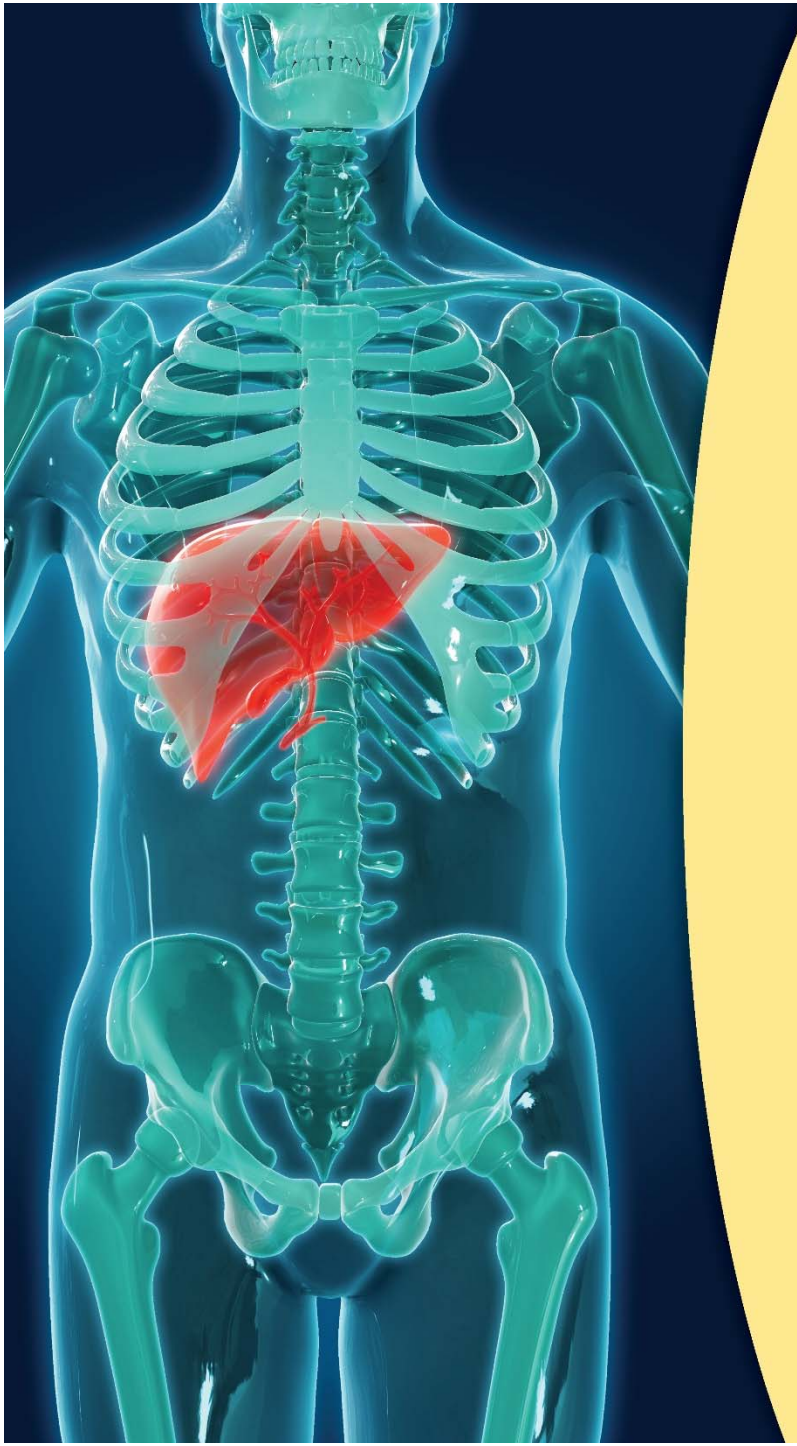

Complimentary CME/CE

Capacity Building in **Hepatitis C:**

Treating Special Populations

Presented by the AGA Institute and Med-IQ.

THE AMERICAN GASTROENTEROLOGICAL ASSOCIATION AGA

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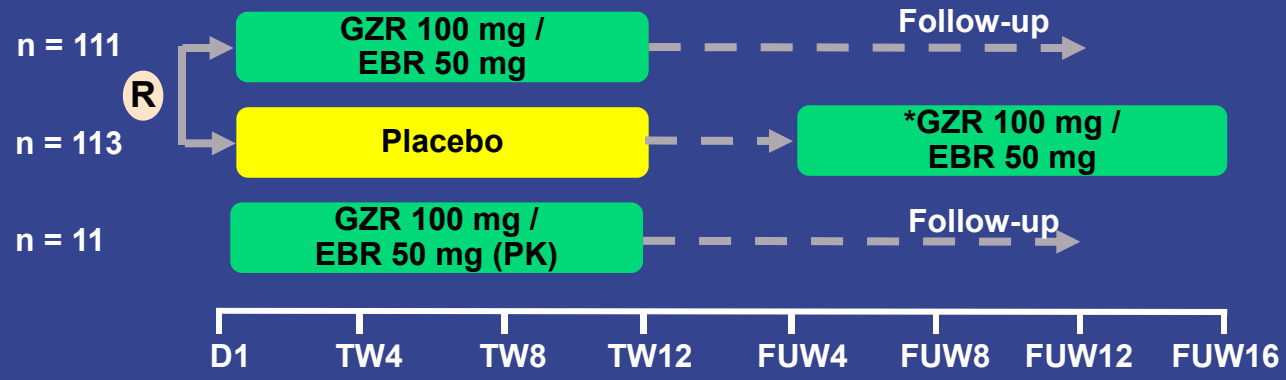
Learning Objective

