

Hepatitis C in The US: Therapy Decision Making

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Case 1



Case: Genotype 1

- 55 yo African-American male having recently found to be anti-HCV positive with birth cohort screening at his PCP's office
- Additional preliminary testing:
 - HCV RNA 4.5 million IU/mL
 - Genotype 1A
 - ALT 60 IU/mL. Prior records show ALT 42 IU/mL 5 years ago



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Additional History and Exam

- Source of HCV acquisition unknown: No history of IDU, blood transfusions, etc. Served in military but no combat.
- Rare alcohol use (<1/month)
- PH: Overweight, controlled HT, diet controlled diabetes, GERD
- Meds: amlodipine and prn omeprazole
- Exam: BMI 31; mild hepatomegaly, palmar erythema; otherwise normal



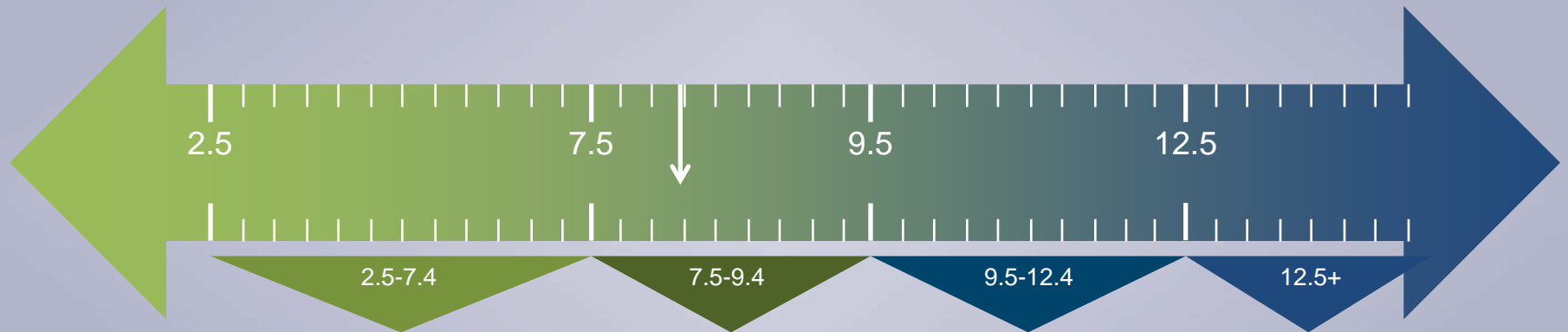
Additional Work-Up

- CBC: WBC 4.5, Hgb 12.2, Plts 142K; INR: 1.2
- AST 55, ALT 43, ALP 112, TB 0.7, Alb 3.3, TP 7.4, BUN 11, creatinine 1.1
- Hgb A1C 6.4, triglycerides 245, LDL/HDL cholesterol normal
- Iron studies normal, HAV and HBV immune
- Fib4 score is 0.53
- APRI = 0.49
- Fibroscan: 8.0



Fibroscan Score

8.0 kPa



F0/F1

**NO, OR MILD
FIBROSIS**

Indicates no or minimal liver fibrosis and no evidence of progressive liver disease

F2

**MODERATE
FIBROSIS**

Indicates significant liver fibrosis and evidence of progressive liver disease

F3

**SEVERE
FIBROSIS**

Indicates severe liver fibrosis and high risk progression to cirrhosis

F4

CIRRHOSIS

Indicates extensive liver fibrosis consistent with cirrhosis

Next Steps....

- Treatment candidate?
 - Insurance type?
- Additional testing needed?
 - Based on insurance
 - Labs within 30 days
 - Drug testing, alcohol testing
- Counseling messages?
 - PPI use?



Highest Priority

- Advanced fibrosis or compensated cirrhosis
- Organ transplant
- Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis)
- Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis



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Highest priority

- Fibrosis (Metavir F2)
- HIV-1 or HBV coinfection
- Other coexistent liver disease (eg, [NASH])
- Debilitating fatigue
- Type 2 Diabetes mellitus (insulin resistant)
- Porphyria cutanea tarda



Treatment Options

1. Ledipasvir/Sofosbuvir x 12 weeks
2. Paritaprevir/r/ombitasvir + dasabuvir + ribavirin x 12 weeks
3. Daclatasvir + sofosbuvir X 12 weeks
4. Simeprevir + sofosbuvir x 12 weeks
5. Sofosbuvir + ribavirin X 24 weeks



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LIVER AND BILIARY

What if:

- Genotype 1B?
 - 3D without RBV?
- Albumin 2.7, total bilirubin 2.1, creatinine 1.2?
 - Can you use any protease inhibitor?
- Prior treatment failure with telaprevir/P/R?
 - Data supporting which regimens?



