Epatiti virali e Profilassi pre-esposizione

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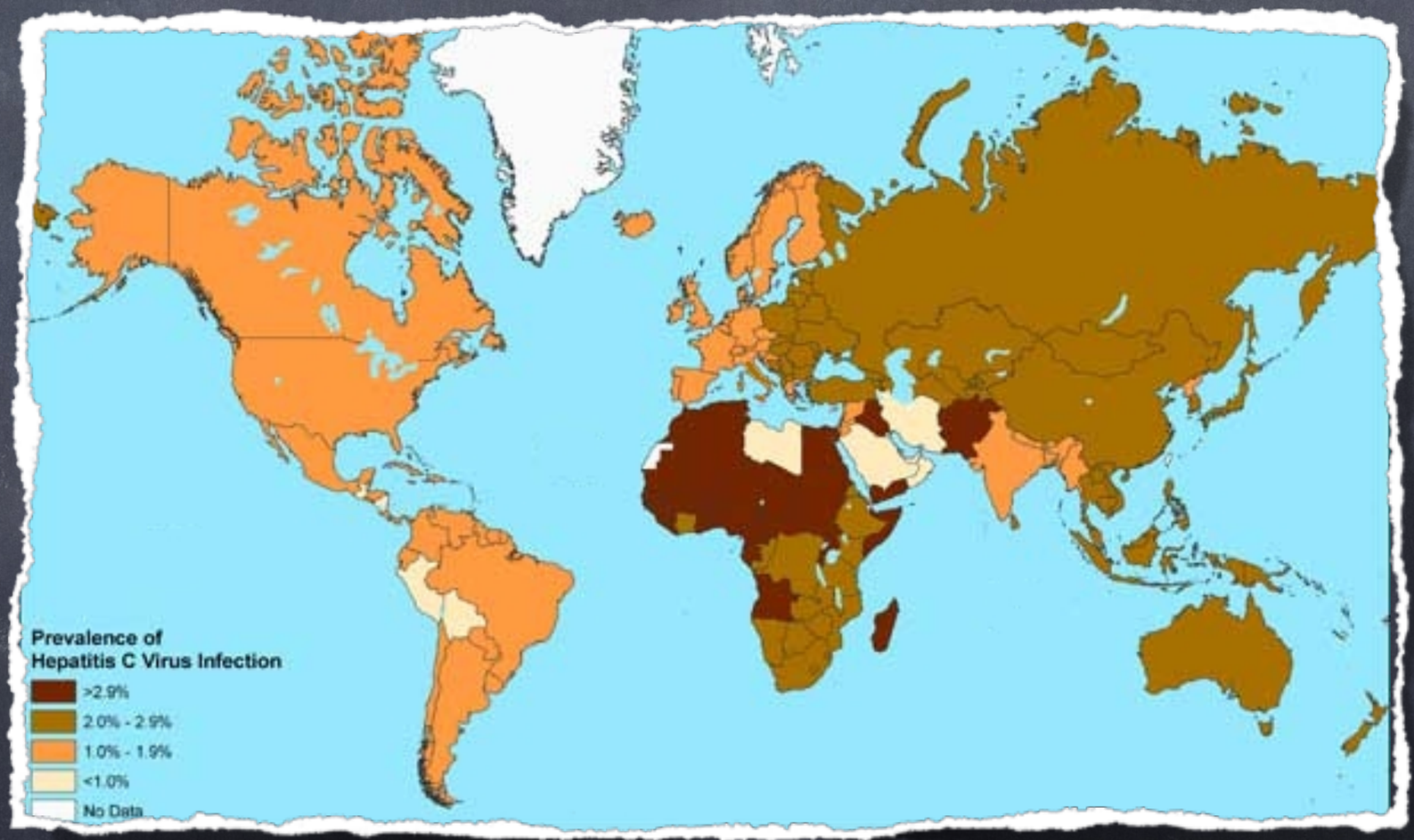
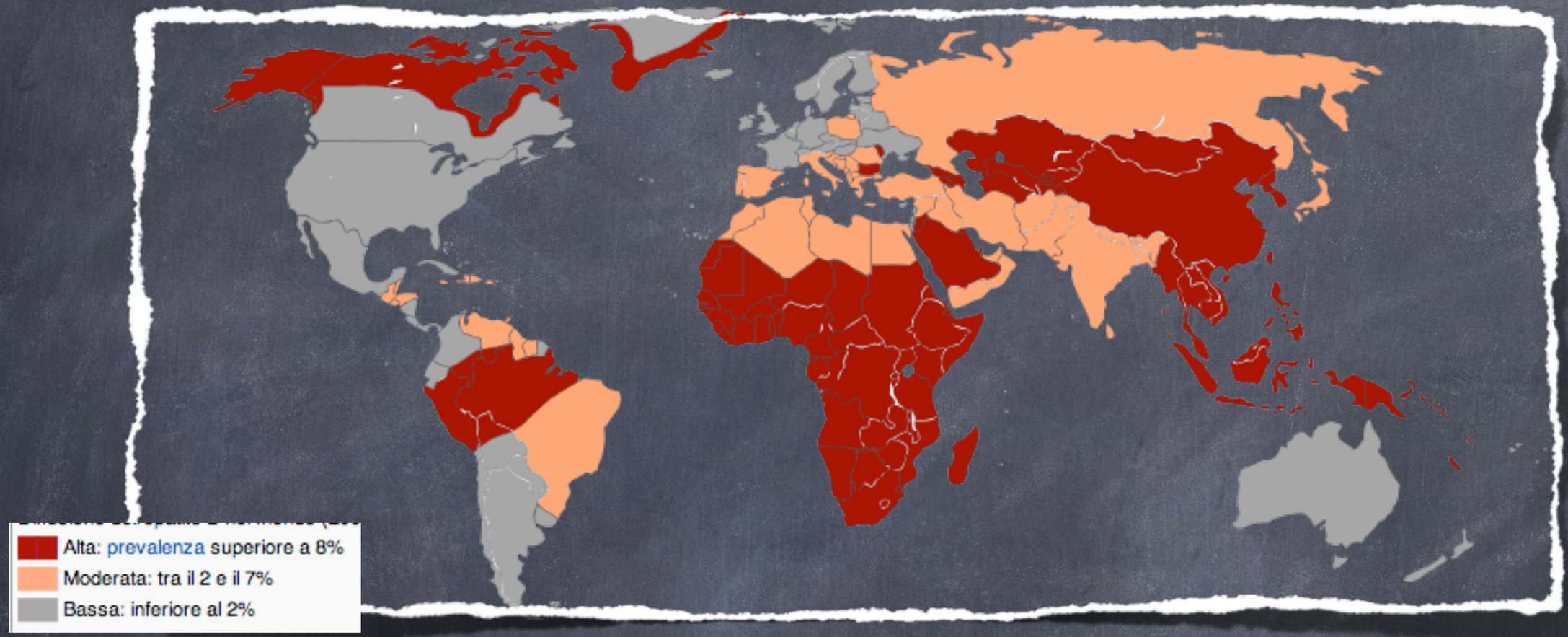
Epatiti virali

Introduzione

- Nel mondo, 170 milioni di persone hanno un'infezione cronica da HCV
- 2,8 milioni di HIV+ sono anche HCV+
- 350.000 persone muoiono ogni anno per le conseguenze dell'infezione

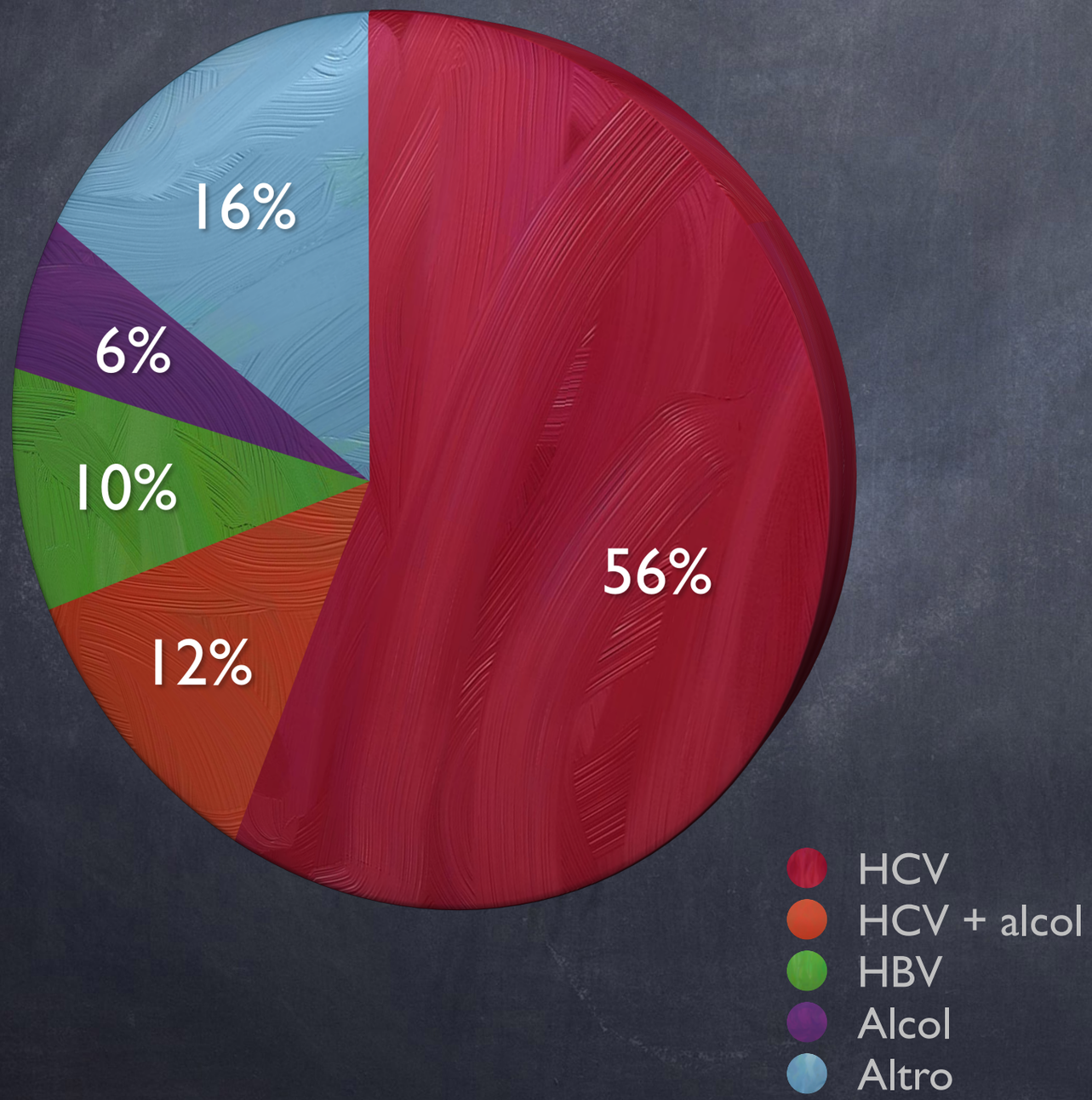


Introduzione



- Circa 350 milioni di persone nel mondo vivono con un'infezione cronica da HBV.
- Le conseguenze dell'infezione acuta e cronica provocano nel mondo più di 600.000 morti all'anno.
- Esiste un vaccino sicuro ed efficace
- Tutti i soggetti HBsAg positivi sono a rischio di infezione con HDV (e vanno quindi screenati per tale infezione) virus difettivo a RNA che utilizza HBsAg per l'assemblaggio del virione.

Introduzione

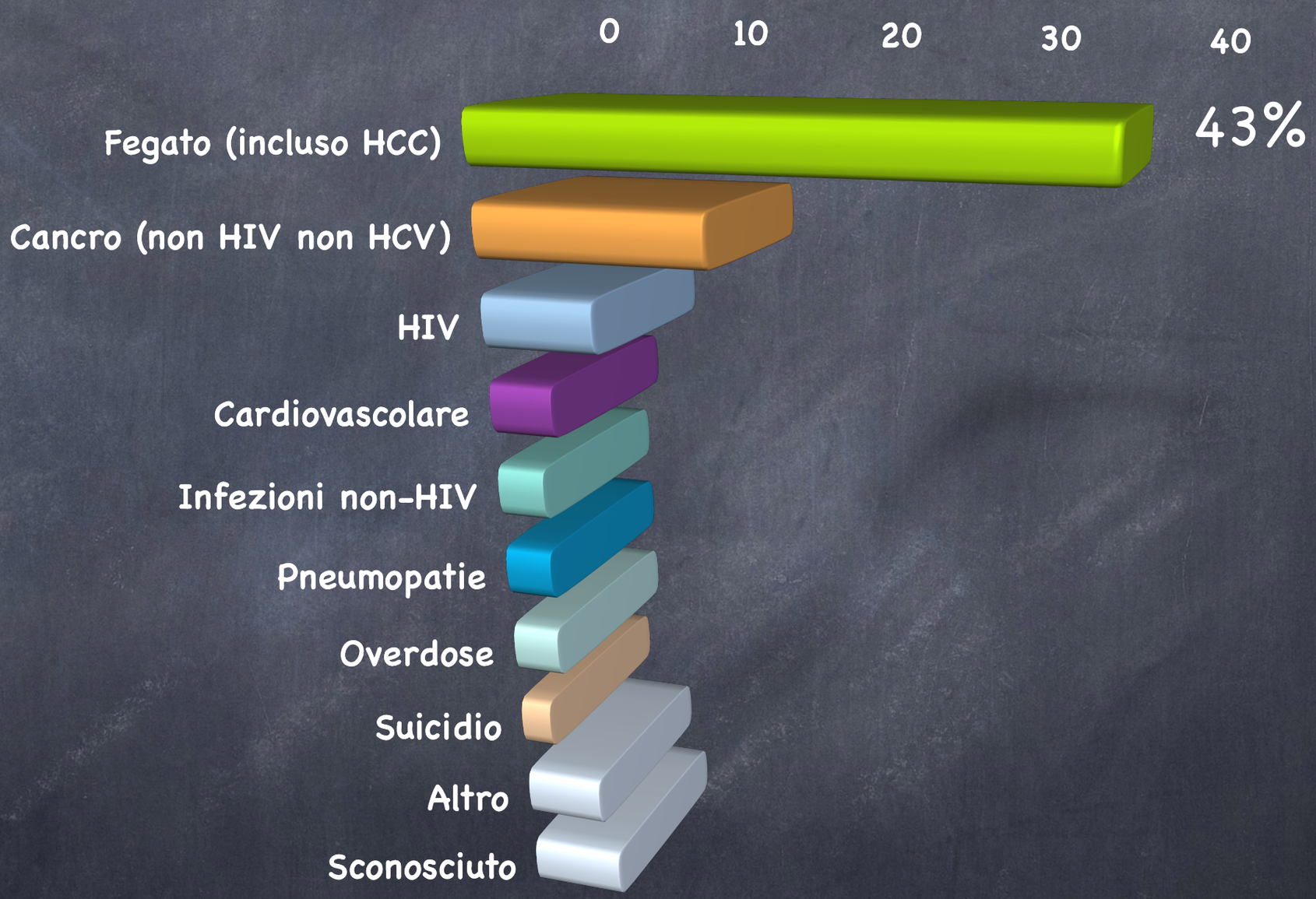


- In Italia, HCV è responsabile, da solo o in associazione con l'alcol, del 68% dei casi di epatopatia cronica
- HBV di circa il 10%
- prevalenza
  HCV 2-3%
  HBV 1,5%

Sagnelli et al., J Med Virol 2005

Introduzione

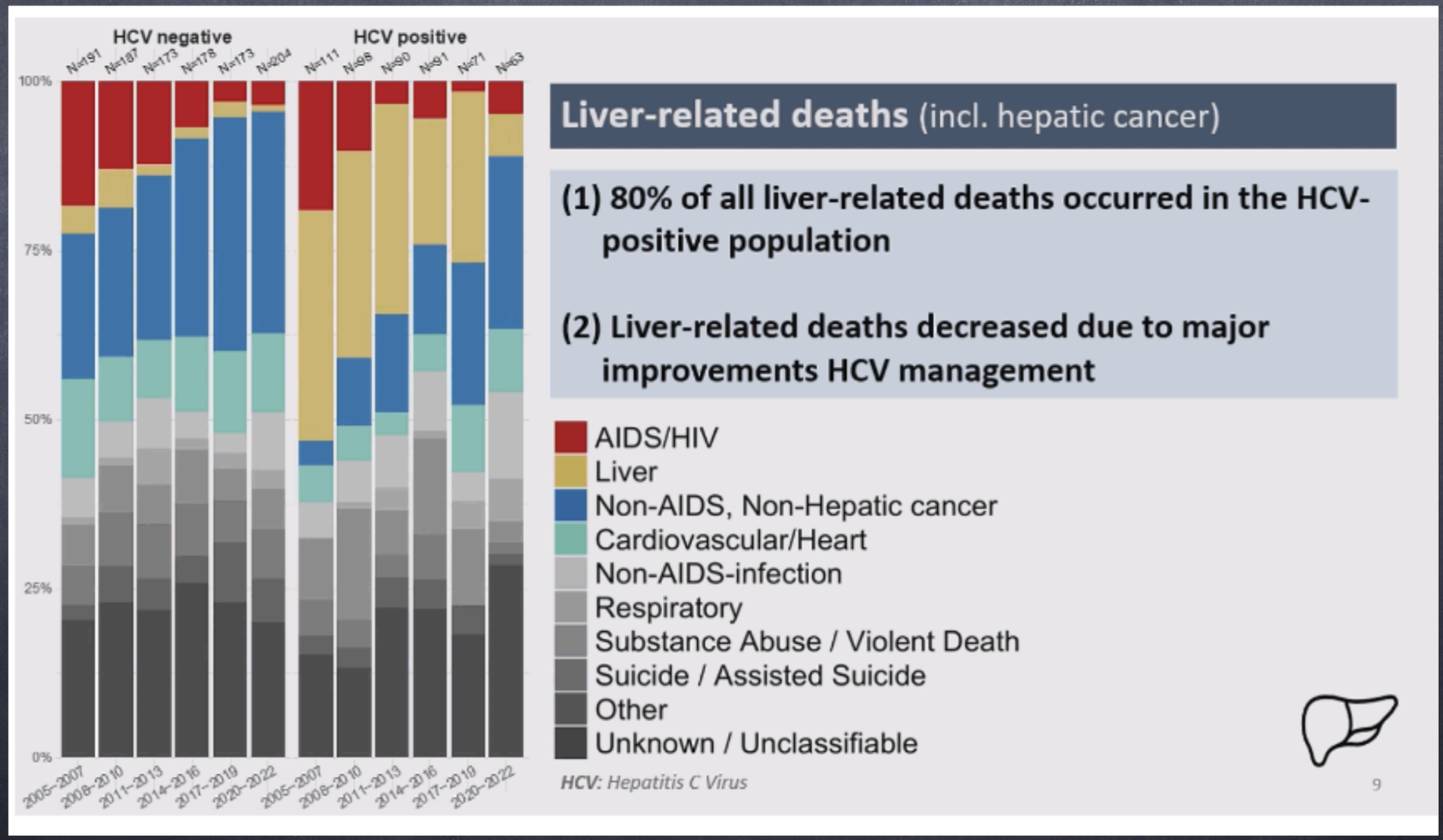
Cause di morte nella popolazione HIV+ HCV+ in Francia



Lacombe K et al. 7th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2013). June 30–July 3 2013. Kuala Lumpur, Malaysia. Abstract WEPL0104.

Introduzione

Cause di morte nella popolazione HIV+ in Svizzera



Mascolini M. Et al. Time trends in causes of death in people with HIV: insights from the Swiss HIV Cohort Study. 19th European AIDS Conference October 18th-21st , 2023 Warsaw, Poland

Epidemiologia

- Vie di trasmissione:

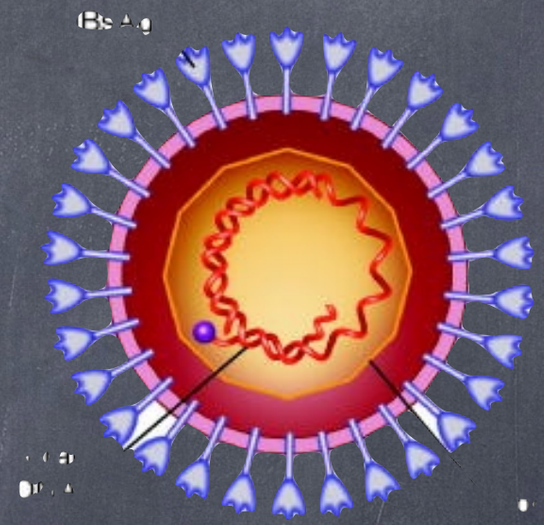
  - parenterale classica (trasfusioni, TD e.v., personale sanitario);
  - parenterale inapparente (rasoi, spazzolini da denti, piercing, cure odontoiatriche, ecc.);
  - sessuale (B > C);
  - materno-fetale.

- Serbatoio rappresentato dai malati in fase acuta e, soprattutto, dai portatori cronici.
- La cronicizzazione di HBV si verifica nel 90% dei casi di trasmissione materno-fetale, nel 20-50% dei soggetti che si infettano in età infantile e in meno del 5% dei soggetti infettati in età adulta.
- La cronicizzazione di HCV si verifica nel 60-85% dei soggetti esposti.
- L'infezione acuta da HBV guarita lascia immunità, da HCV no.

Marker sierlogici HBV

HBsAg

È la proteina principale prodotta dal virus. La sua presenza nel sangue indica l'infezione in corso (acuta o cronica)



HBsAb

Anticorpo contro HBsAg, che conferisce immunità protettiva.

HBcAb

Anticorpi prodotti solo in caso di infezione naturale

HBV-DNA o viremia

Genoma virale circolante. Esprime la presenza di infezione e la contagiosità.

I livelli correlano con la gravità di malattia.

Qualche esempio...