After completing this educational activity, participants should be able to:

- Use patient characteristics and preferences to select HCV treatment strategies that maximize the potential of achieving a cure

GZR/EBR in Treatment-Naïve and -Experienced Patients With HCV Genotype 1 and CKD

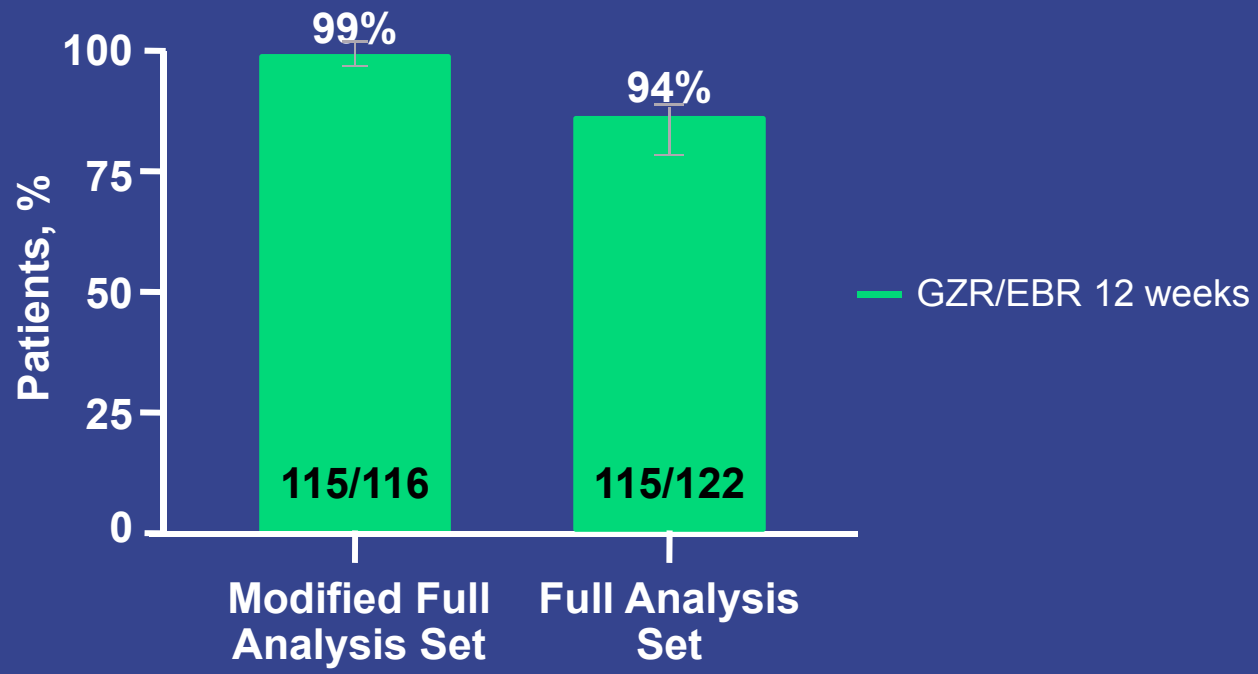


- Randomized, parallel-group, multisite, placebo-controlled trial
- Stratification by diabetes and hemodialysis status
- 224 patients randomized to immediate treatment with GZR/EBR or deferred treatment with placebo for 12 weeks then open-label GZR/EBR starting at FUW4
- 11 patients in open-label GZR/EBR arm underwent intensive PK sampling

*Deferred open-label treatment arm (all randomized patients remained blinded to treatment until FUW4). GZR and EBR were administered as separate entities in the immediate and PK arms and as a fixed-dose combination in the deferred arm.

Roth D, et al. *Lancet*. 2015;386:1537-45.

SVR12: Immediate Treatment Group



Relapse	1*	1
Discontinued unrelated to Tx	0	6†

MFAS = primary efficacy analysis; FAS was a secondary analysis.
*Noncirrhotic, IFN-intolerant patient with HCV GT 1b infection relapsed at FW12.
†LTFU, n = 2; n = 1 each for death, noncompliance, withdrawal by subject, and withdrawal by physician (due to violent behavior).

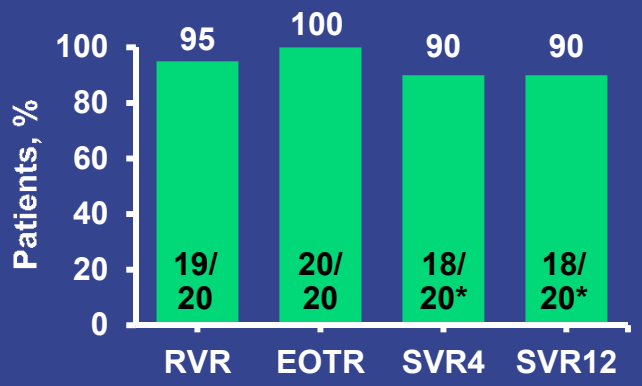
Roth D, et al. *Lancet*. 2015;386:1537-45.