Case 2



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UT HEALTH SCIENCE CENTER
WE HEAR, LIVE BETTER
LAX AND DALLAS

72 Year Old Woman with Compensated Cirrhosis

- HCV genotype 1b
- Probably acquired 40 years ago when transfused for postpartum hemorrhage
- Cirrhosis (Metavir F4) on biopsy in 2011
- Had virologic breakthrough during course of PEG/RBV and telaprevir in 2011
- Complains of chronic fatigue
- Physical examination: palpable spleen tip
- Labs: ALT 58 U/L, AST 71 U/L, albumin 3.5 g/dL, platelets 90,000 cells/mm³, hemoglobin 11.8 g/dL, AFP 13 ng/mL
- MRI nodular liver contour, no focal liver lesions, spleen 16 cm



Treatment-Experienced GT1 Cirrhotic

Would you do anything else to assess hepatic fibrosis?

- Fibroscan 24 kPa

Any other measures while arranging treatment?

- EGD: Grade 1 varices, too small for banding
- Would you start beta blockers?

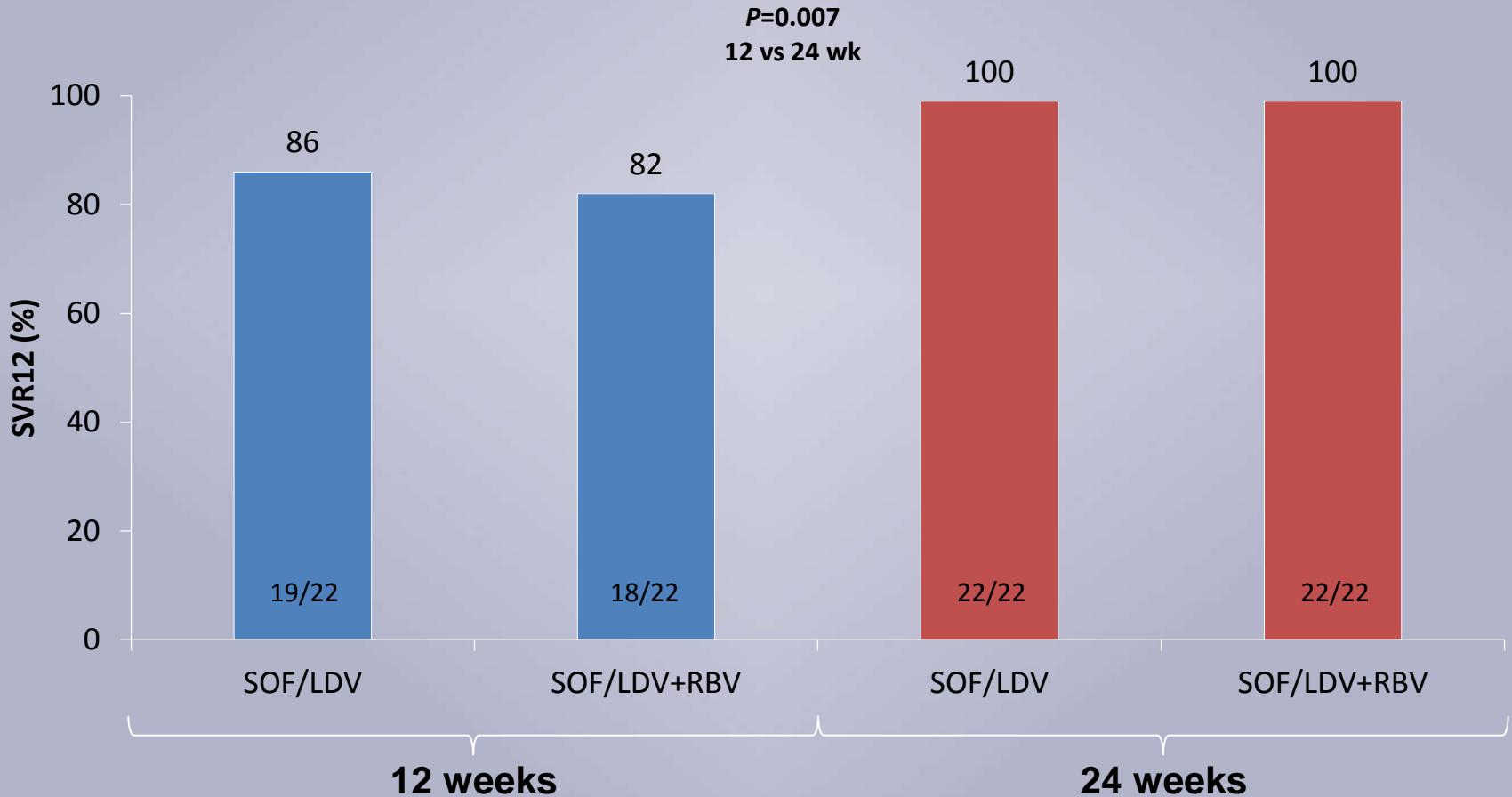


Question

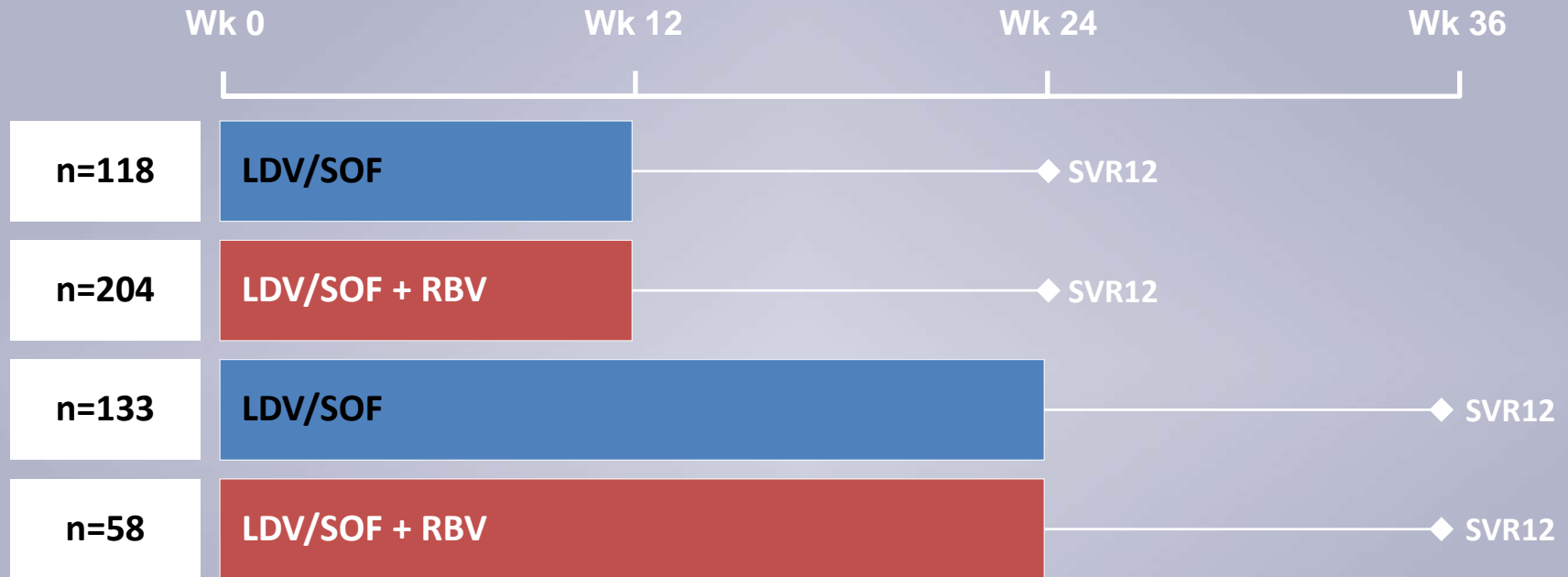
- How would you treat this patient?
 - Ledipasvir/sofosbuvir 24 weeks
 - Ledipasvir/sofosbuvir + RBV 12 weeks
 - Paritaprevir/ritonavir/ombitasvir + dasabuvir 12 weeks
 - Simeprevir plus sofosbuvir 24 weeks
 - Daclatasvir plus sofosbuvir 24 weeks
- Would your decision be different if she had failed PEG/RBV without a protease inhibitor?

ION-2: Ledipasvir + Sofosbuvir ± RBV

Genotype 1 Treatment Experienced Patients With Cirrhosis



Integrated Analysis of Cirrhotic Patients From the Ledipasvir/Sofosbuvir Development Program



- 513 patients with HCV GT 1, compensated cirrhosis
- Pooled data from Phase 2 and 3 LDV/SOF ± RBV studies
 - LONESTAR, ELECTRON, ELECTRON-2, 337-0113, ION-1, ION-2, SIRIUS
- Primary efficacy endpoint: SVR12



