

TAF for Pre-Exposure Prophylaxis: Now FDA approved!

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Disclosures

No conflicts of interest or relationships to disclose

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FDA NEWS RELEASE

FDA approves second drug to prevent HIV infection as part of ongoing efforts to end the HIV epidemic

How will this approval change your practice?

1. I plan to prescribe F/TAF for PrEP for all patients at risk
2. I will change F/TDF to F/TAF for PrEP for all patients at risk
3. 1 & 2
4. I plan to prescribe F/TAF for MSM/transwomen only
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6. I am not an early adopter and will not use F/TAF yet

FTC/TAF vs FTC/TDF for PrEP

DISCOVER: Background

- FTC/TAF effective & now standard of care for treating HIV
- Lower plasma levels → reduced renal and bone adverse effects over time, as compared to FTC/TDF
- However, lower levels in rectal and cervicovaginal tissues so can't assume effective for PrEP¹

FTC/TAF vs FTC/TDF for PrEP

DISCOVER: Study Design

Study Features

- Phase 3, multinational, double blind, active controlled trial designed to assess safety and efficacy of FTC/TAF for PrEP
- Enrolled high-risk* cisgender MSM and transgender women (TGW)
- Exclusions: HIV, HBV, eGFR <60 (prior PrEP allowed)
- All received counseling & condoms at entry and every 3 months
- Primary endpoint: HIV incidence/100 person-years of follow-up (PYFU)

1:1

FTC/TDF daily
n = 2,694

FTC/TAF daily
n = 2,694

100% at 48 weeks
50% at 96 weeks

* ≥ 2 episodes condomless anal sex within past 3 months or bacterial STI within past 6 months

Source: Hare B et al. CROI 2019, Seattle, WA.



