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Special issue: First reports from CROI 2018

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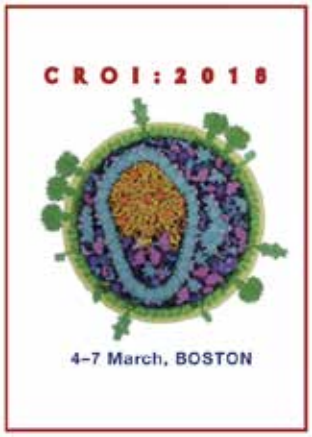

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EDITORIAL

This edition of HTB includes the first reports from CROI 2018, with additional reports following in subsequent issues.

Important themes this year included cure-related research, TB coinfection, PrEP and new antiretroviral drugs.

As usual, webcasts and conference material are already online.

Also, news that after more than a decade in development, the monoclonal antibody ibalizumab has been approved in the US as a treatment for multidrug resistant HIV.

This drug will be a life-saving option for some people, although it is still dependent on being used in combination with other active HIV drugs.

As we went to press it was still unclear whether there are plans to apply for approval in the EU.

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All help is appreciated.

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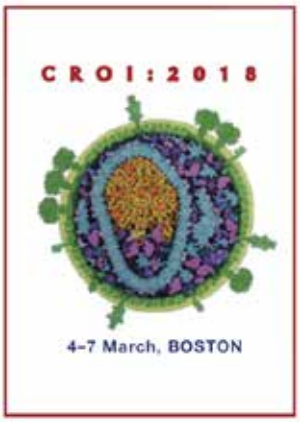
CONFERENCE REPORTS

25th Conference on Retroviruses and Opportunistic Infections (CROI 2018)

4–7 March 2018, Boston

Introduction



This year CROI was squeezed between a north east storm that disrupted travel into Boston, knocking out power to a million US homes, and a snow on the last day of the meeting that also cancelled flights, at least to much of the rest of the US.

And in between the weather, around 1100 scientific studies were presented on every aspect of HIV research. And remarkably, almost as soon as each study was presented the abstract was available online with webcasts for oral presentations and PDF files for posters.

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

Cure-related research was a main theme this year, with many presentations on approaches to define and shift the reservoir of latently infected CD4 cells, including important proof-of-principle results in animal studies.

Other major themes included new and better treatments (including global access), HIV prevention (including PrEP) and important studies on managing coinfections and complications (important studies on TB).

The full programme is now available online and abstracts and webcasts from oral presentations will become available immediately after the presentations. Approximately 1100 new studies were selected for the conference this year.

http://www.croiconference.org

Reports from CROI 2018 is this issue include:

- Inching towards an HIV cure: bNAb and TLR-7 agonist reduce viral rebound off-ART in macaques
- No HIV evolution in plasma or lymph nodes on suppressive ART and no impact of dolutegravir intensification
- Dual therapy can reduce TB prophylaxis from nine months to one: fewer side effects and more people complete treatment
- Twice-daily dolutegravir effective and tolerable with rifampicin
- Once-daily tenofovir alafenamide appears sufficient when dosed with rifampicin
- Efavirenz 400 mg can be given with anti-tuberculosis treatment
- Bictegravir studies at CROI 2018: switching and drug resistance analyses
- PrEP at CROI 2018 (part 1): Access in Australia and the US
- PrEP at CROI 2018 (part 2): Animal studies for future drugs
- BHIVA best of CROI feedback workshops

As with previous years, BHIVA will be organising a series of post CROI feedback meetings. Please register online to reserve a free place.

www.bhiva.org/Croi2018ConferenceRegistration.aspx

CROI 2018: CURE RESEARCH

Inching towards an HIV cure: bNAb and TLR-7 agonist reduce viral rebound off-ART in macaques

Simon Collins, HIV i-Base

Press-released before the results were presented in full, CROI 2018 highlighted the importance of cure research with results from a proof-of-principle study in macaques showing that treatment with broadly neutralising antibodies (bNAbs) might play a role in key stages for an HIV cure.

These are early results, and these are animal data, but they are encouraging for showing a delay in viral rebound in half the animals after stopping SHIV treatment, with significantly slower rates of viral rebound and to lower levels.

Top-line results were presented by Dan Barouch study from Beth Israel Deaconess Medical Center, Boston, using the bNAb PGT121 combined with the TLR-agonist GS-9620 (an investigational compound in development by Gilead). Full results were presented on Tuesday morning. [1]

Dan Barouch at CROI 2018 press conference

The study involved infecting 44 rhesus macaque monkeys with SHIV, and treating them with daily ART (dolutegravir/TDF/FTC) from day seven (during acute infection) for two years. The animals were then randomised to one of four groups (each n=11):

1. 10 mg/kg PGT121 by infusion (every 2 weeks x 5 doses).
2. 0.15 mg/kg GS-9620 by oral gavage (every 2 weeks x 10 doses).
3. Both PGT121 and GS-9620.
4. Placebo (sham) controls.

ART was then discontinued 16 weeks after the last intervention and viral load monitored.

PGT121 antibody levels were detected throughout treatment and SHIV DNA was significantly lower in the dual vs placebo animals (p=0.004), but became undetectable (in blood, lymph nodes and colorectal tissue) eight weeks before ART was stopped.

Viral load rebounded in all animals in the placebo arm at median 21 days (IQR 21 to 42), compared to only 6/11 animals in the dual therapy intervention rebounding by 140 days (p=0.03), with significantly longer time to rebound, median 112 days (IQR 84 to 140+), (p=0.0005). Peak viral load and viral setpoint were also significantly lower by –2.54 log and –1.52 log, respectively (both p<0.0005). Intermediate responses were seen with each or the single therapy interventions. See Table 1.

Additional details on this study are included in press releases from NIAID who sponsored this study and Gilead who are developing GS-9620. [2, 3]

Table 1: Responses after stopping ART in placebo vs dual arms

	Placebo	PGT121 + GS-9620	p
No. with rebound	11/11	6/11	0.03
Med, time to rebound (days)	21 days (IQR 21 to 42)	112 days (IQR 84 to 140+)	0.0005
Setpoint VL	12,500	< 400 c/mL	–1.52 log difference p<0.0001)

C O M M E N T

These results show that bNAbs can significantly impact viral dynamics when ART is started in acute infection and later discontinued. The researchers stressed however that these are very preliminary results in relation to an HIV cure.

The mechanism for the impact observed on viral dynamics is not well understood. Importantly, these compounds stimulate general CD4 responses, rather than specifically targeting HIV-infected cells in the reservoir.

Also, it is uncertain how results obtained against the lab-created SIV-HIV chimeric virus SHIV-SF162P3 (which has mostly been used for prevention experiments) will translate to HIV in humans.