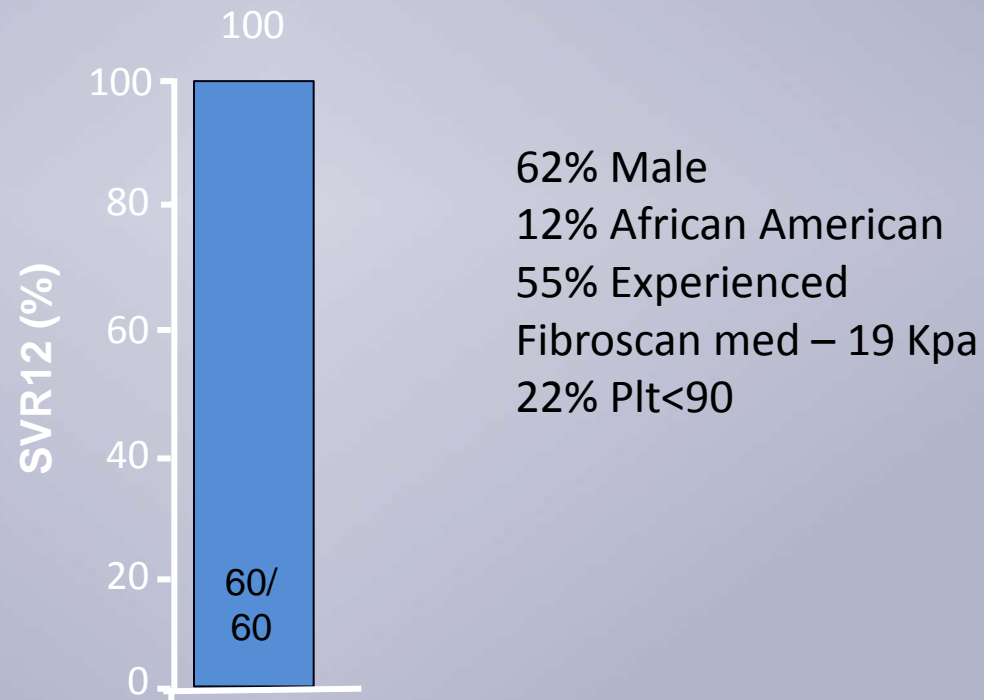
Integrated Analysis: SVR12 by Treatment Regimen

		Total	Treatment Naïve	Treatment Experienced
Overall SVR12		96%	98%	95%
Duration	12 wk	95%	97%	94%
	24 wk	98%	99%	98%
Regimen	LDV/SOF	95%	96%	95%
	LDV/SOF + RBV	97%	99%	96%
Duration/ ± RBV	LDV/SOF 12 wk	92%	96%	90%
	LDV/SOF + RBV 12 wk	96%	98%	96%
	LDV/SOF 24 wk	98%	97%	98%
	LDV/SOF + RBV 24 wk	100%	100%	100%

SVR12, %

TURQUOISE III: RBV-free 12 week option for G1b cirrhotics

Paritaprevir/r + ombitasvir + dasabuvir x 12 weeks **WITHOUT** RBV
In **G1b** naïve/experienced cirrhotics



Case 3



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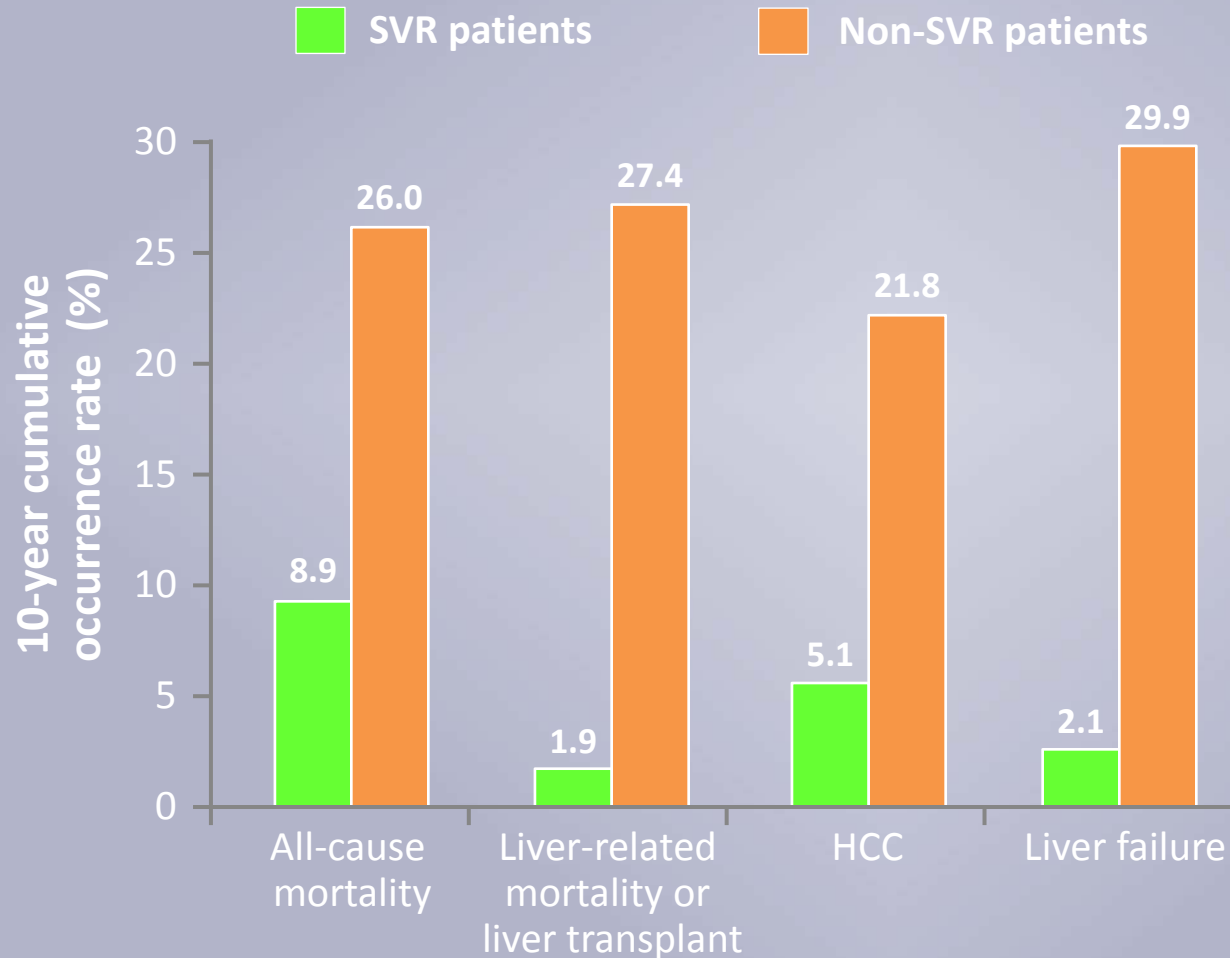
54 Year Old Woman with Compensated Cirrhosis and Small HCC

