# *Traitements des patients atteints de cirrhose*

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

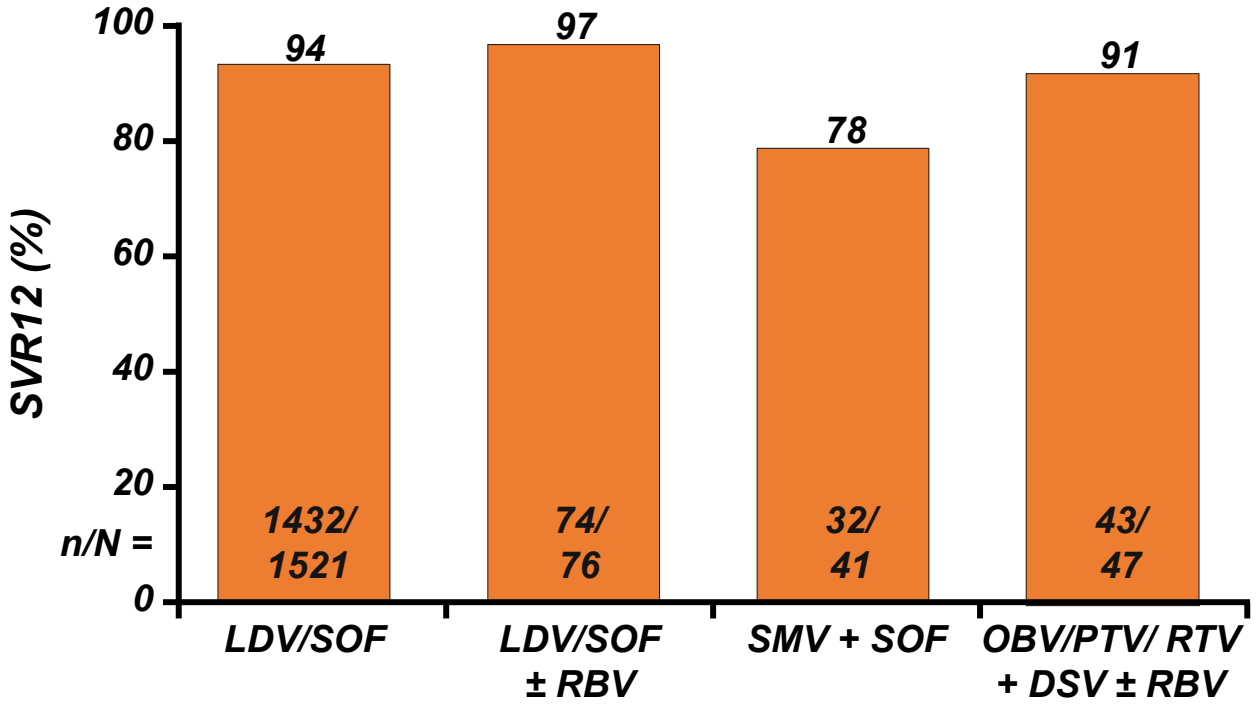
*2. Dans tout les cas les patients atteints de cirrhose hépatique doivent-eux recevoir une thérapie antivirale?*

*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)



