

# Genotype 2 and 3 Hepatitis C

## Standard of The Care and Future Directions

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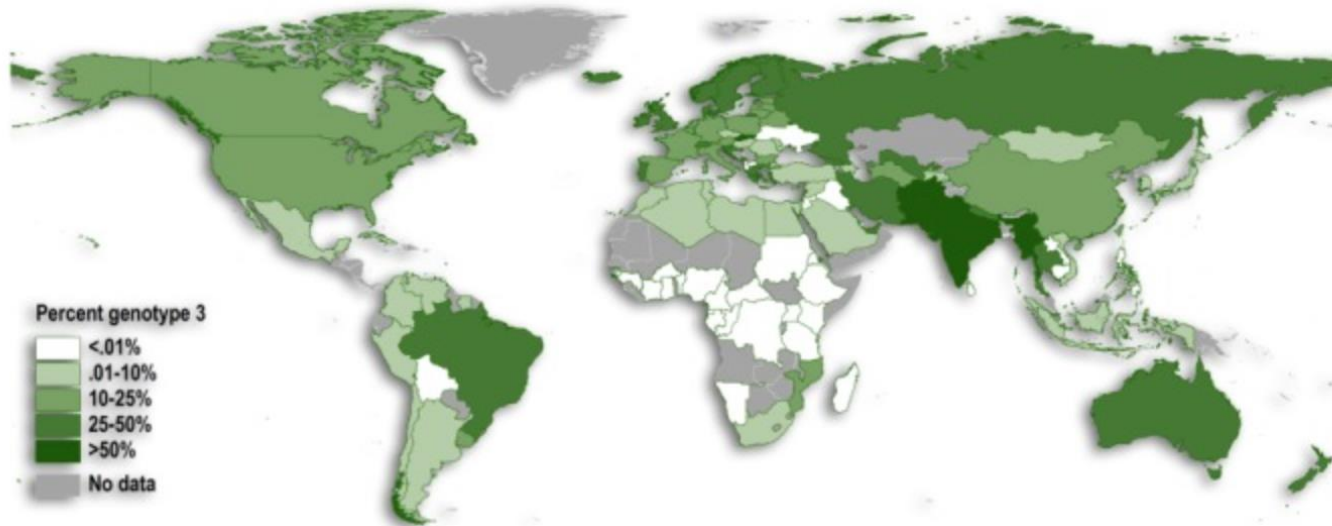
# Disclaimer

- Speaker has had relations in the form of
  - Speaker
  - Member of advisory board
  - Consultant
  - Clinical trials

