Anti-HCV Therapy: standard of care and current guidelines

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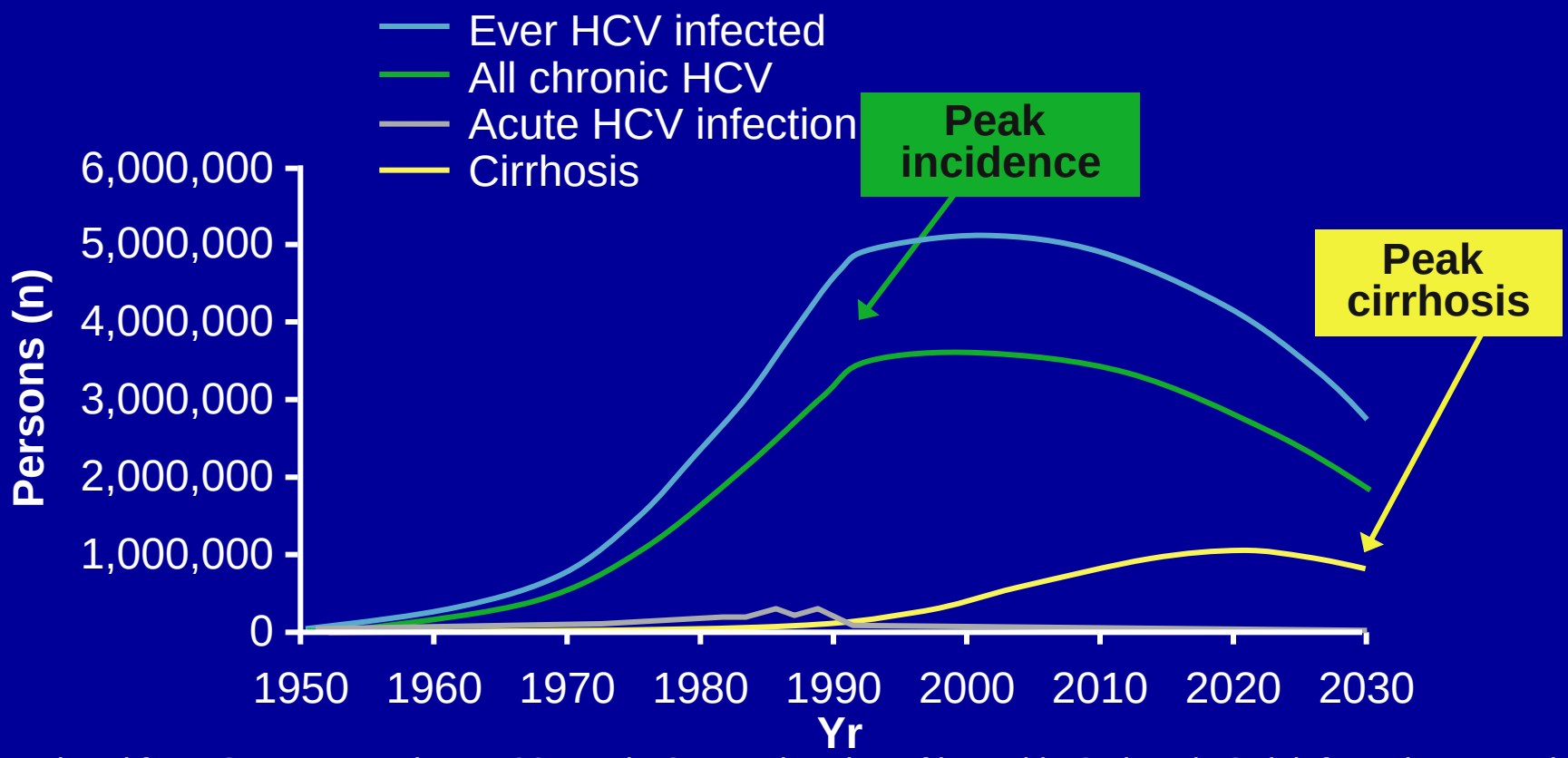
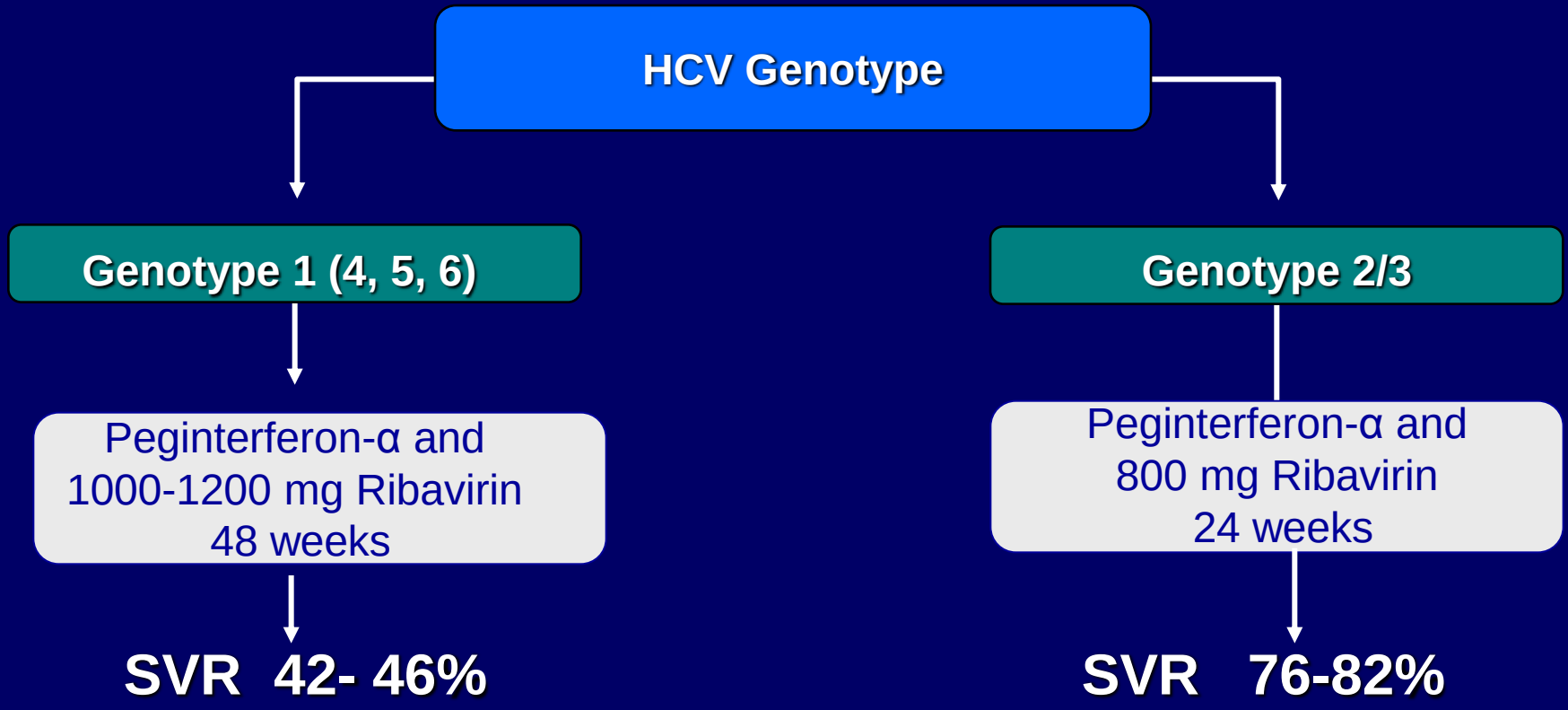
The Changing Face of HCV in the US



Reprinted from Gastroenterology, 138, Davis GL, et al, Aging of hepatitis C virus (HCV)-infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression, 513-521, Copyright 2010, with permission from Elsevier.

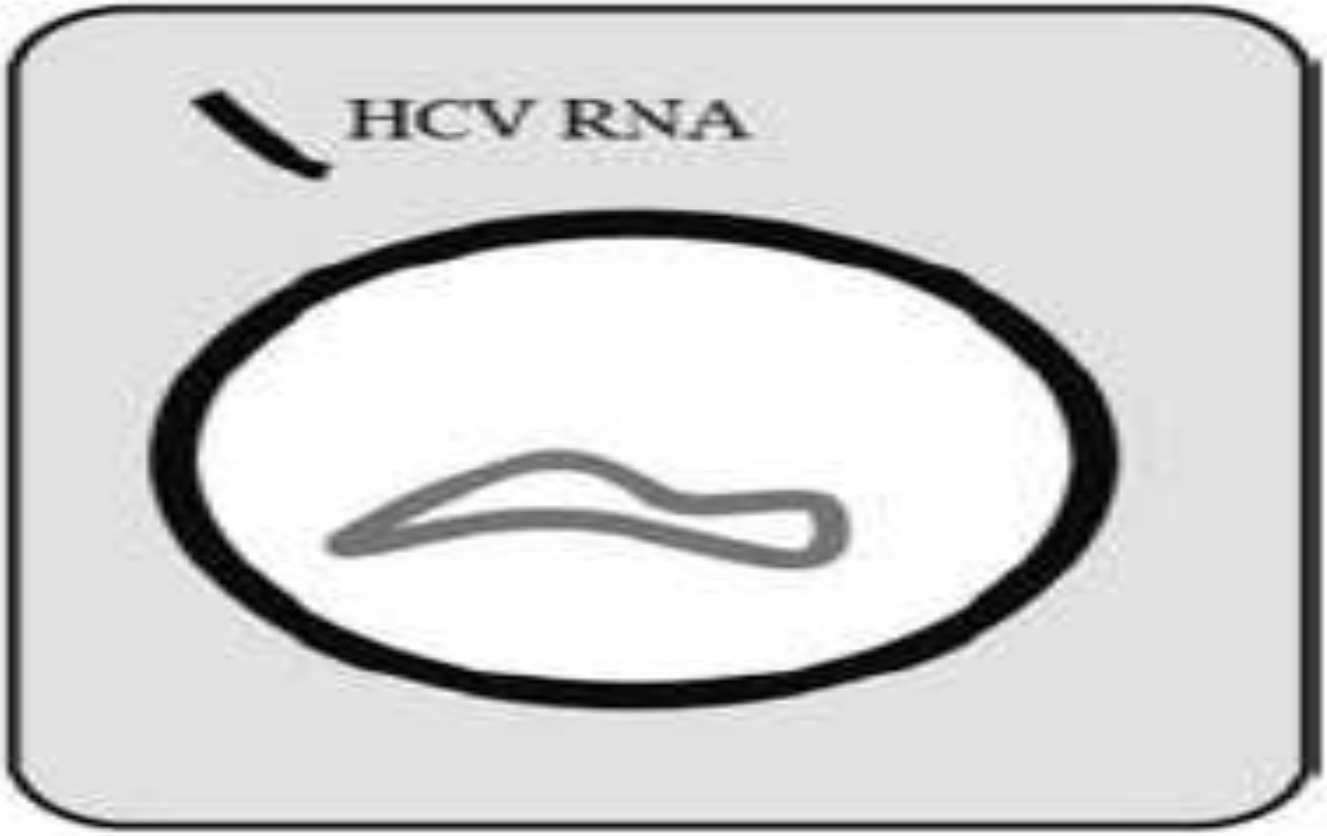
Standard Treatment of HCV Peginterferon α and Ribavirin



