

Hepatitis C In The Native Community

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Chronic Liver Disease in Aboriginal North Americans

- Aboriginal North Americans
 - American Indians/Alaska Natives(AI/AN)
 - Canadian First Nations
 - Native Greenlanders
- Disproportionately affected by chronic liver disease (CLD)
- USA mortality chronic liver disease
 - Twelfth leading cause of death in general population
 - Fifth leading cause of death in AI/AN
- USA mortality rate(1990-1998)
 - 4.5% decrease in general population
 - 11% increase in AI/AN
 - Second leading cause of death AI/AN 25-44

Epidemiology of Chronic Liver Disease

- Alcohol
- Viral Hepatitis
 - Hepatitis B
 - Hepatitis C
- Non Alcoholic Fatty Liver Disease (NAFLD)
- Autoimmune Liver Disease
- Primary Biliary Cirrhosis (PBC)

HCV Infection: Magnitude of the Problem

- Approximately 3.9 million persons in United States infected
 - Approximately 35,000 new cases yearly
 - 85% of new cases become chronic
- 10,000-20,000 HCV-related deaths per year
 - Number expected to triple in next 10-20 years
- Leading cause of
 - Chronic liver disease
 - Cirrhosis
 - Liver cancer
 - Liver transplantation

CDC. MMWR Morb Mortal Wkly Rep. 1998;47;1-39.

NIH Consensus Conference Statement. Available at: <http://consensus.nih.gov/2002/2002HepatitisC2002116html.htm>. Accessed August 19, 2008.

Rustgi VK. J Gastroenterol. 2007;42:513-521.

Hepatitis C in AI/AN

- Common cause of CLD
- Incidence varies with population studied
 - .8%-32%
- Route of transmission similar to general population
- Genotype distribution
 - Type 1 60%(72% in general pop.)
 - Type 2 23%(15% in general pop.)
 - Type 3 14%(6% in general pop.)
- Treatment response data is limited due to small numbers of AI/AN in studies

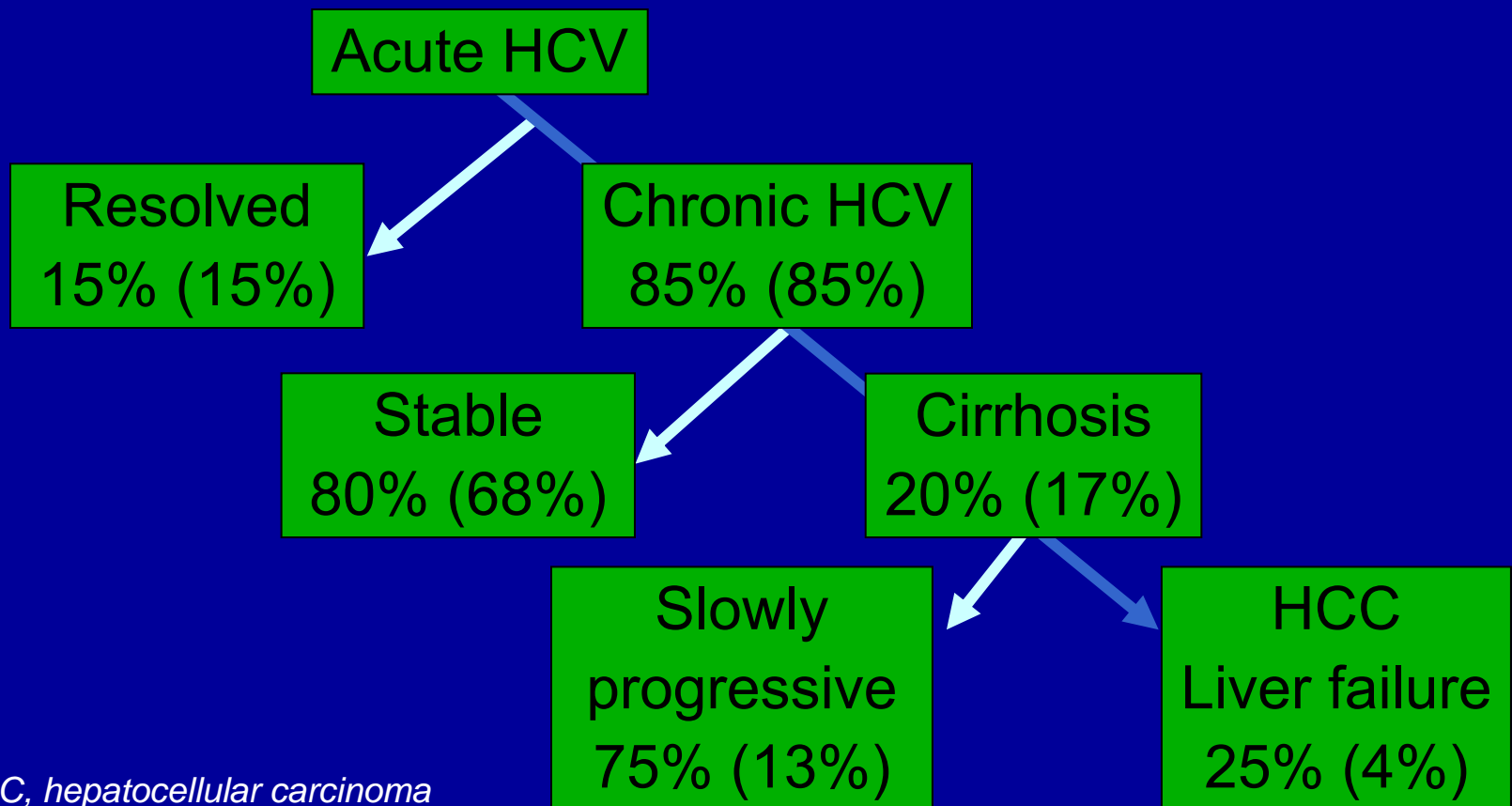
Hepatitis C Virus Infection

Population at Risk

- Transfusion of blood products before 1992
- Intravenous drug use
- Nasal inhalation of cocaine
- Chronic renal failure on dialysis
- Incarceration
- Occupational exposure to blood products
- Transplantation of an organ/tissue graft from an HCV-positive donor
- **Body piercing and potentially tattoo**

