Approved Regimes for Non-Cirrhotic Patients

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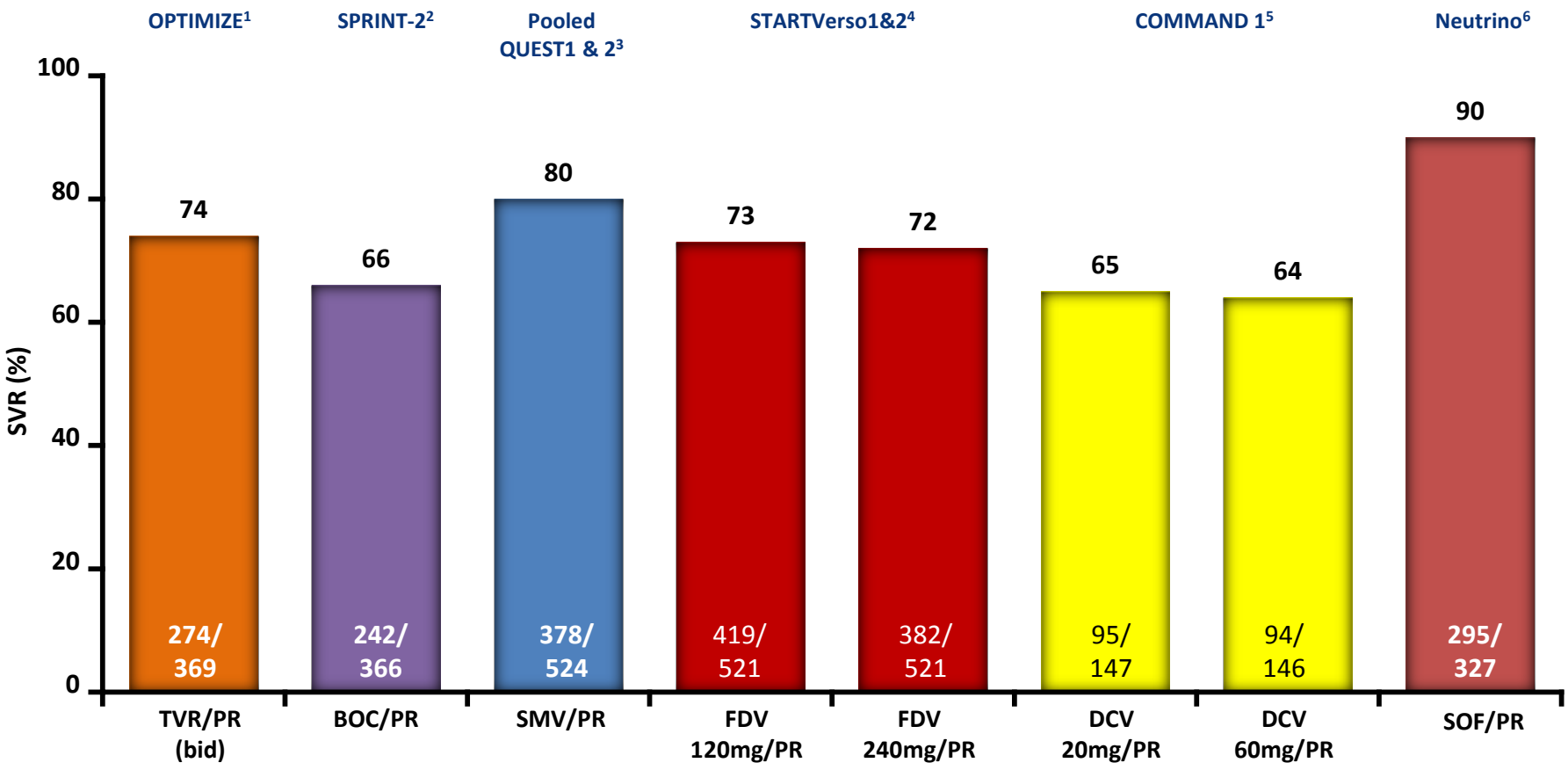
Conflicts of Interest

- Speaker and consultancy fees received from
- AbbVie, BI, BMS, Gilead, Janssen, Roche, Merck, Novartis, Springbank, Achillion, Idenix

HCV – Approved Regimes (G1)

- Regimes for the poor

IFN-based options for genotype 1 treatment-naïve patients



1. Buti M, Gastroenterology 2014;146:744–53
2. Boceprevir SmPC; 3. Jacobson I, et al. AASLD 2013. Poster 1122
4. Jensen DM, et al. AASLD 2013. Abstract 1088
5. Hézode, et al. AASLD 2012: Abstract 755;
6. Lawitz E, et al. N Engl J Med 2013;368:1878–

Cross comparison of studies cannot be carried out
SMV: simeprevir; FDV: faldaprevir; DCV: daclatasvir
SOF: sofosbuvir

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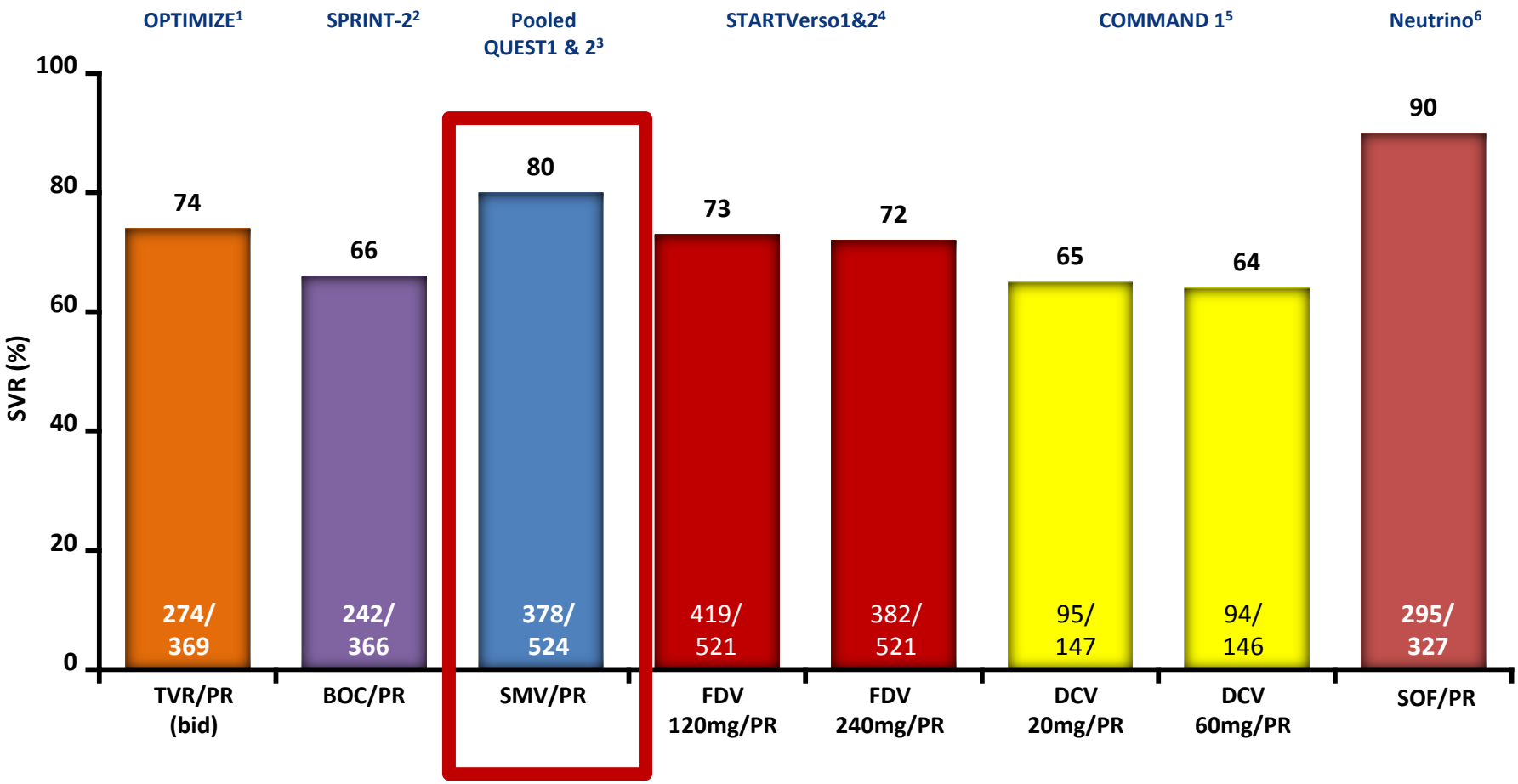

