How to improve the access to therapy in South and East: Romania

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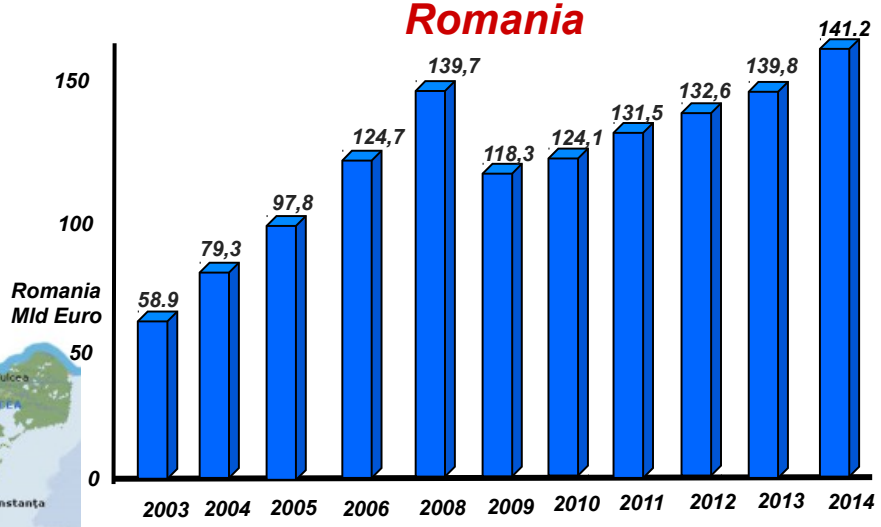
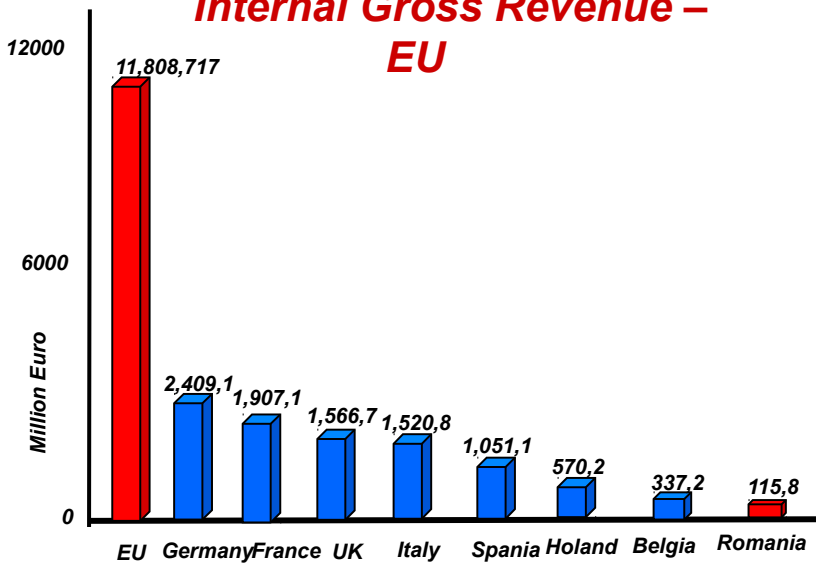
Romania

20 mil. Habitants;
5.6% HCV prevalence
99.5% GT1b

Internal Gross Revenue - Romania



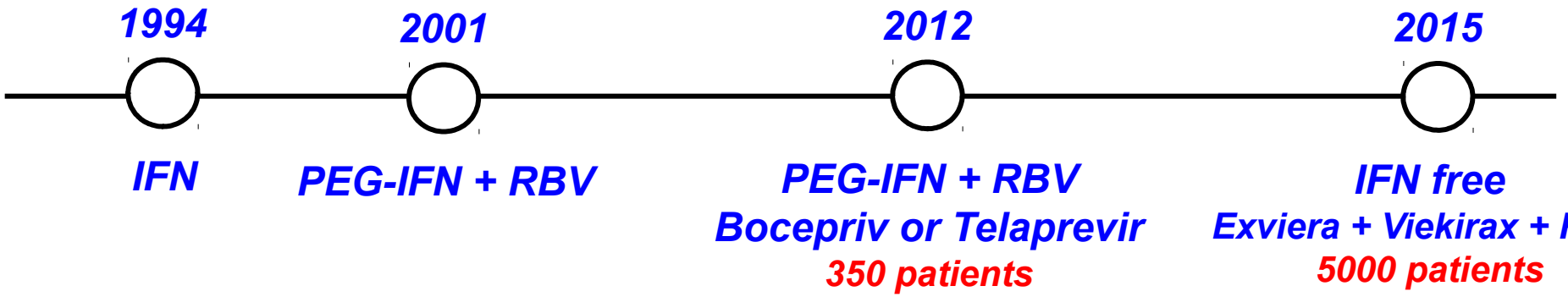
Internal Gross Revenue – EU



- Romania was financially exhausted and affected by poverty after the collapse of the communist regime. The budget allocated to Healthcare system was constantly low (4.5%), a reflection of a reduced Internal Gross Revenue comparing to Western countries (2 – 3 times less).

