HCV: Interferon Free Therapy In Treatment Experienced Patients

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Disclosures

David R Nelson, MD,

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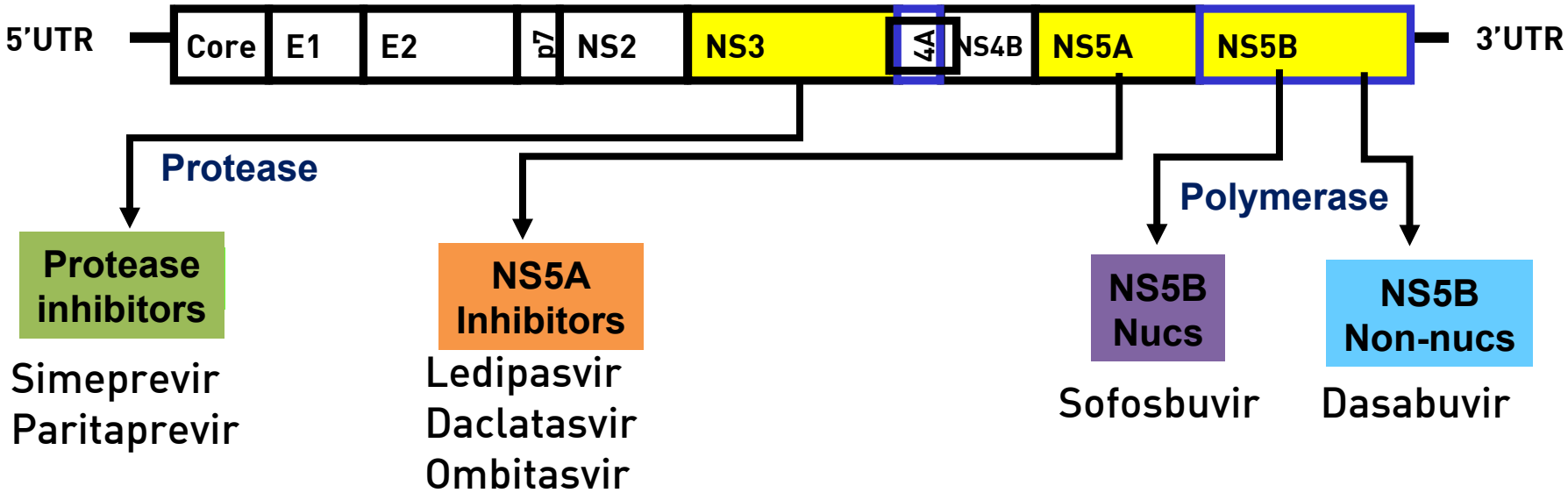
- Additional research support: NIH, DOD, DOH grants

Outline

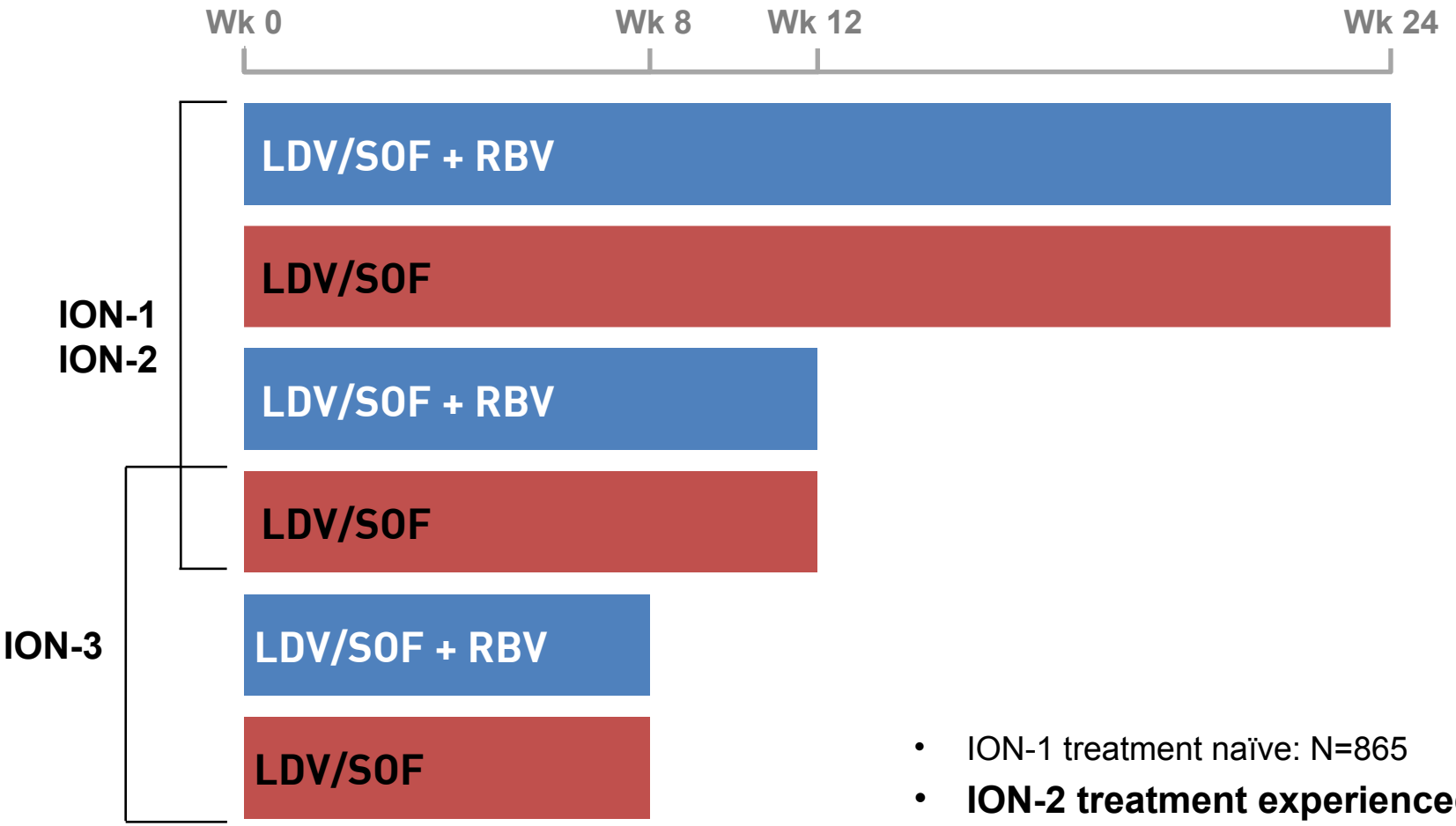
- Overview of drug development
  - Direct acting antiviral drugs
  - Treatment regimens
- Approach to treatment experienced
  - Genotype 1 clinical trials data
  - Treatment algorithms
- Future regimens

