Pre-Exposure Prophylaxis

PrEP

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Faculty Disclosure

None to Report

seeblue.

Educational Need/Practice Gap

Gap

Most providers are not familiar with standards related to the efficacy and prescribing of PrEP.

Need

Despite some advances related to the prevention of HIV, infections continue to occur across the US.

Objectives

Upon completion of this educational activity, the learner will be able to:

1. Explain the underlying premise of pre-exposure prophylaxis.
2. Prescribe pre-exposure prophylaxis.

Expected Outcome

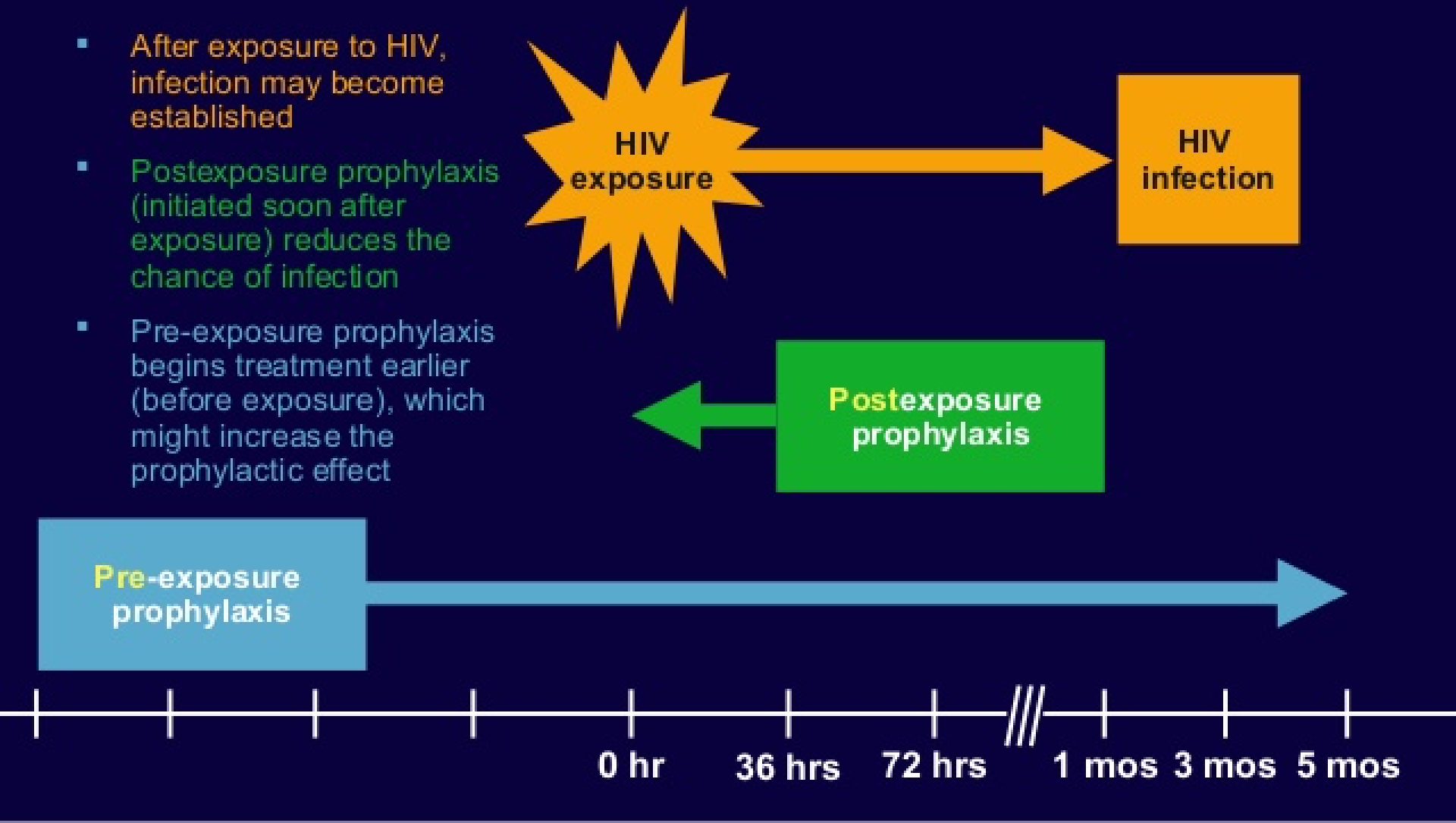
- Providers will be comfortable prescribing PrEP for high risk patients.