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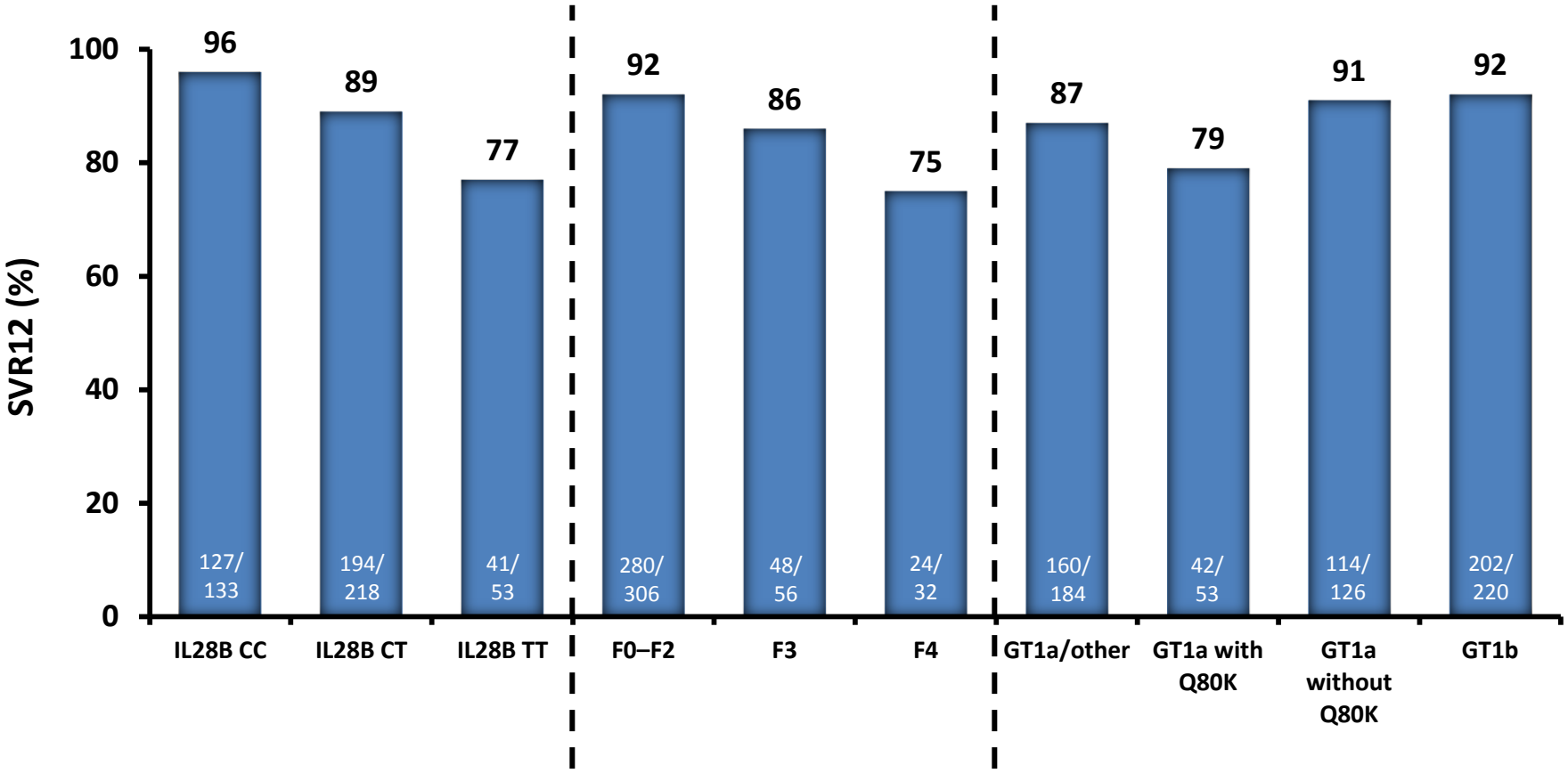
Simeprevir – In treatment naïve patients

- Treat for 4 weeks and assess
- If no response – abandon
- If responding treat for total of 24 weeks

SMV + PR: Not all patients are equal



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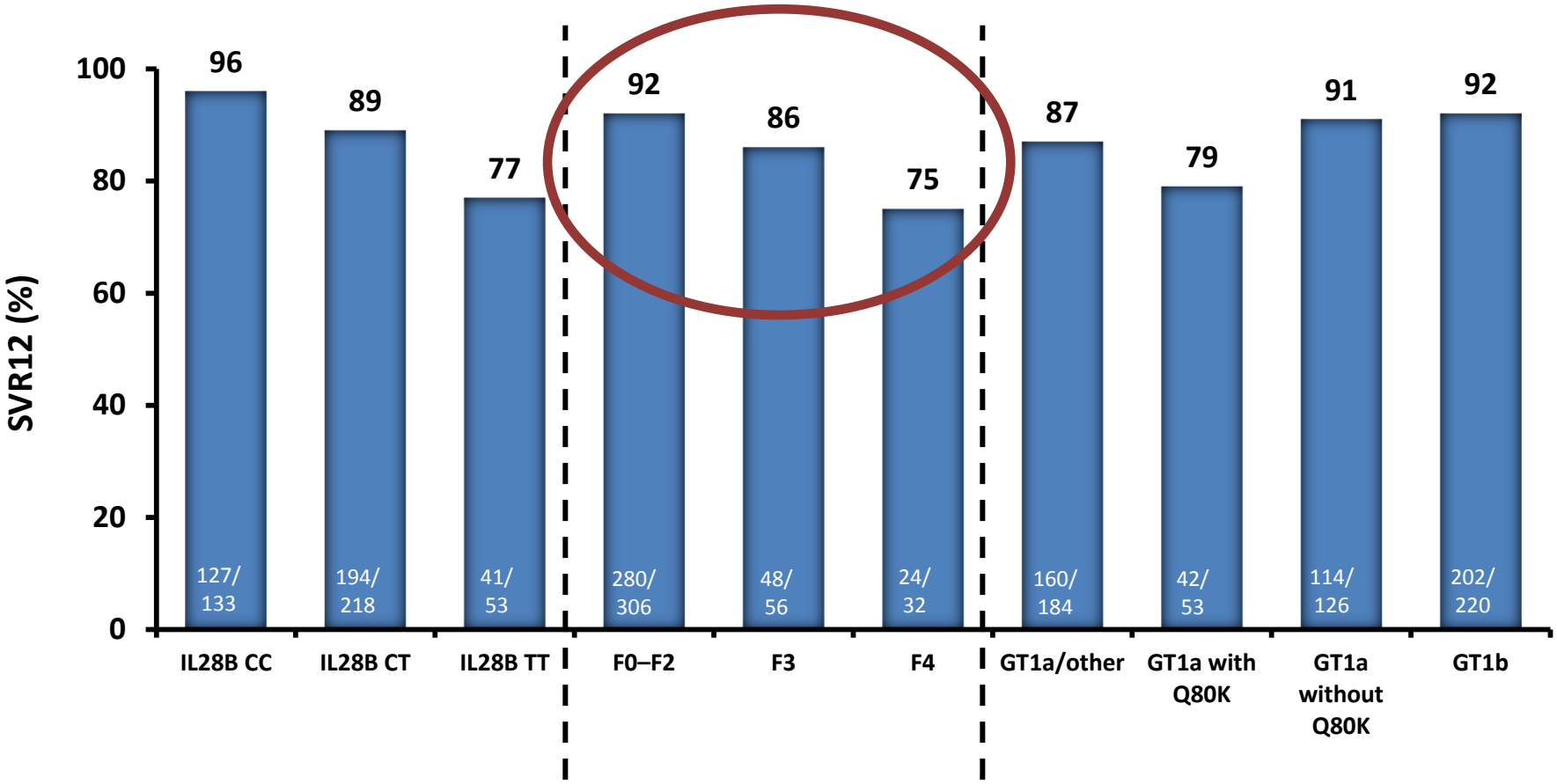