Insufficient Response, Multiple Adverse Events, and Expensive

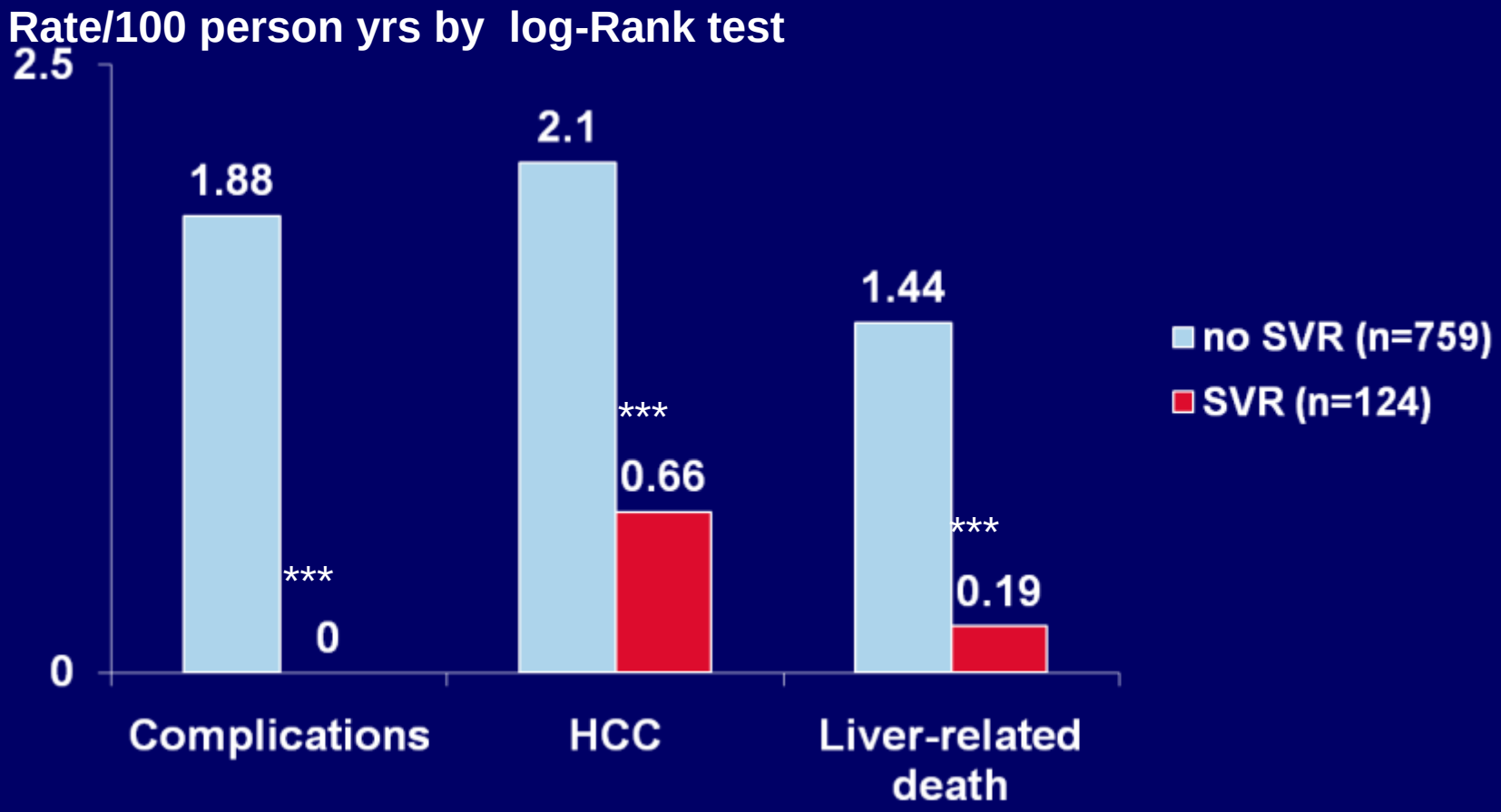
Manns et al., *Lancet* 2001 358:958-965 Fried et al., *N Engl J Med* 2002;347:975-982

Hepatitis C is a Curable Disease



Reduction in Clinical Outcomes after SVR

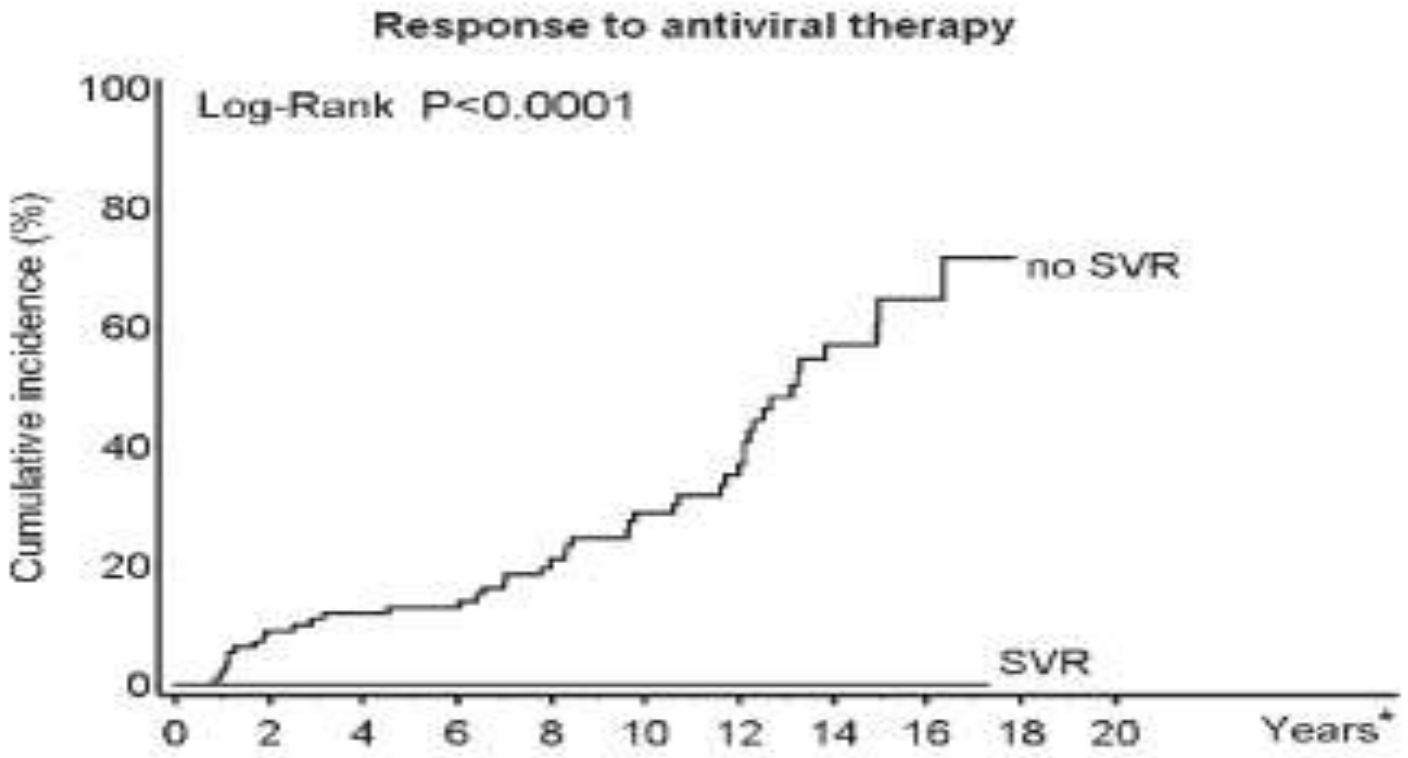
920 patients, 142 had SVR, all with cirrhosis, G-1 73%, F/U mean 96 mo.



***p<0.001

Bruno S et al, Hepatology 2007; 45: 579-87

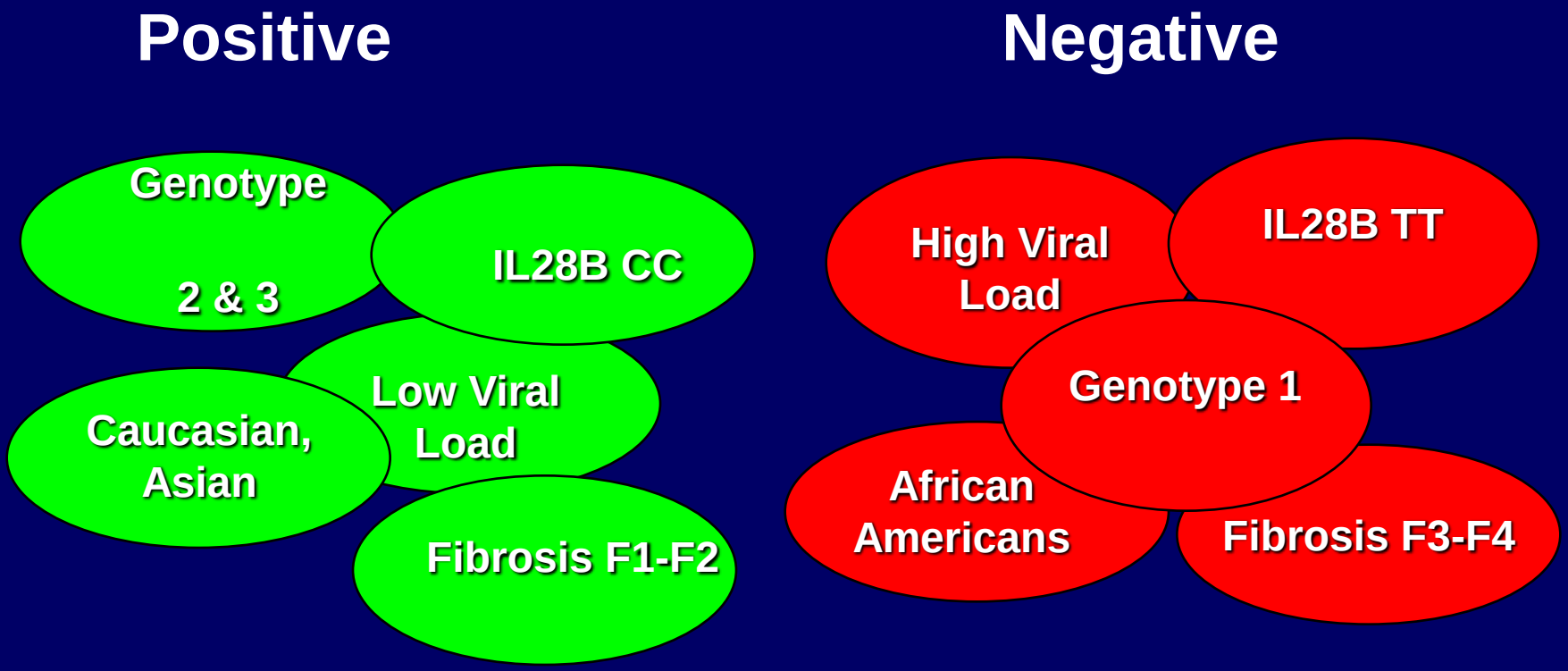
Incidence of Esophageal varices in 149 treated patients with compensated, HCV-related liver cirrhosis according to response to therapy



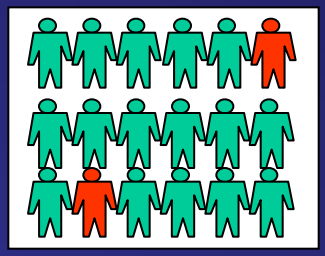
Bruno S et al. Hepatology 2010

Predictive Factors of Therapy Response

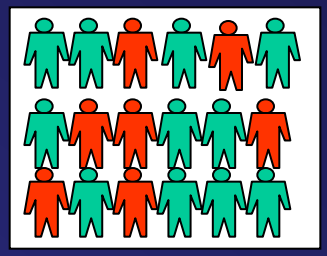
Baseline Factors



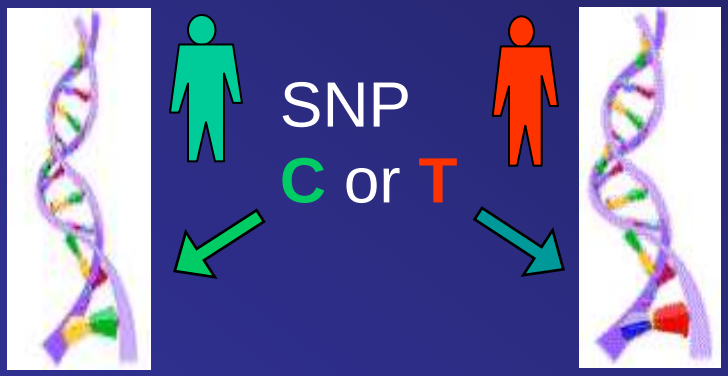
What are Genome wide association scans (GWAS)?



