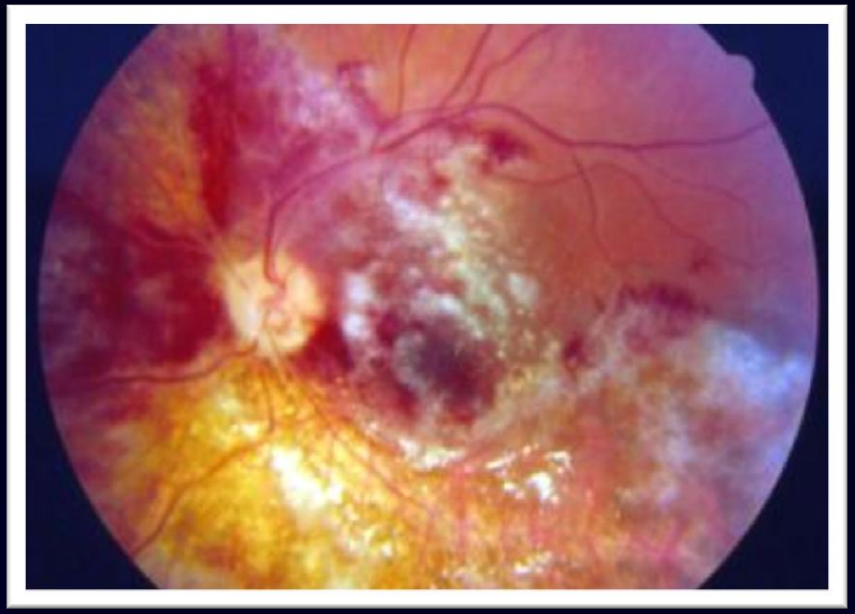
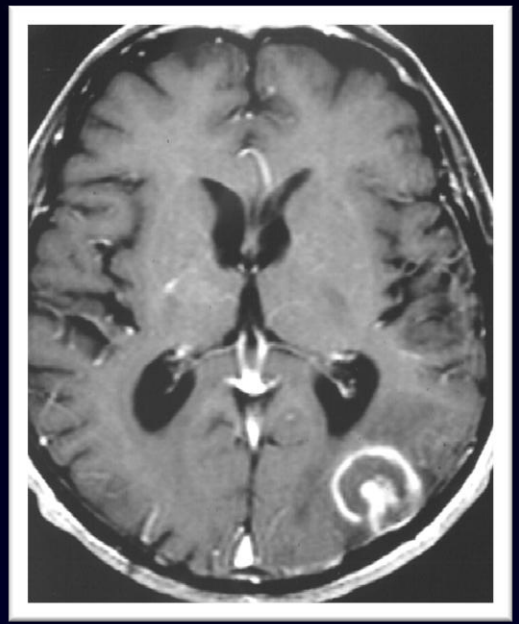
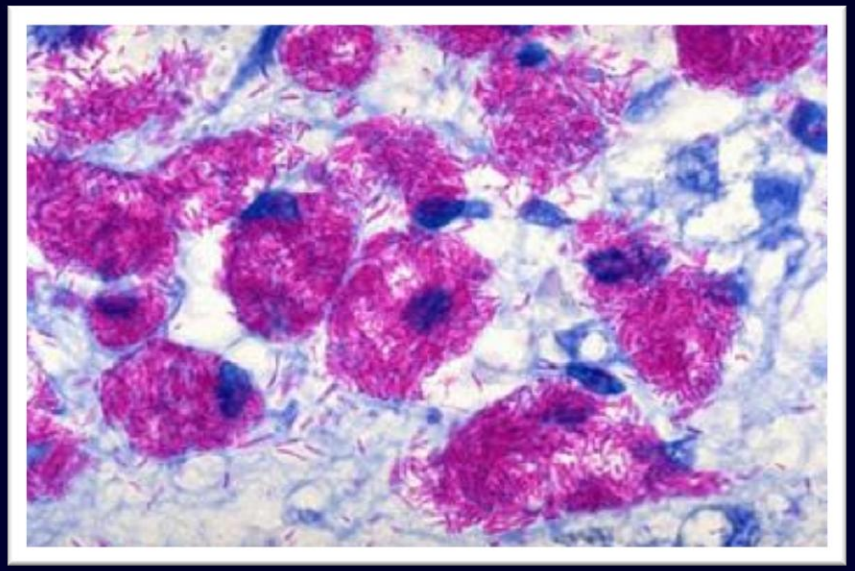
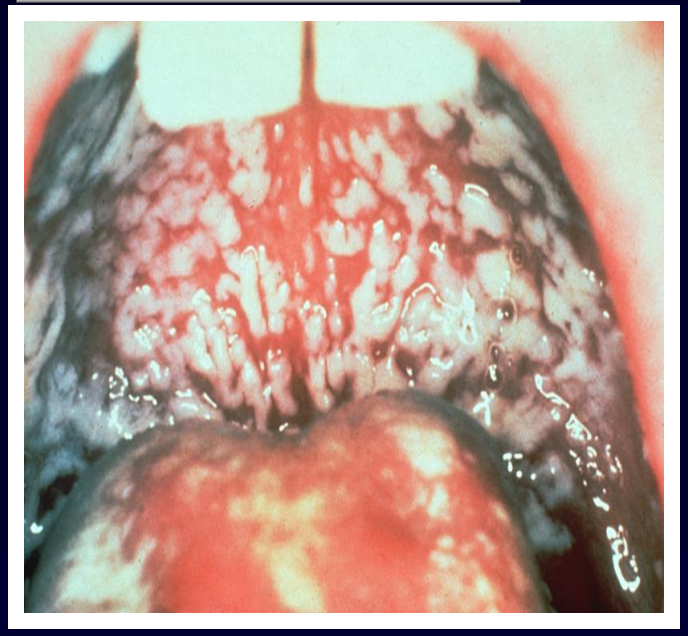
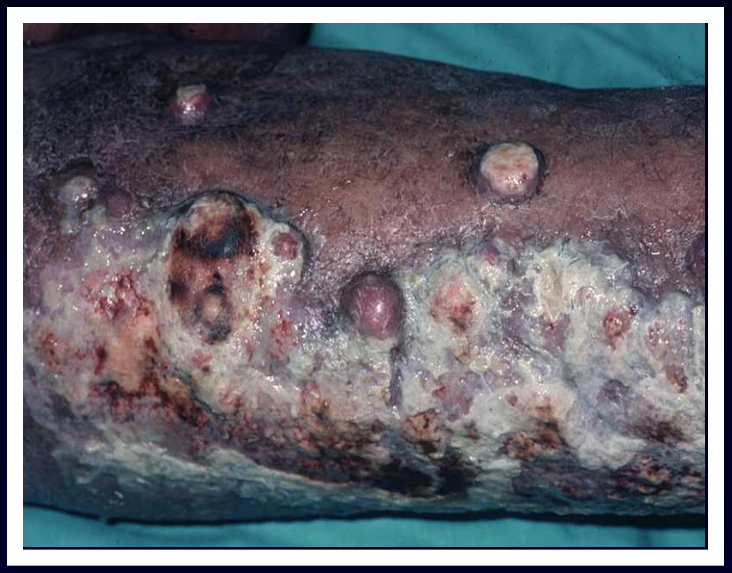

Aids makes us equal
AIDS
Protect yourself

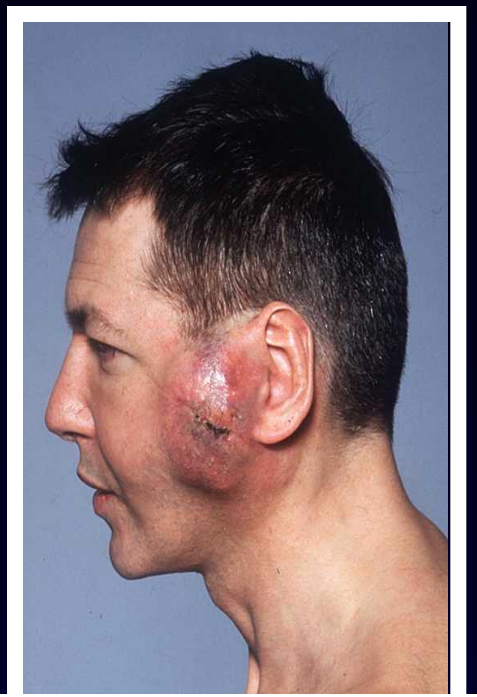


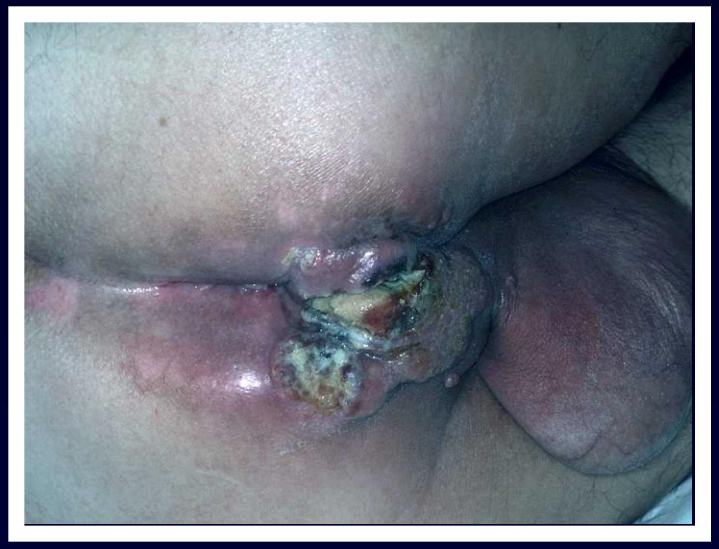


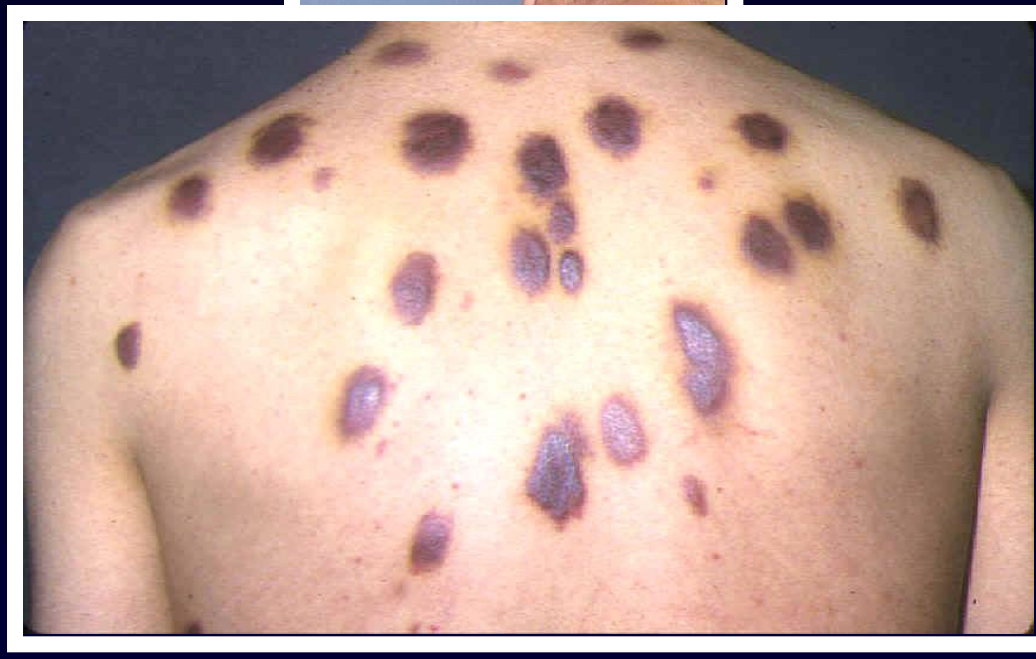








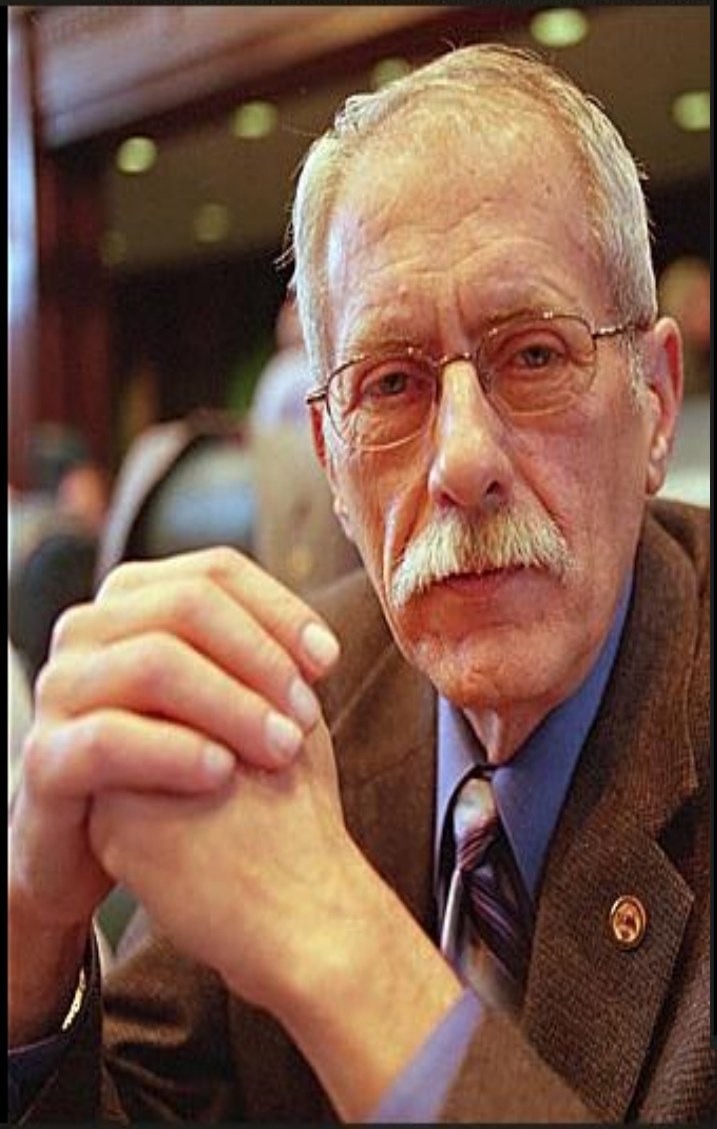




TIME

The Graying of AIDS

More Americans are living with HIV into middle age a



The personal is political

Larry McKeon, 61, is currently serving his fifth term as a state legislator in Illinois. He is the state'
and HIV-positive legislator and jokes that his tenure comes with built-in term limits. Photograph b
/ Aurora for TIME

TIME

The Graying of AIDS

More Americans are living with HIV into middle age and beyond.

Email This

TIME

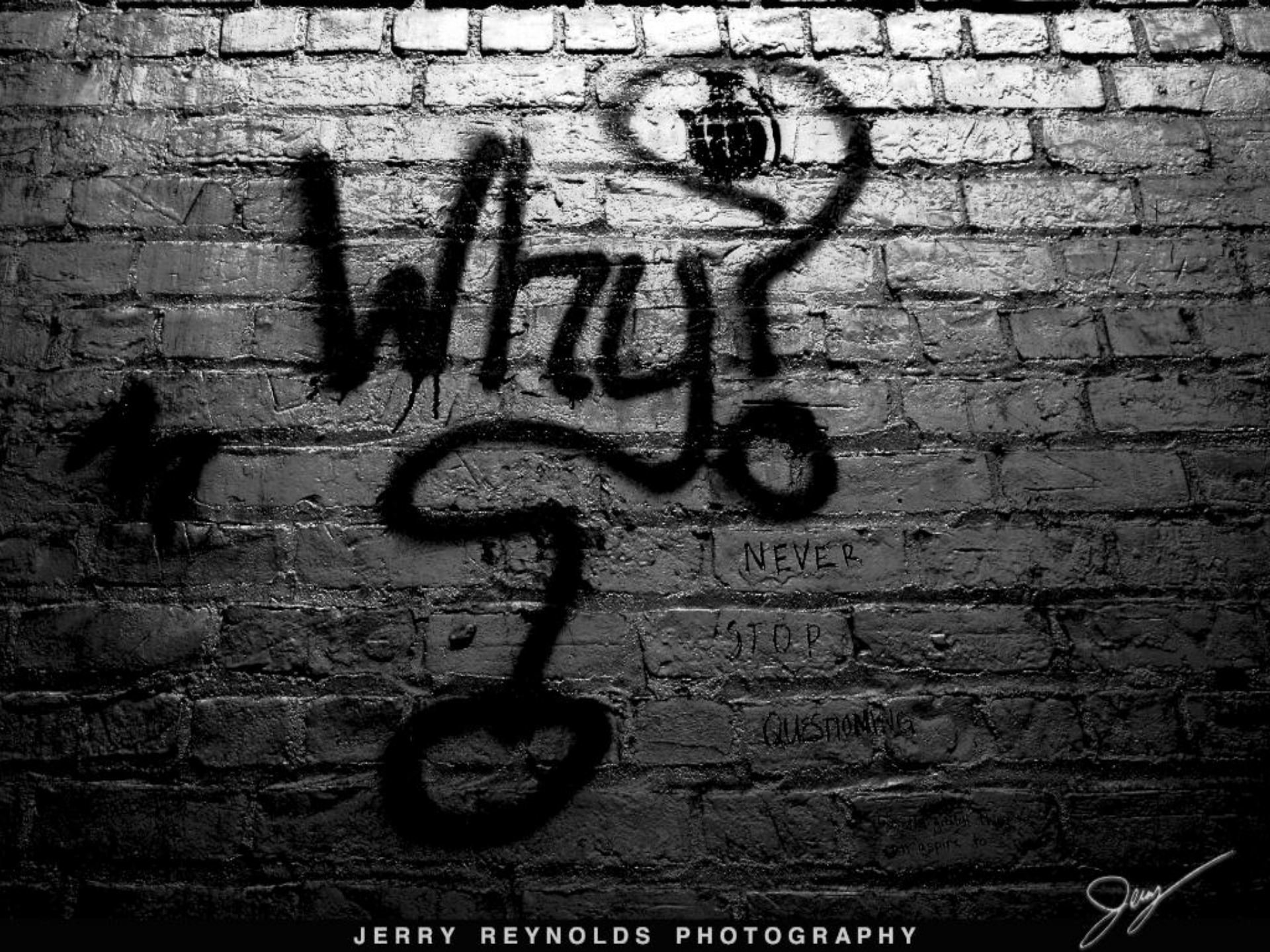
The Graying of AIDS

More Americans are living with HIV into middle age and beyond.

Email This

Pioneer

Bill Rydwels, 73, was diagnosed with HIV in 1985. Like many gay men of his generation, Bill buried his partner and then waited to die himself. Photograph by Katja Heinemann / Aurora for TIME


NEVER
STOP
JERRY REYNOLDS PHOTOGRAPHY

Available Antiretrovirals 2013

NRTIs

- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

NNRTIs

- Efavirenz
- Nevirapine
- Etravirine
- Rilpivirine

Protease Inhibitors

- Atazanavir
- Darunavir
- Fos-Amprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

New Classes

Fusion Inhibitors

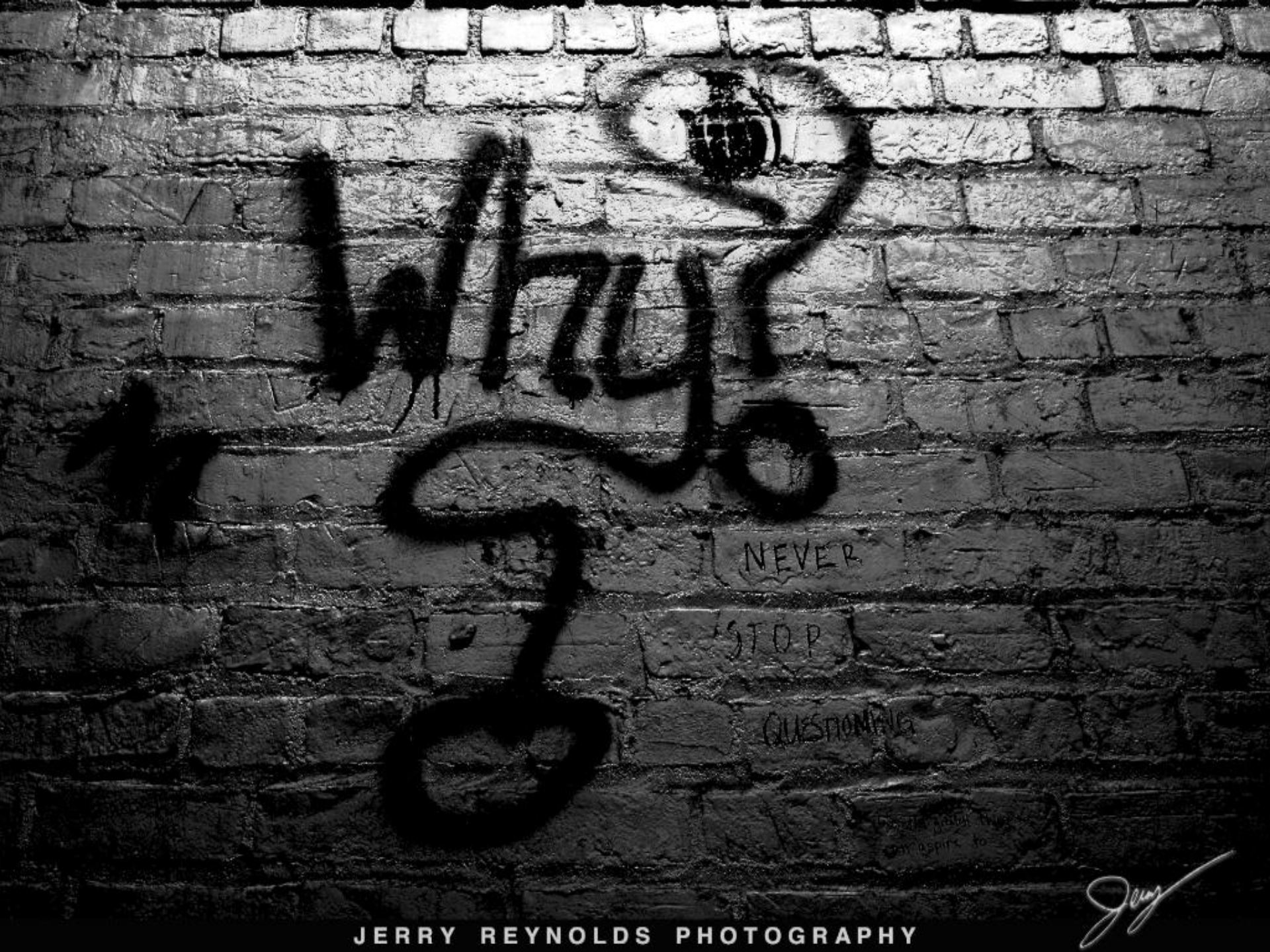
- Enfuvirtide

R5 Inhibitors

- **Maraviroc**

Integrase Inhibitors

- Raltegravir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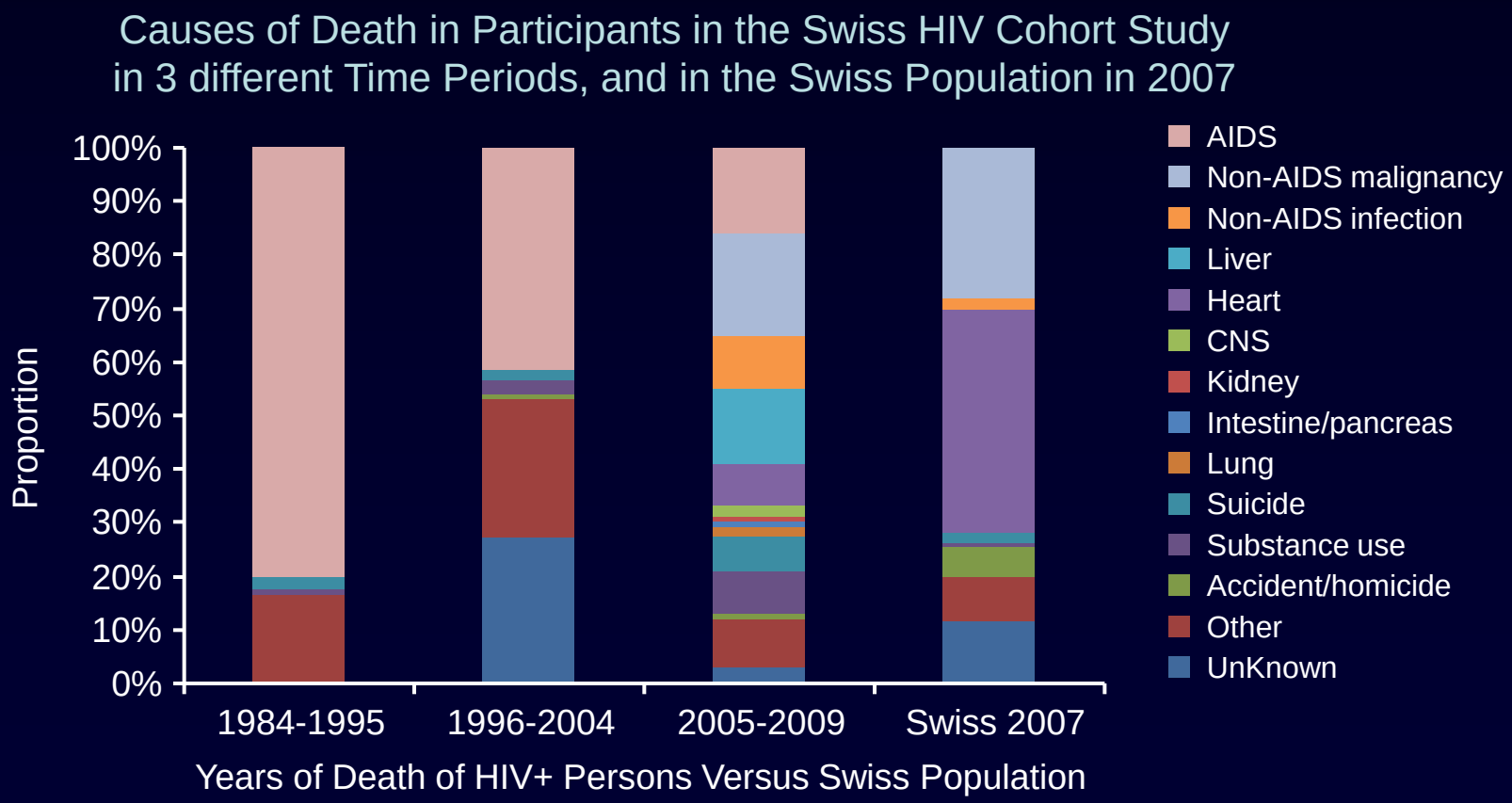
- **Maraviroc**

Integrase Inhibitors

- Raltegravir

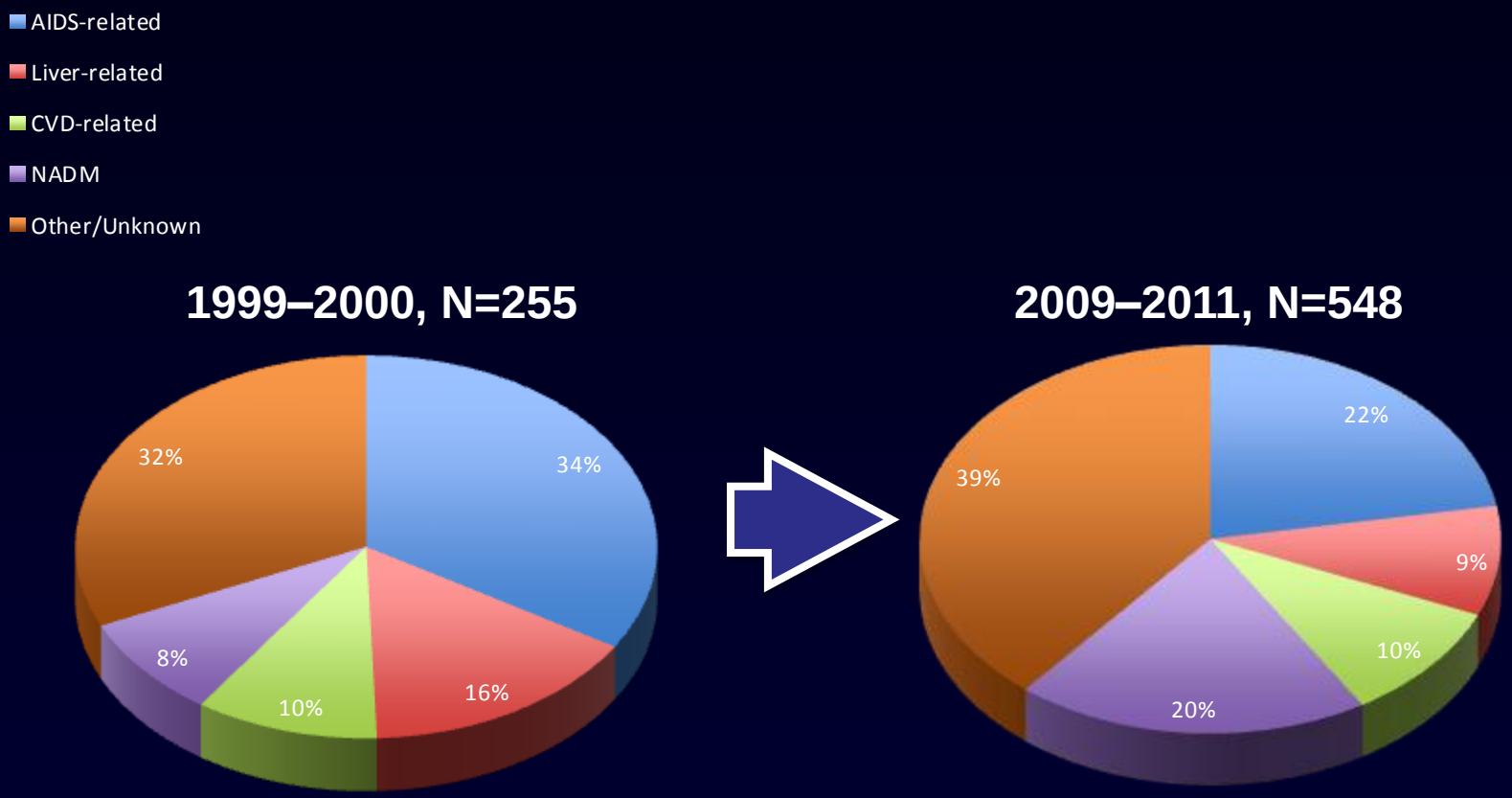
Changing Patterns of the Causes of Death in a Swiss Cohort (SHCS)

- SHCS is a prospective observational cohort
- Characteristics of participants that died from 2005-2009
- 459 deaths/9,053 participants (5.1%)



Ruppik M, et al. 18th CROI; Boston, MA; February 27-March 2, 2011. Abst. 789.

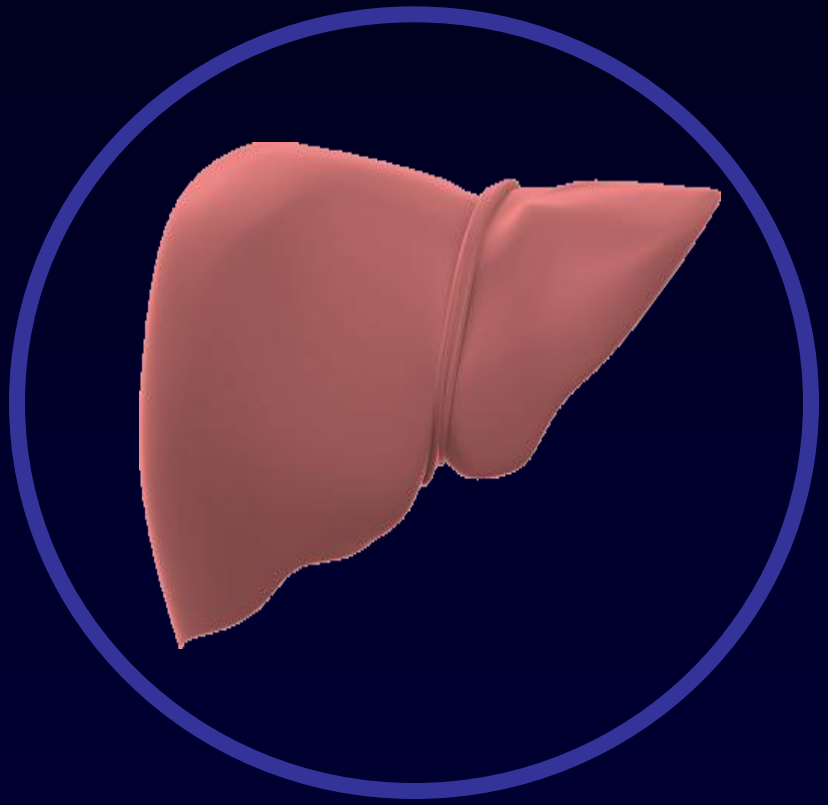
Changes in Causes of Death Over Time in PLWH



Death rate fell from 17.4 deaths per 1000 per year in 1999-2000 to 8.3 deaths in 2009-2011

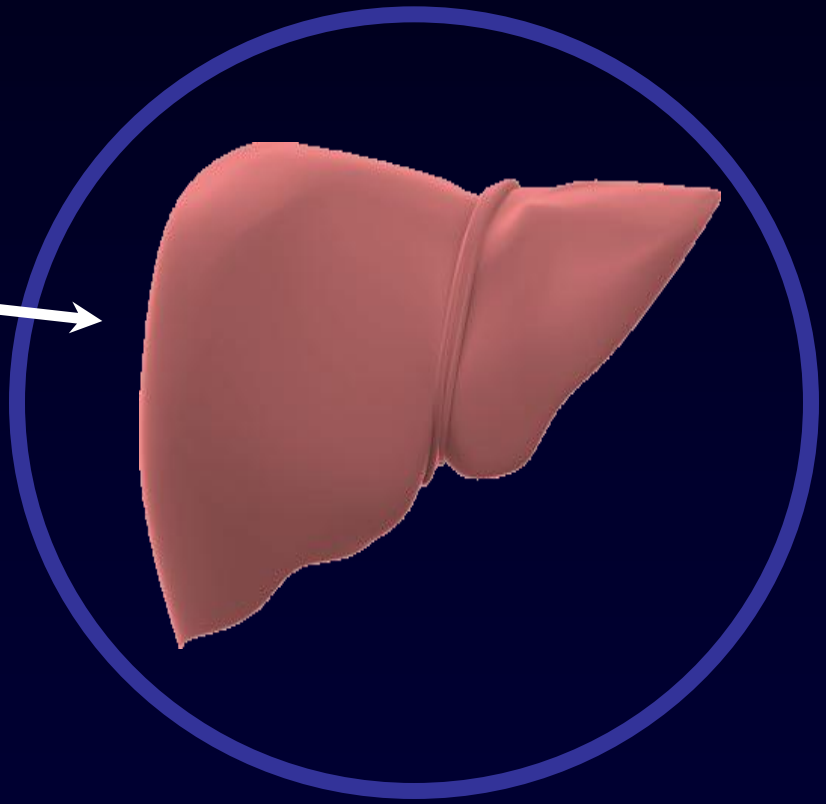
PLWH, people living with HIV; NADM, non-AIDS defining malignancies

Weber R, et al. 19th IAC; Washington, DC; July 22-27, 2012; Abst. THAB0304.



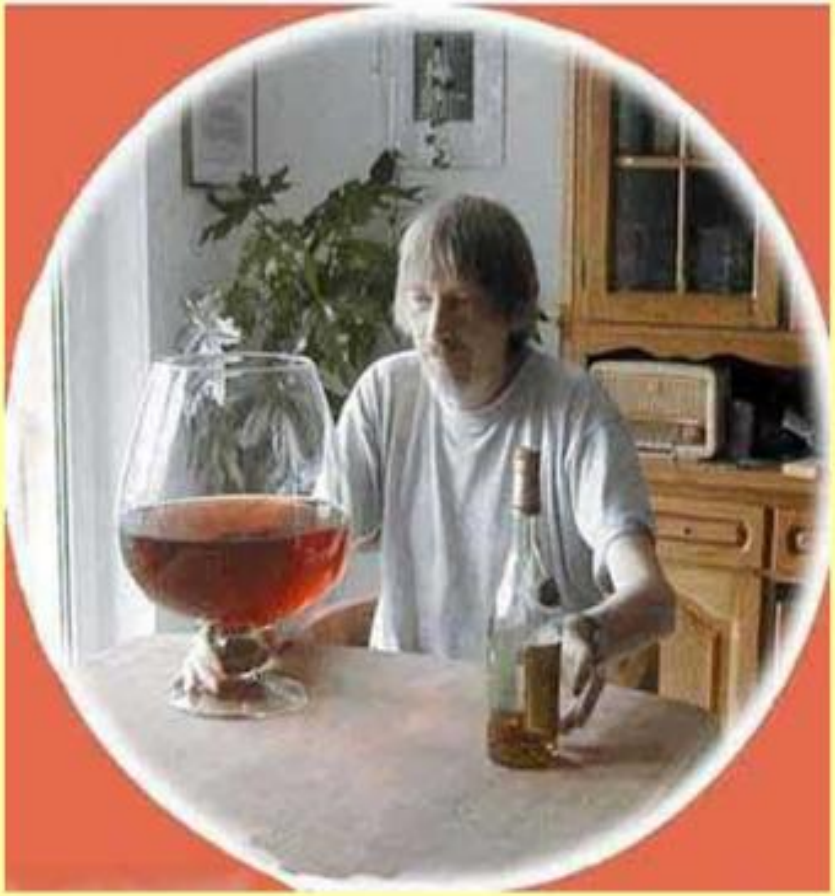
Mark Nelson: Personal communication

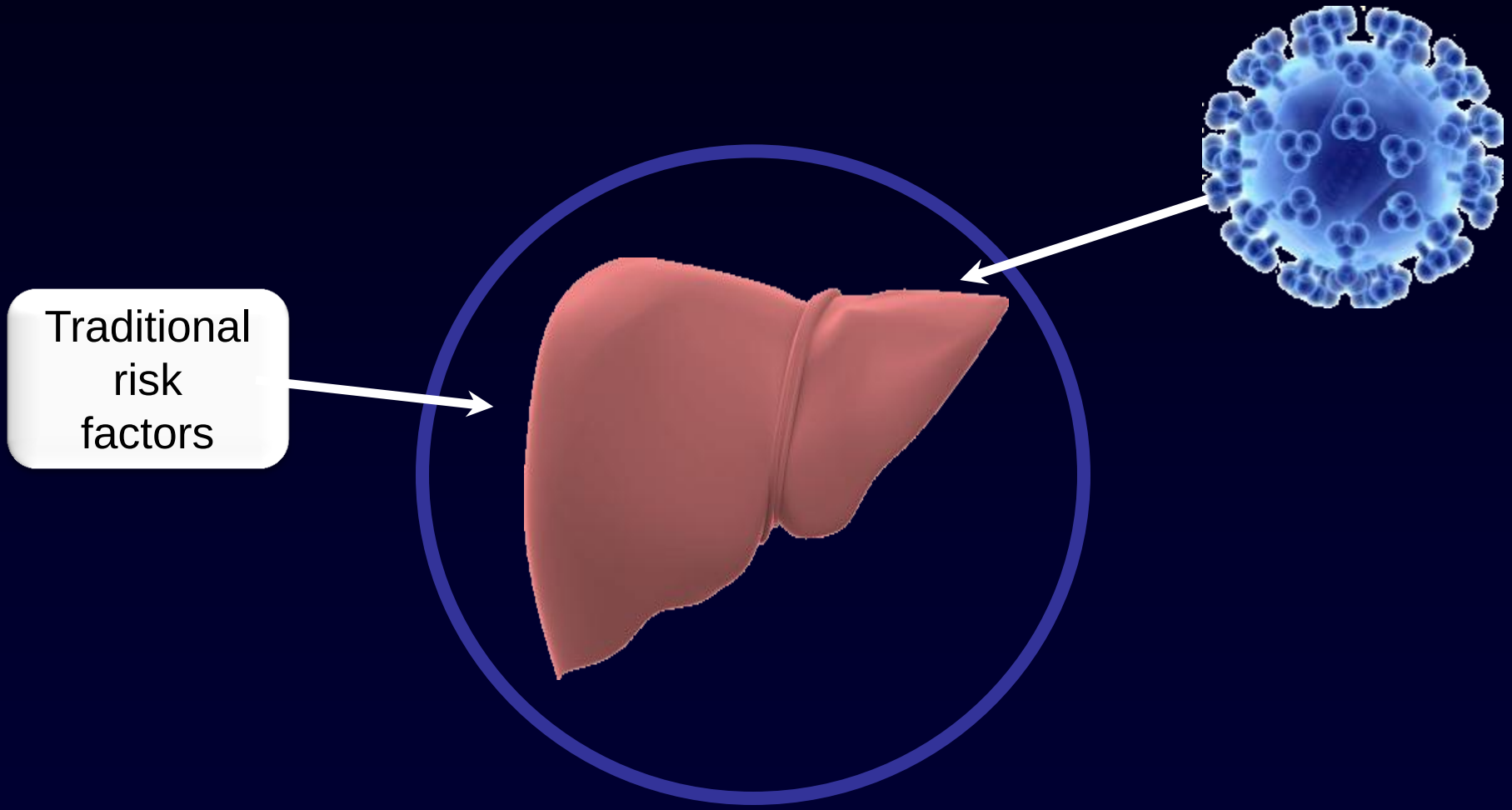
Traditional risk factors



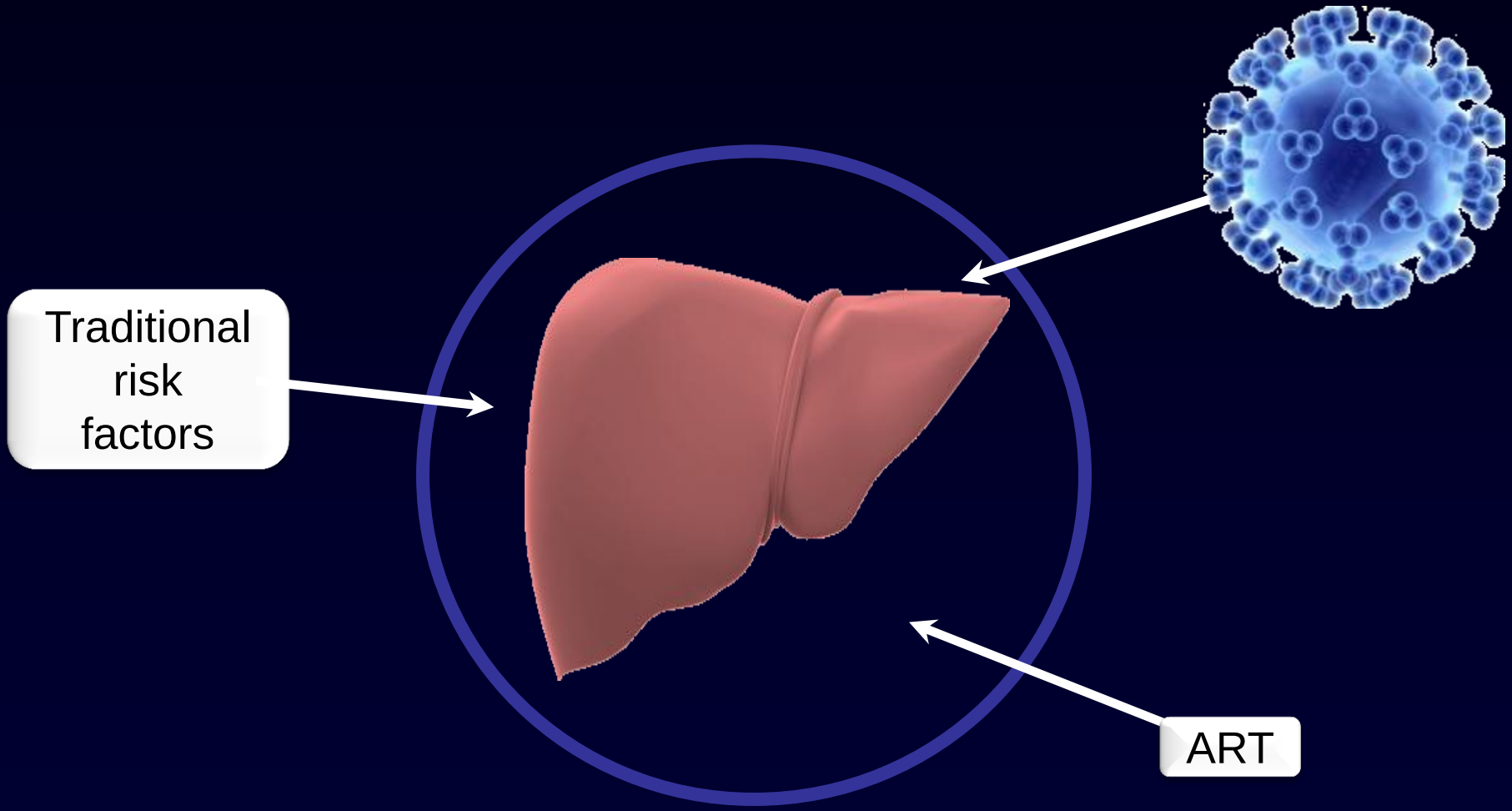
Mark Nelson: Personal communication

My Doctor said "Only 1 glass of alcohol a day". I can live with that.