Definitions

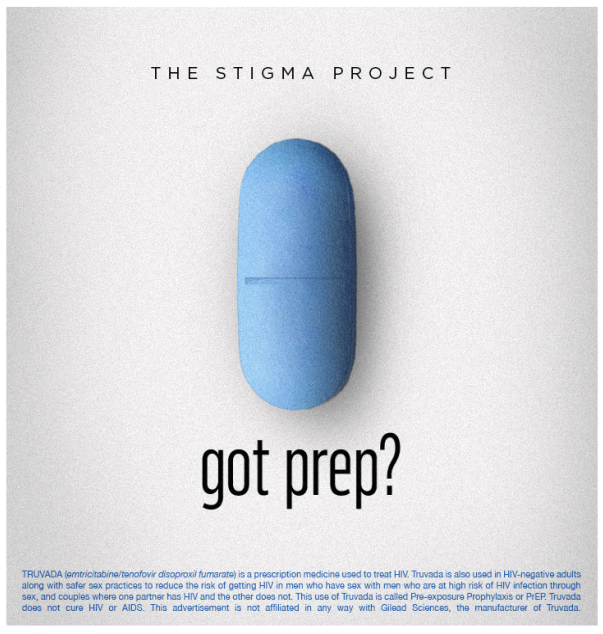
- TasP
- PrEP
- PEP
- nPEP
- U=U

Pre- vs Postexposure Prophylaxis

- After exposure to HIV, infection may become established
- Postexposure prophylaxis (initiated soon after exposure) reduces the chance of infection
- Pre-exposure prophylaxis begins treatment earlier (before exposure), which might increase the prophylactic effect




CONDOMS
Education
HIV
TRANSMISSION
Perinatal
Prophylaxis
Needle Exchange
Circumcision
ARV TREATMENT
see blue.



US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV 2017 UPDATE A CLINICAL PRACTICE GUIDELINE

PrEP
Background

- **Was** controversial
- Highly effective (75-96%)
- Efficacy predicated on adherence
- 2 ARVs (Truvada®) once daily

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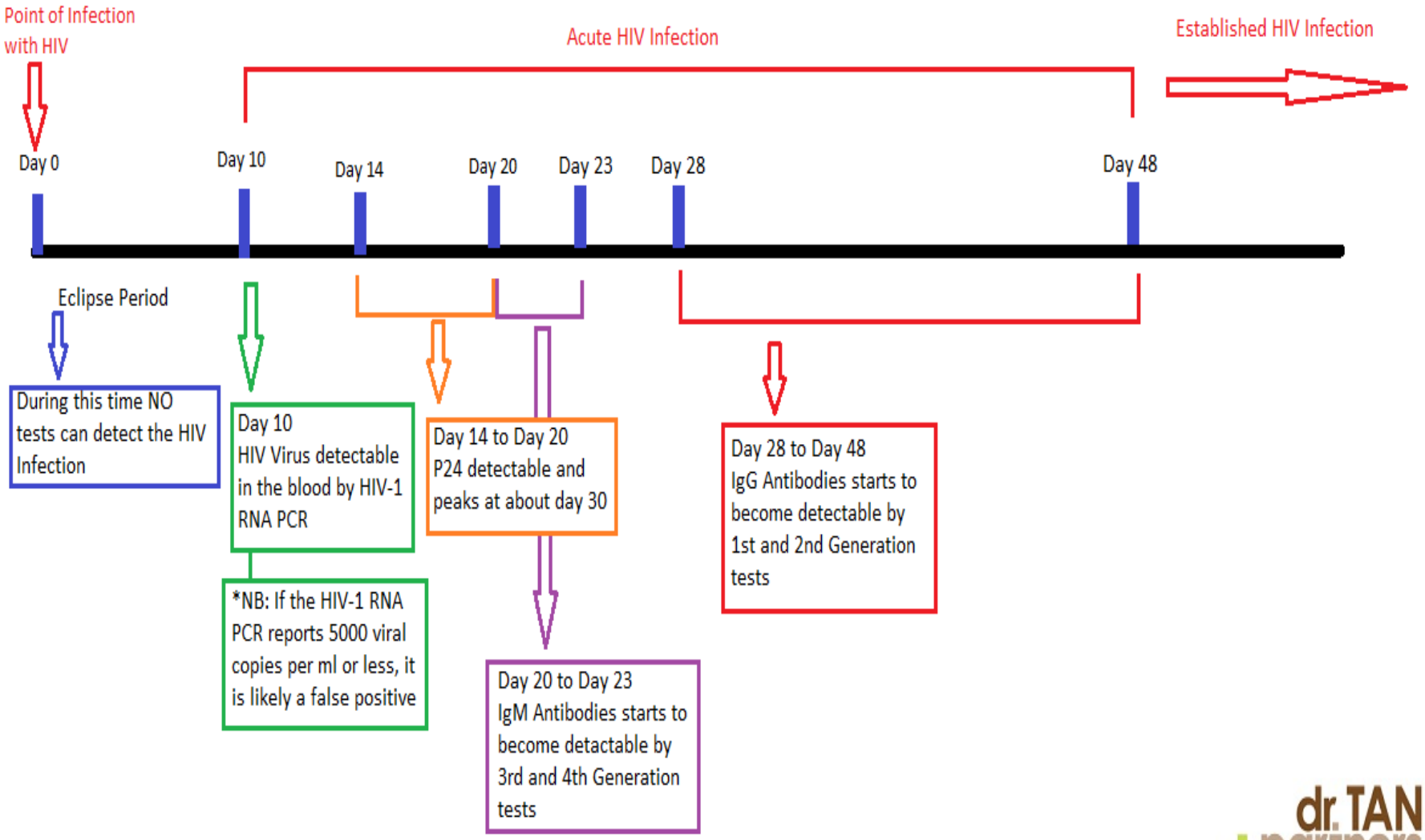
HIV Testing Window Period - Updated June 2014



