Management of CHC G1 patients who are relapsers or non-responders to Peg IFN and RBV therapy: Wait or Triple Therapy?

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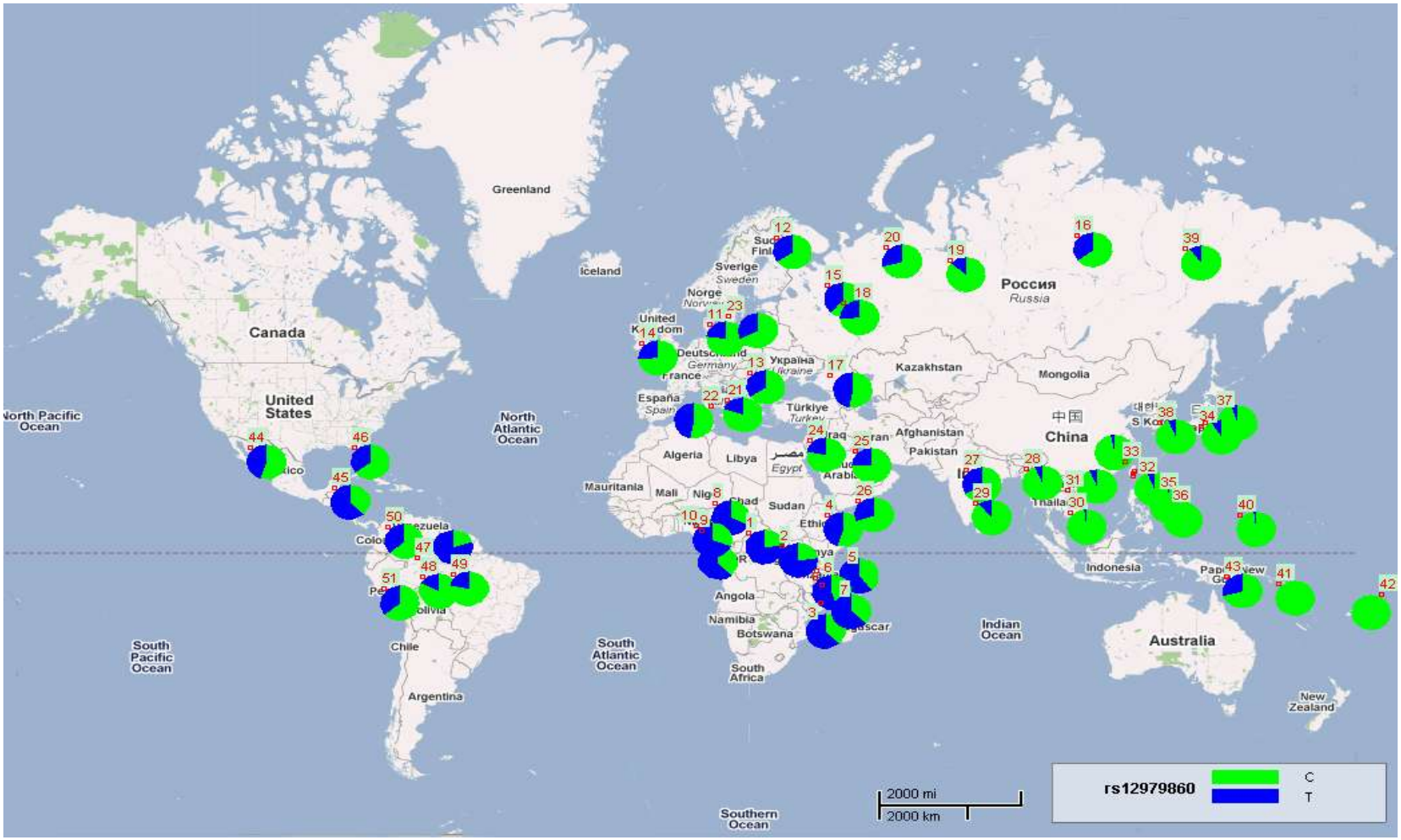
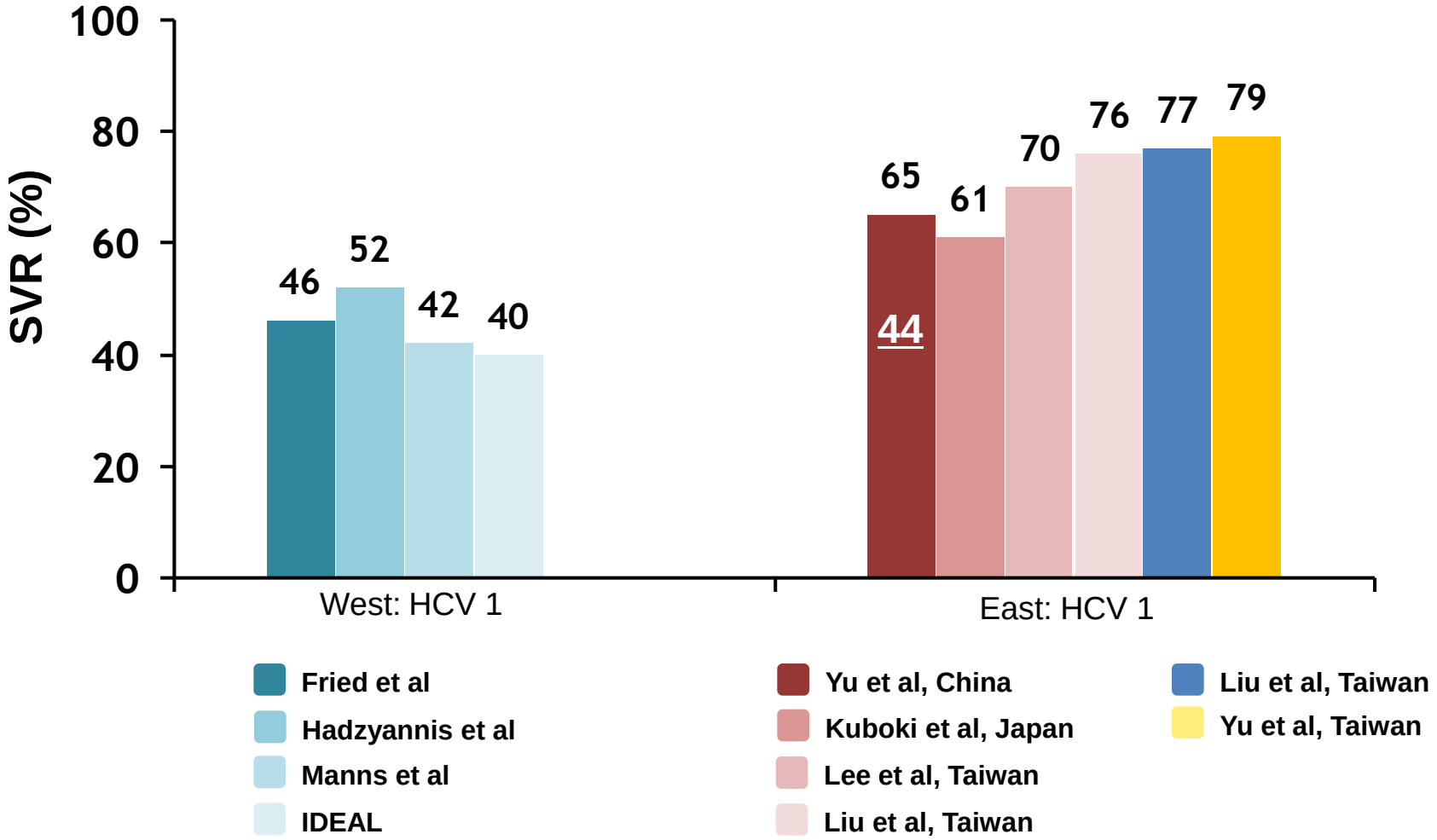
Good SVR rates in Asia are likely due to the high prevalence of the favorable *IL28B* CC genotype



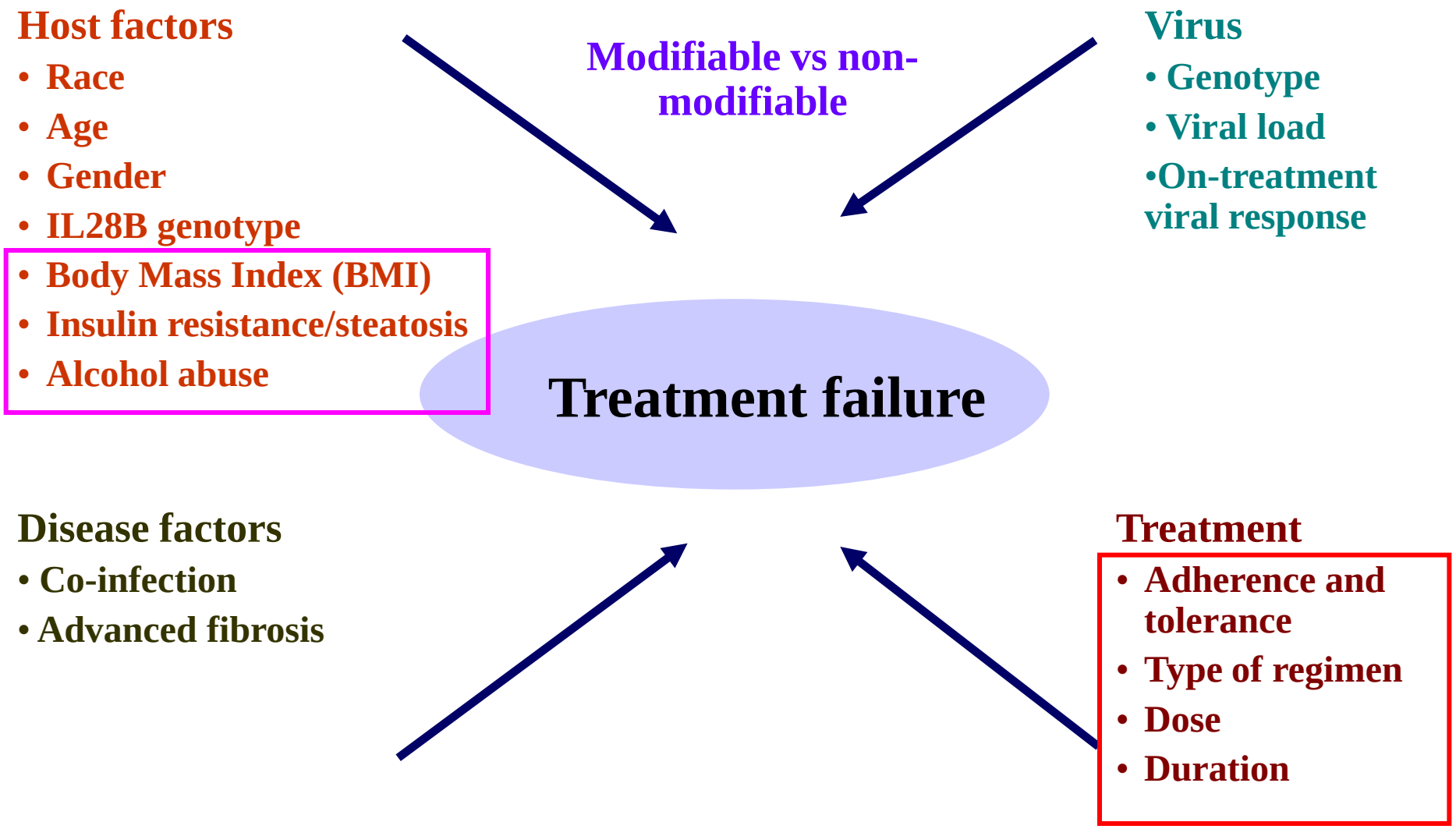
Thomas DL, et al. Nature 2009; 461: 798–801