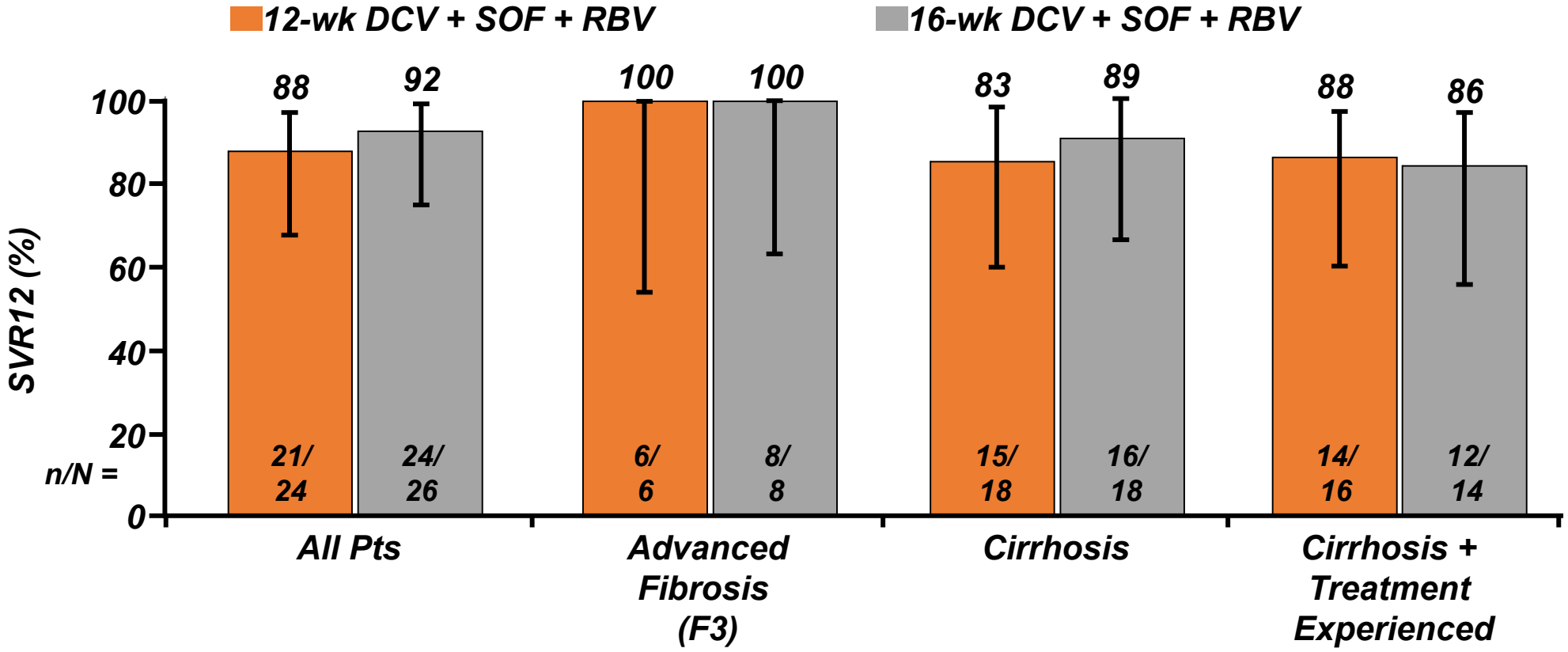

| Factors Associated With Lower SVR Rate | P Value |
|---|---|
| Platelet count < 100K/mL | < .001 |
| Cirrhosis | < .001 |
| Prescribing outside of FDA-approved labeling* | < .001 |
| Male sex | .008 |

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

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

# Virologic Efficacy

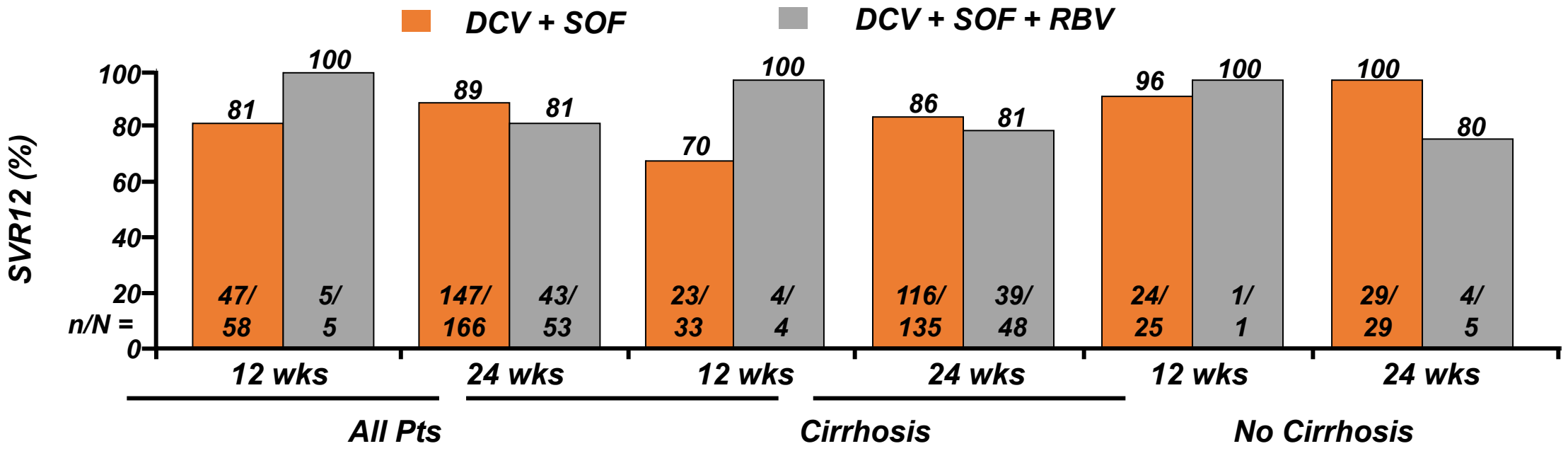
- **No virologic failures or AE-related discontinuations**