with the following companies

Gilead, Bristol Myer Squibb, AbbVie, Merck, Bayer-Sanofi, Salix, Intercept

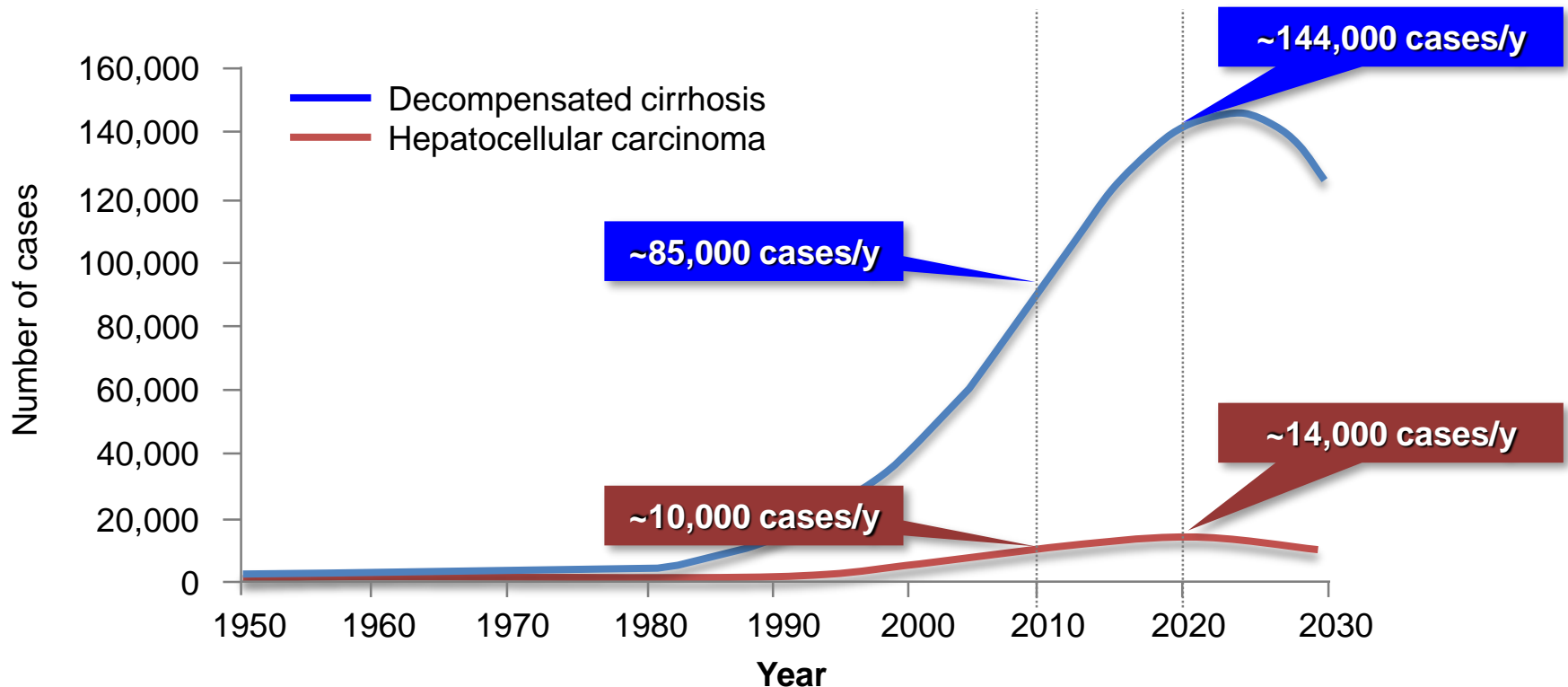
# GT3, a Global Issue



Higher risk of cirrhosis and hepatoma with GT3

*J Viral Hepat.* 2011 Nov;18(11):745-59

# Hepatoma & Decompensated Cirrhosis Due to HCV

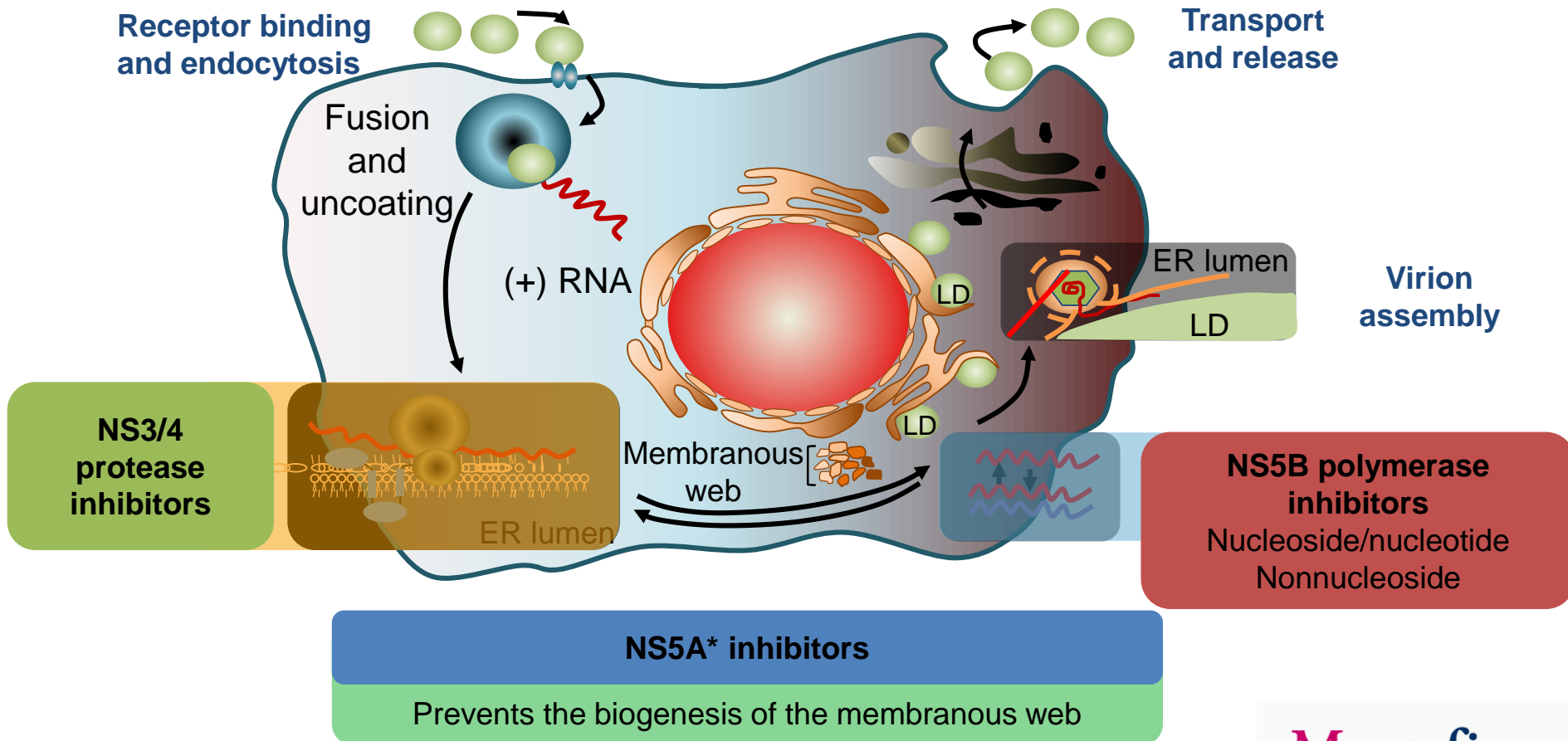


➤ **As of 2007, more people die from HCV than HIV**

*Davis GL, et al. Gastroenterology. 2010;138:513-21.*

*Ly KN, et al. Ann Intern Med. 2012;156:271-278.*

# HCV Life Cycle and DAA Targets



Manns MP, et al. Nat Rev Drug Discov. 2007;6:991-1000.

# ABC of DAAs (Direct Acting Antivirals)

## ➤ Protease Inhibitors

- ✓ revirs (paritaprevir, simeprevir, grazoprevir)
  - ✓ Hepatotoxicity, no GT2 and 3 activity at this time

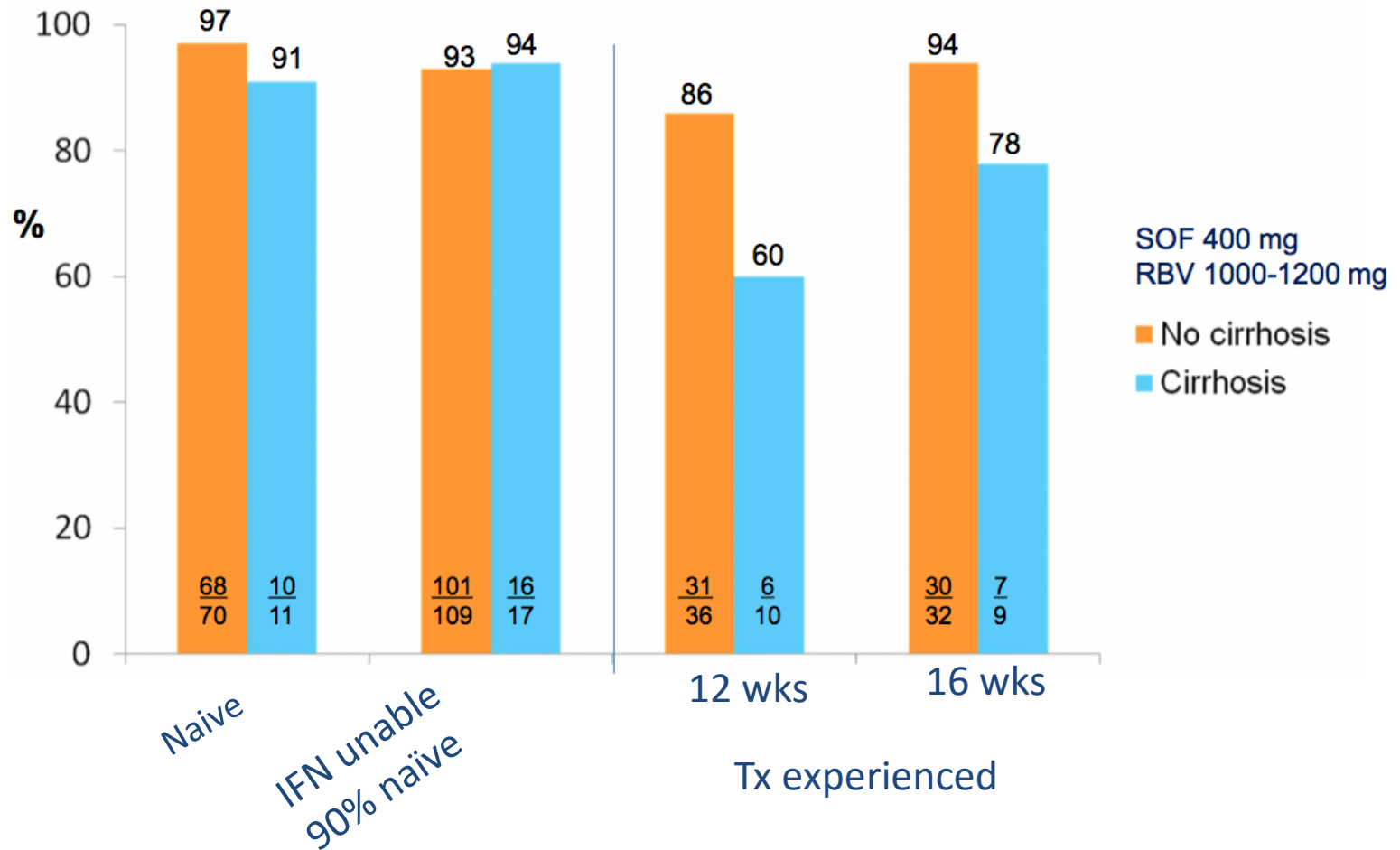
## ➤ NS5B Polymerase inhibitors

- ✓ buvirs (sofosbuvir)
  - ✓ Very potent, no resistance, pan-genotypic

## ➤ NS5A Polymerase Inhibitors

- ✓ asvirs (daclatasvir, ledipasvir, velpatasvir)
  - ✓ Risk of resistance, even at baseline

