy of MK-8591 at doses of 0.25 to 2.25 mg QD, in combination with doravirine and lamivudine through 24 weeks in treatment-naïve adults with HIV-1 infection. 10th IAS Conference on HIV Science (IAS 2019), 21-24 July 2019, Mexico City. Late breaker post abstract LBPED46.
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http://programme.ias2019.org/Abstract/Abstract/4843

Dual therapy with islatravir (MK-8591) plus doravirine: 24 week results as switch strategy

Simon Collins, HIV i-Base

A late-breaking oral abstract at IAS 2019 included the first results of a new dual therapy of the investigational NRTTI islatravir plus the NNRTI doravirine, compared to triple therapy with additional lamivudine (3TC). [1]

This was part of a phase 2b study for treatment naïve participants who initiated ART with islatravir, doravirine and 3TC and who switched to dual ART at week 24 if viral load was undetectable (<50 copies/mL). Participants taking longer than 24 weeks were able to switch when then did become undetectable. Week 24 results were already presented at IAS 2019 and reported separately. [2, 3]

This was a randomised, double-blind, comparator-controlled, dose-ranging trial (using 0.25 mg, 0.75 mg or 2.25 mg once-daily doses of islatravir). This compound has a long intracellular half-life ~120 hours with potential for weekly and perhaps monthly dosing.

Primary efficacy endpoints included the overall proportion of participants at week 48 with viral load < 50 copies/mL by FDA snapshot analysis. The results at 48 weeks (following 24 weeks on dual ART) were presented by Jean-Michel Molina from St Louis Hospital, Paris.

Baseline characteristics included mean age 31 years, 93% male. Mean CD4 count was 492 cells/mm^3(SD: 188) and 22% had viral load >100.000 copies/mL. Race included 76% white and 20% black but the study also referred to approximately half the participants being Hispanic or Latin American. Approximately 40% were treated in sites in North America, 30% in South American and 25% in Europe.

At week 48, five participants in the islatravir arms (4 rebound, 1 non-response) vs one in the control arm (viral rebound) had viral load levels that were >50 copies/mL. However, no participants had viral load rebound >200 copies/mL and all were reported as being <80 copies/mL. This was below the threshold to test for drug resistance and new drug resistance was reported. Mean CD4 increases were similar in all groups.

Tolerability was generally good. Drug-related AEs were reported less frequently for the combined dual therapy arms compared to triple drug control group (7.8% vs 19.4%).

From week-48 all participants in the islatravir groups were changed to the 0.75 mg dose (for follow up until week-96) – although the dose to take forward into phase 3 studies has not yet been announced.

The study concluded that dual therapy would continue to be studied.

Table 1: Viral load responses after week 48: dual ART for 24 weeks,

	ISL 0.25mg + DOR	ISL 0.75 mg + DOR	ISL 2.25 mg + DOR	doravirine /3TC/TDF
n	29	30	31	31
d/c before wk 24	0	0	4	3
d/c wk 24-48	2	1	3	2
<50 c/mL wk 48	89% (26/29)	90% (27/30	77% (24/31)	84% (26/31)
> 50 c/mL wk 48	7% (2/29)	7% (2/30)	13% (4/31)	7% (2/31)
No data at wk 48	3% (1/29)	3% (1/30)	10% (3/31)	10% (3/31)

References

1. Molina J-M et al. MK-8591 at doses of 0.25 to 2.25 mg QD, in combination with doravirine establishes and maintains viral suppression through 48 weeks in treatment-naïve adults with HIV-1 infection. 10th IAS Conference on HIV Science (IAS 2019), 21-24 July 2019, Mexico City. Late-breaker oral abstract WEAB0402LB. http://programme.ias2019.org/Abstract/Abstract/4789
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3. Collins S. Islatravir (MK-8591) in new fixed dose combination (FDC) with doravirine plus lamivudine: 24 week results. HTB July 2019. http://i-base.info/htb/36398

Fostemsavir: 96-week follow-up in people with multi-drug resistance

Simon Collins, HIV i-Base

Fostemsavir is a gp-120 attachment inhibitor that has had a long development history as an investigational compound for people with HIV multidrug resistance.

