Genotype 2 , What's new ?

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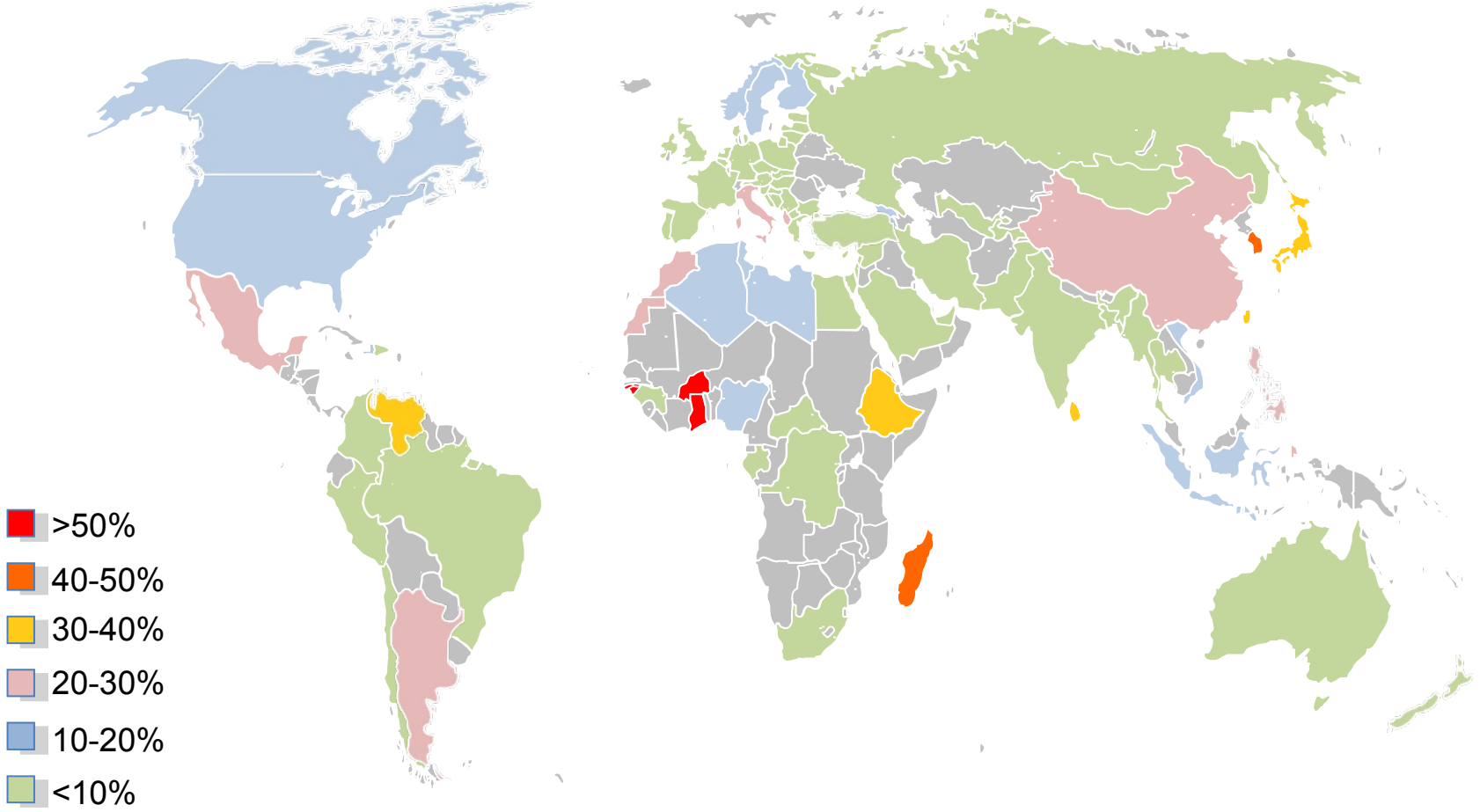
Disclosures

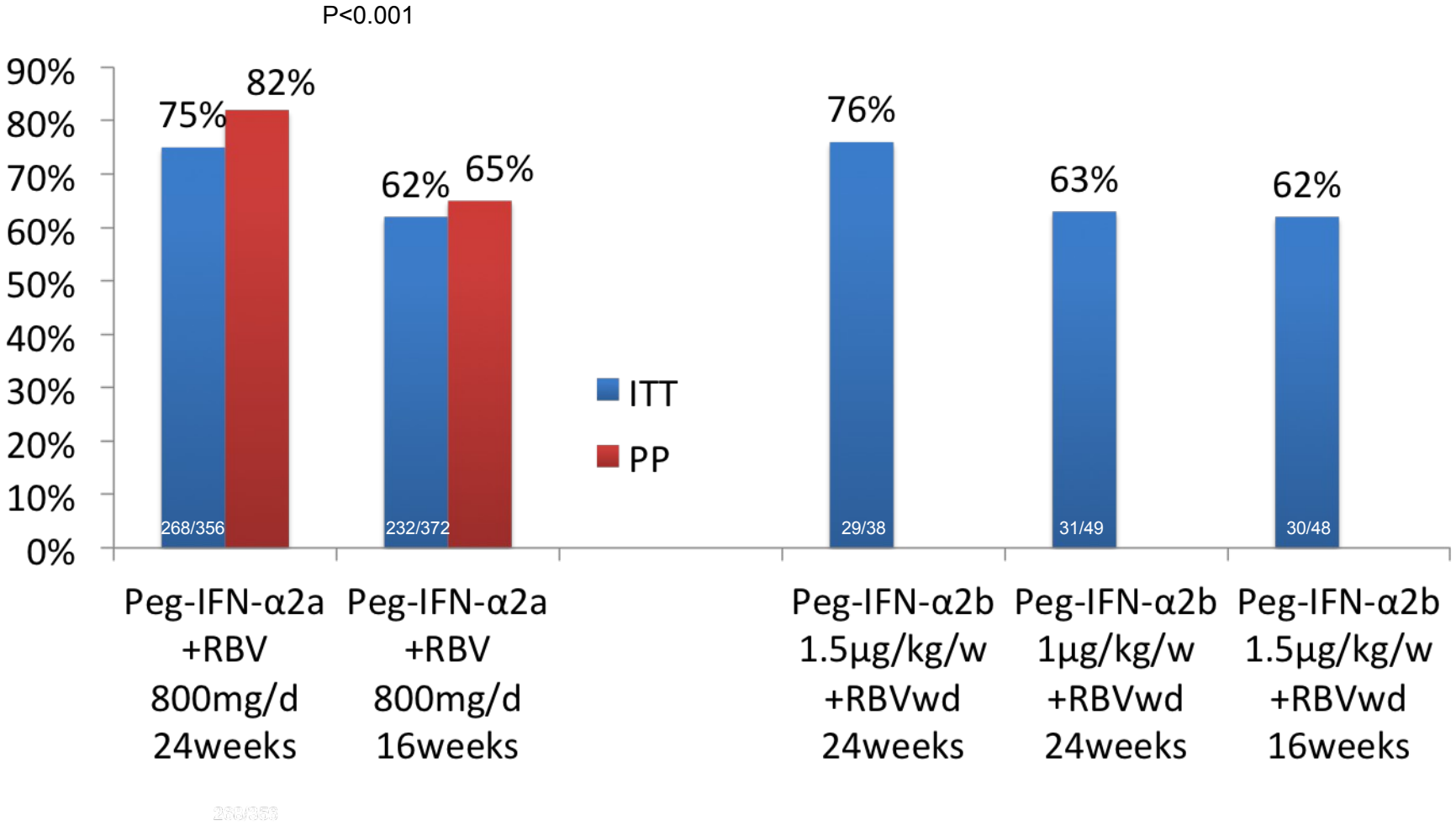
- Board member for : Schering-Plough, Merck, Janssen, Gilead, Boehringer Ingelheim, BMS, Novartis, Roche, Abbott, GSK, Vertex, Idenix
- Speaker for : Roche, Schering-Plough, Merck, Janssen, Gilead, BMS, Abbvie

Genotype 2 prevalence worldwide (13%)



Gower R et al. J Hepatol 2014: 61: S45-S57
Mohd Hanafiah K et al. Hepatology 2013: 57: 1333-42..

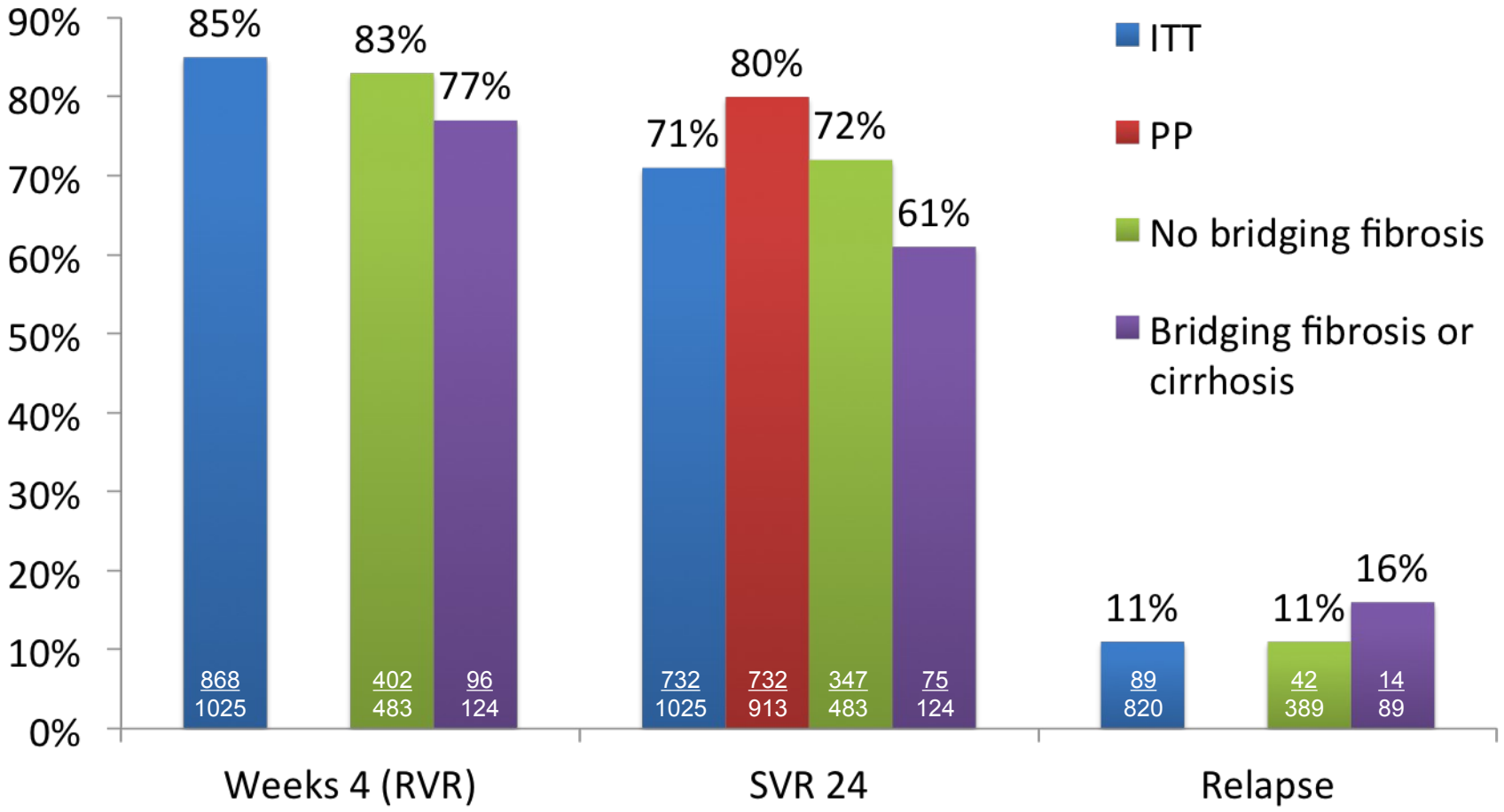
Pegylated IFN + Ribavirin for GT-2 in clinical trial