Multiple Validated Drug Targets in 2015



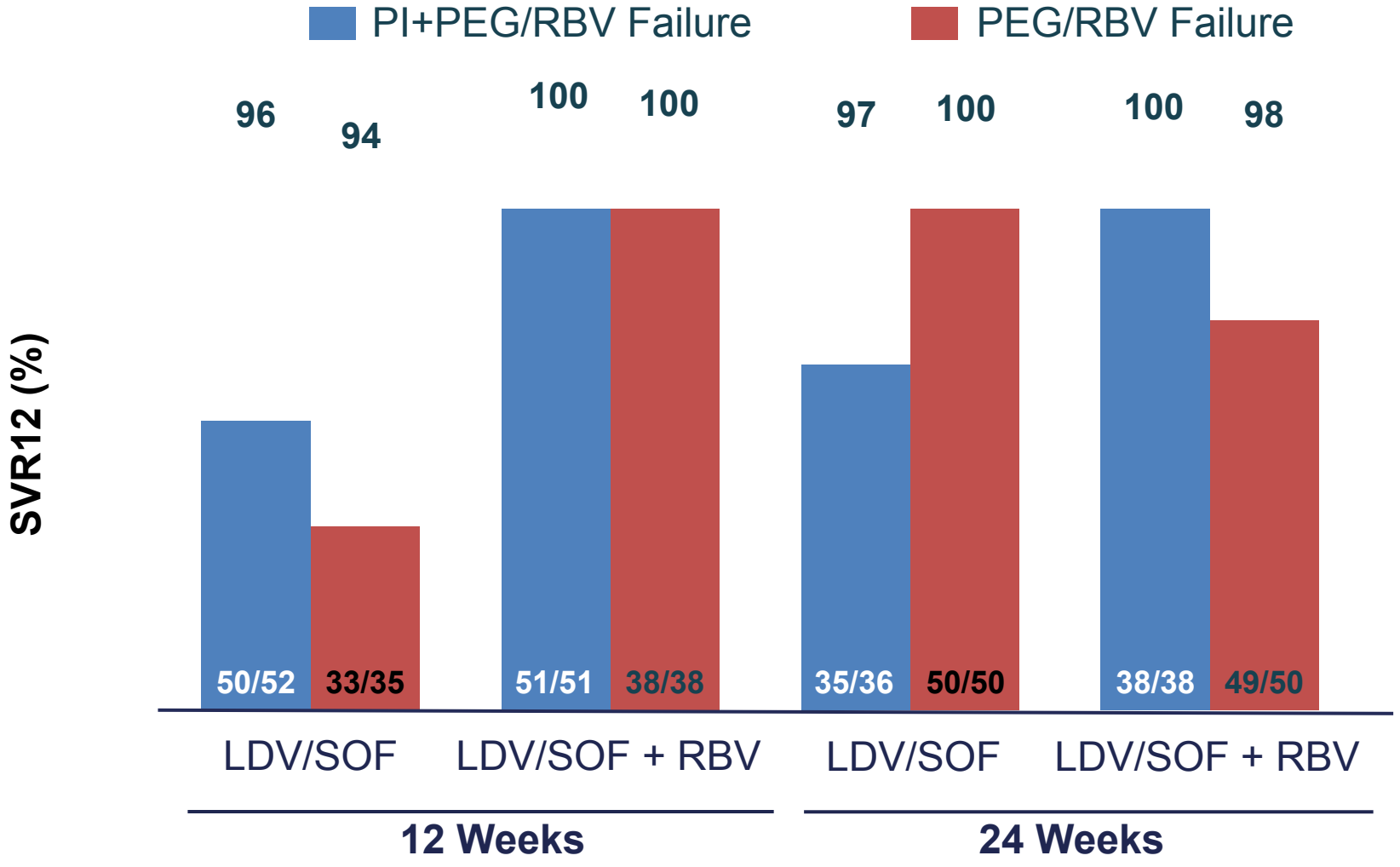
	Regimens in Use	Direct Acting Antiviral Class
Current	PEG/RBV + sofosbuvir	NUC
	Sofosbuvir + RBV	NUC
	Sofosbuvir + simeprevir	NUC + PI
	Sofosbuvir + ledipasvir	NUC + NS5A Inhibitor
	Paritaprevir + Ombitasvir+ Dasabuvir +/- RBV	PI + NS5B + NNI
In EU	Sofosbuvr + daclatasvir	NUC + NS5A Inhibitor