Sustained Viral Response (SVR) HCV 1 treated with PegIFN/Ribavirin
Caucasian vs Asian



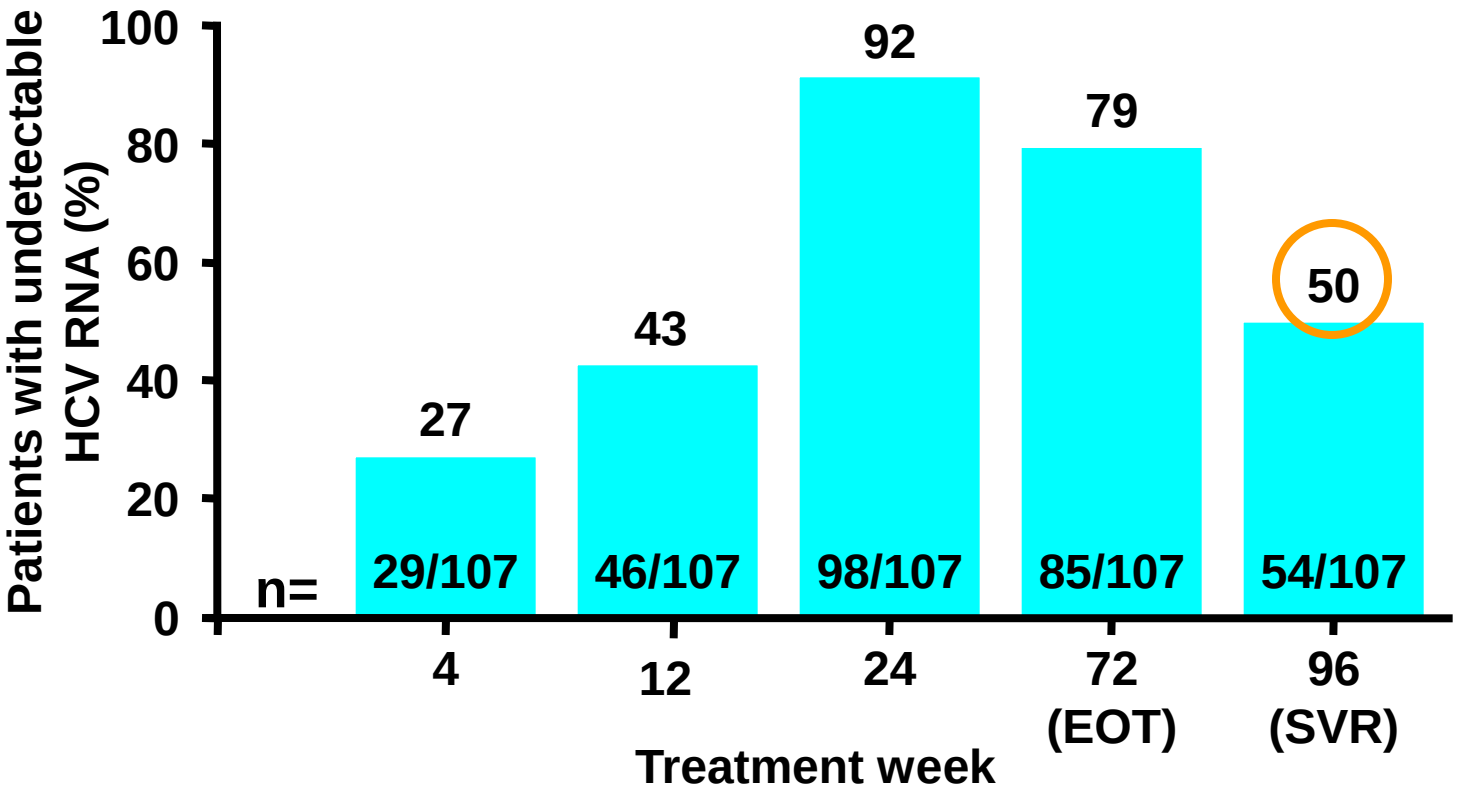
Adapted from Yu ML, Chuang WL. J Gastroenterol Hepatol 2009;24:336-45

Predictors of treatment response



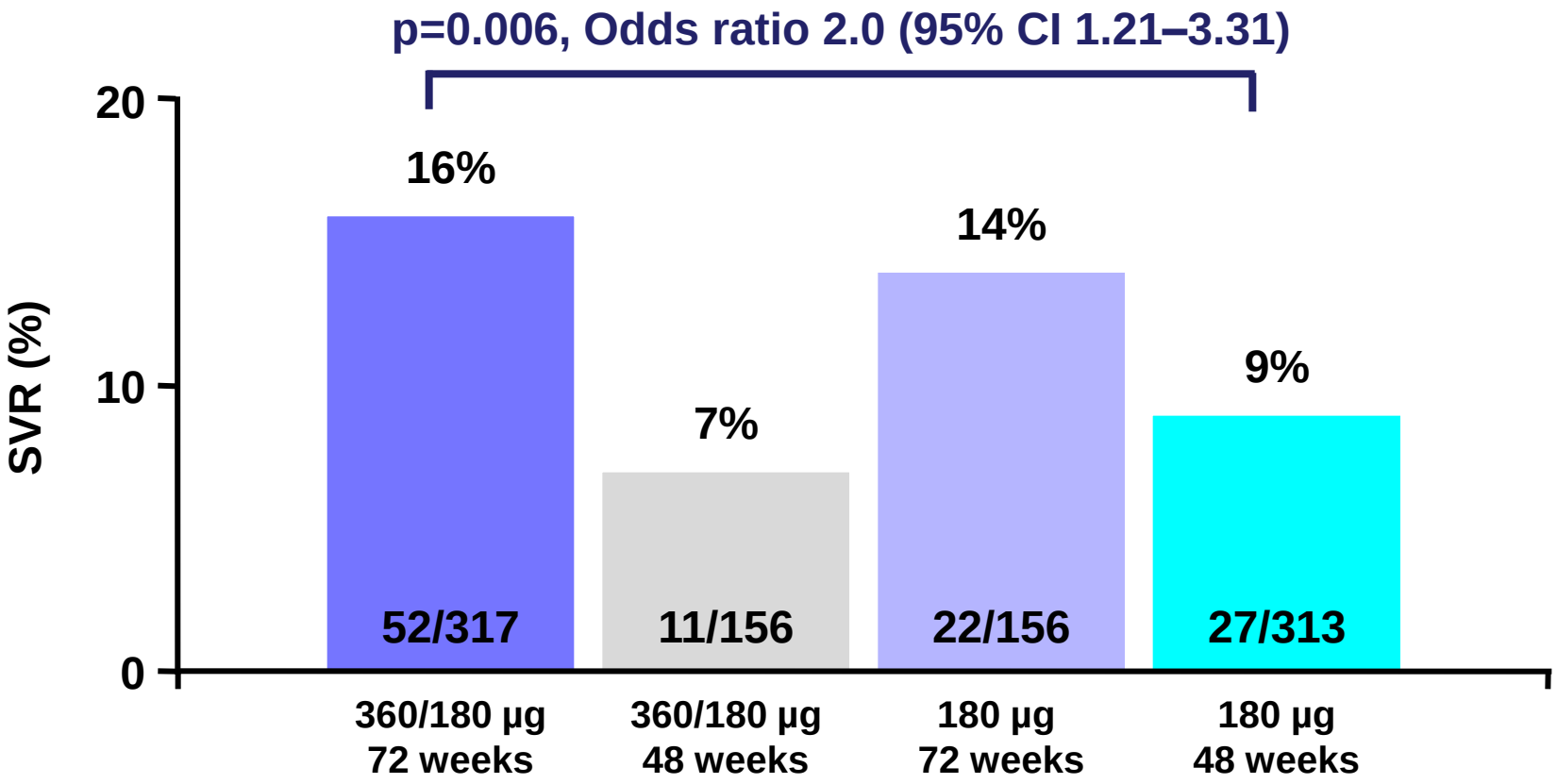
Adapted from Pol & Bourliere, Antiviral Therapy 11:955-970

SVR rate of 50% achieved in relapsers re-treated for 72 weeks with PegIFN alfa-2a/RBV