Several research groups are leading interventions using bNAbs with potential for prevention (PrEP and vaccine strategies) and treatment. While current bNAbs have interesting though limited application, development of more potent and broad compounds are expected, and use in combinations provides exciting potential for future research.

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No HIV evolution in plasma or lymph nodes on suppressive ART and no impact of dolutegravir intensification

Simon Collins, HIV i-Base

Two studies with implications for cure research were included in the CROI 2018 press conference on Sunday, with full presentations on Tuesday. Both support the idea that ART reaches everywhere in the body that it needs to, and that residual HIV replication comes from HIV infected cells that were archived before ART was started.

Mary Kearney at CROI 2018 press conference

The first, summarised by Mary Kearney from the US NIH, Maryland, looked at whether viral evolution occurs in the context of suppressive ART in both plasma and lymph nodes. {1]

This question is important for cure research, to know whether the latently infected cellular reservoir is a fixed or moving target. Other groups have produced supportive evidence that this is likely, including a paediatric study by Lisa Frenkel in 2005 showing no viral evolution over seven years in a group of children with undetectable viral load. [2]

The current study is notable for prospectively collecting matched PBMC and lymph node samples before ART and again after 4.3 to 12.9 years. It involved five participants, with two provided lymph nodes (an invasive procedure).

Proviral populations and expression were characterised by cell associated RNA- and DNA- single genome sequencing, with sequences compared phylogenetically.

Overall, analysis of 176 samples from PBMCs and 234 from lymph nodes, showed no increase in branch length, diversity, or divergence from pre-ART plasma or PBMC due to ongoing viral replication in either location. There was no evidence of differences between compartments with proviruses with identical sequences at both sites.

This led the researchers to conclude that their findings were not compatible with a theory that the reservoir was maintained by ongoing active replication in either PBMCs or lymph nodes during suppressive ART.

The second study, presented by Thomas Rasmussen from Aarhus University Hospital, Denmark looked at whether intensification of suppressive ART with dolutegravir could further reduce viral replication. [3]

Again, this is an issue that has been looked at by many other research groups, including by Frank Maldarelli in 2008 using PIs and NNRTIs to intensify ART and by Steve Deeks in 2011 using the integrase inhibitor raltegravir (also looking at gut tissue).

The study at CROI 2018 randomised 40 HIV positive adults who had been on suppressive ART for at least three years to add either daily dolutegravir (50 mg) or matched placebo for 56 days.

There were no differences between groups for the primary outcome of level of 2-LTR circles at day 7 (p=0.17), or at any other timepoint. Median (IQR) fold-change from baseline to day 7 in 2-LTR circles was –0.17 (–0.90 to +0.90) and –0.26 (–1.00 to +1.17) in the in the dolutegravir and placebo groups, respectively. There was no consistent difference

in the levels of cell-associated unspliced HIV RNA, total and integrated HIV DNA on a single copy assay, T-cell activation markers or plasma levels of sCD14, d-dimer, IL-6 or hs-CRP. However, PD-1 expression in CD4 cells declined slightly after 56 days in placebo recipients compared to dolutegravir (p=0.03).

These researchers also concluded that this data supported a lack of ongoing residual viral replication in people on suppressive ART.

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CROI 2018: TB COINFECTION

Dual therapy can reduce TB prophylaxis from nine months to one: fewer side effects and more people complete treatment

Simon Collins, HIV i-Base

New results from a large international study using a simplified approach to prevent TB have the potential to dramatically improve outcomes for HIV positive people, cutting prophylaxis from nine months to one.

Richard Chaisson at CROI 2018 press conference

The BRIEF-TB study randomised 3000 adults with either latent TB or at high risk of TB infection to either one month of daily isoniazid (H) 300 mg plus rifapentine (P) 450 - 600 mg or to the standard of care nine-month regimen with daily isoniazid 300 mg.

The study included three years follow-up with primary endpoints of incidence rates (IR) of active TB, TB death or death by unknown cause, and stratified participants by ART use.

This was a non-inferiority study with lower margin of 1.25/100 patient years, based on an assumed IR of 2.0/100 PY in the nine-month arm. Results were presented by Richard Chaisson from Johns Hopkins University.

The study recruited participants from May 2012 to November 2011 in 45 sites in 10 countries.

Baseline demographics included 54% women (n=1614), median age 35 years (IQR 28-43), with 66% black and 24% Hispanic. Median CD4 count was 470 cells/mm^3 (IQR 346 to 635) and 50% were on ART at entry. Median BMI was 23.5 (IQR 20.9 to 27.1). Approximately 20% (n=634) had latent TB defined by positive TST or IGRA.

After three years of follow-up, there was no significant difference in the rate of primary events: in 34 vs 35 participants in the one vs nine month arms respectively. TB incidence rates were 0.69 vs 0.72/100 person years respectively (difference –0.025, upper 95% CI: 0.31).

Rates were higher for participants not on ART at entry and those with a positive TST/IGRA, but with no difference between treatment arms. Higher incidence in the one-month arm with baseline CD4 count <250 cells/mm3 was not statistically significant (p=0.12). See Table 1.

Although higher serious adverse events in the nine-month arm (7.1% vs 5.6%) were not statistically significant (p=0.1), targeted safety events was significantly lower with one month of treatment (3.3 vs 5.1/100 person years, p=0.03). Importantly the one-month course was more likely to be completed (97% vs. 90%, p<0.01).

There was one case of rifampin-resistant TB in each arm and one case of isoniazid-resistant TB in the nine-month arm.

The researchers concluded that once daily isoniazid plus rifapentine was non-inferior to nine-months isoniazid, with fewer side events, and higher completion rates.

C O M M E N T

The effectiveness of current TB prophylaxis for people with HIV is limited by the difficulties of taking nine months of isoniazid – despite their dramatically higher need for this protection.

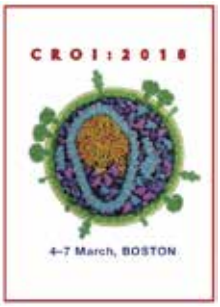
These results are likely to change management of HIV in people with latent TB or in high TB incidence settings.

Reference

Swindells S et al. One month of rifapentine/isoniazid to prevent TB in people with HIV: BRIEF-TB/A5279. CROI, 3-6 March 2018. Late breaker oral abstract 37LB.

Twice-daily dolutegravir is effective and tolerable with rifampicin

Polly Clayden, HIV i-Base



Dolutegravir 50 mg twice daily is effective and well-tolerated in adults with HIV/TB receiving rifampicin-based TB treatment. This is based on 24 weeks interim results from the INSPIRING study presented at CROI 2018. [1]

Treating TB and HIV is complicated by drug interactions, overlapping toxicities, and immune reconstitution inflammatory syndrome (IRIS). Dolutegravir (DTG) is poised to become a massively-used antiretroviral worldwide – including in settings were TB is common.