Extended 96-week results from the phase 3 international BRIGHTE study were presented as an oral abstract at IAS 2019 and in a poster. [1, 2]

Because of the difficulty that many potential participants had in constructing background regimens to use with fostemsavir, this study included both a randomised cohort (RC; n=272) for those with some options and an open-label cohort (non-RC: n=99) for people who didn't meet entry criteria.

Although the primary endpoint for this study was viral reduction after a short 8-day period of virtual monotherapy, and the main secondary endpoint was viral efficacy at week 24, the continued follow-up is important to understand the sustained results.

Median baseline characteristics have been previously reported but in the RC group this included median (range) CD4 and viral load that were approximately 100 cells/mm^3 (0 to 1160) and 4.7 log copies/mL (1.6 to 6.9), respectively. Thirty per cent of the group were women.

Baseline characteristics were similar for the open-label group, with the important exception that 80% had no active drugs in the optimised backgroundregimen (OBR) and 20% had only one active drug. Median CD4 count was 41 cells/mm^3 in the non-RC group. [3]

Discontinuations during the study occurred in 22% (n=59) in the RC vs 38% (n=38) in the non-RC group, mainly due to lack of efficacy (n=12 vs 6), non-adherence (n=11 vs 6), adverse events (n=7 vs 4), withdrawn consent (n=5 vs 1) and loss to follow up (n=8 vs 1). However, there were 24 deaths (n=9 vs 15), reflecting the very advanced HIV and limited options at baseline. All comparison are RC vs non-RC).

This left 213 (78%) and 61 (62%) in the RC and non-RC arms. At week 96, RC participants had a mean CD4 increase of 205 cells/mm^3 with, 60% achieving virologic suppression (an increase of 6% from week 48). Of RC with baseline CD4 < 50, 58% of the RC group increased this to ≥200 cells/mm^3. See Table 1.

Overall, 38% participants had a serious adverse event (SAE); 3% were drug related and 7% discontinued due to AE. There were higher rates of severe events in the Non-RC vs RC: SAE (48%/34%), Grade 3-4 AEs (49%/29%), and deaths (16%/4%). Most deaths were related to advanced HIV infection and acute infection.

Results from a substudy of the RC arm was also presented at a poster at IAS 2019. [2]

This reported significant increases in mean CD4 increases for all sub-groups including by age, gender, ethnicity, baseline CD4 and viral load and active ARVs in the background combination. Virological responses were good in all subgroups except those with no other active ARVs in the optimised background combination.

No data have been presented on risk or development of resistance to fostemsavir in participants who continued with detectable viral load on treatment.

C O M M E N T

The long development of this compound were related for manufacturing and formulation issues that has delayed regulatory submission and blocked availability of a named-patient expanded access programme.

Results from the primary endpoint viral suppression at week 24 were presented at EACS in 2017. [3] Several analyses at week 48 were also presented at the Glasgow Conference in 2018. [4, 5]

FDA submission is now expected by the end of 2019 in the US and not until 2020 in the EU. [6]

References

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http://i-base.info/htb/35310
6. Personal communication. See HIV pipeline report 2019. HTB supplement, July 2019.
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Table 1: Viral response rates over time by snapshot and observed analysis

	Randomised (n=272)		Non-randomised (n=99)	
	Snapshot n (%)	Observed n (%)	Snapshot n (%)	Observed n (%)
Week 24	144 (53)	141/246 (57)	37 (37)	37/89 (42)
Week 48	146 (54)	145/233 (62)	38 (38)	40/83 (48)
Week 96	163 (60)	170/214 (79)	37 (37)	39/66 (59)

Dolutegravir/lamivudine dual therapy non-inferior to triple ART at week-96

Simon Collins, HIV i-Base

Results out to 96-weeks using the dual combination of dolutegravir/lamivudine as first-line therapy were presented as a late-breaking oral abstract at IAS 2019. The dual combination continued to show non-inferiority compared to the three-drug combination of dolutegravir plus TDF/FTC.

Dolutegravir/lamivudine was approved as a dual fixed dose combination (FDC) was approved by the FDA and EMA in April and July 2019, respectively, with tradename Dovato.

Combined results from the GEMINI 1 and 2 phase 3 studies were presented as a late-breaker oral abstract by Pedro Cahn from Fundación Huesped, Buenos Aires. [1] Week 48 results presented at the IAS 2018 conference last year. [2]

Overall, 1433 participants were randomised to either dual or triple ART. Baseline characteristics have been previously described and included median age 32 years (range 18 to 70); 15% women/85% men; and race included 69% white, 12% African American and 10% Asian.

