

Viral hepatitis and HIV coinfection

Dr Greg Dore

**Head, Viral Hepatitis Program
National Centre in HIV Epidemiology and Clinical Research
The University of New South Wales, Sydney, Australia**

St Vincent's Hospital HIV/Immunology/Infectious Diseases Clinical Services Unit

Co-infection: HIV and viral hepatitis

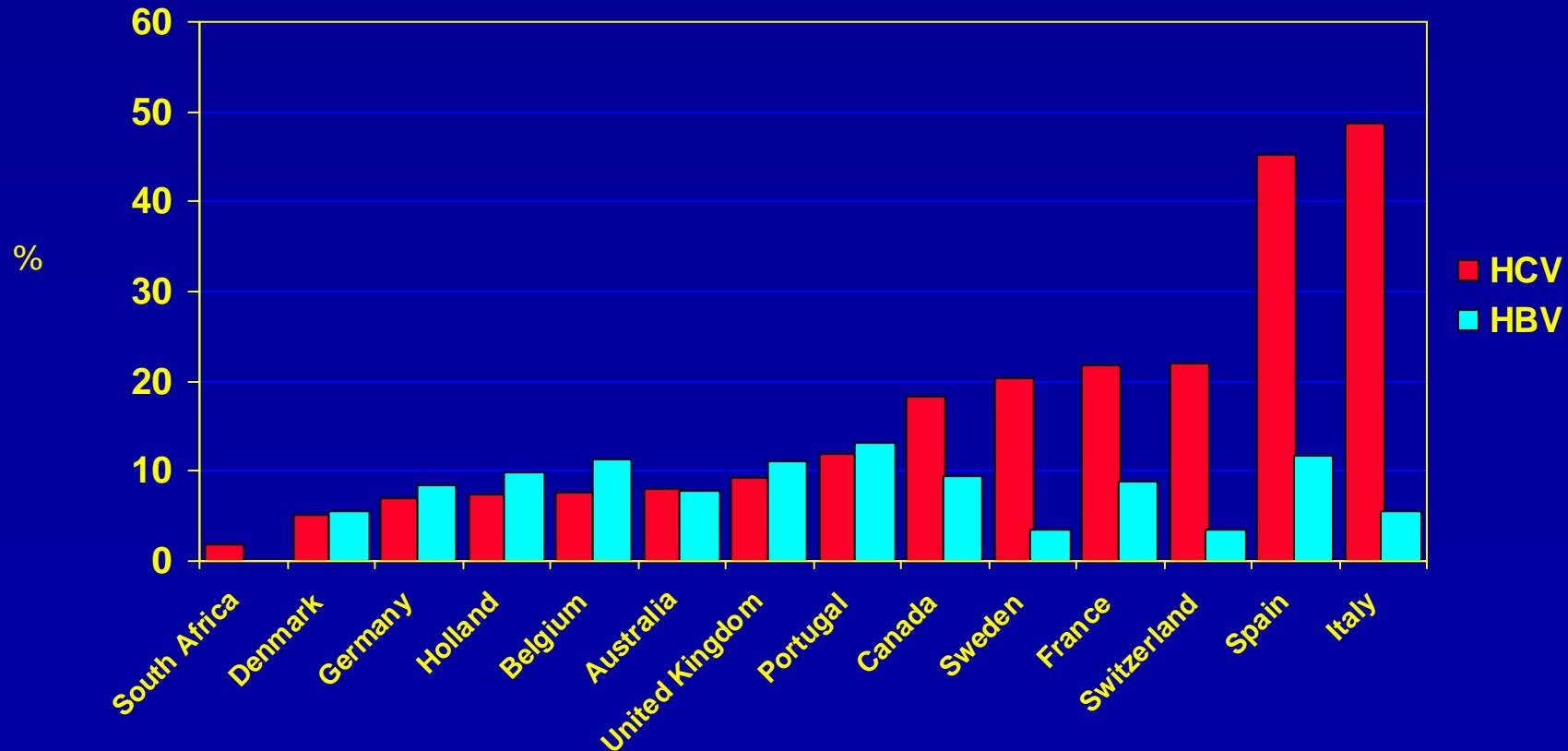


- Prevalence
- Natural history
- Therapeutic strategies

Coinfection: HIV and viral hepatitis



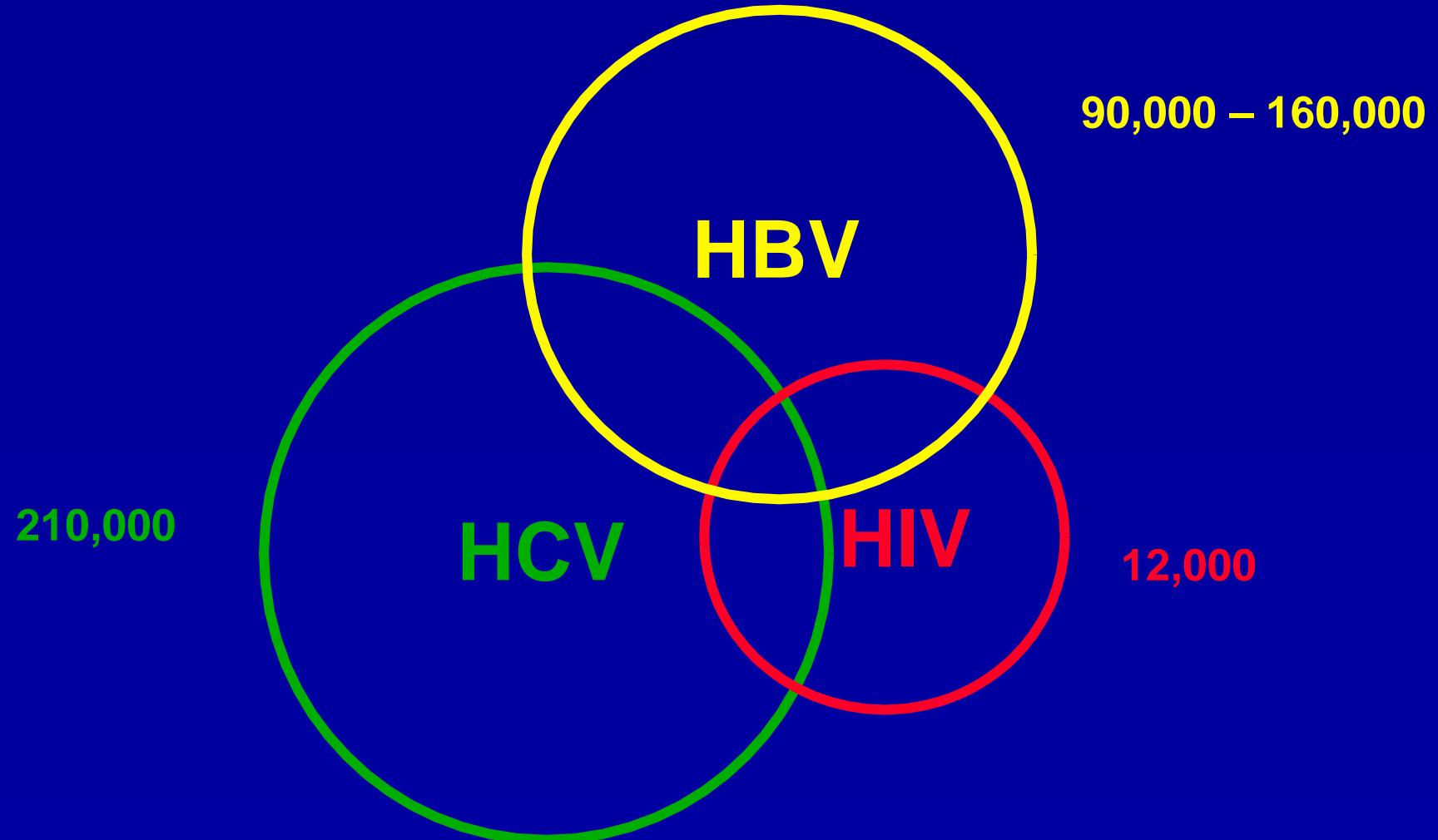
Prevalence of HIV/HBV and HIV/HCV coinfection (CAESAR study)



Co-infection: HIV and viral hepatitis



Australian BBV estimates



HIV and hepatitis coinfection



Prevalence in Australian HIV Observational Database (AHOD)

	Tested	% positive (tested)	% positive (total cohort)
HIV/HBV (HBsAg)	1605/2086 (77%)	6.3	4.8
HIV/HCV (HCV Ab)	1704/2086 (82%)	13.1	10.1

Coinfection: HIV and viral hepatitis



Prevalence of HIV/HBV and HIV/HCV coinfection in AHOD

Exposure category	HIV/HBV (%)	HIV/HCV (%)
MSM (n=1159, 1236)	6.7	8.7
MSM + IDU (n=92, 102)	9.5	50.0
IDU (n=33, 36)	3.1	63.9
Heterosexual (n=136, 142)	6.3	9.9
Other/Unknown (n=171, 174)	4.9	11.5
Total (n=1605, 1704)	6.3	13.1

Co-infection: HIV and hepatitis B



Impact of HIV on hepatitis B

- Higher chronic infection
- Higher eAg positivity
- Higher HBV DNA levels
- Higher rate of reactivation
- Lower ALT levels
- More rapid liver disease progression

Co-infection: HIV and hepatitis B



Liver disease mortality in MACS cohort

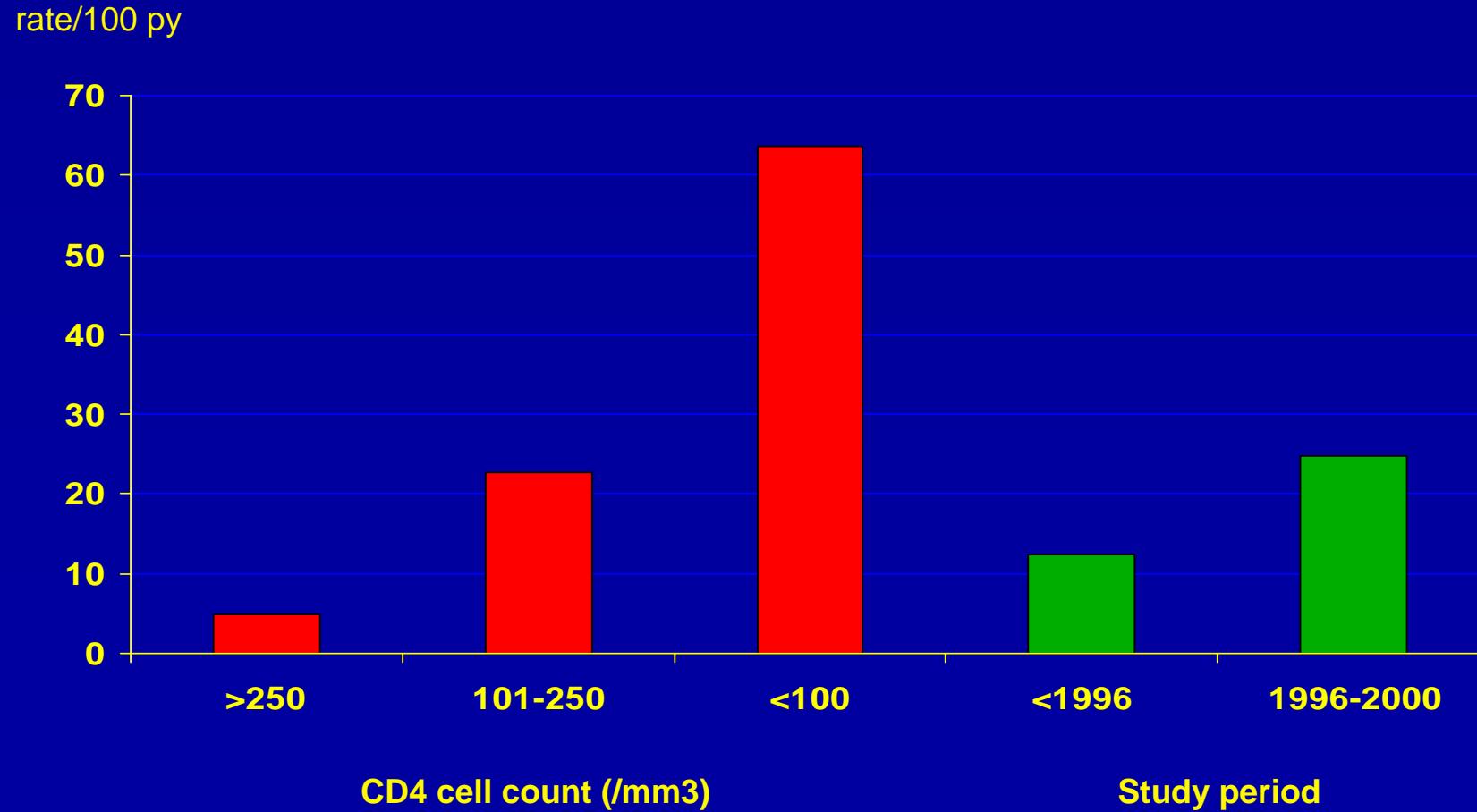


Thio et al Lancet 2002

Co-infection: HIV and hepatitis B



Liver disease mortality in HIV/HBV (MACS)