# Sofosbuvir + Ribavirin for Genotype 2



# Treatment Options GT2

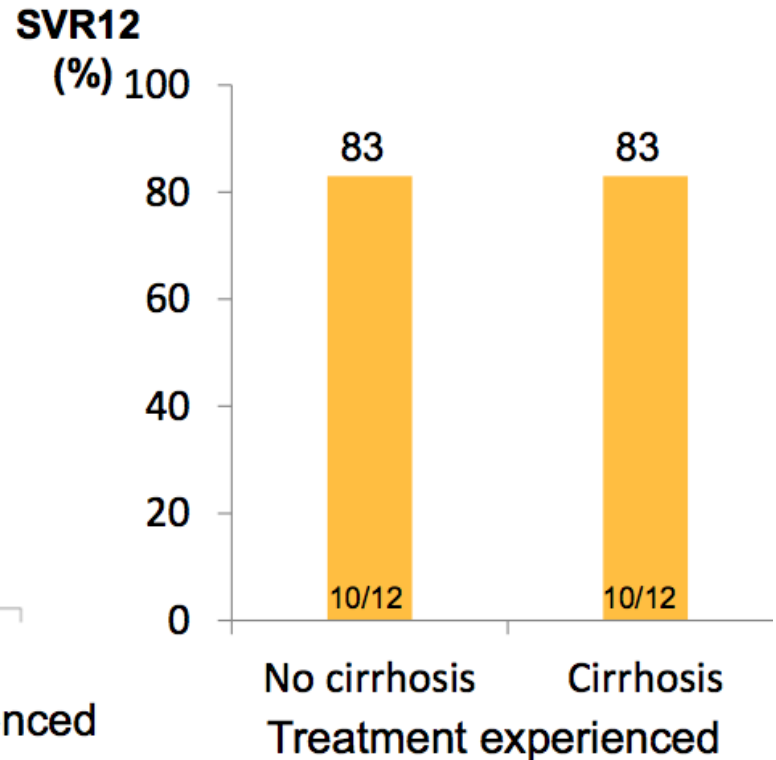
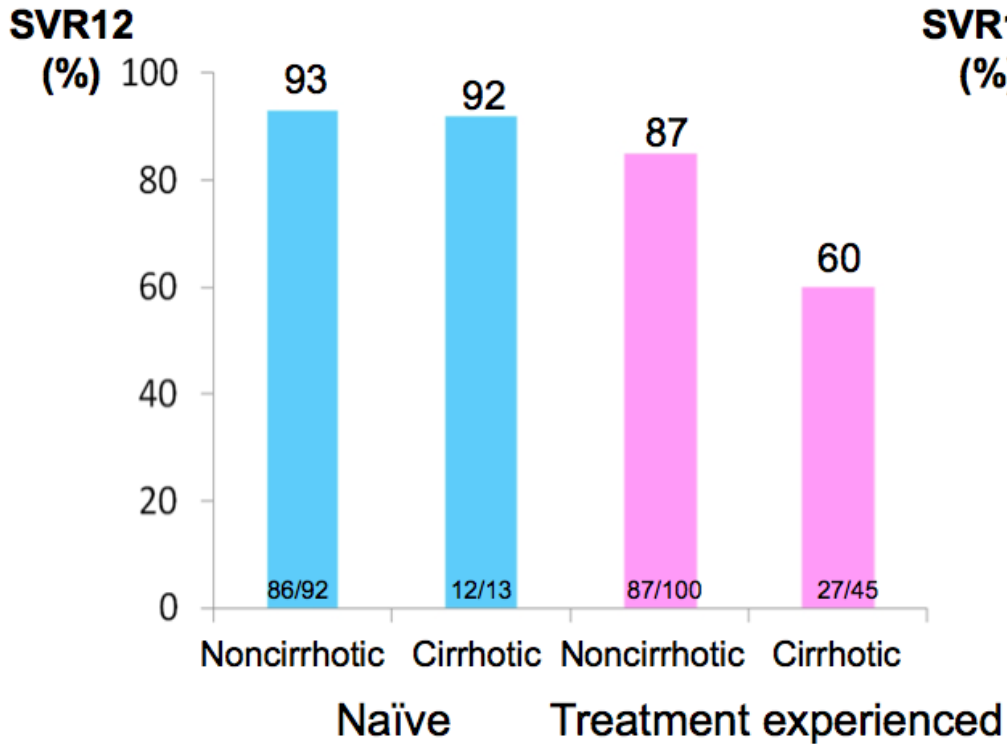
- SOF-VEL 12 wks is the AASLD recommended regimen
- DCV-SOF for 12-24 weeks as an alternative
- SOF-RBV is no longer recommended by AASLD, though it is highly effective in patients without cirrhosis
- TARGET data showed a good SVR for SOF-RBV in pts with cirrhosis