Shiffman. ML et al N Engl J Med 2007: 357: 124-34

Manns. M et al. J Hepatol 2011; 55: 554-63.

Pegylated IFN + Ribavirin for GT-2 in "real life" : PROPHESYS (2007-2011)



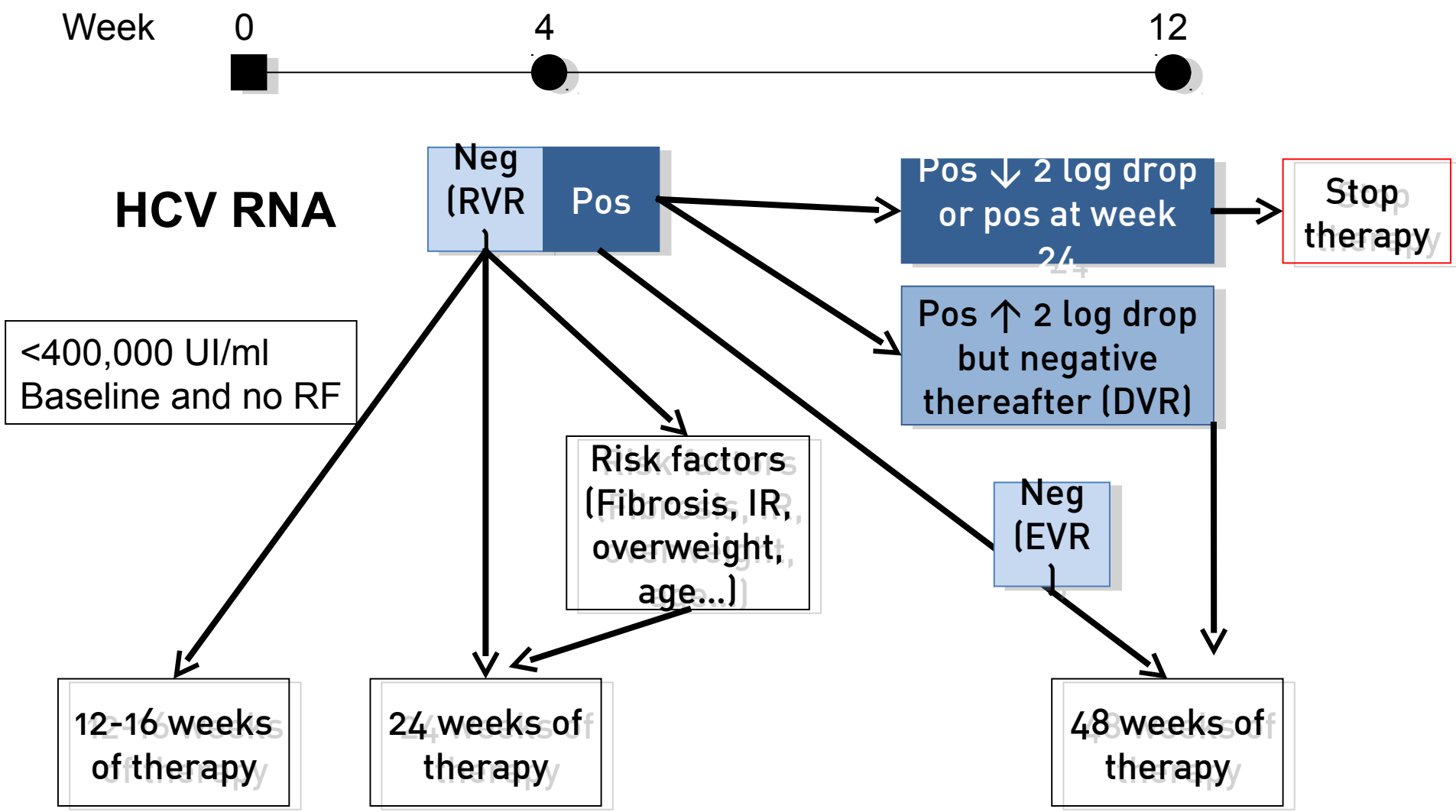
86% Peg-IFN-α2a, 14% Peg-IFN-α2b, 96% 24 weeks, 3.5% 48 weeks

Marcellin. P et al. Hepatology 2012; 56: 2039-50

Predictors of response to PR for GT-2 patients

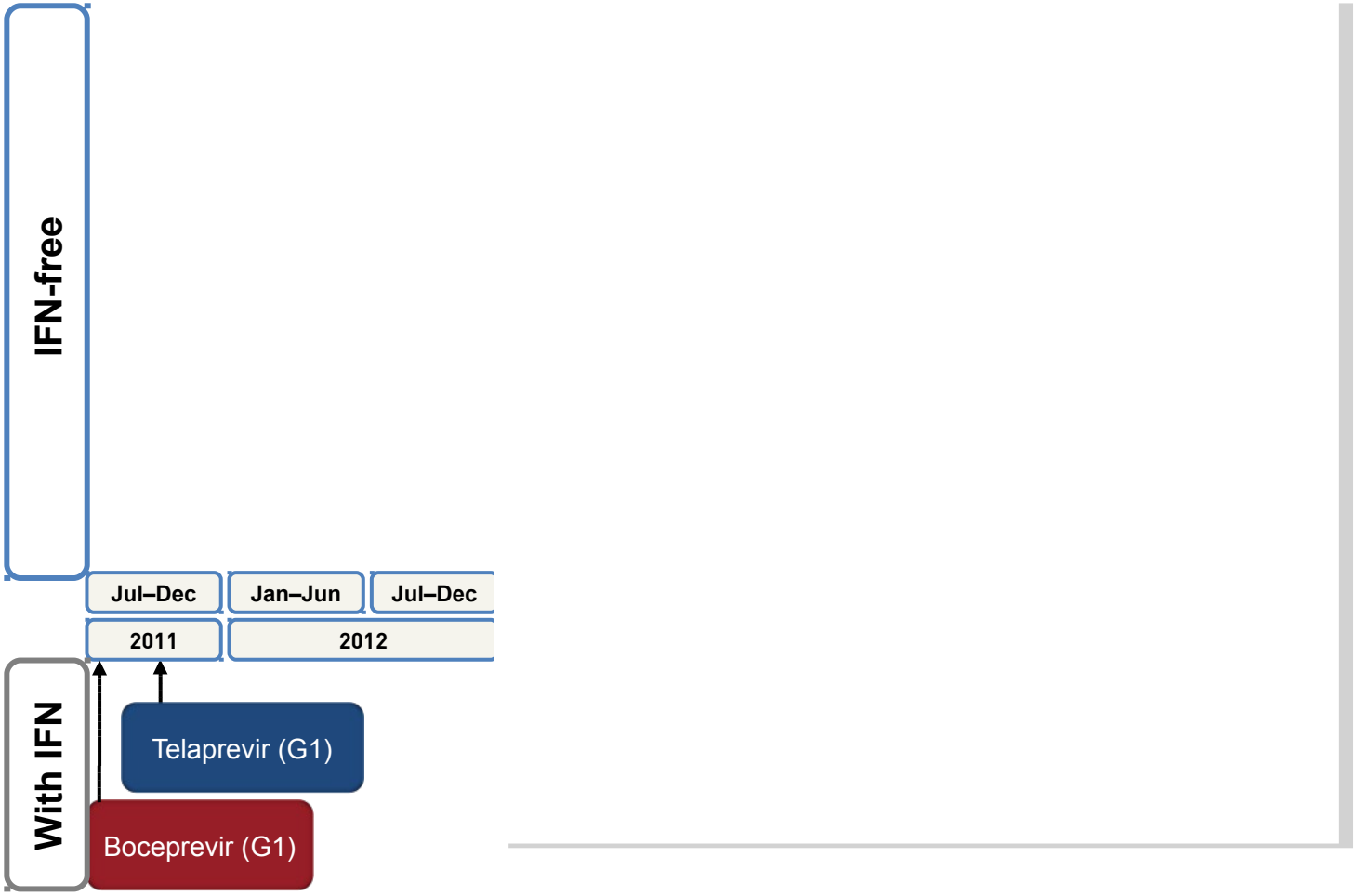
- Baseline lower viral load : slight effect
  - (Andriulli A et al. Dig Liv Dis 2006: 38: 741-8)
  - (Marciano S et al. Liver Int 2014; 34(S1): 13-7)
- Absence of bridging fibrosis or cirrhosis : slight effect
  - (Marcellin P et al. Hepatology 2012; 56: 2039-50)
- IFNLambda3/IL28B polymorphism in non RVR :
  - In non RVR : SVR rate in IL28B CC 66% vs 45% in non CC
    - (Mangia A et al. Gastroenterology 2010; 139: 821-7.)
- **RVR 4: Strongest predictive factor of SVR**
- RVR 2 : Highest positive predictive value for SVR (85% for the 25% patients with RVR 2)
  - (Marcellin P et al. Hepatology 2012; 56: 2039-50)