- Bureaucracy and poor management of resources amplified dramatically the deficit.

- Romania is one among other European countries where detection, prevention and treatment policies on viral hepatitis were implemented with a delay.



1994 ⟶ starts INF therapy: 4.000 patients

2001 ⟶ starts PEG INF + RIBA: 26.000 patients / 10 years

In 2013 The European Liver Patients Association (ELPA) has commissioned the independent Swedish Institute for Economic Analysis Quantify Research to conduct a study which estimates the economic burden of HCV in Romania and make recommendations. (Thanks to Achim Kautz and M. Voiculescu who provided the data).

2013 – PI first generation 350 patients.

2015 – Start the IFN free therapy with Exviera and Viekirax for 5000 patients.

For the moment, Government Insurance Fund provides funding only for treatment of patients with advanced fibrosis (F4). We expect very soon to extend the indication to F3.

Until now 1230 patients complete the tests, but only 750 were considered eligible.

Solutions to increase the patient's access to treatment

- *a better government funding;*
- *goals' efficiency by defining priorities and methodologies.*
- *better regional coordination concerning the screening of the diseases;*
- *simplifying and cost-accessibility of the detection and treatment*
- *measure results and implement corrective actions*
- *keeping the political decidents constantly aware in order to improve the system especially under the circumstances of the extended immigration.*

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Traitements des patients atteints de cirrhose

1. Quelle sont les bénéficies réele d'un traitement antivirale pour les patients atteints de cirrhose hépatique?

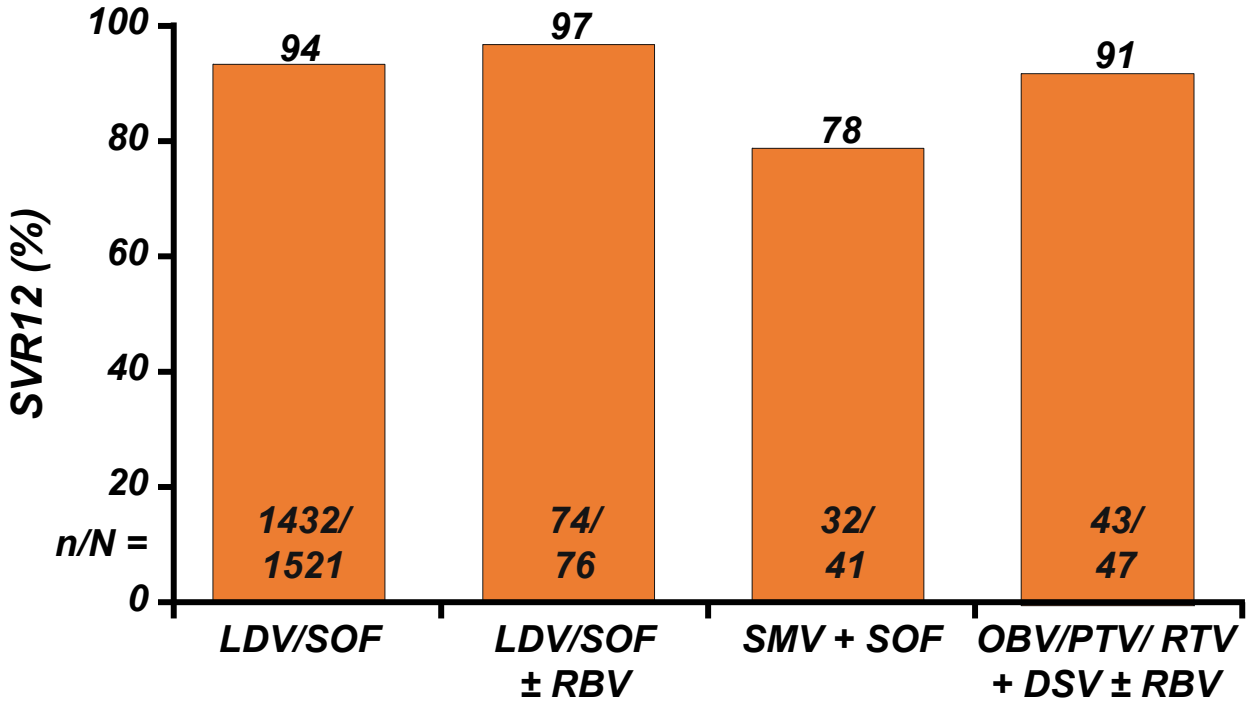
2. Dans tout les cas les patients atteints de cirrhose hépatique doivent-eux recevoir une thérapie antivirale?

