

Long-term PrEP- what to monitor and how best to do it? Case based discussion



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David

- 44 year old bisexual male currently in a relationship with male HIV positive partner.
- Previous PWID last injected 2014, currently stable only on methadone and carbamazepine for seizures following car accident in 2001.
- Started on truvada PrEP and attends regularly for blood monitoring.

● Do Not Coadminister ■ Potential Interaction ▲ Potential Weak Interaction ◆ No Interaction Expected

Results Key

	FTC/TDF
Carbamazepine	◆
Methadone	◆

Renal function and Tenofovir DF

UrPCR monitored (early marker for renal tubular loss with TDF) and Creatinine Clearance. Normal or first 12 months then.....

- **Ur PCR 35mmol/L. CrCl 68mls/min**

Called back in one month:

- **Stable UrPCR at 32mmol/L. CrCl 66mls/min**

One month later again:

- **UrPCR 36mmol/L. CrCl 66mls/min**

Decision made to continue but monitor frequently.

NB. Diclofenac bought over the counter stopped and switched to paracetamol

Truvada film-coated tablets

Gilead Sciences Ltd

[contact details](#)

Active ingredient

tenofovir disoproxil fumarate

emtricitabine

Table 1: Dosing recommendations in adults with renal impairment

	Treatment of HIV-1 infection	Pre-exposure prophylaxis
Mild renal impairment (CrCl 50-80 mL/min)	Limited data from clinical studies support once daily dosing (see section 4.4).	Limited data from clinical studies support once daily dosing in HIV-1 uninfected individuals with CrCl 60-80 mL/min. Use is not recommended in HIV-1 uninfected individuals with CrCl < 60 mL/min as it has not been studied in this population (see sections 4.4 and 5.2).
Moderate renal impairment (CrCl 30-49 mL/min)	Administration every 48 hours is recommended based on modelling of single-dose pharmacokinetic data for emtricitabine and tenofovir disoproxil in non-HIV infected subjects with varying degrees of renal impairment (see section 4.4).	Not recommended for use in this population.
Severe renal impairment (CrCl < 30 mL/min) and haemodialysis patients	Not recommended because appropriate dose reductions cannot be achieved with the combination tablet.	Not recommended for use in this population.

However....

ALT comes back at **292** with all other LFT's normal

- **HCV Antigen positive**
- **PCR 789,000iu/mol**
- **Genotype 1a**
- **Normal Fibroscan**

David tells us he has had a bereavement and has been injecting heroin again.

He is shocked by HCV diagnosis and asks about treatment

HCV direct-acting antivirals (DAAs) + tenofovir-DF

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Results Key

	FTC/TDF
Elbasvir/Grazoprevir	◆
Glecaprevir/Pibrentasvir	◆
Ledipasvir/Sofosbuvir	■
Sofosbuvir/Velpatasvir	■

Potential Interaction

Ledipasvir/Sofosbuvir

Tenofovir-DF

Summary:

Coadministration of tenofovir (in combination with efavirenz/emtricitabine or rilpivirine/emtricitabine) increased tenofovir exposure. Tenofovir concentrations may also be increased when given with ledipasvir/sofosbuvir and an HIV protease inhibitor/ritonavir or with ledipasvir/sofosbuvir and elvitegravir, cobicistat and emtricitabine. The safety of increased tenofovir concentrations in these settings has not been established. If coadministration of ledipasvir/sofosbuvir and tenofovir with an HIV protease inhibitor/ritonavir is necessary, monitor for tenofovir-associated adverse reactions, including frequent renal monitoring. Note, coadministration of ledipasvir/sofosbuvir and tenofovir with elvitegravir, cobicistat and emtricitabine is not recommended.

Co-administration of ledipasvir/sofosbuvir increased tenofovir C_{max}, AUC and C_{min} by 79%, 98% and 163%, respectively.

David has no baseline RAVs

- 5 months later is treated with Zepatier for 12 weeks
- Achieves SVR

He becomes concerned about his kidneys and reads the truvada could be making things worse



What is PrEP?

PrEP is a pill that protects you from HIV. It's a course of tablets that you take before and after sex.

[Find out more →](#)



Bradley Hare of UCSF presenting data at CROI 2019 from the DISCOVER trial of Descovy vs. Truvada as PrEP.
Benjamin Ryan

TREATMENT NEWS

Descovy PrEP Works Equally Well, May Be Safer for Kidneys and Bones

Truvada and Descovy are both highly effective and generally safe options for HIV prevention.

Attends clinic and tells us he has bought Descovy online and wants to start it ASAP

However.....

Carbamazepine is a P-gp inducer and decreased TAF AUC and Cmax by 55% and 57%.

NOT RECOMMENDED

David is referred to neurology and over a period of 3 months, CBZ is switched to **Leviteracetam**.

Do Not Coadminister	
Emtricitabine/Tenofovir alafenamide (FTC/TAF)	
Carbamazepine	

Quality of Evidence: Moderate ⓘ

Summary:

Coadministration is not recommended as it decreases tenofovir alafenamide plasma concentrations which may result in loss of therapeutic effect and development of resistance. Co-administration of carbamazepine (titrated from 100 mg to 300 mg twice a day) with emtricitabine/tenofovir alafenamide (200/25 mg once daily) decreased tenofovir alafenamide AUC and Cmax by 55% and 57%, respectively.