Thio et al Lancet 2002

Co-infection: HIV and hepatitis C



Impact of HIV on hepatitis C

- Higher chronic infection (85% vs 75%)
- Higher HCV RNA levels
- Higher infectiousness (e.g. perinatal)
- Comparable ALT levels
- More rapid liver disease progression

Co-infection: HIV and hepatitis C



Natural history: survival among haemophilia cohort

	Death (all cause)	Death (liver disease)
HCV (20 years)	8% (4-13%)	3% (0.4-6%)
HIV/HCV (13 years / 20 years)	57% (48-66%)	21% (13-31%)

Co-infection: HIV and hepatitis C



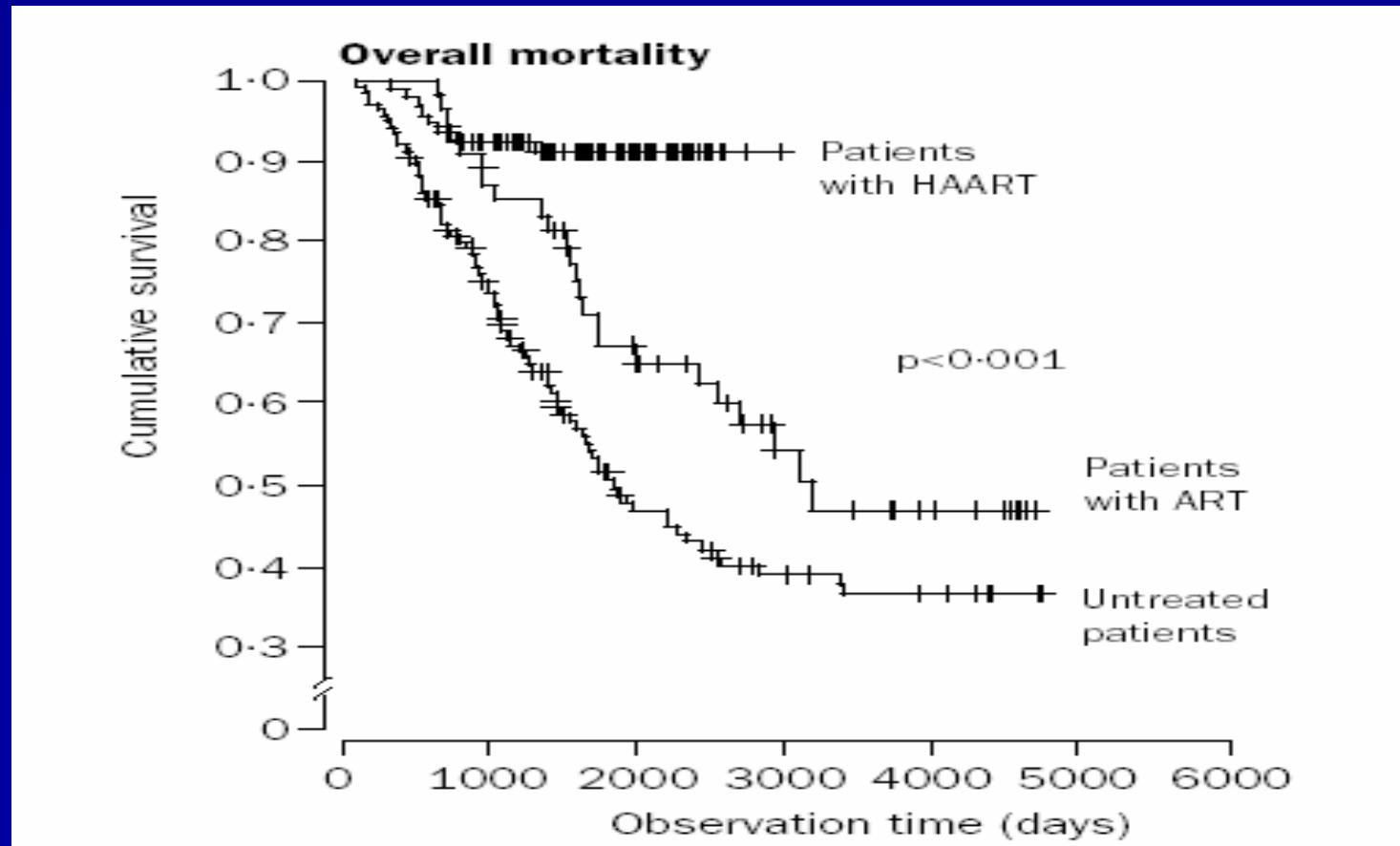
Meta-analysis of impact of HIV on HCV disease progression

	Cirrhosis	ESLD
Makris et al	3.9 (1.4-10.8)	4.2 (1.0-18.4)
Soto et al	1.9 (0.9-4.1)	
Pol et al	2.6 (1.1-5.9)	
Benhamou et al	1.5 (0.8-2.8)	
Eyster et al		3.2 (0.6-17.0)
Telfer et al		21.4 (2.6-174.5)
Lessens et al		7.4 (2.2-25.5)
Meta-analysis	2.1 (1.4-3.1)	6.1 (2.9-13.2)

Co-infection: HIV and hepatitis C



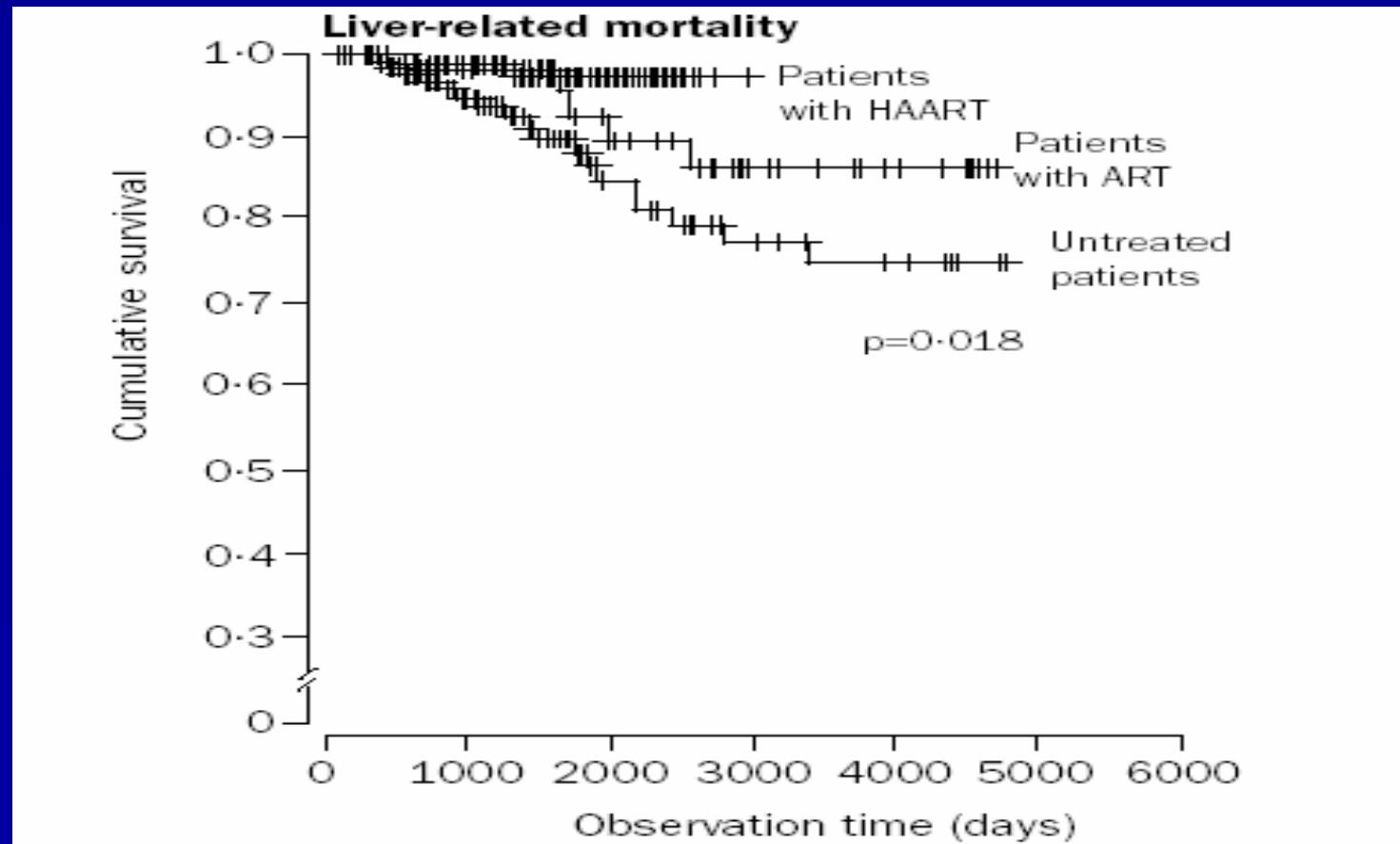
Impact of HAART on mortality in HIV/HCV coinfection