3. Pour les patients atteints de cirrhose hépatique le rapport risque/ bénéfices justifie-t-il un traitement antivirale?

4. RBV est elle nécessaire dans le traitement de patients atteints de cirrhose?

TRIO: real-world analysis of predictors of DAA-based Tx failure in GT1 HCV

- Data obtained on GT1 HCV from Trio Health program
  - Includes pts with GT1 HCV who received 12-wk LDV/SOF, OBV/PTV/RTV + DSV, or SMV + SOF-based Tx 10/2014-3/2015 (N = 1685)



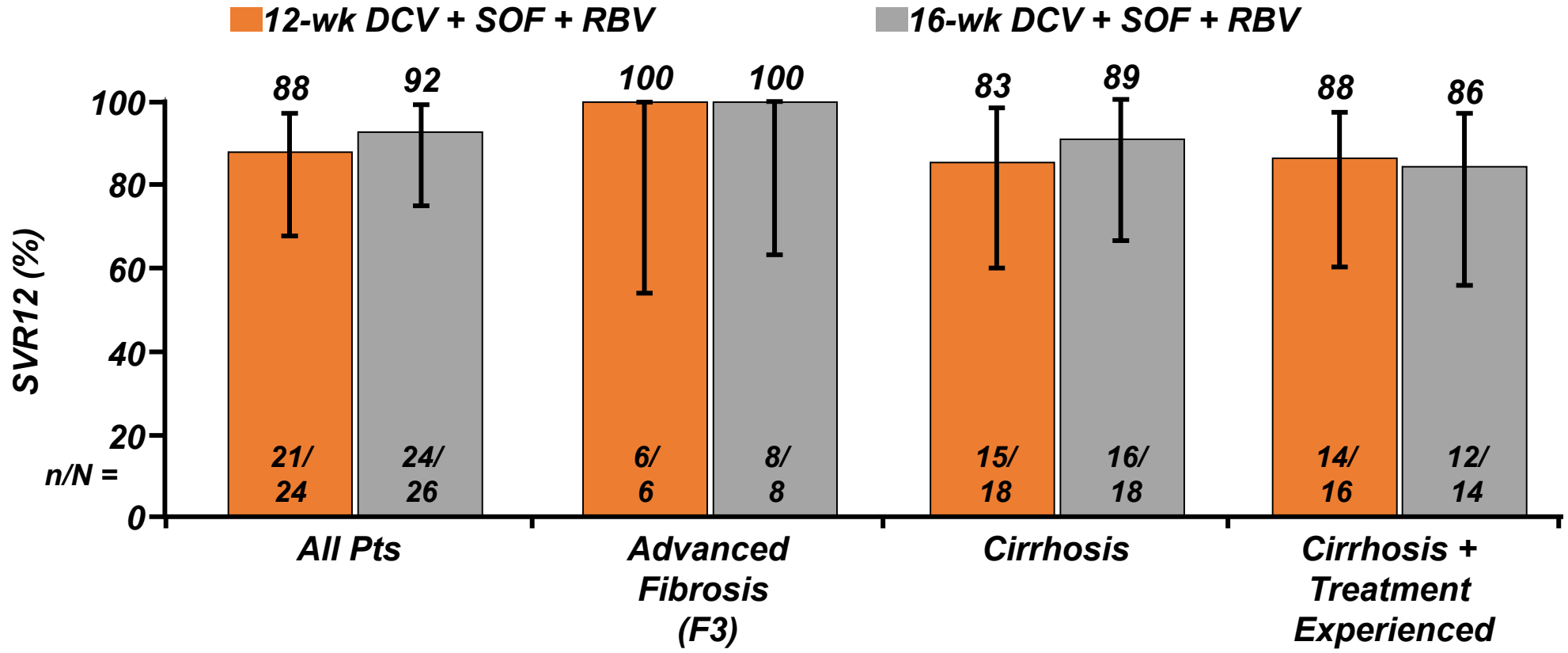
Factors Associated With Lower SVR Rate	P Value
Platelet count < 100K/mL	< .001
Cirrhosis	< .001
Prescribing outside of FDA-approved labeling*	< .001
Male sex	.008

*149/1685 pts treated outside of FDA-approved labeling.