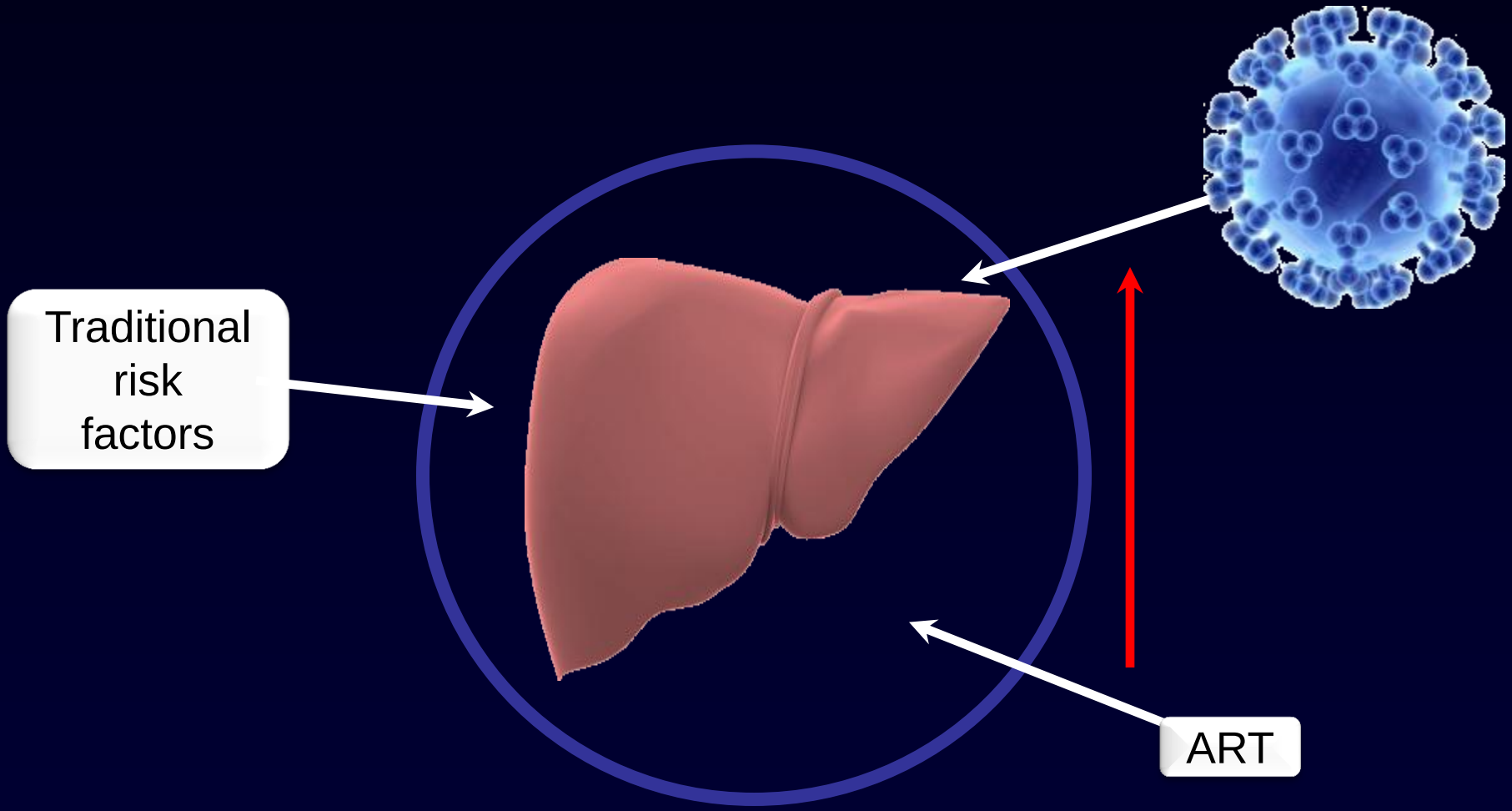




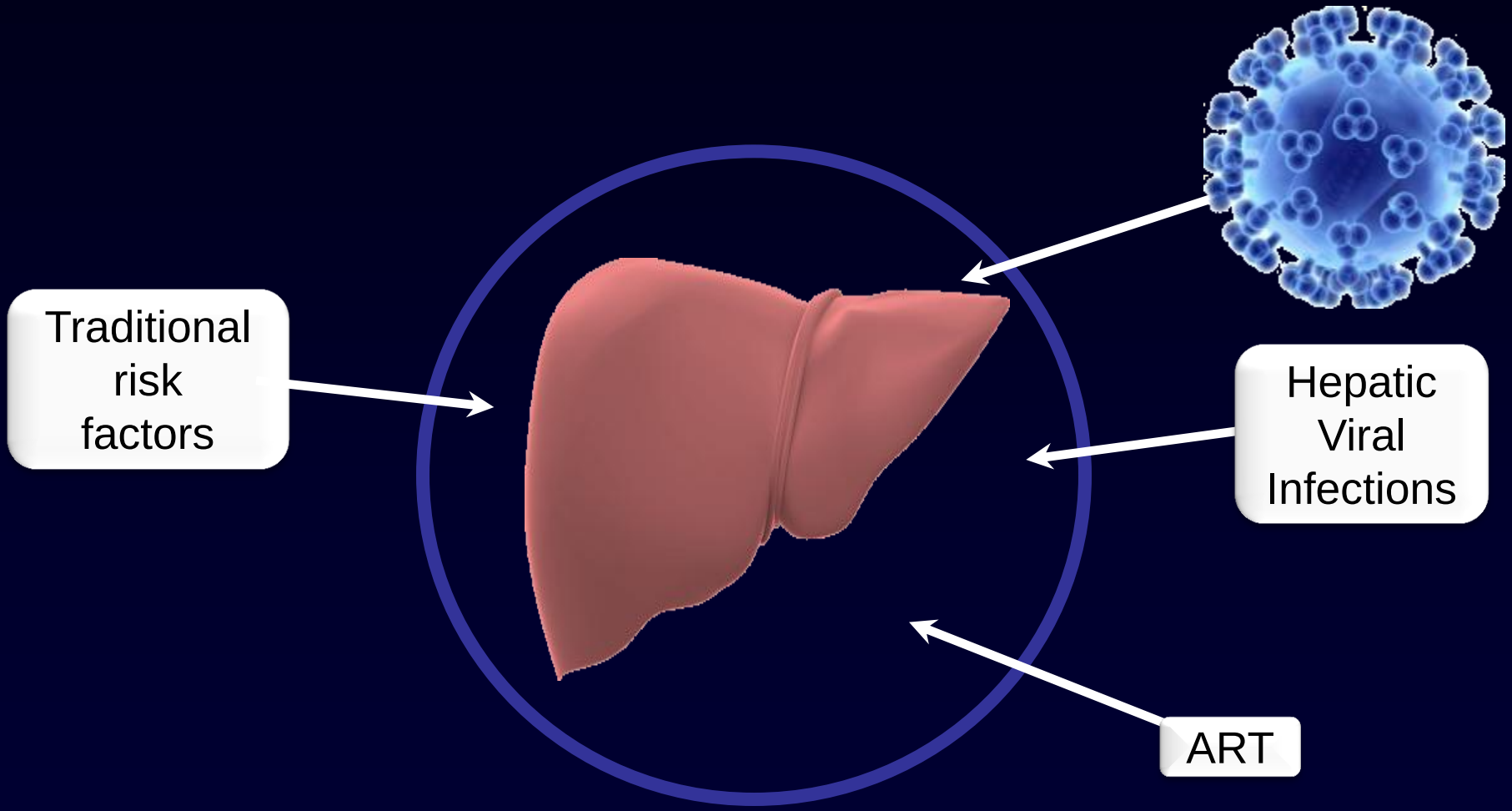
Mark Nelson: Personal communication

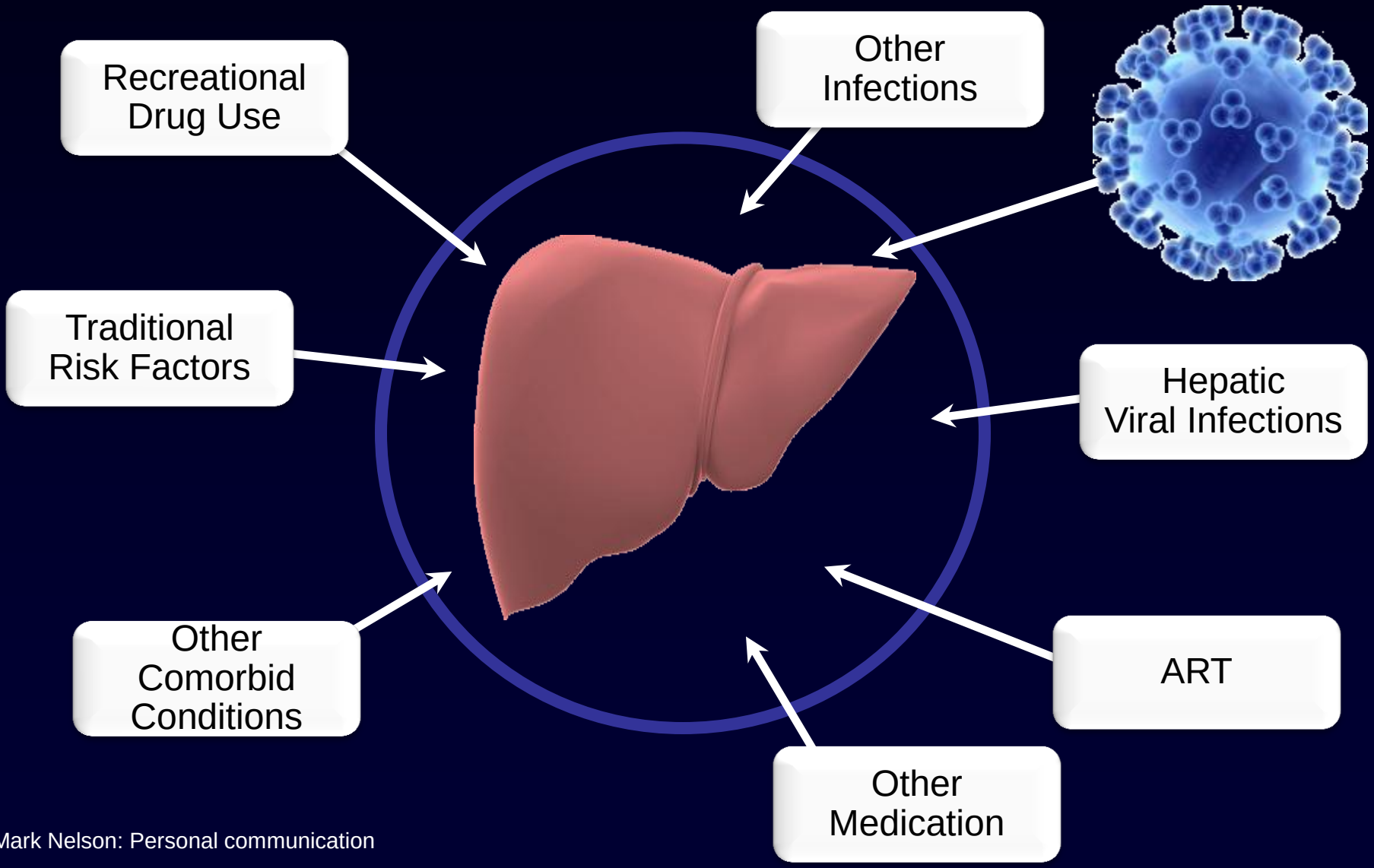


Mark Nelson: Personal communication



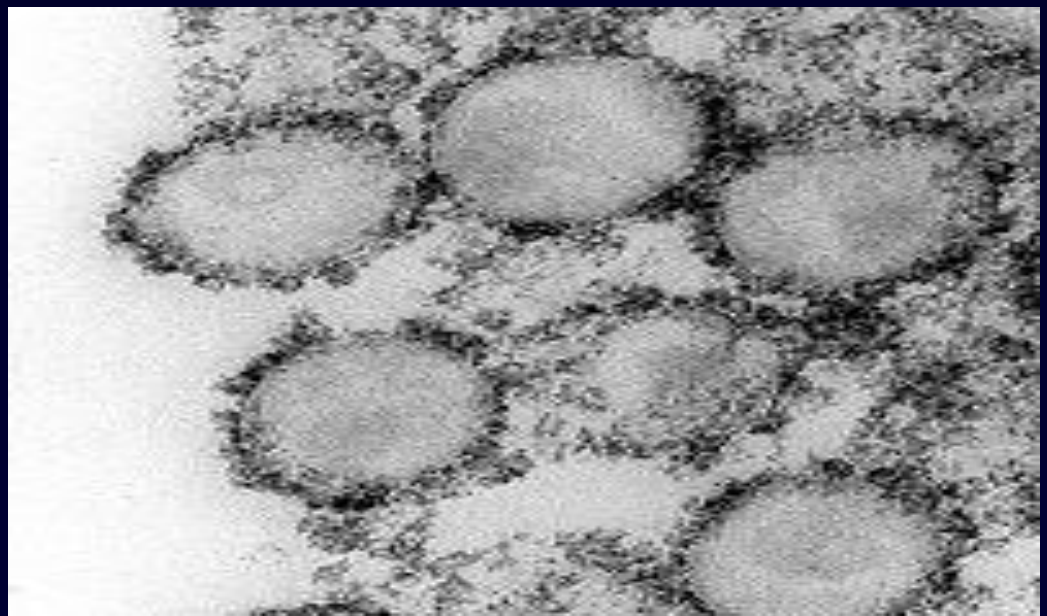
Mark Nelson: Personal communication

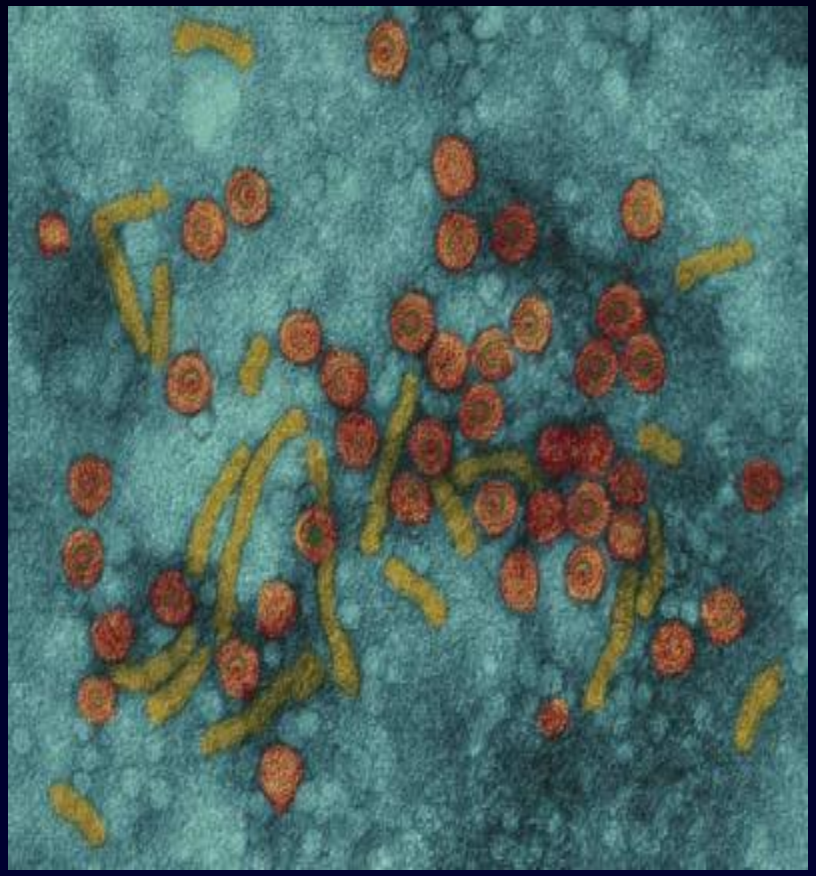

Traditional risk factors
Hepatic Viral Infections
ART



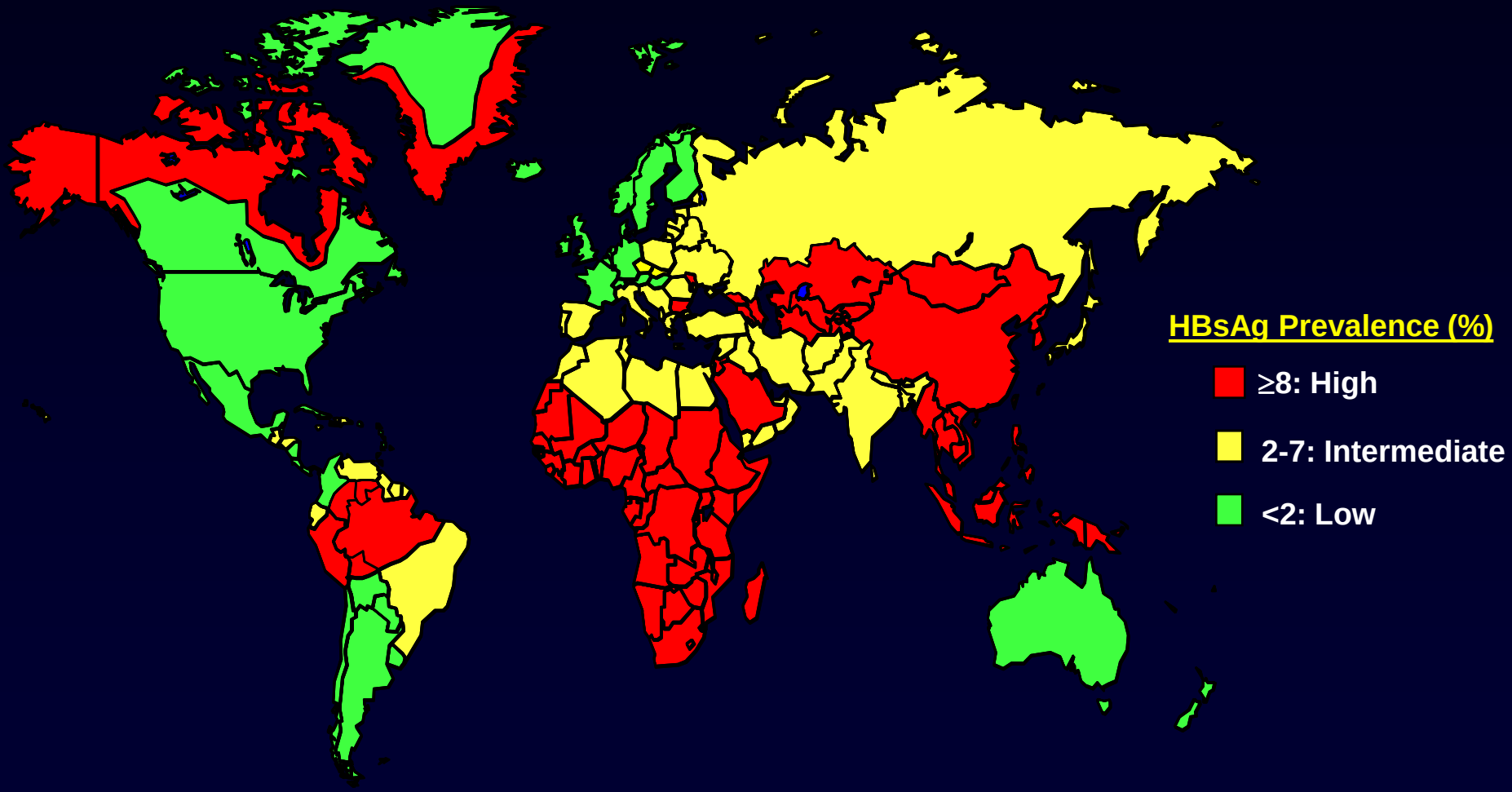
Mark Nelson: Personal communication


A
B
C



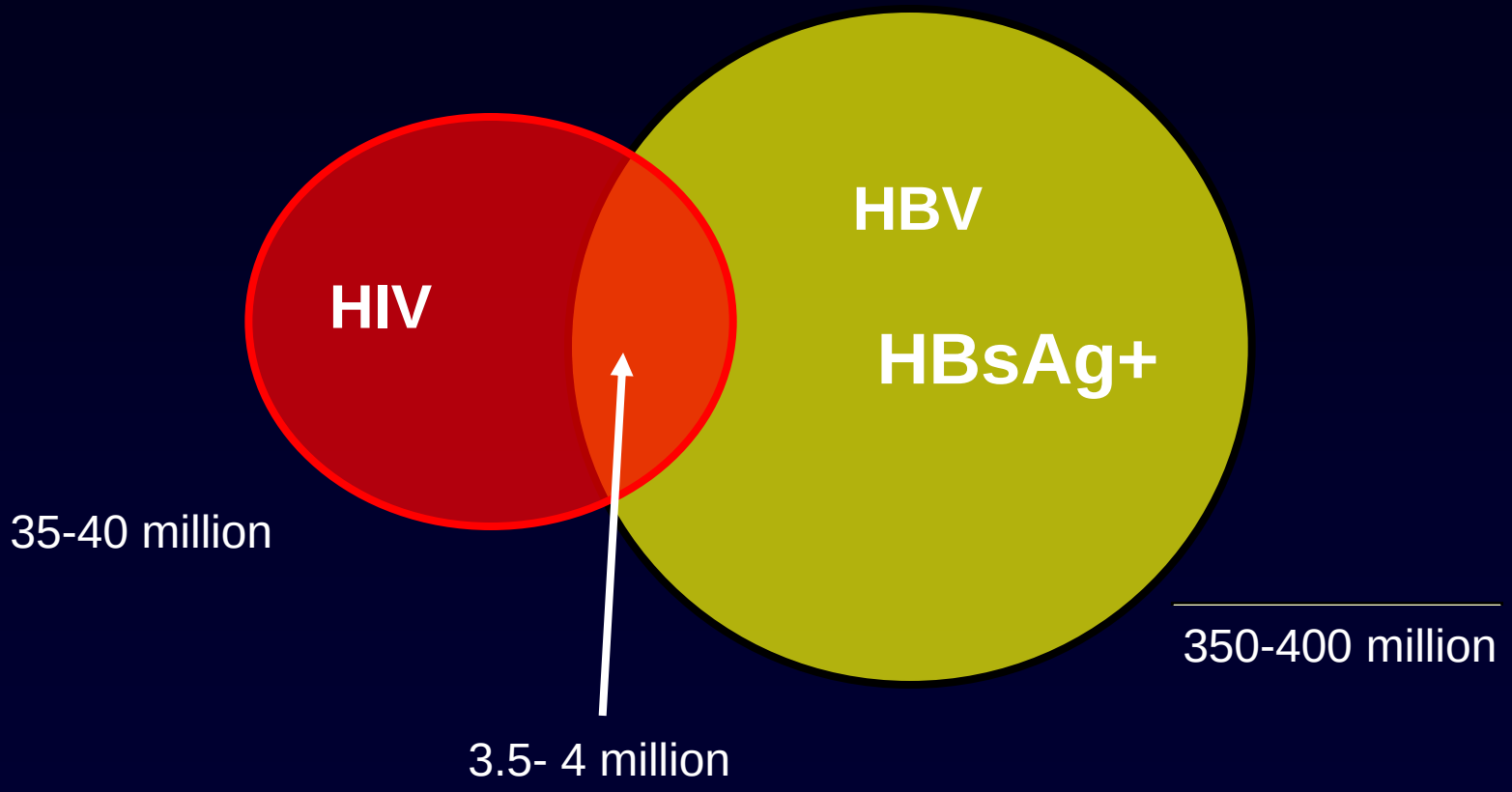


Worldwide Prevalence of Chronic Hepatitis B

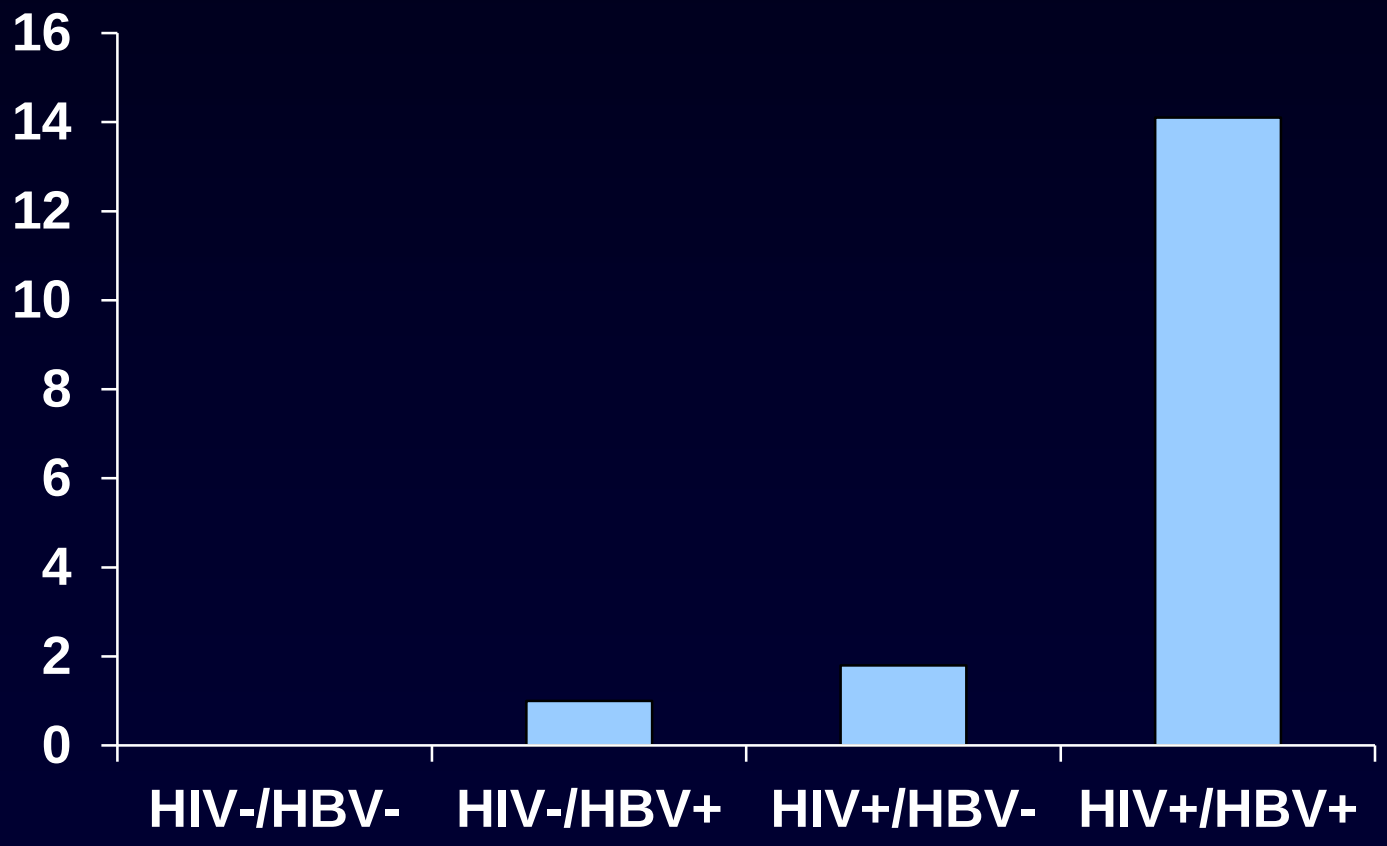


World Health Organization
Centers for Disease Control and Prevention.

Overlapping HIV and HBV Epidemics



Liver Mortality Rate (per 1000 PY) MACS



Thio et al. Lancet 2004

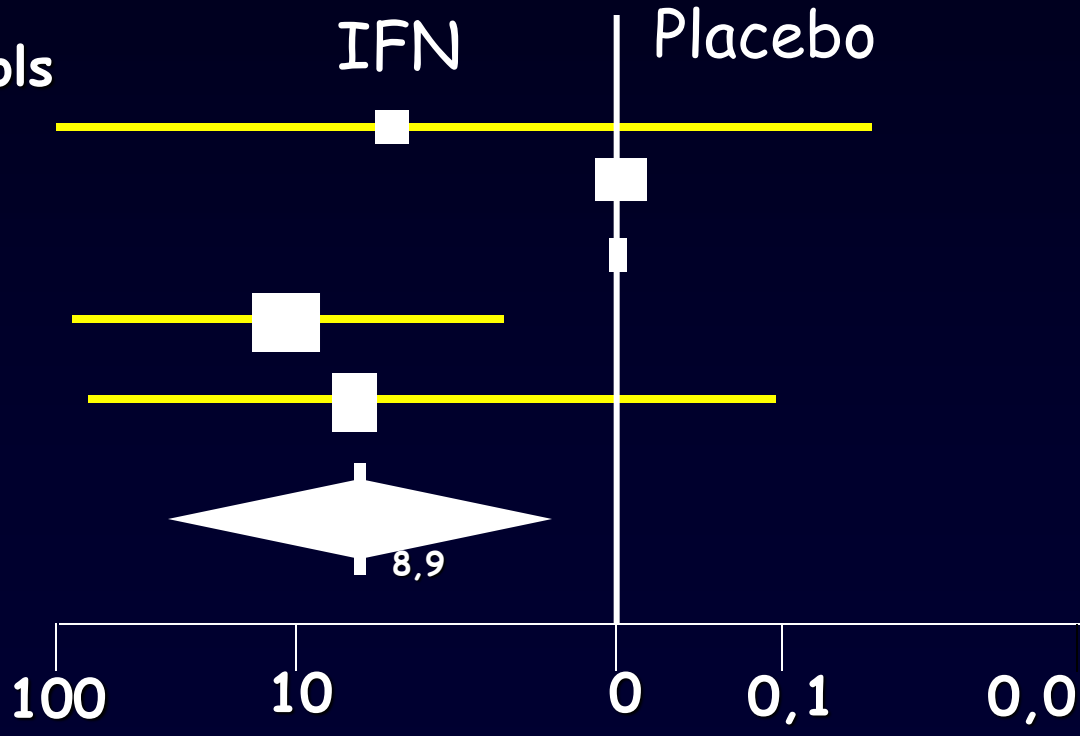
Anti-HBV Therapies

Immune modulators	Polymerase Inhibitors
IFN-alpha	Lamivudine
Pegylated-Interferon-alpha	Adefovir
	Entecavir
	Telbivudine
	Tenofovir
	Emtricitabine

IFN-α in HBV /HIV co-infection

16 RCT IFN-α *vs* placebo 837 HBsAg+ - 107 HIV+ included in 5 studies

Author(Yr.)	n. Tx	n. Controls
Hoofnagle(88)	10	4
Brook (89)	16	6
Brook (89)	6	9
Pol (92)	16	14
Wong (95)	13	13
All	61	46



HBe seroconversion/negativation : HIV+ *vs* HIV: - 0.38 (CI 0.06-0.7 *P* =.02)

Puoti et al. personnal comm.

Anti-HBV Therapies

Immune modulators

IFN-alpha

Pegylated-Interferon-alpha

Polymerase Inhibitors

Lamivudine

Adefovir

Entecavir

Telbivudine

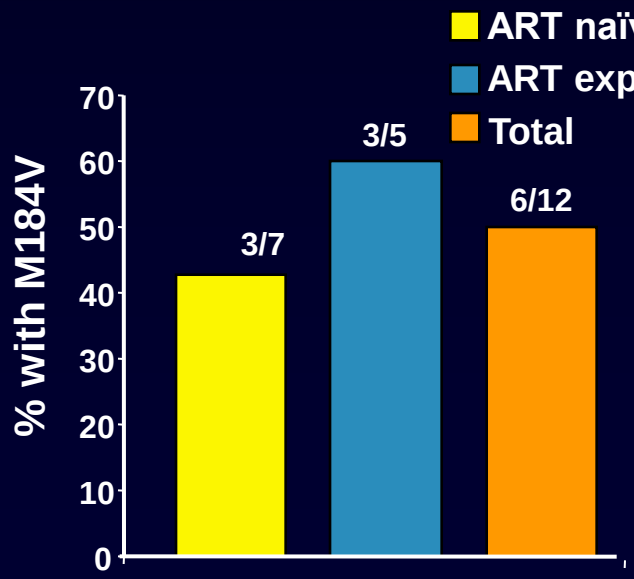
Tenofovir

Emtricitabine

Anti-HIV activity of entecavir

- 17 HIV/HBV coinfected pts (10 naïve, 7 treatment-experienced from US and Australia) who received entecavir (ETV) monotherapy for HBV therapy
- ETV monotherapy results in clinically significant reduction in HIV RNA in the majority but not all pts and can select for the M184V mutation even in naive pts
- HIV/HBV coinfected individuals should not receive ETV monotherapy

Selection of M184V following ETV treatment



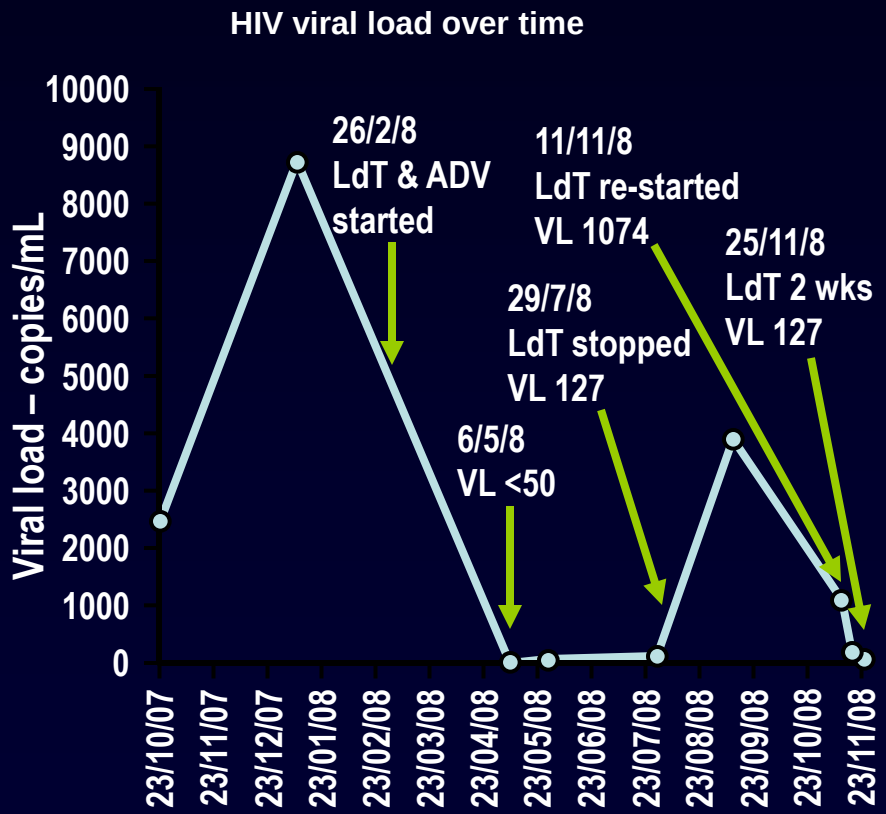
Median time to M184V 148 days 98 days

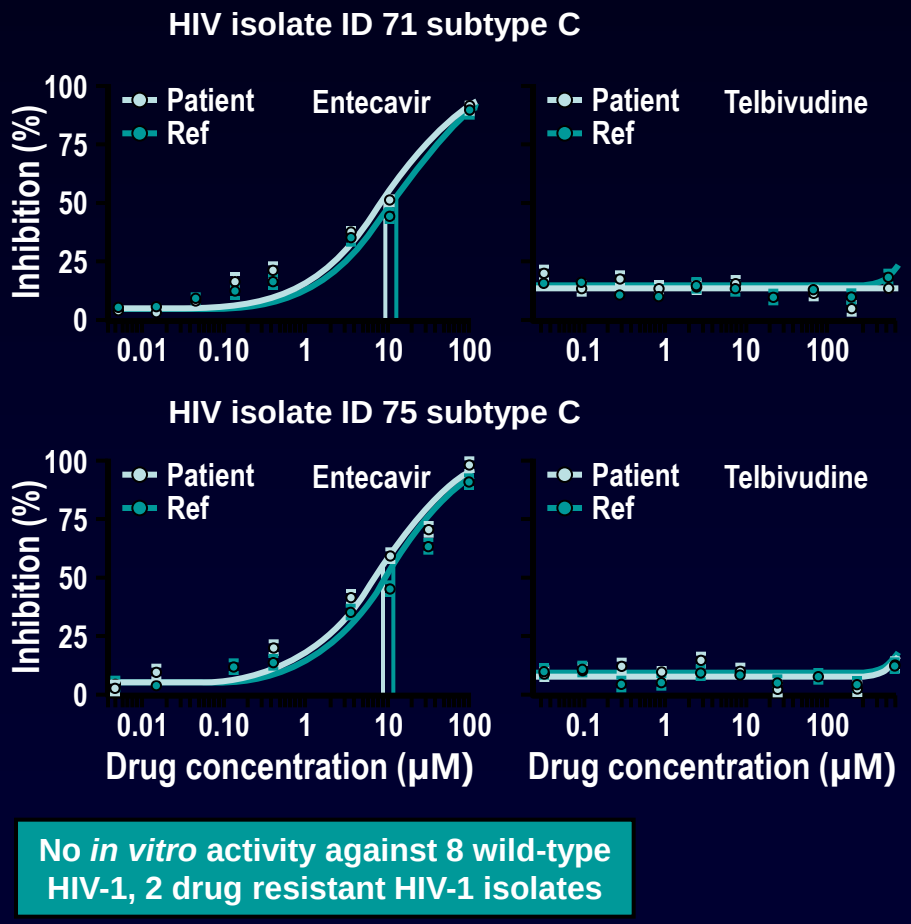
Univariate analysis for selection of M184V

Risk factor	p value
Total duration on ETV	0.05
Magnitude of HBV DNA reduction on ETV	0.04
HIV RNA pre-ETV therapy	0.87
HBV DNA pre-ETV therapy	0.69
Nadir CD4+ count	0.20

Audsley J, *et al. 15th CROI*, Boston 2008, #63

Telbuvidine – ?anti-HIV activity



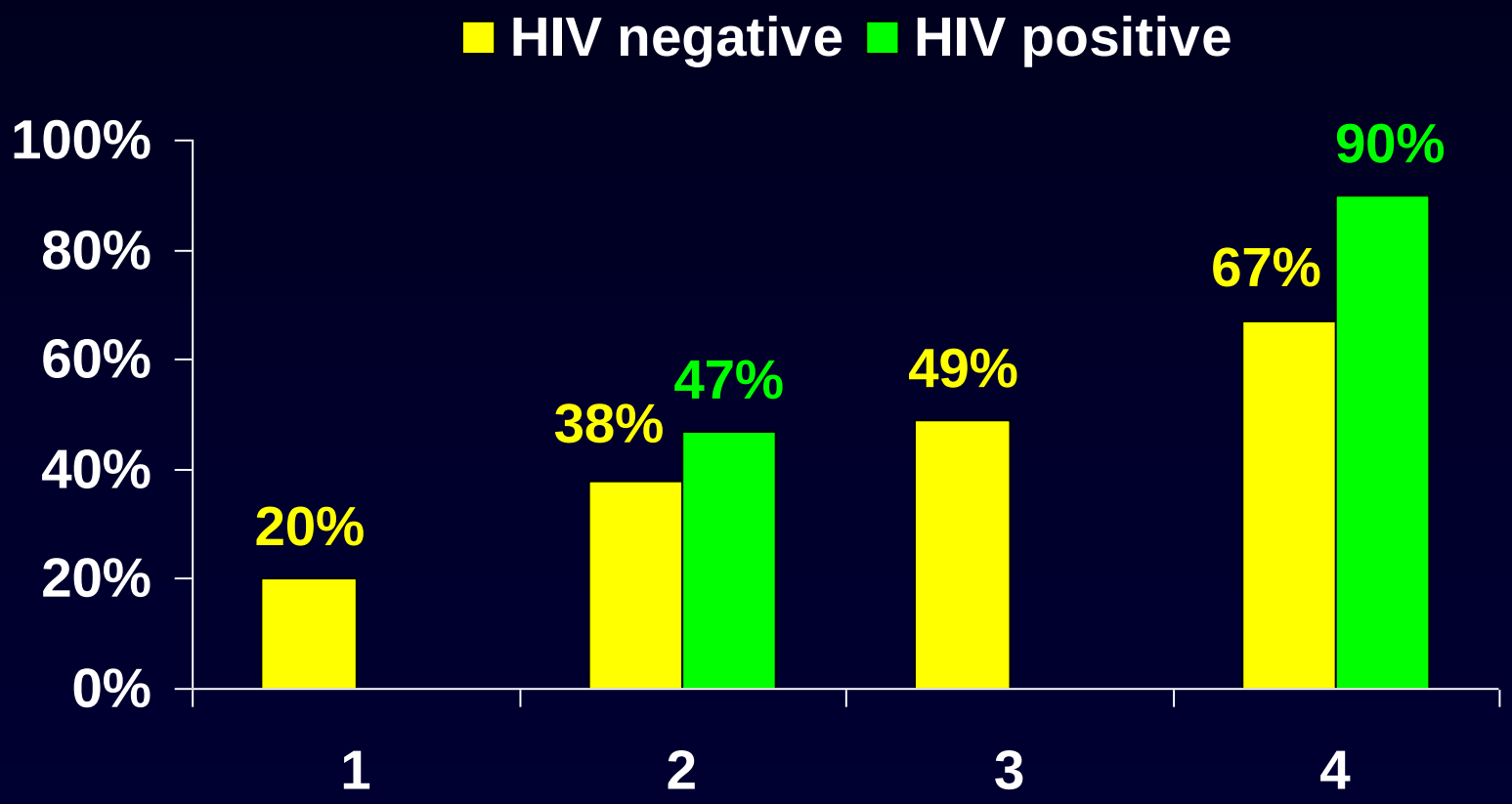


No *in vitro* activity against 8 wild-type HIV-1, 2 drug resistant HIV-1 isolates

E Low, *et al.* CROI 2009;P813a

C Avila, *et al.* CROI 2009;P813b

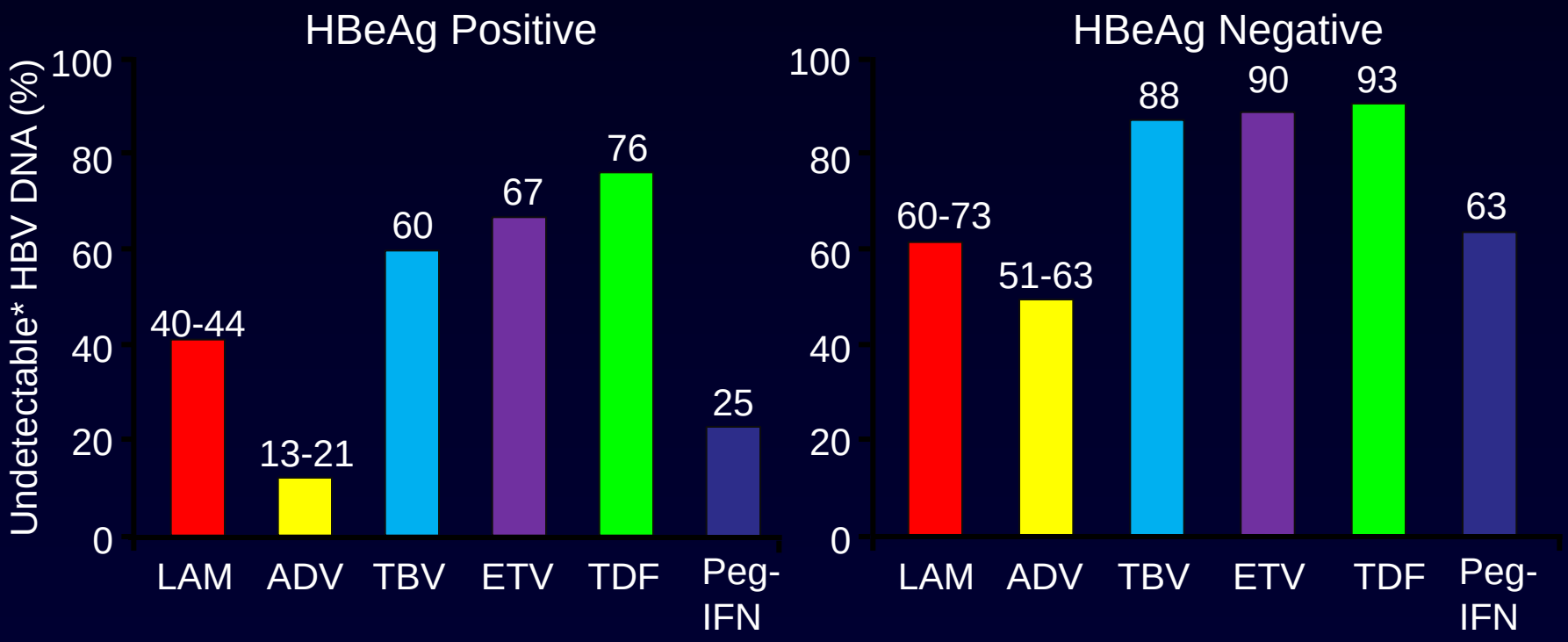
Incidence of LAM Resistance in HBV and HBV/HIV Patients



Benhamou Y et al Hepatology 1999;30:1302-6.

Undetectable* HBV DNA in HBV Patients After 1 Year of Treatment

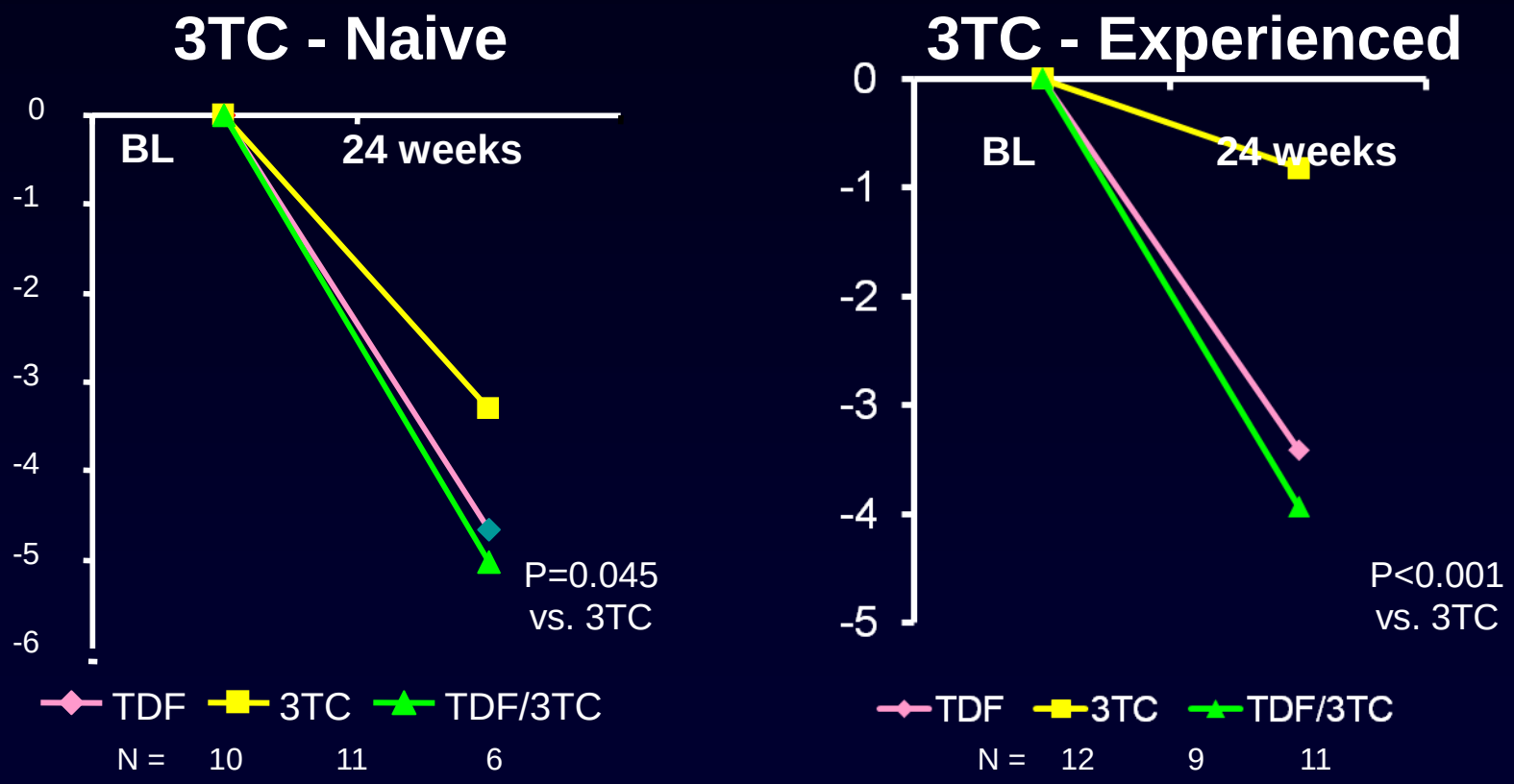
Not head-to-head trials; different patient populations and trial designs



*By PCR-based assay (LLD ~ 50 IU/mL) except for some LAM studies.

Lok AS, et al. Hepatology. 2007;45:507-539. Lok AS, et al. Hepatology. 2009;50:661-662.

TDF vs. TDF/3TC vs. 3TC in HIV/HBV Co-infected

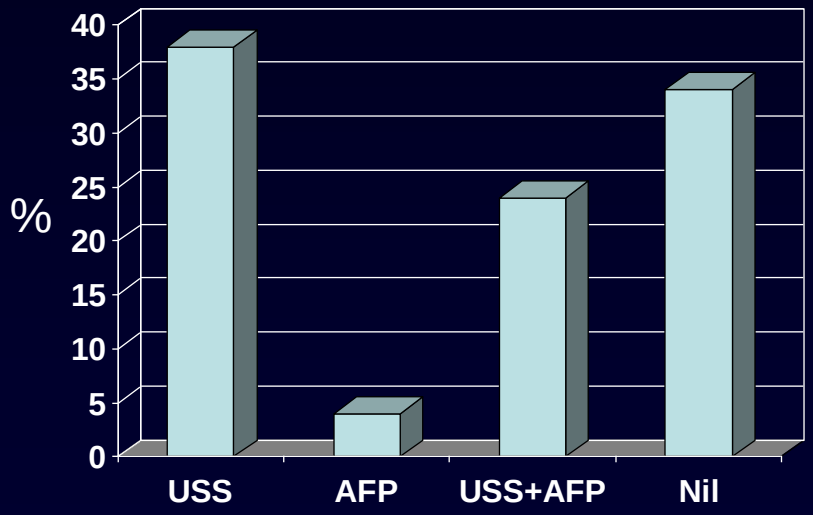


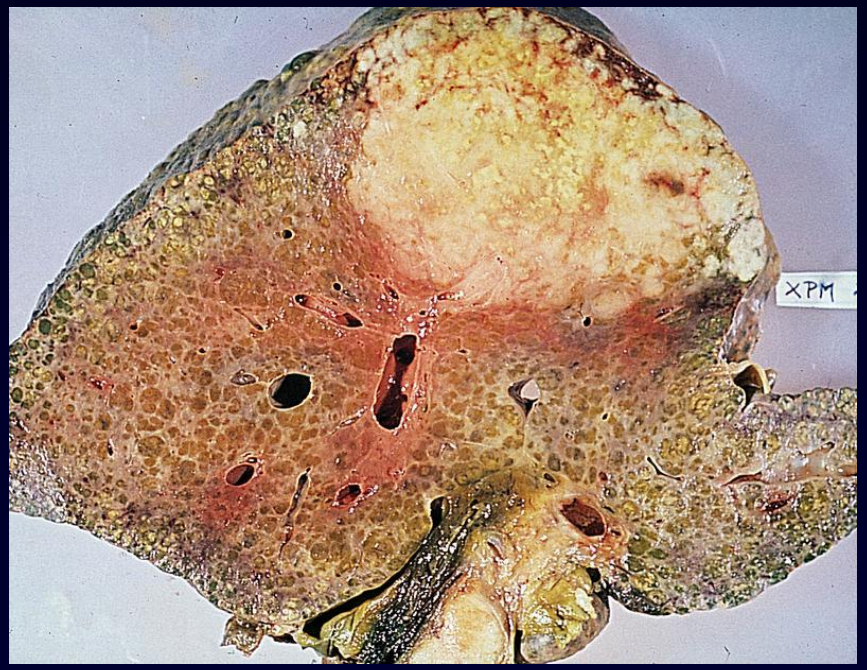
Conclusion:

- TDF/3TC superior to 3TC alone but not TDF in HBV naïve
- No benefit continuing 3TC in experienced HBV viraemic patients
- No difference between adding or switching TDF

Nelson M et al. *13th CROI.* Denver, CO, February 5-8, 2006; Abst. 831.

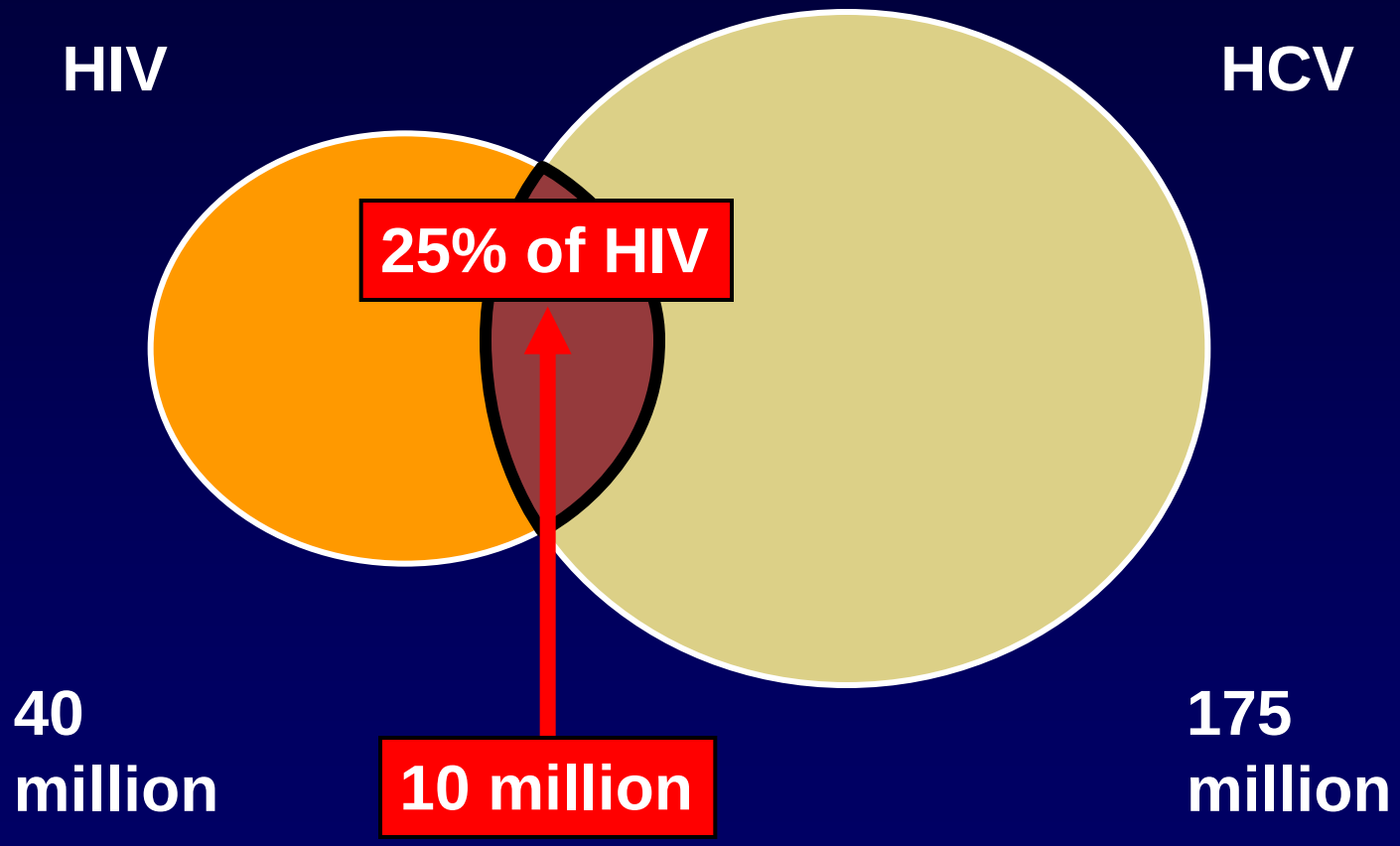
Screening for Hepatoma



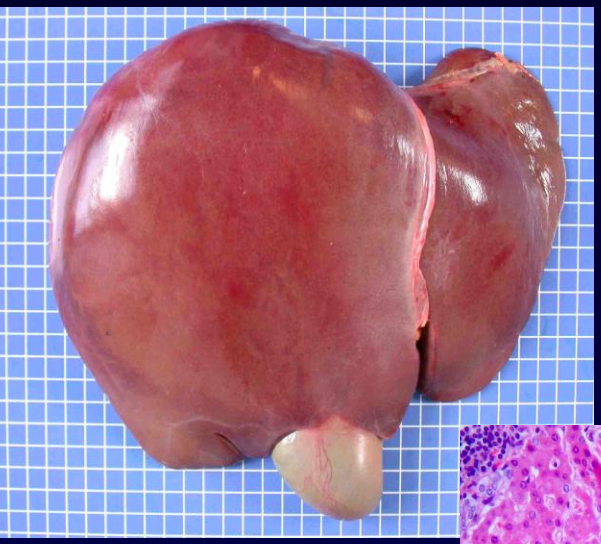


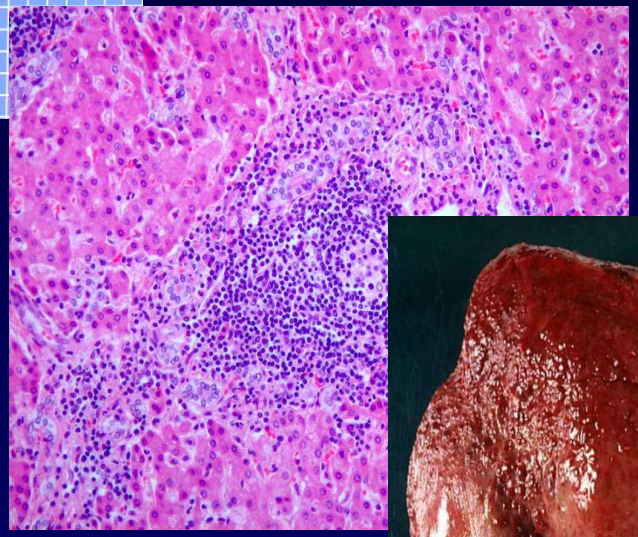

STAMP OUT
HIV / HCV
Co-Infection

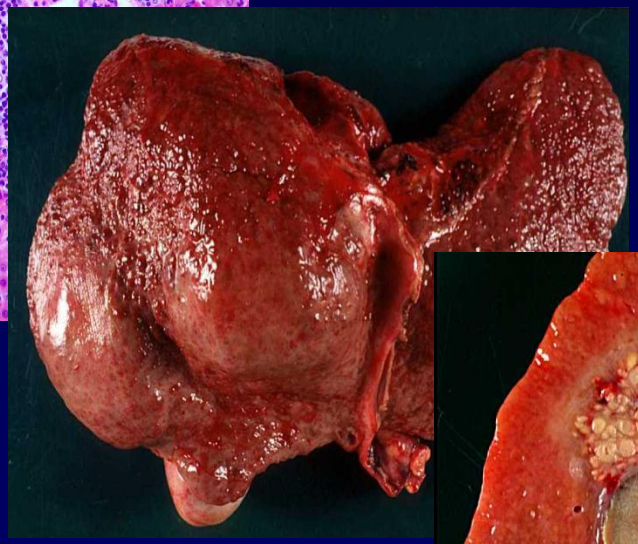
Overlapping HCV & HIV epidemics

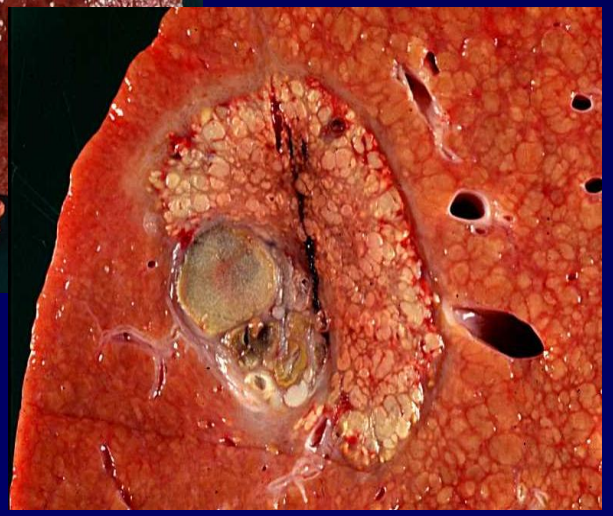


Natural History of HCV Liver Disease









Liver failure (2 – 5% / yr)

~55-85%

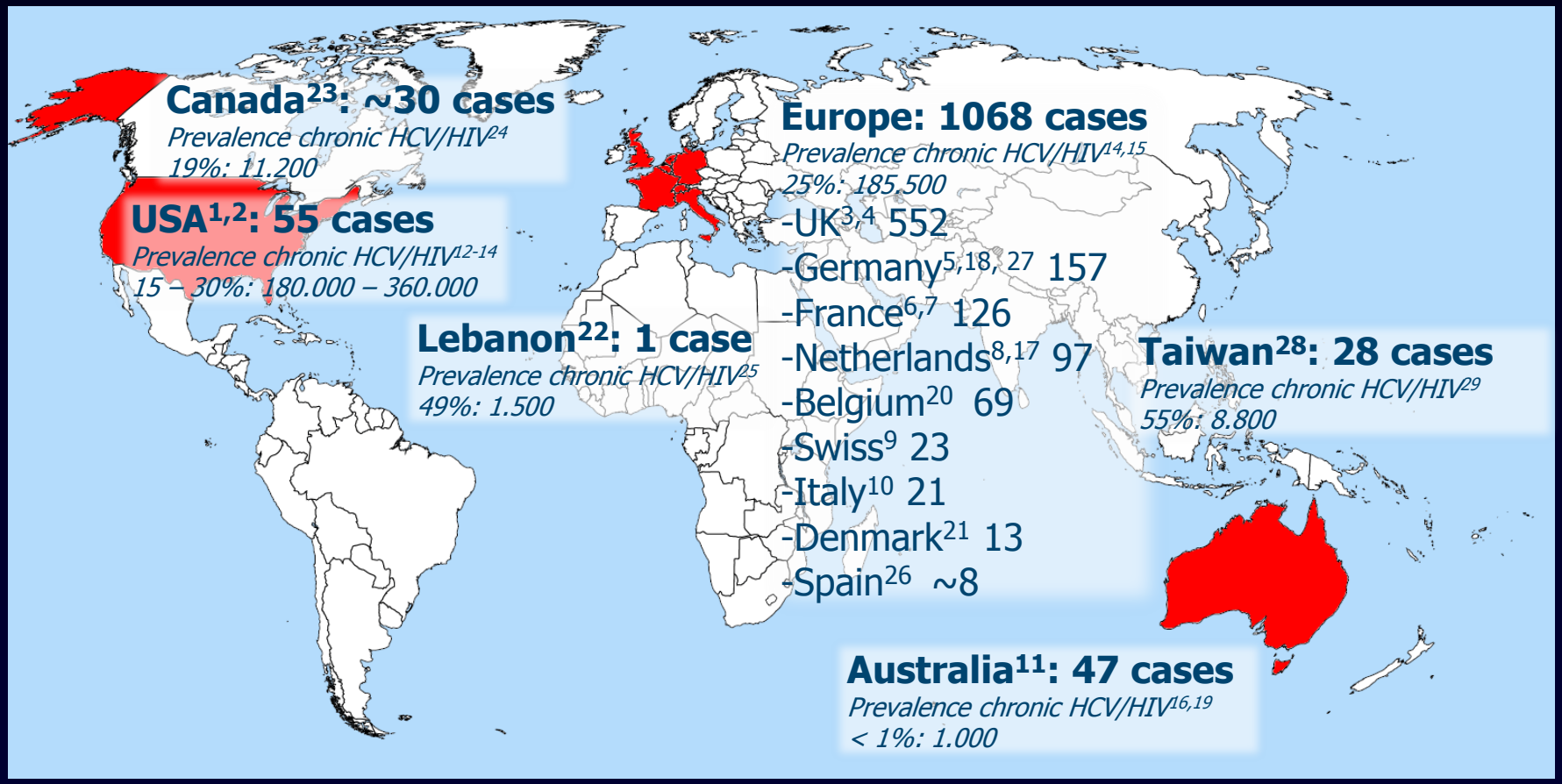
25-30 yrs

2 - 4% / yr

Why do you not want to catch hepatitis C

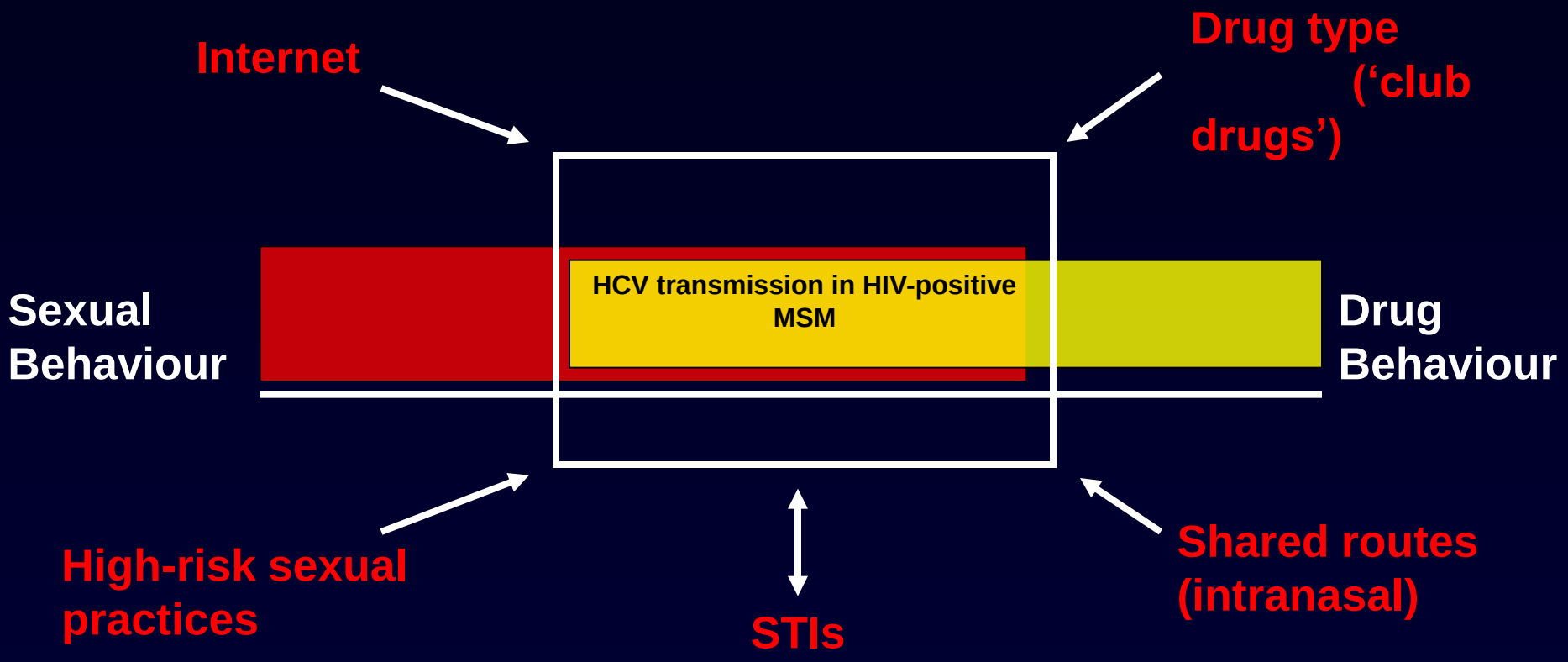
- Transmission

Acute HCV among HIV+ MSM

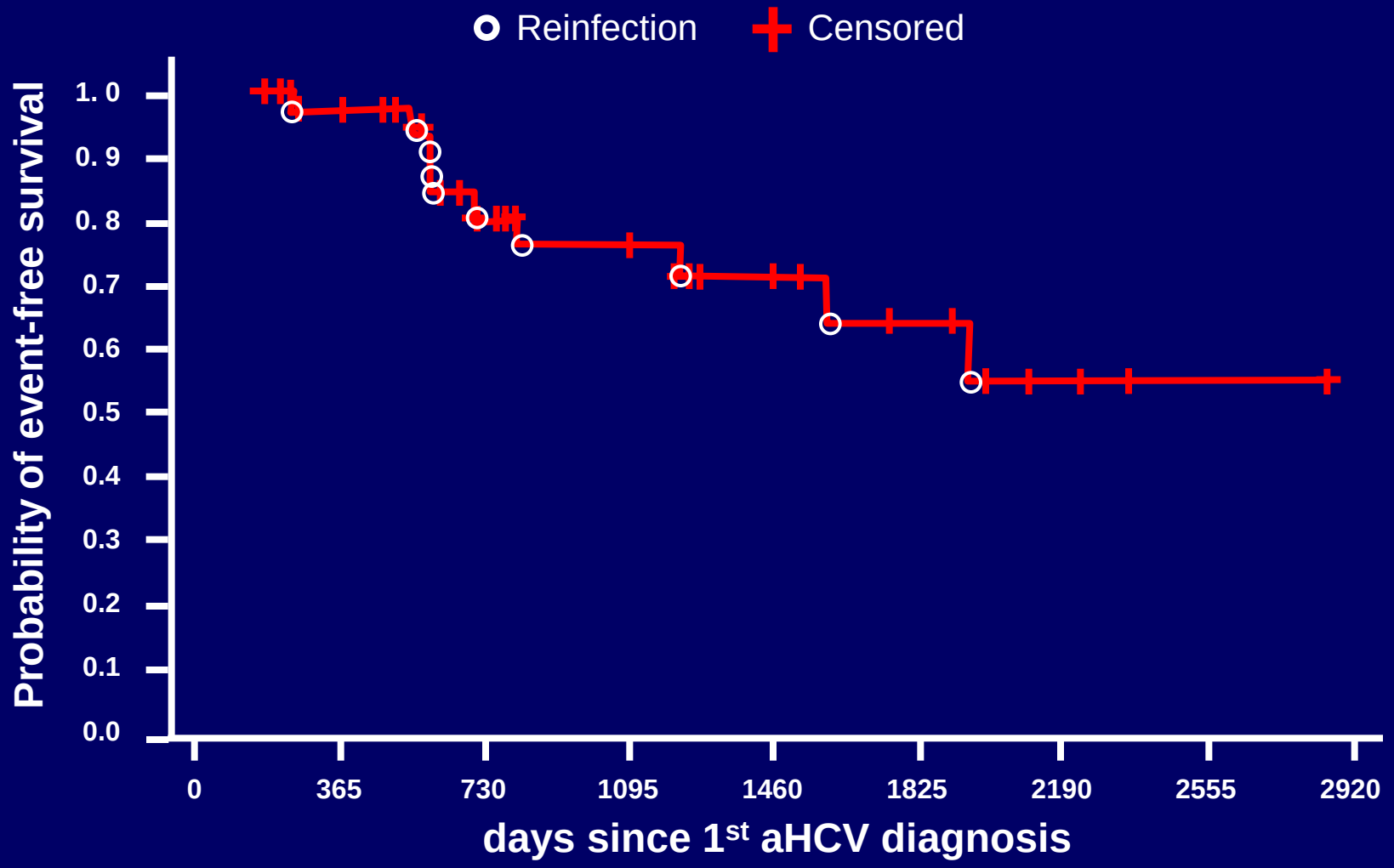


1:Luetkemeyer JAIDS 2006; 2:Cox Gastroenterology 2008; 3:Giraudon Sex Transm Infect 2008; 4:Ruf Eurosurveill 2008; 5:Vogel CID 2009; 6:Gambotti Euro Surveill 2005; 7:Morin Eur J Gastro Hepat 2011; 8:Urbanus AIDS 2009; 9:Rauch CID 2005; 10:Gallotta 4th Works. HIV & Hep. Coinf. 2008; 11:Matthews CID 2009; 12:Sherman CID 2002; 13:Backus JAIDS 2005; 14:UNAIDS Report 2008; 15:Soriano JID 2008; 16:Matthews CID 2011; 17:Arends Neth J Med 2011; 18:Neukam HIV Med 2011; 19:Pfafferott PLoS One 2011; 20:Bottieau Euro Surveill 2010; 21:Barfod Scand JID 2011; 22:Dionne-Odom Lancet Infect Dis 2009; 23:Hull personal conversation 2011; 24:Remis Public Health Agency of Canada 2002; 25:UNGASS Country progress Report 2010; 26:Soriano personal conversation 2011; 27:Boesecke 18thCROI Boston 2011 abstract #113; 28:Sun Liver International 2011; 29:Lee J F Med Assoc 2008

Summary

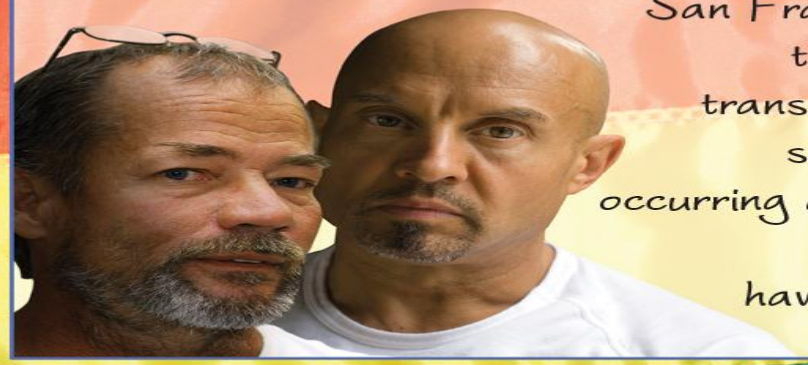

Internet
Drug type ('club drugs')
Sexual Behaviour
HCV transmission in HIV-positive MSM
Drug Behaviour
High-risk sexual practices
STIs
Shared routes (intranasal)

Time from first to second episode of acute HCV infection in 45 subjects with HCV clearance



Stellbrink HJ, *et al. Journal of the International AIDS Society* 2010; 13(Suppl 4): Poster #200.