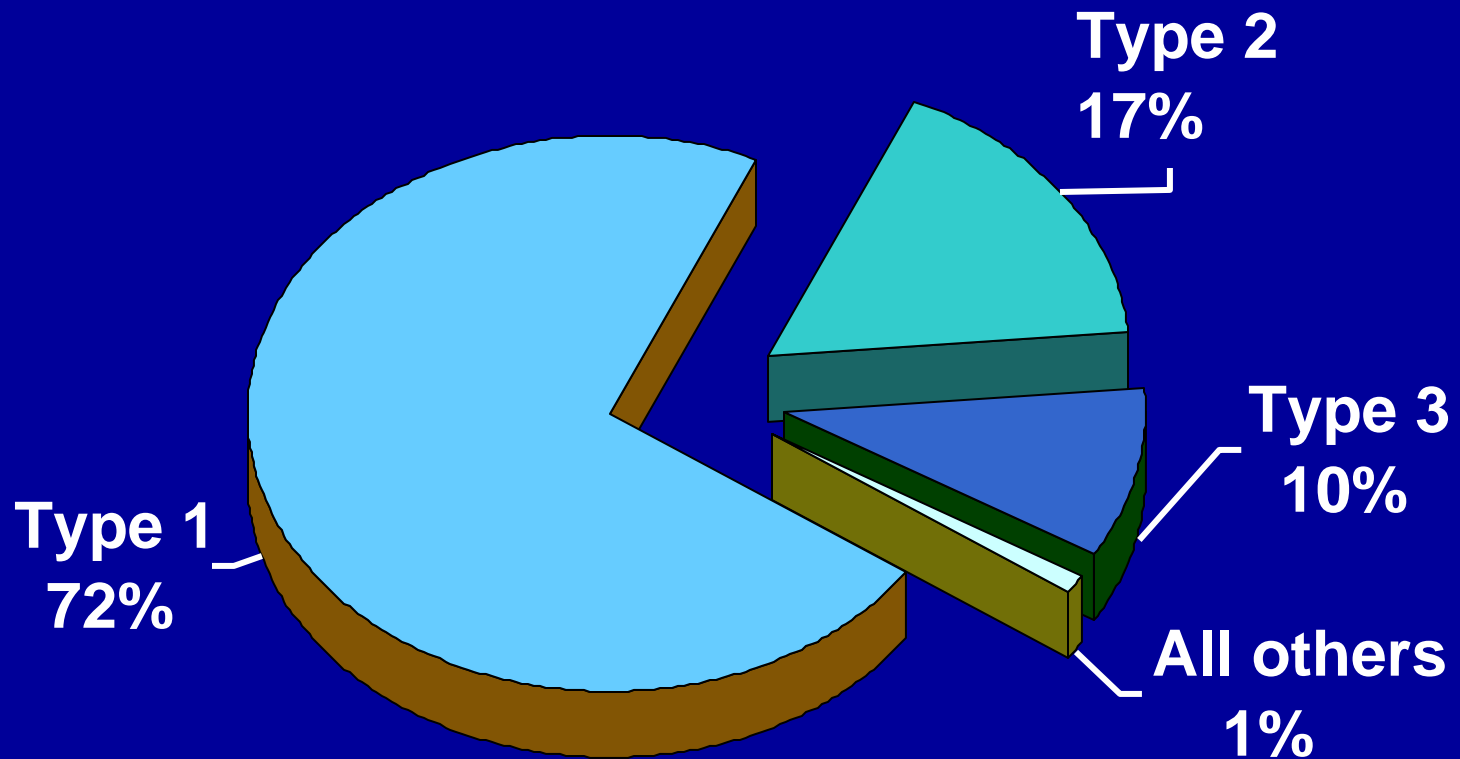
Hepatitis C Virus Infection

Natural History

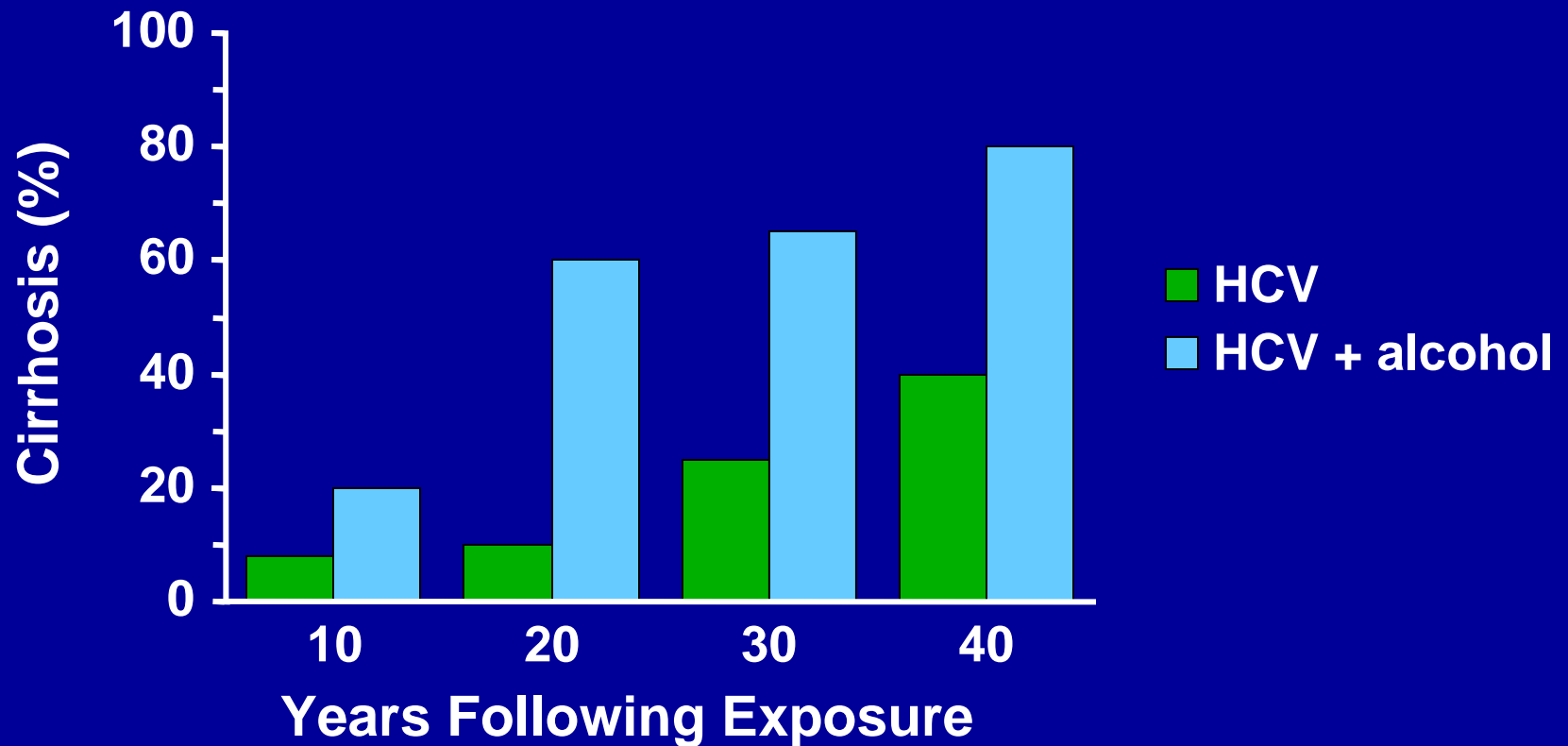


HCC, hepatocellular carcinoma

Hepatitis C Virus *Genotypes in the USA*



HCV and Alcohol *Risk of Cirrhosis*



Excessive alcohol intake characterized as > 40 g/day for women and > 60 g/day for men.