Co-infection: HIV and hepatitis C



Impact of HAART on liver-related mortality in HIV/HCV coinfection



Co-infection: HIV and viral hepatitis



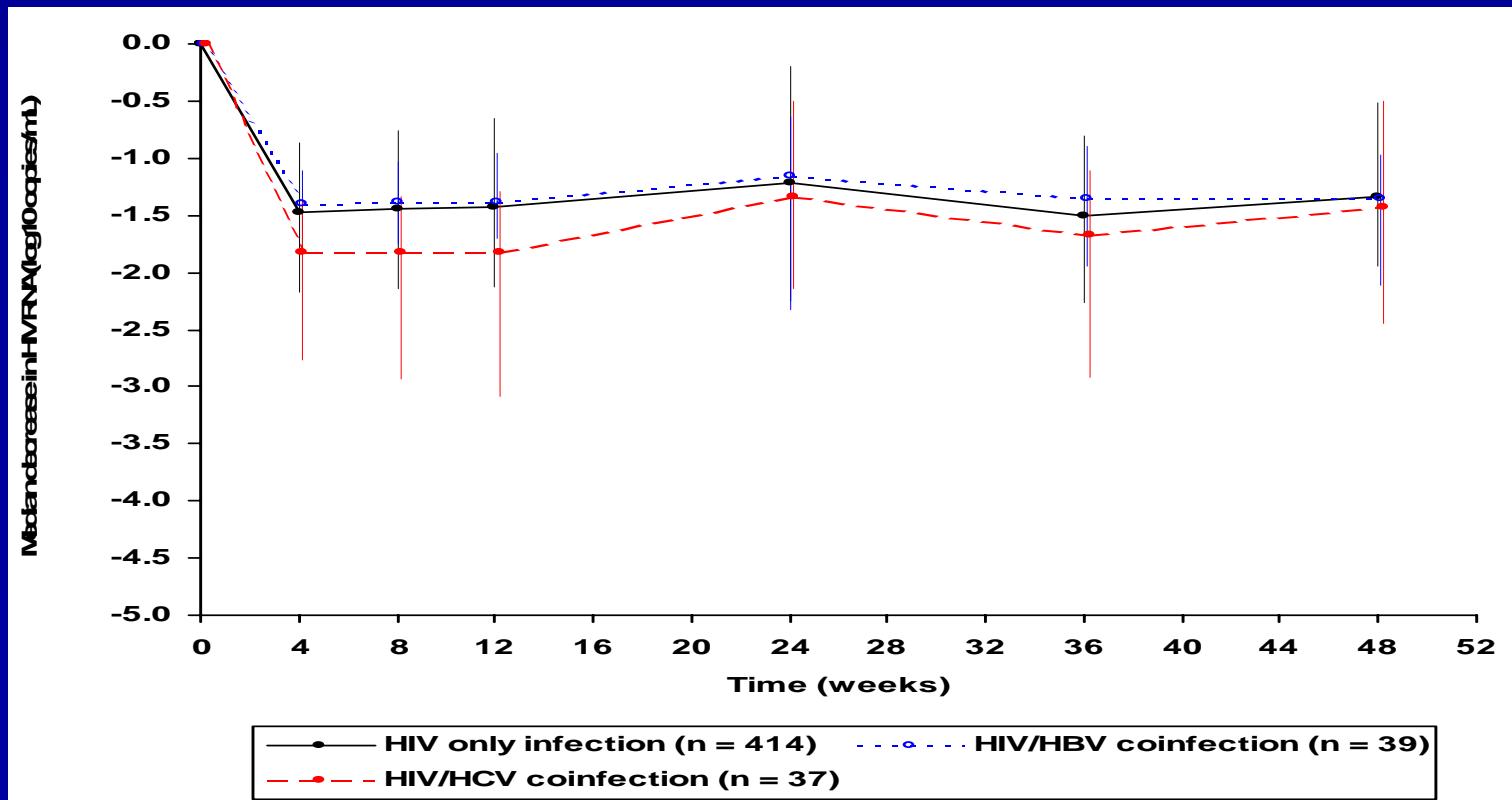
Impact of hepatitis B and C on HIV disease progression

- No impact on HIV viral suppression
- Some impact on CD4 recovery following HAART
- No impact on HIV disease progression

Coinfection: HIV and viral hepatitis



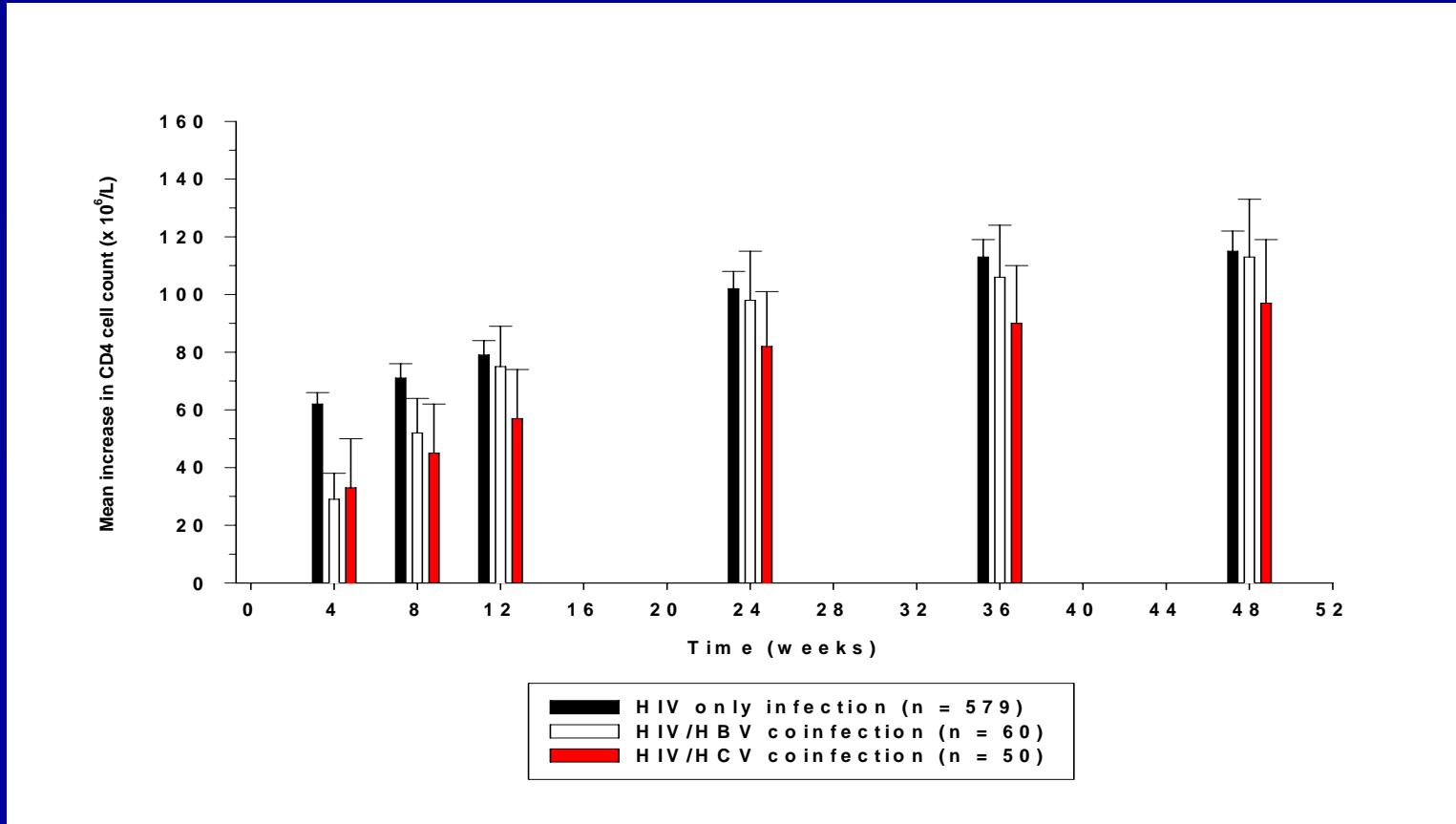
Impact of HBV and HCV on HIV viral suppression (HIV-NAT cohort)



Coinfection: HIV and viral hepatitis



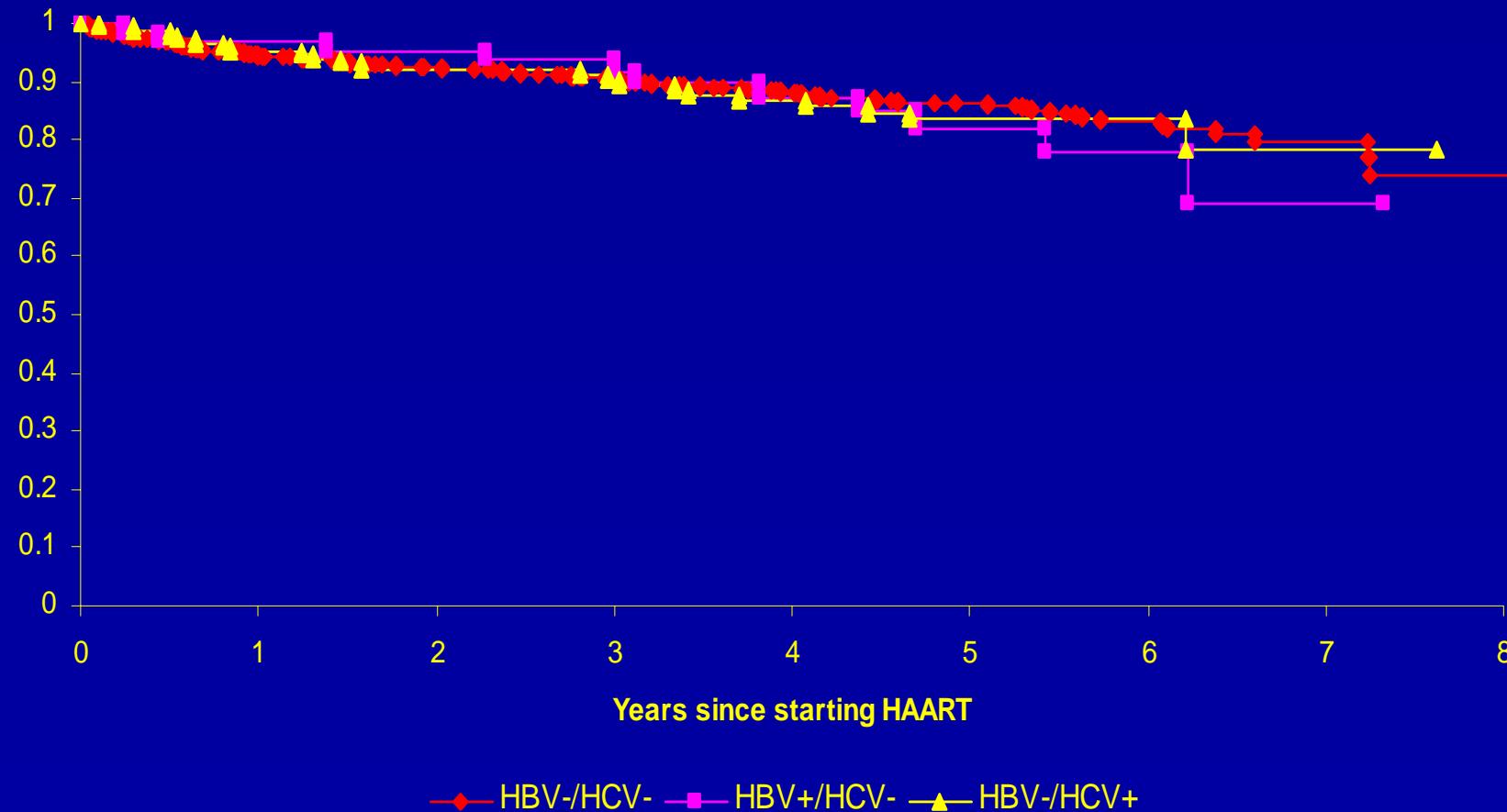
Impact of HBV and HCV on CD4 recovery (HIV-NAT cohort)



Coinfection: HIV and viral hepatitis



Impact of HBV and HCV on HIV disease progression (AHOD)