Responders

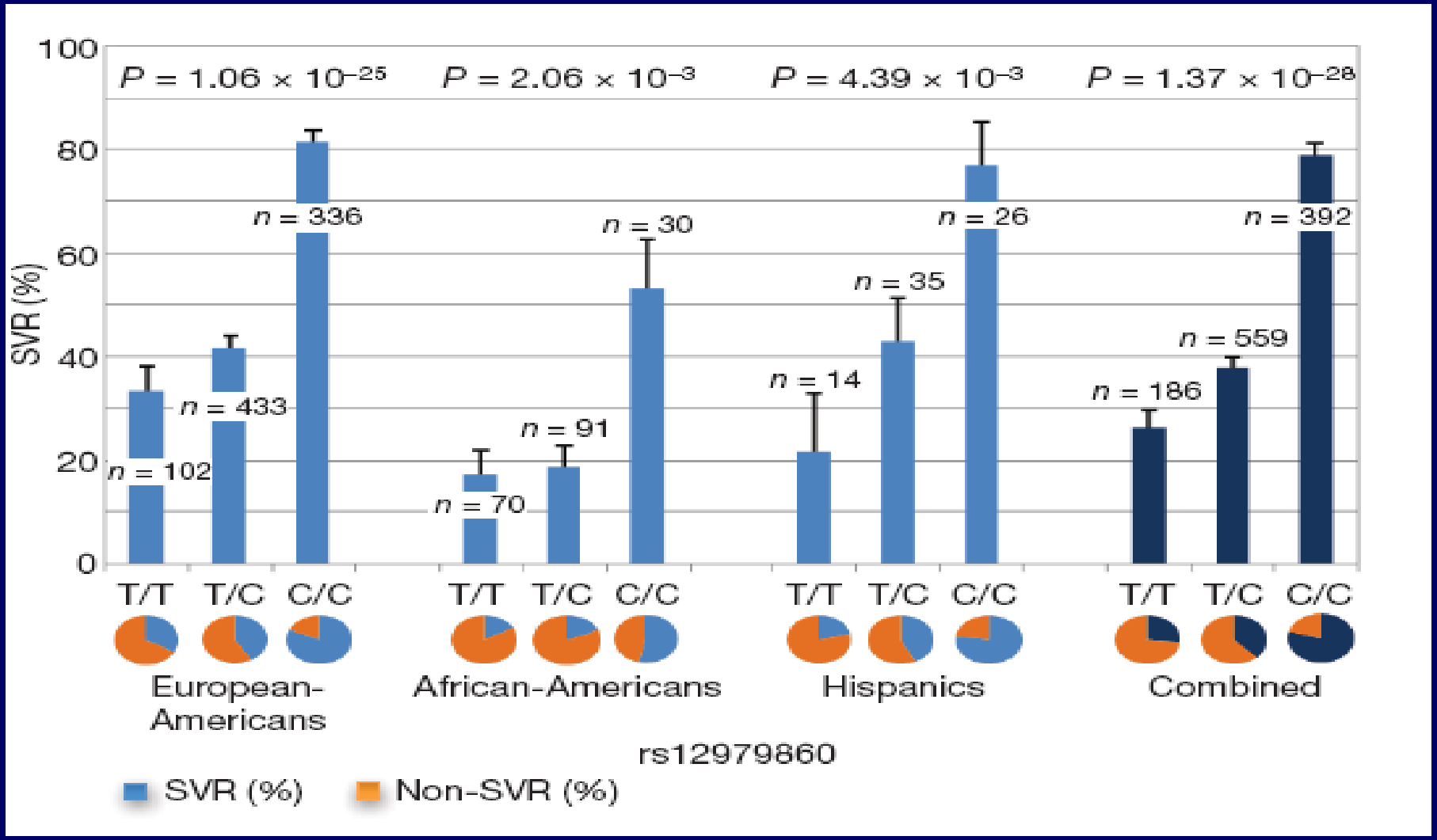


Non-responders



Pharmacogenetic Analysis of the rs12979860 C allele

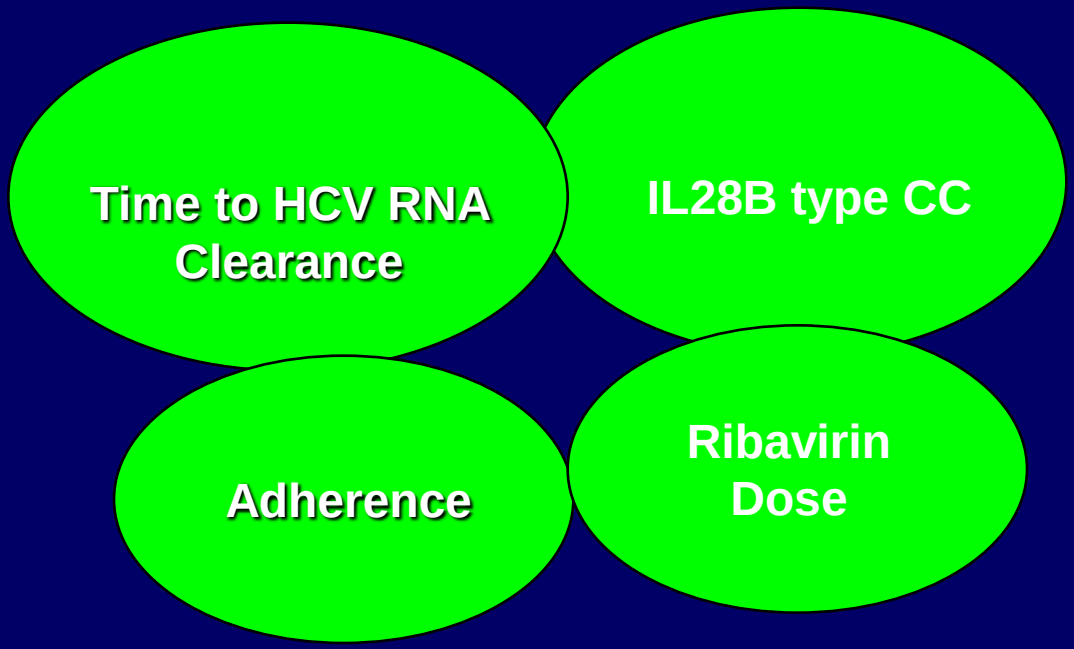
Genetic variation in IL28B predicts SVR in Genotype 1 Patients