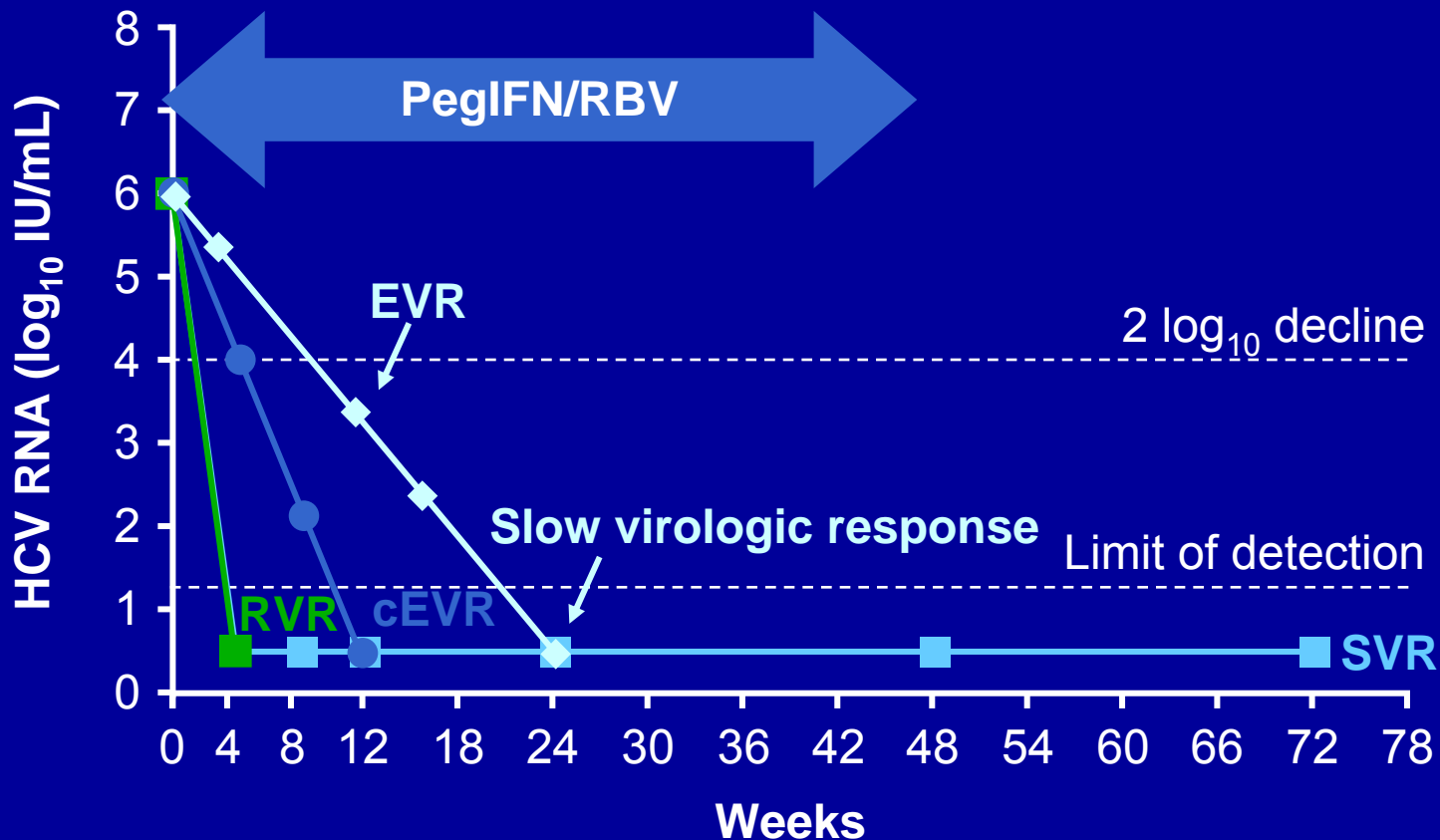
Goals of HCV Therapy

- Primary goal of treatment is to eradicate the virus
- Additional goals
 - Slow disease progression
 - Minimize risk of HCC
 - Improve liver histology
 - Enhance quality of life
 - Prevent transmission of virus
 - Reduce extrahepatic manifestations

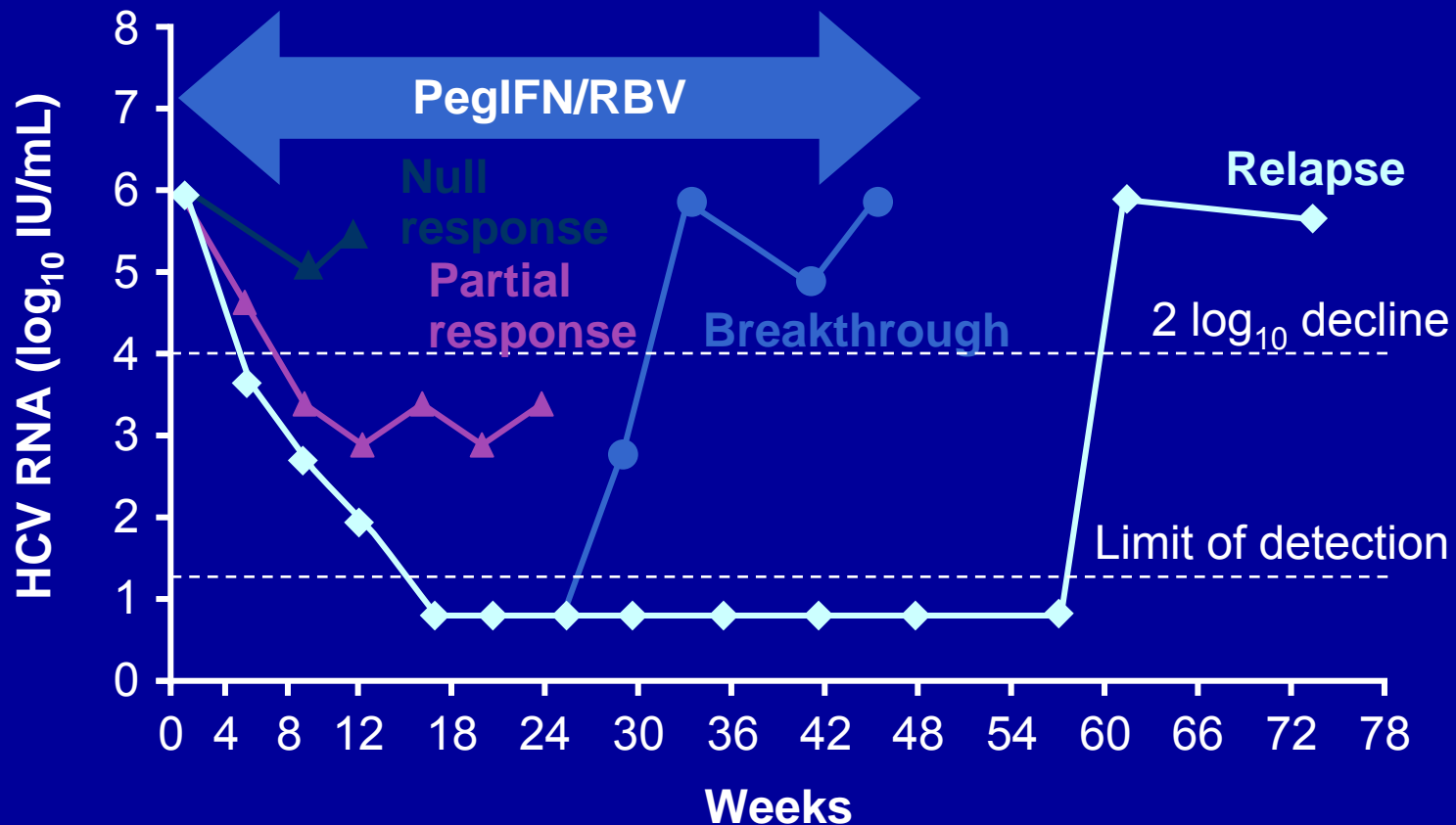
Important Definitions Used in Treatment of Hepatitis C