Afdhal NH, et al. AASLD 2015. Abstract LB-17. Reproduced with permission.

Virologic Efficacy

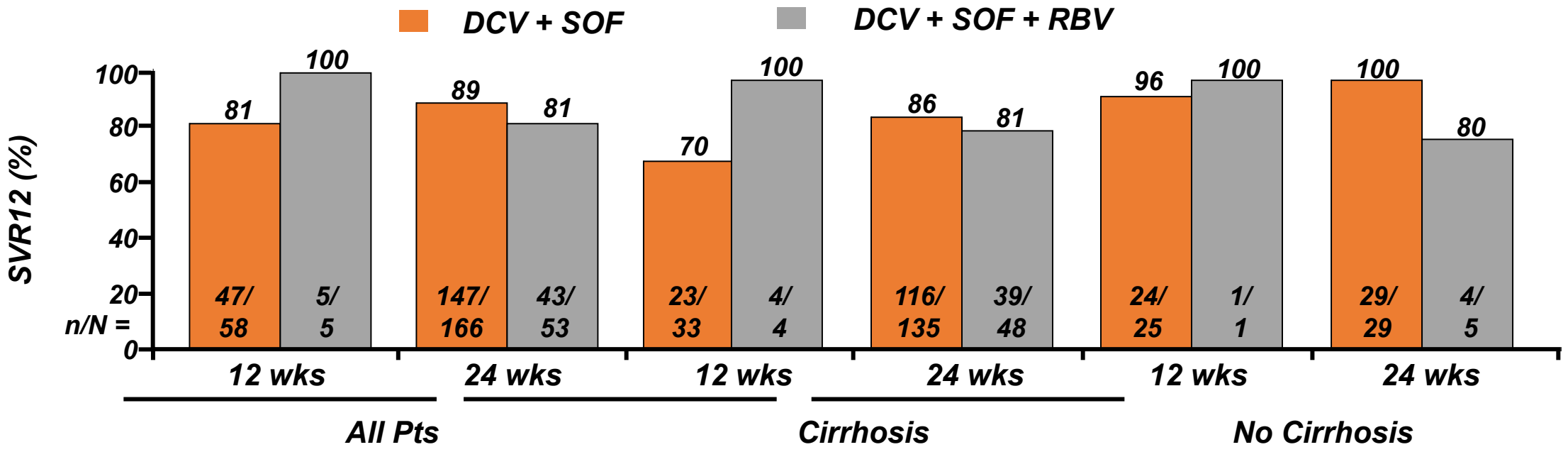
- **No virologic failures or AE-related discontinuations**



Leroy V, et al. AASLD 2015. Abstract LB-3. Reproduced with permission.

Interim Analysis: Daclatasvir + Sofosbuvir ± RBV in GT3 HCV in French CUP

- *Pts treated with DCV 60 mg + SOF 400 mg QD for 24 wks; RBV added or duration shortened to 12 wks per physician discretion*
- *Most common AEs: asthenia, sleep disorder, headache*
  - *Tx-related serious AEs (n = 1 each): hepatic decompensation, allergic dermatitis*