In healthy volunteers, rifampicin (RIF) reduced DTG concentrations considerably but this is likely overcome by giving DTG 50 mg twice daily. [2]

The INSPIRING study is being conducted to look at safety and efficacy of DTG in ART naive adults with HIV/TB. It is a phase 3b, non-comparative, active control, randomised, open-label study in HIV positive adults with at least 50 CD4 cells/mm3 and drug-sensitive TB.

Table 1: Incidence of primary events by baseline characteristics

Characteristics	One-month (H+P) Event / PY (IR/100PY)	Nine-month (H) Event / PY (Rate/100PY)	IR difference: 1-9 month (95%CI) *All p=NS between groups*
All participants	34/4923 (0.69)	35/4884 (0.72)	–0.025 (–0.36 to +0.31)
Baseline ART			
Yes	14/2378 (0.59)	14/2397 (0.58)	0.005 (–0.43 to +0.44)
No	20/2545 (0.79)	21/2487 (0.84)	–0.059 (–0.55 to +0.44)
TST/IGRA status			
Positive	11/1107 (0.99)	12/1133 (1.06)	–0.066 (–0.90 to +0.77)
Negative	23/3816 (0.60	23/3751 (0.61)	–0.01 (–0.36 to +0.34)
Baseline CD4			
<250 c/mm^3	14/619 (2.26)	7/627 (1.12)	1.15 (–0.30 to +2.59)
>250 c/mm^3	20/4304 (0.46)	28/4256 (0.66)	–0.19 (–0.51 to +0.12)
Sex			
Men	12/2300 (0.52)	17/2285 (0.74)	–0.22 (–0.68 to +0.24
Women	22/2622 (0.84)	18/2599 (0.69)	0.15 (–0.33 to +0.62)

Participants receiving rifampicin-based TB treatment for up to eight weeks were randomised (3:2) to receive DTG (50mg twice daily during and for two weeks after finishing TB treatment, followed by 50mg once daily) or efavirenz (EFV 600mg once daily), with two investigator-selected NRTIs for 52 weeks.

For the 24-week interim analysis, the investigators evaluated the proportion of participants with viral load <50 copies/mL using the modified FDA Snapshot algorithm in the intent to treat exposed population. They also assessed safety in all participants who received study drug. An independent adjudication committee looked at IRIS events. The study was not powered for non-inferiority. Kelly Dooley from Johns Hopkins University, Baltimore presented the results on behalf of the investigators.

INSPIRING enrolled 113 participants, across 37 sites in seven countries. The majority were from South Africa (n=65), other participating countries were: Peru, Brazil, Mexico, Russia, Argentina and Thailand. The study started in January 2015 and took about 21 months to fully enrol.

The participants were median age of 33 years and about 60% were male (TB is more common in men so this reflects incidence). Approximately 55–60% had a viral load >100,000 copies/mL and 20–30% CD4 <100 cells/mm3. They received TB treatment for about 30 days before starting ART. The most common ART backbone was TDF/XTC.

There were 69 and 44 participants randomised to the DTG and EFV arms respectively. Virological suppression <50 copies/mL was achieved in 56 (81% [95% CI 79 to 98]) and 39 (89% [95% CI 72 to 90]) participants in the respective arms.

There were 7 (10%) and 3 (7%) virological non-responders in the DTG and EFV arms respectively. Dr Dooley noted that among 5 participants who were not suppressed to <50 copies/mL in the DTG arm, 4 were between 50 and 400 copies/mL and 3 achieved suppression at later visits. Five (7%) of non-responders in the DTG arm were due to discontinuations for non-treatment reasons (mainly lost to follow up while suppressed).

Pharmacokinetics in INSPIRING are shown in Table 1.

Table 1: INSPIRING pharmacokinetic data

Time	n	DTG concentration (ng/mL) GM (90%)
Pre-dose concentration: DTG 50 mg twice daily + RIF		
Week 8	41	852 (208 to 2340) 118
Week 24	22	942 (19 to 3380) 276
Pre-dose concentration: DTG 50 mg once daily (post TB treatment)		
Week 36	16	1143 (80 to 4370) 151
Week 48	12	591 (19 to 3310) 359

Median CD4 cell increases at week 24 were 146 cells/mm3 (IQR 71–214) for DTG and 93 cells/mm3 (IQR 47– 178) for EFV.

Adverse events were common, occurring in 72% in the DTG arm and 91% of participants in the EFV arm. There were only two serious adverse events, both TB IRIS, one in each arm.

Of participants with events sent to IRIS adjudication committee 6% in the DTG arm and 9% in the EFV arm met the criteria for TB-associated IRIS. No one permanently discontinued their treatment due to IRIS.

Two participants had grade 3 liver toxicity; there was one in each arm and neither had to discontinue.

One participant met viral withdrawal criteria and no DTG resistance was detected.

Interim week 24 results from this ongoing study suggest that DTG 50 mg twice daily seems effective and well-tolerated in HIV/TB co-infected adults receiving RIF-based TB therapy. The investigators concluded that these data support the use of a DTG based regimen in HIV/TB co-infection.

COMMENT

The DTG label already recommends twice-daily dosing in the presence of RIF based on the previous drug-drug interaction study in HIV negative participants. This study was not powered to make a comparison with EFV but conducted to obtain some data in people with HIV/TB.

New antiretroviral options for people with HIV/TB are very welcome, as are all new data to support the imminent widespread use of DTG across populations.

For large scale programmes such as South Africa, the logistical issues involved in procuring and dispensing DTG single tablets in addition to DTG-based fixed-dose combinations (which are less vulnerable to stock outs etc), might prove too complex. Another strategy could be to switch to an EFV-based fixed-dose combination during TB treatment and back to DTG after this is completed. How countries approach HIV/TB co-treatment is likely to vary according to the size and capacity of the programme.

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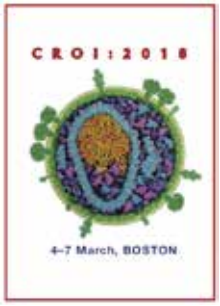
Once-daily tenofovir alafenamide appears sufficient when dosed with rifampicin

Polly Clayden, HIV i-Base



Plasma concentrations of tenofovir alafenamide AUC were decreased by 55% and intracellular tenofovir-diphosphate concentrations by 36% when given with rifampicin. But intracellular concentrations were still 76% higher than those with standard dose tenofovir disoproxil fumarate. [1]

These data from RIFT, a pharmacokinetic (PK) study of once-daily tenofovir alafenamide (TAF) with rifampicin (RIF) conducted by Maddalena Cerrone and colleagues from Chelsea and Westminster Hospital, London, UK, The Johns Hopkins University, Baltimore, MD, USA, University of Liverpool, Liverpool, UK, University of Cape Town, Cape Town, South Africa, were presented at CROI 2018. The study is the first to measure PK of once-daily TAF with RIF and compare it directly to tenofovir disoproxil fumarate (TDF).