HBsAg	positivo
HBsAb	negativo
HBcAb	positivo

HBsAg	negativo
HBsAb	positivo
HBcAb	negativo

HBsAg	negativo
HBsAb	positivo
HBcAb IgG	positivo

Marker sierlogici HCV

anti-HCV o HCV-Ab

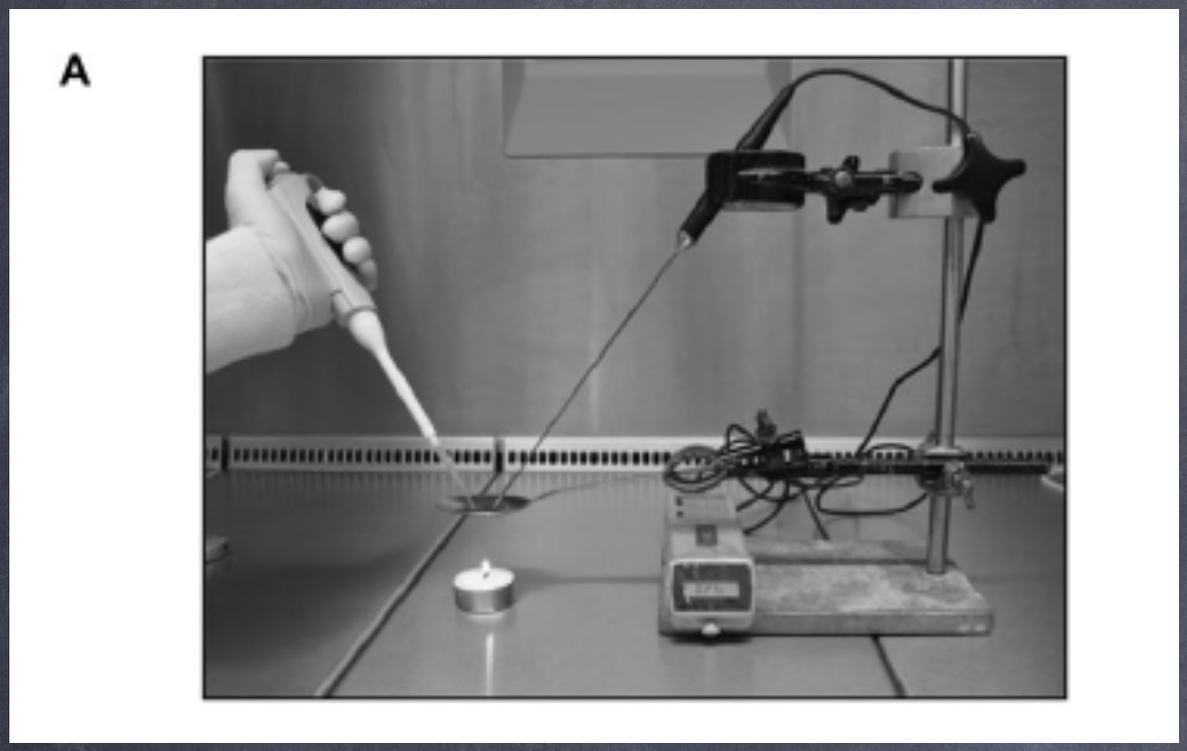
Anticorpi anti-HCV, che esprimono il pregresso contatto con il virus (quindi nel 60-85% una forma cronica).

Restano positivi per tutta la vita, ma non sono protettivi.

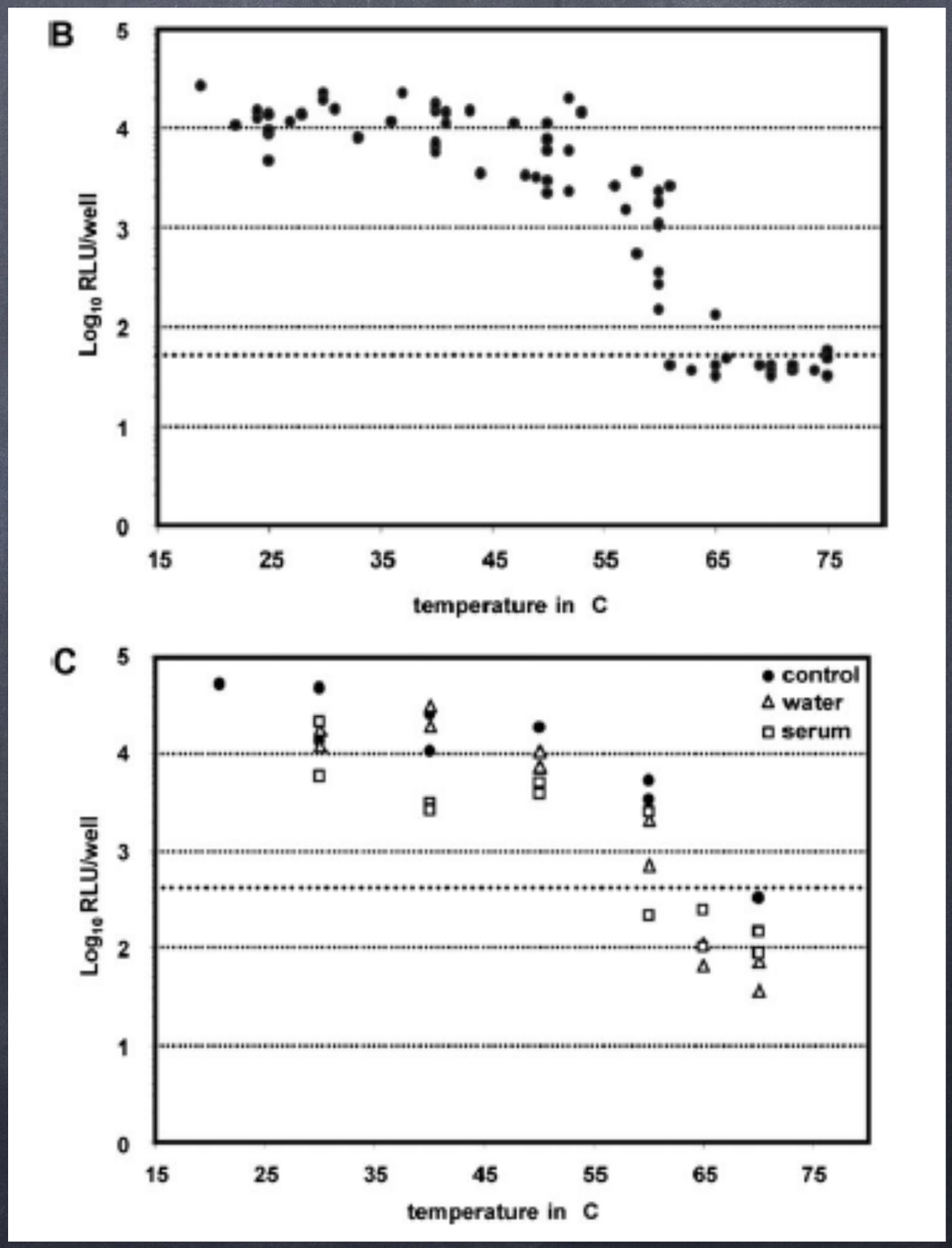
HCV-RNA o viremia

Genoma virale circolante. Esprime la presenza di infezione e di contagiosità. I livelli NON correlano con la gravità di malattia.

HCV nella materia inerte

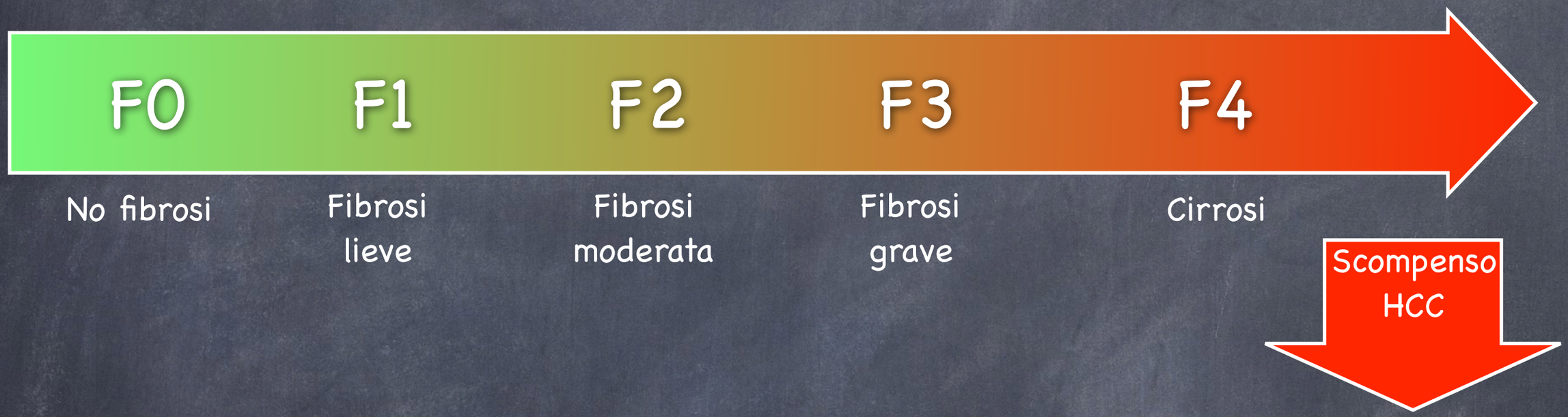


- Per inattivare HCV servono temperature di almeno 65°C per 80-95 secondi



Doerrbecker et al., JID 2011

Storia naturale



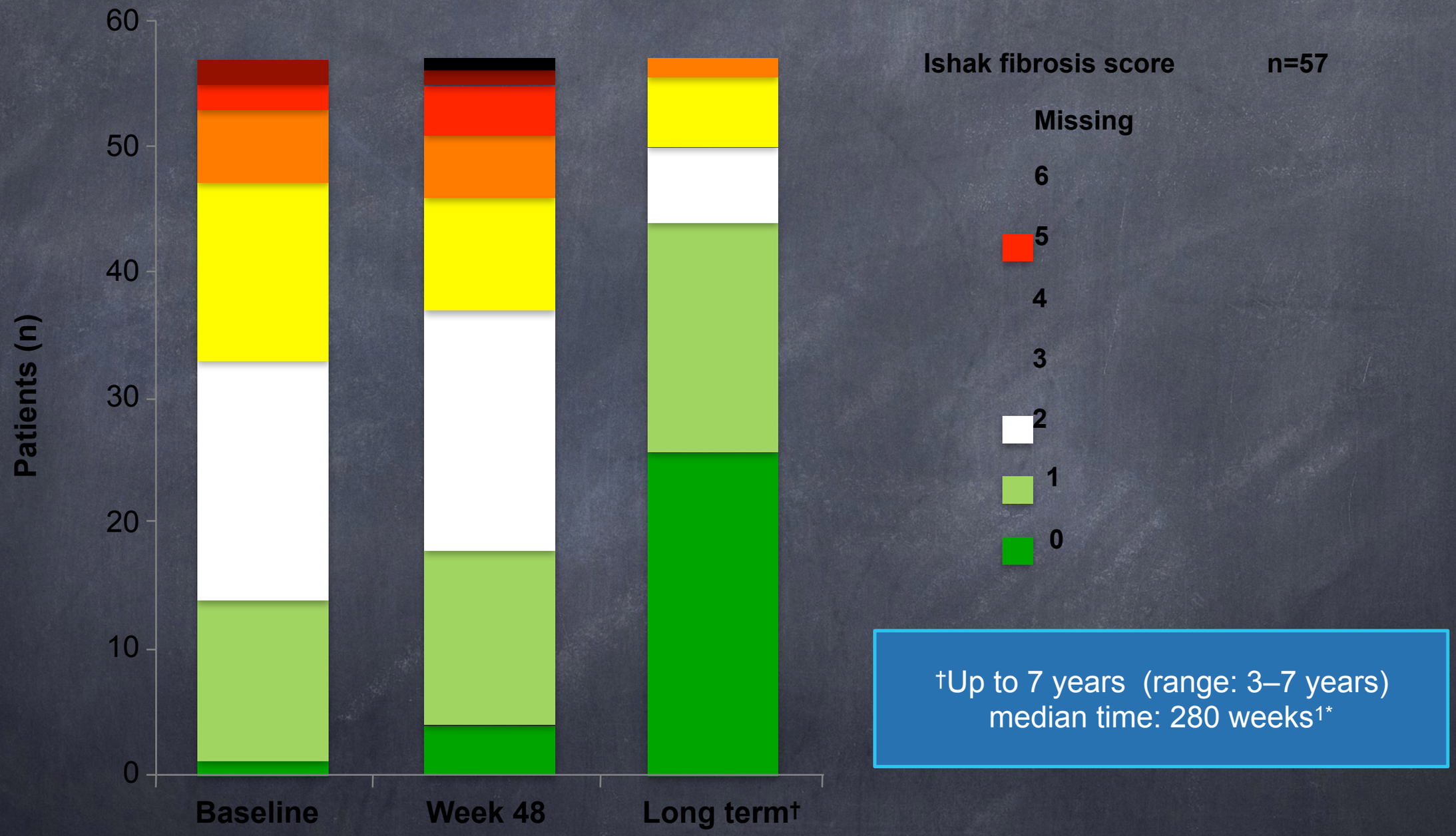
- La presenza di HCV e/o HBV è un fattore di rischio per cirrosi, scompenso ed epatocarcinoma
- Fattori di rischio aggiuntivi (HIV, alcol, dismetabolismo) accelerano il processo

La terapia anti-HBV

Trattamento "curativo" - PEG-IFN alfa2a

Trattamento "soppressivo" - Entecavir, Tenofovir

Miglioramento della fibrosi dopo terapia con Entecavir



†Up to 7 years (range: 3–7 years) median time: 280 weeks[1*]

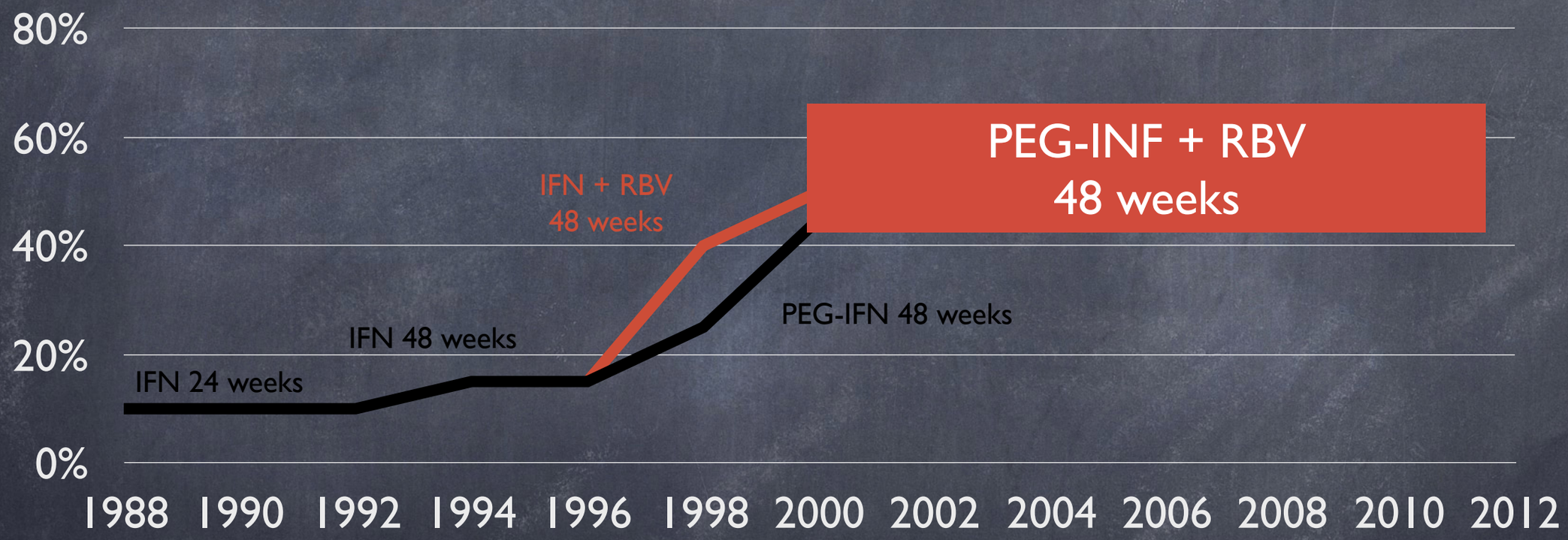
*In the randomised, controlled studies, patients received 0.5 mg ETV. In the 901 rollover study, patients received 1 mg ETV. Please refer to the SmPC for further information on the treatment regimen.[2]

1. Adapted from Chang T-T, et al. *Hepatology* 2010;52:886–93; 2. Baraclude® (entecavir) SmPC May 2011.

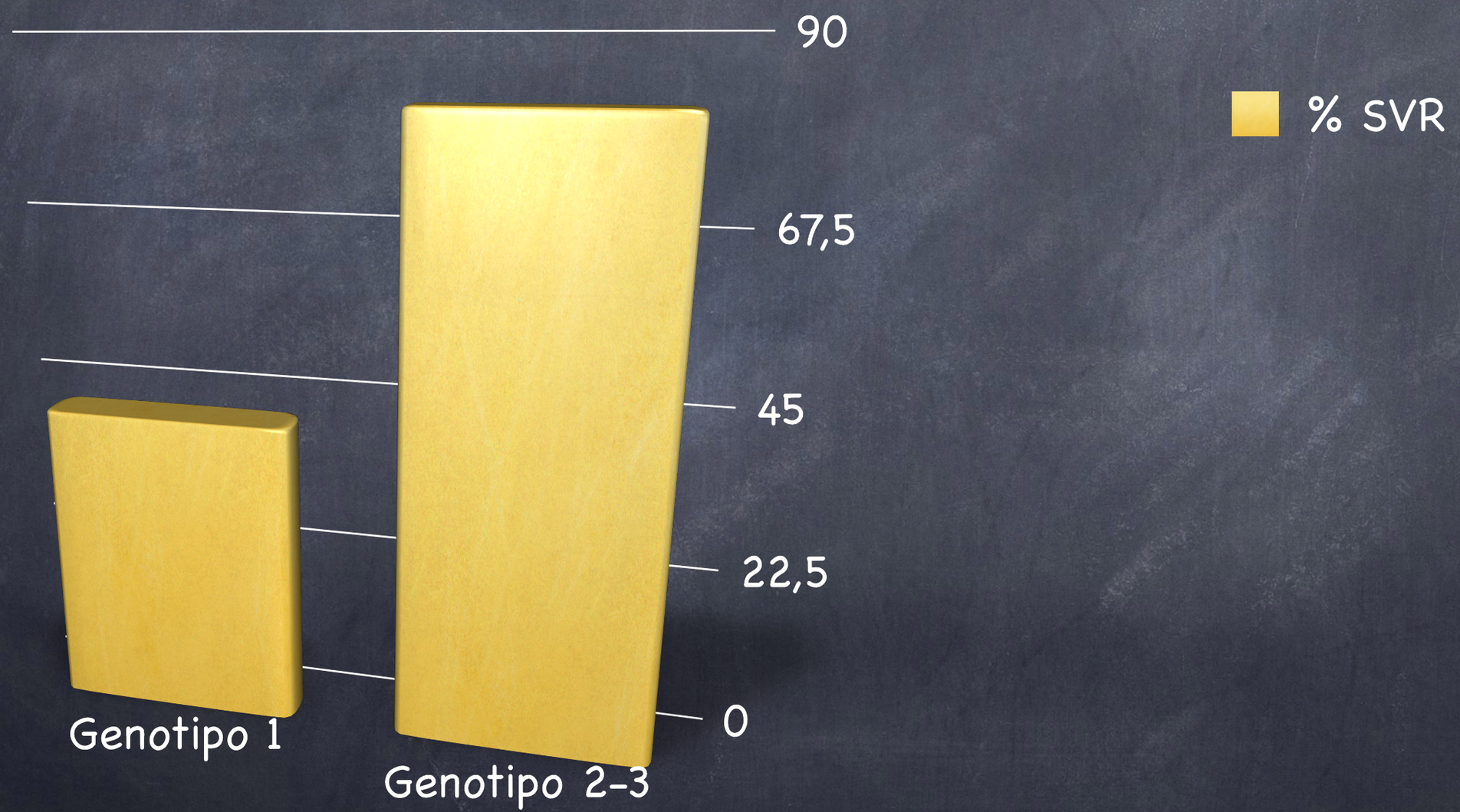
La terapia anti-HCV

- Il passato remoto: interferoni e ribavirina
- Il passato prossimo: triplice terapia
- Il presente: farmaci antivirali diretti
- Il futuro: ??