RUBY-I: OMV/PTV/RTV + DSV ± RBV in GT 1 Patients With Severe Renal Impairment or ESRD

Multicenter, Open-Label, Phase 3b Study: Interim Results

Once-daily dosing of OMV/PTV/RTV + DSV twice daily + RBV four times daily for GT 1a only

Patients	OMV/PTV/RTV + DSV ± RBV n = 20
Male, n (%)	17 (85)
HCV genotype, n (%) 1a/1b	13 (65)/7 (35)
Degree of fibrosis, n (%) F0-F1/F2/F3	10 (50)/6 (30)/4 (20)
HCV viral load, log_{10} (IU/mL), median (range)	6.6 (5.5-7.6)
Hemoglobin, g/dL, mean (SD)	12.6 (1.8)
CKD stage, n (%) 4/5	7 (35)/13 (65)
eGFR, mL/min/1.73m^2, median (range)	10.9 (5.4-29.9)
Creatinine, mg/dL, median (range)	6.2 (2.2-10.8)

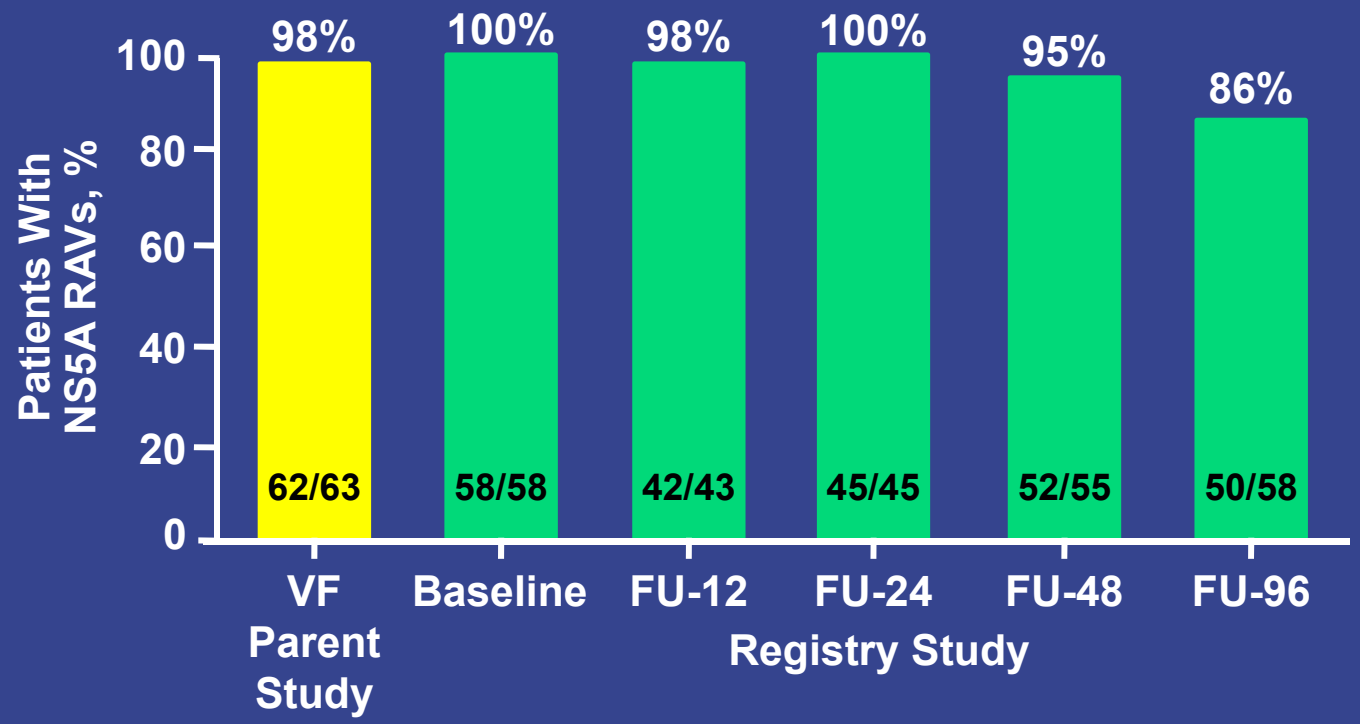


Safety
- AEs more frequent in patients on RBV
- No treatment-related SAEs
- No study discontinuations

*One death, one relapse.

Pockros PJ, et al. EASL 2015; Oral LO1;
Pockros PJ, et al. AASLD 2015; Abstract 1039.