TAF achieves lower plasma and higher intracellular tenofovir (TFV) concentrations than TDF, but it is a substrate of drug transporters so has potential for drug interactions, especially with inducers like RIF.

A recent parallel design PK study showed when twice-daily TAF was given with RIF intracellular TFV-diphosphate (DP) decreased by 24% and plasma TAF by 15% compared with once-daily TAF alone. [3, 4]

RIFT is a phase 1, open label, single arm, single centre evaluation in 23 HIV negative participants (21 completed). Participants received TAF/ FTC 25/200mg once daily (28 days) with food, followed by TAF/FTC + RIF 600mg once daily (28 days, RIF on empty stomach followed by TAF/ FTC with meal after 30 mins), followed by TDF 300mg once daily (28 days) with food.

The investigators performed intensive PK sampling on days 28 (TAF/FTC), 56 (TAF/FTC+RIF) and 84 (TDF). Plasma TAF, TFV, FTC and intracellular TFV-DP and FTC-triphosphate (FTC-TP) concentrations were measured by validated LC-MS methods.

Participants were genotyped for polymorphisms.

Twenty-one participants completed all PK phases. Geometric mean ratios (GMR) for the main PK parameters are shown in Table 1.

FTC-TP PK parameters were not affected by RIF. There were no significant associations with any polymorphisms.

There were two grade 3 adverse events and 2/23 participants discontinued: one case of transient hyper transaminitis during administration of TAF/FTC only (the investigators judged this to be unlikely drug related); one gastrointestinal symptoms (judged likely RIF-related).

The investigators concluded that although RIF co-administration decreased the plasma TAF by 55% and intracellular TFV-DP AUC by 36%, intracellular TFV-DP AUC were 76% higher with TAF + RIF than with TDF (300 mg once daily) alone.

Table 1: PK once-daily TAF + RIF vs TAF vs TDF

PK parameter	TAF + RIF vs TAF GMR (90% CI)	TAF + RIF vs TDF GMR (90% CI)
Plasma TAF		
Cmax ng/mL CV	0.50 (0.42–0.61)	
AUC0–24 ng*h/mL CV	0.45 (0.33–0.60)	
Plasma TFV		
Cmax ng/mL CV	0.35 (0.30–0.42)	
AUC0–24 ng*h/mL CV	0.46 (0.40–0.52)	
C24h fmol*h/10^6 CV	0.45 (0.42–0.50)	
Intracellular TFV-DP		
Cmax ng/mL CV	0.62 (0.52–0.74)	0.23 (0.17–0.30)
AUC0–24 ng*h/mL CV	0.64 (0.54–0.75)	0.24 (0.18–0.32)
C24h fmol*h/10^6 CV	0.57 (0.47–0.71)	0.24 (0.18–0.32)

C O M M E N T

These data support further evaluation of TAF + RIF in people with HIV and TB.

Unlike the previous TAF + RIF PK study, because of the comparison of intracellular TFV-DP concentrations with TAF + RIF to those with TDF alone, this evaluation suggests that doubling dose of TAF when coadministered with RIF is unnecessary.

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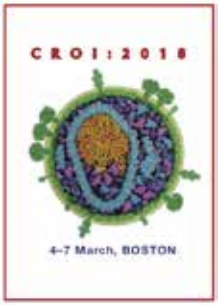
Efavirenz 400 mg can be given with anti-tuberculosis treatment

Polly Clayden, HIV i-Base



Isoniazid/rifampicin in HIV positive people without TB was associated with limited changes in efavirenz 400 mg exposure in a pharmacokinetic study presented at CROI 2018. Efavirenz concentrations were sufficient to maintain virological suppression.

WHO recommends efavirenz 400 mg (EFV400) as an alternative first-line antiretroviral with the caveat that there are

Table 1: PK EFV400 alone and with INH/RIF

	EFV GM (95% CI)			EFV GMR (90% CI)		
PK parameter	EFV400 (PK1)	EFV400 + INH/RIF day 42 (PK2)	EFV400 + INH/RIF day 98 (PK3)	PK2/PK1	PK3/PK2	PK3/PK1
Cmax ng/mL CV%	3257 (2554 to 4154) 83	2953 (2293 to 3804) 80	2791 (2020 to 3857) 87	0.91 (0.83 to 0.99)	0.95 (0.86 to 1.05)	0.84 (0.75 to 0.93)
C24h ng/mL CV%	1703 (1180 to 2457) 124	1441 (948 to 2191) 128	1301 (790 to 2141) 133	0.85 (0.72 to 0.99)	0.88 (0.75 to 1.03)	0.75 (0.62 to 0.92)
AUC0-24 ng*h/mL CV%	52259 (38284 to 71335) 107	47618 (33979 to 66732) 106	44004 (29442 to 65767) 113	0.91 (0.79 to 1.05)	0.92 (0.83 to1.01)	0.84 (0.72 to 0.99)

no data on EFV400 with TB treatment. Many HIV positive people need TB treatment with isoniazid (INH) and rifampicin (RIF) that affect cytochrome P450 and antiretroviral exposure.

Maddalena Cerrone and colleagues from Chelsea and Westminster Hospital, London, Imperial College London, London and University of Liverpool performed an evaluation of EFV400 in the presence of INH and RIF in HIV positive people without TB.

This open-label study investigated the pharmacokinetics (PK), efficacy, CYP2B6 pharmacogenetics of EFV400 and INH/RIF in participants previously stable on tenofovir disoproxil fumarate (TDF), emtricitabine (FTC) and EFV 600 mg (EFV600) for at least 12 weeks with a viral load <50 copies/mL.

Stopping criteria was predefined as EFV concentrations below 20% of the minimum effective concentration (MEC) of 1000 ng/mL on three visits.

After switching from EFV600 to EFV400 alone, intensive PK was performed at day 14 (PK1), INH/RIF was then co-administered and intensive PK was repeated at day 42 (PK2) and day 92 (PK3).

The investigators also evaluated weekly therapeutic drug monitoring (TDM), safety, virological efficacy, and polymorphisms associated with increased steady state EFV exposure.