FTC/TAF vs FTC/TDF for PrEP

DISCOVER: Baseline Demographics & Risk Factors

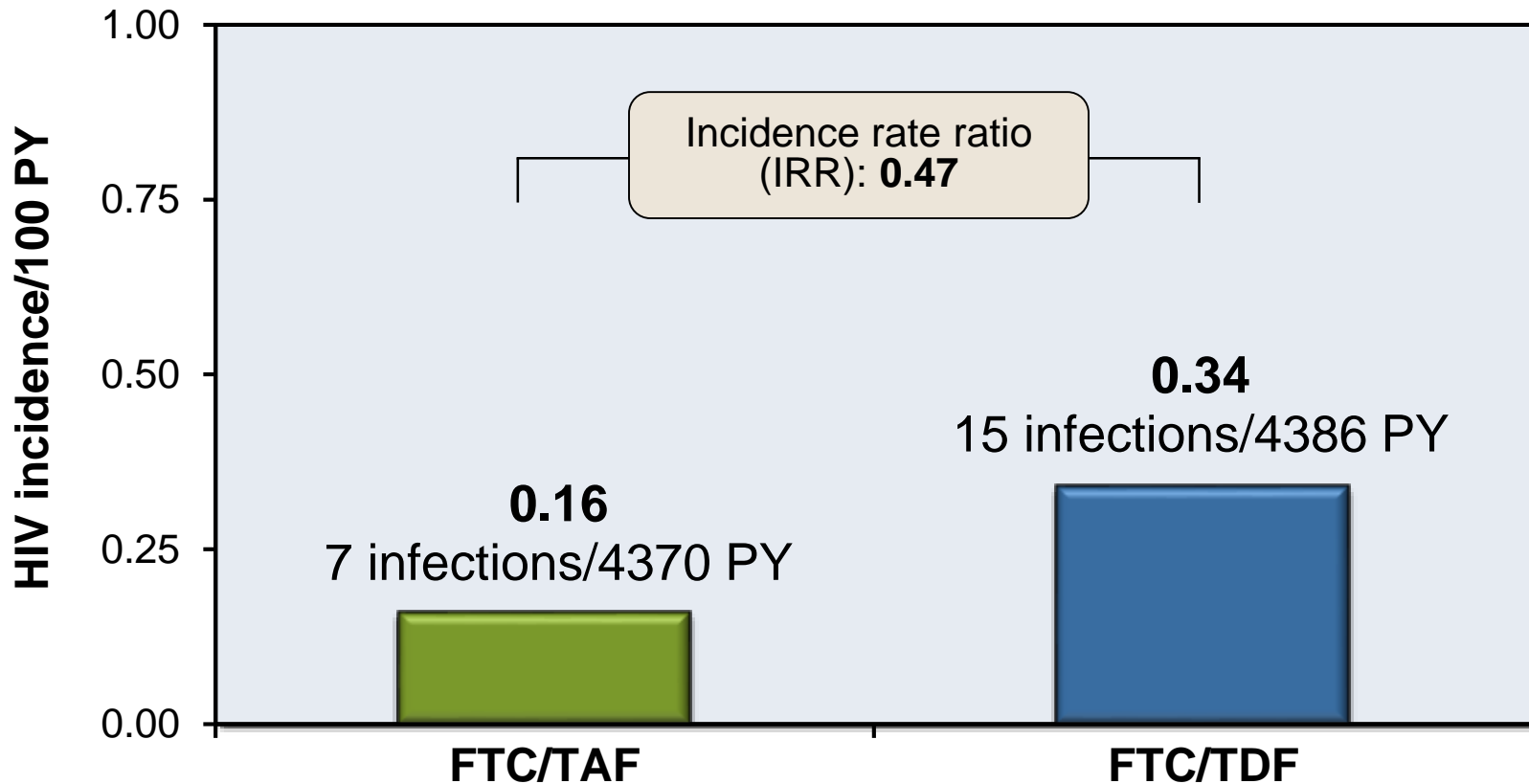
	FTC/TAF (n = 2,694)	FTC/TDF (n = 2,693)
Demographics		
Median age, y (range)	34 (18-76)	34 (18-72)
White, n (%)	2,264 (84)	2,247 (84)
Black, n (%)	240 (9)	234 (9)
TGW, n (%)	45 (2)	29 (1)
HIV risk factors (%)		
≥2 episodes condomless anal sex (receptive), past 12w	60	58
Rectal GC, past 24w	10	10
Rectal CT, past 24w	13	12
Syphilis, past 24w	9	10
Recreational drug use, past 12w	67	67
FTC/TDF PrEP at baseline	17	16

Source: Hare B et al. CROI 2019, Seattle, WA.



FTC/TAF vs FTC/TDF for PrEP

DISCOVER: Primary Endpoint Result



Pre-specific criteria for non-inferiority: IRR <1.62
Excluding baseline HIV infections (1 FTC/TAF, 4 FTC/TDF), IRR: 0.55
1 new infection in each arm occurred with adequate drug levels

FTC/TAF vs FTC/TDF for PrEP

DISCOVER: Secondary Endpoint Results

	FTC/TAF	FTC/TDF
Drug-related AE's		
AE's leading to stoppage	1	2
Mean change (%), spine BMD	0.50*	-1.12
Mean change (%), hip BMD	0.18*	-0.99
Mean change (mL/min), eGFR	1.8*	-2.3
STI's		
GC (any site), n (n/100PY)	1053 (47.1)	1059 (45.3)
CT (any site), n (n/100PY)	1049 (41.9)	1071 (41.6)
Syphilis, n (n/100PY)	365 (10.3)	370 (9.5)