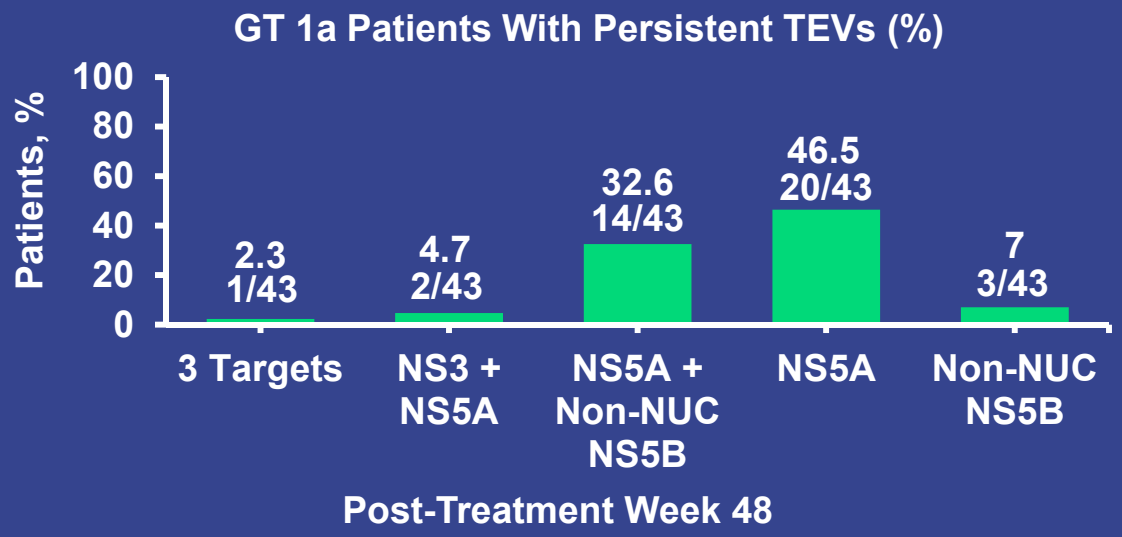
Long-Term Persistence of NS5A Variants After Treatment With LDV



- NS5A RAVs in patients who failed LDV treatment without SOF
- Positions 24, 28, 30, 31, 32, 58, and 93 that confer > 2.5-fold reduced susceptibility to LDV in vitro were included

Dvory-Sobol H, et al. *J Hepatol*. 2015;62:S221[Abstract O059].

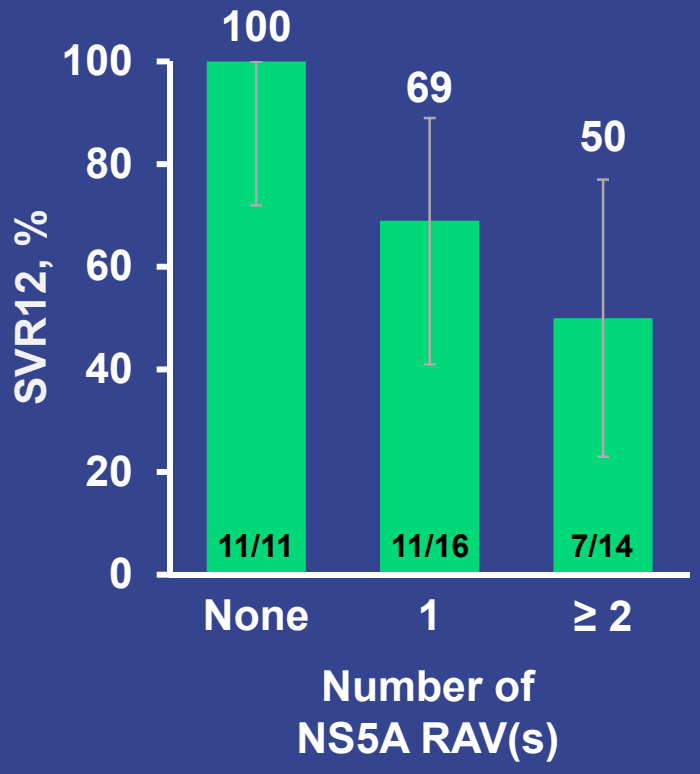
Most NS5A and Non-Nucleoside NS5B Variants Persist Post-Treatment

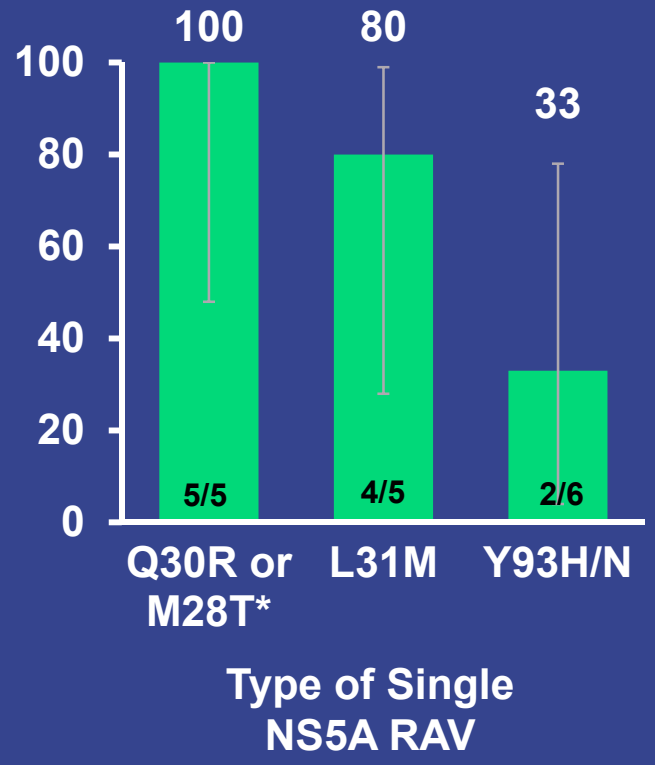


- Patients with TEVs by population sequencing (cut-off 20%) in nine OMV/PTV/RTV + DSV ± RBV trials
- In GT 1a patients, NS3 (9%), NS5A (96%), and non-NUC NS5B (57%) TEVs were still detectable to post-treatment week 48
- Similar to first-generation PIs, NS3/4A variants resolve over 48 weeks

Krishnan P, et al. *J Hepatol*. 2015;62:S220[Abstract O057].