There were 34 participants screened and 26 baselined, 22 completed PK2 (3 participants withdrew for EFV400 TDM results <800 ng/mL in >3 consecutive visits, as per stopping rule, and 1 for of non-drug related liver toxicity). And 18 completed PK3 (2 withdrew for liver toxicity, 1 for low EFV levels and 1 became pregnant).

Participants were 64% male, a median of 47 years of age (range 22–60) and CD4 591 cells/mm3; 45% were black African and 18% slow metabolisers. All participants had viral load <50 at baseline, which was maintained throughout the study.

EFV Cmax, C24h and AUC0-24 were respectively 9%, 15% and 9% lower after four weeks of co-administration with INH/RIF (PK2) vs EFV400 alone (PK1). After another eight weeks (PK3) these respective values were 5%, 12% and 8% lower compared with PK2 and 16%, 25% and 16% lower compared with PK1. Table 1 shows PK parameters of EFV400 alone and co-administered with INH/RIF.

Co-administration of EFV400 with INH/RIF was well-tolerated in 20/22 participants but resulted in >grade 3 ALT elevations in the remaining two. Two participants (extensive metabolisers) had low EFV levels and discontinued before receiving INH/RIF. Two more discontinued after two weeks on INH/RIF.

The plasma concentrations of EFV400 with INH/RIF were maintained above the cut-off extrapolated from the ENCORE1 study regardless of metaboliser status. All participants maintained viral load <50 copies/mL.

The investigators concluded that EFV400 can be co-administered with anti-TB treatment and this is being confirmed in people with HIV/TB coinfection.

COMMENT

EFV is likely to remain an alternative first-line option even in the era of widespread dolutegravir (DTG) use – for reasons of tolerability, patents and price.

Using an EFV-based fixed-dose combination (FDC) during TB treatment could be a simpler option with programmatic advantages than adjusting the DTG dose.

The first FDC with EFV400 was tentatively approved by the FDA in March 2017.

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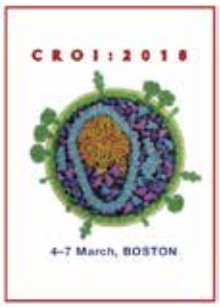
CROI 2018: ANTIRETROVIRALS

Bictegravir studies at CROI 2018: switching and drug resistance analyses

Simon Collins, HIV i-Base



As the most recently approved integrase inhibitor (February 2018 in the US, still pending in the EU) reports about bictegravir were included both in an oral presentation and in several posters. Bictegravir is only available in a fixed dose combination (FDC) with F/TAF.

Switching to bictegravir/F/TAF from dolutegravir plus 3TC/ABC

Jean Michel Molina from St. Louis Hospital, Paris presented results from a double-blind, placebo-controlled phase 3 study that randomised 563 participants on stable dolutegravir (DTG)-based ART to either switch to B/F/TAF or the DTG/3TC/abacavir FDC.

The primary endpoint was viral load suppression <50 copies/mL at 48 weeks, with non-inferiority defined using 4% margin for 95%CI 4%.

Baseline demographics included 88% men and 73% white, with median CD4 count of approximately 700 cells/mm^3 and eGFR 101 mL/min (IQR: 84 to 122).

Results are relatively easy to report, with high efficacy and safety in both arms and few significant differences.

At week 48, viral load was <50 copies/mL in 93.6% vs 95.0% (p=0.59) in the bictegravir vs dolutegravir arms, with 1.1% vs 0.4% (p=0.62) having detectable viral load. This showed a marginal, non-significant numerical difference in favour of the dolutegravir arm of 0.7% (95%CI: –1.0 to +2.8), but still meeting the criteria for non-inferiority for bictegravir.

There were few serious side effects, with 2% (n=6) vs 1% (n=2) stopping treatment in the bictegravir vs dolutegravir groups, respectively. Two deaths were both in the bictegravir group, but not related to study drugs. The only CSF-related events were in the bictegravir arm: one report of suicidal ideation (also not judged related) and one report of abnormal dreams.

Side effects of any grade were reported by about 80% of each group, mainly mild, with the most common reports being equally balanced: upper respiratory tract (10% vs 10%), nasopharyngitis (7 vs 8%), headache (7% vs &%), diarrhoea (9% vs 5%), all bictegravir vs dolutegravir respectively. Of these, side effects assigned as relating to study medication did favour the bictegravir arm (8% vs 16%, p=0.01).

Laboratory abnormalities were mild and overall were reported more often with bictegravir (17% vs 11%). These were mainly higher LDL (5% each arm), increased ALT or amylase (both 2% vs 0) and CK (2% each). There were no drug-related grade 3/4 lab changes.

The bictegravir arm also had a small early increase in eGFR by week 4 that was sustained to week 48 (+1.0 vs –1.8 mL/min) that was statistically significant (p<0.001). This was reported as being linked to greater inhibition of tubular secretion of creatinine with dolutegravir. There were no significant differences in measure of quantitative proteinuria at week 48, showing high level of renal safety in both groups, and no significant changes in bone density (measured at the hip and spine) or for lipids.

Switching to bictegravir/F/TAF in women and adolescents on stable ART

A greater amount of data on women switching to B/F/TAF was presented as a poster from a randomised phase 3 switching study conducted in Uganda, Russia, Thailand, USA and Dominican Republic.. This study randomised 470 women 1:1 to either remain on current ART, largely elvitegravir-based (E/C/F/TAF n=125; E/C/F/TDF n=98; atazanavir/r+FTC/TDF n=13); or change to B/F/TAF.

Demographics included greater ethnic diversity (37% black, 28% white, 21% Asian). As with the study above, CD4 count and eGFR were high (approximate median >700 cells/mm3 and 100 mL/min respectively).

At week 48, viral load remained undetectable (<50 copies/mL) in 96% vs 95% in the B/F/TAF group vs. control arm group, with no significant difference in rate of viral failure (0.1, 95% CI –2.9 to +2.99), meeting criteria for non-inferiority.

Results on switching to B/F/TAF in adolescents on stable ART (viral load <50 copies/mL for > 6 months) were presented from a small prospective single arm study. [3]

Baseline demographics for the 24 participants included median age 15 years (range 12-17), median weight 48.9 kg (range 36.1 to 88.6 kg), 79% women, 52% black and median CD4 count 708 cells/mm^3.

Drug levels for all three components were similar to those achieved in adult studies, with pharmacokinetic parameters generally falling within the expected acceptable geometric mean.

The most common treatment emergent side effect was upper respiratory tract infection (21%, 5 of 24) but side effects reported in more than two participants were mild-moderate and not related to study drug, and no related discontinuations. The only grade 3/4 laboratory abnormality was haematuria in four young women, coinciding with menses in 3/4 cases.

However, median changes in eGFR ranged from –8.0 to –14.0 mL/min/1.73 m2 between week 2 and 24, but this was not considered clinically significant.