Baseline median (range) viral load and CD4 count were 4.4 log copies/mL (1.6 to 6.3) and 430 cells/mm^3(19 to 1497). Approximately20% participants started with viral load >100,000c/mL and 8% with a CD4 count < 200 cells/mm^3.

At week-48, 91% vs 93% in the dual vs triple groups had viral load <50 copies/mL. These levels were largely sustained at week 96 by ITT analysis: 86% vs 89%. respectively. Non-inferiority was also maintained between the two arms (difference:–3.4 (95%CI: –6.7 to 0.0). See Table 1.

As the proportion of participants with viral load >50 copies/mL was the same at week-96 as week-48 (3% vs 2%), the differences between the two timepoints were explained by lack of virologic data:11% vs 9% at week-96 compared to 6% vs 5 % at week 48, in the dual vs triple arm. Over the second year, approximately another 10 people in each arm discontinued due to side effects but more people in the dual therapy arm discontinued for other reasons (n=27 vs 16).

There were no new cases of treatment emergent drug resistance in participants who had protocol defined viral failure during the second year (n=5 vs 3).

Overall, similar adverse events (AE) were reported for the two groups: any drug-related side effect (20% vs 25%), AE leading to withdrawal (3% vs 3%) and serious AE (9% vs 9%).

Increased weight was reported as an AE in 13 (1.8%) vs 10 (1.4%) participants in the dual vs triple arms. Overall, the mean change in weight from baseline was +3.1 kg vs +2.1 kg in the dual vs triple arms.

Changes in renal and bone biomarkers were significantly improved in the dual compared to the triple arms, as expected for non-TDF vs TDF containing ART, although the clinical implications from these changes was not presented.

Conversely, lipid differences significantly favoured the triple therapy arm linked to use of TDF, but again with limited likely clinical significance.

Further results supporting this dual combination was included in a poster reported no differences in the likelihood of low level viral blips over the first 48-weeks. [3]

By all definitions, there were no differences between arms – whether single blips to between 50 - 200, with or without rebound to >200 once - or >200 twice (ie confirmed viral withdrawal, CVW). See Table 2. Risk of blips was not related to baseline viral load being above r below 100,000 copies/mL

** One CVW in DTG+TDF/FTC arm was only confirmed at week 60, so is counted in category 2a.

Earlier this year, a presentation at CROI 2019 also reported no differences between the two arms when looking at participants with viral load <40 copies/mL having either a target detected (TD) or target not detected (TND) result. At the primary 48 week endpoint and at all earlier time points there were no significant differences between the 2D vs 3D arms for TND: 77% vs 73% (adjusted difference: 3.8%, 95% CI –0.6%, 8.2%). [4]

References

1. Cahn P et al. Durable efficacy of dolutegravir (DTG) plus lamivudine (3TC) in antiretroviral treatment-naïve adults with HIV-1 infection - 96-week results from the GEMINI studies. 10th IAS Conference on HIV Science (IAS 2019), 21-24 July 2019, Mexico City. Late-breaker oral abstract WEAB0404LB. http://programme.ias2019.org/Abstract/Abstract/4767

Table 1: Viral responses at week 96 in phase 3 GEMINI studies

	GEMINI 1	GEMINI 2	Pooled
DTG+3TC	300/356 (84%)	316/360 (88%)	616/716 (86%)
DTG+TDF/FTC	320/358 (89%)	322/359 (90%)	642/717 (90%)
Adj. diff. (95% CI)	4.9 (–9.8 to 0)	–1.8 (–6.4 to + 2.7)	–3.4 (–6.7, 0)

Table 2: Low level viral blips in GEMINI studies by week-48

	DTG+3TC (N=716)	DTG+TDF/FTC (N=717)
1. VL 50-200 (after <50 c/mL)	98 (14%)	101 (14%)
a. VL 50-200 c/mL with adjacent values <50 c/mL ("blips")	83 (12%)	93 (13%)
b. ≥ 2 consecutive VL 50-200 c/mL	15 (2%)	8 (1%)
2. VL ≥200 c/mL after <50 c/mL	19 (3%)	22 (3%)
a. Single VL ≥200 with adjacent VL<200 c/mL	14 (2%)	19 (3%)
b. ≥ 2 consecutive VLs ≥200 c/mL (CVW)	5* (0.7%)	3** (0.4%)
3. VL never <50c/mL (most had only baseline visits.	8 (1%)	7 (1%)
Total (all categories)	125	130

* One CVW in DTG+3TC was also counted in category 3.