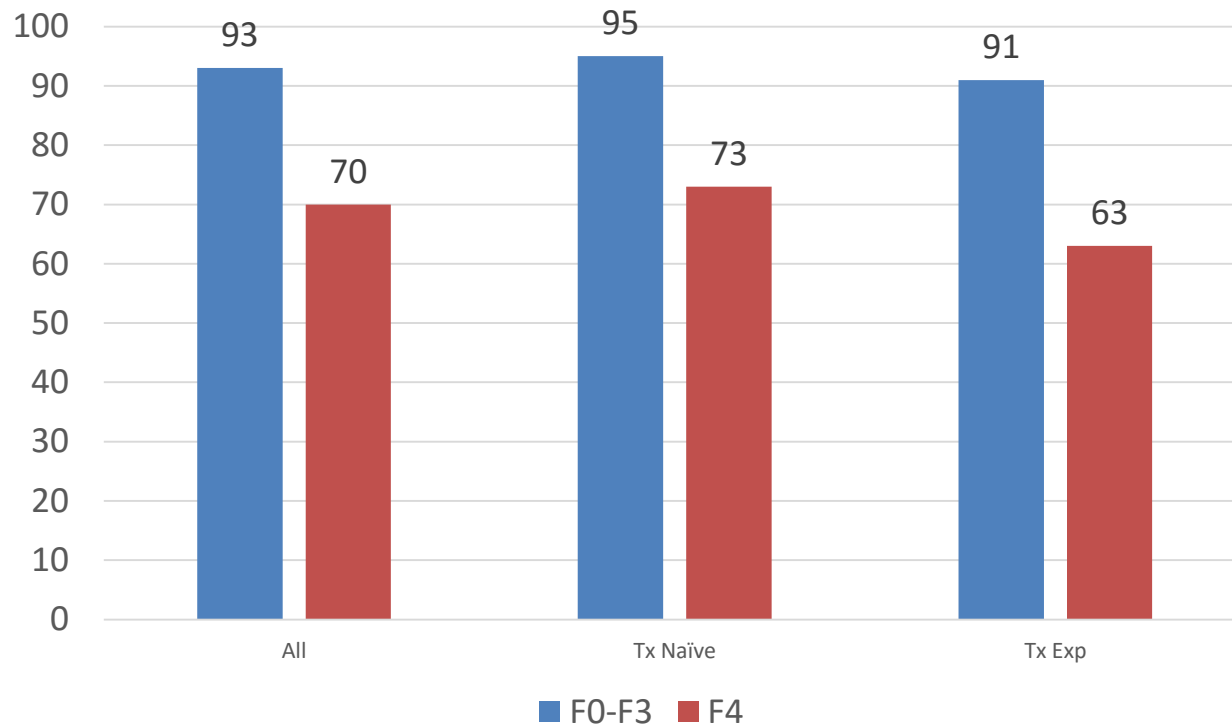
# Treatment of Genotype 3

**VALENCE: 24 weeks**  
SOF+RBV

**LONESTAR-2: 12 weeks**  
PEG IFN + SOF + RBV

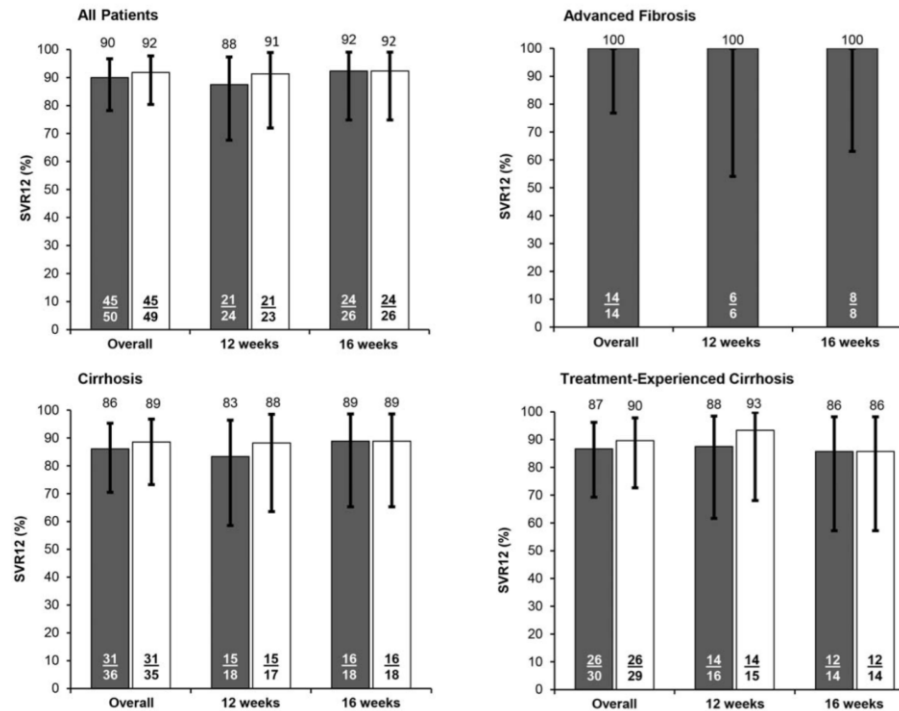


# Daclatasvir-Sofosbuvir 12 wks (ALLY 3)

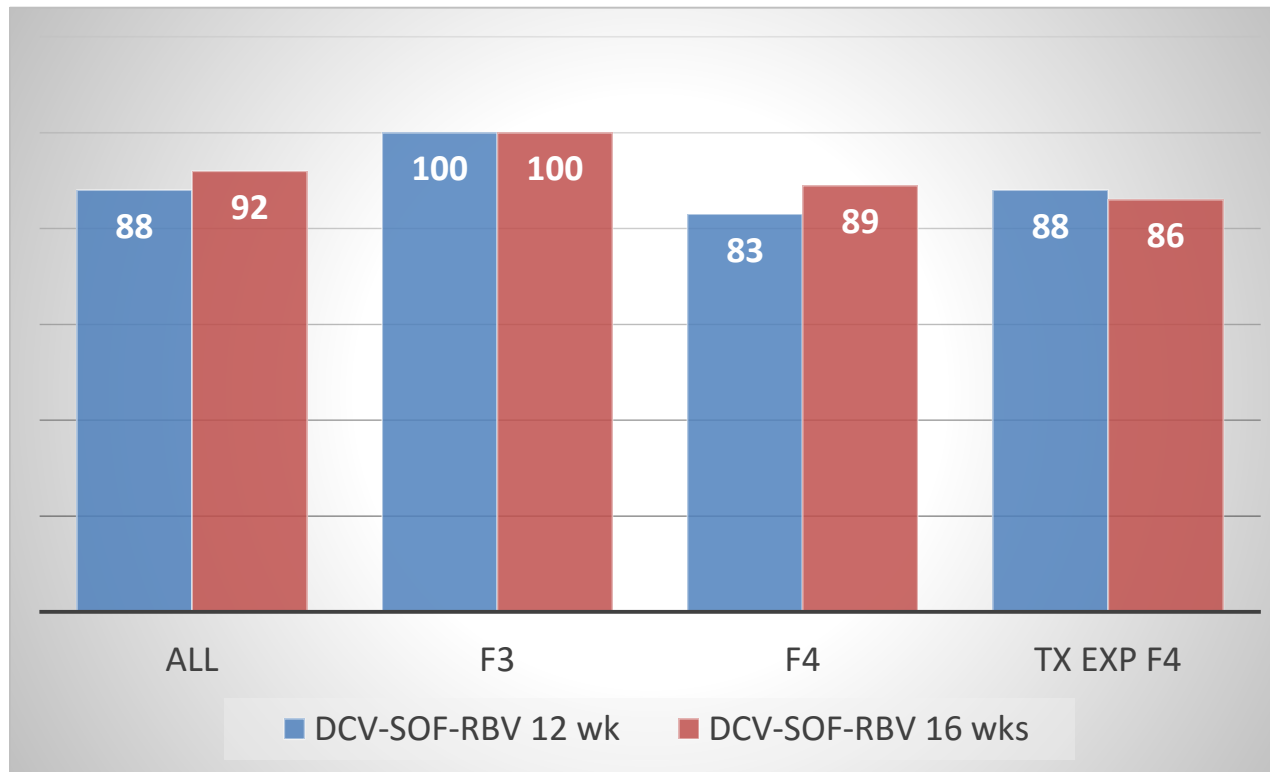


# Daclatasvir, Sofosbuvir, and Ribavirin for Hepatitis C Virus Genotype 3 and Advanced Liver Disease: A Randomized Phase III Study (ALLY-3+)