SVR12 by Baseline NS5A RAV: 24 Weeks of LDV/SOF After Failing 8 or 12 Weeks of LDV/SOF-Based Therapy





*M28T (n = 1).

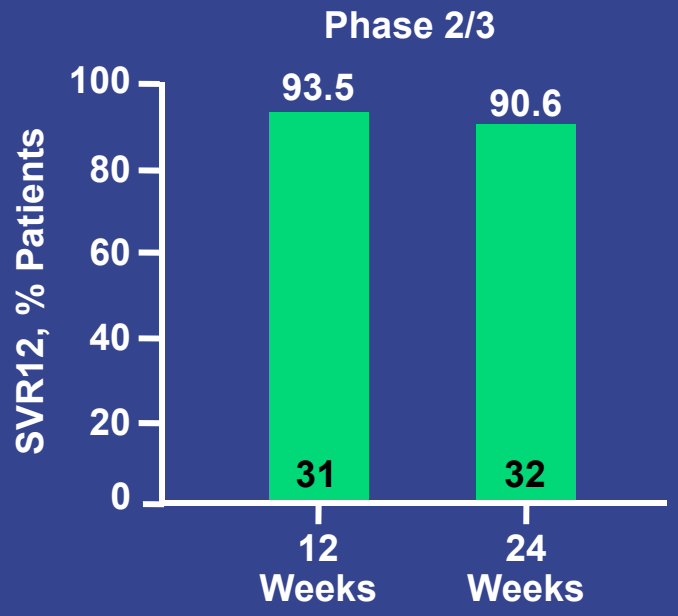
Lawitz E, et al. *J Hepatol.* 2015;62:S192[Abstract O005].

Annual Age-Adjusted Mortality Rates From HBV, HCV, and HIV

Ly KN, et al. *Ann Intern Med.* 2012;156:271-8.

TURQUOISE-I: PTV/r + OMV + DSV + RBV (3D + RBV)

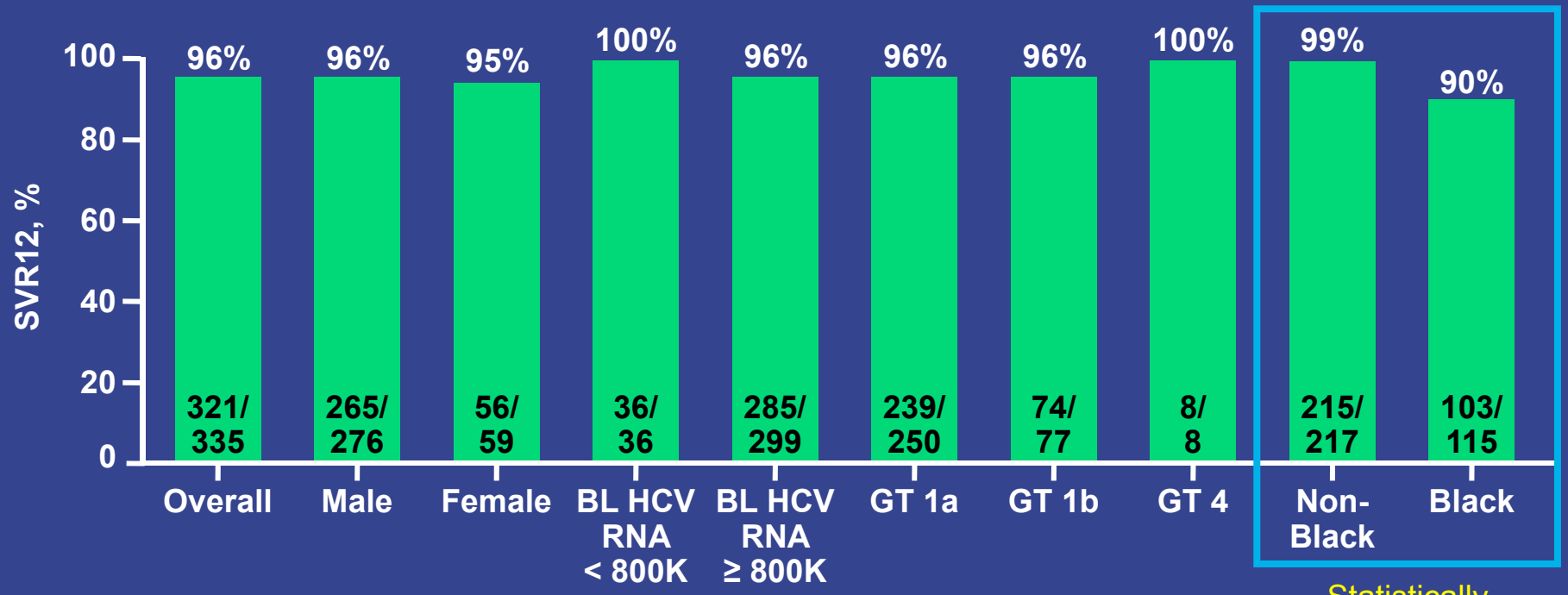
- HCV GT 1
- HIV-1
- Included HCV treatment-naïve, treatment-experienced, cirrhotic, and noncirrhotic patients
  - 3D: Co-formulated Paritaprevir/ritonavir/ombitasvir (150 mg/100 mg/25 mg) + dasabuvir (250 mg)
  - RBV: 1,000-1,200 mg daily, weight-based
  - Patients on atazanavir for HIV were instructed to discontinue their stand-alone ritonavir during 3D therapy