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

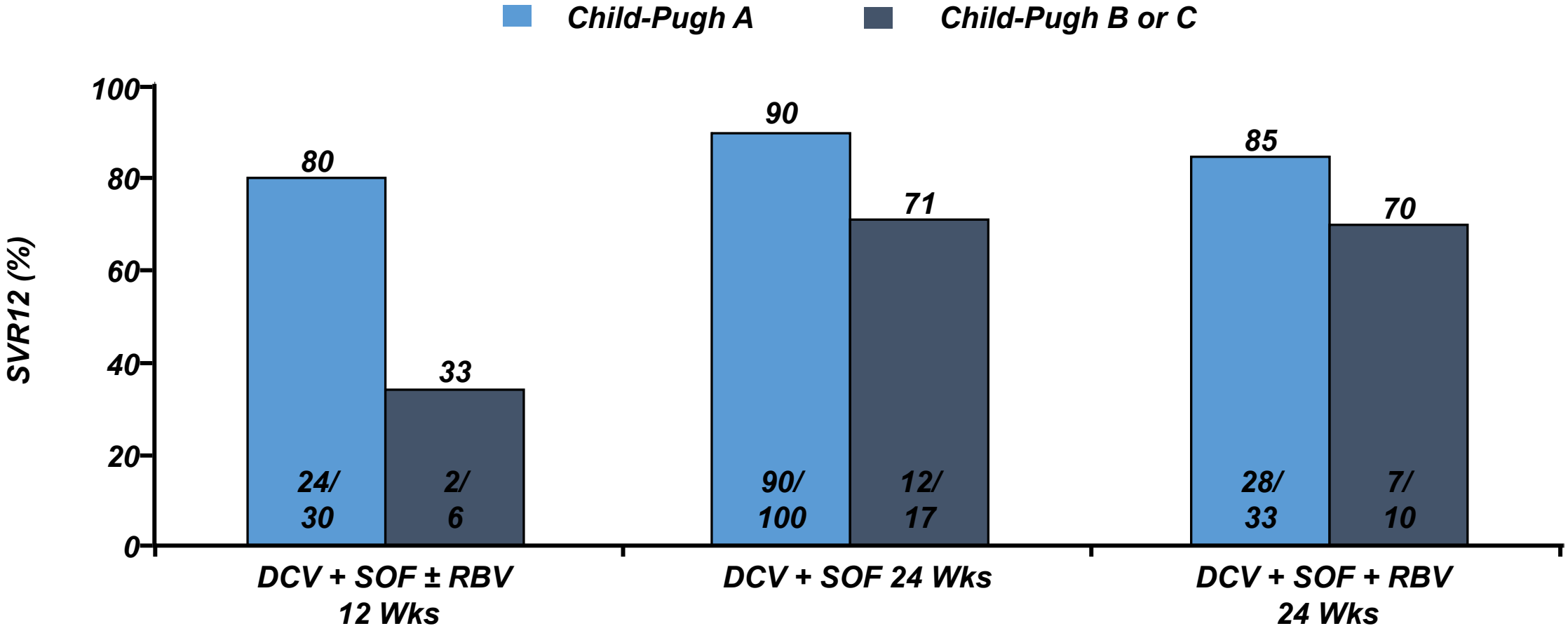
# *Interim Analysis: Daclatasvir + Sofosbuvir ± RBV in GT3 HCV in French CUP*

- *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*




*Hezode C, et al. AASLD 2015. Abstract 206. Reproduced with permission.*

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




Hezode C, et al. AASLD 2015. Abstract 206. Reproduced with permission.