Sofosbuvir + Ledipasvir (HARVONI) Genotype 1 Phase III Trials



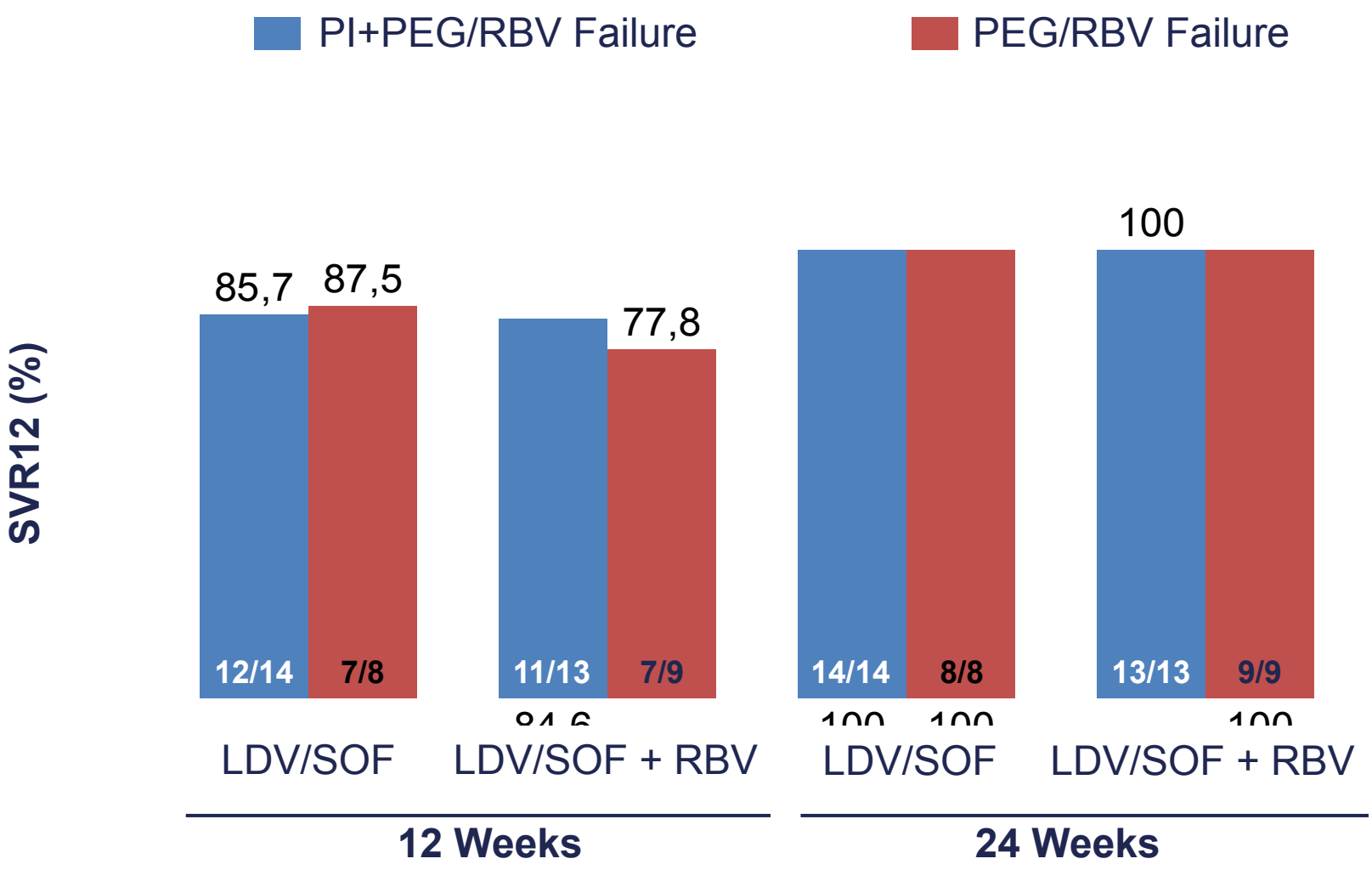
- ION-1 treatment naïve: N=865
- **ION-2 treatment experienced: N=440**
- ION-3 treatment naïve: N=647

ION-2: GT1 Treatment-experienced Non-cirrhotic Patients
Ledipasvir/Sofosbuvir ± RBV for 12 vs 24 Weeks