- RVR(rapid virologic response)
 - Absence of virus by PCR 4 weeks after starting therapy
 - Indicates better prognosis for SVR(cure) and perhaps shorter course of therapy(genotype 1)
- EVR(early virologic response)
 - Absence of virus by PCR 12 weeks after starting therapy
 - IF no EVR chance for SVR less than 5% and therapy is stopped
 - If partial response ie. Atleast a 2 log drop can continue for 24 weeks if virus is then absent can continue for 48 weeks?72 weeks
- ETR (end of treatment response)
 - Absence of virus at end of treatment
 - Associated with high SVR
- SVR (sustained virologic response)
 - Cure !!

Virologic Responses

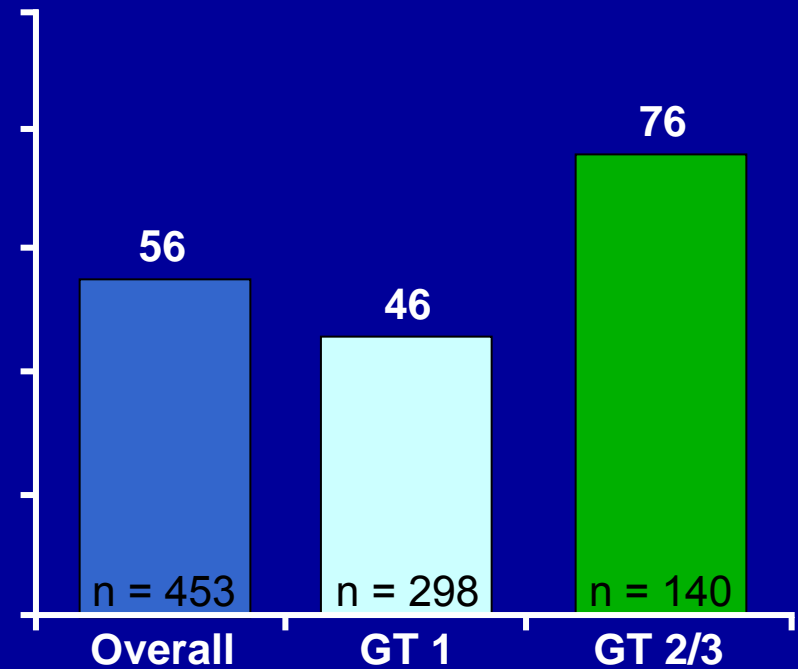
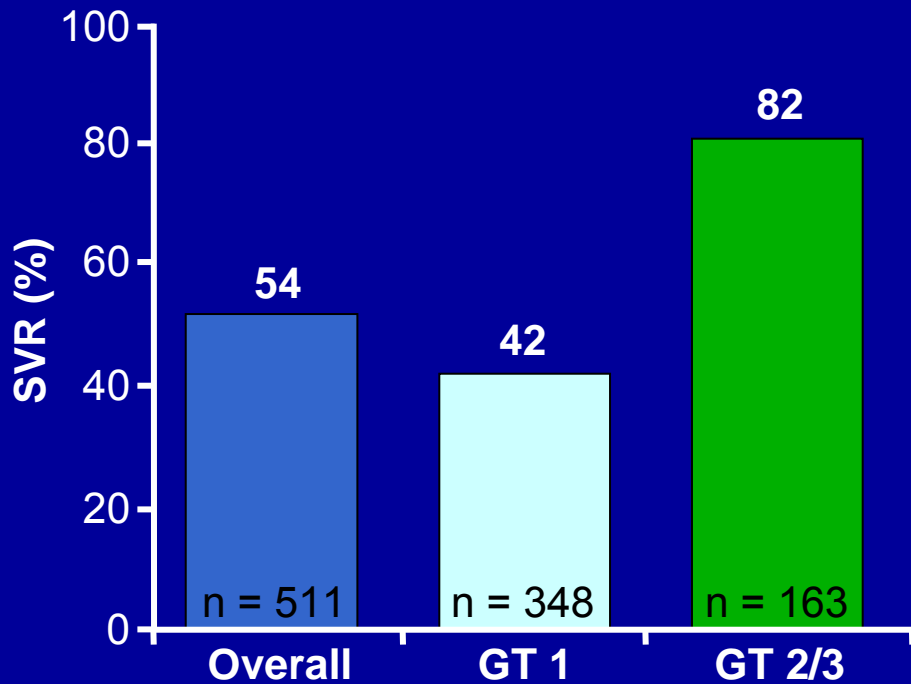


Suboptimal Virologic Responses



SVR With PegIFN: > 50% of GT 1 Patients Do Not Respond

- PegIFN alfa-2b 1.5 µg/kg/week + RBV 800 mg/day for 48 weeks^[1]
- PegIFN alfa-2a 180 µg/week + weight-based RBV (1000 or 1200 mg/day) for 48 weeks^[2]