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HCV – Approved Regimes (G1)

- Regimes for the rich (and wise)
- Sofosbuvir based regimes
- Protease based regimes

Sofosbuvir based regimes

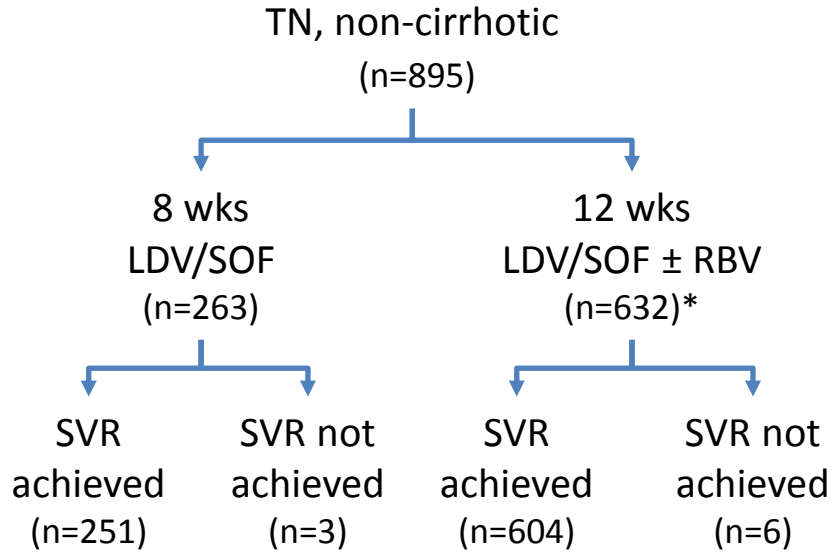
- You can add sofosbuvir to anything and HCV dies
- (Simeprevir, daclatasvir, Channel No 5)

(One of the above is wrong)

Real-world experience from the TRIO Network:

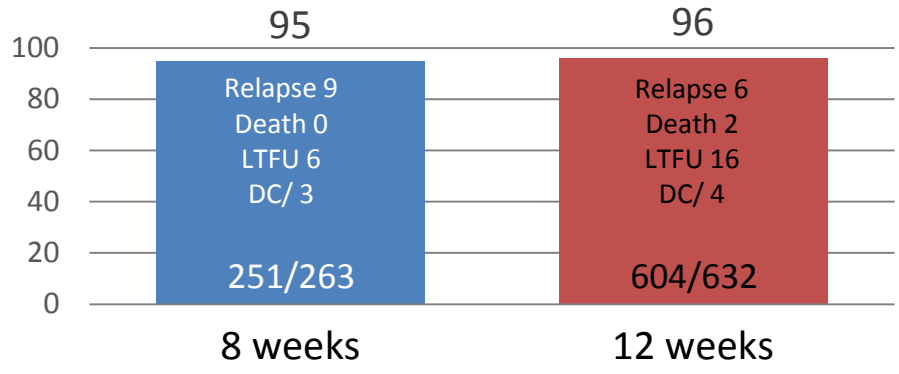
Effectiveness of 8 or 12 week LDV/SOF in treatment-naive patients with non-cirrhotic, G1 HCV