Afdhal et al. *N Engl J Med* 2014;370:1483-93

ION-2: GT 1 Treatment-experienced Cirrhotic Patients Ledipasvir/Sofosbuvir ± RBV for 12 vs 24 Weeks



Afdhal et al. *N Engl J Med* 2014;370:1483-93

Relapse Rates in Treatment Experienced

	LDV/SOF 12 Weeks (N=108)	LDV/SOF 24 Weeks (N=109)
Relapse Rate in Patients Without Cirrhosis	5% (4/86)	0% (0/90)
Relapse Rate in Patients With Cirrhosis	**14% (3/22)**	0% (0/19)

Indications and Usage (Harvoni)

Genotype 1 Patient Populations	Treatment Duration
Treatment experienced without cirrhosis	12 weeks
Treatment experienced with cirrhosis	24 weeks

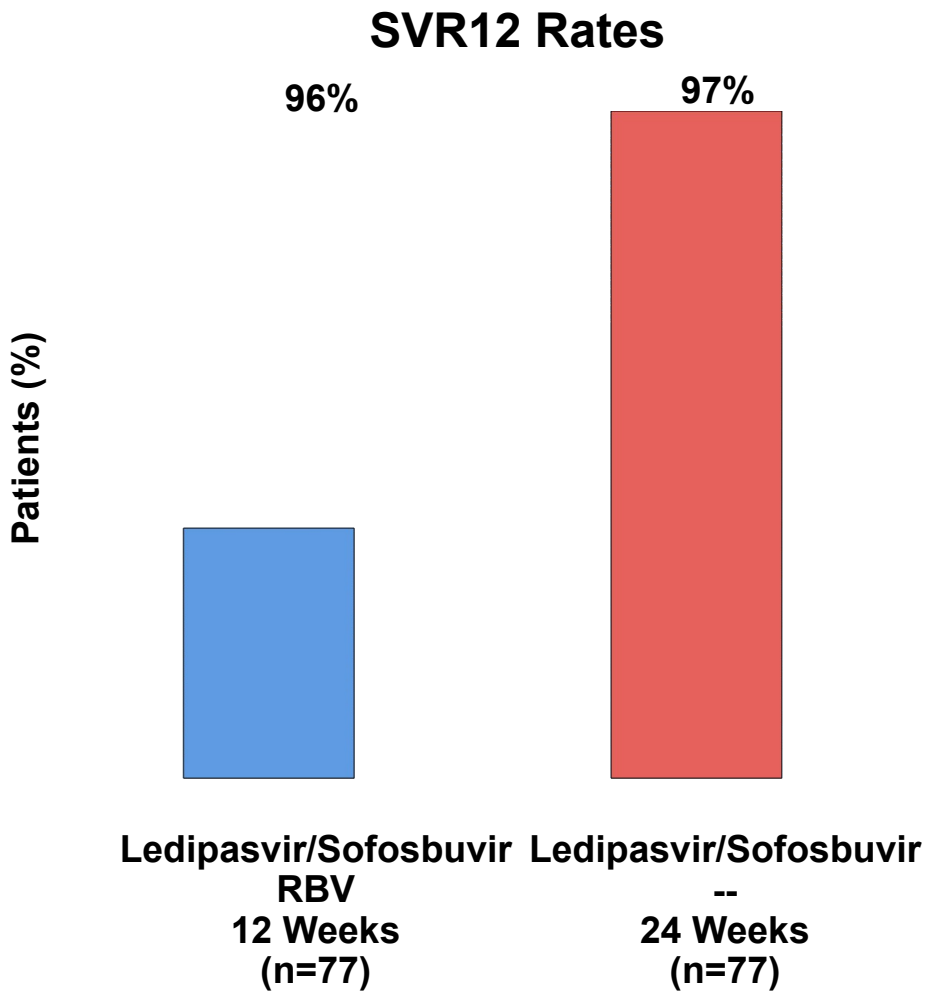
Source: *Harvoni* Prescribing Information. Gilead Sciences