Description:

The co-administration of Descovy is not recommended with carbamazepine. Co-administration of oxcarbazepine, a P-gp inducer, may decrease tenofovir alafenamide plasma concentrations, which may result in loss of therapeutic effect and development of resistance. Co-administration of carbamazepine (titrated from 100 mg to 300 mg twice a day) and emtricitabine/tenofovir alafenamide (200 mg/25 mg once daily, dosed as Descovy and taken with food) decreased tenofovir alafenamide AUC and Cmax by 55% and 57%.

Descovy Summary of Product Characteristics, Gilead Sciences Ltd, April 2016.

Coadministration is expected to decrease concentrations of tenofovir alafenamide and is not recommended.

Descovy US Prescribing Information, Gilead Sciences Inc, April 2016.

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	FTC/TAF
Carbamazepine	●
Methadone	◆

Differences in the DDI Profile of TDF & TAF

	TDF	TAF	Potential Mechanism
Aspirin			NSAIDS and Renal
Celecoxib			NSAIDS and Renal
Diclofenac			NSAIDS and Renal
Ibuprofen			NSAIDS and Renal
Mefenamic acid			NSAIDS and Renal
Naproxen			NSAIDS and Renal
Nimesulide			NSAIDS and Renal
Acetazolamide	<p style="text-align: center;">TAF More renal friendly</p>		Renal transport
Cefalexin			Renal transport
Dacarbazine			Renal transport
Flucloxacillin			Renal transport
Mycophenolate			Renal transport
Probenecid			Renal transport
Verapamil			P-gp/absorption
Topiramate			
Oxaliplatin			Renal toxicity
Sirolimus			Renal toxicity
Penicillamine			Renal toxicity
Tacrolimus			Renal dysfunction
Zoledronic acid			Renal dysfunction

Differences in the DDI Profile of TDF & TAF

	TDF	TAF	Potential Mechanism
Rifabutin		NR	Induction of P-gp
Rifampicin		NR*	Induction of P-gp
Rifapentine		NR	Induction of P-gp
Carbamazepine		CA	Induction of P-gp
Oxcarbazepine		CA	Induction of P-gp
Phenobarbitone		CA	Induction of P-gp
Phenytoin		CA	Induction of P-gp
St John's Wort		NR	Induction of P-gp

NR = Not Recommended
CA = Consider Alternative

Next year....

Unfortunately David did not continue his Descovy and was lost to follow up for 10 months where he tested HIV positive.

- CD4 896 VL 42,000iu/ml
- Commenced on Triumeq
- Re-engages in care
- Still intermittent heroin use

Attends clinic 4 weeks later with a new partner who is 25 weeks pregnant

- Partner tests HIV negative by UPSI
- David VL down to 7200iu/ml, forgetting a few doses
- Discussed risk to new partner by
- Mum offered PrEP, regular testing
- David re-committed on importance of compliance

PrEP is Safe for Pregnant Women Who Want the HIV Prevention Drug, a New Study Finds



Mum continues on PrEP

- Misses some appointments but tests HIV-ve at 36 weeks
- David misses appointment, last VL is 923
- Delivery plan ? PEP for baby

BHIVA pregnancy guidelines start with a positive mum so no official guidance.....

HIV MEDICINE

BHIVA
British HIV Association

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ORIGINAL RESEARCH

National audit of perinatal HIV infections in the UK, 2006–2013: what lessons can be learnt?

- 23 transmissions related to seroconversion late in pregnancy or during breast feeding
- Unclear if women had HIV test in late pregnancy
- Most defined on basis of maternal tests after delivery
- ‘window’ period transmission can happen but seem rare

Adult PEP/PrEP benefits almost always outweigh the risk of medicine

Vs.

Neonatal PEP

- Lack of PK data (particularly in non first line options)
- Lack of drug options
- Potentials side effects potentiated if baby pre-term ie deaths associated with Kaletra use

Plan

- Extra input to David- ensure VL down
- Engage mum- access to rapid tests
- Neonatal PEP plan only in event of transmission

Mum negative at delivery and 3 months later

Resources



HIV Drug Interactions



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LIVERPOOL

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Access our comprehensive, user-friendly, free drug interaction charts. Providing clinically useful, reliable, up-to date, evidence-based information

Start Now →

● Do Not Coadminister ■ Potential Interaction ◆ No Interaction Expected ◆ No Clear Data
● Do Not Coadminister ■ Potential Interaction ◆ No Interaction Expected ◆ No Clear Data

	Atazanavir	Darunavir	Dolutegravir	Efavirenz	Raltegravir	Rilpivirine	Tenofovir-DF
Amiodarone	■	●	◆	■	◆	■	■
Antacids	■	◆	■	◆	■	■	◆
Atazanavir		◆	◆	■	◆	■	■
Cannabis	■	◆	◆	■	◆	◆	◆

Drug Drug Interactions and 90/90/90/(90)

