HIV and Hep B and C co-infection

Dr. Mark Nelson

Chelsea & Westminster Hospital

Executive Committee of the British HIV Association (BHIVA)

GreenShoots FOUNDATION

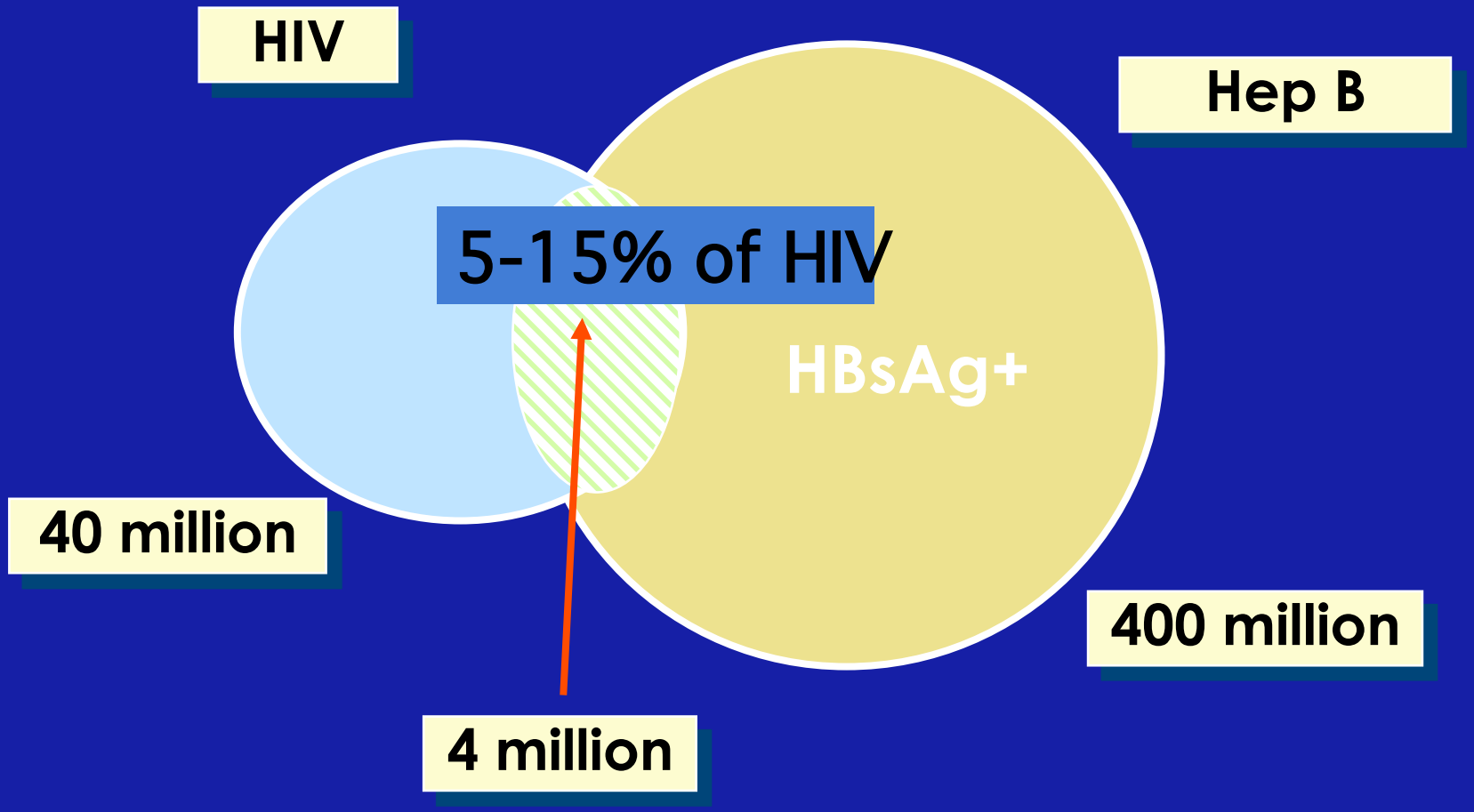
“Support needing populations through medical assistance and the transfer of knowledge to local medical practitioners.”

Our vision for the

Medical Assistance & Medical Education (MAME) Programs

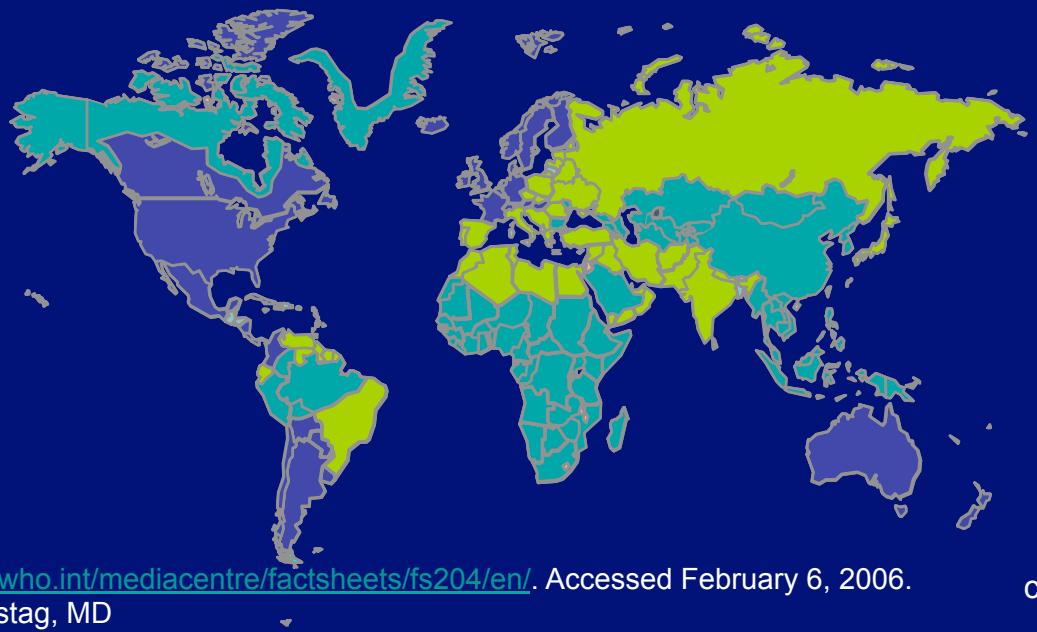
GreenShoots FOUNDATION

Overlapping HBV & HIV Epidemics



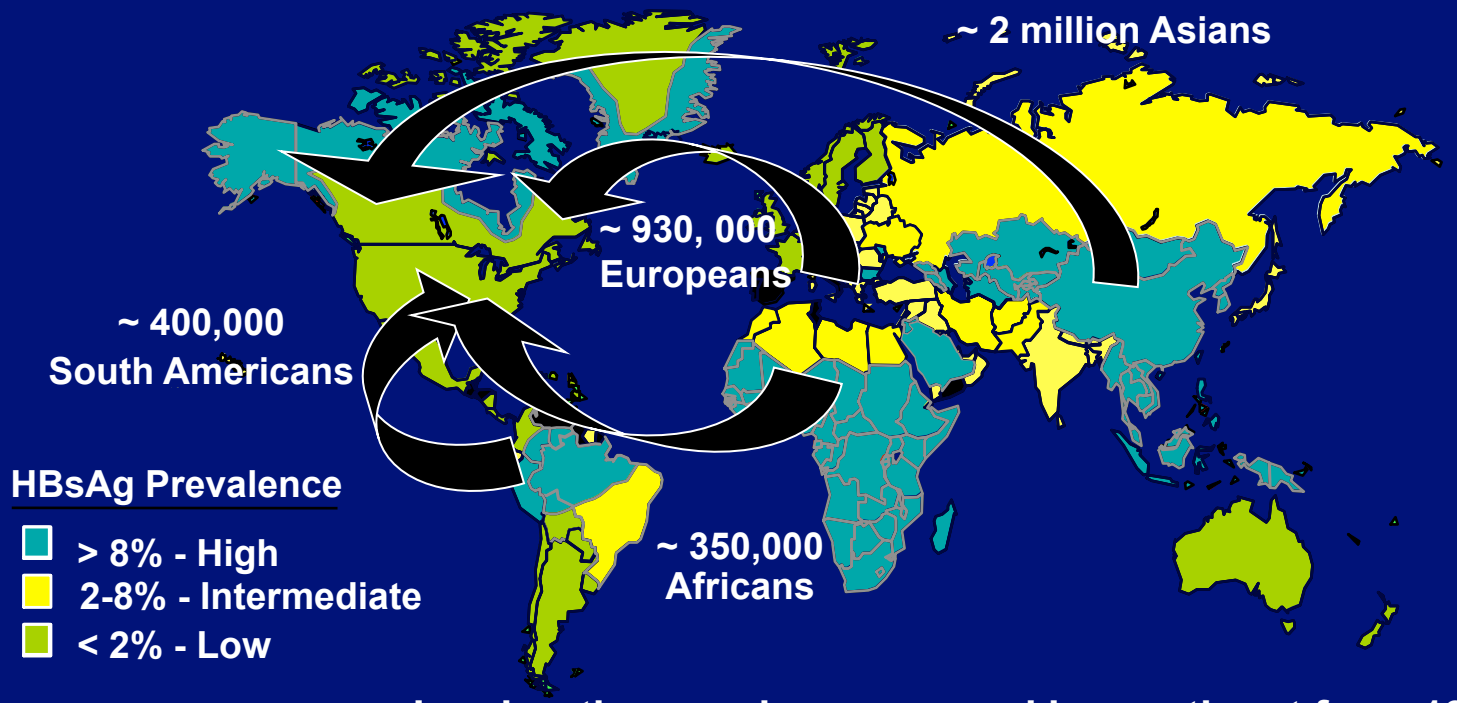
Clinical-Epidemiologic Correlations

HBV Endemicity	Location	Age of Infection	Mode of Transmission	Chronicity	HCC Risk
High 10-15%	Asia Sub-Sahara Africa	Birth Toddler	Perinatal Horizontal	Likely	High
Low < 2%	N. America W. Europe Scandinavia	Early Adulthood	Percutaneous Sexual	Rare	Low



Available at: http://www.who.int/mediacentre/factsheets/fs204/en/. Accessed February 6, 2006.
Designed by Jules Dienstag, MD

Prevalence of Chronic Hepatitis B



Immigration numbers summed by continent from 1996-2002

Centers for Disease Control. Hepatitis B fact sheet. Available at: http://www.cdc.gov/hepatitis. Accessed January 31, 2006. Mahoney FJ. Clin Microbiol Rev. 1999;12:351-366. Hepatitis B Foundation. Hepatitis B statistics. Available at: http://www.hepb.org/hepb/statistics.org. Accessed January 31, 2006.

Anti-HBV Therapies

Immune modulators

IFN-alpha

Pegylated-Interferon-alpha

Polymerase Inhibitors

Lamivudine

Adefovir

Entecavir

Telbivudine

Tenofovir

Emtricitabine

Anti-HBV Therapies

Immune modulators

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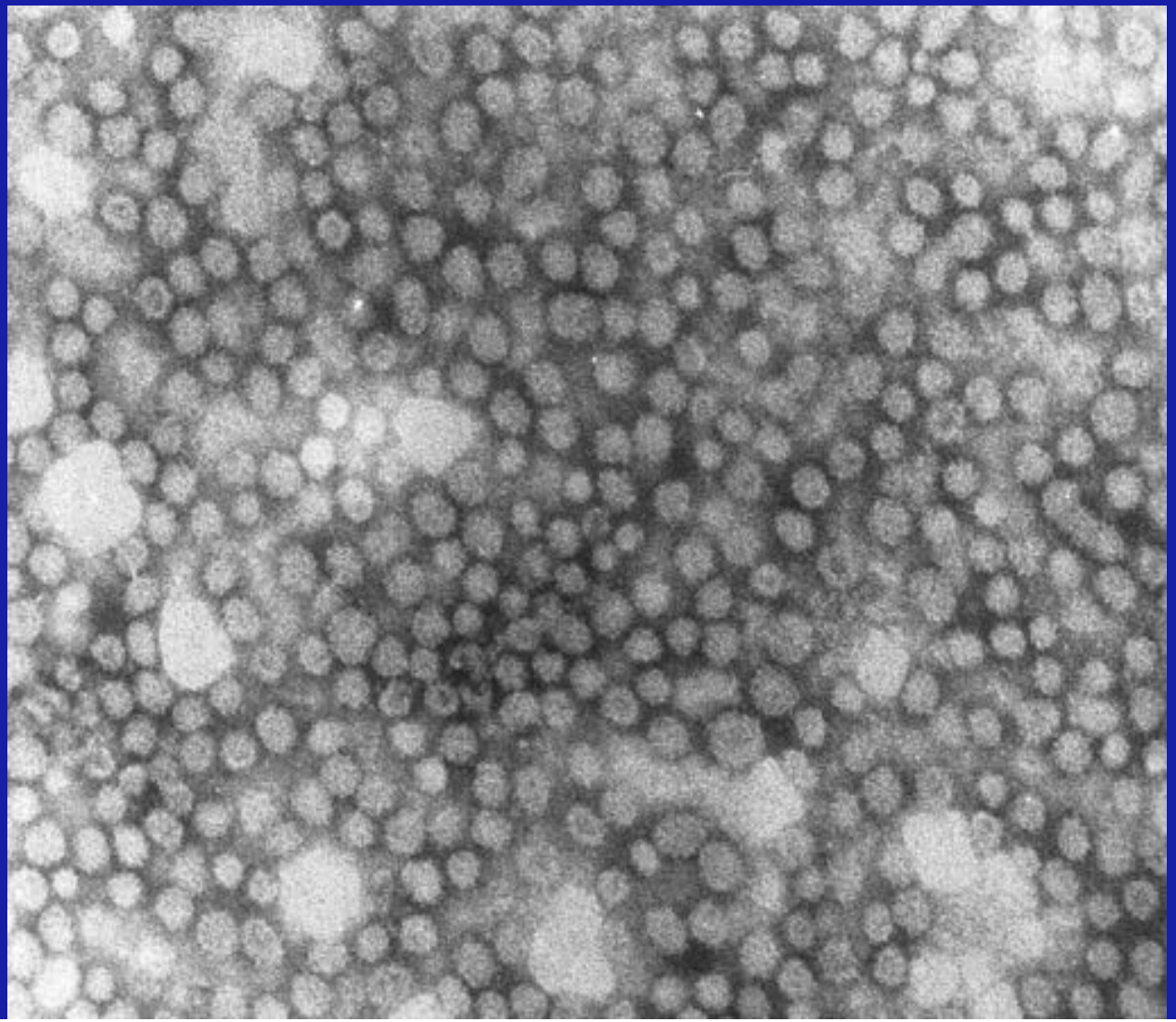
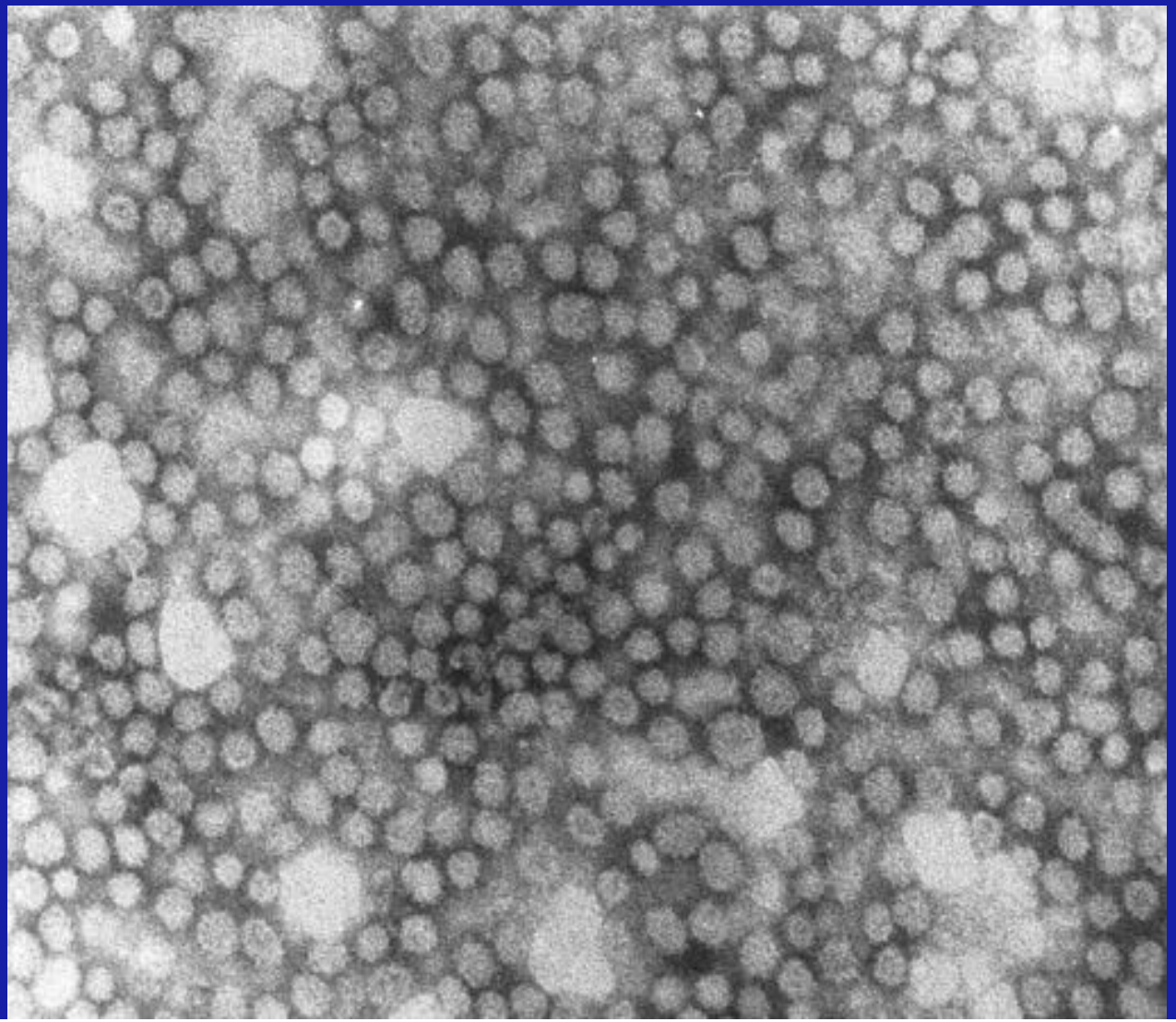
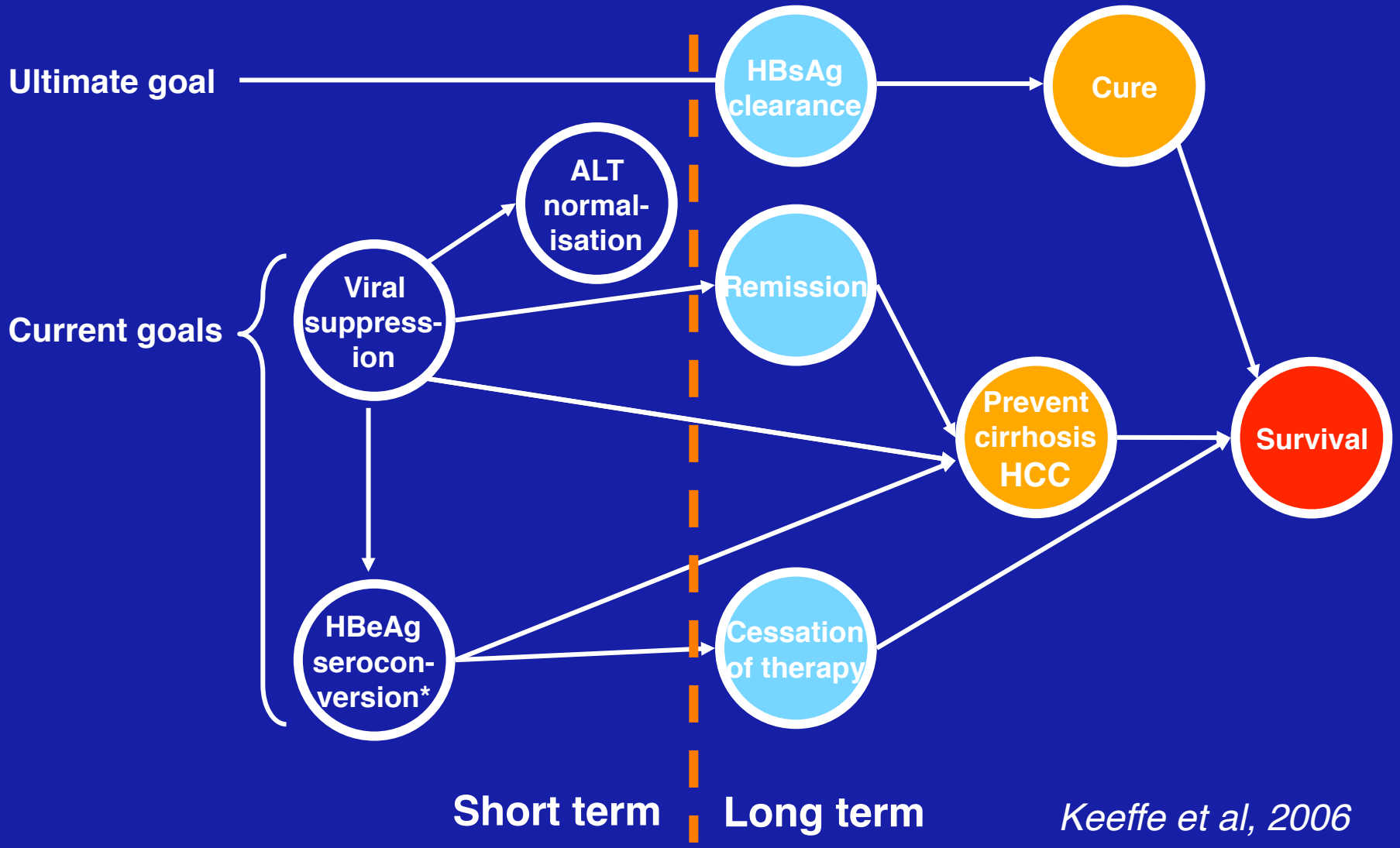


Hepatitis B Therapy



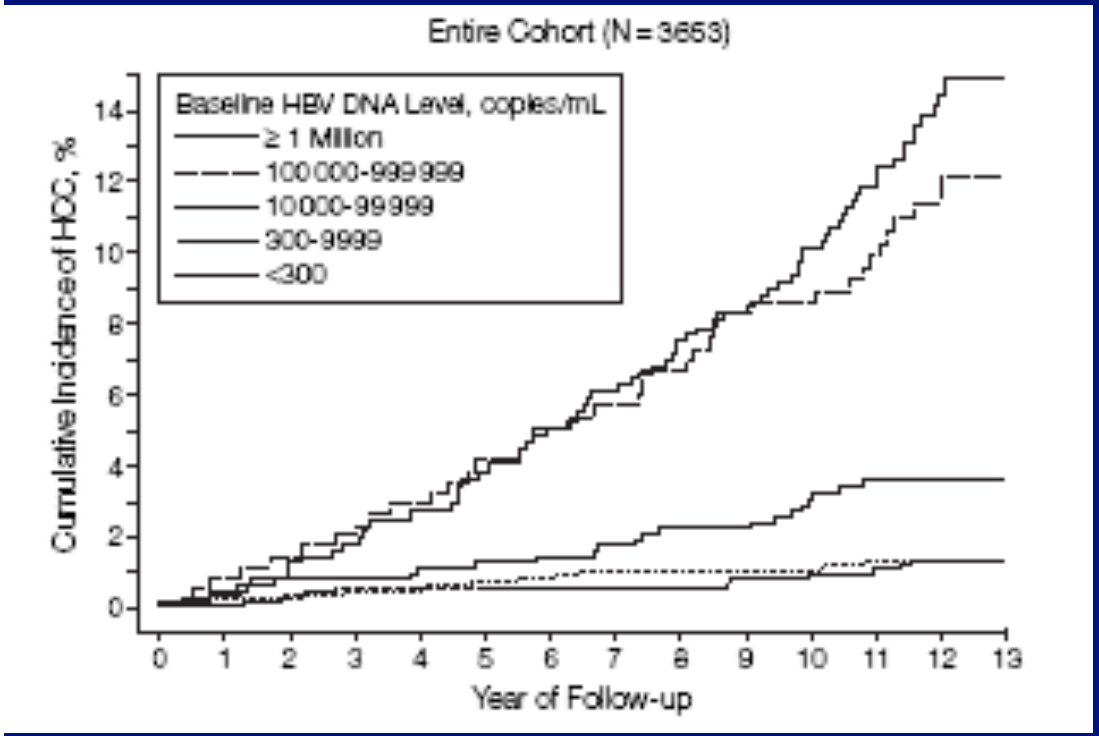
Outcomes to Consider and Goals to Achieve



*HBeAg positive patients only

Keeffe et al, 2006
Lok & McMahon, 2007

HBV DNA Level and Risk of HCC



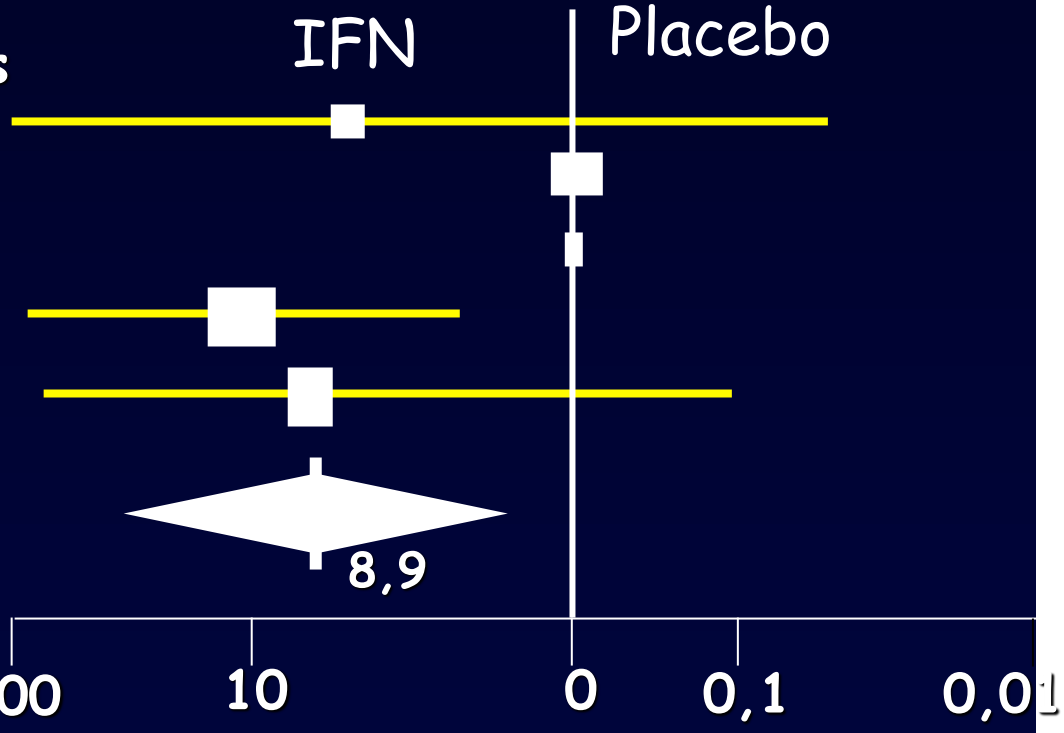
HBV DNA (copies/ml)	Cumulative incidence of HCC
<300	1.30
300-9999	1.37
10,000-99,999	3.57
100,000-999,999	12.17
>1 million	14.89

Chen C-J. *JAMA* 2006; 295:67-73.

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



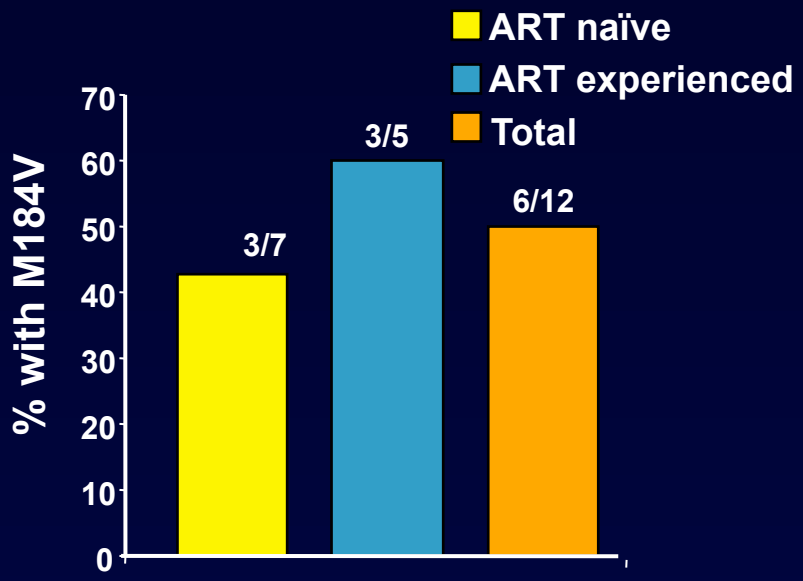
HBe seroconversion/negativation : HIV+ *vs* HIV: - 0.38 (CI 0.06-0.7 *P* =.02)

Puoti et al. personnal comm.

Anti-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

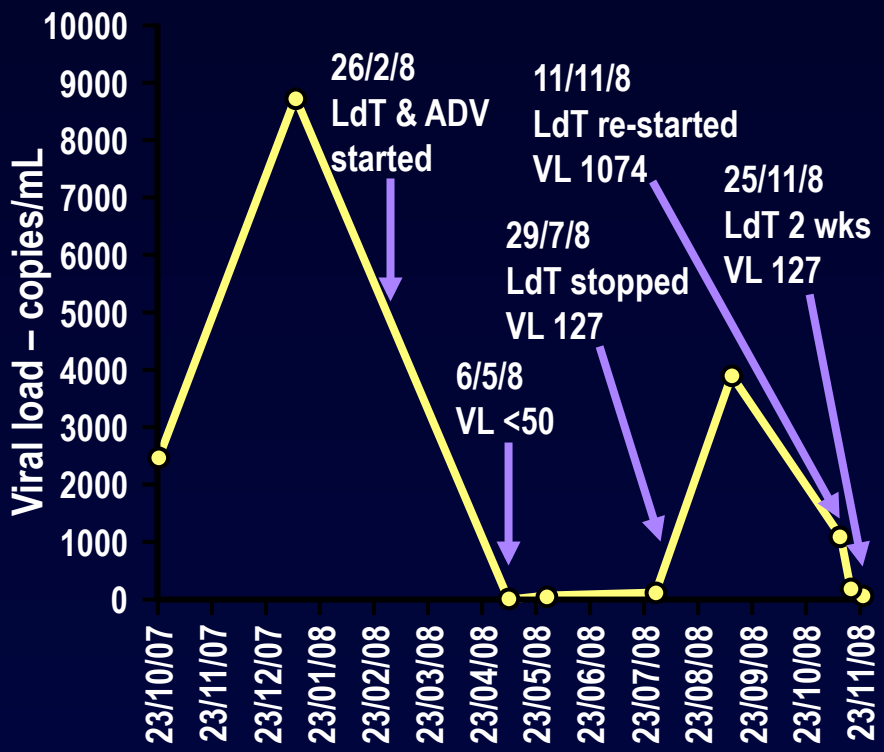


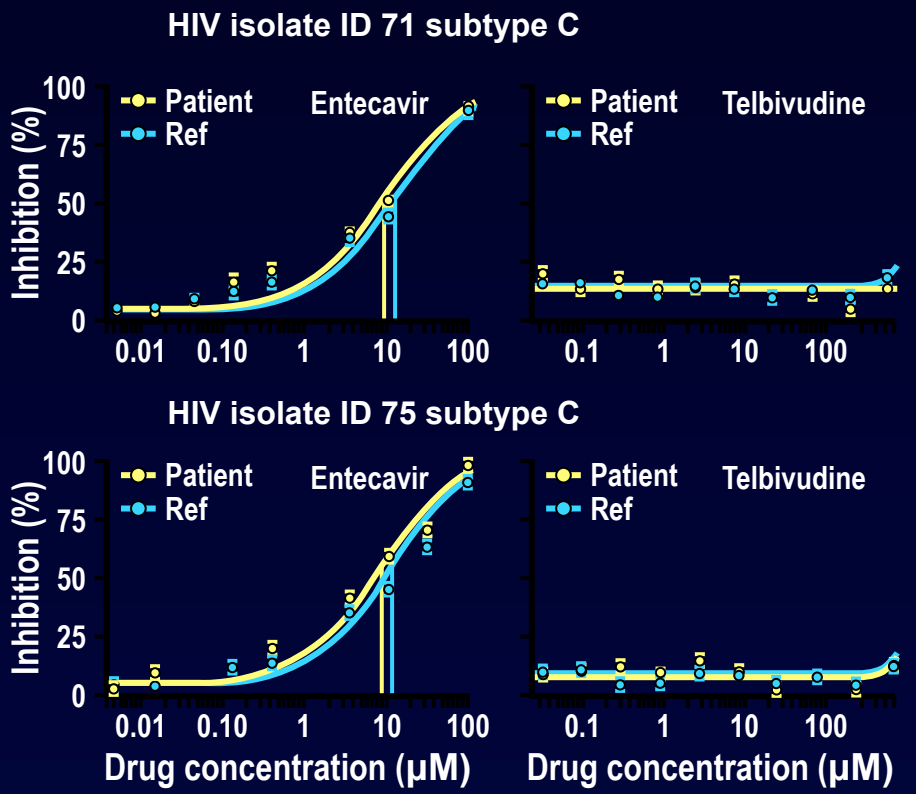
Univariate analysis for selection of M184V

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



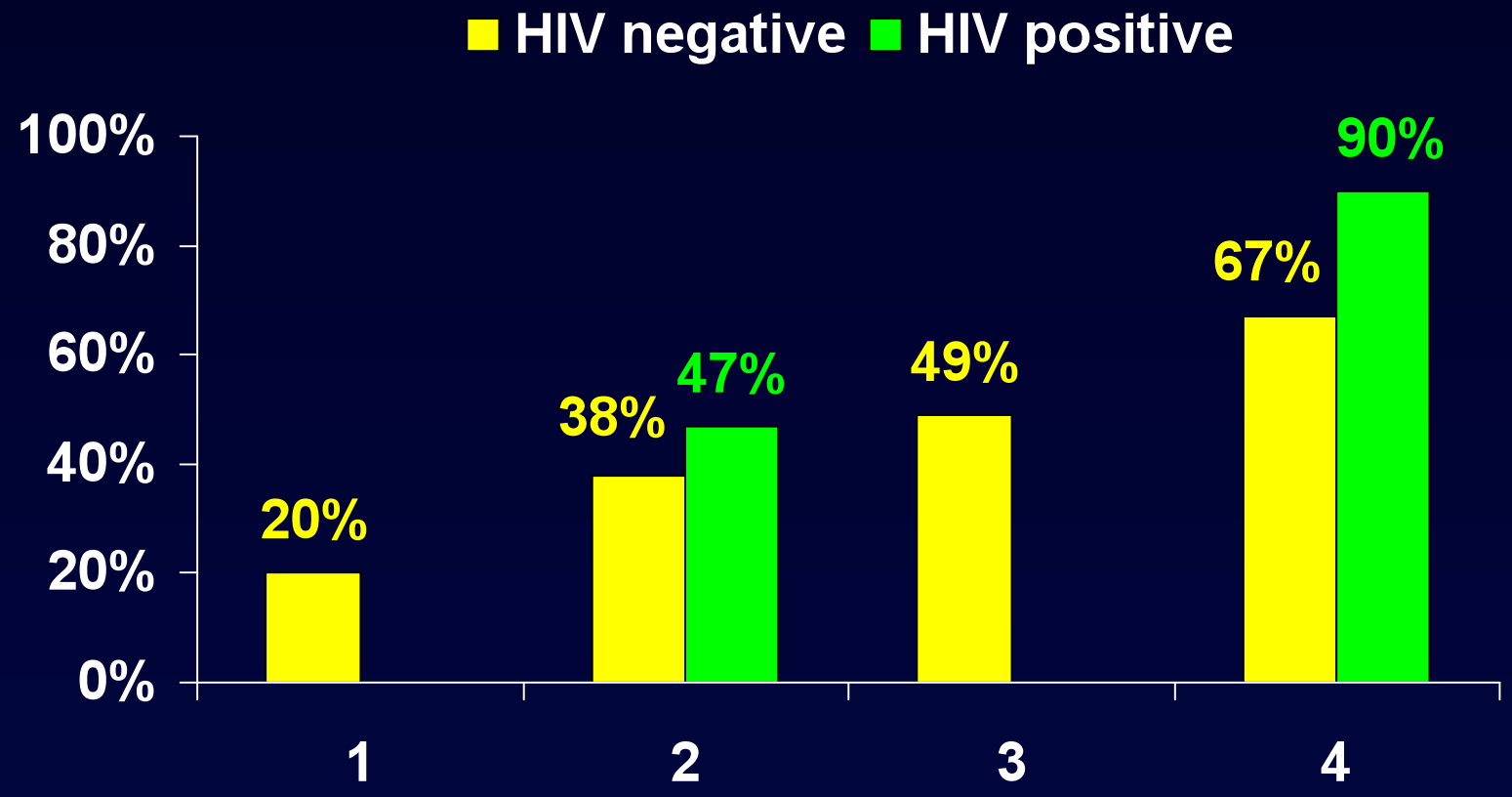


No *in vitro* activity against 8 wild-type HIV-1, 2 drug resistant HIV-1 isolates