Kaiser S, et al. Hepatology 2008; 48 (4, Suppl); 1140A

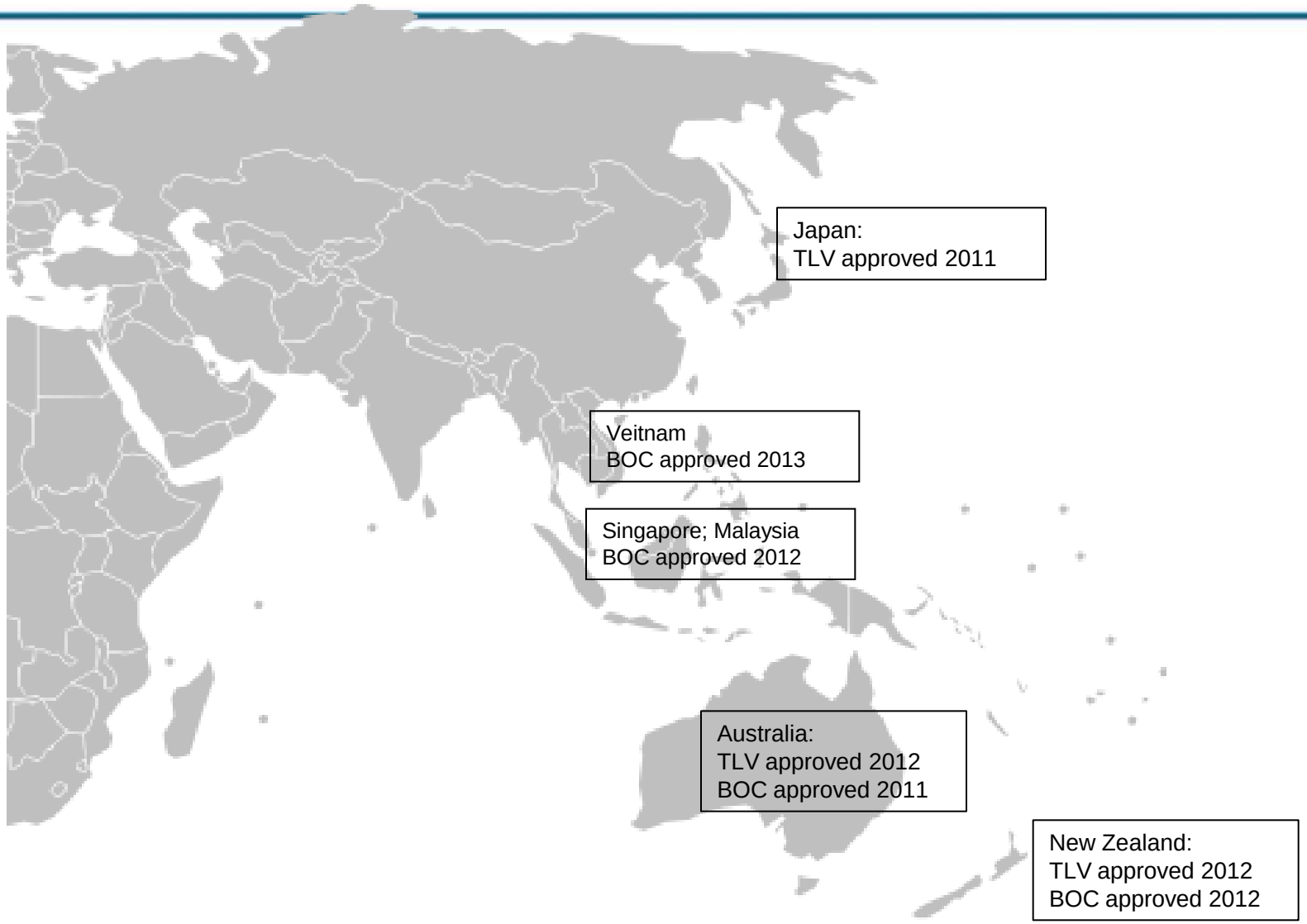
REPEAT: PegIFN/Ribaviin re-treatment in HCV genotype 1 non-responders



Assessed by Cochran-Mantel-Haenszel test stratified by region, HCV genotype and histological stage
Non-responder patients previously treated with pegylated interferon alfa-2b plus ribavirin

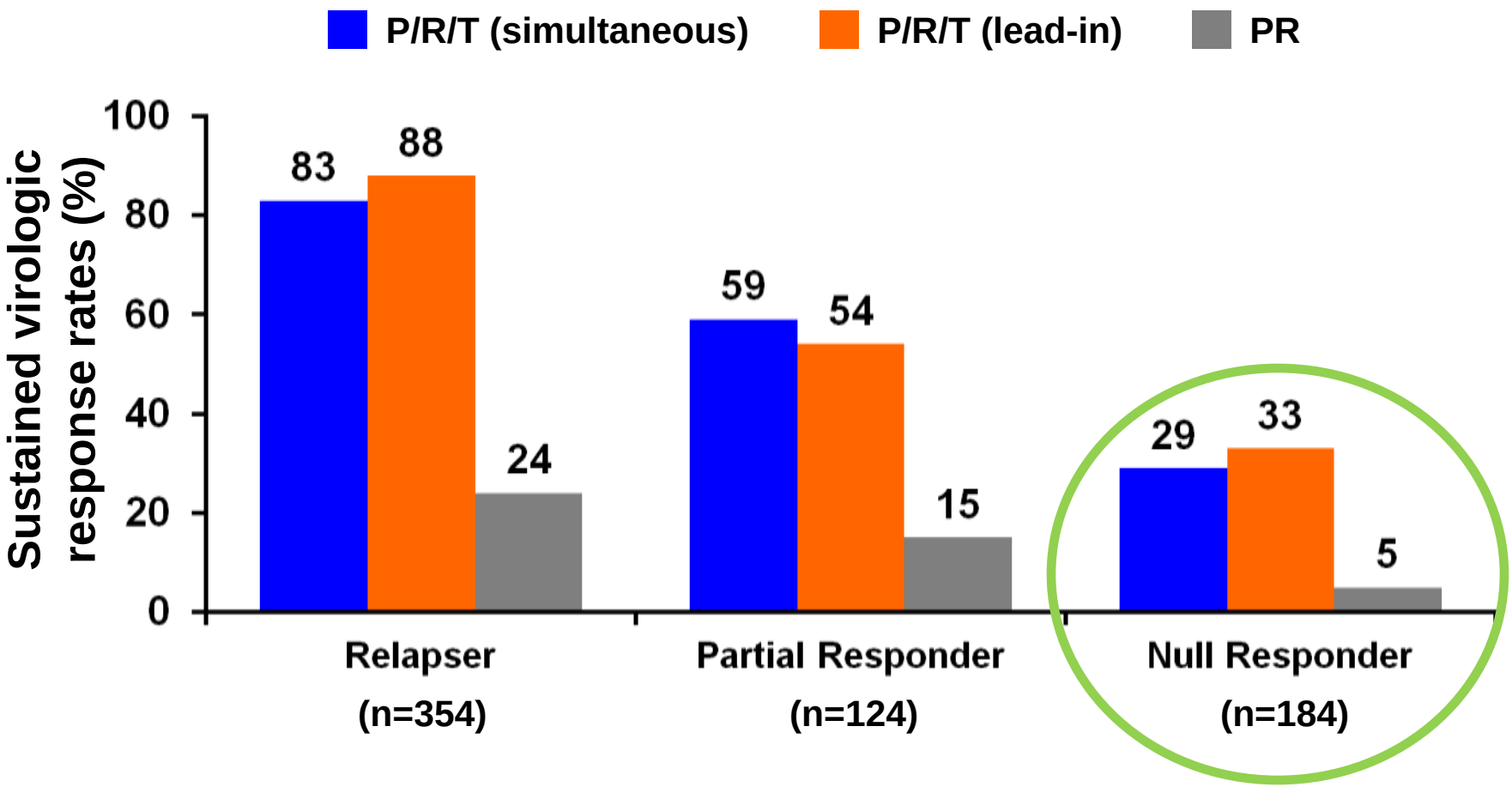
Jensen D, et al. 58th AASLD 2007; Abstract LB4

Regional approval status for BOC and TLV



BOC = boceprevir; TLV = telaprevir

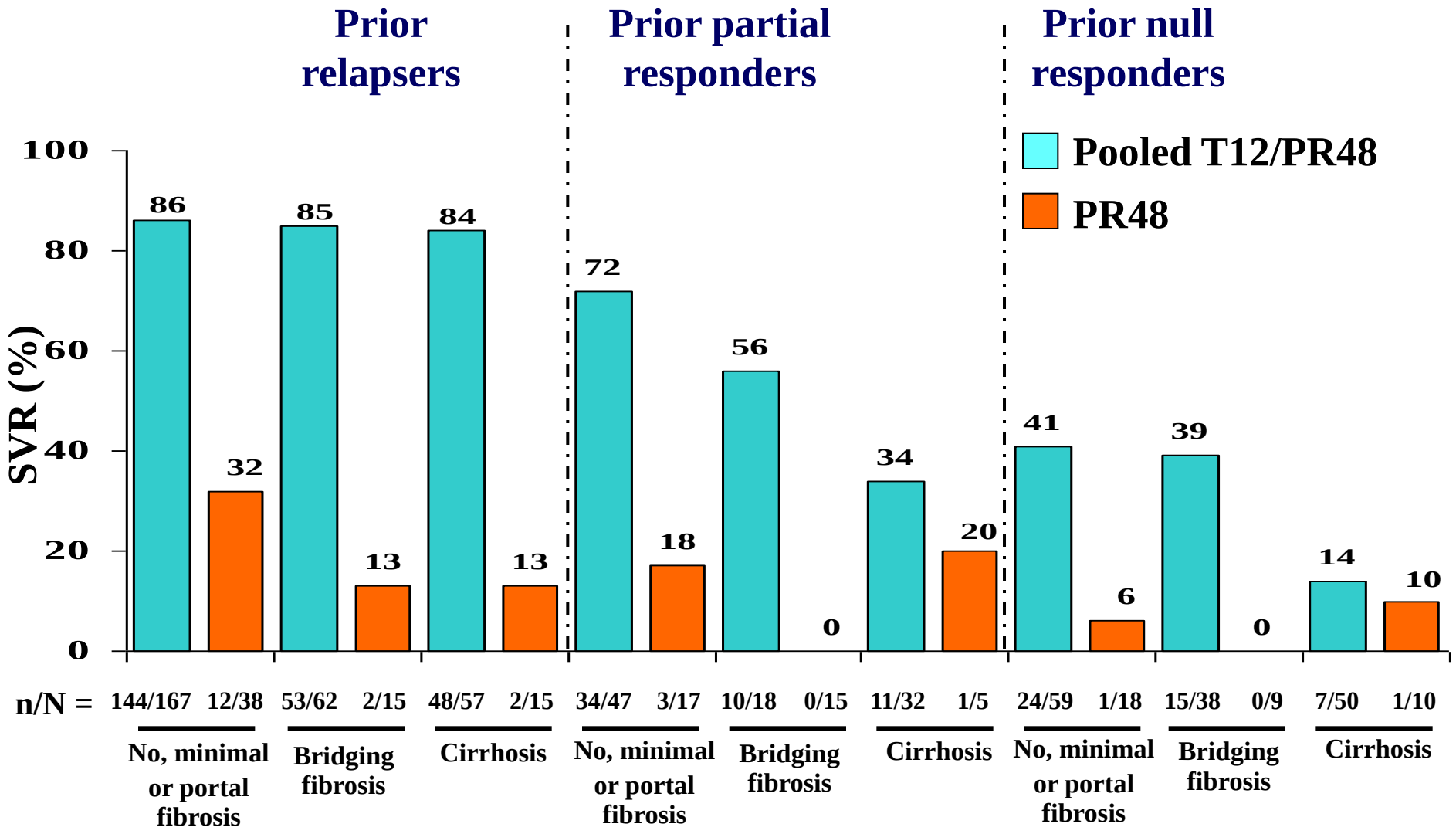
REALIZE: Phase 3 Trial in Tx-Experienced HCV-1 Infected Patients