Response–guided therapy in GT-2 patients receiving PR therapy



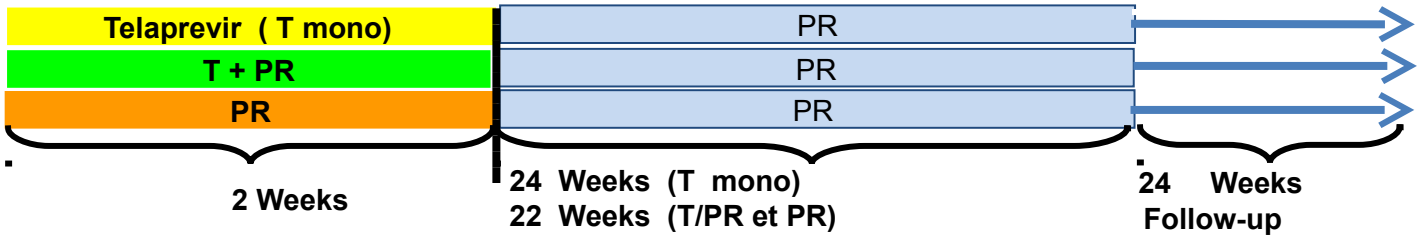
EASL Clinical Practice Guidelines. J Hepatol 2014; 60: 392-420

DAAs Combinations approved by EMA

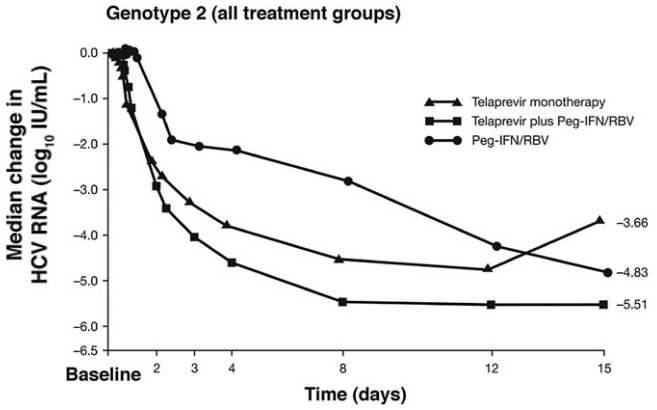


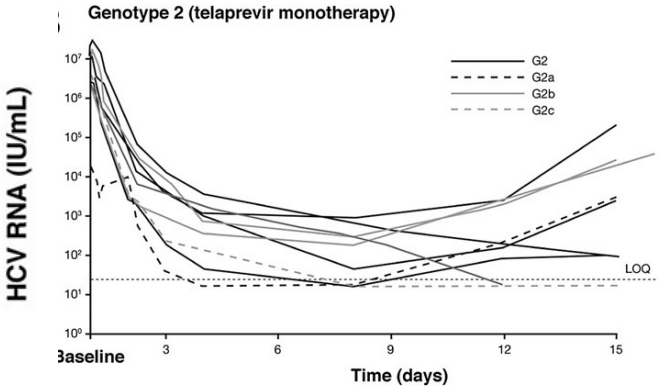
Telaprevir in naive genotype 2 patients

- Phase IIa randomized trial, controlled , partially double blind study.



Genotype 2





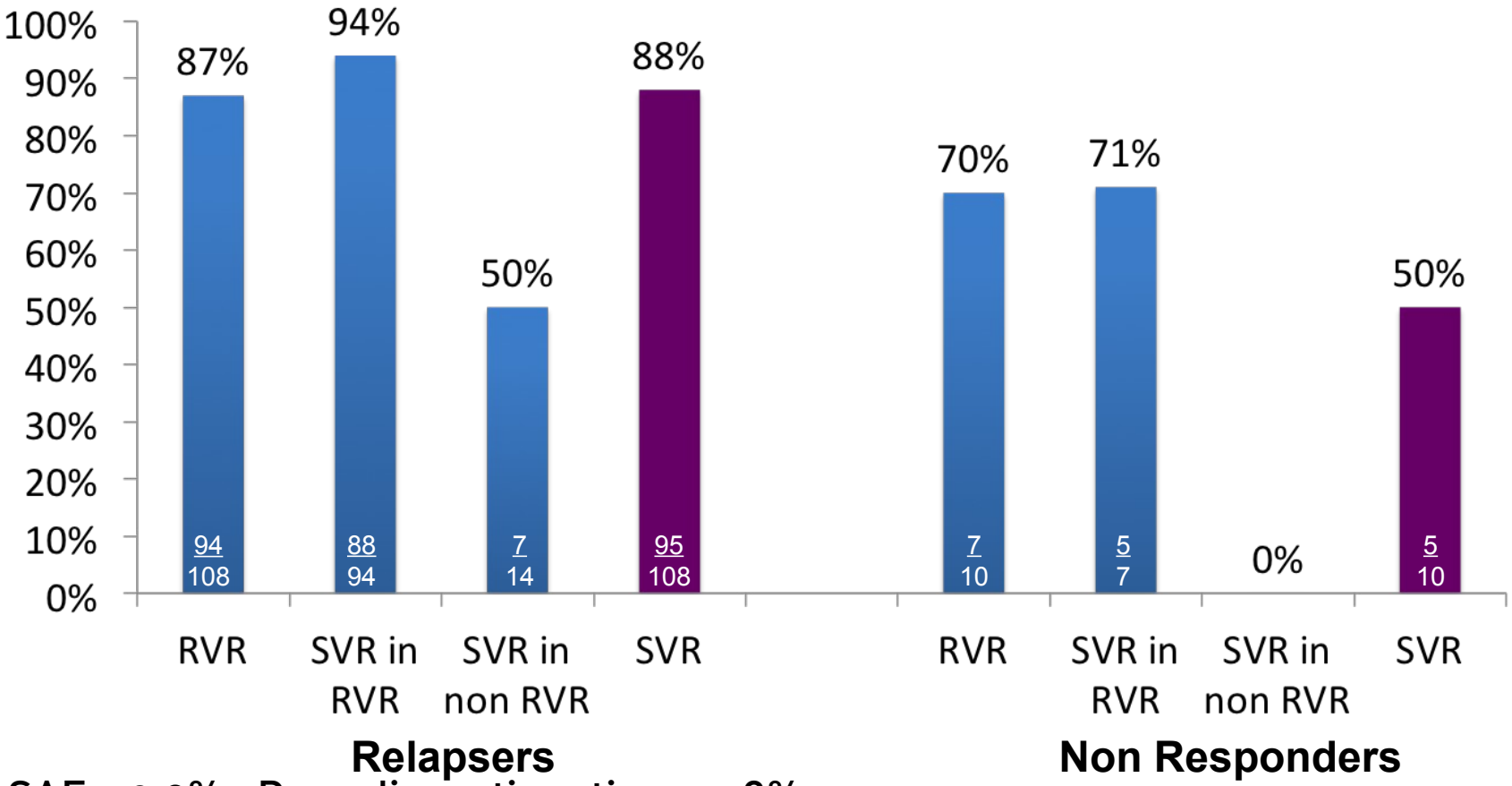
SVR

T mono : (5/9) 56%
T + PR : (5/5) 100%
PR : (8:9) 89%

Forster G et al. Gastroenterology 2011; 141: 881-889.

Telaprevir in genotype 2

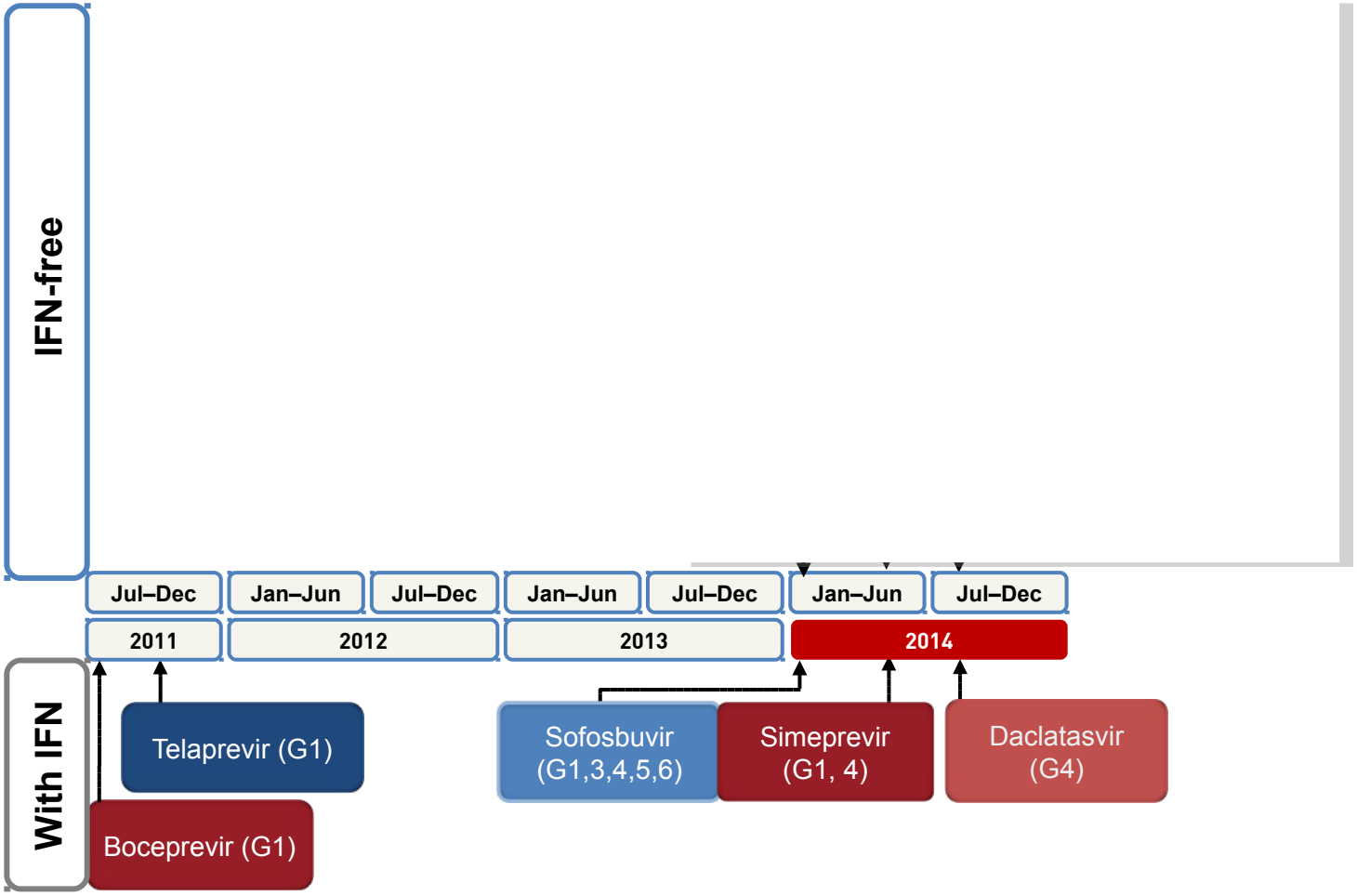
- Phase III study : 118 treatment-experienced GT-2 patients (108 relapsers, 10 non responders)
- Telaprevir 750mg/8H for 12 weeks + PR for 24 weeks