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

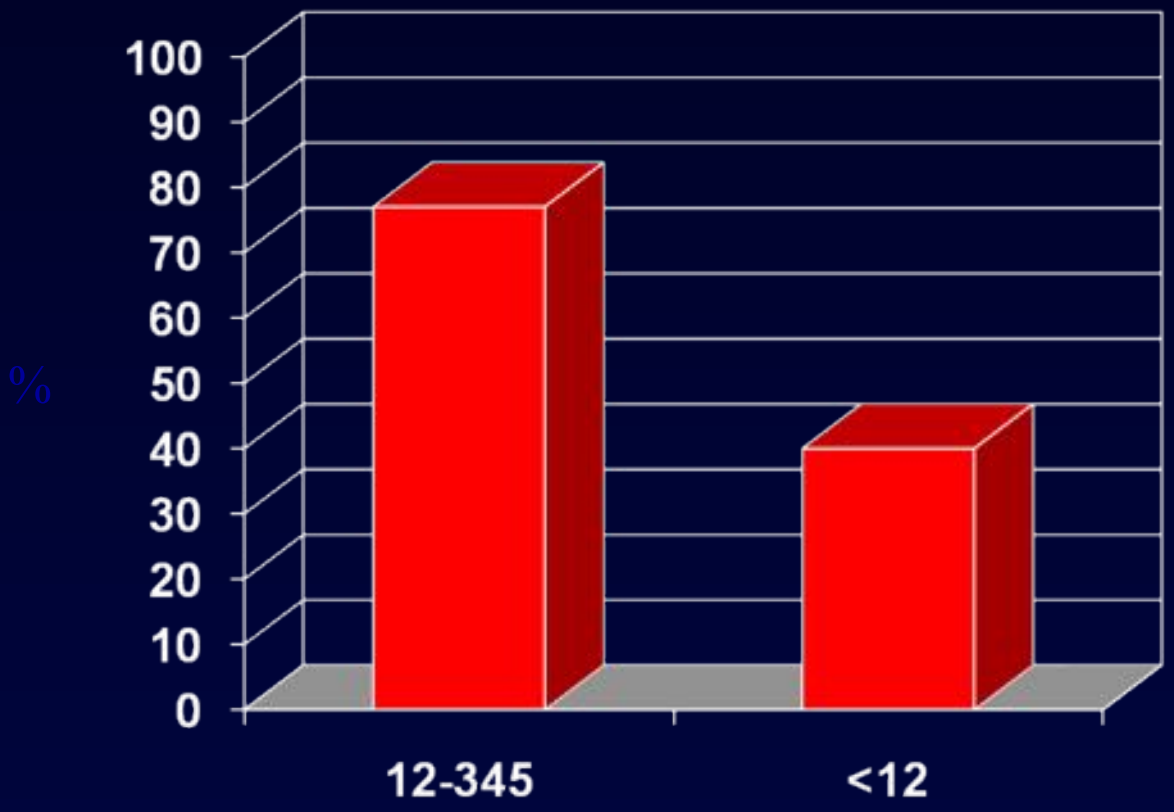
C Avila, *et al.* CROI 2009;P813b

Incidence of LAM Resistance in HBV and HBV/HIV Patients



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

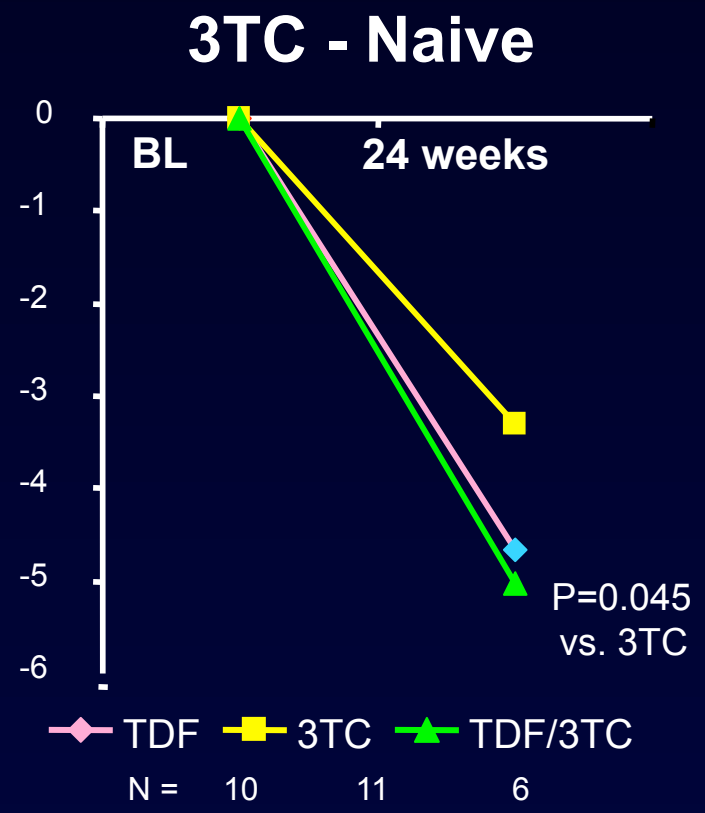
Resistance to Lamivudine even at Very Low Viral Load

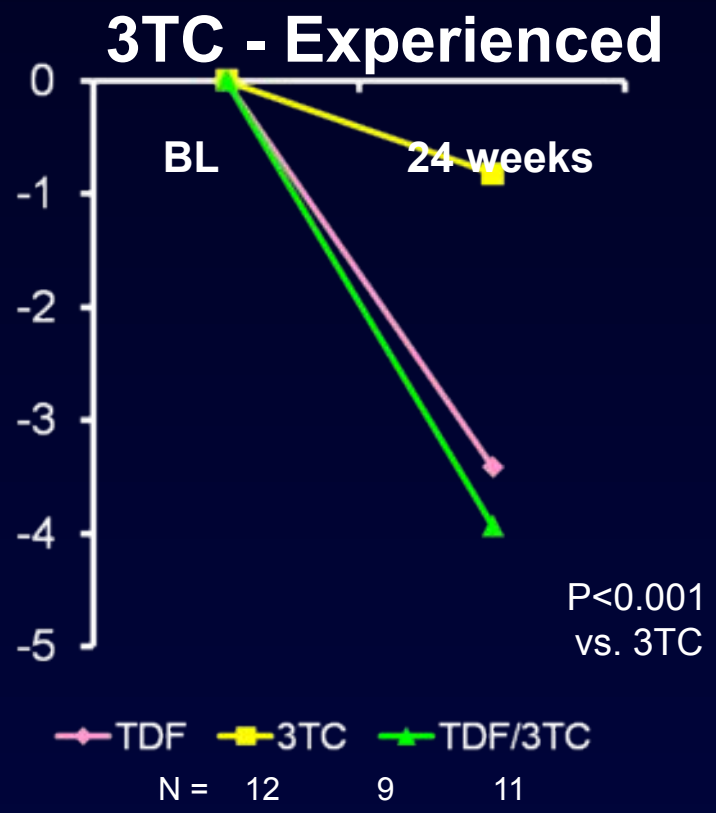


Hepatitis B Viral Load IU/ml

Perno Interntional Drug Resistance Workshop 2009

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





Conclusion:

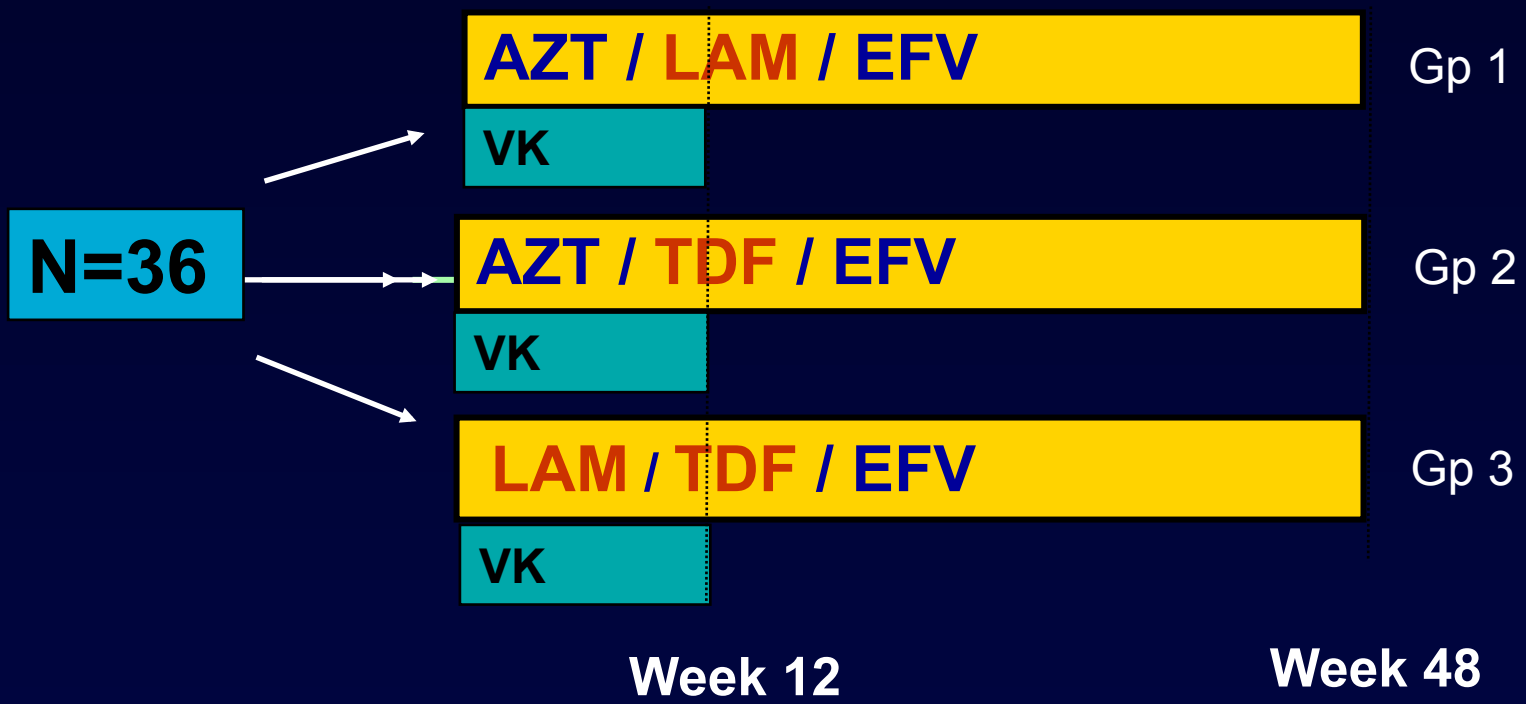
- TDF/3TC superior to 3TC alone but not TDF in HBV naïve
- No benefit continuing 3TC in experienced HBV viraemic patients
- No difference between adding or switching TDF

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

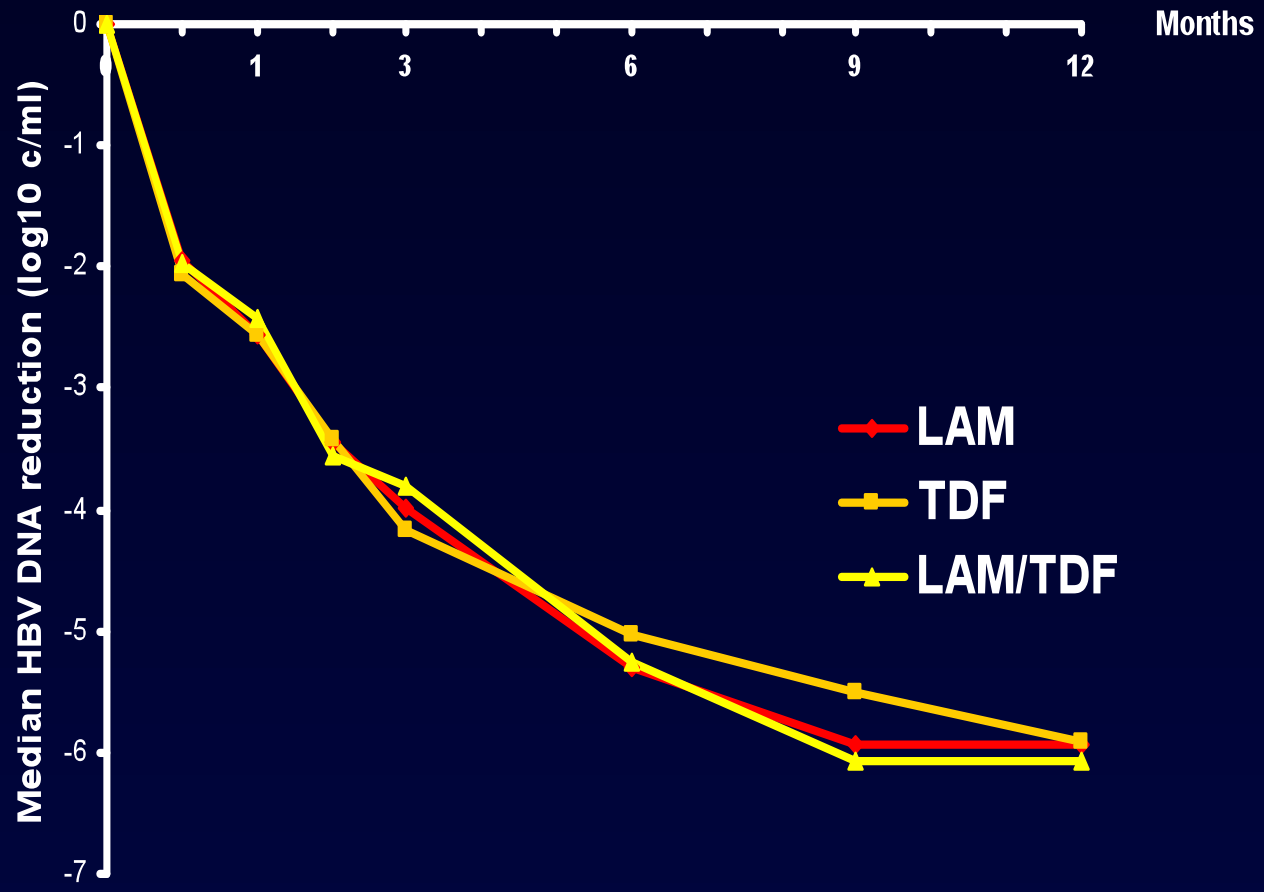
Study design

Primary objective

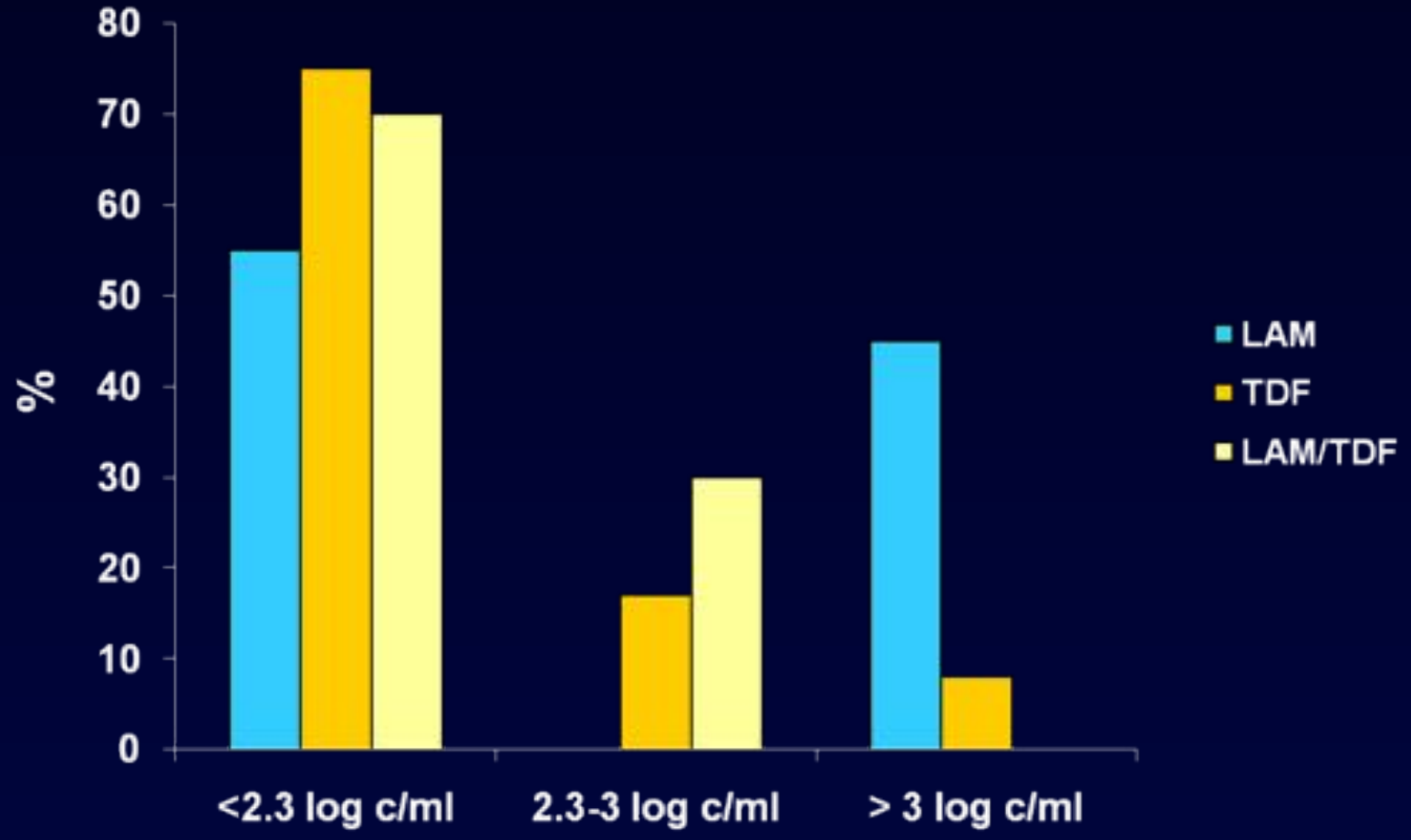
To compare the safety and efficacy of tenofovir (TDF) to lamivudine (LAM) and to combination TDF/LAM in treating HBV in ARV- naive patients with HIV/HBV co-infection over 48 weeks



Median HBV reduction 48 weeks



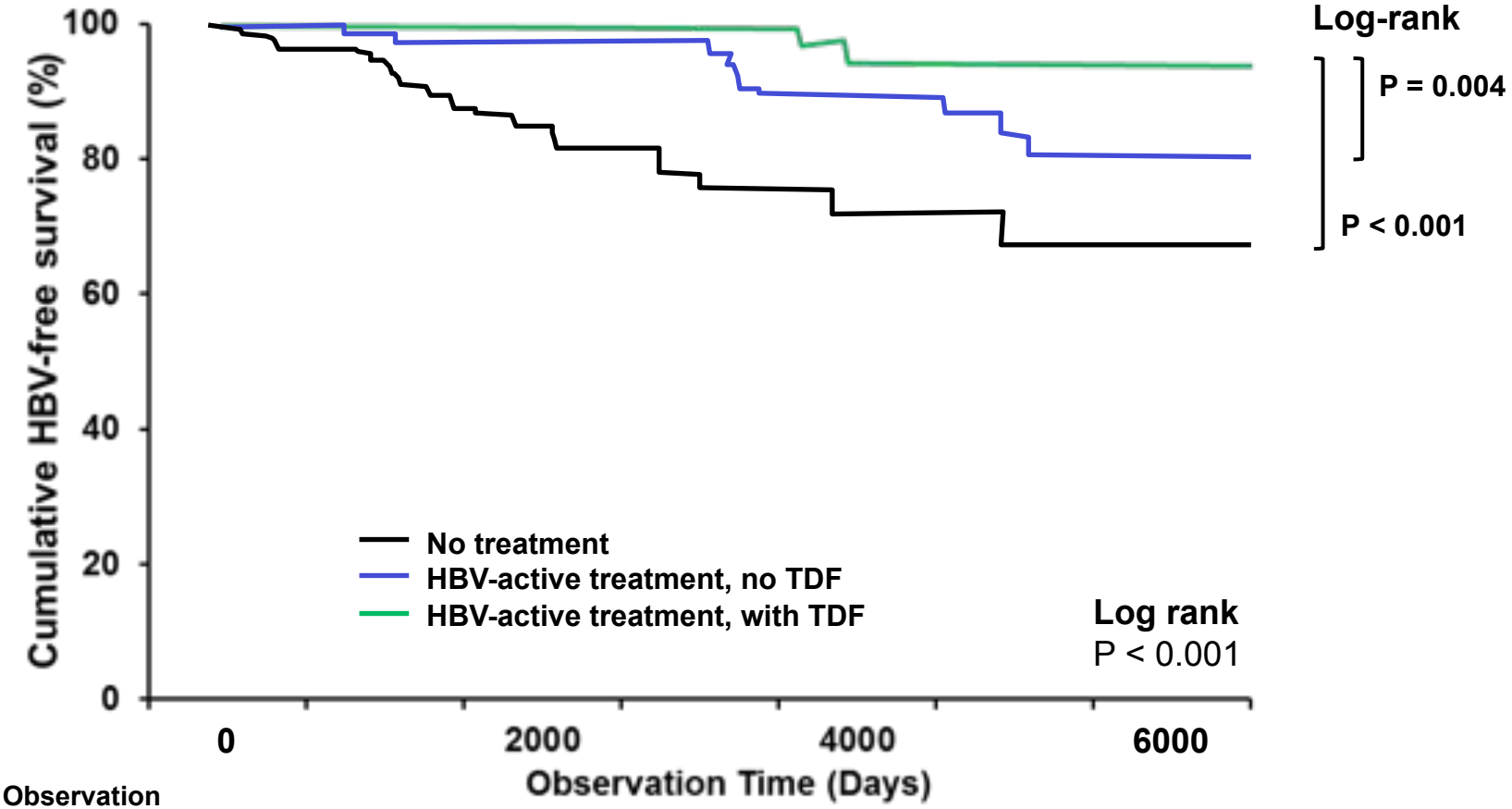
HBV DNA suppression at 48 w



P=0.016

On treatment

Kaplan Meier: HBV-free survival (MSM)

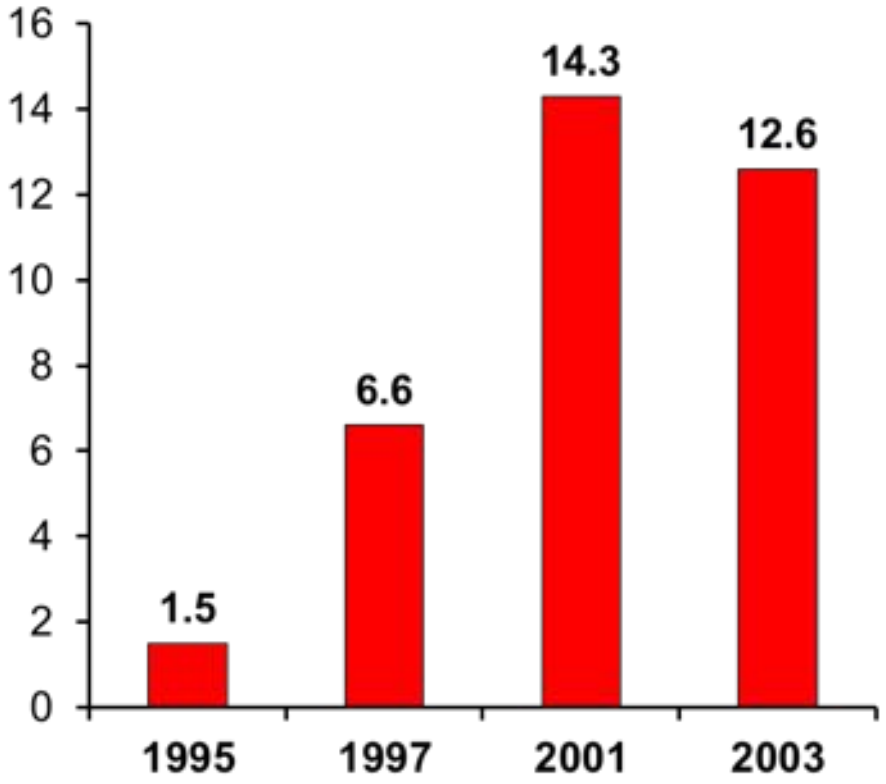


Numbers in Observation				
No Treatment	107	50	19	8
Treatment, No TDF	86	67	36	16
Treatment, with TDF	189	49	38	12

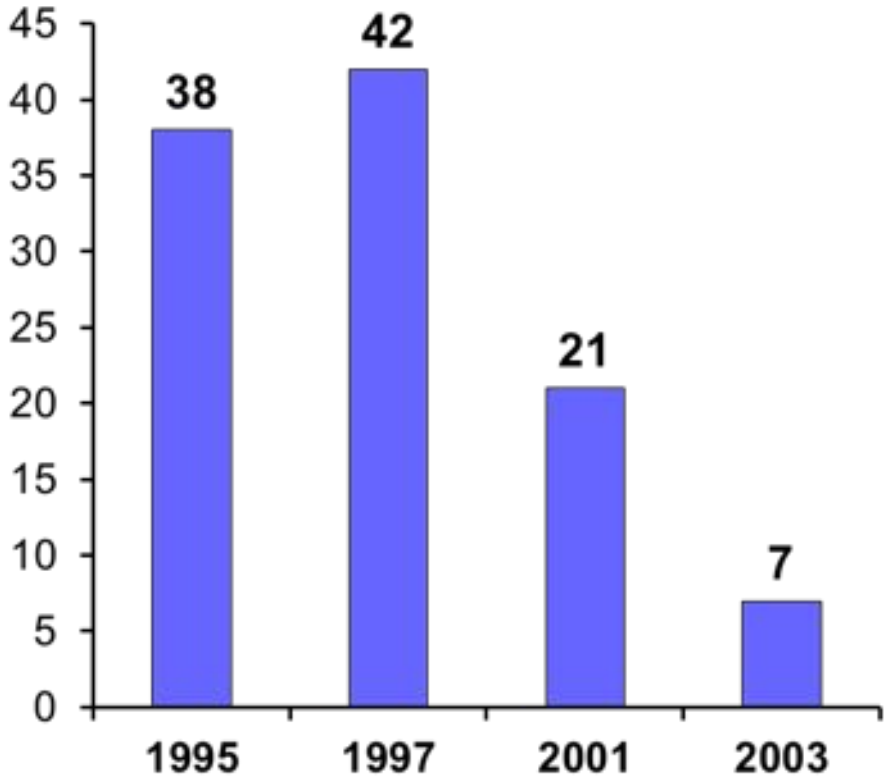
Brinkman K, et al. 20th CROI; Atlanta, GA; 2013. Abstract 33

Liver disease associated mortality in HIV 1995–2003 GERMIVIC

- ESLD associated death: % total mortality



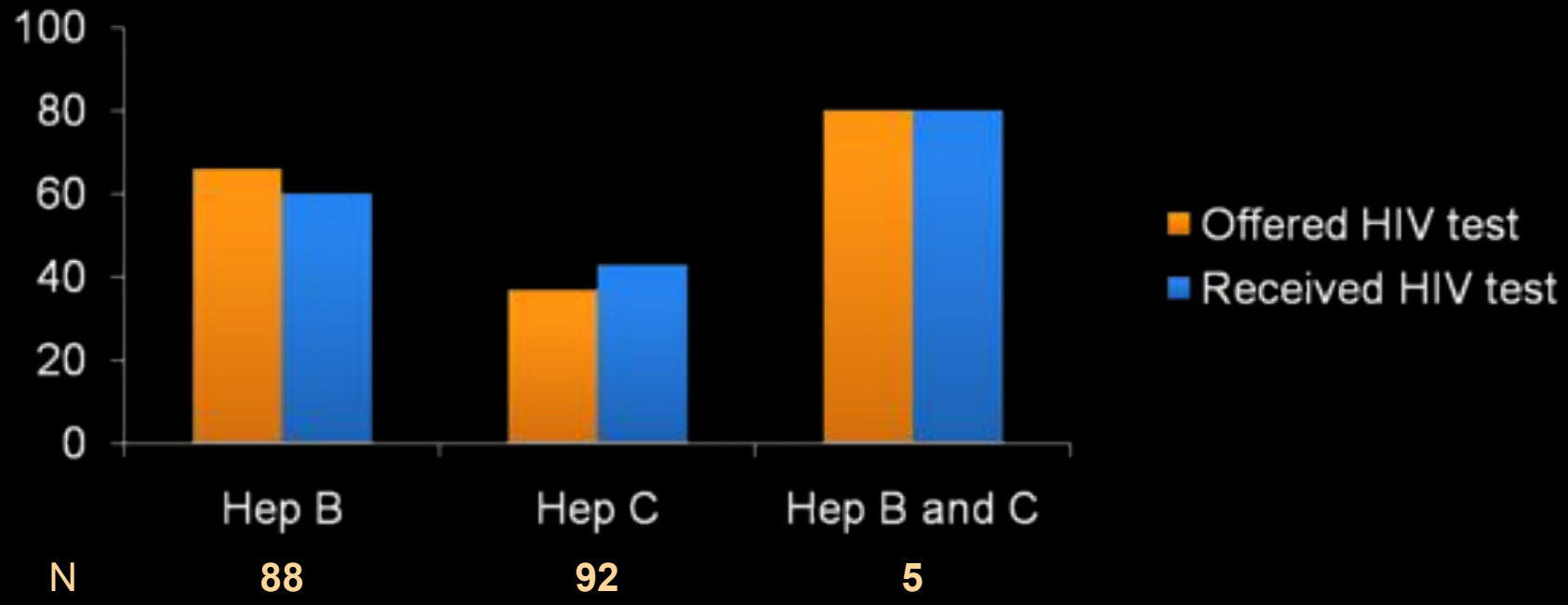
- ESLD associated death: % HBsAg+



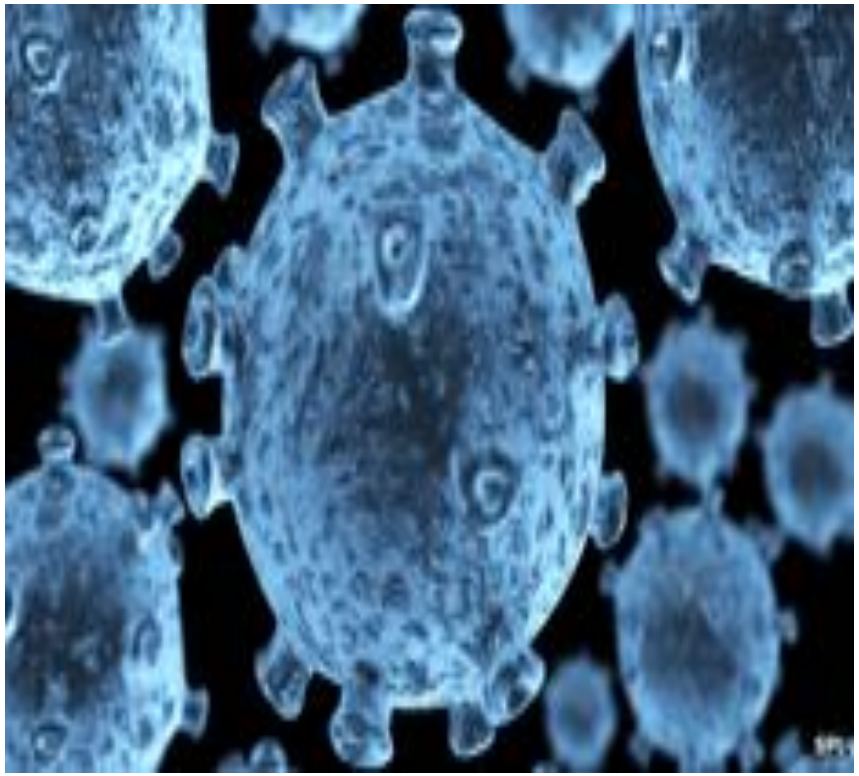
Rosenthal E, et al. J Viral Hepat 2007;14:183–8

Hepatitis and HIV testing

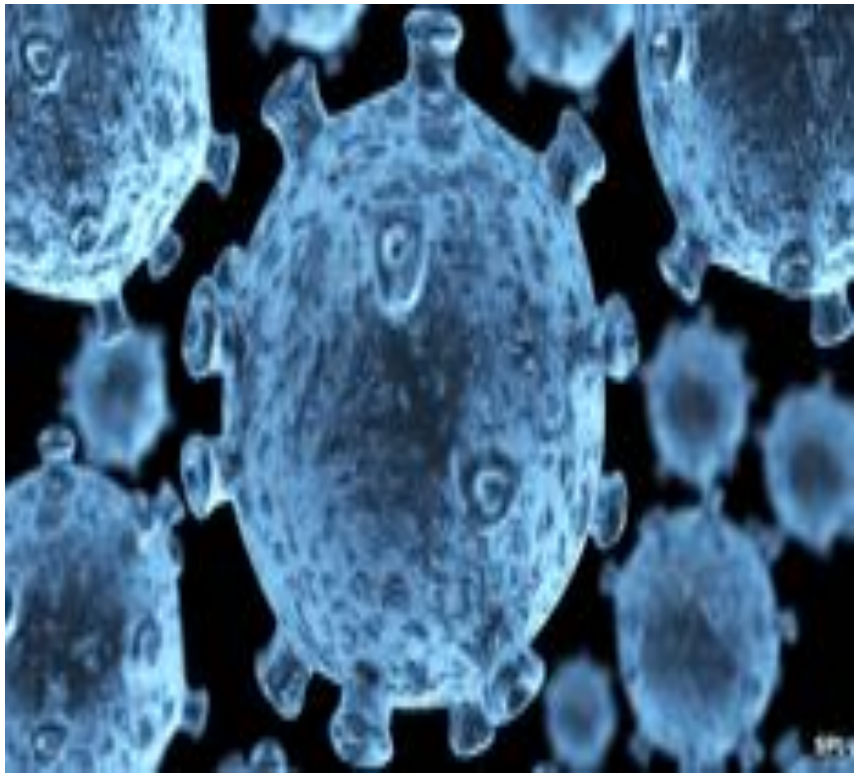
- Aim of study was to identify rates of HIV testing in patients with HBV and/or HCV and to assess HIV testing practice in a large UK teaching hospital
- Retrospective case note review of 185 individuals with known hepatitis infection



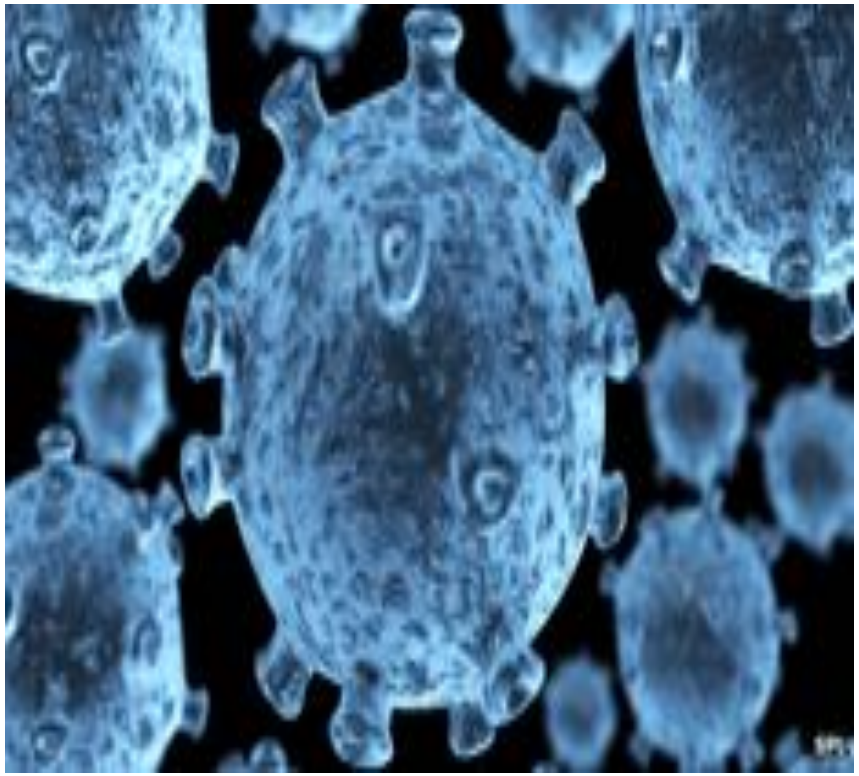
Perera S, *et al. HIV Med*, 2011; **12** (Suppl. 1):87-91.