Protect Yourself and Others



Reports from Europe and more recently New York and San Francisco suggest that hepatitis C transmission through sexual activity is occurring among gay and other men who have sex with men.

This information is provided by the Hepatitis C Support Project / HCV Advocate and Project Inform.

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A special thanks to Matt Sharp who convened the discussion that produced the document

HCV ADVOCATE www.hcvadvocate.org

Hepatitis C Support Project / HCV Advocate Website
PO Box 427037, San Francisco, CA 94142

Executive Director, Editor-in-Chief
Alan Franciscus
HCV Advocate Website: www.hcvadvocate.org

Managing Editor / Webmaster
C.D. Mazoff, PhD

Design and Production
Leslie Hoex, Blue Kangaroo Design
www.bluekangaroodesign.com

PROJECT INFORM

Project Inform
1375 Mission Street, San Francisco, CA 94103–2621
415-558-8669 fax 415-558-0684

National HIV/AIDS Treatment Hotline:
800-822-7422 (toll-free) or 415-558-9051
(San Francisco Bay Area/international)
Monday–Friday, 10am–4pm (Pacific Time)

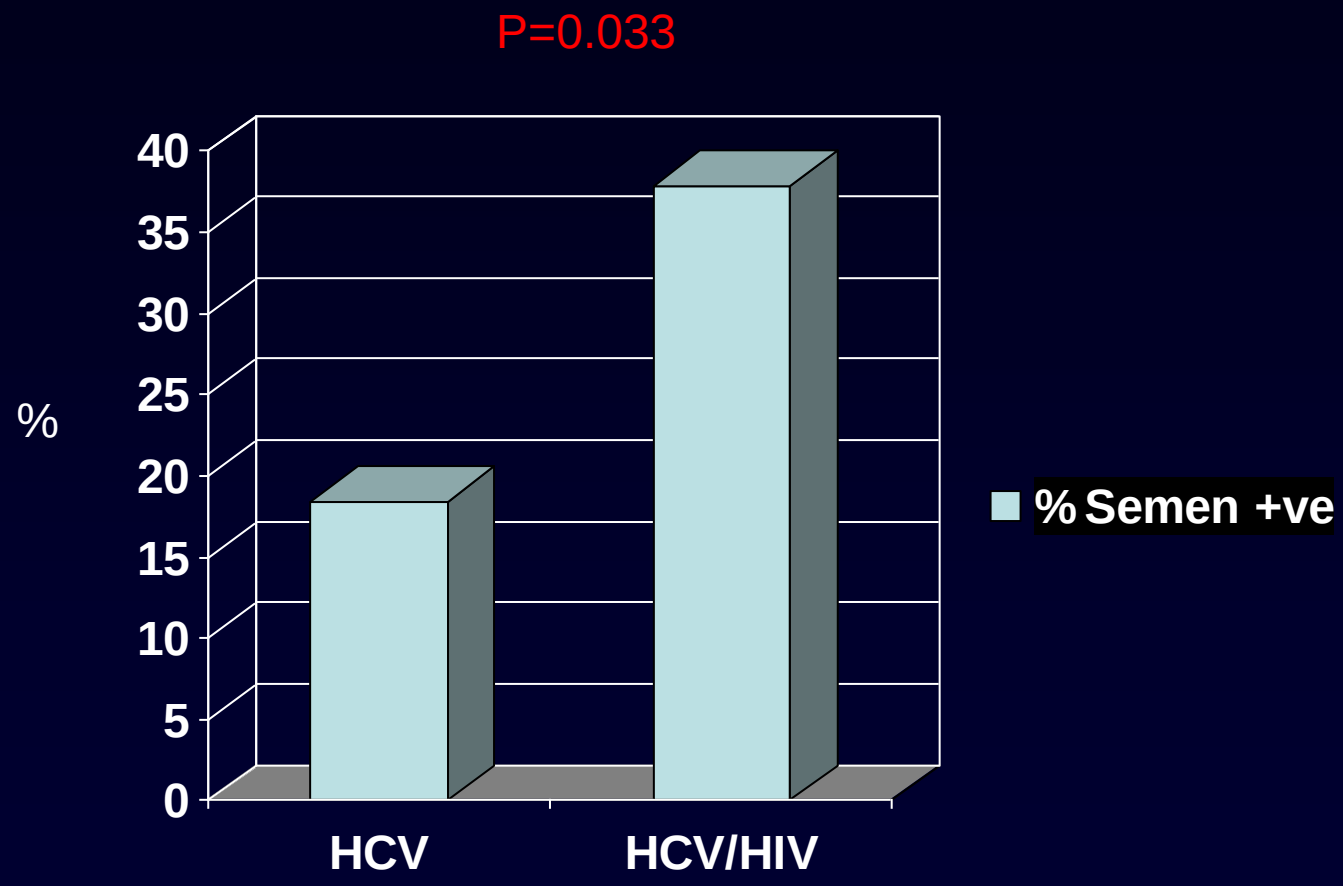
Executive Director
Dana Van Gorder
www.projectinform.org

Gay Men and Hepatitis C

Useful Facts


OK
OK
Don't swallow
OK
Danger! Use condom
OK
Don't swallow
OK
OK
OK
OK
Safety First !
Don't swallow
OK
OK
www.PREVAIDS.org
OK
OK
Danger! Use condom
OK
Don't swallow
OK
Danger! Use condom
OK
OK

Seminal Positivity for HCV



Hepatitis C Genotype

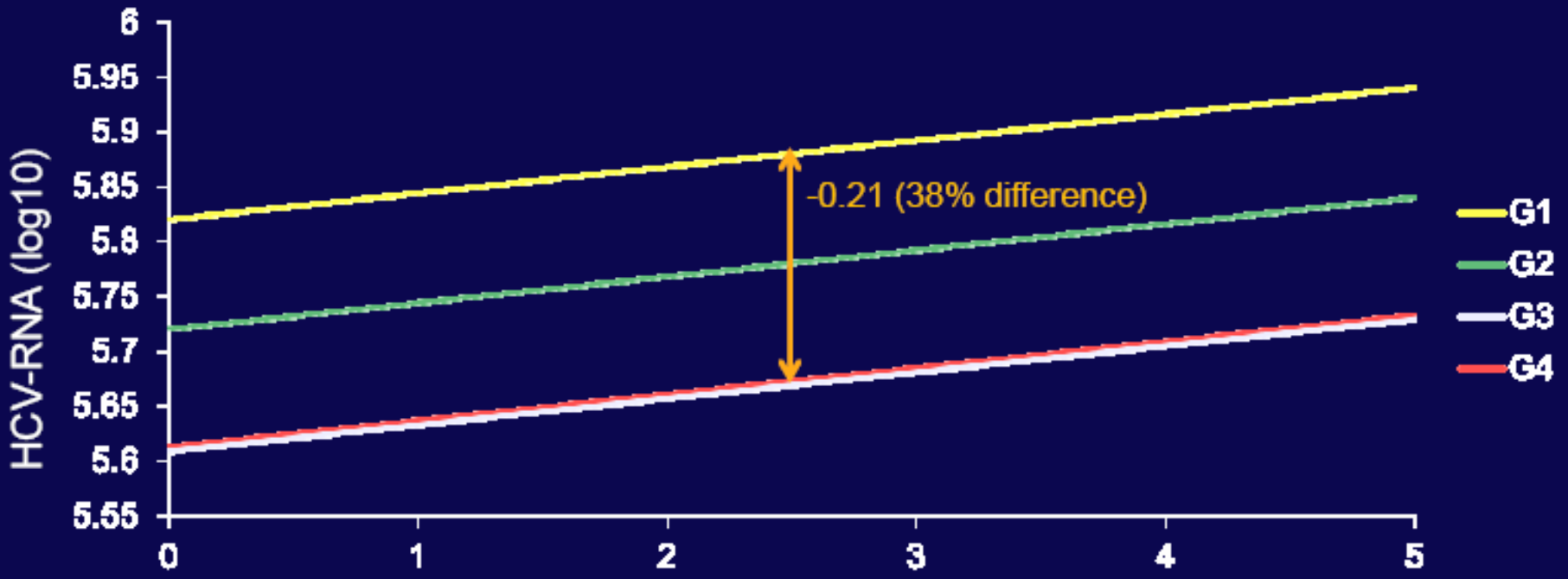
Genotype	NEAT	EUROSIDA
1	66	53
2	3	4
3	13	29
4	18	15

Other small series have reported a prepondrance of hepatitis C genotype 1

Results: Genotype

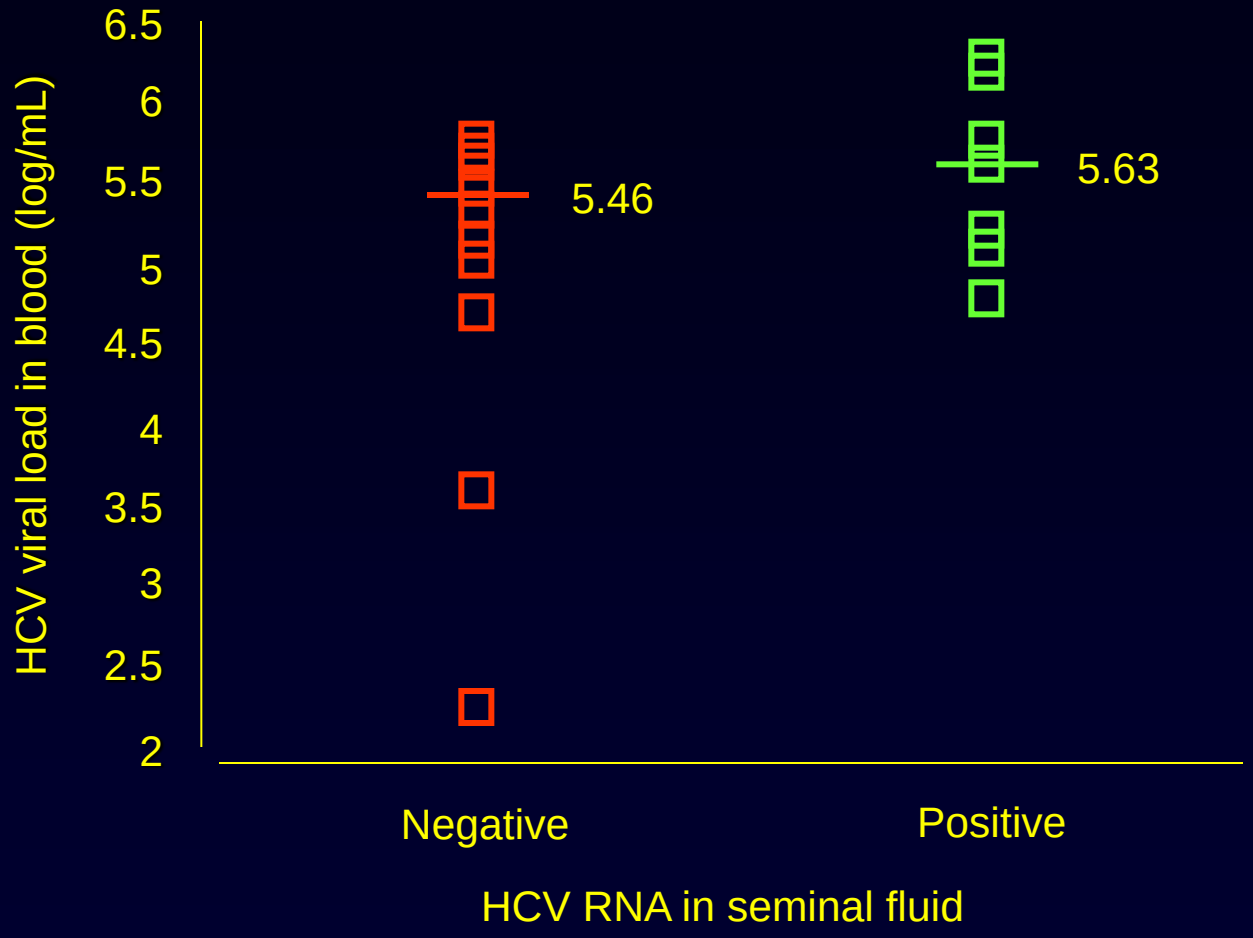
Multivariate Model*

Variable	Estimate (log10)	95% CI	p-value
Time from baseline (years) [SLOPE]	0.024	(0.0042, 0.043)	0.017
HCV Genotype			
1	0		
2	-0.10	(-0.35, 0.15)	0.42
3	-0.21	(-0.31, -0.12)	<0.0001
4	-0.21	(-0.34, -0.084)	0.0012



*Adjusted for: age, gender, race, region, HIV-RNA, CD4, HCV genotype, HCV assay, HBsAg, HIV risk group, cART, HCV infection date.

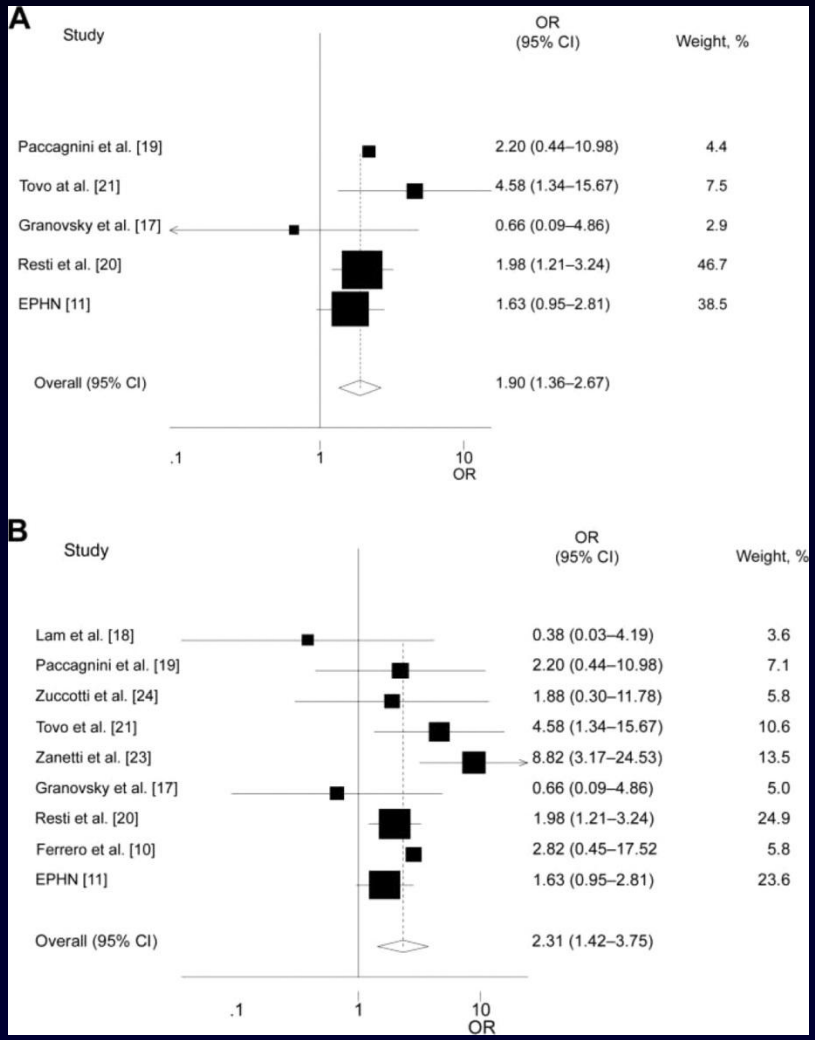
EuroSIDA



Comparison of HCV blood viral load between patients presenting with HCV RNA positive seminal fluid (n=7) and patients presenting with HCV RNA-negative seminal fluid (n=11)

The bar indicates the median

Increased risk of MTC Transmission HCV with HIV.



Polis C B et al. Clin Infect Dis. 2007;44:1123-1131

Clinical Infectious Diseases

Why do you not want to catch hepatitis C

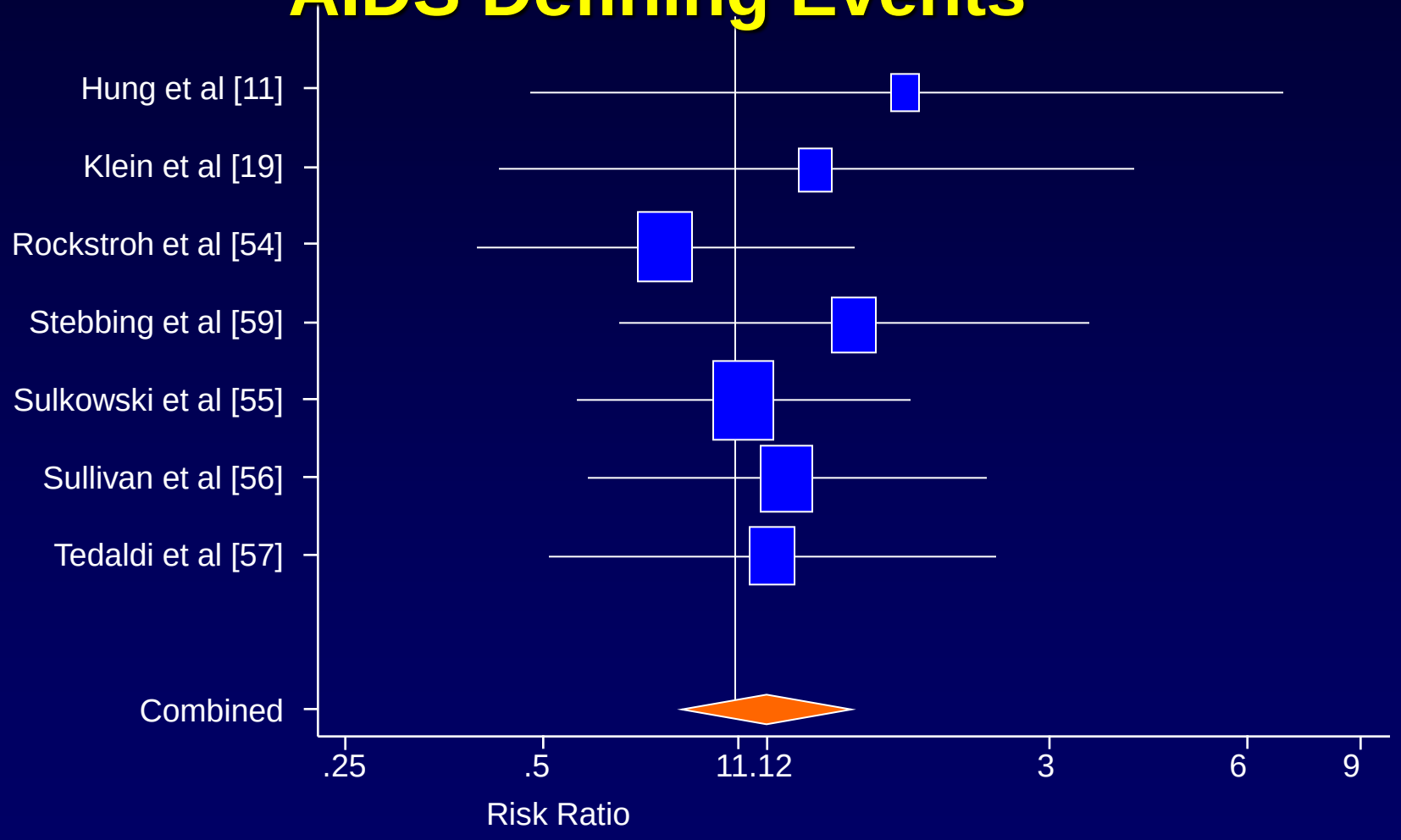
- Transmission
- Stigma

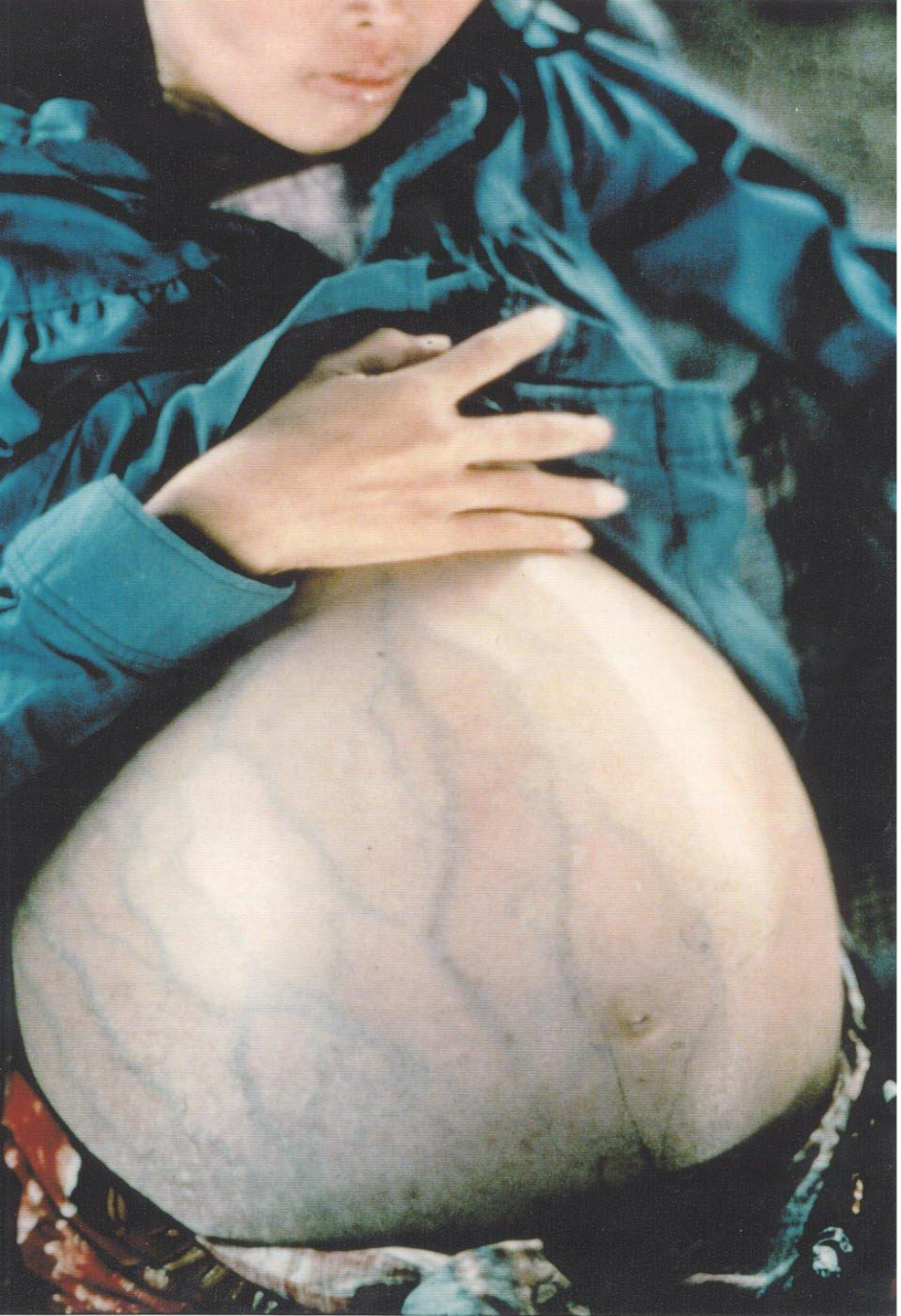

LOVE·MY·VIRUS

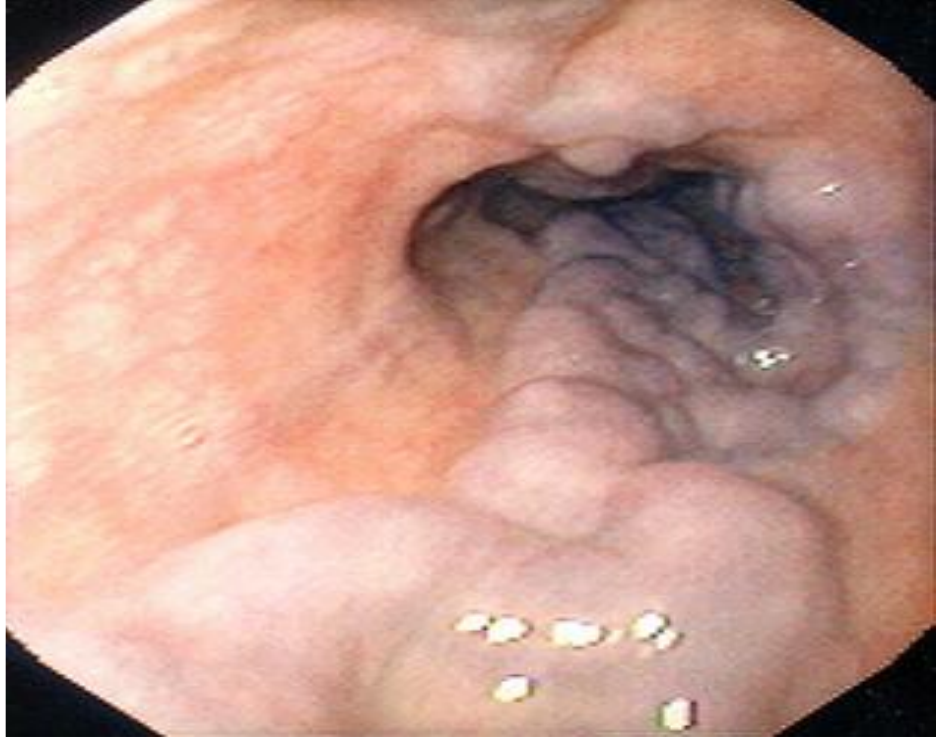
Why do you not want to catch hepatitis C

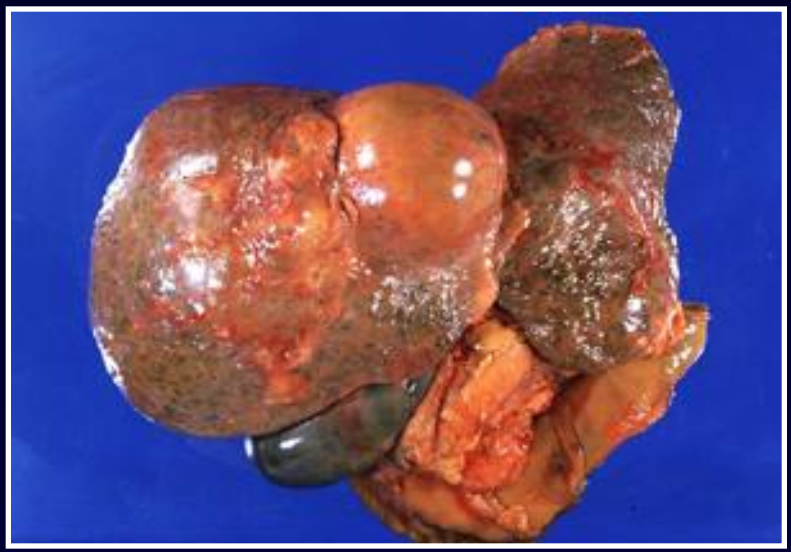
- Transmission
- Stigma
- More Rapid Progression of disease

No Association of Hepatitis C with AIDS Defining Events

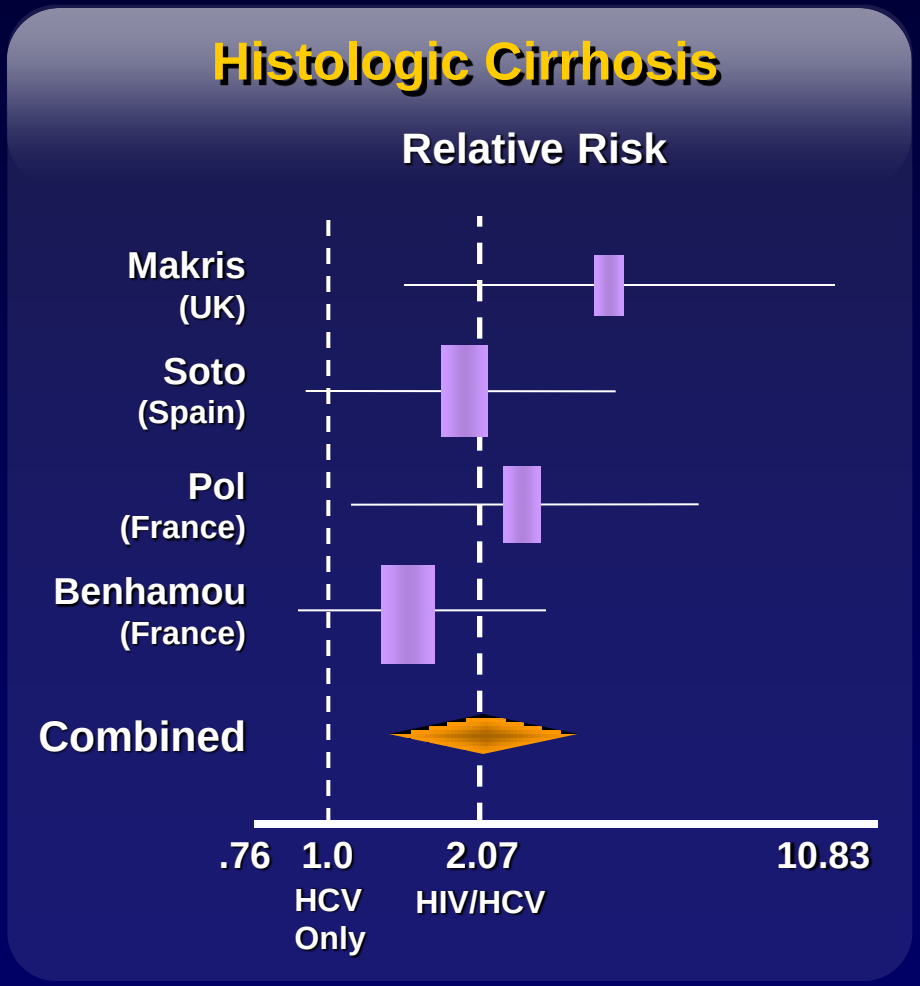


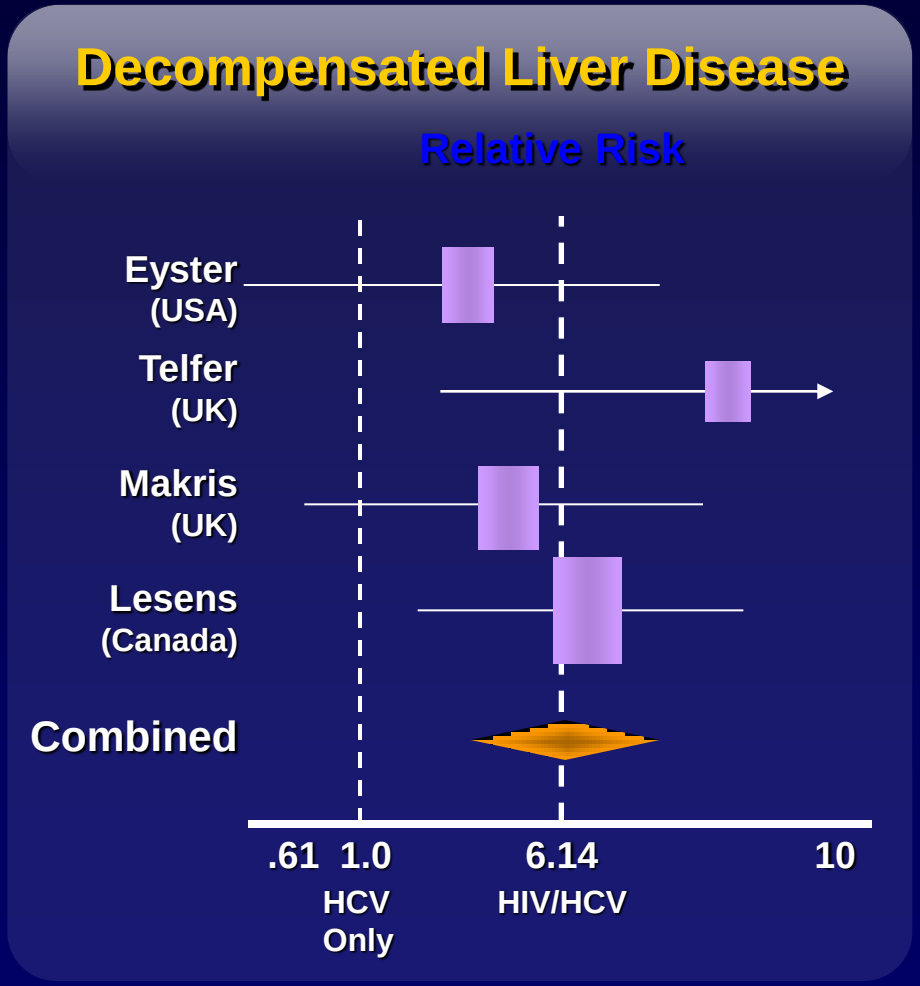






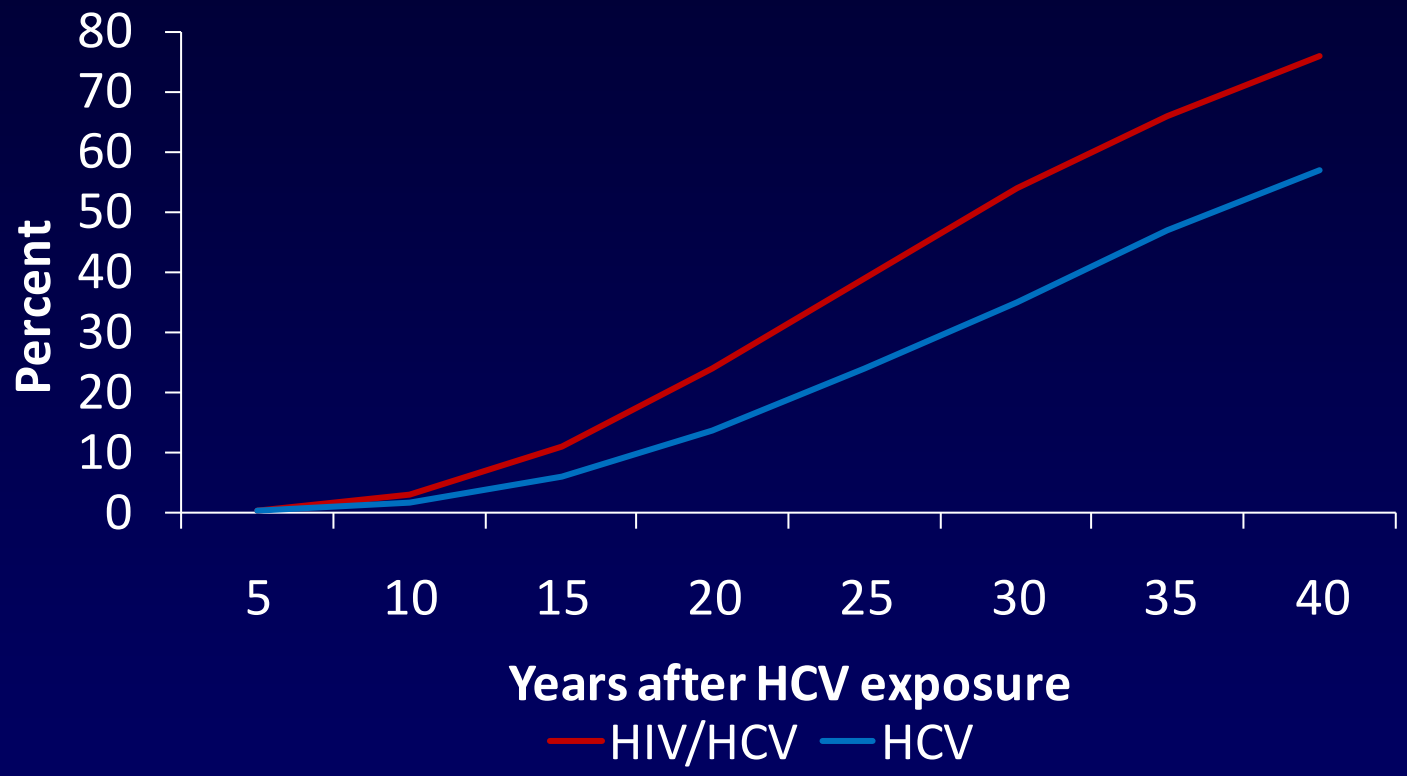
Increased Risk of Cirrhosis and ESLD Due to HIV/HCV Coinfection



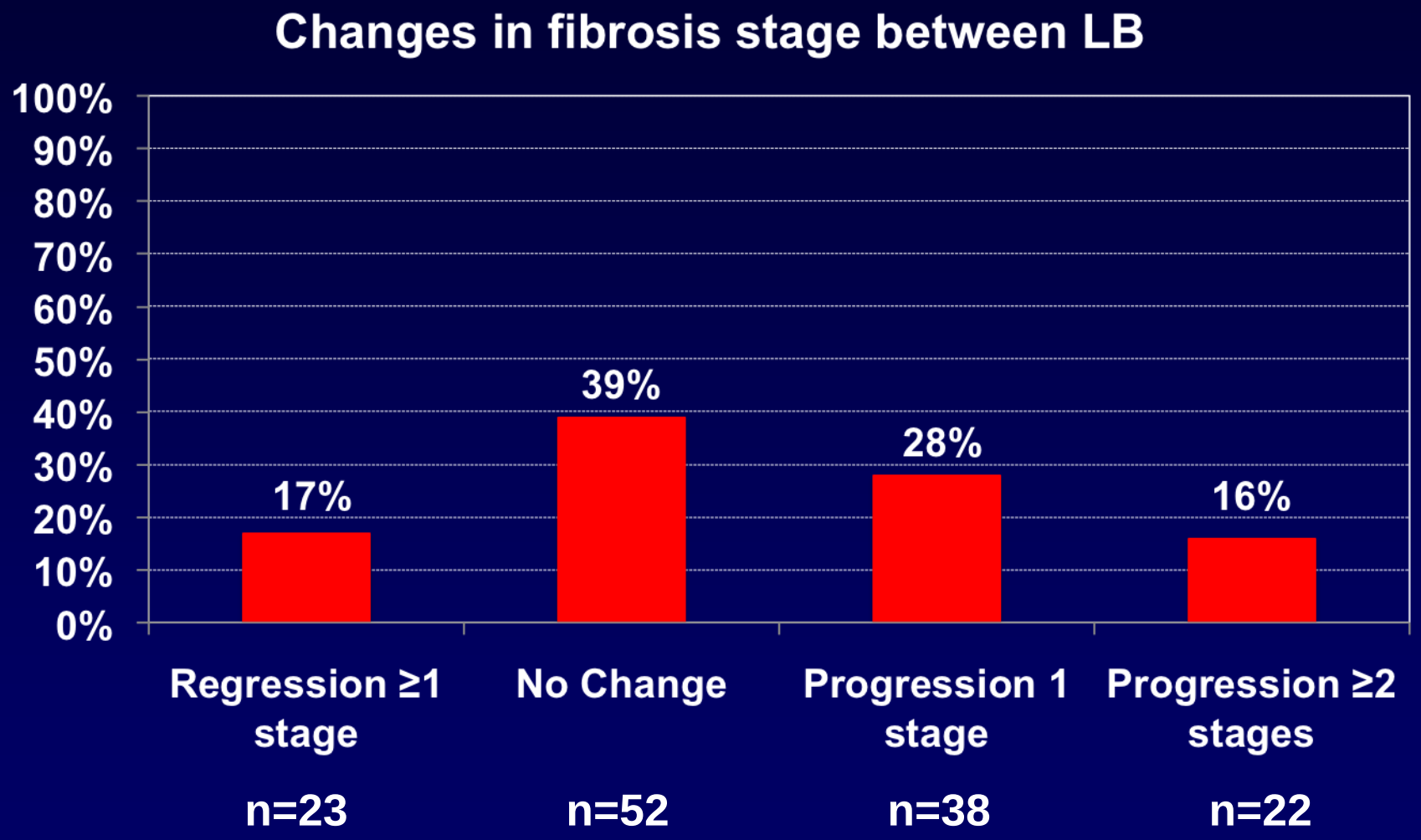


Graham CS, et al. *CID.* 2001;33:562-569.

Results: Cumulative probability of cirrhosis



RESULTS (III)



Median (Q1-Q3) time between LB: 3.3 (2-5.2) years

Why do you not want to catch hepatitis C

- Transmission
- Stigma
- More Rapid Progression of disease
- Increase in now known HIV related comorbidities

Top 12
Ways to Avoid a Heart Attack

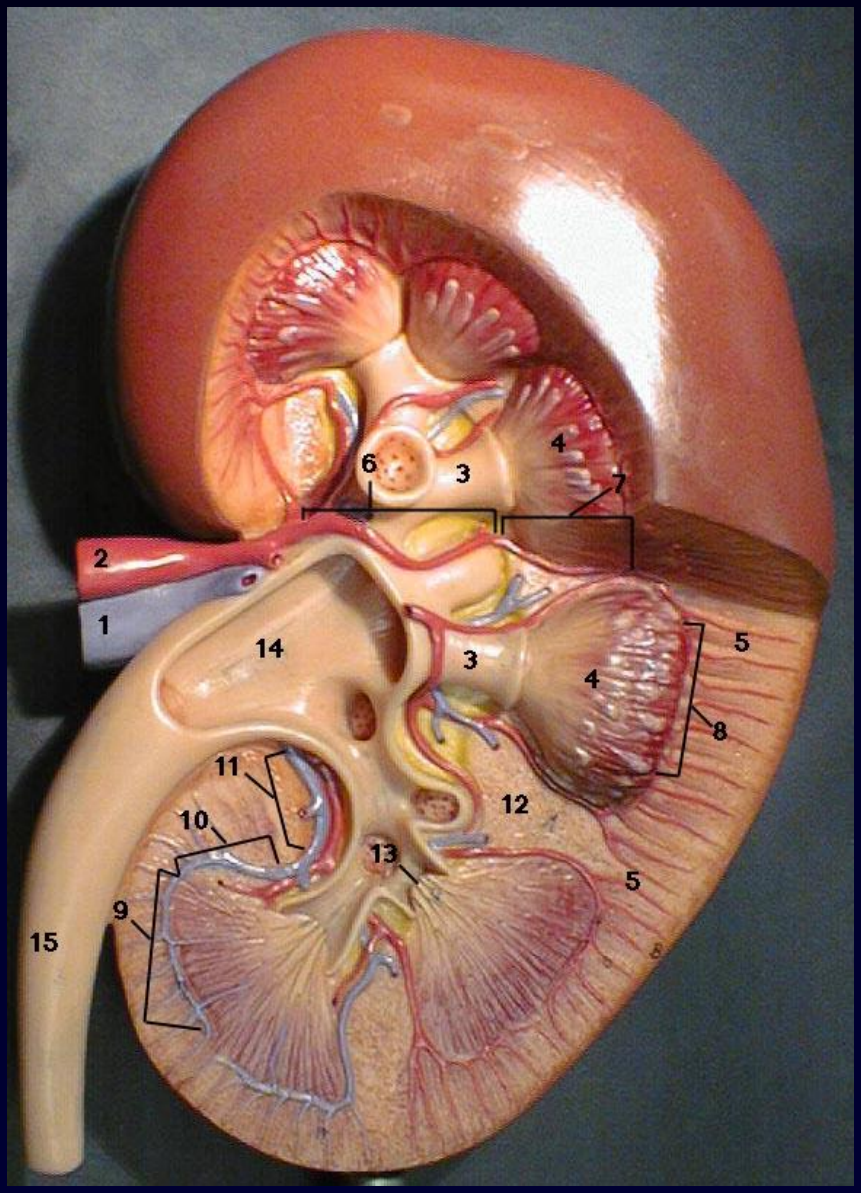
Defrim Kërçagu, MD

DIABETES

The Essential Guide

Need
– 2 –
Know

Sue
Marshall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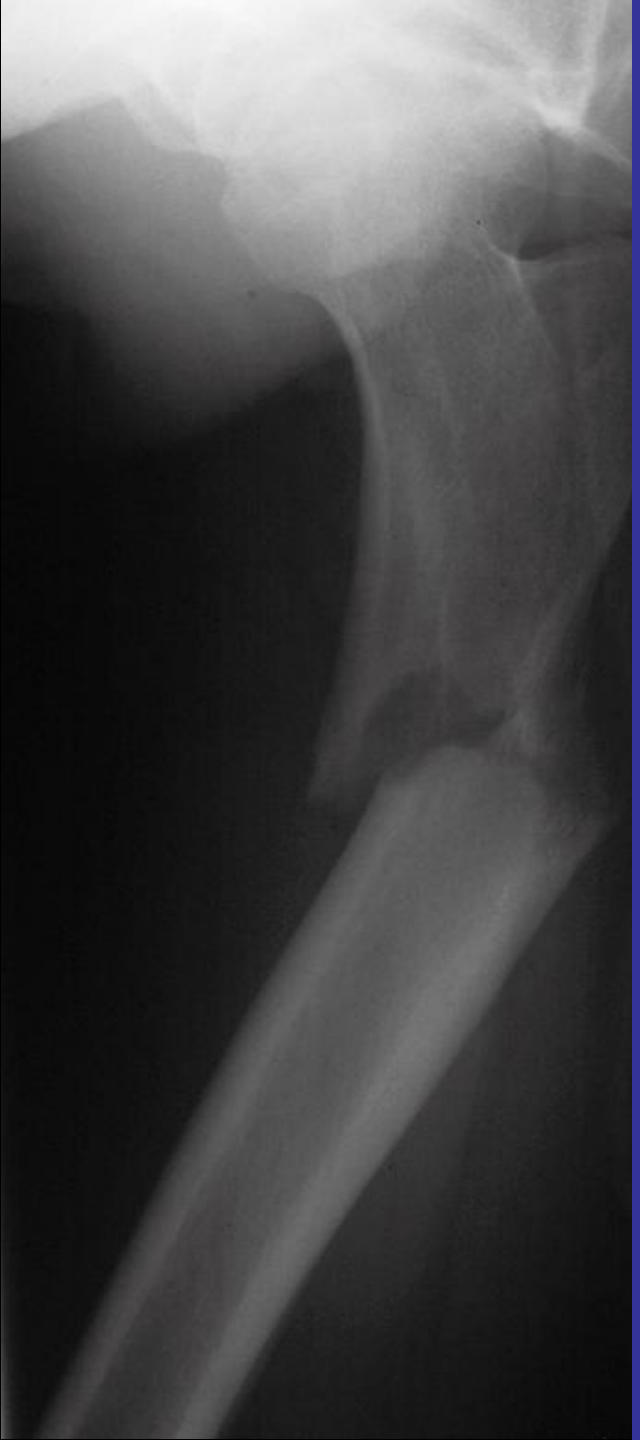
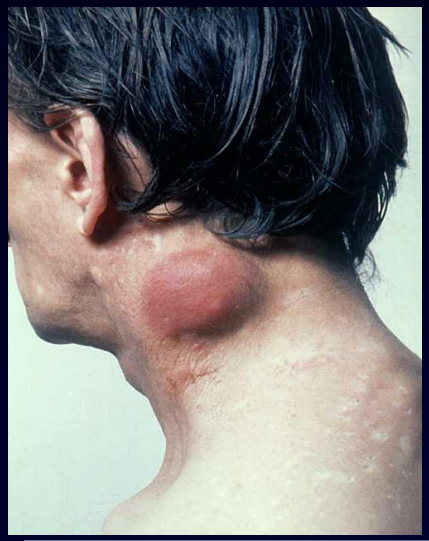
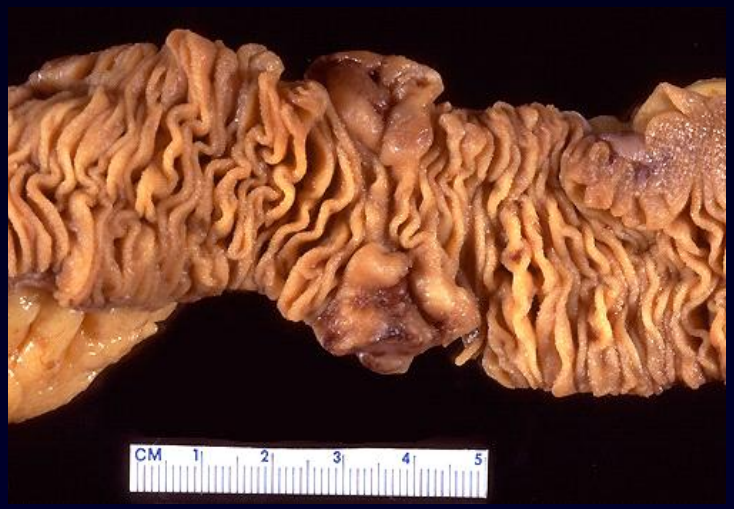
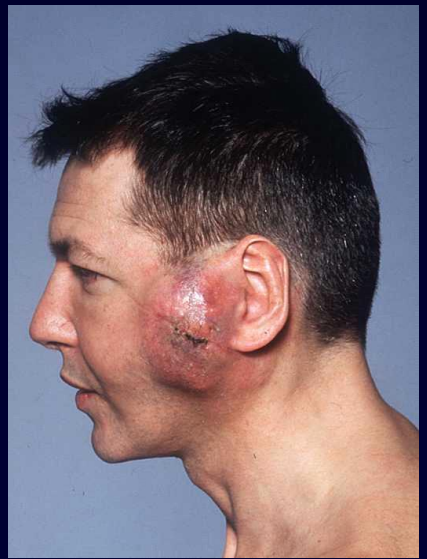
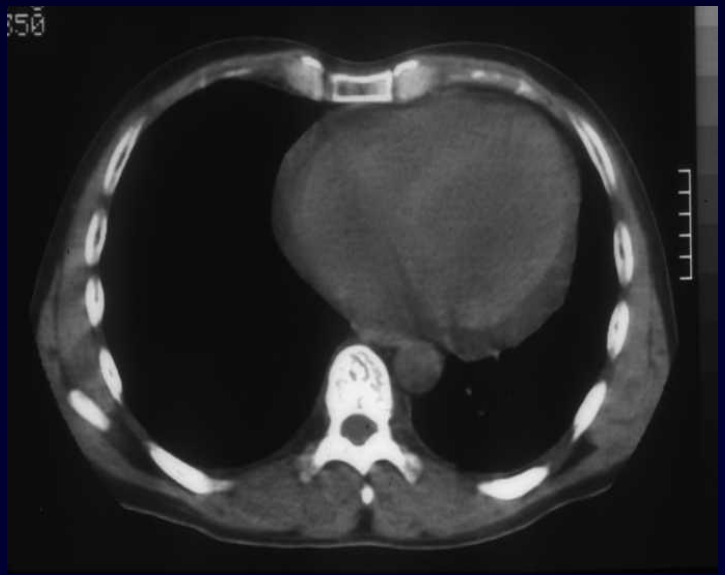



