

# Dolutegravir with tenofovir disoproxil fumarate-emtricitabine as HIV post-exposure prophylaxis in gay and bisexual men

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## Introduction

- Antiretroviral drugs as HIV nonoccupational postexposure prophylaxis (NPEP) is recommended by the World Health Organisation<sup>1</sup>
- Up to one-third of gay or bisexual men (GBM) do not complete 28 days of NPEP<sup>2</sup>
- Adverse events (AEs) are the likely primary cause of NPEP non-completion
- Co-formulated TDF/FTC (Truvada; TVD) is the preferred NRTI backbone for NPEP<sup>3,4</sup>
- Choices for a 3<sup>rd</sup> drug include PIs, integrase inhibitors, NNRTIs and entry inhibitors<sup>5,6,7,8</sup>
- 3-drug NPEP discontinuation
  - higher with LPVr, DRVr or MVC NPEP
  - lower with raltegravir (RAL), rilpivirine (RPV)<sup>5,6,7,8</sup>
- Limitations of current NPEP regimens
  - PIs: GI side-effects, drug-drug interactions and act after HIV integration<sup>5,6</sup>
  - RAL can cause acute muscle toxicity and twice-daily dosing is required<sup>6</sup>
  - RPV must be taken with food<sup>7</sup>
- Dolutegravir (DTG) is an attractive 3<sup>rd</sup> drug for NPEP:
  - dosed once-daily
  - potent
  - safe and well tolerated
  - relatively few drug/drug interactions
  - T<sub>max</sub> 2-4 hours post-dose; and
  - mode of action pre-HIV integration<sup>9,10</sup>
- DTG not previously evaluated for NPEP
- We investigated the completion rate, safety and adherence to TVD + DTG as 3-drug NPEP

## Methods

- Open-label, single-arm study at 3 sexual health clinics and 2 emergency departments in Australia
- One hundred HIV-uninfected GBM requiring 3-drug PEP received DTG plus TVD for 28 days
- The primary endpoint was PEP failure (premature cessation or primary HIV infection through Week 12)
- Additional endpoints were: adherence by self-report (n=98); pill count (n=55); plasma tenofovir levels (n=82); plasma DTG levels (n=80); and safety (clinical and laboratory adverse events [AEs])
- Adherence and adverse events (laboratory & clinical) assessed at Week 1, 2 and 4