Il passato: interferoni e ribavirina



Risultati della terapia



Manns et al., 2001

Effetti collaterali di PEG-IFN e RBV

Somatici

- Sindrome influenzale
- Astenia
- Nausea
- Manifestazioni cutanee (reazioni locali all'iniezione, xerosi, prurito, eczema)
- Tireopatie
- Perdita di peso, calo della libido, perdita di capelli
- Disordini autoimmuni

Psichici

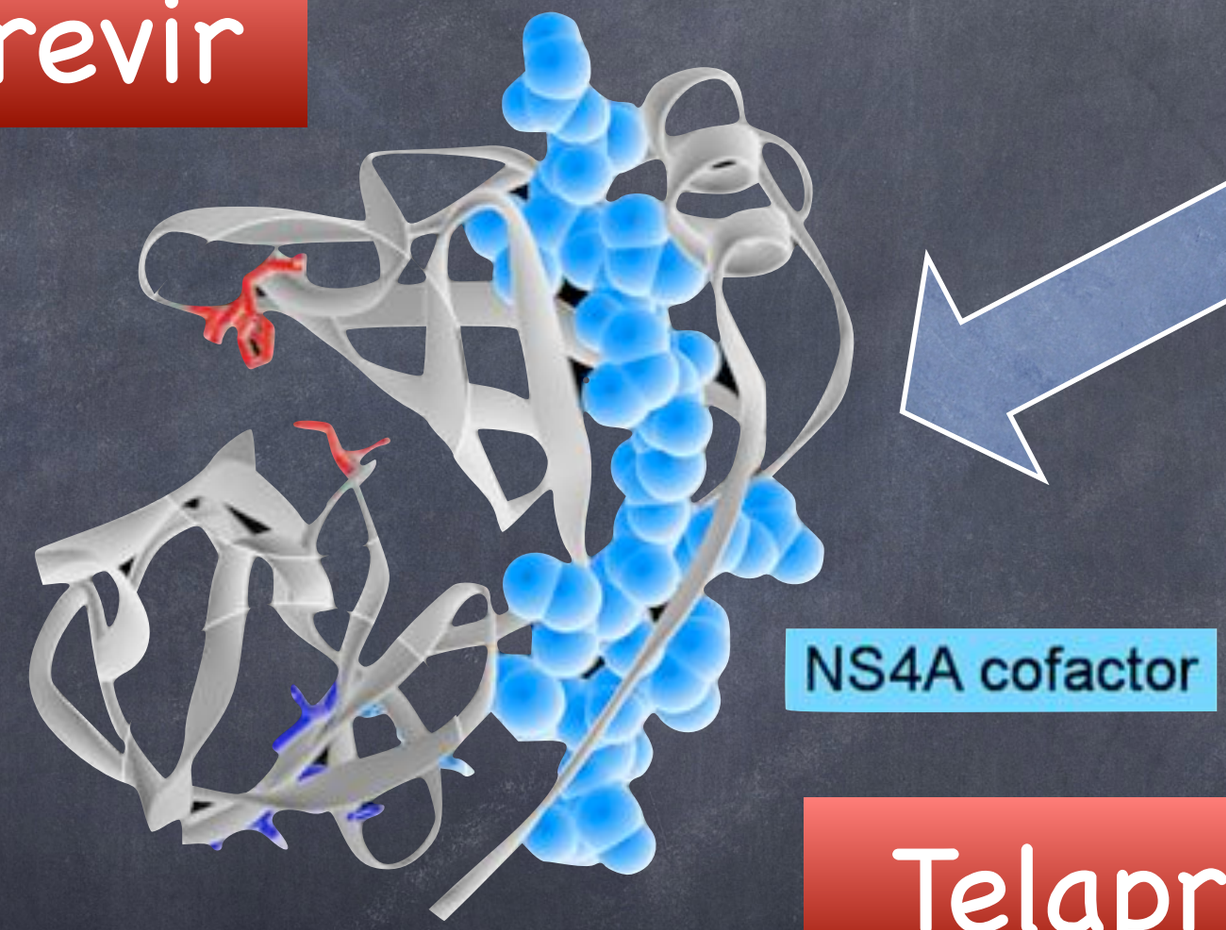
- Insonnia
- Fragilità emozionale e affettiva
- Ansia e irritabilità
- Decadimento cognitivo
- Apatia, abulia, depressione franca

Ematologici

- Leucopenia
- Anemia
- Trombocitopenia

La triplice terapia

Boceprevir



Telaprevir

DAAs
Inibitori della proteasi NS3/4A
Inibitori della polimerasi NS5B
Inibitori di NS5A

NS3/4A è una serina-proteasi virale, essenziale per il clivaggio della poliproteina

"Note dolenti"
PI di I generazione

- Bassa barriera genetica ⟶ neccessario "backbone" di PEG-IFN e RBV
- Attivi solo su genotipo 1
- Problemi farmacocinetici / farmacodinamici
  Telaprevir: 6 cp/die con pasto grasso,
  Boceprevir: 12 cp/die a stomaco pieno
- Effetti collaterali

I nuovi farmaci

NS3/4A ...previr	NS5A ...asvir	NS5B ...buvir	IFN- lamb	nibitori lofillina
Serina-proteasi, essenziale per il clivaggio post-traslazionale della poliproteina	Fosfoproteina di membrana multifunzionale, componente essenziale del complesso di replicazione dell'HCV-RNA	RNA polimerasi RNA-dipendente, HCV specifica	Un interf tipo III distri rec orta a una	mana, lla CV NS5A
Boceprevir Telaprevir Paritaprevir/r Sovaprevir Asunaprevir Simeprevir Faldaprevir Danoprevir Glecaprevir Grazoprevir Voxilaprevir	Daclatasvir Ledipasvir PPI-668 AZ-689 BMS-824393 PPI-461 Ombitasvir Velpatasvir Elbasvir Pibrentasvir	Inibitori nucleosidici Sofosbuvir Mericitabina VX-135 Inibitori non nucleosidici BI-207127 Dasabuvir ABT-072 BMS-791325 Tegobuvir Setrobuvir VX-222 Filibuvir	BMS-914143	porivir SCY-635

Possibili schemi terapeutici

- SOF/VEL (Epclusa) 1 cp al giorno per 12 settimane
- SOF/VEL/VOX (Vosevi) 1 cp al giorno per 8 - 12 settimane
- GLE/PIB (Maviret) 3 cp al giorno per 8 settimane
- ELB/GRZ (Zepatier) 1 cp al giorno per 12 settimane

E nelle persone con

The indications are the same in HCV-monoinfected and HIV coinfected patients. However, treatment alterations or dose adjustments may be needed in the latter due to drug-drug interactions

La prescrizione dei DAA in Italia fino al 2016

- Riservata ai Centri specialistici di Malattie Infettive, Gastroenterologia e Medicina Interna

- Rimborsabilità regolata dai celebri "criteri AIFA" che recitano: "Con l'obiettivo finale di favorire l'accesso alle nuove terapie per tutti i pazienti affetti da epatite C cronica e garantire al tempo stesso la sostenibilità del SSN, si è reso inizialmente necessario individuare una strategia di accesso modulata sulla base dell'urgenza clinica al trattamento. Di conseguenza, l'AIFA, tramite la Commissione Tecnico Scientifica (CTS), ha individuato i criteri di rimborsabilità prioritaria al trattamento con i nuovi DAAs sulla base dei risultati emersi dai lavori del Tavolo tecnico epatite C istituito presso l'Agenzia."

La prescrizione dei DAA in Italia fino al 2016

- I criteri di prioritizzazione individuano i seguenti gruppi di pazienti:

1 Pazienti con cirrosi in classe di Child A o B e/o con HCC con risposta completa a terapie resettive chirurgiche o loco-regionali non candidabili a trapianto epatico nei quali la malattia epatica sia determinante per la prognosi.

2 Epatite ricorrente HCV-RNA positiva del fegato trapiantato in paziente stabile clinicamente e con livelli ottimali di immunosoppressione

3 Epatite cronica con gravi manifestazioni extra-epatiche HCV-correlate (sindrome crioglobulinemica con danno d'organo, sindromi linfoproliferative a cellule B).

4 Epatite cronica con fibrosi METAVIR F3 (o corrispondente Ishack)

5 In lista per trapianto di fegato con cirrosi MELD <25 e/o con HCC all'interno dei criteri di Milano con la possibilità di una attesa in lista di almeno 2 mesi.

6 Epatite cronica dopo trapianto di organo solido (non fegato) o di midollo con fibrosi METAVIR ≥2 (o corrispondente Ishack).

La prescrizione dei DAA in Italia dal 30/03/2017

- I criteri di prioritizzazione sono stati ampliati inserendo i seguenti:

7 Epatite cronica con fibrosi METAVIR F2 (o corrispondente Ishak) e/o comorbilità a rischio di progressione del danno epatico [coinfezione HBV, coinfezione HIV, malattie croniche di fegato non virali, diabete mellito in trattamento farmacologico, obesità (body mass index ≥30 kg/m_2), emoglobinopatie e coagulopatie congenite]

8 Epatite cronica con fibrosi METAVIR F0-F1 (o corrispondente Ishak) e/o comorbilità a rischio di progressione del danno epatico [coinfezione HBV, coinfezione HIV, malattie croniche di fegato non virali, diabete mellito in trattamento farmacologico, obesità (body mass index ≥30 kg/m_2), emoglobinopatie e coagulopatie congenite].

9 Operatori sanitari infetti.

10 Epatite cronica o cirrosi epatica in paziente con insufficienza renale cronica in trattamento emodialitico.

11 Epatite cronica nel paziente in lista d'attesa per trapianto di organo solido (non fegato) o di midollo.

La prescrizione dei DAA in Italia dal 30/03/2017

- I farmaci possono essere prescritti e concessi gratuitamente a tutti i pazienti affetti da epatite cronica C

Epatite acuta C

Sex Transm Infect. 2004 Aug; 80(4): 3
doi: 10.1136/sti.2003.008532

Increased numbers of acute he... infections in HIV positive homosexual men; is sexual tra...

R Browne, D Asboe, Y Gilleece, M Atkins, S Mand...

AIDS. 2007 May 11;21(8):983-91.

Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours.

Danta M[1], Brown D, Bhagani S, Pybus OG, Sabin CA, Nelson M, Fisher M, Johnson AM, Dusheiko GM; HIV and Acute HCV (HAAC) group.

ORI

Hepatitis C virus sero... men who have sex... injection drug u...

Ann N Burchell PhD[1,2], Sandra L C...
Vanessa G Allen MD[3], Ahmed M ...
Robert S Remis MD MPH[2,3], W...
on behalf c...

Poster Sessions – Abstract P106

Acute hepatitis C virus (HCV) infection in the setting of HIV coinfection: a single-centre 10-year follow-up

Ingiliz, Patrick; Steininger, Katharina; Schuetze, Marcel; Dupke, Stephan; Carganico, Andreas; Krznaric, Ivanka; Wienbreyer, Andreas and Baumgarten, Axel

Infectiology, Medical Center for Infectious Diseases, Berlin, Germany.

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 60 / No. 28
July 22, 2011

Sexual Transmission of Hepatitis C Virus Among HIV-Infected Men Who Have Sex with Men — New York City, 2005–2010

Epatite acuta C

- Rischio di trasmissione negli eterosessuali molto basso (0,6-5% delle coppie)
- In costante aumento negli MSM HIV+ in Europa (rischio 0,59% -> 2,23% dal 2002 al 2013)
- Rischio HIV+ circa 4 volte HIV-
- Durante la fase acuta si è molto più contagiosi

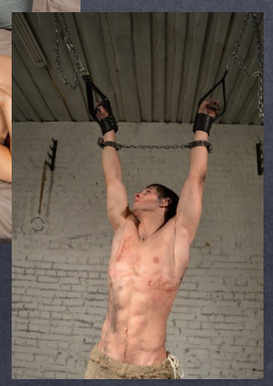
Epatite acuta C

Fattori di rischio

- Rapporti anali senza condom

- Condivisione di sex-toys

- Uso di clisteri prima del sesso anale passivo



- Sesso di gruppo
- BDSM
- Serosorting
- Chemsex

Epatite acuta C

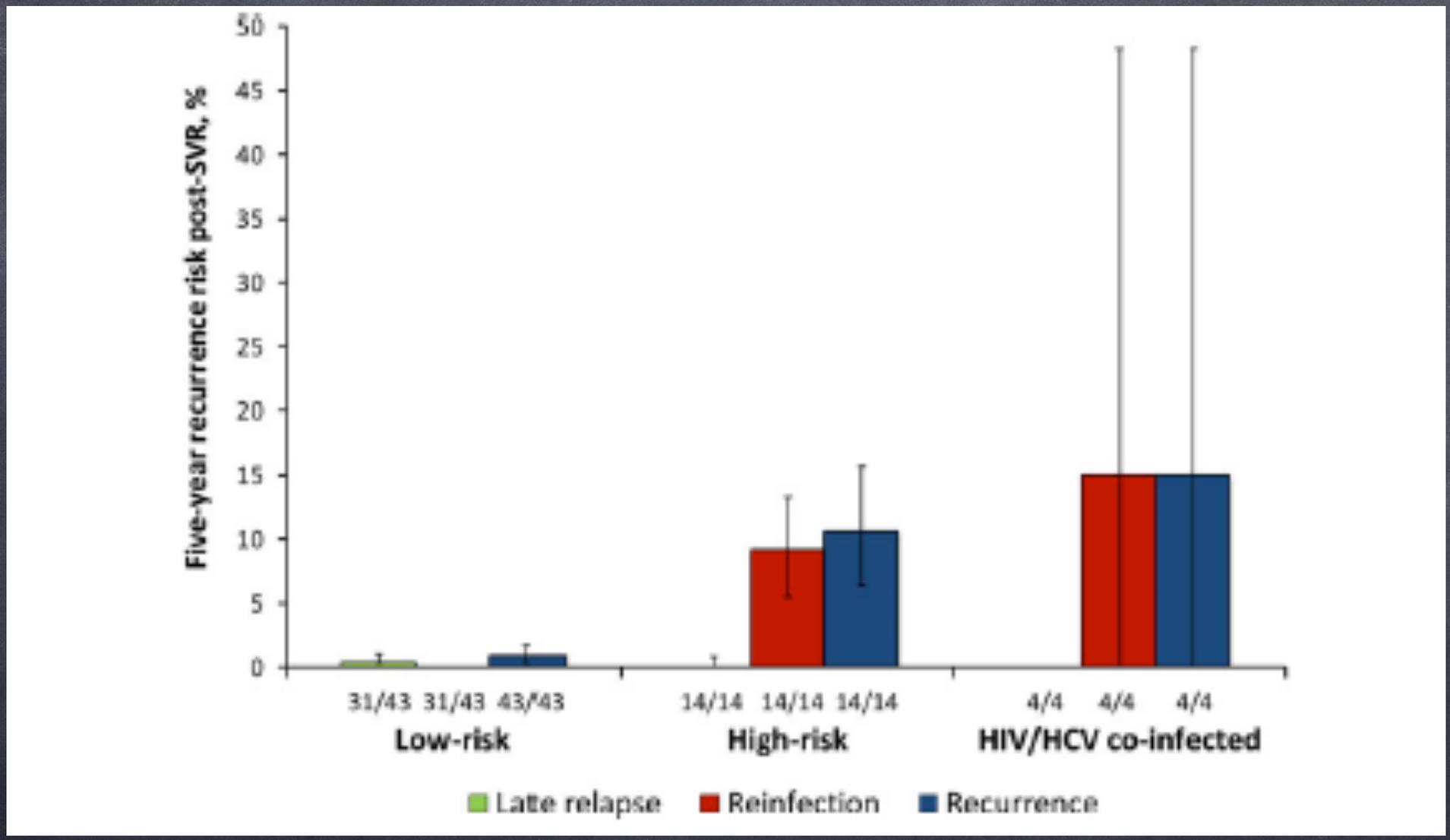
- In confronto agli HIV-negativi, gli HIV-positivi hanno
  - più spesso una forma asintomatica (fino al 92%)
  - un minor controllo precoce della replica di HCV
  - più facilmente virus presente nello sperma (37.8% vs. 18.4%)
  - più probabilità di cronicizzare

QUINDI....

Epatite acuta C

- Devono essere trattati (?)
- E come?

Reinfezione



Simmons et al., CID 2016

Epatite A ed Epatite E

- Epatiti virali a trasmissione oro-fecale
- Tipiche dei paesi in via di sviluppo
- Pericolose soprattutto in chi ha un danno epatico pre-esistente; HEV anche nella donna in gravidanza (mortalità 15-25%)
- Non cronicizzano negli immunocompetenti; HEV può cronicizzare negli immunodepressi

Epatite delta

- HDV è un virus difettivo, che necessita della presenza contemporanea di HBV per replicare
- Condivide le vie di trasmissione con HBV
- Può infettare insieme a HBV (coinfezione) o successivamente in chi ha cronicizzato HBV (sovrainfezione)
- Peggiora drasticamente il decorso dell'epatite B

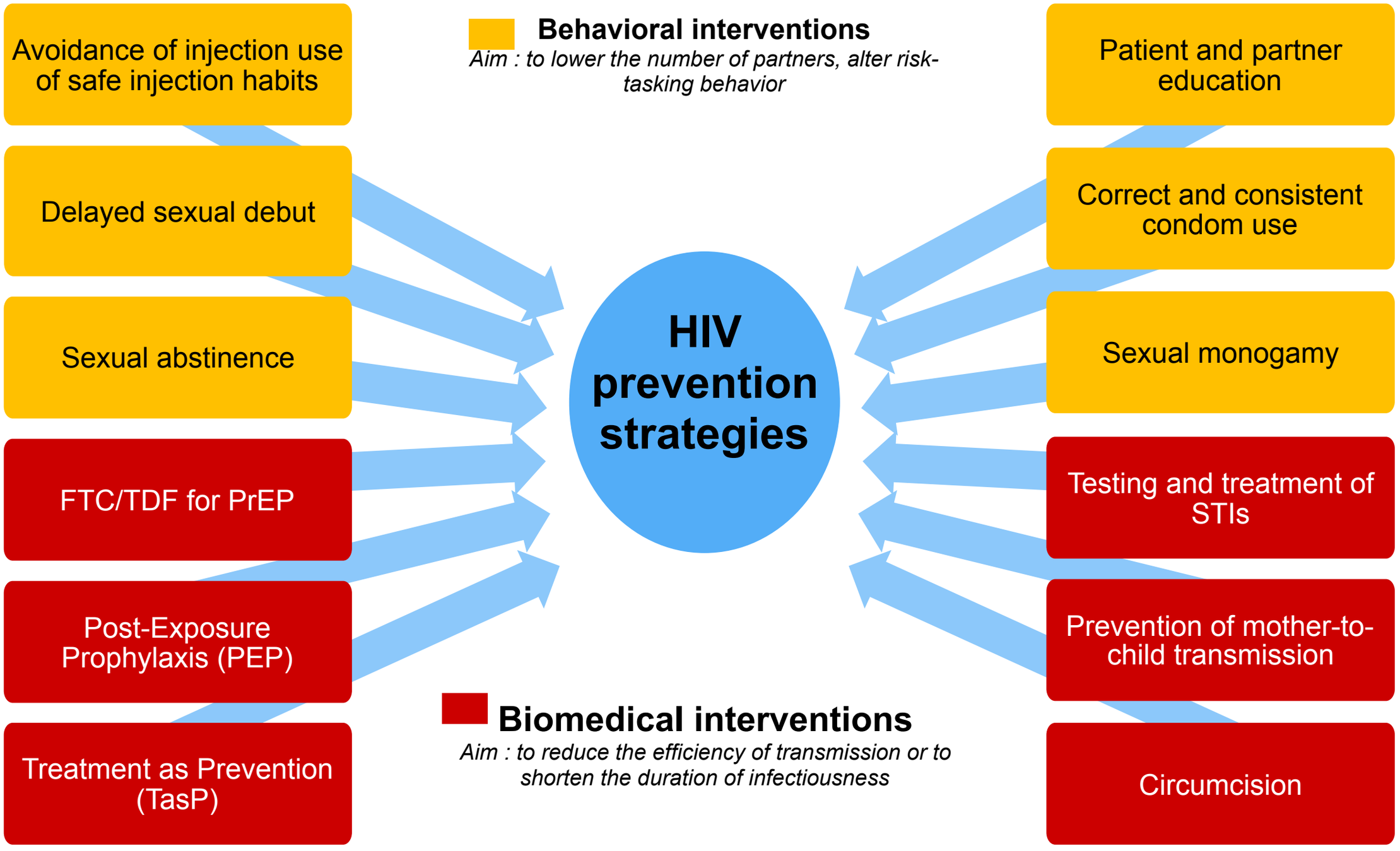
Profilassi Pre-esposizione per HIV

Relative risk of HIV infection according to exposure type

Exposure	Risk per 10,000 Exposures
Needle sharing	67
Receptive anal intercourse	50
Needle stick (occupational exposure)	30
Receptive vaginal intercourse	10
Insertive anal sex	6.5
Insertive vaginal sex	5
Receptive oral intercourse	1
Insertive oral intercourse	0.5

http://www.aidsinfo.nih.gov/contentfiles/NonOccupationalExposureGL.pdf

HIV Prevention incorporates multiple interventions



Cohen M, et al. *J Int AIDS Soc.* 2008;11:4. (adapted)
Cohen M, et al. Sexual HIV Transmission and Its Transmission. www.medscape.org/viewarticle/416415. Accessed March 10, 2016.

Studi clinici a supporto della PrEP

Efficacy results from PrEP clinical trials

Studies supporting TVD label for PrEP

Clinical trial	Participants	Number	Drug	mITT [a] efficacy of % reduction in acquisition of HIV infection [b]		Adherence-adjusted efficacy based on TDF detection in blood [c]	
				%	(95% CI)	%	(95% CI)
iPrEx[1]	Men who have sex with men (MSM)	2499	TVD*	44	(15-63)	**92**	(40-99)
Partners PrEP [2]	HIV discordant couples	4747	TDF	67	(44-81)	**86**	(67-94)[9]
			TVD*	75	(55-87)	**90**	(58-99)[9]
TDF2 [3]	Heterosexually active men and women	1219	TVD*	62	(21-83)	**78**	(41-94)
Bangkok Tenofovir Study [4]	IDU	2413	TDF	49	(10-72)	**84**	(73-99)
PROUD [5]	MSM	544	TVD*	86	(64-96)	-----	-----
IPERGAY [6]	MSM	400	on demand TVD*	86	(40-98)	-----	-----
Fem-PrEP [7]	Heterosexually active women	2120	TVD*	NS	-----	**< 40%**	-----
VOICE [8]	Heterosexually active women	5029	TVD*	NS	-----	**<30%**	-----

1. Grant RM & al. *N Engl J Med* 2010; 363:2587-99
2. Baeten JM & al. *N Engl J Med* 2012;367:399-410
3. Thigpen M, et al. *N Engl J Med* 2012;367:423-34
4. Choopanya K & al. *Lancet* 2013;381, 2083-90
5. McCormack S. & al. *Lancet* 2016;387,53-60
6. Molina JM & al. *N Engl J Med* 2015;373,2237-46
7. Van Damme L, et al. *N Engl J Med* 2012;367:411-22
8. Van der Straten A, et al. *AIDS* 2012;26(7):F13-F19
9. New York State Department of Health AIDS Institute PrEP Guidance 2015, Available at http://www.hivguidelines.org/wp-content/uploads/2016/02/PrEP-Guidance_10-14-15.pdf
10. MarrazzoJM et al. *N EnglJ Med*. 2015 Feb 5;372(6):509-18

***TVD = FTC/TDF**

a. Modified Intent to Treat
b. Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up visit or HIV test
c. The percentage of reduction in HIV incidence among those with TFV detected in blood, compared with those without detectable TFV

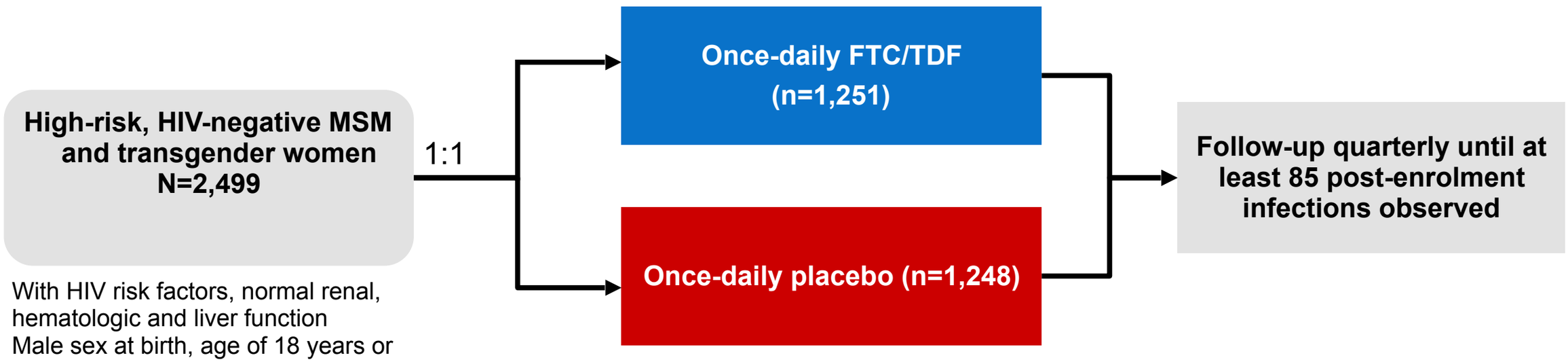
"On-demand" regimen constitutes: FTC/TDF or 2 placebo < 24 hrs prior to sexual intercourse exposure 1 FTC/TDF or placebo dose 24 hrs after; and a final dose 48 hrs after sexual intercourse