ELLIS
48




CM 1 2 3 4 5

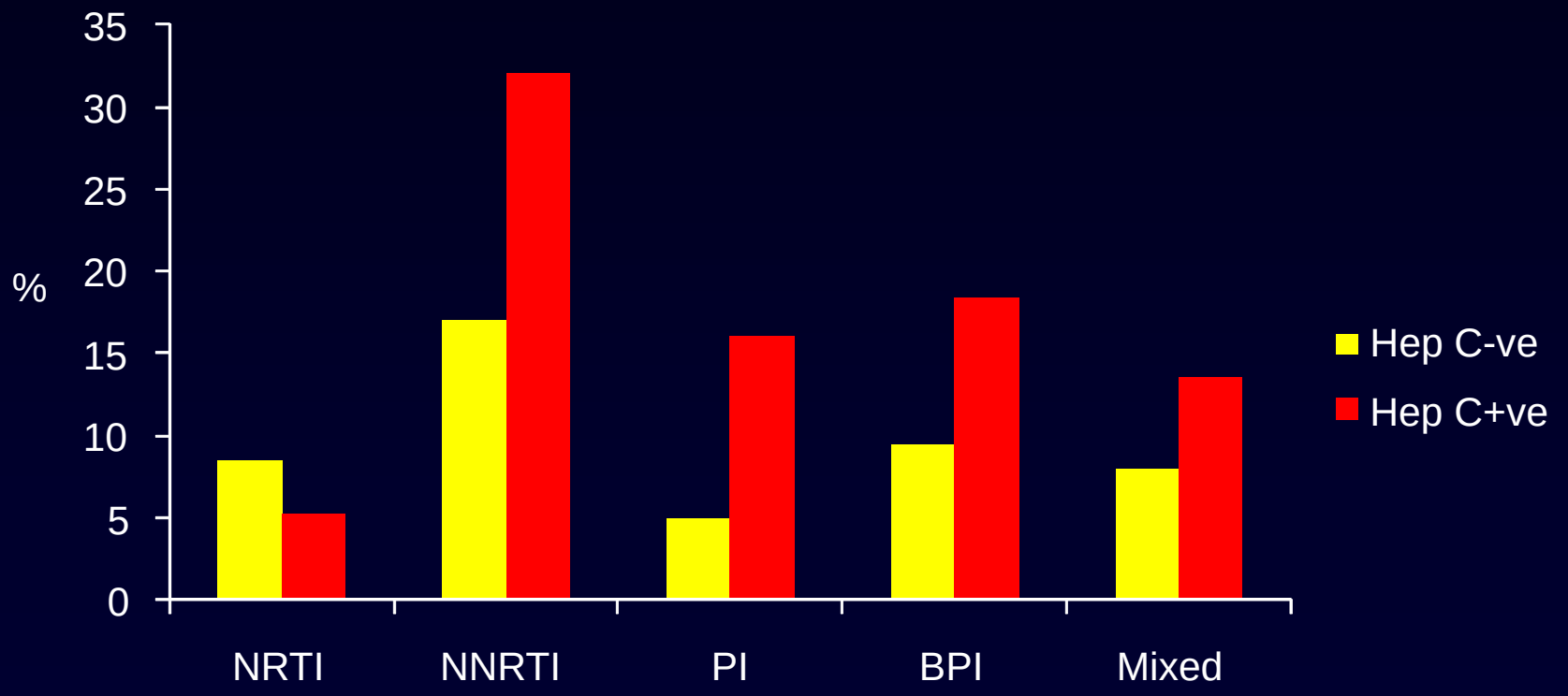




Why do you not want to catch hepatitis C

- Transmission
- Stigma
- More Rapid Progression of disease
- Increase in now known HIV related comorbidities
- Increase in HAART toxicity

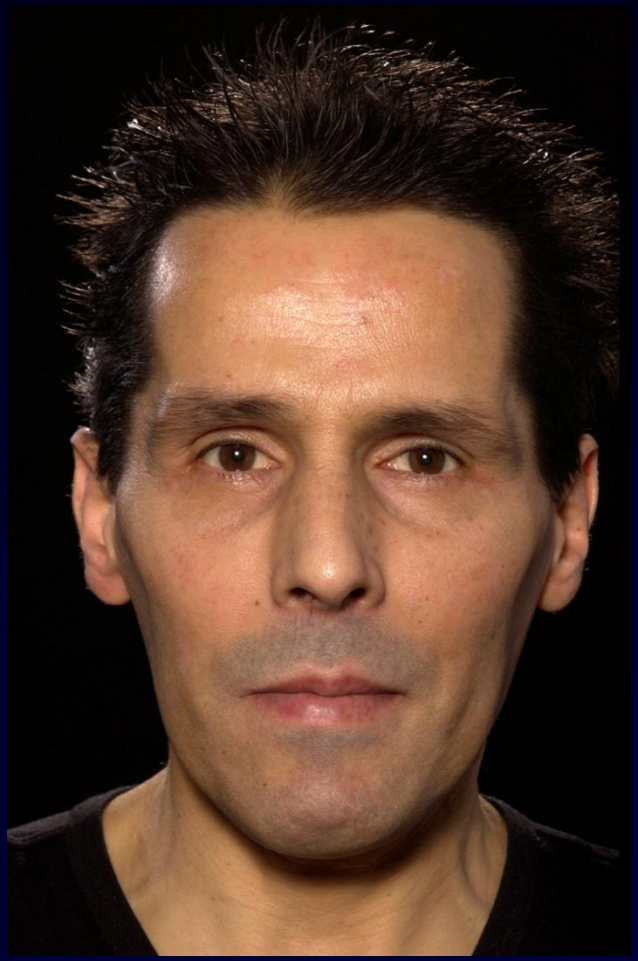
Incidence of Grade 2 or Above Liver Enzyme Elevation

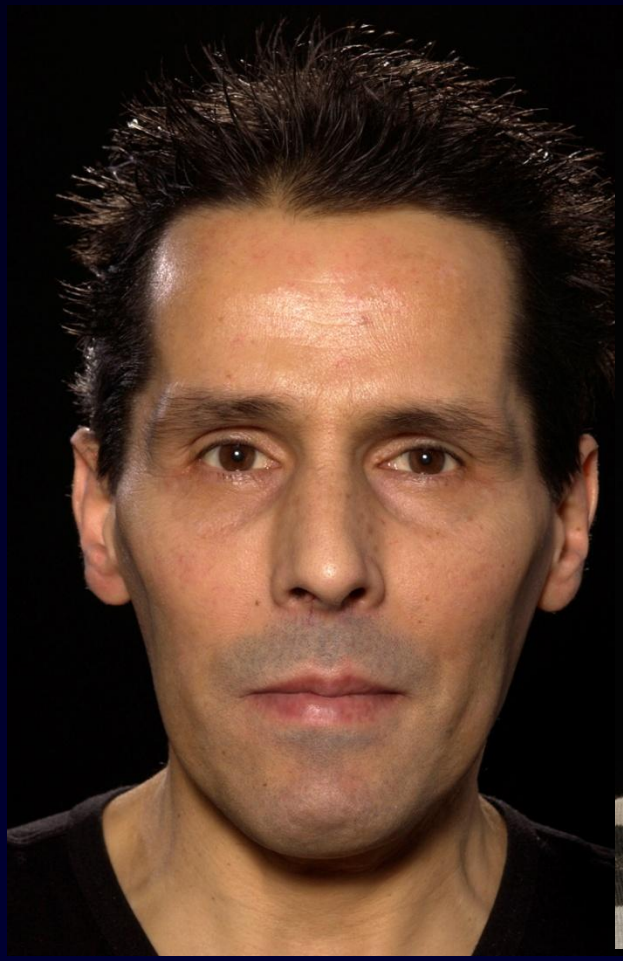
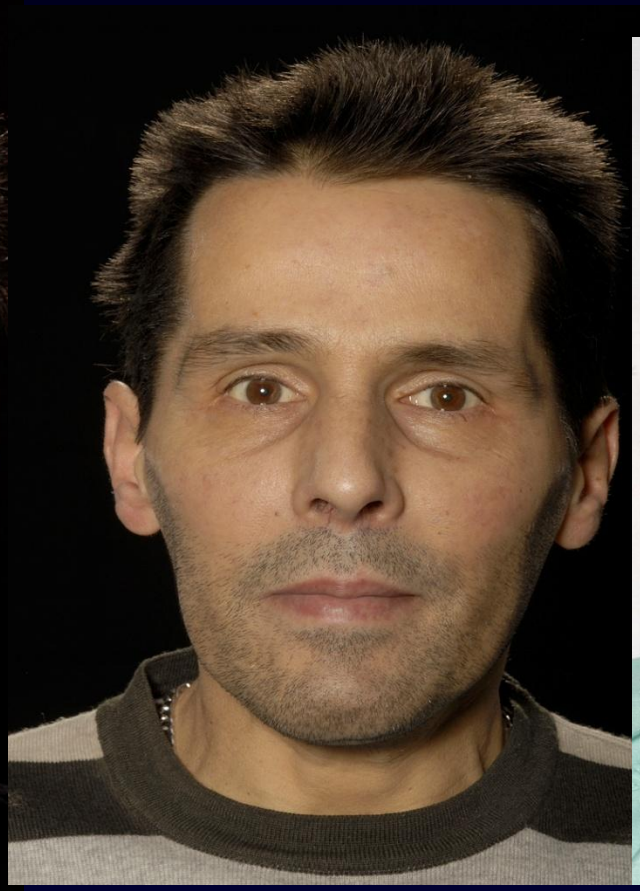
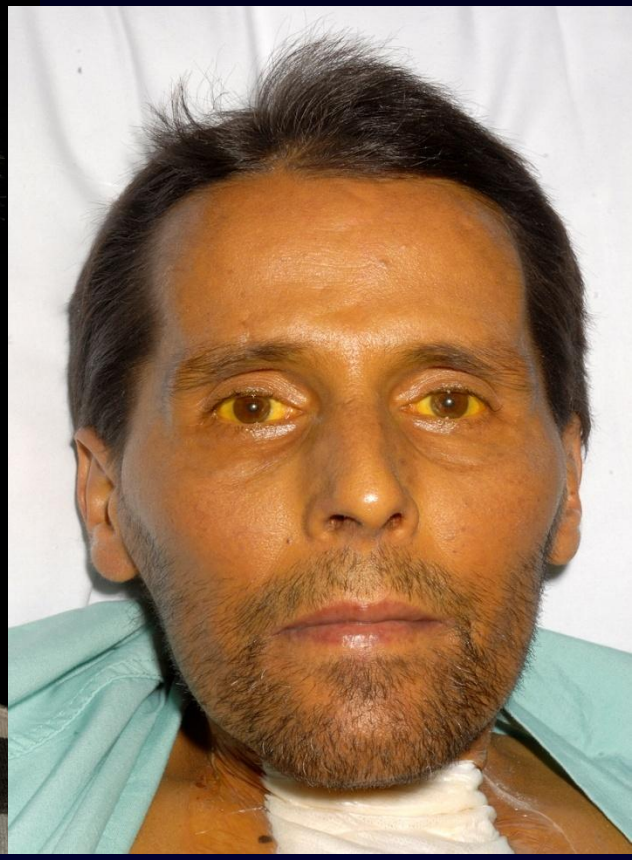


Benhamou Y, et al. 13th CROI 2006. Abstract 88.

Why do you not want to catch hepatitis C

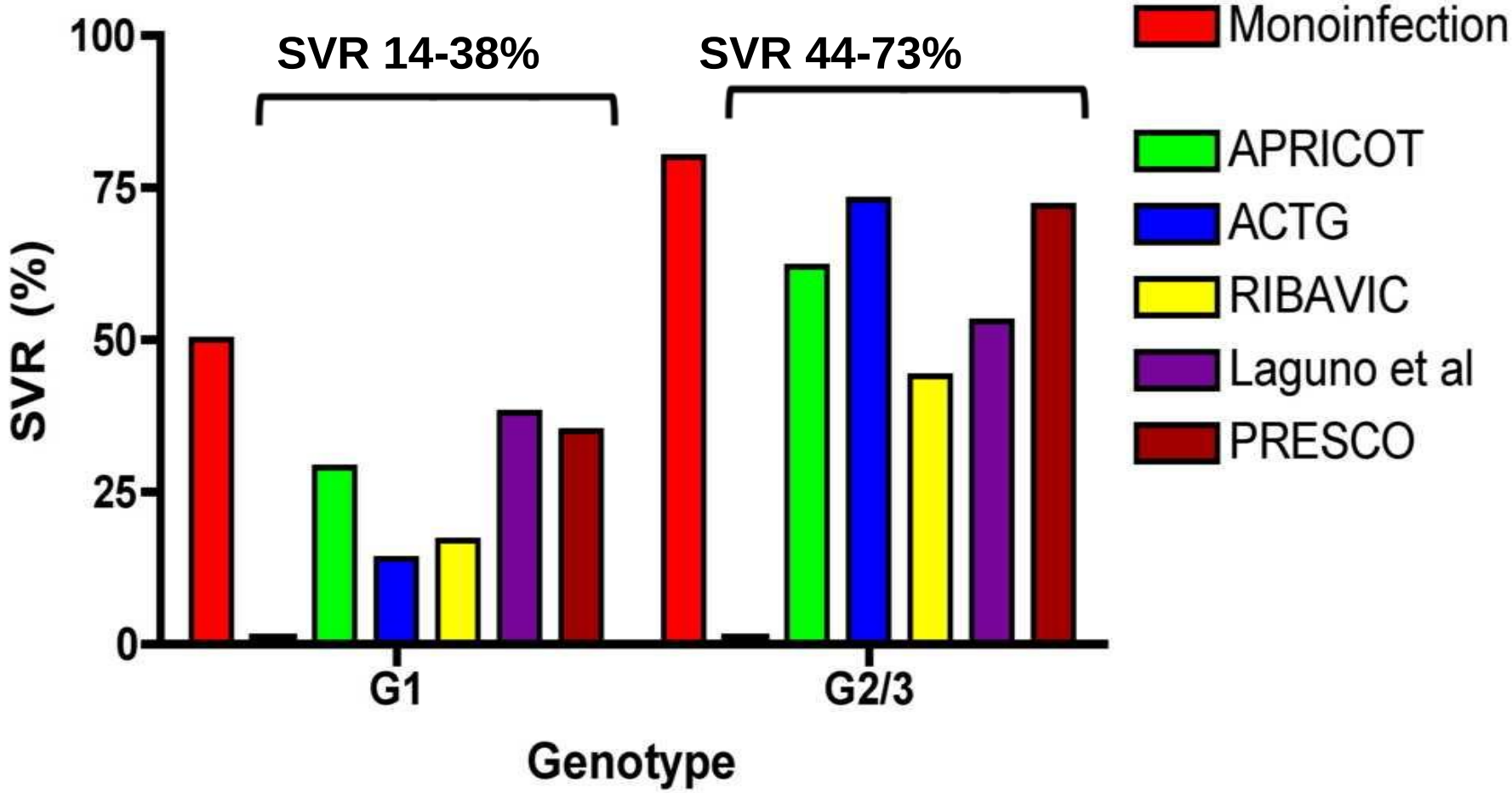
- Transmission
- Stigma
- More Rapid Progression of disease
- Increase in now known HIV related comorbidities
- Increase in HAART toxicity
- People die




peginterferon alfa-2a
PEGASYS® Prefilled Syringe Sterile
For Subcutaneous Injection Only (US Govt. Lic. No. 0136)
Hoffmann-La Roche Inc., Nutley, New Jersey 07110

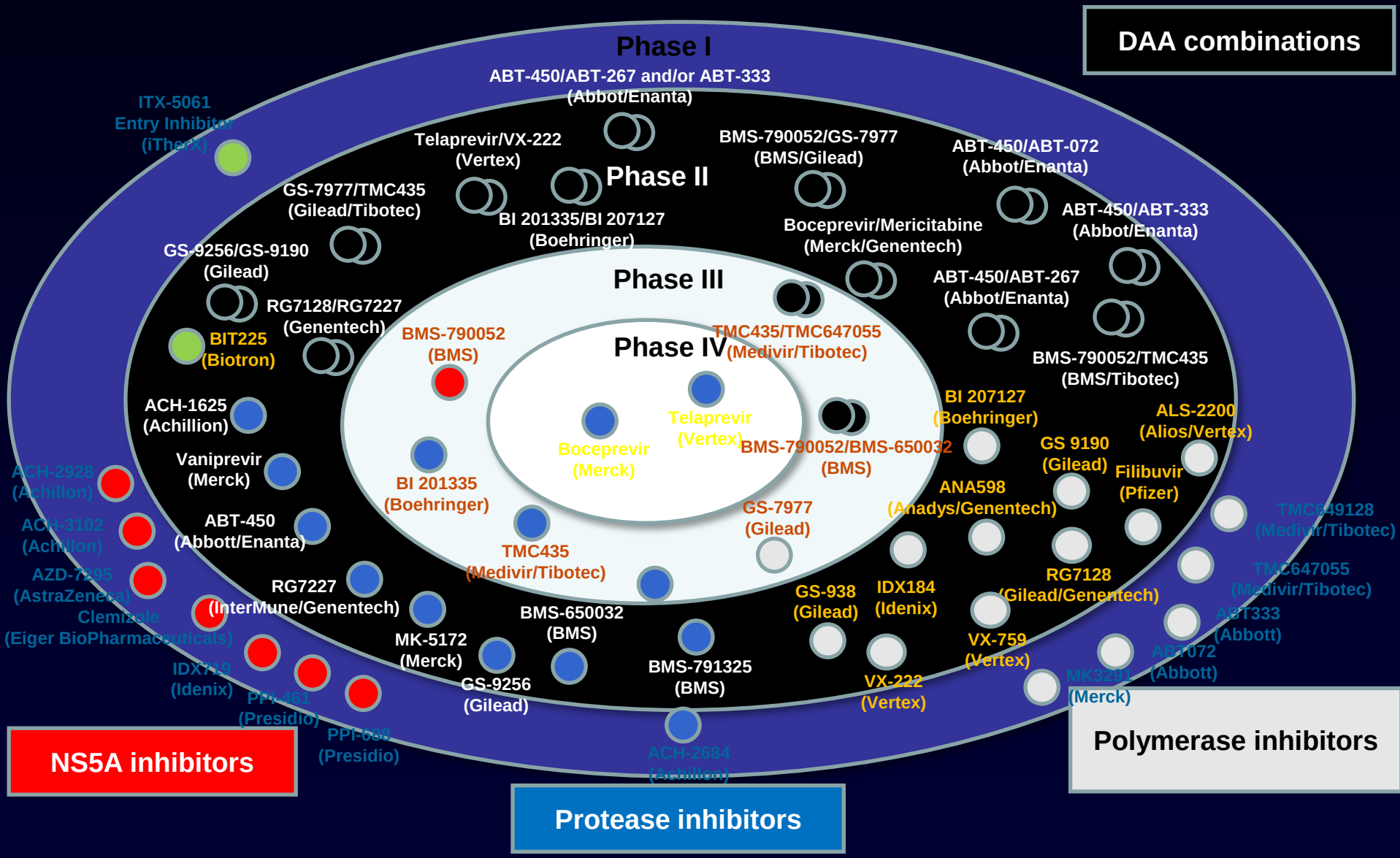
HCV/HIV TREATMENT OUTCOMES



Why lower response rates to anti-HCV therapy in HIV+ patients?

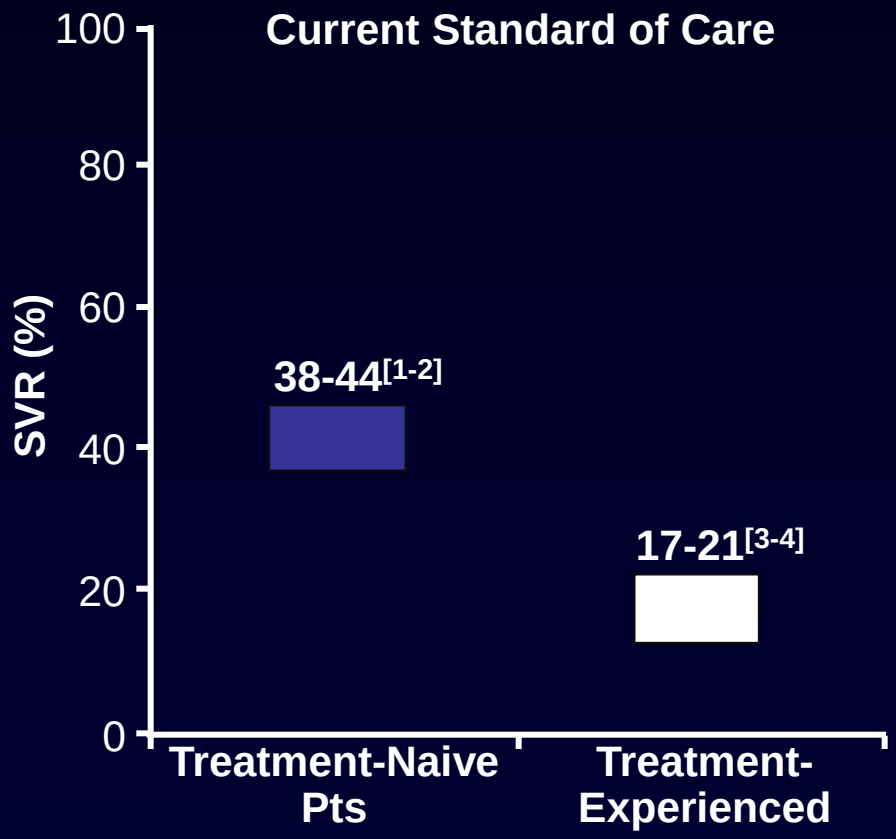
- More advanced fibrosis grade.
- Higher rate of steatosis (NRTIs, etc)
- Unfavorable HCV virological features.
- Higher discontinuation due to side effects.
- Lower drug compliance.
- Lower initial HCV-RNA clearance.
- Higher relapse rates.

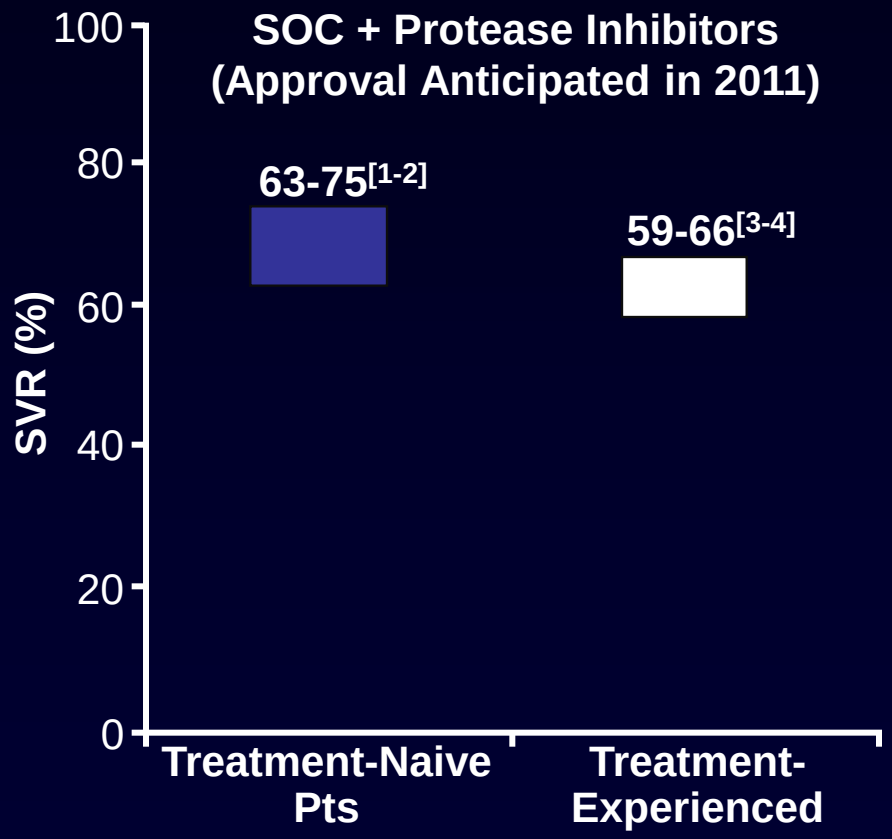
Hepatitis C pipeline



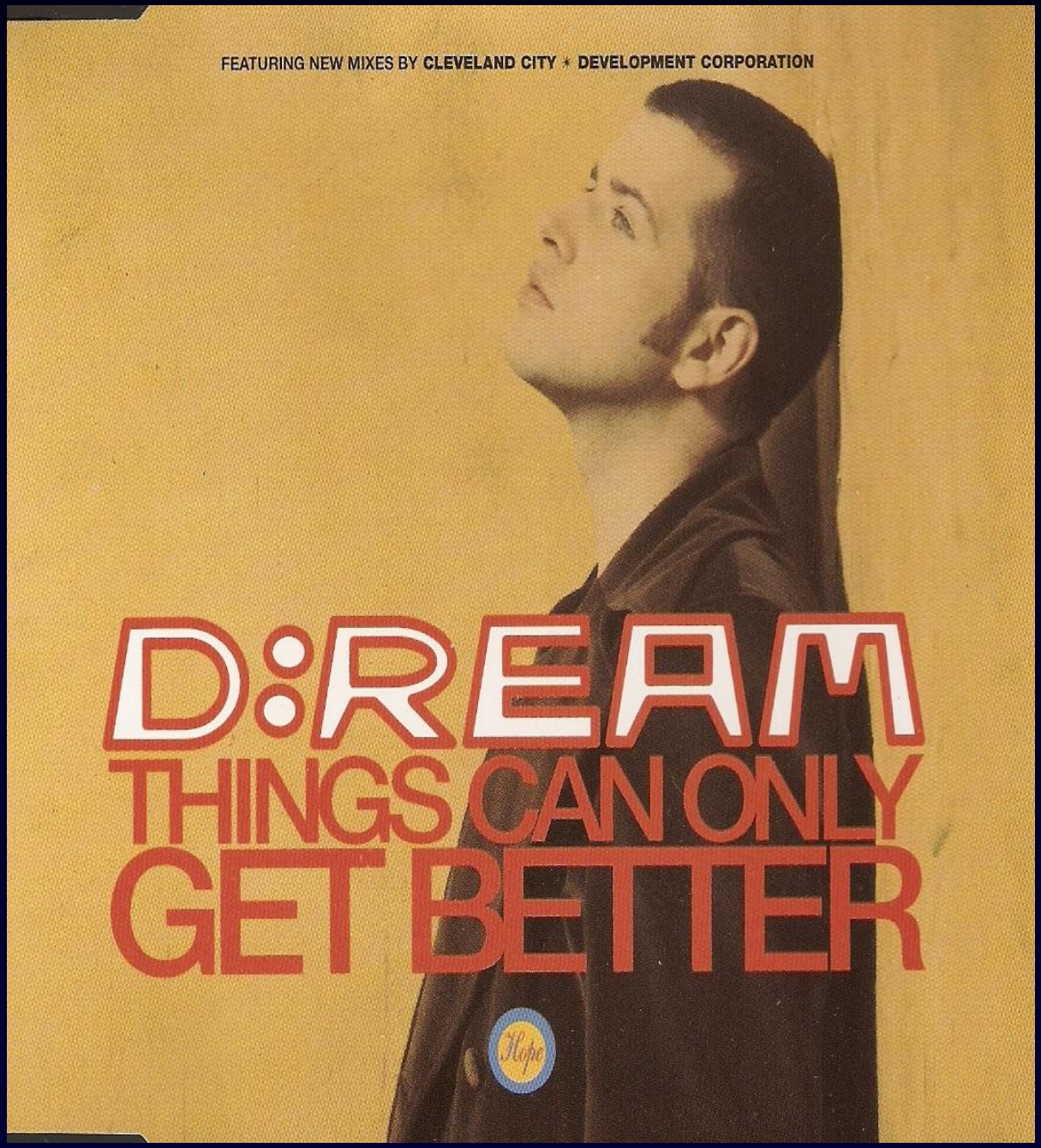
Franciscus, A. Hepatitis C Treatments in Current Clinical Development, 17 October 2012, available at: http://www.hcvadvocate.org/hepatitis/hepC/HCVDrugs_2012.pdf

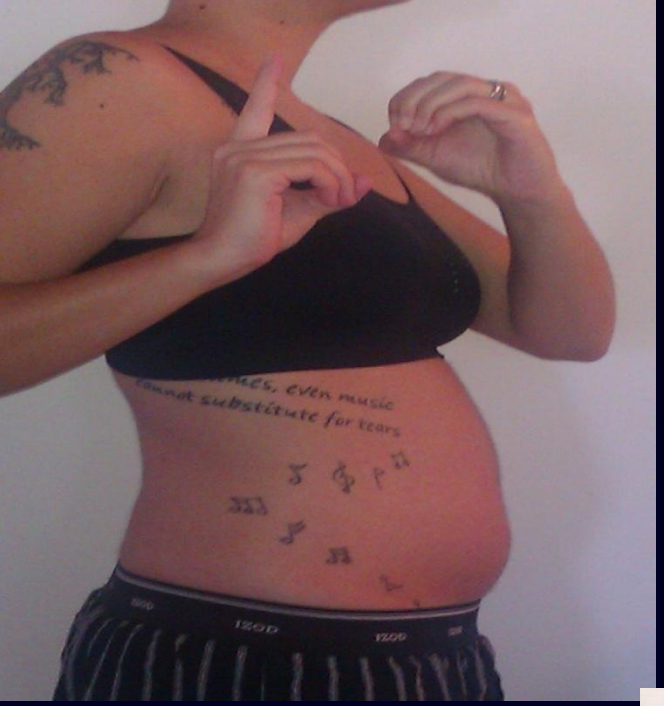
SVR Rates With BOC and TPV in GT1 Treatment-Naive and -Experienced Pts



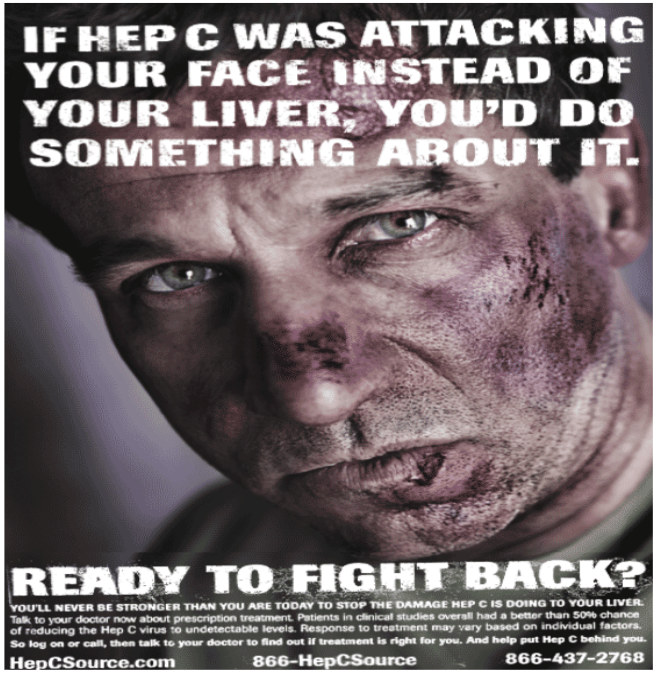


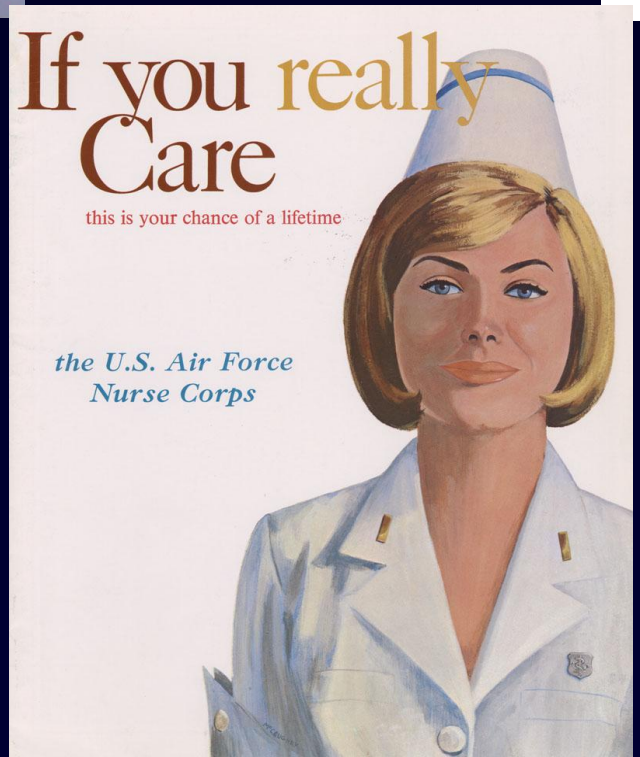
1. Poordad F, et al. AASLD 2010. Abstract LB-4. 2. Jacobson IM, et al. AASLD 2010. Abstract 211. 3. Bacon BR, et al. AASLD 2010. Abstract 216. 4. Foster GR, et al. APASL 2011. Abstract 1529.

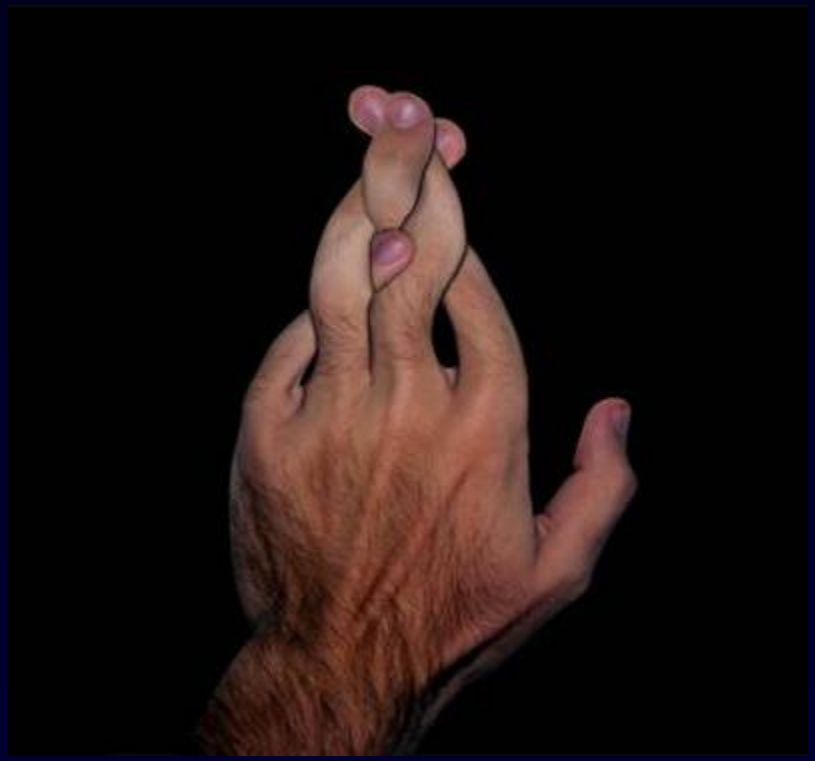

FEATURING NEW MIXES BY CLEVELAND CITY * DEVELOPMENT CORPORATION
D:REAM
THINGS CAN ONLY GET BETTER
Hope


cannot substitute for tears

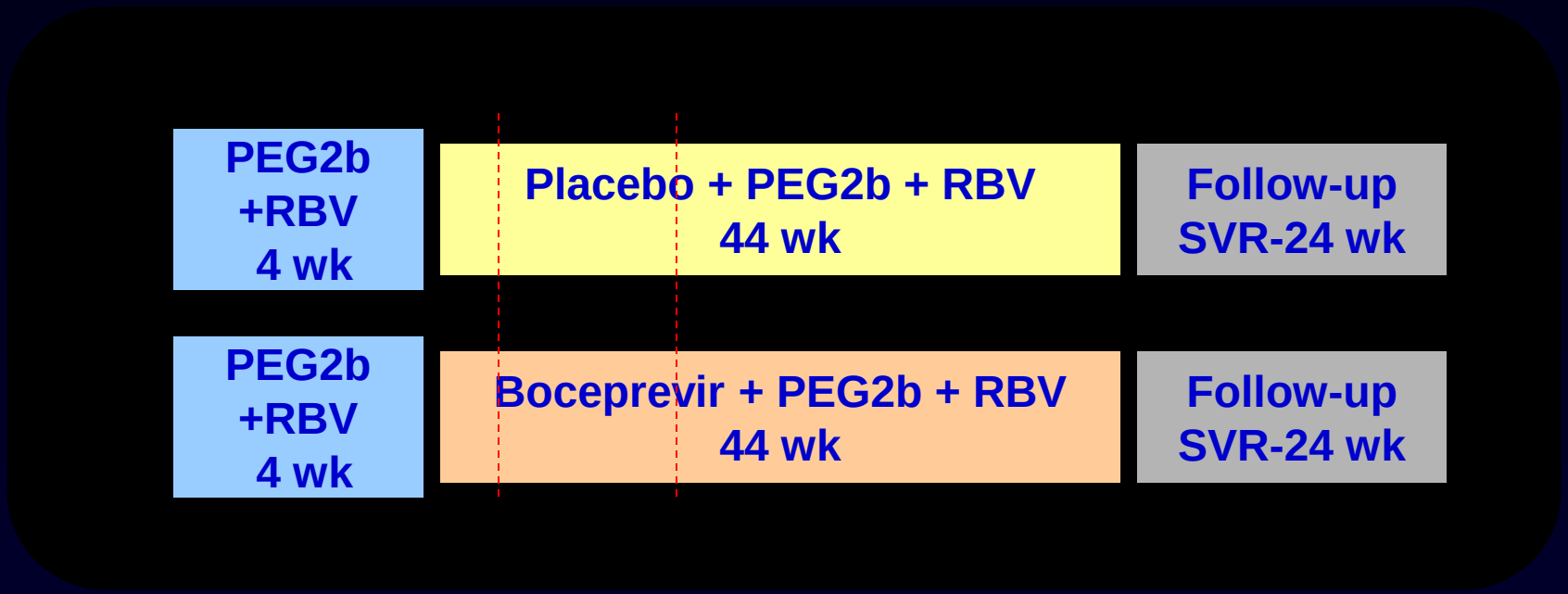
Treat Now


IF HEP C WAS ATTACKING YOUR FACE INSTEAD OF YOUR LIVER, YOU'D DO SOMETHING ABOUT IT.
READY TO FIGHT BACK?
YOU'LL NEVER BE STRONGER THAN YOU ARE TODAY TO STOP THE DAMAGE HEP C IS DOING TO YOUR LIVER.
Talk to your doctor now about prescription treatment. Patients in clinical studies overall had a better than 50% chance of reducing the Hep C virus to undetectable levels. Response to treatment may vary based on individual factors. So log on or call, then talk to your doctor to find out if treatment is right for you. And help put Hep C behind you.
HepCSource.com
866-HepCSource
866-437-2768


If you really Care
this is your chance of a lifetime
the U.S. Air Force
Nurse Corps

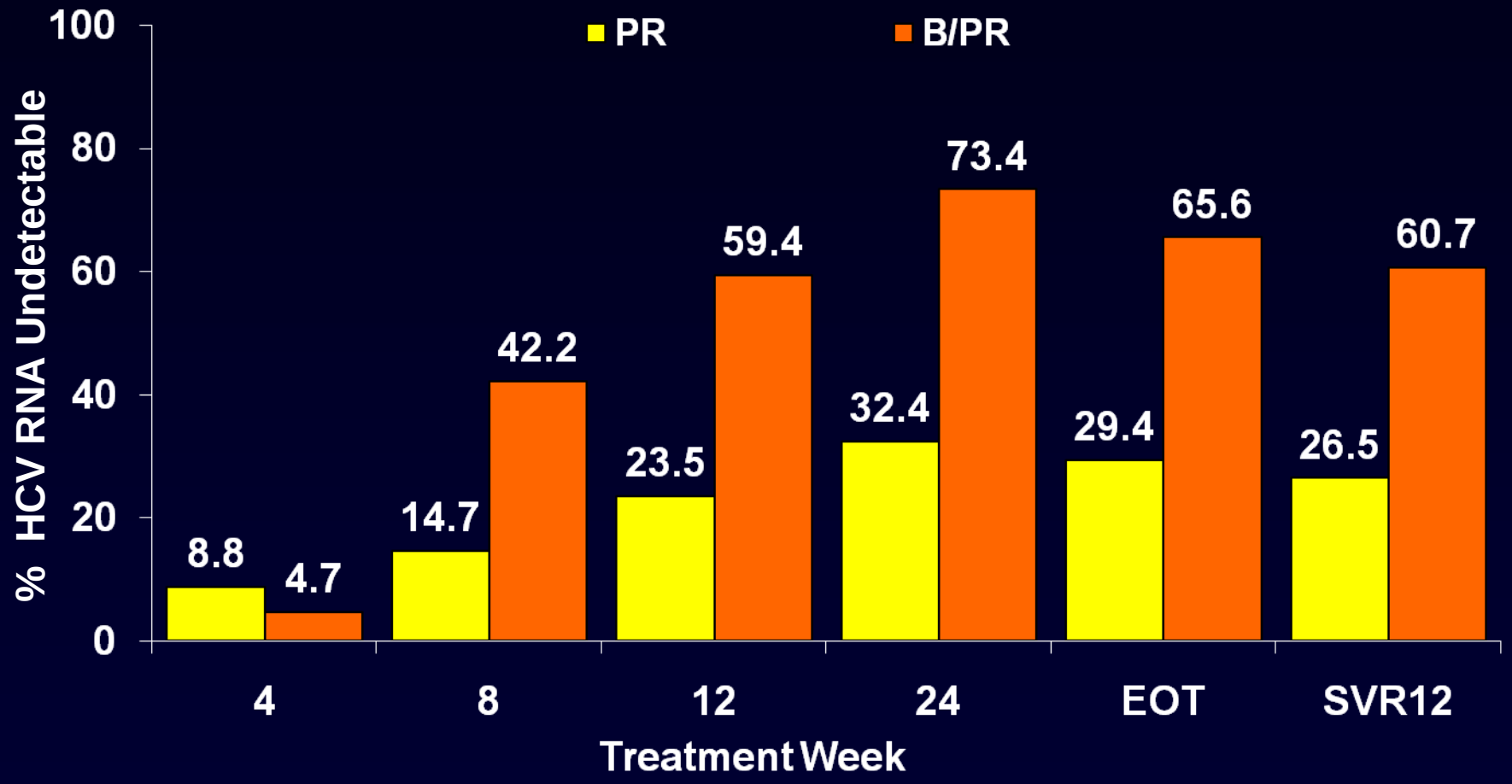


Study Design



- Two-arm study, double-blinded for BOC, open-label for PEG2b/RBV
  - 2:1 randomization (experimental: control)
  - Boceprevir dose 800 mg, TID
- 4-week lead-in with PEG2b/RBV for all patients
  - PEG-2b 1.5 µg/kg QW; RBV 600-1400 mg/day divided BID
- Control arm subjects with HCV-RNA ≥ LLQ at TW 24 were offered open-label PEG2b/RBV+BOC via a cross-over arm

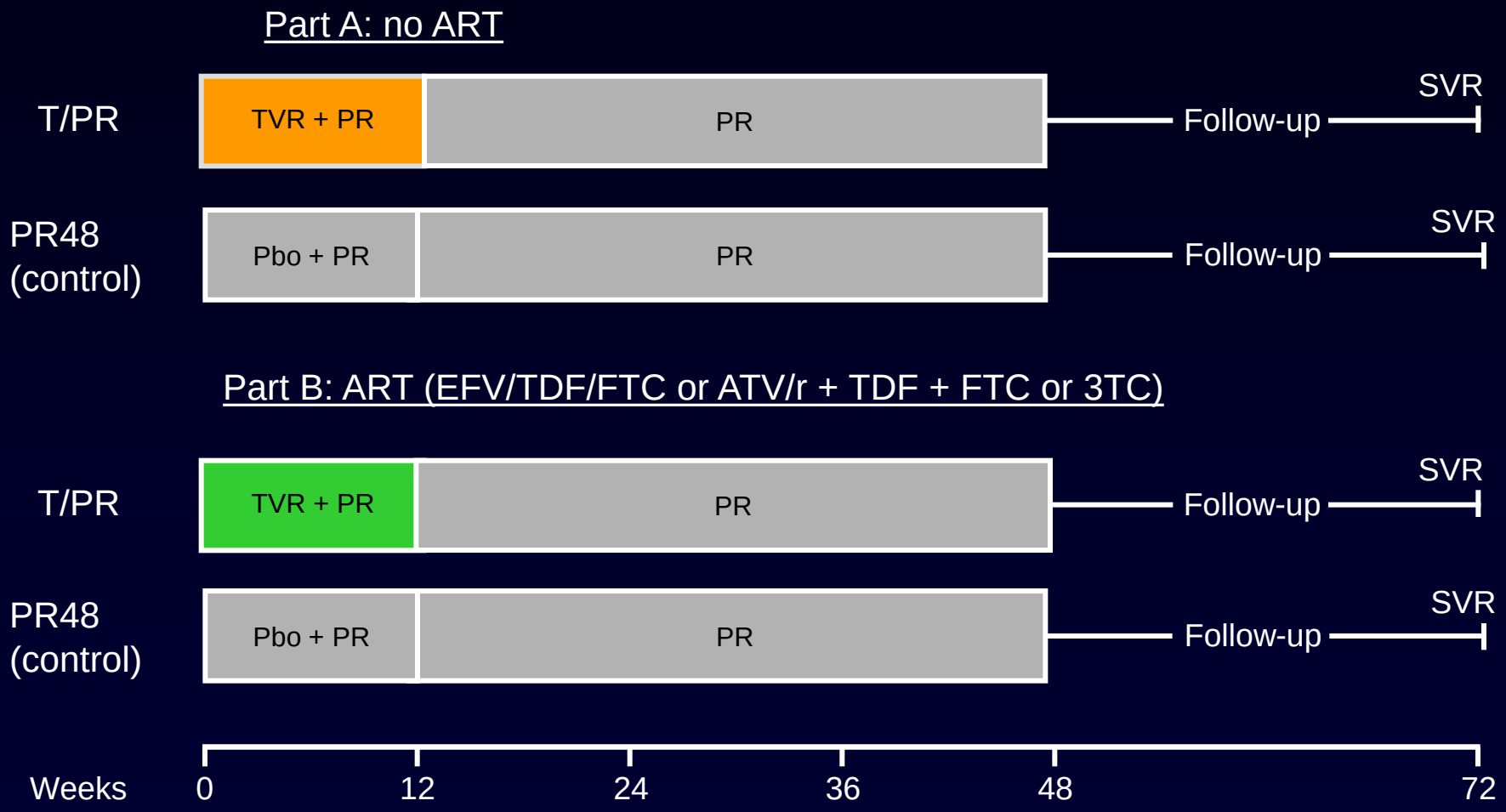
Virologic Response Over Time†



† Three patients undetectable at FW4 have not yet reached FW12 and were not included in SVR12 analysis.

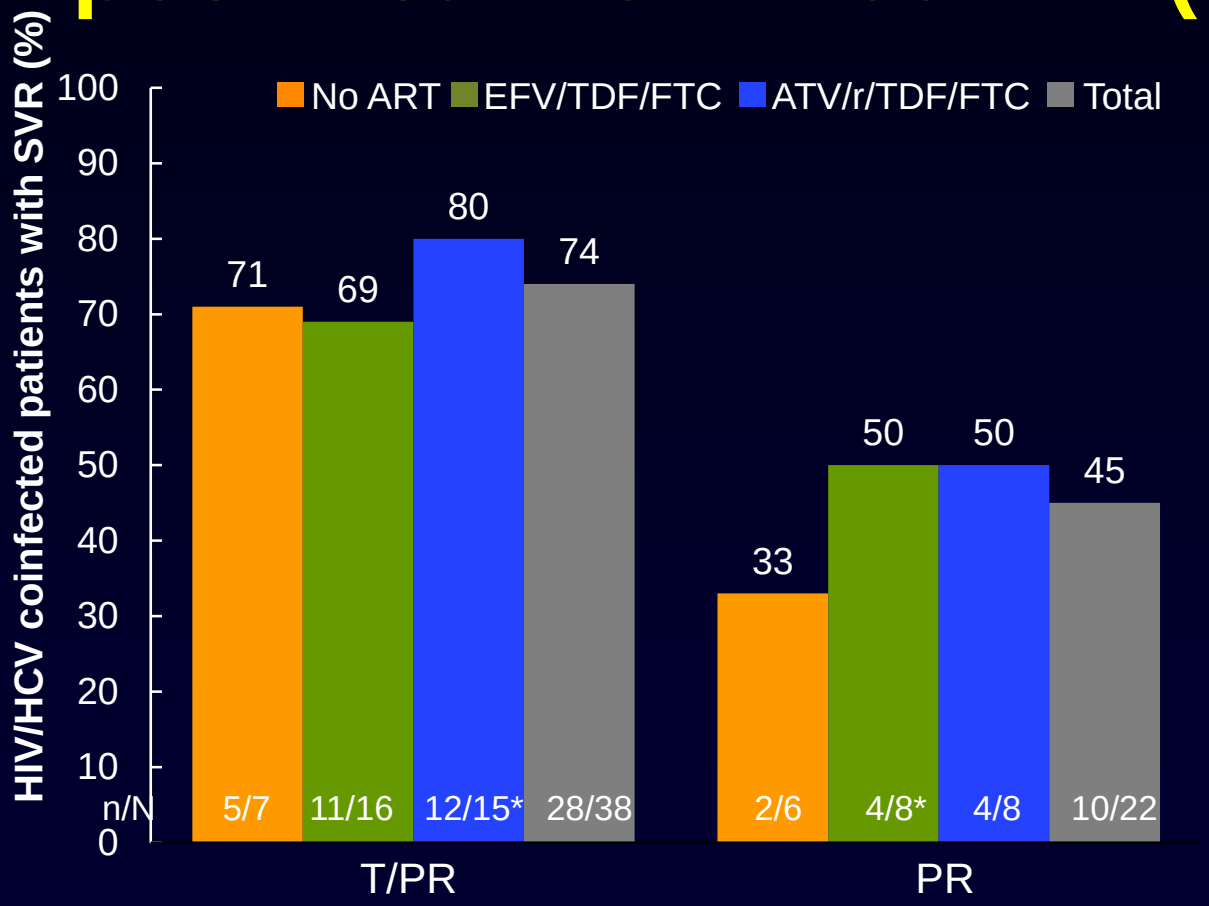
Sulkowski M et al., 19th CROI; Seattle, WA; March 5-8, 2012. Abst. 47

Study Design



(EFV)=efavirenz; (TDF)=tenofovir; (FTC)=emtricitabine; (ATV/r)=ritonavir-boosted atazanavir; (3TC)=lamivudine;
(T) TVR=telaprevir 750 mg q8h or 1125 mg q8h (with EFV); Pbo=Placebo; (P) Peg-IFN=pegylated interferon alfa-2a (40 kD) 180 µg/wk; (R) RBV=ribavirin 800 mg/day or weight-based (1000 mg/day if weight <75 kg, 1200 mg/day for if weight ≥75 kg; France, Germany)
Roche COBAS® TaqMan® HCV test v2.0, LLOQ of 25 IU/mL (pts with values below 25IU/mL were reported as <25 detectable or undetectable)

HIV/HCV coinfected patients: SVR at post-treatment week 24 (SVR_{24})

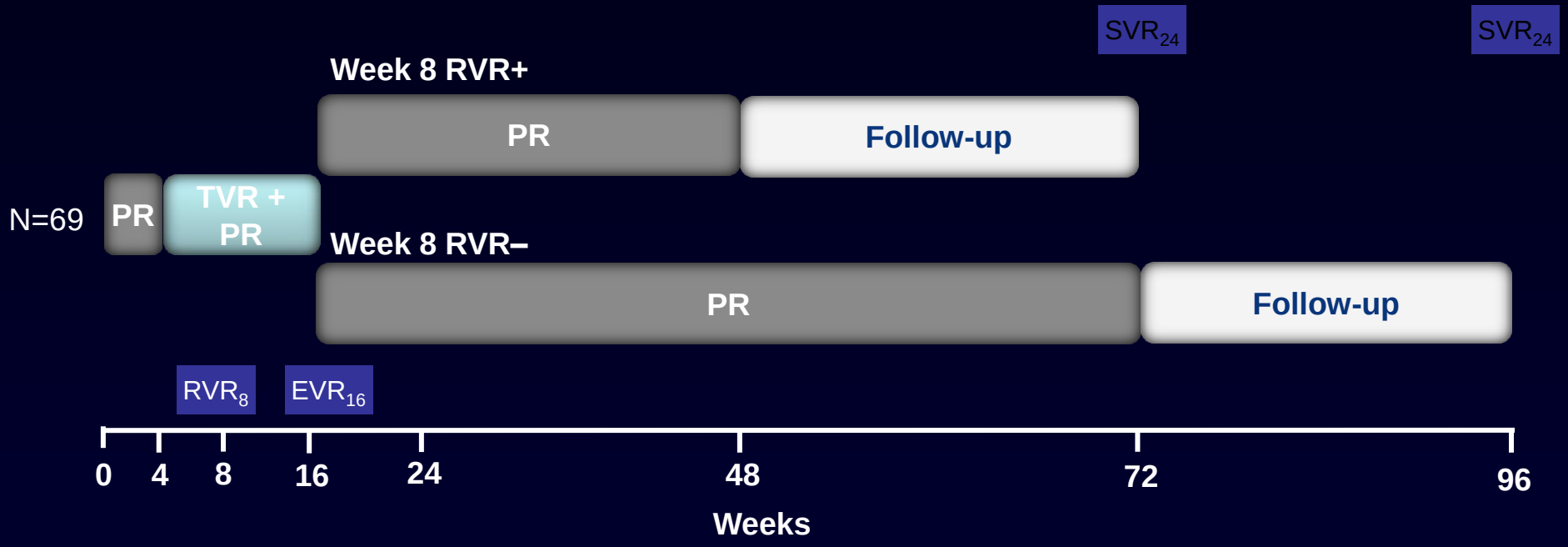


*Prior to Week 24 visit, 1 patient in this cohort was lost to follow up. SVR24 was imputed based on SVR12 for this patient.