dr. TAN + partners MEDICAL CENTRE

What we know …

- Biologic and logistical advantages over PEP
- **TF:**

  Potent; rapid onset; long intracellular $t_{1/2}$; QD dosing; few DIs; est safety/tolerability
- **Non-human primate studies:**

  Oral & topical TF with or without FTC/3TC given QD or intermittently → 70%-100% protection (dose dependent)

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What we know …

- TF/FTC > efficacy than TF alone
- PO TF dosing results in ↑ colonic [ ] vs vaginal [ ] (reverse is true for FTC) PO TF/FTC 10-fold colonic vs cervical drugs [ ]s → ramifications for adherence thresholds?

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Optimal PrEP Frequency

- Underlying premise: PrEP is a ‘time limited prevention strategy’
- Dosing and timing relative to intercourse?
- ~**21 days** to ss (females); ~**7 days** to ss (males)
- Conservative DC lag ~28 days following last high risk exposure in all cases
- Potential for less than daily FTC/TF dosing? 2-1-1-?

  (trials on-going/difficult to compare to placebo [ethics])

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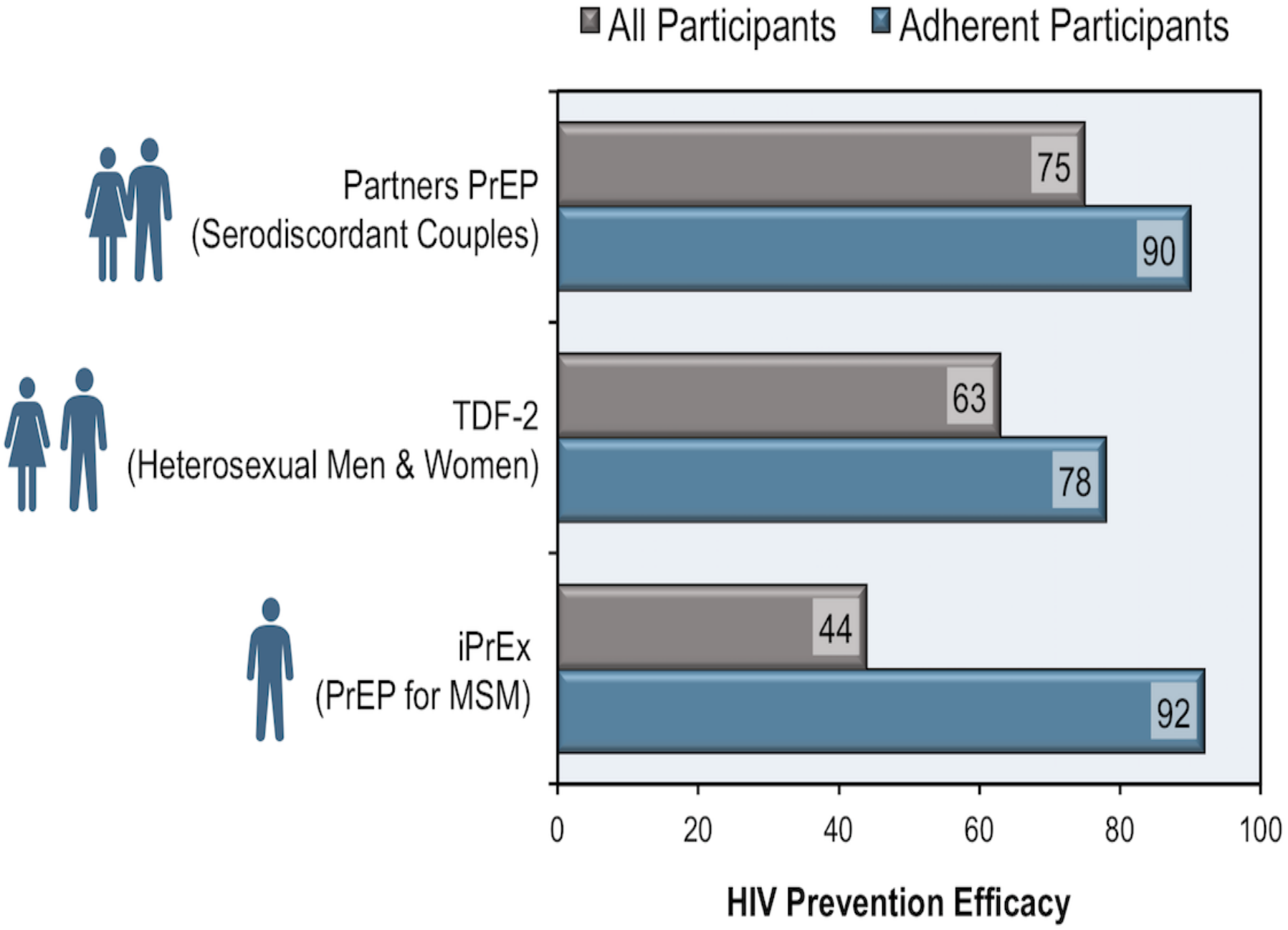
Overview of Major PrEP Trials