*P <0.001; also true for mean % change in urine RBP:Cr ratio and b2M:Cr ratio

FTC/TAF vs FTC/TDF for PrEP

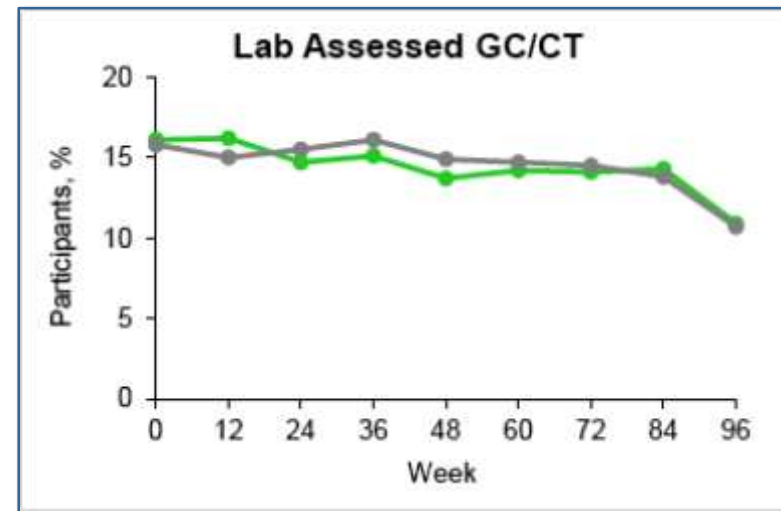
DISCOVER: Conclusions & Concerns

- Investigator conclusions:

- FTC/TAF non-inferior to FTC/TDF for PrEP in high-risk cis-MSM & TGW
- Both drugs well tolerated but bone & renal outcomes favored FTC/TAF
- High-risk sexual behavior constant with no e/o risk compensation

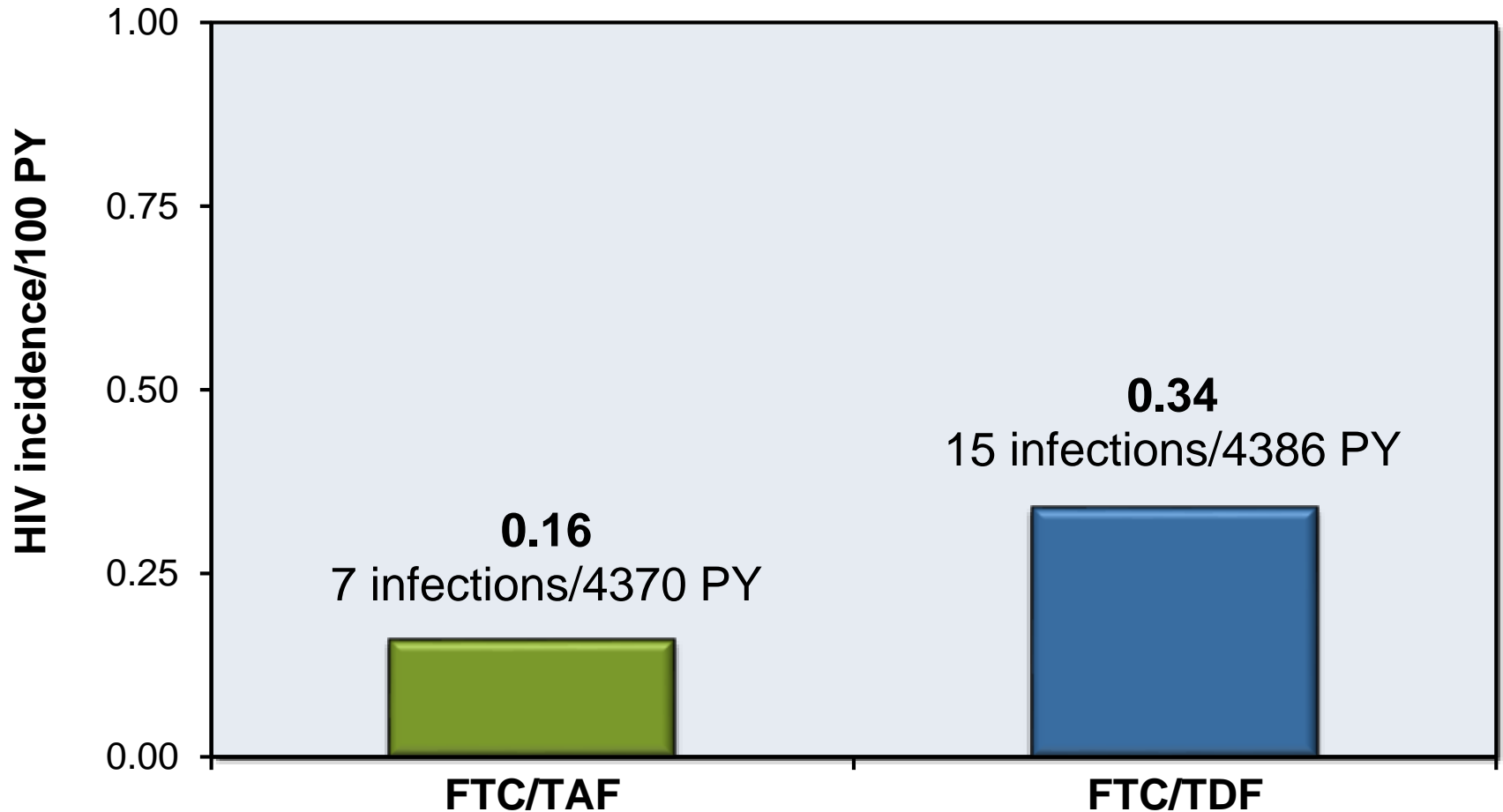
- Concerns:

- Limited follow-up and low event rate
- No participant with renal dysfunction
- Generalizability



FTC/TAF vs FTC/TDF for PrEP

DISCOVER Update at IAS: Is TAF better than TDF??



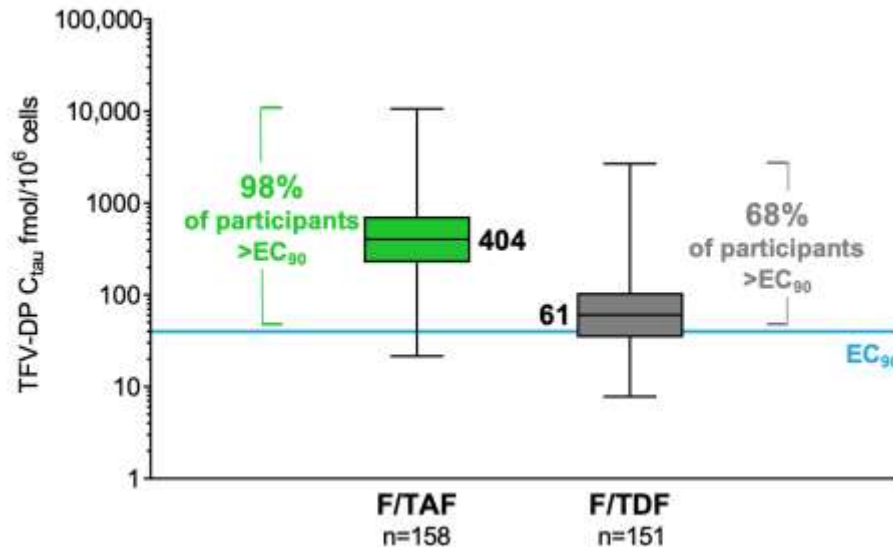
Source: Spinner CD et al. IAS 2019, Mexico City.



FTC/TAF vs FTC/TDF for PrEP

DISCOVER Update at IAS: Is TAF *better* than TDF??