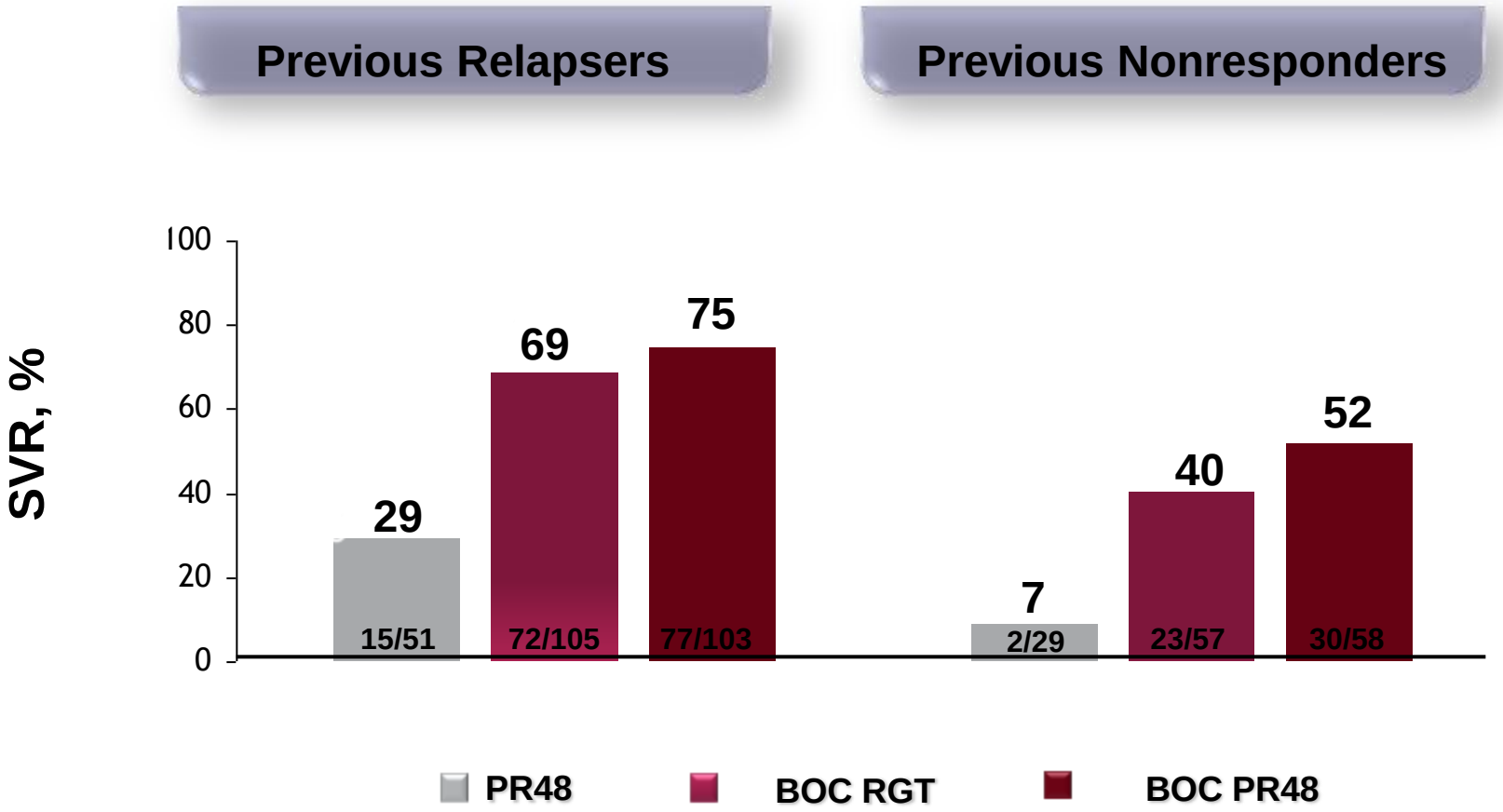
Peginterferon alfa 180 µg qw
Ribavirin 1000-1200 mg/day
Telaprevir750 mg q8h

Zeuzem et al., NEJM 2011

REALIZE: SVR by Baseline Fibrosis Stage and Prior Response



BOC/PR Triple Therapy Significantly Increased SVR Rates vs PR Alone in Previous Treatment Failures

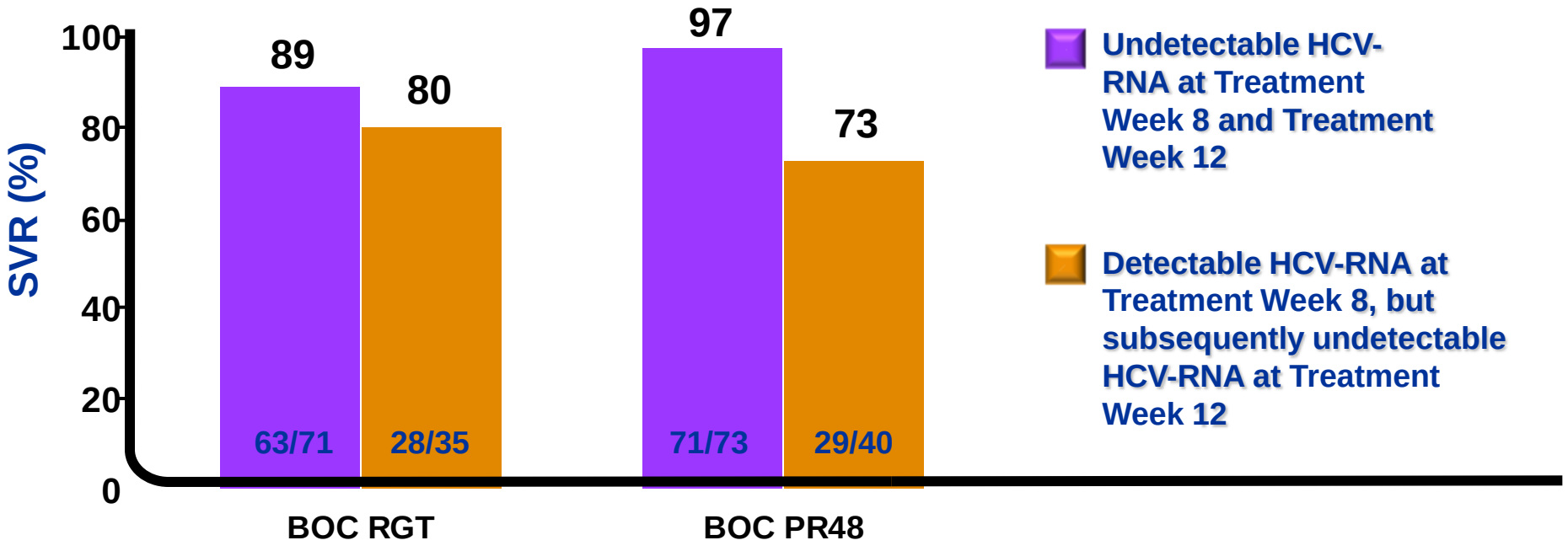


PR = peginterferon alfa and ribavirin; RGT = response-guided therapy; SVR = sustained virologic response.

