BHIVA

British HIV Association

Autumn Conference

Friday 25th November 2022

ROYAL COLLEGE OF PHYSICIANS, LONDON

BHIVA WORLD AIDS DAY

WORLD AIDS DAY

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BHIVA: review of the year

Chair:

Dr Nicola Mackie

This educational event is supported by

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Highlights of the last year

Dr Matthew Page

University Hospitals Birmingham NHS Foundation Trust

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A Year in HIV: 2022 Edition

Dr. Matthew Page

University Hospitals Birmingham, NHS FT

Conflict of Interest

I have previously received conference support, speakers fees and advisory board honoraria from Gilead, Janssen, MSD, and ViiV.

I have received research support from Gilead.

Speakers are required by the Federation of the Royal Colleges of Physicians to disclose conflicts of interest at the beginning of their presentation, with sufficient time for the information to be read by the audience. They should disclose financial relationships with manufacturers of any commercial product and/or providers of commercial services used on or produced for patients relating to the 36 months prior to the event. These include speaker fees, research grants, fees for other educational activities such as training of health professionals and consultation fees. Where a speaker owns shares or stocks directly in a company producing products or services for healthcare this should also be declared. Finally, other conflicts of interest including expert functions in health care or healthcare guidance processes should be declared (eg if the professional is a member of a health board). The Federation considers it good practice to also make speakers' disclosures available in digital format(s) relating to the educational event.

A Year in HIV:

2022

EDITION

Dr Matthew Page
Sexual Health & HIV Consultant
University Hospitals Birmingham, NHS FT

CROI
Conference on Retroviruses and Opportunistic Infections

BHIVA
British HIV Association

BASHH
British Association for Sexual Health and HIV

AIDS 2022
29 July – 2 August

HIV Drug Therapy
GLASGOW 2022 | HYBRID
30 YEARS

Overview

- Where are we with PrEP: “beyond TDF/FTC”
- Promise of self-administration for LA injectables
- Dolutegravir and Neural Tube Defect: Tsepamo Update
- HIV Cure Cases
- Islatravir – back in business?
- Fostemsavir – commissioning update
- Birmingham HIV/AIDS Memorial

Dawn of a new horizon

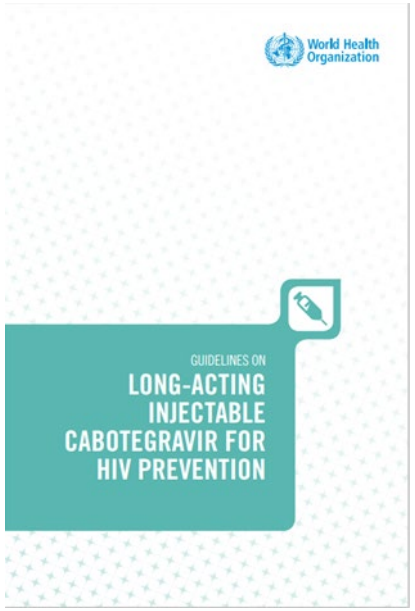
FDA NEWS RELEASE

FDA Approves First Injectable Treatment for HIV Pre-Exposure Prevention

Drug Given Every Two Months Rather Than Daily Pill is Important Tool in Effort to End the HIV Epidemic

Share | Tweet | Linkedin | Email | Print

For Immediate Release: December 20, 2021



HPTN 084
Long-acting Injectable For the Epidemic

VS.

- RCT double-blinded, double-dummy study
- IM LA CAB 600mg (every 8wks) vs daily TDF/FTC as PrEP for **cis-women** not living with HIV in Sub-S Africa aged 18-45 (n = 3224)
- 5wks oral CAB, then IM CAB wk 5 & 9, then e8wk (experimental arm)

- **Headline: CAB LA sup. to daily TDF/FTC HR 0.11 [95%CI 0.05-0.24] (89% less HIV seroconversions in CAB group vs TDF/FTC)** ***(blinded & unblinded phase)***

- 56 incident HIV infections – daily FTC/TDF group
- 6 incident HIV infections – CAB group

Of CAB group
- 4 were positive at enrolment, 1 discontinued oral lead-in CAB then tested positive, 1 – Seroconverted 106wks after last dose

- **No "on-injection" seroconversions**

Delaney-Moretlwe S, Hughes J, Bock P, et al. Long acting injectable cabotegravir is safe and effective in preventing HIV infection in cisgender women: interim results from HPTN 084. Presented at HIV R4P 2021. and undated info presented at CROI 2022

HPTN 083
an HIV prevention clinical trial

vs.