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

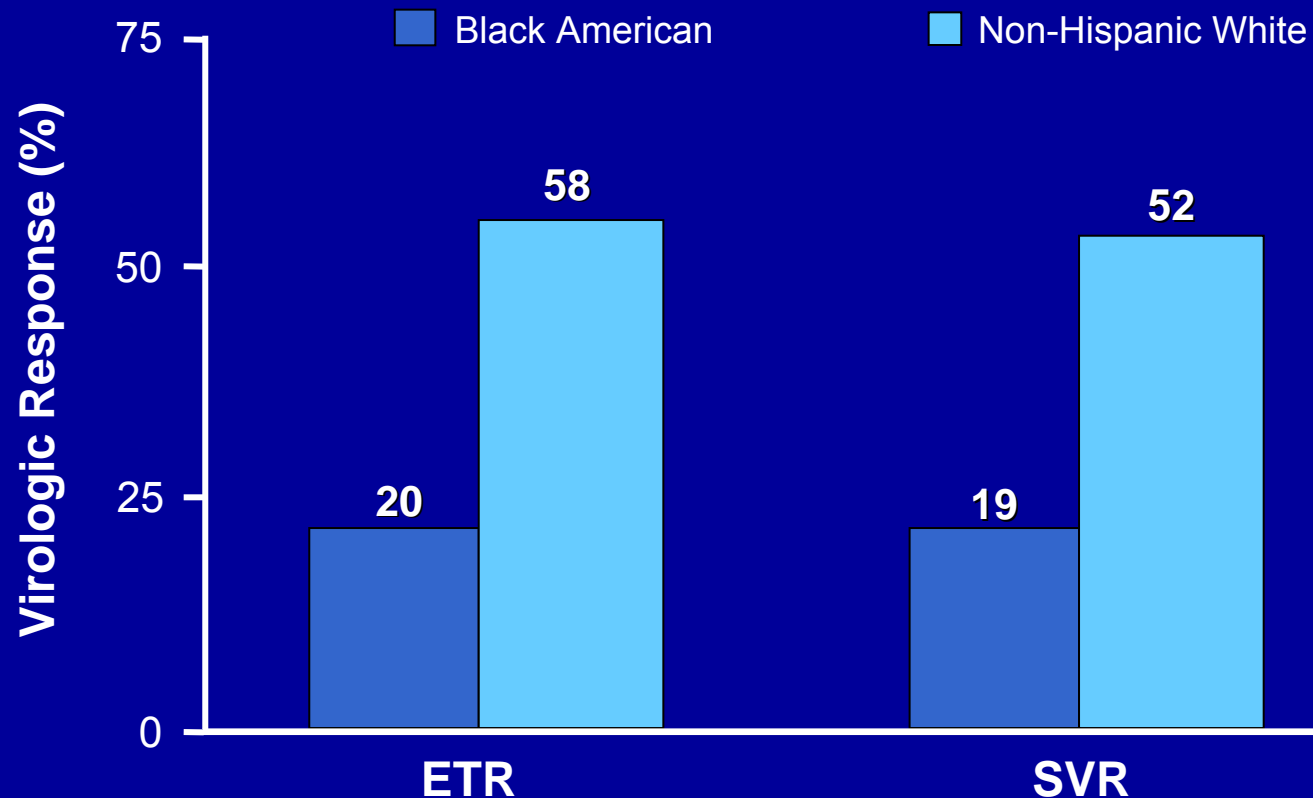
Black Americans and HCV Infection

- HCV infection more common in black Americans than in whites
 - Risk factors the same
- Predominantly genotype 1
- Disease severity or progression may be different
- Rate of HCC increased
- Lower response rate
- Mechanism unknown

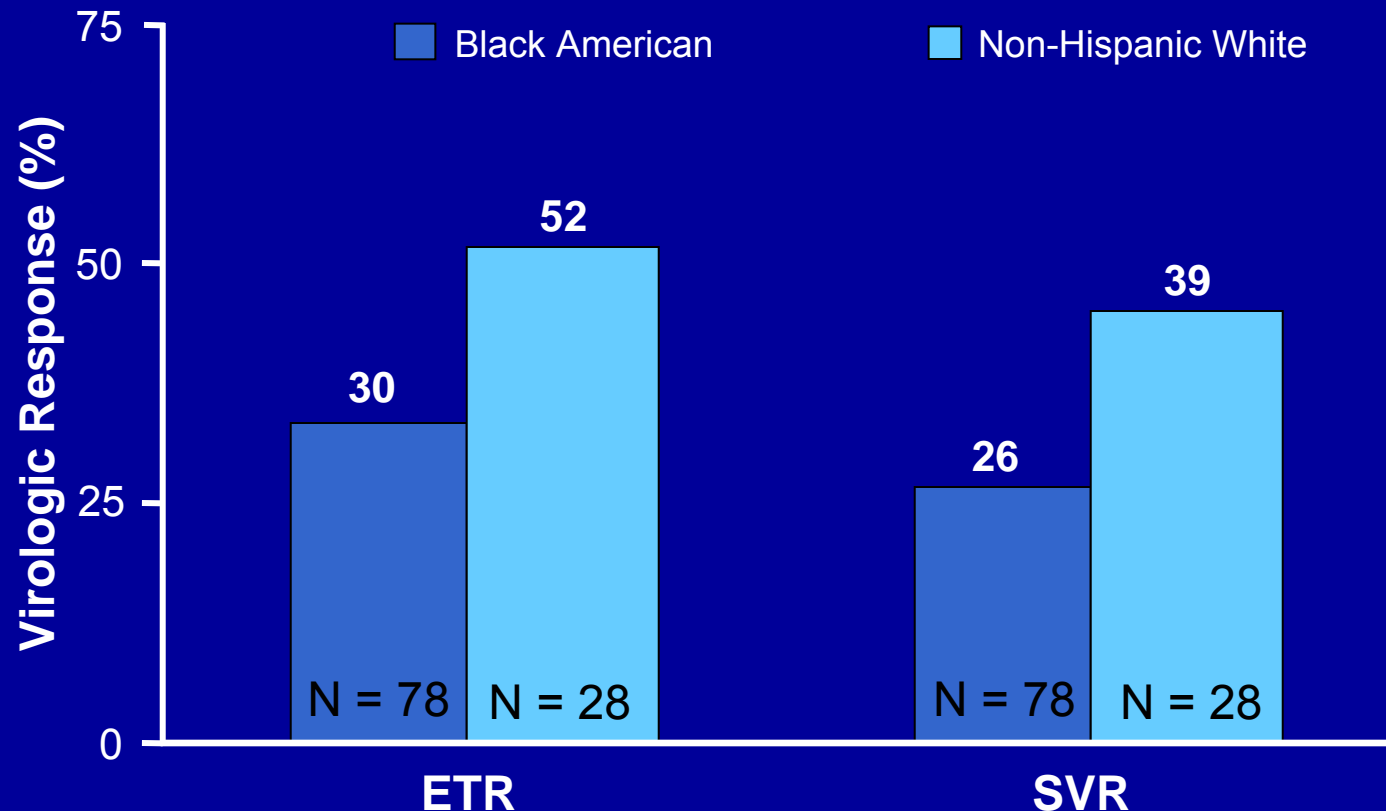
HCV Treatment Considerations in Black Americans

- Two prospective, clinical trials of peginterferon and ribavirin were undertaken to better determine actual response rates in African Americans.
- Patient groups were balanced for genotype and histologic severity