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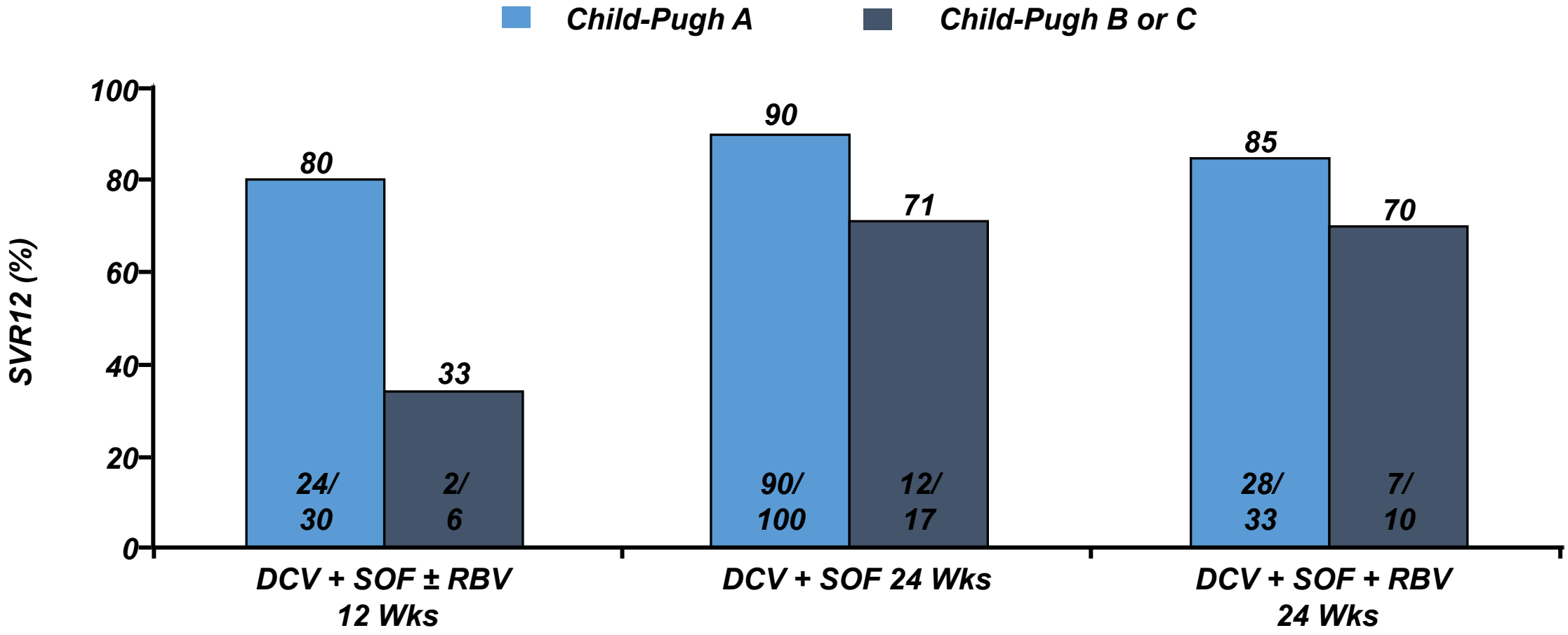
Interim Analysis of French CUP: SVR12 by Child-Pugh Score



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HCC risk after SVR With PegIFN ± RBV

- Retrospective VA cohort study of HCV-infected pts treated with pegIFN ± RBV from 1999-2009 (N = 22,028)
- HCC incidence rate 3.27/1000 PY with SVR vs 13.2/1000 PY without SVR (HR: 0.358)

Predictor of HCC Following SVR*	HR (95% CI)	P Value
Cirrhosis at time of SVR	4.45 (2.53-7.82)	< .0001
Age at SVR, yrs (vs younger than 55 yrs)		
• 55-64	2.40 (1.53-3.77)	.0002
• 65 or older	4.69 (2.04-10.78)	.0003
Diabetes	2.07 (1.35-3.20)	.0010
HCV GT (vs GT1)		
• 2	0.56 (0.32-1.01)	.0522
• 3	1.91 (1.14-3.18)	.0131

*Cox proportional hazards model adjusted for competing risk of death.

El-Serag HB, et al. AASLD 2015. Abstract 90. Reproduced with permission.