TDF is not licensed for PrEP
FTC/TDF is only licensed as a daily dosage for PrEP

‡

iPrEx : Preexposure Prophylaxis Initiative trial

Placebo-controlled, double-blind, randomised, multicentre study in the Americas, South Africa, and Thailand



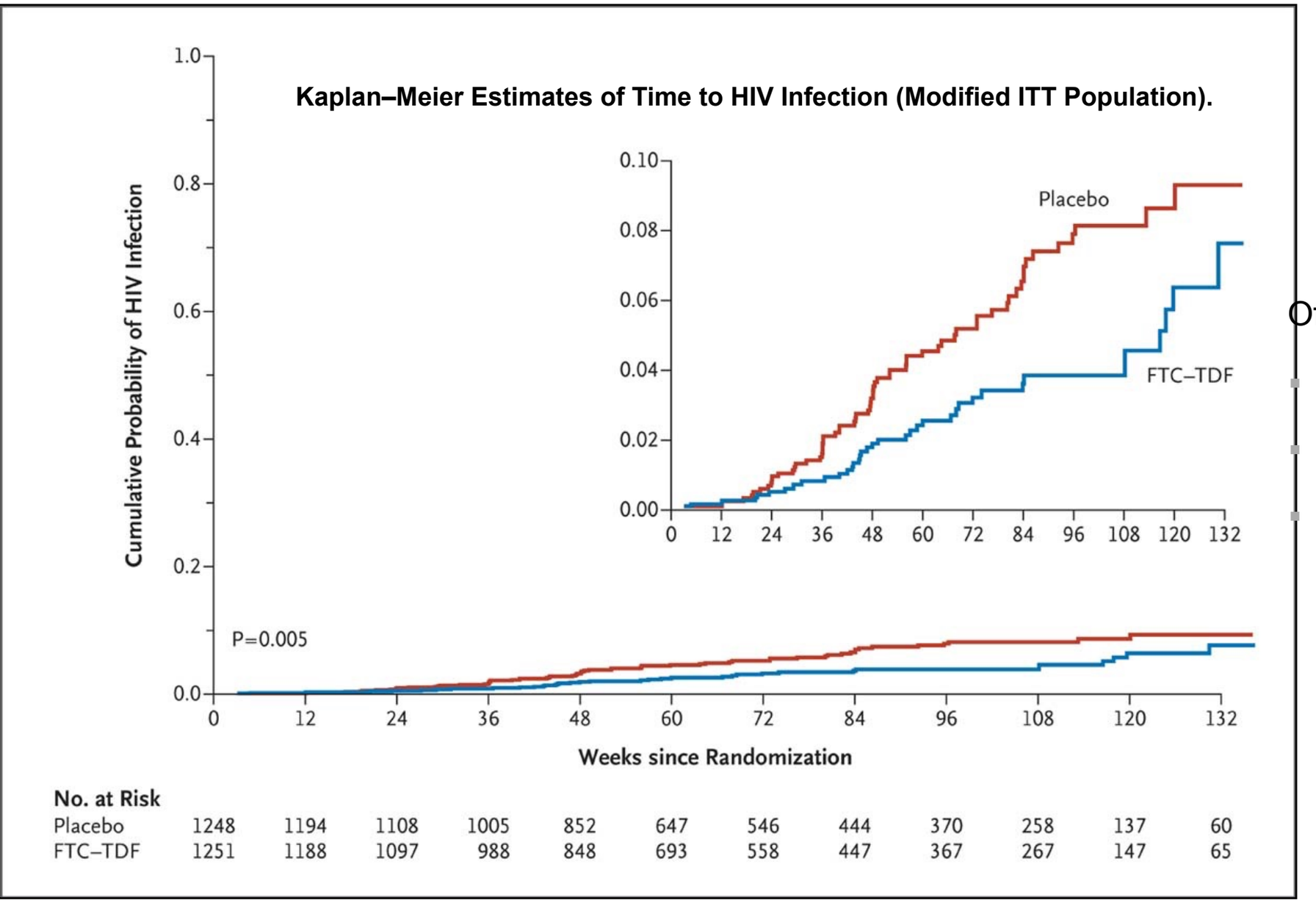
ClinicalTrials.gov Identifier: NCT00458393

- **Objective** : to determine whether once-daily use of FTC/TDF versus placebo can prevent HIV-1 infection in 2,499 MSM who also receive HIV counselling, condoms, and treatment for STIs
- **Primary endpoint**: HIV seroconversion between randomisation and Month 12
- **Secondary endpoints**: safety, adherence, sexual behaviour, resistance development

Grant RM et al. *N Engl J Med* 2010;363:2587–2599
Michael NL. *N Engl J Med* 2010;363:2663–2664

MSM : Men who have Sex with Men

Efficacy results



Of the 100 incident infections:

- **64** infections in the placebo group
- **36** infections in the FTC/TDF group

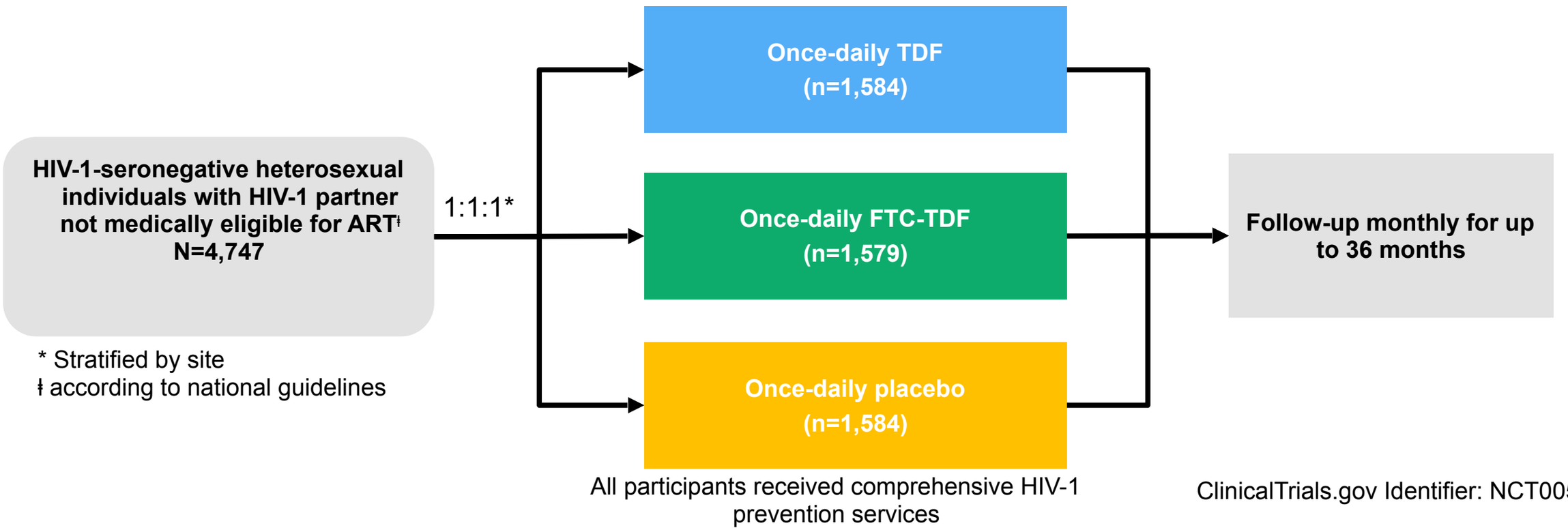
No resistance to FTC or TDF was detected among these individuals

Once-daily oral FTC/TDF provided 44% additional protection from HIV among MSM who received a comprehensive package of prevention services

Grant RM & al. *N Engl J Med* 2010; 363:2587-99

Partners PrEP

Randomised, double-blind, placebo-controlled study in Africa (Kenya and Uganda)



ClinicalTrials.gov Identifier: NCT00557245

- **Study objective**: to determine whether once-daily use of FTC/TDF vs placebo can decrease the acquisition of HIV-1 infection in 4,747 serodiscordant heterosexual couples
- **Primary endpoints**: incidence of HIV-1 seroconversion among HIV-1-negative participants, adherence
- **Secondary endpoints**: safety, sexual behaviour, resistance development, sexual transmitted infections (STI)

Baeten JM et al. *N Engl J Med* 2012;367:399-410

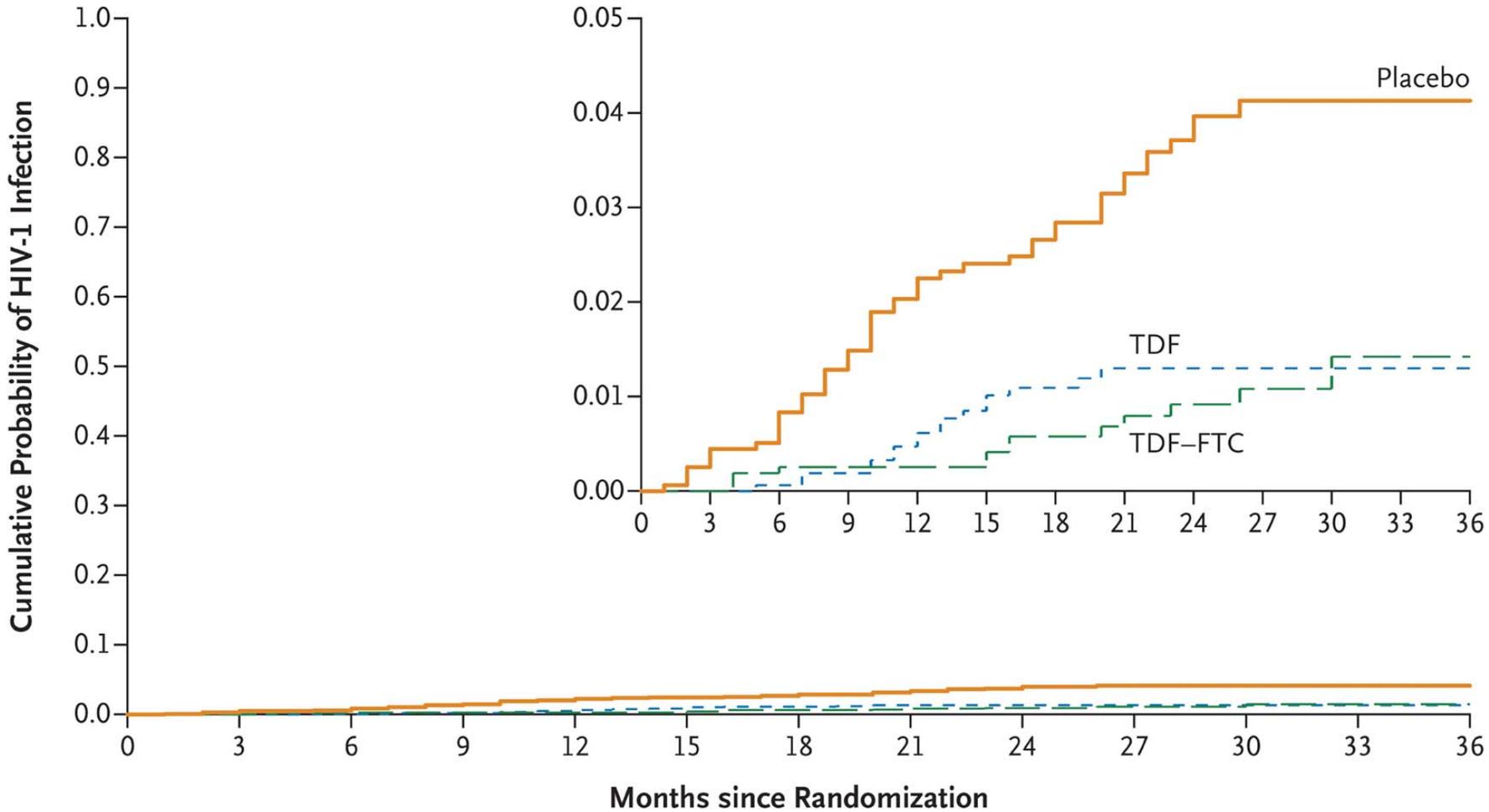
TDF is not licensed for PrEP

Efficacy results

Of the **82** incident infections:

- **17** occurred in TDF group
- **13** in the FTC/TDF group
- **52** in the placebo group

Kaplan–Meier Estimates of the Primary End Point in the Modified ITT Analysis, according to study treatment.



No. at Risk													
TDF	1572	1559	1547	1498	1350	1223	1062	902	735	510	287	108	15
TDF–FTC	1568	1557	1546	1493	1371	1248	1059	901	743	525	291	114	16
Placebo	1568	1557	1544	1487	1347	1224	1061	902	744	523	295	120	18

TDF and FTC/TDF were efficacious in preventing HIV-1 acquisition among negative individuals part coupled with an HIV-1 positive partner

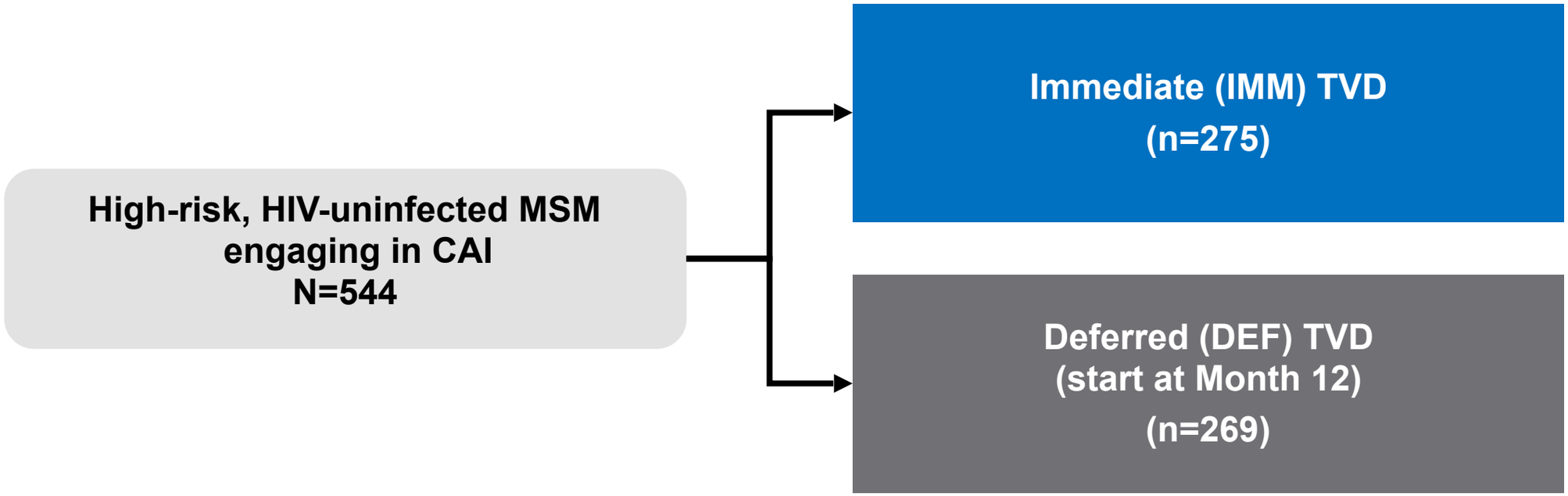
Baeten JM et al. *N Engl J Med* 2012;367:399-410

TDF is not licensed for PrEP

PROUD: Pragmatic Open-Label Randomized Trial of Pre-Exposure Prophylaxis

PROUD

Randomised, multicentre, open-label pilot study in the UK



ClinicalTrials.gov Identifier: NCT02065986

All subjects received comprehensive HIV prevention services, including condoms, risk-reduction counseling, testing and treatment for sexually transmitted infections, and HIV pre- and post-test counseling

Primary endpoint: HIV seroconversion between randomisation and Month 12

Secondary endpoints: Safety, adherence, sexual behavior, resistance development

Oct 2014: the PROUD Trial Steering Committee announced that participants on the deferred arm of the study, who had not yet started PrEP, would be offered the opportunity to begin PrEP ahead of schedule

McCormack S. & al. *Lancet* 2016;387,53-60

CAI: Condomless anal intercourse

Efficacy results

HIV Incidence

Group	Infections, n	Follow-up (PY)	Incidence/100 person-years (90% CI)
Overall	23	465	- *
Immediate	3	243	1.2 (0.4-2.9)
Deferred	20	222	9.0 (6.1-12.8)

* The overall incidence was 4.9 infections/100 person-years, 90%CI (3.4-6.8) at 1st communication in McCormack S, et al. CROI 2015; Seattle, WA. #22LB

- Use of post-exposure prophylaxis by arm:
  - IMM: 12 subjects (4.4%); 14 prescriptions
  - DEF: 85 subjects (31.5%); 174 prescriptions

86% (90% CI: 64-96) Relative Risk Reduction; *p*=0.0001

Number needed to treat to avert one HIV infection = 13 (90% CI: 9-23)

McCormack S. & al. *Lancet* 2016;387,53-60

‡

IPERGAY

Randomised, multicentre, double-blind study in France and Québec

High-risk, HIV-uninfected MSM with Condomless anal sex with ≥2 partners within 6 months
N=400

eGFR > 60 mL/min

« On-demand » TVD (n=199)

« On-demand » TVD placebo (n=201)

All participants received a package of preventative measures:
- counseling
- repeated HIV testing
- screening & treatment for other STIs
- HBV and HAV vaccination
- condoms and gel

"On-demand" regimen constitutes:
- 2 TVD or 2 placebo 2 - 24 hrs prior to sexual intercourse exposure
- 1 TVD or placebo 24 hrs after first intake
- 1 TVD or placebo 48 hrs after first intake

Primary endpoint: HIV seroconversion

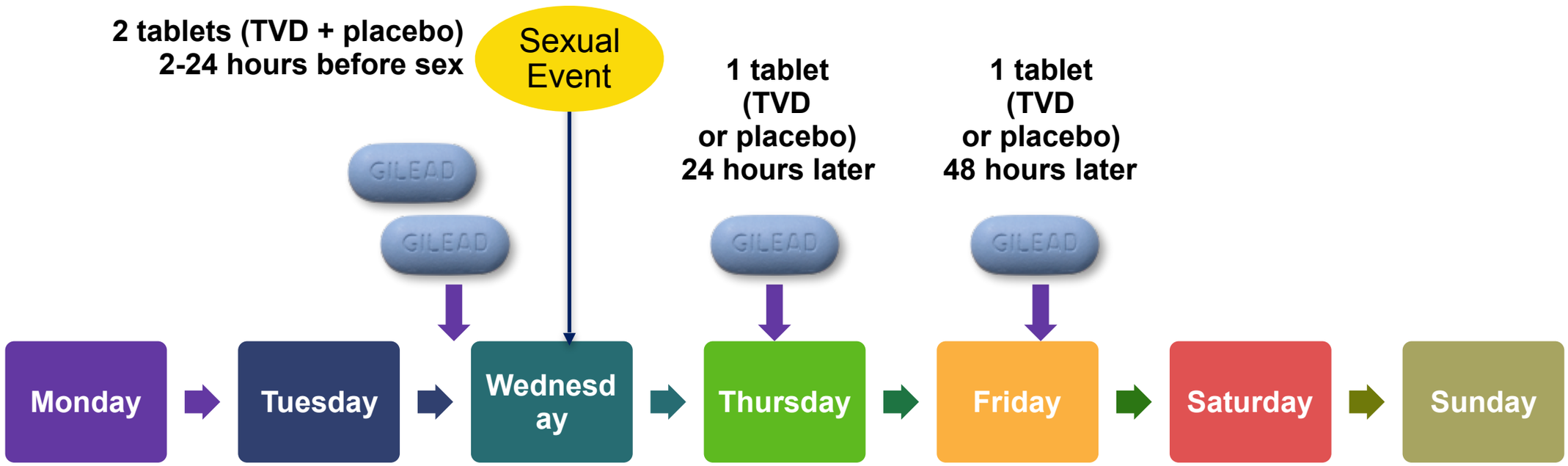
Secondary endpoints: Sexual behavior, safety events, adherence

Oct. 2014, the DSMB recommended that the placebo arm be discontinued and patients be offered switching into the treatment arm.