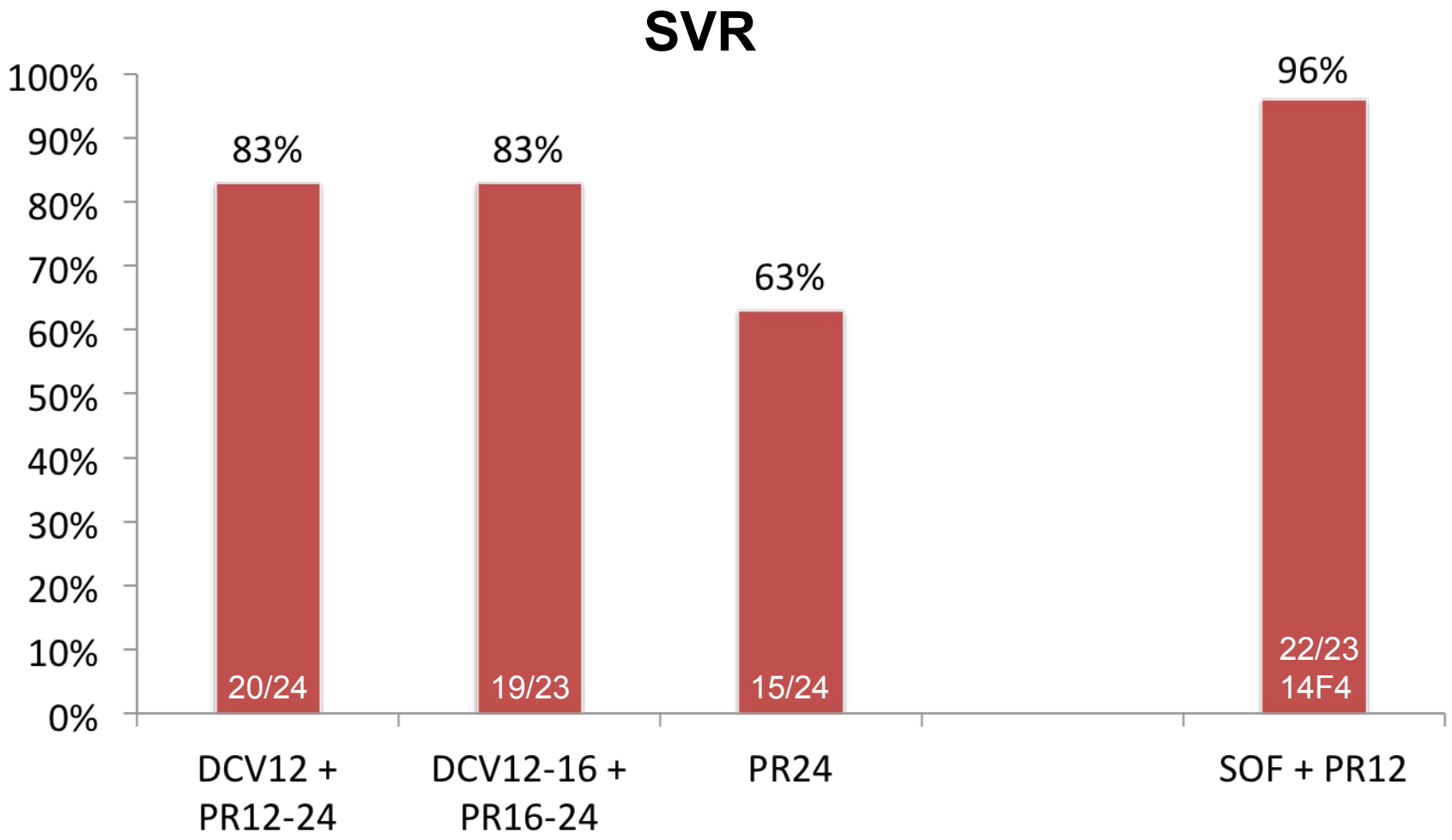
SAE: 10.2% , Drug discontinuation: 17.8%