Which was discovered first?

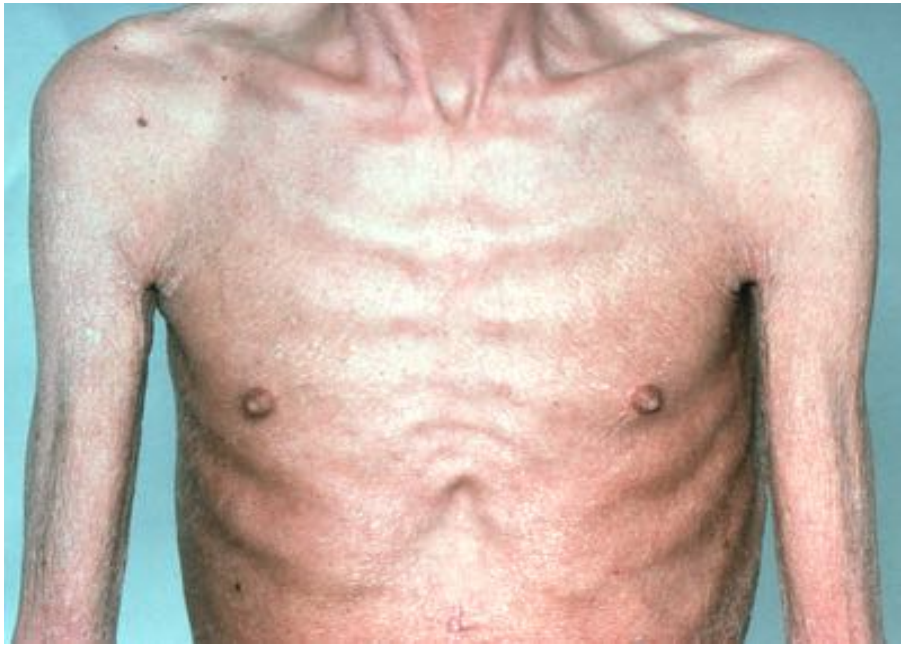


1983



1989


Aids makes us equal
AIDS
Protect yourself




TIME
The Graying of AIDS
TIME
The Graying of AIDS
Email This
TIME
The Graying of AIDS
Email This
The personal is political
Pioneer

Available Treatments for Hepatitis C 2014(UK)

Interferon

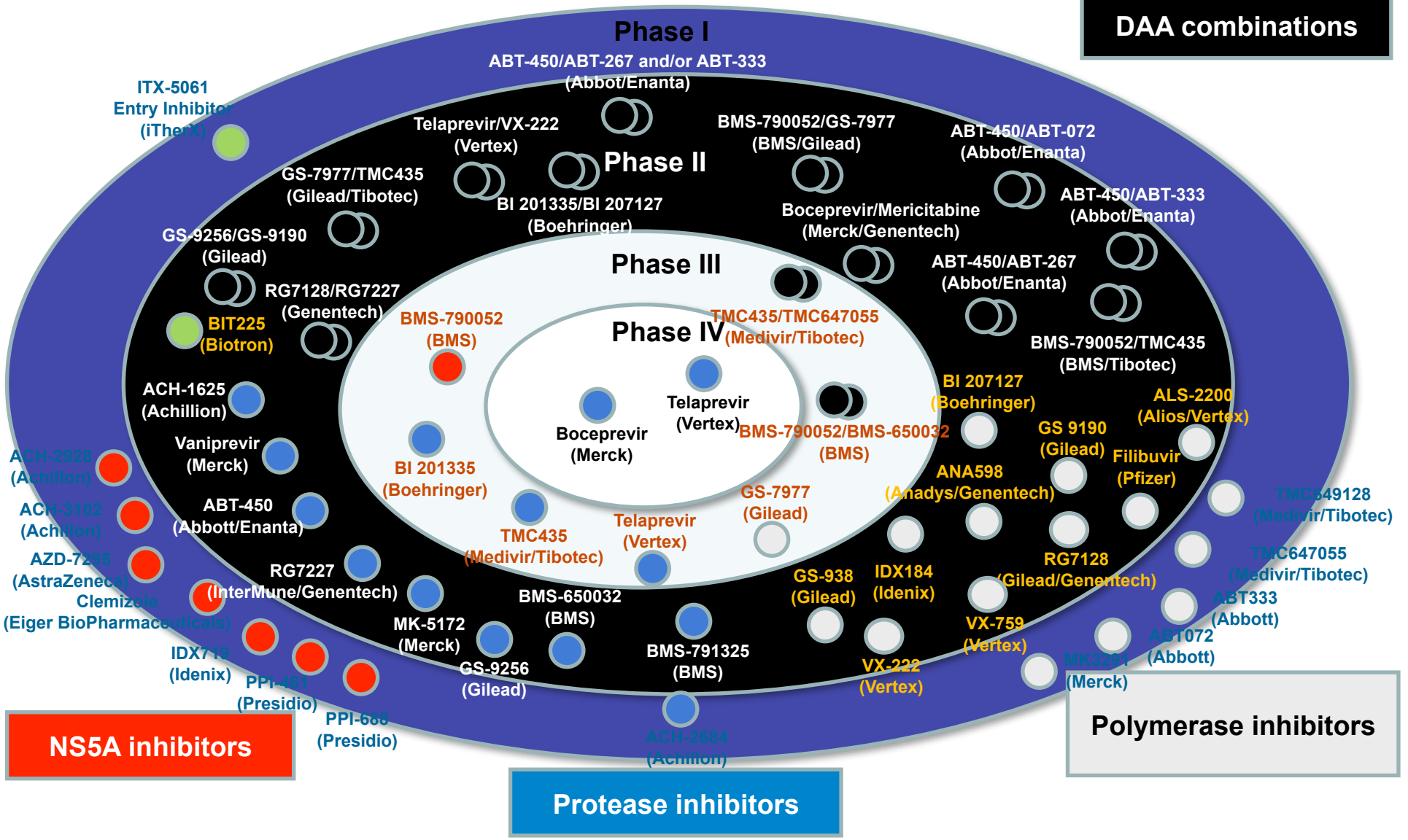
Ribavarin

Protease Inhibitors

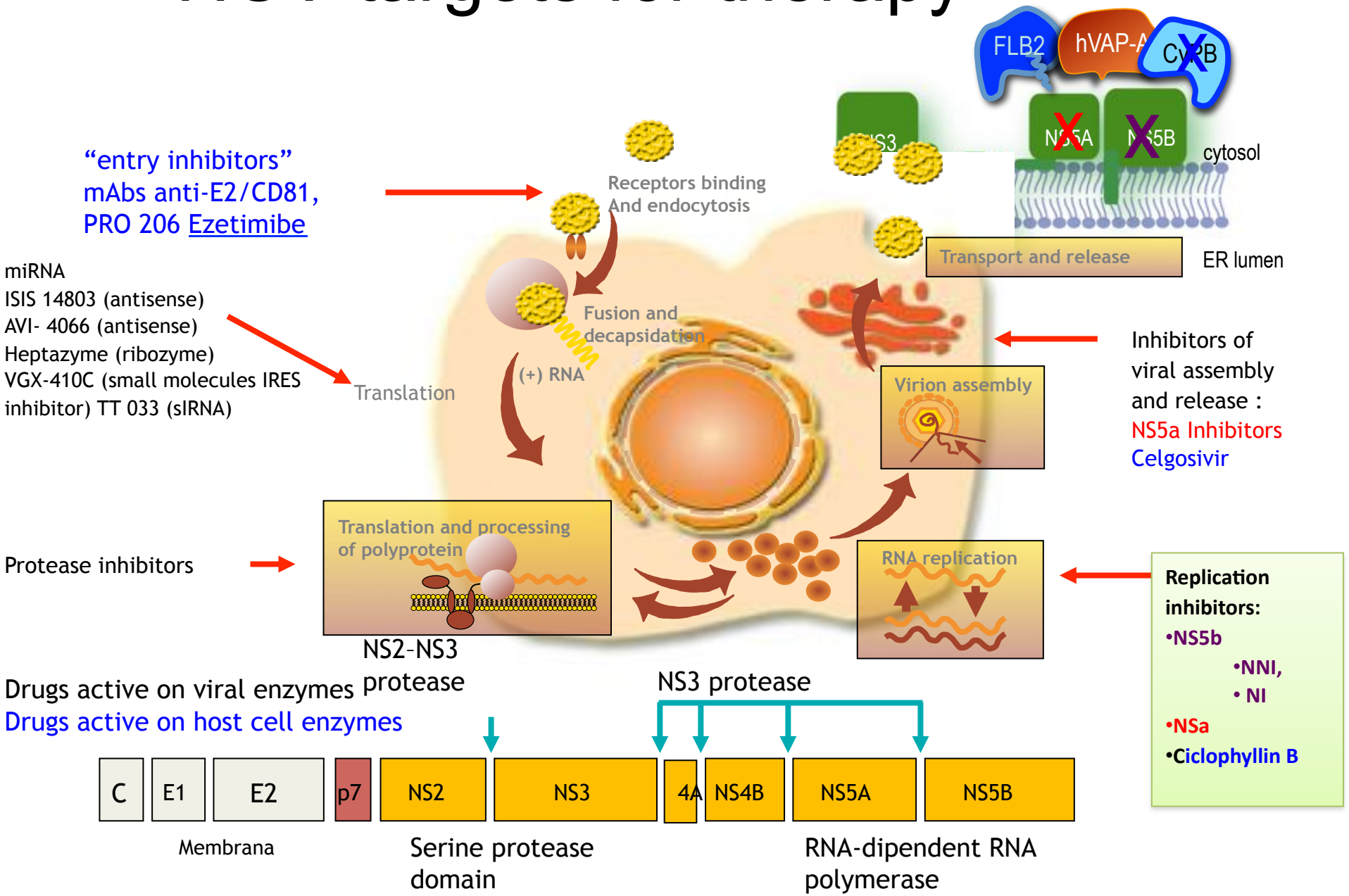
- Telaprevir
- Boceprevir


THE WINDS OF CHANGE
EARTH BOUNCE

Hepatitis C pipeline

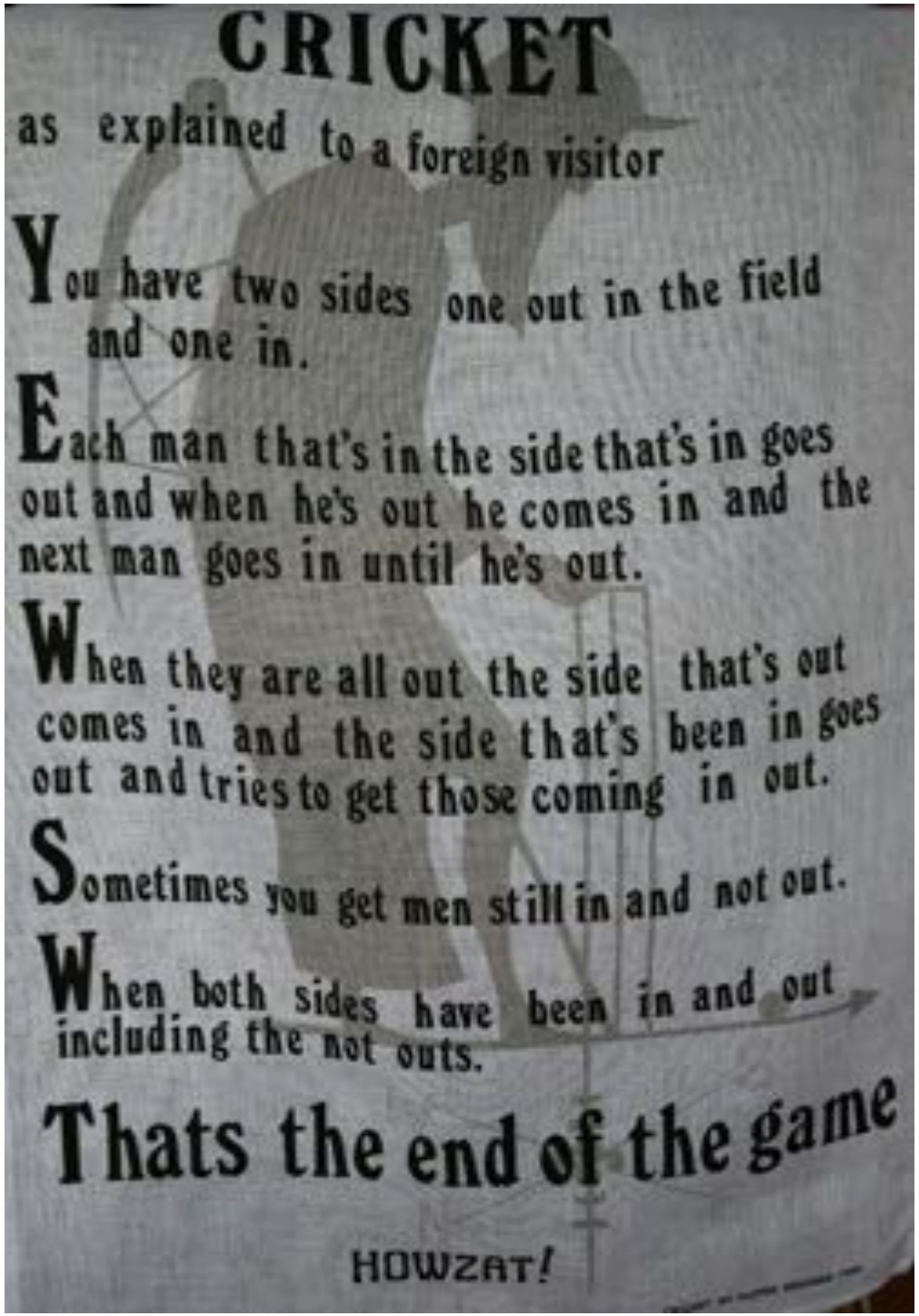


HCV targets for therapy



1. Lindenbach BD & Rice CM. Unravelling hepatitis C virus replication from genome to function. *Nature* 2005;436:933-938


LOST
CONFUSED
UNSURE
UNCLEAR
PERPLEXED
DISORIENTED
BEWILDERED

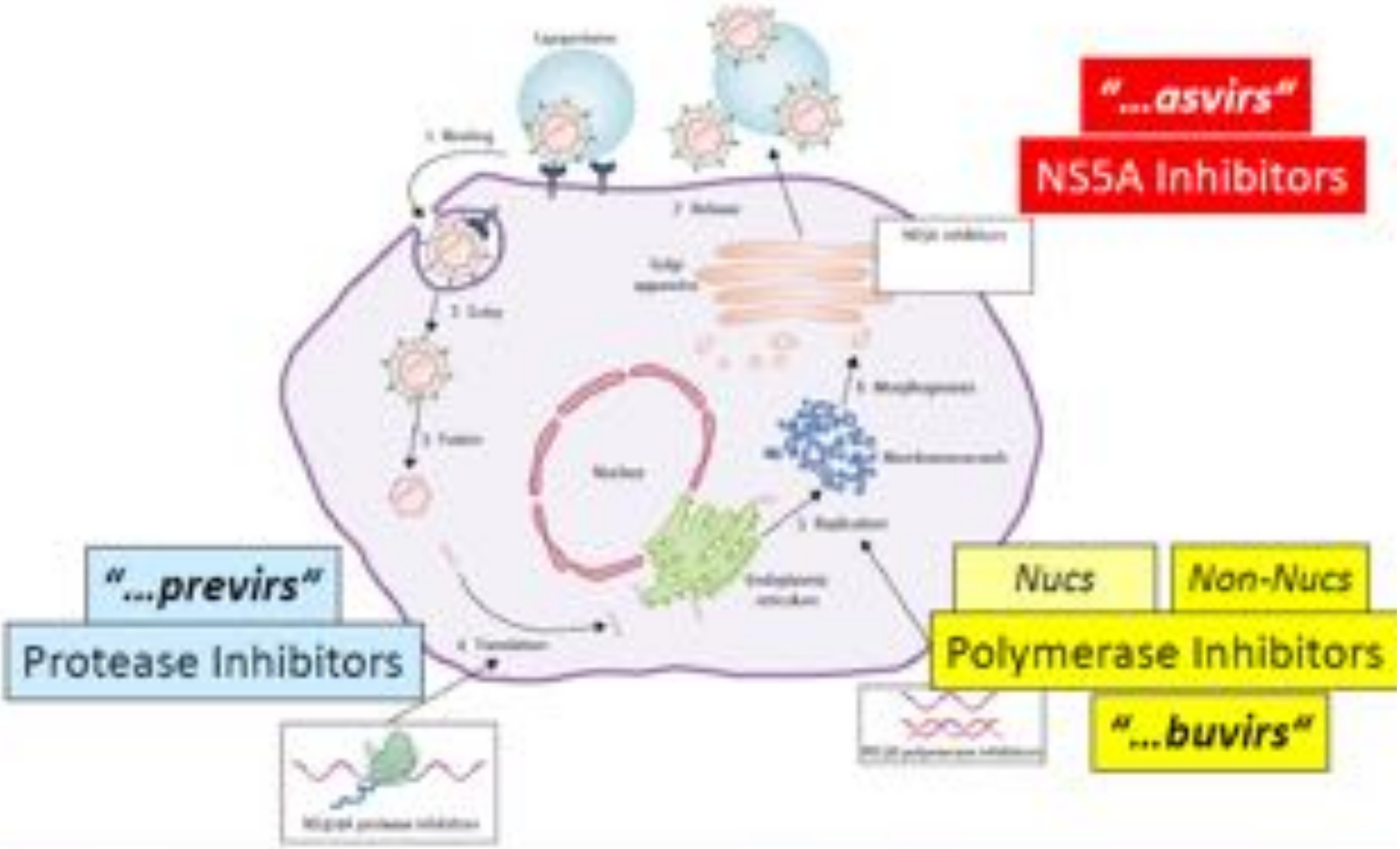

CRICKET
as explained to a foreign visitor
You have two sides one out in the field and one in.
Each man that's in the side that's in goes out and when he's out he comes in and the next man goes in until he's out.
When they are all out the side that's out comes in and the side that's been in goes out and 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

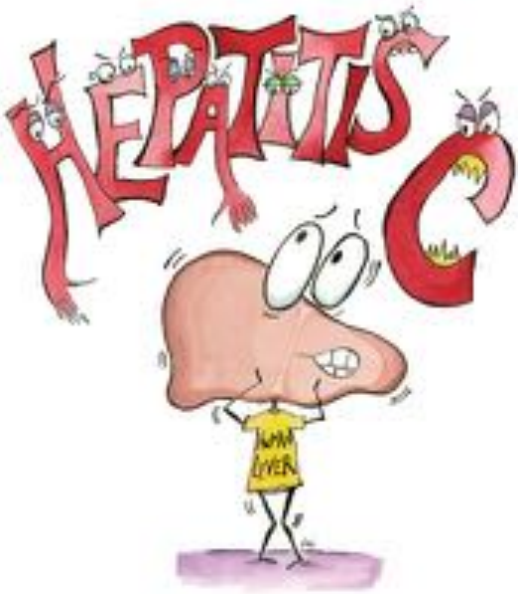

Cricket
Play Har


£7.95
RT

Direct Acting Antivirals against HCV



Manns, von Hahn, Nat Rev Drug Discov 2013



No Liver, No Life.

Hepatitis C (HCV) could be attacking your liver and you may not even know it. Without a liver, you can't live. To find out more information about this deadly disease, visit www.cdc.gov/hepatitis

CDC


TOXIC

Drug Resistance


©Vincent Desjardins 2009
MILK
MILK
inter
actions


PUSH DOWN AND UNSCREW
CLOSE RIGHT


A
B
C

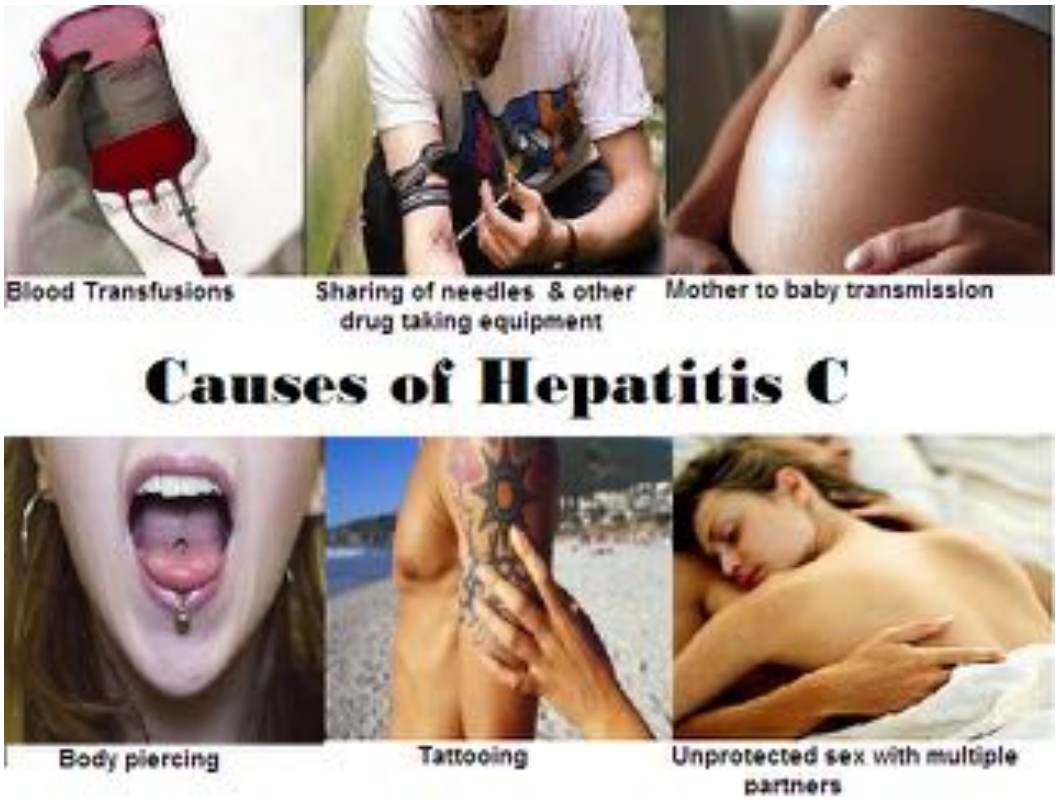

IF HEP C WAS ATTACKING YOUR FACE INSTEAD OF YOUR LIVER, YOU'D DO SOMETHING ABOUT IT.
READY TO FIGHT BACK?


NOPE

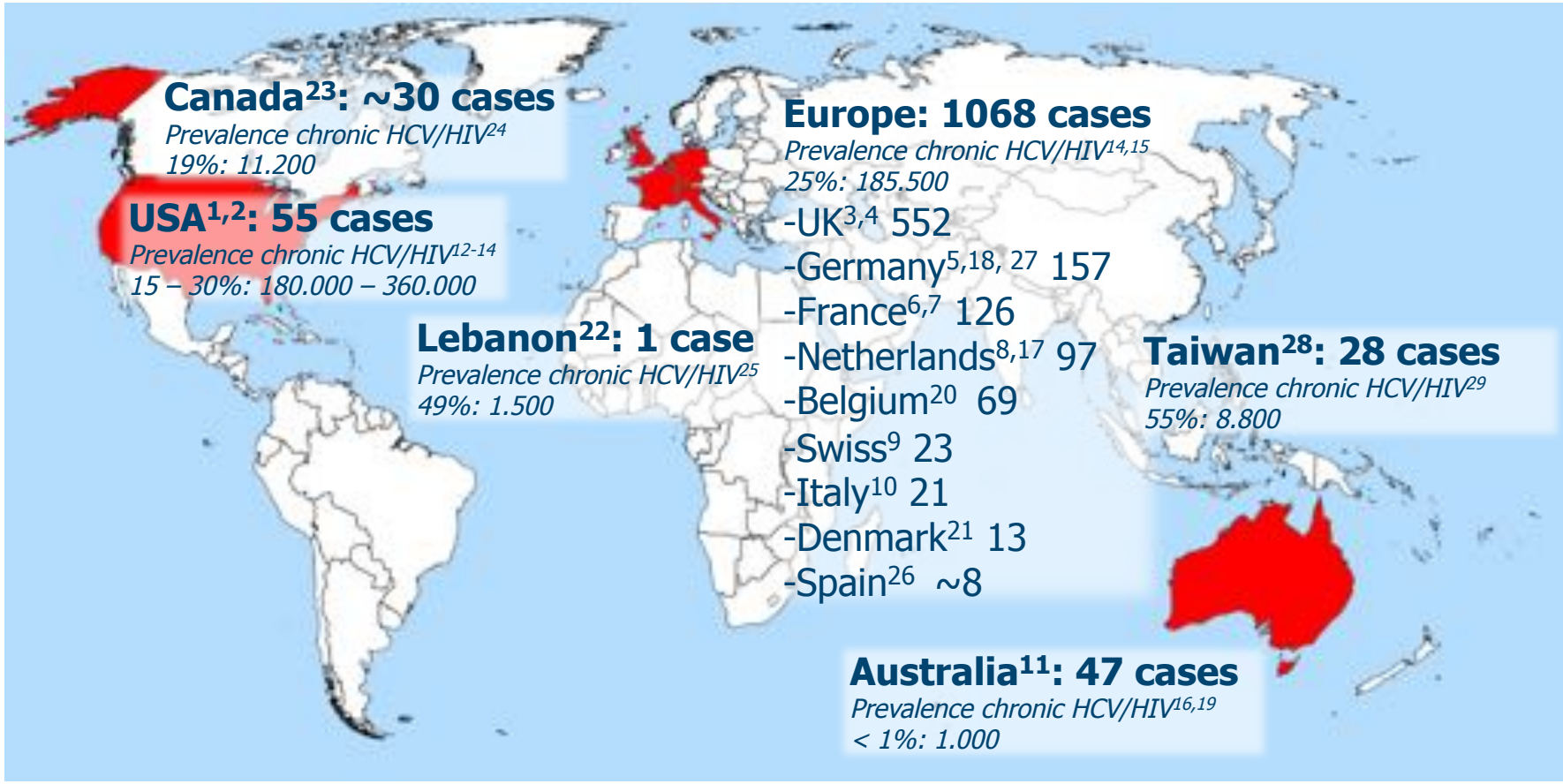
Why do you not want to have hepatitis C and HIV

Why do you not want to have hepatitis C and HIV

- Transmission

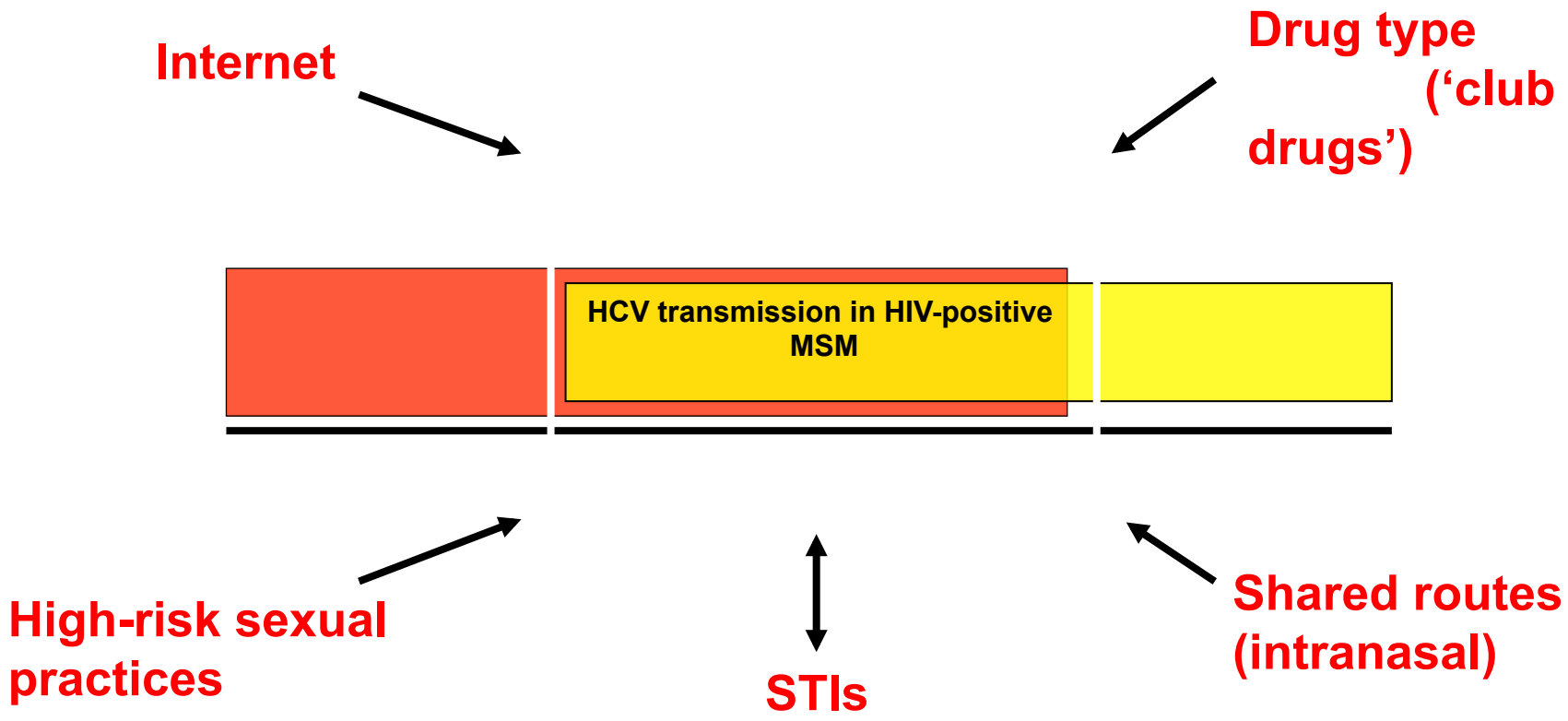


Acute HCV among HIV+ MSM



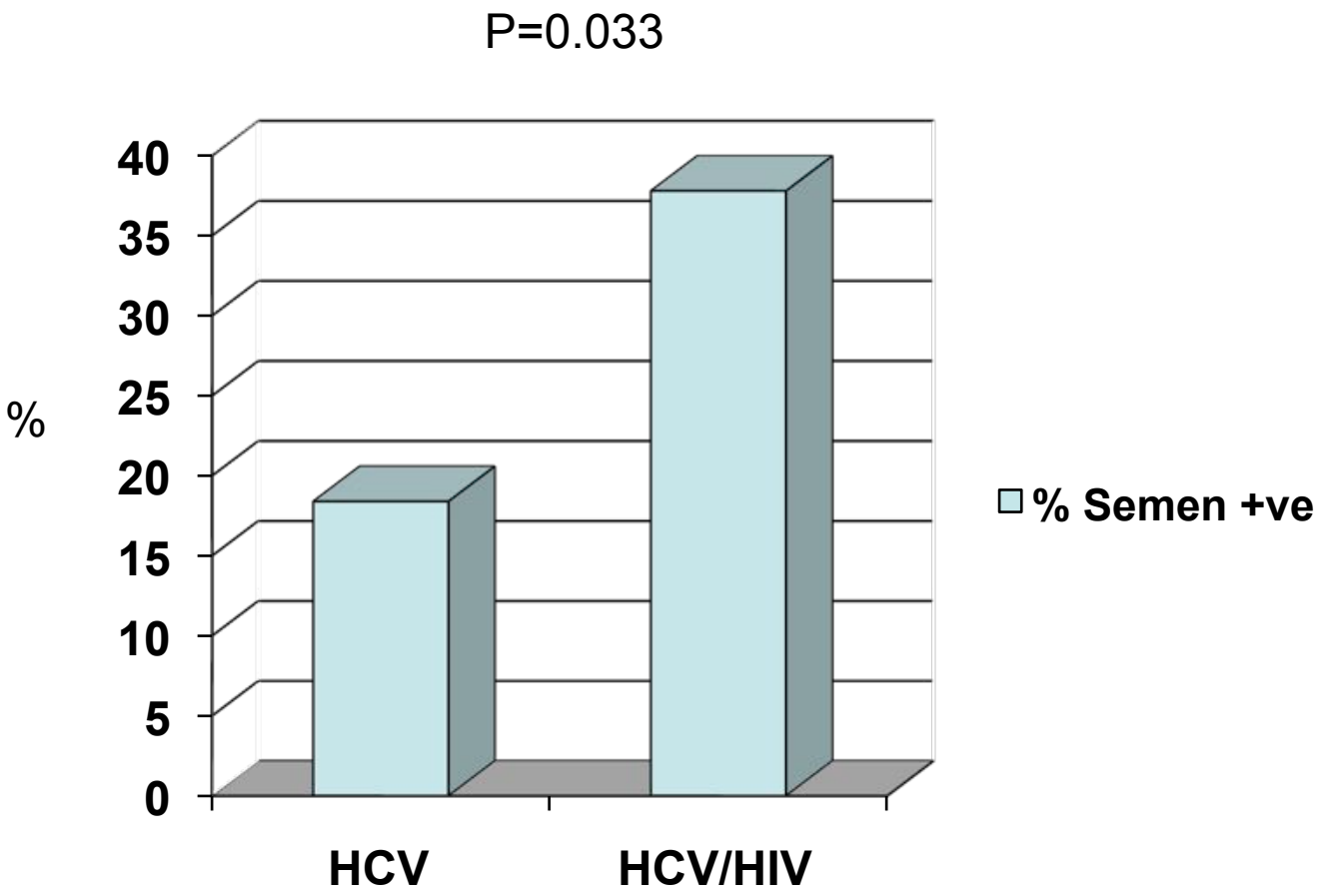

GRINDR
GRINDR
Meet Guys Near You
On The World's Largest All-Male
Location Based Social Network