Molina JM et al. CROI 2015; Seattle, WA. #23LB
Molina JM & al. *N Engl J Med* 2015;373,2237-46

FTC/TDF is only licensed as a daily dosage for PrEP

Event-driven PrEP



- IPERGAY results provide the first evidence that an event-driven regimen was effective among high-risk MSM with frequent sex (median of 10 sex acts per month and 8 partners every two months).
  - In this study overall, available data suggest that men were taking PrEP an average of three to four days per week.
- CDC cautions that researchers do not yet know if this regimen will work among MSM who have sex less frequently or among other populations at high risk for HIV infection.
- CDC continues to recommend daily dosing of PrEP and urges people at substantial risk for HIV infection and their health care providers to continue to follow current CDC guidelines

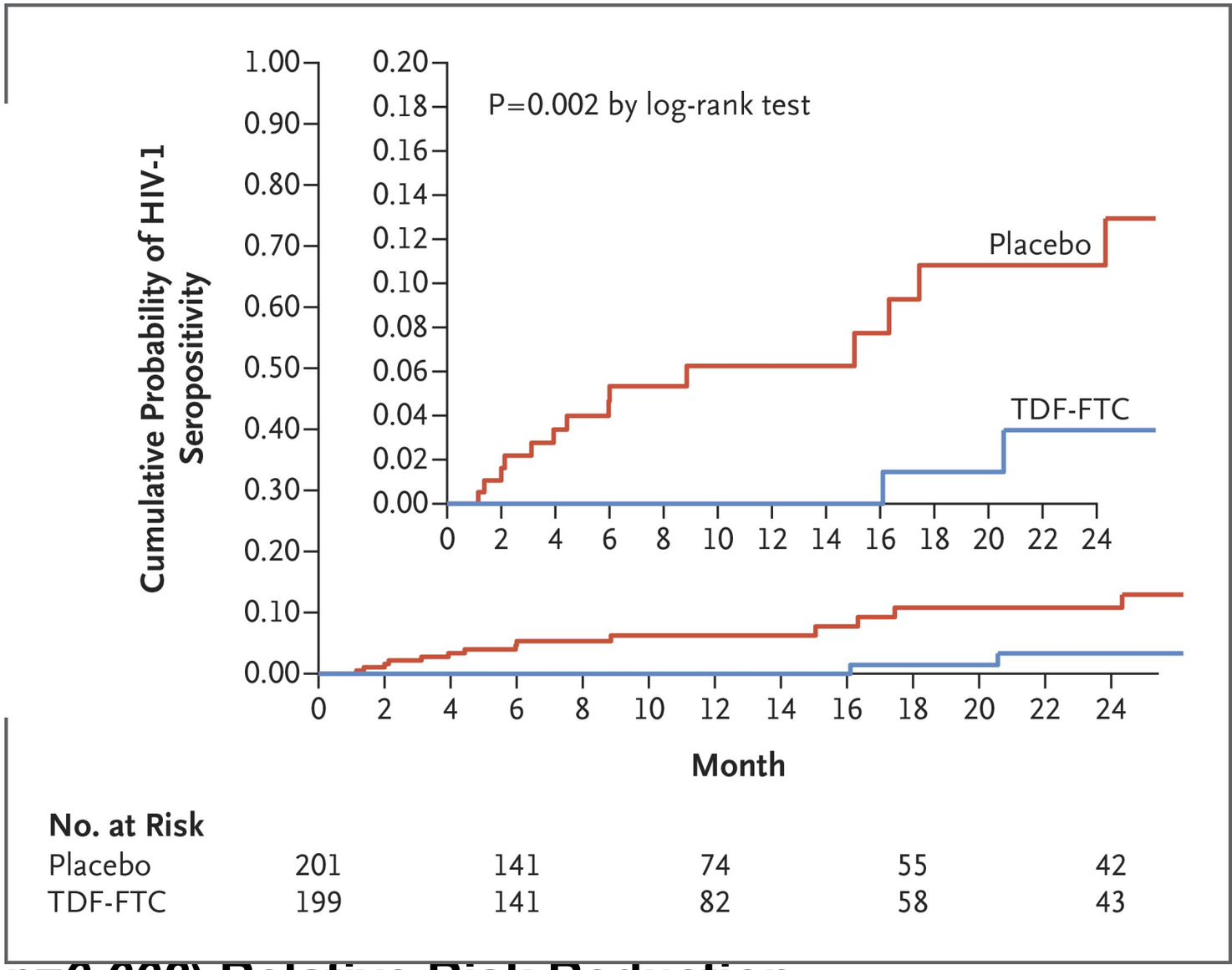
Molina JM et al. CROI 2015; Seattle, WA. #23LB
Molina JM & al. *N Engl J Med* 2015;373,2237-46
http://www.cdc.gov/nchhstp/newsroom/2015/IPERGAY-2015-Media-Statement.html

FTC/TDF is only licensed as a daily dosage for PrEP

Efficacy results

- **16 subjects infected**
  - **Placebo = 14** (incidence: 6.60/100 PY)
  - **FTC/TDF =2** (incidence: 0.91/100 PY)
- Mean follow-up= **9.3 months** (IQR 4.9-20.6)
- Average **15 pills / month**
  (TVD : IQR 11-21; PBO : IQR 9-21)
- 56 subjects received post-exposure prophylaxis :
  - PBO = 25
  - TVD = 31

p=0.37

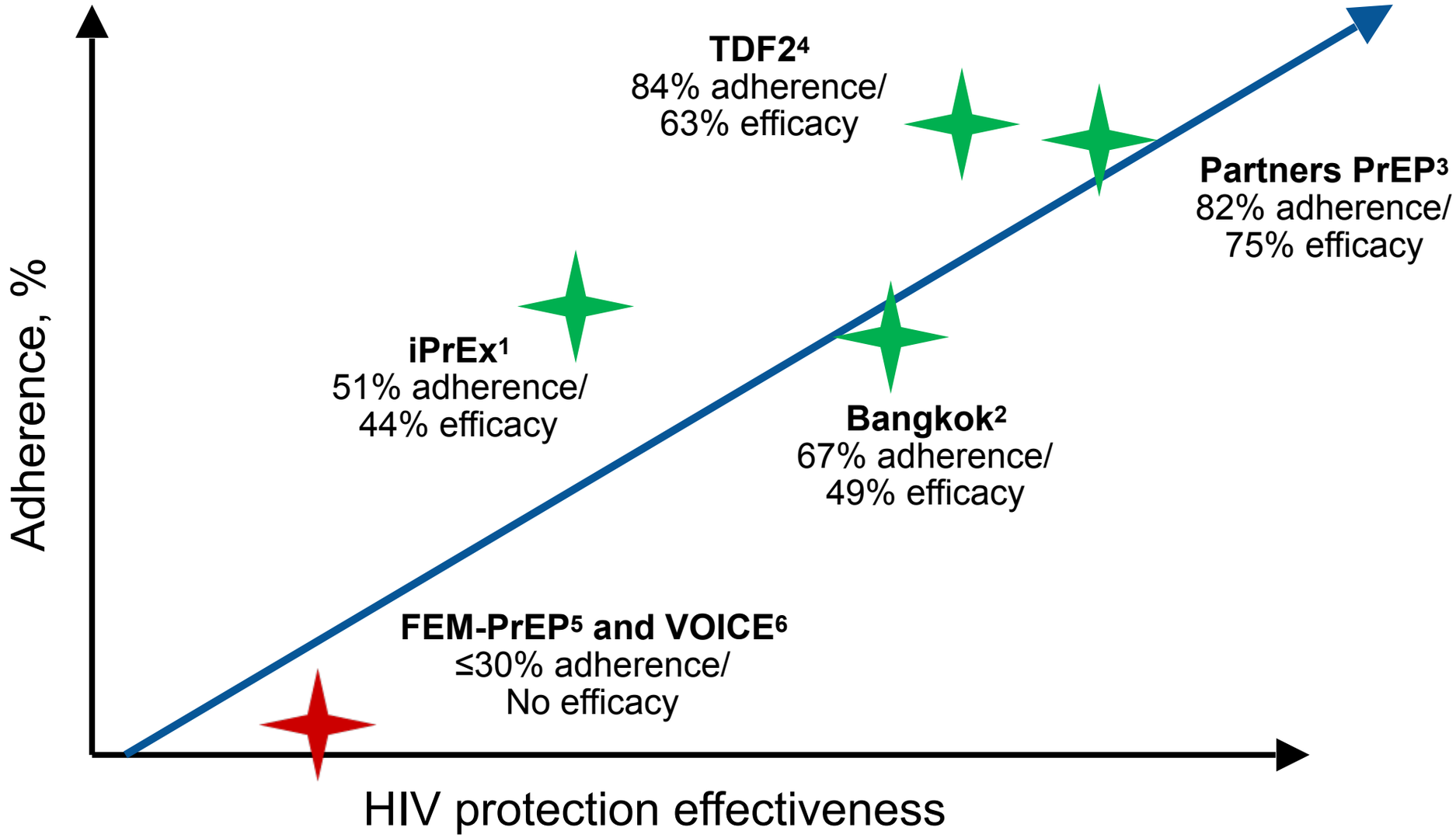


86% (95% CI: 40-98, *p=0.002*) Relative Risk Reduction
Number needed to treat for 1 year to avert 1 HIV infection: 18 (95% CI : 11-50)

Molina JM et al. CROI 2015; Seattle, WA. #23LB
Molina JM & al. *N Engl J Med* 2015;373,2237-46

FTC/TDF is only licensed as a daily dosage for PrEP

PrEP: Better adherence correlates with higher efficacy

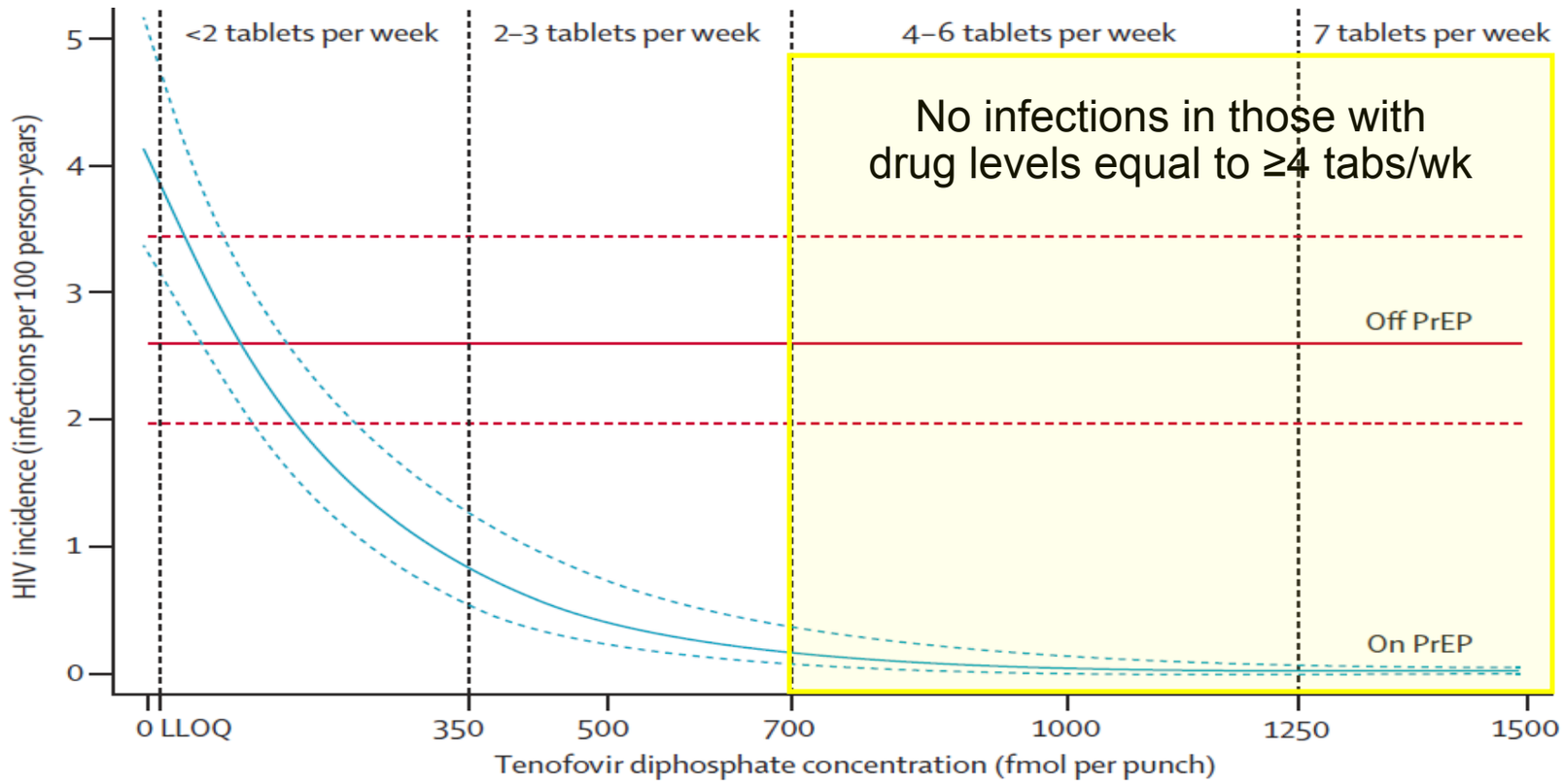


Trials where the majority of subjects were adherent demonstrated HIV protection, with higher protection estimates when more of the population was adherent

1. Grant R, et al. *N Engl J Med* 2010;363:2587-99. 2. Choopanya K, et al *The Lancet*. June 13, 2013. 3. Baeten J, et al. *N Engl J Med* 2012;367:399-410. 4. Thigpen M, et al. *N Engl J Med* 2012;367:423-34. 5. Van Damme L, et al. *N Engl J Med* 2012;367:411-22. 6. Van der Straten A, et al. *AIDS* 2012;26(7):F13-F19

HIV incidence & drugs concentrations in MSM

Modeling data from subjects in randomized placebo-controlled iPrEx, ATN 089, or US PrEP safety trials were enrolled in the 72-week open label extension (iPrEx OLE)



Drug Concentration	none	<2 pills/week	2-3 pills/week	≥ 4 pills/week	7
HIV Incidence per 100 PY (95%CI)	*4.7 (2.99-7.76)*	*2.25 (1.19-4.79)*	*0.56 (0.00-2.50)*	*0*	
Risk Reduction (95%CI)		*44% (-31-77)*	*84% (21-99)*	***100% (86-100***	

The recommended dose of TVD for PrEP in HIV-1 uninfected adults is one tablet once daily taken orally with or without food[3]

1. Grant RM, et al. Lancet ID 2014;14(9):820-829
2. Grant RM et al. AIDS 2014, TUAC0105LB
3. EMA Truvada SmPC, September 2016

Seroconversion rates in demonstration projects
(July 2012 to May 2016)

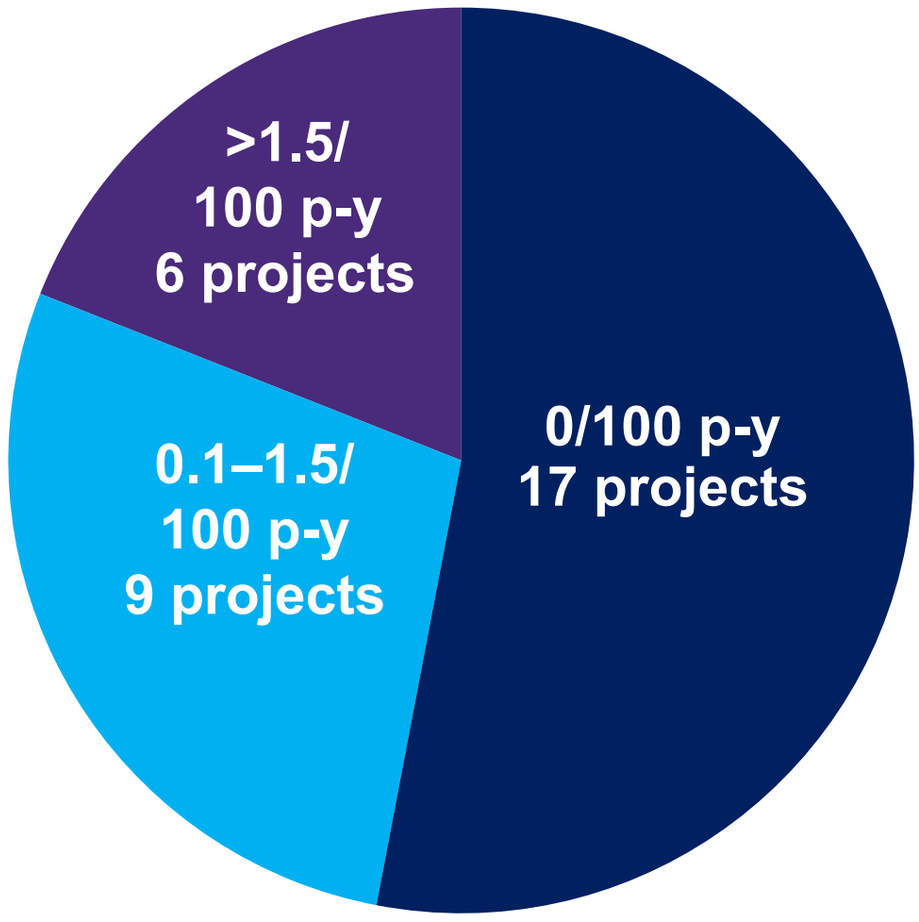
32 individual studies of FTC/TDF for PrEP

- 8,478 participants:
  - 7,002 men
  - 1,388 women
  - 76 transgender
- 7,061 cumulative person-years of FTC/TDF exposure

Results

- 67 HIV-1 seroconversions
- 0.95/100 p-y seroconversion rate (95% CI: 0.74, 1.21)

Seroconversion Rates From 32 Projects



IPERGAY control arm: 6.6/100 p-y
PROUD control arm: 9/100 p-y

Mera, R. AIDS 2016. Durban, South Africa. Oral #TUAX0105LB
McCallister, ASM Microbe 2016, Abs 371LB

‡

Characteristics of seroconverters in demo projects

Seroconversion Rates By Sex/Gender

	Men n=7002	Women n=1388	Transgender Women* n=76
Total exposure, p-y	6214	788	48
Number of HIV-1 seroconversions	64	2	1
Rate/100 p-y (95% CI)	**1.03** (0.80-1.32)	**0.25** (0.03-0.92)	**2.07** (0.05-11.52)

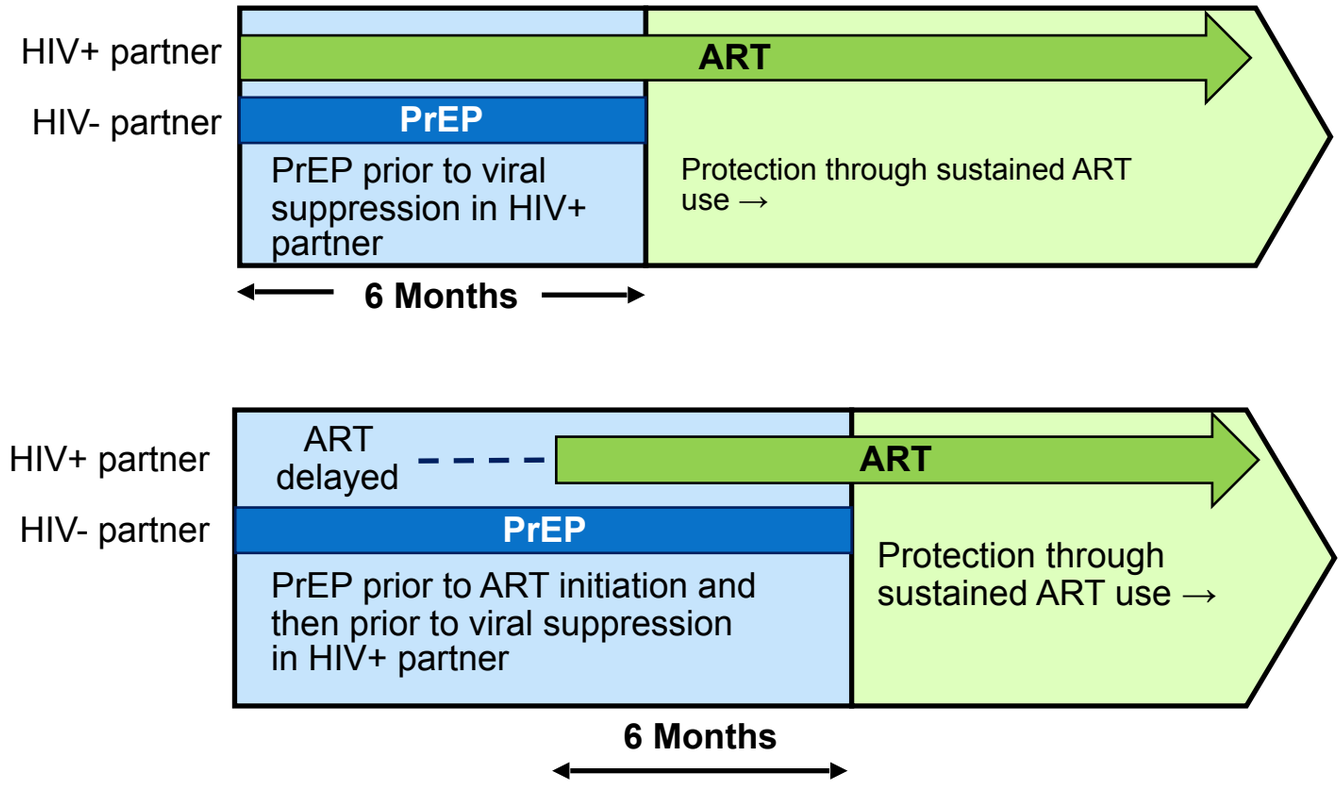
Mera, R. AIDS 2016. Durban, South Africa. Oral #TUAX0105LB
McCallister, ASM Microbe 2016, Abs 371LB

‡

PrEP + TasP for HIV serodiscordant couples

Open-label, prospective interventional study of integrated ART and PrEP delivery for HIV prevention among N=1013 heterosexual high risk HIV serodiscordant couples

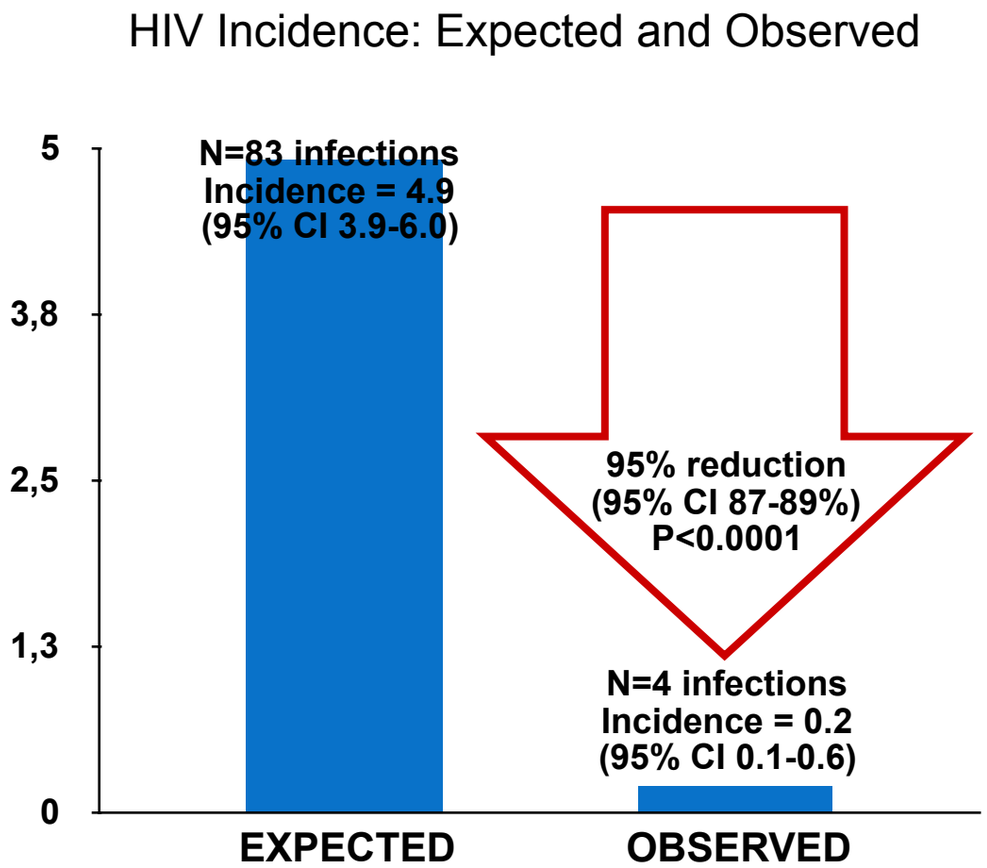
- Residual risk of HIV-1 transmission can continue for the first 6 months of ART, prior to viral suppression
- For couples initiating ART at enrollment, PrEP is offered through 6 months, then stopped
- Couples in which the infected partner delays or declines ART, PrEP is continued until 6 months after ART initiation