Patient disposition

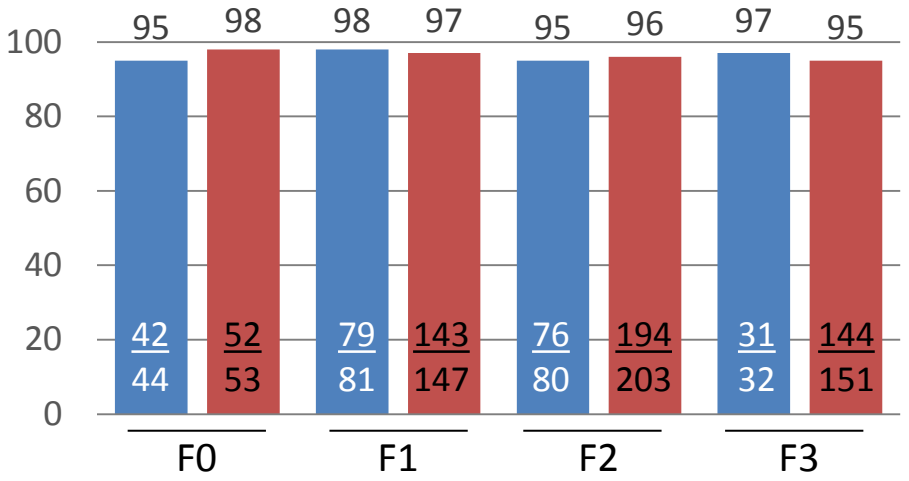


*21 Patients were on 12 weeks of LDV/SOF+RBV

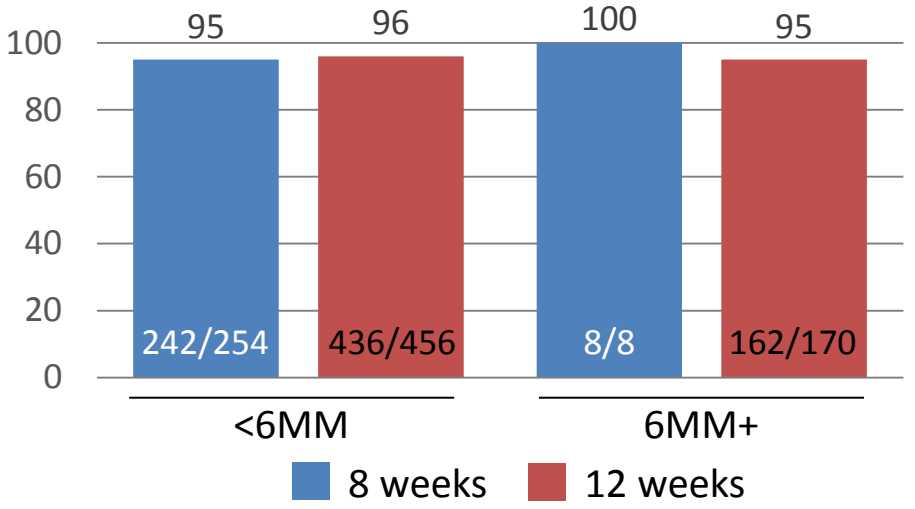
SVR12 by duration



SVR12 by fibrosis



SVR12 rates by baseline viral load

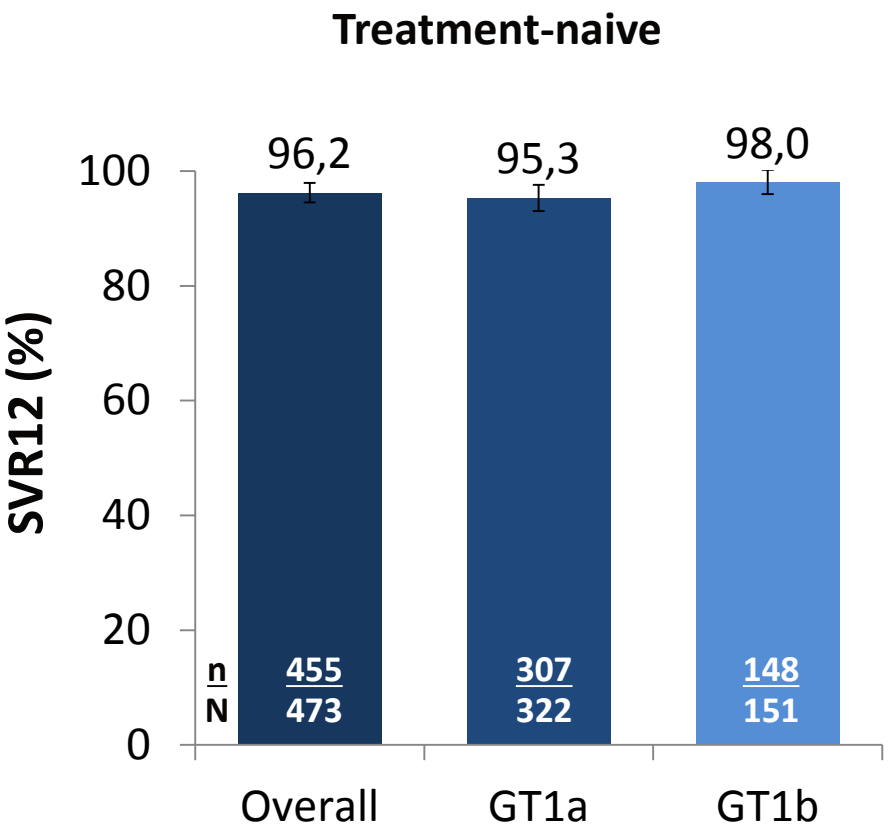


Curry M, et al. AASLD 2015, San Francisco. #1046

HCV – Approved Regimes (G1)

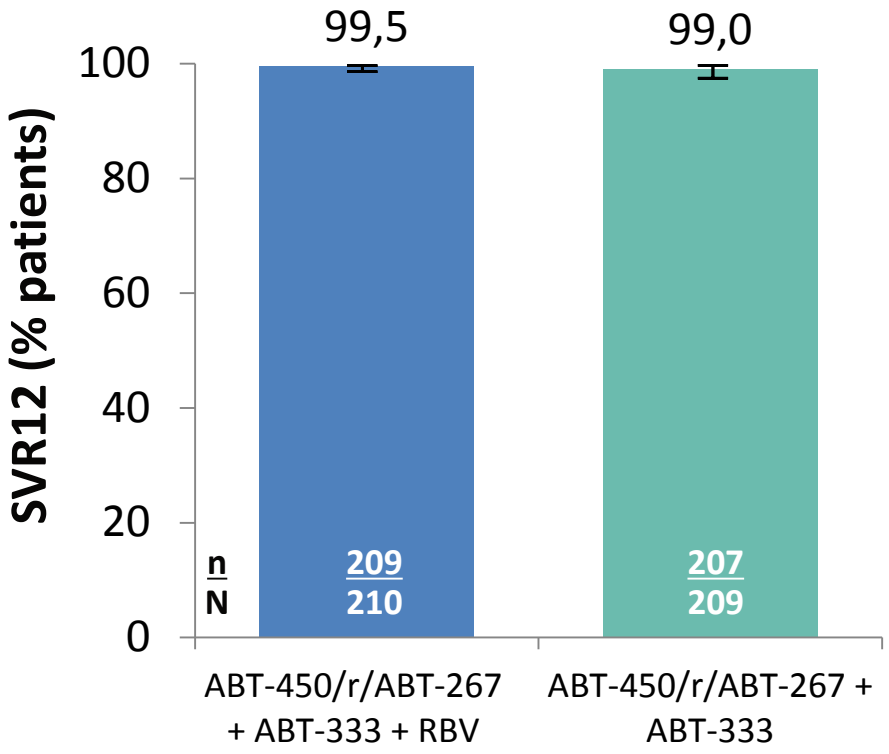
- Regimes for the poor (and wise)
- Sofosbuvir based regimes
- Protease based regimes

SAPPHIRE-I: GT1 treatment-naive patients — Paritaprevir (R) /Ombitasvir/Dasabuvir



Error bars: 95% CI.

PEARL-III: SVR rates with 3D ± RBV in GT1b treatment-naive patients



- Error bars: 95% CI.

- Ferenci P, *et al. NEJM 2014;370:1988*].

Genotype 1 HCV

- Sorted!

- Independent assessment of cost effectiveness (NICE) recommends that ALL patients get treated

Emerging Issues - Resistance

- Current story is that Resistance Associated Variants (RAVs) have no impact on SVR

- Is this really true?

HCV – Approved Regimes (G2)

- 80% of Genotype 2 patients respond to 24 weeks of Peg + Riba

- (Patients who respond rapidly may have duration reduced to 12 weeks)

Genotype 2
Sofosbuvir + Ribavirin for 12 weeks

NAIVE		EXPERIENCED			
G2		G2 12 WEEKS		G2 16 WEEKS	
Non Cirrhosis	Cirrhosis	Non Cirrhosis	Cirrhosis	Non Cirrhosis	Cirrhosis
92%	94%	96%	60%	100%	78%

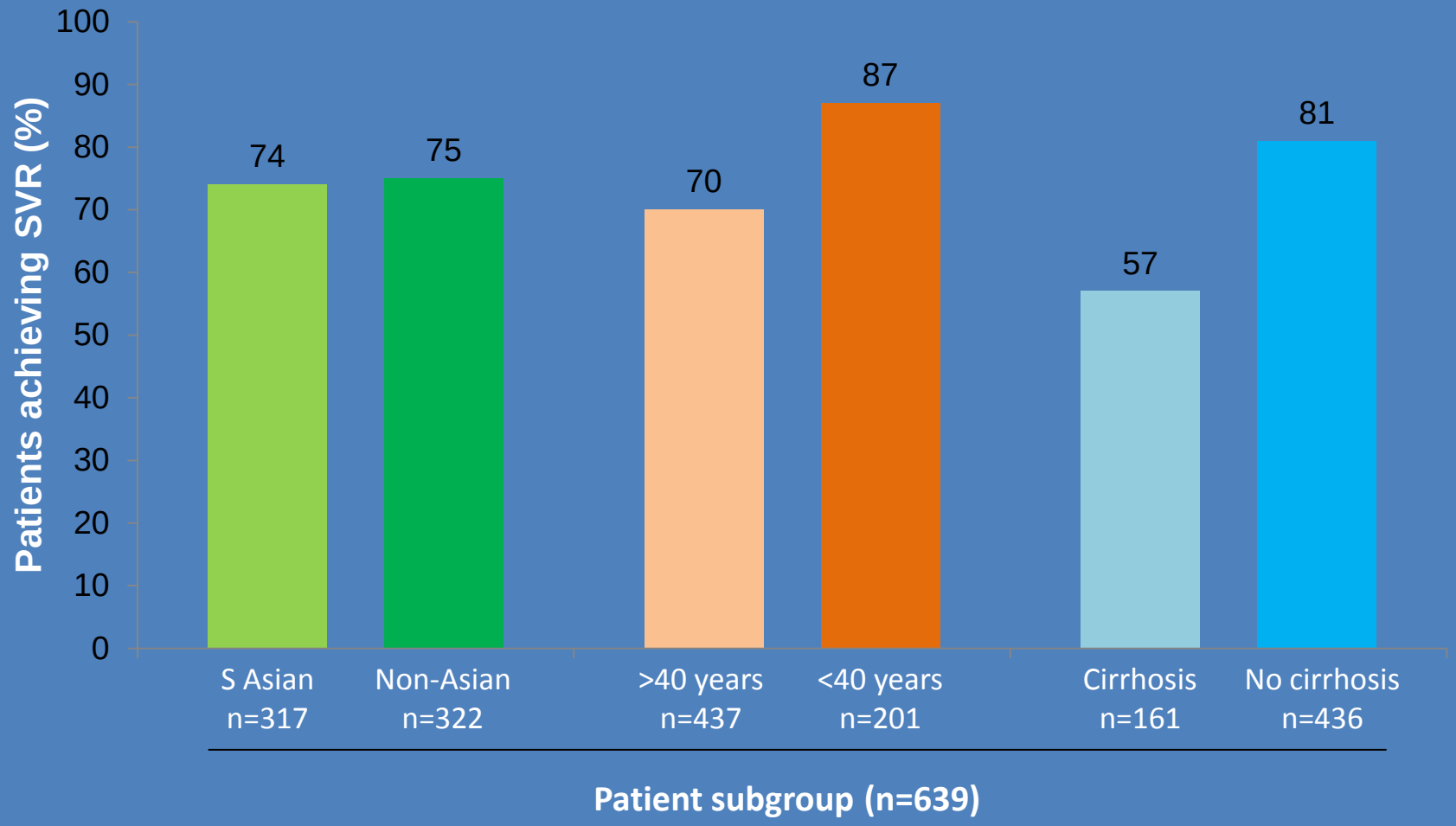
Jacobson NEJM 2013

HCV – Approved Regimes (G3)