T/PR, telaprevir in combination with peginterferon alfa-2a and ribavirin; PR, peginterferon alfa-2a and ribavirin

Sulkowski M S, et al. AASLD, 2012. Presentation #54

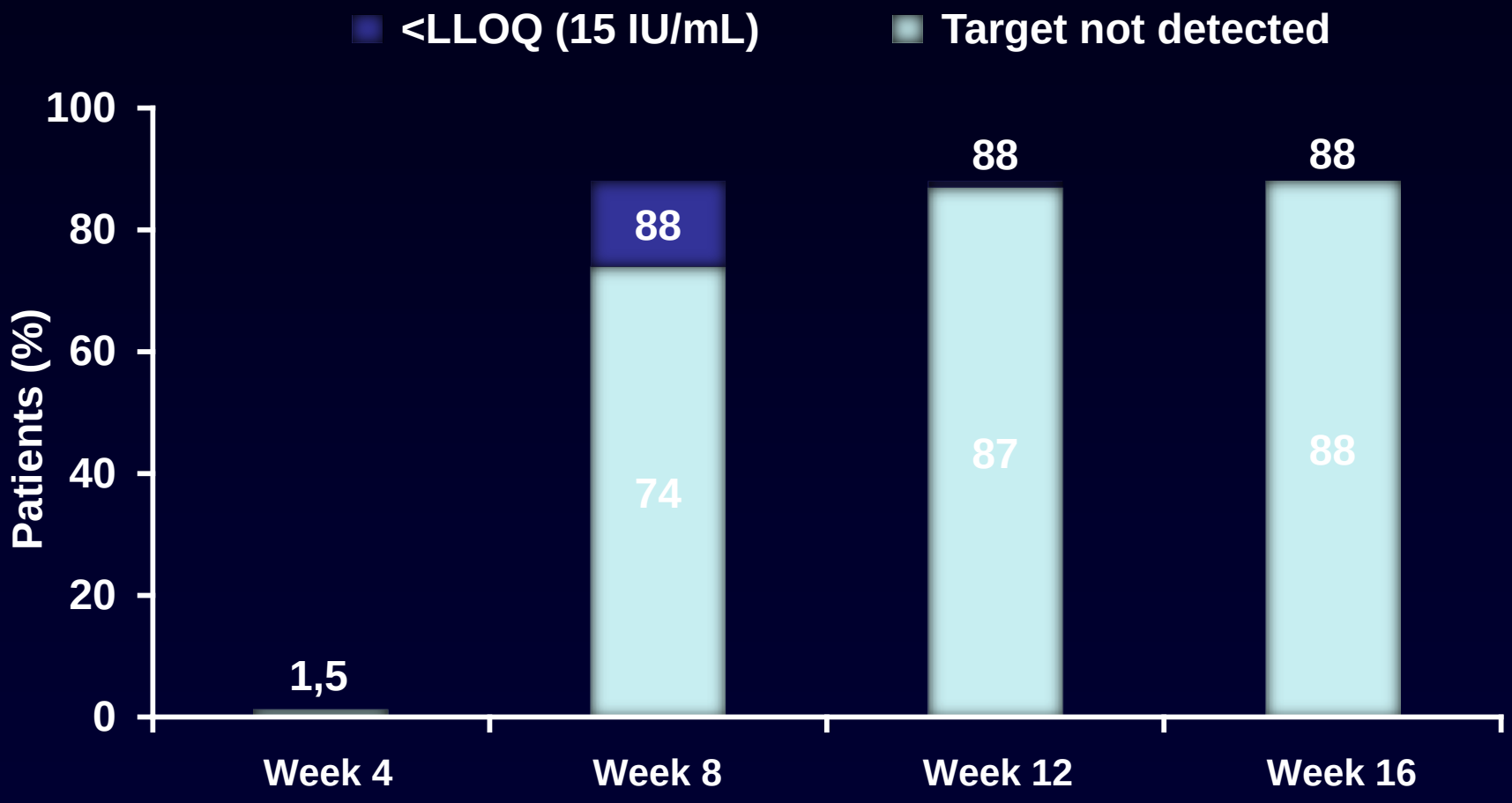
ANRS HC26 TelapreVIH study* in G1 HCV/HIV1 co-infected treatment-experienced patients



- HIV <50 copies/mL, CD4 ≥200/mm^3 and ≥15%
- Patients were also administered ART
  - Authorized drugs: ATV, ATV/r, EFV, RAL, TDF, FTC, 3TC

*Null responders with cirrhosis were excluded
T: telaprevir 750 mg tid (1125 mg tid with EFV); P: Peg-INF-2a: 180 µg/wk; R: ribavirin 1000–1200 mg/day
Primary objective: SVR24
ART: antiretroviral therapy; ATVr: atazanavir + ribavirin; EFV: efavirenz
RAL: raltegravir; TDF: tenofovir; FTC: emtricitabine; 3TC: lamivudine

TelapreVIH: virological response (ITT, n=69)

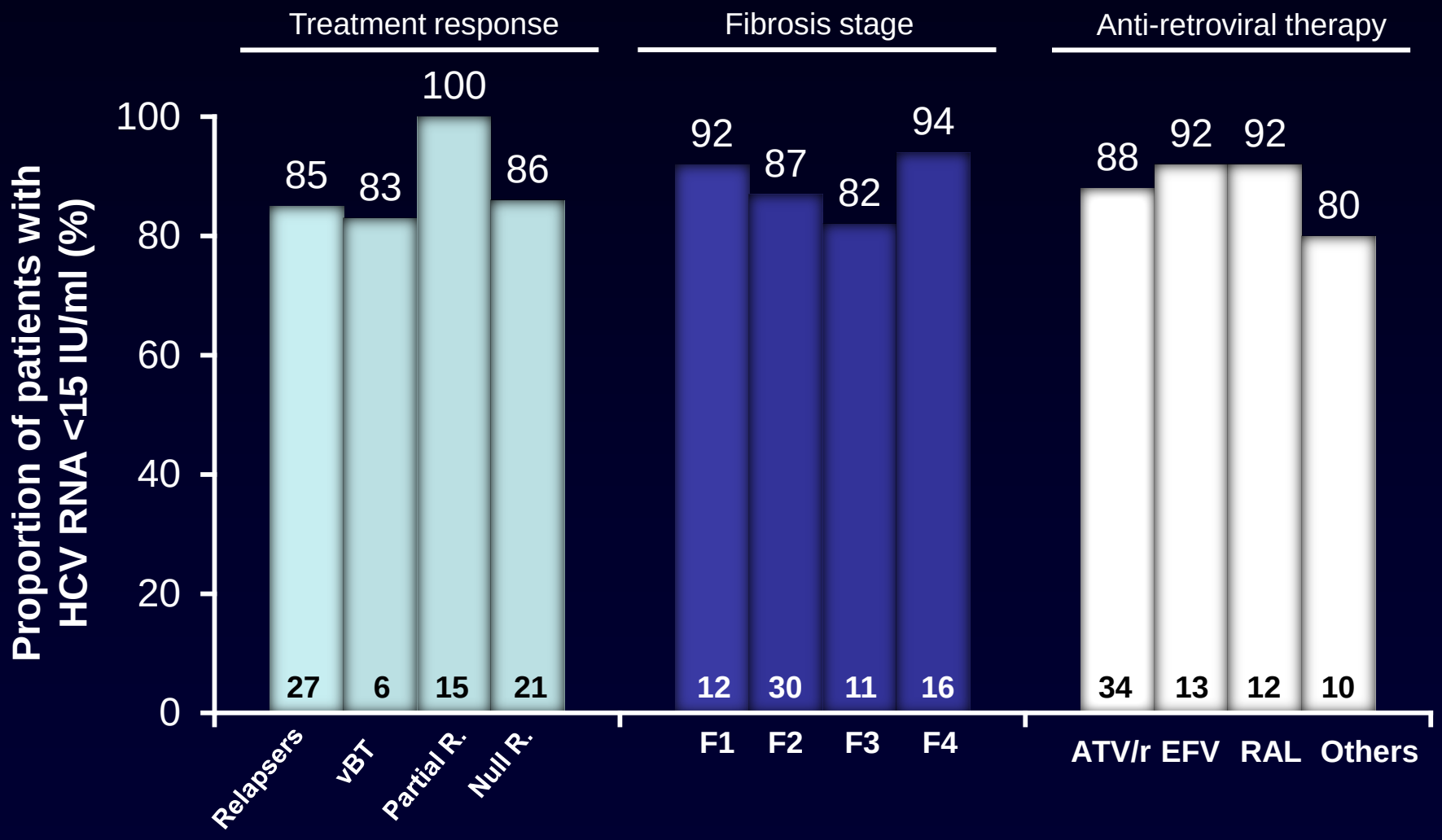


Only 3 patients did not achieve RVR8 and were assigned a 72 week treatment duration

ITT: intent-to-treat ; LLOQ: lower limit of quantification

Cotte L, et al. CROI 2013, Abstract 36

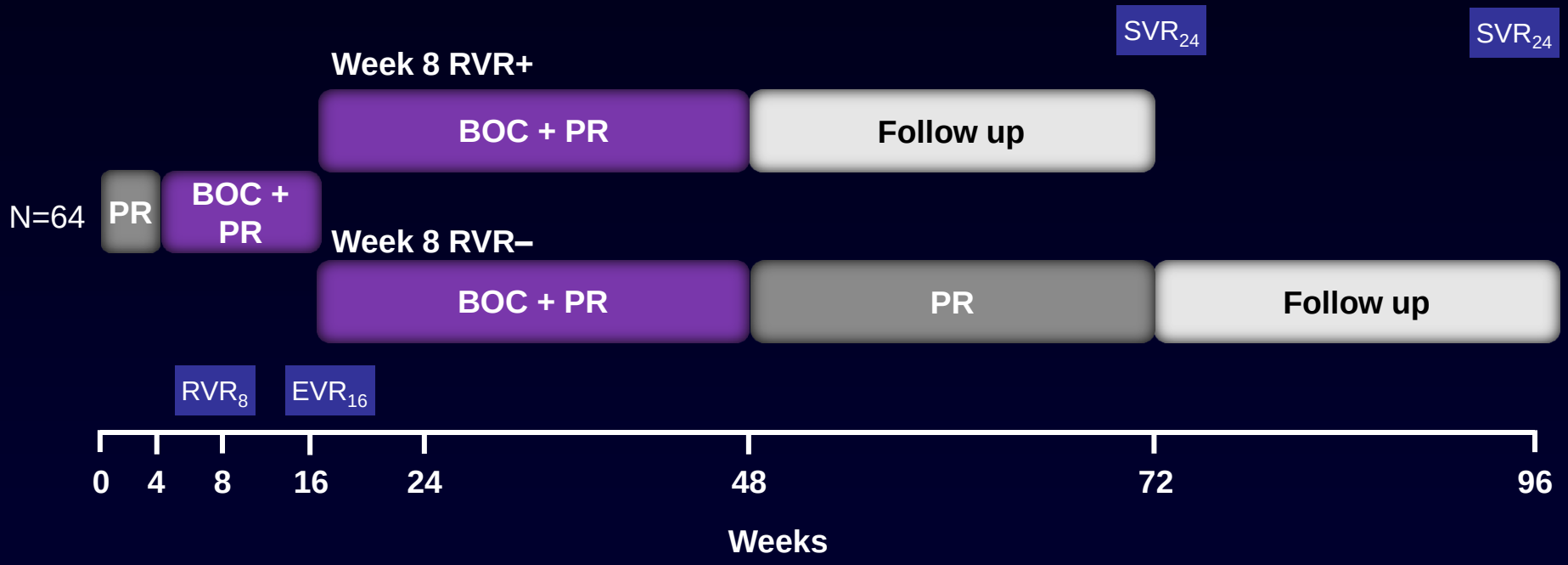
TelapreVIH: Week 16 virologic response



vBT: viral breakthrough

Cotte L, et al. CROI 2013, Abstract 36

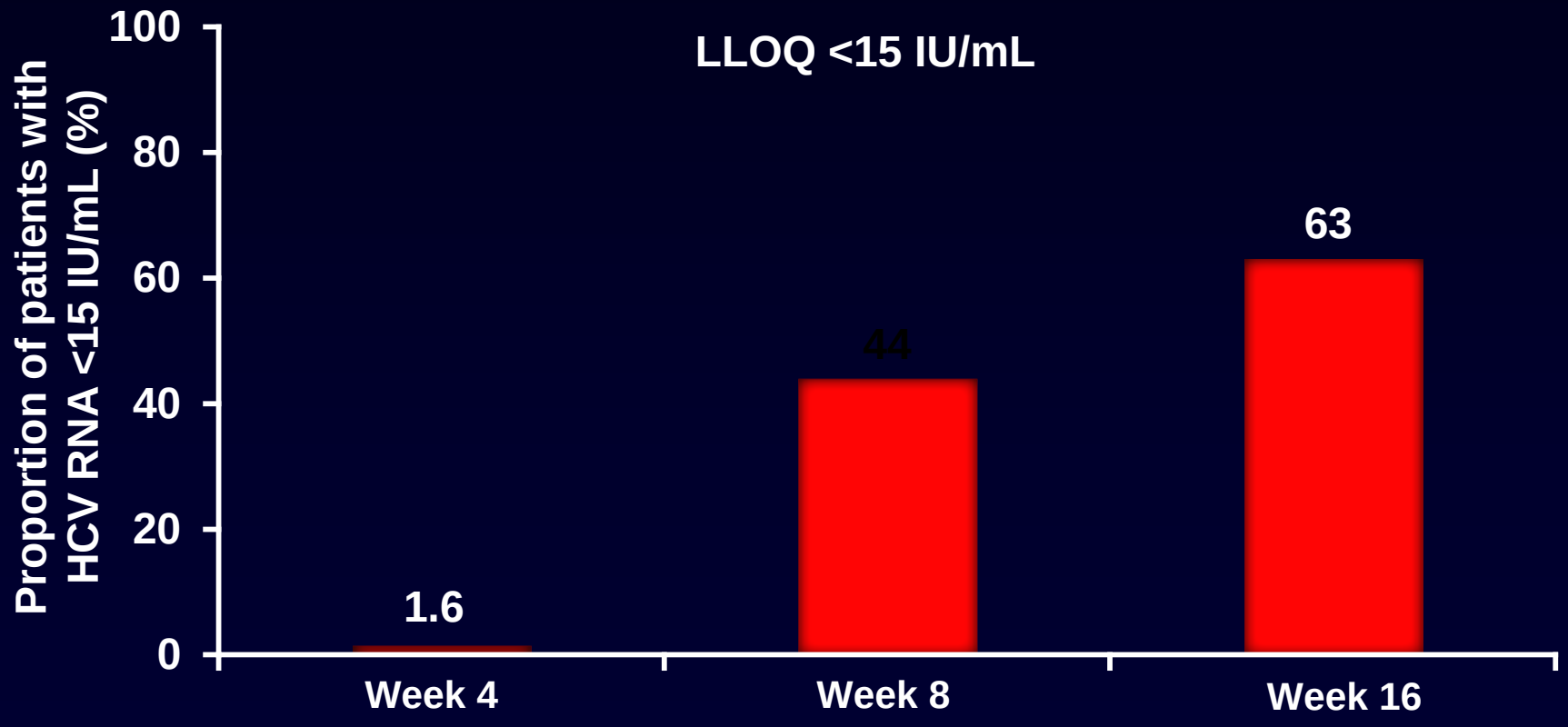
Treatment-experienced HCV/HIV co-infected patients: ANRS HC27 BocepreVIH study*



- HIV <50 copies/mL, CD4 ≥200/mm^3 and ≥15%
- Patients were also administered ART
  - Authorized drugs: ATV, ATV/r, RAL, TDF, ABC, FTC, 3TC

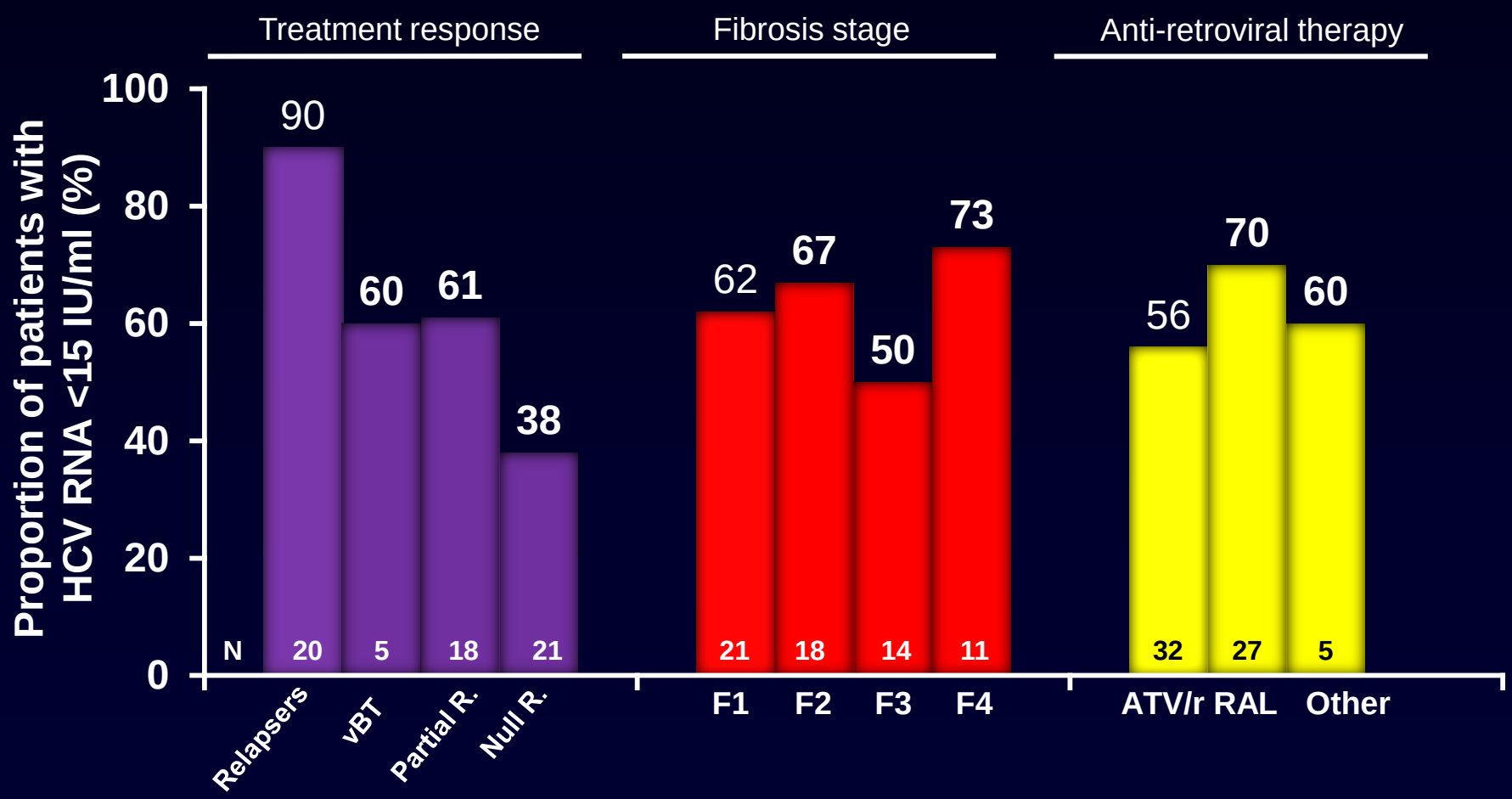
*Null responders with cirrhosis were excluded
Primary objective: SVR24
BOC: 800 mg tid; P: Peg-INF-2b: 1.5 µg/kg/wk; R: RBV 1000–1200 mg/day

BocepreVIH: virologic response (ITT, n=64)

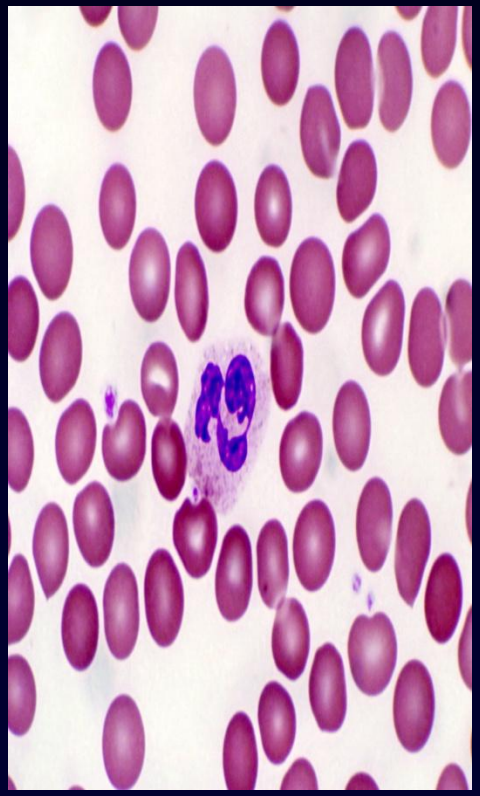


Poizot-Martin I, et al. CROI 2013, Abstract 37

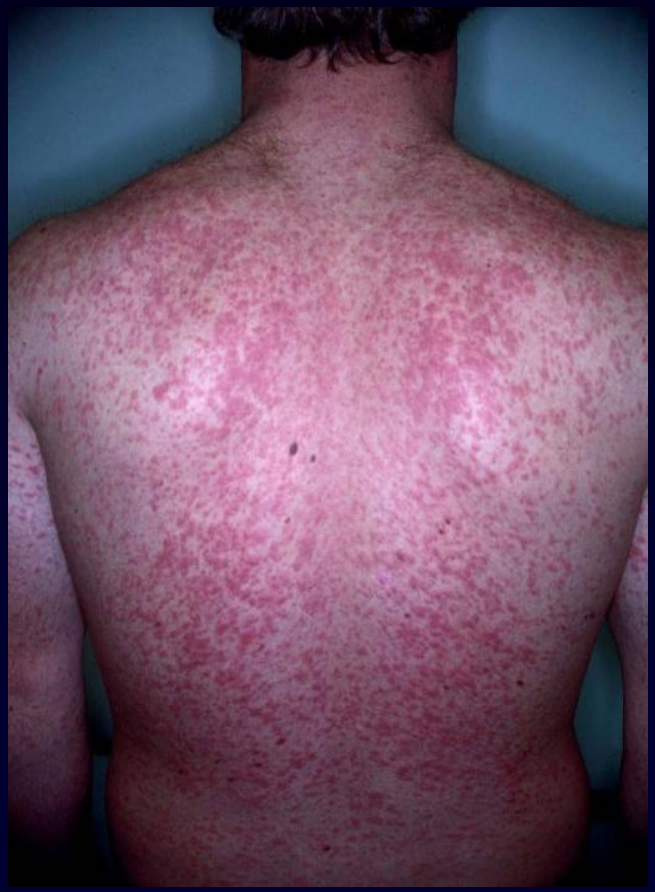
BocepreVIH: Week 16 virologic response



Boceprevir

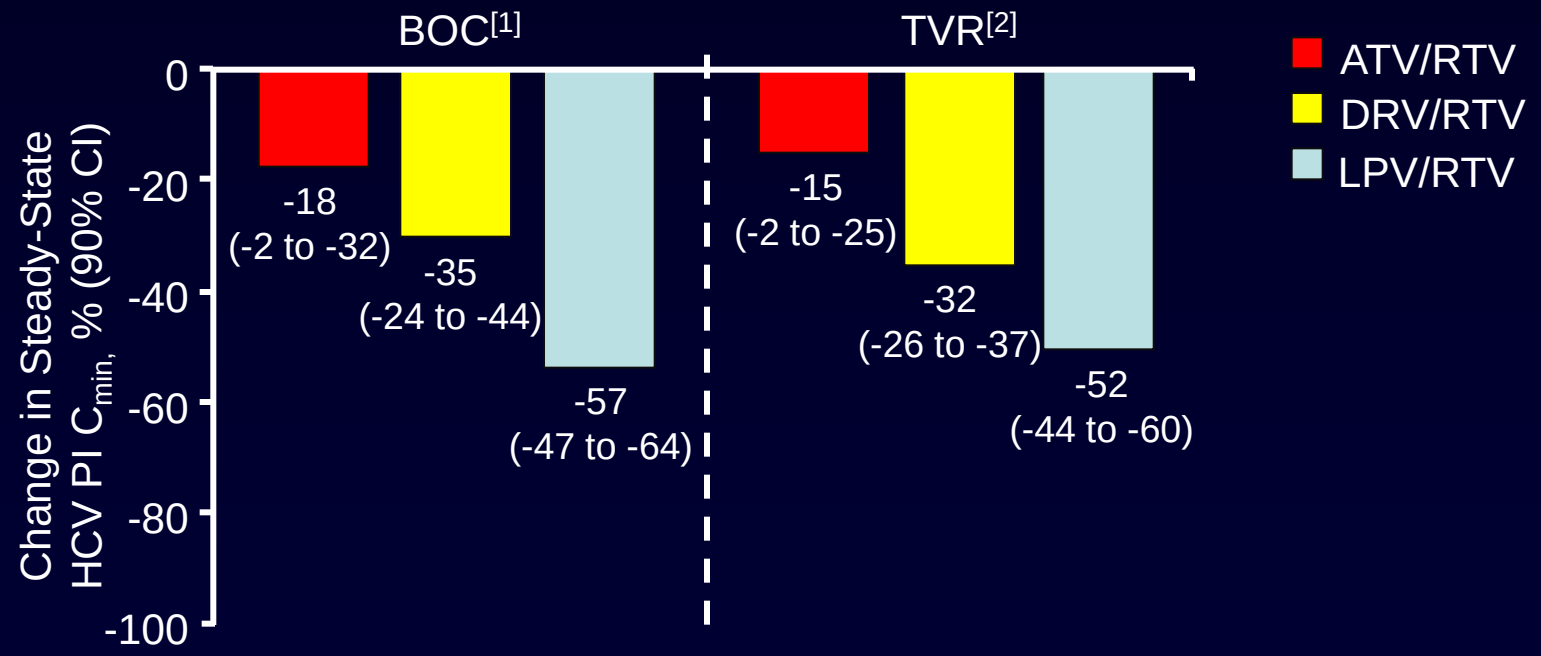


Telaprevir



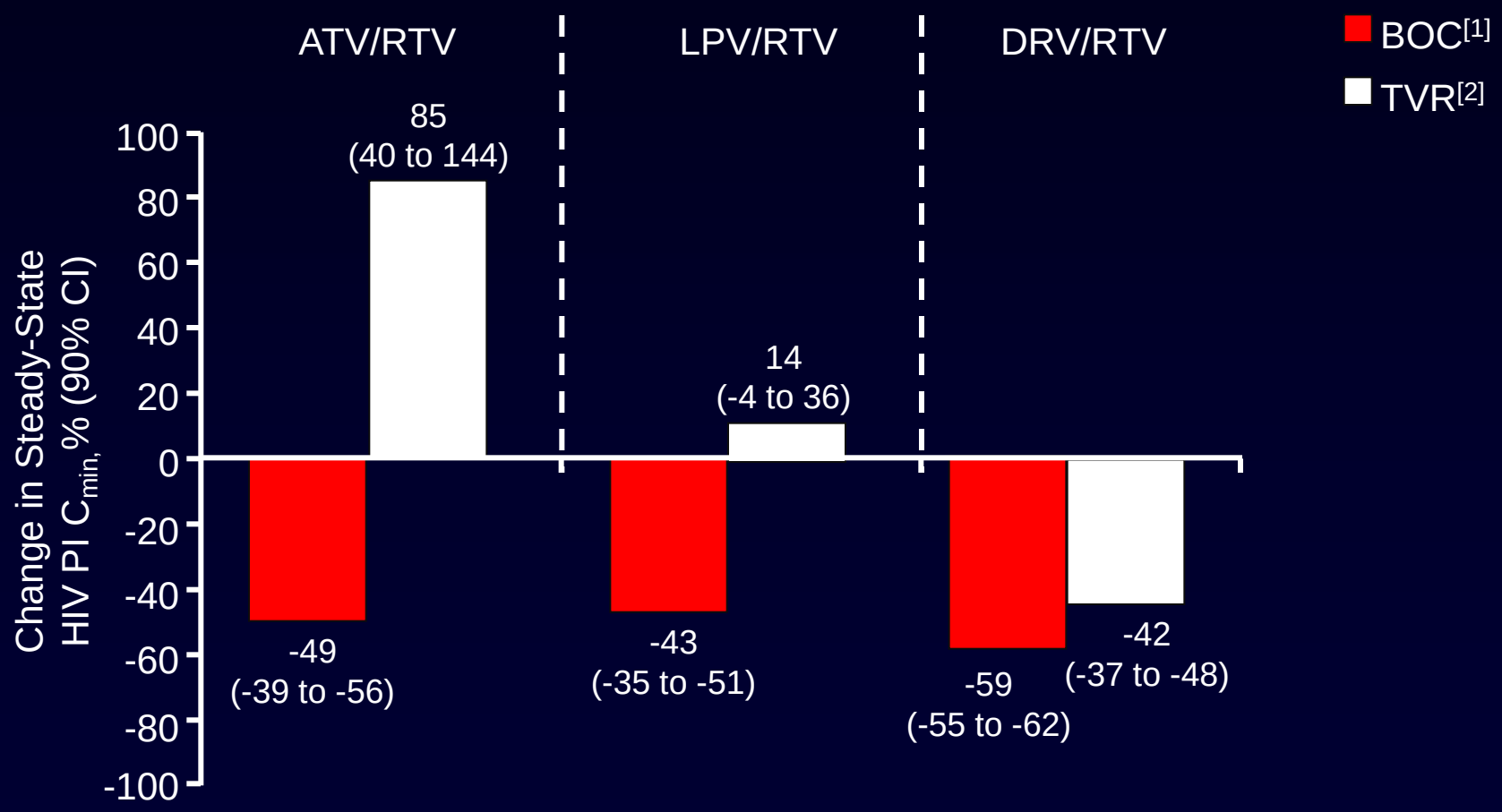
Pharmacokinetic Effects of RTV-Boosted HIV PIs on BOC and TVR

- Similar reductions in BOC and TVR exposures observed with coadministration of ATV/RTV, DRV/RTV, and LPV/RTV
- Prescribing information for TVR does not recommend coadministering TVR with DRV/RTV, FPV/RTV, or LPV/RTV; prescribing information for BOC does not recommend coadministering BOC with any HIV PI



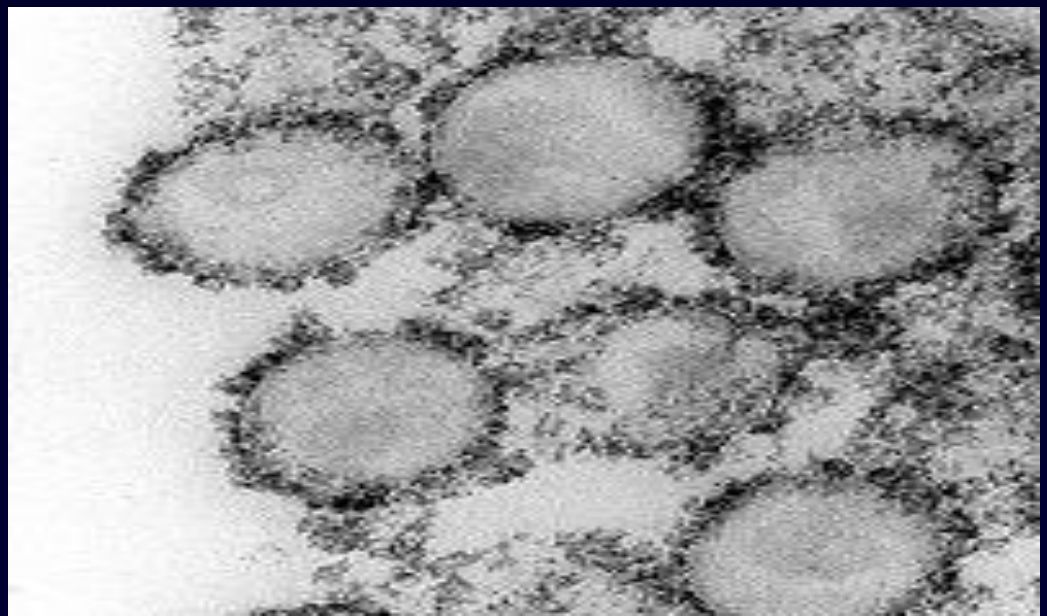
1. Hulskotte EGJ, et al. CROI 2012. Abstract 771LB. 2. van Heeswijk R, et al. CROI 2011. Abstract 119.

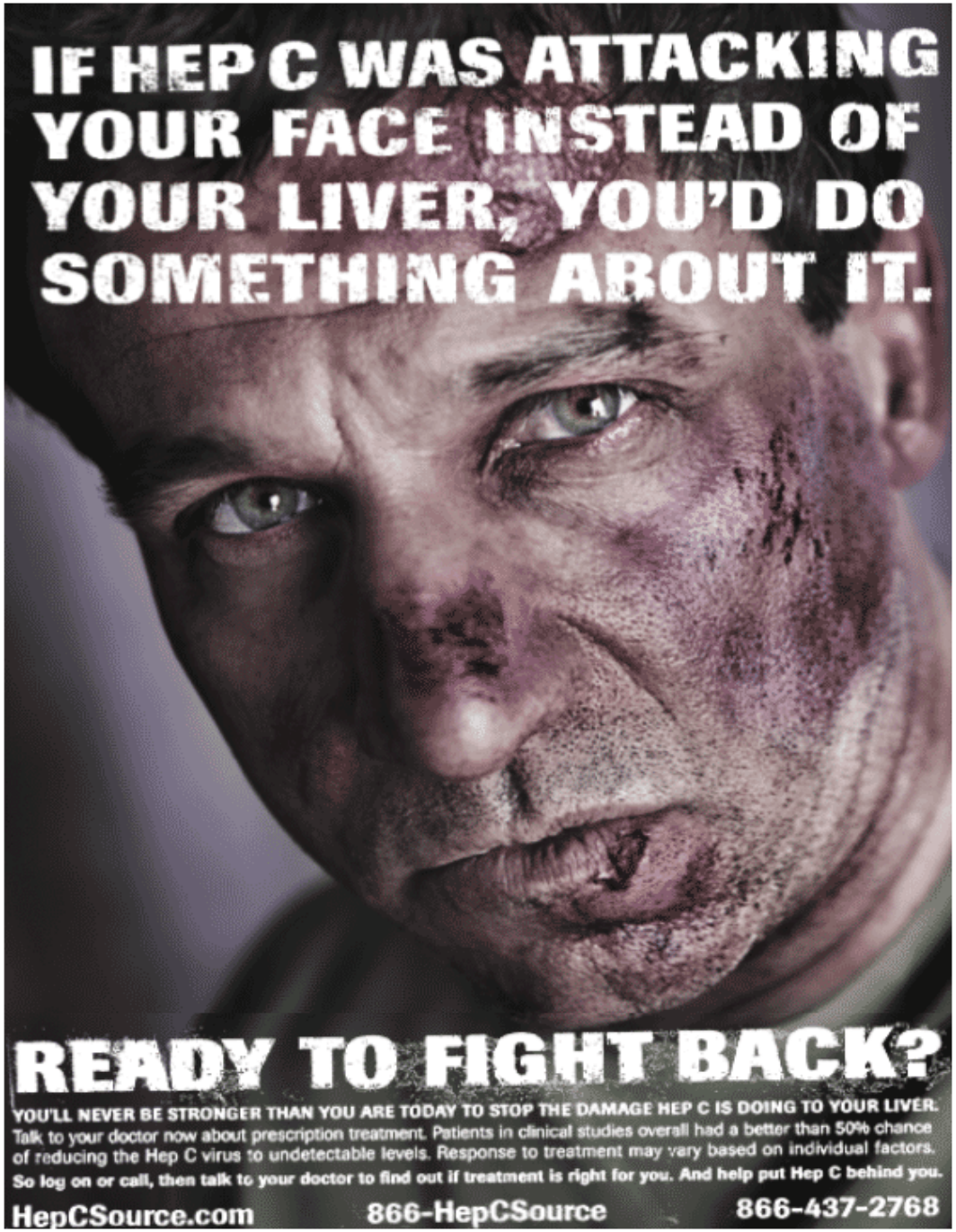
Pharmacokinetic Effects of BOC and TVR on RTV-Boosted HIV PIs



1. Hulskotte EGJ, et al. CROI 2012. Abstract 771LB. 2. van Heeswijk R, et al. CROI 2011. Abstract 119.

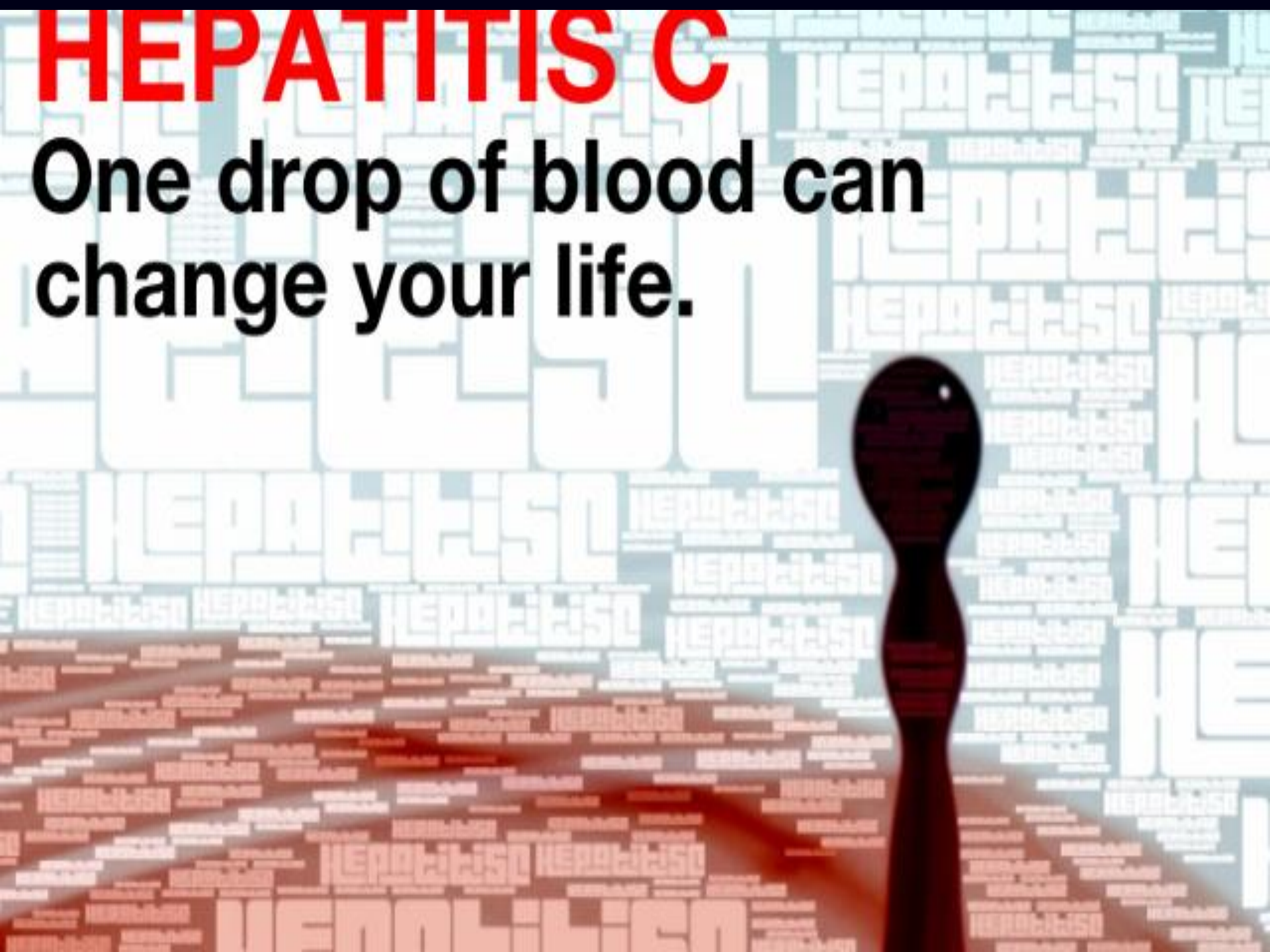

A
B
C

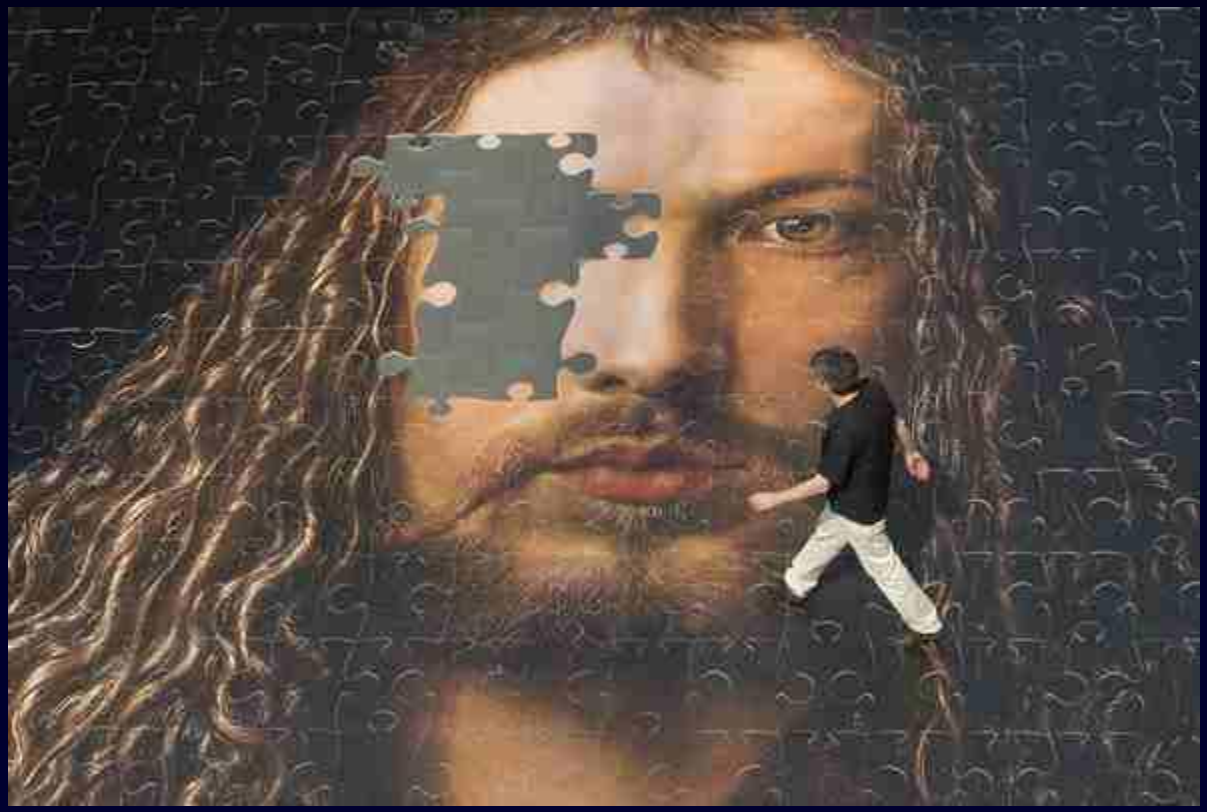


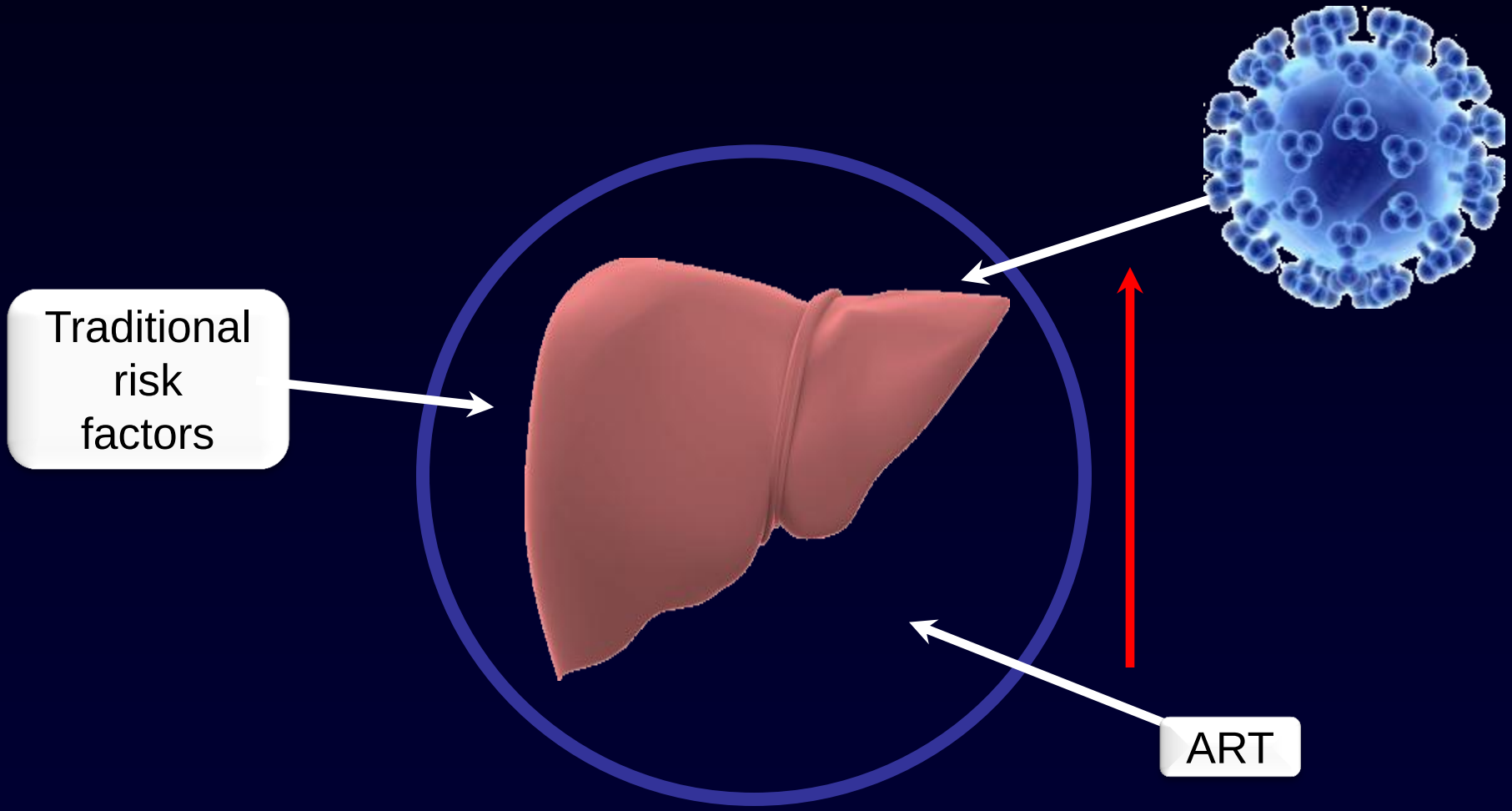

IF HEP C WAS ATTACKING YOUR FACE INSTEAD OF YOUR LIVER, YOU'D DO SOMETHING ABOUT IT.
READY TO FIGHT BACK?
YOU'LL NEVER BE STRONGER THAN YOU ARE TODAY TO STOP THE DAMAGE HEP C IS DOING TO YOUR LIVER.
Talk to your doctor now about prescription treatment. Patients in clinical studies overall had a better than 50% chance of reducing the Hep C virus to undetectable levels. Response to treatment may vary based on individual factors.
So log on or call, then talk to your doctor to find out if treatment is right for you. And help put Hep C behind you.
HepCSource.com
866-HepCSource
866-437-2768

HEPATITIS C

One drop of blood can change your life.







Mark Nelson: Personal communication

Available Antiretrovirals 2013

NRTIs

- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

NNRTIs

- Efavirenz
- Nevirapine
- Etravirine
- Rilpivirine

Protease Inhibitors

- Atazanavir
- Darunavir
- Fos-Amprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

New Classes

Fusion Inhibitors

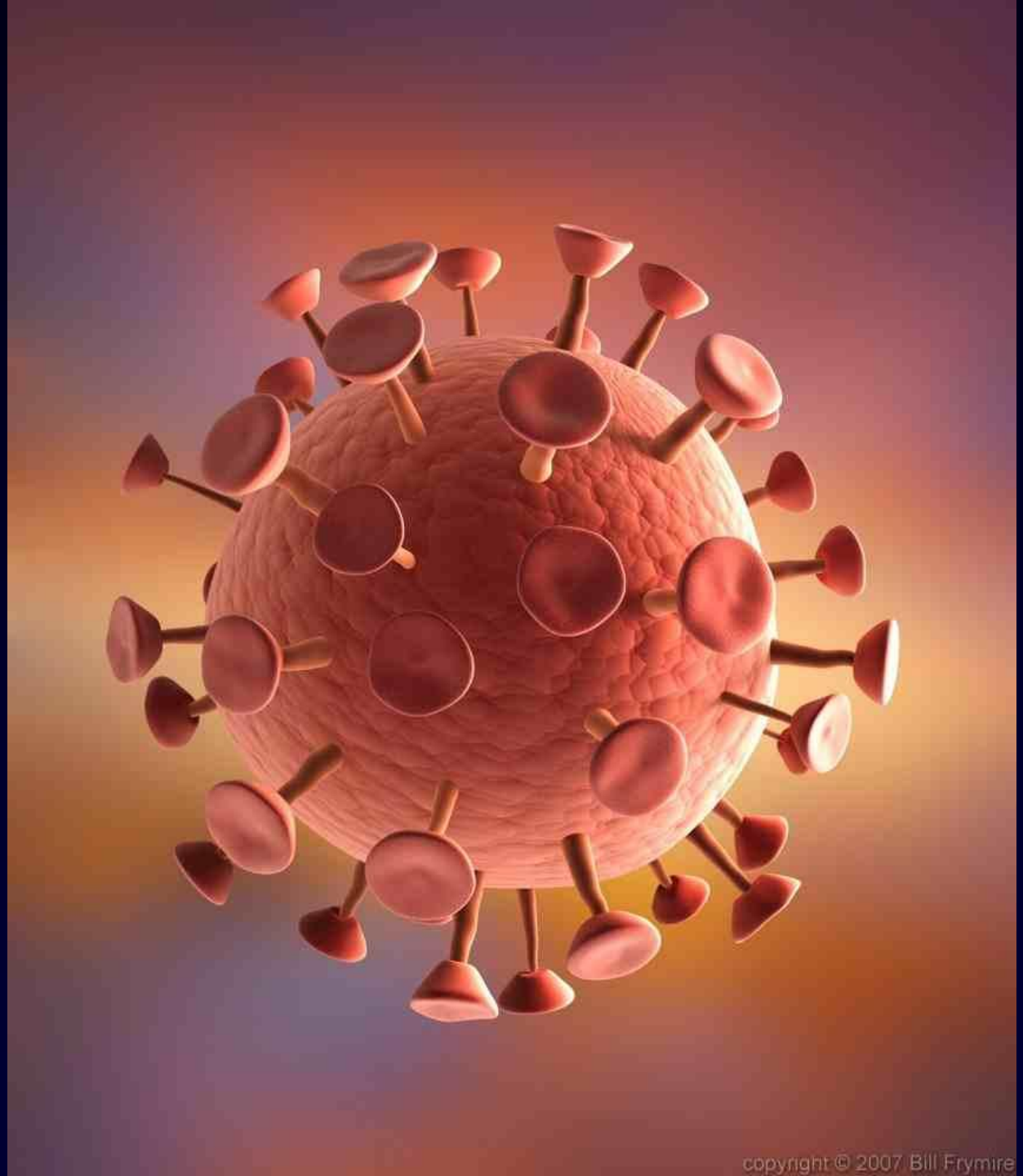
- Enfuvirtide

R5 Inhibitors

- **Maraviroc**

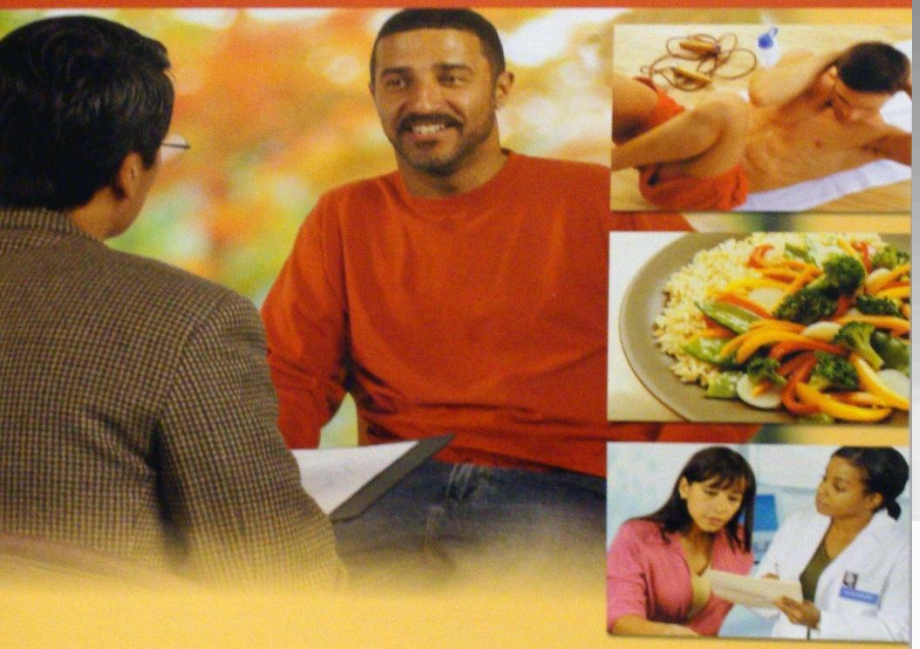
Integrase Inhibitors

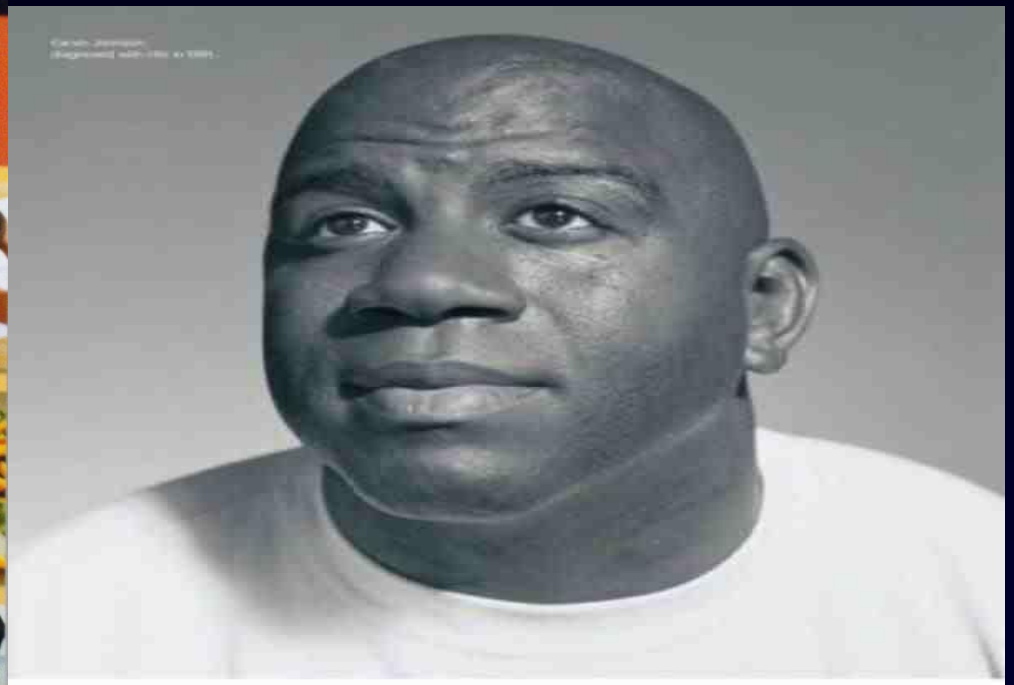
- Raltegravir


copyright © 2007 Bill Frymire

Self-Care Handbook

Living Well with HIV





For me, staying healthy with HIV is about a few basic things:

A positive attitude. Partnering with my doctor. Taking medicine every day.

One of the keys to living with HIV is finding a treatment plan that may be right for you – then sticking with it. For some people, getting through the first few months of HIV therapy can be tough, so discuss it with your doctor. The decisions you make today can make a huge difference for years to come.

For information about living with HIV, call 1-888-TREAT HIV, or visit www.TreatHIV.com.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ANDREW WATKINS/AFP/GETTY IMAGES

CRICKET

as explained to a foreign visitor

You have two sides one out in the field and one in.

Each man that's in the side that's in goes out and when he's out he comes in and the next man goes in until he's out.

When they are all out the side that's out comes in and the side that's been in goes out and tries to get those coming in out.

Sometimes you get men still in and not out.

When both sides have been in and out including the not outs.

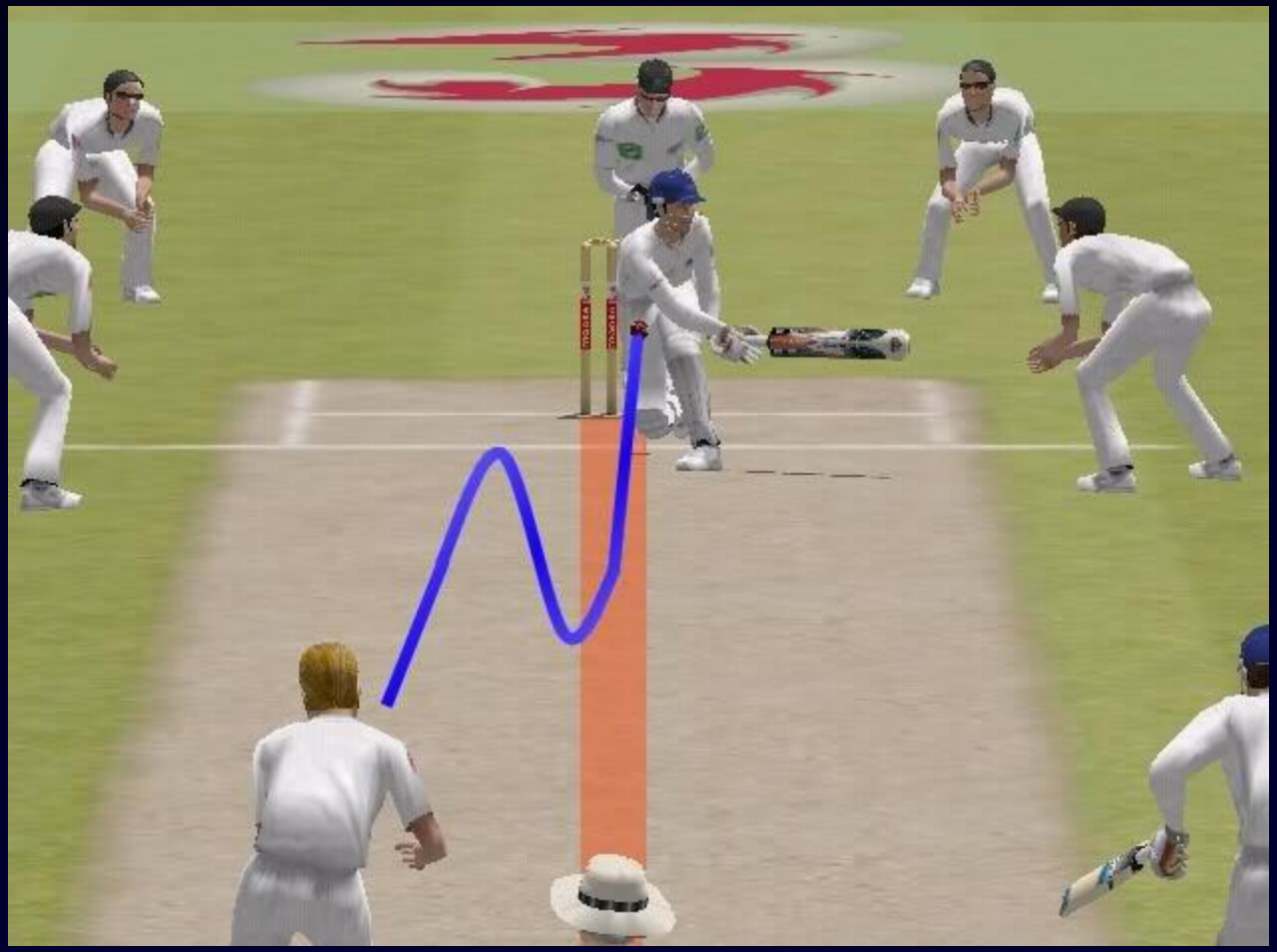
Thats the end of the game

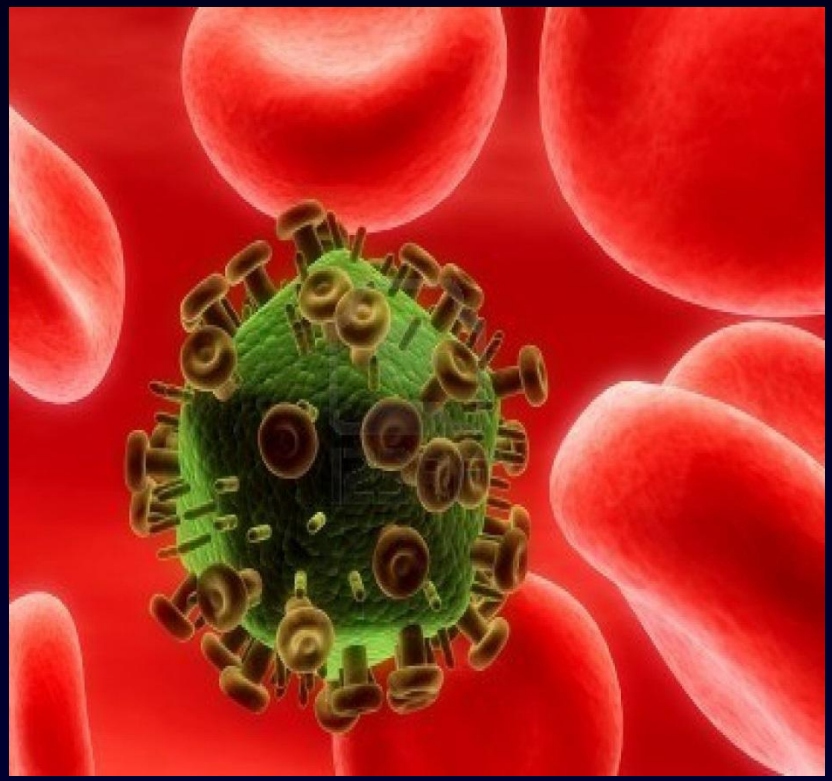
HOWZAT!