Coinfection: HIV and hepatitis B



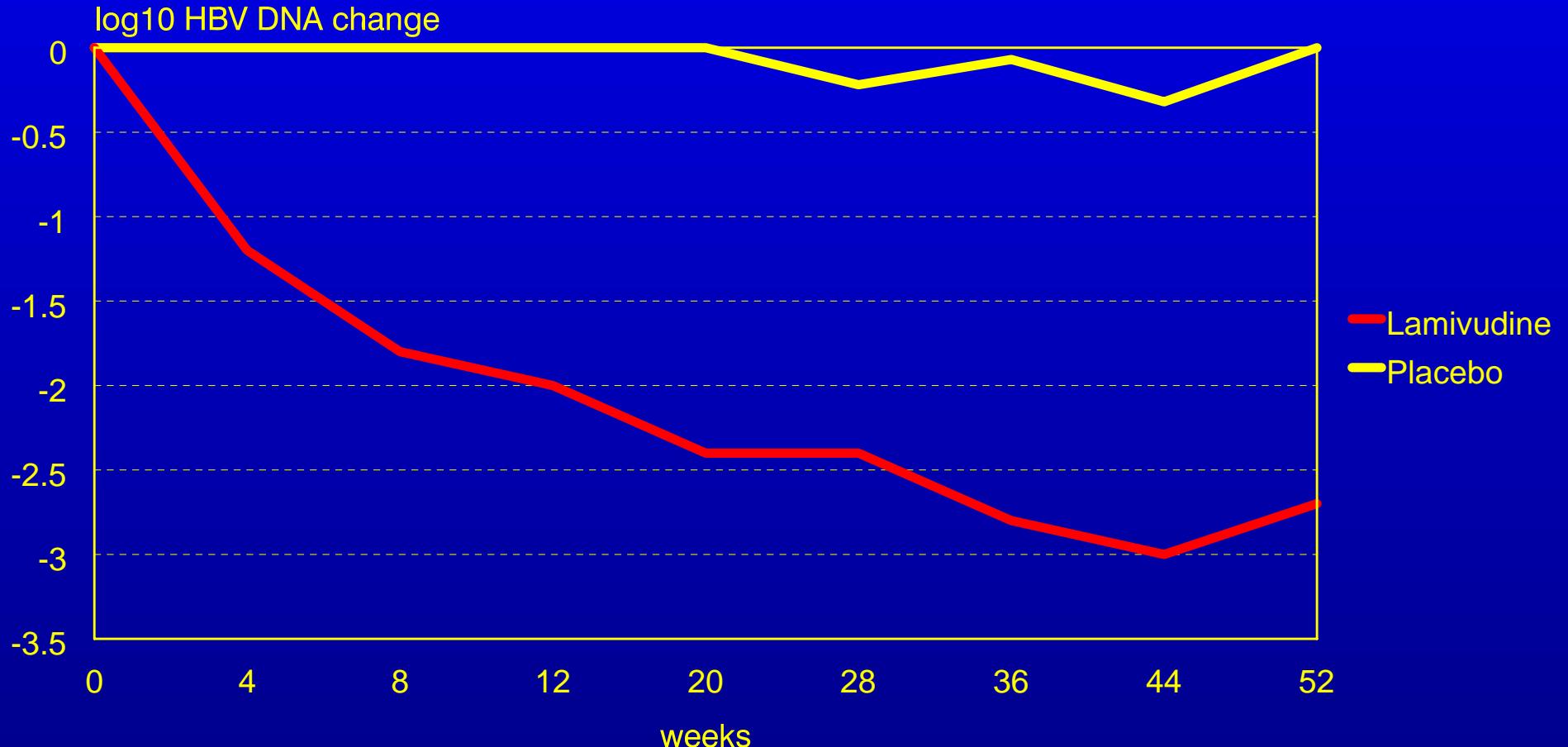
Antiviral therapy

- **Lamivudine (150 mg bd): clear anti-HBV virological and biochemical efficacy, but development of resistance**
- **Adefovir (10 mg daily): evidence of efficacy including lamivudine resistant strains**
- **Tenofovir (300 mg daily): evidence of efficacy including lamivudine resistant strains**
- **Limited data on combination anti-HBV therapy**
- **HAART induced HBeAg seroconversion documented, but relatively uncommon**



HIV & HBV coinfection

Impact of lamivudine on HBV viral load (CAESAR study)



Source: Dore et al JID 1999

Coinfection: HIV and hepatitis B



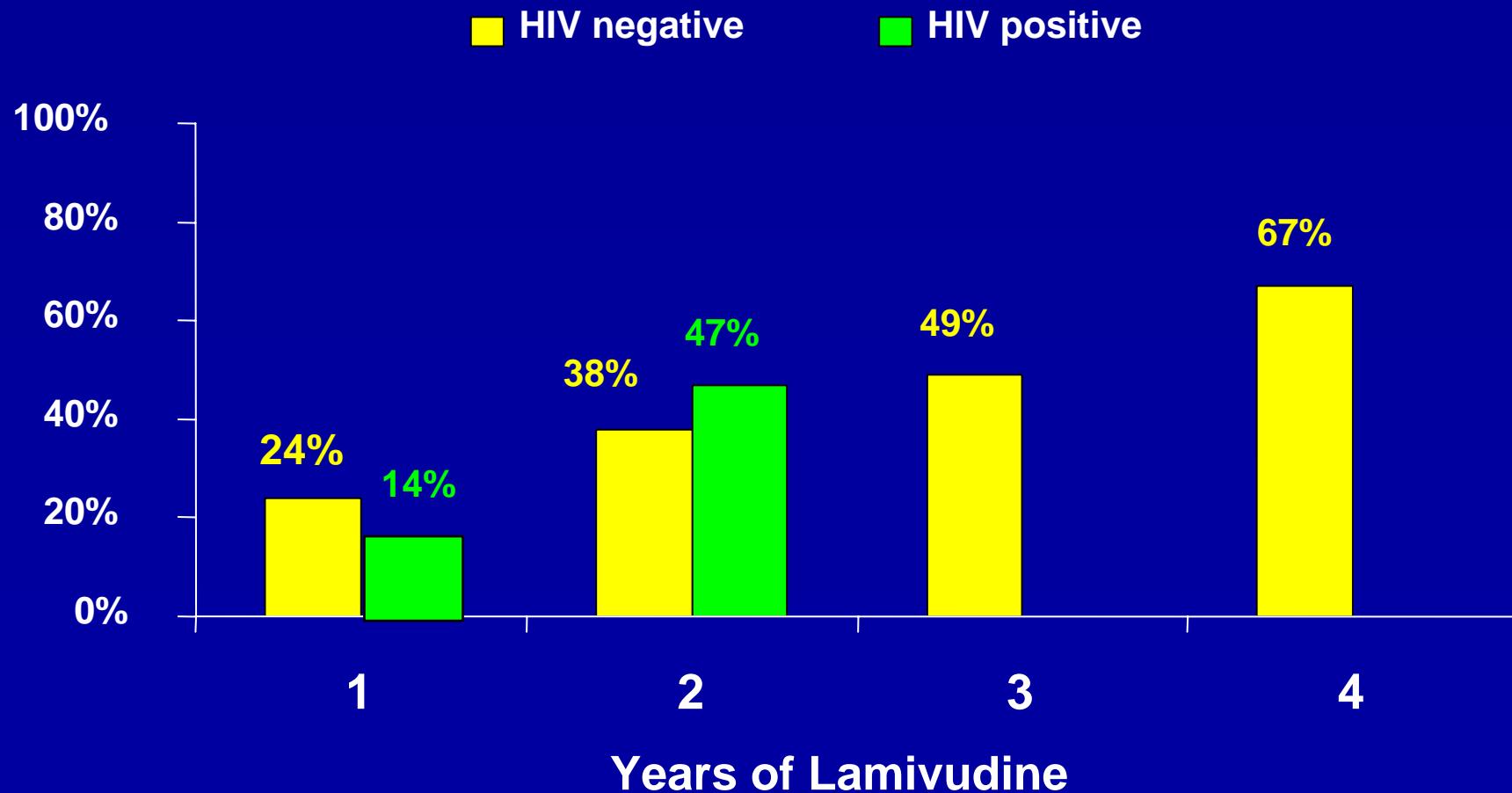
Antiviral therapy: lamivudine

- HBeAg seroconversion similar to HIV -ve (15- 20%)
- Predictors of HBeAg seroconversion: low HBV viral load, high CD4 count
- YMDD resistance in 14% at 1 year and 50% at 2 years
- Should it be used as monotherapy in HIV/HBV patients?

Coinfection: HIV and hepatitis B



Lamivudine resistance

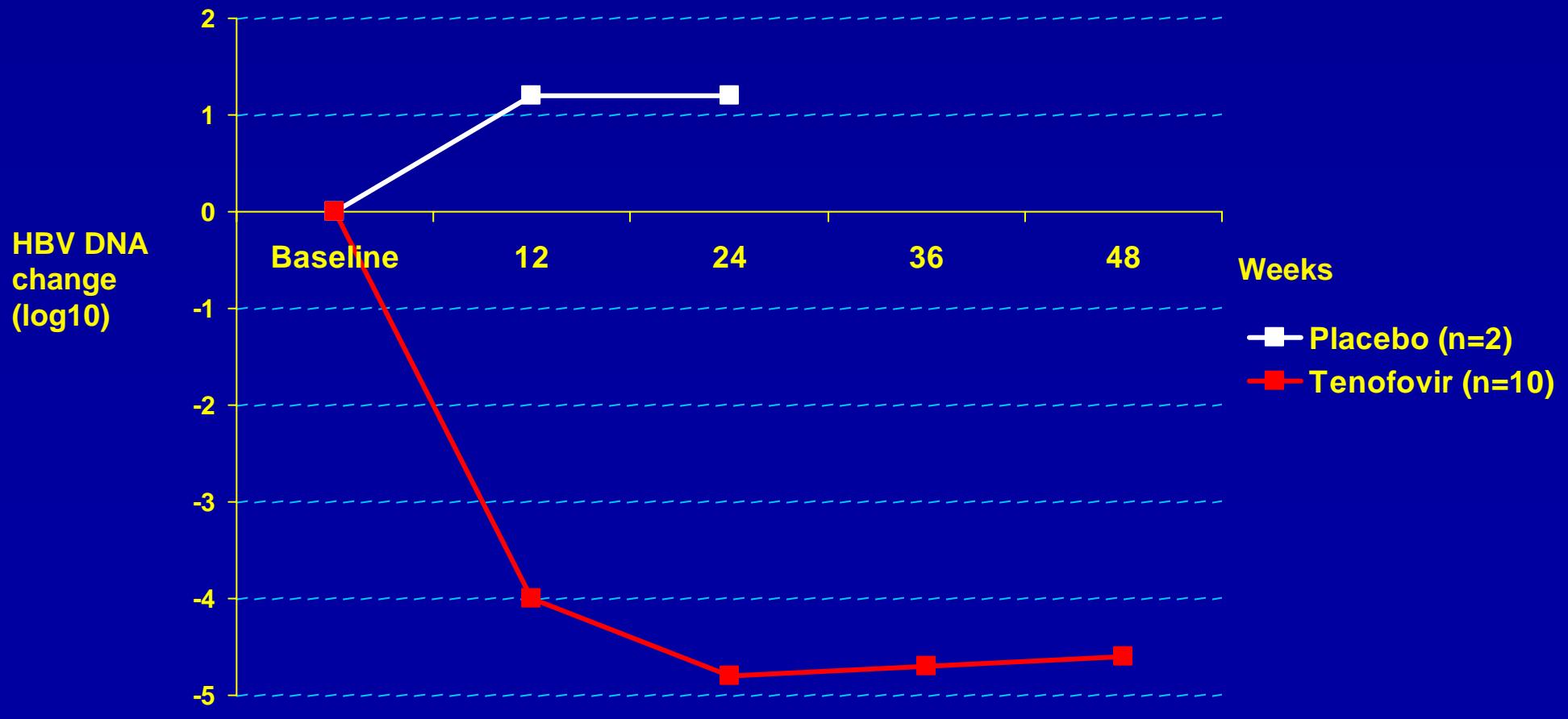


Lai C et al 1998, Leung NW et al 1999, Chang T et al 2000, Pillay et al 2000, Benhamou Y et al 1999

Coinfection: HIV and hepatitis B



Efficacy of tenofovir in ART-experienced HIV/HBV (Study 907)