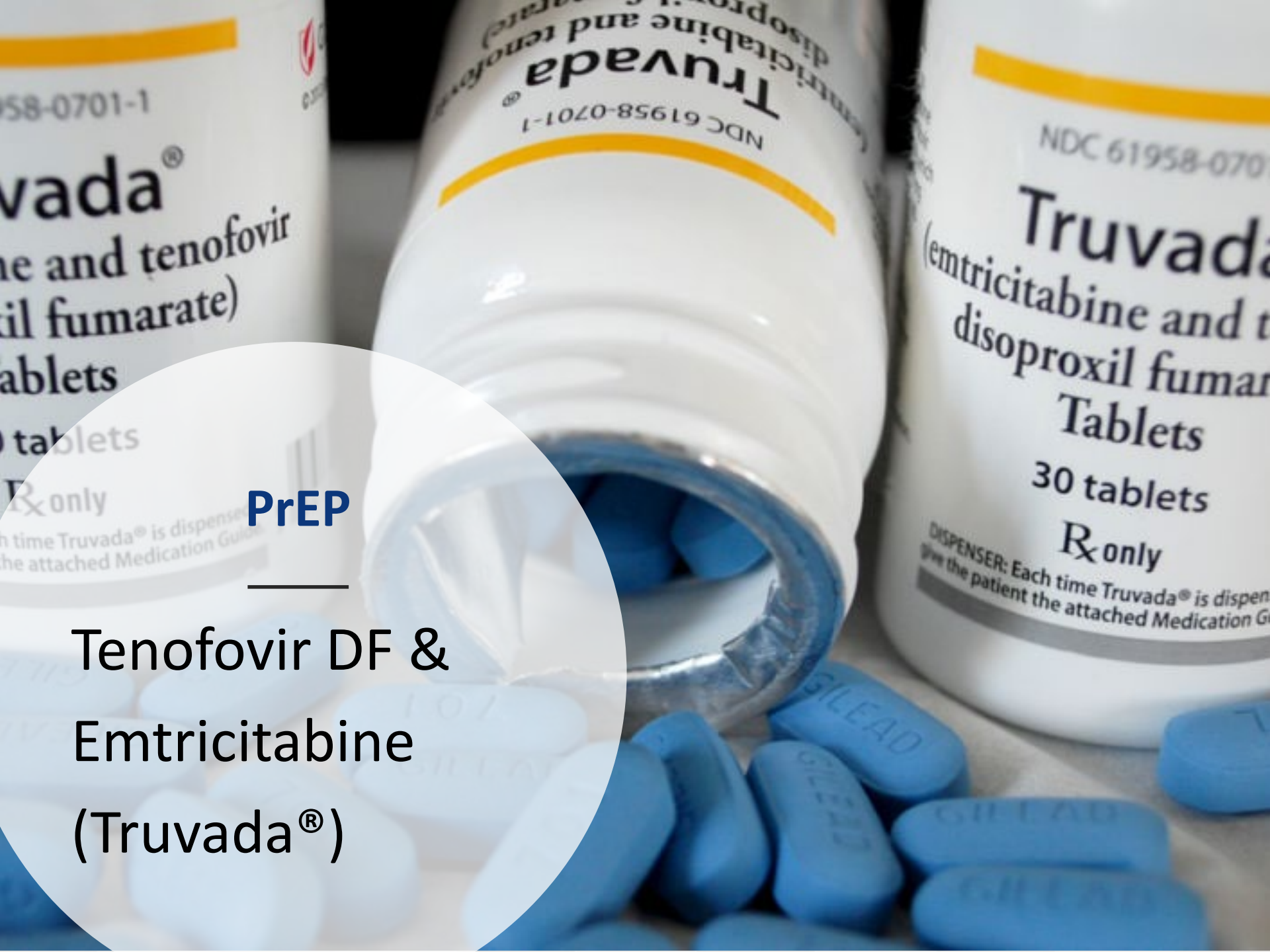
Clinical Trial	Participants	Medication(s)	mITT Efficacy % (CI)	Adjusted for Adherence % (CI)
Bangkok TDF	Injection drug users	TDF	49 (18-90)	74 (17-94)
Partners PrEP	**Heterosexual discordant couples**	**TDF** **TDF/FTC**	**67 (44-81)** **75 (55-87)**	**86 (67-94)** **90 (58-98)**
TDF2	Heterosexual men/women	TDF/FTC	63 (21-83)	85 (NS)
iPrEx	**Men who have sex with men**	**TDF/FTC**	**44 (15-63)**	**92 (40-99)**
Fem-PrEP	Heterosexual women	TDF/FTC	NS	
VOICE	Heterosexual women	TDF TDF/FTC	NS NS	

*Adapted from Centers for Disease Control and Prevention (CDC). Preexposure prophylaxis for the prevention of HIV infection in the United States - 2014. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2014.

Divergence in Efficacy

ADHERENCE


All Participants
Adherent Participants
Partners PrEP
(Serodiscordant Couples)
75
90
TDF-2
(Heterosexual Men & Women)
63
78
iPrEx
(PrEP for MSM)
44
92
0
20
40
60
80
100
HIV Prevention Efficacy


PrEP
Tenofovir DF &
Emtricitabine
(Truvada®)
Truvada
30 tablets
Rx only

Candidates?

- MSM @ substantial infection risk
- Heterosexual @ substantial infection risk
- IVDU @ substantial infection risk
- Serodiscordant couples

What's "substantial?"

- HIV+ sexual partner
- Recent bacterial STI
- High # of sex partners
- Hx of inconsistent or no condom use
- Commercial sex work
- Sharing injection equipment

Recommended Laboratory Testing and Frequency for Patients Taking PrEP

Laboratory test	Baseline	Every 3 months	At least every 6 months	Notes
HIV screening assay	✔	✔		Consider need for HIV RNA PCR
HBV antibody panel and HCV antibody	✔			Offer HBV vaccination if not immune
Serum creatinine	✔		✔	Avoid PrEP if eCrCl <60 mL/min
STI testing	✔		✔	Include oral/rectal screen for MSM if risk
Pregnancy test for women*	✔	✔		

Åbbreviations: eCrCl = estimated creatinine clearance; STI = sexually transmitted infections
*The safety of PrEP in pregnancy has not been established

PrEP Initiation

- Education = STIs
- Adherence Counseling
- Truvada® 1 PO QD x 90d

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PrEP Discontinuation

- HIV+ → resistance testing
- Hep B+ → consult/appropriate FU meds
- HCG+ → prenatal provider referral, med exposure
- On-going risk-reduction and support