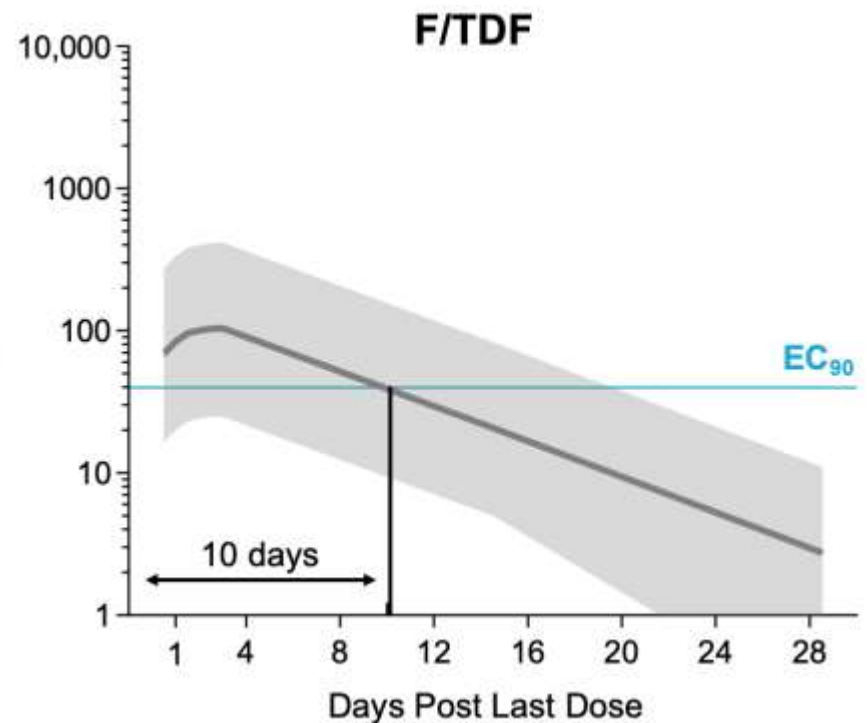
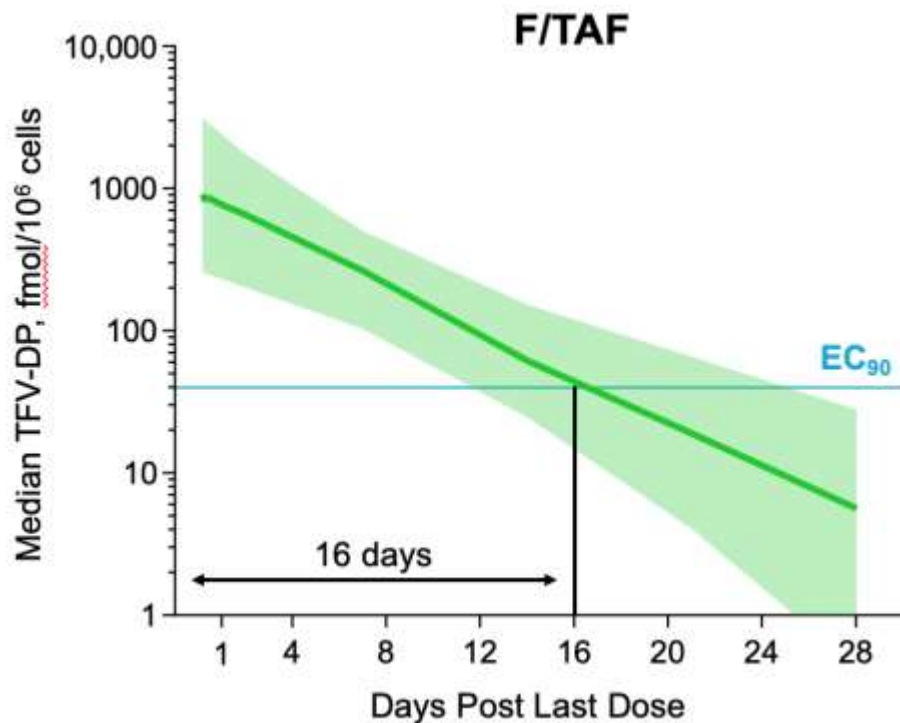
- No differences in reported adherence or pill count in the entire study
- TFV-DP levels 6.3 fold higher in F/TAF vs T/TDF
- % of participants with TFV-DP levels above protective threshold 98% F/TAF vs 68% F/TDF ($p < 0.001$)



FTC/TAF vs FTC/TDF for PrEP

DISCOVER Update at IAS: Is TAF *better* than TDF??

- Median duration of protection longer after last dose with F/TAF



Source: Spinner CD et al. IAS 2019, Mexico City.