Coinfection: HIV and hepatitis B



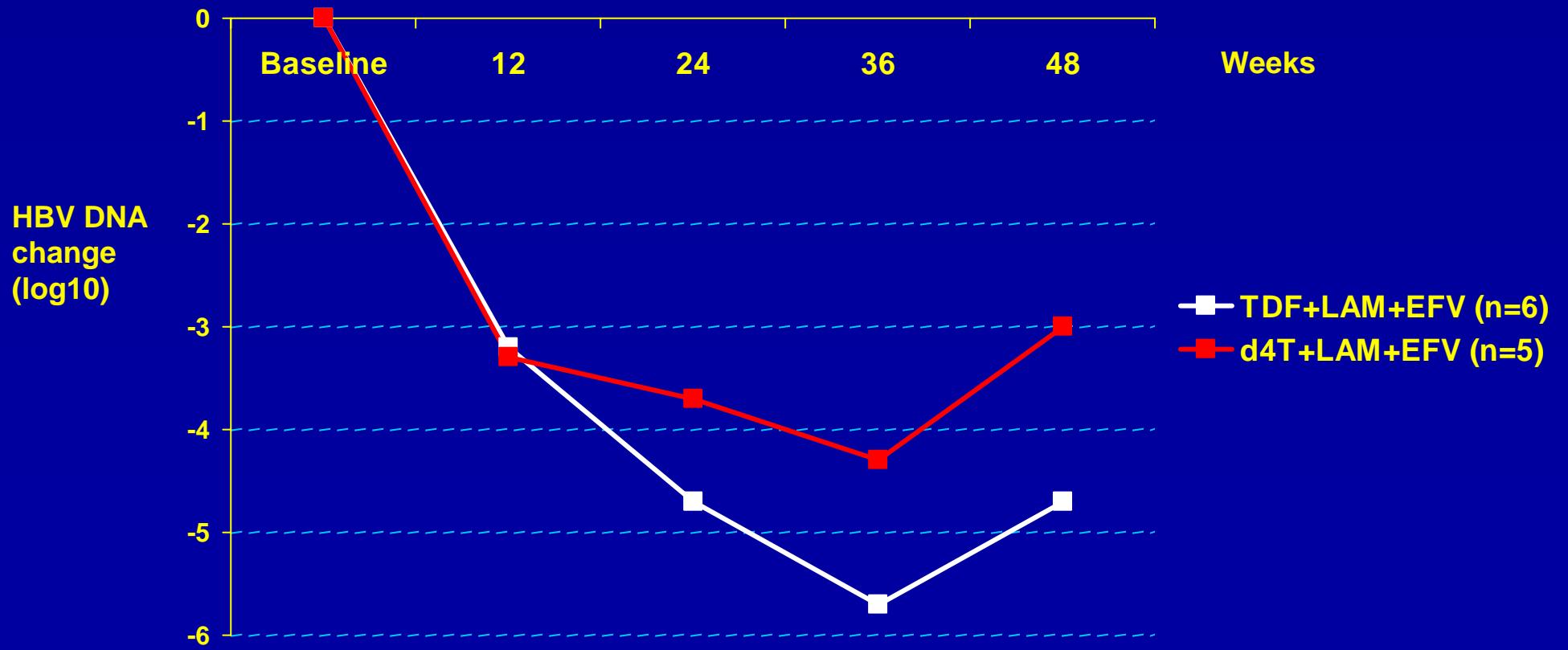
Study 907: HBV DNA change by genotype

	Wild-type (N=4)	LAM-R (N=6)
Baseline	9.7	8.5
Week 24	-5.4	-4.6

Coinfection: HIV and hepatitis B



Efficacy of tenofovir in ART-naive HIV/HBV (Study 903)



Dore et al JIID 2004

Co-infection: HIV and hepatitis B



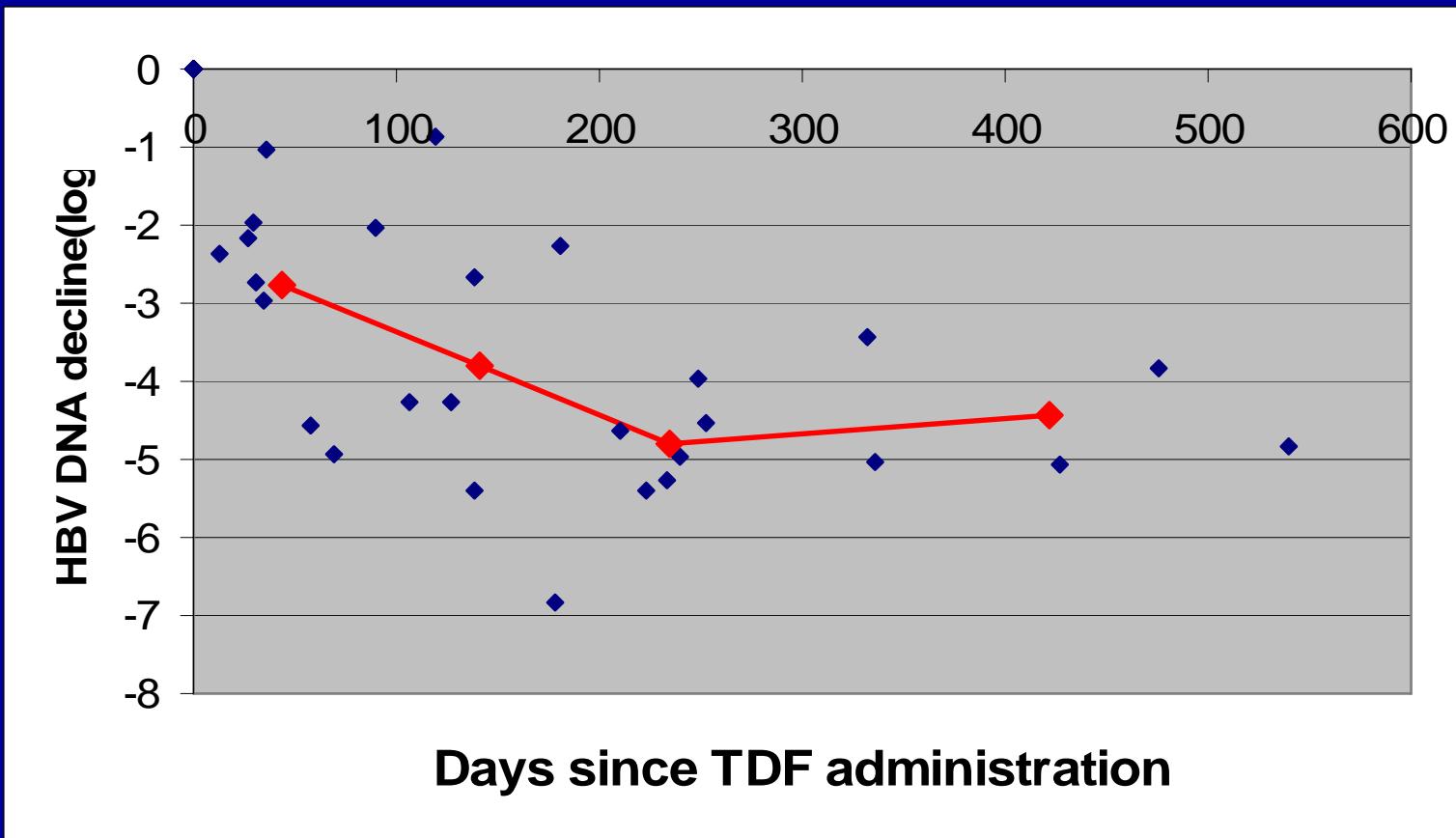
Week 48 outcomes in study 903 substudy

	LAM (n=6)	LAM/TDF (n=5)
Mean change in HBV DNA	- 3.0	- 4.7
HBV DNA > 1,000 copies/mL	5	1
LAM resistance	4	0
HbeAg seroconversion	1	1
Mean ALT change	- 22	- 55



Coinfection: HIV and hepatitis B

St Vincent's Hospital Tenofovir Cohort: 2001 – 2003 (n=17)



Coinfection: HIV and hepatitis B



Therapeutic strategy

- HBV testing in all people with HIV
- HBV DNA and liver biopsy if HBsAg+ with abnormal ALT
- Low HBV DNA (<100,000 copies/ml) and early liver disease
 - LAM-containing HAART
- High HBV DNA and/or more advanced liver disease
 - LAM/TDF-containing HAART
 - (close monitoring for hepatic decompensation)
- Only use HBV active antiretrovirals within HAART regimen

Coinfection: HIV and hepatitis C



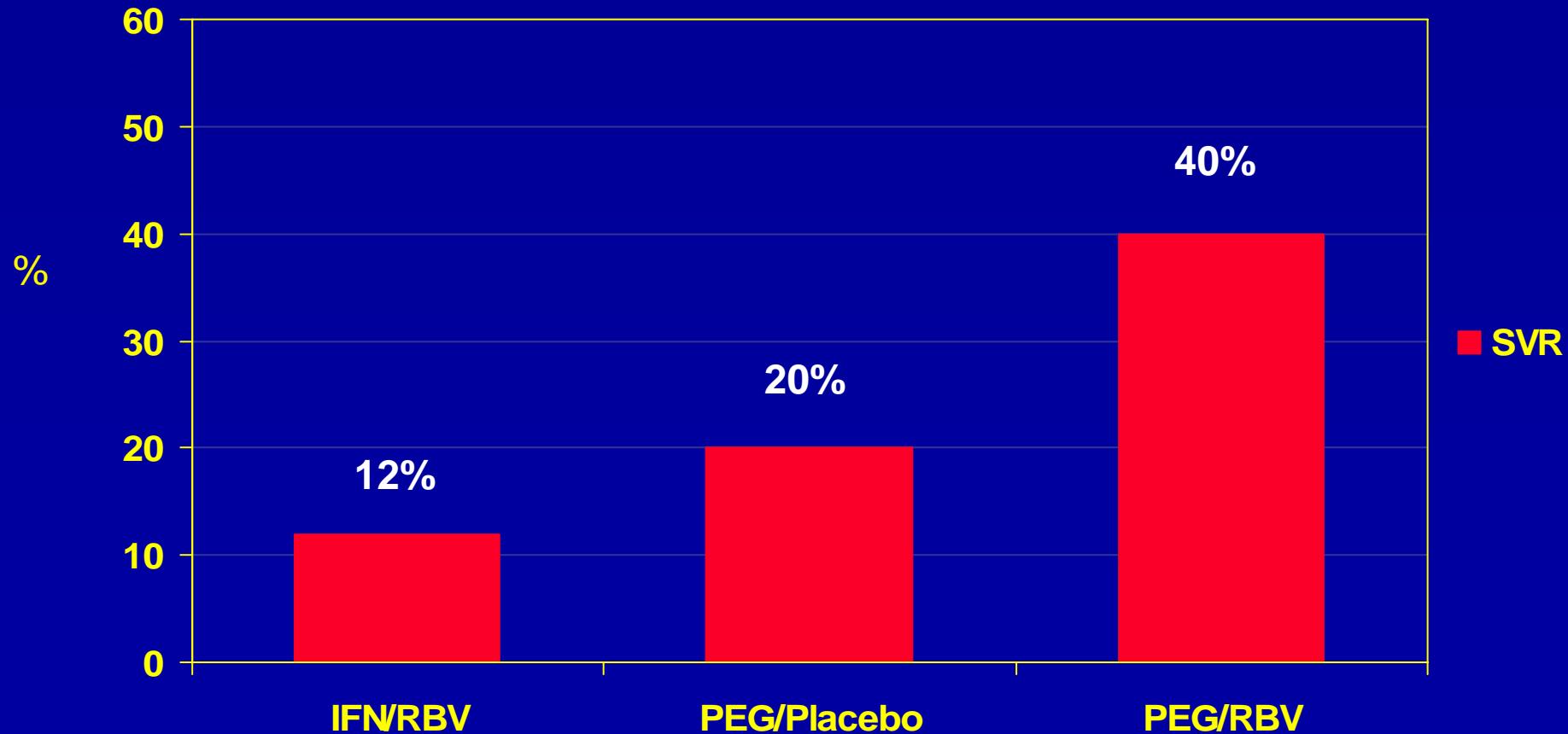
Antiviral therapy

- **IFN monotherapy poorly effective (15% SVR)**
- **Combination IFN + ribavirin enhanced efficacy**
- **Pegylated IFN + ribavirin further improvement**
- **SVR rates 15-20% lower than HCV monoinfection**
- **Need for improved therapeutic strategies, particularly for HCV genotype 1**