- 2 patients in the 24-week group had reinfection, not relapse.

Sulkowski MS, et al. *JAMA*. 2015;313:1223-31.

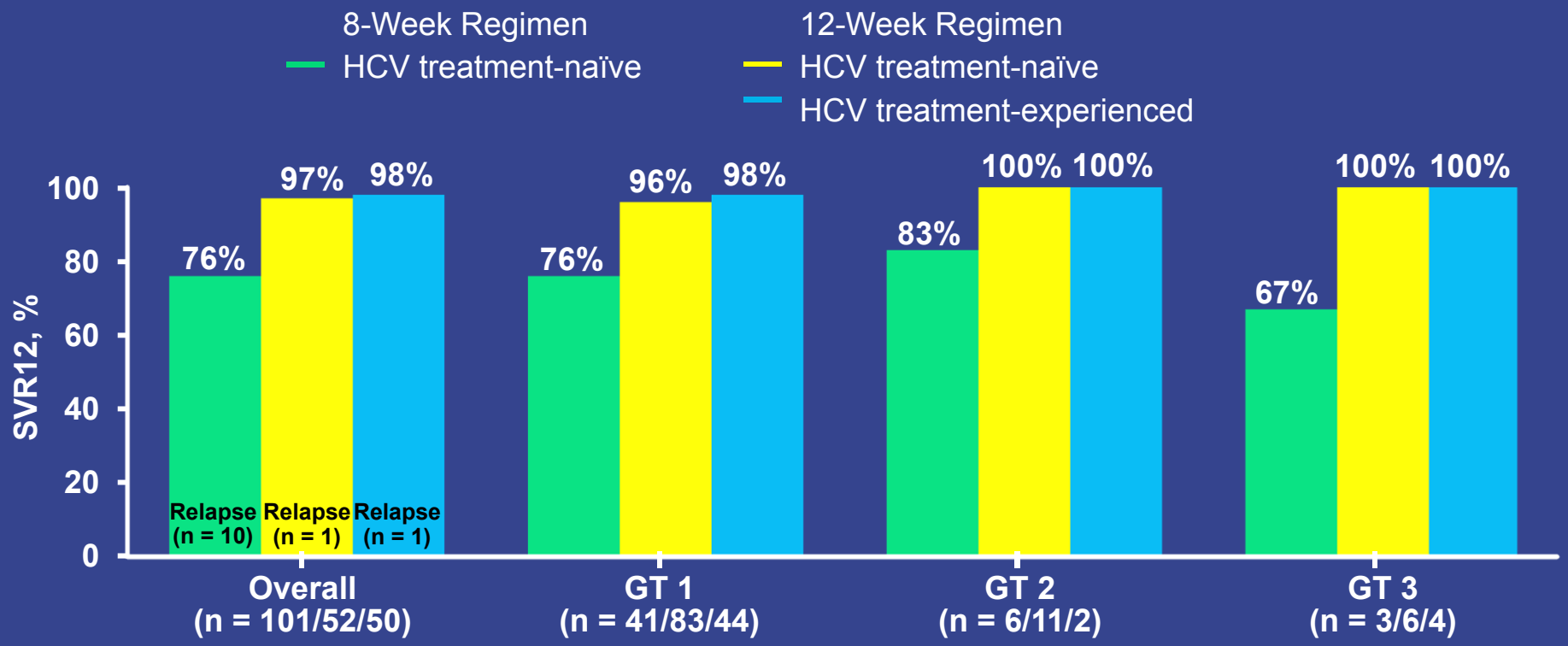
ION-4: SVR12 Rates by Subgroup and Baseline Characteristics for 12 Weeks of LDV/SOF in HIV/HCV Coinfection



- All relapsers in the Black cohort had cirrhosis
- AEs included headache, fatigue, and diarrhea

Naggie S, et al. *N Engl J Med.* 2015;373:705-13.