PrEP is offered as a 'bridge' for the first 6 months after ART initiation by the HIV-infected partner

Mujugira A, et al. CROI 2015; Seattle, WA. #989
Baeten J, et al. AIDS 2016. Durban, South Africa. Oral #WEAC0105

Integrated delivery of PrEP and ART: sustained near elimination on HIV transmission in African HIV serodiscordant couples



4 incident HIV seroconverters :

- No TFV detected in plasma (n=3) or PrEP declined (n=1)
- No resistance for TFV or FTC

- **Integrated delivery of ART and PrEP in HIV serodiscordant couples demonstrated,**
  - **95% reduction in observed HIV incidence compared to expected**
  - **time-limited PrEP as a bridge to ART is feasible and highly effective in preventing HIV transmission**

Baeten J, et al. AIDS 2016. Durban, South Africa. Oral #WEAC0105

Renal and bone safety

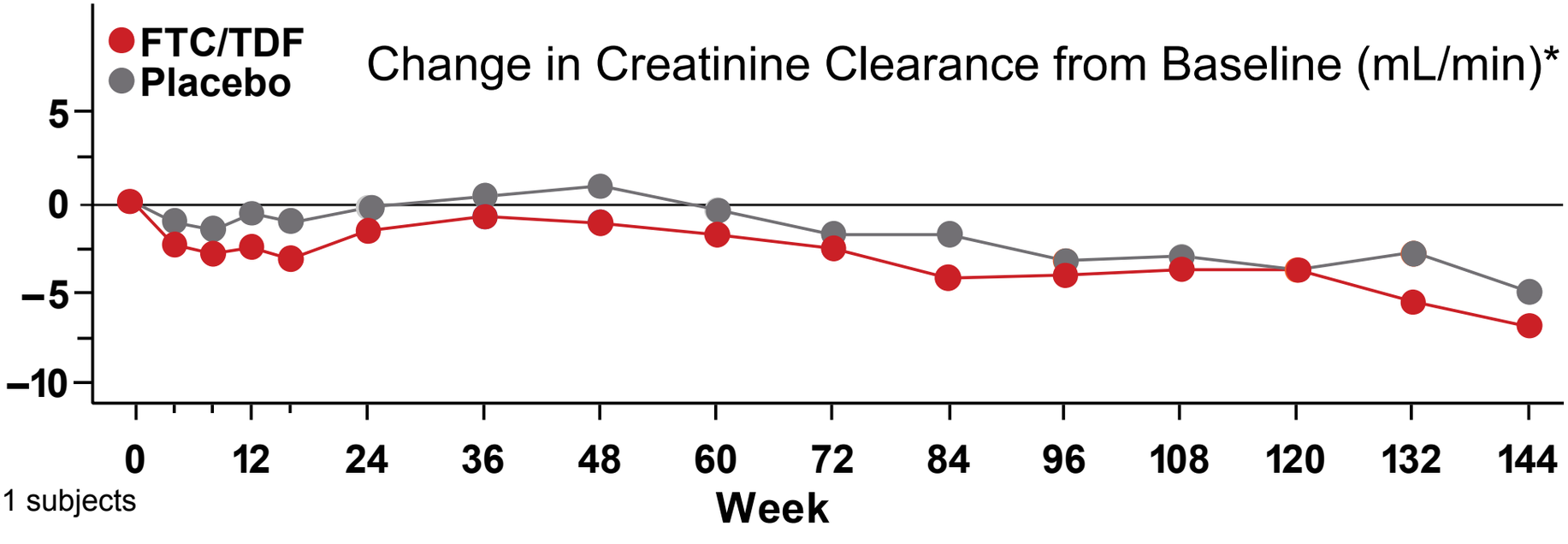
‡

Renal Safety

Renal safety assessment of 2499 HIV-negative subjects in iPrEx study

- A mild, non-progressive decrease in creatinine clearance (Cockcroft-Gault), that was reversible and readily managed with routine monitoring
  - Did not vary by race, age, or HTN history
  - Affected by NSAID use
    - -3.4 mL/min (+NSAID) vs. -0.3 mL/min (no NSAID), *p* = 0.04

Mean Change in CrCL (mL/min)	TVD	Placebo	*p-value*
Wk 4	-2.4	-1.1	0.02
Last visit on treatment	+0.3	+1.8	0.02
Post stopping treatment	-0.1	0.0	0.83



* in 1,131 subjects

Solomon M, et al. *AIDS* 2014;28(6):851-9

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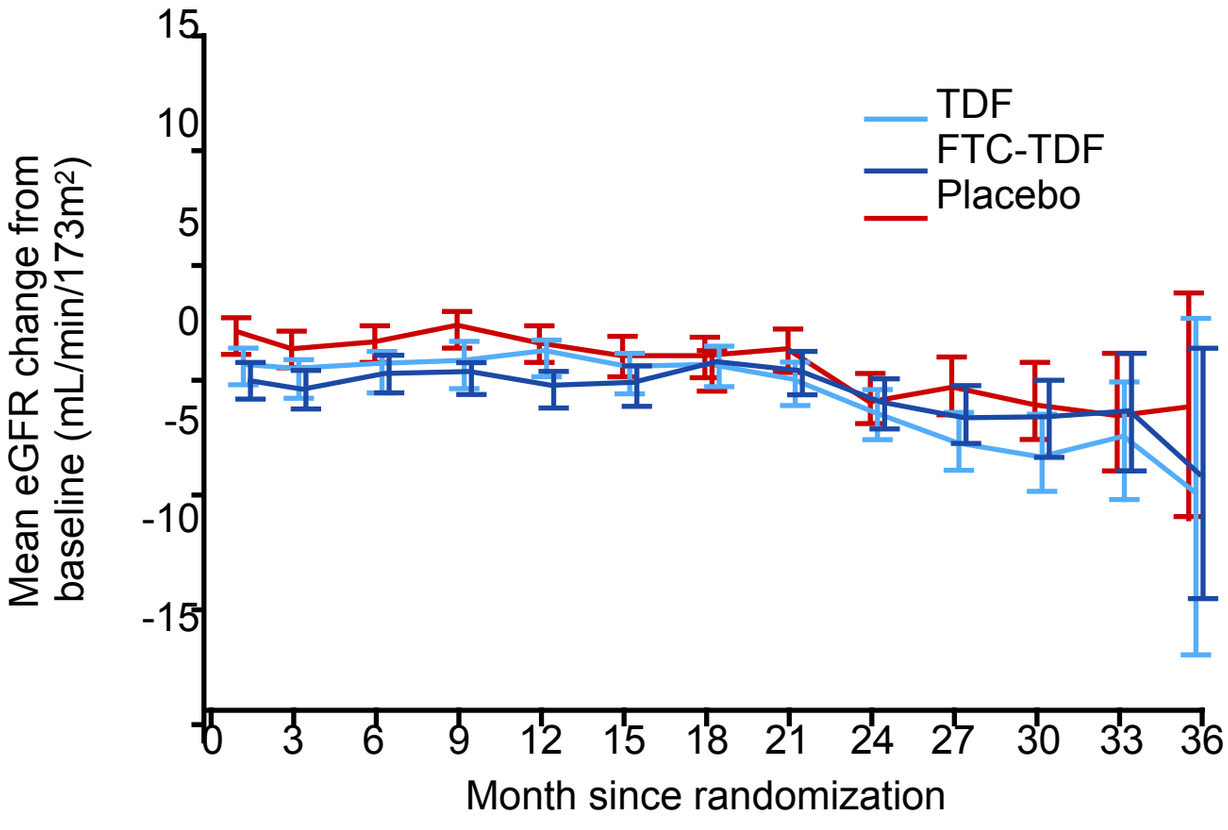
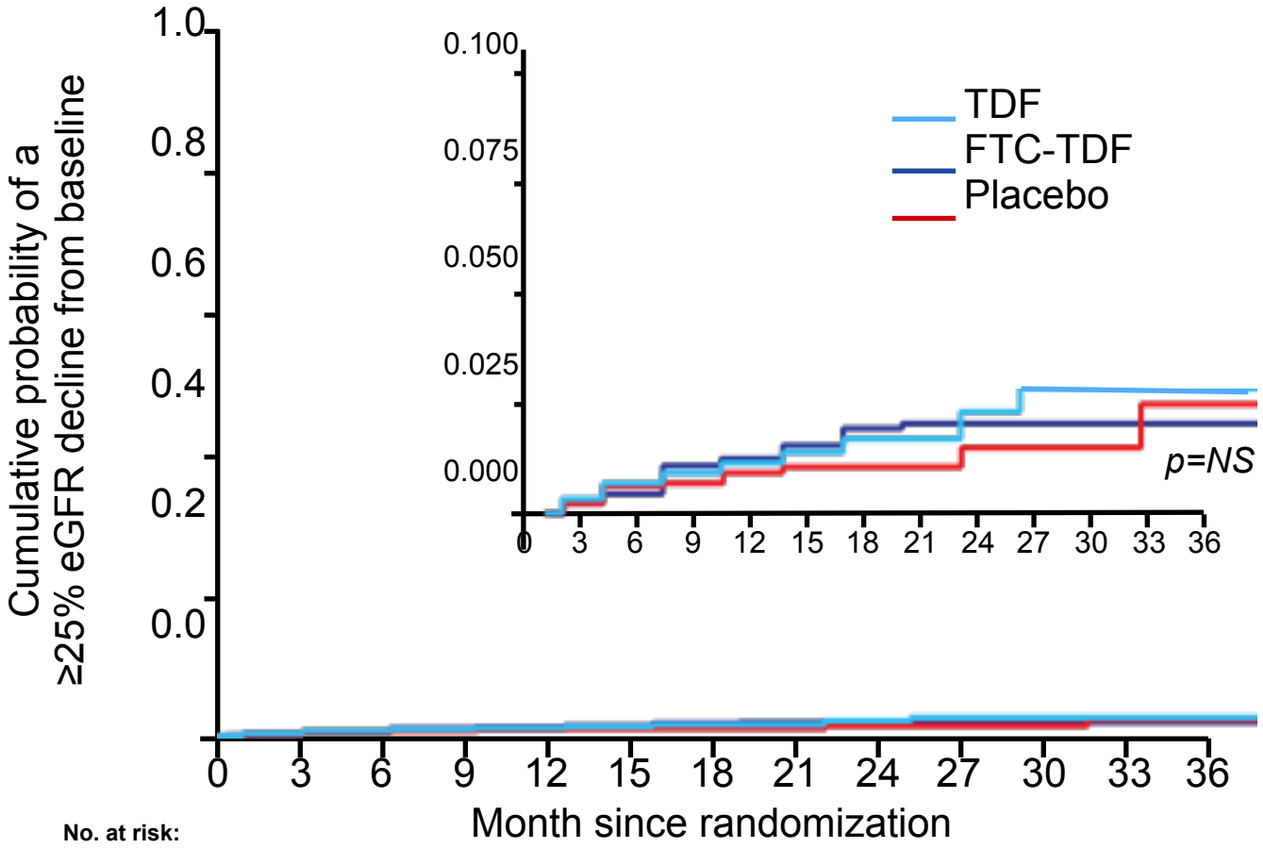
Renal safety

Variation over time in crude mean eGFR change from baseline, according to treatment group



TDF	1568	1523	1495	1443	1307	1187	1029	872	717	502	286	107	15
FTC-TDF	1558	1522	1498	1448	1334	1204	1029	870	727	516	288	112	16
Placebo	1570	1530	1511	1446	1317	1190	1037	885	737	516	295	119	18

Cumulative probability of a ≥25% eGFR decline from baseline, according to study treatment



No. at risk:

TDF	1548	1479	1399	1305	1146	1019	872	724	579	400	237	86	10
FTC-TDF	1545	1491	1420	1326	1191	1063	893	740	602	420	235	89	12
Placebo	1547	1480	1409	1311	1166	1039	893	752	613	425	233	97	16

- **Both TDF** (-1.23mL/min/1.73m², 95%CI, -2.06 to-0.40, p=0.004) **and FTC/TDF** (−1.59 mL/min/1.73m², 95%CI, −2.44 to −0.74; P < .001) **were associated with significant decline in eGFR vs placebo after a median follow-up of 18 months**
- **The difference in mean eGFR between PrEP and placebo appeared by 1 month after randomisation and was stable through 12 months**

FTC/TDF as PrEP resulted in a small but non-progressive decline in eGFR

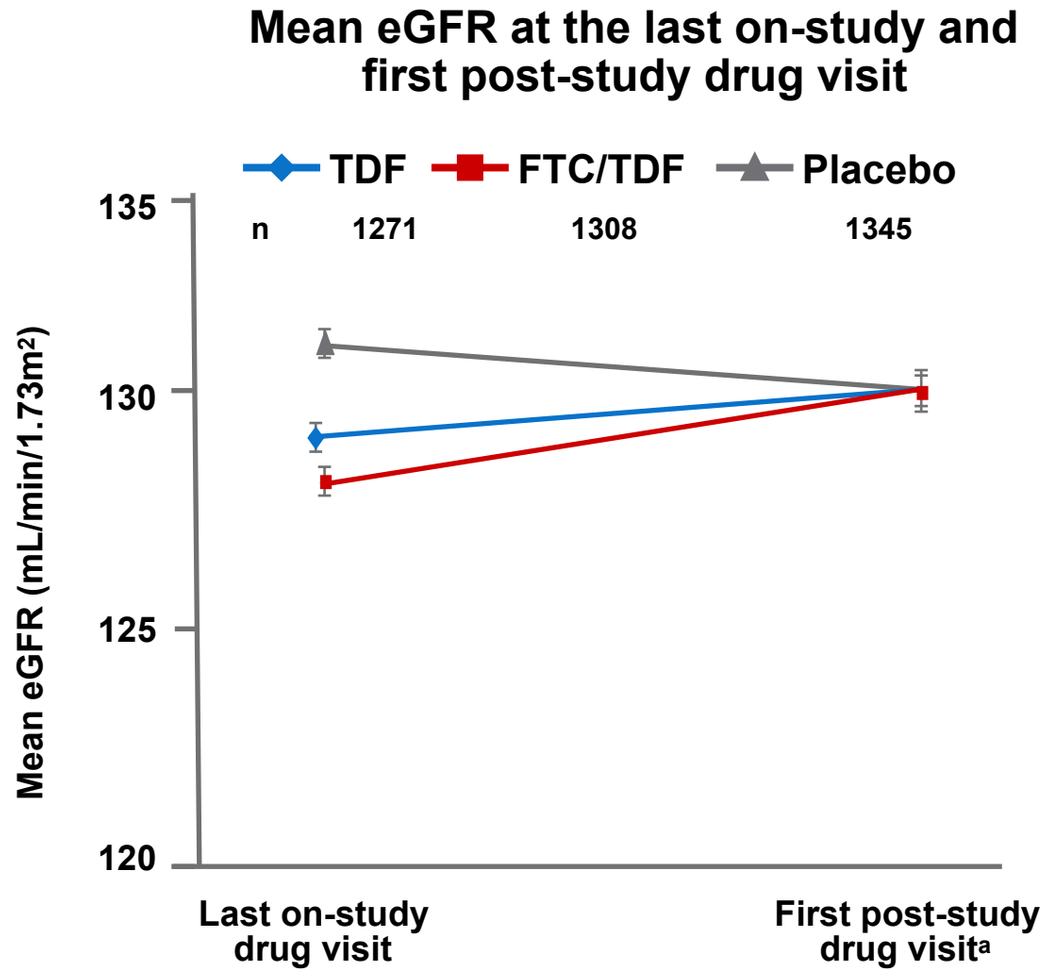
Mugwanya K et al. *JAMA* Intern Med 2015;175(2):246–254

TDF is not licensed for PrEP

Decline in eGFR resolves within weeks of discontinuing TDF or FTC/TDF for PrEP

- Phase 3, randomised trial of daily oral TDF PrEP vs. FTC/TDF PrEP vs. PBO among African HIV-negative men and women (N=4747) with normal baseline renal parameters
  - SCr was assessed quarterly while on study medication, and at 2 monthly visits after d/c
  - eGFR was calculated using CKD-EPI[a]

- **Mean eGFR was 2-3 mL/min lower on PrEP vs. PBO (*P*<0.01) at first post-study drug visit**
- **>96% of participants had >75% eGFR reversion to baseline levels by 8 weeks of study drug discontinuation**



[a] Chronic Kidney Disease Epidemiology Collaboration Equation.
[b] Median time from the last on-study drug visit to the first post-study drug visit was 4 weeks (IQR: 3 - 5), which was similar across treatment groups.

Mugwanya, K. CROI 2015, Seattle, WA #981

TDF is not licensed for PrEP

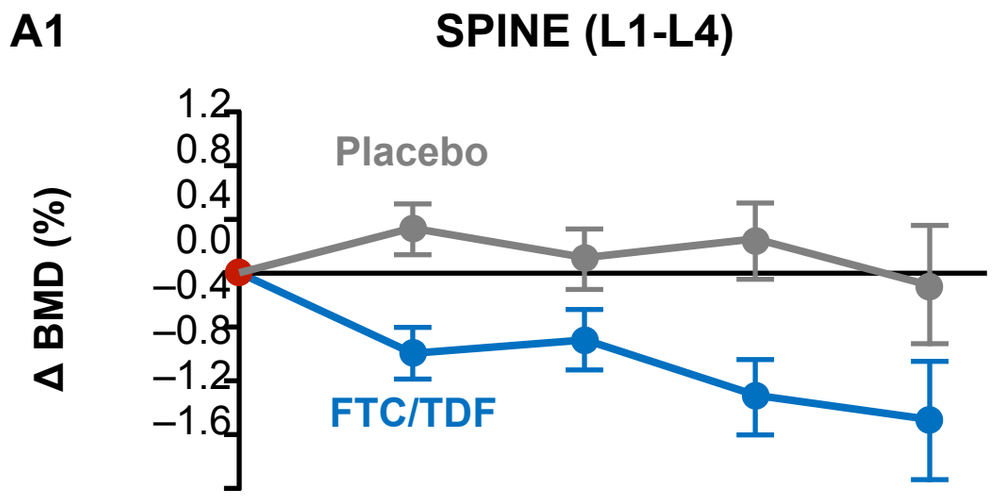
Renal Monitoring for PrEP

- It is recommended that estimated creatinine clearance be assessed in all individuals prior to initiating therapy and as clinically appropriate during therapy with FTC/TDF:
  - **FTC/TDF should only be used in individuals with creatinine clearance (CrCl) <80 mL/min if the potential benefits are considered to outweigh the potential risks.**
  - **Do not use FTC/TDF in HIV-uninfected individuals for PrEP if CrCl is below 60 mL/min**. If a decrease in CrCl is observed in uninfected individuals while using FTC/TDF for PrEP, evaluate potential causes and re-assess potential risks and benefits of continued use.
- Renal impairment, including cases of acute renal failure and Fanconi syndrome, has been reported in association with the use of TDF
- FTC/TDF should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high-dose or multiple NSAIDs)

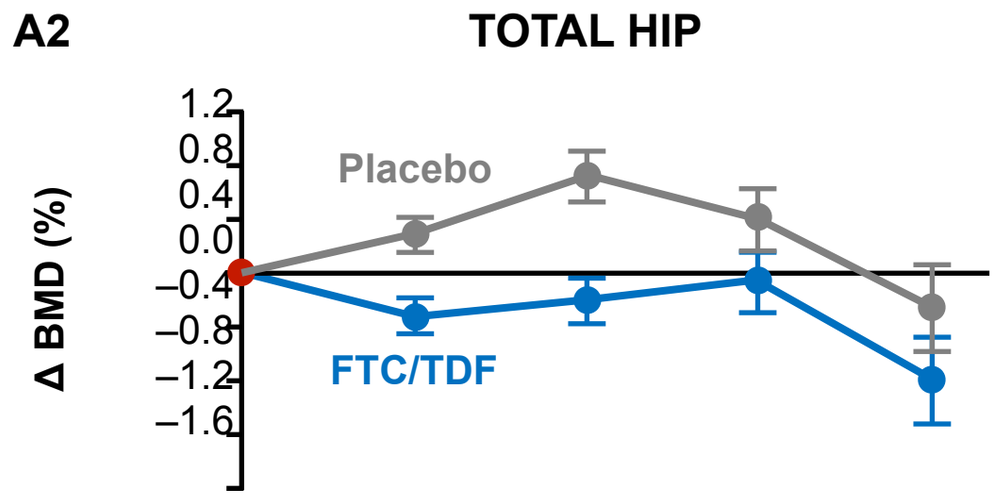
TRUVADA EU SmPC, August 2016.