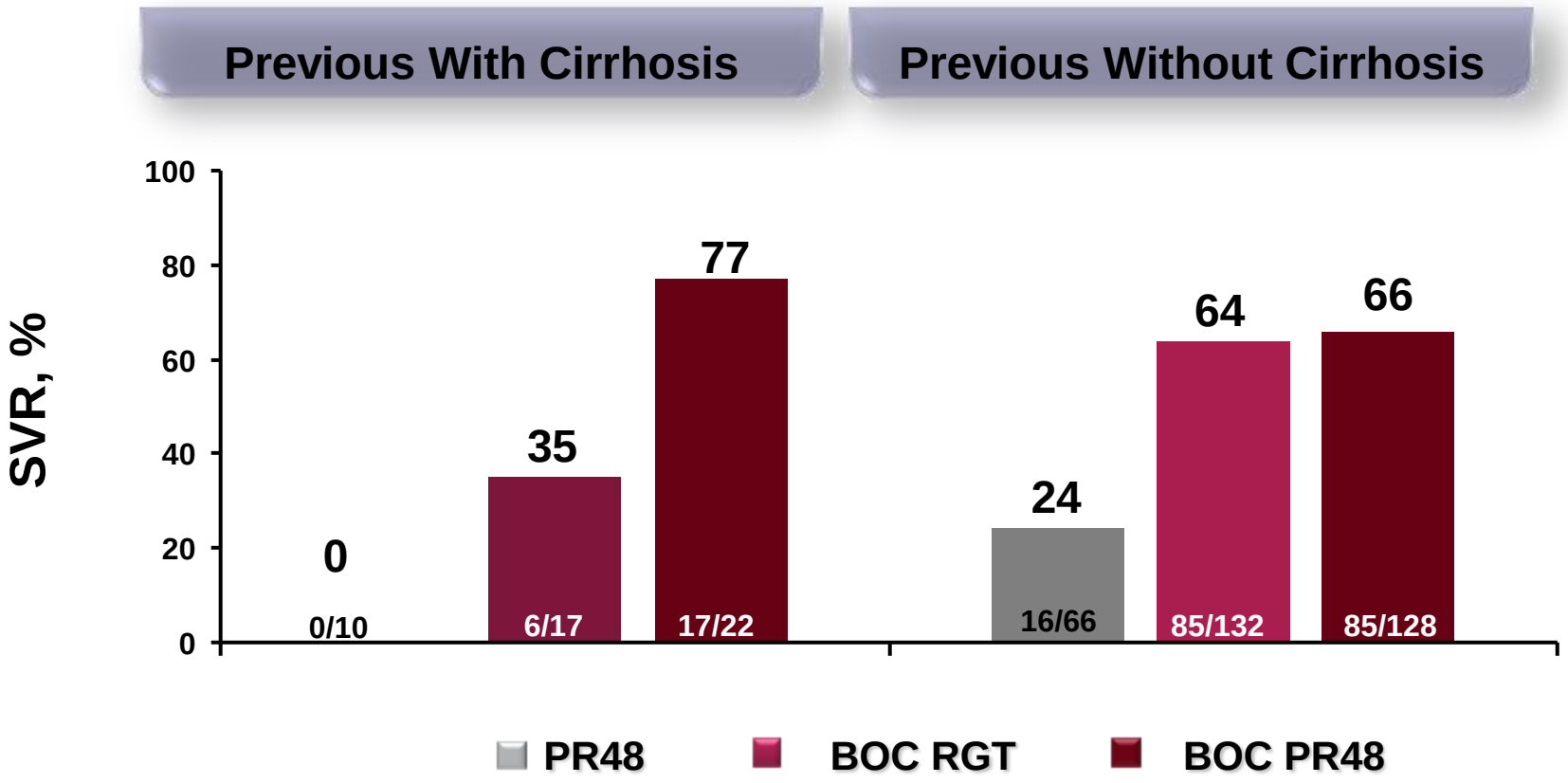
Bacon BR et al. N Engl J Med. 2011;364:1207–1217.

Subjects who failed previous therapy: Boceprevir plus PR achieved > 89% SVR rates in subjects with undetectable viral load at treatment week 8 and treatment week 12

- 44% (71/162) of subjects in the BOC RGT group and 45% (73/161) of subjects in the BOC PR48 group were early responders, with undetectable HCV-RNA at Treatment Week 8 (early responders) and Treatment Week 12
- 22% (35/162) of subjects in the BOC RGT group and 25% (40/161) of subjects in the BOC PR48 group were late responders, with detectable HCV-RNA at Treatment Week 8 but subsequently undetectable at Treatment Week 12

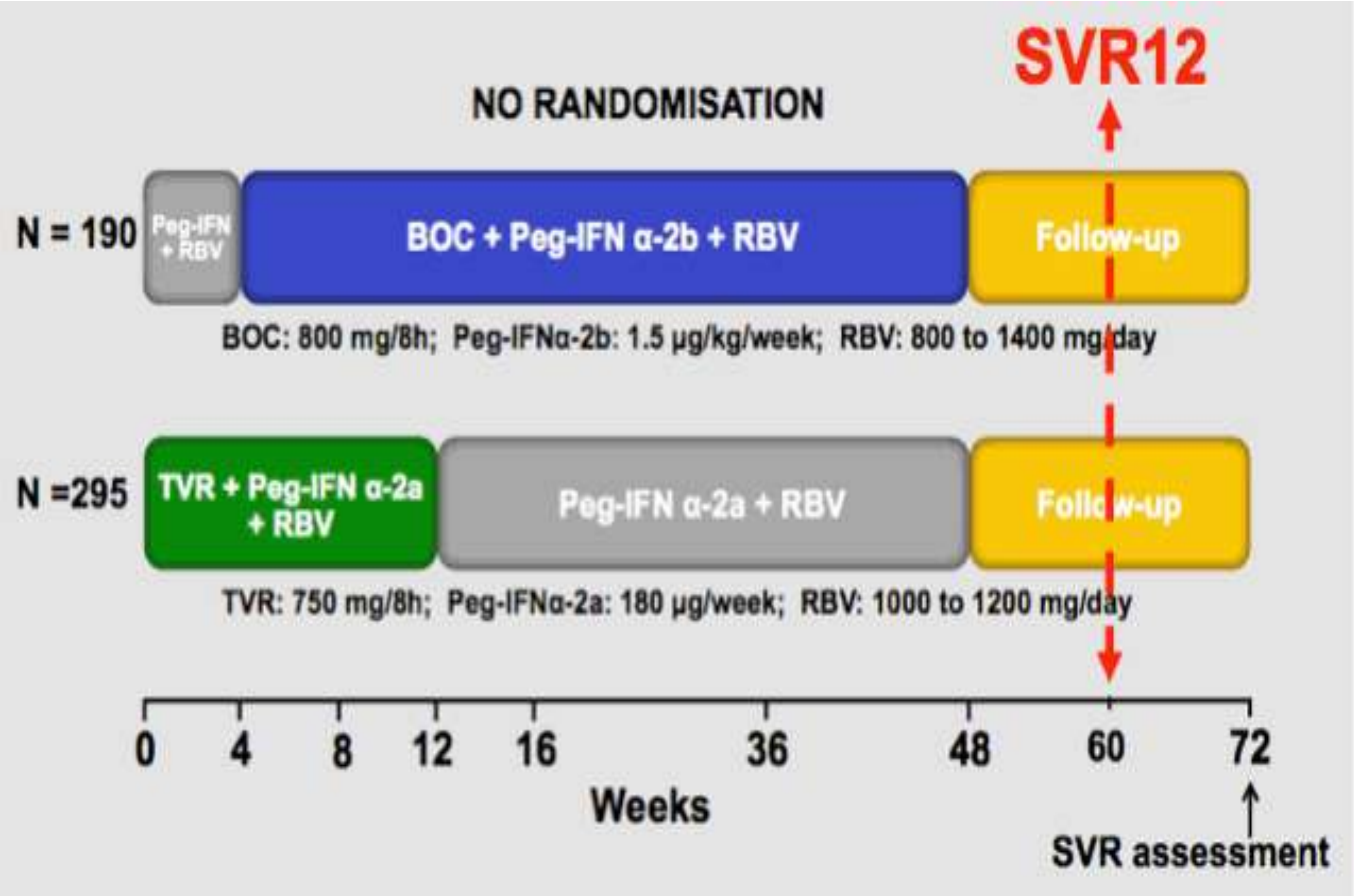


Longer duration of combination therapy with Boceprevir was associated with higher SVR in previous treatment failures with cirrhosis



Bacon BR et al. N Engl J Med. 2011;364:1207–1217.

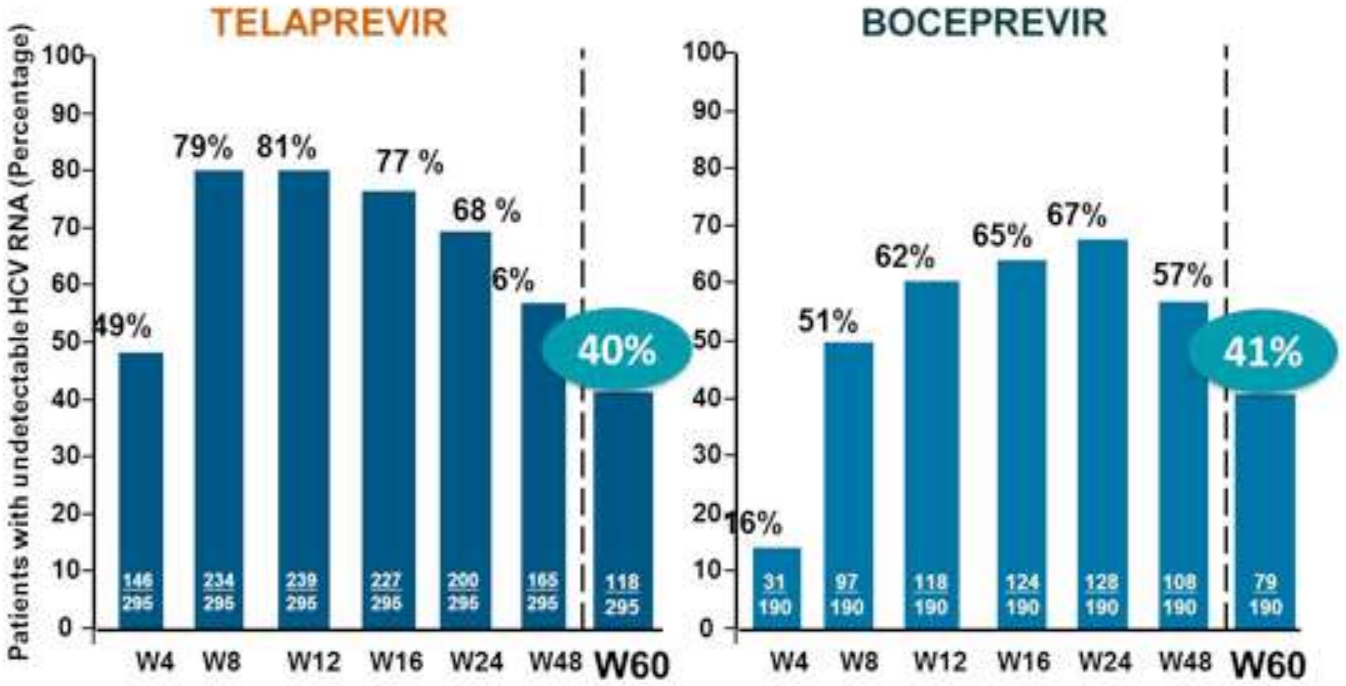
CUPIC: Treatment regimen



Fontaine H. etal. EASL 2013.