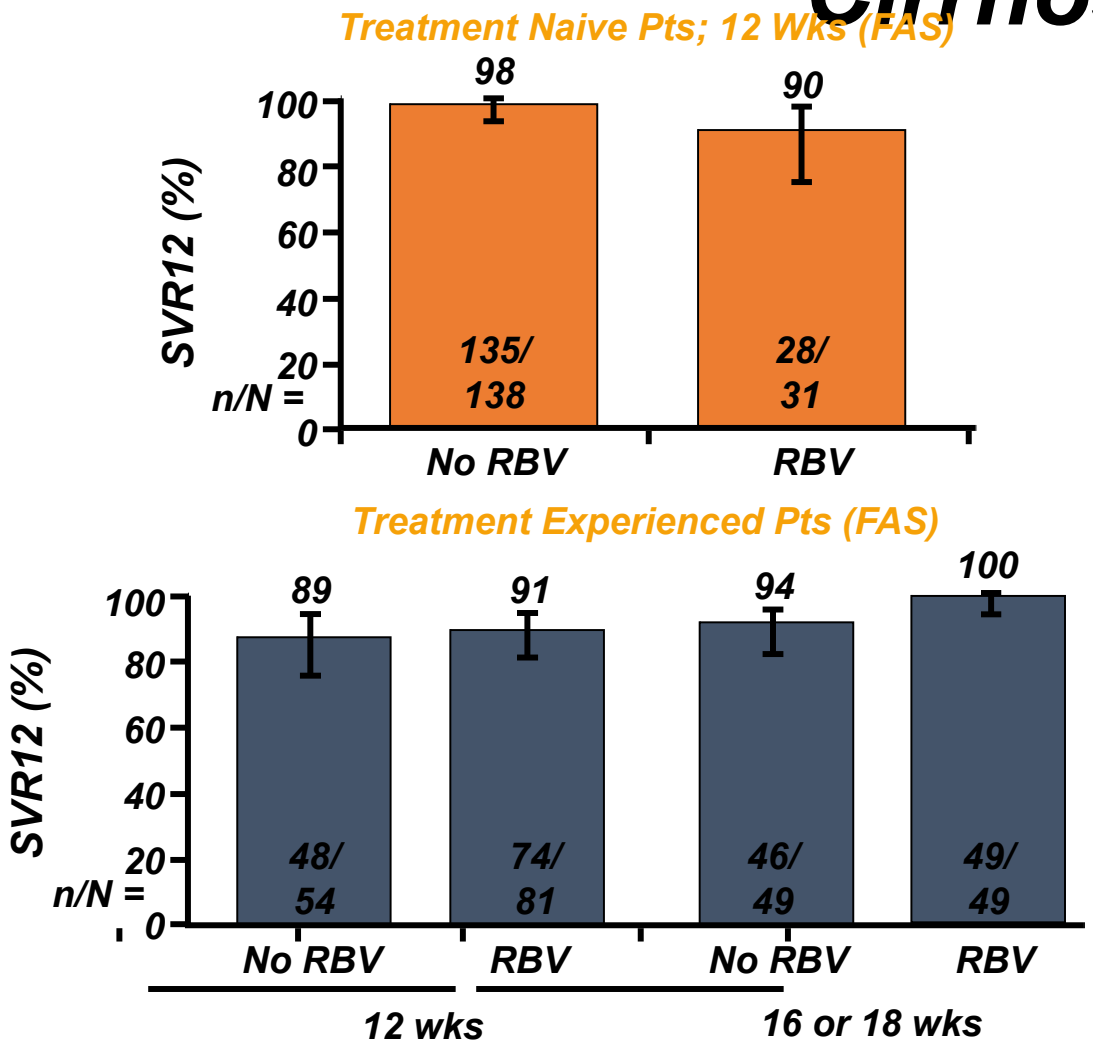
Elbasvir/Grazoprevir in compensated Cirrhosis: pooled analysis of Ph II/III data

- *Includes pts with Child-Pugh A cirrhosis and GT1, 4, or 6 HCV who received elbasvir/grazoprevir ± RBV in phase II/III trials*
  - *Treatment-naive pts treated for 12 wks (n = 169)*
  - *Treatment-experienced pts treated for 12, 16, or 18 wks (n = 233)*
  - *FAS: all randomized pts who received ≥ 1 dose of drug*
  - *Modified FAS: FAS, excluding pts who discontinued for reasons unrelated to study drug*

HCV Genotype, n (%)	*Pts (N = 402)*
1a	*219 (54.5)*
1b	*152 (37.8)*
1 other	*5 (1.2)*
4	*23 (5.7)*
6	*3 (0.8)*

Jacobson IM, et al. AASLD 2015. Abstract 42.

Elbasvir/Grazoprevir in compensated Cirrhosis: SVR12



- Treatment-naive pts: SVR12 rates similar regardless of RBV use, HCV subtype in FAS and regardless of platelets, cirrhosis determination method, FibroScan score in mFAS
  - SVR12 rate range across subgroups treated without RBV: 96% to 100%
- Previous relapsers (mFAS): SVR12 rates not affected by treatment duration or RBV use
- Previous nonresponders (mFAS): SVR12 rates lower with 12-wk, no RBV vs 16/18-wk, + RBV treatment
  - GT1: 92% vs 100%
  - GT4: 67% vs 100%

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Elbasvir/Grazoprevir in compensated Cirrhosis: safety

Safety Outcome (FAS), %	Elbasvir/Grazoprevir (n = 264)	Elbasvir/Grazoprevir + RBV (n = 193)
Drug-related AE	42.0	73.1
Serious AE	3.0	3.1
Serious drug-related AE	0.4	0
Discontinuation for AE	0.4	2.1
Discontinuation for lab abnormality*	0.4	0
Death†	0.4	0.5
AEs in > 10% pts		
• Fatigue	15.2	30.6
• Headache	16.7	20.7
• Nausea	4.2	13.5

*ALT elevation with increased eosinophils. †Coronary artery disease (n = 1), car accident (n = 1).