Summary


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


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

Seminal Positivity for HCV



Briat AIDS 2005

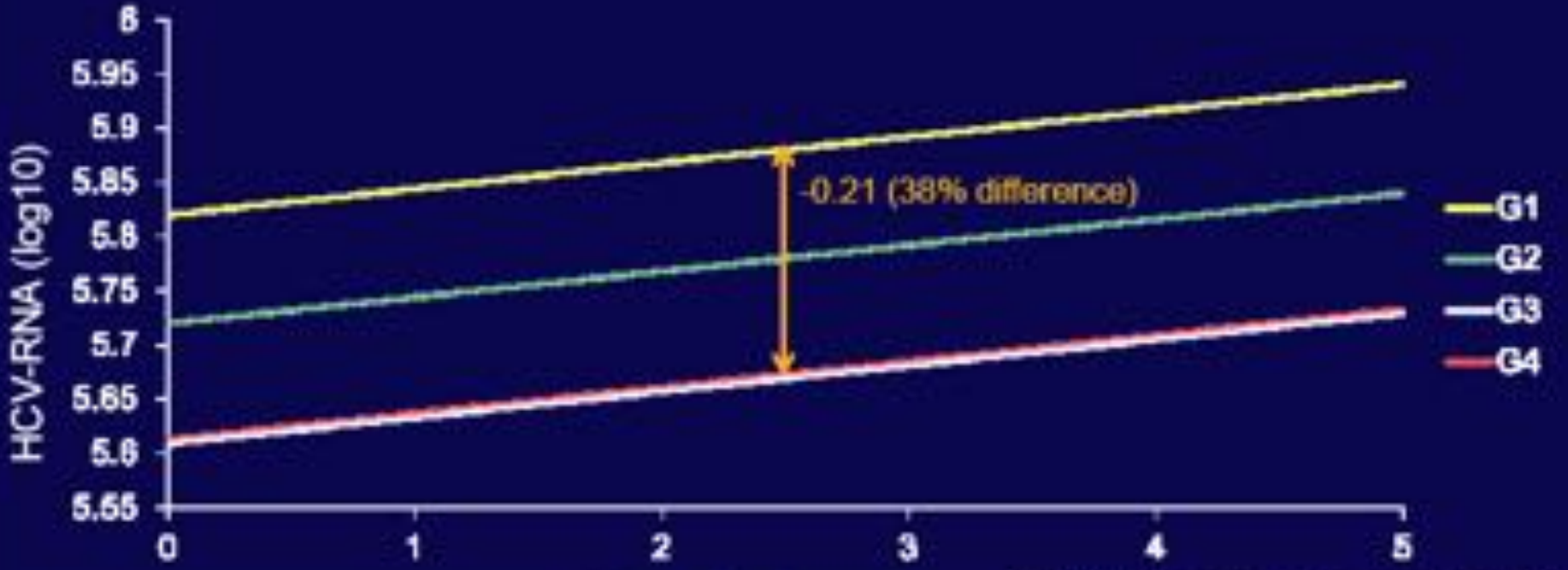
Hepatitis C Genotype

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

Results: Genotype

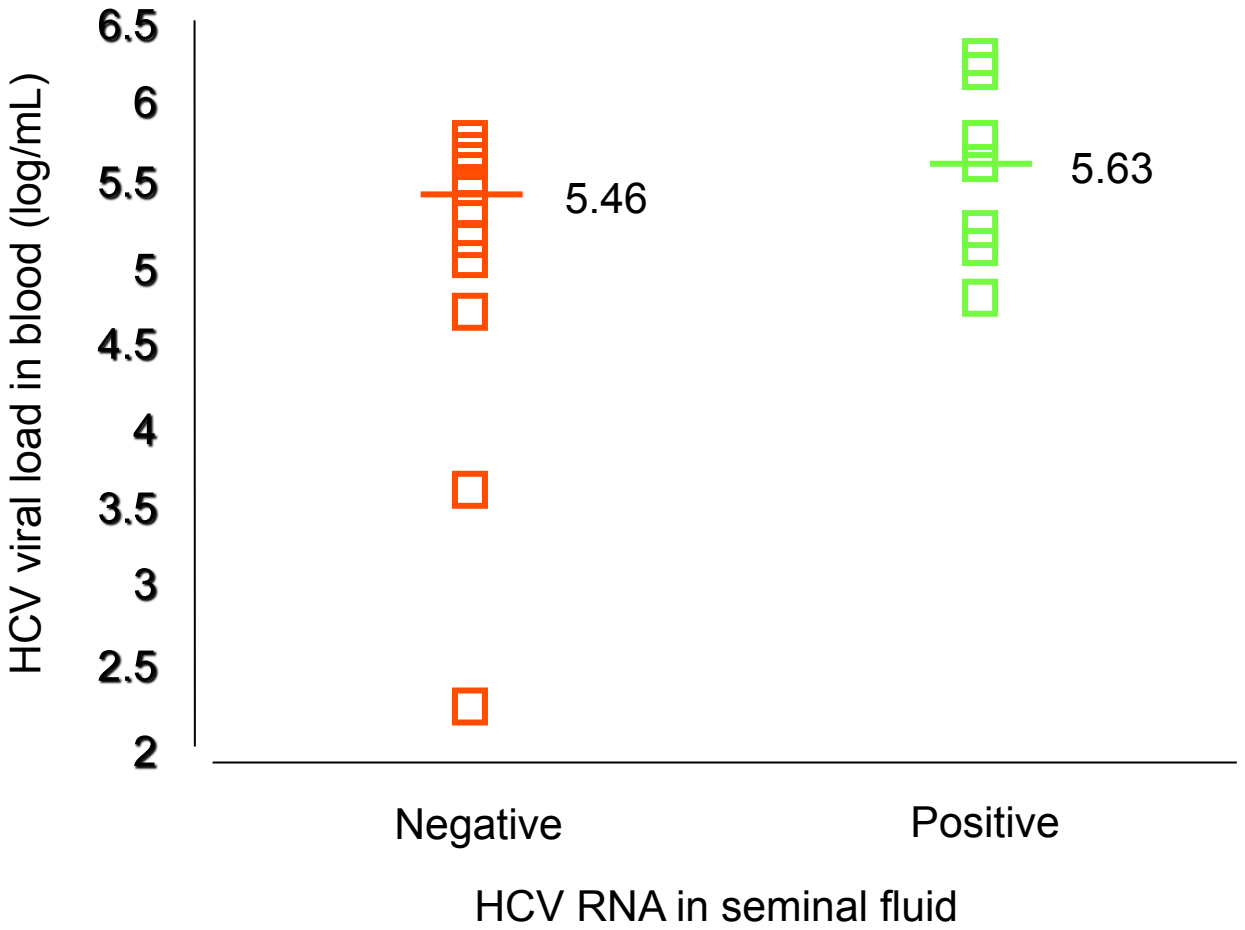
Multivariate Model*

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



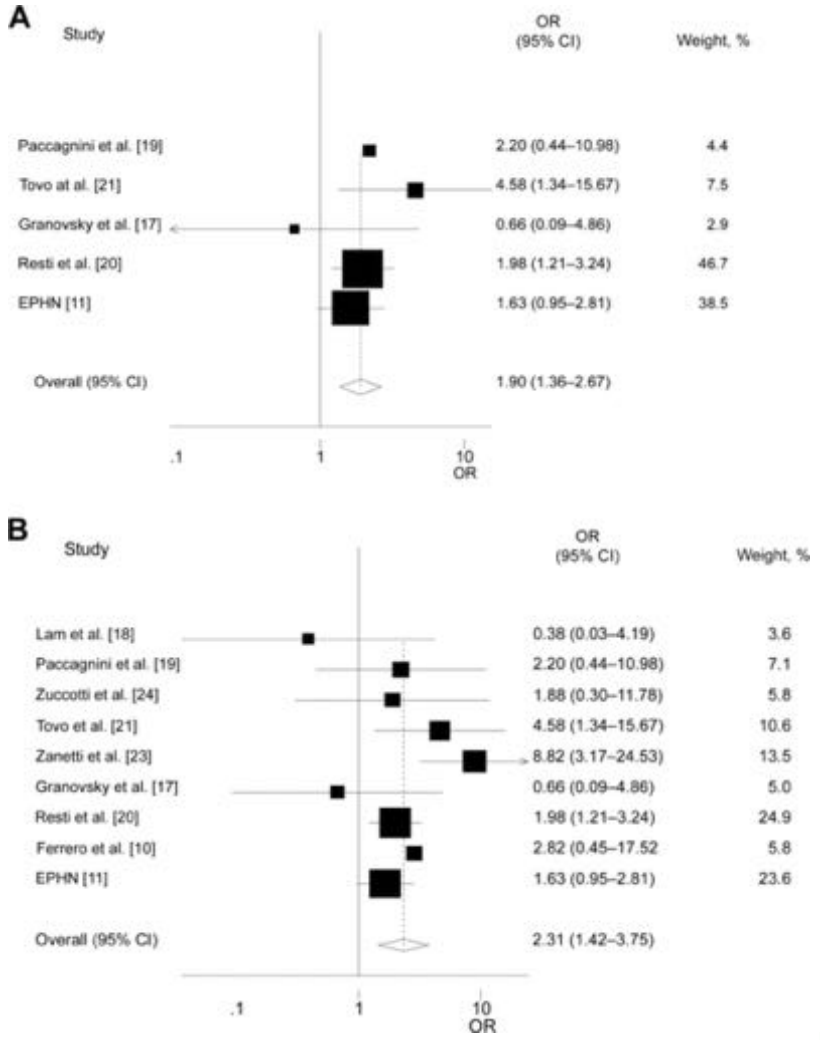
EuroSIDA

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



Briat AIDS 2005

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 have hepatitis C and HIV

- Transmission
- Stigma

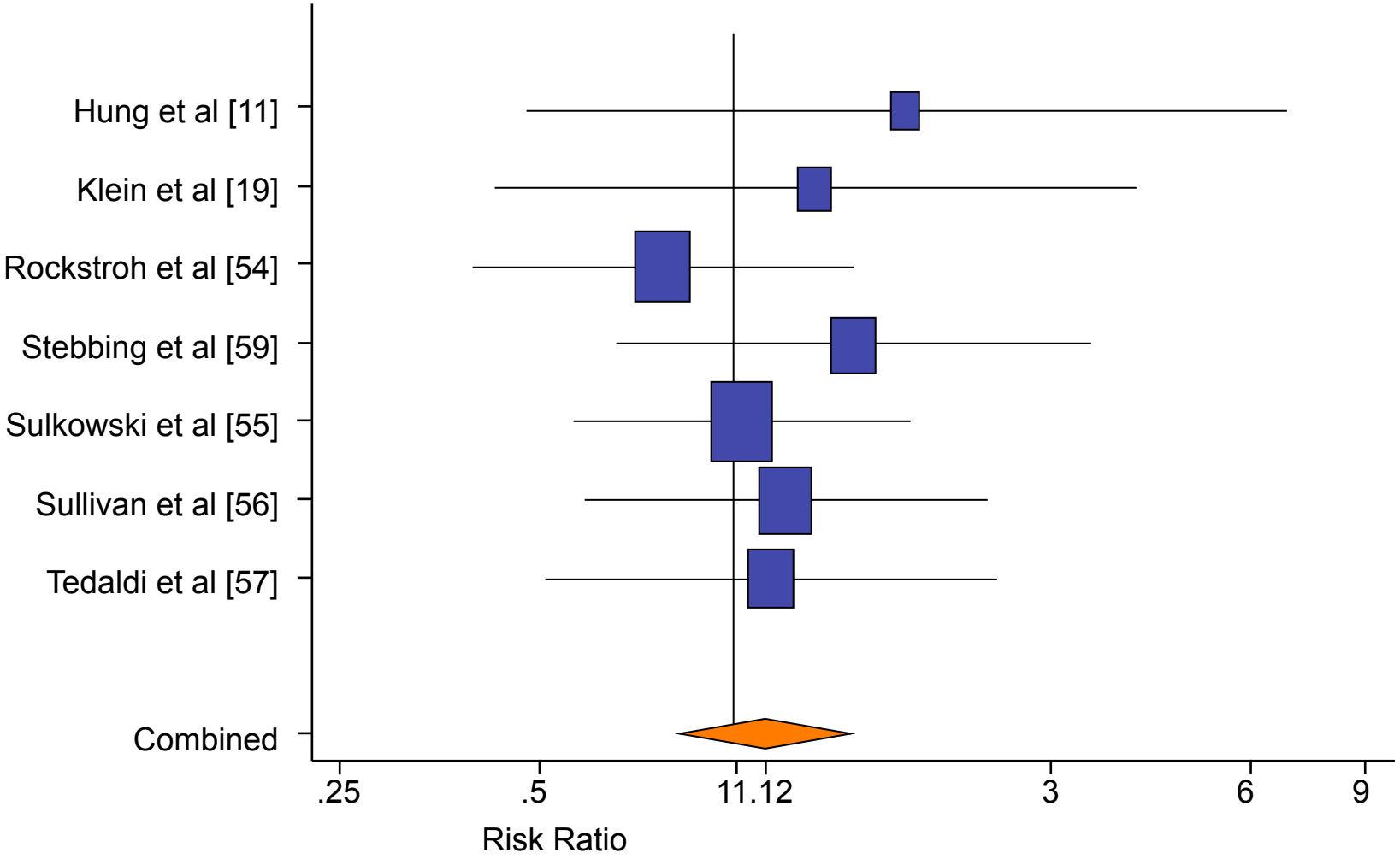

I Have
hiv
JOE BOXER
JOE BOXER
JOE BOXER

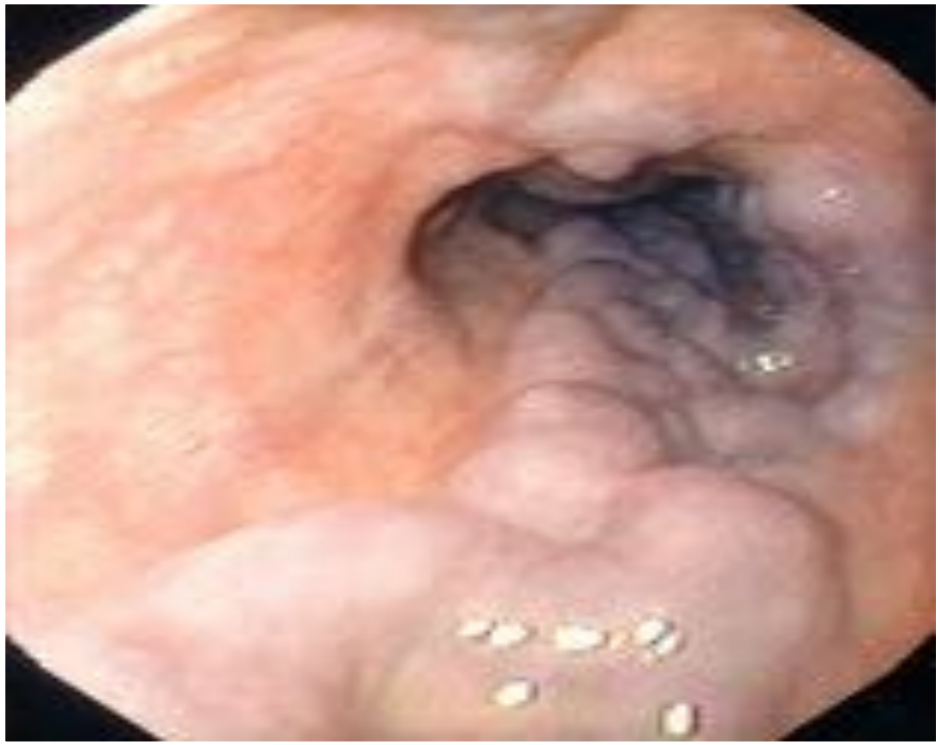

LOVE·MY·VIRUS

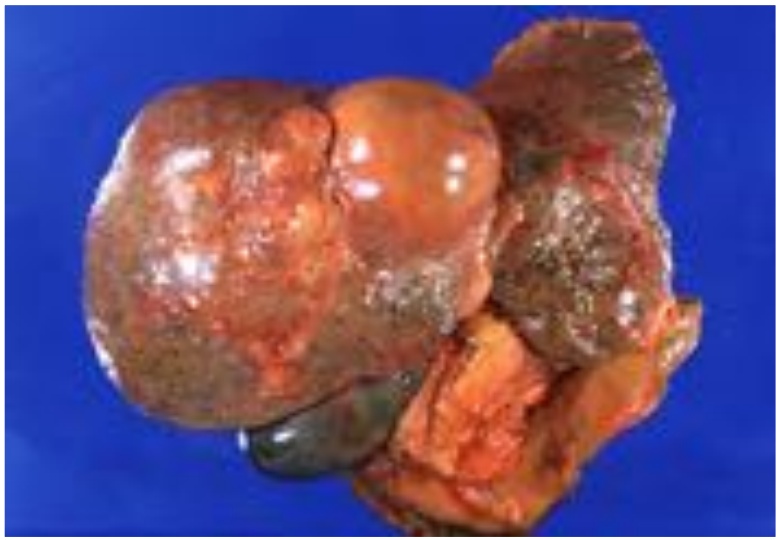
Why do you not want to have hepatitis C and HIV

- Transmission
- Stigma
- More Rapid Progression of disease

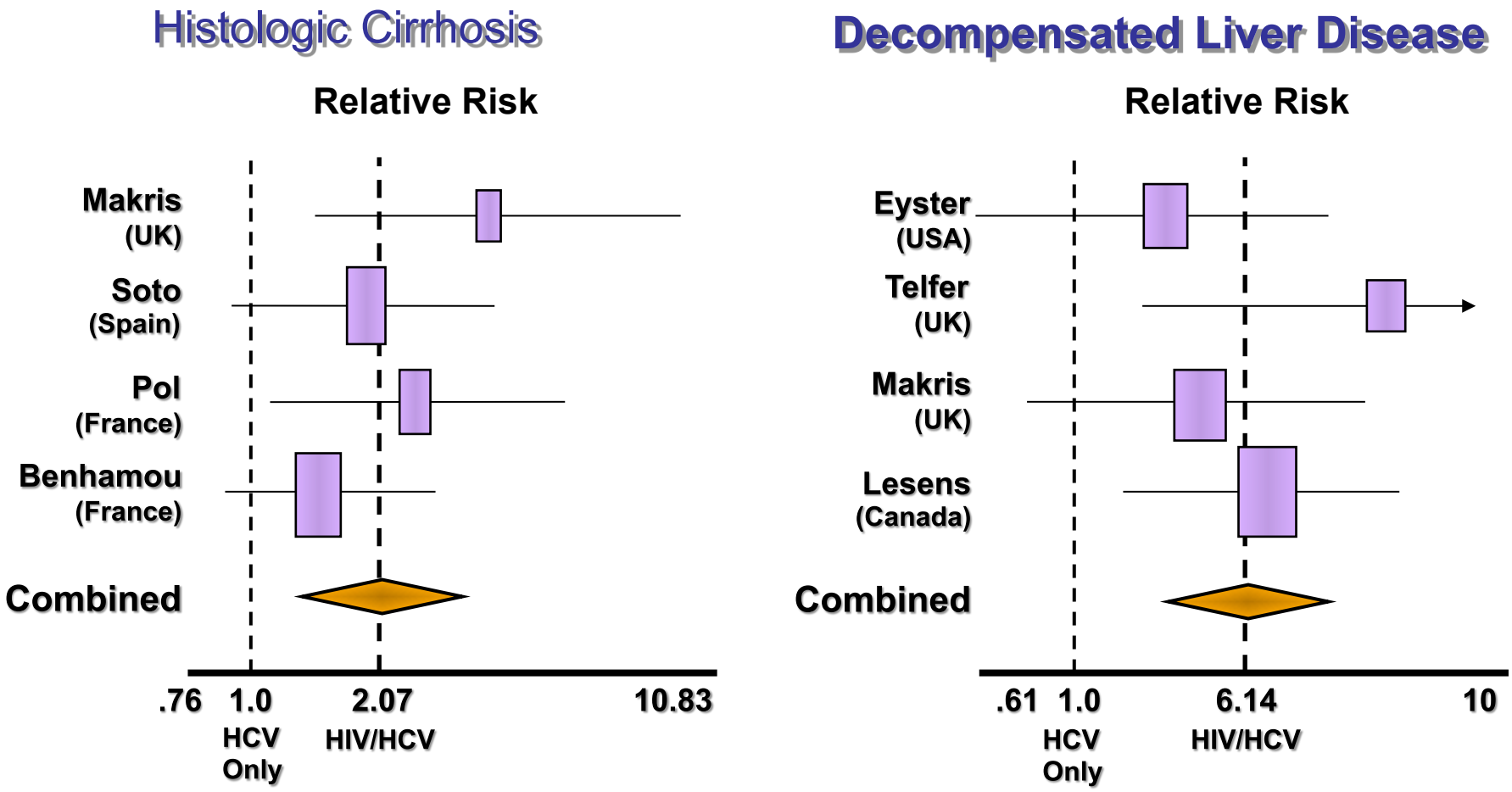
No Association of Hepatitis C with AIDS Defining Events







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

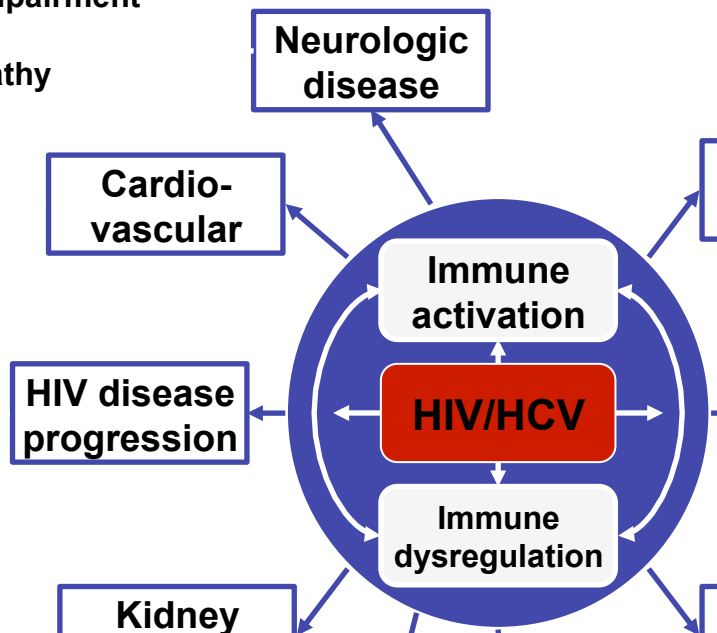


Graham CS, et al. *CID*. 2001;33:562-569.

Why do you not want to have hepatitis C and HIV

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

HIV/HCV co-infection may result in multi-systemic disorders



- Global cognitive impairment
- Cognitive-motor impairment
- Dementia
- Peripheral neuropathy

Neurologic disease

- Cerebrovascular disease
- Acute myocardial infarction

Cardio-vascular

- Diabetes mellitus
- Insulin resistance

Metabolic disorders

- Opportunistic infections
- Wasting syndrome

HIV disease progression

- Steatosis
- Fibrosis
- Cirrhosis
- End-stage liver disease
- Liver-related death

Liver disease

- Proteinuria
- Acute renal failure
- Chronic kidney disease

Kidney disease

- Microbial translocation

GI tract

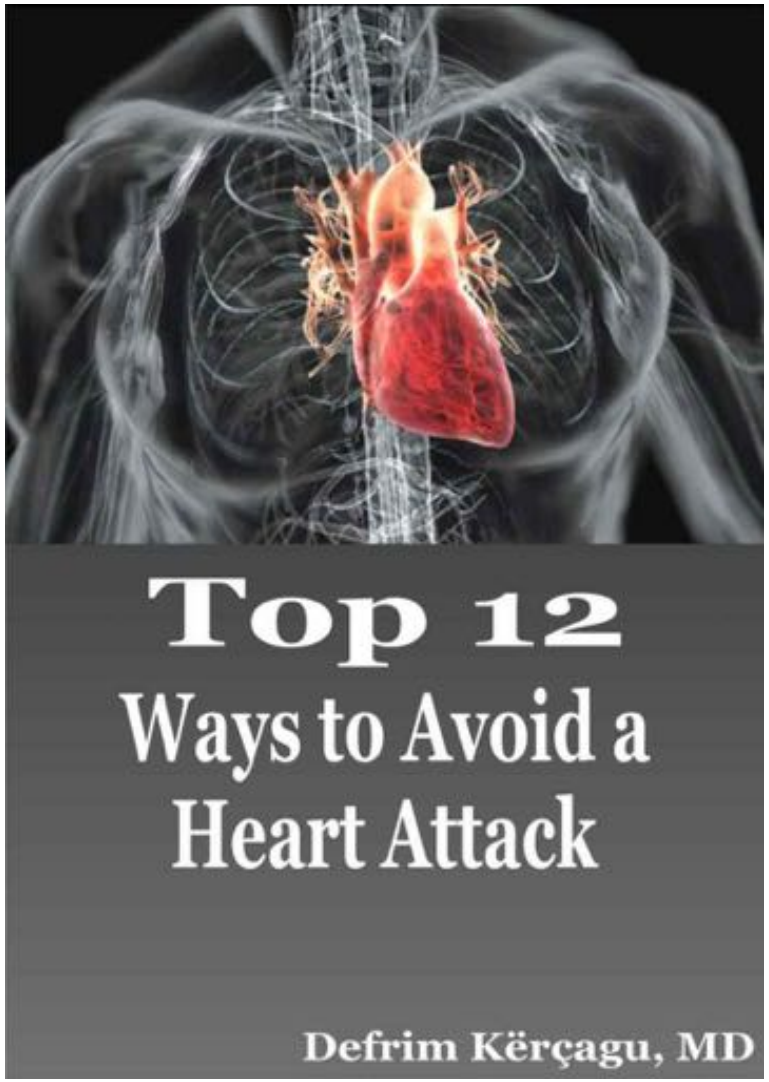
- Osteonecrosis
- Osteoporosis
- Bone fracture

Bone disorders

- CD4 apoptosis
- Abnormal T-cell responses and cytokine production
- Cytotoxic T-cell accumulation in liver
- CD4 recovery post-HAART
- Severe immunodeficiency

GI: gastrointestinal; HAART: highly active antiretroviral therapy

Operskalski EA & Kovacs A. Curr HIV/AIDS Rep 2011;8:12–22

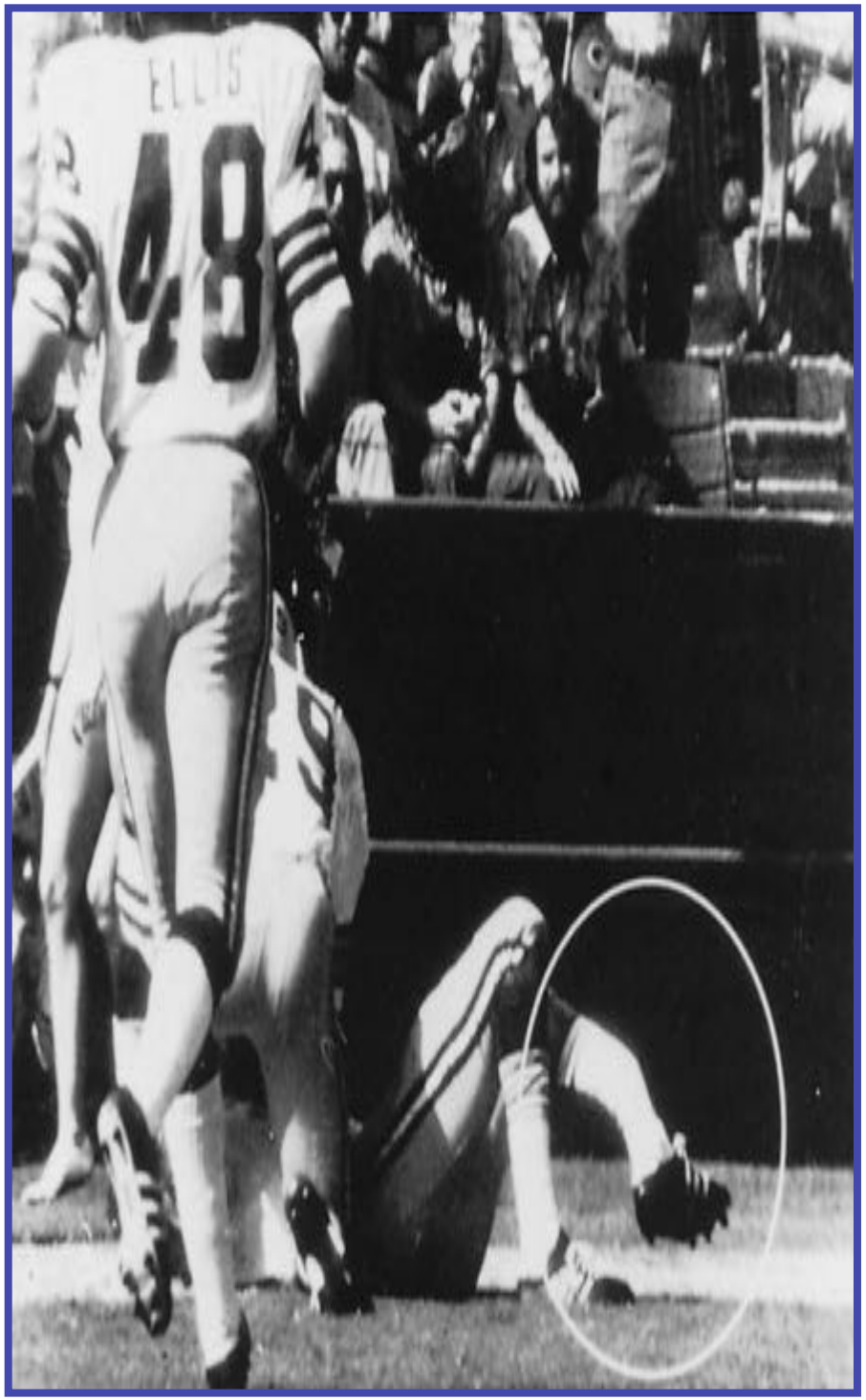

Top 12
Ways to Avoid a
Heart Attack
Defrim Kërçagu, MD

DIABETES

The Essential Guide

Need – 2 – Know

Sue Marshall


ELLIS
48


CM 1 2 3 4 5

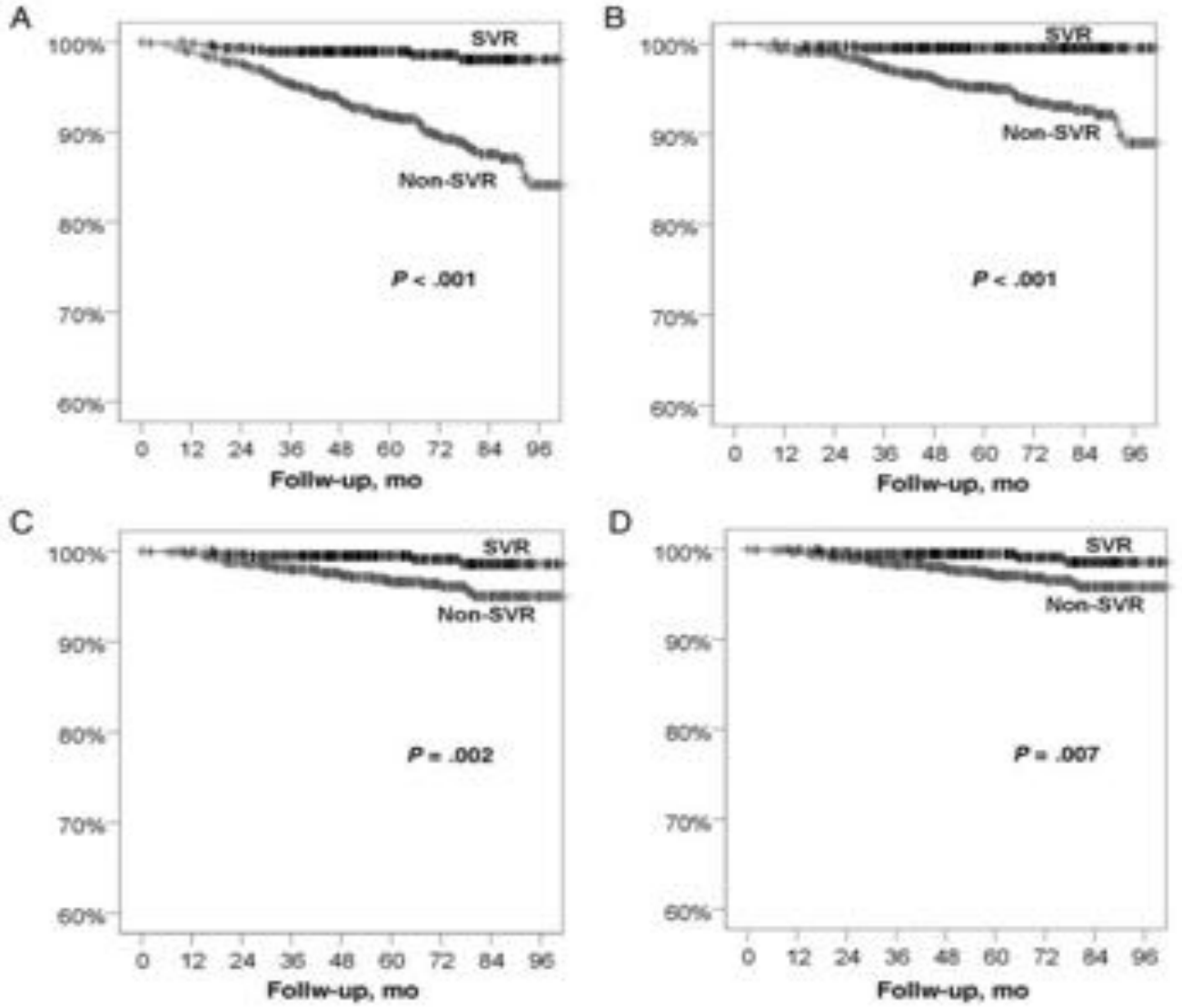
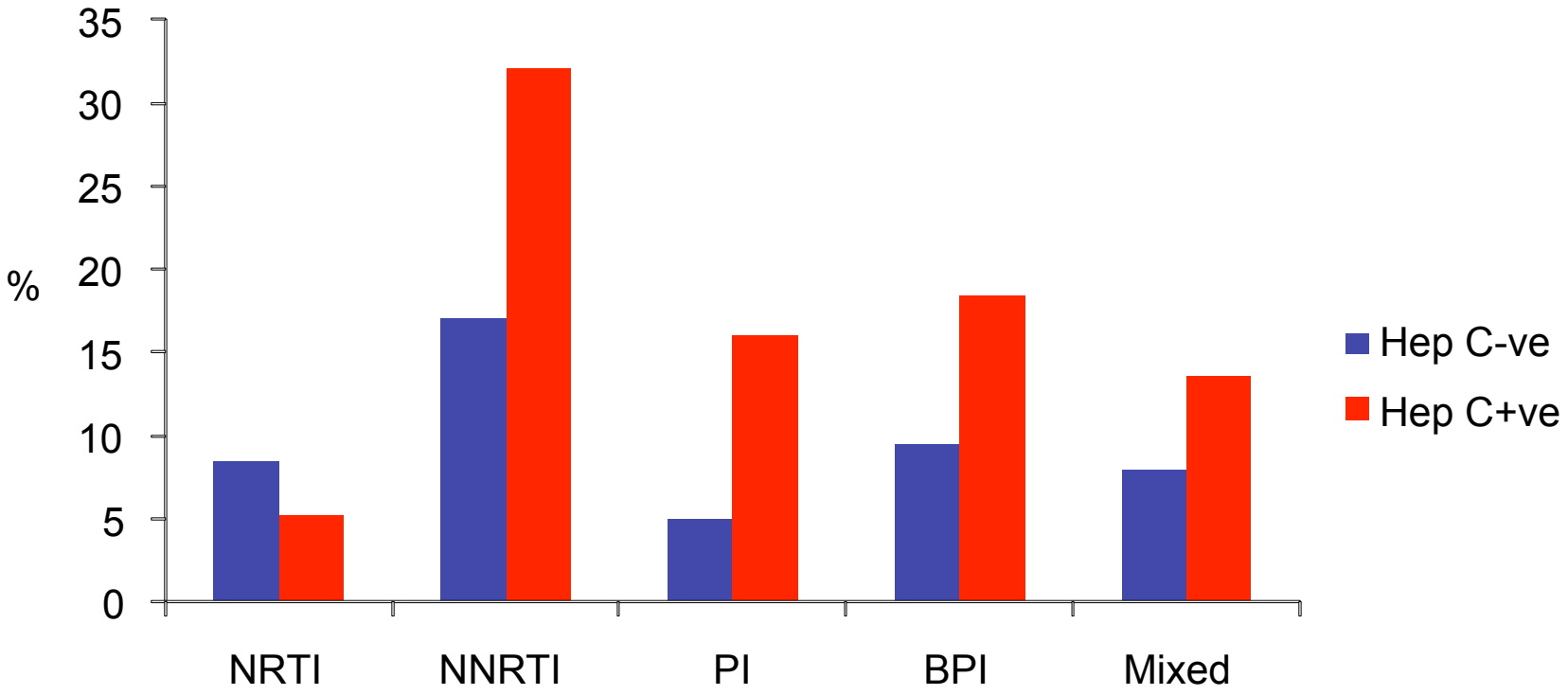


Figure 1. Kaplan-Meier curves showing the occurrence of overall deaths (*A*), liver-related deaths (*B*), non–liver related deaths (*C*), and non–liver-related, non–AIDS-related deaths (*D*) in 1599 patients coinfected with human immunodeficiency virus and hepatitis C virus, with or without sustained virological response after therapy with interferon plus ribavirin. Abbreviation: SVR, sustained virological response.