Change from baseline in bone mineral density (BMD)

Changes from baseline in BMD during treatment in the spine and hip



Week	0	24	48	72	96
N Placebo	251	211	168	112	56
N FTC/TDF	247	210	165	107	55
pvalue		.001	.064	.004	.111



Week	0	24	48	72	96
N Placebo	251	211	167	112	56
N FTC/TDF	245	207	162	105	55
pvalue		.001	<.001	.176	.246

A decrease in BMD was observed for both spine (p=0.001) and hip (p=0.001) in the FTC/TDF group vs placebo within 24 weeks

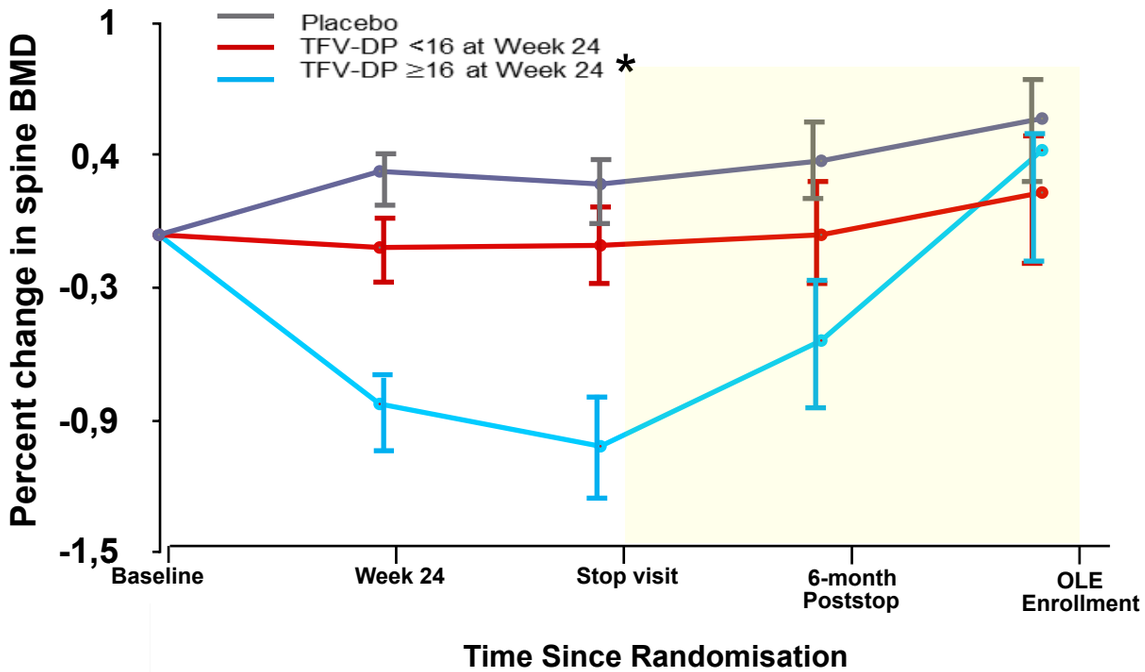
There were no differences in bone fractures between the FTC/TDF and placebo groups (p=0.62)

DEXA, dual-energy X-ray absorptiometry
Mulligan K et al. *Clin Infect Dis* 2015;61(4):572–580

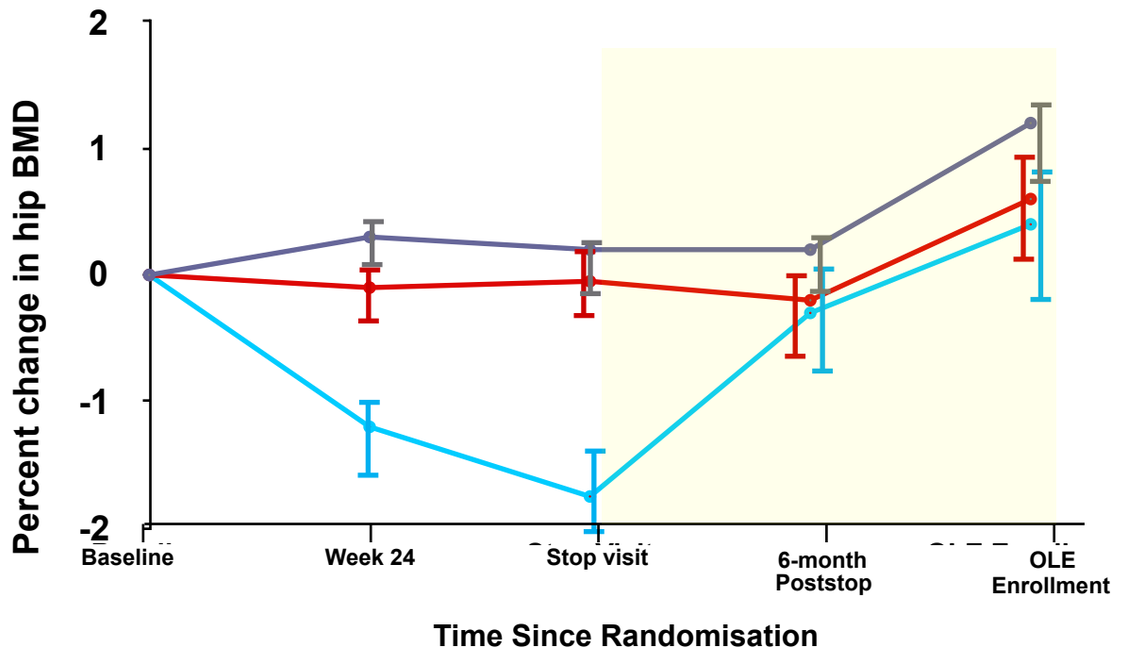
Bone mineral density (BMD) extension study

498 MSM and TGW, BMD measured every 24 weeks during the iPrEx study, 24 weeks after stopping PrEP and at the beginning of the iPrEx open-label extension (OLE)

Change in spine BMD from iPrEx enrolment



Change in hip BMD from iPrEx enrolment



* Drug concentration in PBMCs to evaluate adherence. (fmol/M viable PBMCs)

16 fmol/M viable PBMCs is the TDF concentration associated with a 90%-reduction in HIV infection risk (EC_{90})

- **BMD recovered (to placebo levels) by 6 months in spine when TVD discontinuation**
- **BMD recovered completely by enrolment in iPrEx OLE (median 73 weeks) in both spine and hip**

Grant R et al. CROI 2016, Boston, MA, Oral #48LB: http://betablog.org/9038-2/ (accessed June 2016)

‡

BMD changes in 18-24yo MSM after discontinuing TVD PrEP

Extension Phase (EPH)

- DXA scans at 48 weeks after discontinuing PrEP study, i.e. 48 weeks on FTC/TDF followed by 48 weeks off FTC/TDF
- N=72 individuals followed-up through the EPH

BMD change (mean)	From BL to Wk 48 (on FTC/TDF)	From Wk 48 to end of EPH (off FTC/TDF)	Overall change from BL to end of EPH
Hip	**-1.43%***	**+1.02%***	-0.35%
Whole Body	**-0.63%***	**+0.64%***	-0.11%
Lumbar Spine 1-4	-0.25%	**+1.15%***	**+0.87%***

***p<0.05**

- **There is evidence of impact on bone density caused by exposure to TDF/FTC used as PrEP over 48 weeks in 18-22 year old males**
- **Discontinuation of exposure to TDF/FTC leads to a trend to recovery of bone density changes over a 48 week follow-up period**

Mulligan K, et al. AIDS 2016, Durban, South Africa. Oral #WEAC0305LB

Risk compensation

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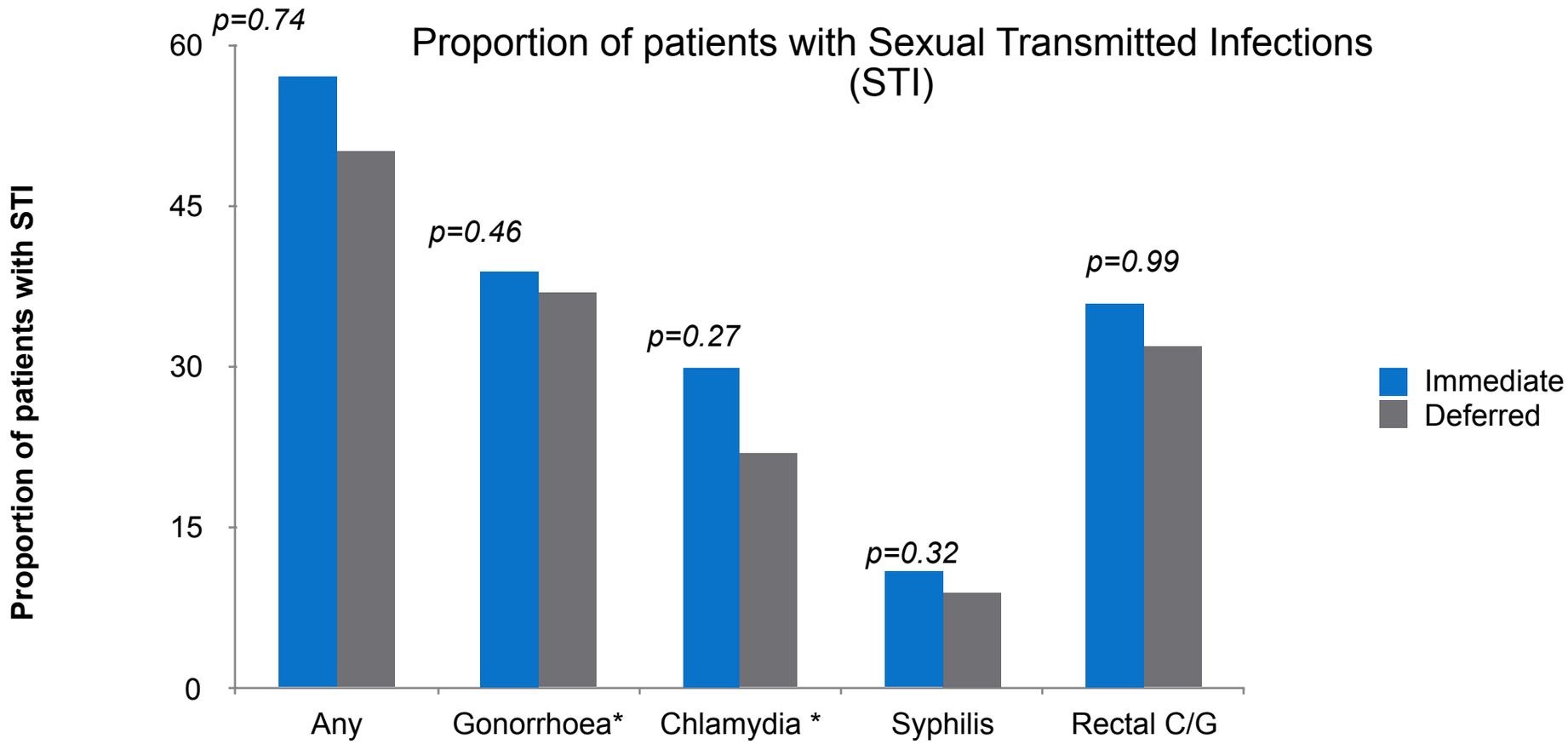
Risk compensation



- **The proportion of sexually transmitted infections did not differ significantly between groups** despite a suggestion of risk compensation among a small proportion of PrEP recipients.
- However, the number of screens differed between groups, eg. rectal C/G :
  - 974 in immediate arm
  - 749 in deferred arm
- 6 incidents Hepatitis C (3 in each group)

STI, Sexuallly Transmitted Infections
C/G Chlamydia or Gonorrhoea
* Detected in throat, urethra or rectum

McCormack S, et al. CROI 2015; Seattle, WA. #22LB
McCormack S. & al. PROUD_Lancet 2016;387,53-60

‡

HIV incidence (mITT analysis), adherence and sexual behavior

	Open-label	Double-blind	
	FTC/TDF	FTC/TDF	PBO
HIV Incidence per 100py (95%CI)	**0.19** (0.01-1.08)	**0.91** (0.11-3.30)	**6.60** (3.60-11.1)
Total Follow-up, py	515	219	212
Median follow-up, months (IQR)	18.4 (17.5-19.1)	9.3 (4.9-20.6)	
Adherence Measures:			
Median pills/month, no. (IQR)	18 (11-25)	15 (11-21)	
Participants with plasma TFV >40ng/ml, %	55	46	
Correct* PrEP use at last sexual intercourse, %	50 *p=0.007*	42	
Sexual Behavior:			
Change in No. reporting condomless AI, %	77→86 (p=0.0003)	No significant change	
Incidence rate of first STI , /100py	40.6	35.2	
Participants with any STI, %	58	37	

*At least one pill 24h before and one pill 24h after sex event

mITT, Modified Intention-to-Treat Population
py, patient years
STI, sexually transmitted infection

On Demand PrEP with oral TDF/FTC remained highly effective in at-risk MSM
97% relative reduction in HIV incidence vs. Placebo

Molina JM, et al. AIDS 2016. Durban, South Africa. Oral #WEAC0102
Molina JM. N Engl J Med 2015; 373:2237-2246.

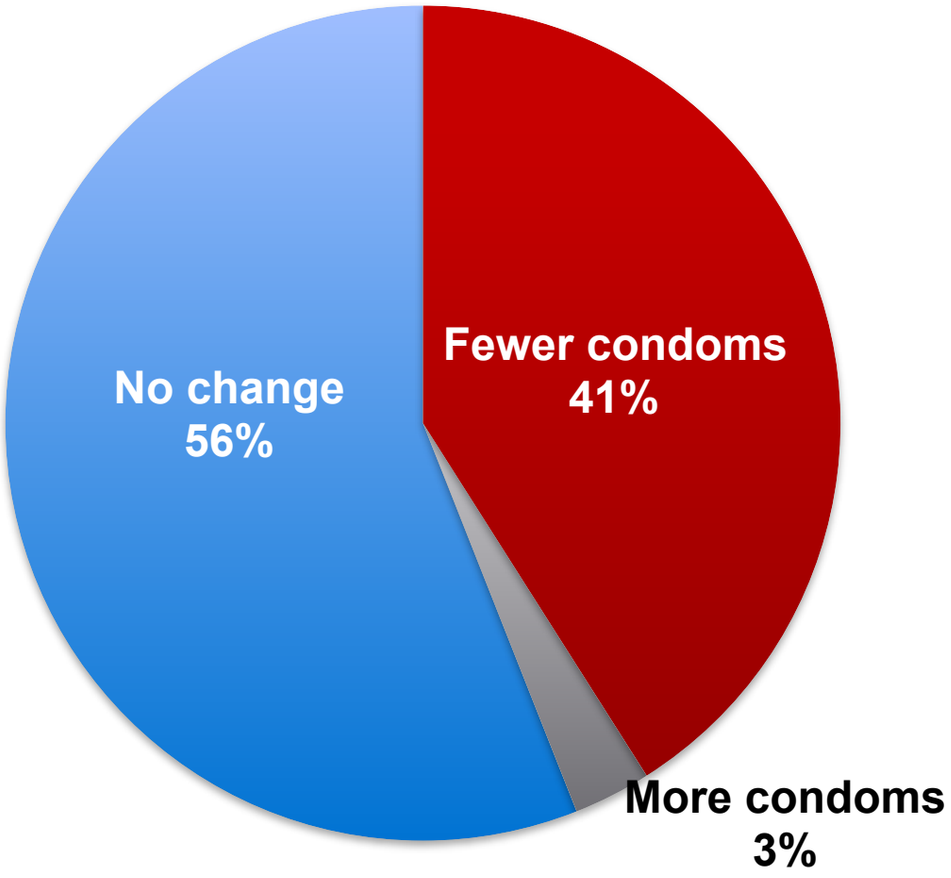
FTC/TDF is only licensed as a daily dosage for PrEP

‡

Behaviour change after starting PrEP

A total of 143 individuals taking PrEP completed a survey relating to use of condoms after 6 months of PrEP use

Changes in reported condom use after starting PrEP (n=143)



No association with:

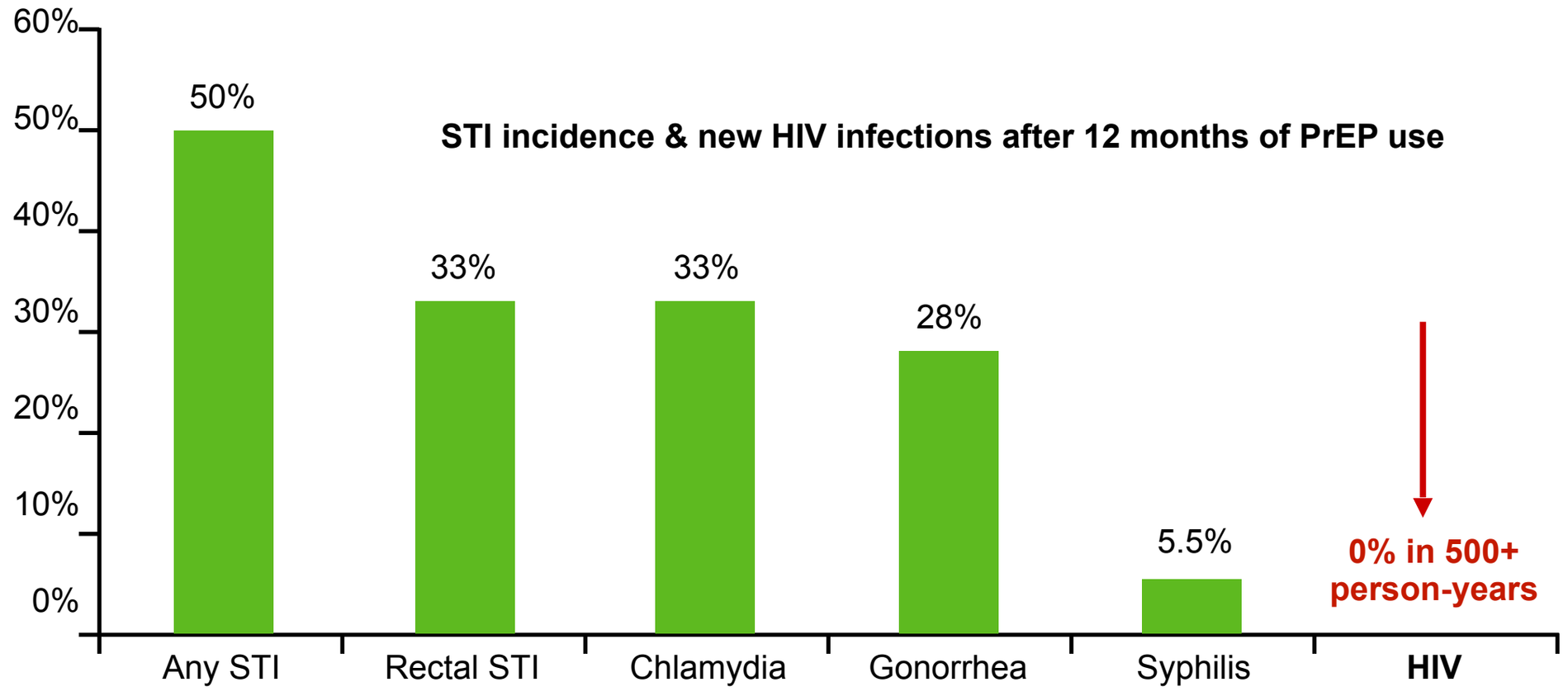
- Age
- STI history
- Condoms 3 months before PrEP use
- HIV-positive partner
- Methamphetamines/cocaine
- Adherence

A decrease in self-reported use of condoms was observed in PrEP users

Volk JE et al. *Clinical Infectious Diseases* 2015;61(10):1601–1603

Incidence of STIs among PrEP users

Cohort of 657 PrEP users (mostly MSM) from 2012–2015 within the Kaiser Permanente integrated healthcare system, San Francisco (US)



- Of those taking part in the study, 187 were diagnosed with at least 1 STI during follow-up, and 78 individuals were diagnosed with multiple STIs
- 2 cases of sexually-acquired HCV

Volk JE et al. *Clinical Infectious Diseases* 2015;61(10):1601–1603

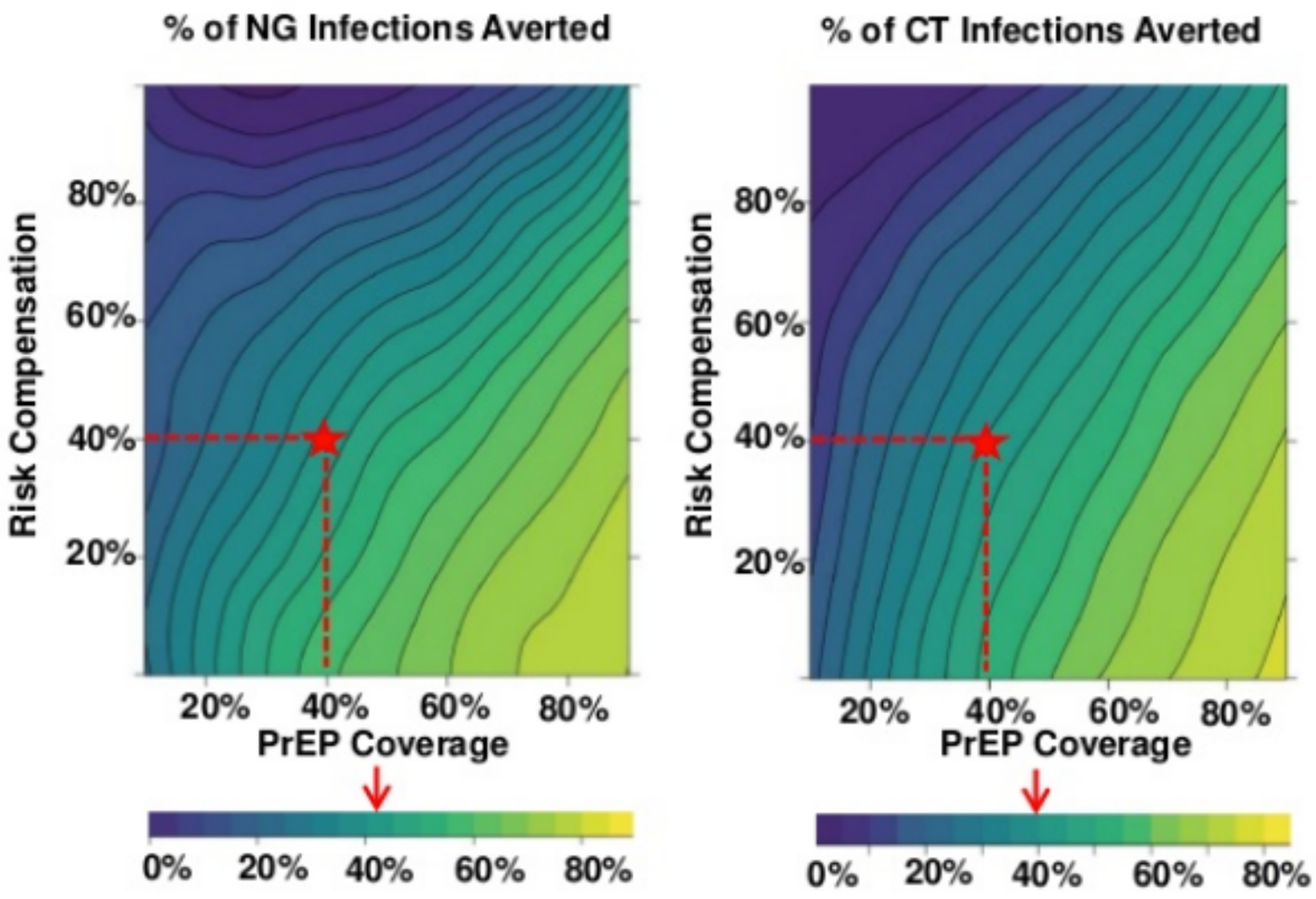
Combining TRUVADA for PrEP with STI Screening Could Decrease STI Rates

Model of co-circulating HIV, gonorrhea (NG), and chlamydia (CT) infections among MSM in the United States based on social networks

Method: TRUVADA indications modeled based on CDC guidelines, adherence based on the PrEP Demo Project, efficacy based on iPrEx.