High rates of acceptance of the pill size was reported with high adherence (88% taking >95% of medication over 24 weeks. The poster also showed the smaller physical size of the bictegravir FTC, being smaller than both E/C/F/TAF and DTG/3TC/ABC.

Drug resistance with bictegravir

Two posters at CROI 2018 presented results of resistance analyses, in the few people with viral failure at week 48 in bictegravir development studies.

The first poster reported on combined efficacy and resistance result from two phase 3 treatment-naive studies (n=634 on

B/F/TAF, n= 325 on DTG + F/TAF and n=315 DTG/ABC/3TC). Entry criteria included baseline screening for drug resistance, although not for integrase resistance. This poster also provided a breakdown for the 10% of participants who had non-B HIV sub-type. [4]

In the small numbers of people with viral failure at week 48 (n=17, all sub-type B), there were no cases of development of new drug resistance associated with any of the study drugs. One participant who was later found to have INSTI resistance at baseline (G140S+Q148H) that was phenotypically sensitive to bictegravir and partially sensitive to dolutegravir. This person had undetectable viral load < 50 copies/mL at week 4 and that was maintained through week 72 on B/F/TAF.

The second analysis was from two randomised, placebo-controlled switch studies in participants on stable ART (n=572 on B/F/TAF, n=281 on DTG/ABC/3TC and n=287 on elvitegravir-based STR or PI = 2NRTIs).

There was no detectable new resistance the 1.4% (8/572) of B/F/TAF treated patients experienced viral failure at week 48. This included 40 participants who started with archived NRTI mutations at baseline associated with resistance to FTC or TAF. Of these, 97% (35/36) on B/F/TAF maintained undetectable viral load at week 48: 100% (5/5) with K65R/N, 100% (8/8) with only M184V/I/T (18/18), 92% with M184V and other NRTI-R (12/13), and 100% with ≥2 TAMs (4/4).

There were no cases of new resistance developing in either the bictegravir or dolutegravir groups. [5]

C O M M E N T

Although switch studies to newer HIV drugs have always been used to show differences between combinations, the high efficacy of most modern combinations, generally report modest efficacy differences. ART in 2018 is very good.

Bictegravir was approved in the US in the US in February 2018, in a fixed dose formulation with FTC and TAF, with an EU decision expected later this year. Bictegravir is an integrase inhibitor from Gilead that (unlike elvitegravir) does not need boosting, so in practice will provide a similar option to dolutegravir as both are taken once-daily, with or without food.

The main practical differences between the integrase inhibitors relates to the coformulated NRTIs, with FTC/TAF providing coverage for HBV and abacavir/3TC requiring an HLA B*5701 test to rule out major risk of abacavir hypersensitivity.

In high-income countries, the price for the FDCs. Gilead now coformulates all FDCs with the new version of tenofovir (TAF), a new drug, still in patent, while ViiV matches generic pricing for the dual NRTI components, and also has two large ongoing studies looking at whether dolutegravir/3TC dual therapy might be sufficient to be able to drop abacavir altogether.

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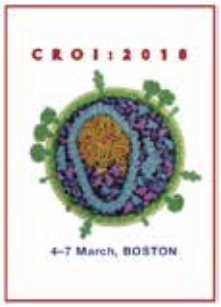
CROI 2018: PREVENTION

PrEP at CROI 2018 (part 1): access in Australia and the US

Simon Collins, HIV i-Base



Strategies to reduce incidence of new HIV infections was one of the key themes at CROI 2018, with at least 80 studies on PrEP included in the programme.

These covered all scientific aspects of PrEP research, new drugs and formulations, current use and acceptability and ways to expand access to PrEP to diverse populations, some studies on adherence and a few looking at STIs.

This report starts with two different approaches to access to PrEP in Australia and the US.

A second linked report covers oral abstract sessions on new drugs presented at the same oral session.

PrEP rapidly reduces HIV incidence in Australia

Positive results from a PrEP implementation study in Australia showed an impressive public health approach in New South Wales. The results, presented by Andrew Grulich from the Kirby Institute, showed that making PrEP widely available can quickly reduce HIV incidence. [1]

This programme was developed as part of the government's policy to eliminate HIV incidence as part of their 90:90:90 target. As approximately 80% of new infections are in gay men, this included the aim to make PrEP widely available within a year to people at high risk, prioritising gay and bisexual men, (less than 1% of participants were trans or other risk). The programme initially planned for 3700 men to use PrEP (based on 2.3% of the population identifying as gay, 8% of who were estimated to have high risks that would make them eligible (recent STI, condomless sex or chemsex). However, when the enrolment goal was reached within eight months, the cap was removed, and uptake steadily increased to reaching more than 9000 men over two years.

This was an adult study, with 8% aged 18-24, 40% aged 25-34, 30% age 35-44 and 26% older than 45. Approximately 90% of participants lived in Sydney, with 40% living in a gay-area postcode. Approximately half the participants accessed PrEP from a public clinic and half from a private GP.

In the first year, HIV diagnoses overall fell by 25% (from n=295 in the year before PrEP to 221 after the first year) and recent infections reduced by 32% (from 149 to 102). However, the overall HIV incidence was lower than predicted (<1/1000 PY compared to the expected rate of 2/100), perhaps linked to other polices including early use of ART.

For Australian, English or Asian participants, HIV incidence dropped in all age groups and geographical regions, but the programme didn't reach non-English speaking men born in other countries, where annual HIV diagnoses increased in this group by 24% (from n=17 to 21). This, together with a greater focus on younger people, are planned.

When asked where the resources for health clinics came from to enable the programme, this was mainly from the drive and belief by health workers to enable this access.

When asked for ideas on how to achieve similar programmes in other countries, Grulich was clear: "the political support to end HIV was essential - and we were clear that it couldn't happen without PrEP".

Inequity of PrEP in the US: those most in need have least access

A more sobering presentation from Dawn Smith from the US CDC, showed that despite PrEP being approved in the US more than five years ago, racial disparities in access meant that those in most need of PrEP are least likely to be using it.

This study used new methodology for compiling local, regional and national estimates of numbers of people with an indication for PrEP, by race, US state and transmission risk group. Updated 2015 estimates for the need for PrEP now used new sub-population data at a state level from the 2016 census that were not previously available. The model estimated that 25% of gay and bisexual men overall would have an indication for PrEP and included recent data, race and other risks (heterosexual, of injecting drugs).

A similar number of people were estimated to need PrEP (1.1 million), but almost doubled the demand for MSM, reducing estimates for heterosexuals and people who inject drugs. A breakdown of this total by race was 44% black (58% of MSM and 64% of heterosexuals) 35% Hispanic and 26% white. The denominator for actual use was a lower underestimate, covering 85% of commercial and mail order pharmacies, but not people in integrated health systems (such as the VA, military etc).