- HCV genotype 3A
- Cirrhosis (Metavir F4) on biopsy in 2010
- Prior treatment with PEG/RBV in 2011 with response but relapse
- Physical examination: palpable spleen tip
- Labs: ALT 58 U/L, AST 71 U/L, albumin 3.5 g/dL, platelets 80,000 cells/mm³, hemoglobin 11.8 g/dL, AFP 113 ng/mL
- MRI nodular liver contour, spleen 16 cm, 2.5 cm hypervascular lesion with washout in right lobe consistent with HCC
- She has been referred for consideration of liver transplantation



SVR and All-cause Mortality in CHC Patients with Advanced Fibrosis

530 patients followed for a median of 8.4 years



Baseline factors significantly associated with all-cause mortality:

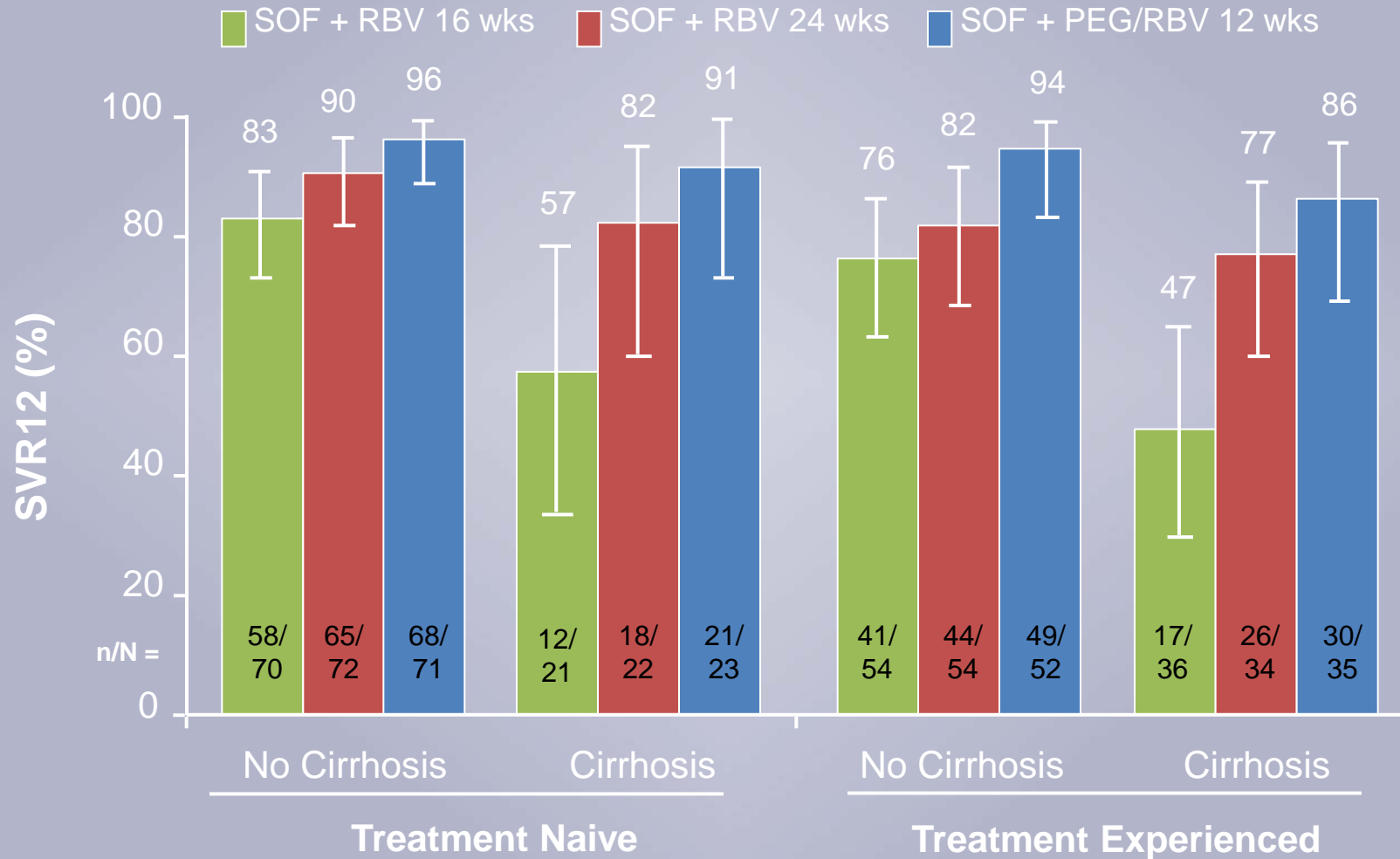
- Older age
- Genotype 3 (2-fold increase in mortality and HCC)
- Higher Ishak fibrosis score
- Diabetes
- Severe alcohol use