Virological response in the CUPIC trial (ITT)

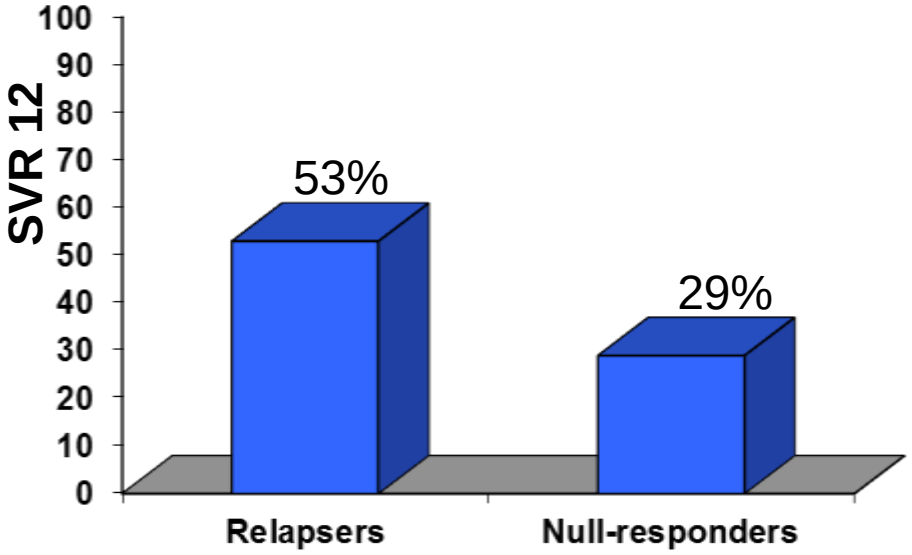
French early access program for cirrhotic previous PR non-responders



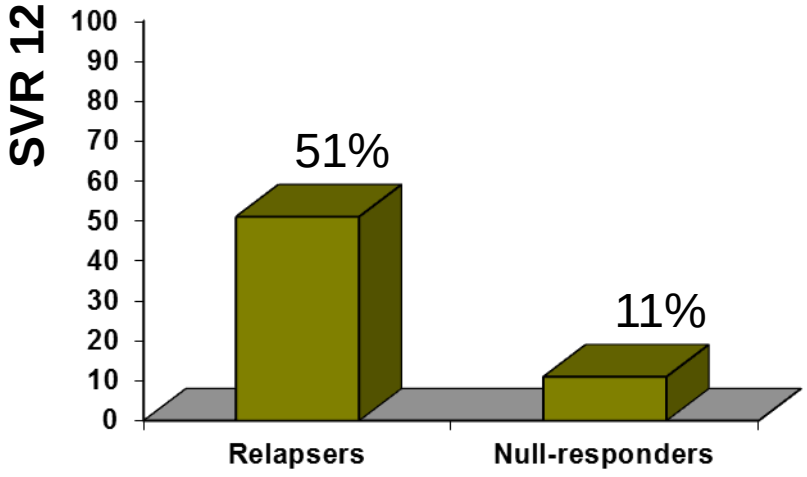
Fontainse H. etal. EASL 2013

Virological response in the CUPIC trial (ITT)

TELAPREVIR



BOCEPREVIR



Fontainse H. etal. EASL 2013

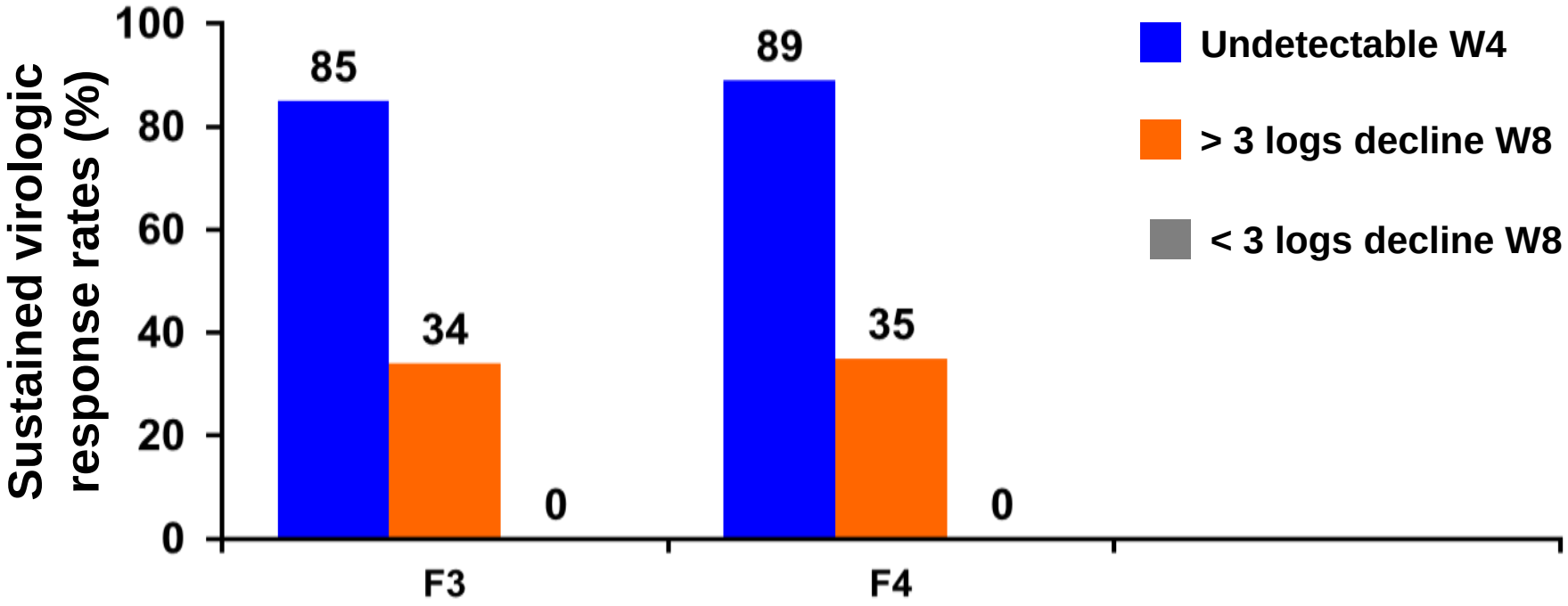
Safety findings in CUPIC up to week 60

Patients, n (% patients with at least one event)	Telaprevir n=295	Boceprevir n=190
Serious adverse events (SAEs)*	535 in 160 patients (54.2%)	321 in 97 patients (51.0%)
Premature discontinuation / due to SAEs	139 (47.1%) / 63 (21.3%)	80 (42.1%)/ 27 (14.2%)
Death	7 (2.4 %)	3 (1.6%)
Infection (Grade 3/4)	27 (9.1 %)	8 (4.2%)
Hepatic decompensation (Grade ¾)	15 (5.1 %)	9 (4.7%)
Anemia (Grade ¾ : Hb < 8 g/dL)	38 (12.9 %)	19 (10%)
Rash (grade 3/SCAR)	16 (5.4 %)/ 2 (0.6 %)	2 (1.0%)/
EPO use / blood transfusion	168 (57 %) / 53 (18 %)	119 (62.6%) / 26 (13.7%)
GCSF use	8 (2.7 %)	13 (6.8%)
TPO use	6 (2 %)	3 (1.6%)

Risk of death or severe complication increased in patients with Platelete < 100,000 /mm3 and Albumin < 35 g/L

Fontaine H. etal. EASL 2013

CUPIC : SVR according to on-treatment virological response



Fontainse H. etal. EASL 2013

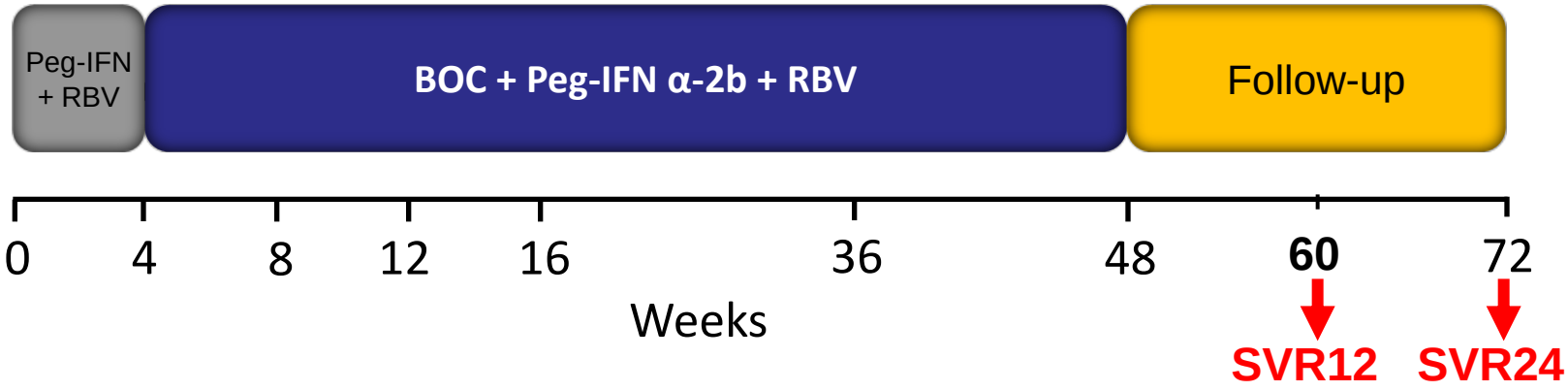
Protocol for BNPP study – global study

Eligibility

- Age>18y
- Previous treatment failure
- Compensated advanced fibrosis or cirrhosis
- Genotype 1
- No contraindications for Peginterferon/ribavirin
- Able to give consent

Exclusions

- Previous boceprevir or PI therapy
- Decompensated liver disease
- Organ transplant
- Co-infection: HIV, HBV
- Prohibited medications
- Substance abuse
- Severe medical illness