Kumada H et al. Hepatol Res 2014

DAAs Combinations approved by EMA



DAAs + PR for GT-2 patients

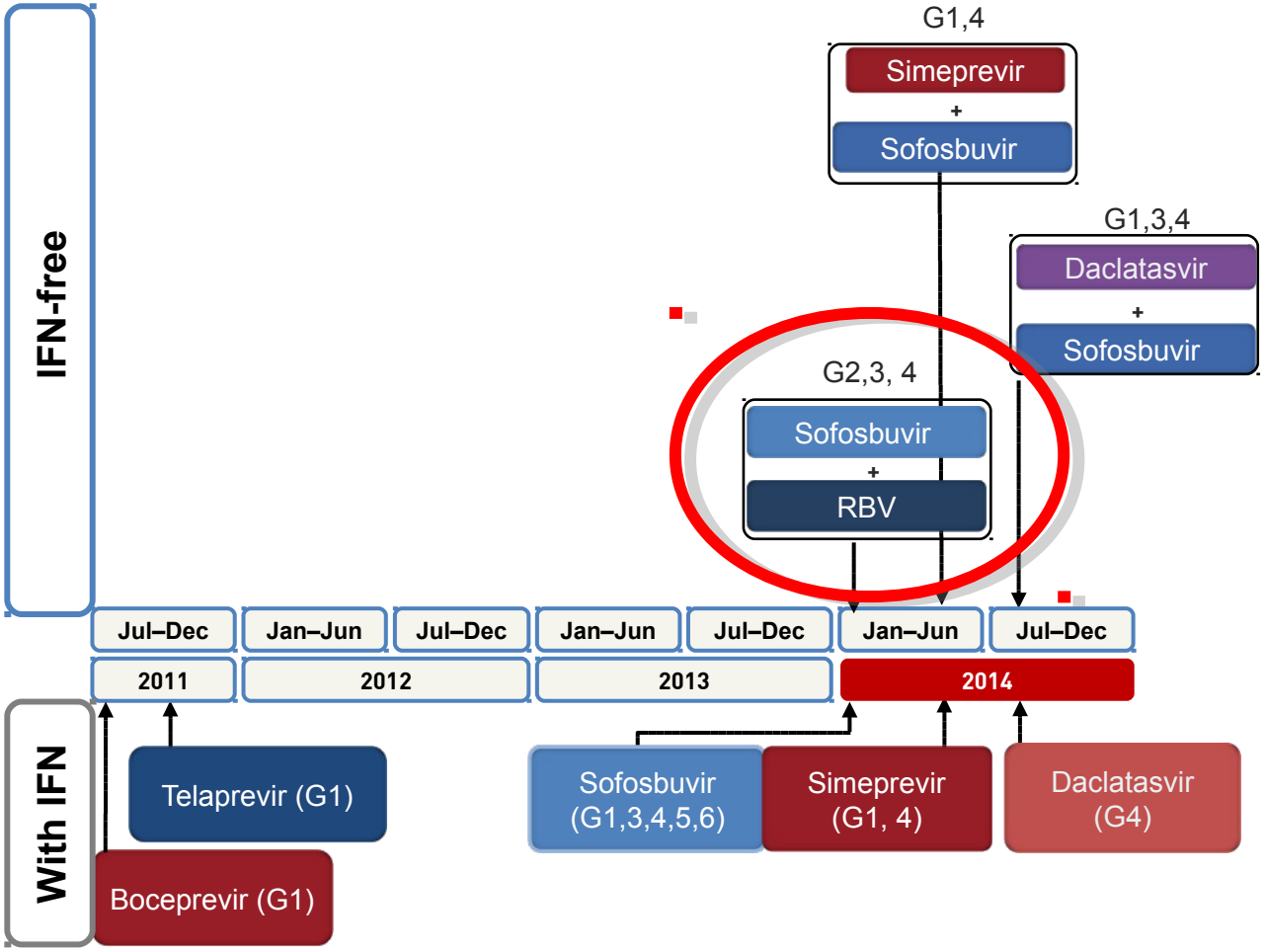


Dore GJ et al. Gastroenterology 2014

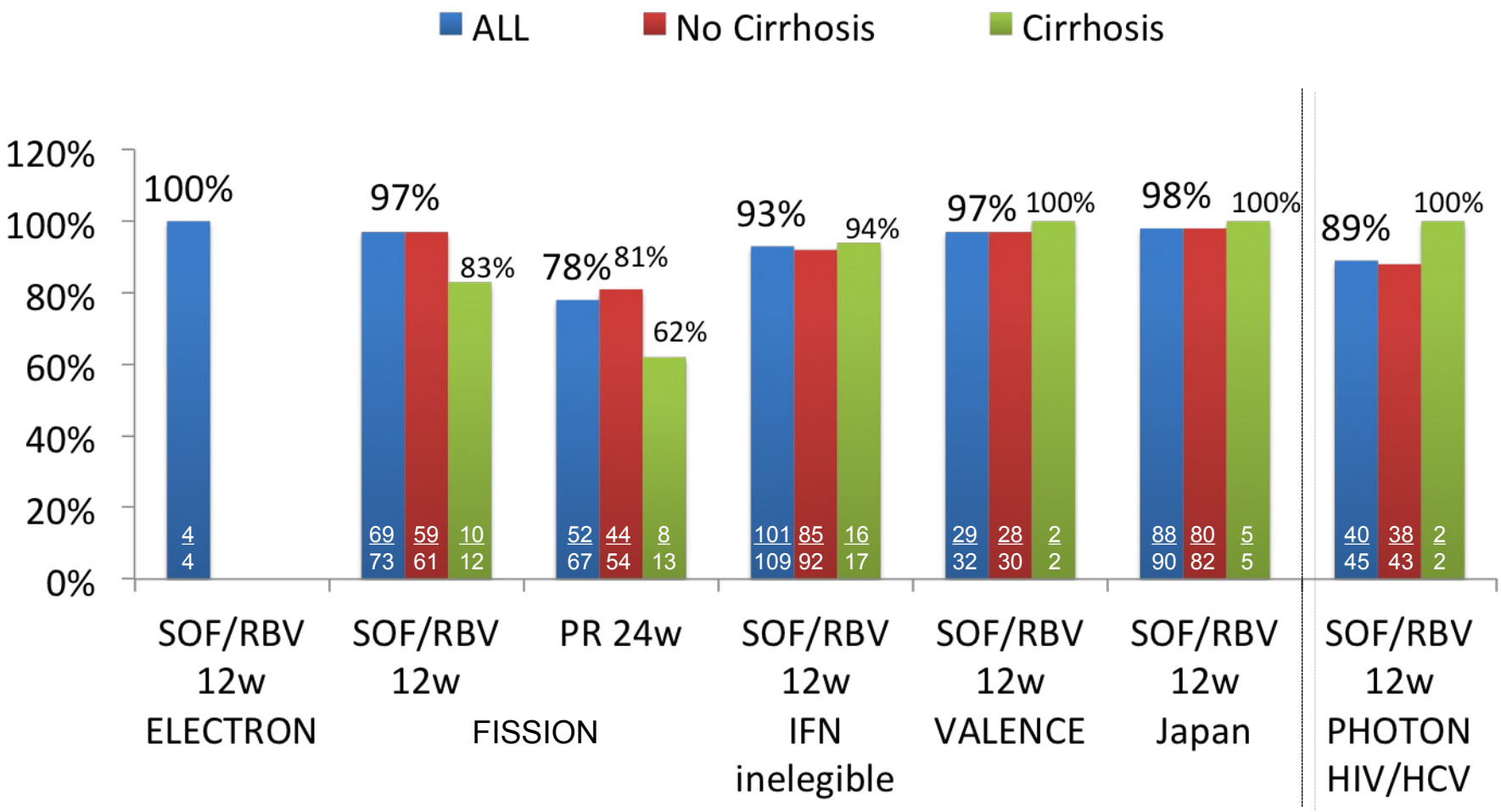
Lawitz E et al. Hepatology 2014

IFN-free DAA regimen for GT-2 patients

DAAs Combinations approved by EMA

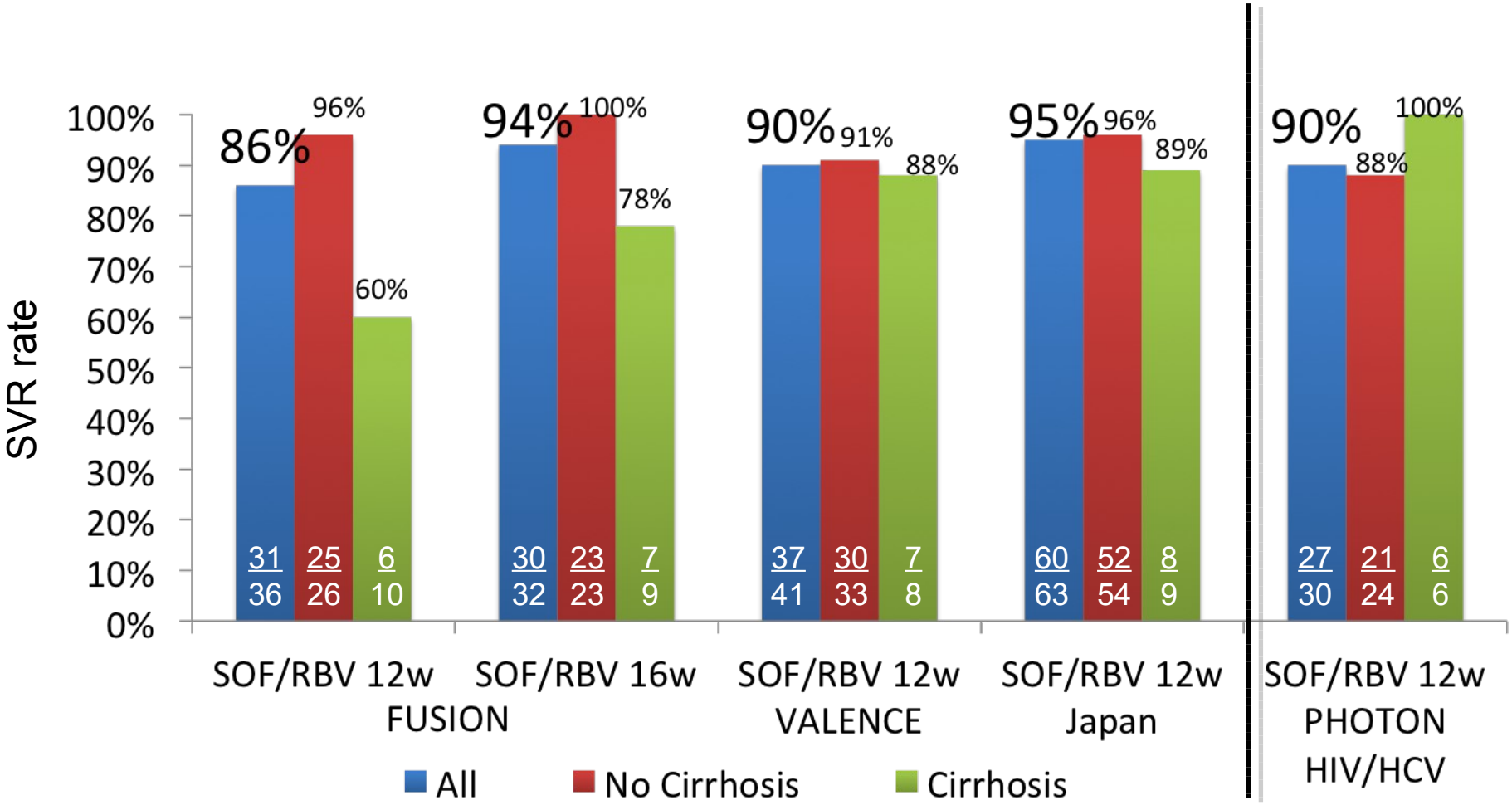


Sofosbuvir + RBV in GT-2 Naïve patients



Gane EJ et al. N Engl J Med 2013; 368:34-44.
Lawitz E et al. N Engl J Med 2013; 368: 1878-87.
Jacobson I et al. N Engl J Med 2013; 368: 1867-77.
Zeuzem S et al. N Engl J Med 2014; 370: 1993-2001.
Omata M et al. J Viral Hep 2014.
Rockstroh J et al. Hepatology 2014 Abst 195.

Sofosbuvir + RBV in GT-2 Treatment-experienced patients



Jacobson I et al. N Engl J Med 2013; 368: 1867-77.
Zeuzem S et al. N Engl J Med 2014; 370: 1993-2001.

Omata M et al. J Viral Hep 2014.
Rockstroh J et al. Hepatology 2014 Abst 195.

Sofosbuvir in «real life »

Target cohort
2 330 patients included
In 53 centers in USA , Canada and Germany

Trio cohort
1 211 patients included
in 231 centers in USA

- Treatment regimen were done according to guidelines

Treatment regimen

Cohort (Nb patients treated)	SOF/Peg/RBV	SOF/RBV	SOF/SMV	SOF/SMV/RBV
Target (2 063)	384	667	784	228
Trio (995)	384	227	320	

→ **Demographics, clinical virological and safety data were collected**

AASLD 2014 – Jensen DM et al., abstr. 45 ; Dieterich D et al., abstr. 46,

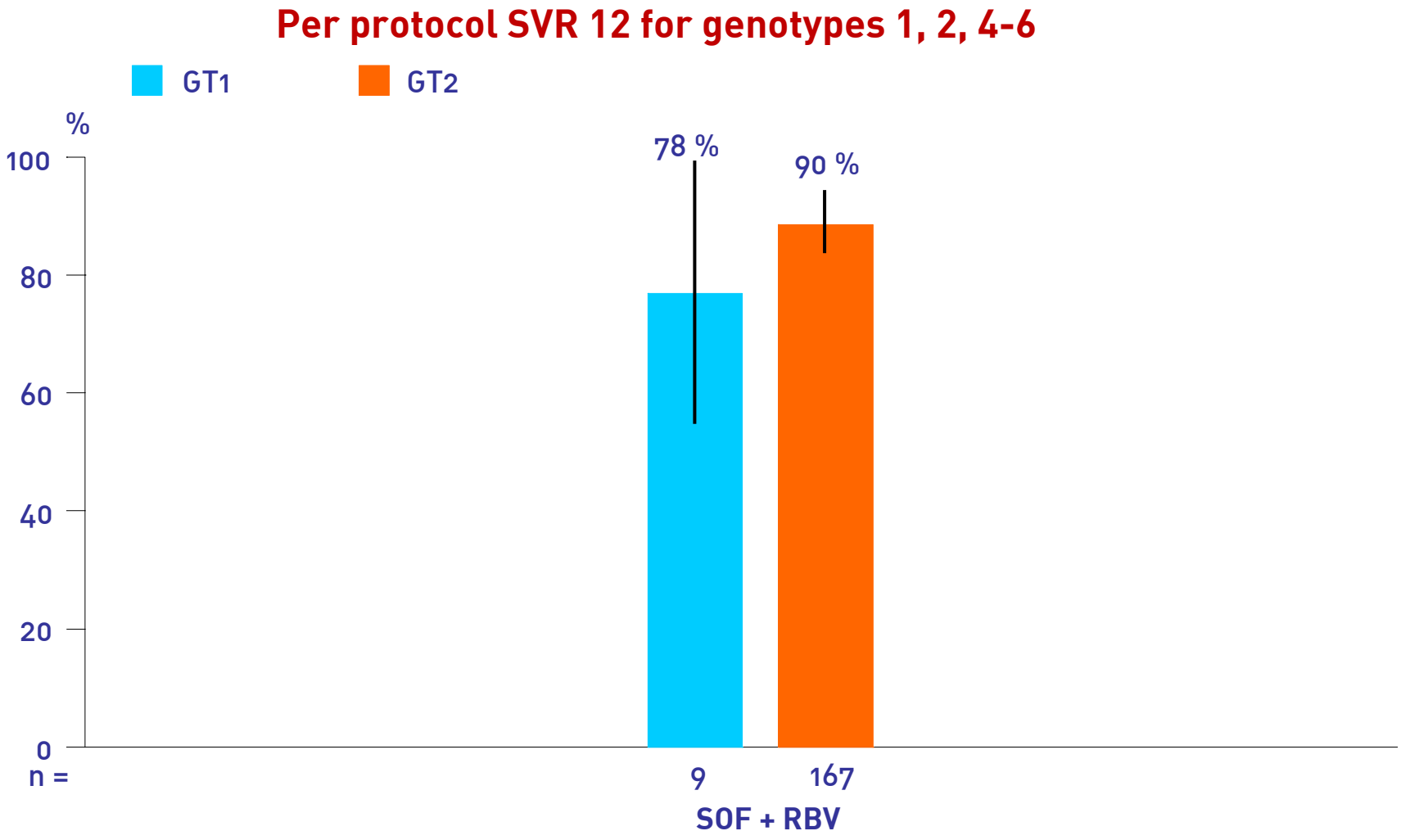
Sofosbuvir in «real life »