■ ITT analysis    □ Observed data\*

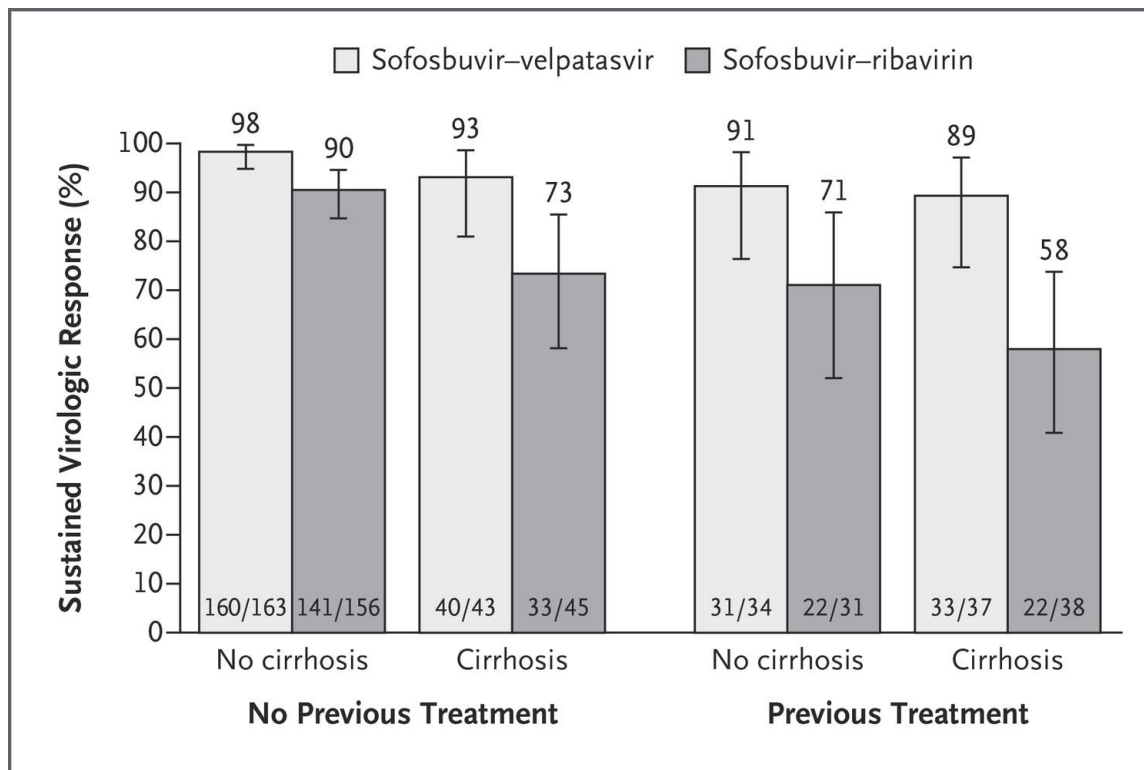


## Daclatasvir, Sofosbuvir, and Ribavirin for Hepatitis C Virus Genotype 3 and Advanced Liver Disease: A Randomized Phase III Study (ALLY-3+)