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Safety

- No significant AEs identified
- GI complaints (~10% of pts)
- iPrEx: 1% decline in BMD [MSM]
- No PrEP trial has demonstrated renal complications
- No reports of teratogenicity from TF or TF/FTC

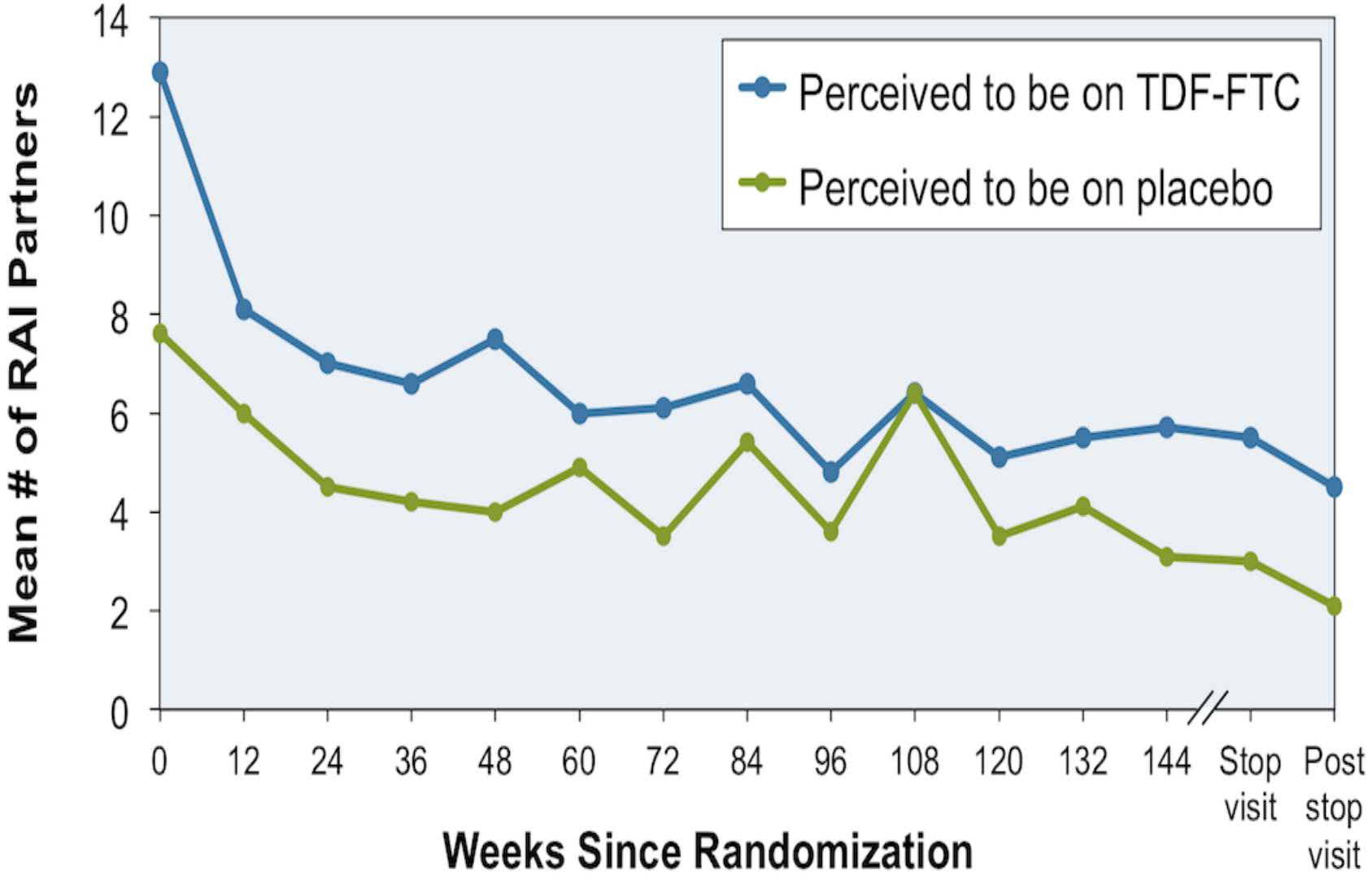
Resistance

- ARV resistance rare
- Incidence sequestered to those with seronegative acute infection at time of randomization
- M184V and K65R most common genotypes

Risk Taking?