Other Options For Shorter Duration: RBV

Ledipasvir/Sofosbuvir in Cirrhotic Patients Who Failed Previous PI-Based Therapy

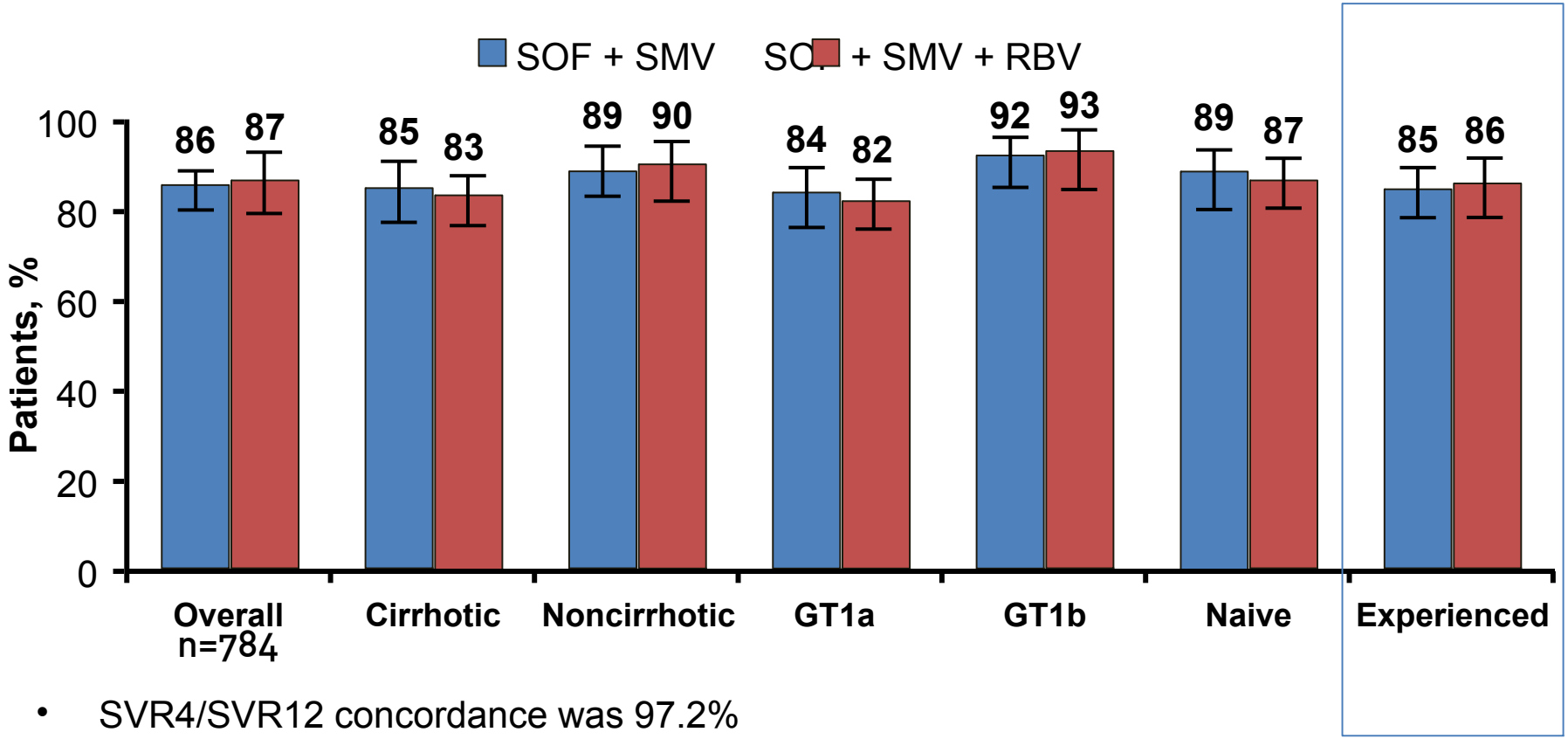
Phase 2 (France)

- Genotype 1
- Compensated cirrhosis
- Treatment experienced
- PR and PI + PR failure



Bourlierre P, et al. *Hepatology.* 2014;60(suppl 1). Abstract LB-6.

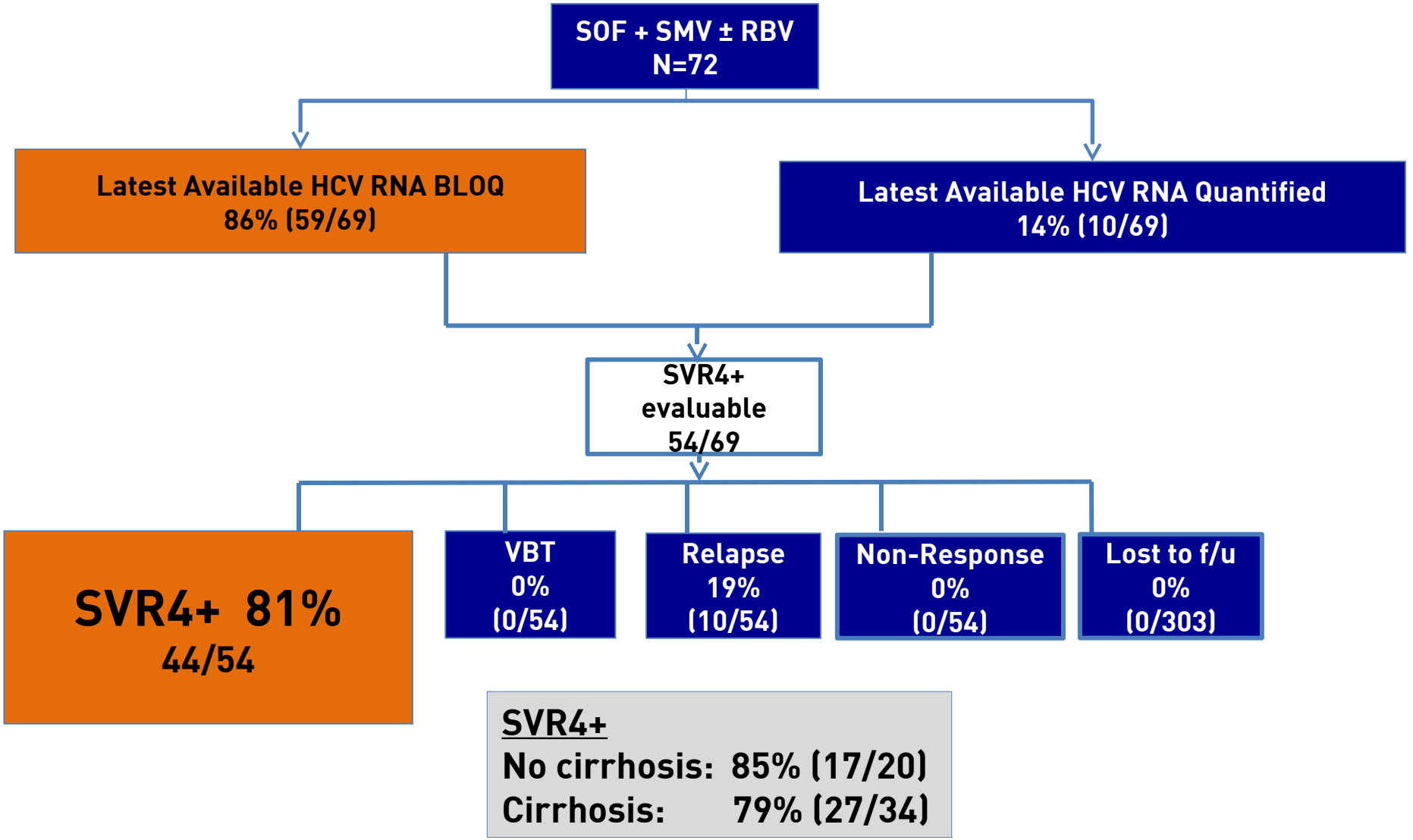
Sofosbuvir + Simeprevir ± RBV
HCV-TARGET: Adjusted SVR4 in GT1