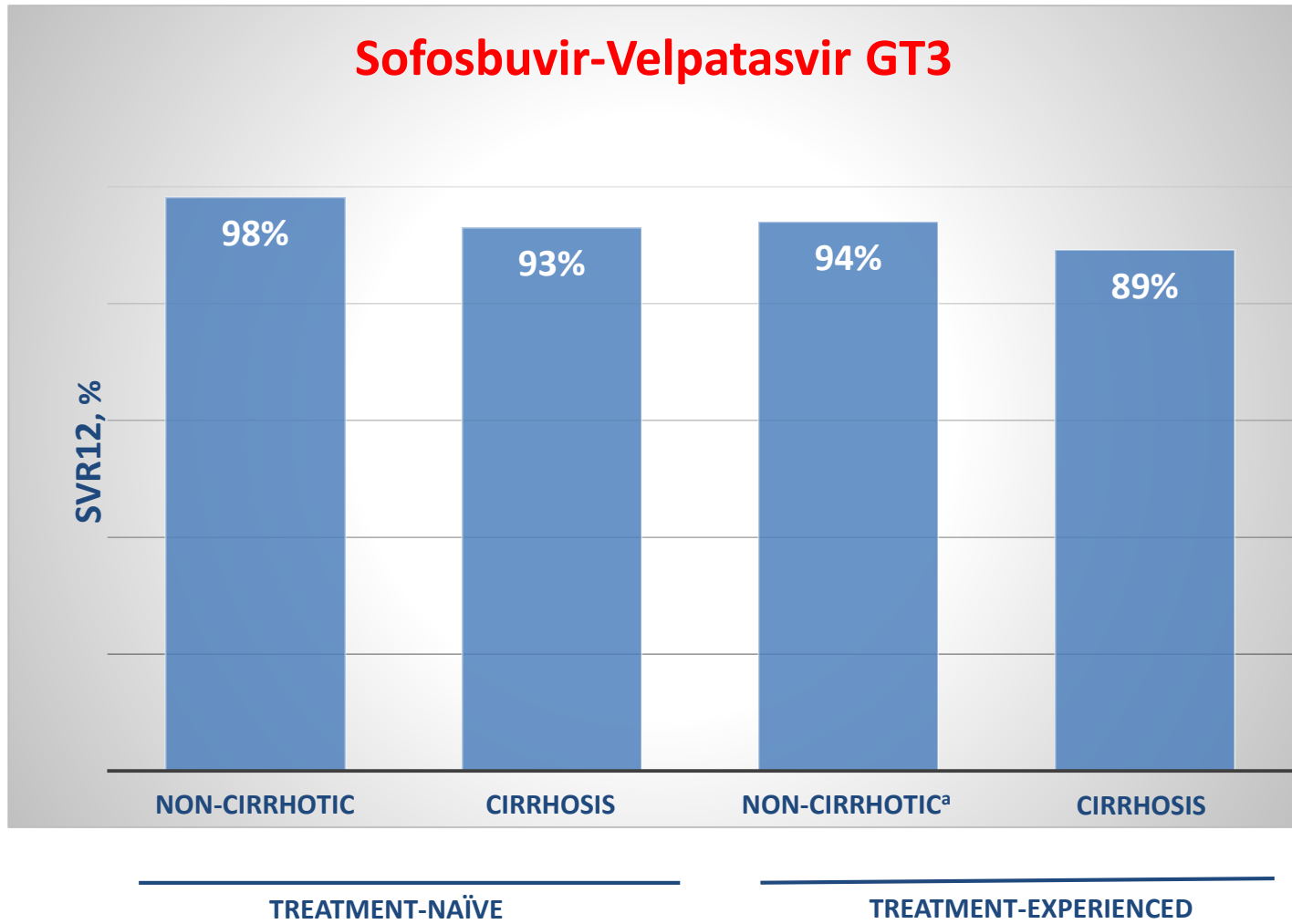


ORIGINAL ARTICLE

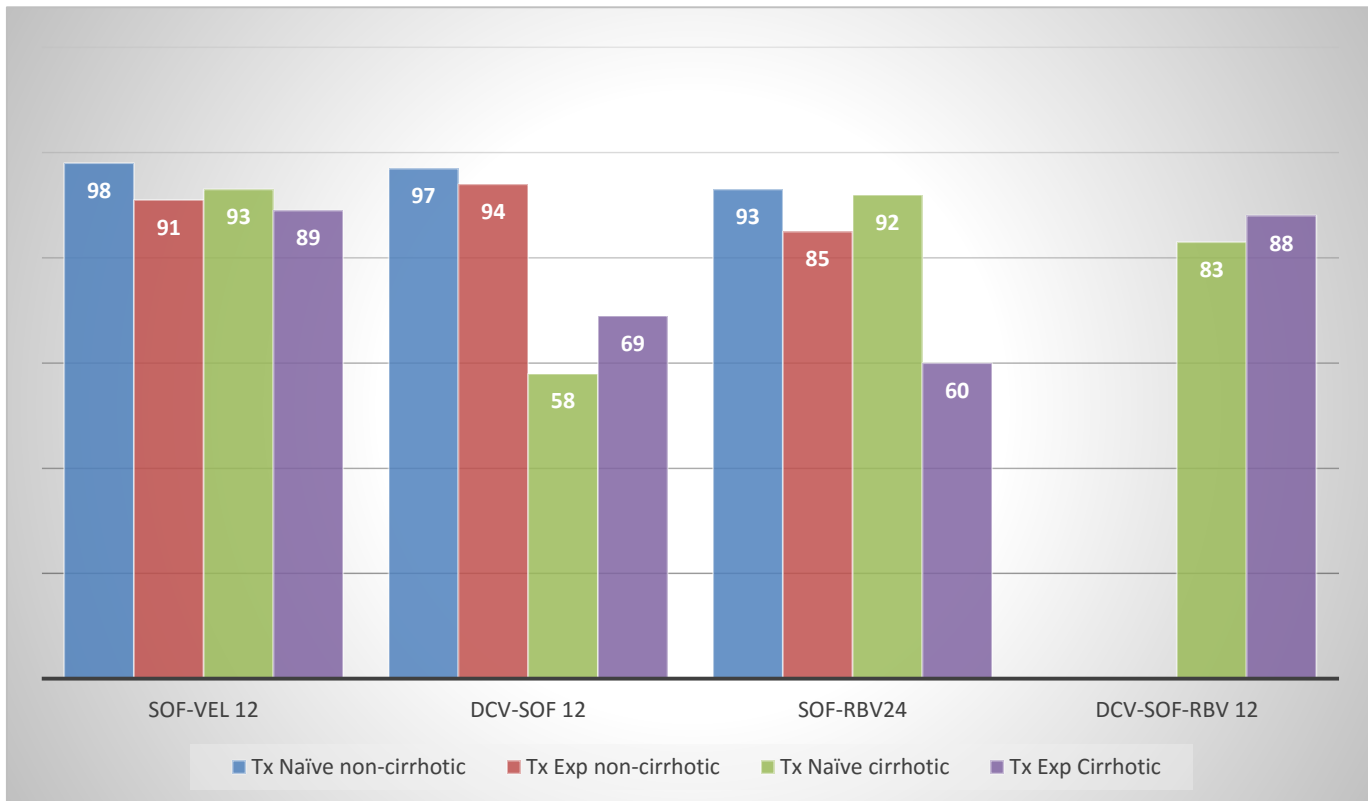
## Sofosbuvir and Velpatasvir for HCV Genotype 2 and 3 Infection