Baseline characteristics

	TARGET (n = 2 063)	TRIO (n = 995)
Age mean (range)	57,6 (20-83)	57 (17-86)
Male	1 300 (63,7 %)	565 (59 %)
Teatment failure	1 077 (52,2 %)	407 (43 %)
– PI failure (TVR/BOC)	193 (17,9 %)	82 (20 %)
Cirrhosis	999 (48,4 %)	291 (30 %)
– prior decompensation	375 (43,1 %)	-
Liver transplantation	227 (11 %)	-
HCC	211 (10,2 %)	-
HIV	47 (2,3 %)	-
Genotypes 1a-1b - 1	-	462 (48 %) – 179 (19 %) – 62 (6 %)
Genotype 2	-	212 (22 %)
Genotype 3	-	7 (1 %)

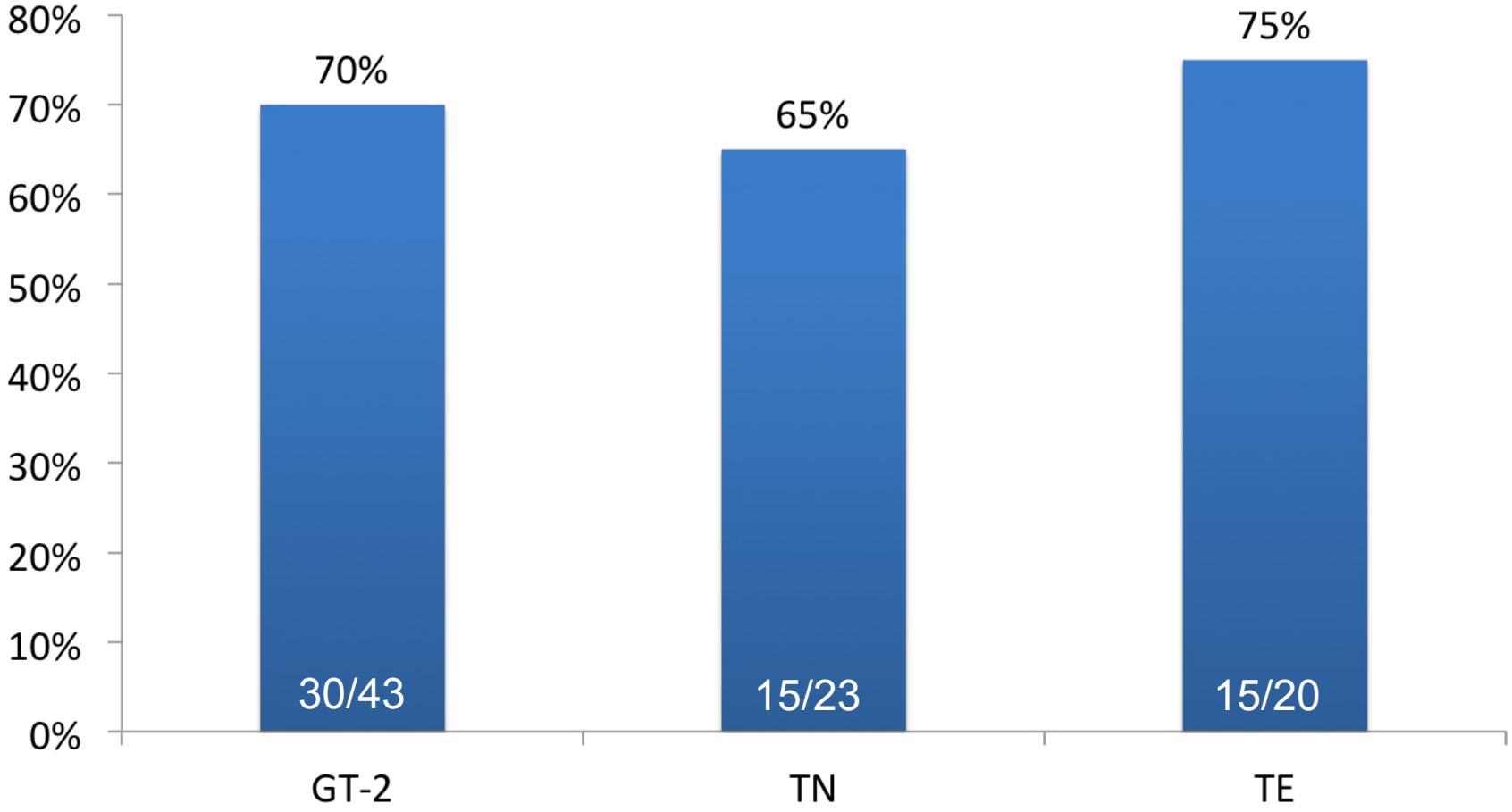
AASLD 2014 – Jensen DM et al., abstr. 45 ; Dieterich D et al., abstr. 46,

TRIO : Real life data from USA : Sofosbuvir + Ribavirin



Dieterich D et al. AASLD 2014, Abs. 46

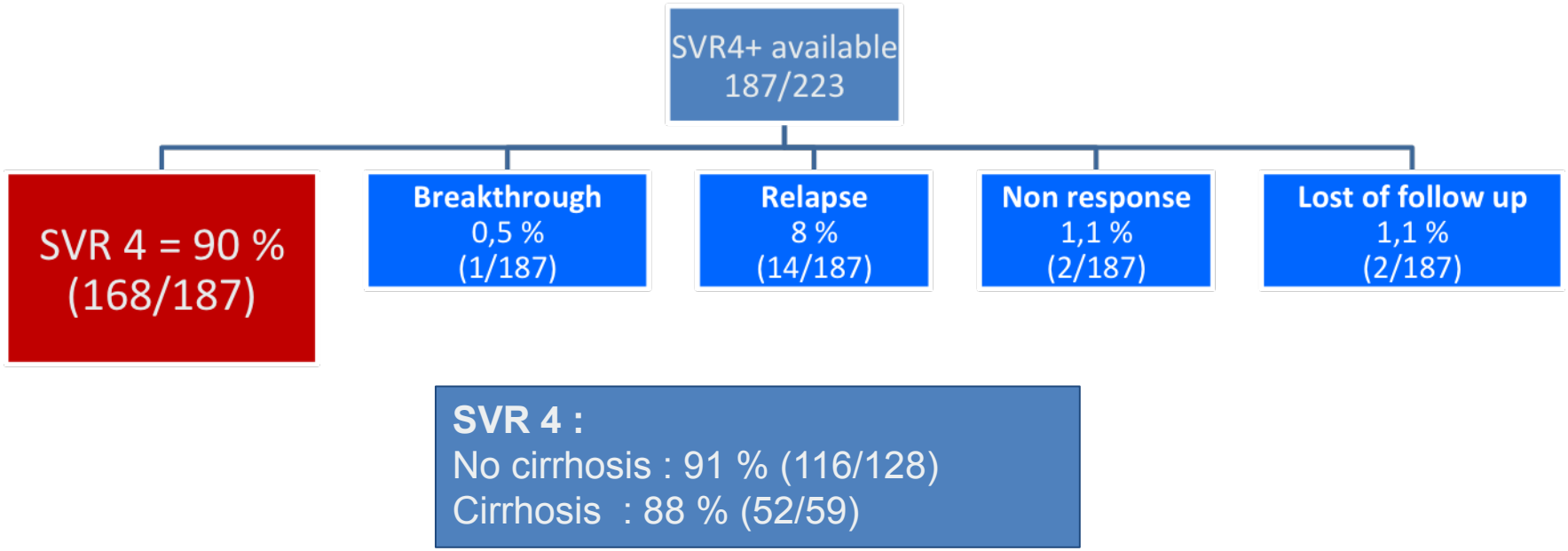
TRIO : Real life data from USA : Sofosbuvir + Ribavirin in GT-2 cirrhotic patients