2. Cahn P et al. Non-inferior efficacy of dolutegravir (DTG) plus lamivudine (3TC) versus DTG plus tenofovir/emtricitabine (TDF/FTC) fixed-dose combination in antiretroviral treatment-naïve adults with HIV-1 infection – 48-week results from the GEMINI studies. AIDS 2018, 23-27 July 2018, Amsterdam. Late breaker oral abstract TUAB0106LB.
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http://www.croiconference.org/sessions/hiv-replication (abstract)

Switching to dolutegravir/lamivudine dual therapy is non-inferior to TAF-based triple therapy at week-48 in TANGO study

Simon Collins, HIV i-Base

Results from a international phase 3 study using the dual fixed dose combination (FDC) dolutegravir/lamivudine (DTG/3TC) as a switch option in treatment experienced participants was presented in a late-breaking oral presentation at IAS 2019.

Although already approved for first-line therapy, the phase 3 TANGO study is the first large randomised study to look at this in treatment-experienced participants.

This study randomised 741 people (1:1) with viral load <50 copies/mL for > 6 months on current TAF-based ART to either switch to DTG/3TC or remain on their current therapy. Entry criteria included not having hepatitis B or prior virologic failure or document major resistance to NRTIs or integrase inhibitors.

The primary endpoint of this ongoing phase 3, non-inferiority trial is viral suppression at week-48, with results stratified by baseline third drug (PI, NNRTI or INSTI), with follow-up out to week 196.

Approximate baseline characteristics included median (range) age 40 years (18 to 74), which 20% older than 50; 8% were women and 20% were defined as "non-white". Baseline median (range) CD4 was about 700 cells/mm3 (119 to 1904) with 9% having a CD4 count <350 cells/mm3.

Most participants were using an integrase inhibitor (79%, mainly elvitegravir), with 14% using an NNRTI (mainly rilpivirine) and 7% were using a boosted PI (mainly boosted darunavir).

Participants had been on ART for a median (range) of 34 months (range: 7 to 201 months).

At week 48, 0.3% vs 0.5% (n=1 and 2) participants had viral load >50 copies/mL in the dual vs triple arms respectively (difference: 0.3: 95%CI: 1.2 to +0.7), meeting criterion for non-inferiority for this primary endpoint, based on 4% margin. The single case in the DTG/3TC arm was a protocol violation before taking study drugs.

Results were very similar for secondary endpoint of suppression < 50 copies/mL: 93% in each arm, again meeting non-inferiority (difference: 0.2; 95%CI: –3.4 to +3.9, margin 8%). Also, 6.5% in each group had no data for this time point. See Table 1.

Adverse events were similar between groups: with 80% reporting any AE, but 12% vs 1% reported drug-related AEs, in the dual vs TDF arms, with 4% (n=13) vs 1% (n=2) discontinuing because of side effects. These were mainly anxiety (n=3), insomnia (n=3), weight gain (n=2) or fatigue (n=2) in the DTG/3TC arm (all (<1%). Serious AEs (SAEs) were report by 6% (n=21) vs 4% (n=16). The single death in the study was due to gunshot wounds and unrelated to HIV treatment.

Small differences in bone and renal markers, and lipid profiles, were unlikely to have clinical significance but continued follow-up to 96- and 148 weeks will provide information about longer-term results.

At week 48, similar weight gains were reported for each group (approximately +0.8 kg).

Table 1: Week 48 study outcome by snapshot analysis

	DTG/3TC (n=369)	TAF-based ART (n=372)
VL <50 c/mL, n (5)	344 (93%)	346 (93%)
VL <50 c/mL, n (5)	1* (0.3%)	2 (0.5%)
No VL data	24 (6.5%)	24 (6.5%)
Discontinue (AE or death)	12 (3.3%)	1 (0.3%)
Discontinue other reasons (VL >50 c/mL	24 (6.5%)	22 (5.9%)

* Discontinued unrelated to treatment.