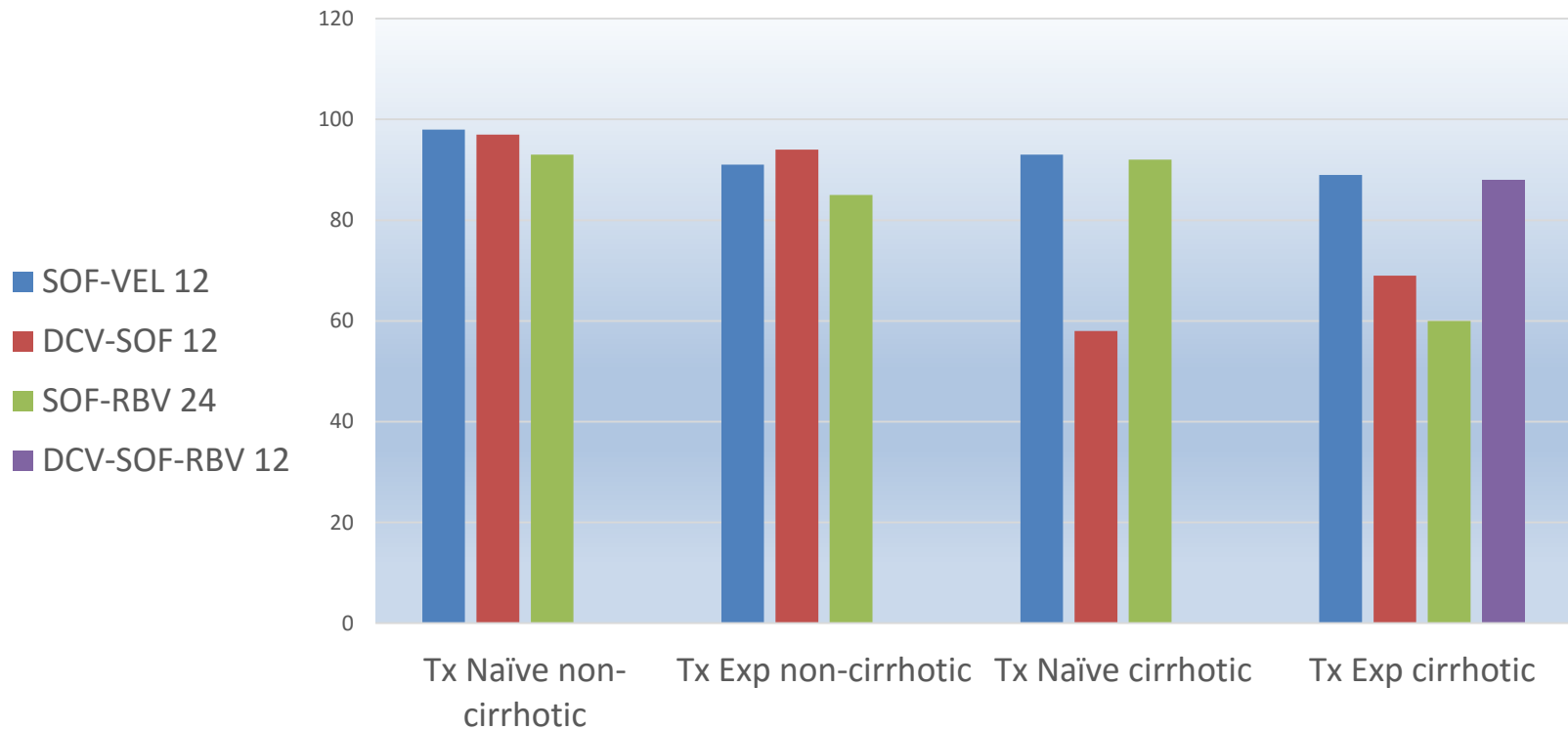
## Sofosbuvir-Velpatasvir GT3



# Treatment options GT3



# Treatment Options, GT3





# REVIEWS IN BASIC AND CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

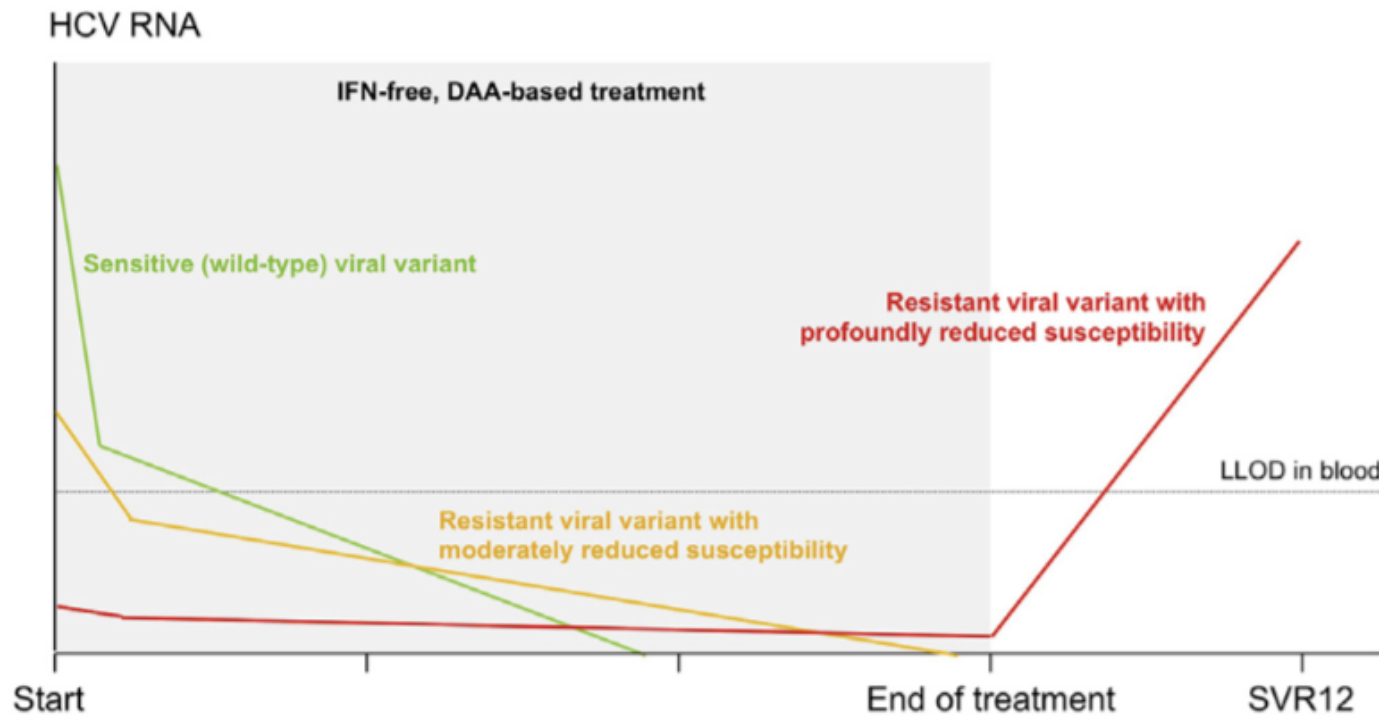
*Ernst J. Kuipers and Vincent W. Yang, Section Editors*