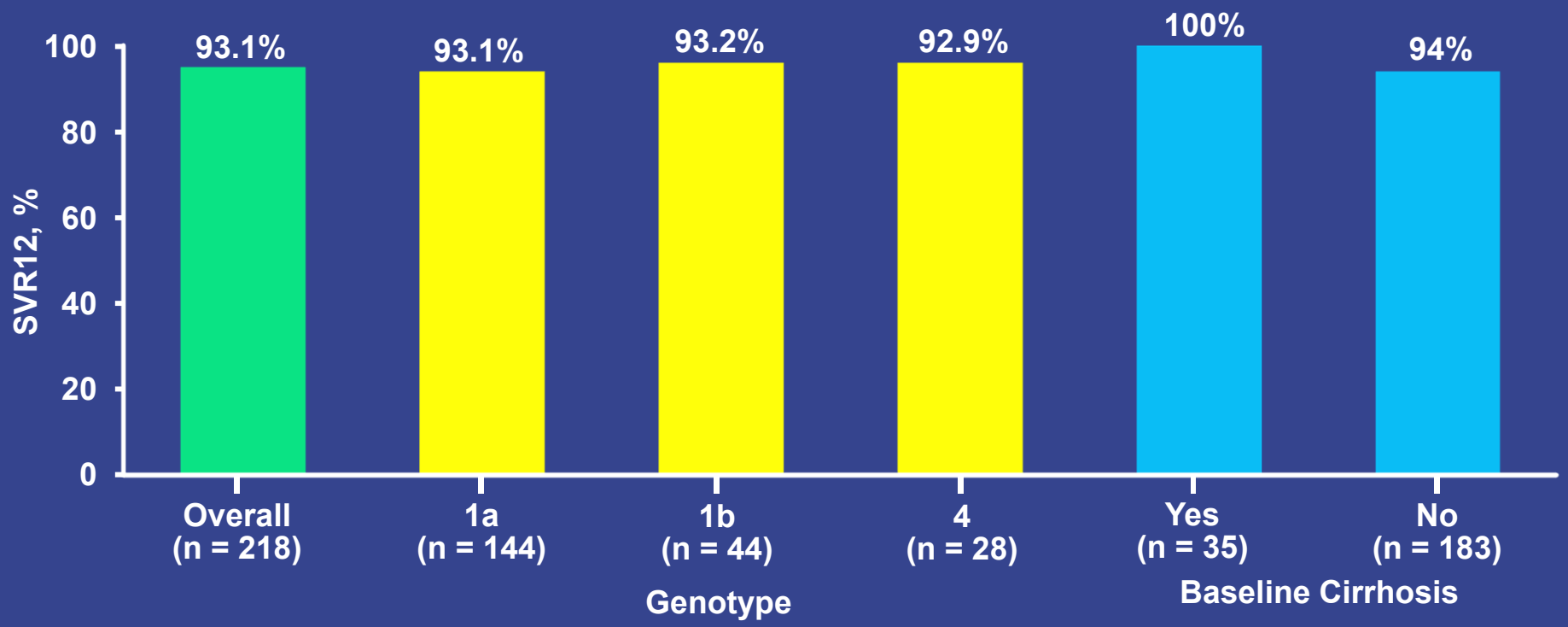
ALLY-2 Study: SVR12 Rates for DCV + SOF in HIV/HCV Coinfection



- 12-week regimen: no impact of race, baseline HCV RNA, cirrhosis, baseline NS5A RAVs, or ART regimens on SVR12
- GT 4 results not shown (n = 3)
- AEs included nausea, fatigue, and headache

Wyles D, et al. *N Engl J Med.* 2015;373:714-25.

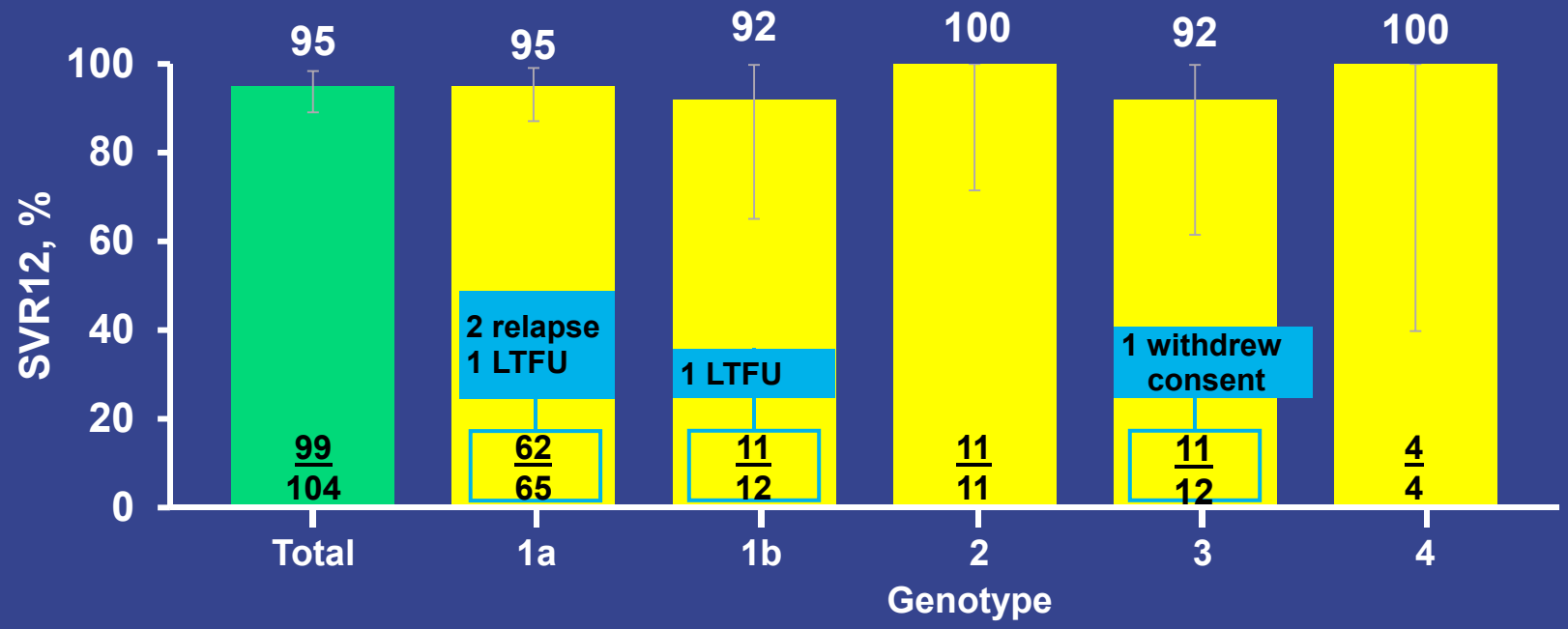
C-EDGE: SVR12 Rates for GZR/EBR in HCV/HIV Coinfection