Virologic Response: PegIFN Alfa-2b + RBV



Virologic Response: PegIFN Alfa-2a + RBV



Obesity, Metabolic Syndrome, and HCV

- Patients with BMI > 30 more likely to have steatosis and fibrosis
- Steatosis is common in HCV (20% to 60%)
 - Related to insulin resistance in genotype 1
 - Related to HCV replication in genotype 3
- Steatosis may lead to progressive fibrosis
- Obesity and steatosis decrease response to HCV treatment
- Weight loss may improve insulin resistance and steatosis
- *Few data on weight loss before treatment to improve results but patients may benefit*

Swain M, et al. AASLD 2005. Abstract 1244. Cesario K, et al. DDW 2005. Abstract M953. Poynard T, et al. Hepatology. 2003;38:75-85. Fartoux L, et al. Gut. 2005;54:1003-1008. Matos C, et al. J Gastro Hepatology. 2006;21:1236-1239. Hourieux C, et al. Gut. 2007;56:1302-1308. Romero-Gomez M, et al. Gastroenterology. 2005;128:636-641. Sanyal AJ, et al. AASLD 2004. Abstract 179A. Younossi ZM, et al. J Clin Gastroenterol. 2004;38:705-709. Hui JM, et al. Gastroenterology. 2003;125:1695-1704. Conjeevaram H, et al. Hepatology. 2007;45:80-87. Tarantino G, et al. Gut. 2006;55:585.

HIV/HCV Coinfection

HIV-infected

- 1 million people have HIV
- Incidence: 40,000/yr
- 15,000 deaths/year
- ~45% are HCV-infected

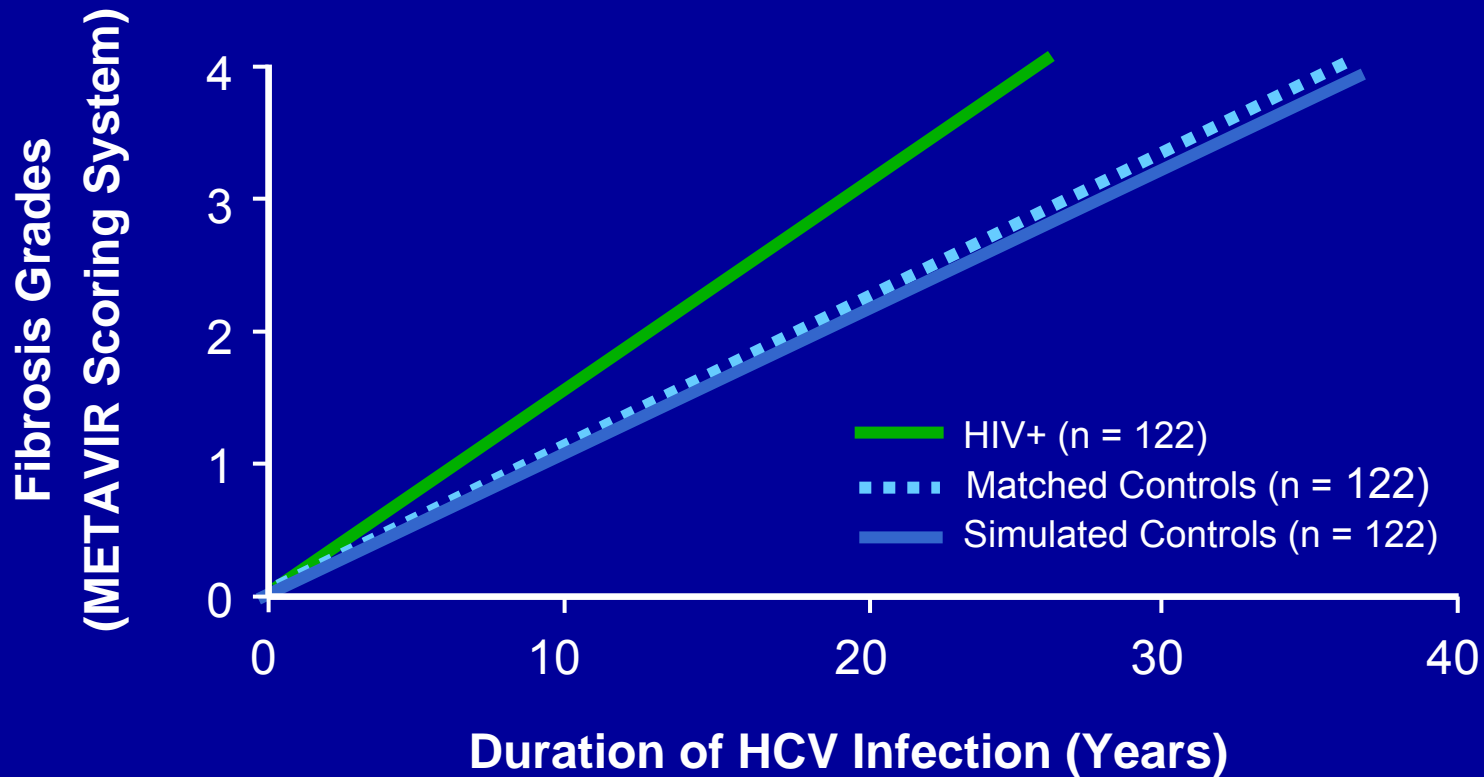
HCV-infected

- 4 million people have HCV
- Incidence: 40,000/yr
- 8000-10,000 deaths/year
- ~10% are HIV-infected

Impact of HCV on HIV Disease Progression

- Prospective cohort study of 3111 patients on HAART between 6/96 to 5/99
- 37% were HCV+
- HIV-related progression and death higher in active IVDU with HCV infection
- HCV associated with blunted CD4 recovery
- Deaths from liver disease 3-fold higher