Co-infection: HIV and hepatitis C



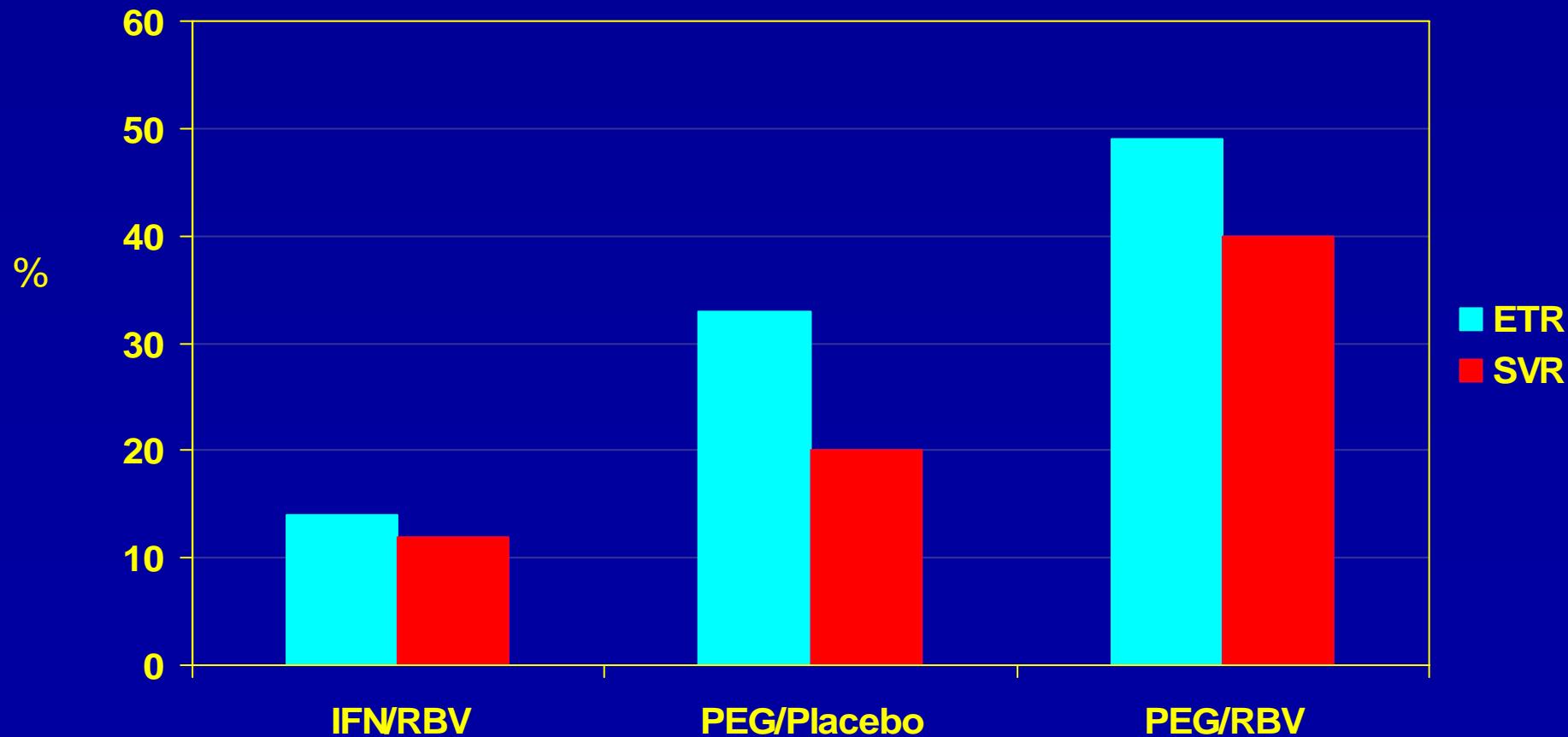
Efficacy of PEG-IFN alfa-2a / RBV combination (APRICOT)



Co-infection: HIV and hepatitis C



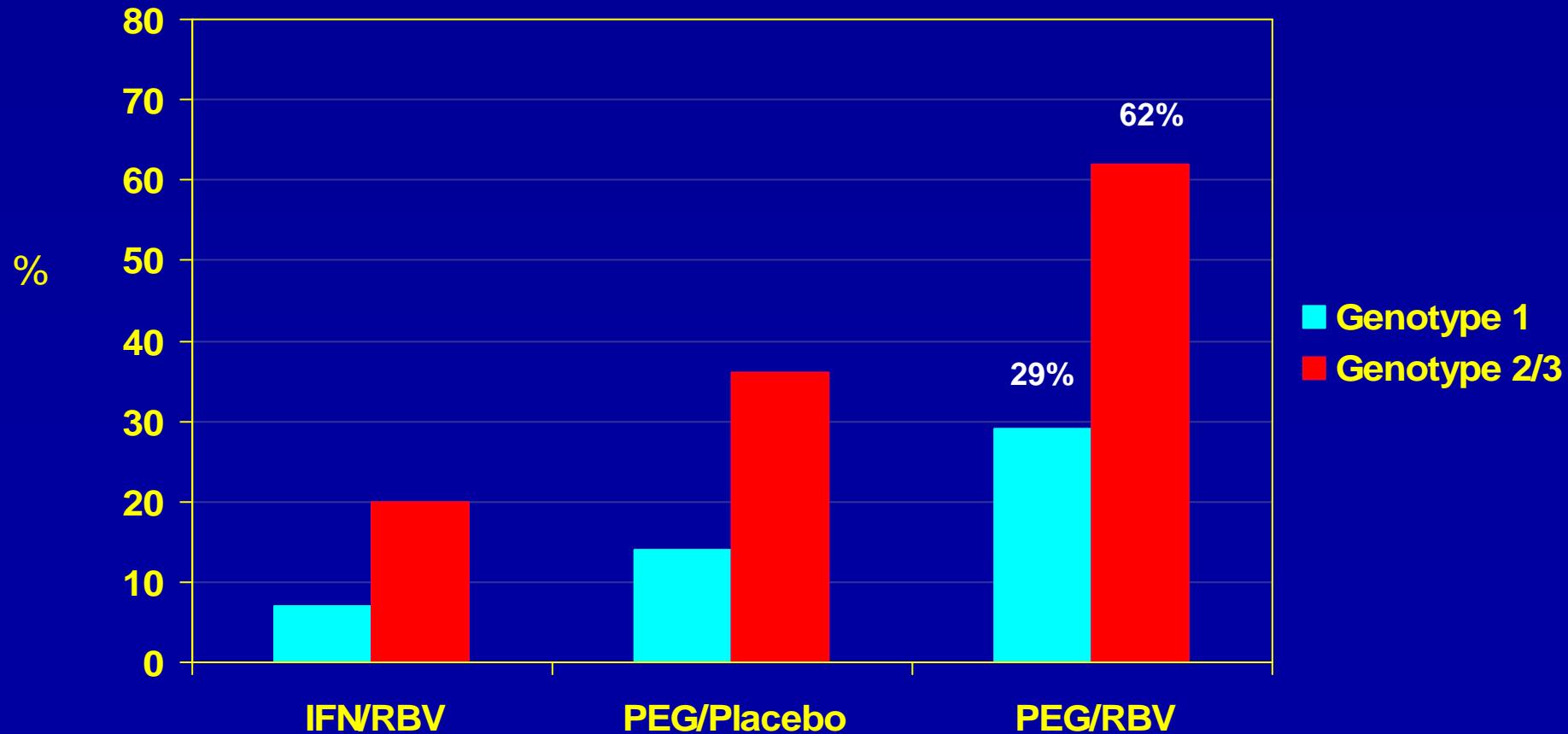
Efficacy of PEG-IFN alfa-2a / RBV combination (APRICOT)



Co-infection: HIV and hepatitis C



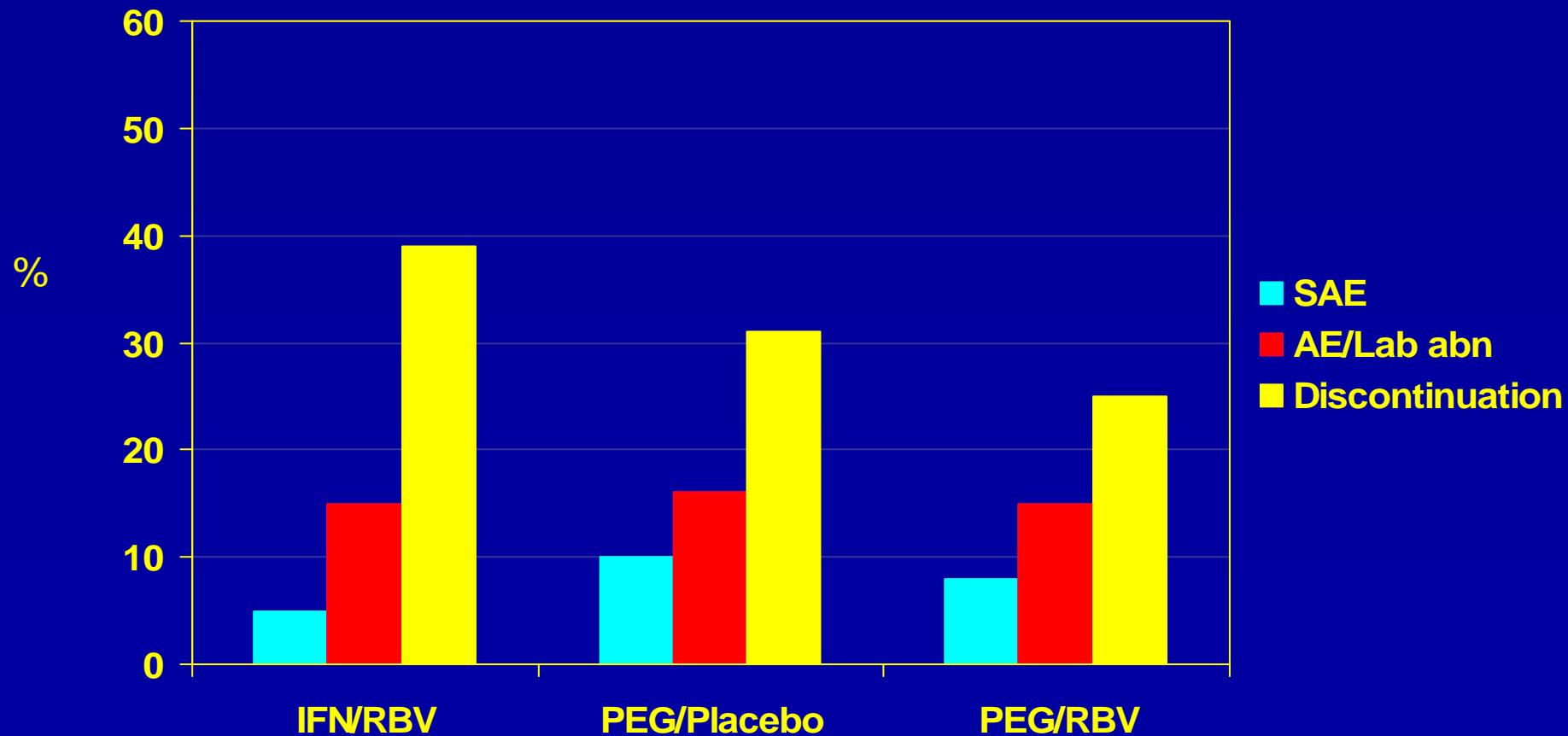
Efficacy of PEG-IFN alfa-2a / RBV combination (APRICOT)