- Examined in 2 trials (iPrEx & Partners PEP)
- Self-reported condom use increases
- STI rates fell in both trials
- Synergism?

Mean # of Receptive Anal Intercourse Partners in Past 3 Months in iPREX



RAI= receptive anal intercourse; TDF-FTC= tenofovir-emtricitabine

Risk Reduction

- Counseling
- Condoms
- Clean needles and equipment
- Access to drug tx programs
- STI testing

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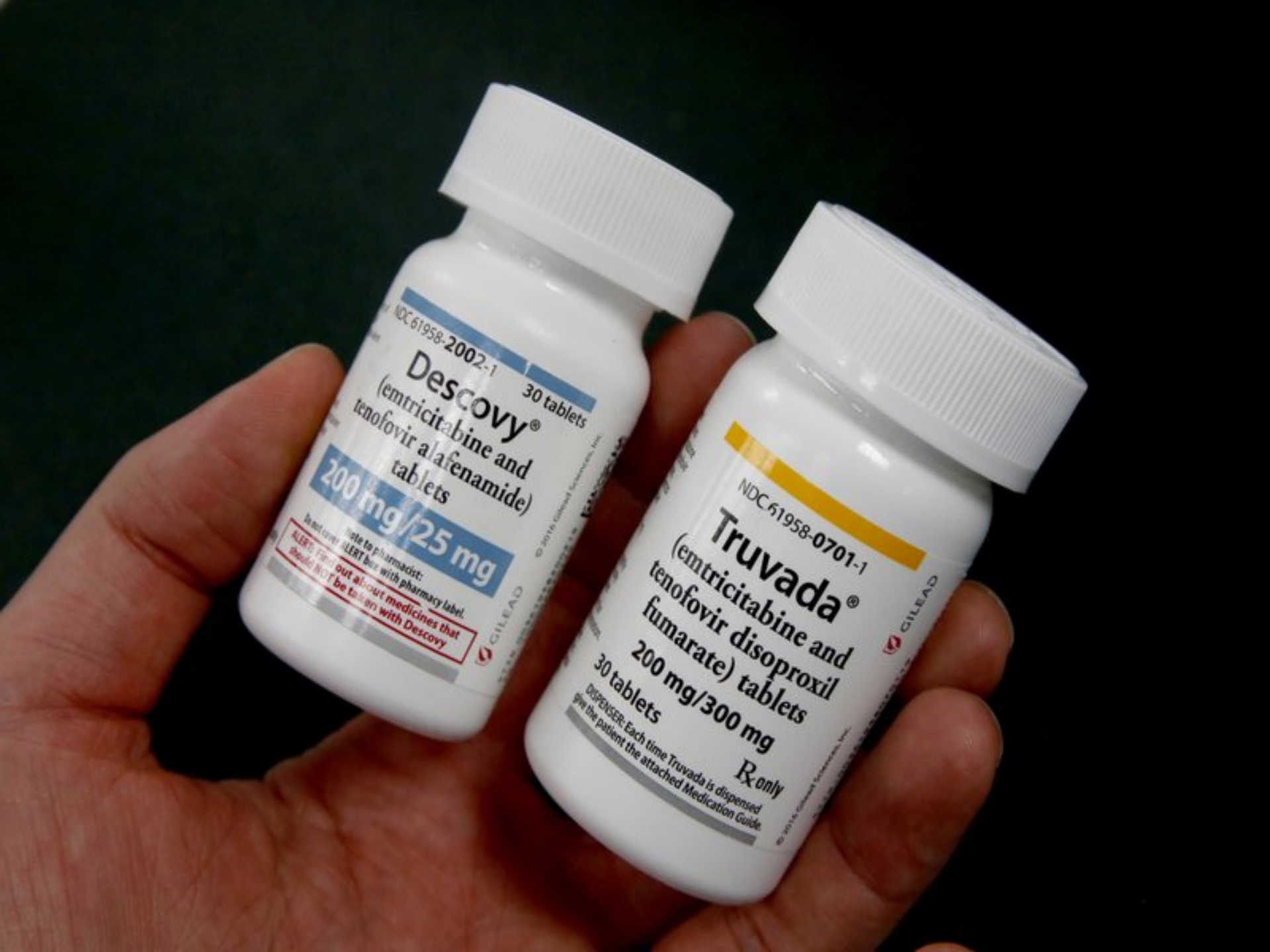
NDC 61958-2002-1
30 tablets
Descovy®
(emtricitabine and
tenofovir alafenamide)
tablets
200 mg/25 mg
GILEAD
NDC 61958-0701-1
Truvada®
(emtricitabine and
tenofovir disoproxil
fumarate) tablets
200 mg/300 mg
30 tablets
Rx only
GILEAD

Truvada® versus Descovy®

- Cost
- Hepatitis B
- Generic Truvada®?