Results:

- Increased uptake of PrEP coupled with routine STI screening and treatment could lead to strong and sustained declines in gonorrhea and chlamydia incidence and prevalence among MSM
- At 40% TRUVADA coverage and 40% Risk Compensation 42% of GC and 40% of CT infections would be averted over 10 years
- A doubling in risk compensation would still result in net STI prevention relative to no TRUVADA
- Performing STI screening at quarterly vs. biannual intervals would result in a further 50% reduction in incidence



The study suggests that the high STI rates among PrEP users may not be attributable to Risk compensation, and may be a result of selection bias (i.e. higher risk population at baseline combined with more frequent screening).

Jenness SM, et al. CROI 2017. Seattle, WA. Poster #1034

Drug resistance and drug-drug interactions

‡

Drug resistance

	Individuals Uninfected at Baseline Who Acquired HIV-1 on Study, n		Unrecognized Baseline Infections, n	
Study	**HIV Infections**	**Resistant to FTC or TDF**	**HIV Infections**	**Resistant to FTC or TDF**
iPrEx	100 (36 on FTC/TDF, 64 on placebo)	0	10 (2 on FTC/TDF, 8 on placebo)	2 on FTC/TDF (M184V/I); 1 on placebo (M184V/I)
Partners PrEP	65 (13 on FTC/TDF, 52 on placebo)	0	9 (3 on FTC/TDF, 6 on placebo)	1 on FTC/TDF (M184V) 2 on TDF (M184V)

Resistance development to FTC or TDF was more likely to occur when FTC/TDF for PrEP was given during unrecognised/acute infection.

US Public Health Services. Preexposure Prophylaxis For The Prevention Of HIV Infection In The United States, 2014. http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf. Accessed June 13, 2014.

Case Reports of PrEP Failure: HIV Infection Despite High Adherence

Patient	PrEP Adherence	Seroconversion	Likely Cause of PrEP Failure
43-yr-old MSM[1]	24 mos, supported by pharmacy records, blood concentration analyses, clinical history	Acquired MDR HIV	Exposure to PrEP-resistant, multiclass-resistant HIV strain
MSM in his 20s[2]	Excellent by self-report, supported by blood and hair concentration analyses	Acquired MDR HIV after 2 x condomless insertive anal sex with 2 different partners within 11 wks before diagnosis	Exposure to PrEP-resistant, multiclass-resistant HIV strain
50-yr-old MSM[3]	Excellent by self-report, supported by blood analyses	Acquired wild-type HIV after 2-5 median condomless anal sex partners per day in each mo following PrEP initiation	Chronic rectal inflammation ± trauma
34-yr-old MSM[4]	Hair sample indicative of high adherence in preceding mos	Acquired MDR HIV	Exposure to PrEP-resistant, multiclass-resistant HIV strain
21-yr-old MSM[5]	Excellent by self-report, supported by blood and hair concentration analyses	Acquired MDR HIV	Exposure to FTC-resistant, but TDF-susceptible HIV strain

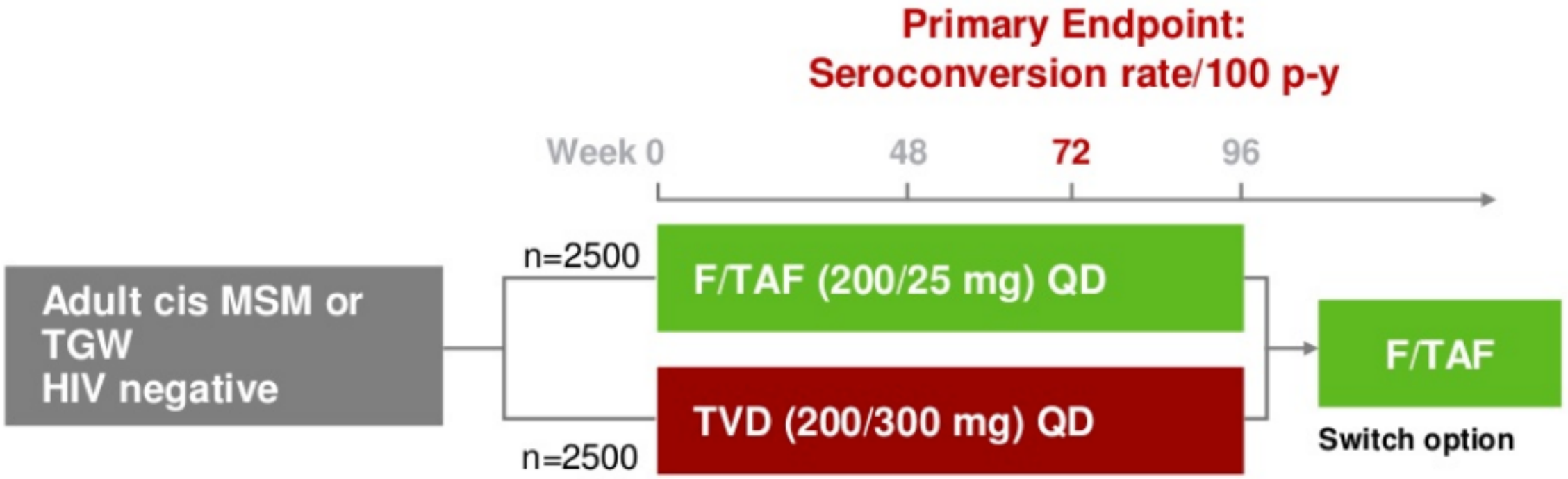
PrEP is not 100% effective, but it is highly protective;
condom use with PrEP optimizes HIV prevention and protects against STIs

1. Knox. NEJM. 2017;376:501. 2. Markowitz. J Acquir Immune Defic Syndr. 2017;76:e104.
3. Hoornenborg. CROI 2017. Abstr 953. 4. Thaden. AIDS. 2018;32:F1. 5. Cohen. IDWeek 2018. Abstr 1298.

Slide credit: clinicaloptions.com

Nuovi farmaci per la PrEP

DISCOVER: Pivotal Study F/TAF vs TVD for PrEP



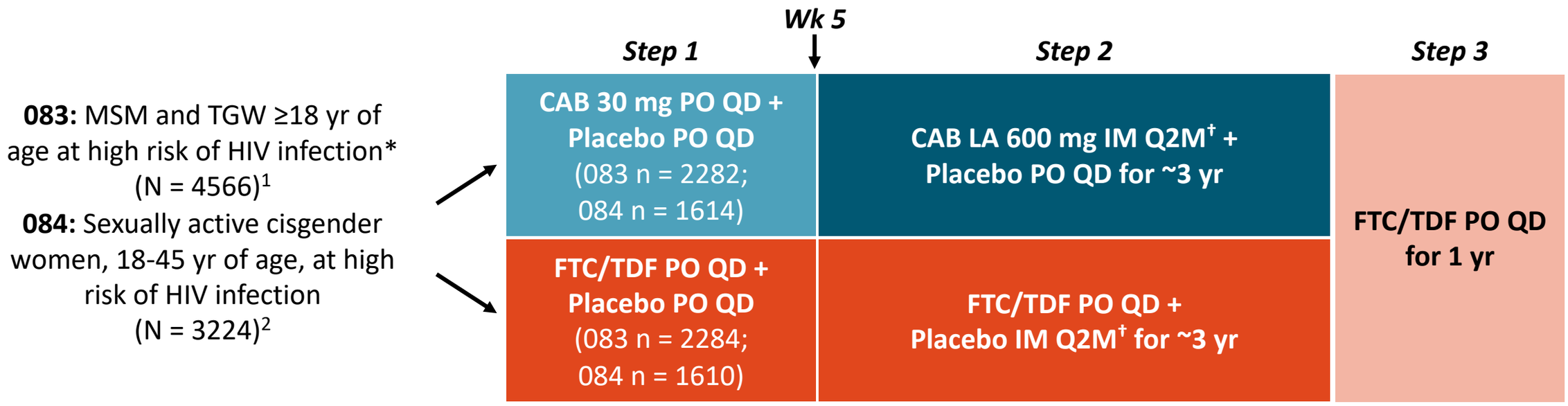
- Eligibility: HIV and HBV negative, eGFR ≥60 mL/min, and at least one o
  - 2+ episodes condomless anal intercourse (past 12 wks),
  - or rectal gonorrhea/chlamydia (past 24 wks)
  - or syphilis (past 24 wks)

Participants, N	
Screened	5,902
Enrolled	5,400
DXA sub-study	373

- Sample size N=5000 to show noninferiority (F/TDF vs F/TAF) assumes 1.4/100 p-y seroconversion rate for F/TDF arm; 144 seroconversions needed to demonstrate NI
- Sites: sexual health clinics, medical offices (North America, EU)

HPTN 083 and 084: Efficacy and Safety of LA Injectable CAB vs Daily Oral FTC/TDF for PrEP

- International, randomized, double-blind phase IIb/III (083) and phase III (084) trials



*Any noncondom receptive anal intercourse, >5 partners, stimulant drug use, incident rectal or urethral STI or incident syphilis in past 6 mo, or SexPro Score ≤16 (US only).
†First 2 doses given in Wk 5 and 9, then every 2 mo thereafter.

1. Landovitz. AIDS 2020. Abstr OAXLB0101. 2. Delany-Moretlwe. HIVR4P 2021. Abstr HY01.02.

Slide credit: clinicaloptions.com

HPTN 083 and 084: HIV Incidence

- LA CAB met criteria for superiority vs FTC/TDF in both 083 and 084[1,2]

Primary Efficacy Endpoint	HPTN 083[1]		HPTN 084[2]	
	CAB (n = 2244)	FTC/TDF (n = 2247)	CAB (n = 1614)	FTC/TDF (n = 1610)
HIV infections, n	13*	39	3†	36
PYFU	3205	3187	1956	1942
HIV incidence per 100 PY	0.41	1.22	0.15	1.85
HR for CAB vs FTC/TDF (95% CI)	**0.34 (0.18-0.62)**		**0.08 (0.03-0.27)**	

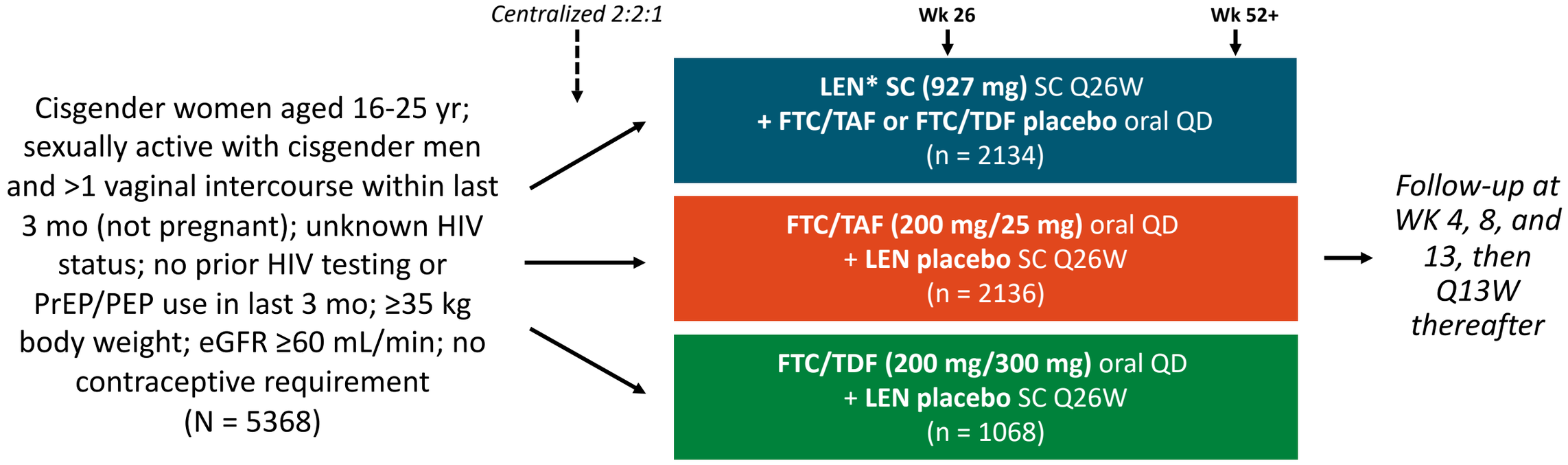
*Includes 1 case readjudicated post hoc as a baseline infection; revised HIV incidence based on readjudication: 0.37 (95% CI: 0.19-0.65), revised HR: 0.32 (95% CI: 0.16-0.58).
†Includes 1 baseline infection.

1. Landovitz. NEJM. 2021;385:595. 2. Marzinke. IAS 2021. Abstr PECLB25.

Slide credit: clinicaloptions.com

PURPOSE 1: Twice-Yearly LEN Injections vs Daily Oral Tenofovir as PrEP in Cisgender Women

- Randomized, double-blind phase III trial in South Africa and Uganda using counterfactual design

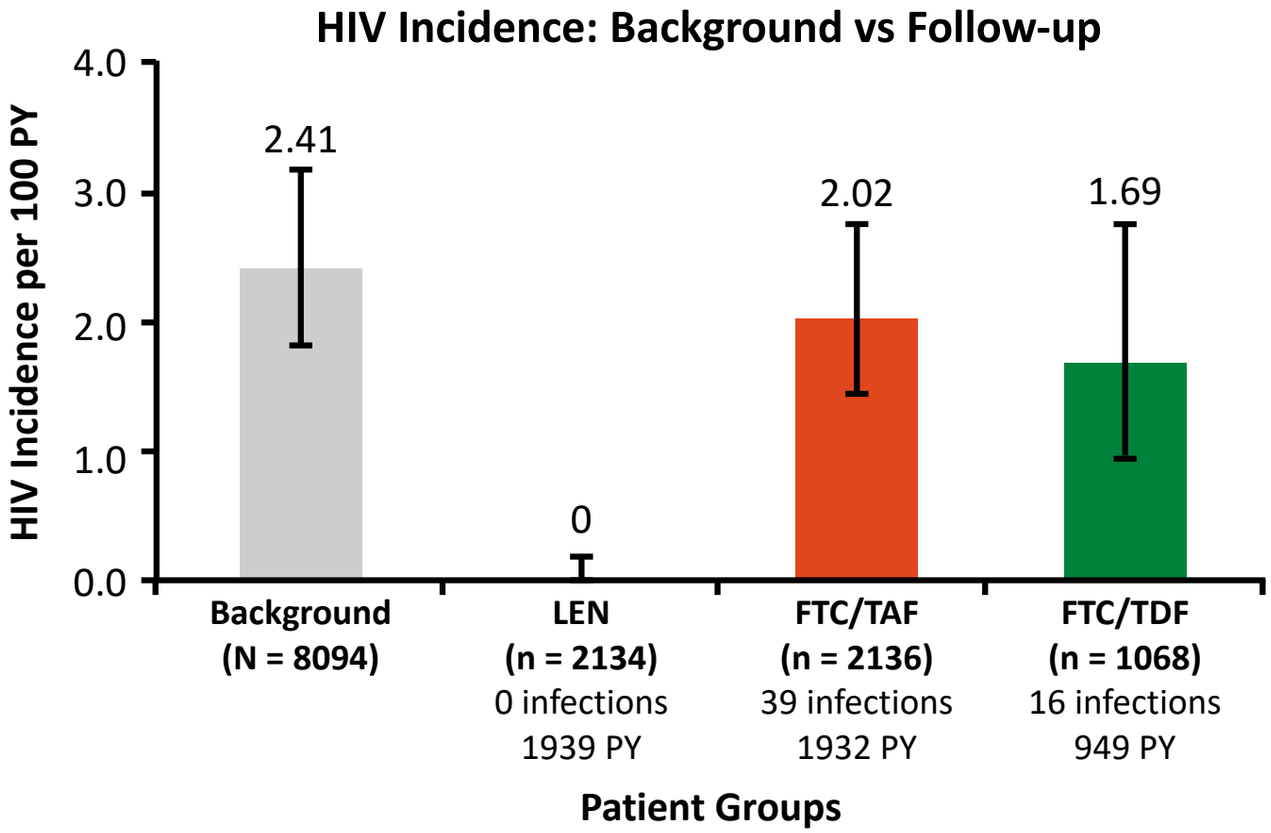


*Participants received a loading dose (300 mg tablets) on Day 1 and Day 2.

- Prespecified interim analysis when 50% of participants completed ≥52 wk
  - **Primary analysis**: LEN vs background HIV incidence, FTC/TAF vs background HIV incidence
  - **Secondary analysis**: LEN vs FTC/TDF HIV incidence, FTC/TAF vs FTC/TDF HIV incidence

Bekker. AIDS 2024. Abstr SS0407. Bekker. NEJM. 2024;[Epub].

PURPOSE 1: HIV Incidence in mITT Population at Interim Analysis



- At baseline, median age 21 yr, 23%-56% aged 16-18 yr, ~25% with any STI

Comparison	HIV Incidence Rate Ratio (95% CI)*	*P* Value
LEN vs background HIV incidence	0 (0.00-0.04)	<.001
FTC/TAF vs background HIV incidence	0.84 (0.55-1.28)	.21
LEN vs FTC/TDF HIV incidence	0 (0.00-0.10)	<.001
FTC/TAF vs FTC/TDF HIV incidence	1.20 (0.67-2.14)	--

*People found to have HIV at study entry excluded from analysis.

- **In LEN arm, zero HIV infections**
- **In oral FTC/TAF arm, HIV incidence no different from background** and treatment adherence was poor

Bekker. AIDS 2024. Abstr SS0407. Bekker. NEJM. 2024;[Epub].

PEP - Profilassi Post-Esposizione

La PEP è….

- L’assunzione di farmaci anti-retrovirali dopo un’esposizione potenziale o certa ad HIV
- Una strategia considerata “d’emergenza”
- Rimborsata dal SSN Italiano

La PEP non è….

- Supportata da solide evidenze scientifiche

Efficacy of Postexposure Prophylaxis after Intravaginal Exposure of Pig-Tailed Macaques to a Human-Derived Retrovirus (Human Immunodeficiency Virus Type 2)

RON A. OTTEN,[1]* DAWN K. SMITH,[2] DEBRA R. ADAMS,[1] JENNIFER K. PULLIUM,[1,3] EDDIE JACKSON,[4] CARYN N. KIM,[1] HAROLD JAFFE,[1] ROBERT JANSSEN,[2] SAL BUTERA,[1] AND THOMAS M. FOLKS[1]

TABLE 1. HIV-2-specific provirus detection in PBMC and serologic status

Study group and macaque	Detection[a]/status[b] at wk post-virus exposure									
	0	1	2	3	4	8	12	16	20	24
Untreated controls										
53-422	−/−	−/−	+/−	+/+	+/+	+/+	+/+	+/+	+/+	+/+
53-443	−/−	−/−	+/−	+/+	+/+	+/+	+/+	+/+	+/+	+/+
83-306	−/−	−/−	+/−	+/−	+/+	+/+	+/+	+/+	+/+	+/+
83-310	−/−	−/−	−/−	−/−	−/−	−/−	−/−	−/−	−/−	−/−
12-h PEP										
83-268	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
83-283	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
83-308	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
83-297[d]	−/−	−/−	−/−	−/−	−[c]/−	NT	NT	NT	NT	NT
36-h PEP										
52-121	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
83-267	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
83-269	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
83-273	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
72-h PEP										
72-34	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
83-285	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	−/−	−/−	−/−
83-305	−/−	−/−	−/−	−/−	−[c]/−	−/−	−/−	+/+	+/+	+/+
83-303[d]	−/−	−/−	−/−	NT	NT	NT	NT	NT	NT	NT

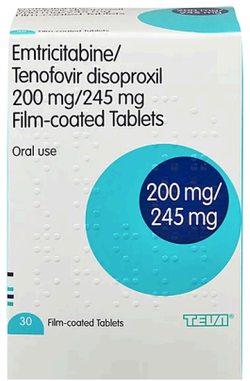
[a] +, nested DNA-PCR amplification and detection of HIV-2 protease gene sequences; −, no HIV-2-specific signal was detected; NT, not tested.
[b] +, confirmed HIV-2-specific seroconversion; −, lack of seroresponse; NT, not tested.
[c] DNA PCRs and virus isolation results were also negative for ILN biopsy specimens.
[d] Longer-term follow-up was not possible due to unanticipated death.

JOURNAL OF VIROLOGY, Oct. 2000, p. 9771–9775
0022-538X/00/$04.00+0

La PEP non è….

- Supportata da solide evidenze scientifiche

Emtricitabina/Tenofovir disoproxil (cp)



+

Un terzo farmaco (inibitore dell’integrasi)

per 30 giorni

PEP

PEP Occupazionale

Modalità esposizione	PEP
• Ferita con ago o altro tagliente	raccomandata
• Contaminazione congiuntivale	raccomandata
• Contaminazione di cute lesa o mucose	considerata
• Ferita da morso	considerata
• Contaminazione di cute integra	sconsigliata

Materiale biologico	PEP
• Sangue, liquidi biologici ematici, liquor, colture virali	raccomandata
• Liquido amniotico, sinoviale, pleurico, pericardico, peritoneale, tessuti, sperma, secrezioni vaginali	considerata
• Urina, feci, vomito, saliva	sconsigliata

Paziente fonte	PEP
• HIV-positivo	raccomandata
• HIV-negativo ma con evento a rischio recente (TD, MST, epatite virale acuta, ecc.)	raccomandata
• Con stato HIV non noto e che rifiuta di sottoporsi al test HIV	raccomandata
• Paziente non noto o non disponibile	considerata
• HIV-negativo	sconsigliata

PEP

PEP Non occupazionale

Fonte / Rapporto	HIV+	Rischio recente	HIV+ undetectable	Rifiuta/Violenza/ Ignoto
Anale recettivo	Sì	Sì	No	Sì
Vaginale recettivo	Sì	Sì	No	Sì
Orale (fellatio) recettivo con eiaculazione	Sì	Sì	No	Sì
Orale (fellatio) recettivo senza eiaculazione			No	
Anale o vaginale insertivo	Sì		No	
Cunnilingus, petting	No	No	No	No

Domande ?