- 70% of Genotype 3 patients respond to 24 weeks of Peg+Riba

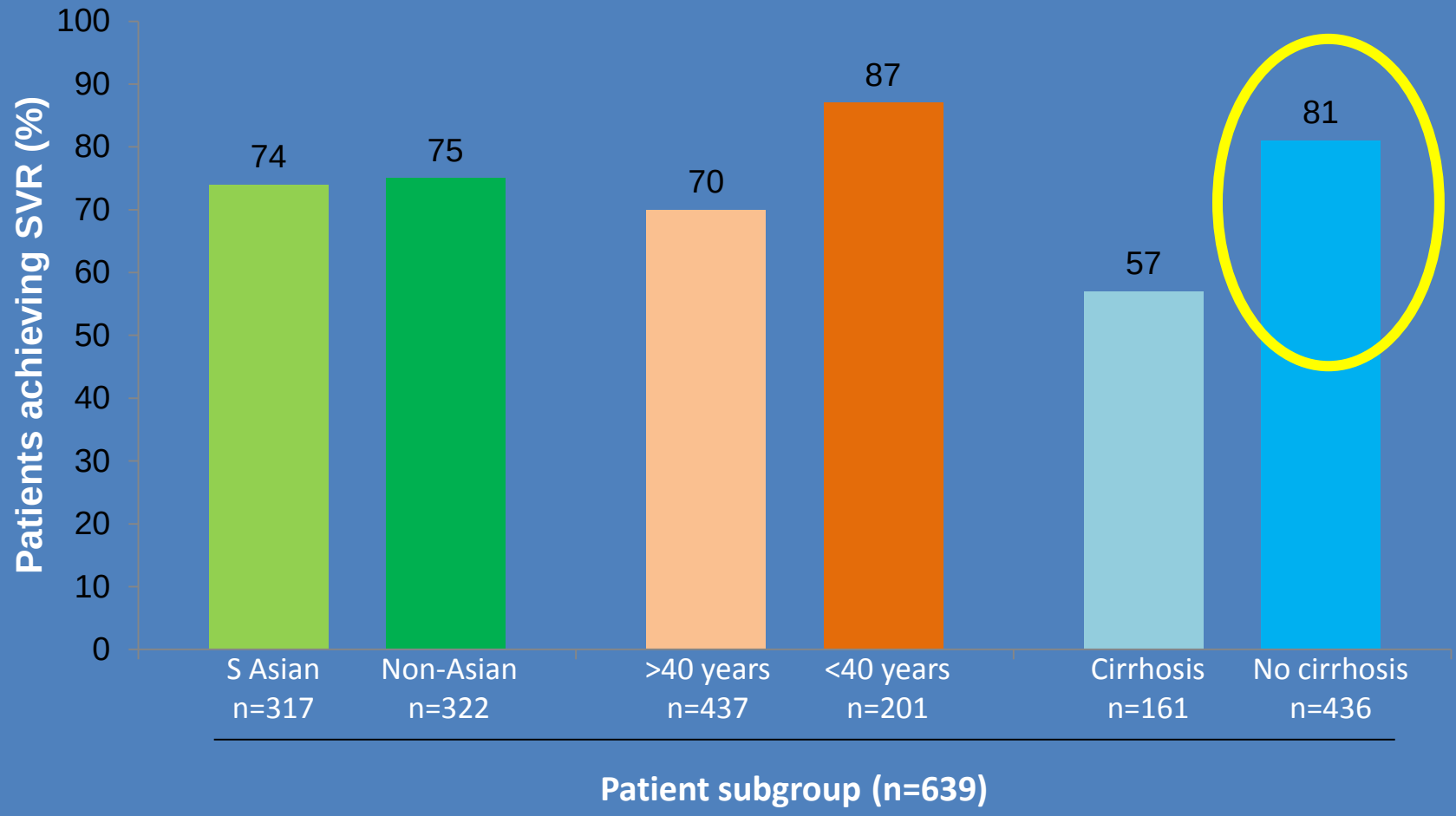
- Cirrhosis is a different game……

Genotype 3
PegIFN + Ribavirin



Data are from an audit of 639 patients tretated with PegIFN/RBV; Shoeb D, et al. *Eur J Gastroenterol Hepatol* 2011;**23**:747–753