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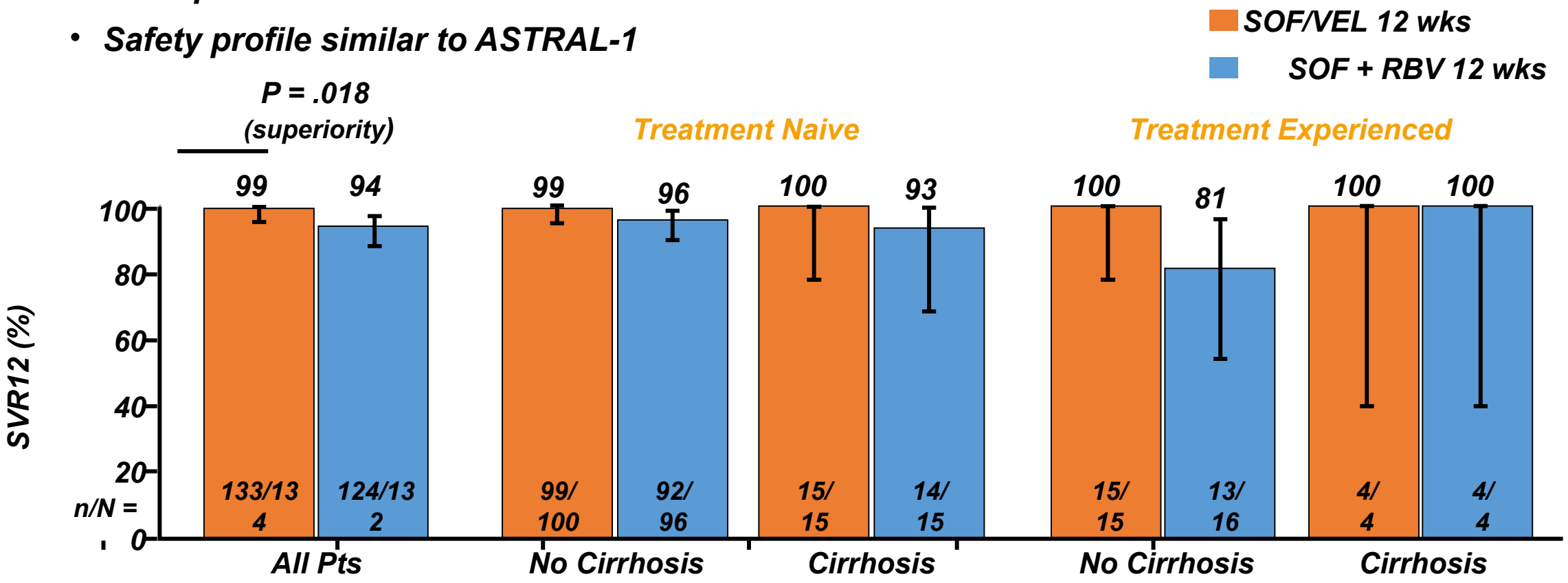
ASTRAL-2 open-label trial: SVR12, safety with Sofosbuvir/Velpatasvir in GT2 HCV

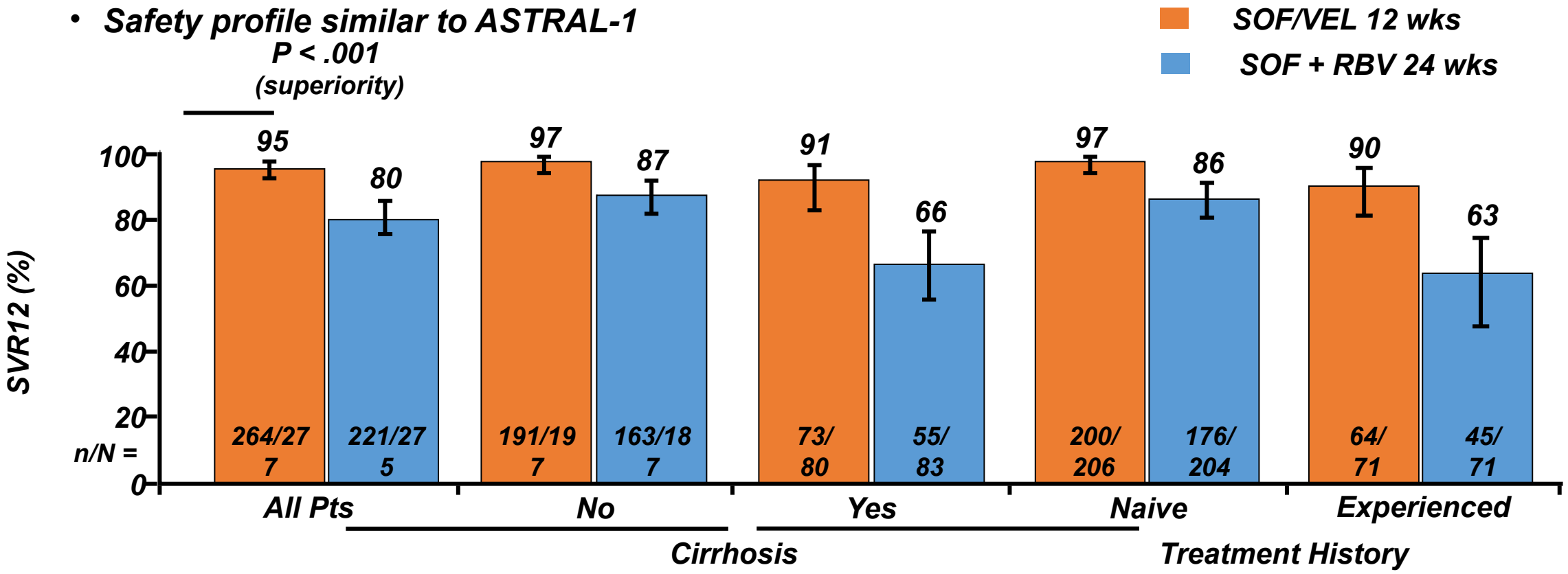
- No impact of BL NS5A RAVs on SVR rates
- Safety profile similar to ASTRAL-1