# 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.

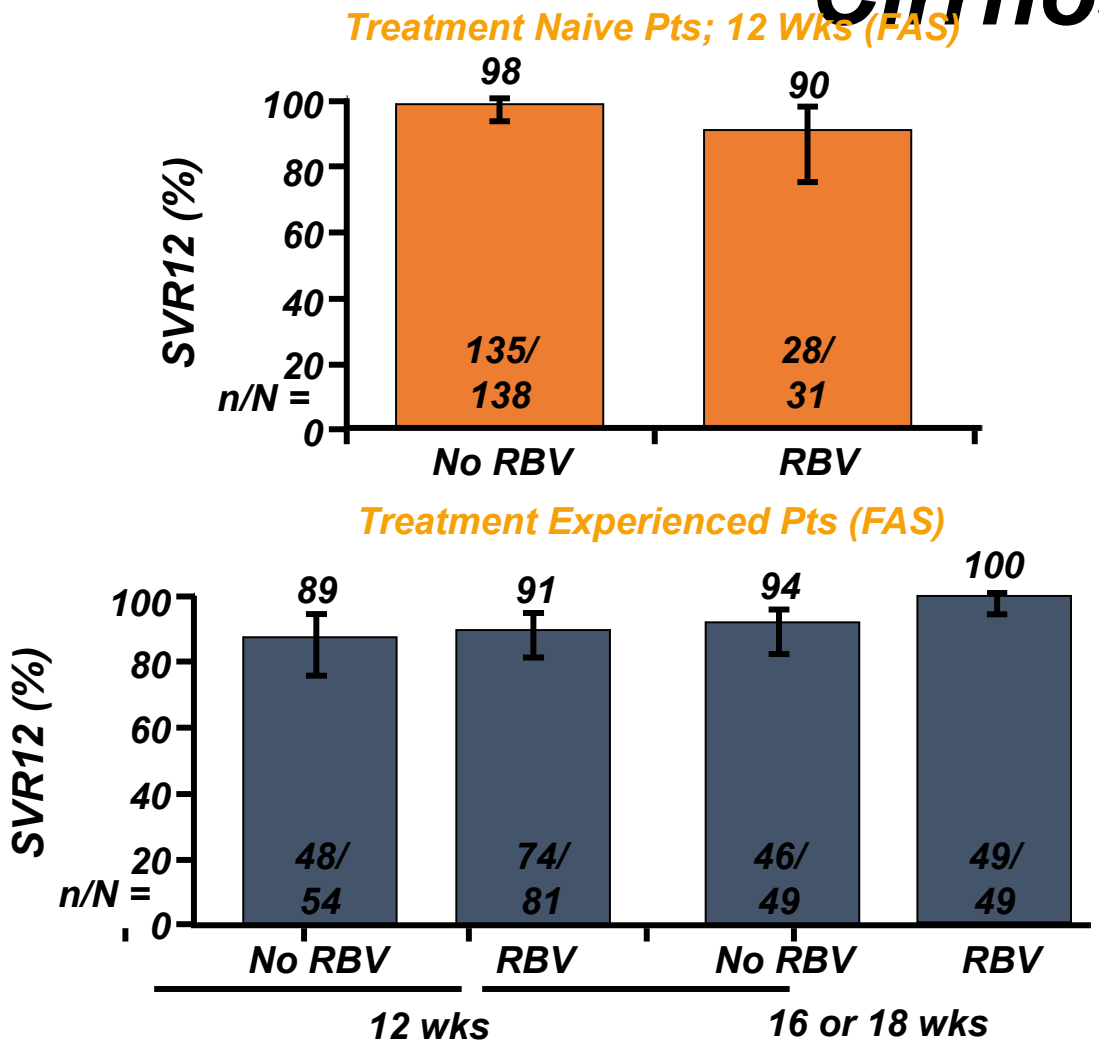
# *Elbasvir/Grazoprevir in compensated Cirrhosis: pooled analysis of Ph II/III data*

- *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%

Jacobson IM, et al. AASLD 2015. Abstract 42. Reproduced with permission.