Why do you not want to have hepatitis C and HIV

- 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 have hepatitis C and HIV

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


SPIRAL


THINK
Positive

HCV: Probability of the presence of viral variants

Hepatitis C virus:	~9600 nucleotides
Error rate during replication:	~10^{-4} – 10^{-5} per copied nucleotide
Viral turnover:	~10^{12} virions produced every day

Number of nucleotide change	Probability of generation after one round of replication	Number of virions with nucleotide change(s) produced per day	Number of all possible nucleotide mutants	Fraction of all possible mutants created per day
0	91%	9.1×10^{11}		
1	8.7%	8.7×10^{10}	2.9×10^{4}	1
2	0.4%	4.2×10^{9}	4.1×10^{8}	1
3	0.001%	1.3×10^{8}	4.0×10^{12}	3.4×10^{-5}

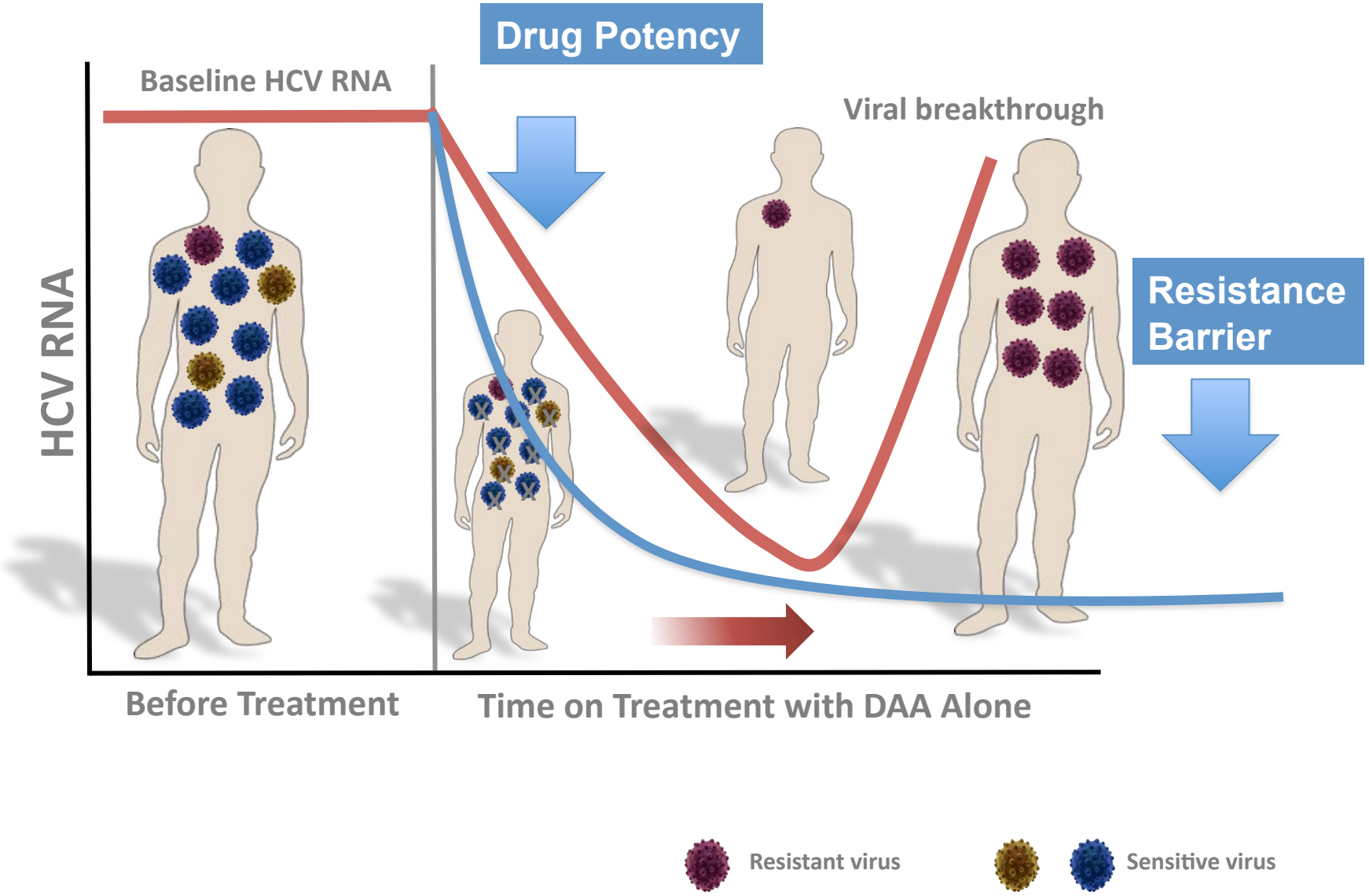
- HCV genome ~ 9600 nucleotides; the average number of changes per genome is 0.096 per replication cycle
- Before treatment, a new virion has a probability of 91% to carry an unmutated genome and 8.7% to carry one substitution

Not all variants survive

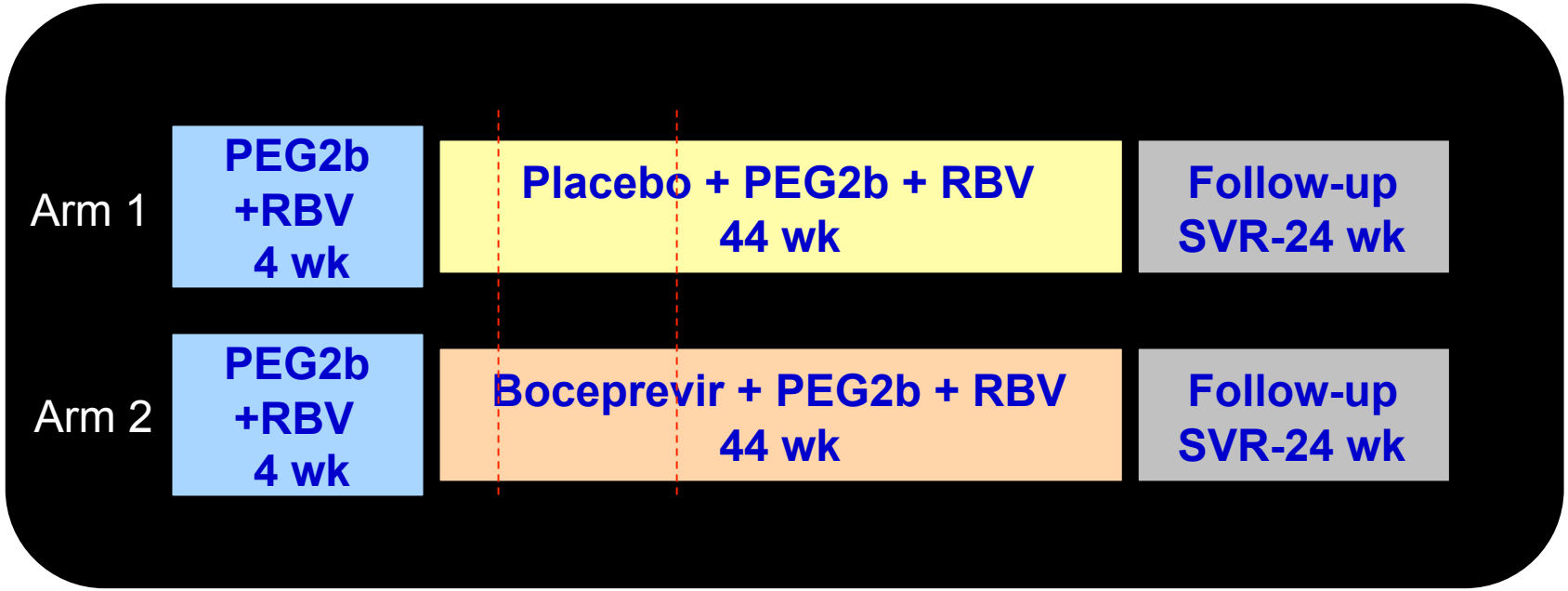
- Dead mutations (variants that can not replicate)
- Immune sensitive mutations (variants eliminated by the immune system)

Rong L, et al, Sci Transl Med 2010;2:30ra32; Neumann AU, et al. Science 1998;282:103–7
Domingo E, et al. Viral Hepatitis Rev 1996;2:247–61; Cuevas JM, et al. J Virol 2009;83:5760–4

Emergence of Pre-existing Resistant Variants During Treatment with DAA

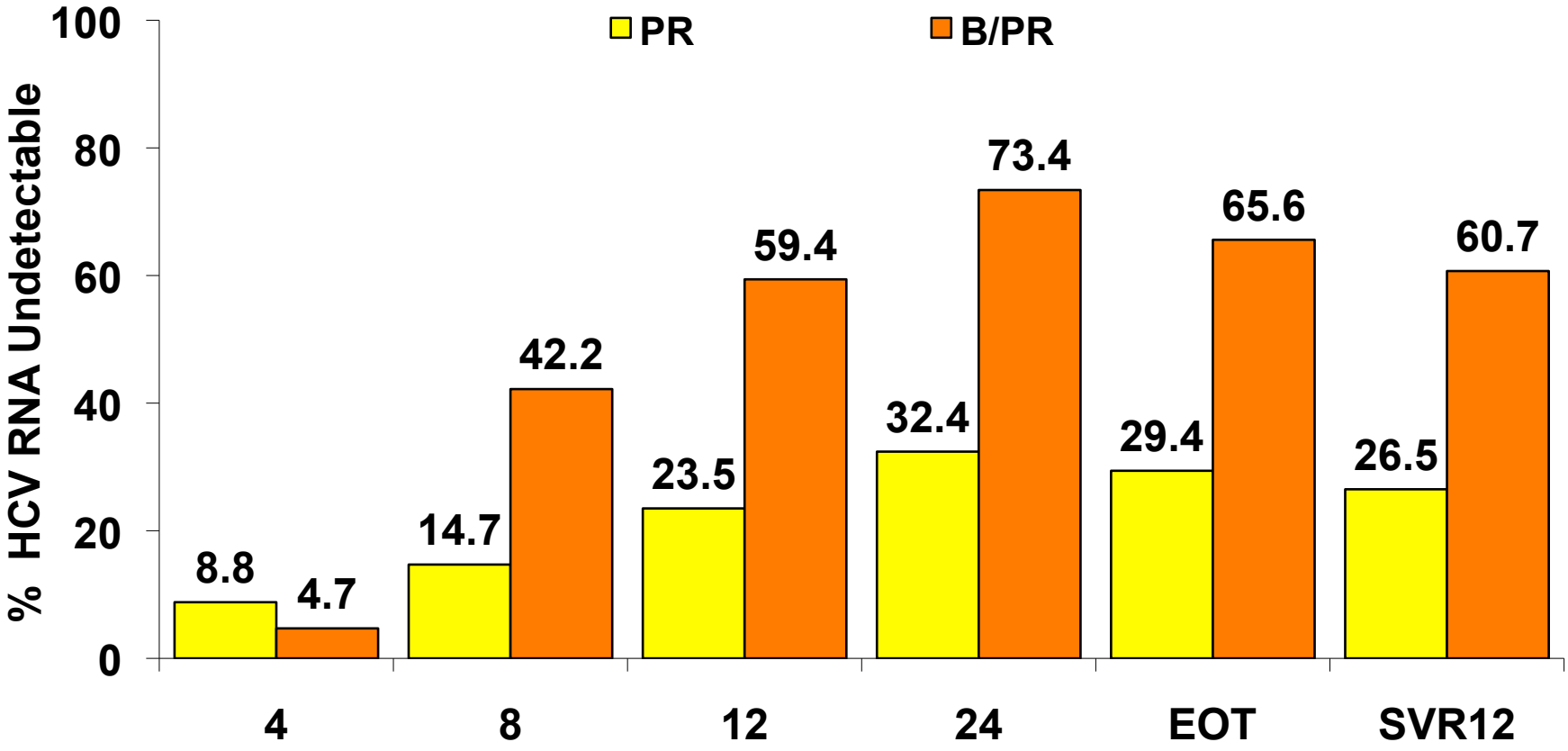


Study Design



- 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†

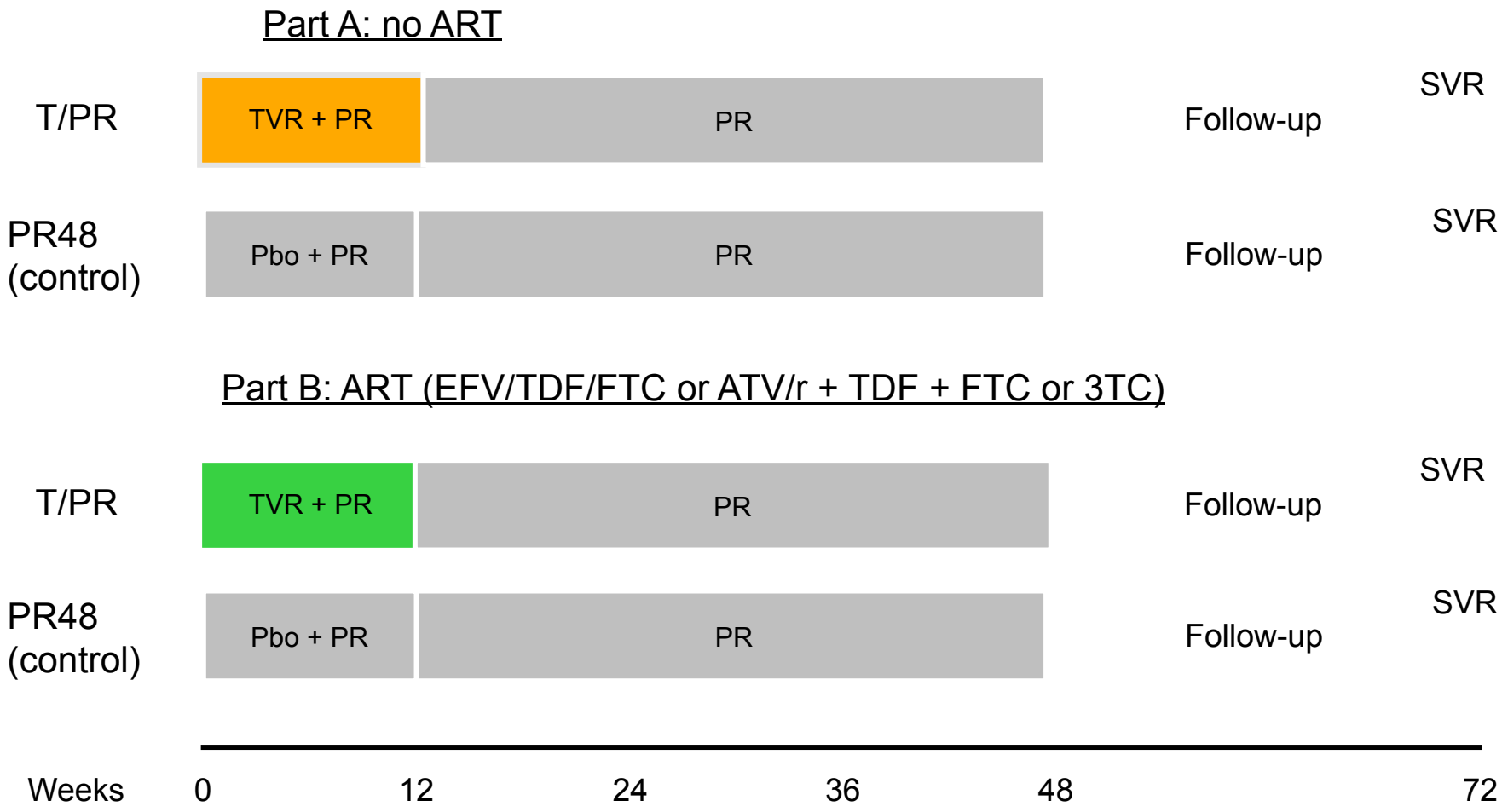


† Three patients undetectable at FW4 have not yet reached FW12 and were not included in SVR12 analysis.

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

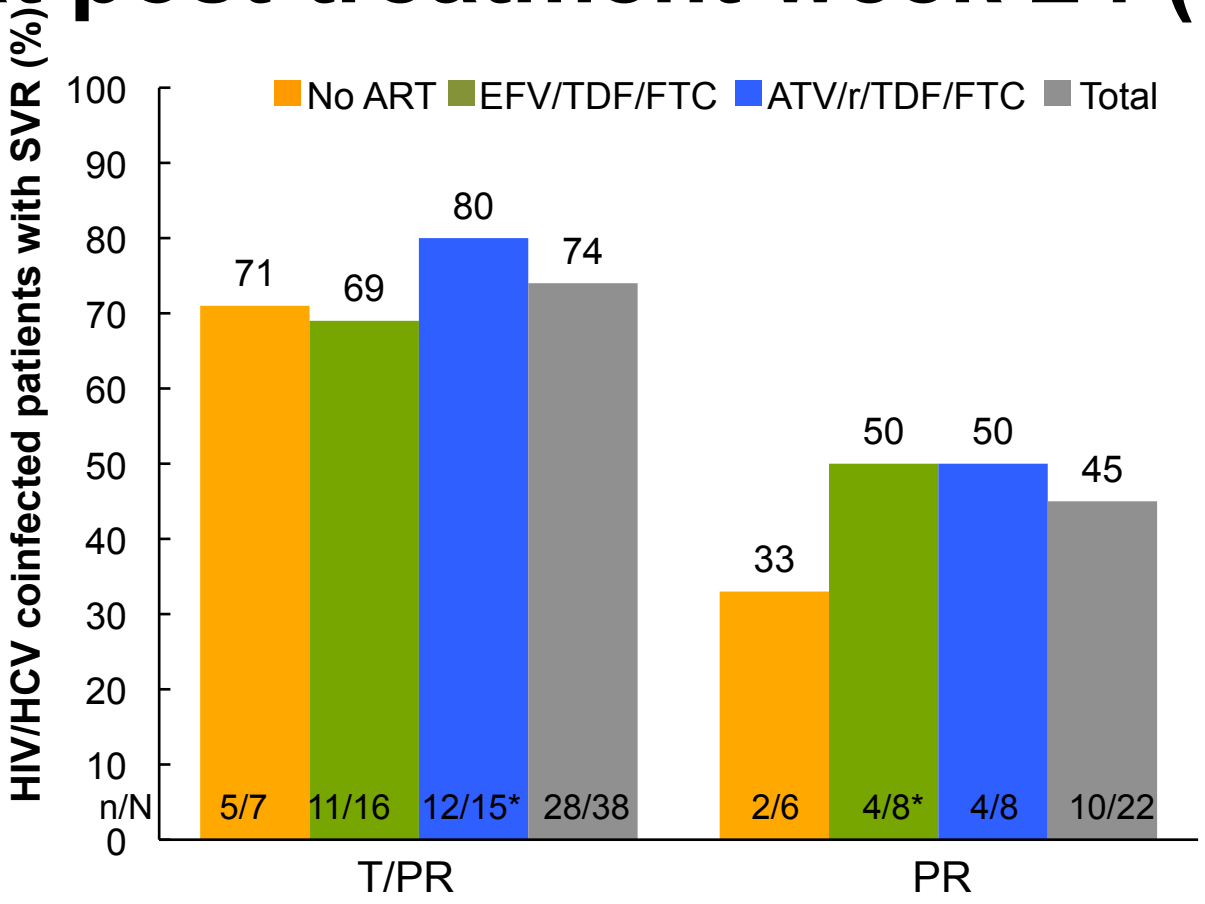
;

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)

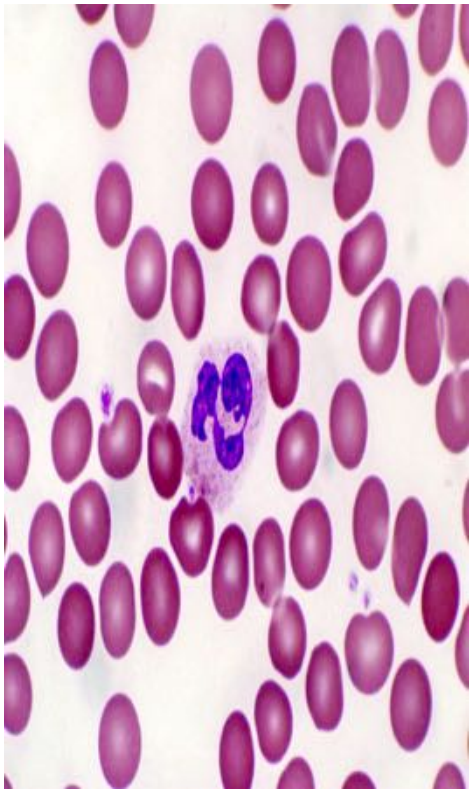
HIV/HCV coinfected patients: SVR at post-treatment week 24 (SVR_{24})



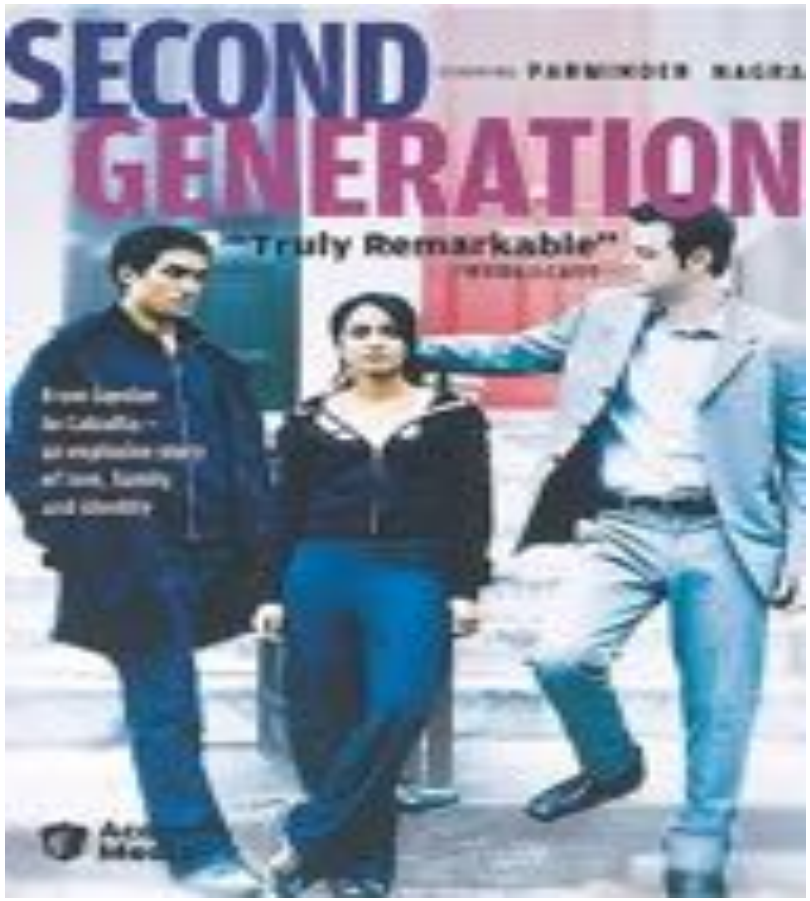
T/PR, telaprevir in combination with peginterferon alfa-2a and ribavirin; PR, peginterferon alfa-2a and ribavirin

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

Boceprevir



Telaprevir


SECOND
GENERATION
"Truly Remarkable"

DAA Classes and Subclasses

Drug Class	Subclass	Potency	Resistance Barrier
Protease inhinbitors	1st Generation first wave i.e. Telaprevir/Boceprevir	**Medium- Low**	**Low**
	1st Generation 2nd wave i.e. Faldaprevir/Simeprevir/Asunaprevir ABT450/r	**Medium**	**Low**
	2nd Generation MK5172 ABT 493	**High**	**High except HCVG3**
NS5a Inhibitor	1st Generation Daclatasvir, Ledipasvi,r ABT 267	**High**	**Medium- High except HCV G3 & 1a**
	2nd Generation MK 8742 GS 5816 ABT530	**High**	**High**
NN Polymerase Inhibitors	ABT 333 GS 9669 Deleobuvir BMS 791325	**Low- Medium**	**Low**
Nucleos/tides Polymerase inhibitors	1st Generation: Mericitabine	**Low**	**High**
	2nd Generation : Sofosbuvir	**High Lower in HCV G1b and 3**	**High**

DAA Classes and Subclasses

Drug Class	Subclass	Potency	Resistance Barrier
Protease inhinbitors	1st Generation first wave i.e. Telaprevir/Boceprevir	**Medium- Low**	**Low**
	1st Generation 2nd wave i.e. Faldaprevir/Simeprevir/Asunaprevir ABT450/r	**Medium**	**Low**
	2nd Generation MK5172 ABT 493	**High**	**High except HCVG3**
NS5a Inhibitor	1st Generation Daclatasvir, Ledipasvi,r ABT 267	**High**	**Medium- High except HCV G3 & 1a**
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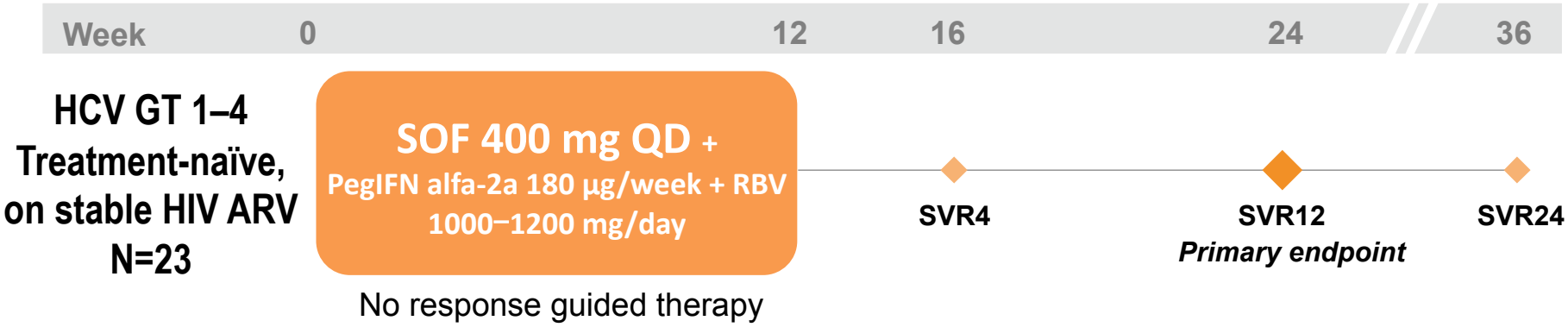
Nucleos/tides Polymerase inhibitors	1st Generation: Mericitabine	**Low**	**High**
	2nd Generation : Sofosbuvir	**High Lower in HCV G1b and 3**	**High**

SOF + PegIFN + RBV in Treatment-Naïve HIV/HCV Co-infected Patients

Phase 2 Study 1910 Design

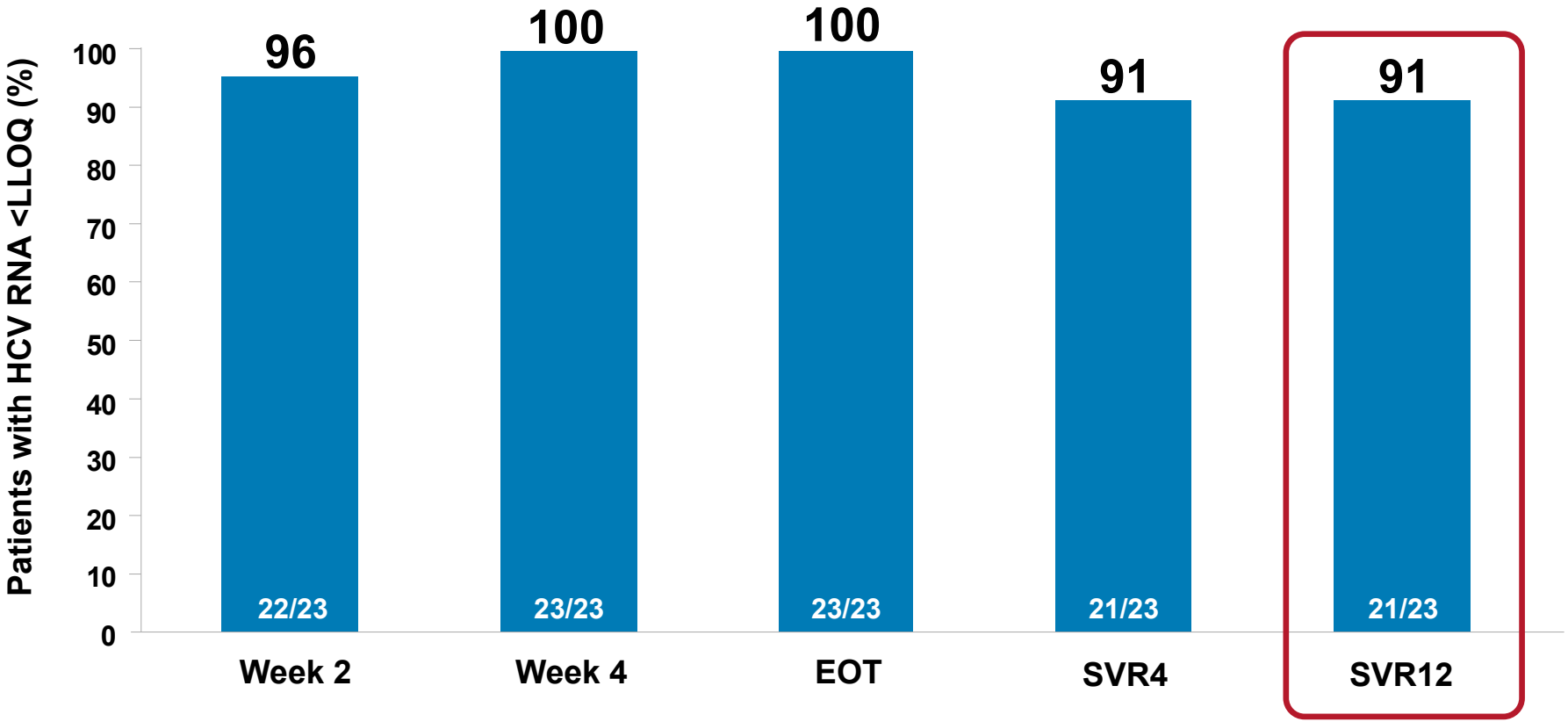
- Single-center, open-label, single-arm trial to assess the safety and efficacy of a 12-week course of SOF + PegIFN + RBV for the treatment of patients with chronic HCV, co-infected with HIV



Rodriguez-Torres M, et al. IDWeek 2013; San Francisco, CA. Poster #714

SOF + PegIFN + RBV in HIV/HCV Coinfection

Virologic Response and SVR12

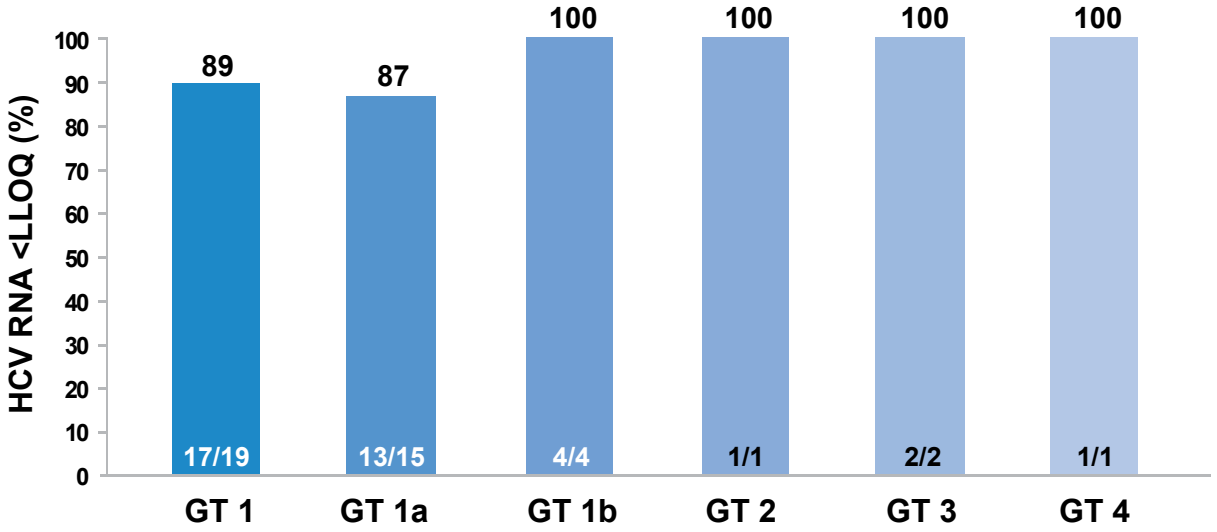


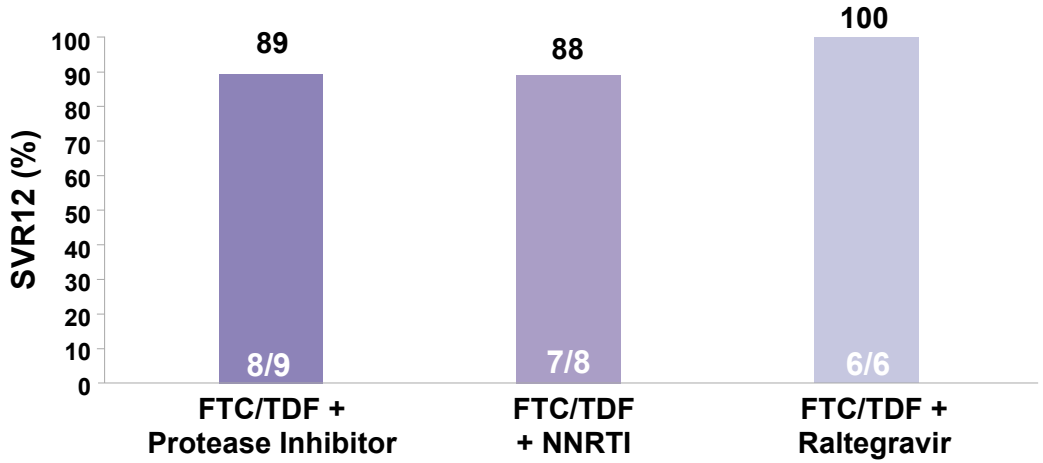
- There was no on-treatment HCV or HIV virologic breakthrough
- Relapse occurred in 1 patient and accounted for all virologic failures
- Two patients discontinued treatment early due to adverse events, one of whom achieved SVR12 after receiving 8 weeks of SOF + PegIFN + RBV