FTC/TAF vs FTC/TDF for PrEP

DISCOVER Update at IAS: Is TAF *better* than TDF??

Conclusions from IAS:

Potentially some benefit of F/TAF if poor adherence

DISCOVER Update IDWeek 2019: Renal Outcomes

- Outcome: Treatment-emergent renal adverse effects
 - Renal AE's leading to discontinuation
 - Investigator-reported proximal renal tubulopathy
- Measures:
 - Proteinuria by urinalysis and UPCR
 - eGFR by Cockcroft-Gault
 - Markers of proximal tubular function
 - β 2M:Cr
 - RBP:Cr

DISCOVER Update IDWeek 2019: Renal Baseline Data

Characteristic	Overall		Baseline F/TDF for PrEP	
	F/TAF n=2694	F/TDF n=2693	F/TAF n=465	F/TDF n=440
Median age, y (range)	34 (18, 76)	34 (18, 72)	36 (19, 73)	36 (19, 71)
Race, n (%)	White	2264 (84)	391 (84)	379 (87)
	Black*	240 (9)	234 (9)	41 (9)
Hispanic/Latinx ethnicity, n (%)	635 (24)	683 (25)	81 (17)	73 (17)
Trans women, n (%)	45 (2)	29 (1)	4 (1)	2 (1)
Median time on F/TDF, y (range)	1 (<1, 6)	1 (<1, 6)	1 (<1, 6)	1 (<1, 6)
Median eGFR _{CG} , mL/min (IQR)	123 (105, 143)	121 (104, 142)	119 (101, 139)	117 (99, 137)
Proteinuria (dipstick) grade ≥1, n (%)	124 (4)	112 (4)	31 (7)	17 (4)
Medical history, n (%)	Diabetes mellitus	79 (3)	10 (2)	22 (5)
	Hypertension	282 (10)	298 (11)	56 (12)
	CV disease	31 (1)	23 (1)	3 (1)
	Hyperlipidemia	311 (12)	320 (12)	51 (11)

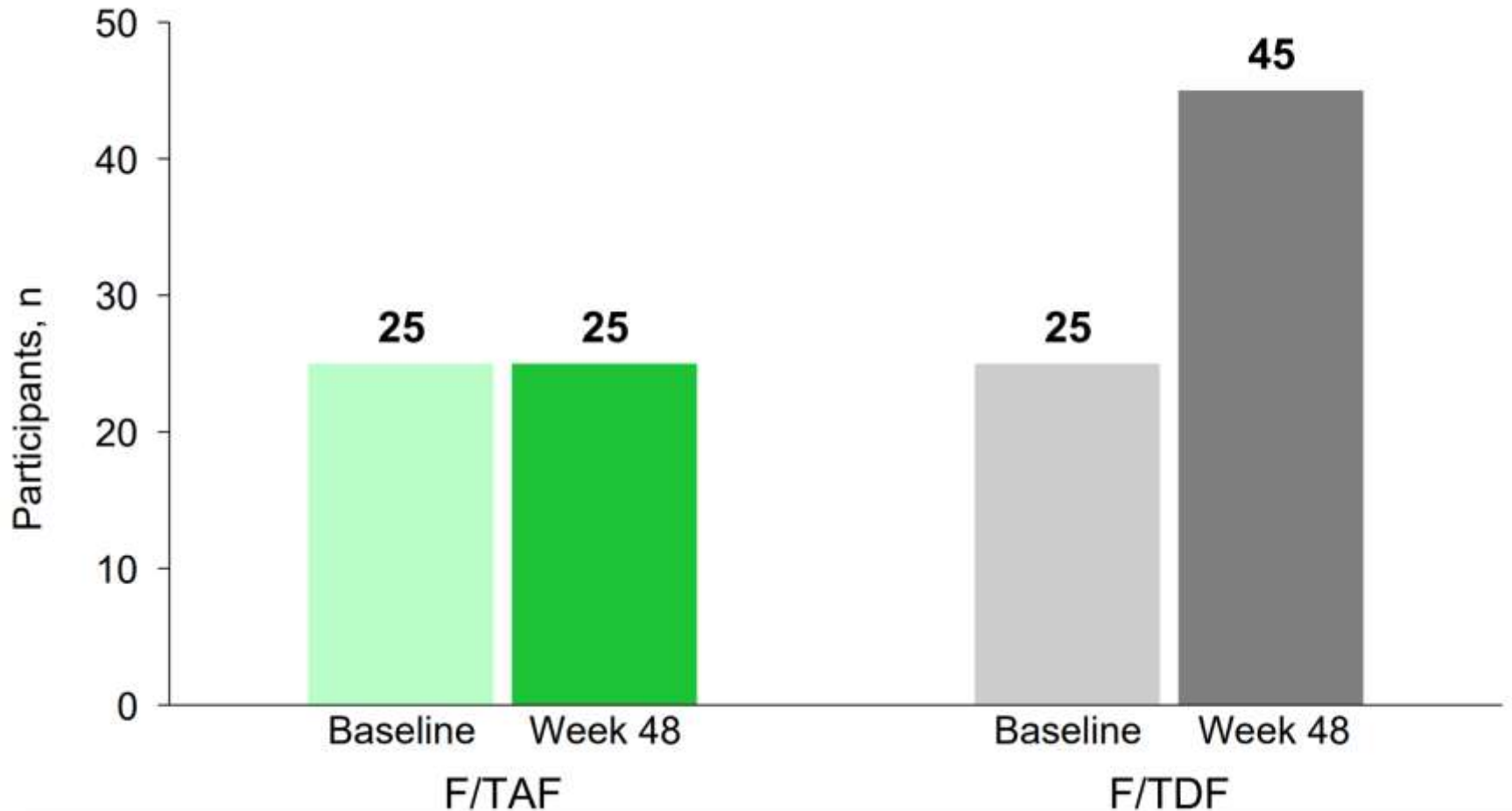
Source: Mills A et al. IDWeek 2019, Washington, DC.