- SVR4/SVR12 concordance was 97.2%
- In multivariate analysis, likelihood of achieving SVR4 was associated with baseline ALB, HCV genotype (1b > 1a), previous decompensation, and history of triple therapy failure

Jensen D, et al. AASLD 2014. Abstract 45.

HCV RNA Outcomes for SOF/SMV±RBV: Genotype 1 Prior Protease Inhibitor Failures



SVR4+
No cirrhosis: 85% (17/20)
Cirrhosis: 79% (27/34)

Jensen D, et al. AASLD 2014. Abstract 45.

Sofosbuvir + Simeprevir
FDA Pooled Analysis from Phase 2 Trials

Relapse Rates

	SOF+SMV 12 weeks	SOF+SMV 24 Weeks
Overall	7%	0%
F0-F3	5%	0%
F4 (cirrhosis)	14%	0%

*Recommended duration of SOF + SMV for GT 1 is:

- F0-F3: 12 weeks
- F4: 24 weeks

*FDA expanded indication granted 11/5/14; Simeprevir (OLYSIO) product label, Janssen

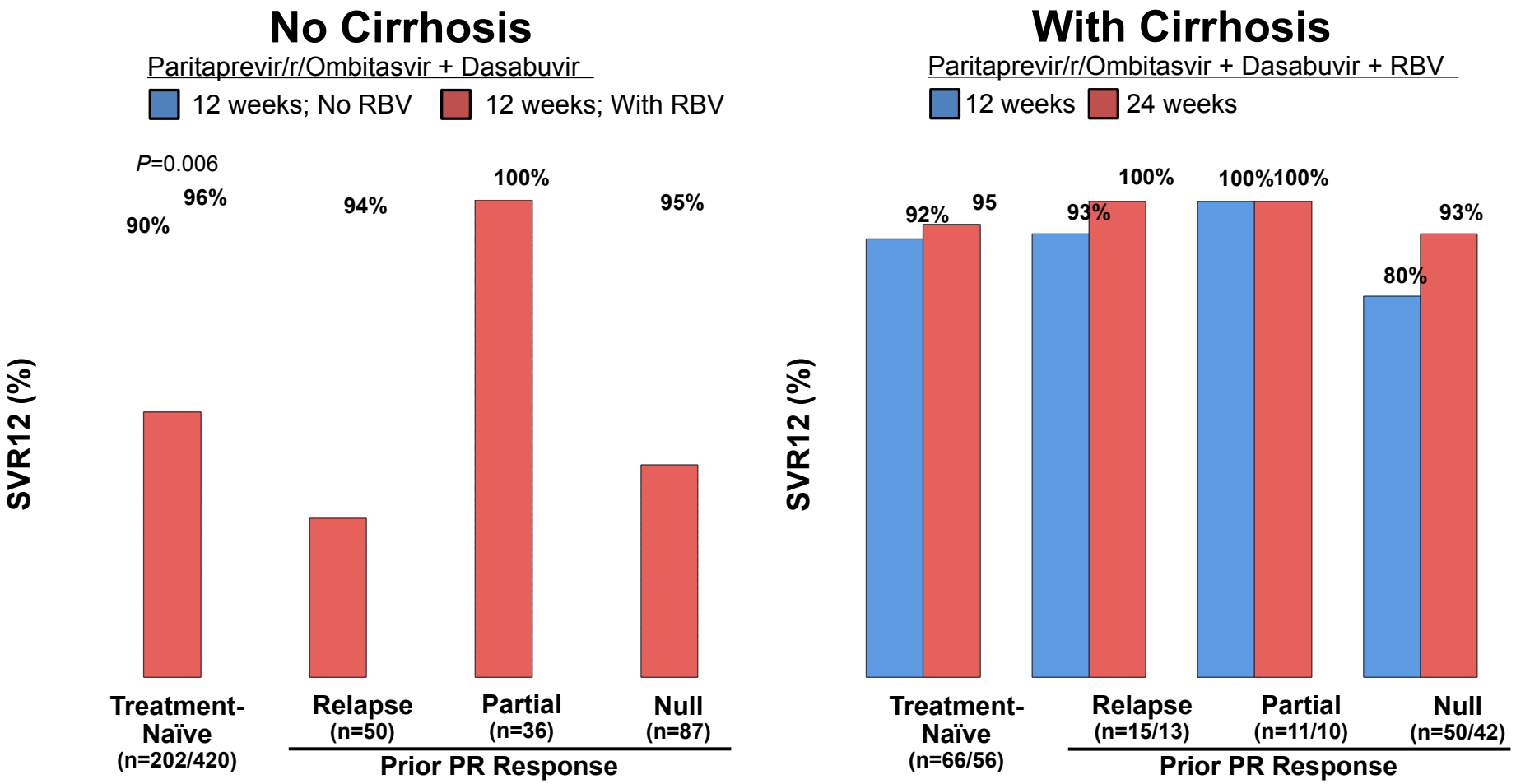
AbbVie Phase III Clinical Results In Treatment Experienced