- RCT double-blinded, double-dummy study
- IM LA CAB 600mg (every 8wks) vs daily TDF/FTC as PrEP for **MSM/TGW** not living with HIV in N & S Amer, Africa, Asia aged 18 or over (n= 4566)
- 5wks oral CAB, then IM CAB wk 5 & 9, then e8wk (experimental arm)

- **Headline: CAB LA sup. To daily TDF/FTC 95% HR 0.34 [0.18-0.62] (66% less HIV seroconversions in CAB group vs TDF/FTC)**

- 39 incident HIV infections – daily FTC/TDF group
- 13 incident HIV infections – CAB group

Of CAB group

- 4 were positive at enrolment, 5 had no recent exposure to CAB when became positive, 3 became positive during CAB OLI

4 HIV seroconversions "on-injection" – appropriate schedule and plasma drug concentration levels

Landovitz RJ, Donnell D, Clement ME, et al. Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women. The New England Journal of Medicine 2021;385:595-608. DOI: 10.1056/NEJMoa2101016

Promise of self-administration for LA injectables?

EPB176

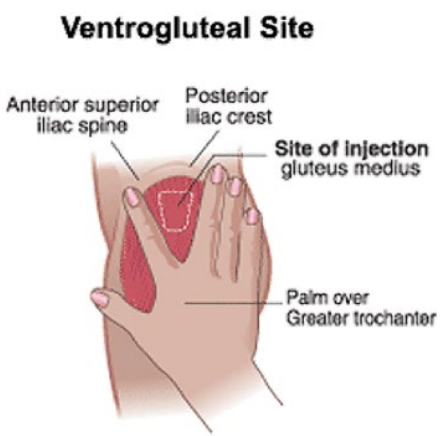
Pharmacokinetics and Tolerability of Cabotegravir and Rilpivirine Long-Acting Intramuscular Injections to the *Vastus Lateralis* (Lateral Thigh) Muscles of ~~Healthy Adult Participants~~ People not living with HIV

- Usually IM injection administered by a HCP into the gluteus medius

- Phase 1 study – assess tol. (ISR, PIN), safety, and efficacy (PK-est) with lat. thigh inj delivery – potential for self-delivery

- OLI → w/o period 10 to 14d →single 3ml injection CAB 600mg & RPV 900mg
- not-PLWH, n=15 (6 female), 47% white, med. BMI 31.4, med. Age 33yrs

- **In brief:**
- Participant biochemistry unchanged from BL
- Participant "pain-on-injection" score (moderately acceptable - 2.9 at peak)
- Pharmacokinetic profile favourable and supports further evaluation
    - Plasma concentrations at weeks 4 and 8 were above the PA-IC_{90} for;
        - CAB (wk4: 15.4-fold above, wk8: 5.3-fold above)
        - RPV (wk4: 4.7-fold above, wk8 2.4 fold-above)



Han AIDS2022 Poster EPB176

Promise of self-administration for LA injectables?

PESUB24

A Study Evaluating the Safety, Tolerability, and Pharmacokinetics of a High-Concentration (CAB 400 mg/mL) Cabotegravir Long-Acting Injectable Formulation Following Subcutaneous and Intramuscular Administration in ~~Healthy Adult Participants~~ People not living with HIV

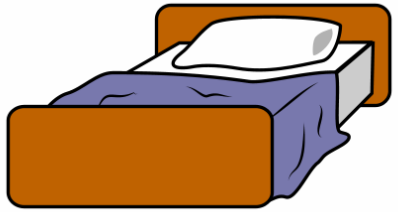
- Usually CAB 200mg/ml IM inj preparation

- Interim phase 1 study – assess tol. (ISR, PIN), safety, and efficacy (PK-est) CAB 400mg/ml IM gluteal, IM lat thigh and s/c abdomen