# Elbasvir/Grazoprevir in compensated Cirrhosis: safety

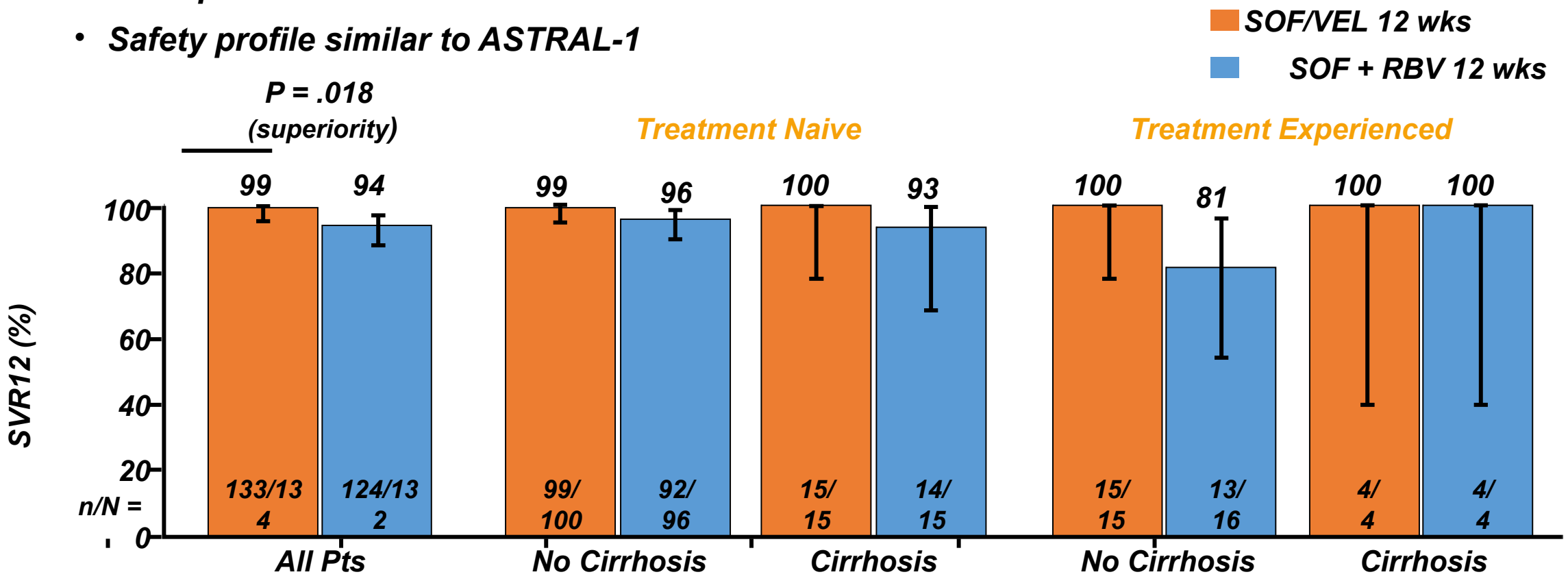
| Safety Outcome (FAS), % | Elbasvir/Grazoprevir (n = 264) | Elbasvir/Grazoprevir + RBV (n = 193) |
|---|---|---|
| Drug-related AE | 42.0 | 73.1 |
| Serious AE | 3.0 | 3.1 |
| Serious drug-related AE | 0.4 | 0 |
| Discontinuation for AE | 0.4 | 2.1 |
| Discontinuation for lab abnormality* | 0.4 | 0 |
| 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).

Jacobson IM, et al. AASLD 2015. Abstract 42. Reproduced with permission.