Study	Patients	Treatment Regimen	SVR 12
PEARL-II *(12 weeks)*	GT1b treatment-experienced *(N=179)*	3D+ RBV (n=88)	**97%**
		3D only (n=91)	**100%**
TURQUOISE-II *(12 & 24 weeks)*	GT1 treatment-naive and treatment-experienced with compensated cirrhosis *(N=380)*	3D + RBV, 12 weeks (n=208)	**92%**
		3D + RBV, 24 weeks (n=172)	**96%**
SAPPHIRE-II *(12 weeks)*	GT1 treatment-experienced *(N=394)*	3D + RBV (n=297)	**96%**

3D: Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir

EASL, 2014 London, April 9-13

3D ± RBV in HCV Genotype 1a Integrated Efficacy Analysis*



*Pooled data from 4 phase III trials of paritaprevir/ritonavir/ombitasvir + dasabuvir ± RBV in cirrhotic and noncirrhotic patients with GT1a HCV

Everson GT, et al. *Hepatology.* 2014;60(suppl 1):239A-240A. Abstract 83.

Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir (*Viekira Pak*) Indications and Usage (Naïve and Experienced)

Patient Populations	Treatment*	Duration
GT1a, without cirrhosis	Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir + Ribavirin	12 weeks
GT1a, with cirrhosis	Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir + Ribavirin	24 weeks*
GT1b, without cirrhosis	Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir	12 weeks
GT1b, with cirrhosis	Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir + Ribavirin	12 weeks

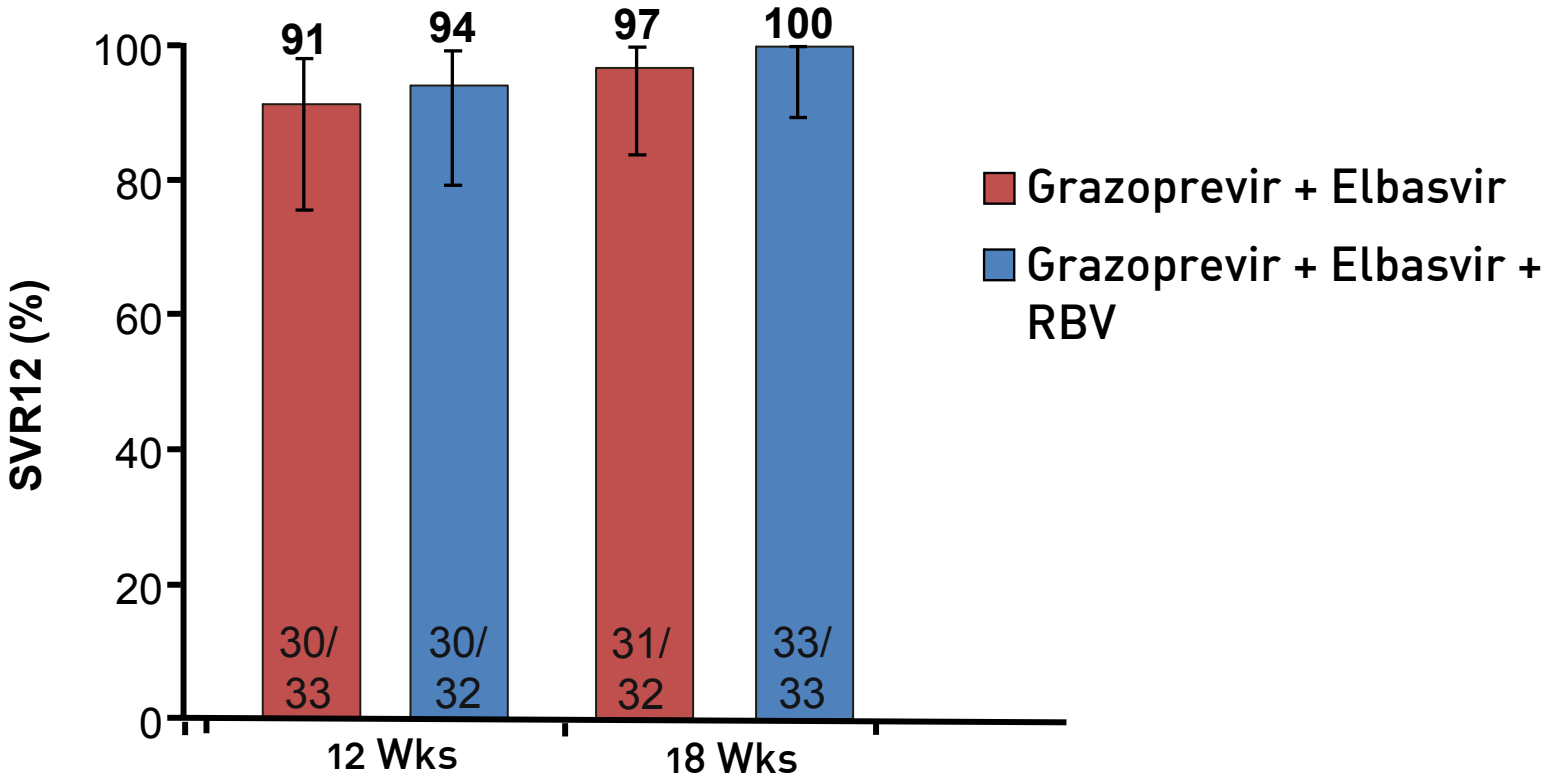
*Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir + ribavirin for 12 weeks may be considered for some patients based on prior treatment history