Genotype 3
PegIFN + Ribavirin



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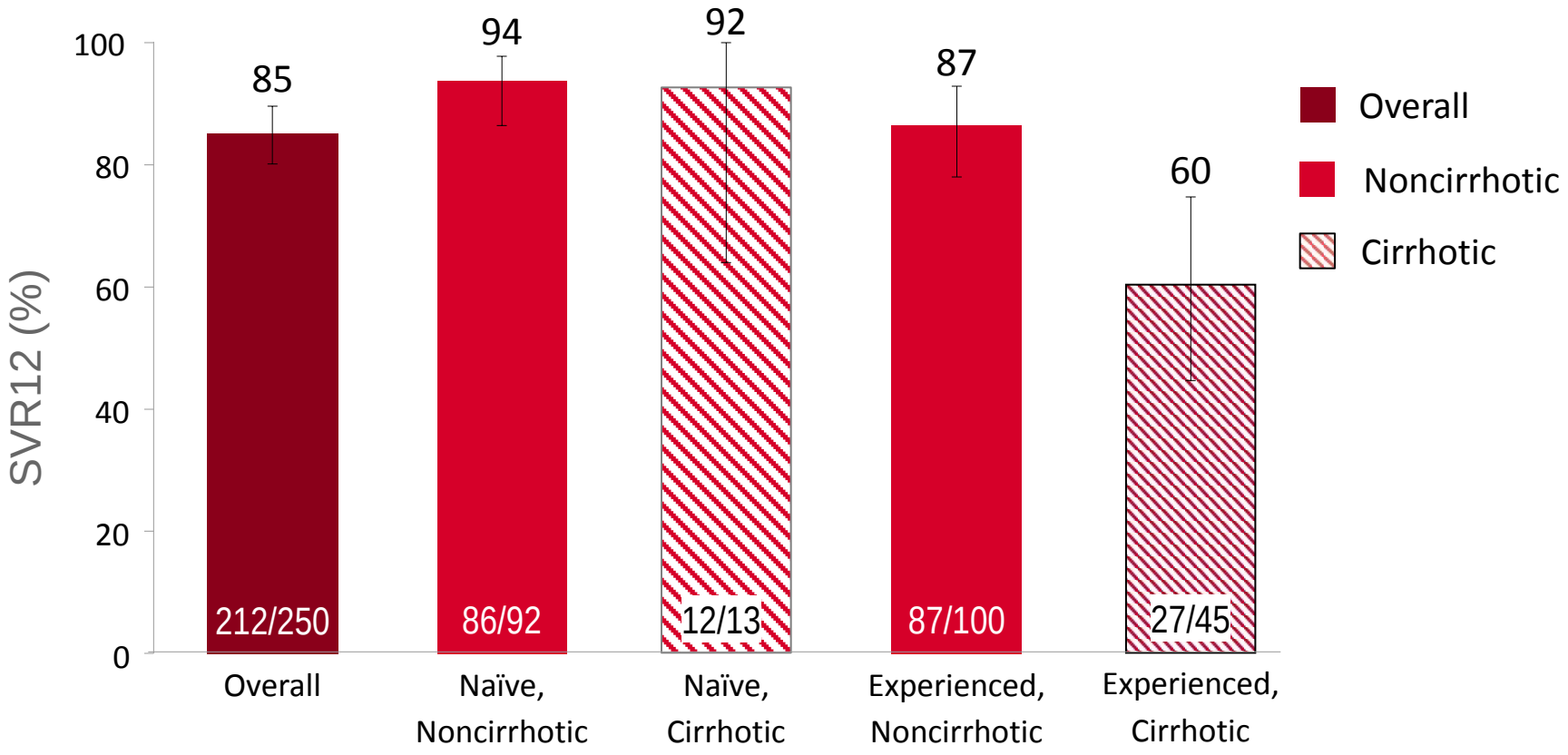
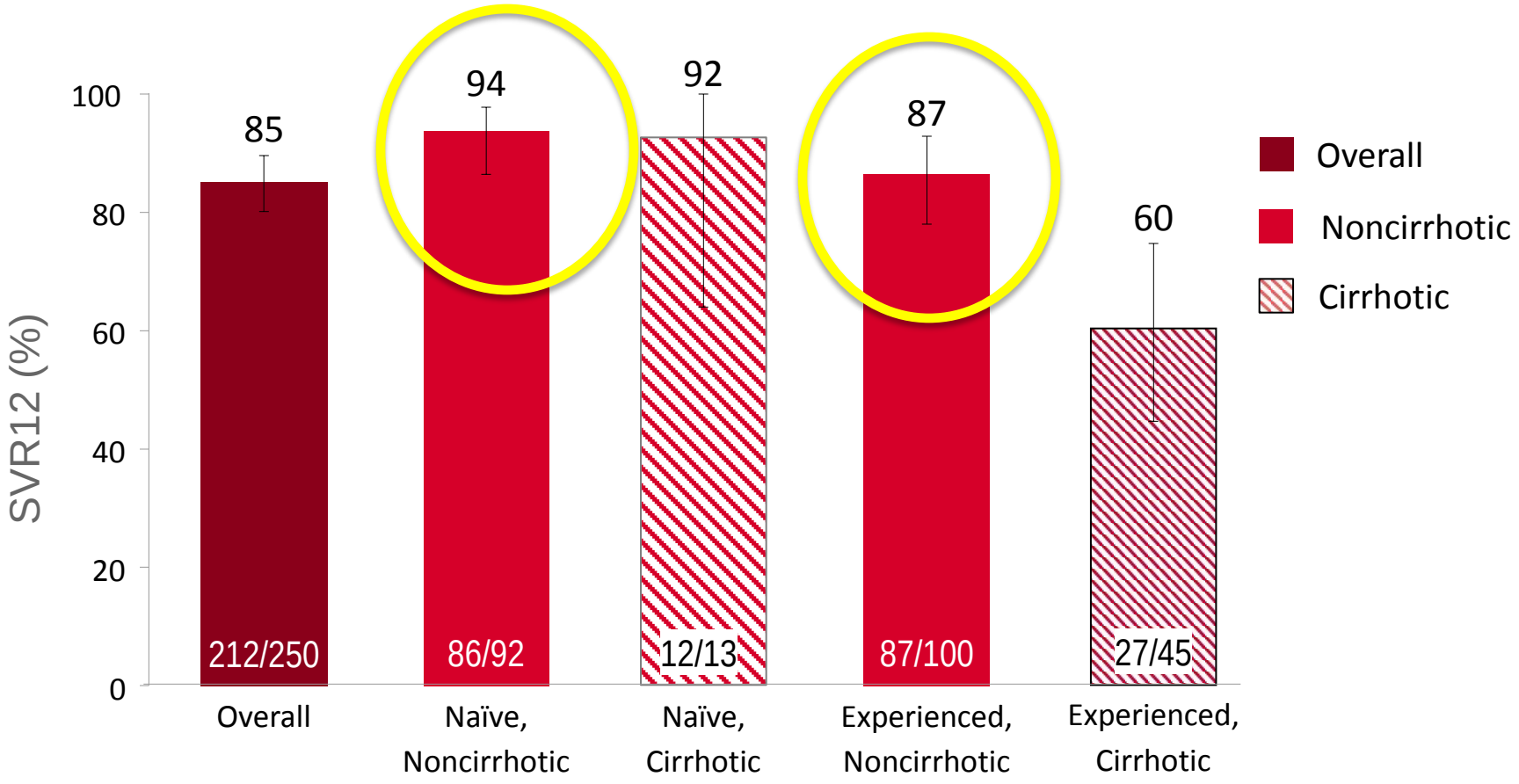
Sofosbuvir for G3 24 weeks therapy



Note – this is not a cheap regime!