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

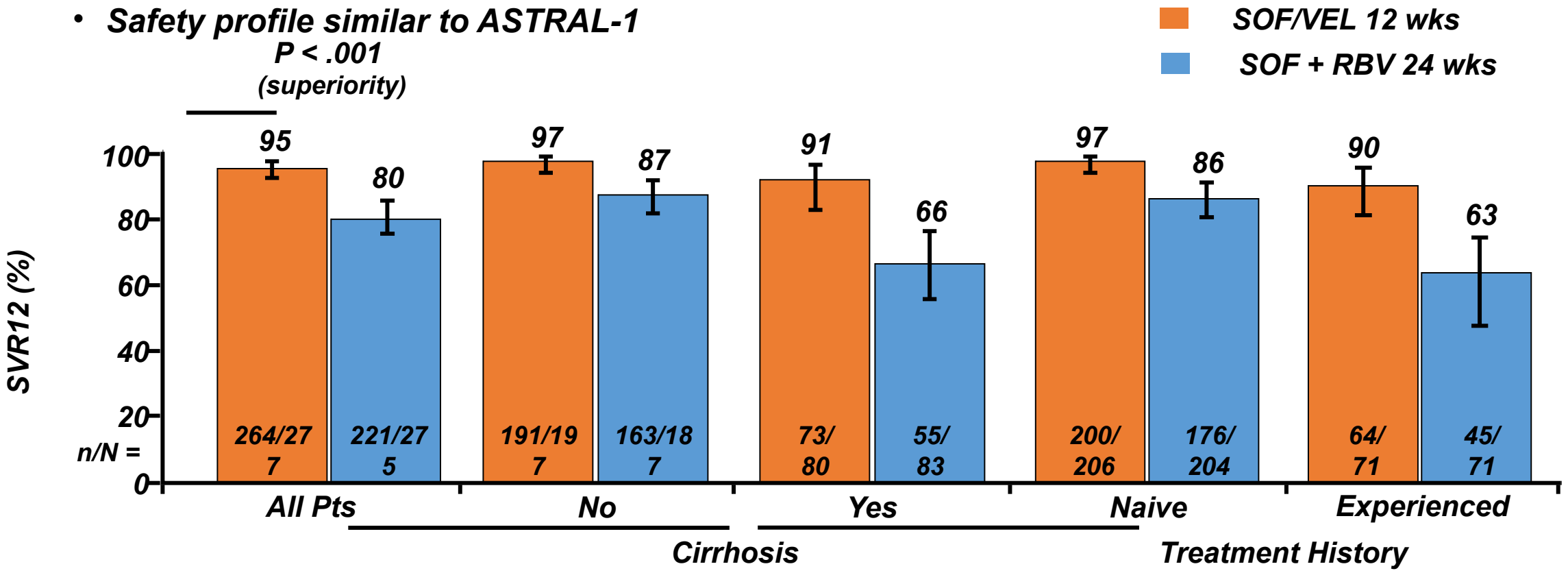
- No impact of BL NS5A RAVs on SVR rates
- Safety profile similar to ASTRAL-1




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

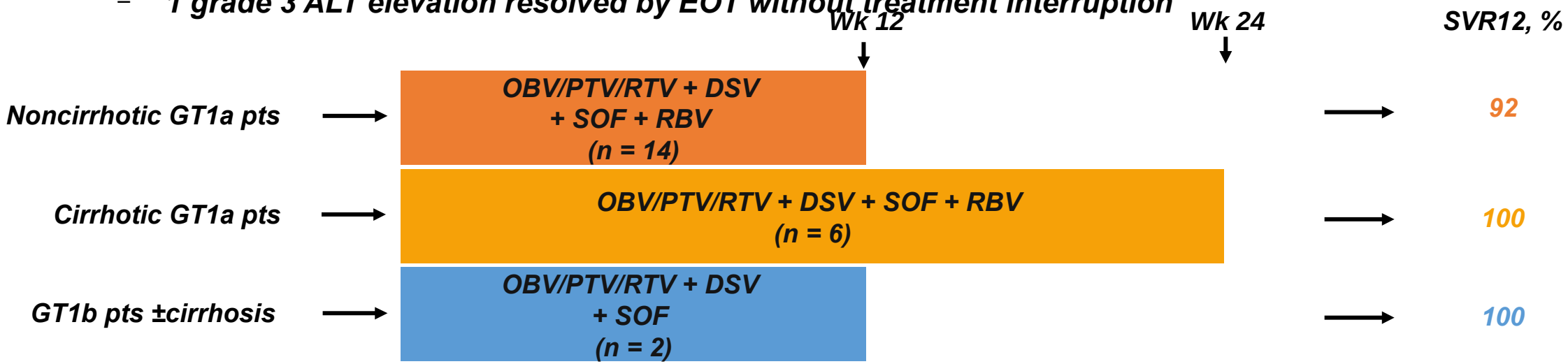
- SVR12 rate numerically lower with vs without BL NS5A RAVs (88% vs 97%)
- Safety profile similar to ASTRAL-1




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.