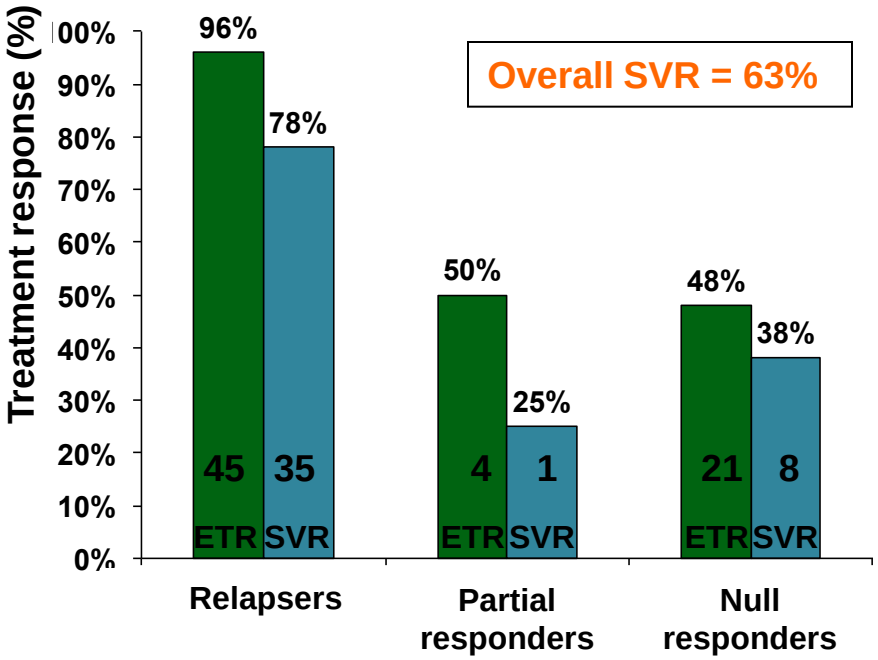


Treatment response according to type of prior treatment failure

BNPP Asian Cohort, n=70/79 (completed FU)

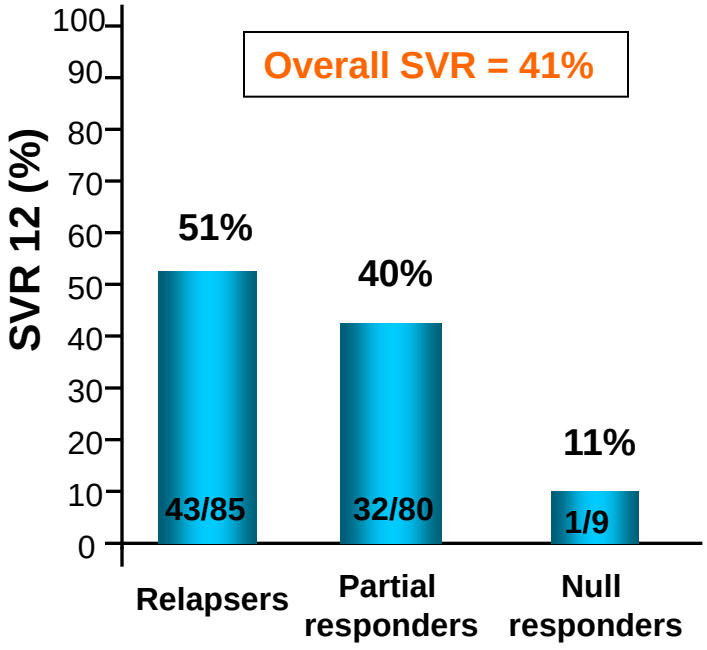
Thailand, Singapore, Malaysia

(provisional data)



Piratvisuth, APASL Liver Week 2013 (updated)

BNPP CUPIC,n= 190 (boceprevir)



Fontaine H. etal. EASL 2013

Serious Adverse Events

Type	n/N	BNPP Asia	CUPIC
All SAEs	16/79	16.5%	51%
Death	0	0	1.6%
Sepsis	3/79	3.8%	4.2%
Decompensation	2/79	2.5%	4.7%
Blood transfusions	11/79	13.9%	13.7%

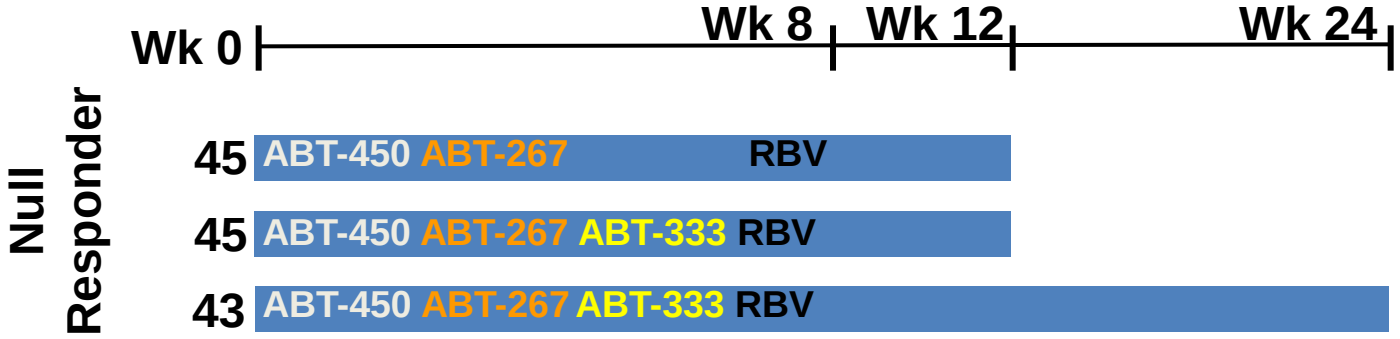
Piratvisuth, APASL Liver Week 2013

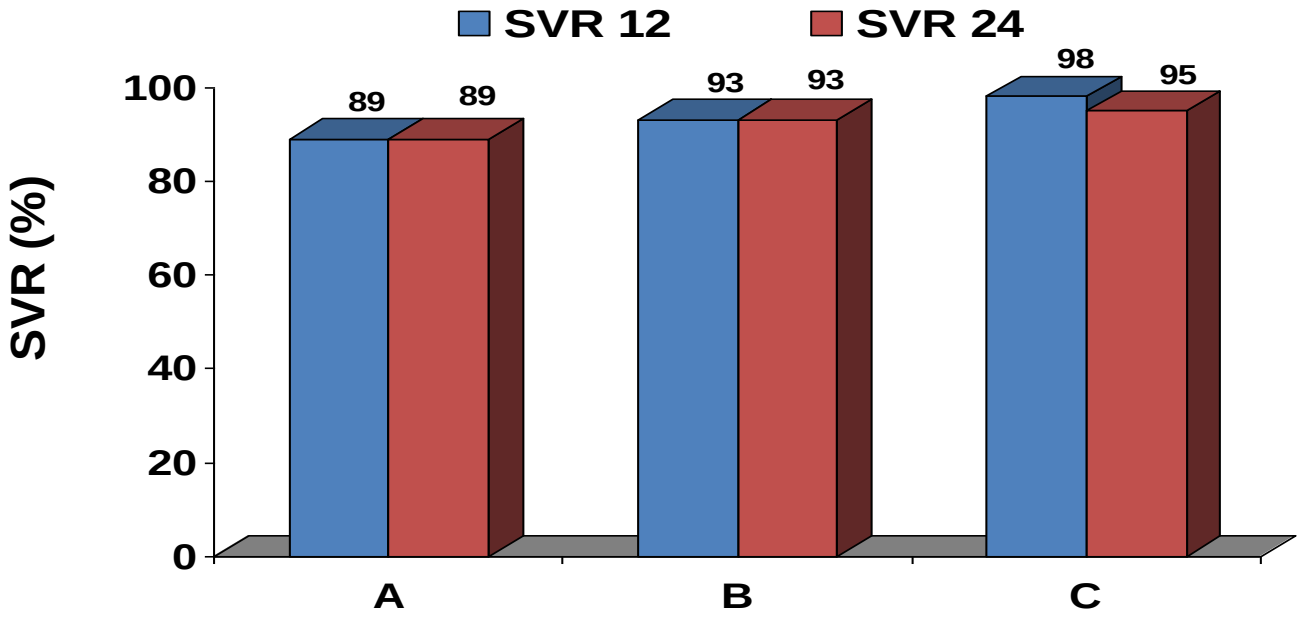
Fontaine, EASL 2013

SAE (16/79 = 20.3%)