Ge D et al. Nature 2009

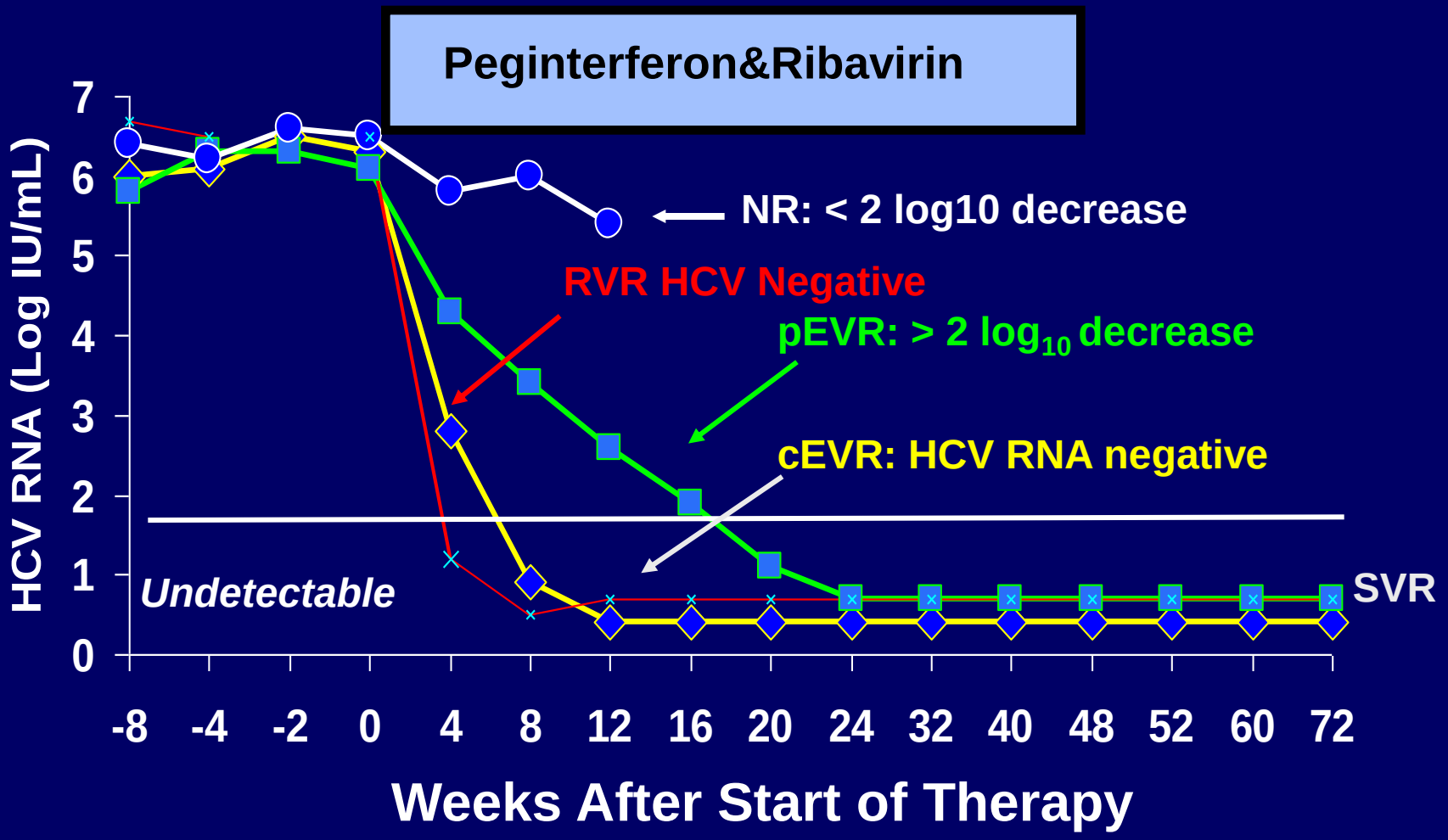
Predictive Factors of Therapy Response

During Therapy

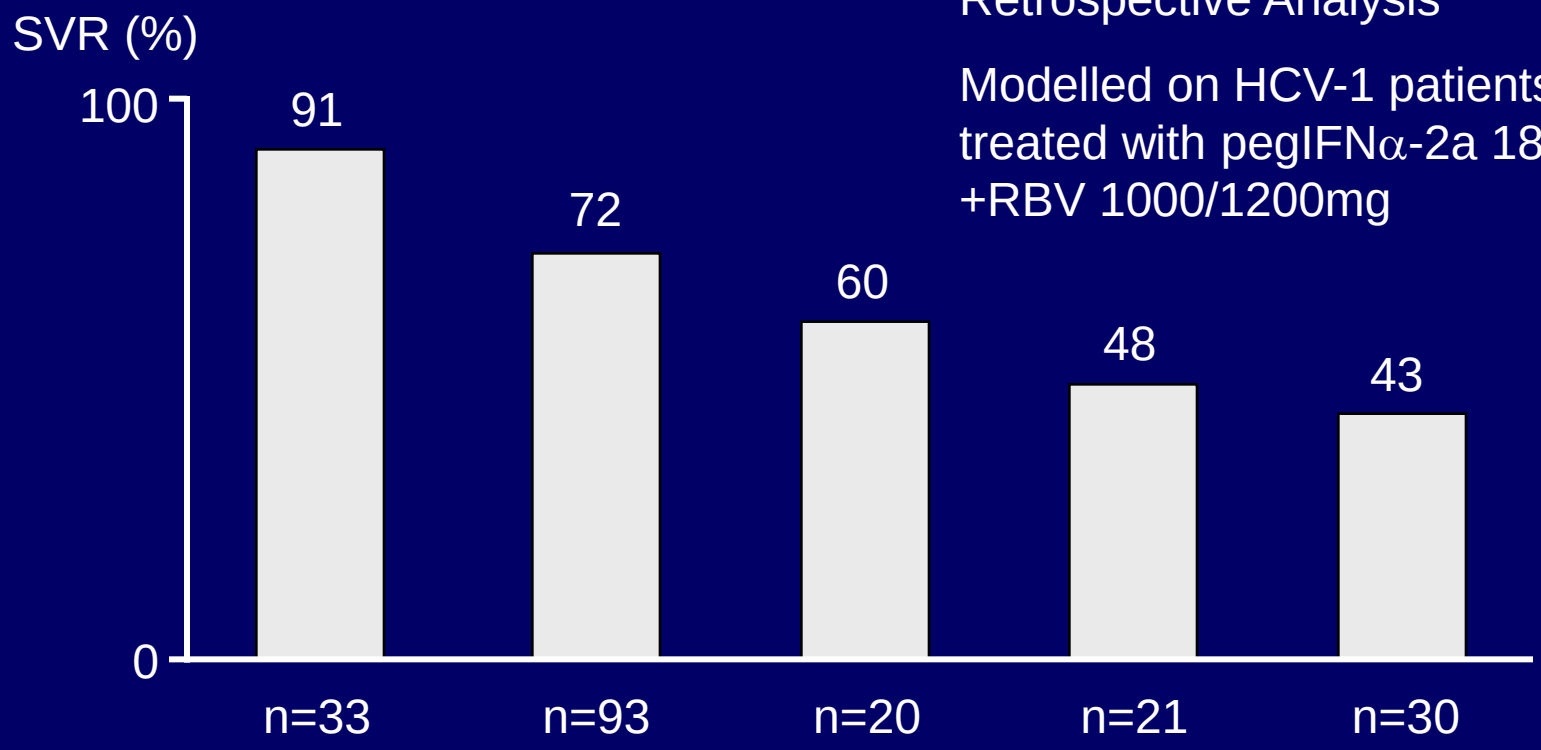


CHRONIC HEPATITIS C

Patterns and Definitions of Virological Response



Rate of achieving undetectable HCV RNA level predicts SVR in genotype 1 patients



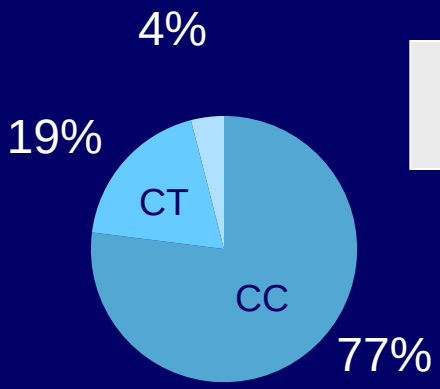
Retrospective Analysis

Modelled on HCV-1 patients treated with pegIFNα-2a 180 µg/wk +RBV 1000/1200mg

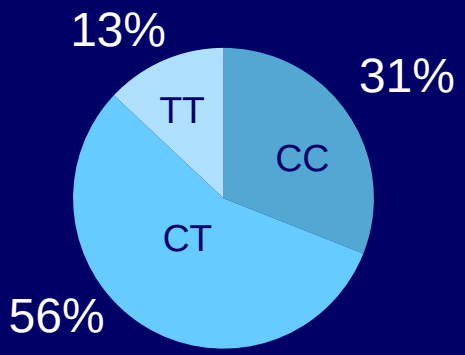
HCV RNA status					
Week 4	Negative	≥2-log ↓	<2-log ↓	≥2-log ↓	<2-log ↓
Week 12	Negative	Negative	Negative	≥2-log ↓	≥2-log ↓
Week 24	Negative	Negative	Negative	Negative	Negative

Ferenci et al, J Hepatol 2005; 43: 45

IL28B-type predicts SVR in Genotype 1 non-RVR patients

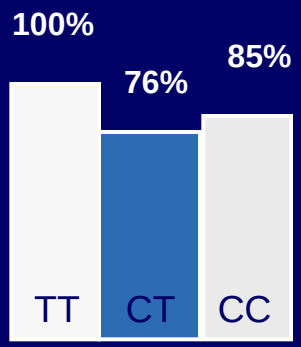


Caucasians
N = 1091

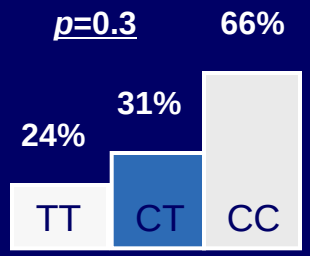


RVR= 14%

Non-RVR = 86%



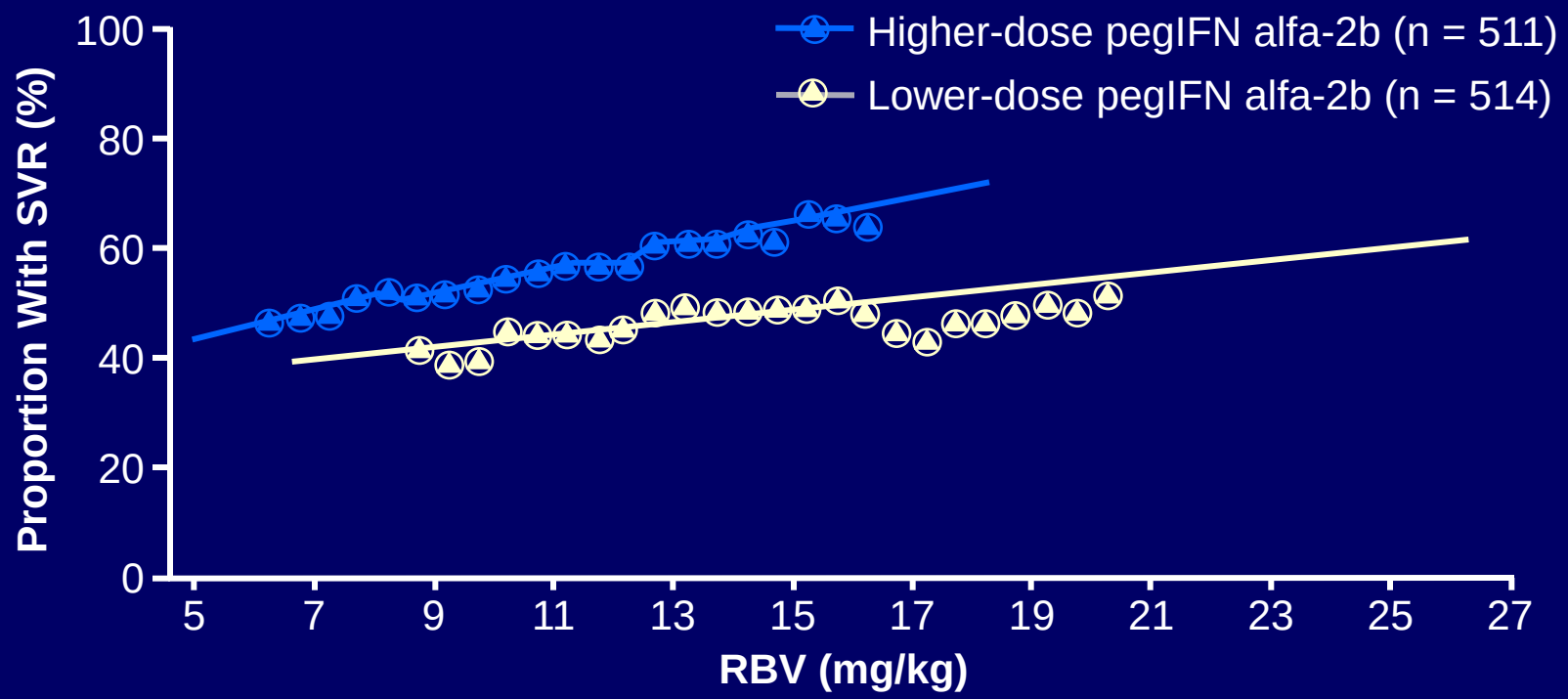
SVR



SVR

Thompson A et al. *AASLD 2009*

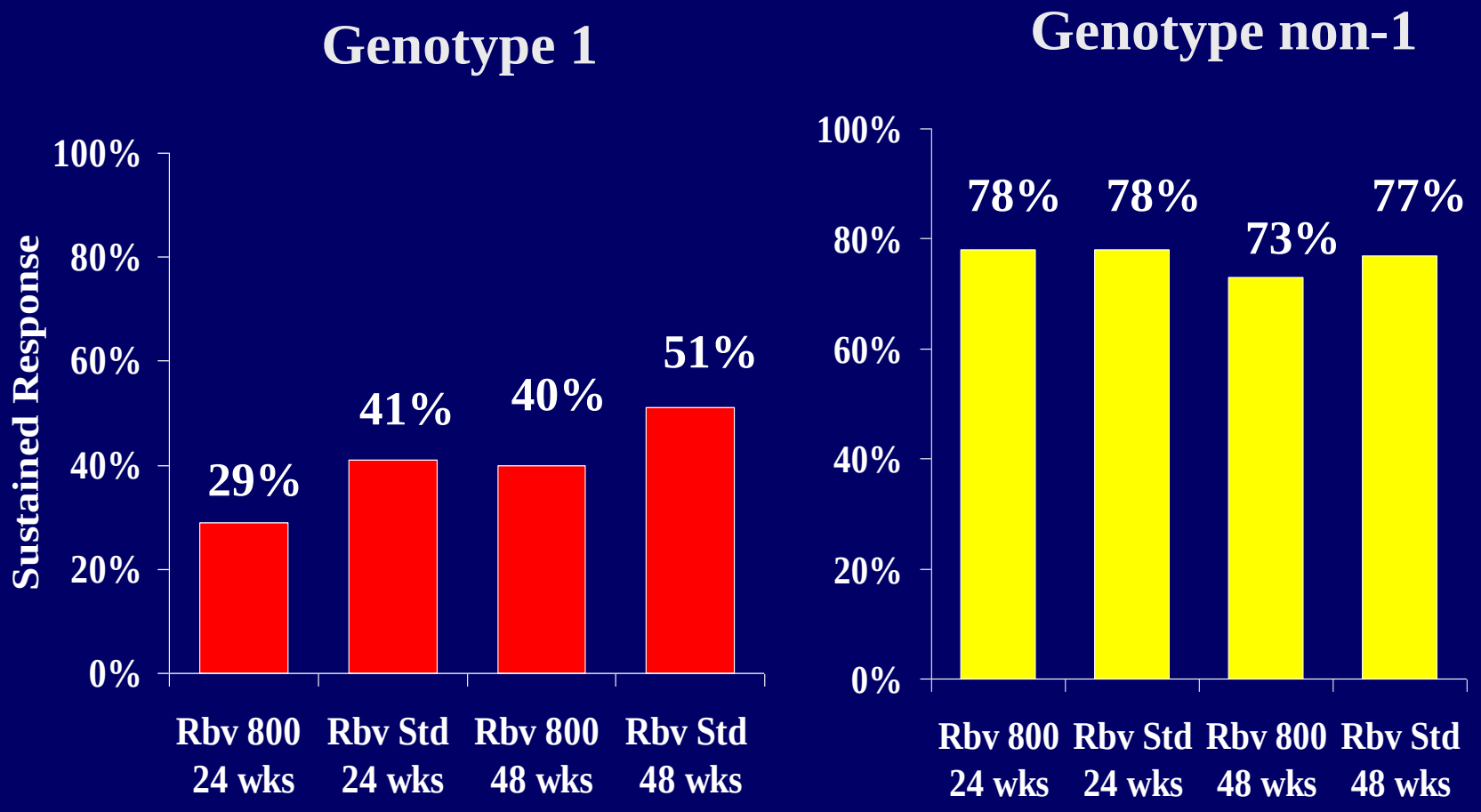
Optimizing RBV Dose When Used With PegIFN



- SVR rate was higher in all groups when the dose of RBV was > 10.6 mg/kg body weight (or > 800 mg/day for a 75-kg person)