DISCOVER Update IDWeek 2019: Renal Adverse Events

n (%)	Overall	
	F/TAF n=2694	F/TDF n=2693
Any renal-specific AE	263 (10)	266 (10)
Study drug-related renal AEs	14 (1)	26 (1)
Grade \geq 3 renal AEs	2 (<1)	3 (<1)
Renal AEs leading to discontinuation	2 (<1)	6 (<1)
Proximal renal tubulopathy	0	1 (<1)

DISCOVER Update IDWeek 2019: Participants with UPCR Elevation > 200mg/g



Source: Mills A et al. IDWeek 2019, Washington, DC.



DISCOVER Update IDWeek 2019: Conclusions

- At 48 weeks, F/TAF vs F/TDF for PrEP was associated with:
 - Significantly better eGFR and renal biomarkers
 - Numerically fewer renal AEs
 - No proximal renal tubular injury (compared to 1 in TDF arm)

F/TAF for PrEP

- Who: Adults and adolescents (≥ 35 kg) at sexual risk of acquiring HIV (**excluding vaginal sex**)
- How: Daily (**not on demand**)

Why not women?

- The FDA panel voted 16–2 in favor of the view that Descovy had been shown to be safe and effective for PrEP against HIV in men and transgender women who have sex with men
- But the FDA panel then split 10–8 on the question of whether available data support approval of a PrEP indication for Descovy for cisgender women

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F/TDF vs F/TAF for PrEP Summary

F/TDF (Truvada)



F/TAF (Descovy)



EFFECTIVENESS

- ✓ for multiple populations

SAFETY

- Small ↓ in eGFR and BMD

COST

- \$1,845/month in 2019
- Generic in 2020



SAFETY / 48 WKS

eGFR (mL/min)

HIP BMD

LDL (mg/dL)

BODY WEIGHT (kg)



EFFECTIVENESS

- ✓ for MSM and transwomen
- ? for other populations

SAFETY

- Small ↑ in LDL and weight

COST

- \$1,845/month in 2019

Acknowledgment

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