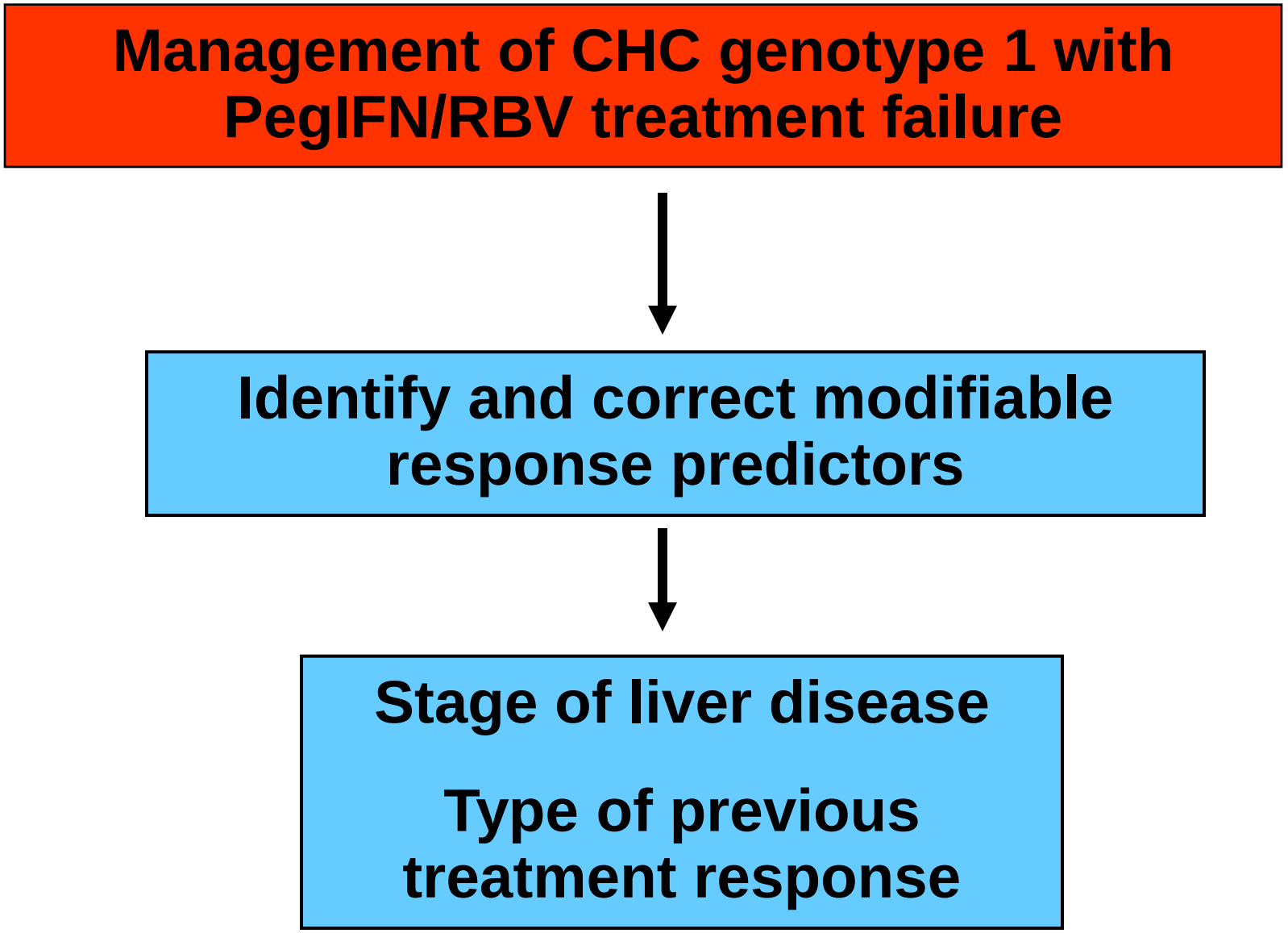
Hospitalization	Sepsis	Blood transfusion	Decompensation	Severe abd pain	Number of patients
yes	yes				1
yes	yes	yes			1
yes	yes	yes	yes		1
yes		yes			1
yes		yes	yes		1
yes			yes		1
yes					2
yes		yes			1
		yes			6
				yes	1

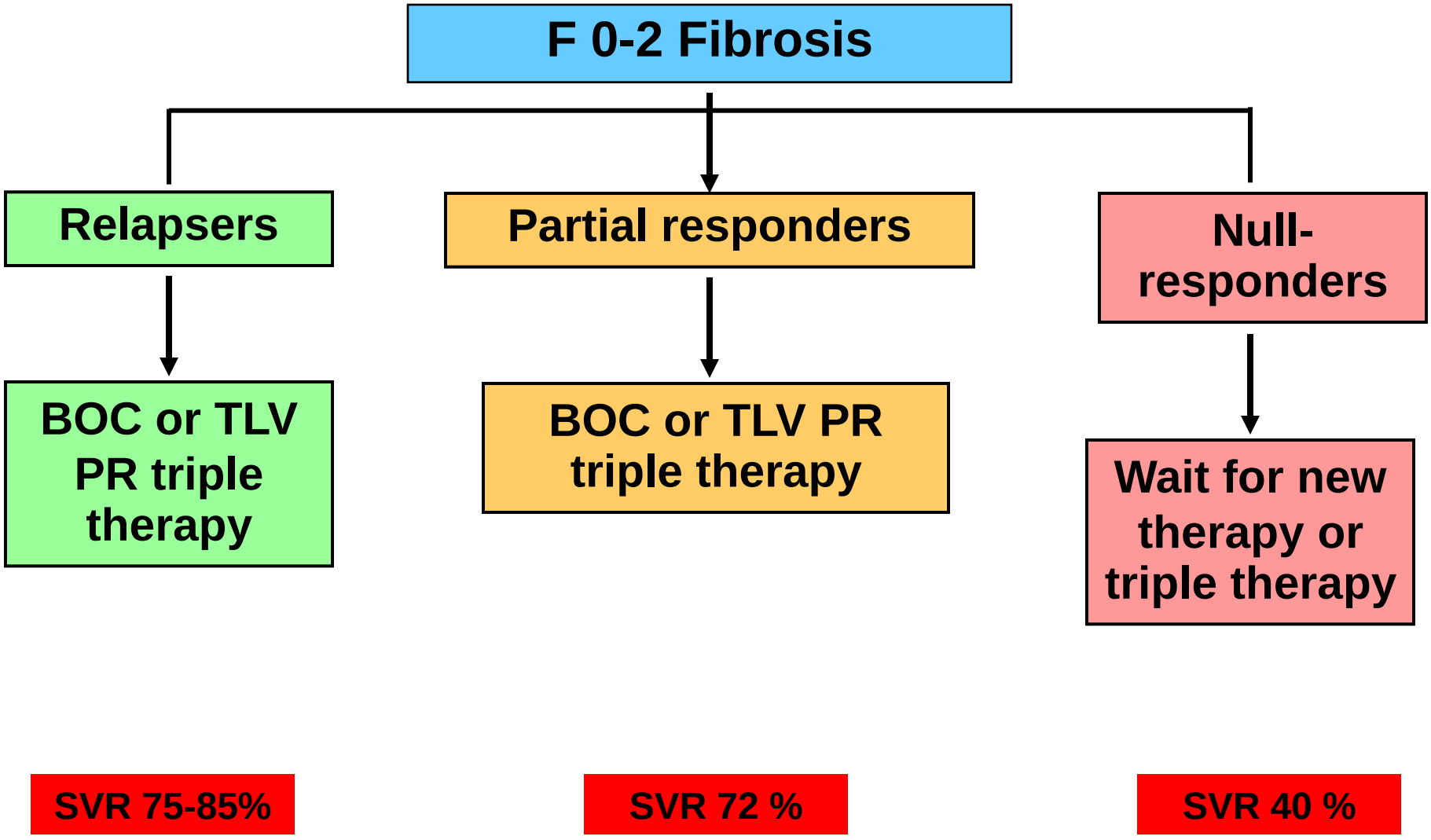
AVIATOR Study: ABT-450/r, ABT-267, ABT-333 +/- RBV in Null Responders

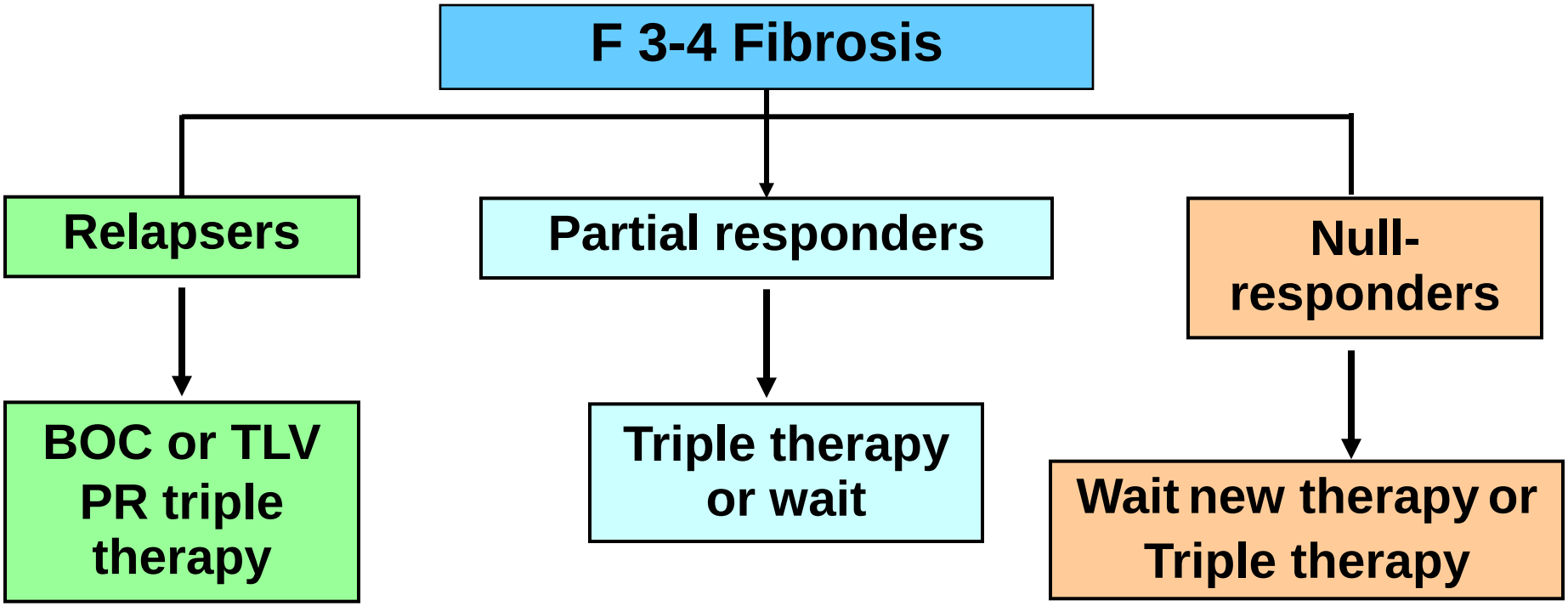




Kowdley K. EASL 2013.
Poorded F. Gastroenterology 2010;139:491-98.


Management of CHC genotype 1 with PegIFN/RBV treatment failure
Identify and correct modifiable response predictors
Stage of liver disease
Type of previous treatment response


F 0-2 Fibrosis
Relapsers
Partial responders
Null-responders
BOC or TLV PR triple therapy
BOC or TLV PR triple therapy
Wait for new therapy or triple therapy
SVR 75-85%
SVR 72 %
SVR 40 %



SVR 75-84%

SVR 34 %

SVR 14 %

Cirrhotic patients with thrombocytopenia and hypoalbuminemia ⇒ wait for new therapy


Thank you