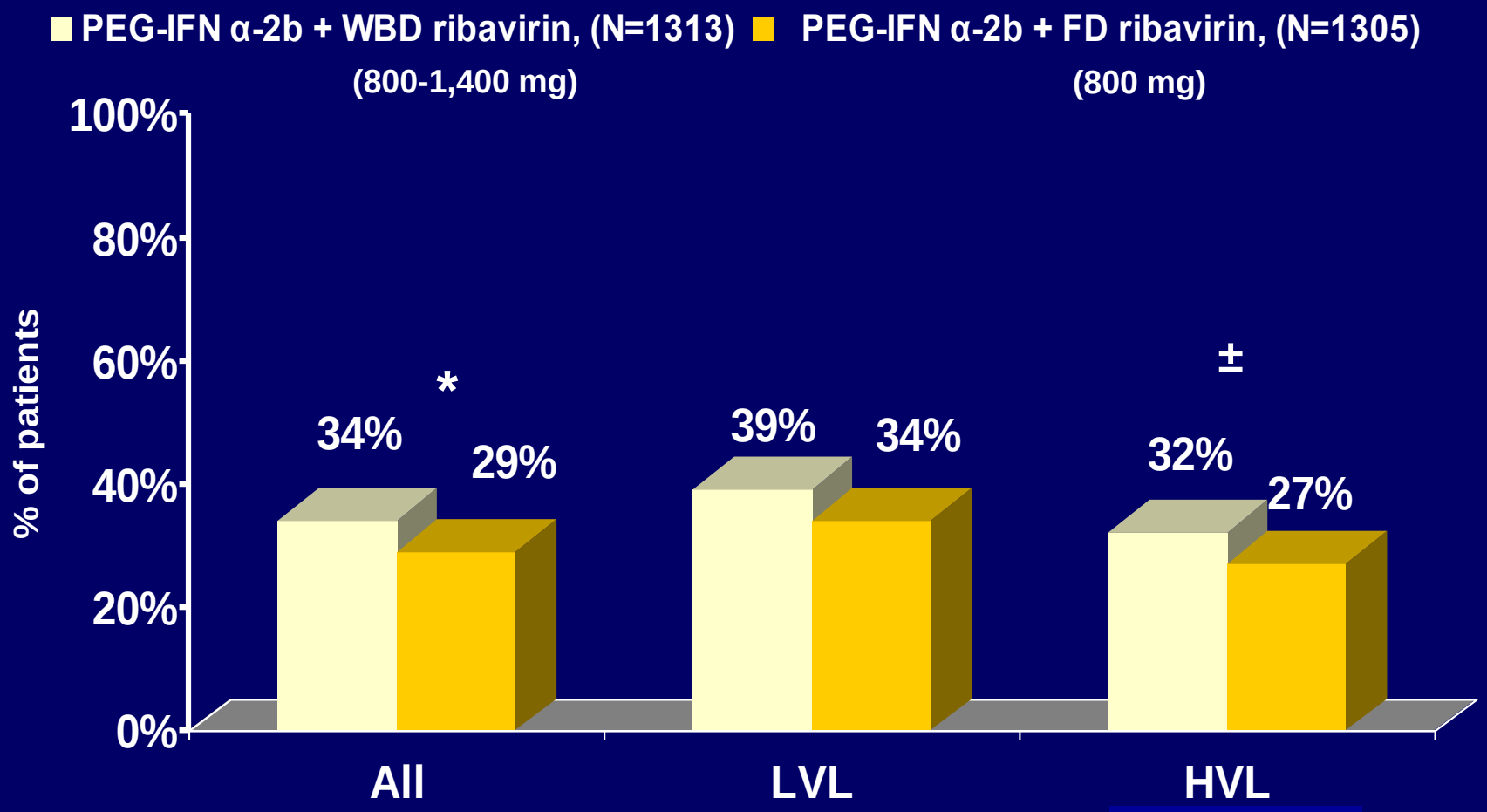
Manns MP, et al The Lancet, 2001, 358,9286,

Peginterferon & Ribavirin for Chronic Hepatitis C



Hadziyiannis et al 2002

Win-R Study. Sustained Virologic Response Genotype 1 (2,628 Patients)



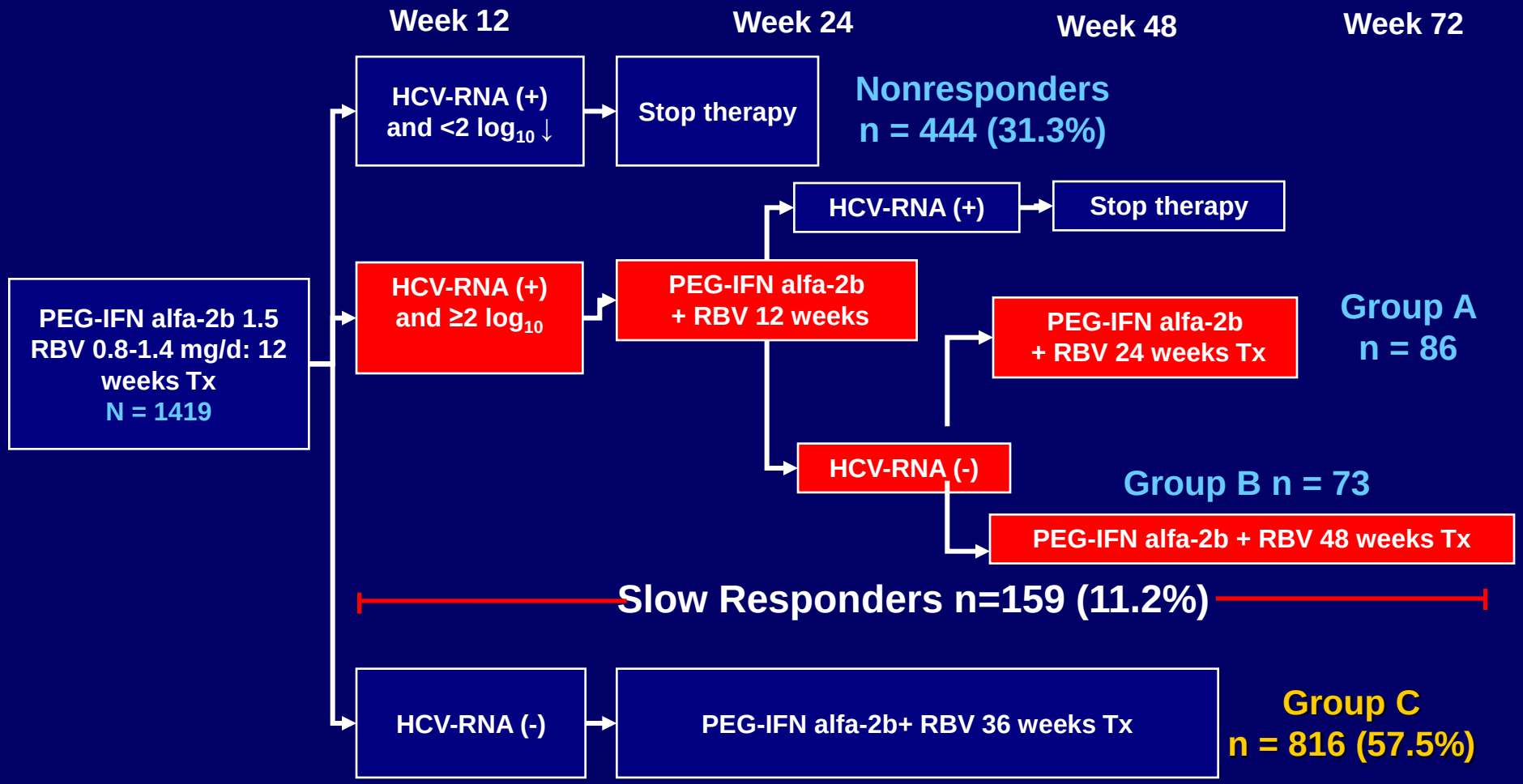
Jacobson I. Hepatology 2007

Can Extended Therapy Duration increase SVR rates?

- **Studies in Genotype 1 Patients**
  - **Heterogeneous**
  - **Different Ribavirin Dosage**
  - **Different criteria for selecting patients for longer therapy**
  - **Retrospective and Prospective**
- **Studies in Genotype 2 and 3**

Success Study: Genotype 1 Patients

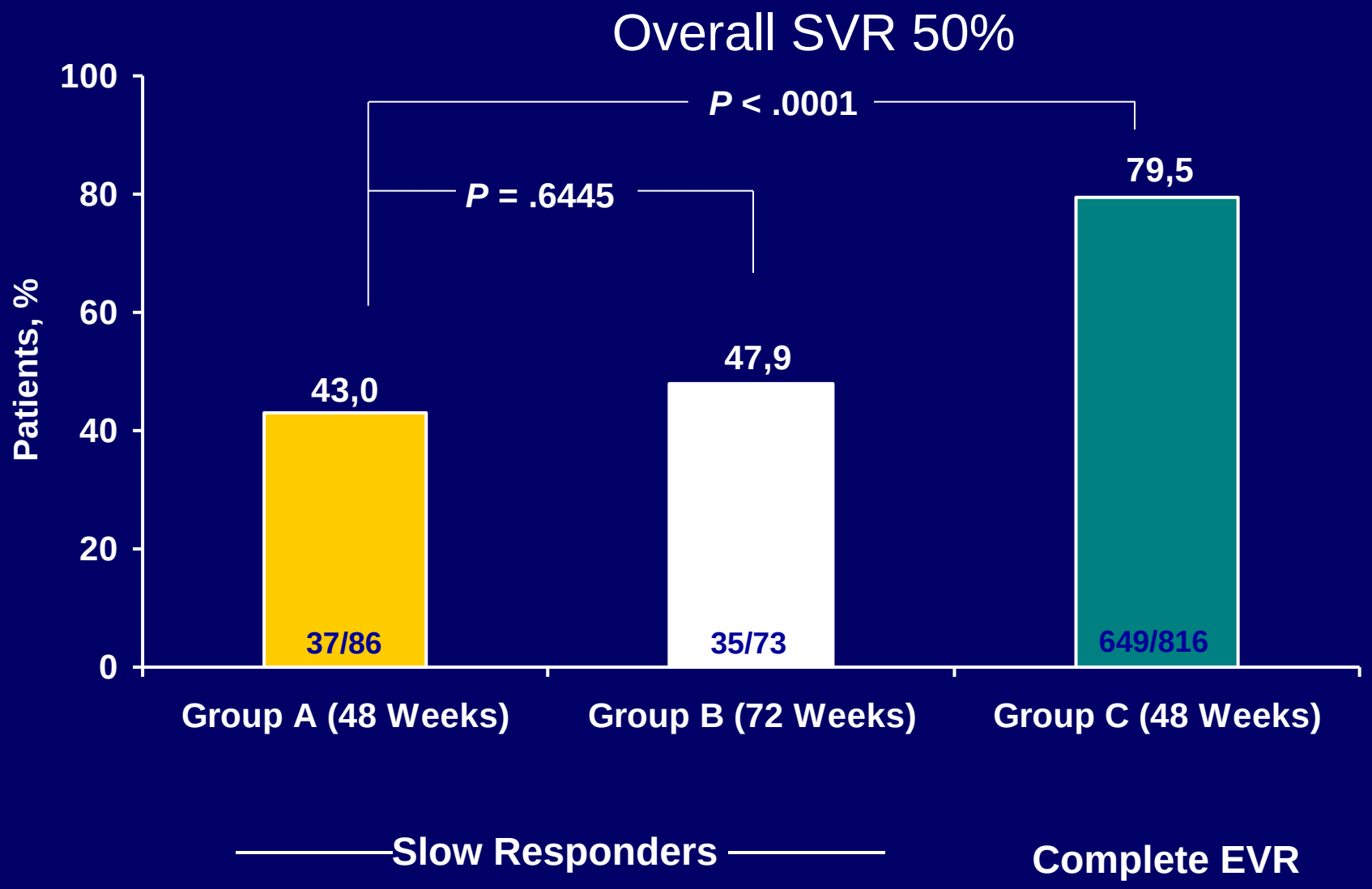
- Enrolled 1,428 treatment-naive patients with chronic HCV G1



HCV-RNA Central lab Roche TaqMan assay (LLQ = 30 IU/mL)

Buti M , Esteban R et al Hepatology 2010

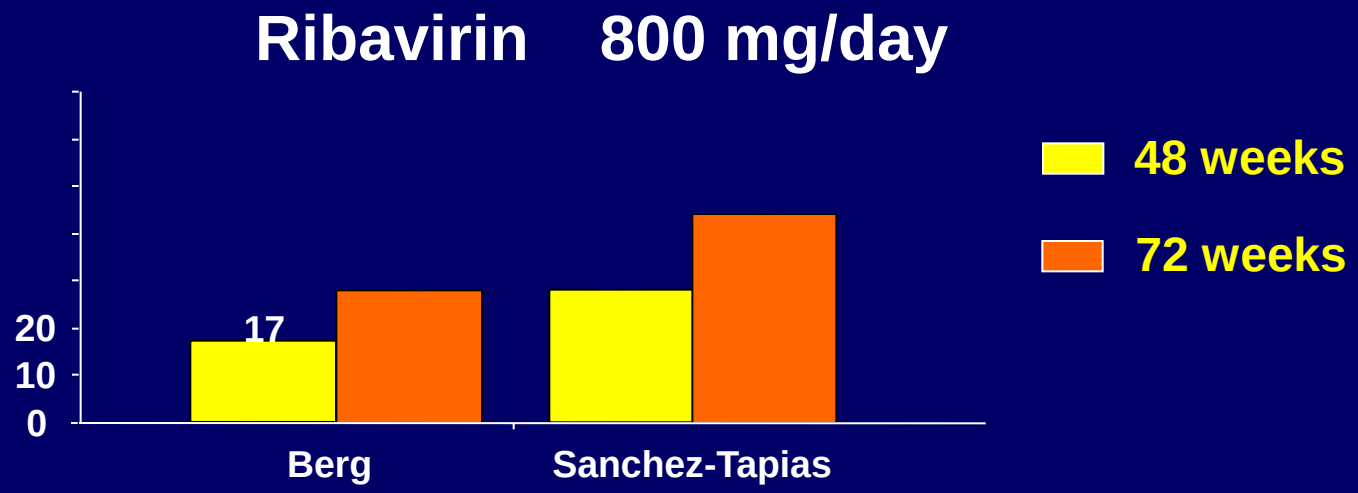
SVR with 72-Week Treatment Was Not Statistically Superior to 48-Week in Slow Responders (ITT Analysis)