Rodriguez-Torres M, et al. IDWeek 2013; San Francisco, CA. Poster #714

SOF + PegIFN + RBV in HIV/HCV Coinfection

SVR12 According to HCV Genotype and HIV ARV Regimen





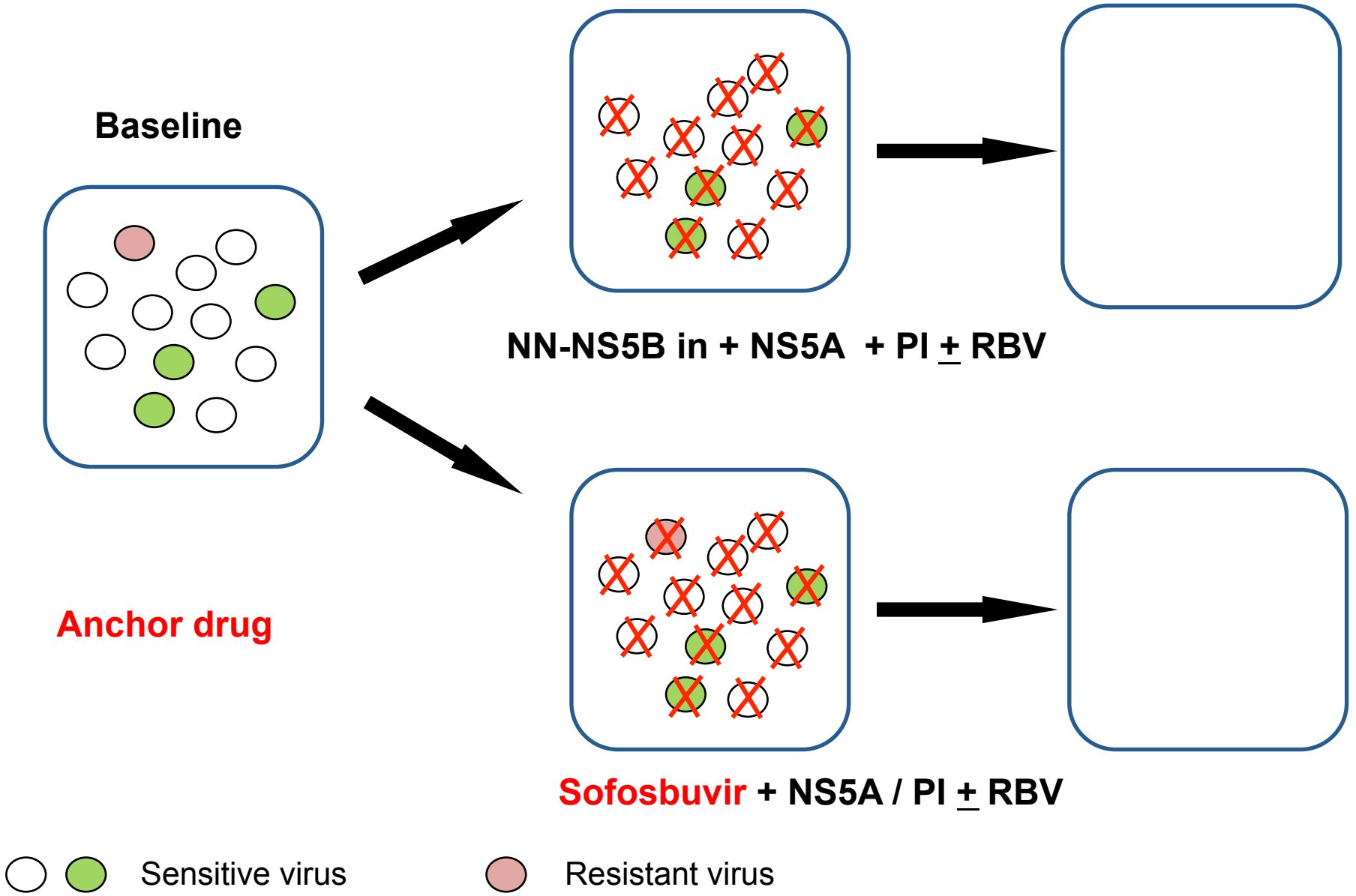
NNRTI, non-nucleoside reverse transcriptase inhibitor

Rodriguez-Torres M, et al. IDWeek 2013; San Francisco, CA. Poster #714

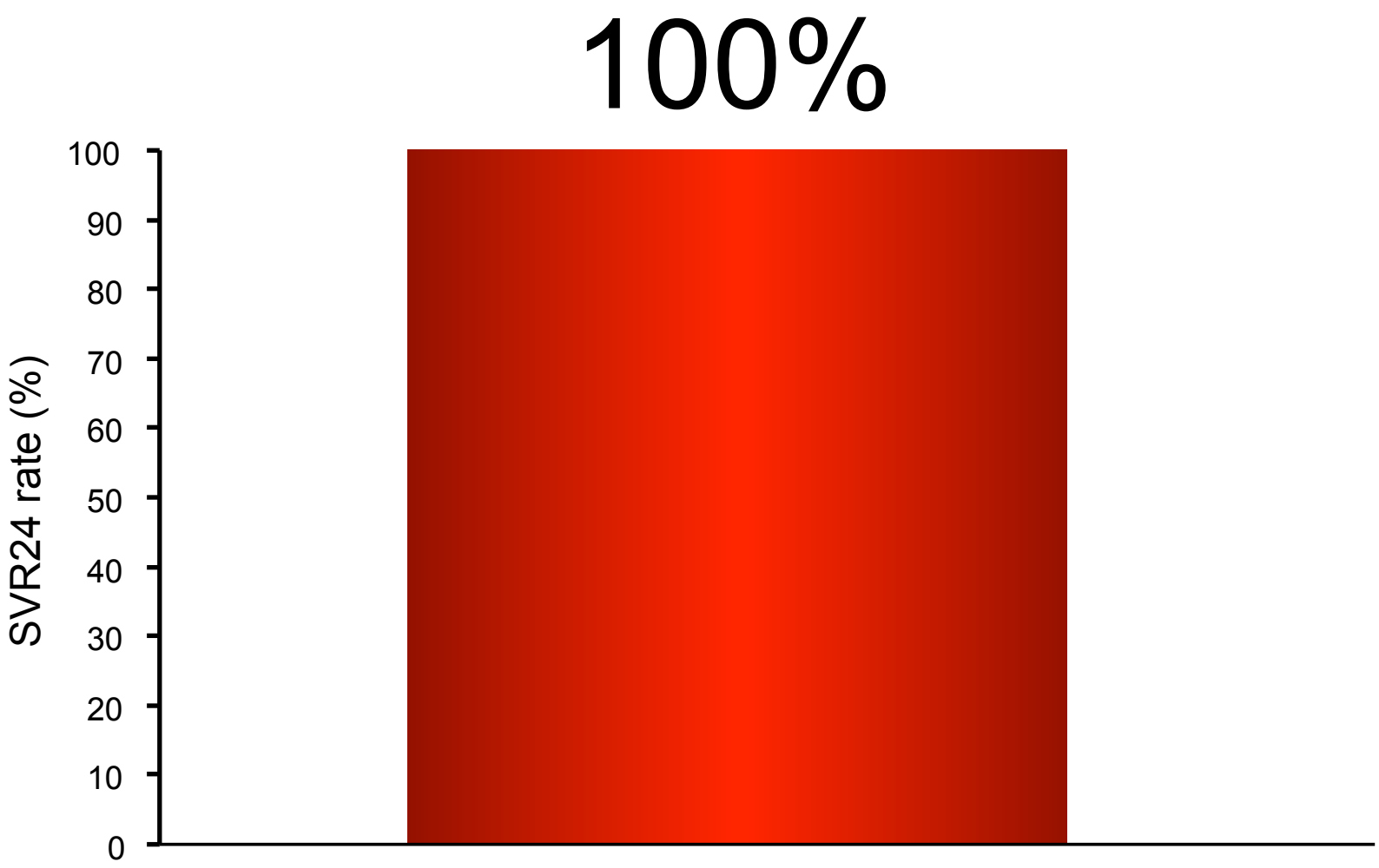

Rx
Interferon

Genetic barrier to resistance can be increased in HCV G1 by combination drug regimens

No relationship with IFN sensitivity no IFN related side effects



Summary of EASL 2014

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© EPA


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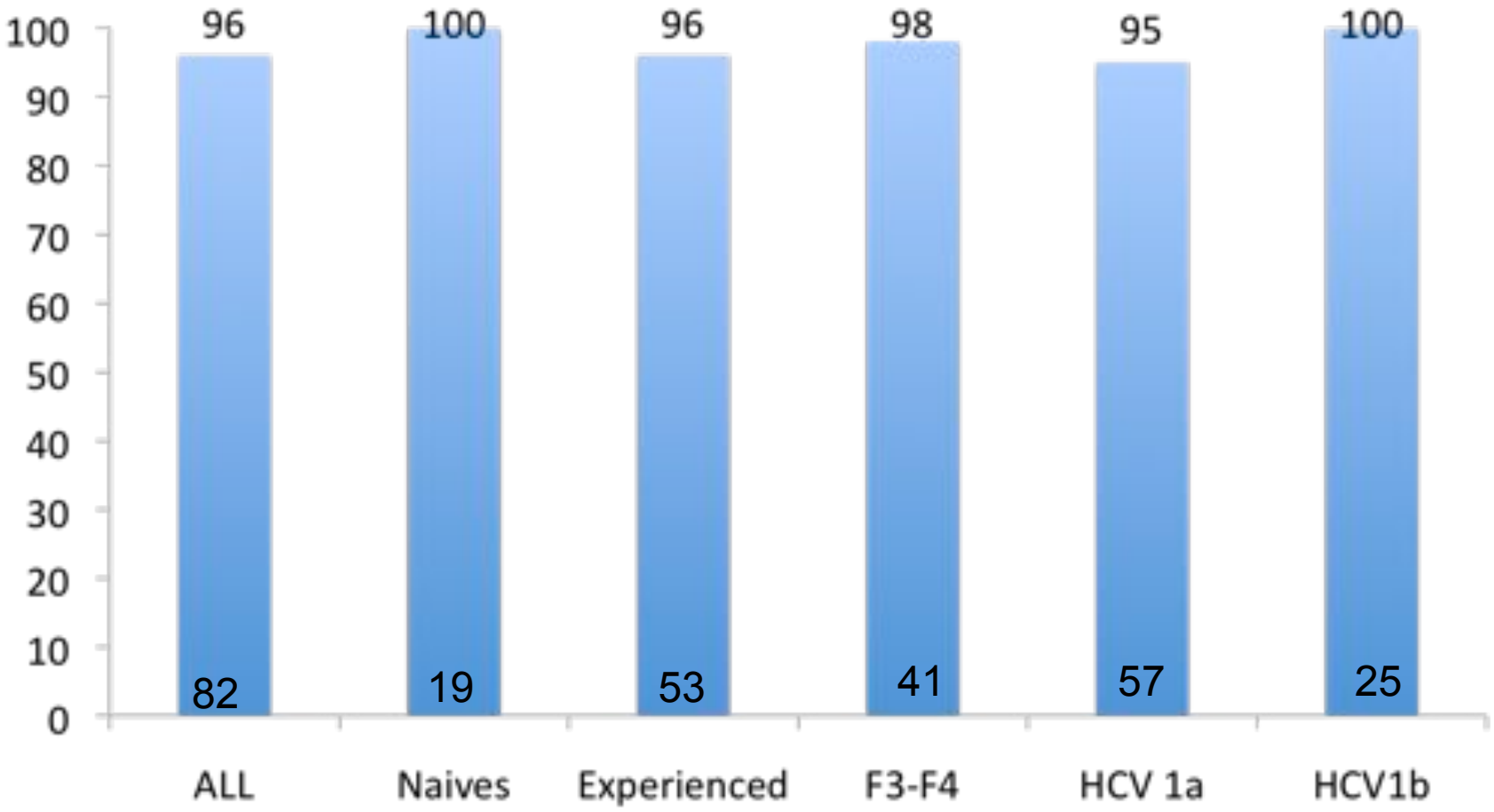
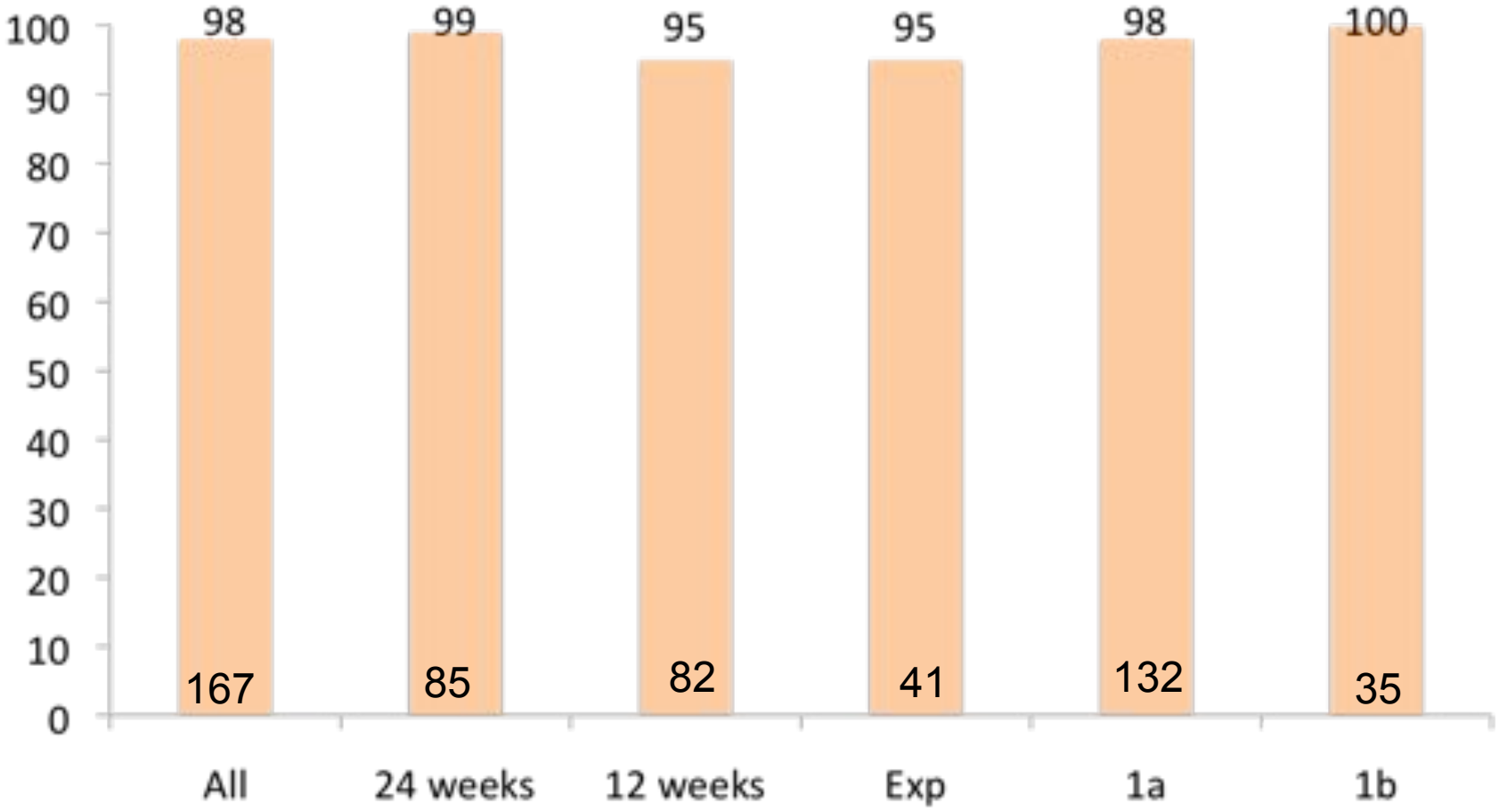
26
8

Sofosbuvir + Simeprevir ± RBV for 12 weeks



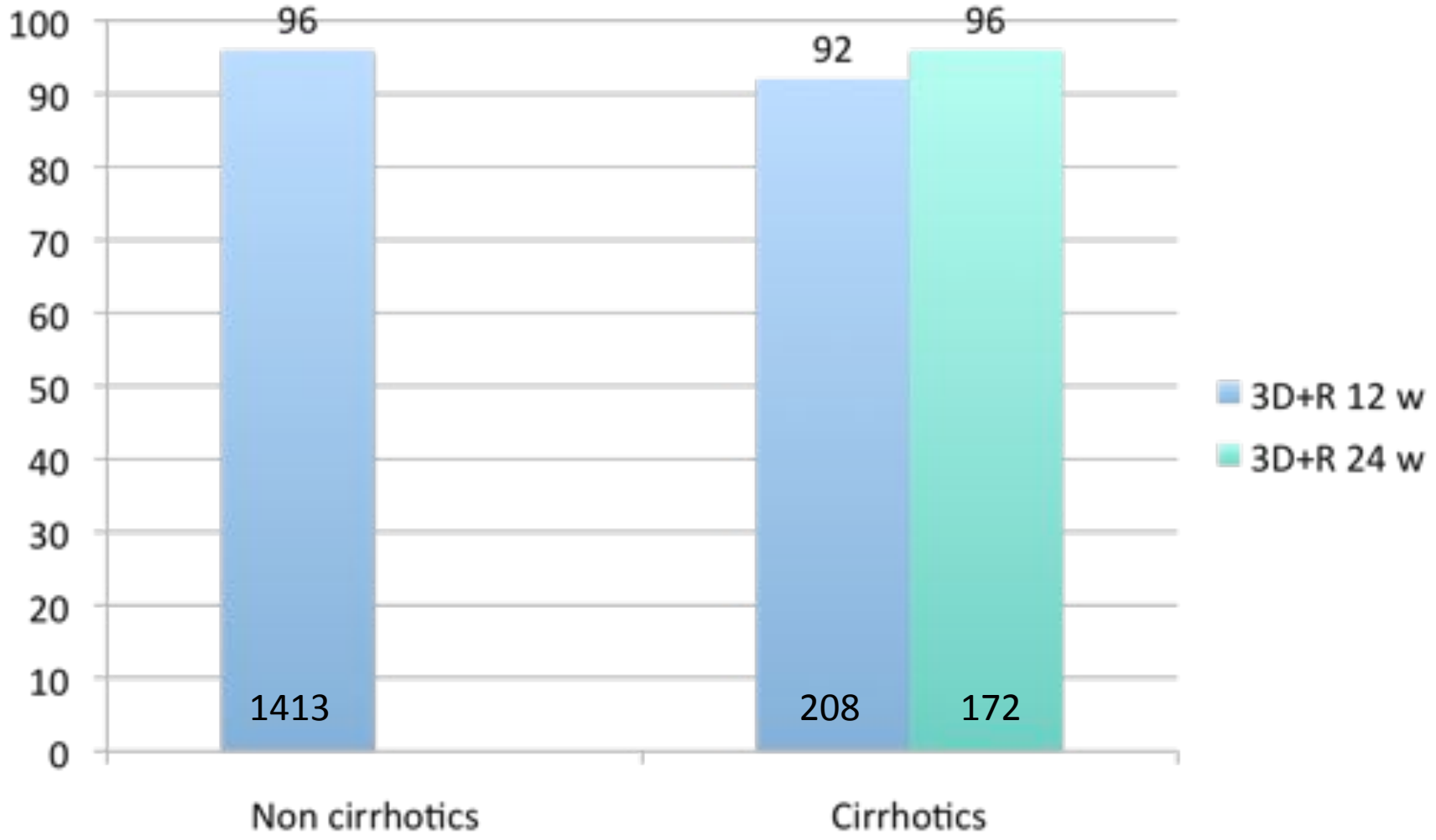
Jacobson IM, et al. AASLD 2013, Washington DC. #LB-3

Sofosbuvir + Daclatasvir ± Ribavirin for 12-24 weeks in 167 HCV G1 (32 F4)



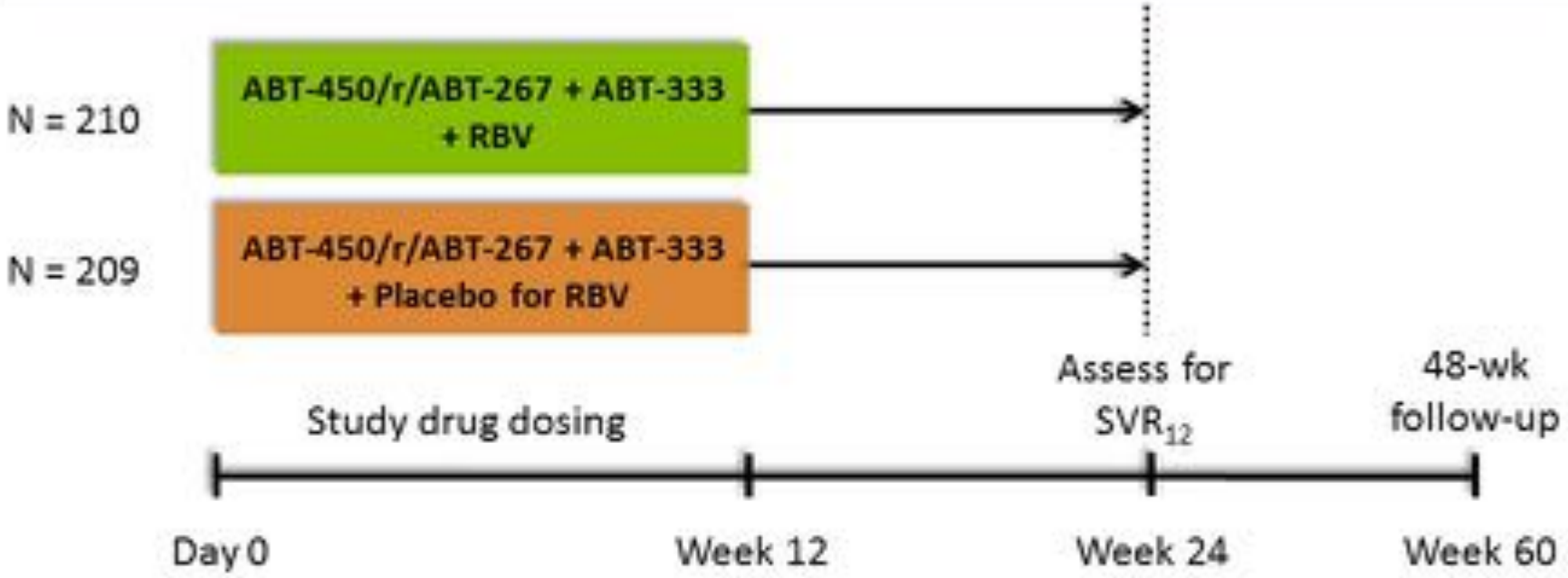
Sulkowski M et al NEJM 2014

3D combo + R in HCV Genotype 1 (1a + 1b; experienced + naives) stratified according to the presence of cirrhosis



Kowdley et al. NEJM 2014; Lawitz et al AASLD 2013; Abbvie Press Release Jan 31st 2014

PEARL-III: Study Design



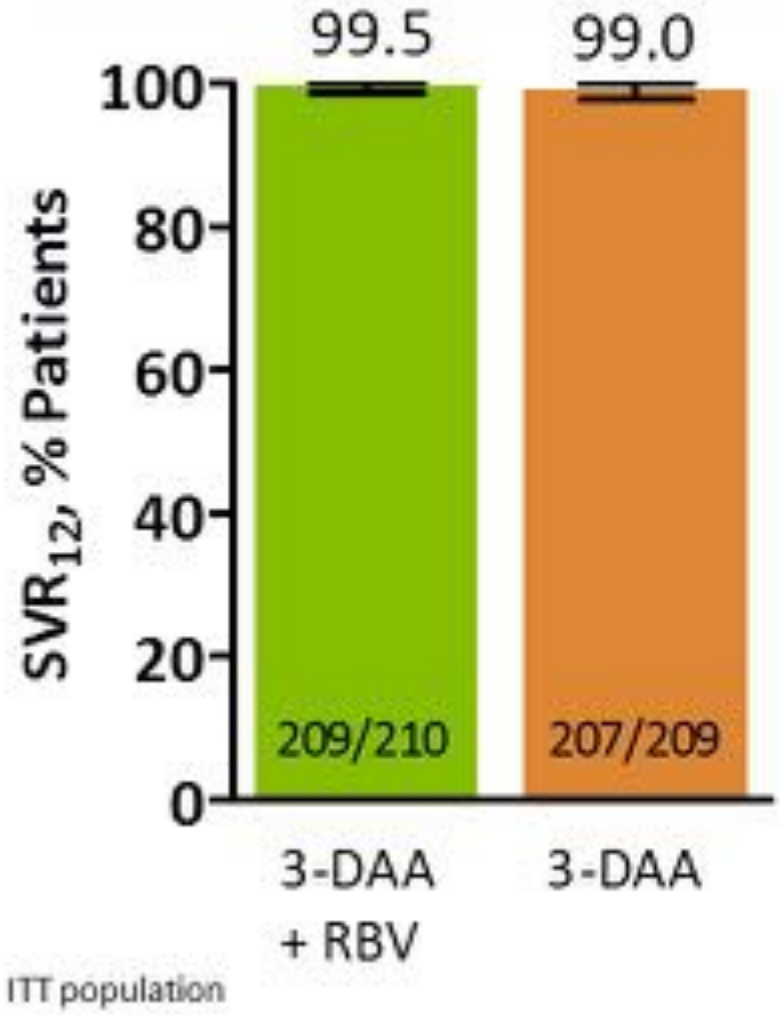
ABT-450/r/ABT-267: 150 mg/100 mg/25 mg QD

ABT-333: 250 mg BID

RBV: 1000 mg if body weight was <75 kg, 1200 mg if body weight ≥75 kg, or matching placebo

Adapted from the K Rajender Reddy presentation at CROI on March 4, 2014

SVR_{12} ≥99% Achieved After 12 Weeks with 3-DAA ± RBV

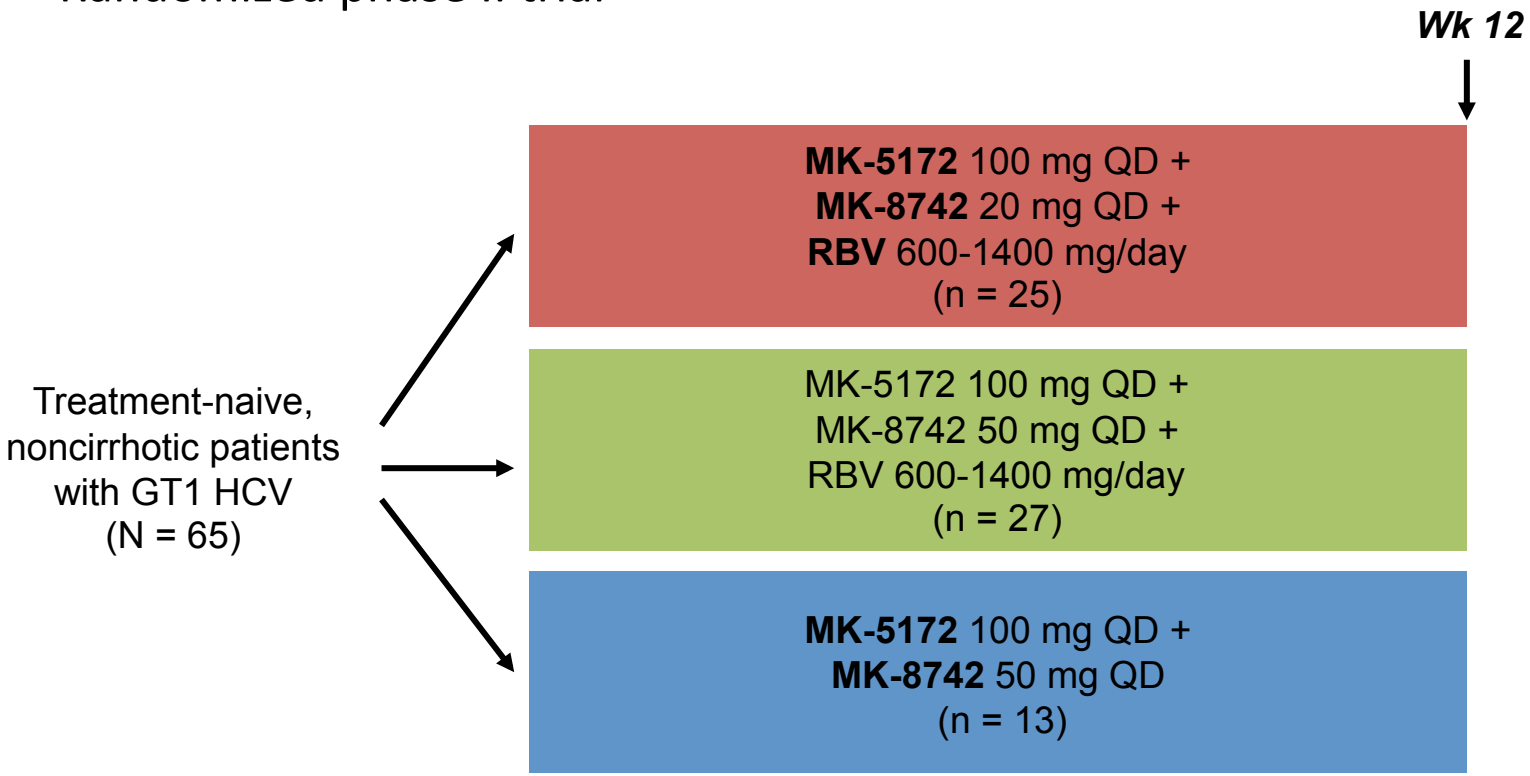


ITT population

Adapted from the K Rajender Reddy presentation at CROI on March 4, 2014

C-WORTHY: MK-5172 (PI)+ MK-8742(NS5a) ± RBV in Treatment-Naive GT1 HCV Pts

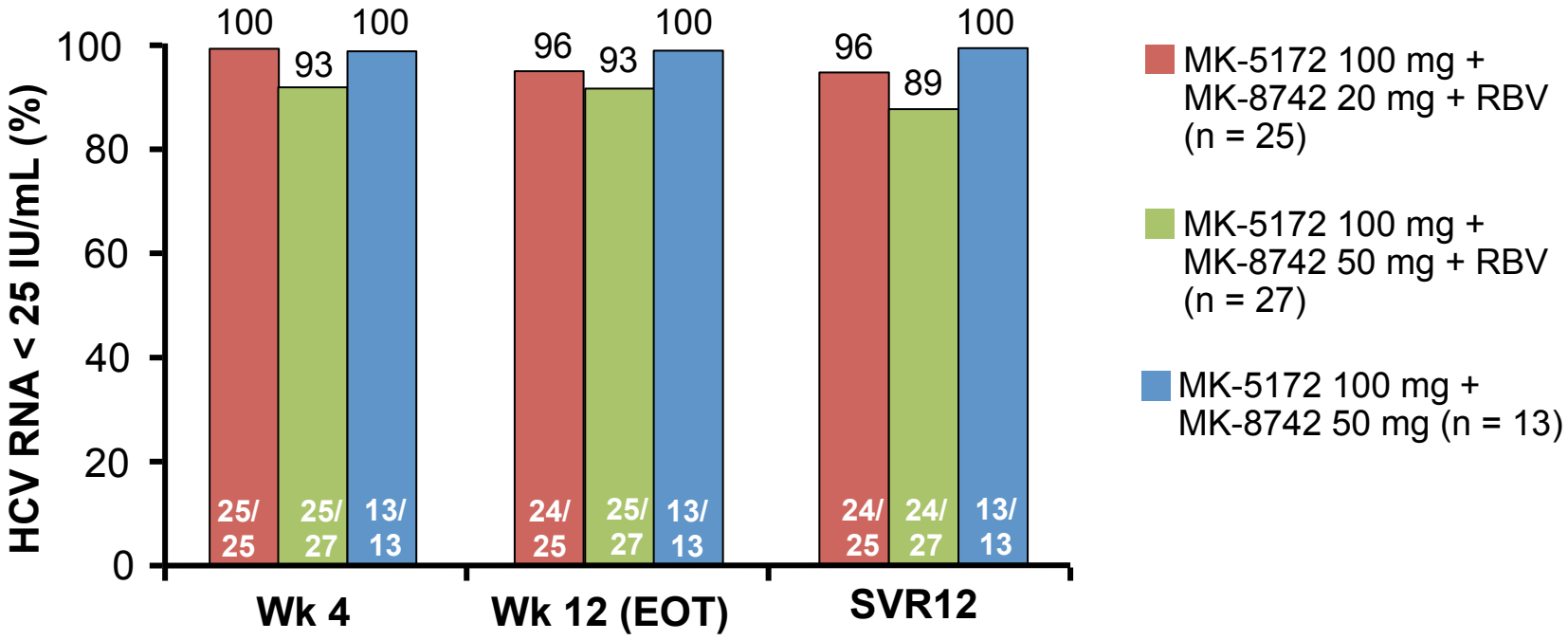
- Randomized phase II trial



Pts with GT1a randomized 1:1 to RBV arms only; patients with GT1b randomized 1:1:2 into all 3 arms

Lawitz E, et al. AASLD 2013. Abstract 76. Reproduced with permission.

C-WORTHY: Virologic Response Rates With MK-5172 + MK-8742 ± RBV

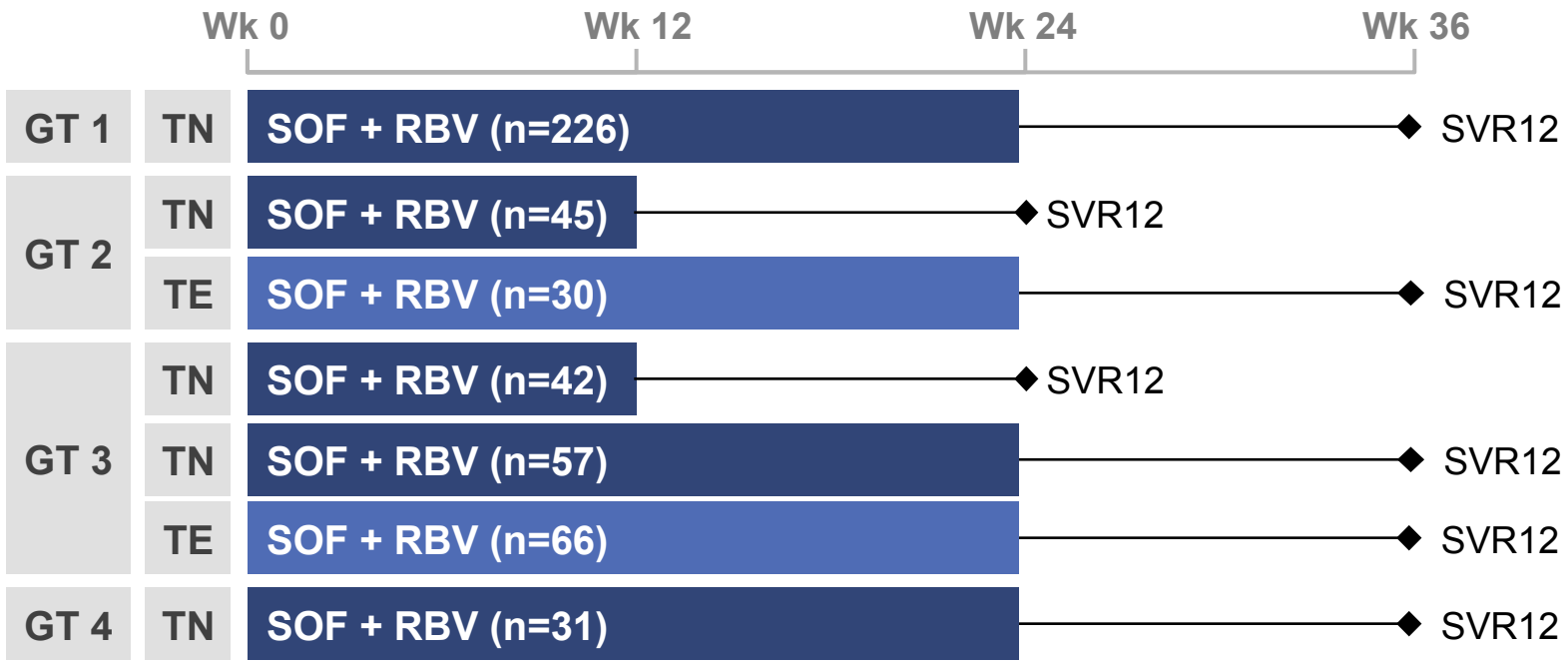


- All treatment regimens safe and well tolerated
- No early discontinuations due to drug-related AEs

Lawitz E, et al. AASLD 2013. Abstract 76. Reproduced with permission.