Flamm et al AASLD 2014: Abst 983

Real Life TARGET cohort

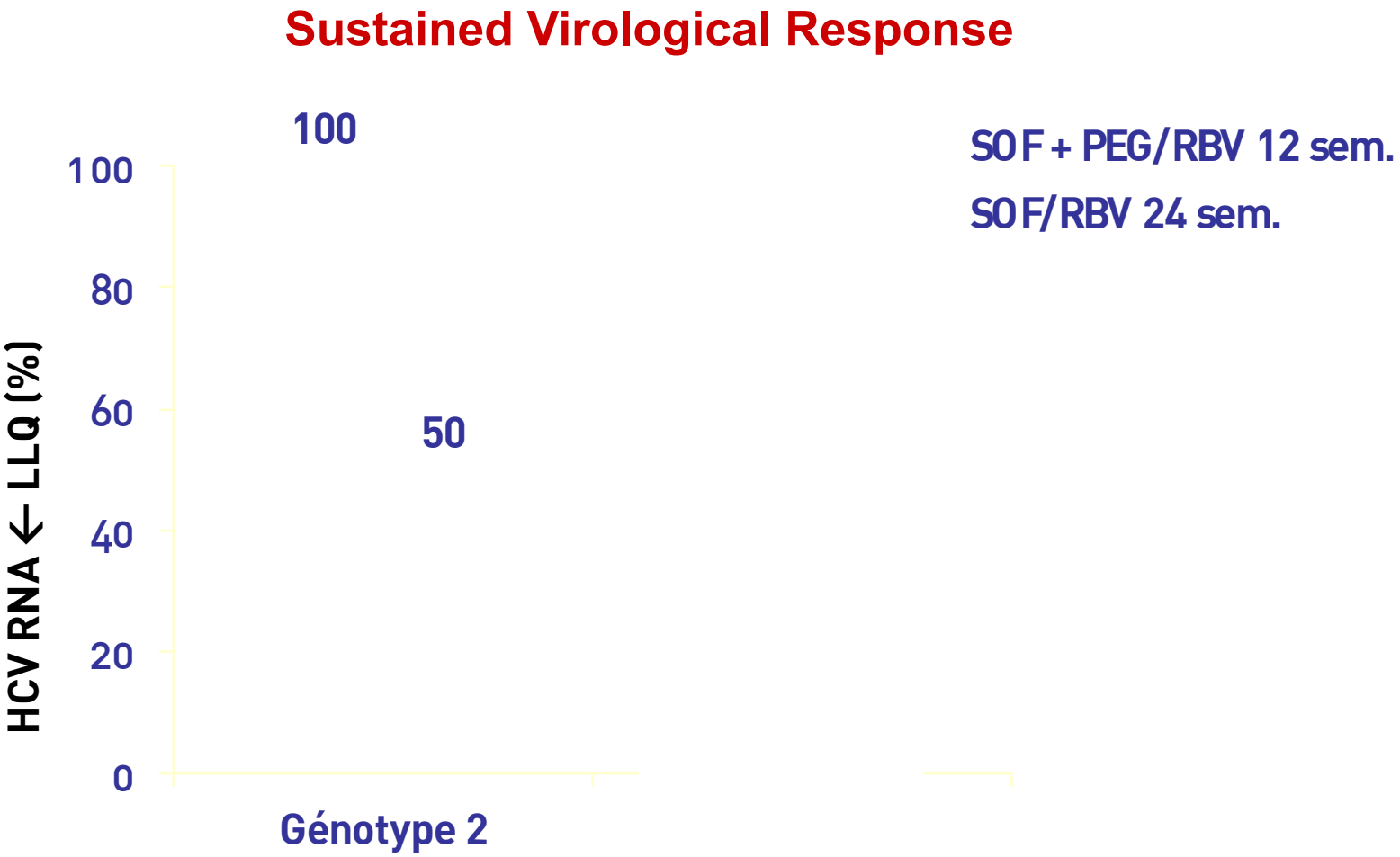
- Genotype 2 :
- SOF + RBV 12 weeks : 235 patients