## Hepatitis C Virus Resistance to Direct-Acting Antiviral Drugs in Interferon-Free Regimens

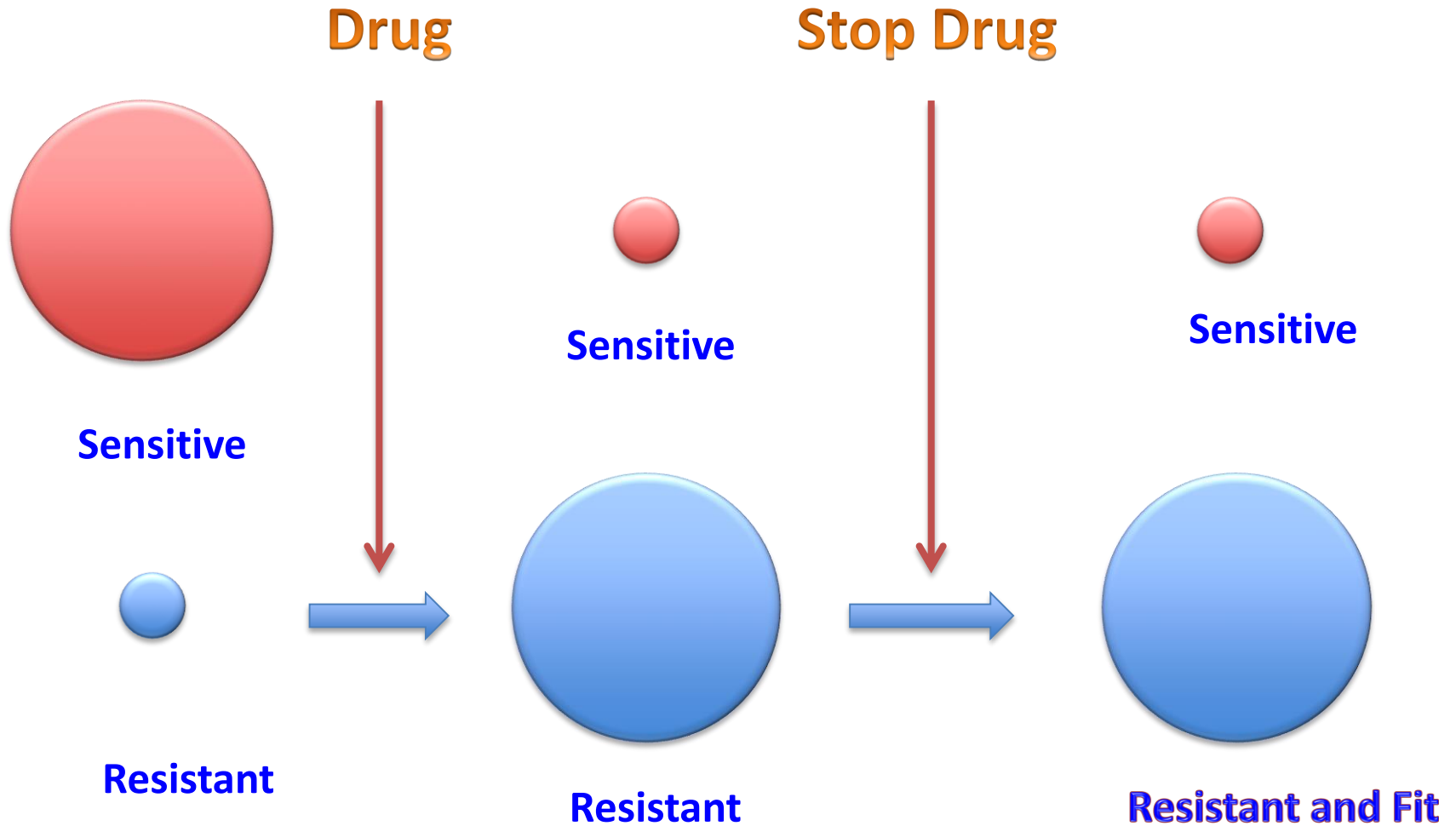


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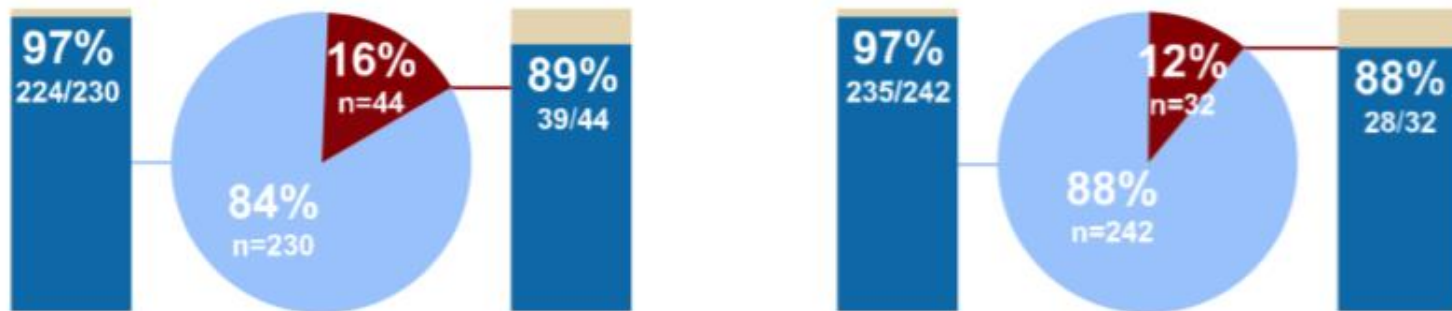
Jean-Michel Pawlotsky<sup>1,2</sup>



# Resistance



# The Impact of NS5A Resistance ASTRAL (Sofosbuvir-Velpatasvir) Data



Deep sequencing: 1% cut off

15% cut off

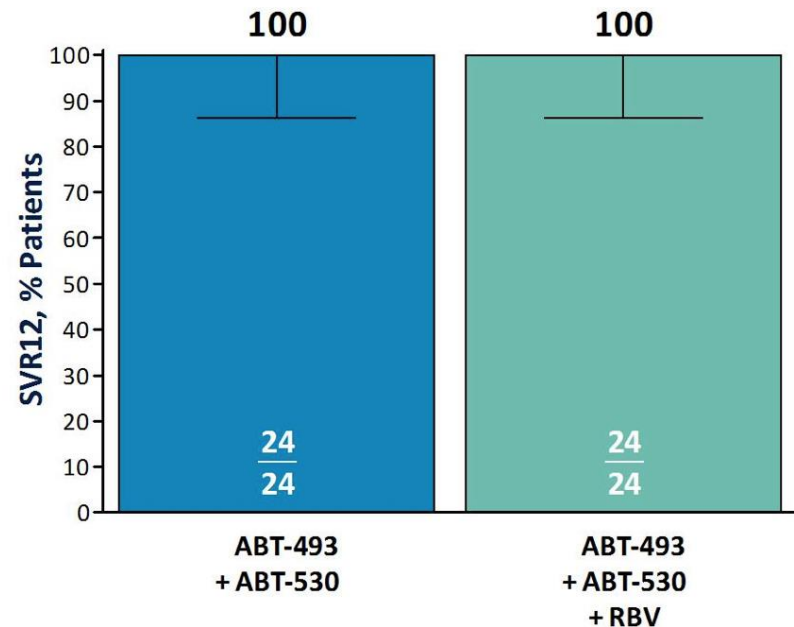
In patients with relapse, Y93H/N is the most commonly seen RAV  
Deep sequencing may not make an impact on the chance of SVR  
Patients with baseline RAV may have lower chance of SVR

Hezode C, R EASL 2016

# ABT-493 + ABT-530

- ✓ ABT-493
  - ✓ Pan-genotypic NS3/4 A
  - ✓ Protease inhibitor
  - ✓ Effective against most PI resistant variants

- ✓ ABT-530
  - ✓ NS5A inhibitors
  - ✓ Effective against common RAVs (28,29,30,93)



Kwo, et al, EASL 2016

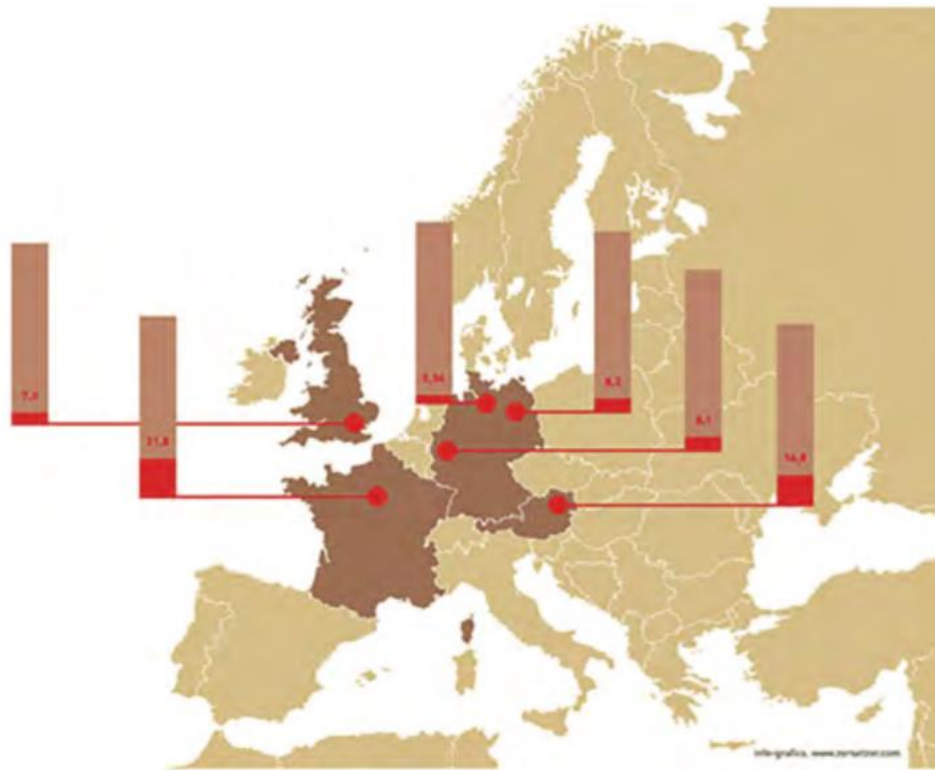
## Risk of Hepatocellular Carcinoma After Sustained Virological Response in Veterans With Hepatitis C Virus Infection

- Annual risk of HCC after SVR in patients with cirrhosis is 1.39%
- The risk does not go down with time
- Patients with diabetes, SVR achieved after the age of 64 and GT3 have higher risk of HCC development
- Patient should be screened for HCC regardless of SVR

## PS006

### HCV REINFECTION INCIDENCE AND OUTCOMES AMONG HIV INFECTED MSM IN WESTERN EUROPE

T.C. Martin<sup>1,2</sup>, P. Ingiliz<sup>3</sup>, A. Rodger<sup>4</sup>, H.J. Stellbrink<sup>5</sup>, S. Mauss<sup>6</sup>,  
C. Boesecke<sup>7</sup>, M. Mandorfer<sup>8</sup>, A. Baumgarten<sup>3</sup>, J. Bottero<sup>9</sup>, S. Bhagani<sup>10</sup>,  
K. Lacombe<sup>9</sup>, M. Nelson<sup>1</sup>, J. Rockstroh<sup>7</sup>, NEAT study group. <sup>1</sup>Chelsea and



- Can we tackle (eliminate) the hepatitis C?
- When there is a will, there is a way