Sulkowski MS, et al. AASLD 2015. Abstract 205. Reproduced with permission. Foster GR, et al. N Engl J Med. 2015;[Epub ahead of print].

ASTRAL-3 open-label trial: SVR12, safety with Sofosbuvir/Velpatasvir in GT3 HCV

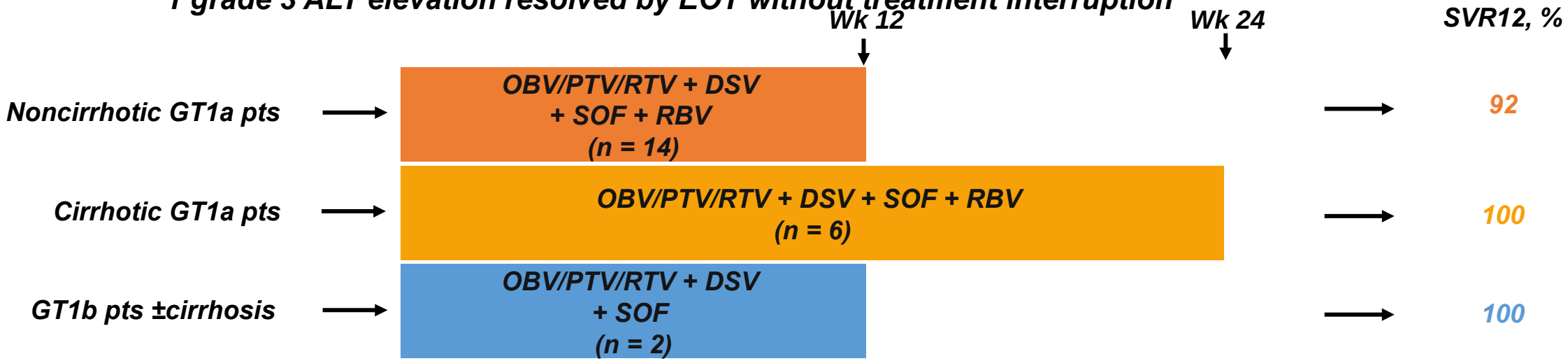
- SVR12 rate numerically lower with vs without BL NS5A RAVs (88% vs 97%)
- Safety profile similar to ASTRAL-1



Mangia A, et al. AASLD 2015. Abstract 249. Reproduced with permission.
Foster GR, et al. N Engl J Med. 2015;[Epub ahead of print].

QUARTZ-I: OBV/PTV/RTV + DSV + SOF ± RBV for DAA-Exp'd pts with GT1 HCV

- Multicenter, open-label, phase II study
  - Previous Tx: 73% OBV/PTV/RTV ± DSV; 9% TPV + PR; 9% SOF + RBV or SOF + PR; 4.5% SMV + SOF; 4.5% SMV + samatasvir + RBV
- Majority of AEs mild to moderate
  - 2 serious AEs not related to study drugs (pneumonia and cellulitis)
  - 1 grade 3 ALT elevation resolved by EOT without treatment interruption



OBV/PTV/RTV 25/150/100 mg QD + DSV 250 mg BID; SOF 400 mg QD; weight-based RBV.

Poordad F, et al. AASLD 2015. Abstract LB-20.