Co-infection: HIV and hepatitis C



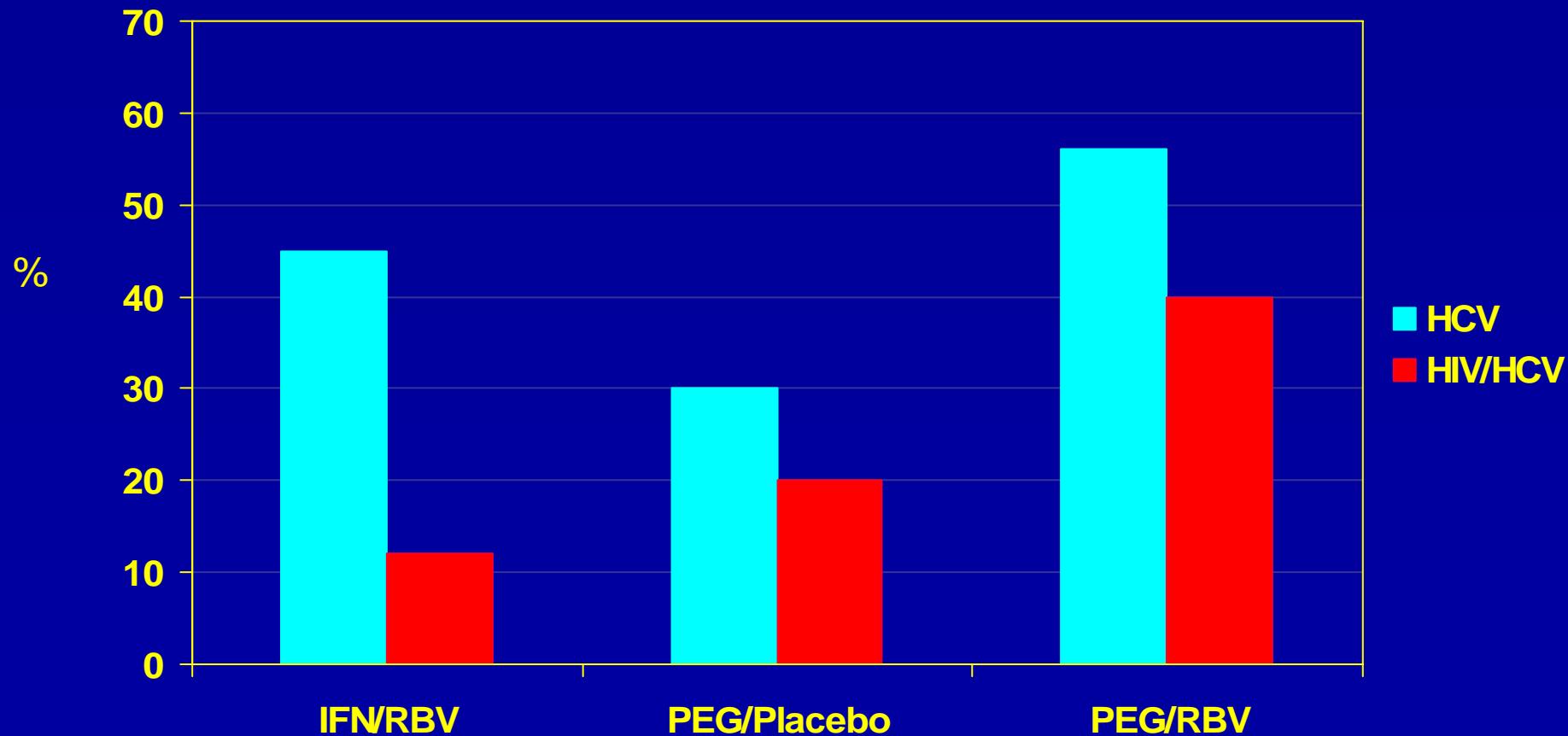
Safety of PEG-IFN alfa-2a / RBV combination (APRICOT)



Co-infection: HIV and hepatitis C



Efficacy of PEG-IFN alfa-2a / RBV combination (impact of HIV)

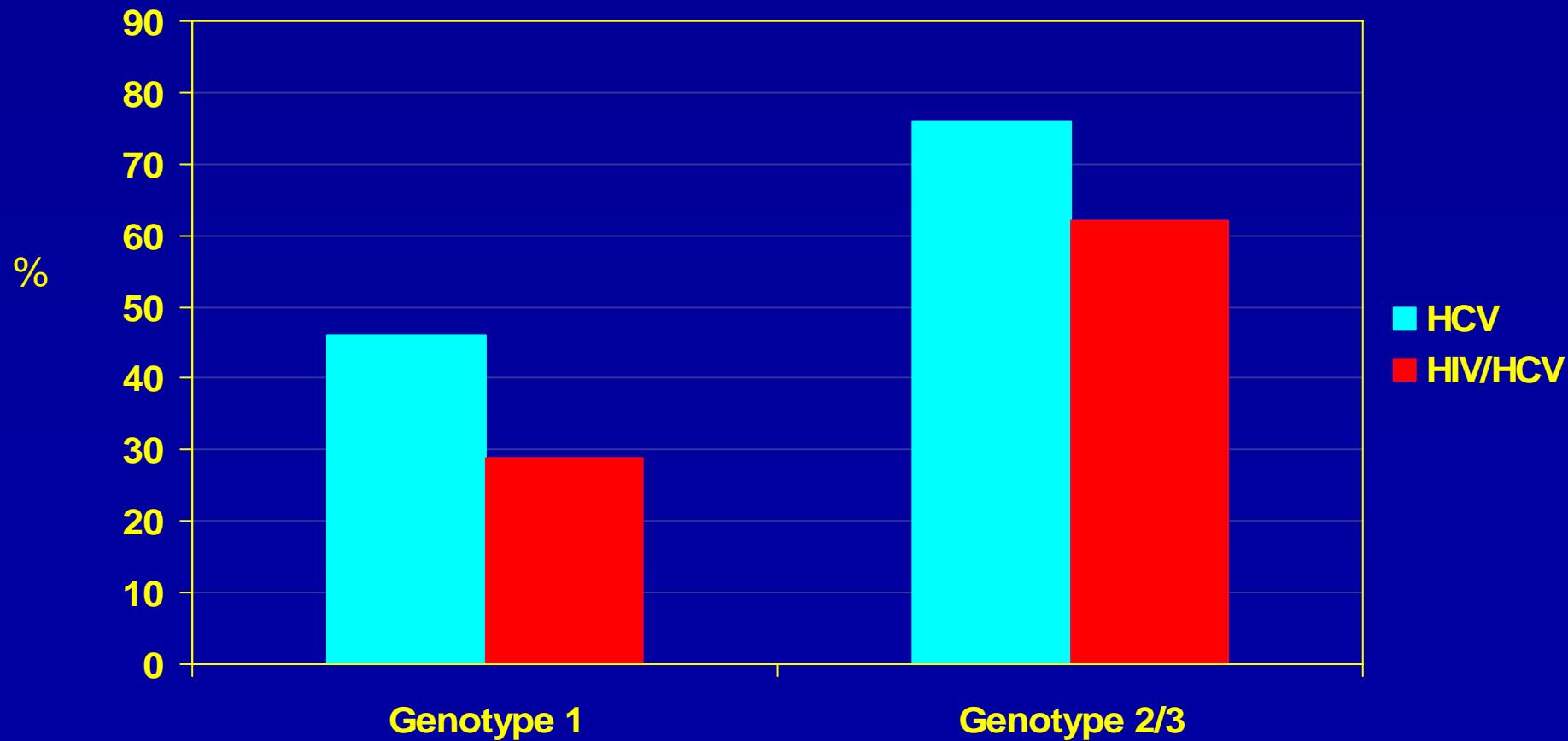


Dietrich et al CROI 2004; Fried et al NEJM 2002

Co-infection: HIV and hepatitis C



Efficacy of PEG-IFN alfa-2a / RBV combination (impact of HIV)



Dietrich et al CROI 2004; Fried et al NEJM 2002

Co-infection: HIV and hepatitis C



Development of treatment strategy for HIV/HCV

- Early versus deferred HCV antiviral therapy ?
- HCV genotype specific strategy ?
- Timing and choice of HAART regimen for treatment naive ?
- Switch to “liver friendly” HAART regimens for treatment experienced ?
- Appropriate strategies to improve treatment adherence ?

Co-infection: HIV and hepatitis C



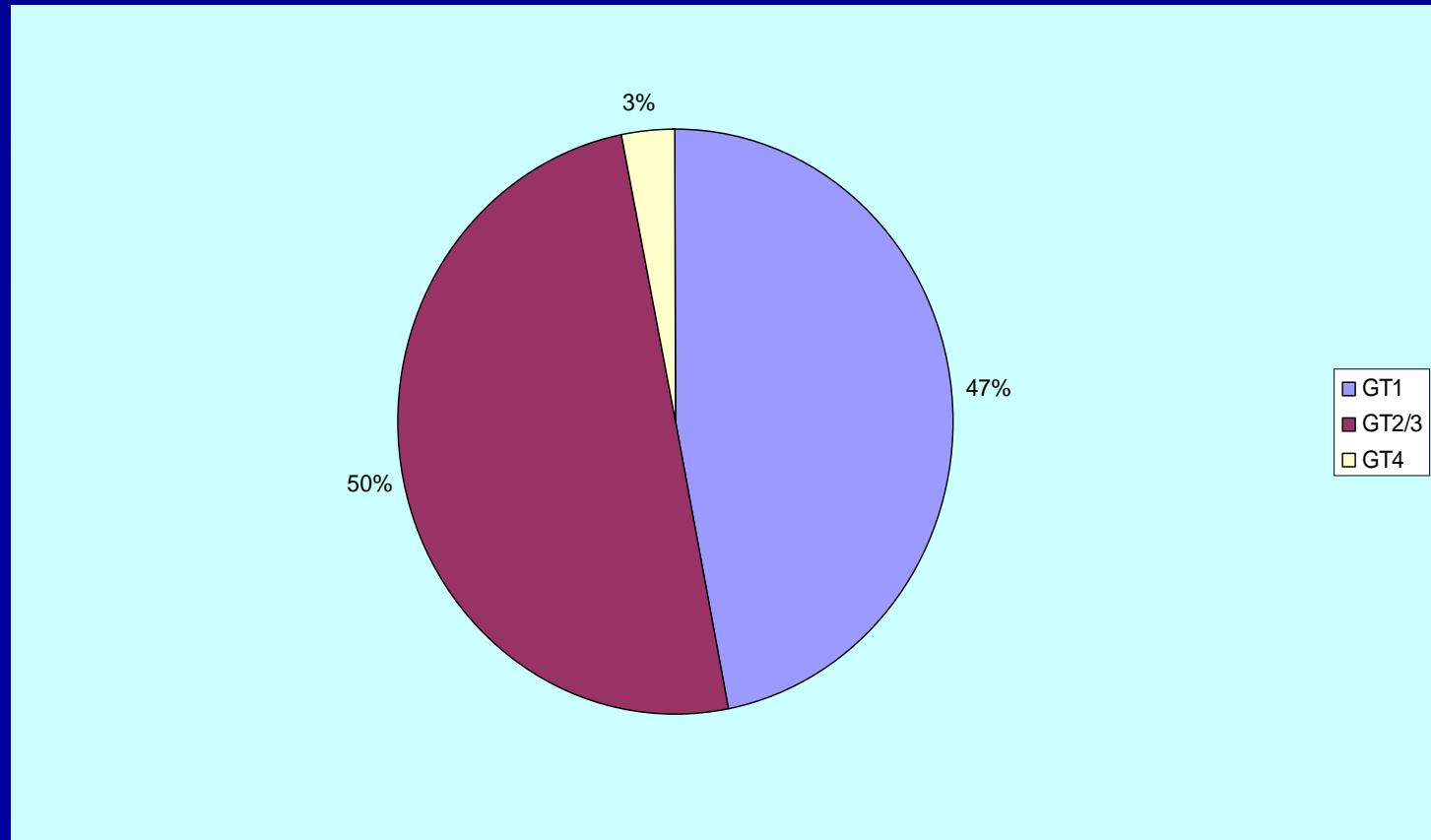
Therapeutic strategy

- Liver biopsy staging if HCV RNA+ and abnormal ALT
- HCV genotype and viral load
- Deferral of treatment if early liver disease, particularly if more advanced HIV disease or HCV genotype 1
- Restoration of immune function prior to treatment
- Earlier treatment for HCV genotype 2 and 3