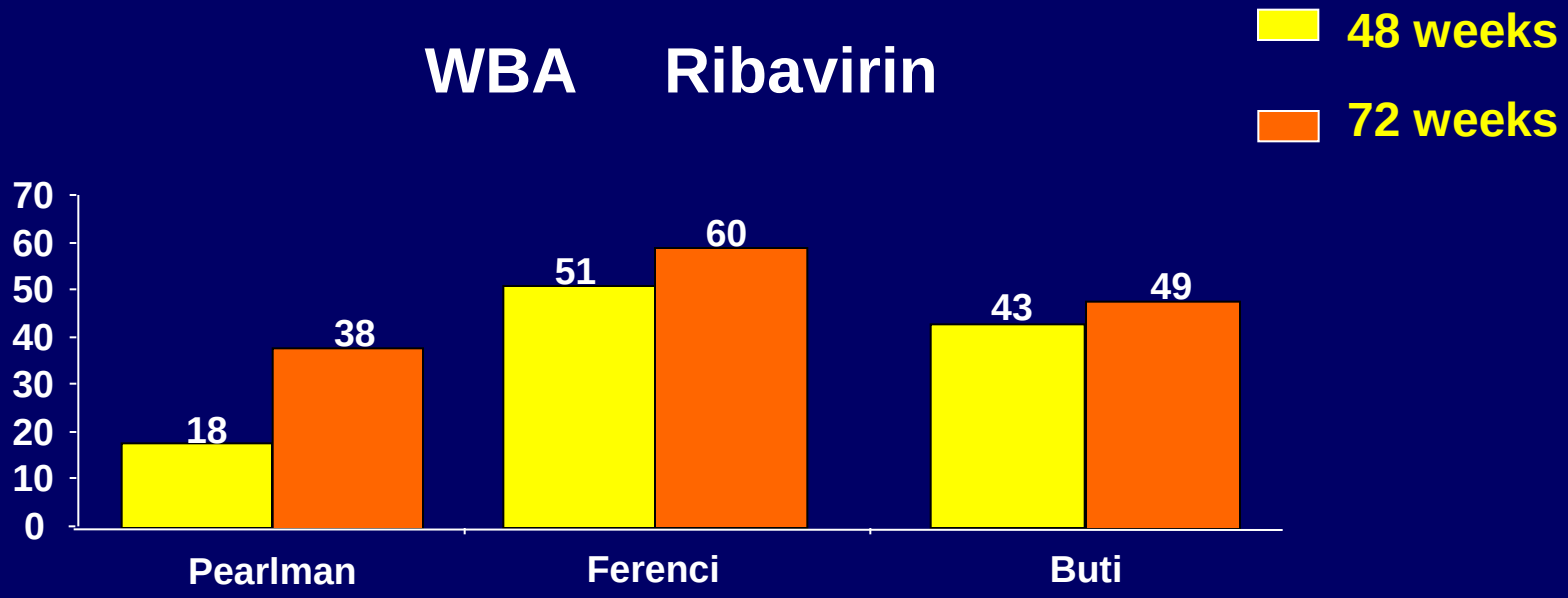


Treatment Discontinuations

Patient, n (%)	Group A 48 Weeks Tx	Group B 72 Weeks Tx	Group C Complete EVR
n	86	73	816
Completed study	78 (90.7)	56 (76.7)	716 (87.7)
Withdrew early	8 (9.3)	17(23.3)	100 (12.3)
Due to AE	3 (3.5)	6 (8.2)	39 (4.8)
Lost to FU	2 (2.3)	1 (1.4)	21 (2.6)
No wish to continue	1 (1.2)	6 (8.2)	16 (2.0)
Noncompliance	2 (2.3)	2 (2.7)	16 (2.0)
Others	0	2 (2.7)	8 (1.0)