2021

- Efficacy
- Renal (60 vs 30)
- Bone Mineral Density
- Lipids

Descovy®

Tenofovir Alfenamide [TAF] plus Emtricitabine [FTC]

- 5,300 MSM
- Recent condomless anal sex or been dx with an STI in last 6 months
- Randomized to Truvada® vs Descovy® QD x 24 months

THE PHASE 3 DISCOVER STUDY: DAILY F/TAF OR F/TDF FOR HIV PREEXPOSURE PROPHYLAXIS. CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS. March 2019, Seattle Washington.

seeblue.

Descovy®

Tenofovir Alfenamide [TAF] plus Emtricitabine [FTC]

- Results:

  7 infections in D group and 15 in T group ($p>0.05$)

  (0.16 and 0.34 incidence rate per 100 cumulative years, respectively)

- Seroconverts: 5 were suspected to already be HIV+ & undetectable; 15 were found to have sub-therapeutic levels of T (adherence)
- Conclusion: non-inferiority

THE PHASE 3 DISCOVER STUDY: DAILY F/TAF OR F/TDF FOR HIV PREEXPOSURE PROPHYLAXIS. CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS. March 2019, Seattle Washington.

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Descovy®

Tenofovir Alfenamide [TAF] plus Emtricitabine [FTC]

- Why the disparity?
- D may be more “forgiving”
- D = faster and higher immune cell drug levels and persistence
- Future implications: on-demand & 2-1-1 regimens
- Will these “small” differences be worth the extra cost in 2021?

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Descovy®
October
2019

FDA APPROVED

PRE-EXPOSURE PROPHYLAXIS

Insufficient data from clinical trials.

EXCLUDES RISK INVOLVING RECEPTIVE VAGINAL INTERCOURSE.

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The California Experiment

- Senate Bill 159
- Targets “pay for delay”
- Authorizes pharmacists to dispense PrEP and PEP without a RX
- 60-day supply max and forbids prior authorization requirements

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On-Demand PrEP?

- The 2-1-1 alternative
- More logical option for those engaging in less frequent sexual exposures?
- 2 does 2-24h before sex then 1 dose 24h hour sex followed by another 24h later
- *KP Study*: PrEP QD pts were sent 2-1-1 info and interested Ms rec phone consultations and switch

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On-Demand PrEP?
The KP Study

- MSM, median age: 43; 56% W
- Most common reason for 2-1-1 = infrequent sex
- 181 M used 2-1-1 exclusively
- 4% reported missing a dose at last sexual encounter
- Median: (1) 2-1-1 course per month
- No infections

Hojilla et al. https://academic.oup.com/cid/article-abstract/doi/10.1093/cid/ciaa474/5850905

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Long-Acting Agents
The HPTN 083 Study

- Cabotegravir: inv integrase inhibitor similar to dolutegravir; packaged within nanoparticles; half-life of 21-50d
- Initial trial = 4,570 MSM (50% AA) with 12% transgender F who have sex with M
- C injections (q 8 weeks) compared to TDF/3TC QD; C was assoc with 70% fewer cases (placebo controlled)
- Evidence of non-inferiority; trial discontinued
- Safety data similar between groups
- HPTN 084 (cis-gendered females) = on-going

https://www.who.int/news-room/detail/20-05-2020-exciting-new-results-from-long-acting-prep-study-show-it-to-be-effective-in-preventing-hiv-acquisition-in-msm-and-transgender-women

PrEP & COVID-19
CDC Guidance

- PrEP = essential healthcare service
- Lab only visits for PrEP FU is advised
- If lab services are unavailable, consider at home-mail-in test kits for HIV/STIs; last resort = HIV swab screen (low sensitivity esp for recent inf)
- Following neg HIV screen consider 90d med supply (versus 30d with 2 ref) to reduce pharmacy visits

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History

Safety

Risk Behavior

Adherence

Acceptance

Efficacy

Resistance

COURTESY G.D. SEARLE & CO. / PHARMACIA CORPORATION

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Myers JE, Sepkowitz KA. *CID 2013;56(11):1604-12*