- OLI 28d→ CAB 400mg/ml e4w at varying volumes at varying sites depending on cohort randomised to
- not-PLWH, ~50% white, ~33% black, ~20% other, ~20-50% female across cohorts

- **In brief:**
- Safety profile similar to CAB 200
- ISRs – esp. erythema/nodules more common with CAB 400
- Plasma concentrations within range of approved CAB 200mg/ml IM gluteal regimens, regardless of the delivery method in the study

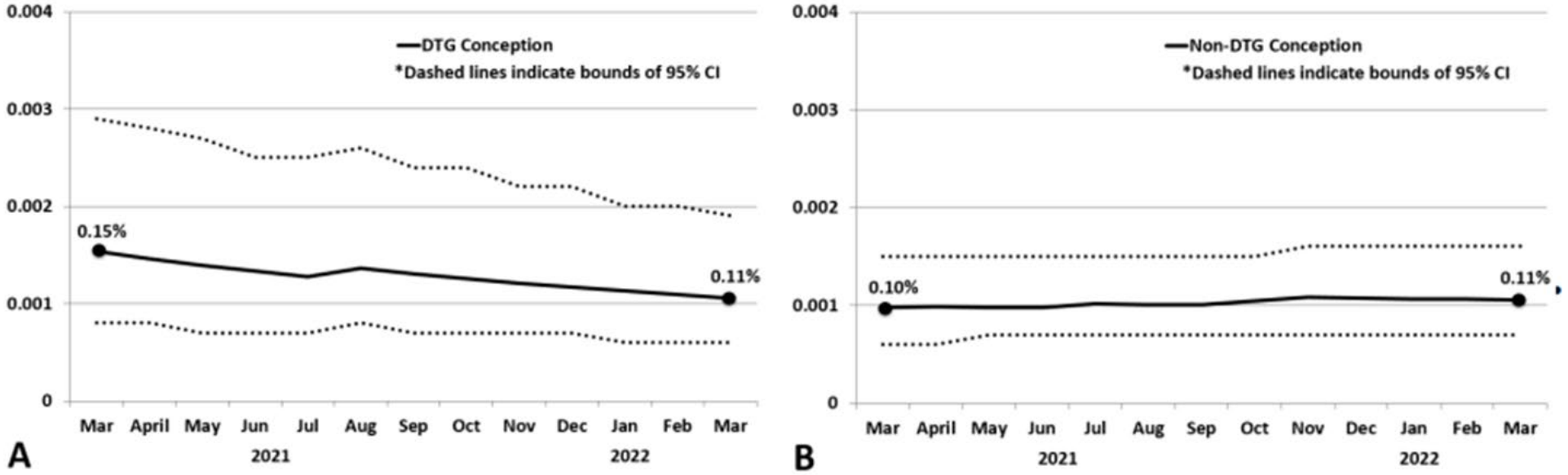
Tsepamo: Can the NTD issue be put to bed?



Birth outcomes study across 8 large maternity centres in Botswana.
223,797 deliveries across sites (Aug 2014 – Mar 2022) included in analysis (99.8% of all)

NTD prevalence with DTG Recap:
May 2018: → 0.94% (vs 0.12% for other ART)
March 2021: → 0.15% (vs 0.10% for other ART)

NTD prevalence on DTG at conception (A) vs NTD on non-DTG regimens at conception (B)



Zash, AIDS 2022 Poster PELBB02

Further HIV functional cure cases

1. CROI 2008: "The Berlin patient" – SCT Leukaemia, >13yrs (RIP 2020)

2. CROI 2019: "The London patient" – SCT HL, >4yrs

3. CROI 2022: "The New York patient" – SCT (adult and cord), Leukaemia, >1.5yrs

4. CROI 2022: "The Dusseldorf patient" – SCT Acute Myeloid Leukaemia, >3yrs

5. AIDS 2022: "The 'City of Hope' (California) patient" – SCT Leukaemia, >1.5yrs

Rare mutation in the donor stem cell
- CCR5-delta 32 deletion
Results in absence of CCR5 co-receptors
HIV (most types) unable to enter T-lymphocyte cells

Islatravir – back in business?