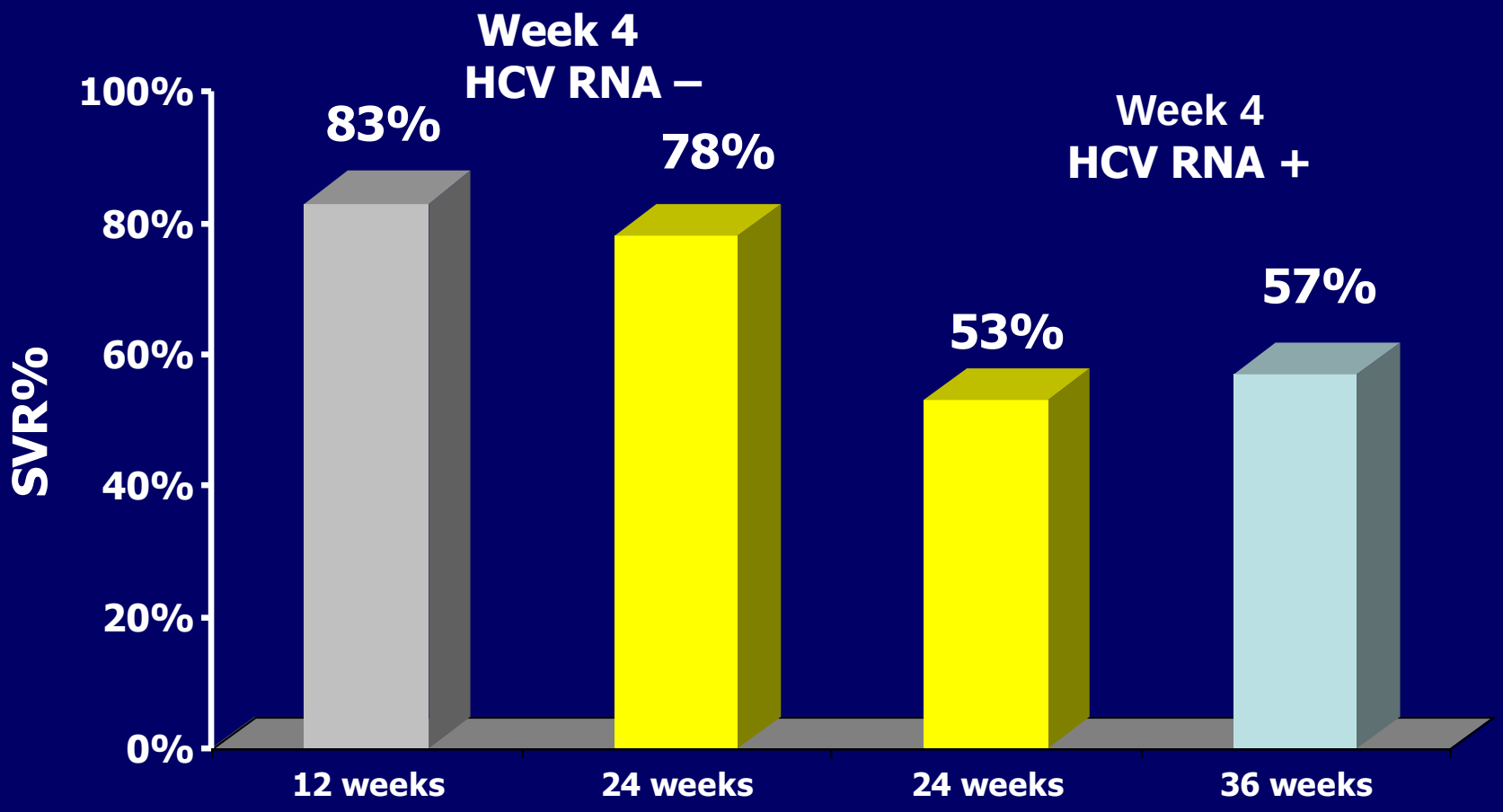
Percentage of SVR in Slow Responders





Sustained Virologic Response in Genotype 2 and 3

PegIFN alfa-2b 1.5 µg/kg + ribavirin 1000- 1200



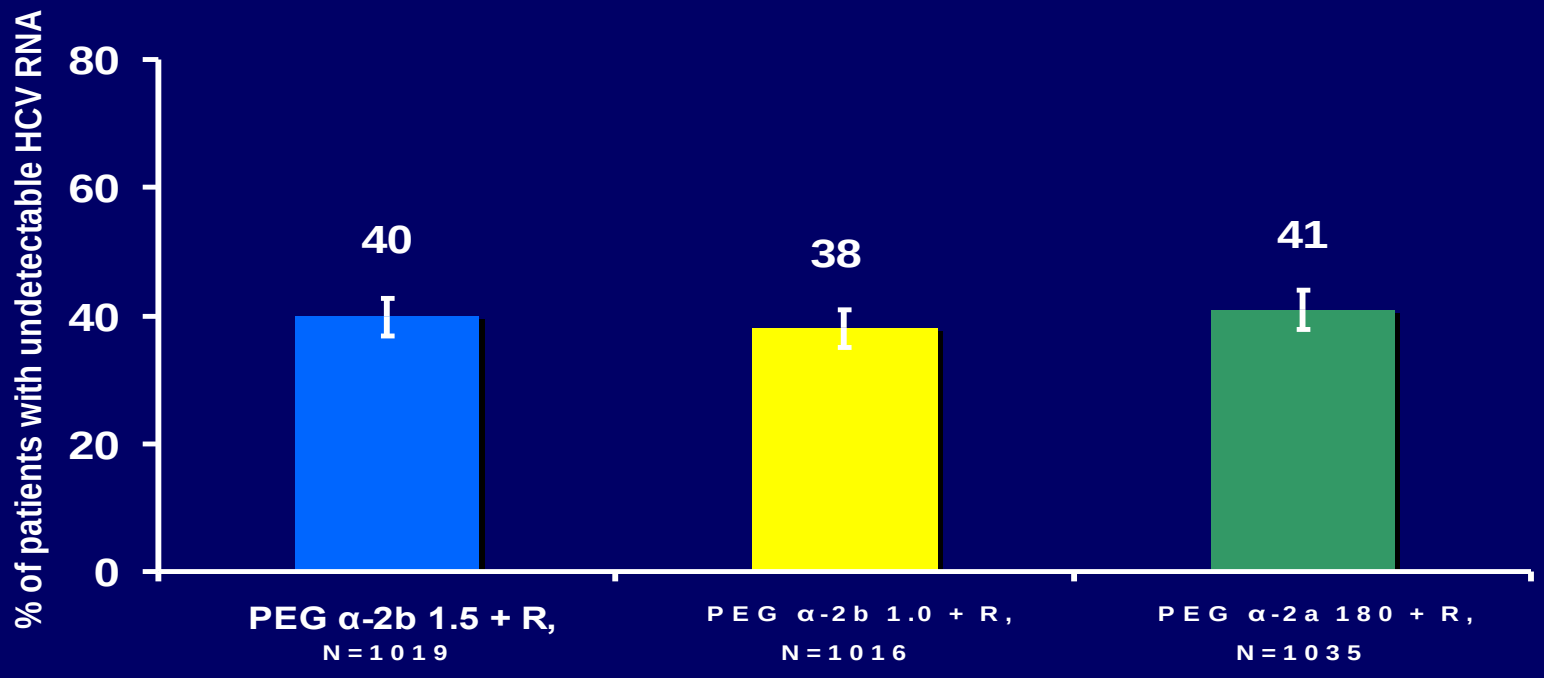
Mangia A et al. AASLD 2009

Optimizing HCV Treatement

Decrease Adverse Events and Discontinuation

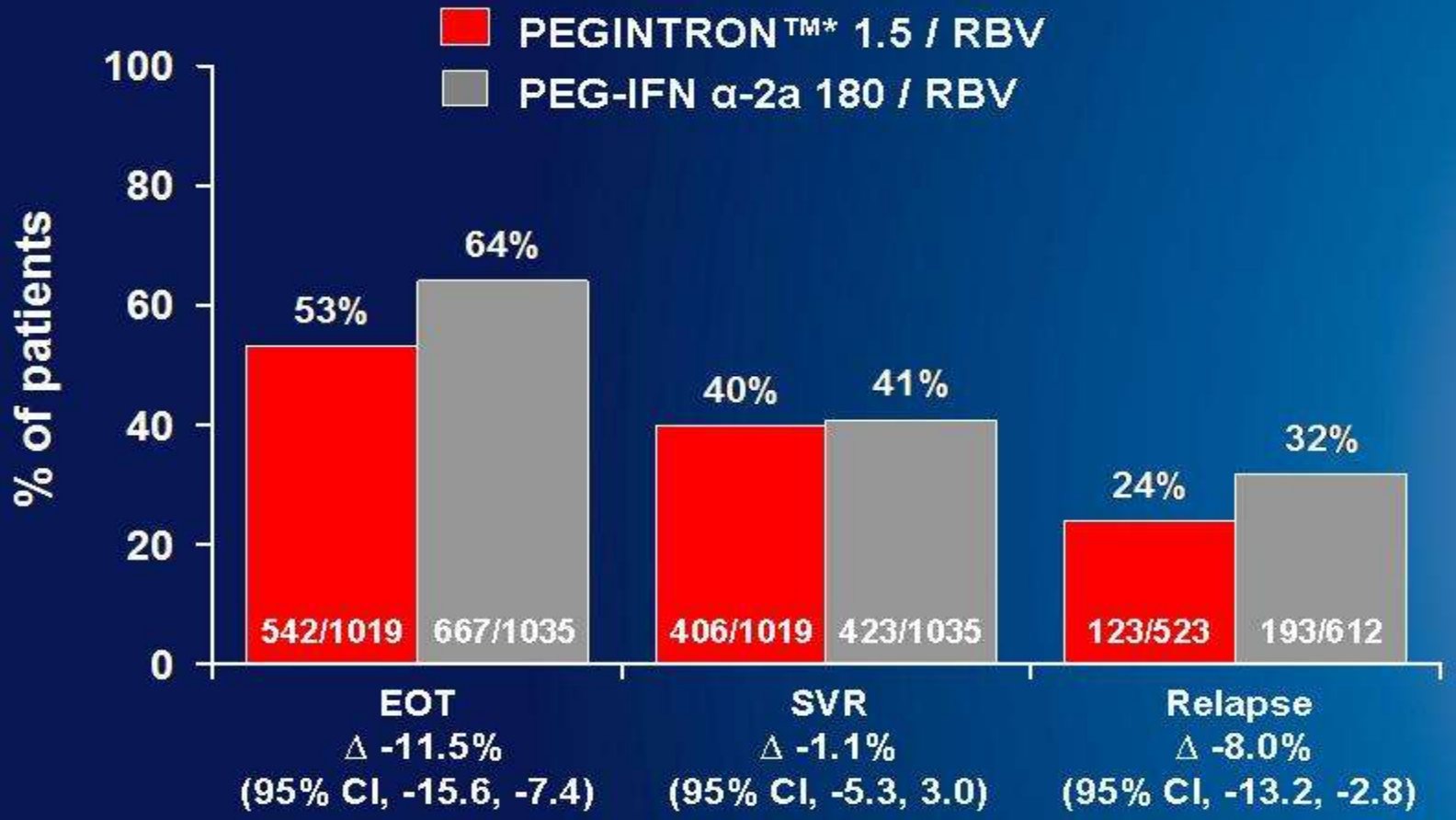
Decreasing Doses of Peginterferon
Shortening Therapy Duration

SVR in U.S. Genotype 1 Patients (ITT)



PEG-IFN α-2b 1.5/RBV vs PEG-IFN α-2a 180/RBV, p-value 0.57.
PEG-IFN α-2b 1.5/RBV vs PEG-IFN α-2b 1.0/RBV, p-value 0.20.

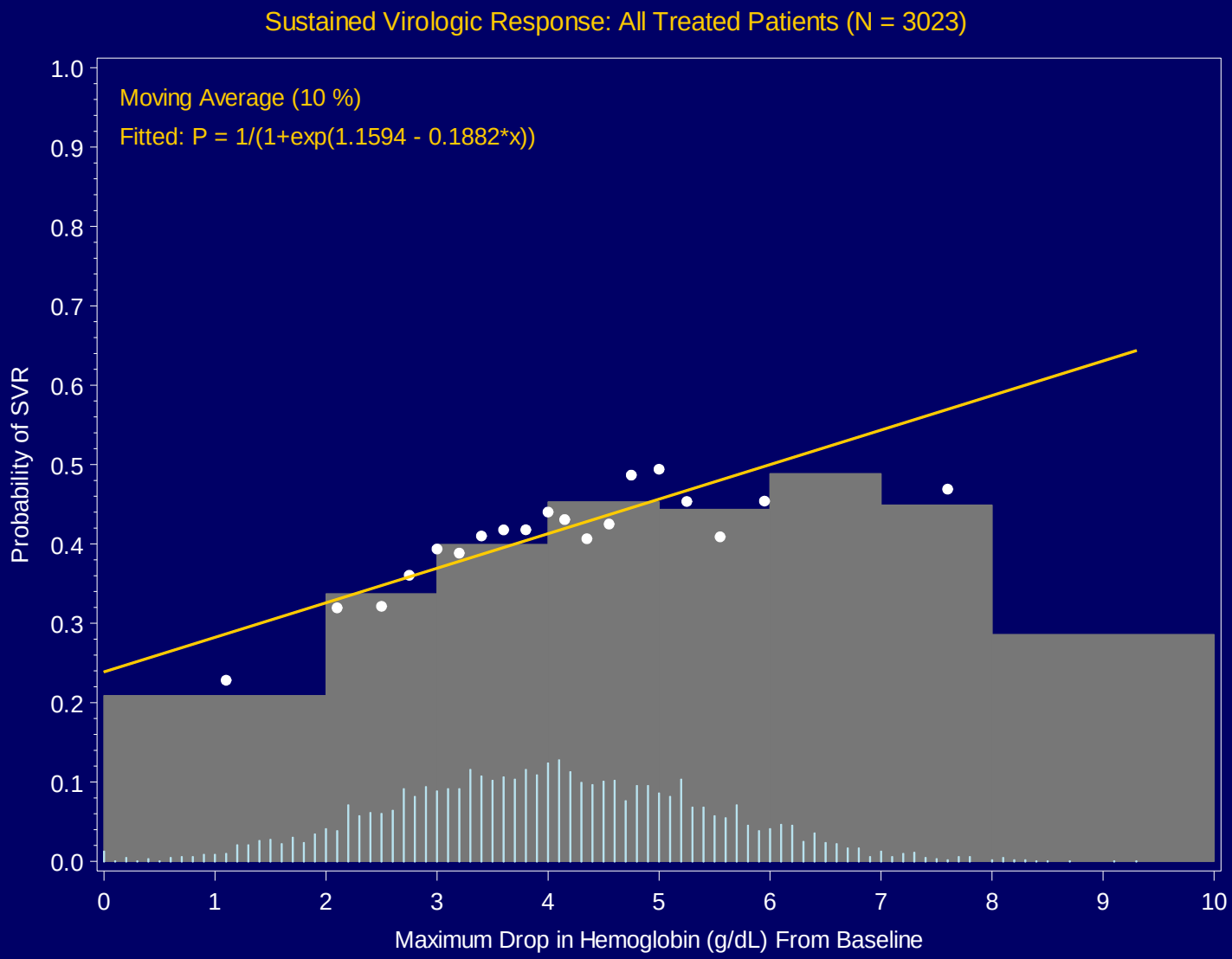
EOT, SVR, and Relapse Rates†



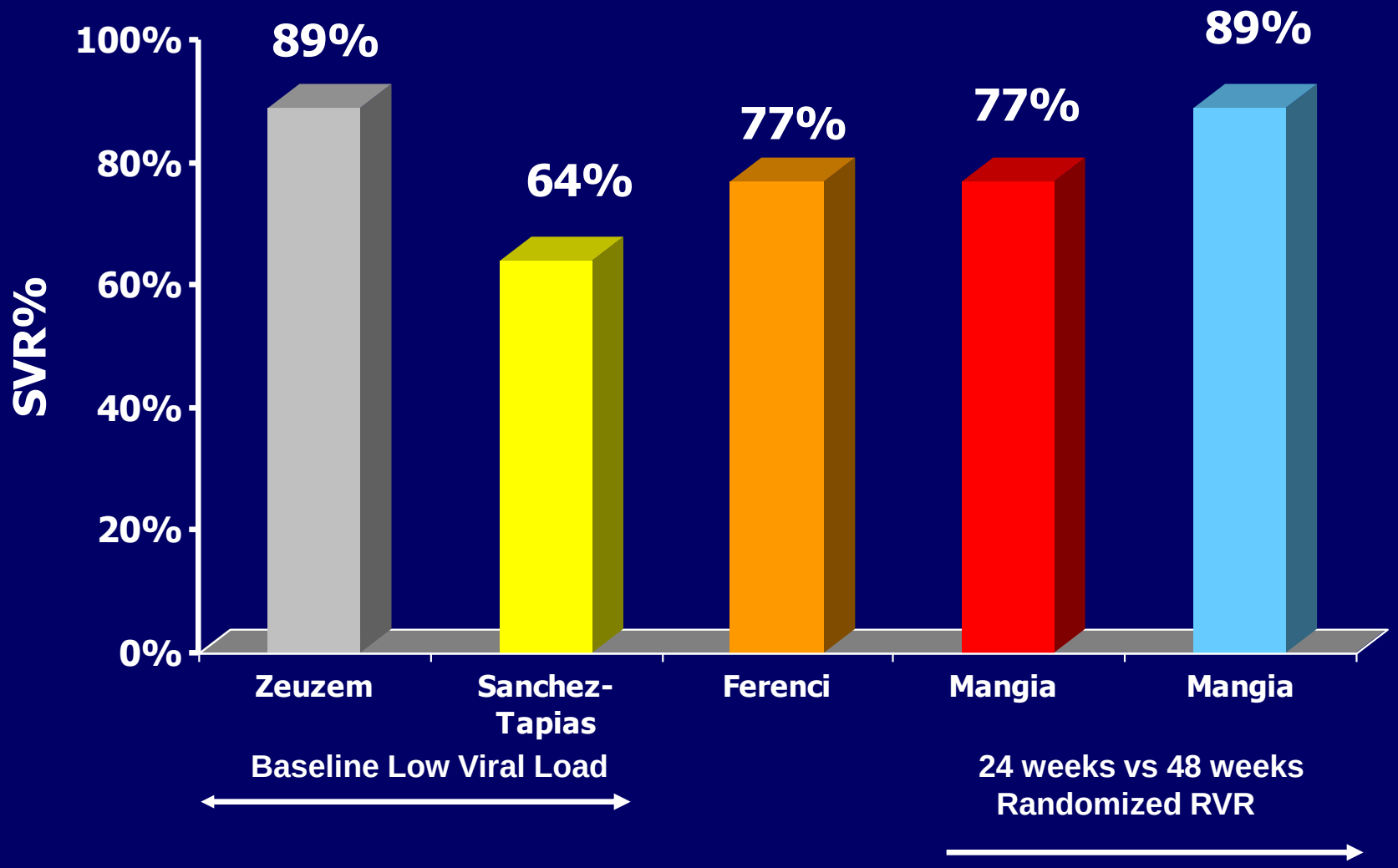
†Relapse rate was a prespecified analysis.

*PEGINTRON™ (Peginterferon alfa-2b) Powder for Injection.
Data on file. Schering Corporation, Kenilworth, NJ.