When the number of PrEP prescriptions during 2015-2016 were compiled using 2015 estimates of indications for PrEP, the disparity of access became even more clear. Nationwide, overall 8% of people with an indication for PrEP were able to access it, but by ethnicity, PrEP was prescribed to 14% of white, 3% of Hispanic and only 1% of black people with an indication for PrEP.

The results were summarised as an essential call to urgent action: "Inequitable access to and use of PrEP by black Americans is an urgent problem that must be addressed. The high need for PrEP among black MSM and women is largely unmet. Until addressed, this situation will continue to result in disparity in new HIV infections".

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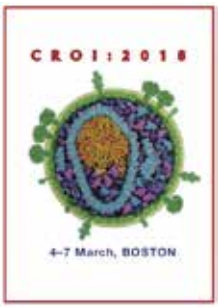
PrEP at CROI 2018 (part 2): Animal studies for future drugs

Simon Collins. HIV i-Base



Part 2 of our PrEP reports from CROI 2018 summarise early stages for promising approaches to future PrEP.

Tiny dose EFdA (MK-8591) protects against rectal SHIV

One of the most exciting potential HIV drugs with an indication for both treatment and prevention is an NRTI called MK-8591. This compound has high potency, retains activity against many NRTI-resistant mutations, and has the potential for formulation in a slow release removal implant that would provide drug coverage for a year.

New data at CROI 2018 included results from an animal PrEP study showing that progressively lower doses of EFdA still remained highly effective as PrEP. [1]

This added to results first presented as a late breaker at the IAS conference last year in Paris showing that weekly dosing (3.9 mg/kg, equivalent to 10 mg/week human dose) of EFdA protected all eight animals following weekly rectal exposure, compared to rapid infection in controls. [2]

The new results at CROI 2018, presented by Martin Markovitz from the Aaron Diamond AIDS Research Centre in New York, continued this study in the same animals, but using steadily lower doses: 1.30, 0.43, 0.10 and 0.025 mg/kg. Each animal received up to four challenges (a week after dosing), with a 4-8 week washout period before moving to the next lower dose.

At the 1.3 and 0.43 mg/kg doses, all eight animals continued to be protected after multiple SHIV rectal challenges. At 0.1 mg/kg, 2/8 animals did become infected (after the third and fourth challenge), although protection was still highly significant compared to control animals (p=0.004). Post infection viral load in these two animals was significantly lower (by 3 to 4 log copies/nL) compared to control animals. At the lowest 0.025 mg/kg dose, all four remaining animals did become infected.

Mean levels of intracellular MK-8591-TP at the time of challenge were 282 and 102 fmol/million PBMCs at the 1.3 and 0.43 mg/kg dosing levels, respectively (compared to 810 at the original 3.9 mg/kg dose). At the 0.1 mg/kg dose levels were not able to be detected, either in plasma or in cells, but were estimated at 24 fmol/mil PBMCs based on linear dynamics. All animals had wild-type HIV after viral break though.

A second oral presentation at CROI 2018 looked at low dosing of EFdA when used as treatment, suggesting daily doses as low as 0.25 mg/day would be effective in daily combinations. [3] At 0.25 mg, EFdA will have to be coformulated to even see it.

Results showing TAF protects against vaginal exposure

Although preclinical animal data in rectal tissue supported TAF use for PrEP, with the ongoing Discover study already enrolled (comparing oral FTC/TDF to FTC/TAF), the first data on vaginal tissue was only presented at CROI 2018.

Ivana Massud presented results from a two-part study in five pigtailed macaques (median age 12 years) showing in part 1 that a 1.5mg/kg TAF dose that resulted in levels that were higher than matched human exposures in plasma but that closely matched intracellular levels in vaginal and rectal tissue . [4]

The efficacy study was similar to previous studies using oral FTC/TDF, with six animals dosed 24 hours before and 2 hours after weekly SHIV exposures for 16 weeks. Control animals all become infected (median 5 weeks) compared to only one animal receiving FTC/TAF (at week 2). This showed 82% efficacy (p=0.042)

The animal that became infected had good levels of active metabolite for FTC in PBMCs throughout 16 weeks, but tenofovir levels were largely below the limit of quantification. Although the cause of these low levels was not explained, it showed the FTC alone was not sufficient for protection. No resistance was detected in this animal.

First animal studies of PrEP in penile tissue: oral TDF/FTC and long-acting cabotegravir

Charles Dobard from the US CDC presented the first data (ever) on PrEP levels in penile tissue. [5]

Although approximately 50% of HIV infections globally are estimated to be from transmission into penile tissue (through the foreskin, glans and urethra), this has never been studied directly in animal or human PrEP studies. However, the effectiveness of PrEP in penile tissue has been proven indirectly in heterosexual studies (TDF-2 and Partners-PrEP).

The model was first validated using the same design as the animal studies that showed oral TDF/FTC protected against vaginal and rectal exposure. Six rhesus macaques were given oral TDF/FTC (24 hours before and 2 hours after) with weekly penile exposure to SHIV, for 12 weeks. All control animals became infected by week 12 (at median 2 weeks), with only one TDF/FTC animal becoming infected (at 7 weeks), showing 92% efficacy (p=0.032).

For the cabotegravir study, six animals were injected with cabotegravir LA (50 mg/kg IM) every month for three months with similar weekly exposures to SHIV for 12 weeks. Weekly inoculation was both directly into the urethra and to the pouch under the foreskin.

The results were also similar. All controls were infected by week 12 (median by two weeks) compared to only one animal in the active CAB-LA (at 12 weeks); matching the 93% efficacy reported in the vaginal and rectal studies (p=0.02).

Very good PK was reported for the protected animals with all protected animals having drug concentrations 4-fold above the protein adjusted IC90. In the animal that became infected drug levels dropped below this level for the fourth week of each cycle.

All eight controls were all infected within 12 weeks, with 50% by 2 weeks, compared to only 1/6 animals in active group (at week 7), producing efficacy of 92% (p=0.032).

Vaginal insert for PrEP against HIV, HSV-2 and HPV: griffithsin/carrageenan (GRFT/CG)

Another animal study included results from using a fast-dissolving vaginal implant design to protect against HIV, HSV-2 and HPV. [6]

GRFT is a small lectin derived from red algae that blocks HIV entry without having cross-resistance to current ARVs and that also has activity against HSV and HPV. This study used a version grown from the tobacco plant. CG is a polysaccharide also derived from algae that has potent activity against HPV.