Question

- How would you treat this patient?
 - Sofosbuvir plus ribavirin for 24 weeks
 - Daclatasvir plus sofosbuvir 24 weeks
 - Daclatasvir plus sofosbuvir plus ribavirin for 12 weeks
 - Sofosbuvir plus peginterferon/ribavirin for 12 weeks
 - Something else

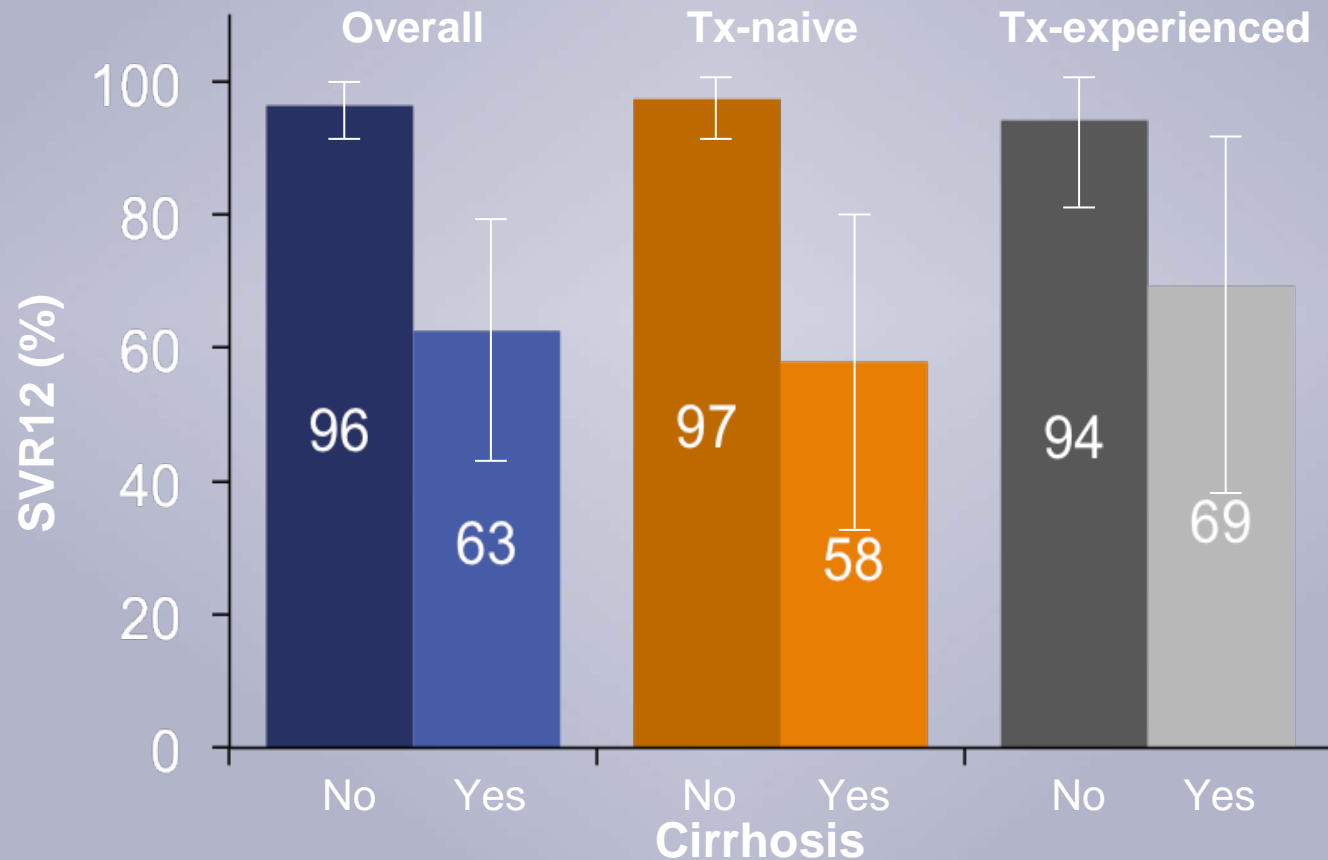


BOSON: SOF/RBV 16 vs 24 vs PEG/SOF/RBV x 12



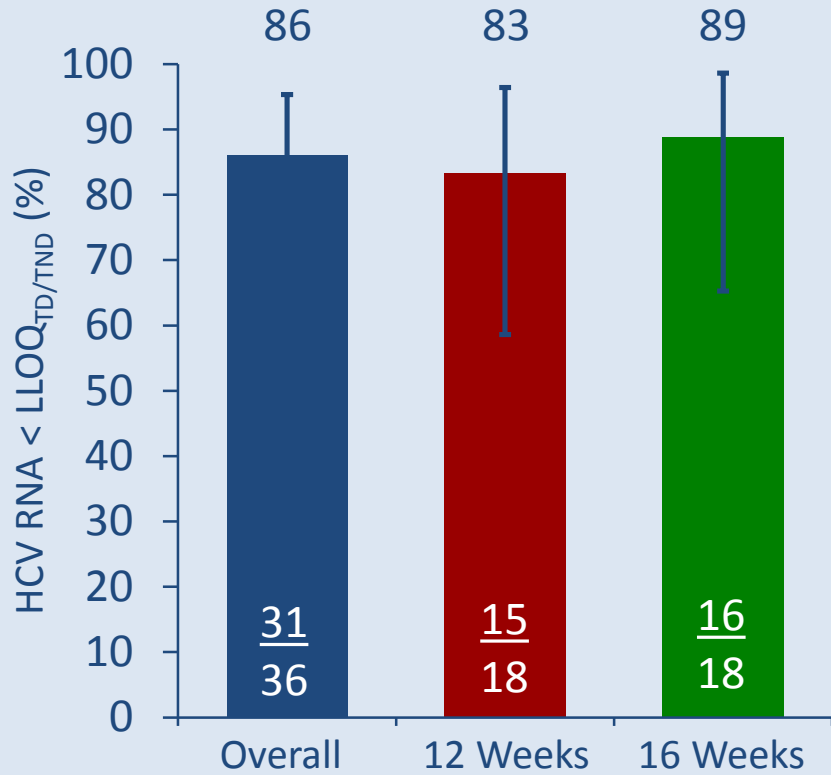
- **Clear advantage to PEG/RBV/SOF – especially in cirrhosis**
- **Only 1 trt-discontinuation – good safety**

DCV/SOF for GT 3: SVR12 in Patients With and Without Cirrhosis Treated for 12 Weeks (ALLY-3)