SVR and Maximum Hb Decline

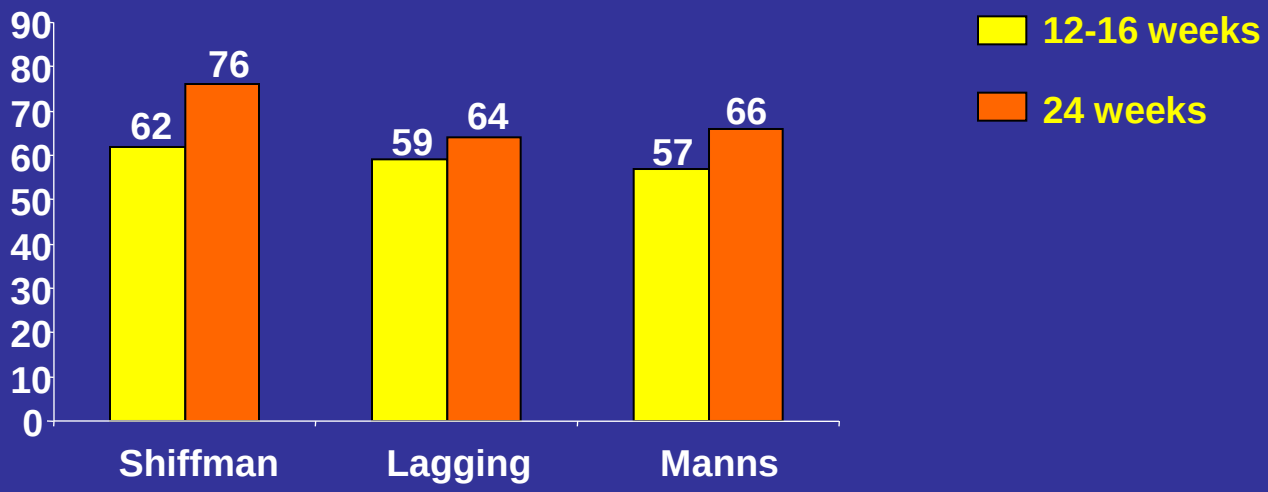


Sustained Virologic Response in Genotype 1 patients with RVR treated for 24 weeks



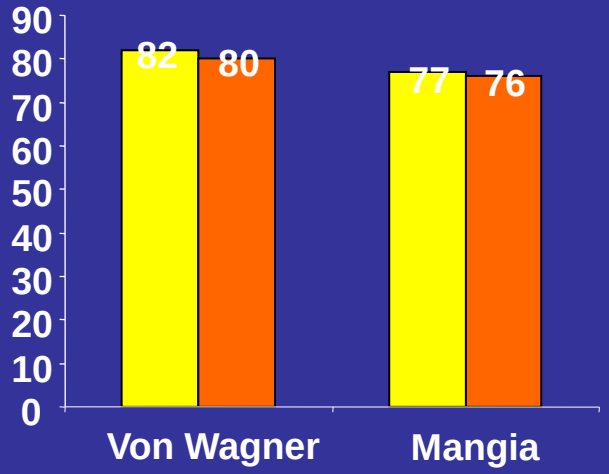
Percentage of SVR in Genotype 2 and 3

Randomization at baseline

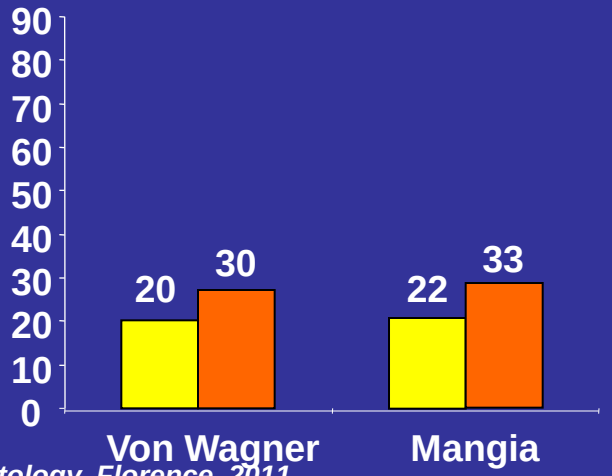


Randomization at week 4

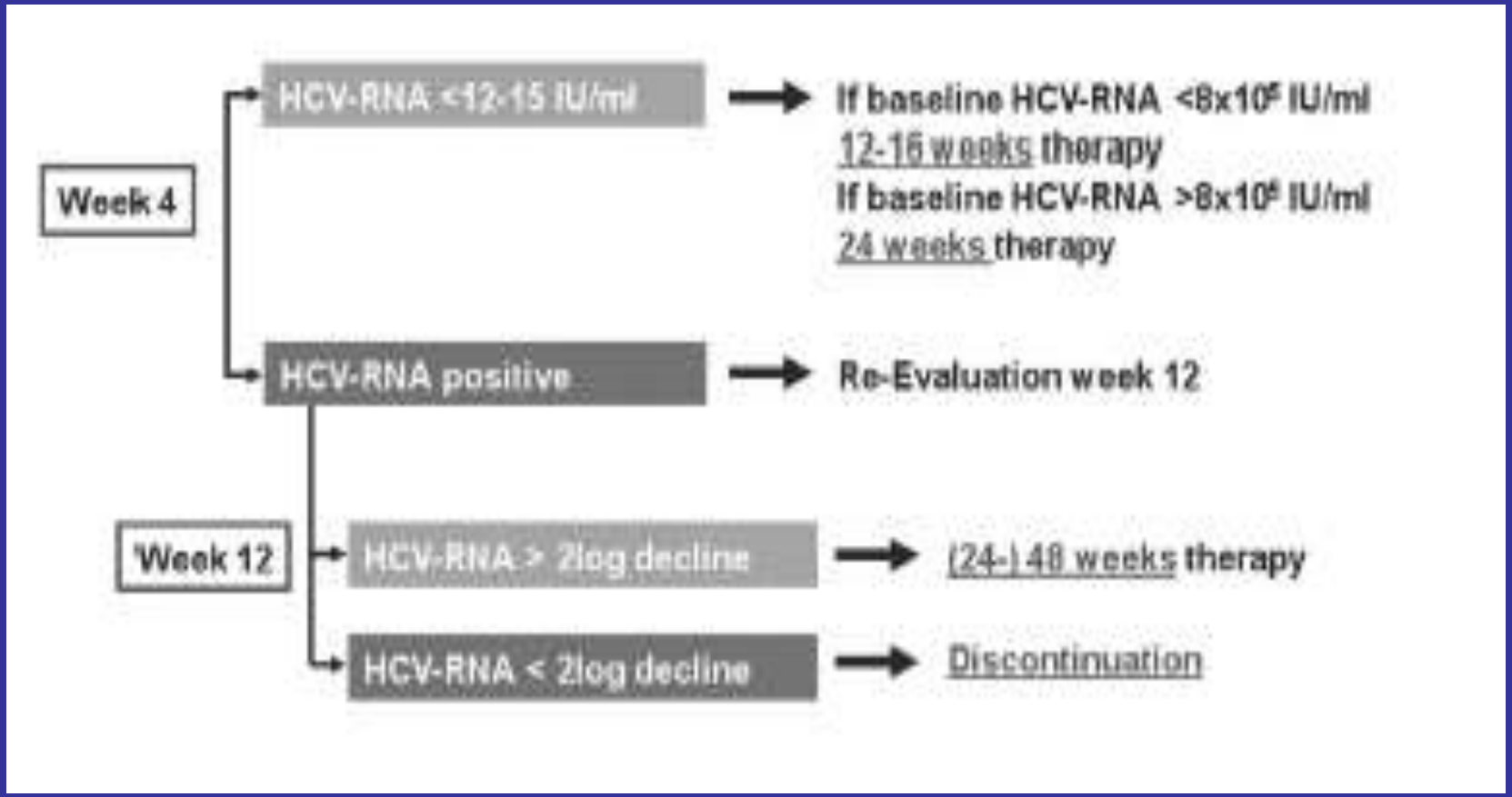
HCV RNA -



HCV RNA +



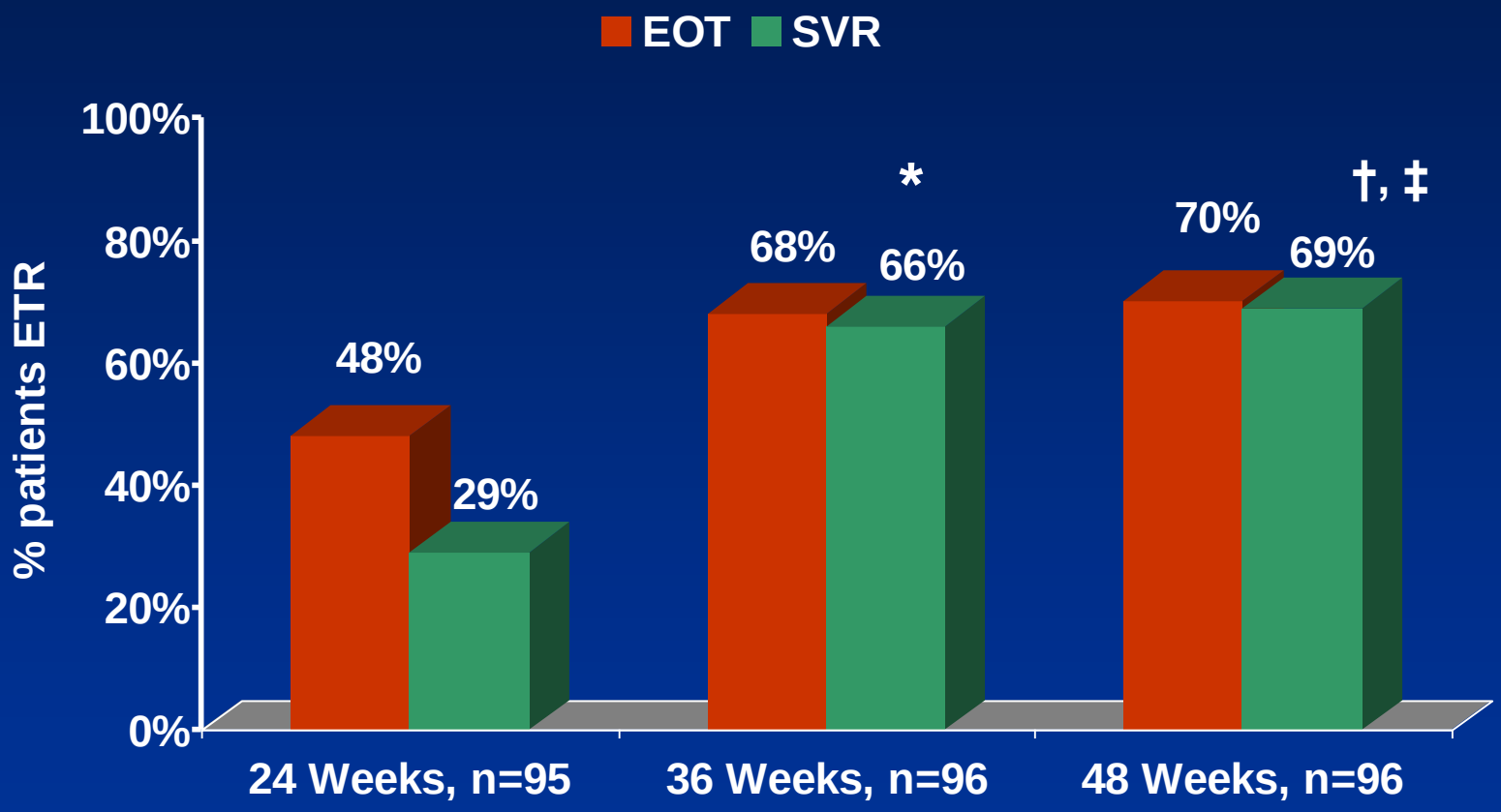
Management of HCV genotype 2 and 3



Therapy of HCV Genotype 4

Patients. Virologic Response Rates

PEG-IFN α-2b 1.5 µg/kg QW + ribavirin 1,000–1,200 mg/day



* p= 0.04 for 36 vs. 24 weeks
† p= 0.4 for 48 vs. 36 weeks
‡ p= 0.02 for 48 vs. 24 weeks

* p= 0.001 for 36 vs. 24 weeks
† p= 0.5 for 48 vs. 36 weeks
‡ p= 0.001 for 48 vs. 24 weeks

Kamal S, et al, Gut 2005;000:1–10.

Summary

- **Peginterferon and Ribavirin is the standard of care**
  - **It is essential an appropriate dose of Ribavirin**
  - **Decreasing Peginterferon dosef is a safe and efficacious option for patients with bad tolerance**
- **Therapy can be individualized**
  - **shortening duration in patients with low viral load, RVR, and probably IL28b CC**
  - **Prolonging HCV therapy can benefit very selected patients, young patients with good adherence, slow virologic response, and probably IL28bCC**
  - **When new DAAs are approved, all that we have learned with the current therapy will be very useful to optimize treatment with the new drugs**