References

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http://programme.ias2019.org/Abstract/Abstract/4903

IAS 2019: PrEP

Potential for islatravir (MK-8591) implant to provide HIV PrEP for more than one year

Simon Collins, HIV i-Base

Also hinted at in previous conferences, IAS 2019 included the first results that a small implant with a slow-release formulation of the newly-named islatravir (MK-8591) might sustain drug levels for over a year.

This was a double-blind placebo-controlled phase 1 trial, using two doses of an islatravir (54 mg or 62 mg) or placebo implant (six participants per arm). Modelling from previous phase 1 and animal studies established a target threshold concentration of 0.05 pmol/10^6 TP in PBMCs.

The implants were removed after 12 weeks, with PK sampling continuing for a further four weeks for free drug and intracellular triphosphate levels. These levels remained above this target with both active implants.

PK results and predicted durability of effect are included in Table 1. This modelled protection for 8-10 months and 12-16 months for the 54 mg and 62 mg implants respectively.

The implants were reported as tolerable, with no serious adverse events or early discontinuations.

Table 1: PK and predicted durability with islatravir implants for PrEP

	54 mg	62 mg
N	6	6
Geometric Mean at day 85 (%GCV) (pmol/10^6 cells)	0.135 (27.3)	0.272 (45.2)
Estimated mean C at one year (pmol/10^6 cells) *	0.02	0.08
Projected duration for protection: range (months)	8-10	12-16

* Target threshold 0.05 pmol/10^6 cells.

COMMENT

In animals studies the effectiveness of islatravir was comparable to that seen with TDF/FTC PrEP. Given the effectiveness of oral PrEP is closely related to adherence to oral pills, a slow release implant could both broaden access to PrEP and increase efficacy on a population level.

This will depend on efficacy studies which have not yet started.

Slow-release removable implants are already widely used in some countries as contraceptive options for women. Actually, the use of a subcutaneous cotton strip for PrEP could easily produce a cult following as popular as piercings or tattoos.

References

1. Matthews RP et al. First-in-human trial of MK-8591-eluting implants demonstrates concentrations suitable for HIV prophylaxis for at least one year. 10th IAS Conference on HIV Science (IAS 2019), 21-24 July 2019, Mexico City. Late breaker post abstract TUAC0401LB. http://programme.ias2019.org/Abstract/Abstract/4843

FUTURE MEETINGS

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

4th European Workshop on Healthy Living with HIV

13 – 14 September 2019. Barcelona

www.virology-education.com

10th International Workshop on HIV & Ageing

10 – 11 October 2019 | New York, NY, USA

www.virology-education.com

International Workshop on HIV Drug Resistance and Treatment Strategies

16 – 18 October 2019

www.hivresistance2019.co.za

21st International Workshop on Comorbidities and Adverse Drug Reactions in HIV

5 – 6 November 2019, Basel, Switzerland

www.intmedpress.com

17th European AIDS Conference

6 – 9 November 2019, Basel, Switzerland

https://eacs-conference2019.com

3rd European Chemsex Forum

14-16 November 2019, Paris

https://ihp.hiv

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 (Dec 2017)
- Guide to HIV, pregnancy & women's health (December 2015)

Pocket guides

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

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

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

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

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

This project was developed with the Kobler Centre in London.

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

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

email: subscriptions@i-base.org.uk

Fax: 0208 616 1250

Other i-Base resources can still be ordered online as usual.

http://i-base.info/forms/order.php

Order publications and subscribe online

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

http://i-base.info/order

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Orders and subscriptions

107 The Maltings,169 Tower Bridge Road, London, SE1 3LJ
Tel: +44 (0) 20 8616 2210

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- **HIV Treatment Bulletin (HTB) every two weeks** ☐ **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 *(July 2019): 32-page A4 booklet* **quantity** _____

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

UK Guide To PrEP *(March 2019): 24-page A5 booklet* **quantity** _____

Introduction to ART *(May 2018): 48-page A5 booklet* **quantity** _____

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

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

Guide to HIV, pregnancy and women's health *(April 2019): 52-page A5 booklet* **quantity** _____

Guide to changing treatment: what if viral load rebounds *(Jan 2018): 24-page A5 booklet* **quantity** _____

- **Other resources**

U=U resources:

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

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

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

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

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