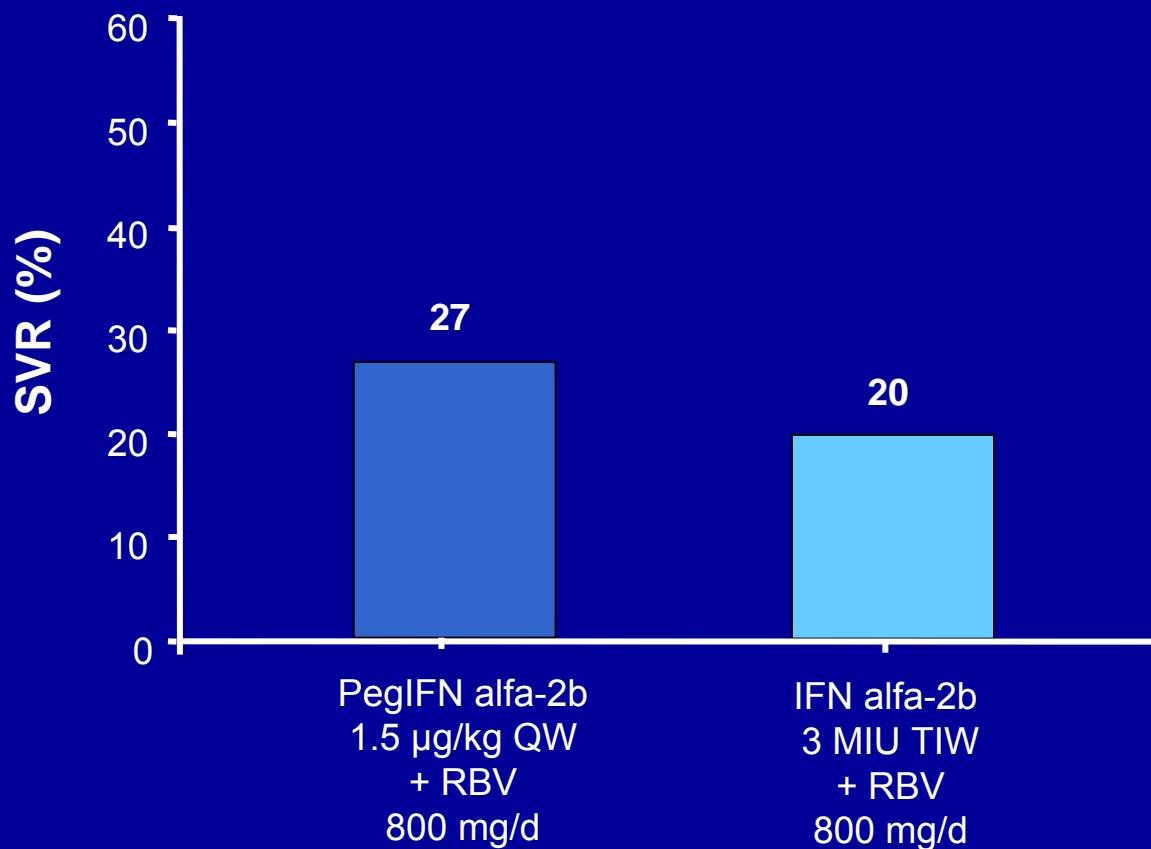
Effect of HIV/HCV Coinfection on Fibrosis Progression Rates



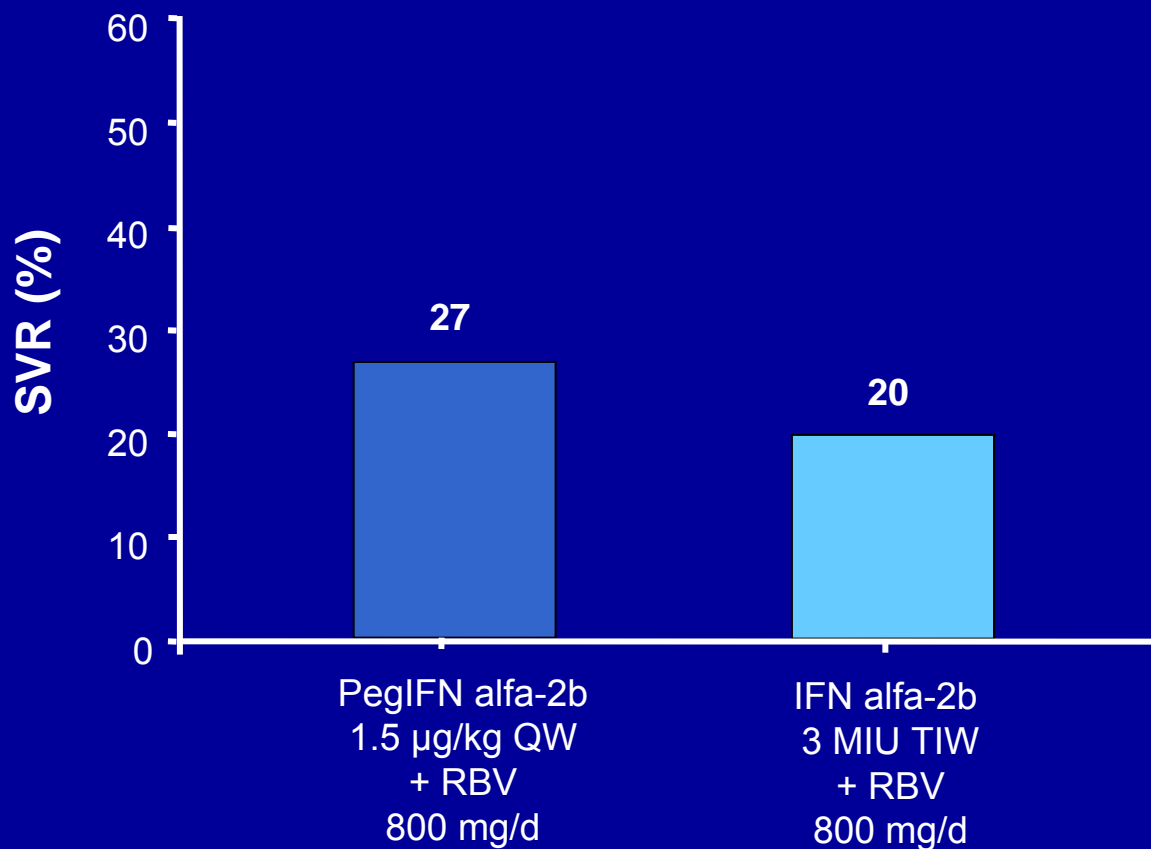
HIV/HCV Coinfection Trials: PegIFN/RBV

Study	Treatment Regimen
RIBAVIC France (N = 412)	PegIFN alfa-2b 1.5 µg/kg QW + RBV 800 mg/d IFN alfa-2b 3 MIU TIW + RBV 800 mg/d
ACTG 5071 USA (N = 133)	PegIFN alfa-2a 180 µg QW + RBV 600 mg → 1 g/d IFN alfa-2a 6 MIU TIW → 3 MIU + RBV 600 mg → 1 g/d
APRICOT International (N = 868)	PegIFN alfa-2a 180 µg QW + RBV 800 mg/d IFN alfa-2a 3 MIU TIW + RBV 800 mg/d PegIFN alfa-2a 180 µg QW + placebo QD