Study Design

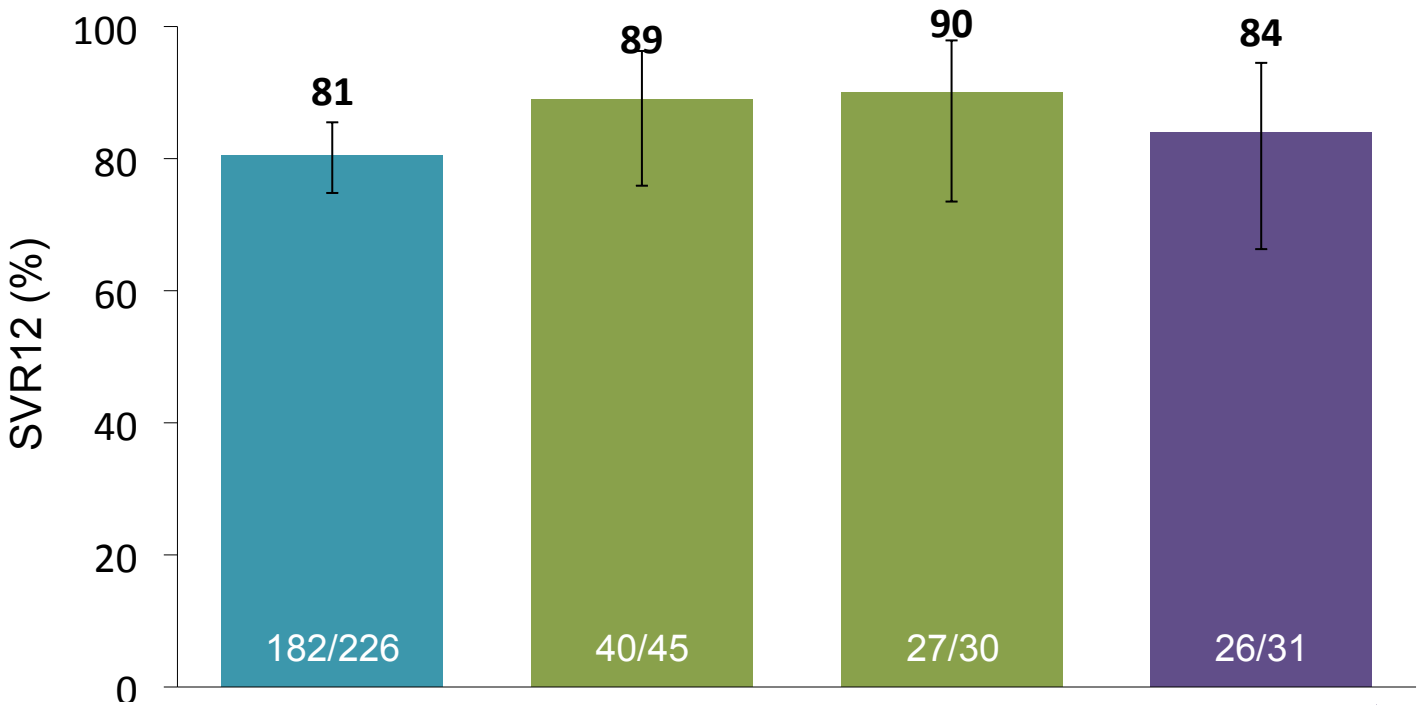
GT 1-4 HIV-HCV (PHOTON-1 and 2)



- Broad inclusion criteria
  - Compensated cirrhosis permitted; no platelet cutoff
  - Hemoglobin: ≥12 mg/dL (males); ≥11 mg/dL (females)
- Wide range of ART regimens allowed
  - Undetectable HIV RNA for >8 weeks on stable ART regimen
- Baseline CD4 count
  - ART treated: >200 cells/μL; ART untreated: > 500 cells/μL

Results: SVR12 for HCV genotype 1, 2 and 4

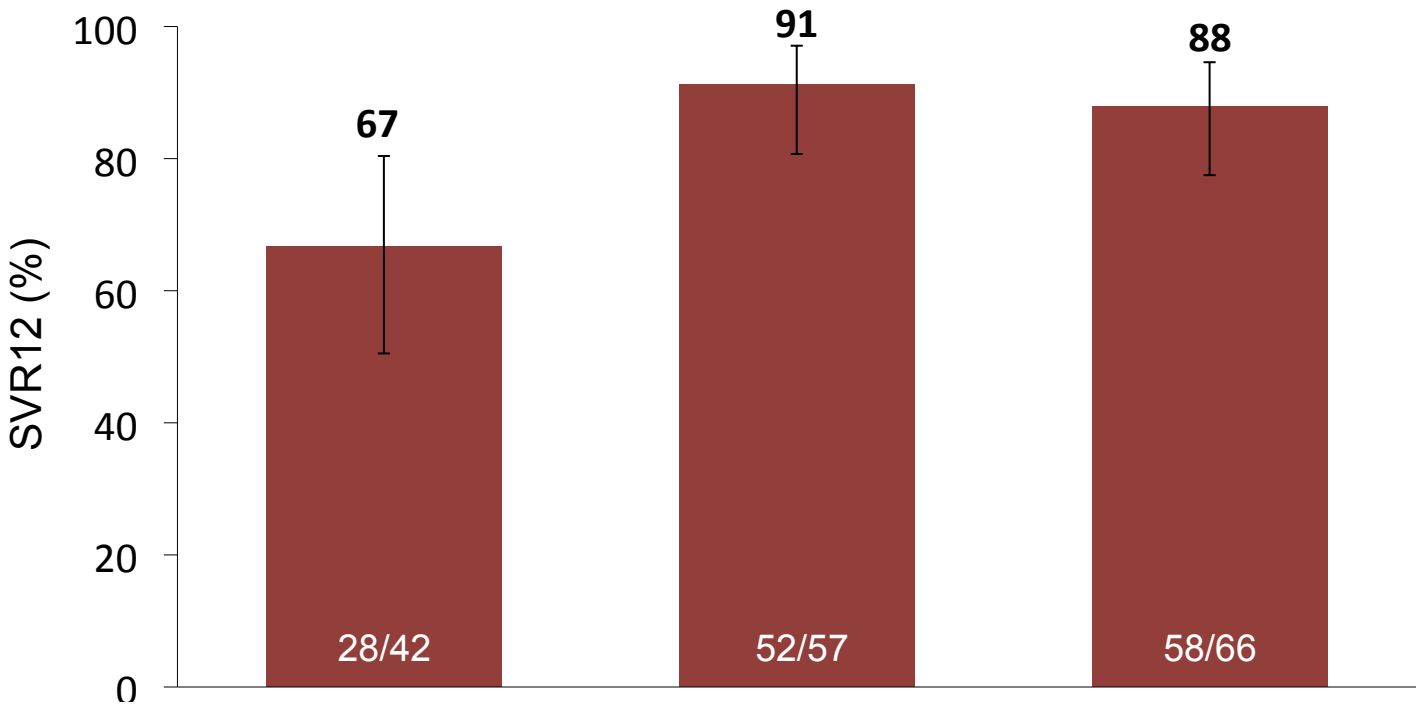
GT 1-4 HIV-HCV (PHOTON-1 and 2)



	GT 1 TN 24 Weeks	GT 2 TN 12 Weeks	GT 2 TE 24 Weeks	GT 4 TN 24 Weeks
Relapse, n (%)	39 (17)	1 (2)	2 (7)	5 (16)
Breakthrough, n (%)	1 (<1)	1 (2)	0	0
Lost to follow-up, n (%)	2 (<1)	1 (2)	0	0
Withdrew consent, n (%)	2 (<1)	2 (4)	1 (3)	0

Results: SVR12 for HCV genotype 3

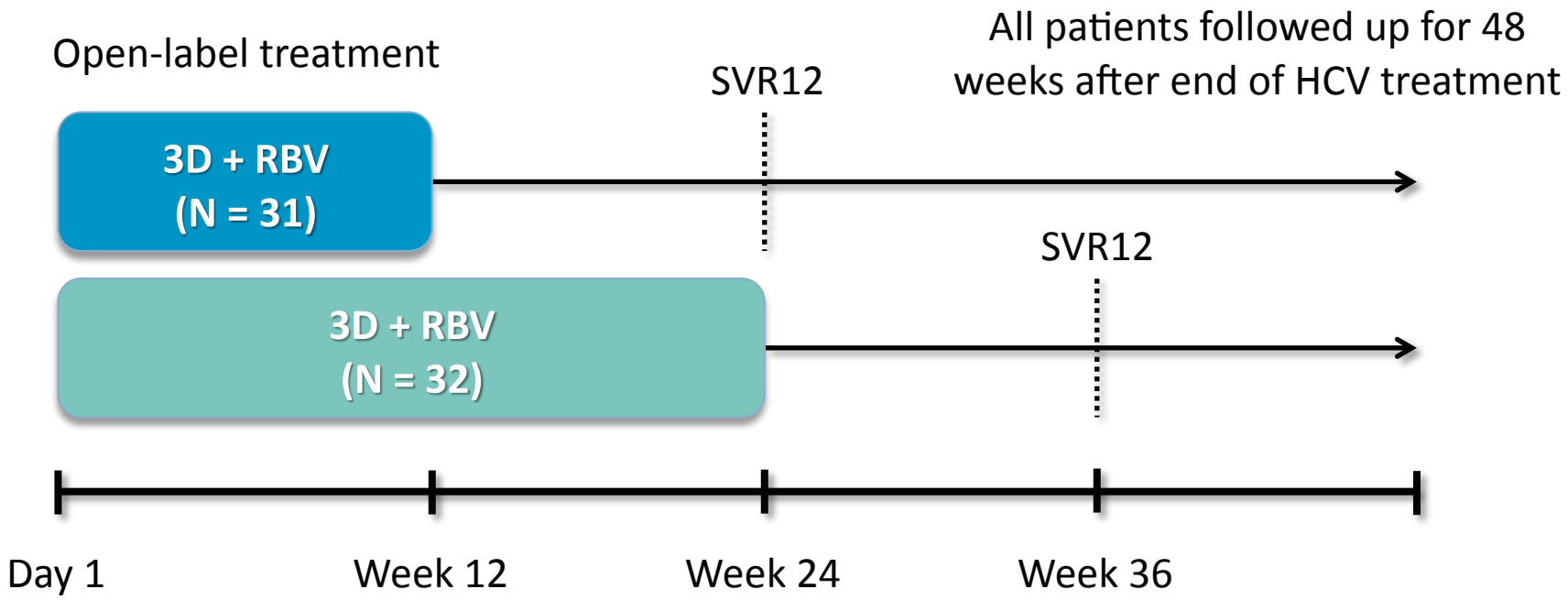
GT 1-4 HIV-HCV (PHOTON-1 and 2)



	GT 3 TN 12 Weeks	GT 3 TN 24 Weeks	GT 3 TE 24 Weeks
Relapse, n (%)	12 (29)	4 (7)	7 (11)
Breakthrough, n (%)	0	0	1 (<1)
Lost to follow-up, n (%)	2 (5)	0	0
Withdrew consent, n (%)	0	1 (2)	0

TURQUOISE-I Methods: Part 1a Study Design (N = 63)

Phase 2/3* multicenter, randomized, open-label study; HCV/HIV-1 coinfected patients

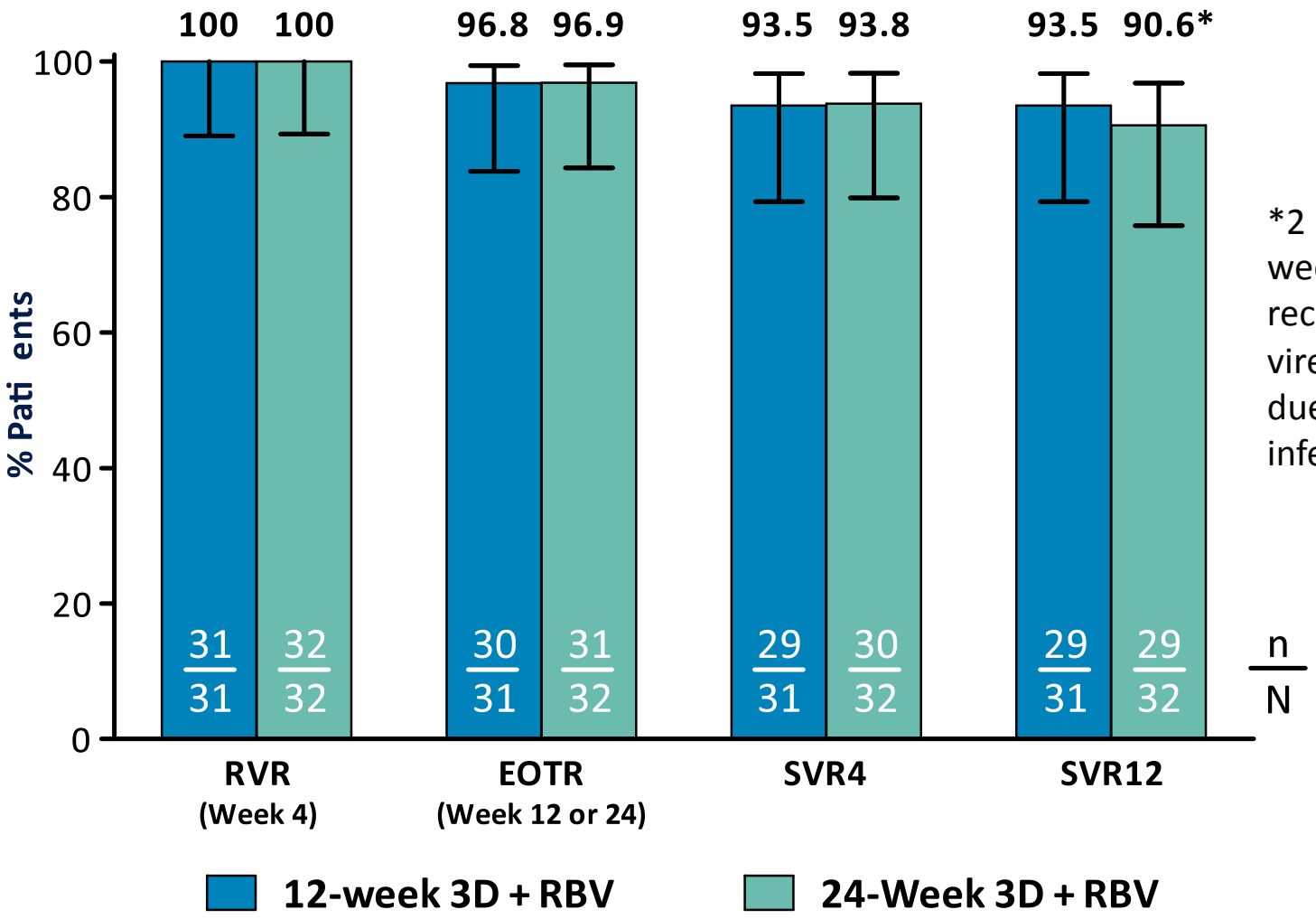


3D: coformulated ombitasvir/ABT-450/r, 25/150/100 mg once daily; dasabuvir, 250 mg twice daily

RBV: 1000 or 1200 mg daily according to body weight (<75 kg and ≥75 kg, respectively) in 2 divided doses

*Part 1: phase 2 pilot cohort (part 1a and part 1b); part 2: phase 3 cohort

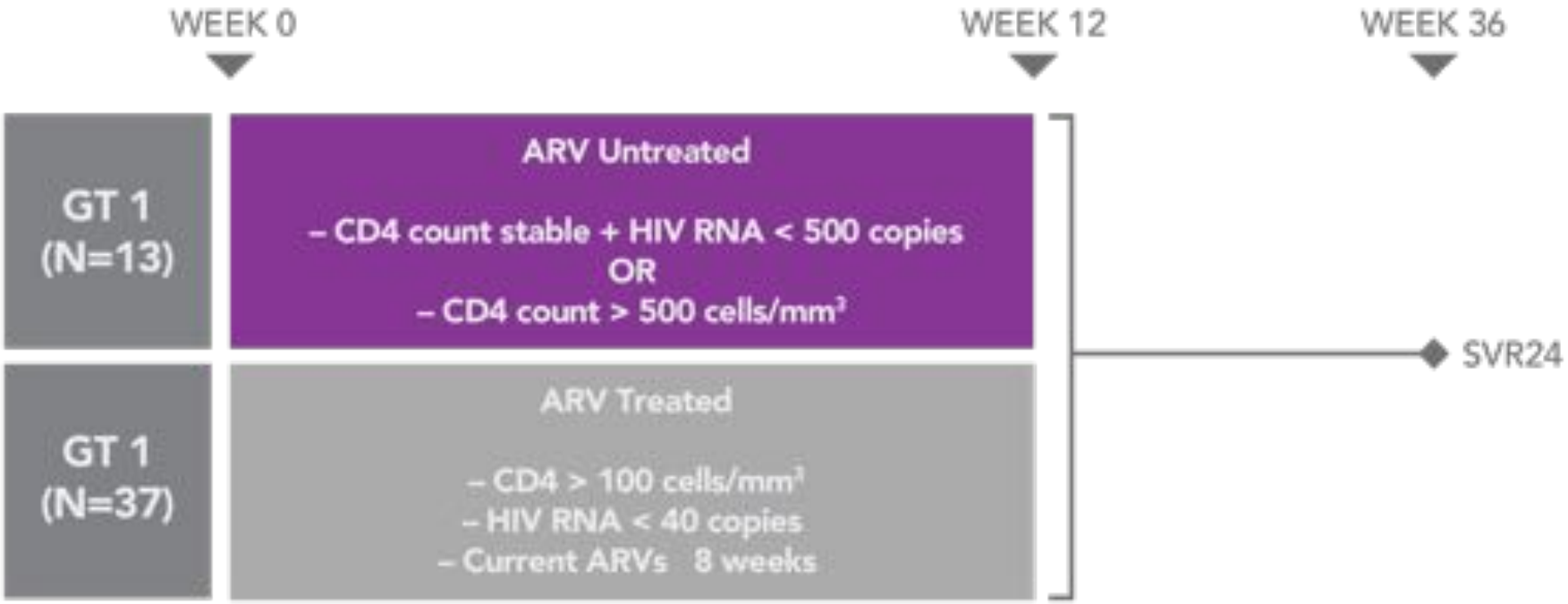
TURQUOISE-I Results: Intent-to-Treat Virologic Response Rates



*2 patients in the 24-week group had recurrence of HCV viremia believed to be due to HCV re-infection

EOTR, end of treatment response; RVR, rapid virologic response.

Study Design



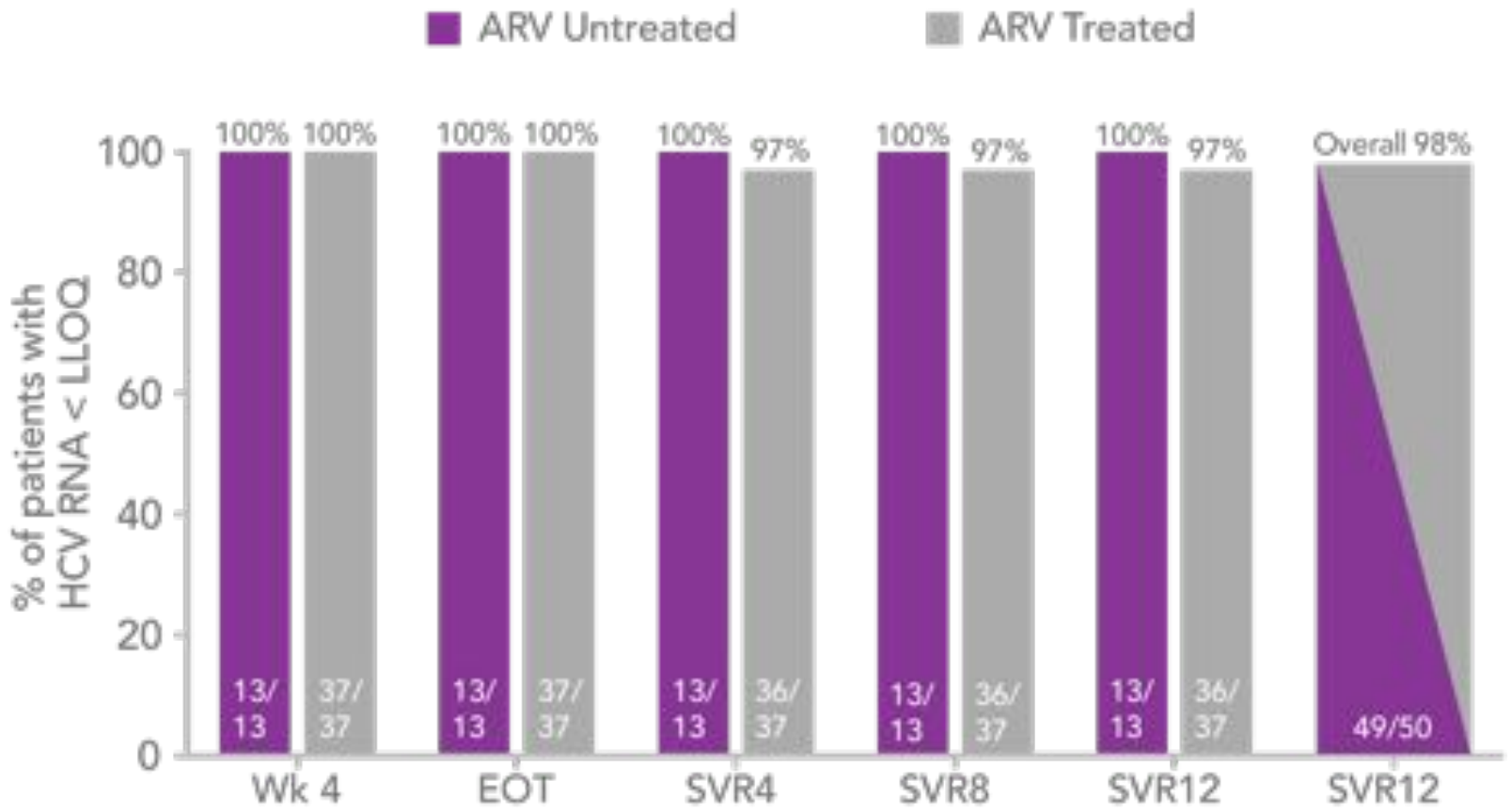
Open label

- **LDV 90mg/ SOF 400 mg STR for 12 wks**

Treatment-naïve GT-1 patients without cirrhosis
No ribavirin administered
ARVs: TDF/FTC, EFV, RILP and RALT

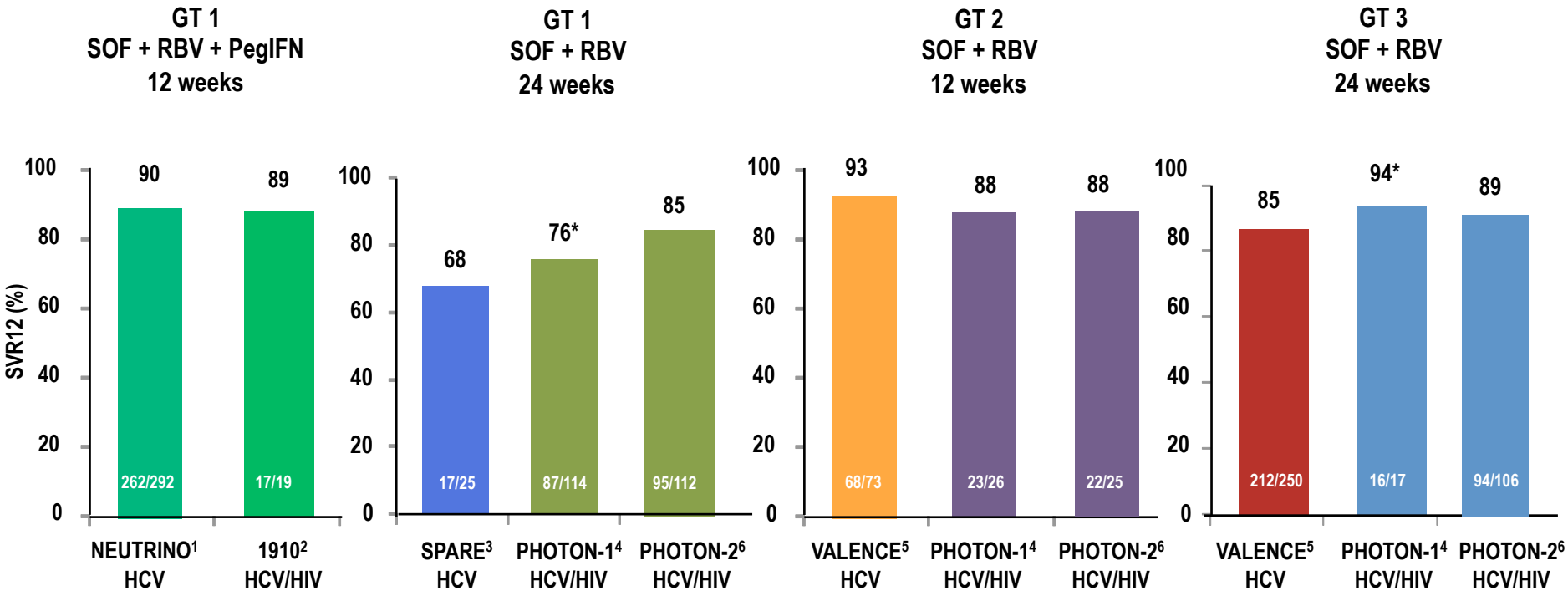
REFERENCES: 1. Osinusi A *et al*, AASLD, 2014. Poster

Treatment Response



REFERENCES: 1. Osinusi A *et al*, AASLD, 2014. Poster

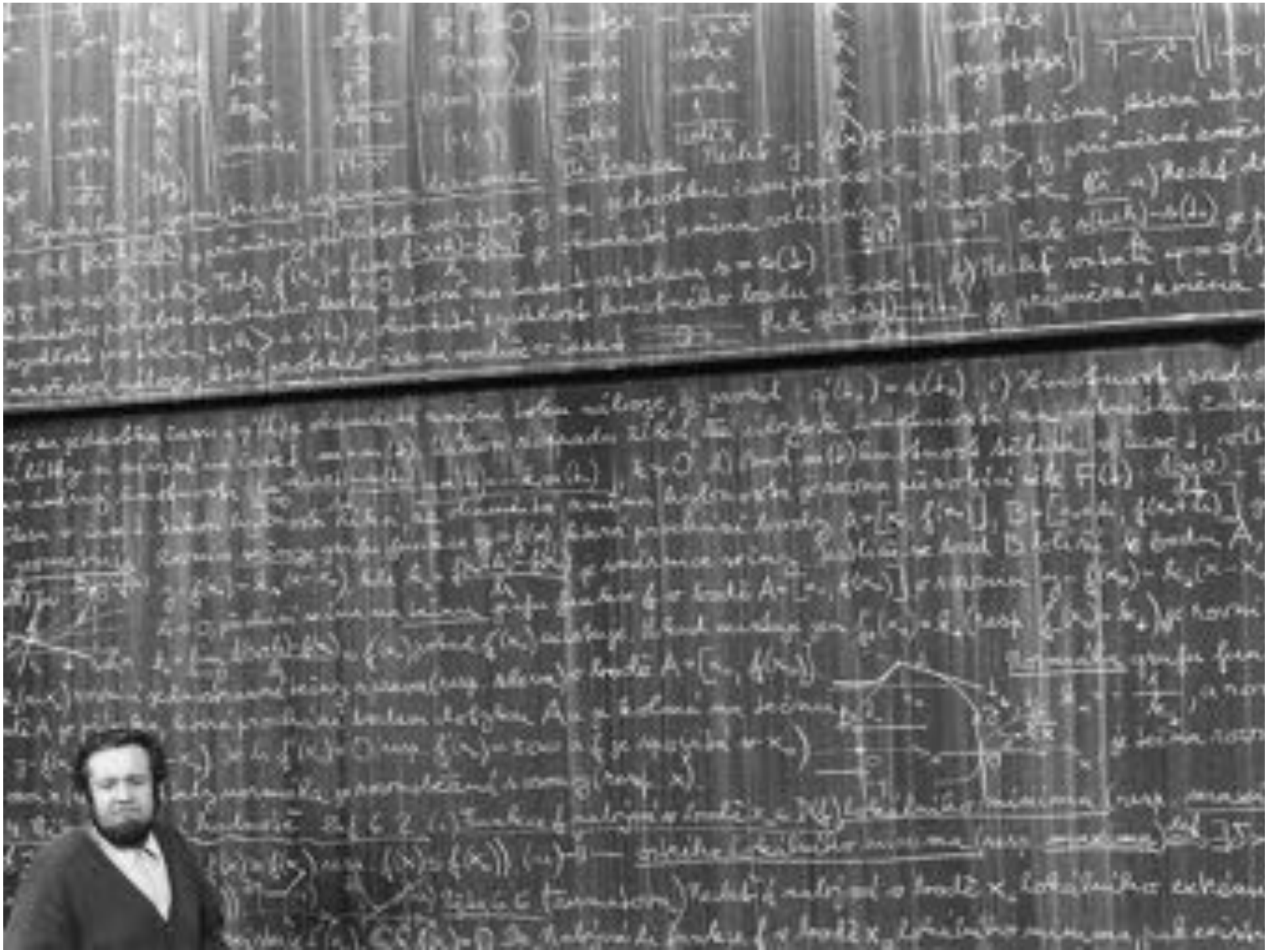
SVR12 in HCV Mono-infected and HCV/HIV Co-infected
SOF + RBV ± PegIFN x 12 or 24 weeks



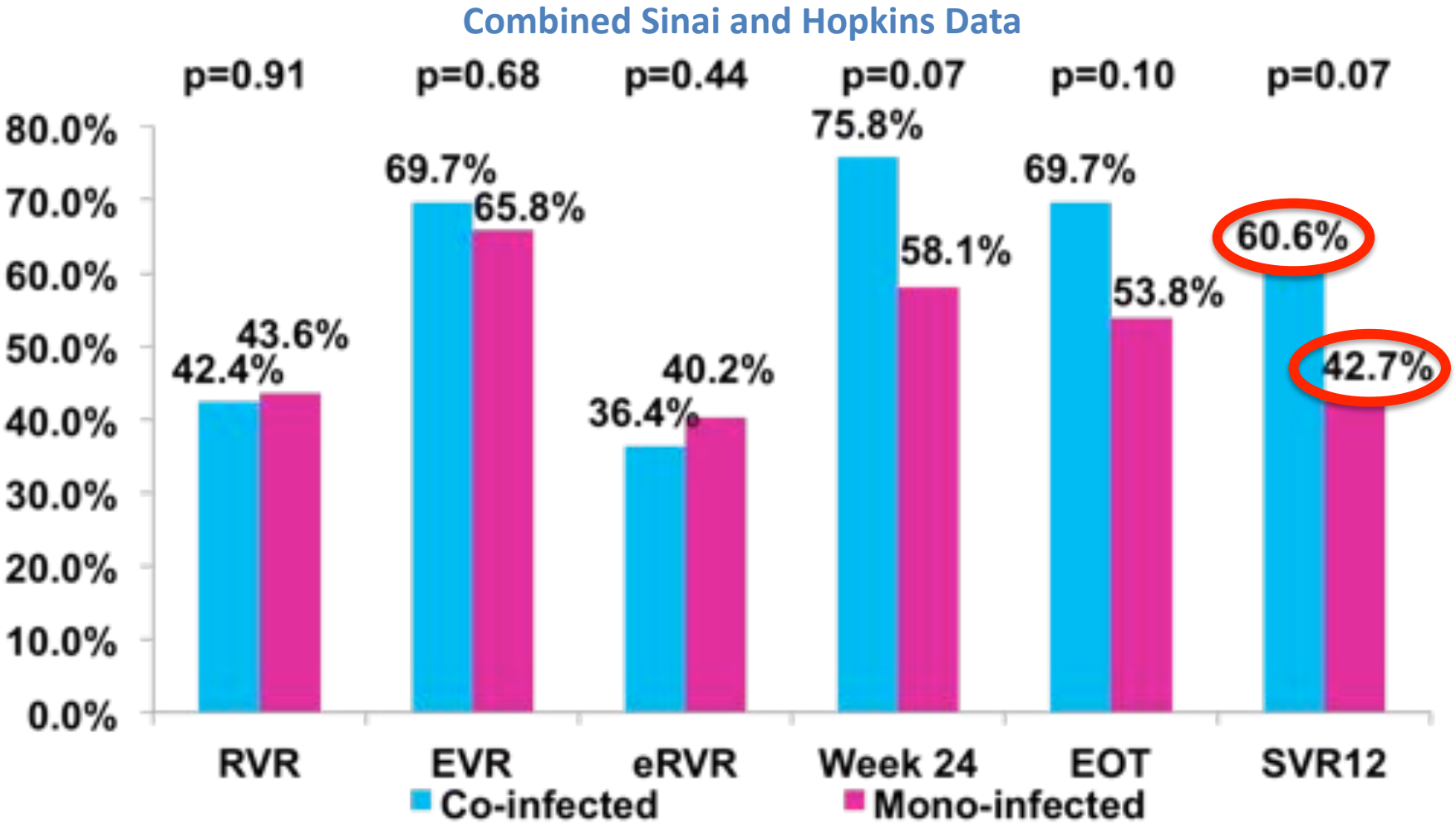
Similar response rates in HCV/HIV co-infected patients compared to HCV mono-infected patients

SVR12 from VALENCE includes pooled analysis from all patients (treatment-naïve and –experienced) by genotype and duration of therapy
*GT1 SVR24 of 75%; GT3 TE SVR24 of 88%

1. Lawitz E, et al. APASL 2013. Singapore. Oral #LB-02. 2. Rodriguez-Torres M, et al. IDWeek 2013; San Francisco, CA. Poster 714. 3. Osinusi A, et al. *JAMA*. 2013;310(8):804-811. 4. Naggie S, et al. CROI 2014. Boston, MA. Oral #26. 5. Zeuzem S, et al. AASLD 2013. Washington, DC. #1085. 6. Molina JM, et al. *IAS Melbourne Abstract* MOAB0105LB



SVR 12 HIV/HCV vs HCV mono-infection



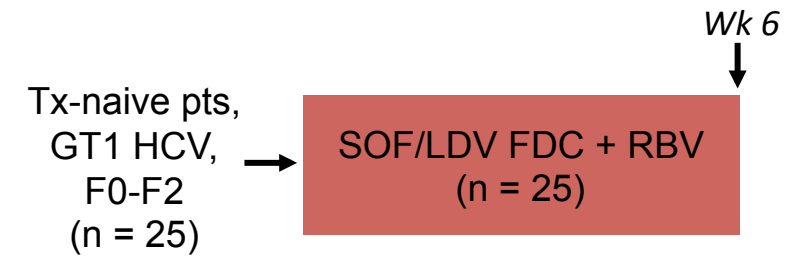
Trend for better virologic responses in co-infected patient is potentially explained by a selection bias

Martel V et al CID 2013

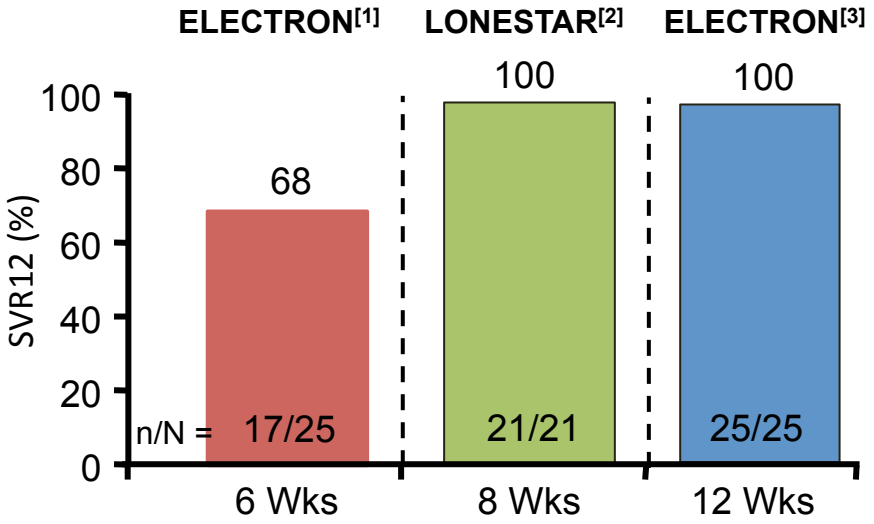

LESS
IS
MORE

ELECTRON: Sofosbuvir/Ledipasvir FDC + RBV for 6 Wks in Naive GT1 HCV Pts

- Open-label phase II trial in GT1 HCV pts
- 68% SVR12 rate with 6 wks of SOF/LDV FDC + RBV lower[1] than SVR rates previously achieved with 8 wks[2] or 12 wks[3] treatment with this regimen