➔ Real life confirm phase III studies

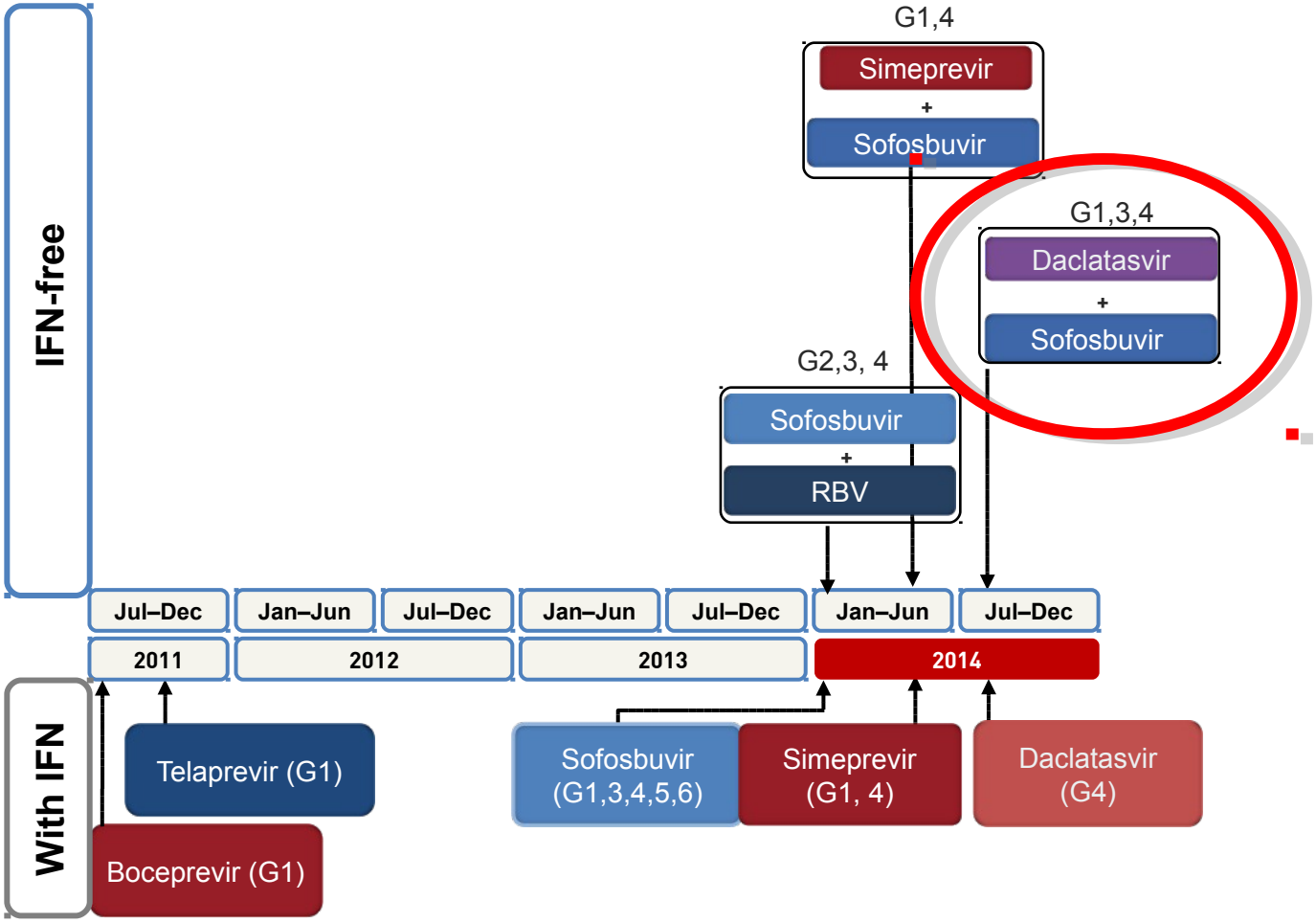
Jensen DM et al. AASLD 2014, Abs. 45

Retreatment of Sofosbuvir-containing regimen failure in genotype 2 patients

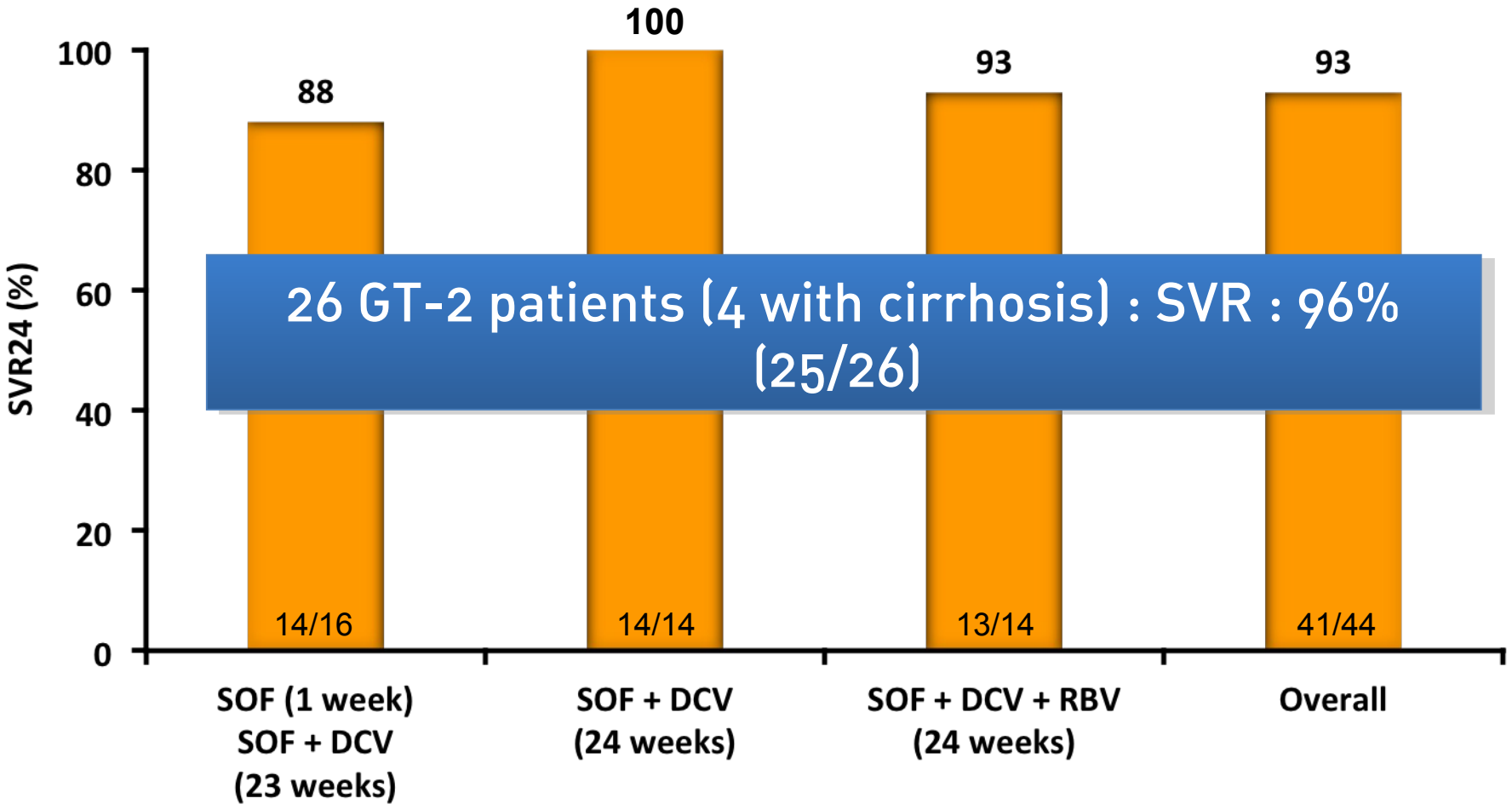


Esteban R, et al. EASL 2014, Abs. 08

DAAs Combinations approved by EMA



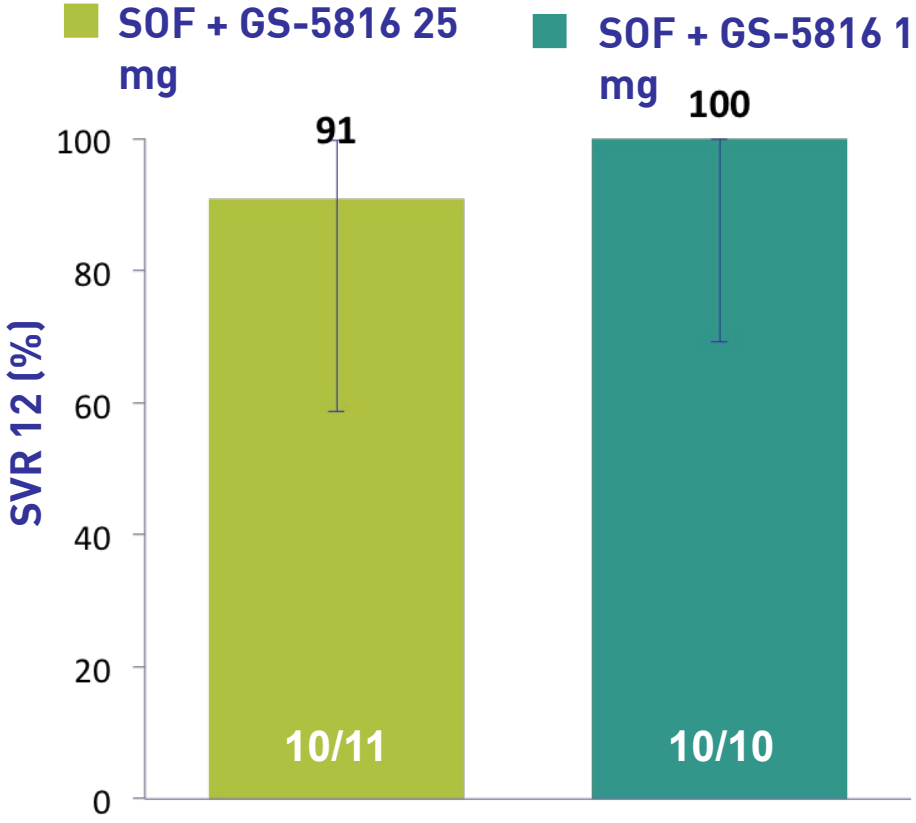
SOF + DCV ± RBV for GT2 and 3 naïve patients



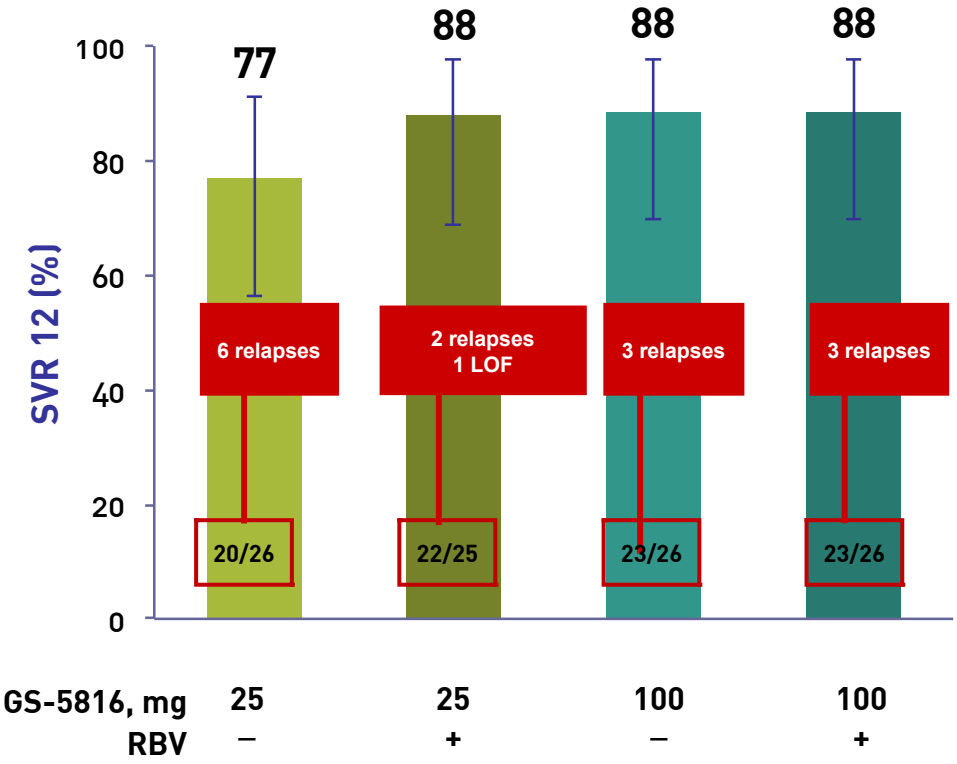
Sulkowski M, et al. New Engl J Med 2014;370:211–21

Sofosbuvir + GS 5816 ± RBV in naïve GT-2 patients without cirrhosis

SVR 12 with 12 weeks treatment duration (no RBV)



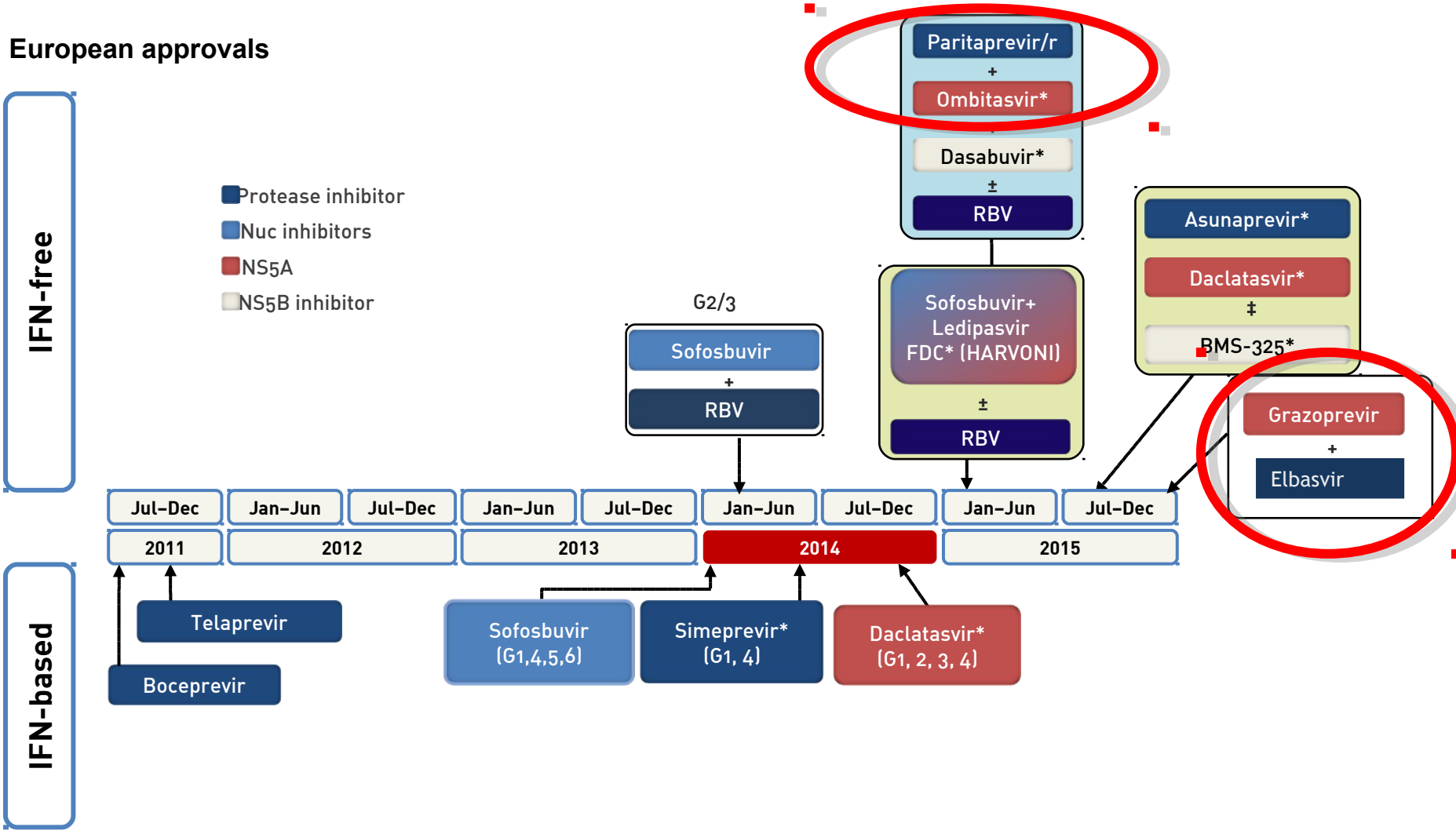
SVR 12 with 8 weeks treatment duration



Tran T et al. AASLD 2014, Abs. 80

Tran T et al. AASLD 2014, Abs. 80

Future from now to 2015, at least within Western countries



Other DAAs combinations for GT-2 patients

- Viekirax (paritaprevir/ritonavir) + Exviera (ombitasvir) ± RBV for 12 weeks :
  - 20 GT-2 naïve non cirrhotic patients
  - ETR : 9/10 with RBV, 8/10 without RBV
  - SVR: 8/10 with RBV, 6/10 without RBV
- Grazoprevir (MK-5172) + Elbasvir (MK-8742) for 12 weeks :
  - Study on-going

Lawitz E et al The Journal of Infection 2014

Current Guidelines for Genotype 2

	AASLD	EASL	Germany	AFEF
Naïve **Recommanded** *alternative*	SOF + RBV 12w 16w for F4 SOF+RBV 48w*	SOF + R BV12w	**SOF + R 12w** *SOF + R 24 w* *PR 12-24w*	**SOF + R 12w** SOF+DCV 24w*
Relapsers **Recommanded** *alternative*	SOF + RBV 12-16w *SOF+PR*	SOF + RBV 12w	SOF + R 12-24w	SOF + R 12w SOF+DCV 12w**
Non Responders	**SOF + RBV** **12-16w** *SOF+PR* SOF+RBV 48w*	SOF + RBV 16 -20w	SOF + R 12-24w	SOF + R 16w SOF +DCV 24w*
Post transplantation	**SOF + RBV 24s**			

* Decompensated cirrhosis
** Sof/RBV failure

Conclusion

- PR can still be an option for GT-2 patients in countries with no access to DAAs
- Sofosbuvir + Ribavirin 12 weeks achieve SVR ↑90%
- It became the SOC for EASL or AASLD guidelines
- TE cirrhotic patients may need other options
- All efforts should be made to reduce the cost of such therapies in order to extend treatment access

Thank you for your attention