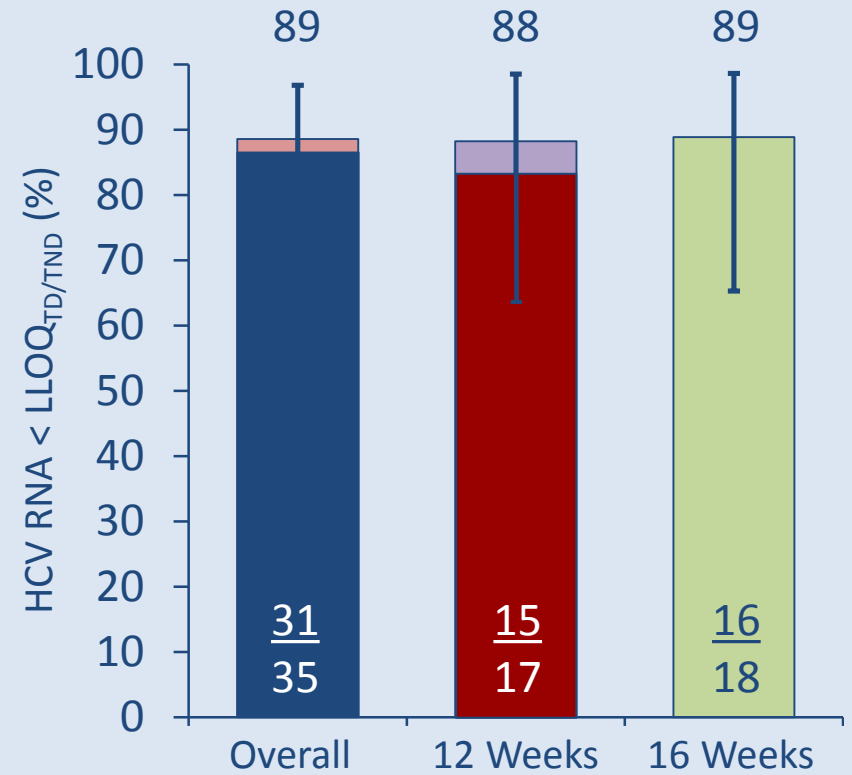
ALLY 3+ SVR12: Patients with Cirrhosis

ITT ANALYSIS



VBT^a	0	0	0
Relapse^b	4	2	2
Death^c	1	1	0

OBSERVED ANALYSIS



VBT	0	0	0
Relapse	4	2	2

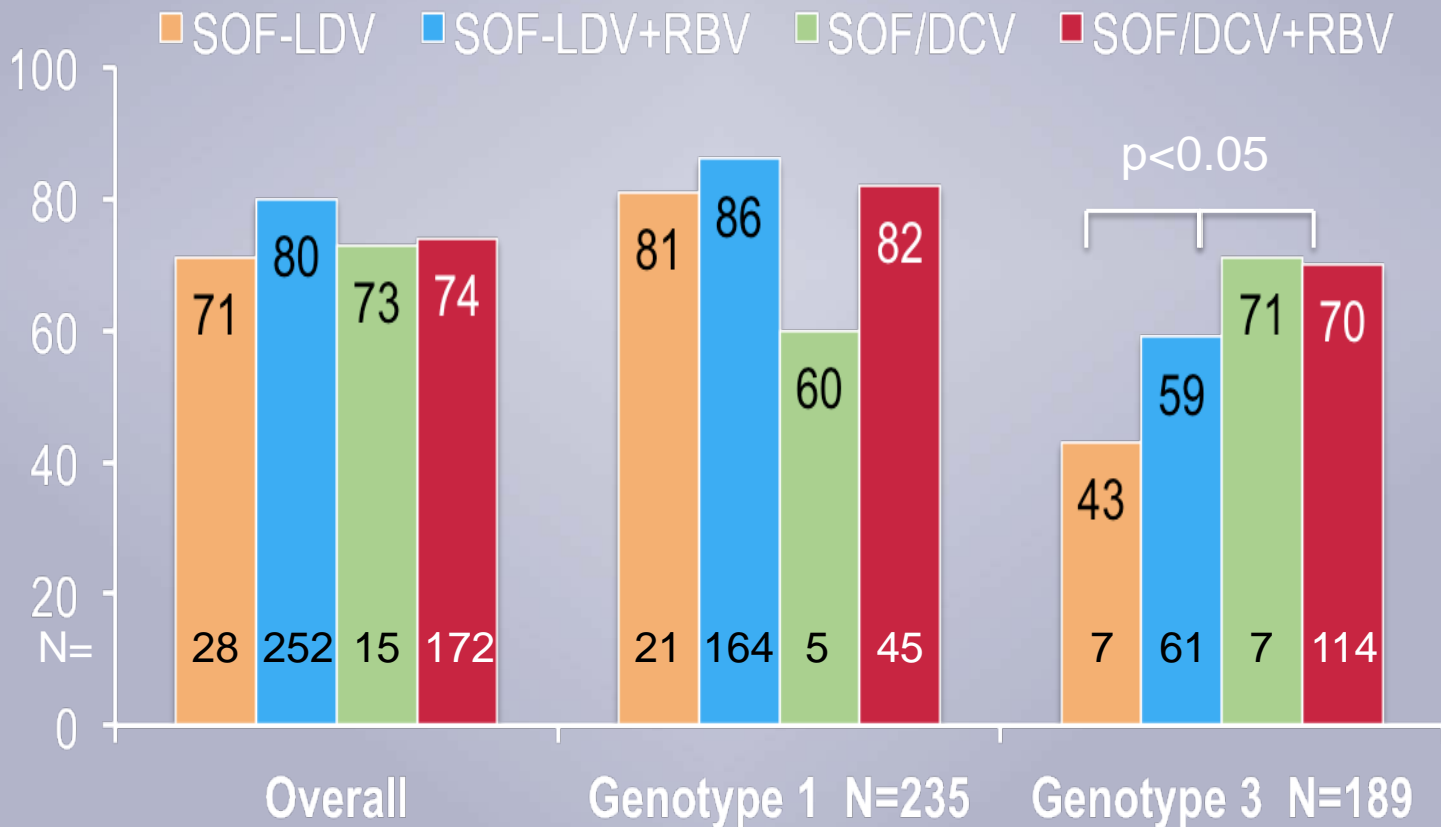
^a **VBT** (virologic breakthrough): confirmed HCV RNA $\geq 1 \log_{10}$ IU/mL above nadir, or \geq LLOQ if previously < LLOQ TD or TND;

^b **Relapse**: confirmed HCV RNA \geq LLOQ at any posttreatment visit following < LLOQ_{TND} at end of treatment;

^c Dilated cardiomyopathy on Day 72, not related to treatment; cirrhosis status diagnosed by liver biopsy (F4) n = 9; FibroScan ≥ 14.6 , n = 27.

SOF Plus NS5A Therapy for 12 Weeks in Decompensated Cirrhosis

UK Compassionate Access Program, 66% CP-B, 34% CP-C



Summary

- Geno 1a: SOF/LDV or 3D/RBV
- Geno 2: SOF/DAC or SOF/RBV
- Geno 3: SOF/DAC +/- RBV
- Geno 4: 2D/Rbv or SOF/LDV/RBV