55


Cricket
Play Har


Indian & Chinese
Gulistan
£7.95
EAT FREE ON SUNDAYS
RT






ROCHE 0246

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Fusion Inhibitors

- Enfuvirtide

R5 Inhibitors

- **Maraviroc**

Integrase Inhibitors

- Raltegravir


HOW LOW CAN YOU GO?
THE AIM IS TO KEEP YOUR VIRAL LOAD UNDER 50, WHAT WE CALL UNDETECTABLE.


HIV
AIDS


TOXIC
©DDY

Drug Resistance


©Vincent Desjardins 2009
PRESCRIPTION STRENGTH
Rx
MILK MILK
inter actions
Rx
Extra Strength


SHN
CLOSE TIGHTLY
PUSH DOWN AND UNSCREW

“Drugs don’t work if people don’t take them”

Former US Surgeon General C. Everett Koop

- **“*Drugs do work if people do take them*”**

Mark R. Nelson

UK Surgeon General

- ***“Crappy Drugs are Crappy and dont work because they are Crap”***

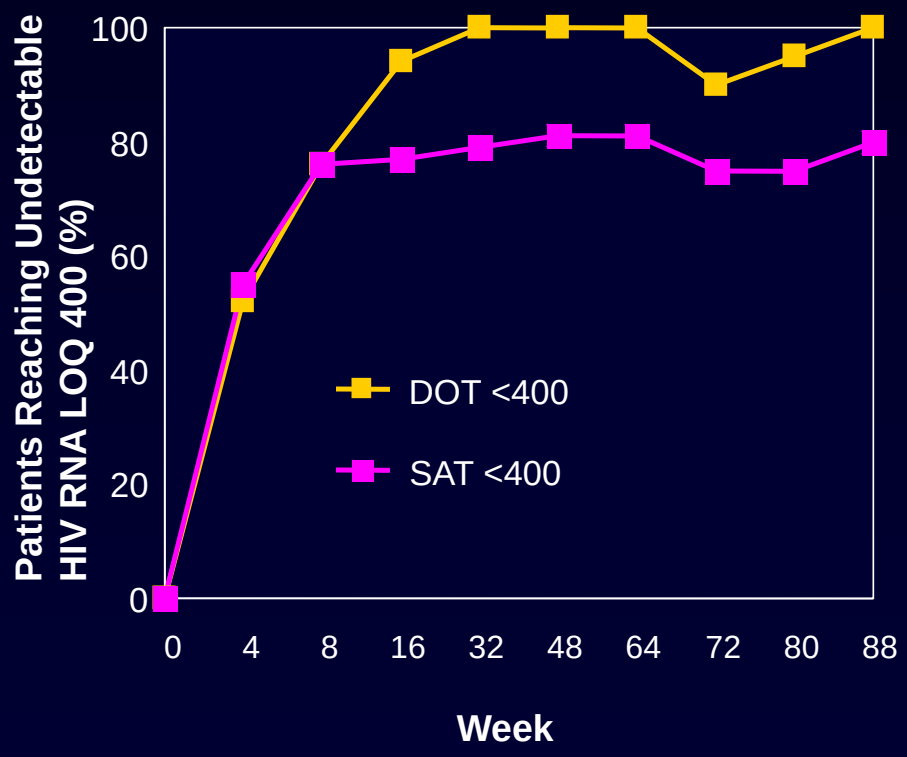
Cassie Workman

Australia

HAART is Highly Effective When Taken as Directed

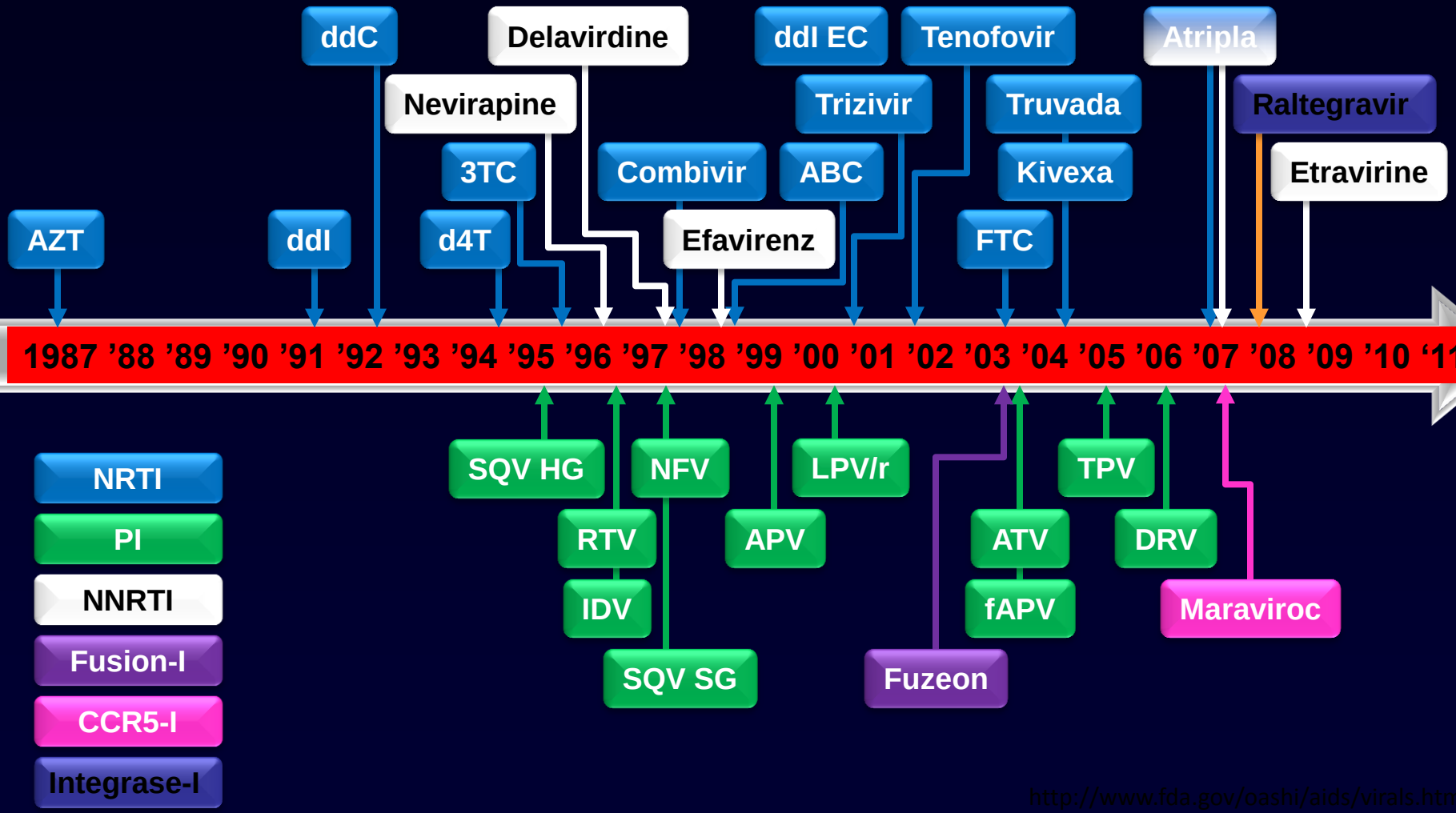
Directly Observed Therapy (DOT) *vs* Self-administered Therapy (SAT)

- Patients: Antiretroviral-naive patients in prison on 3- or 4-drug combinations under DOT *vs* SAT
- Conclusions
  - HAART works when taken properly
  - DOT group superior at all time points
  - Within SAT group, 4-drug regimens had lowest response (57%)
  - EFV-containing regimens had the best virologic response rates
  - Lower toxicity rate in DOT group



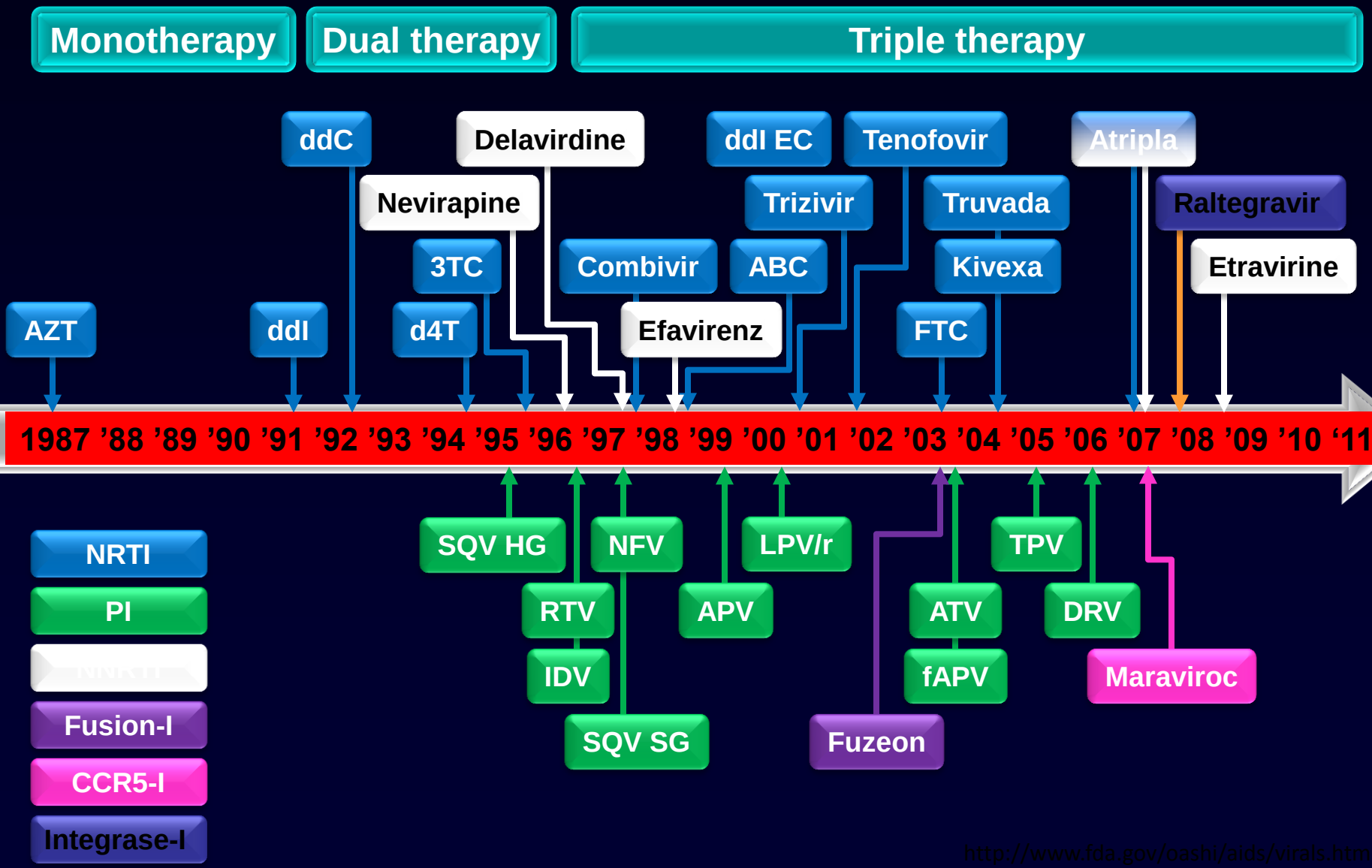
Fischl. 8th CROI; 2001; Chicago. Abstract 528.

ARV adherence milestones



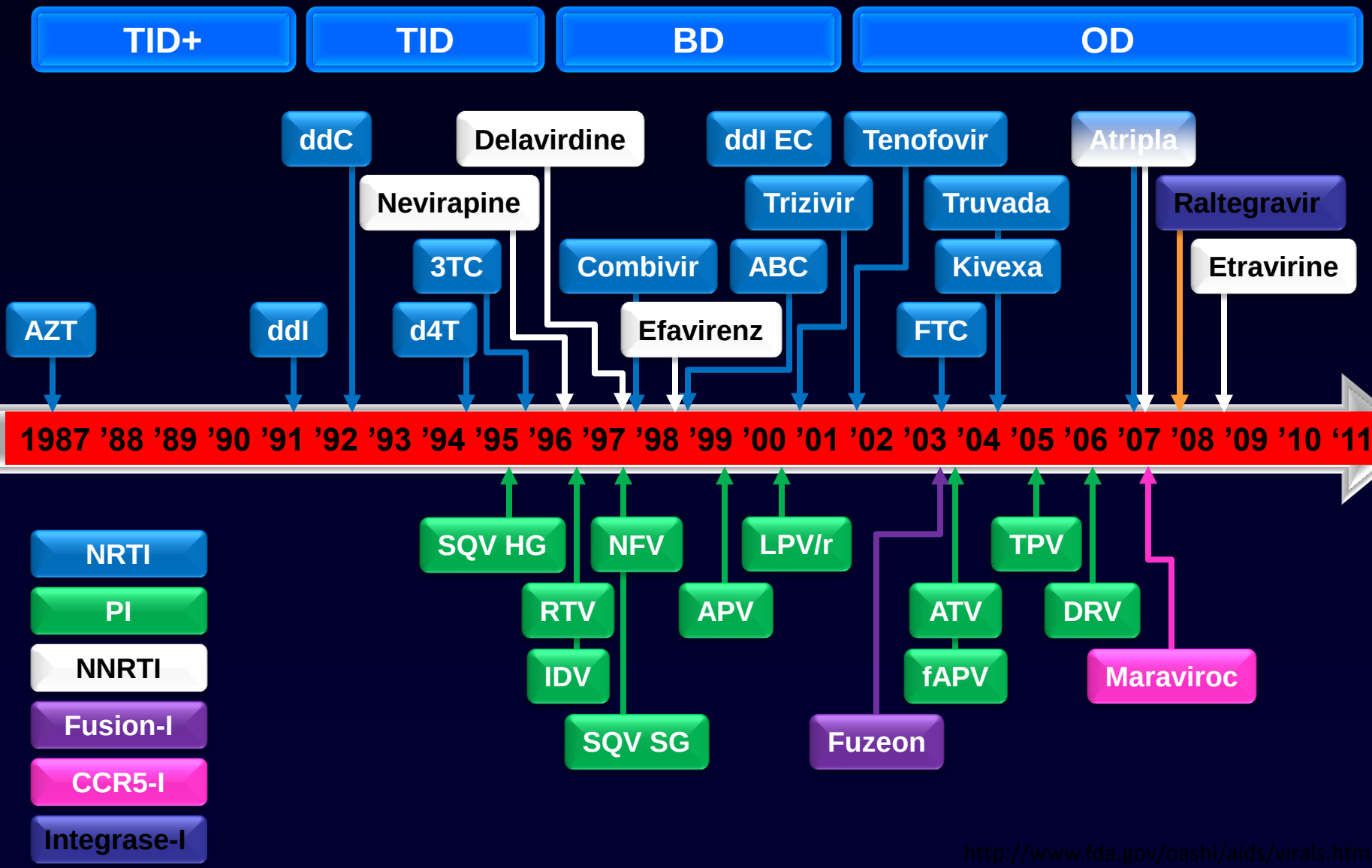
http://www.fda.gov/oashi/aids/virals.html

ARV adherence milestones



http://www.fda.gov/oashi/aids/virals.html

ARV adherence milestones



http://www.fda.gov/oashi/aids/virals.html

Available Once Daily

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- Abacavir
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- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

NNRTIs

- Efavirenz
- Nevirapine
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Protease Inhibitors

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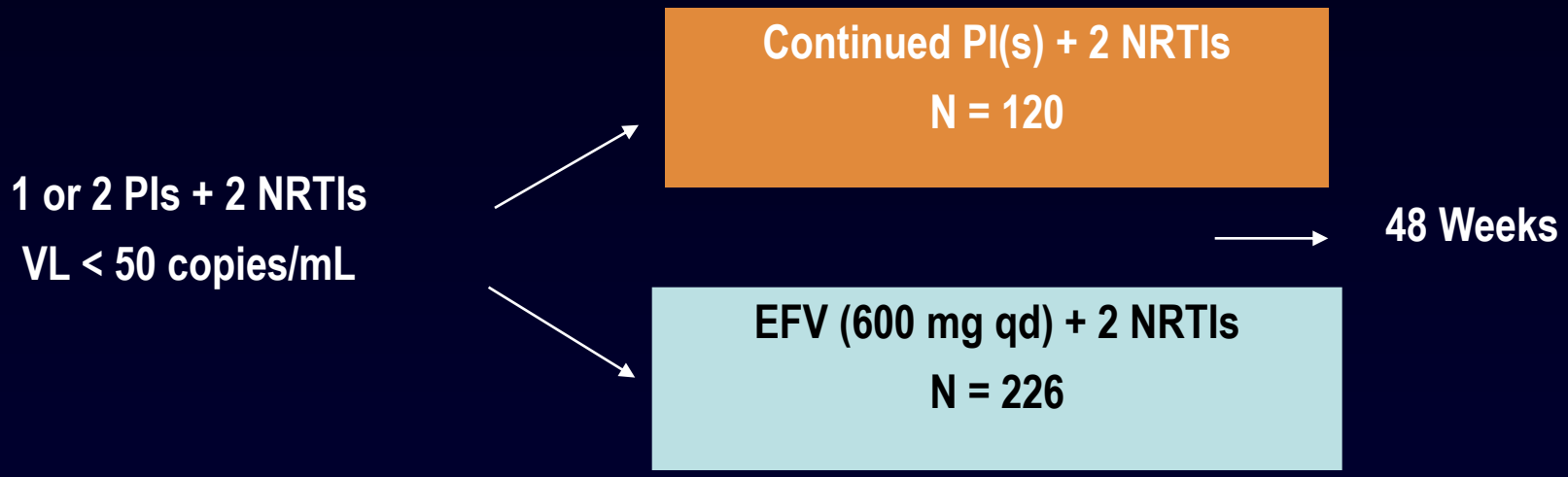
R5 Inhibitors

- **Maraviroc**

Integrase Inhibitors

- **Raltegravir**

Switching from PI to EFV: Design of DMP 049 Study

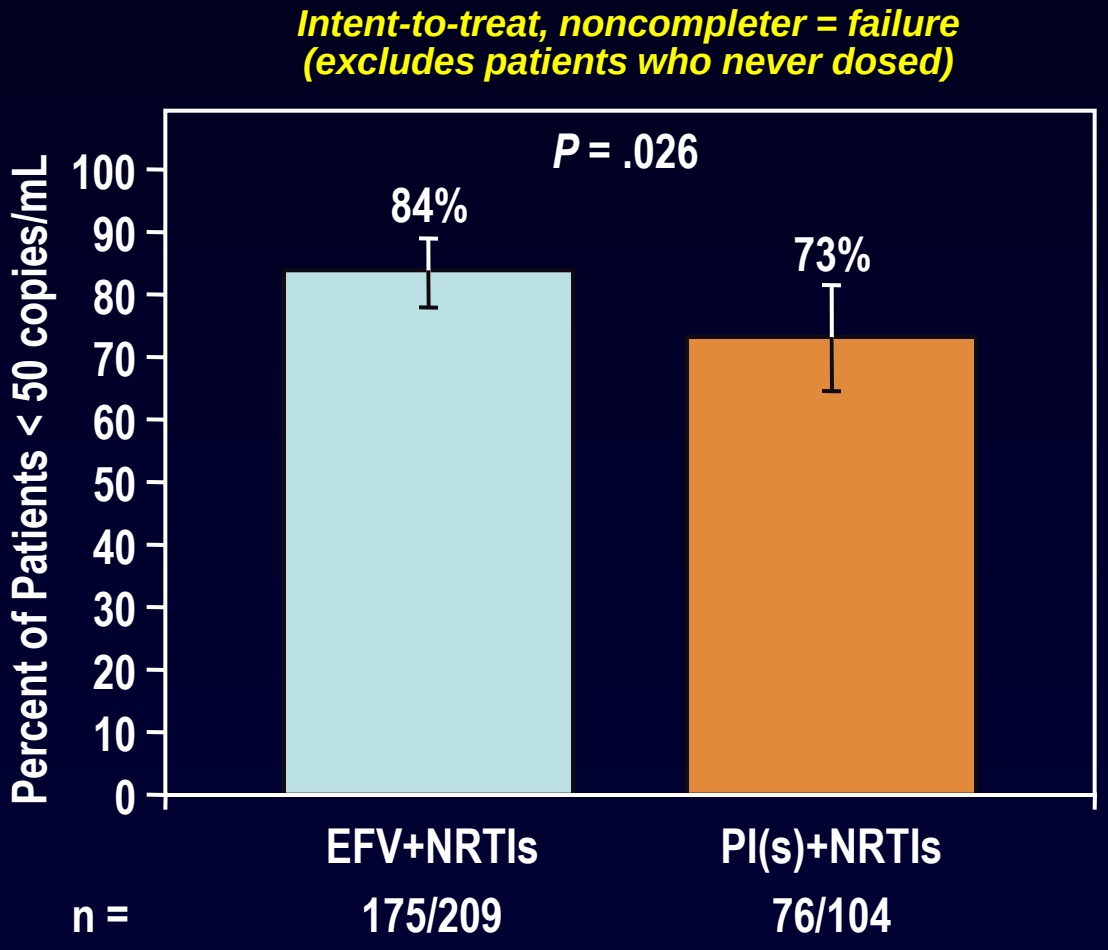


NRTIs remained the same as prior to study entry

* Patients randomized to EFV remained on their PI(s) for 7-day overlap period after starting EFV

Becker et al. 8th CROI. Abstract 20.

DMP 049 Study: Superior Rates of Viral Suppression at Week 48

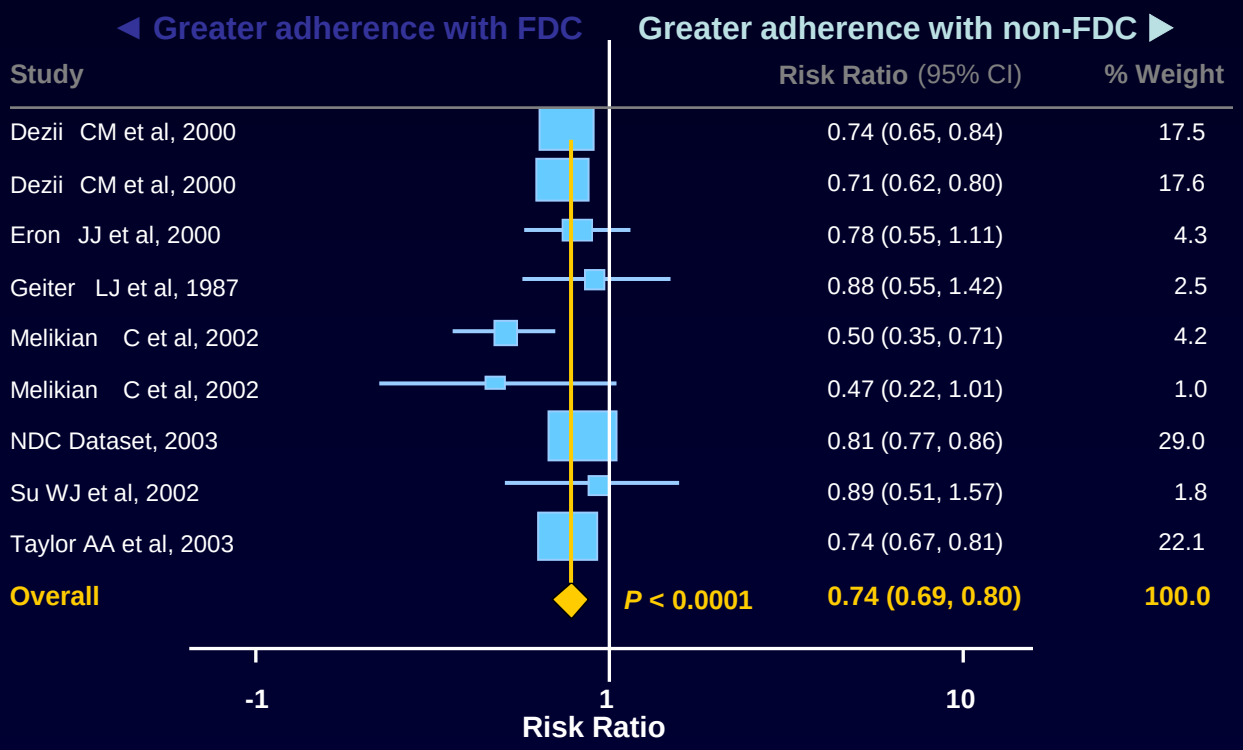


Becker et al. 8th CROI. Abstract 20.

Meta Analysis of Adherence with FDC

Meta-analysis of 9 clinical trials in 4 therapeutic areas (TB, HTN, HIV, DM)
11,925 FDC patients and 8317 non-FDC patients

Effect of FDCs versus non-FDC on risk of non-adherence

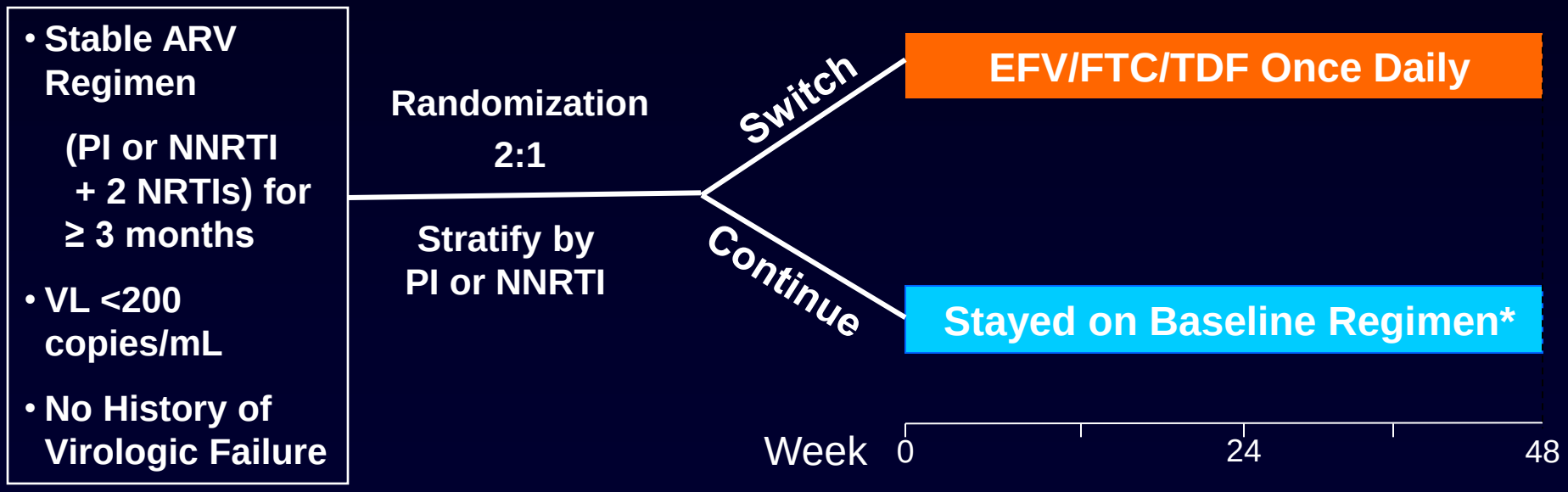


FDC regimens reduce risk of non-adherence by ~25% (compared to dosing with individual pills)

Bangalore S, et al. Am J Med 2007;120:713-9

Study Design

Phase IV, multicenter (55 US sites), open-label study (N = 300)

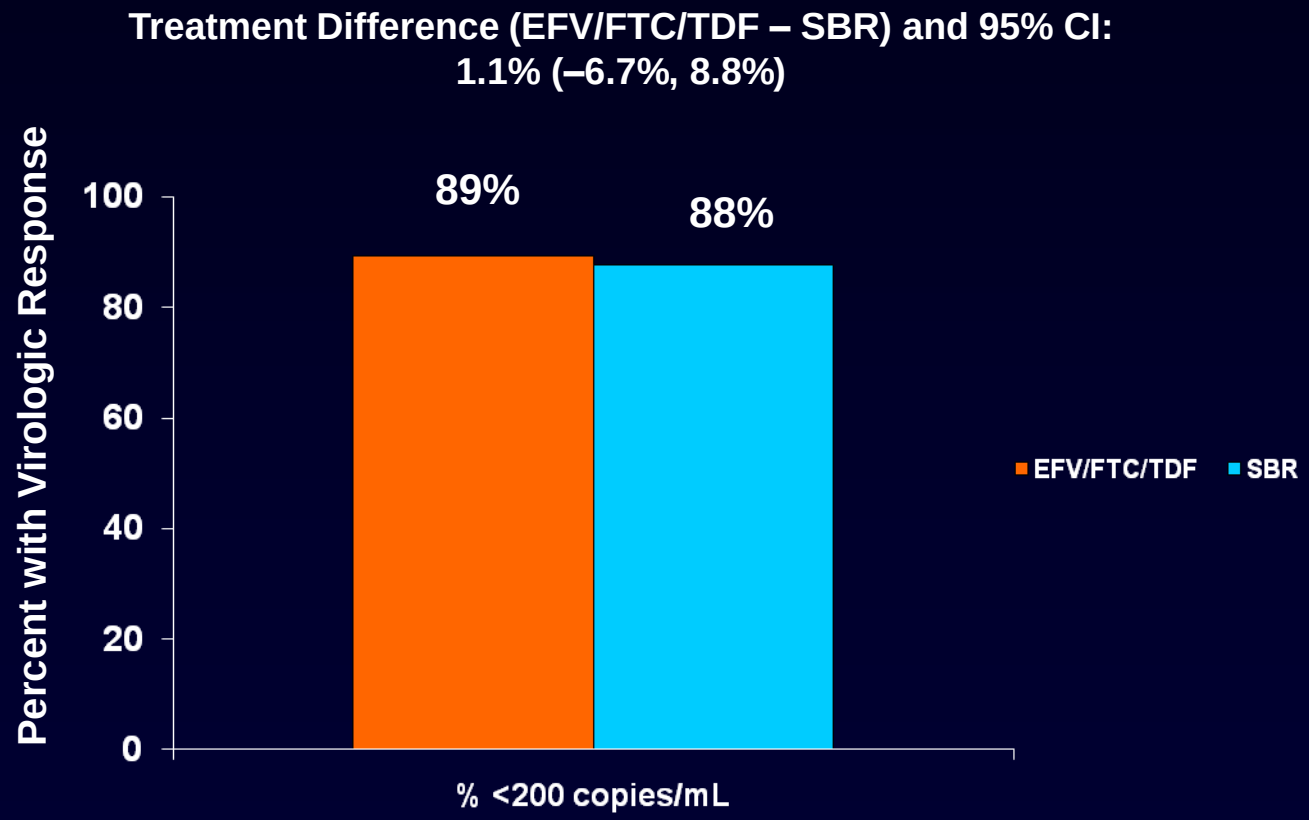


Primary Endpoint: assess non-inferiority of EFV/FTC/TDF vs. SBR in terms of maintenance of HIV-1 RNA <200 copies/mL through Week 48 by TLOVR**analyses

*SBR: stayed on baseline regimen

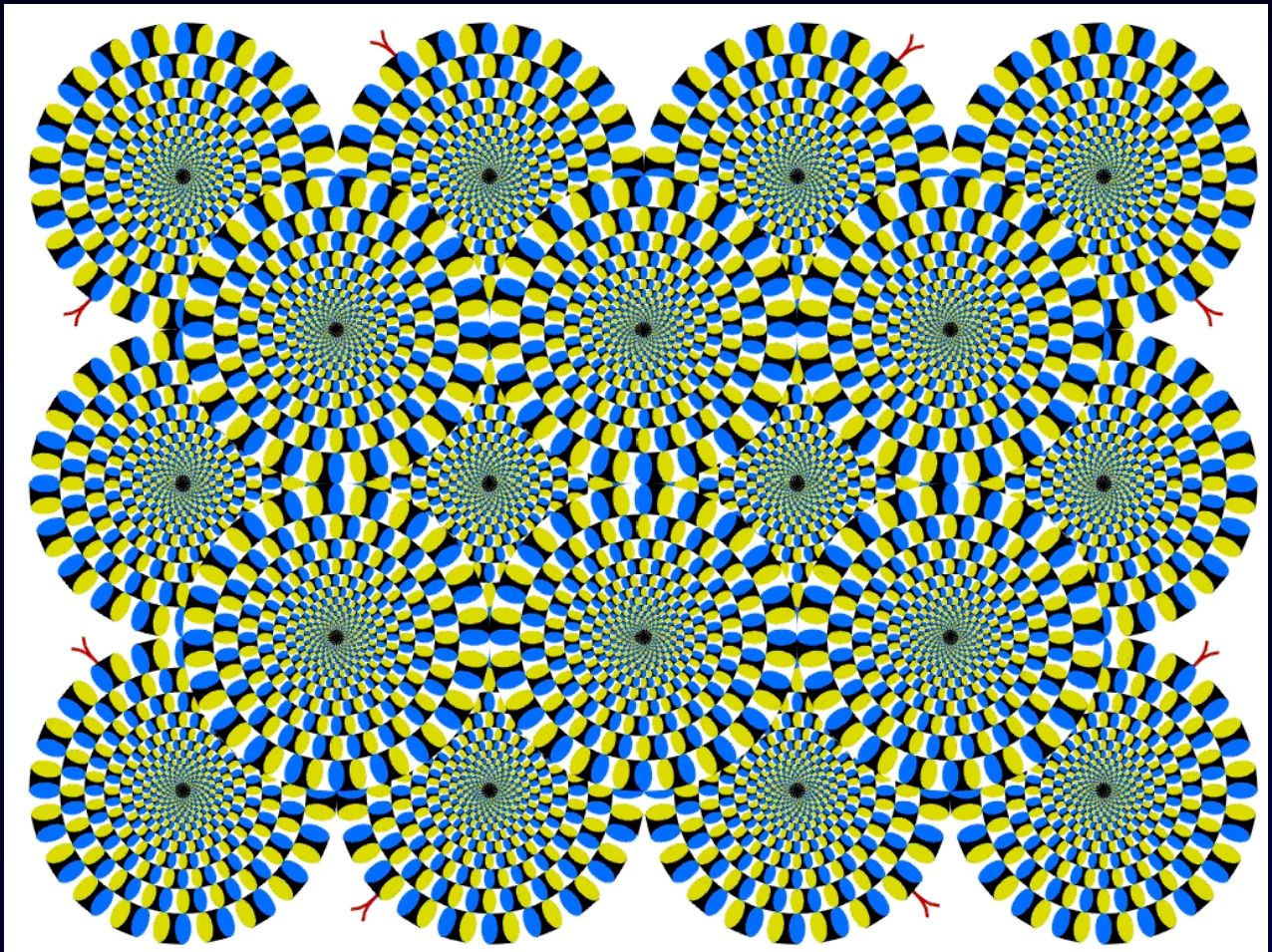
**Time to loss of Virologic Response Algorithm

Primary Endpoint Analysis: Percentage of Patients with HIV-1 RNA <200 copies/mL Through 48 Weeks (TLOVR)



- The primary endpoint of non-inferiority of EFV/FTC/TDF to SBR was demonstrated

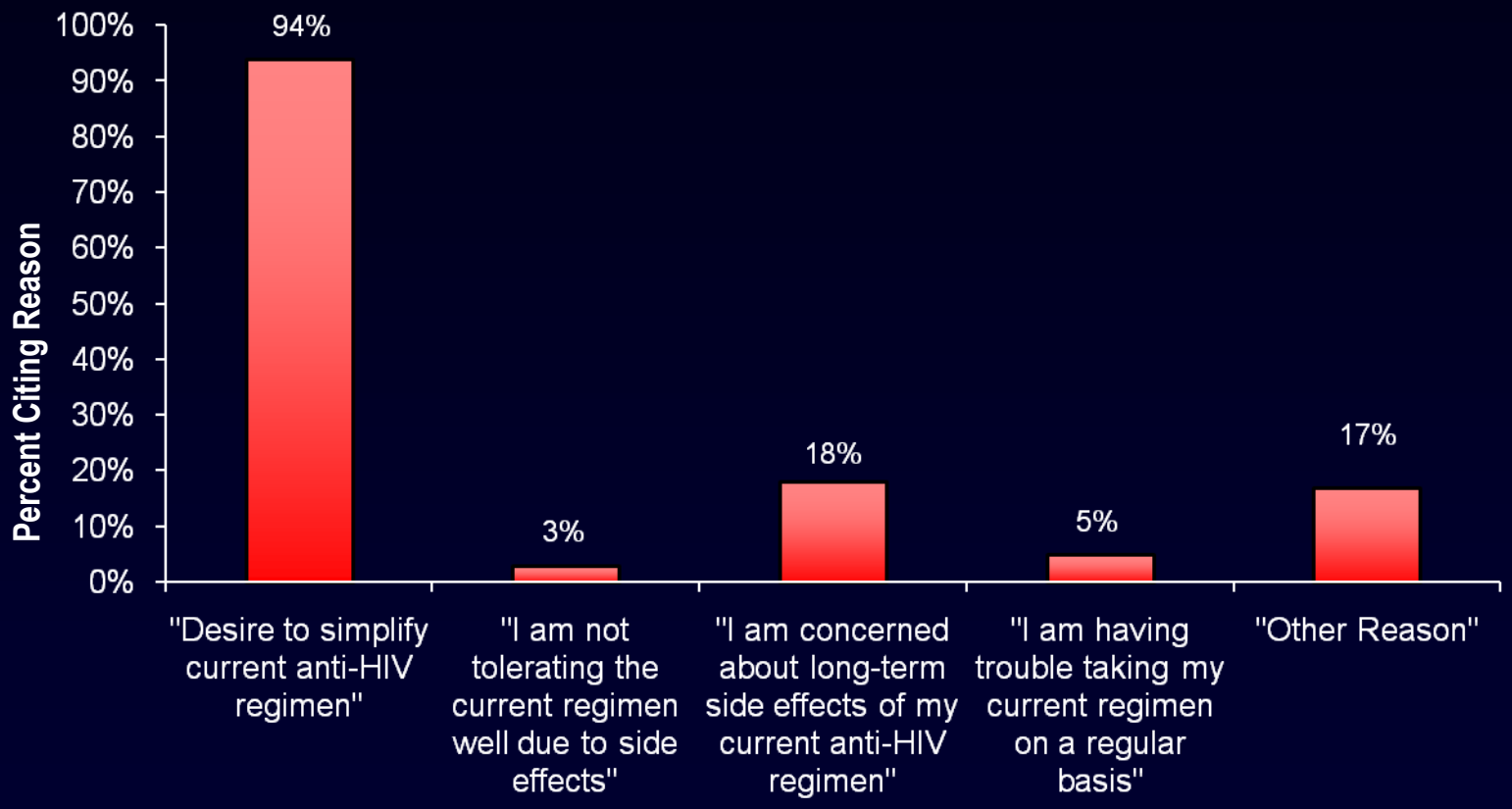
Perception v Reality




HIPHOP POW
HIPHOPPOW.com

Study 073

Enrollment Survey
Reasons for Willingness to Switch

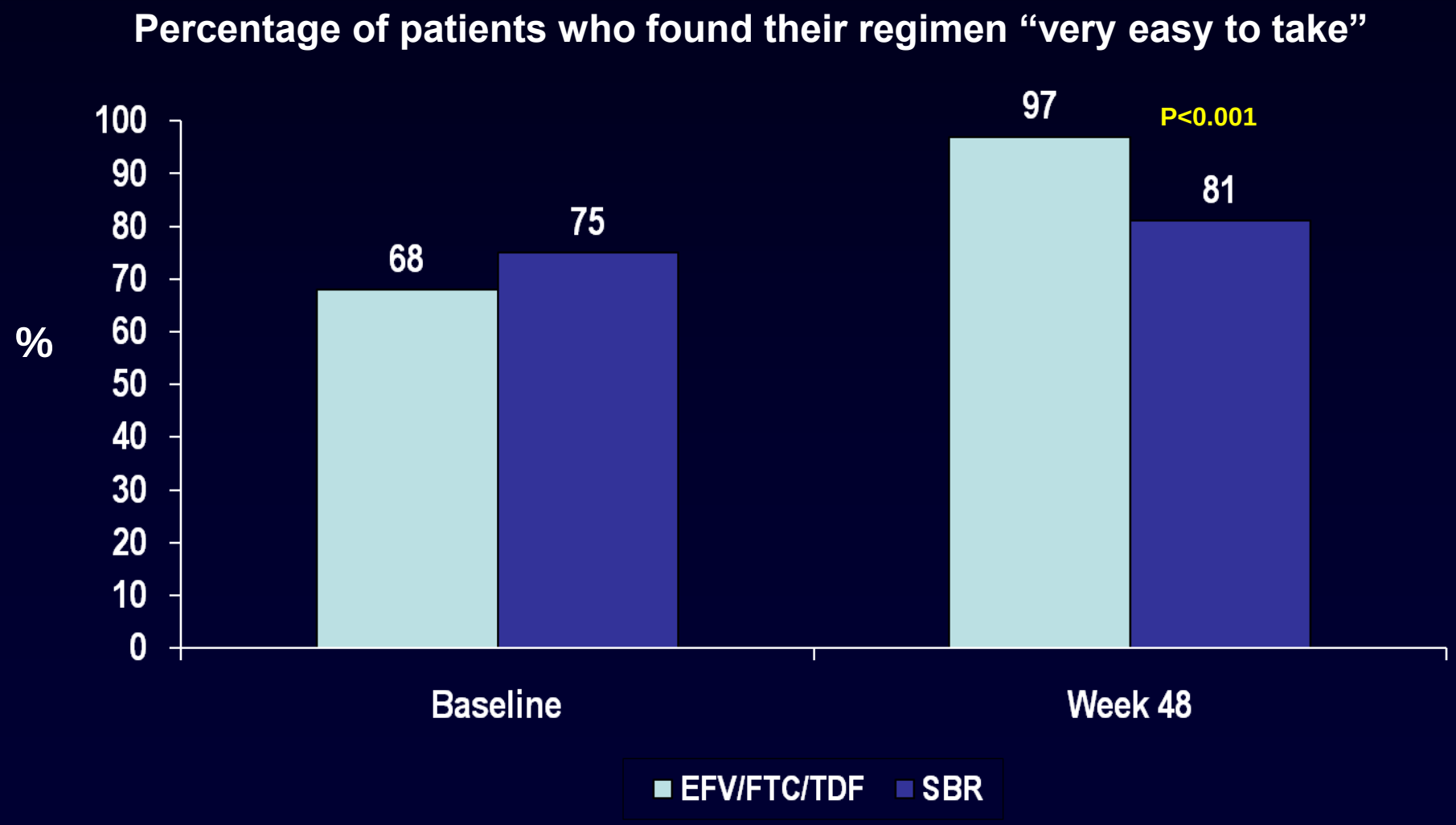


- Other Reasons responses included: “curious,” “cost,” “hope to find a cure,” “interested in research,” “lipoatrophy,” “asked by doctor to participate,” “to help in the understanding of what this could do for others”

Hodder S, et al. 9th International Congress on Drug Therapy in HIV Infection, 2008 #P063

Study 073

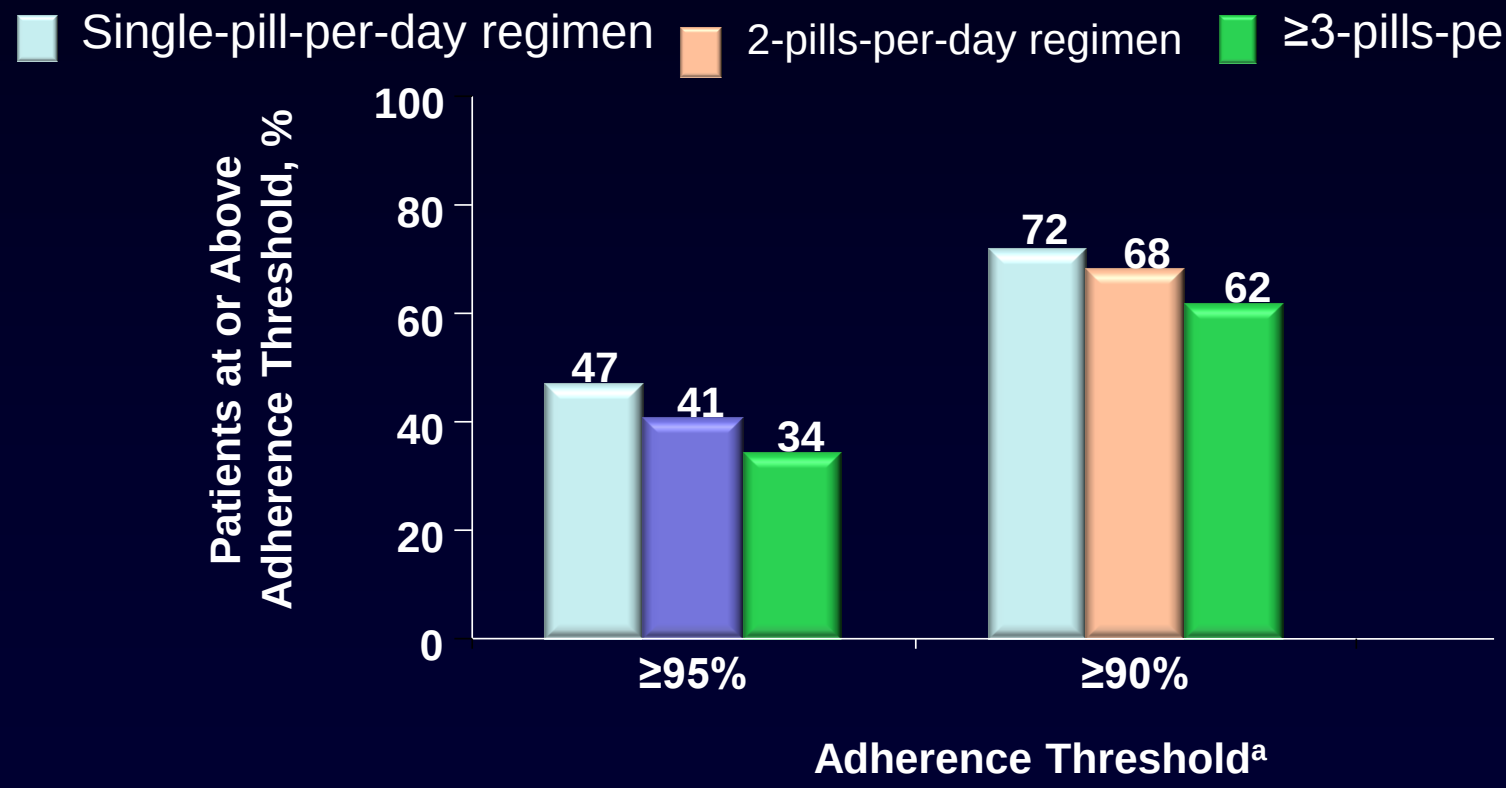
Perceived Ease of the Regimen for Condition (PERC)



DeJesus E, et al. JAIDS. 2009; 51(2):163-174.

LifeLink Database: Impact of Simplified Regimens on Adherence

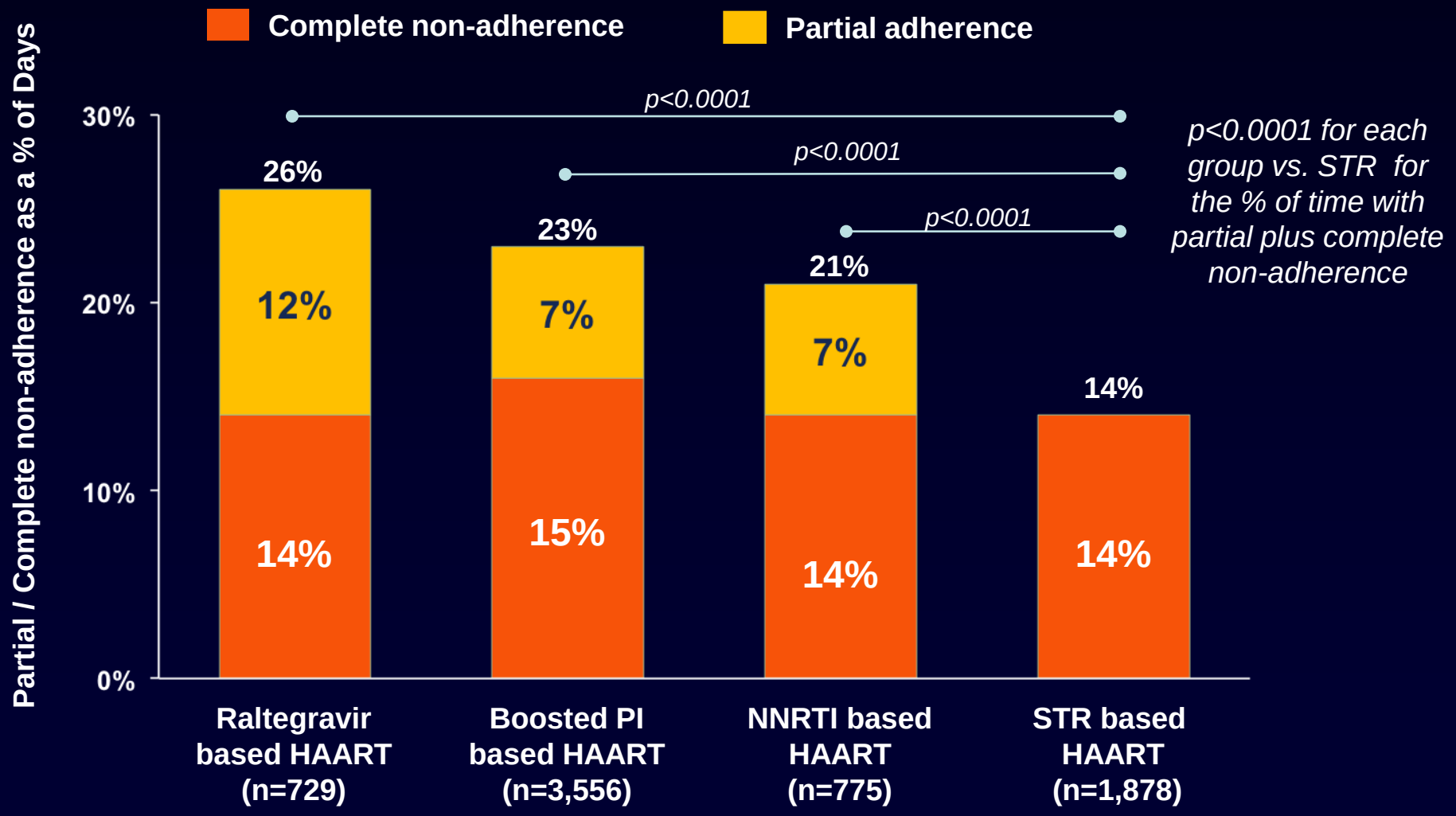
STR associated with 59% greater likelihood of ≥95% adherence vs ≥3 pills per day
STR generally favorable—significantly greater adherence vs more pills per day



[a] *P* <0.05 for single-pill-per-day cohort vs 2- and ≥3-pills-per-day cohorts at all levels of adherence, except vs 2-pills-per-day cohort at 90% level of adherence.

Sax P, et al. HIV10. 2010. Glasgow. Oral #113.; Sax P, et al. *PLoS ONE.* 2012;7:e31591.

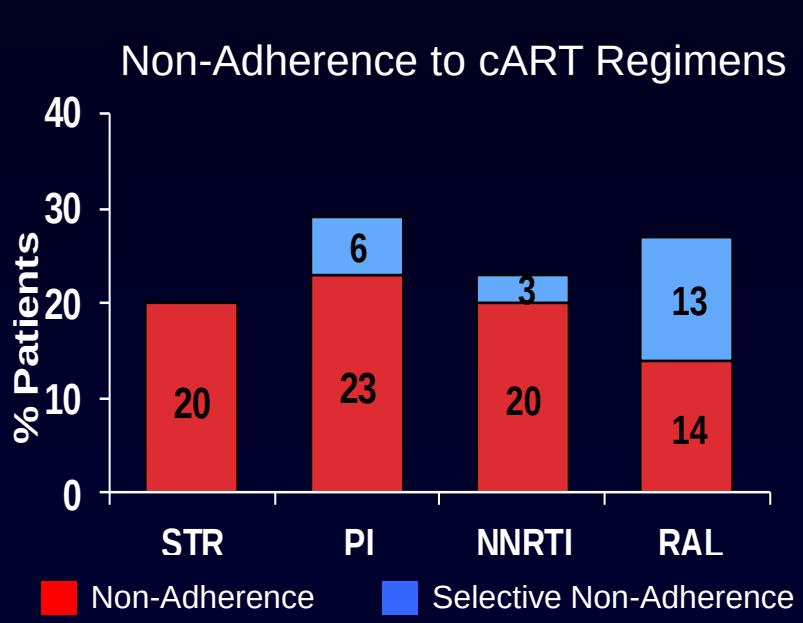
Partial and Complete Non-Adherence to ART

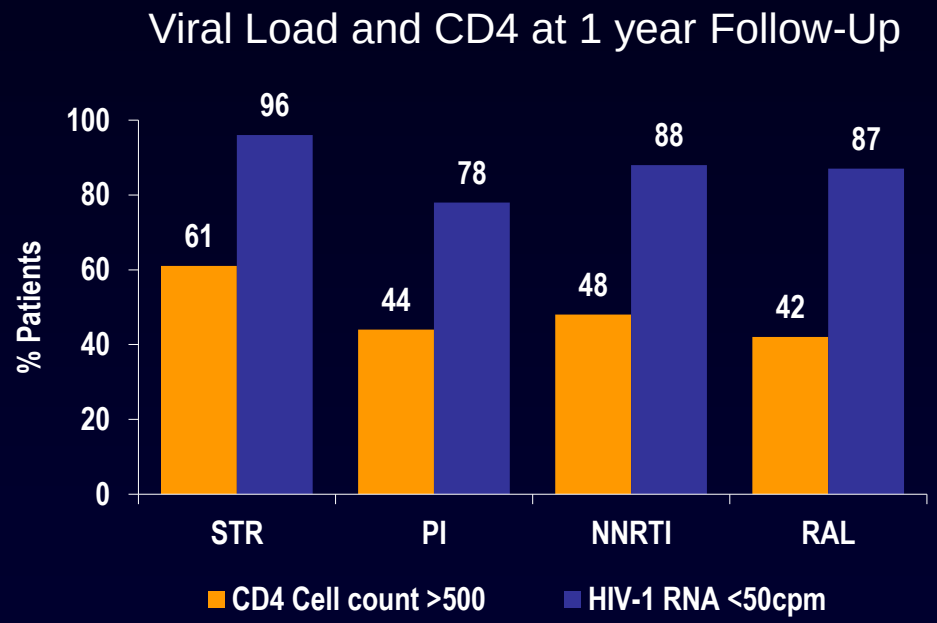


C Cohen. HIV11, Glasgow, UK 2012 #P1

COMPACT
Adherence in pts on an STR or multi-pill regimens

Retrospective, observational cohort analysis in 1,604 HIV+ patients (2008-2010)





SUM: Higher Adherence with the STR vs. multi-pill regimens

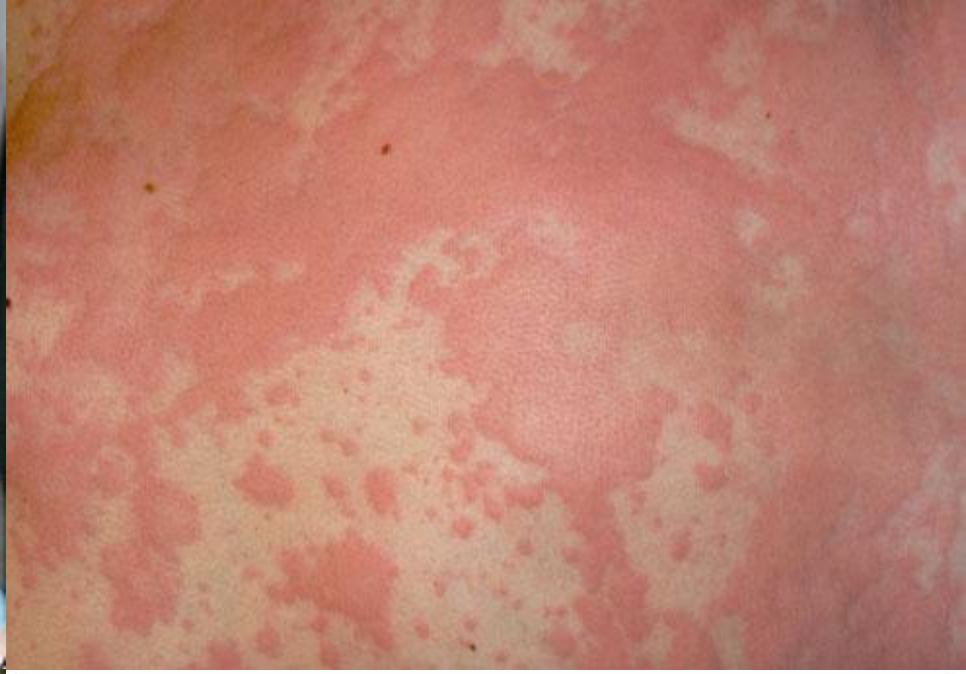
STR associated with a higher rate of

- Virologic suppression (VL<50)
- CD4>500 cells/mm^3

Antinori, et al. HIV-11 2012; Glasgow. Poster

Common Sense

So rare that it's a super power.