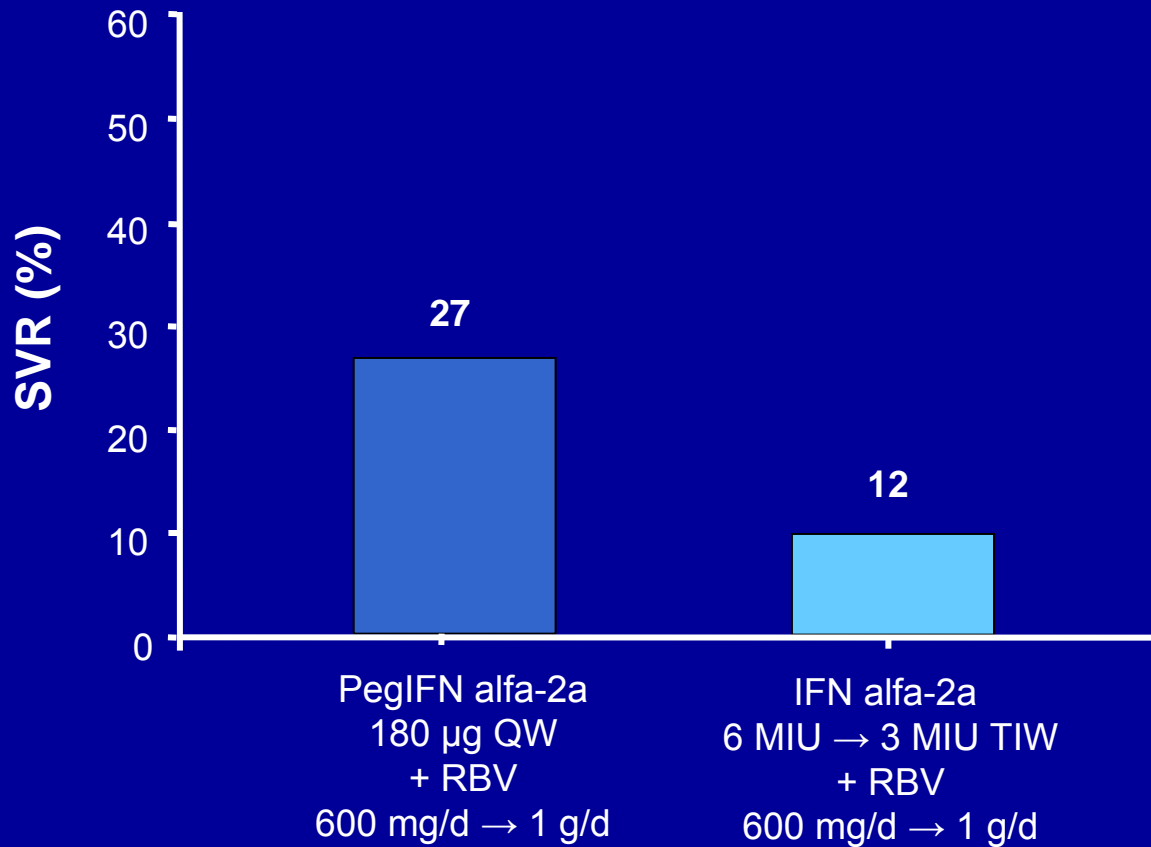
RIBAVIC Study: SVR



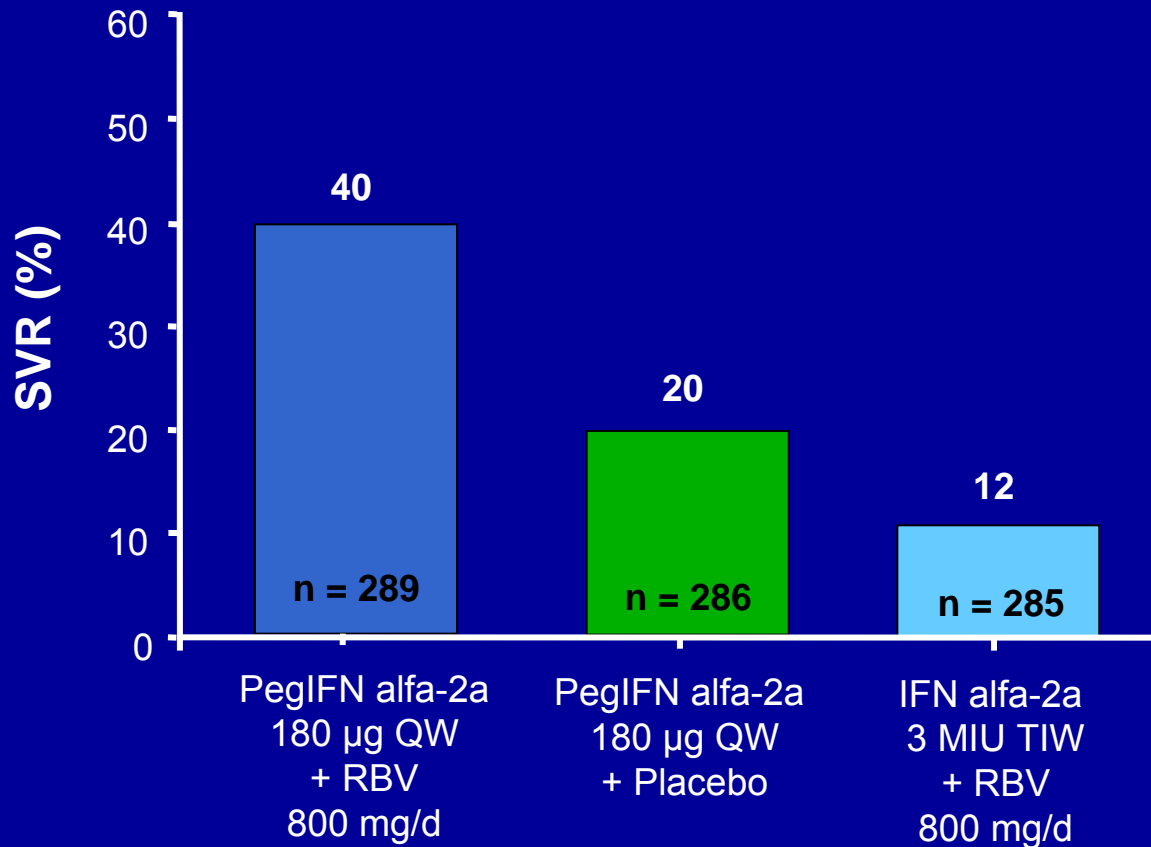
RIBAVIC Study: SVR



ACTG 5071 Study: SVR



APRICOT Study: SVR



HIV/HCV Co-infection

- In 2005, the FDA approved peginterferon alfa-2a and ribavirin as treatment for HCV disease in HCV/HIV coinfection

Potential New Treatments For Hepatitis C

- Not all patients have an SVR (19%-70%)
 - Multiple variables
 - Race
 - Genotype
 - Viral load
 - Liver histology
 - BMI
 - Compliance
- We need better treatment options

Telaprevir Treatment For HCV

- Complicated regimen
 - 12 week lead in with 3 medications
 - High dropout rate due to side effects
 - Severe dermatitis
 - GI intolerance
- SVR only 60-70% (Genotype 1)

Potential New treatments For Hepatitis C

- Protease Inhibitors
 - Telaprevir
 - Complicated regimen
 - Severe side effects
- Helicase inhibitors
- Polymerase inhibitors
- Other agents that interfere with viral replication
- Vaccine against Hepatitis C

Hepatitis C Infection In AI/AN

- Major cause for Morbidity and Mortality
- Treatment is available
 - Preliminary data suggests response rates comparable to non Hispanic Caucasians
 - We need more data to confirm this
 - Comorbidities need to be addressed
 - Coinfection with HIV
 - Alcoholism
 - Obesity
- Prevention
 - Education
 - Addiction services
- Increase availability of treatment(ECHO)