In macaque studies, the fast-dissolving combination insert (developed with PATH in Seattle) produced GRFT target levels 100-fold above the EC90 in cervical vaginal lavage within an hour that were sustained over 24 hours for most animals. The macaque studies also looked at the impact of pretreatment with depot medroxyprogesterone acetate (DMPA) long-acting progestin contraceptive.

Ten animals in each group were challenged by SHIV four hours after the insert was applied. All control animals, using only CG, became infected compared to only 2/10 of the GRFT/CG active group (p=0.003). There were no differences in viral dynamics or immunologic responses between infected and control animals.

Activity against HSV-2 was shown in a mouse study. All 15/15 mice become rapidly infected, showing symptoms within 7 days compared to only 6/15 in the active arm - leaving 60% of the mice receiving GRFT/CG disease-free, (p<0.0001).

HPV protections was shown in mice challenged with HPV-16, with all control animals showing evidence of infection compared to active group (p<00001).

On the basis of these results, the first phase 1 human study is already underway, using a GRFT/CG gel.

Separate phase 2 studies are also underway using CG gel to prevent HPV.

Long-acting PrEP using bNAbs

There is sufficient potential for long-acting broadly neutralising antibodies to be used as PrEP that two large phase 2b studies are already ongoing using VRC01.

A preclinical animal study at CROI 2018 looked at using two different gp120-binding bNAbs – 3BNC117 and 10-1074 – that protected against rectal exposure in animal studies. Both antibodies are more potent than VRC01, though with less broad neutralisation. The new study, presented by David Garber from the US CDC, looked at vaginal protection in three groups of rhesus macaques: (i) 3BNC117 alone (n=6), (ii) BNC117 combined with 10-1074 (n=6) or (iii) a placebo control arm (n=3), followed by weekly SHIV challenges. [7]

All animals did become infected but at significantly different median times with: 2 weeks for the control group, 5 weeks for the single 3BNC117 antibody arm (p=0.002 vs control) and 11.5 weeks for the dual antibody arm (p=0.002 vs control and p=0.0005 vs the mono arm).

The great protections in the dual arm were related to longer persistence of 10-1074 and higher maximum levels after dosing (rather than a longer half-life).

Neither of the antibody groups showed different viral or immunological responses after infection, compared to the control group.

A separate poster was also presented from a phase 1 study using a combination of two different antibodies that were formulated as a vaginal film. [8]

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Unless stated otherwise, all references are to the Programme and Abstracts of the 25th Conference on Retroviruses and Opportunistic Infections (CROI 2018), 4–7 March 2018, Boston.

http://www.croiconference.org

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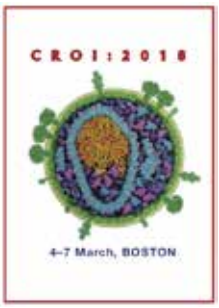
CROI 2018: OTHER NEWS

BHIVA best of CROI feedback workshops

bhiva.org



This year BHIVA will hold six CROI feedback workshops.

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

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

Registration is free, but places are held against a £20 card reservation that is only charged if you do not either attend or cancel by Friday 9 March 2018.

Please register online.

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

ANTIRETROVIRALS

FDA approves ibalizumab in the US to treat multidrug HIV resistance

Simon Collins, HIV i-Base

On 6 March 2018, the US FDA approved ibalizumab as a treatment for HIV positive people with multidrug resistance who are currently on failing ART.

Ibalizumab is a monoclonal antibody that works as an entry inhibitor, interfering with post-attachment steps for HIV to infect a CD4 cell. It is given by intravenous infusion every two weeks and needs to be used in combination with other active HIV drugs. Ibalizumab needs an initial loading dose of 2,000 mg followed by a maintenance dose of 800 mg every two weeks.

Approval is based on results from combined results in only 292 people during the long clinical development phase, which has been ongoing for at least a decade. The most recent TMB-301 study was in 40 highly treatment experienced participants with drug resistance to at least three classes and who were on currently failing ART. Ibalizumab was either added to current failing ART or used as monotherapy for the first week, which led to a 0.5 log reduction in viral load in 80% of participants.

Background ART was optimised to the best available combination based on resistance test results and previous treatment history.

At baseline, median viral load and CD4 cell counts were 35,350 copies/mL and 73 cells/mm^3, respectively. After 24 weeks of use in combination with other drugs, viral load was reduced by a median of 1.6 log and 43% of participants achieved undetectable viral load.

The most common side effects are diarrhoea, dizziness, nausea and rash. Severe side effects include rash and immune reconstitution syndrome.

An analysis of drug susceptibility in this study was also presented at CROI 2018. [2]

For full details please see the US prescribing information. [3]

Ibalizumab was developed by TaiMed Biologics with the trade name Trogarzo. It is marketed in the US and Canada by Theratechnologies.

COMMENT

Approval of this compound will be a life-saving drug for people with multidrug resistance, but it's relatively modest antiretroviral activity is dependent on use with other drugs that are still active.

The US list price for ibalizumab is US $ 118,000 (WAC/Wholesale Acquisition Cost), which doesn't include costs for providing the infusions (the product is not self-administered).

It is unclear whether there are any plans to make ibalizumab available in other countries, or whether the compound will be submitted for EU approval.

The development has been very slow, with Phase 1b efficacy results first reported in 2008. [4]

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FUTURE MEETINGS

Conference listing 2018

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

BHIVA 'Best of CROI' Feedback Meetings 2018

Monday 19 March, London

Tuesday 20 March, Birmingham

Wednesday 21 March, Haydock

Tuesday 27 March, Cardiff

Wednesday 28 March, Wakefield

Thursday 29 March, Edinburgh

www.bhiva.org/BestofCROI2018.aspx

4th Joint BHIVA/BASHH Spring Conference

17 – 20 April 2018, Edinburgh

www.bhiva.org

12th INTEREST

29 May – 1 June 2018, Kigali

interestworkshop.org

International Workshop on Clinical Pharmacology of Antiviral Therapy 2018

Tbc May 2018, Washington

www.virology-education.com

22nd International AIDS Conference (AIDS 2018)

23 – 27 July 2018, Amsterdam

www.aids2018.org

International Workshop on HIV & Aging

13 –14 September 2018, New York, USA.

www.virology-education.com

Australasian HIV&AIDS Conference 2018

24 – 26 September 2018, Sidney

www.hivaidsconference.com.au

HIV Glasgow 2018

28 – 31 October 2018, Glasgow

www.hivglasgow.org

PUBLICATIONS & SERVICES FROM i-BASE

i-Base website

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

http://www.i-Base.info

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

Publications and regular subscriptions can be ordered online.

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

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

i-Base treatment guides

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

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

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

New pocket guides

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

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

We hope these are especially useful as low literacy resources.

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

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

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