Co-infection: HIV and hepatitis C



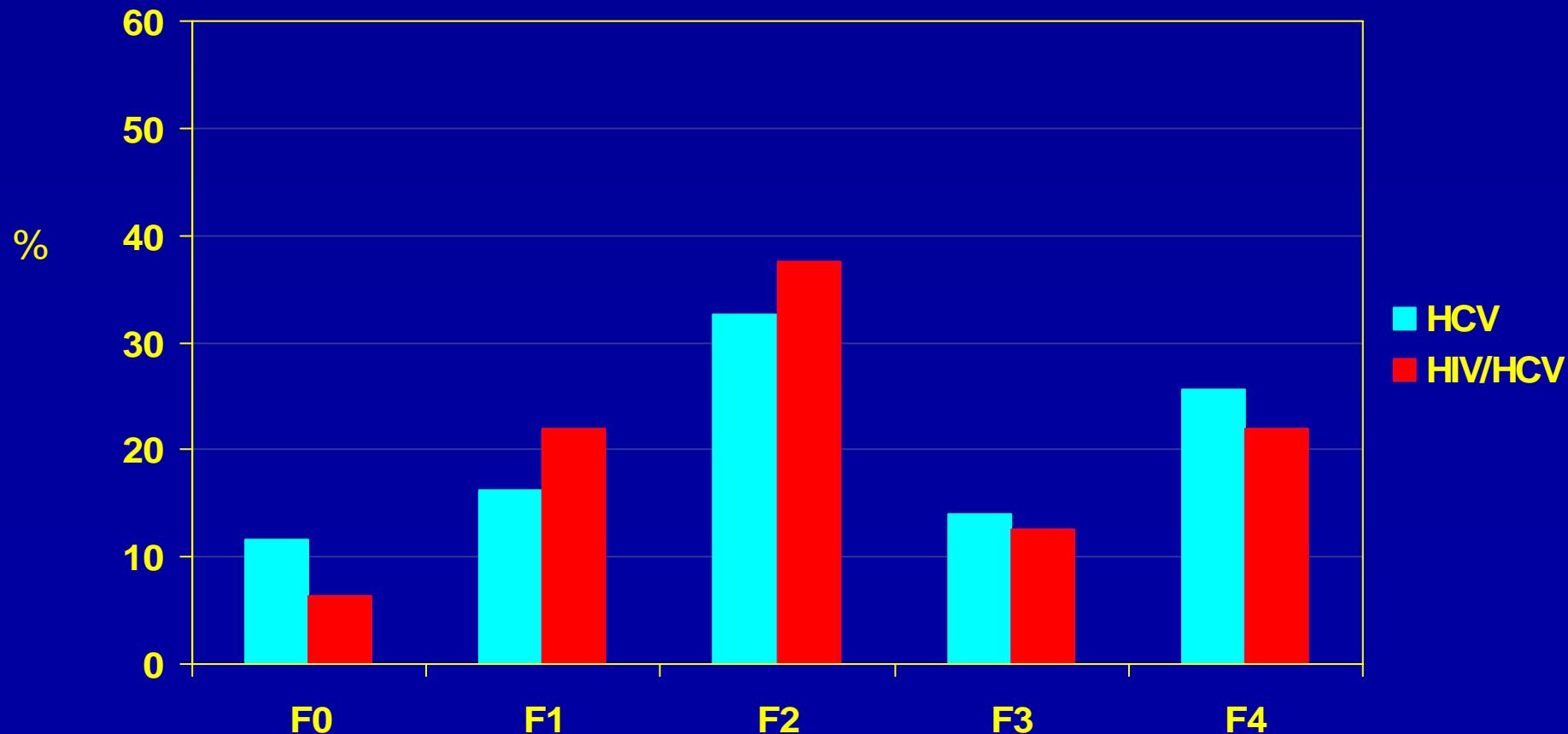
St Vincent's Hospital 2000-2004 (n=32): HCV genotype distribution



Co-infection: HIV and hepatitis C



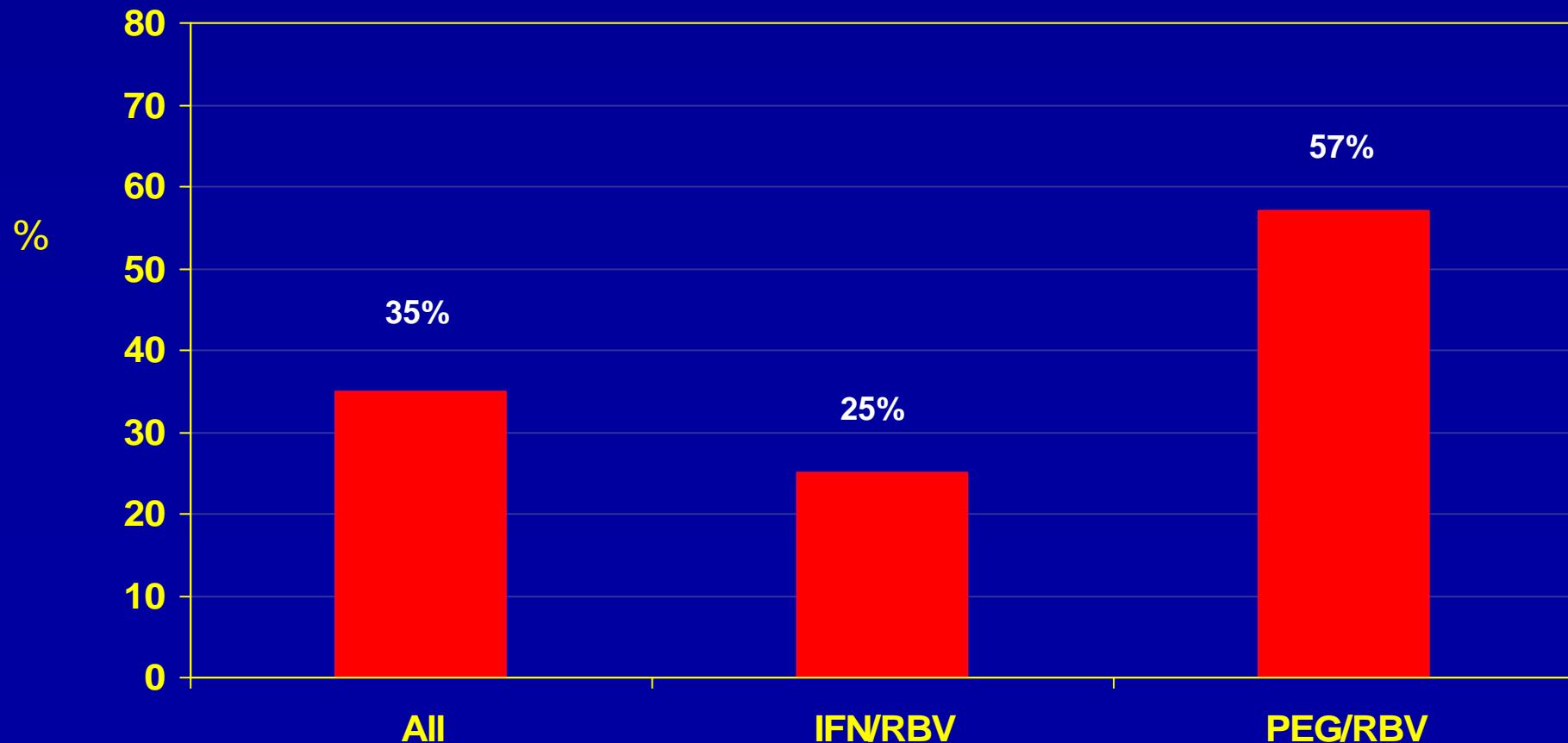
St Vincent's Hospital 2000-2004: Liver fibrosis distribution



Co-infection: HIV and hepatitis C



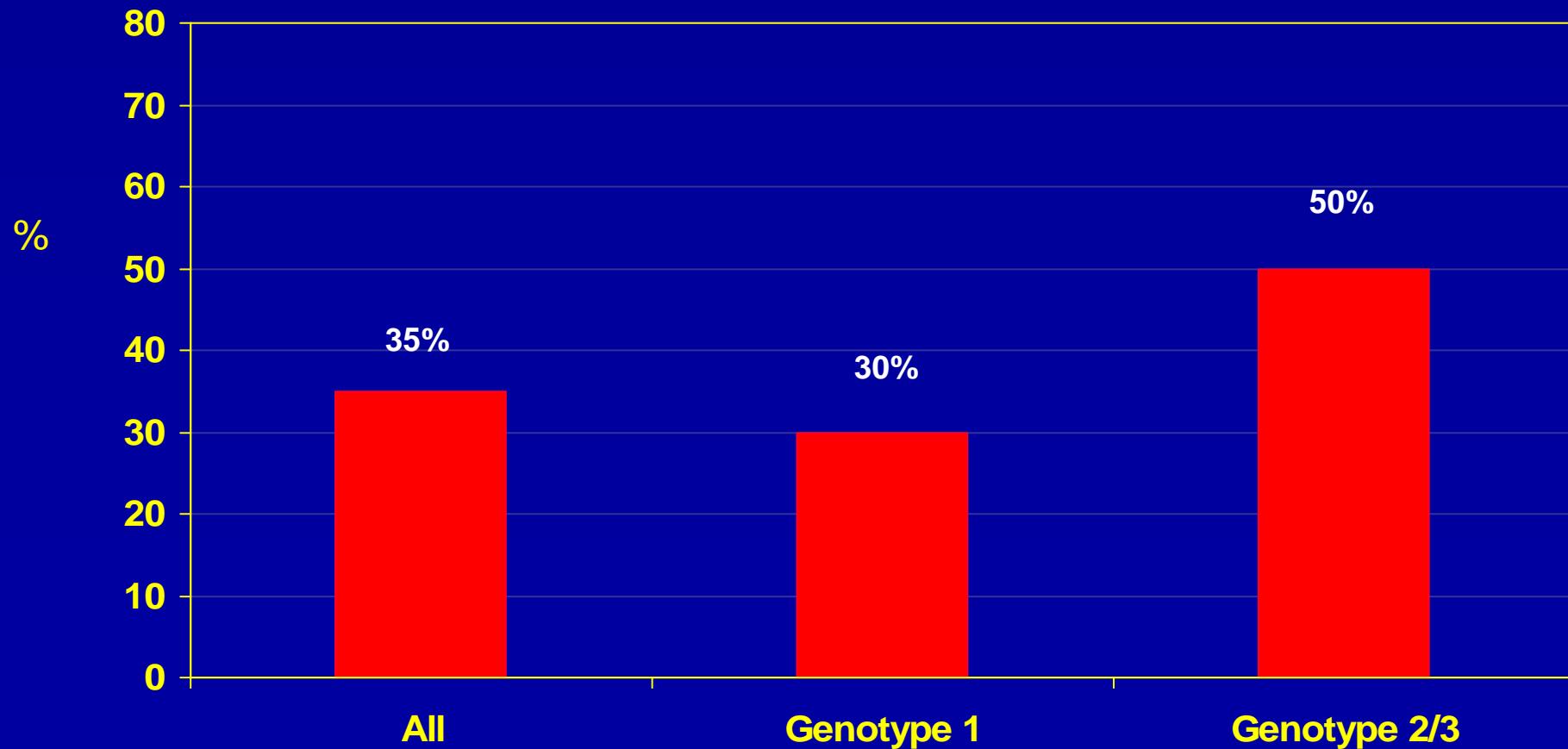
St Vincent's Hospital 2000-2004: Sustained Virological Response



Co-infection: HIV and hepatitis C



St Vincent's Hospital 2000-2004: SVR by genotype



Co-infection: HIV and hepatitis C



St Vincent's Hospital: 2000-2004

- **6/32 patients withdrawn from therapy**
 - 1 nausea
 - 1 vasculitis
 - 1 hypomania
 - 1 non-compliance / IDU
 - 2 decompensation
- **CD4 count declined by 150 by end-of-treatment, but rebounded by 6 months post-treatment**
- **Dose reductions: RBV 5/32, IFN 5/32**

Coinfection: HIV and viral hepatitis



Acknowledgments

- NCHECR
 - Janaki Amin
 - Gail Matthews
 - Philip Law
 - David Cooper
- HIVNAT
 - Philip Law
 - Kiat Ruxrungtham
 - Chris Duncombe
 - Mark Boyd
 - David Cooper
- St Vincent's Hospital
 - Gail Matthews
 - John McAllister
 - Zoe Potgeiter
 - David Cooper
- Other Collaborators
 - Stephen Locarnini
 - Sharon Lewin
 - Joe Sasadeusz