## Acknowledgements

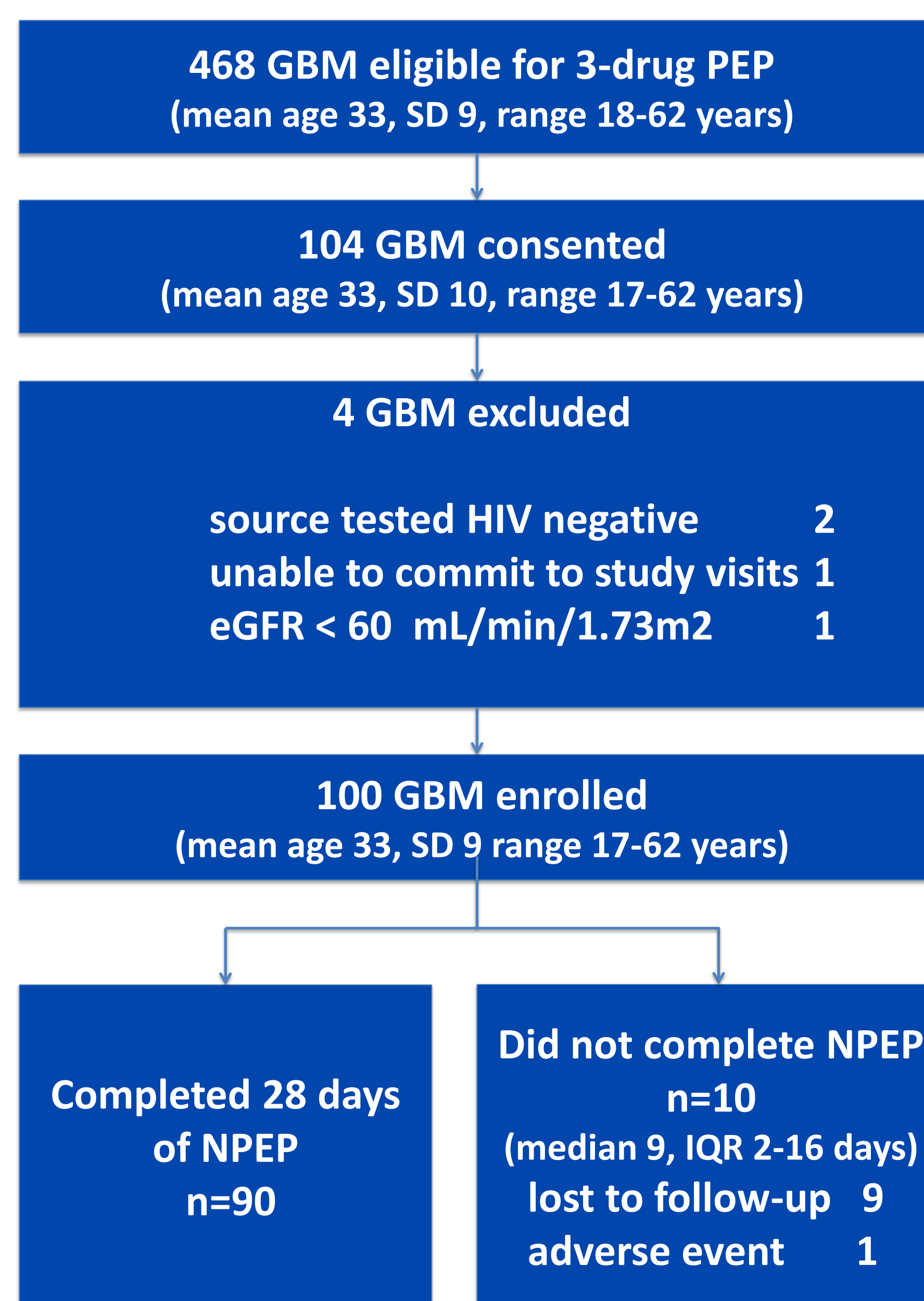
- Study funded by ViiV Healthcare

## Results

### Baseline characteristics

- Recruitment 1<sup>st</sup> August 2014 – 30<sup>th</sup> October 2015
- Prior NPEP 41%
  - Mean doses 1 (SD 2)
- Risk behaviour
  - receptive anal sex 82%
  - substance use 61%
  - condomless sex 70%
  - HIV+ source 40%
    - HIV RNA detectable 10%
    - HIV RNA not detectable 8%
- Time from exposure (hours)
  - to assessment 25 (IQR 14-39)
  - to 1<sup>st</sup> NPEP dose 27.5 (IQR 17-40)

### Completion



### Adherence

Self-report % (n=98)	Pill count % (n=55)	Day-28 plasma drug level ≥ inhibitory quotient (TDF ≥40ng/mL; n=82) (DTG ≥64ng/mL; n=80)
TVD 98%	TVD 98%	TNV 85%
DTG 98%	DTG 98%	DTG 99%

# measured a mean 15 (SD 8) hrs after last dose of DTG or TVD

### Safety / adverse events

#### Clinical AEs (n=98)

- 67 (68%) reported 144 subjective AEs possibly attributable to study drug
- 98% of AEs were grade 1-2
- There were no unexpected AEs and no serious AEs
- 1 pt ceased NPEP because of grade-3 headache

#### Subjective AEs possibly related to NPEP occurring in ≥5%

Subjective AEs	Percent
Fatigue	26%
Nausea	25%
Diarrhoea	21%
Headache	10%
Abdominal pain/cramps	9%
Flatus	9%
Vivid dreams	7%

#### Laboratory AEs

Laboratory test	Grade 1 – Grade 2	Grade 3 – Grade 4
<b>Chemistries [n (%)]</b>		
↑Creatinine	10/93 (11)	
Hyperglycaemia	1/91 (1)	
Hypophosphataemia	5/91 (5)	
↑Bilirubin	4/93 (4)	1/89 (1)
↑Alanine aminotransferase	22/89 (25)	1/93 (1)
↑Creatine kinase	8/92 (9)	1/92 (1)
↑Lipase	7/92 (8)	1/84 (1)
↑Amylase	7/92 (8)	1/85 (1)
Hyperlactataemia	8/91 (9)	1/89 (1)
<b>Urinalysis [n (%)]</b>		
Proteinuria	10/88 (11)	
Haematuria	1/88 (1)	
Glycosuria	2/88 (2)	

- No pt ceased NPEP for any lab AE
- Most common laboratory AE was raised alanine aminotransferase (25%)
  - only 1 pt had a Grade 3 or 4 ALT
  - no clinical hepatitis
  - no pt with serum bilirubin ≥2xULN had abnormal level of conjugated or unconjugated bilirubin

- Mean eGFR decrease at Day 28 was 14 mL/minBSAc (SD 17, p=0.001)
  - eGFR <60 mL occurred in 3 pts

#### HIV infection

- No HIV infection through Week 12

## Conclusions

- DTG + TVD were well tolerated as NPEP with high levels of completion (90%) and adherence**
  - Rates similar to those using single-tablet NPEP with TDF-FTC-RPV
- Adherence 98% by self report and pill count, but only 85% had plasma tenofovir ≥40ng/mL at Day 28**

## References

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