Valence NEJM 2014

Sofosbuvir for G3 24 weeks therapy



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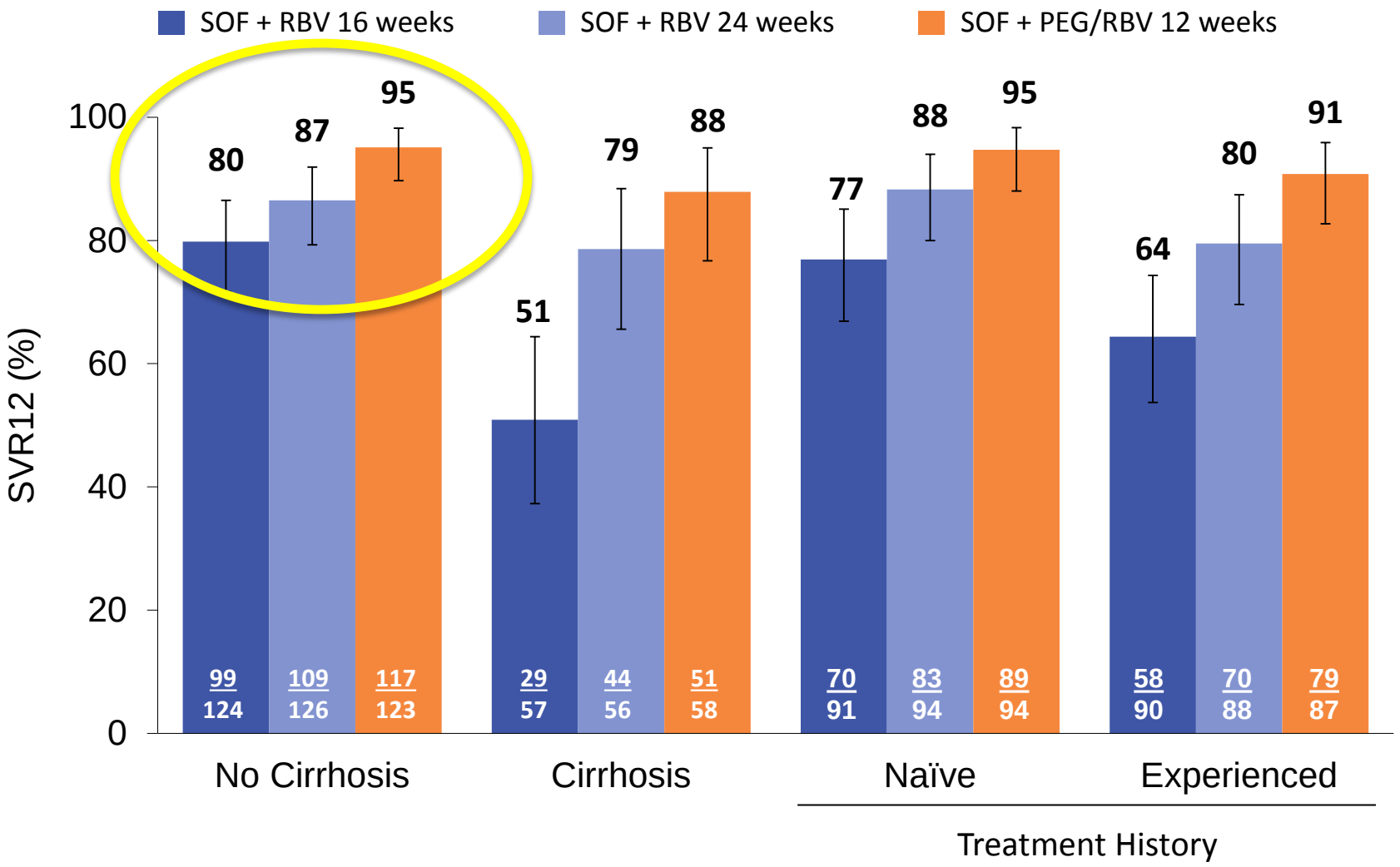
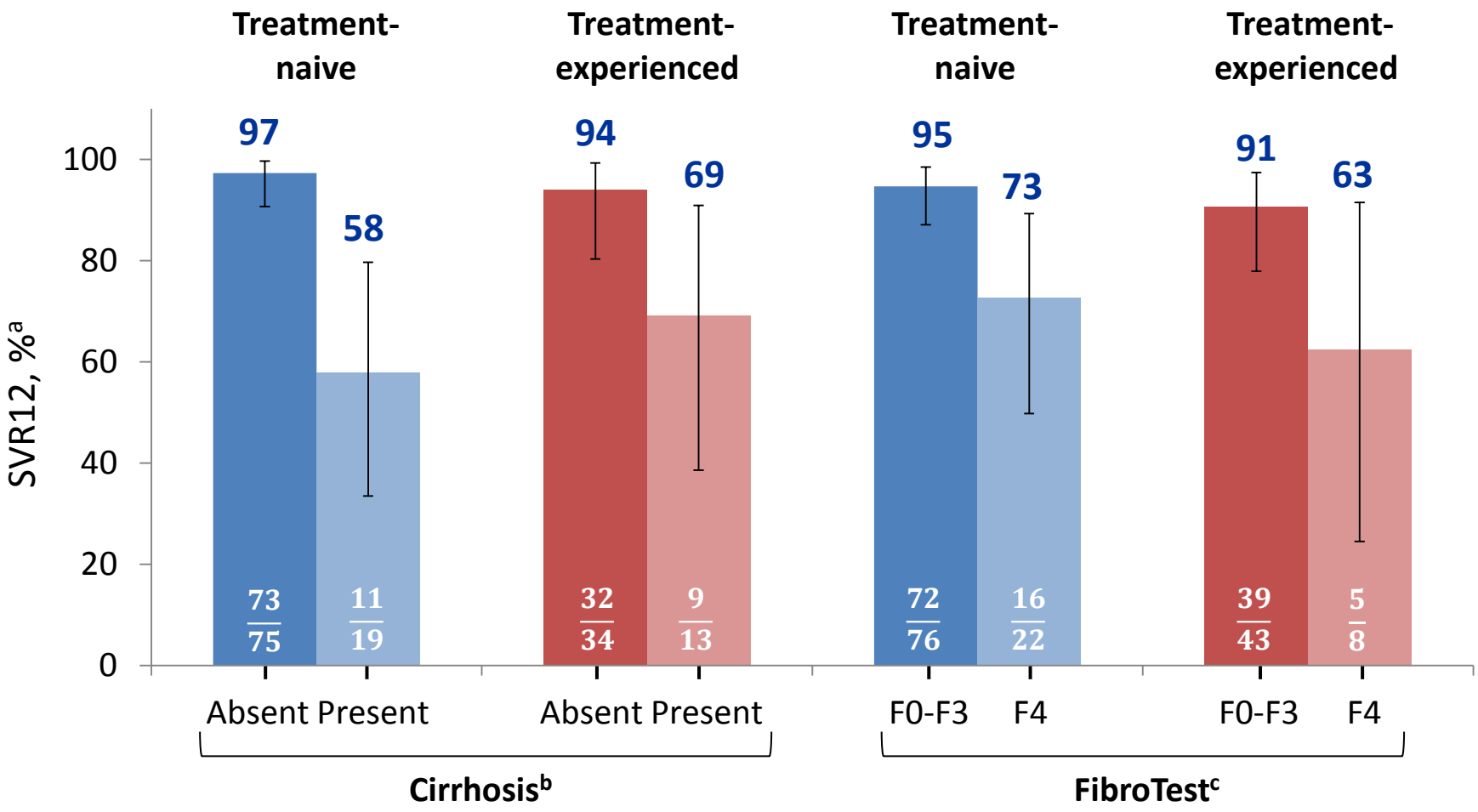
Results: SVR12 in GT 3



- intervals.

G3 Without Interferon



[a] HCV RNA < LLOQ (25 IU/mL); error bars reflect 95% confidence intervals.

[b] Cirrhosis determined by liver biopsy (METAVIR > F3), FibroScan (> 14.6 kPa), or FibroTest score ≥ 0.75 and aspartate aminotransferase to platelet ratio index > 2.

[c] FibroTest assessments could have been performed up to Day 1 (baseline).

Genotype 3

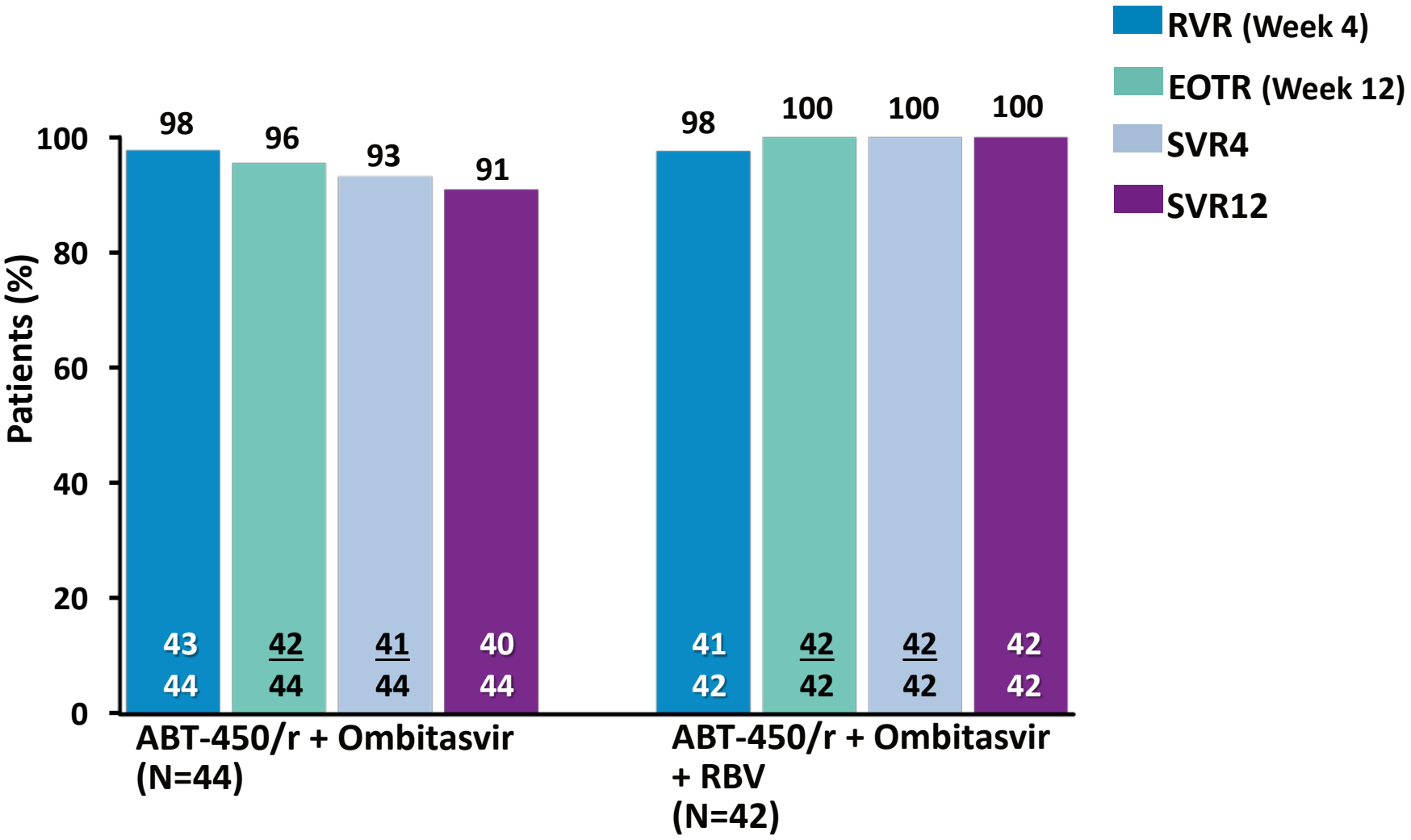
- For non-cirrhotic Genotype 3 most options work well:-