24 and 12 weeks of treatment with VIEKIRA PAK with RBV was +6% with 95% confidence interval, -0.1% to +13% with differences varying by pretreatment history.

Source: *Viekira Pak* Prescribing Information. AbbVie Inc.

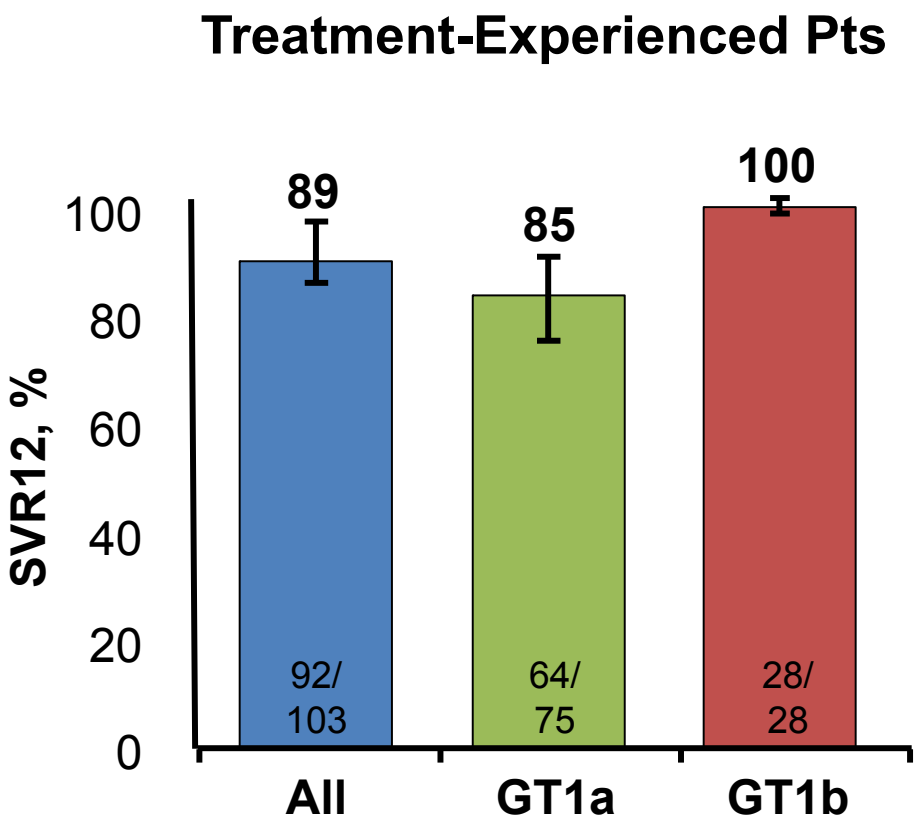
C-WORTHY: Efficacy of Grazoprevir + Elbasvir ± RBV x 12 or 18 Wks

Null Responders With or Without Cirrhosis



Lawitz E, et al. AASLD 2014. Abstract 196.

UNITY-1: 12 weeks of Daclatasvir + Asunaprevir + Beclabuvir in Noncirrhotic, GT1



Poordad F, et al. AASLD 2014. Abstract LB-7.

Overall Summary

- Multiple IFN-free options are available
  - Treatment experienced duration
    - Non-cirrhosis: 12 weeks
    - Cirrhosis: 24 weeks
  - Increased efficacy (SVR > 90%)
  - RBV not required for many regimens
  - Fewer side effects and drug-drug interactions
- All oral regimens preferred