DIARREA
LA DIARREA ES MUY PELIGROSA
DELE A SU NIÑO (A)
SUERO ORAL
MINSA
PCI-NICARAGUA
USAID

ARV Toxicity – Do Doctors and Patients Think Alike?

Rank	Patient (N=95)	HCP (N=58)
1 (most distressing)	Lipodystrophy	Nausea and vomiting
2	Sleep disturbances	Effect on sexual function
3	Increased risk of MI/stroke	Sleep Disturbance
4	Nausea and vomiting	Diarrhoea
5	Effect on sexual function	Lipodystrophy
6	Itchy rash	Weight gain
7	Jaundice	Increased drowsiness
8	Increased drowsiness	Increased risk of MI/stroke
9	Diarrhoea	Jaundice
10 (least distressing)	Weight gain	Itchy rash

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2	Sleep disturbances	Effect on sexual function
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5	Effect on sexual function	Lipodystrophy
6	Itchy rash	Weight gain
7	Jaundice	Increased drowsiness
8	Increased drowsiness	Increased risk of MI/stroke
9	Diarrhoea	Jaundice
10 (least distressing)	Weight gain	Itchy rash

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5	Effect on sexual function	Lipodystrophy
6	Itchy rash	Weight gain
7	Jaundice	Increased drowsiness
8	Increased drowsiness	Increased risk of MI/stroke
9	Diarrhoea	Jaundice
10 (least distressing)	Weight gain	Itchy rash

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6	Itchy rash	Weight gain
7	Jaundice	Increased drowsiness
8	Increased drowsiness	Increased risk of MI/stroke
9	Diarrhoea	Jaundice
10 (least distressing)	Weight gain	Itchy rash

ARV Toxicity – Do All Patients Think Alike?

Rank	Patient UK (N=95)	Patient Uganda (N=64)
1 (most distressing)	Lipodystrophy	Diarrhoea
2	Sleep disturbances	Nausea and Vomiting
3	Increased risk of MI/stroke	Lipodystrophy
4	Nausea and vomiting	Itchy Rash
5	Effect on sexual function	Effect on sexual function
6	Itchy rash	Increased drowsiness
7	Jaundice	Jaundice
8	Increased drowsiness	Increased risk of MI/stroke
9	Diarrhoea	Sleep Disturbance
10 (least distressing)	Weight gain	Weight gain

Mackenzie Nelson J AIDS 2011

ARV Toxicity – Do All Patients Think Alike?

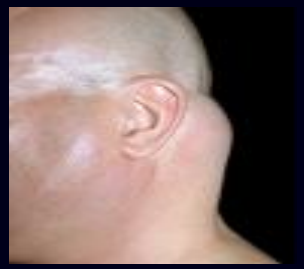
Rank	Patient UK (N=95)	Patient Uganda (N=64)
1 (most distressing)	Lipodystrophy	Diarrhoea
2	Sleep disturbances	Nausea and Vomiting
3	Increased risk of MI/stroke	Lipodystrophy
4	Nausea and vomiting	Itchy Rash
5	Effect on sexual function	Effect on sexual function
6	Itchy rash	Increased drowsiness
7	Jaundice	Jaundice
8	Increased drowsiness	Increased risk of MI/stroke
9	Diarrhoea	Sleep Disturbance
10 (least distressing)	Weight gain	Weight gain

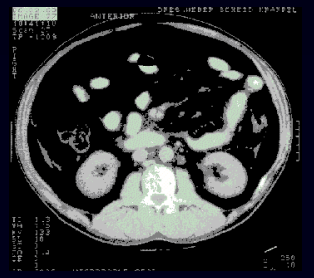
ARV Toxicity – Do All Patients Think Alike?

Rank	Patient UK (N=95)	Patient Uganda (N=64)
1 (most distressing)	Lipodystrophy	Diarrhoea
2	Sleep disturbances	Nausea and Vomiting
3	Increased risk of MI/stroke	Lipodystrophy
4	Nausea and vomiting	Itchy Rash
5	Effect on sexual function	Effect on sexual function
6	Itchy rash	Increased drowsiness
7	Jaundice	Jaundice
8	Increased drowsiness	Increased risk of MI/stroke
9	Diarrhoea	Sleep Disturbance
10 (least distressing)	Weight gain	Weight gain

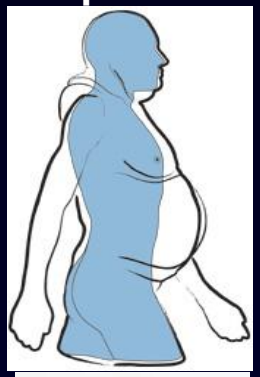
Glucose metabolism impairment

Dyslipidaemia

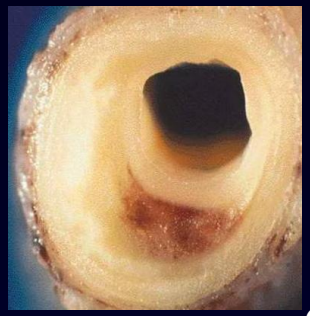


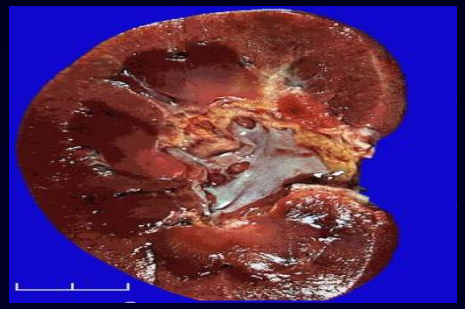


Abnormalities of body composition



HAND



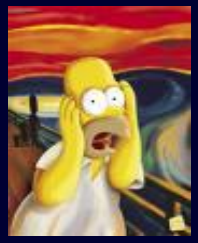


CVD

Body image alterations

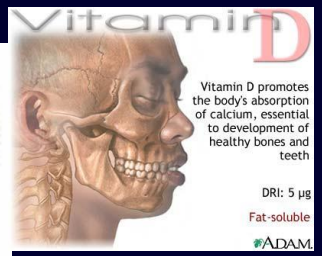
Hepatic steatosis

Bone & Kidney disease



Depression

Hypertension



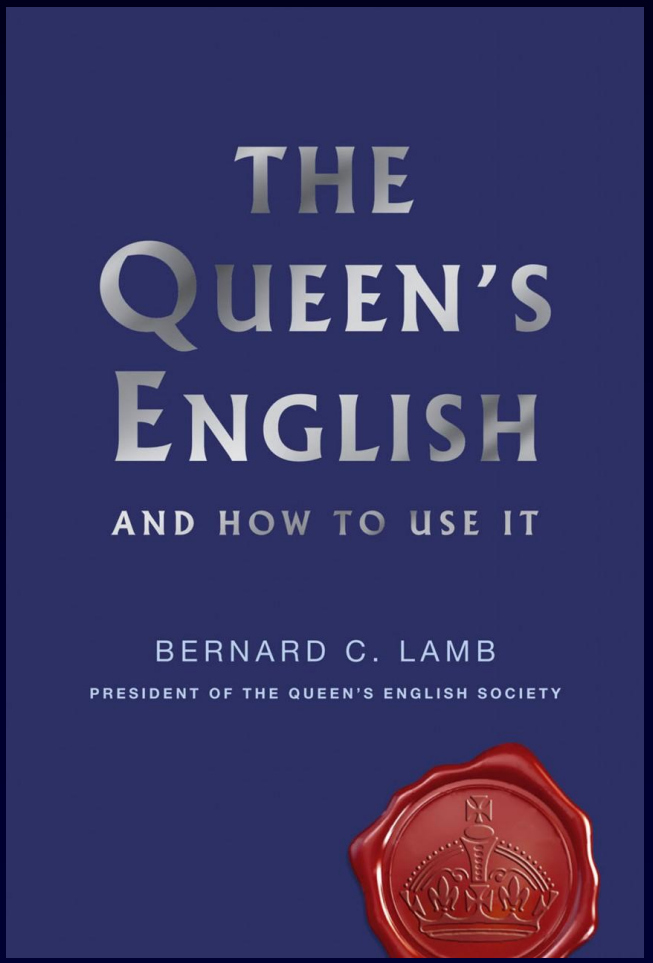
Vitamin D

Type 2 diabetes

Cancer

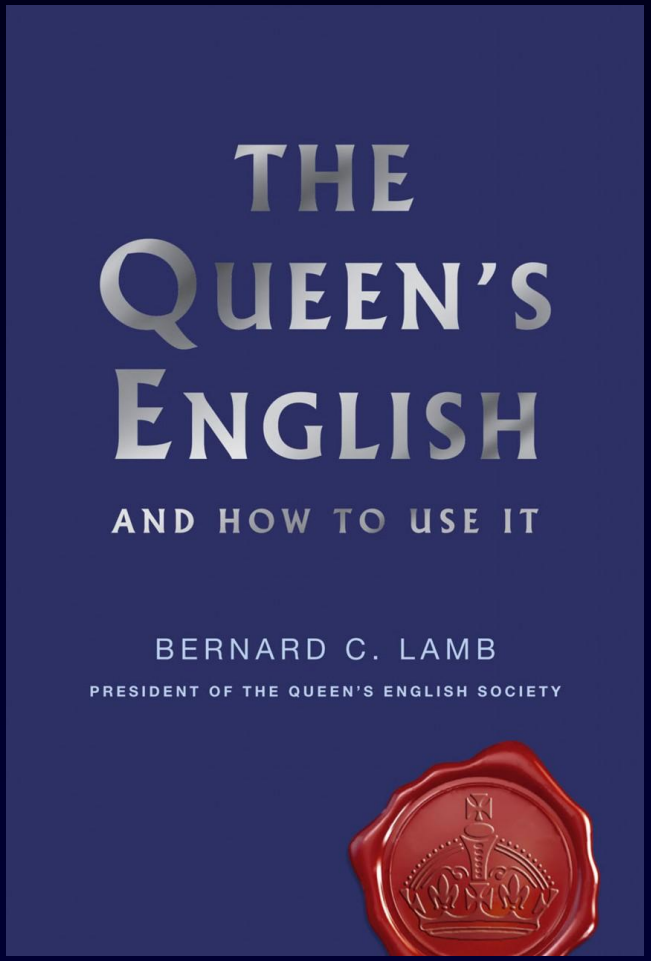
Sexual Dysfunction

To Tolerate

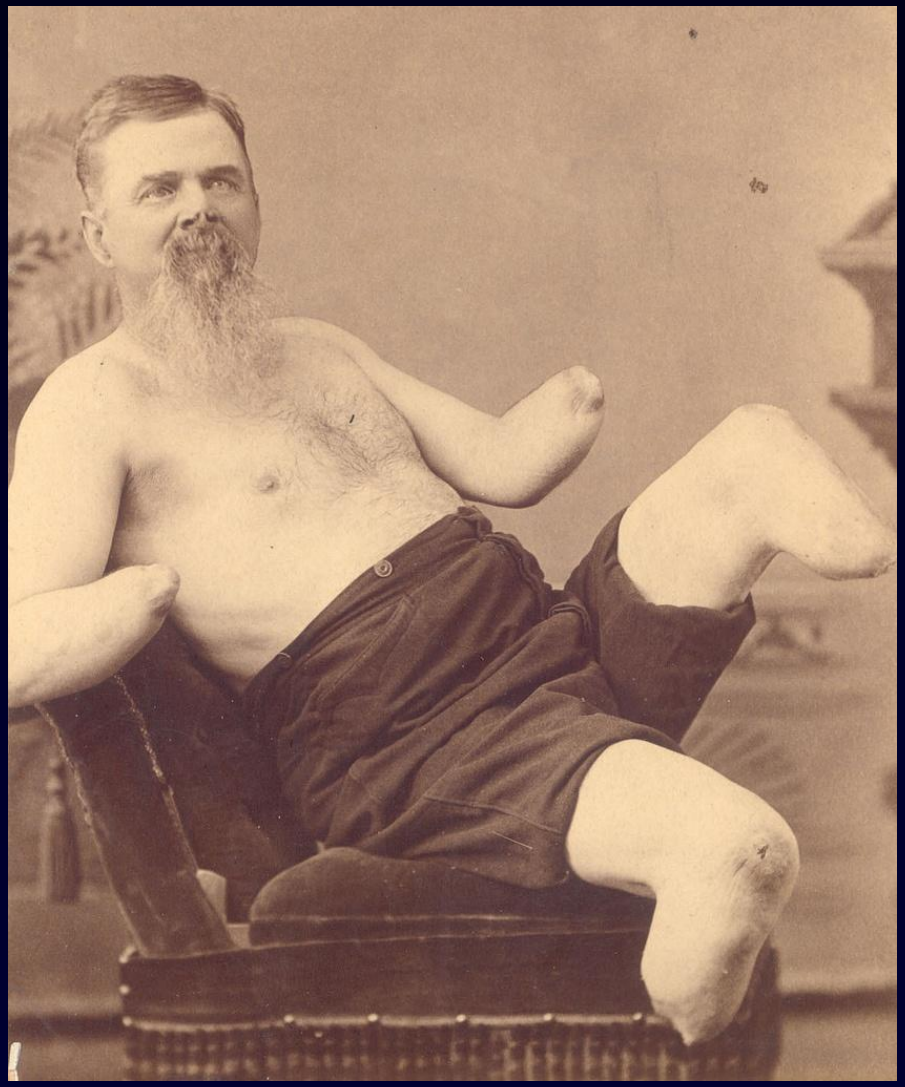

THE QUEEN'S ENGLISH
AND HOW TO USE IT
BERNARD C. LAMB
PRESIDENT OF THE QUEEN'S ENGLISH SOCIETY

To Tolerate

- To endure



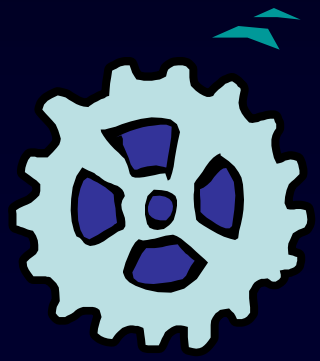

ROYAL NAVY
GORE-TEX
multimat




Bruce in New Zealand

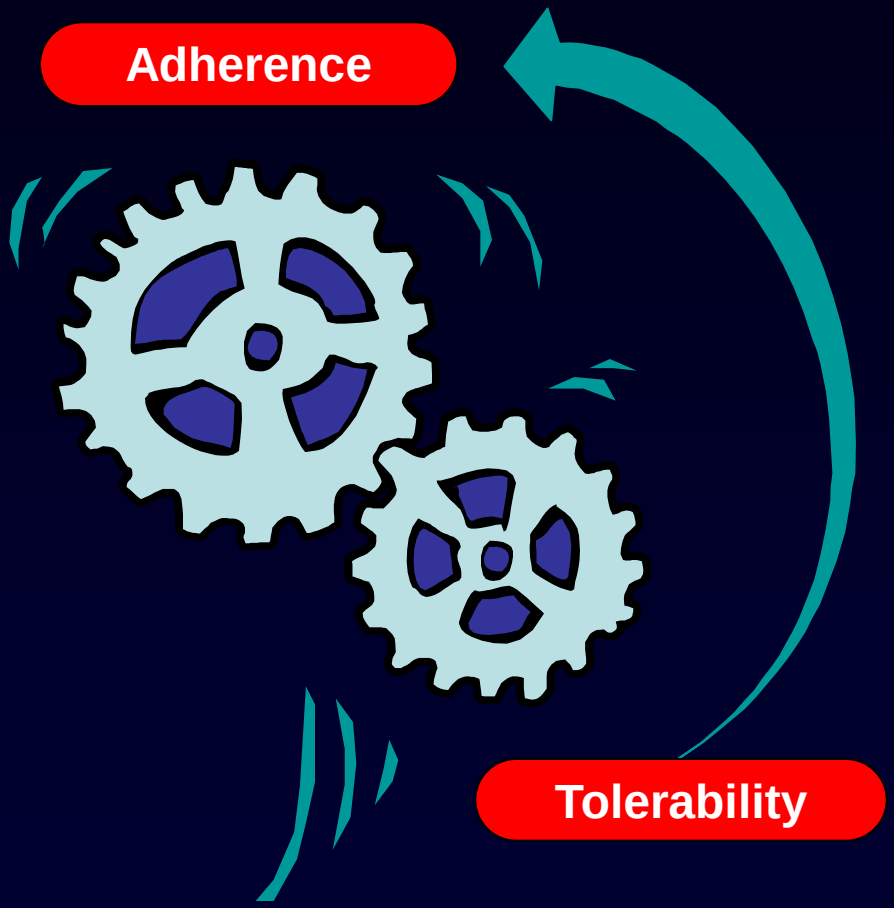
HELLY HANSEN
KODEN
Canon
dubarry

Tolerability drives adherence, which drives efficacy

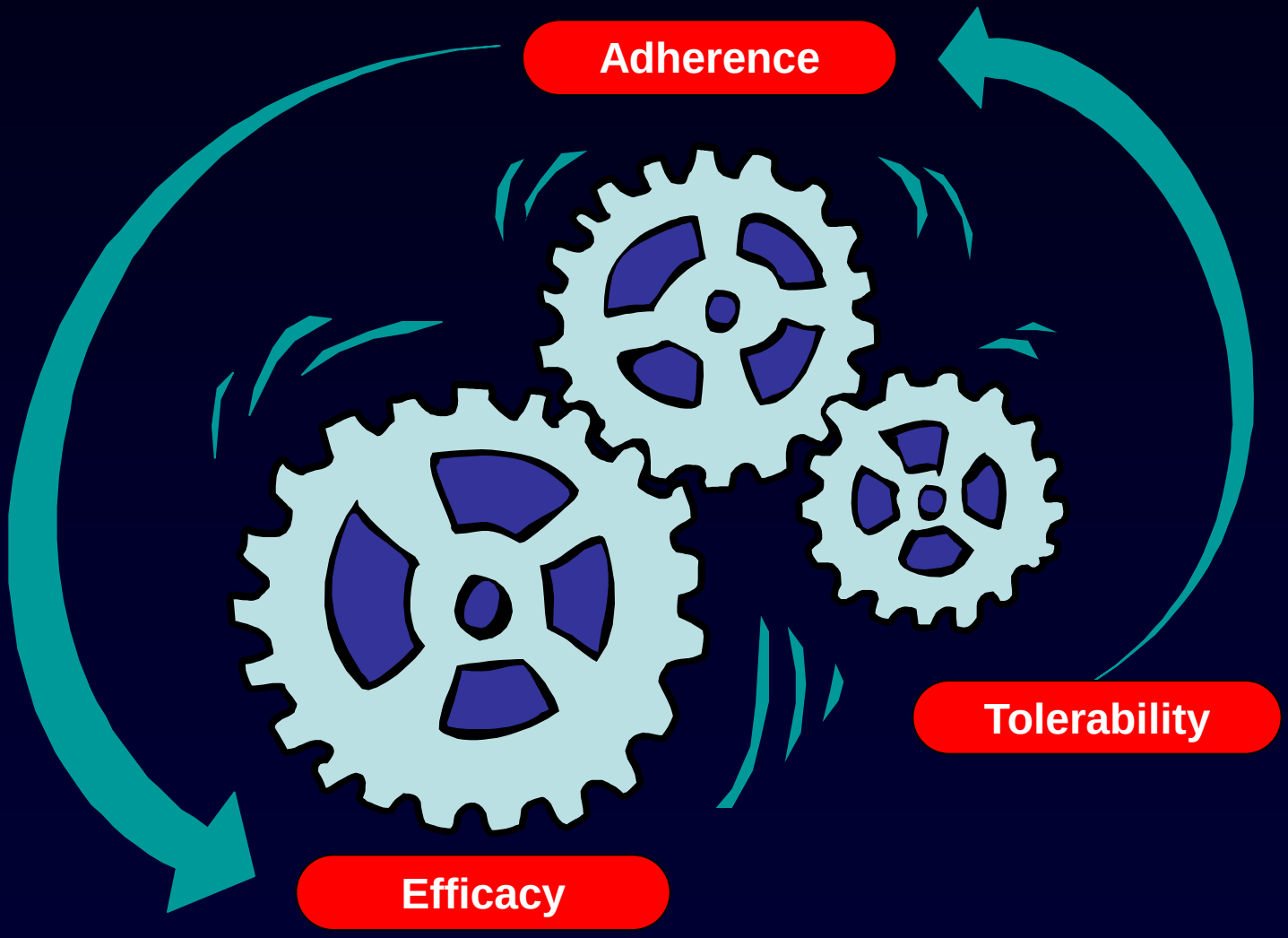


Tolerability

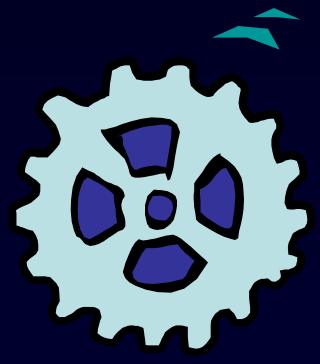
Tolerability drives adherence, which drives efficacy



Tolerability drives adherence, which drives efficacy

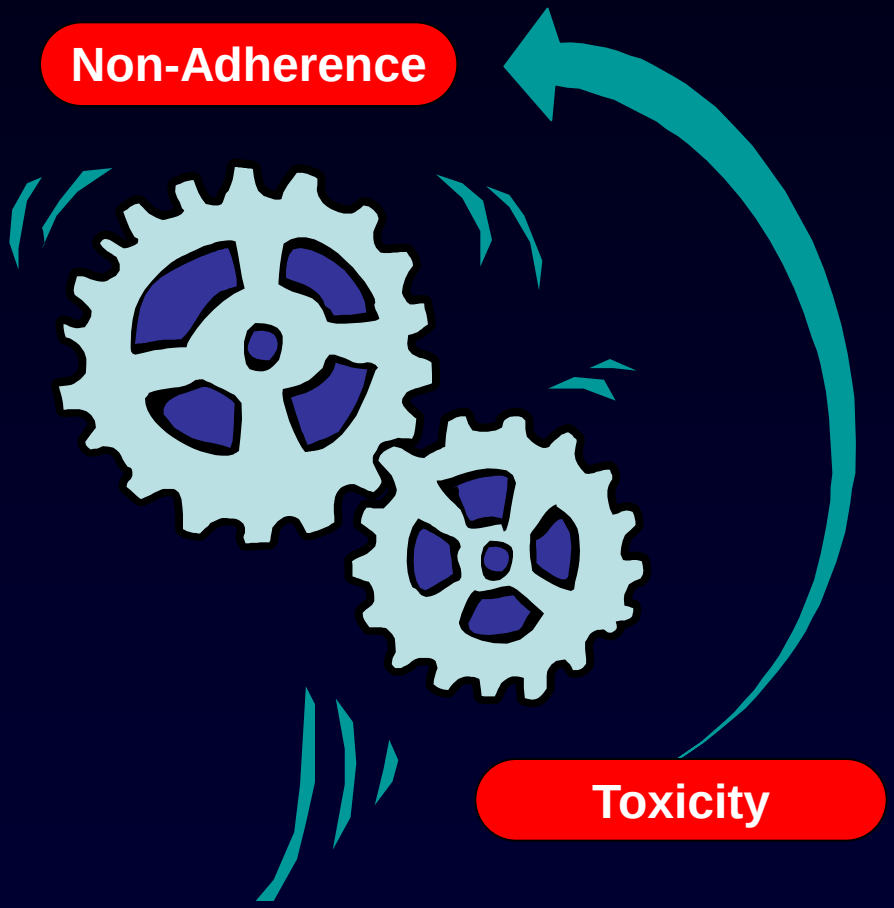


Toxicity drives non-adherence, which drives failure

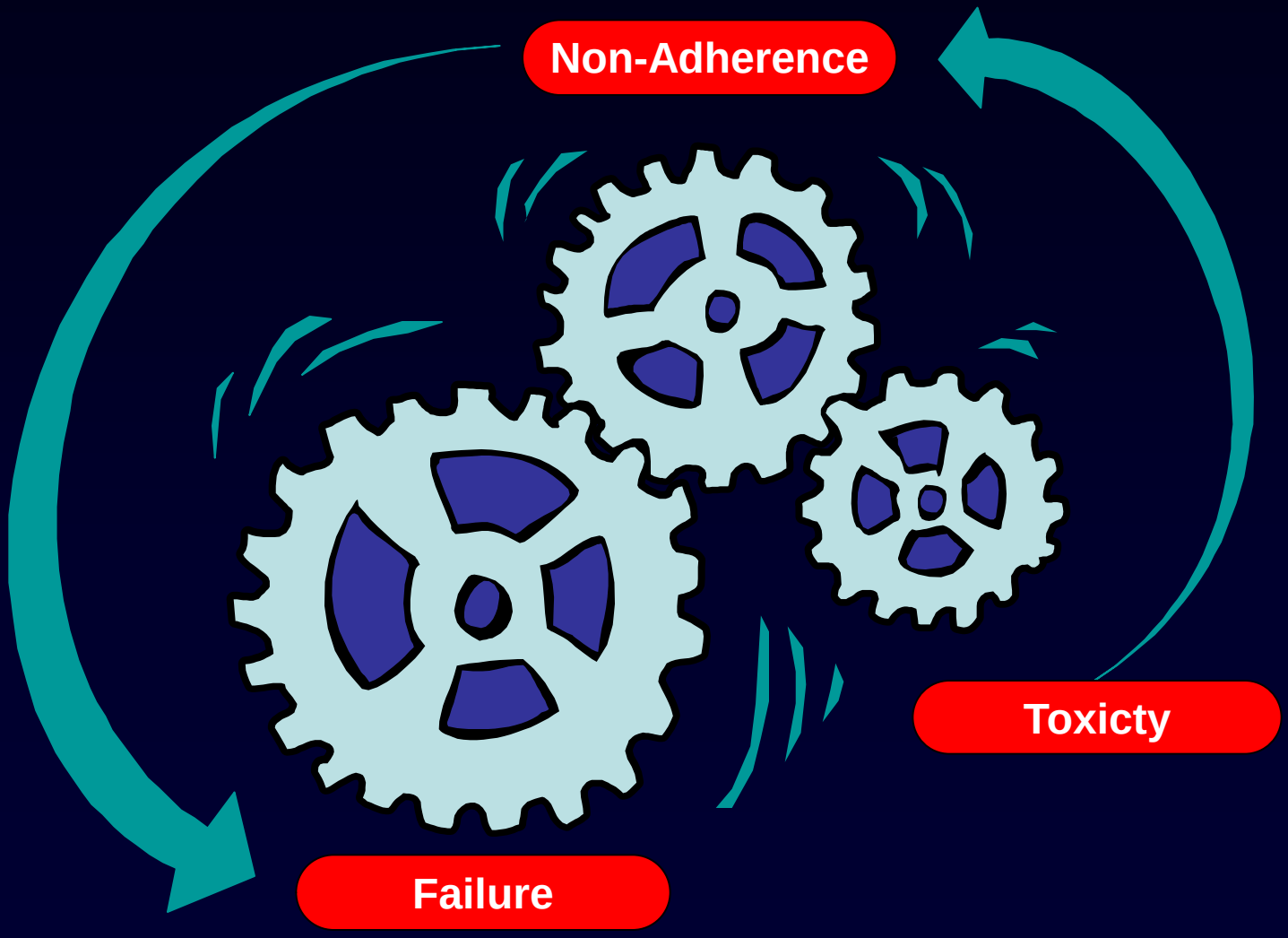


Toxicty

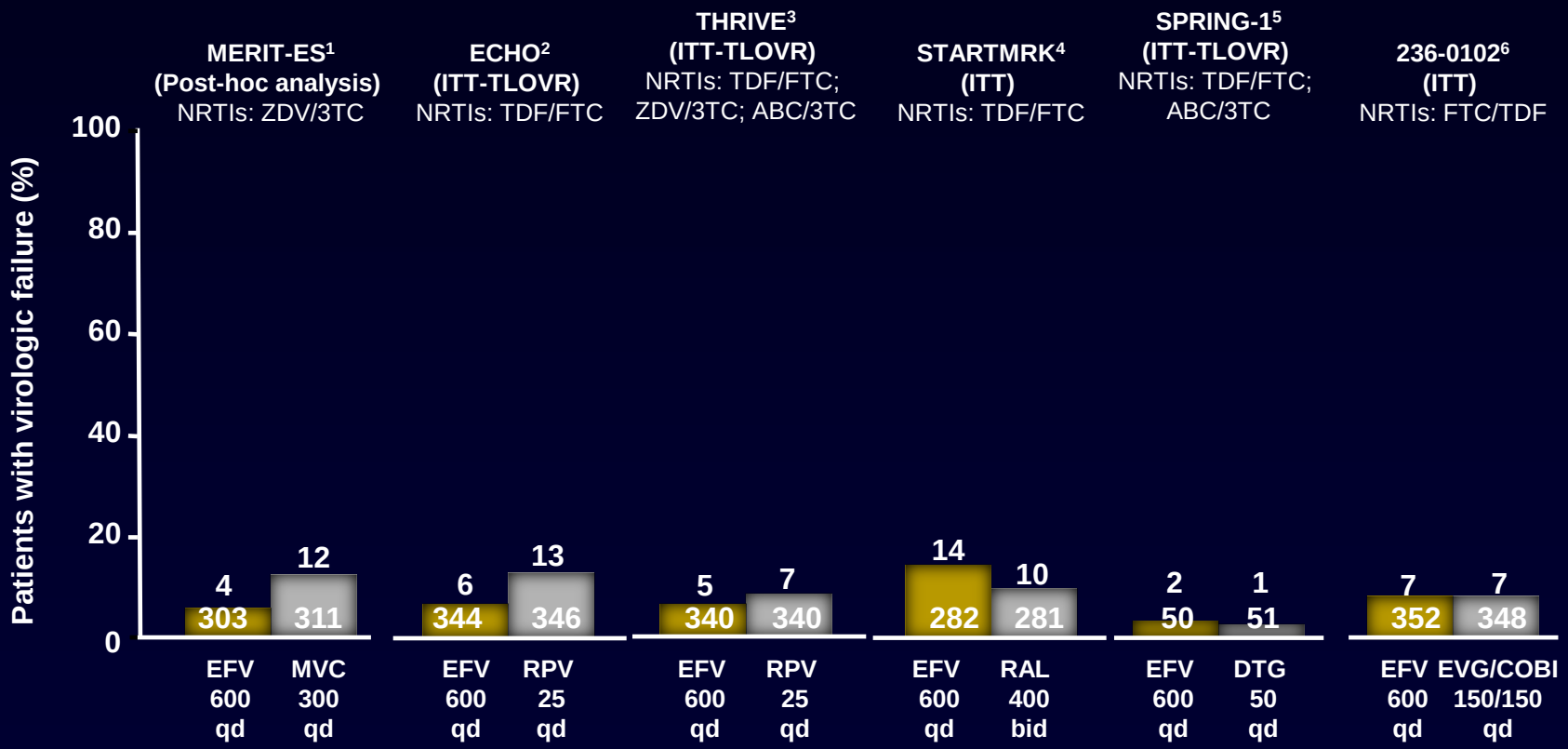
Toxicity drives non-adherence, which drives failure



Toxicity drives non-adherence, which drives failure



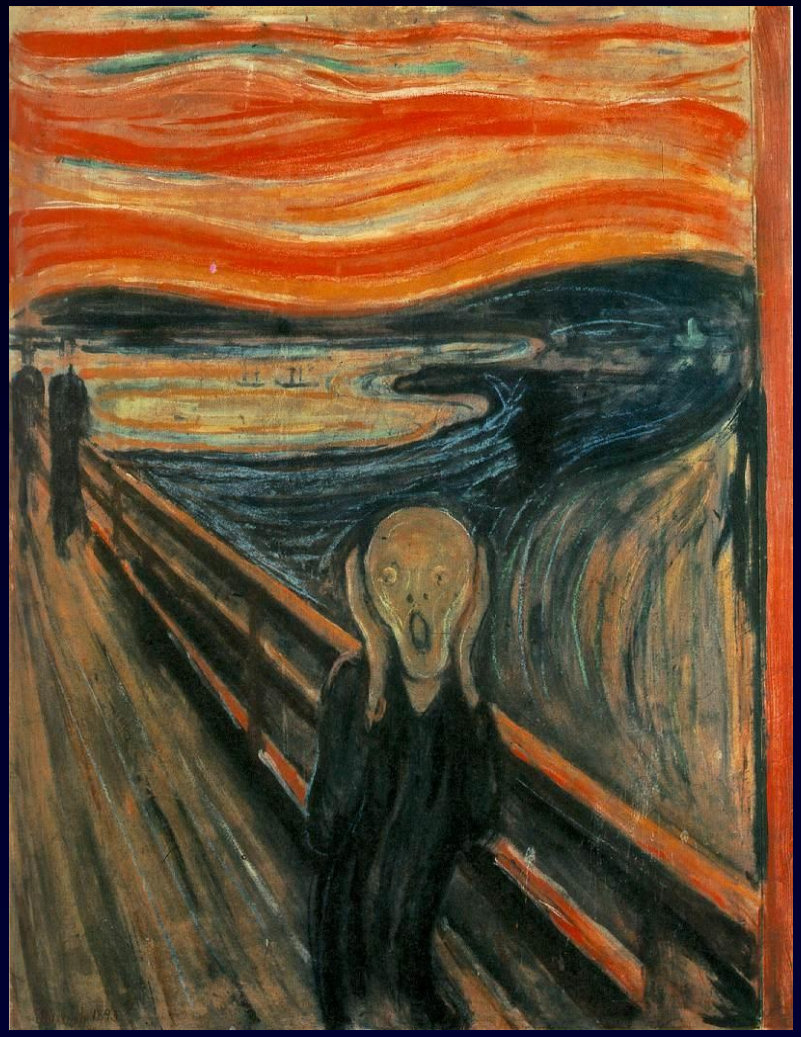
Rates of Virologic Failure at Week 48



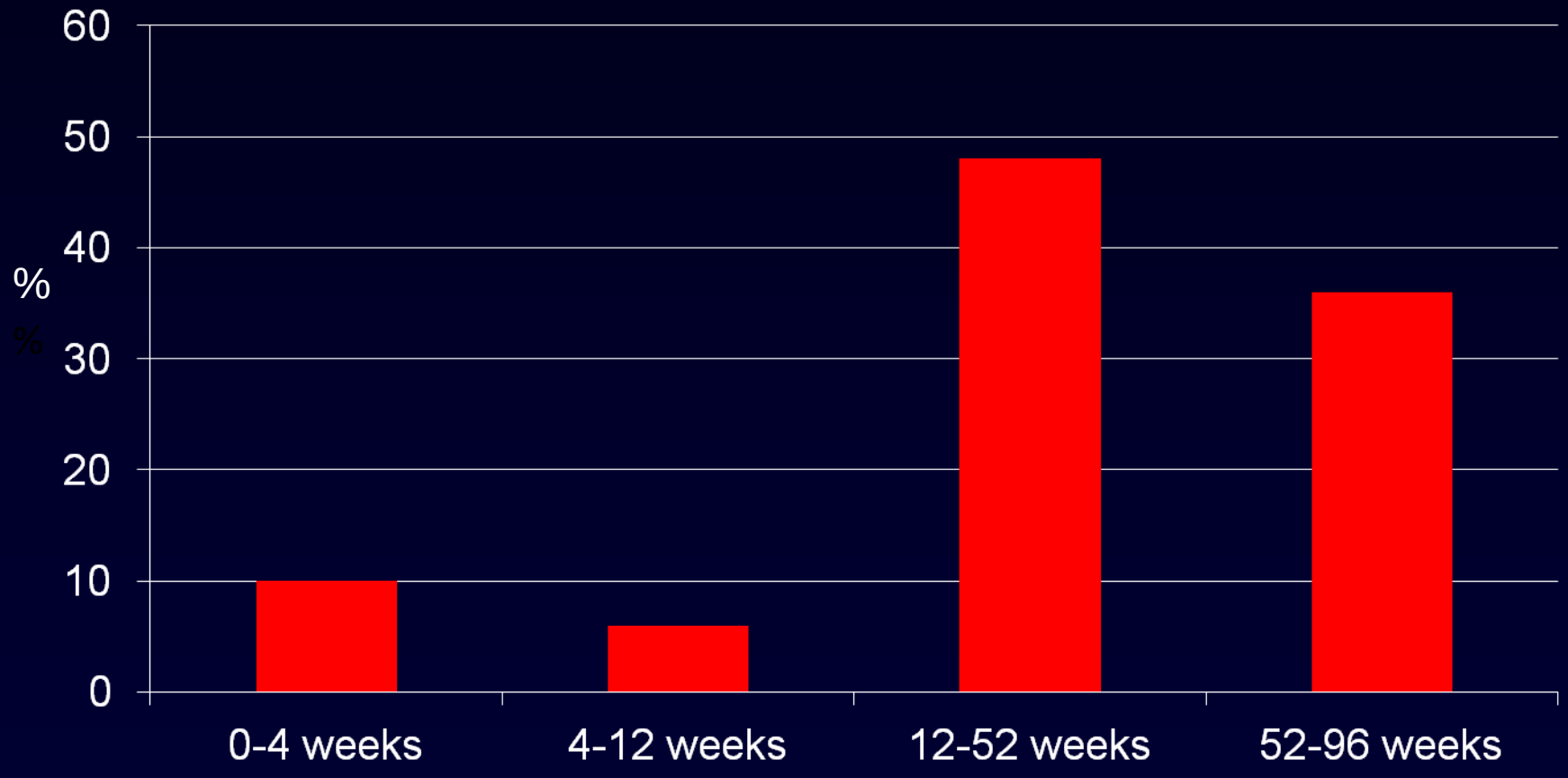
VL=viral load; ITT=intent-to-treat; TLOVR=time-to-loss of virologic response
EVG=elvitegravir; COBI=cobicistat; DTG= dolutegravir

1.Cooper DA, et al. J Infect Dis 2010;201:803–13; 2. Molina JM, et al. Lancet 2011;378:238–46
3. Cohen CJ, et al. Lancet 2011;378:229–37; 4. Lennox JL, et al. Lancet 2009 5;374:796–806
5. van Lunzen J, et al. IAS 2011. Abstract TUBA0102; 6. Sax P, et al. CROI 2012. Abstract 101


ATRIPLA
WORSHIP OR DIE

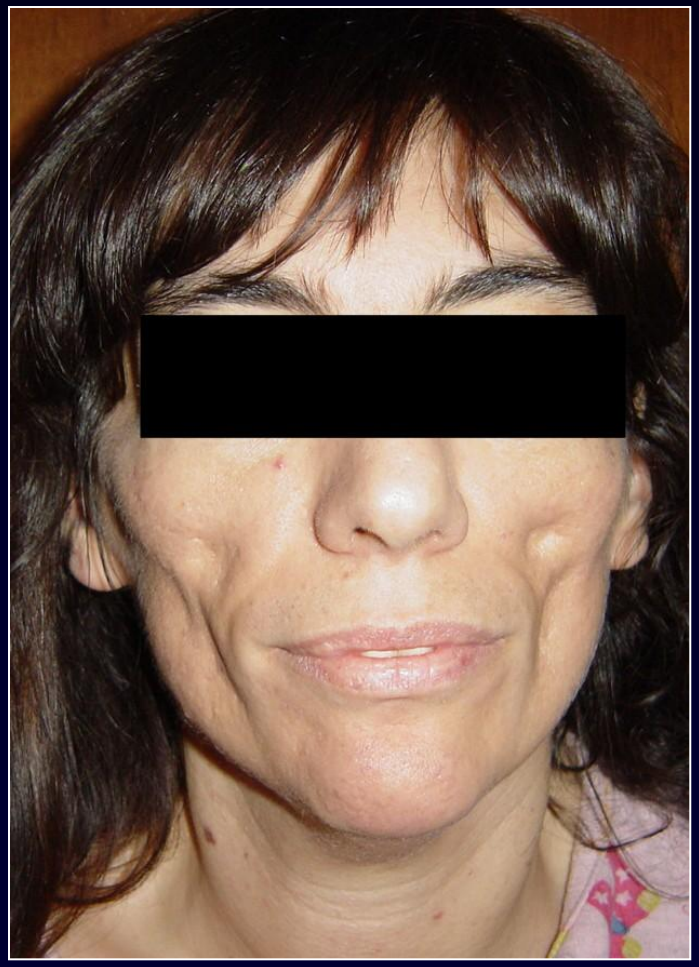


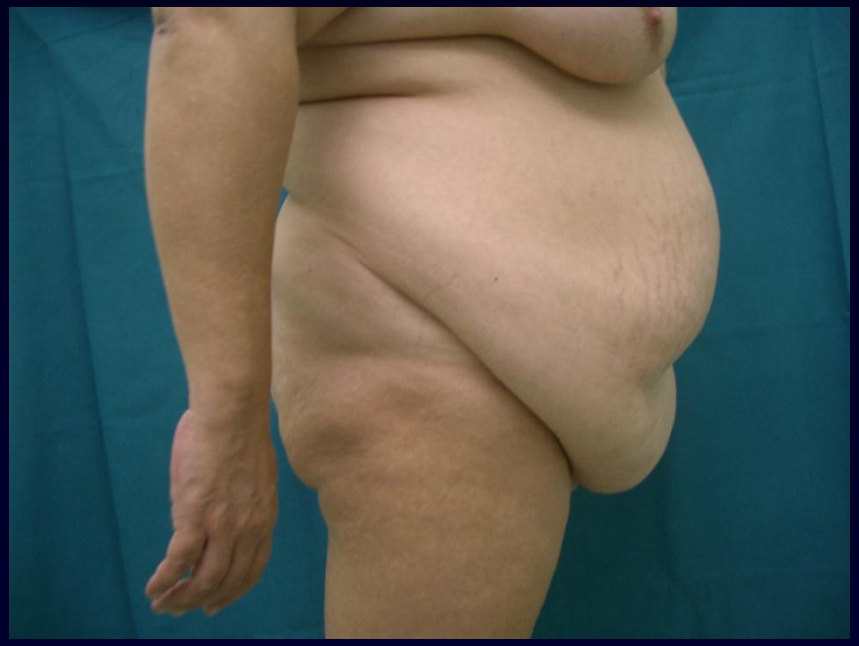
Time to switch for CNS toxicity

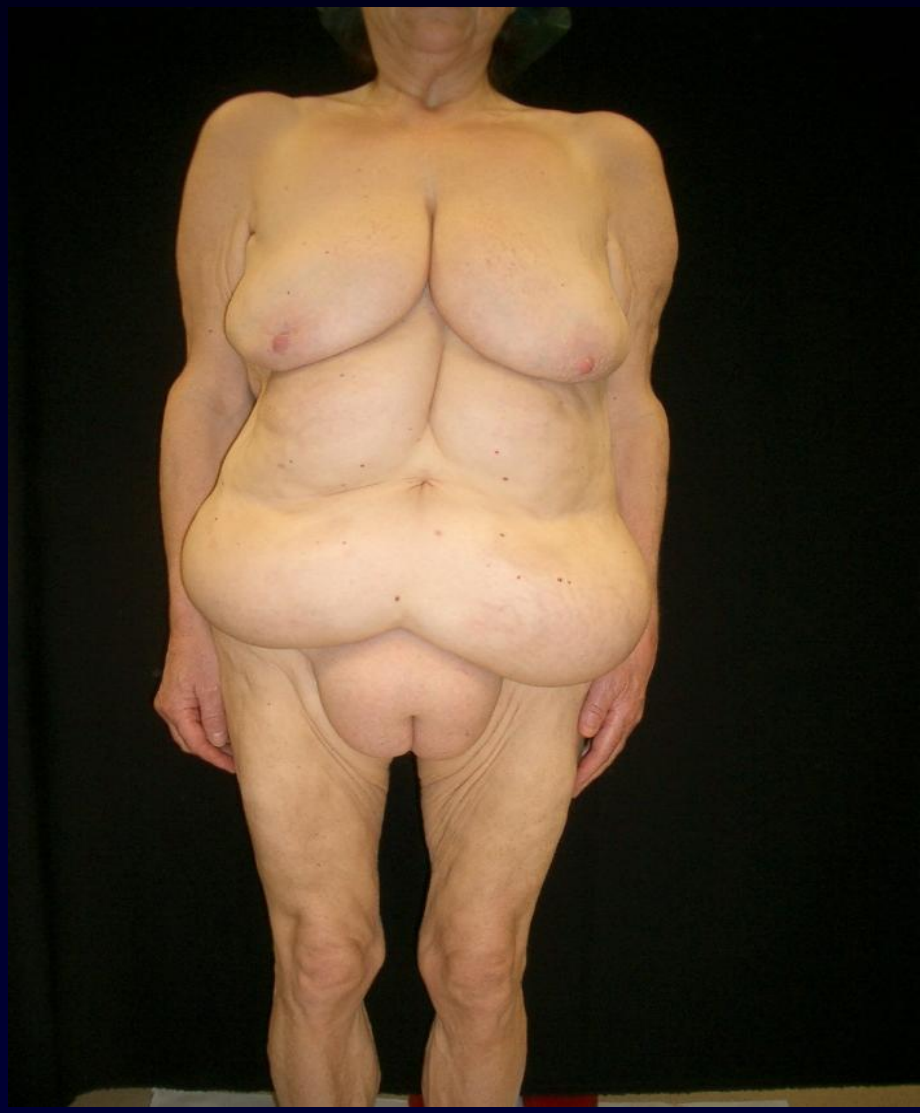


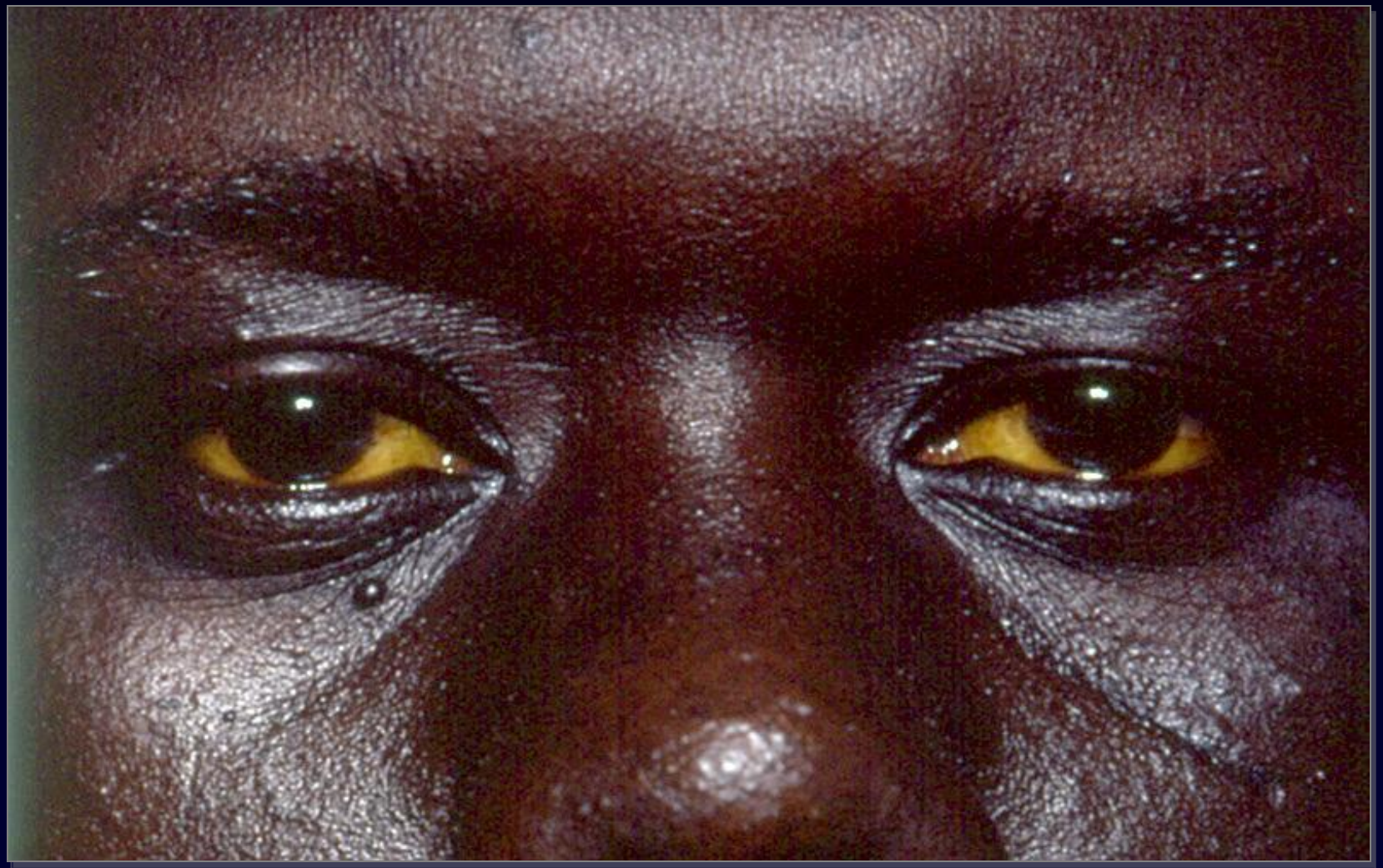
Zheng ICAAC 2011

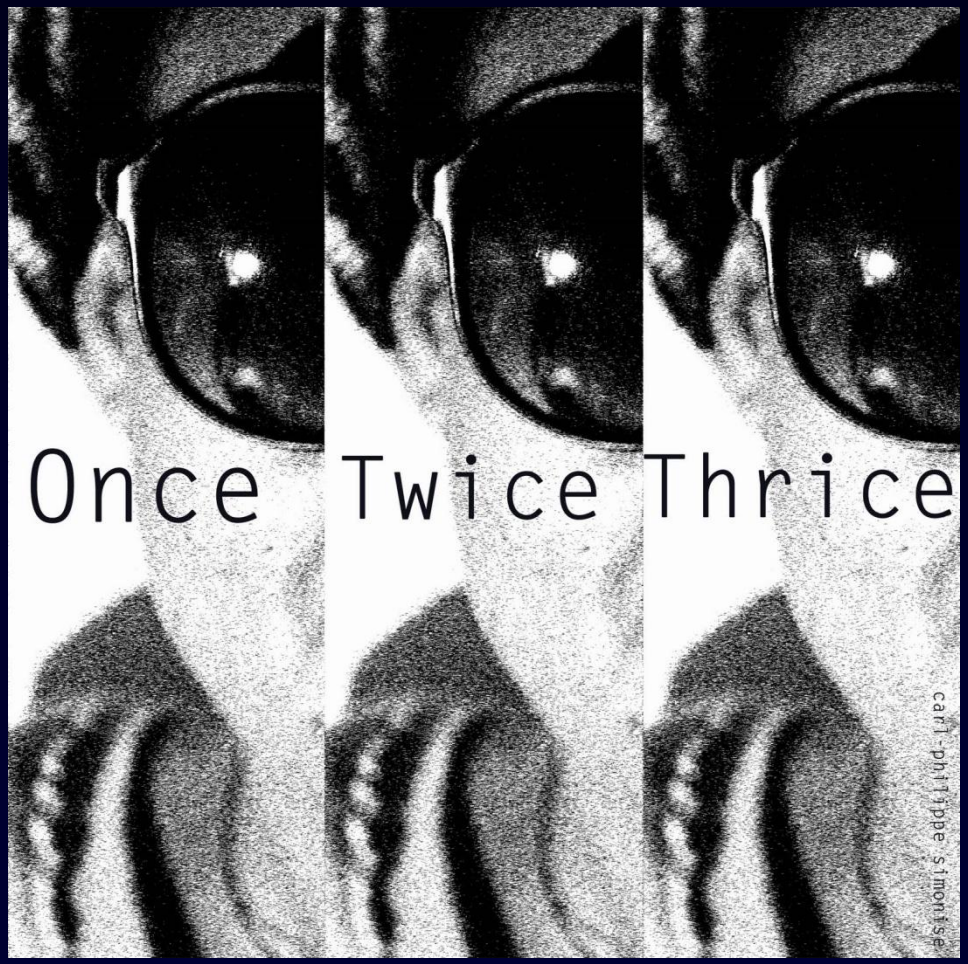

+ Against Bipartisanship, by Frank Rich p.30 / The Myth of the Independent Voter p.32
NEW YORK
REBECCA BLACK
p.71
OCTOBER 3, 2011
Is She Just Too Old For This?
New parents over 50—child-rearing's final frontier.
By Lisa Miller










Once
Twice
Thrice
carl-philippe simonise


CZUMGA
18

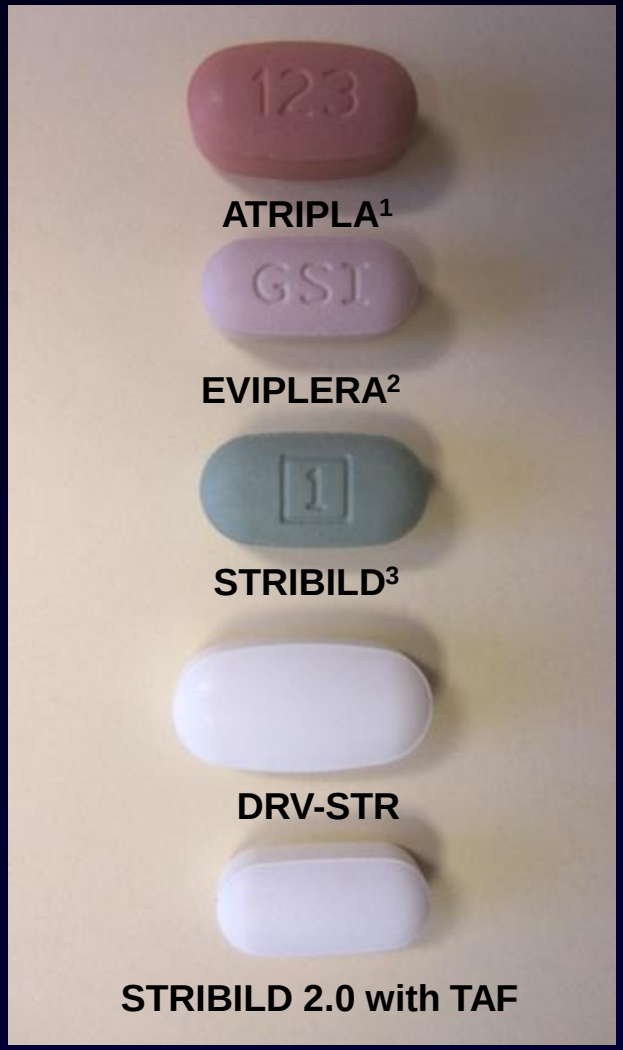
Single Tablet Regimens (STRs)