Sofosbuvir 400 mg QD;/ledipasvir 90 mg QD;
weight-based RBV 1000-1200 mg/day

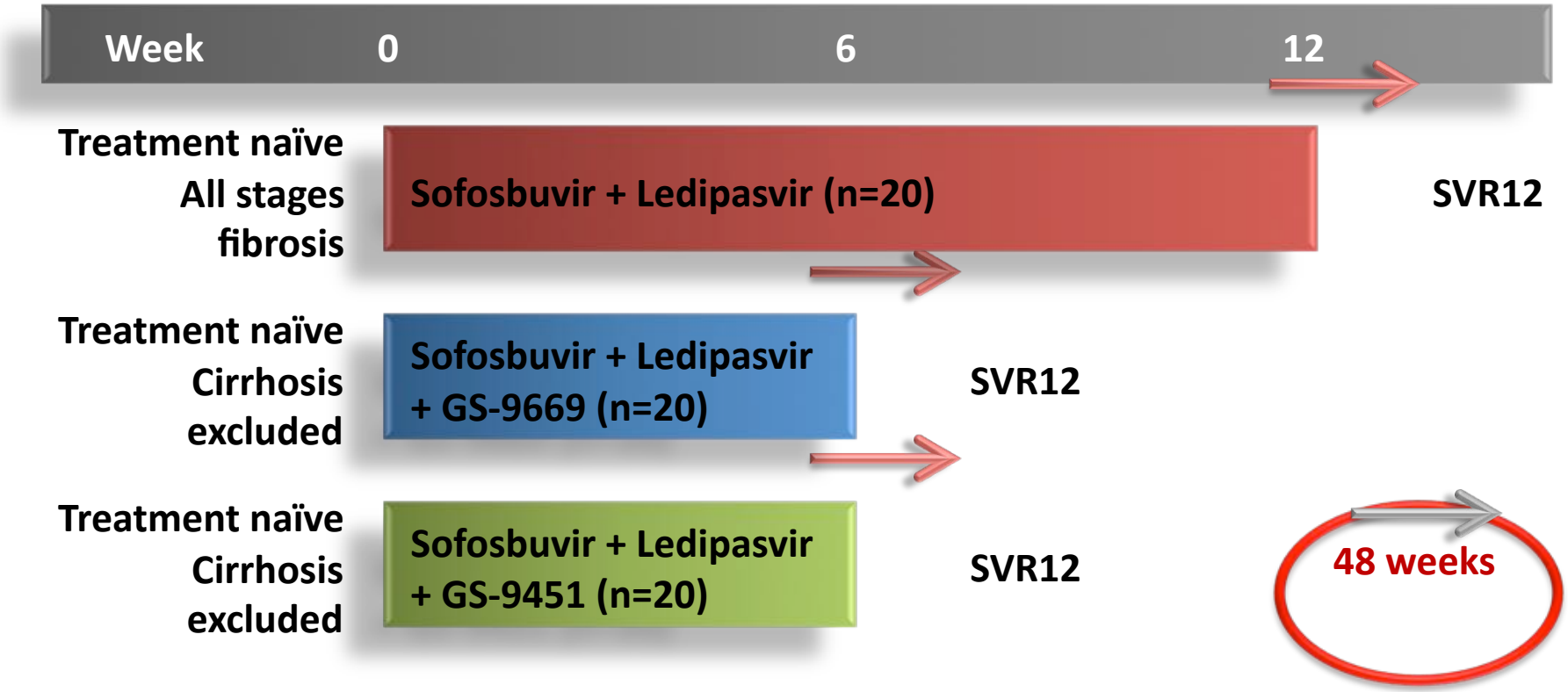


Duration of SOF/LDV + RBV in Tx-Naive Pts

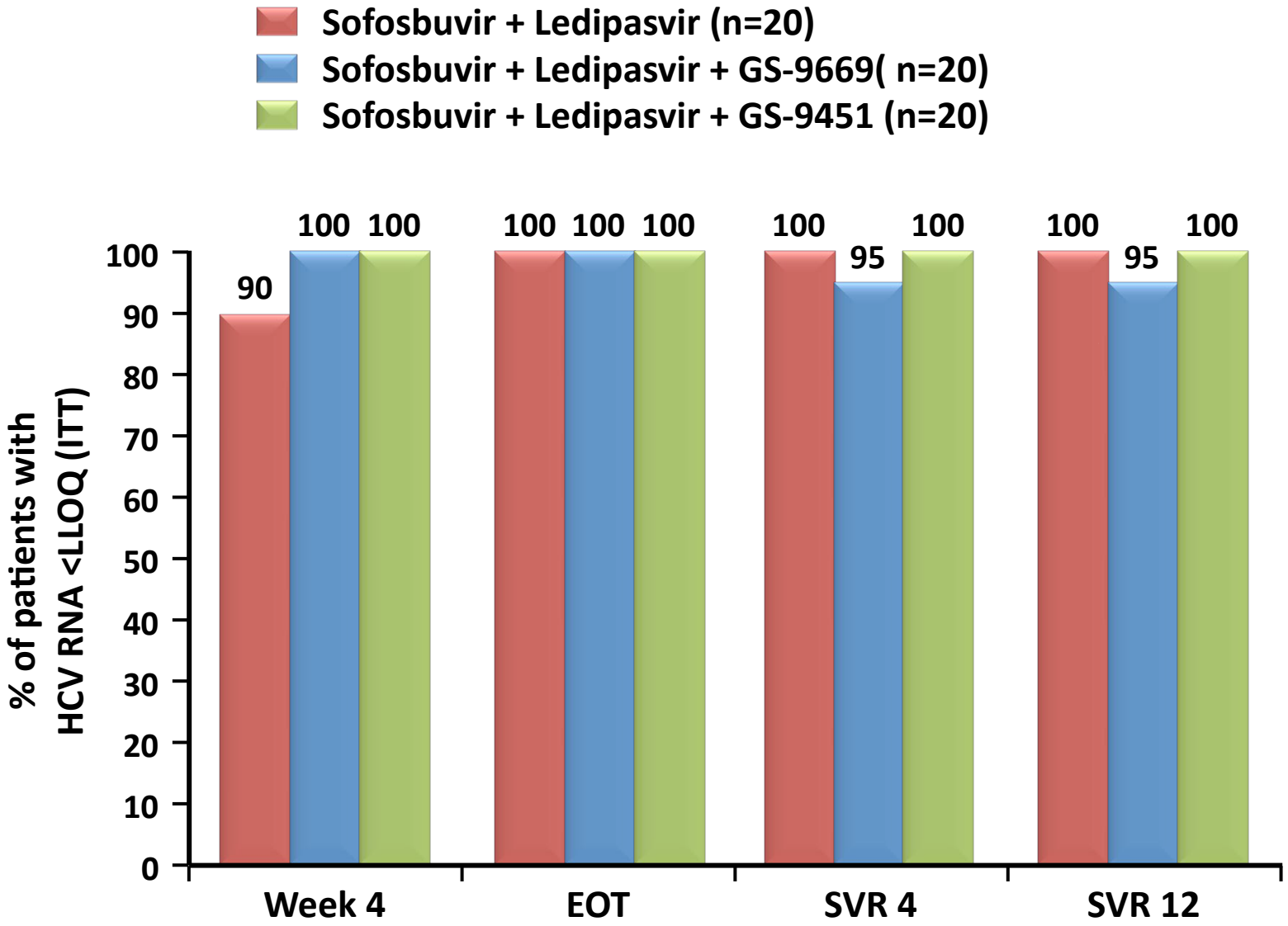
1. Gane EJ, et al. AASLD 2013. Abstract 73. Reproduced with permission.
2. Lawitz E, et al. AASLD 2013. Abstract 215. 3. Gane EJ, et al. EASL 2013. Abstract 14.

Study Design

- Sofosbuvir (nucleotide NS5B inhibitor) 400 mg / ledipasvir (NS5A inhibitor) 90 mg once daily
- GS-9669 (non-nucleoside NS5B inhibitor) 500 mg once daily
- GS-9451 (a protease NS3/4 inhibitor) 80 mg once daily



Treatment Response (ITT)



HIV TREATMENT AS PREVENTION…WHAT ABOUT HCV?

The NEW ENGLAND JOURNAL of MEDICINE

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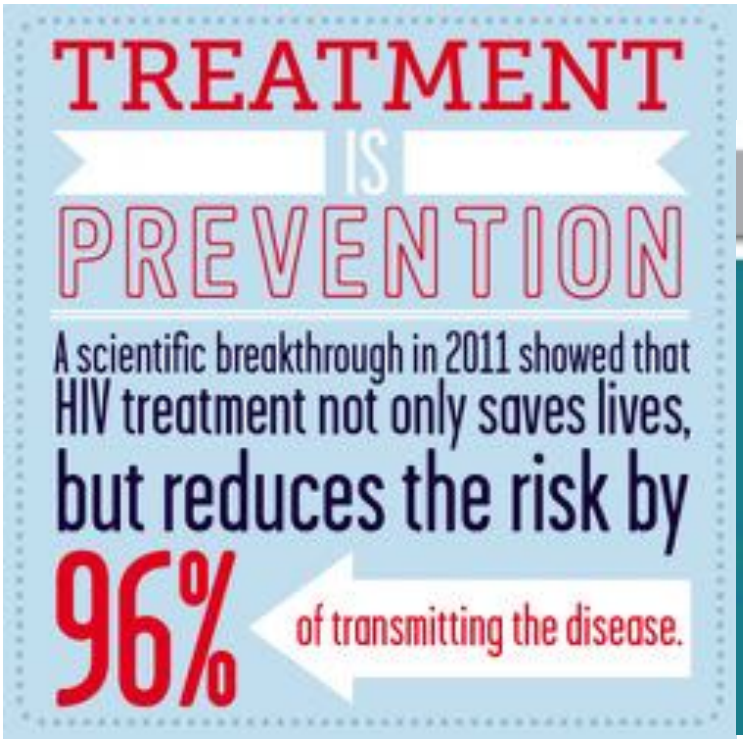
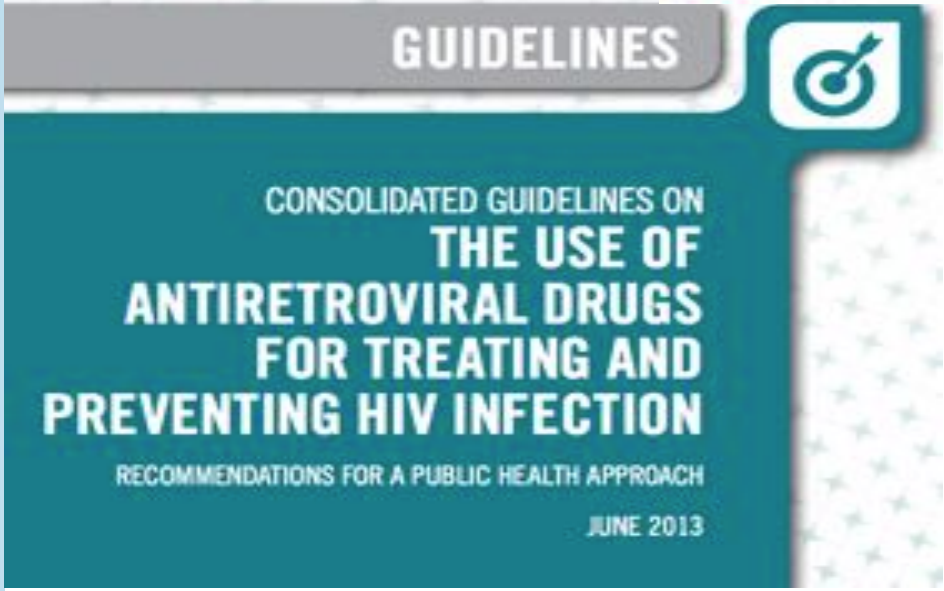
ORIGINAL ARTICLE

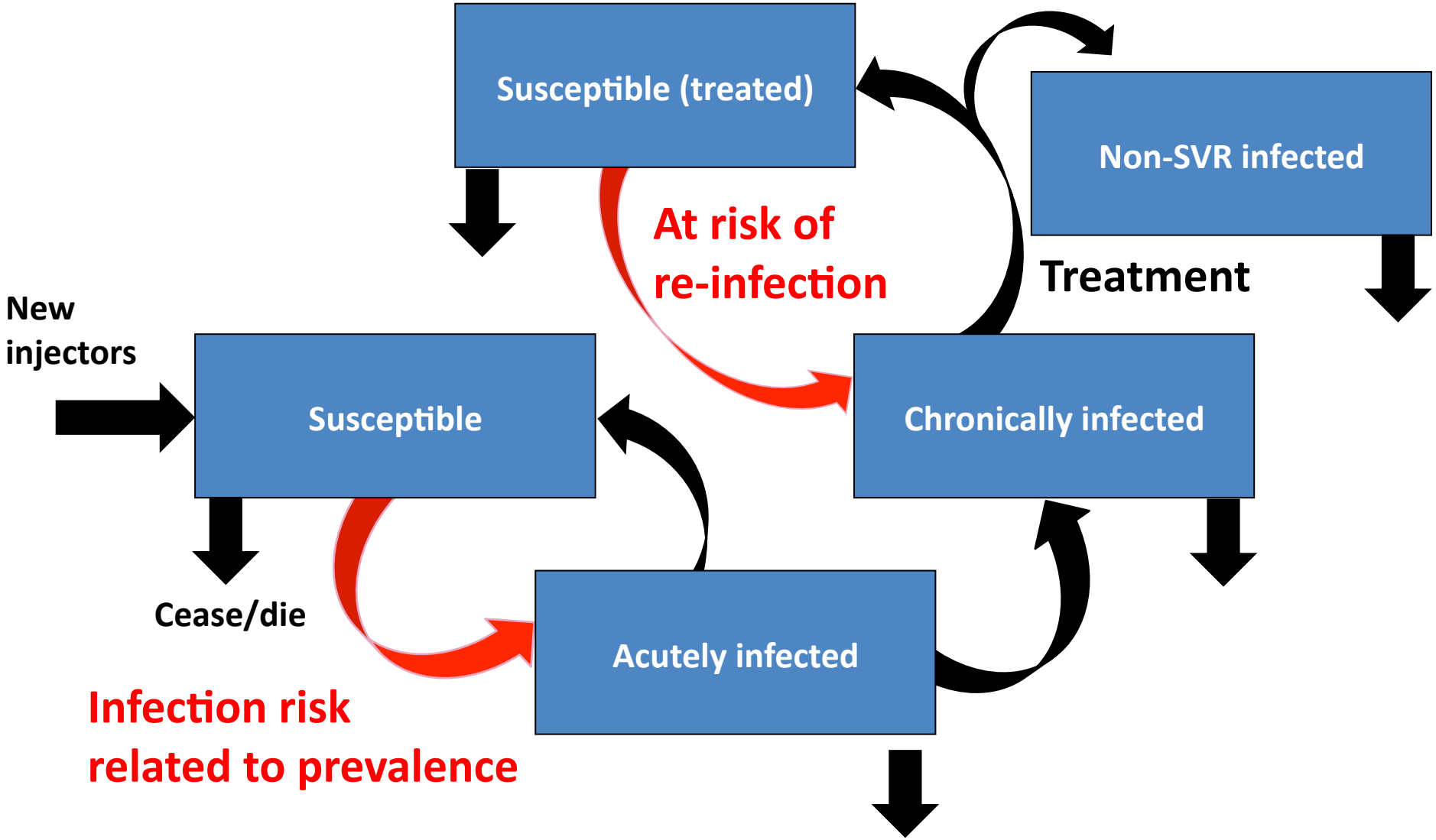
Prevention of HIV-1 Infection with Early Antiretroviral Therapy

Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D., Mina C. Hosseinipour, M.D.,





NEED DYNAMIC TRANSMISSION MODEL TO ASSESS IMPACT OF TREATMENT ON PREVALENCE/INCIDENCE



Martin NK, et al. *Hepatology* 2013; 55(1):49-57

Martin NK, et al. *J Hep* 2011; 54:1137-44

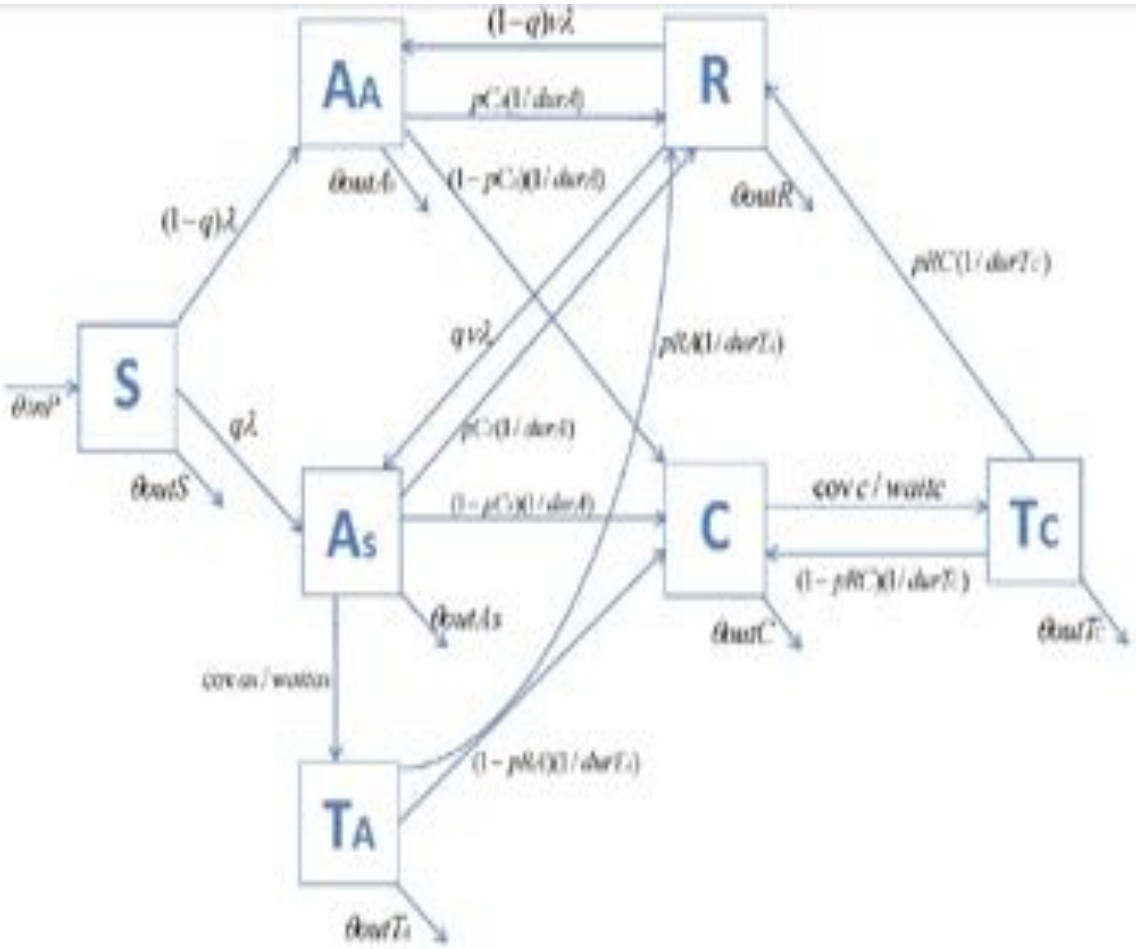
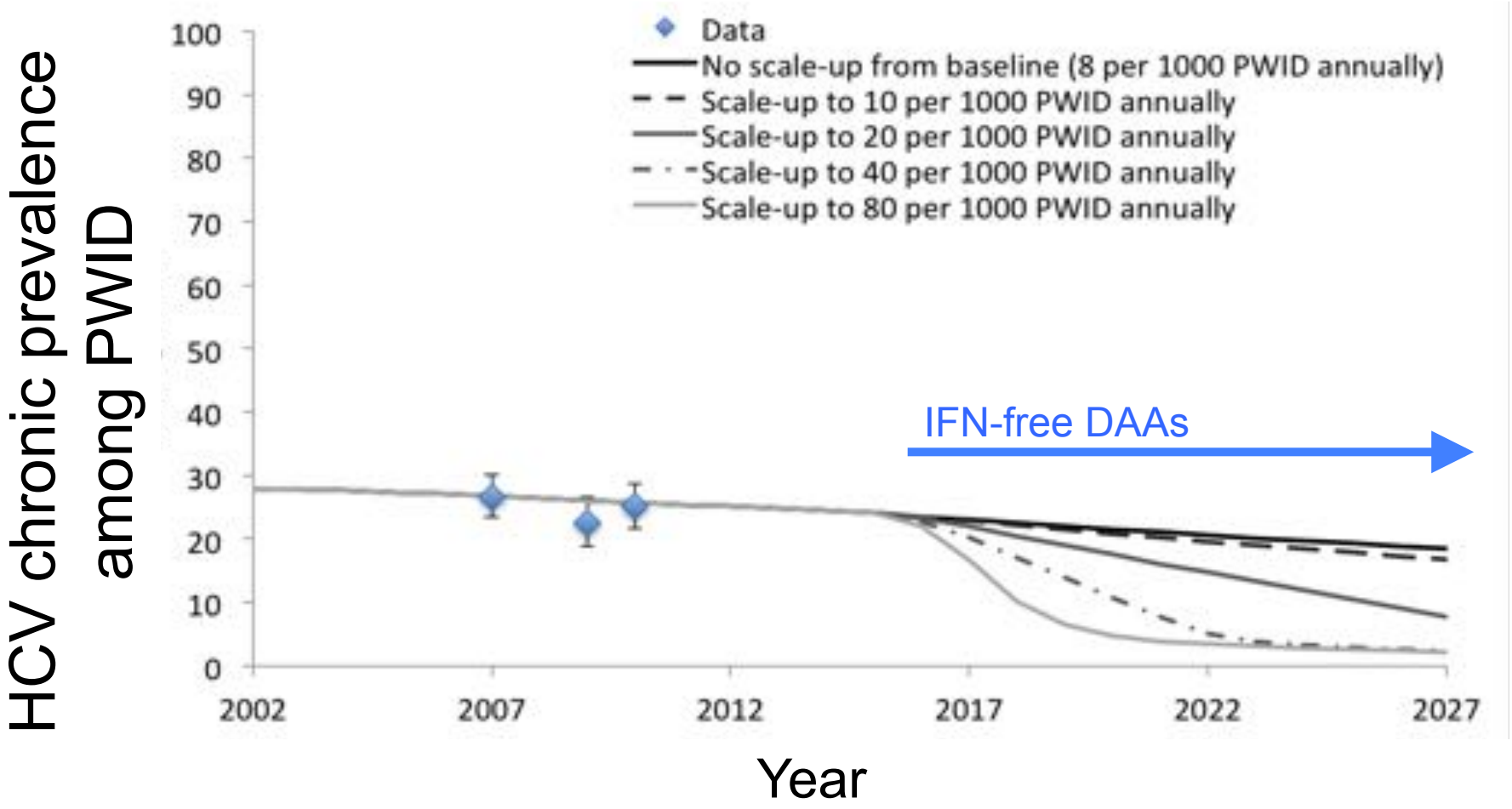
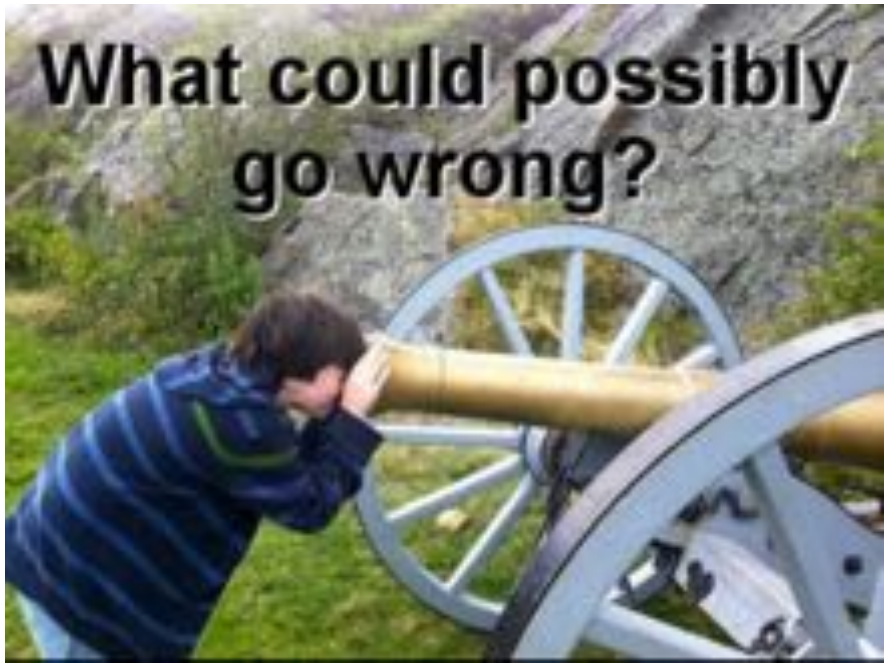


Figure 1. Model schematic. S: Susceptible individuals; A_A: Acute asymptomatic cases; A_S: Acute symptomatic cases; T_A: Treated Acute symptomatic cases; R: Recovered infections; C: Chronic infections; T_C: Treated Chronic infections.
doi:10.1371/journal.pone.0034548.g001

MODELLING PROJECTIONS: TOWARDS ELIMINATION IN EDINBURGH WITH DAA THERAPY



Martin NK, et al. *Hepatology* 2013; 55(1):49-57


What could possibly
go wrong?

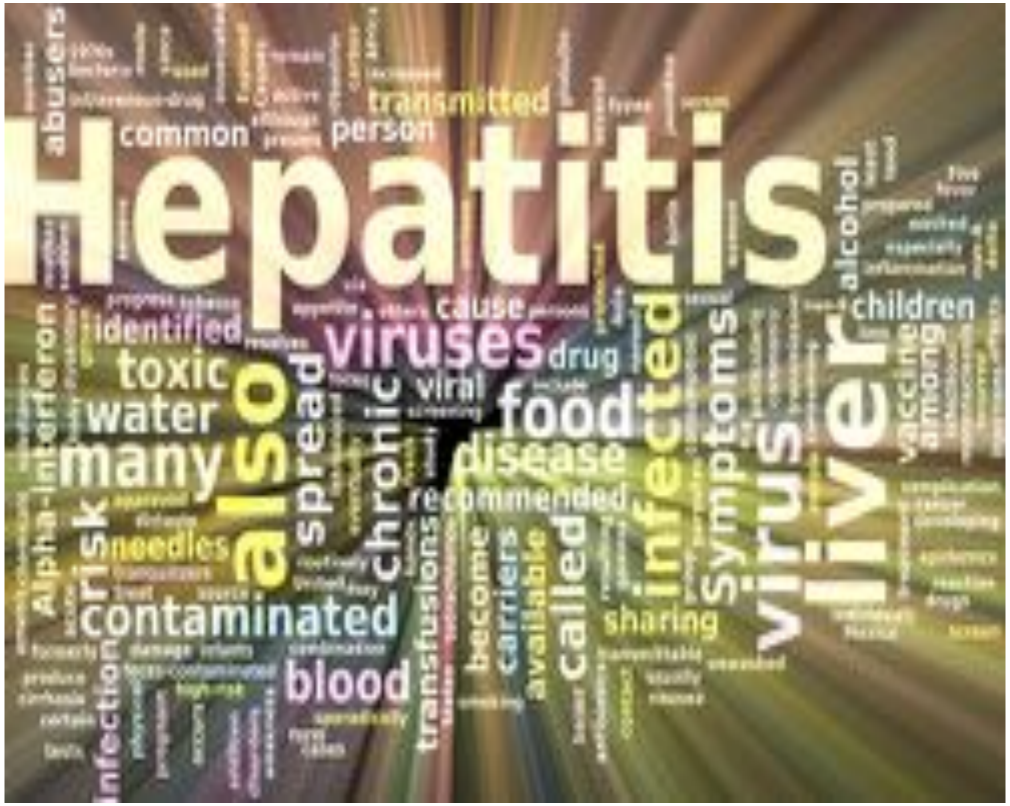

.Real life is overrated.

S.Khoo, 15th Intl. W'shop, 2014

Your EKG is showing a huge financial strain are you alright?

How shall we frighten them this year?

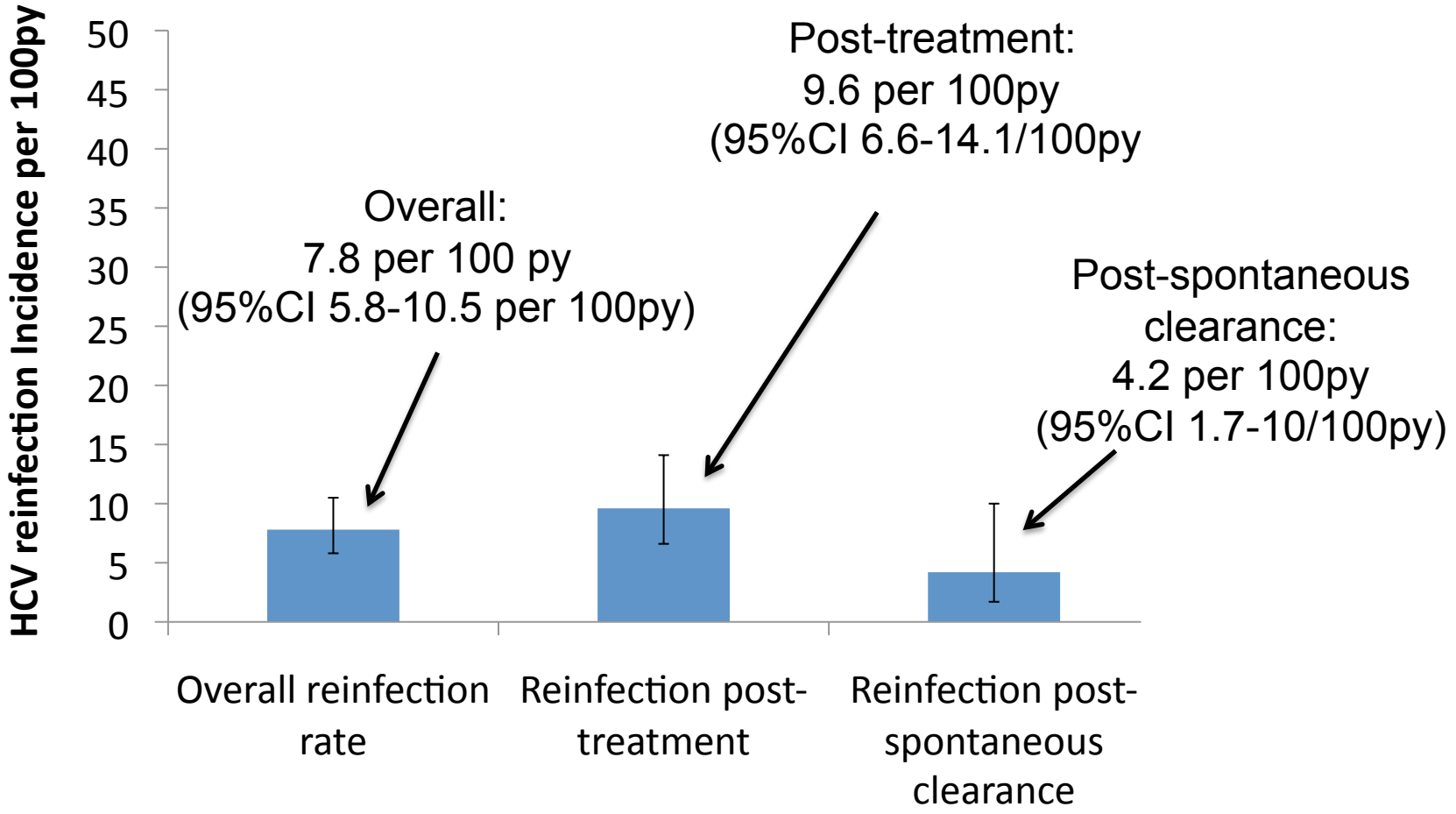

$5,000,000


Hepatitis
common
person
transmitted
abusers
alcohol
children
identified
viruses
cause
drug
toxic
water
many
also
spread
chronic
viral
food
infected
Symptoms
virus
liver
vaccine
among
disease
recommended
needles
risk
Alpha-interferon
contaminated
transfusions
become
carriers
available
called
sharing
blood
infection

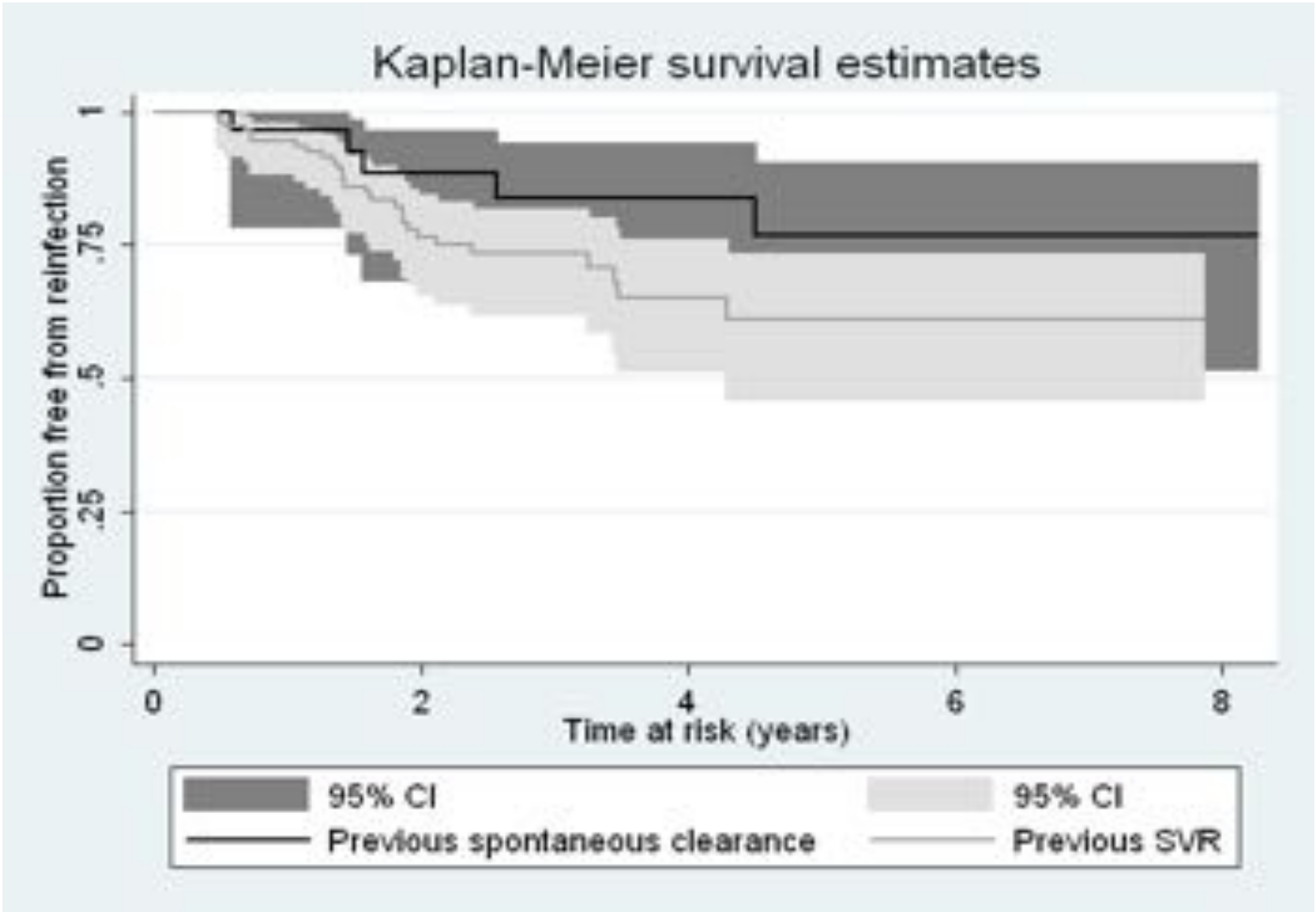

once infected
twice dead

Episode	Genotype	Treatment	Outcome
1	1	PEG/RBV	ETR
2	4	PEGRBV	SVR
3	1	NIL	Clearance
4	1	NIL	Clearance (?)
5	4	PEG/RBV	SVR
6	3	PEG/RBV	SVR
7	1	PEG/RBV	Null Response(?)
8	1	PEG/RBV/PI	SVR
9	1	PEG/RBV/TPV	?

HCV Reinfection Incidence



- Comparing reinfection post-treatment versus post-spontaneous clearance: p=0.15


Kaplan-Meier survival estimates
Proportion free from reinfection
0
.25
.5
.75
1
0
2
4
6
8
Time at risk (years)
95% CI
Previous spontaneous clearance
95% CI
Previous SVR

Thank you

For further information please contact :

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