What is it?
Islatravir (EFdA, MK-8591) is a NRTTI with a long half-life
Hopes for use in LA treatment and prevention of HIV (PrEP implant & pill)

Studies
Showing promise as daily 2DR with Doravirine in suppressed switch and naive patients, as a once weekly LA 2DR with Lenacapavir, and also with experimental agent MK-8507

Set-back
Nov 2021 – Islatravir studies were put on hold following revelations of decreases in total lymphocyte and CD4 counts being observed

Redemption?
HIV Glasgow 2022:
- Post-hoc analysis of P011 study – established CD4 declines dose-dependent, and not sig. at 0.25mg ISL
- Modelling & Simulation of optimal ISL dosing predicted adequate ISL drug levels to be active against HIV at 0.25mg dose vs standard of care ART

Using lower doses of ISL 0.25mg (prev. 0.75mg) & abandoning its use for PrEP, and not exploring monthly or yearly dosing schedules

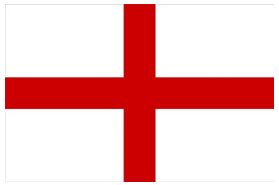
✓ OD ISL + DOR back up and running (ISL 0.25mg)

✓ Plans to resume weekly ISL + LEN (ISL 0.25mg)

Fostemsavir – commissioning update

- 1st in class attachment inhibitor (interferes with interaction between gp120 & CD4 receptor)
- Use: to optimise virological control in people with multi-drug resistant HIV-1 infection. It has no cross-resistance with other ARV classes
- Evidence: BRIGHTE study: wk240 –reductions in viral load and CD4 improvement vs placebo

WHEN



As of Oct 2022 – available in England as a routine commissioning treatment option
Lots of criteria to be met, MDT approval

Clinical Commissioning Policy
Fostemsavir for multi-drug resistant HIV-1 infection (adult) (URN 2108) [201008P]

NHS England

Inclusion criteria

- Individuals are either:
  - Not virally suppressed with existing ART regimen[1] **OR**
  - Are virally supressed but on a highly complex regimen with concerns of tolerance, resistance or safety where the addition of fostemsavir could simplify the regimen and optimise patient outcome and experience

AND must meet all the following five criteria:

- The use of fostemsavir has been discussed and agreed with the patient (through shared decision making, this can be through various mediums including verbal as well as written shared decision-making tools, translated and Easy Read materials) and the HIV specialist multi-disciplinary team (MDT) **AND**
- Individuals are adult patients[2] **AND**
- Fostemsavir is to be added to an optimised background ART regimen **AND**
- Individuals have multi-drug resistant (MDR)-HIV-1 infection[3] **AND**
- Individuals have limited or no therapeutic ART options remaining[4]

Exclusion criteria

- Individuals with contraindications to fostemsavir, as outlined in the summary of product characteristics (EMA. 2021 EMEA/H/C/005011) **OR**
- Individuals with a past trial of fostemsavir with no clinical response[5] **OR**
- Individuals determined not to be suitable for fostemsavir by the HIV specialist MDT

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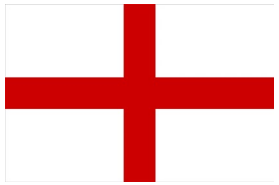

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Independent Funding Request

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Birmingham HIV/AIDS Memorial

The Brainchild

- Gary Jones – Birmingham-based artist, inspired to create the sculpture, noting that there was nothing in Birmingham to remember the loved and lost to HIV/AIDS
- Dr Steve Taylor – HIV Clinician and Medical Director of Saving Lives charity, whose mission is to increase awareness, testing, and reduce late diagnosis, transmission and stigma

The Concept

- 6 metre (~20ft) tall, steel permanent structure “The Ribbons”
- Entwined/embracing ribbons representing HIV/AIDS of the past and of the future – remembering those we have lost, and celebrating those living with HIV
- The sculpture will also act as a reminder of the work still needed to be done (education, end stigma and discrimination)

The Reveal

- World AIDS Day, outside the Birmingham Hippodrome
- Thursday 1st December 2022 @ 1800

thank you

Special thank you to Dr Laura Waters & Dr Tristan Barber for their help with inspiring some of the content for this presentation

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Summary & close

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2023 Spring Conference

Mon 24th - Wed 26th April

Gateshead, UK

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