Current

- **ATRIPLA (1550 mg)**
- **EVIPLERA (1150 mg)**
- **STRIBILD (1350 mg)**

Future

- **DRV-STR (1550 mg)**
  - DRV/COBI/FTC/TAF
- **STRIBILD 2.0 (1050mg)**
- **DOLUTEGRAVIR/ABACAVIR/LAMIVUDINE**



1. Mathias AA, et al. JAIDS;2007;46(2):167-73
2. Mathias AA, et al. IAC 2010; Vienna. THLBPE17
3. German P, et al. JAIDS 2010;55:323–329

ECHO and THRIVE – Phase 3 Studies Study Designs

Randomized, double-blind, double-dummy, multicenter, 96-week study

ECHO (TMC278-C209)

690 patients

ARV-naïve
HIV RNA > 5,000 c/mL
No NNRTI RAMs†
Sensitivity to the NRTIs‡

678 patients

THRIVE (TMC278-C215)

- **RPV 25mg qd + EFV placebo qd + TDF/FTC qd (n=346)**
- **EFV 600mg qd + RPV placebo qd + TDF/FTC qd (n=344)**
- **RPV 25mg qd + EFV placebo qd + 2NRTIs* (n=340)**
- **EFV 600mg qd + RPV placebo qd + 2NRTIs* (n=338)**

*** Investigator's choice: TDF/FTC (60%); ZDV/3TC (30%); ABC/3TC (10%)**

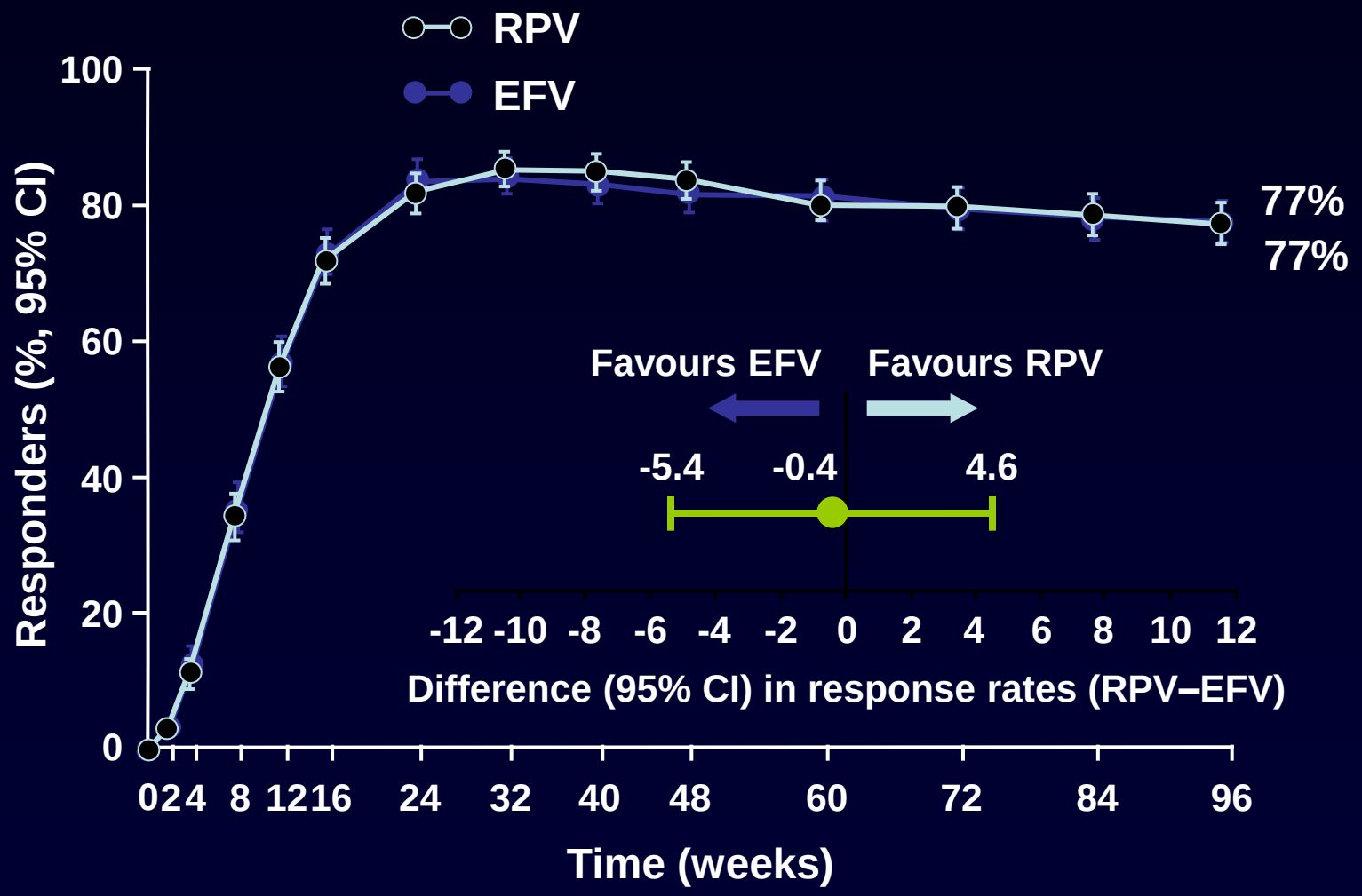
- **Primary objective: to demonstrate non-inferiority (12% margin) vs. EFV in confirmed virologic response (viral load [VL] <50 copies/mL, ITT-TLOVR) at Week 48**

† From 39 NNRTI RAMs based on list of 44[1]; ‡ Based on Virco®TYPE HIV-1 test

[1] Rambuyzer L et al. Antivir Ther 2009;14:103–9

Adapted from Cohen C et al. HIV10 2010. Glasgow. Oral Abstract O432

Viral load <50 c/mL (ITT-TLOVR)



Nelson M, et al. EACS 2011;Belgrade. Poster LBPE7.3/7

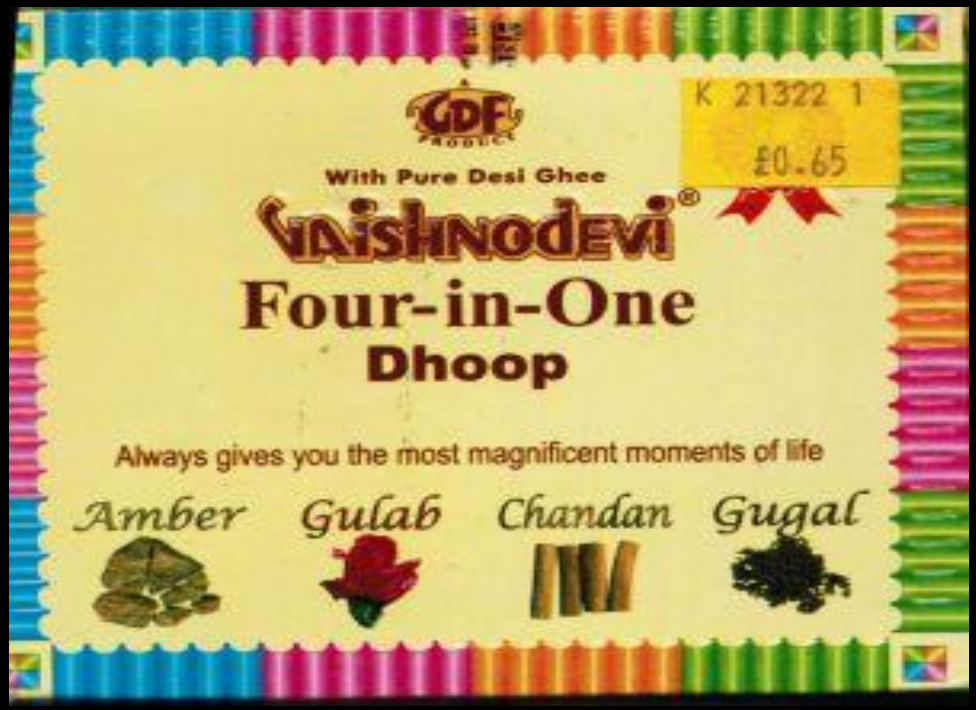
Pooled ECHO & THRIVE (wk 96 FTC/TDF Dataset) Virologic Outcome* by Baseline VL

SNAPSHOT

%	Pooled	
	RPV N=550	EFV N=546
Virologic Response (VL <50 c/mL)	77.3	76.7
Virologic Failure	14.4	8.4
VL ≥ 50 copies/mL at Week 96	3.5	3.3
Virologic failure leading to discontinuation	6.7	2.0
Discontinued due to other reason with last VL ≥ 50 c/mL	3.6	3.1
No Viral Load Data in 96 week window	8.4	14.8
Discontinued due to AE/death	3.6	8.8
Discontinued due to other reason and last available VL < 50 c/mL (or missing)	4.4	5.7
Missing data during window but on study	0.4	0.4

*ITT Snapshot analysis uses last viral load value in the Week 96 window (90–103 weeks)

Adapted from Nelson M et al. EACS 2011. Belgrade. Poster LBPE7.3/7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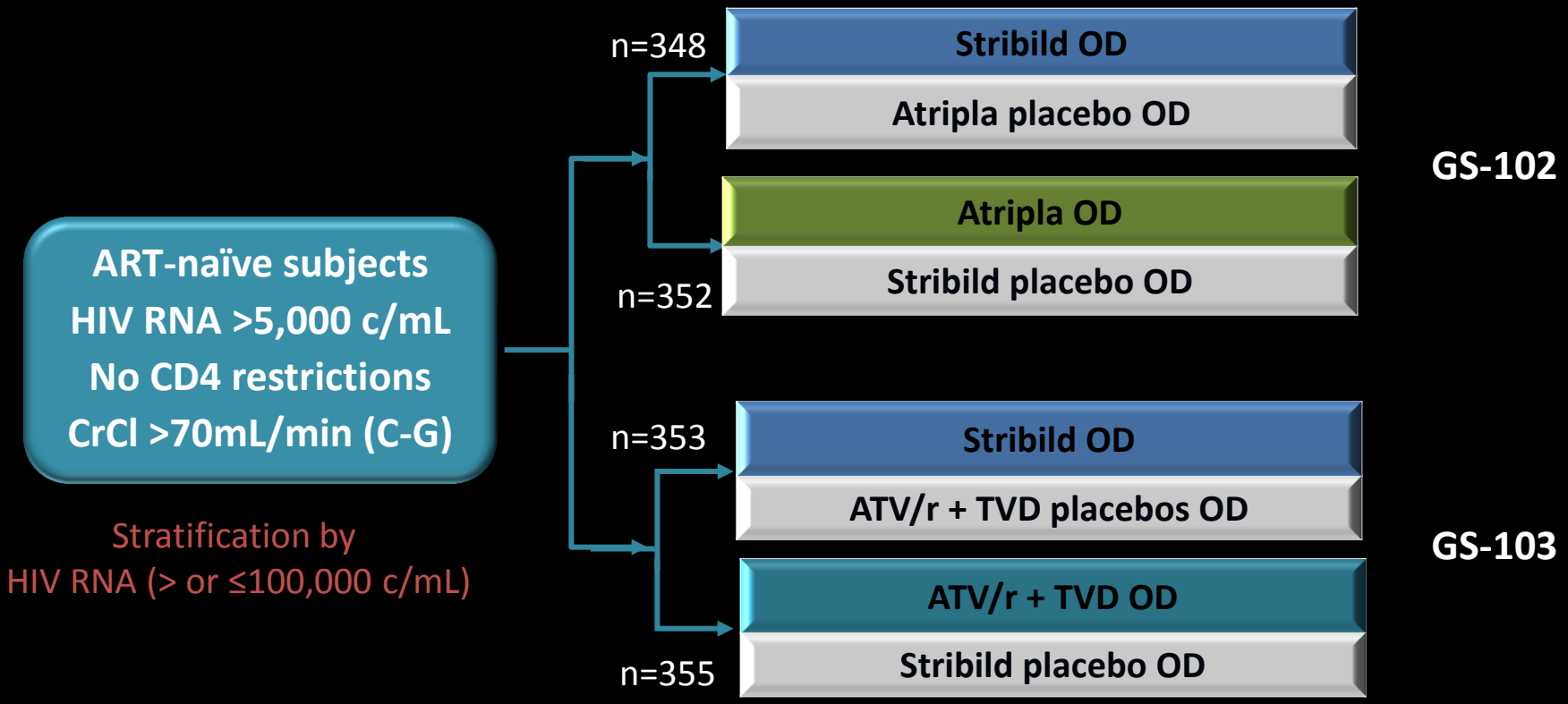
Amber
Gulab
Chandan
Gugal

Study Design
Stribild Phase 3 Studies

- **Multicentre, randomised, Phase 3, blinded, 192-week studies**



Primary endpoint: HIV-1 RNA <50 c/mL at Week 48;
FDA Snapshot analysis with non-inferiority margin of 12%

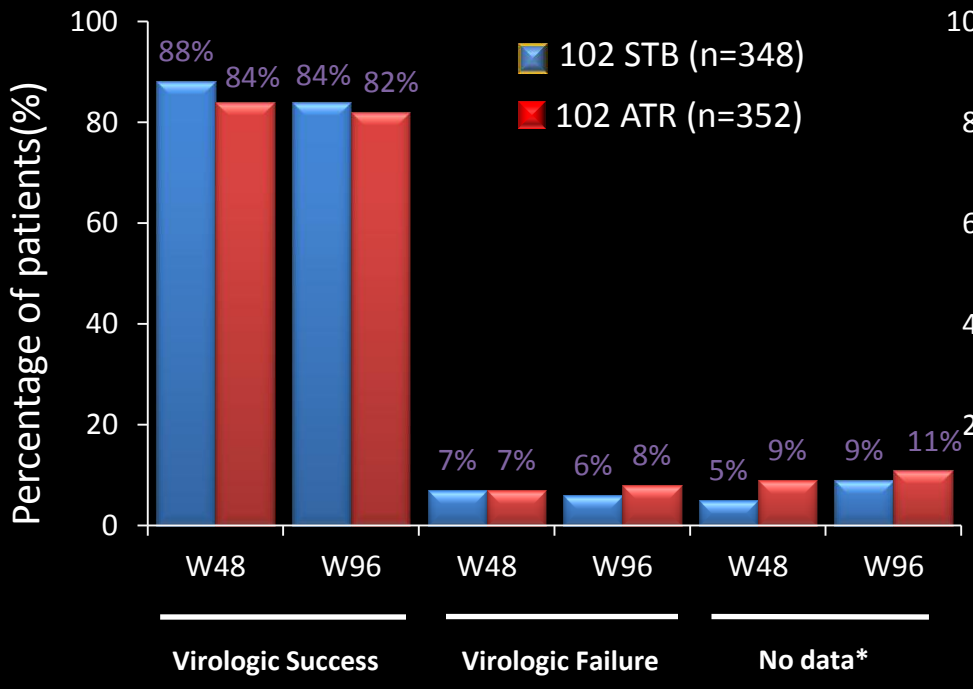
Sax P et al. Lancet 2012; 379: 2439–48
DeJesus E et al. Lancet 2012; 379: 2429–38

C-G: Cockcroft-Gault

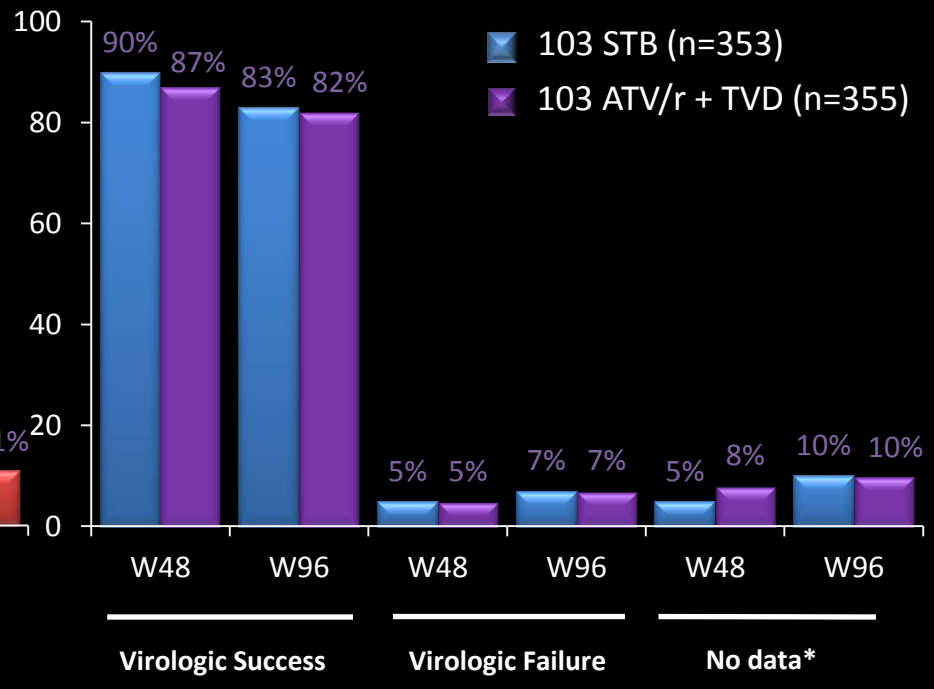
HIV-1 RNA <50 c/mL

Week 96

Phase 3 GS-102 : STB vs. ATR



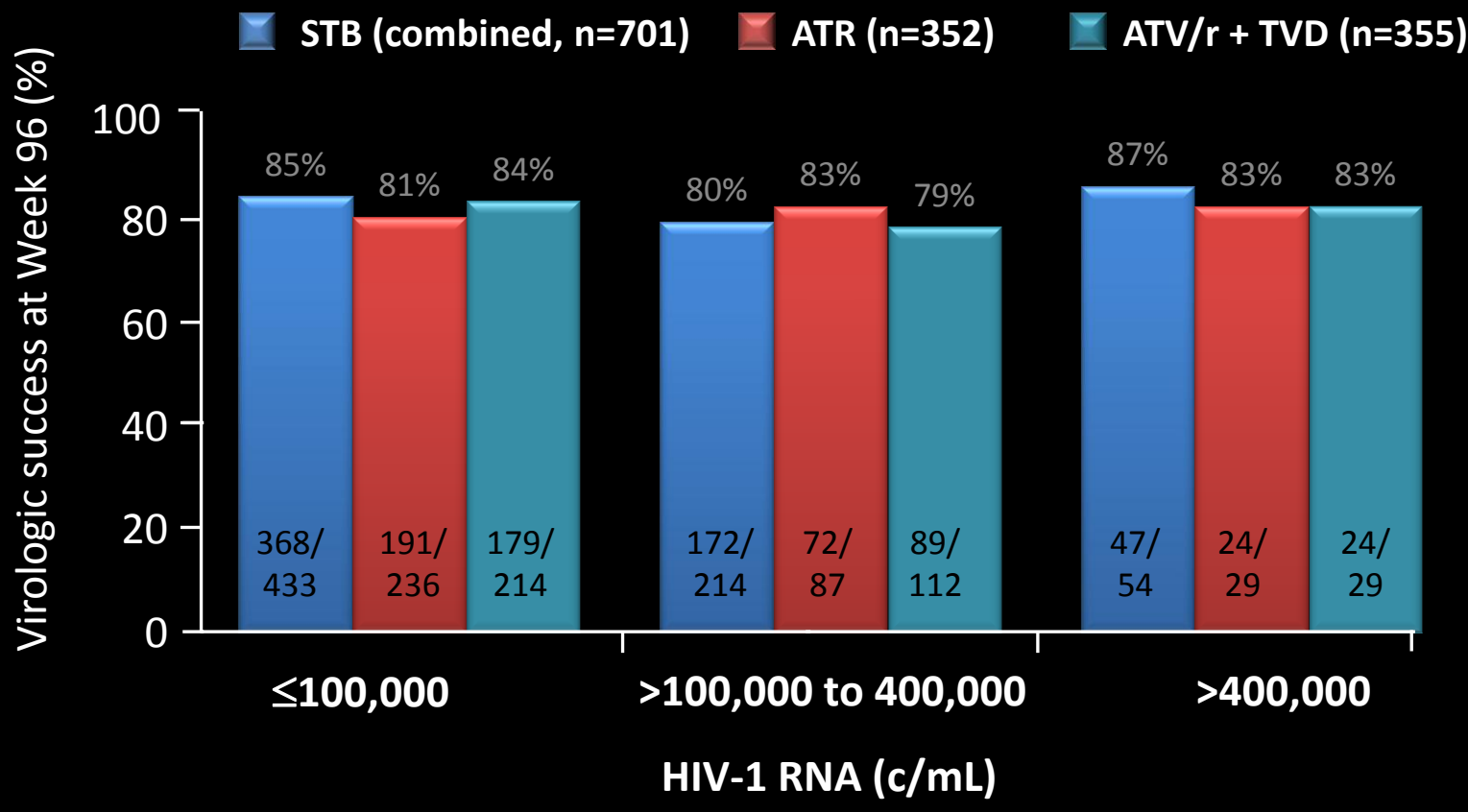
Phase 3 GS-103: STB vs. ATV/r + TVD



No virologic data in window defined as: missing HIV RNA data but on study, discontinued drug due to AE or death, or discontinued drug for reasons other than AE, death, and lack/loss of efficacy with last HIV RNA <50 copies/mL
For the Week 96 virologic success, the analysis window is defined as from Study 631-714

Zolopa A. Presented at CROI 2013, poster 553

Efficacy by Baseline HIV-1 RNA Subgroup
Combined Study GS-102 and -103 – Week 96



Virologic success (HIV-1 RNA <50 c/mL) as defined by FDA Snapshot algorithm
p-value for all comparison vs. STB: non-significant (>0.05)

Zolopa A. Presented at CROI 2013, poster 553

Summary of Common Adverse Events
Combined Study GS-102 and -103 – Week 96

Adverse event *	STB (combined, n=701)		ATR (n=352)		ATV/r + TVD (n=355)	
	Wk 48	Wk 96(Δ)	Wk 48	Wk 96(Δ)	Wk 48	Wk 96(Δ)
Diarrhoea	22%	+3%	19%	+5%	27%	+4%
Nausea	20%	+1%	14%	+1%	19%	+2%
Rash event	17%	+4%	28%	+3%	18%	+5%
Upper respiratory infection	15%	+6%	11%	+6%	16%	+4%
Headache	15%	+2%	10%	+2%	12%	+3%
Fatigue	13%	+1%	13%	+2%	13%	+3%
Depression	8%	+3%	11%	+3%	6%	+5%
Insomnia	8%	+2%	14%	+2%	5%	+2%
Nasopharyngitis	7%	+3%	5%	+3%	8%	+3%
Abnormal dreams	9%	+0.1%	27%	+1%	4%	+0.3%
Sinusitis	6%	+2%	8%	+3%	5%	+3%
Dizziness	6%	+1%	24%	+1%	7%	+1%
Ocular icterus	0.3%	0	0	0	14%	0

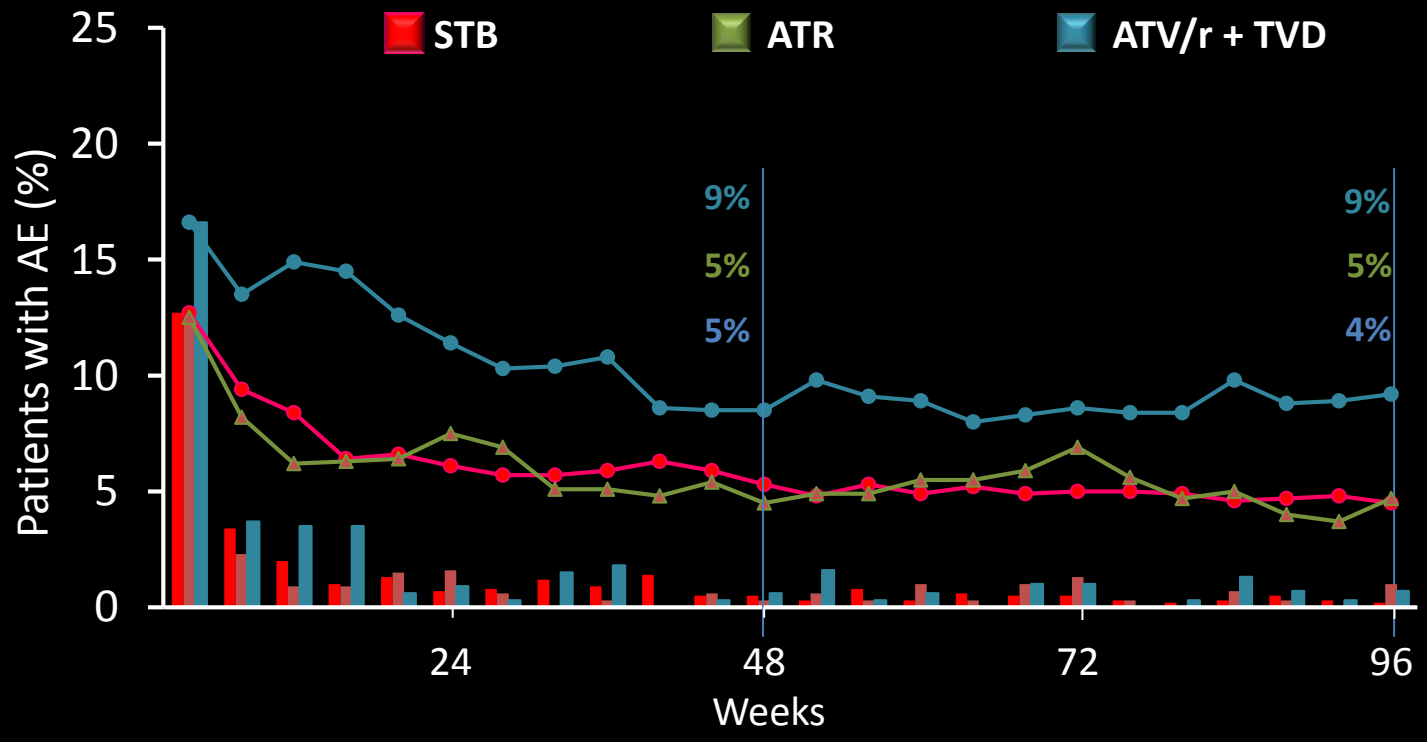
* >10% of patients in any group over 96 weeks

Zolopa A. Presented at CROI 2013, poster 553

Common Gastrointestinal AEs (All Grades)

Combined Study GS-102 and -103 – Week 96

Diarrhoea

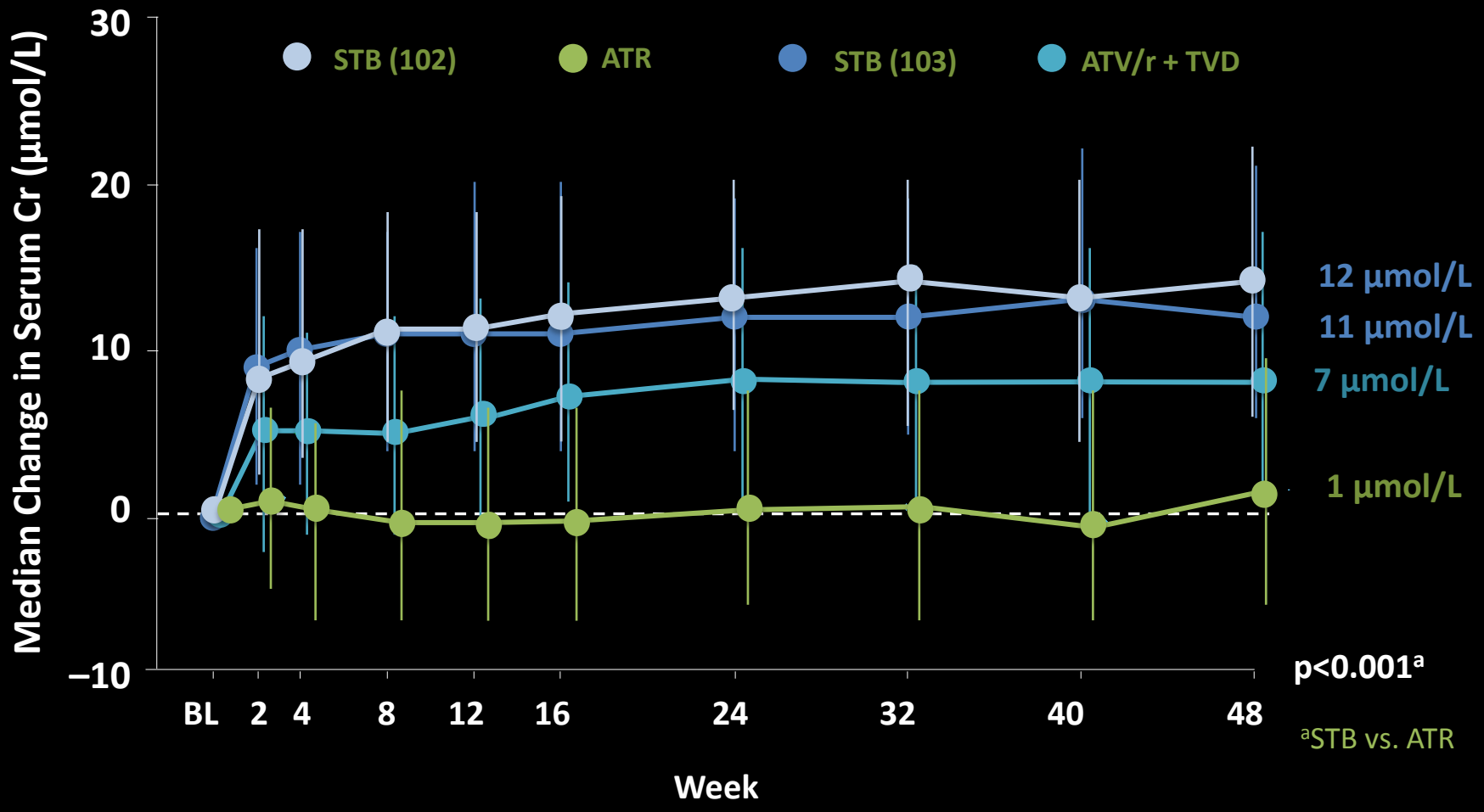


Most were Grade 1 (STB 74% vs. ATR 73% vs. 68% ATV/r + TVD)

Bar (incidence): Patients with new onset or worsening AEs at each 4-week window
Line (prevalence): Patients with ongoing events in the window

Zolopa A. Presented at CROI 2013, poster 553

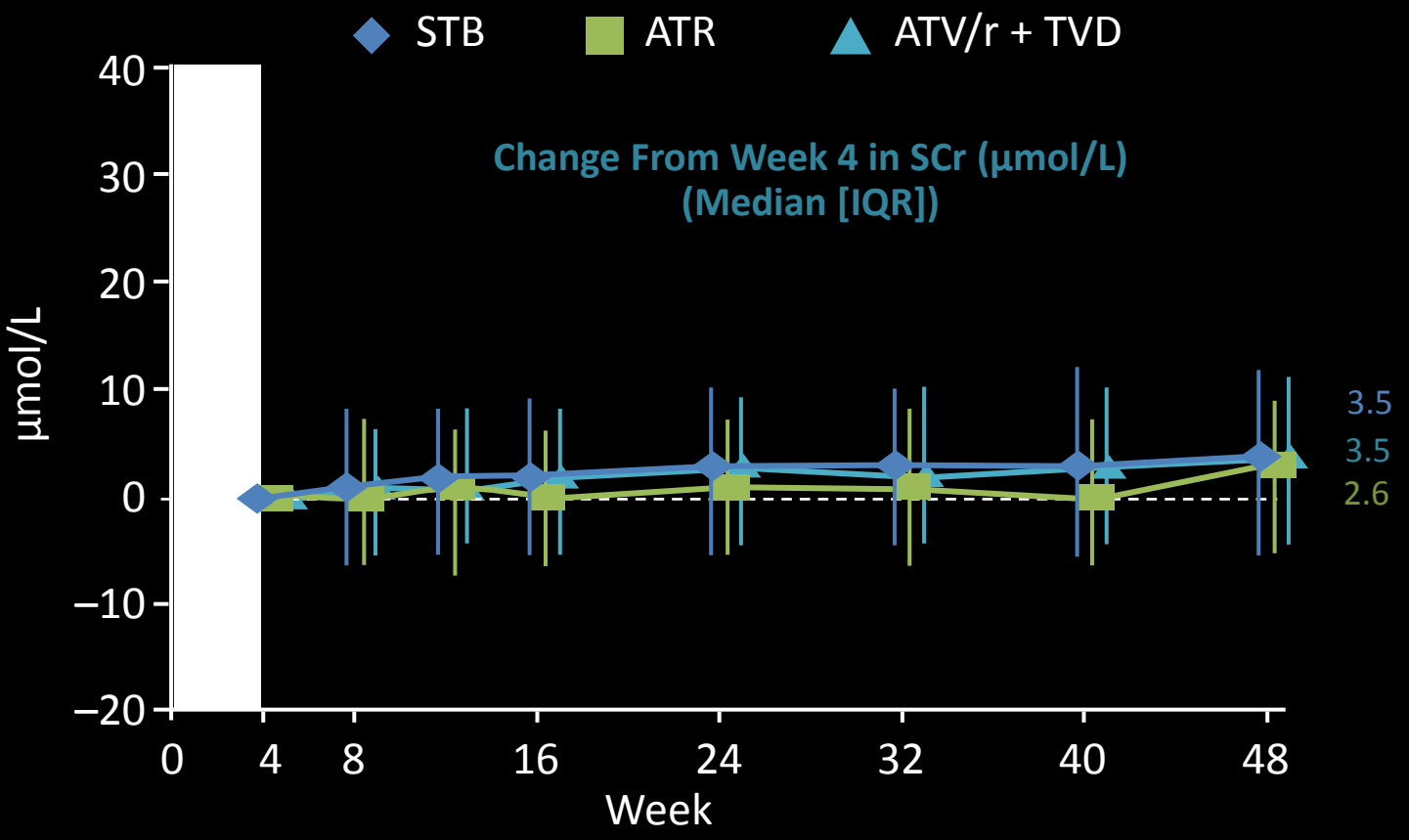
Median (IQR) Change From Baseline in Serum Creatinine Combined GS-102 and -103 Stribild vs. ATR or ATV/r + TVD



DeJesus E et al. Lancet 2012;379:2429–38
Sax PE et al. Lancet 2012;379:2439–48

Studies 102, 103 & 104: Renal Safety Analysis

Changes in serum creatinine from Week 4

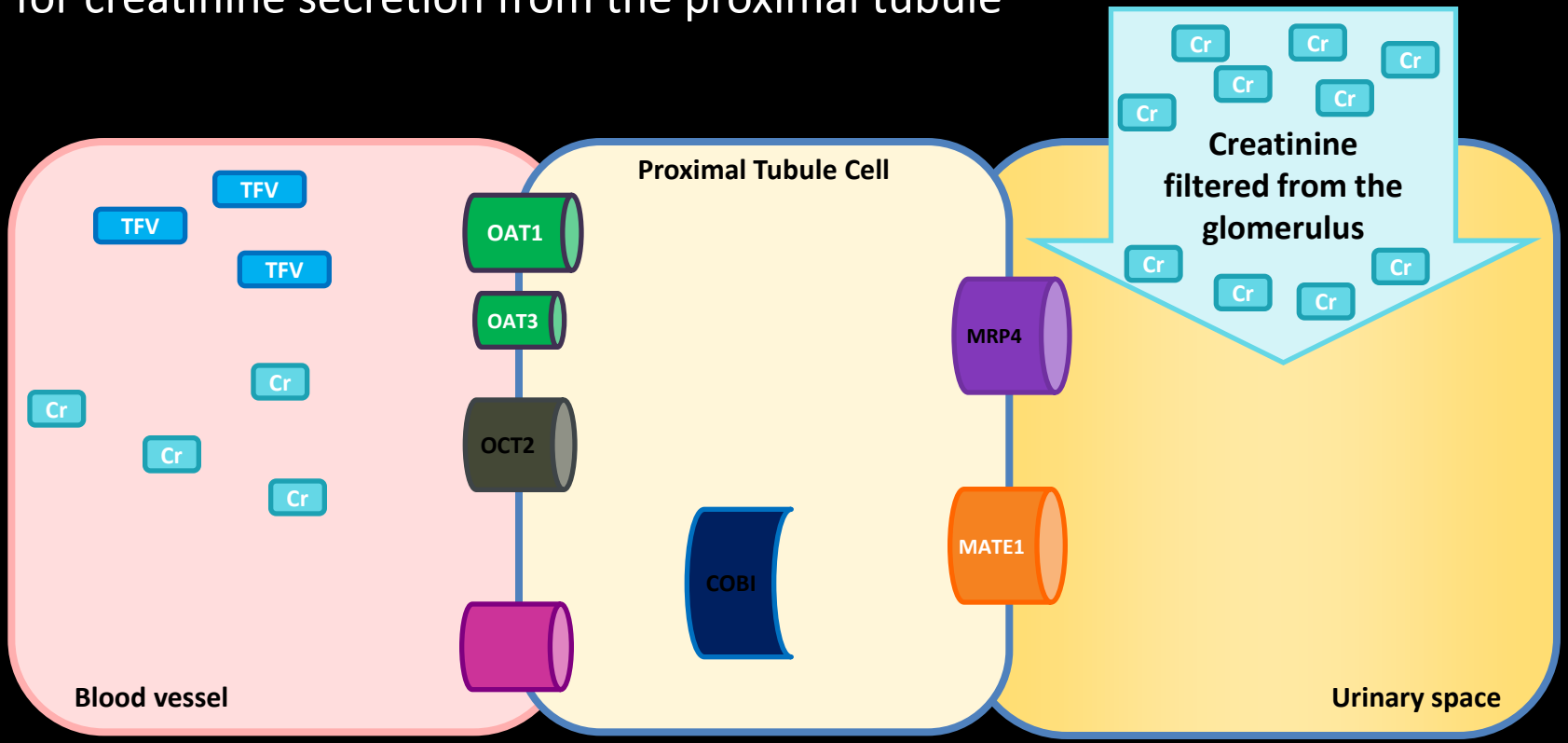


Benson P et al. Presented at ICAAC 2012; #H-891
Ward D, et al. Presented at ICAAC 2012; Oral H-555

Cobicistat Inhibits Active Tubular Secretion of Creatinine

Resulting in Increased Serum Creatinine

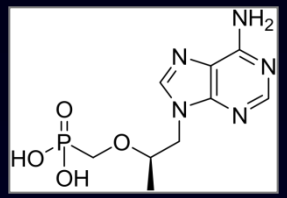
- Preclinical studies indicate that cobicistat blocks a transport pathway used for creatinine secretion from the proximal tubule



German P et al. J Acquir Immune Defic Syndr 2012;61:32–40
Lepist EI, Ray AS. Expert Opin Drug Metab Toxicol 2012;8:433–48

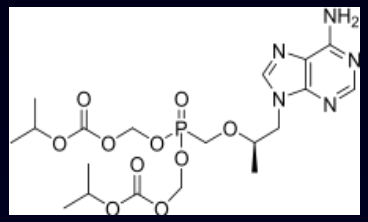
Tenofovir Alafenamide (TAF)

Next Generation Prodrug of Tenofovir-increased liver, lymph concentration



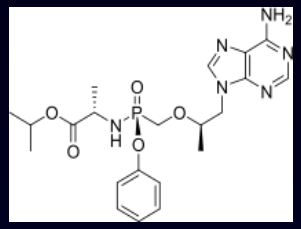
TFV

Tenofovir



TDF

Tenofovir Disoproxil Fumarate

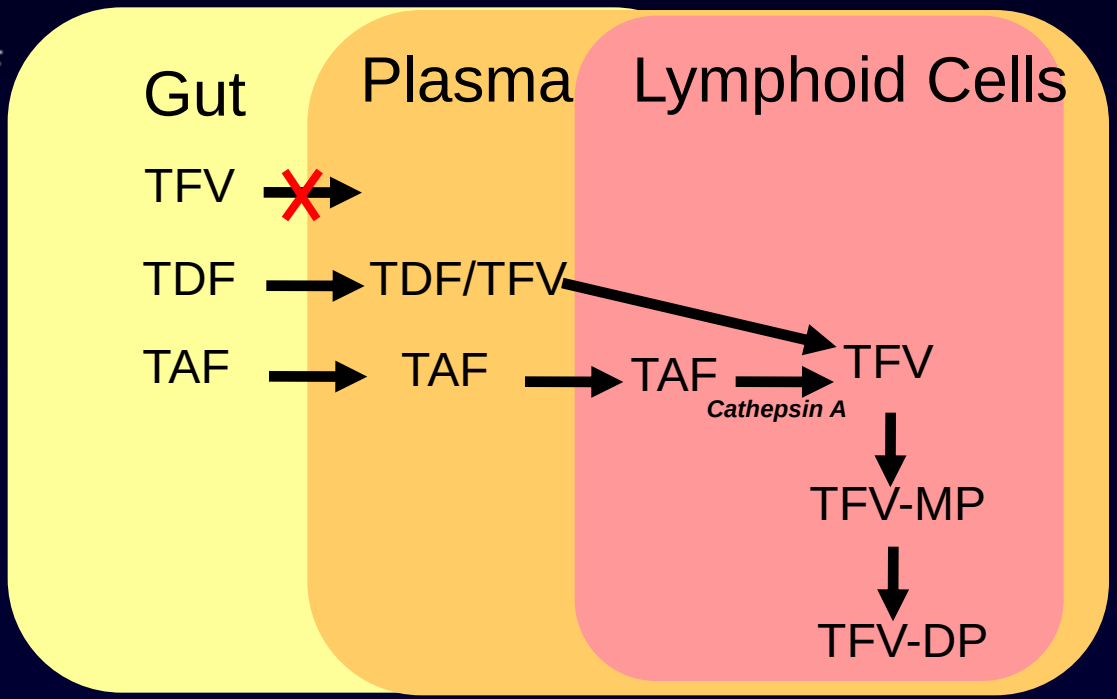


TAF

Tenofovir Alafenamide

TAF 10mg in E/C/F/TAF has PK comparable to TAF 25mg alone[2]

- COBI ↑ TAF levels ~2.2-fold



Relative to TDF 300 mg, TAF 25 mg has[1]:

- Increased anti-HIV-1 activity in Phase 1
- Increased intracellular TFV-DP levels by ~7-fold
- Decreased circulating plasma TFV levels by ~90%
- Lower levels of TFV in kidney and bone tissue expected

[1]P Ruane, et al. CROI 2012; Paper # 103

[2]S Ramanathan, et al. IWCPHT 2012; Abstract O_13

A Zolopa, et al., CROI 2013; Paper # 99LB

Virologic Response (M=F, ITT)
GS-US-292-0102 – Week 24 Analysis

Resistance

3 subjects met protocol-specified criteria for resistance analysis

Confirmed >400 copies/mL of HIV-1 RNA at Week 24 or the discontinuation visit

E/C/F/TAF arm (n=1)

1 subject with Week 24 rebound

No resistance detected

STB arm (n=2)

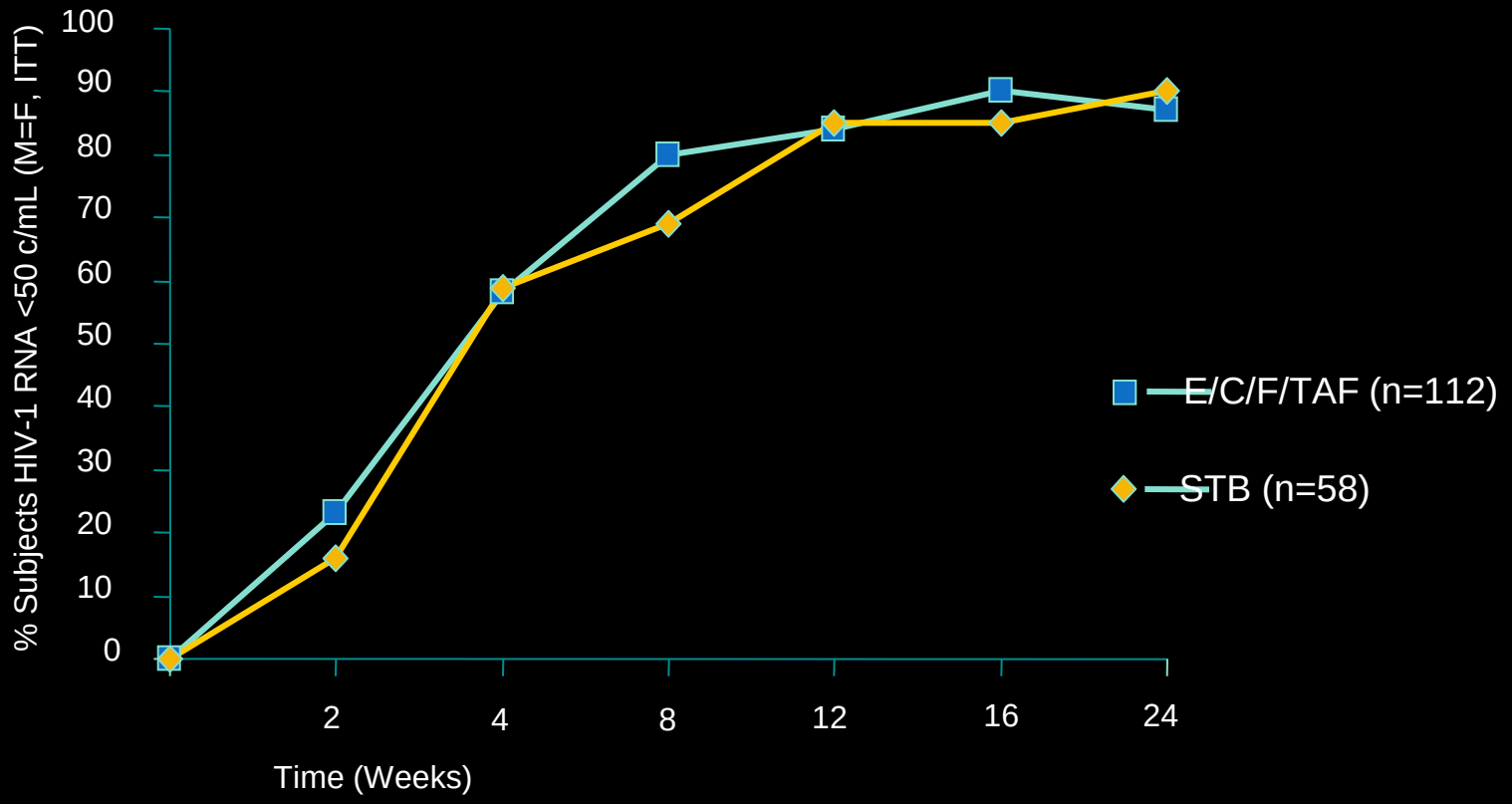
1 subject with persistent viremia

NRTI resistance (M184V + K70E)

No EVG resistance

1 subject with late rebound

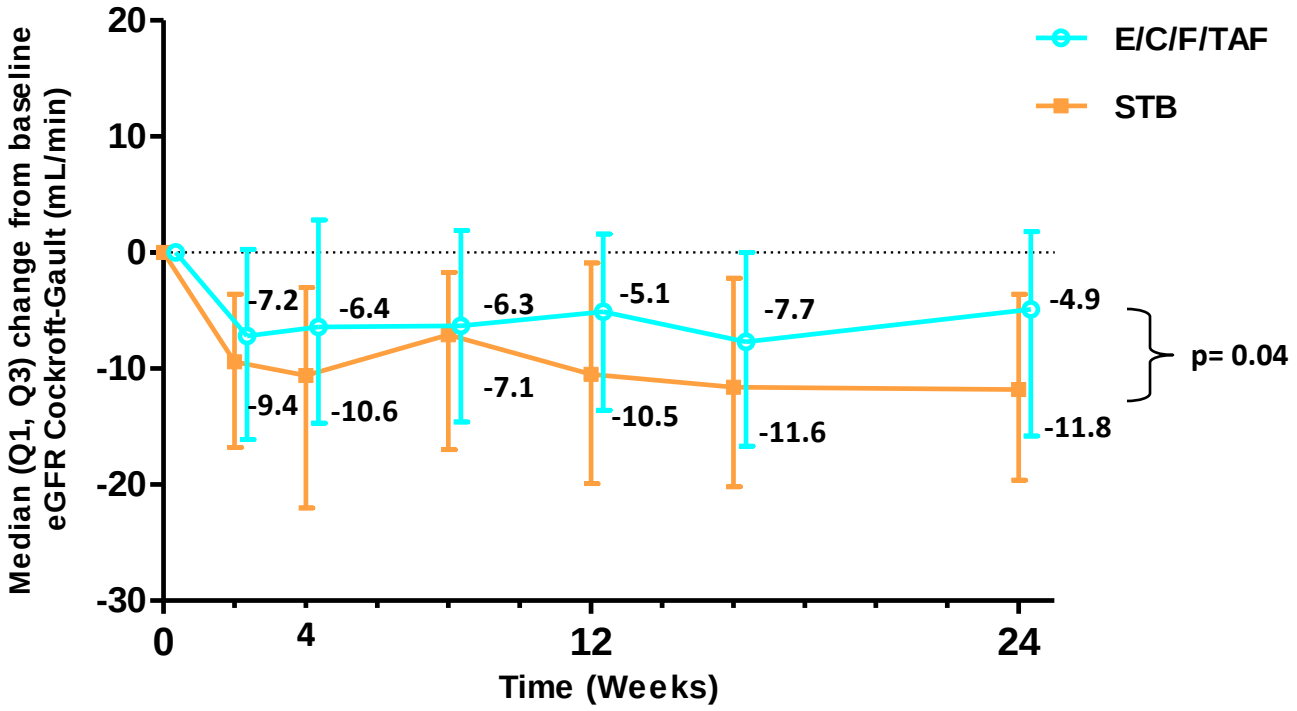
No resistance detected



ϕ **Mean change from baseline CD4+ cell count:**
E/C/F/TAF, +163 cells/μL
STB, +177 cells/μL (p = 0.76)

Median Estimated GFR (Cockcroft-Gault)

GS-US-292-0102 – Week 24 Analysis

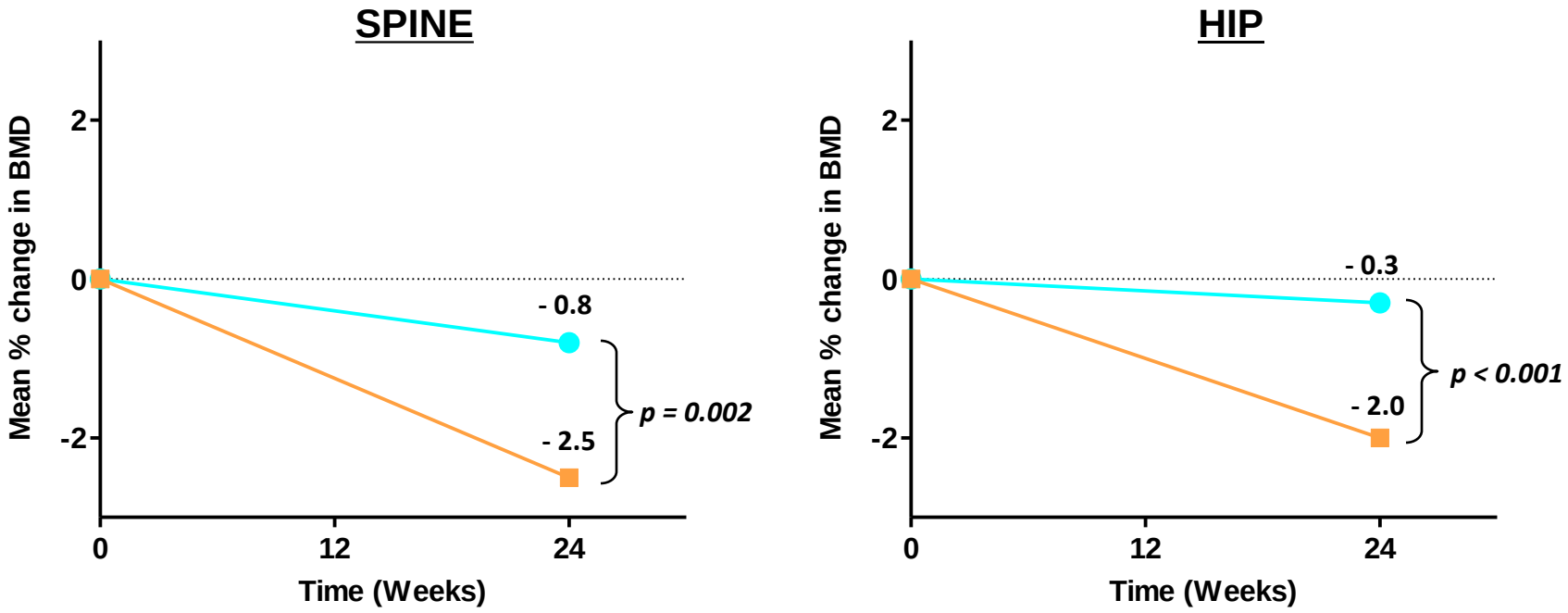


- ***Change in eGFR at Week 24***
  - ***E/C/F/TAF: -4.8 mL/min***
  - ***STB: -11.8 mL/min (p=0.04)***

A Zolopa, et al., CROI 2013; Paper # 99LB

Percent Change in Bone Mineral Density (DEXA)

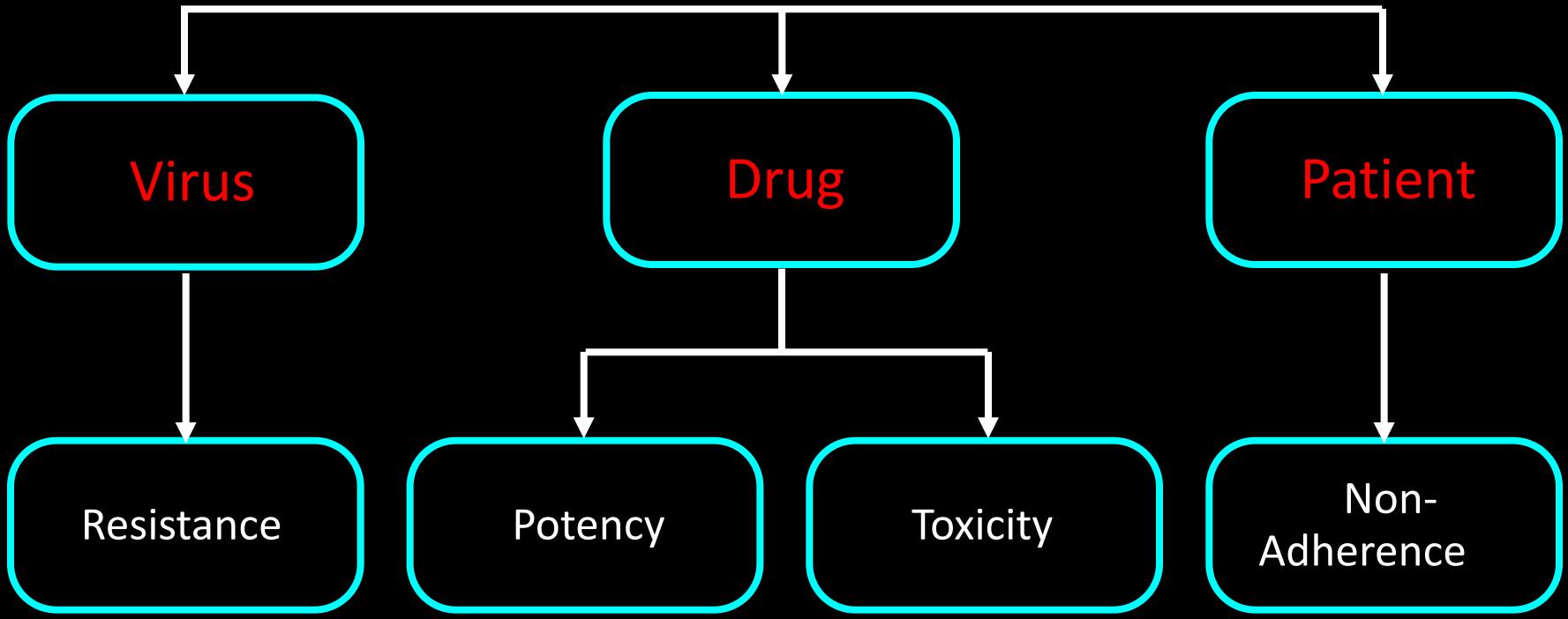
GS-US-292-0102 – Week 24 Analysis



- ***Proportion of subjects with <u>no decrease</u> in BMD***
  - ***Spine: E/C/F/TAF, 38%; STB, 12%***
  - ***Hip: E/C/F/TAF, 41%; STB: 23%***

A Zolopa, et al., CROI 2013;
Paper # 99LB

Why do therapies fail?




L.F.C.