- Peg/Riba 24 weeks
- Peg/Riba/Sof 12 weeks
- Sof/riba 24 weeks
- Sof/Dac 12 weeks

Genotype 4

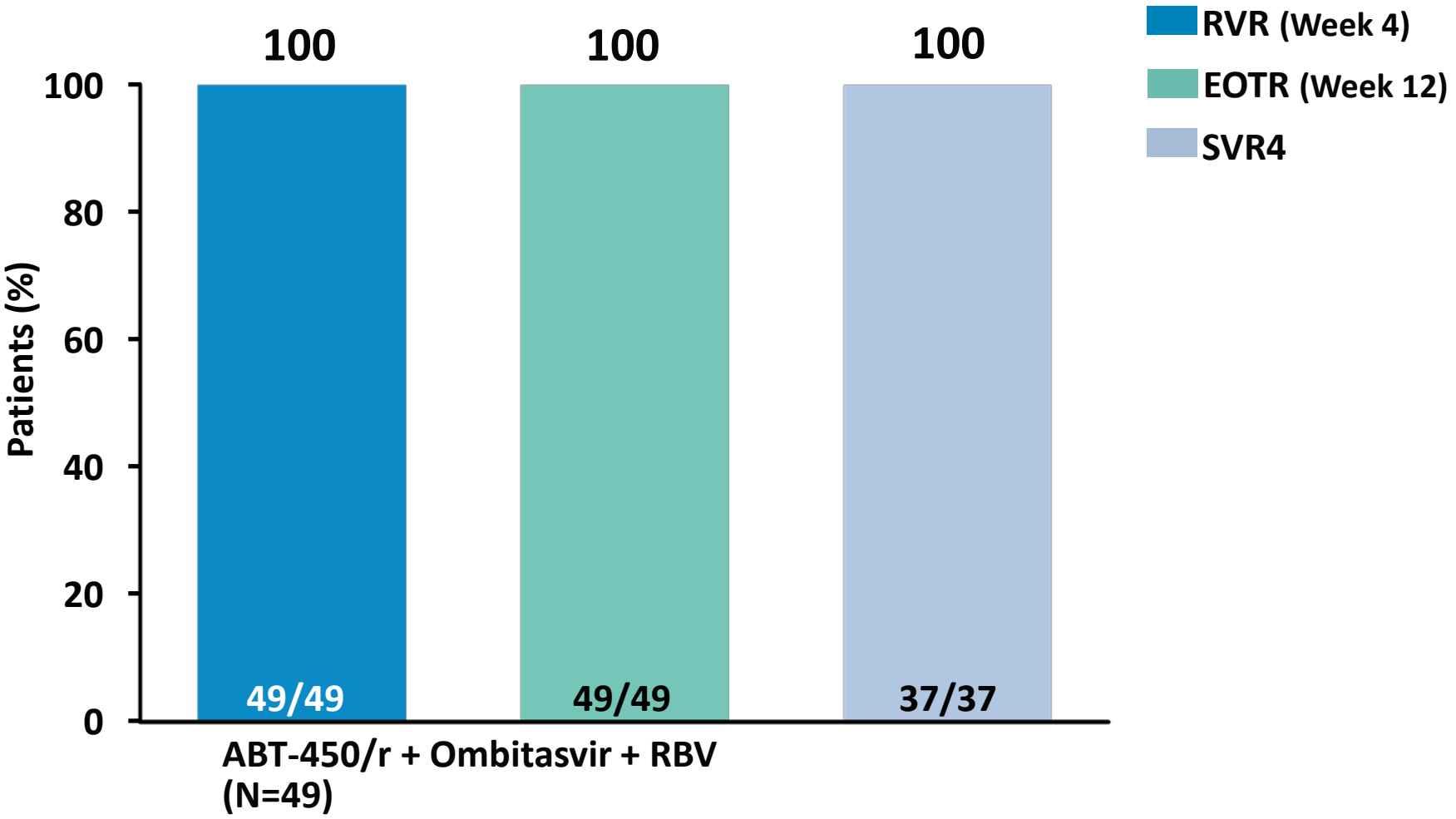
- Options are:-
- AbbVie 2D
- Sofosbuvir + ledipasvir

PEARL-I: GT4-Infected Treatment-Naïve Patients Paritaprevir (R)/Ombitasvir



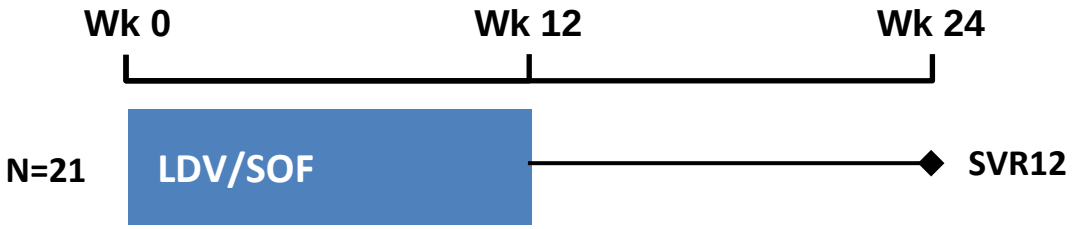
Hezode C, *et al.* EASL 2014

PEARL-I: GT4-Infected Treatment-Experienced Patients
ITT Efficacy Analysis

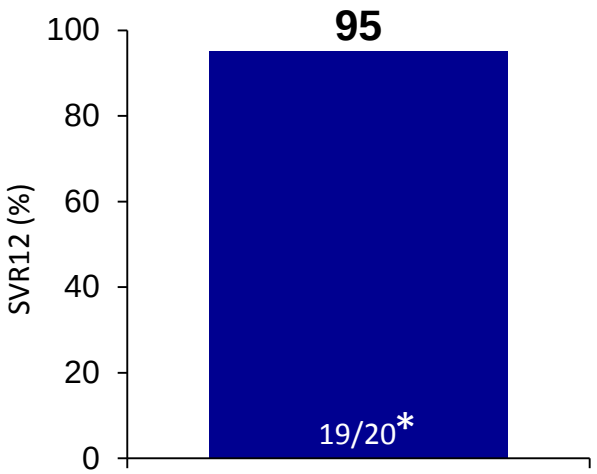


Hezode C, *et al.* EASL 2014

SYNERGY: Phase 2a study of LDV/SOF in GT 4 patients: interim results



Demographics	
Age	55 ± 10
Male, n (%)	14 (67)
Black, n (%)	9 (43)
Country of origin	
Egypt, n (%)	6 (29)
USA, n (%)	5 (24)
Ethiopia, n (%)	4 (19)
Cameroon, n (%)	3 (14)
HCV RNA > 800,000 IU/mL, n (%)	13 (62)
Treatment experienced, n (%)	8 (38)
Cirrhotic, n (%)	7 (33)



95% SVR12 with LDV/SOF for GT 4 HCV – No patient discontinued due to an AE**

- Kapoor R, et al. AASLD 2014; Oral #240.

- *One patient has not reached SVR12 time point yet;
- **One discontinuation in a patient who reported taking one dose of medication

Genotypes 5 & 6

- Nothing licensed

- Limited data with:-
- Peg/riba/sofosbuvir
- Sofosbuvir/ledipasvir
- Sofosbuvir/daclatasvir

Licensed Therapies for HCV

- Excellent all oral therapies are now available for all patients with HCV

- For most genotypes there are alternatives which provides both challenges and opportunities