- SVR12 by ART containing: abacavir (95.7%), tenofovir DF (97.5%), raltegravir (96.4%), dolutegravir (100%), rilpivirine (94.6%)
- AEs included fatigue, headache, and nausea

Rockstroh JK, et al. *The Lancet HIV*. 2015;2:e319-27.

ASTRAL-5: SVR12 Rates for 12 Weeks of SOF/VEL* in HIV/HCV Coinfection



- Error bars represent 95% confidence intervals
- AEs included fatigue, headache, arthralgia, diarrhea, upper respiratory tract infection, nausea, and insomnia

*Investigational.

www.natap.org/2016/EASL/EASL_32.htm. Accessed May 24, 2016.

What About New Therapies? ASTRAL-4: SOF/VEL Fixed-Dose Combination for HCV in Patients With Decompensated Liver Disease

- Open-label, randomized (1:1:1) US study
- GT 1-6 treatment-naïve or -experienced patients with CPT B cirrhosis
- Eligibility criteria: CrCL > 50 mL/min, platelets > 30,000 x 10^3/µL; no HCC or liver transplant
- Weight-based RBV dosing (1,000 or 1,200 mg/day)
- AEs included fatigue, nausea, headache, and anemia

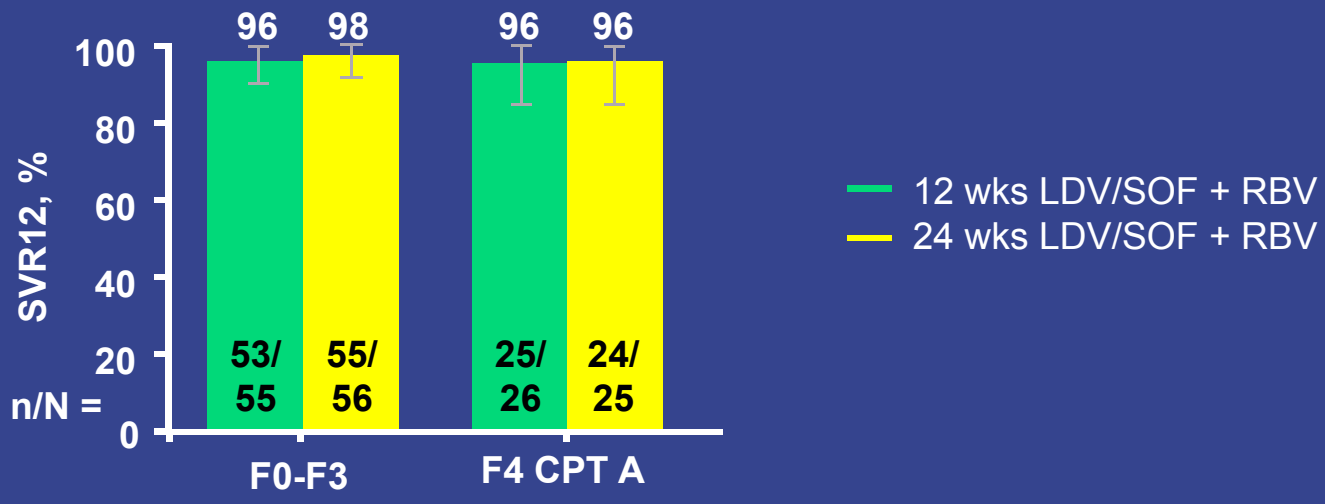
Curry MP, et al. *N Engl J Med*. 2015;373:2618-28.

Results: SVR12 in ASTRAL-4 Study

	SVR12			
	GT 1	GT 3	GT 2, 4, or 6	Overall
SOF/VEL 12 weeks	88	50	100	83 (95% CI, 74-90)
SOF/VEL + RBV 12 weeks	96	85	100	94 (95% CI, 87-98)
SOF/VEL 24 weeks	92	50	86	86 (95% CI, 77-92)

Curry MP, et al. *N Engl J Med.* 2015;373:2618-28.

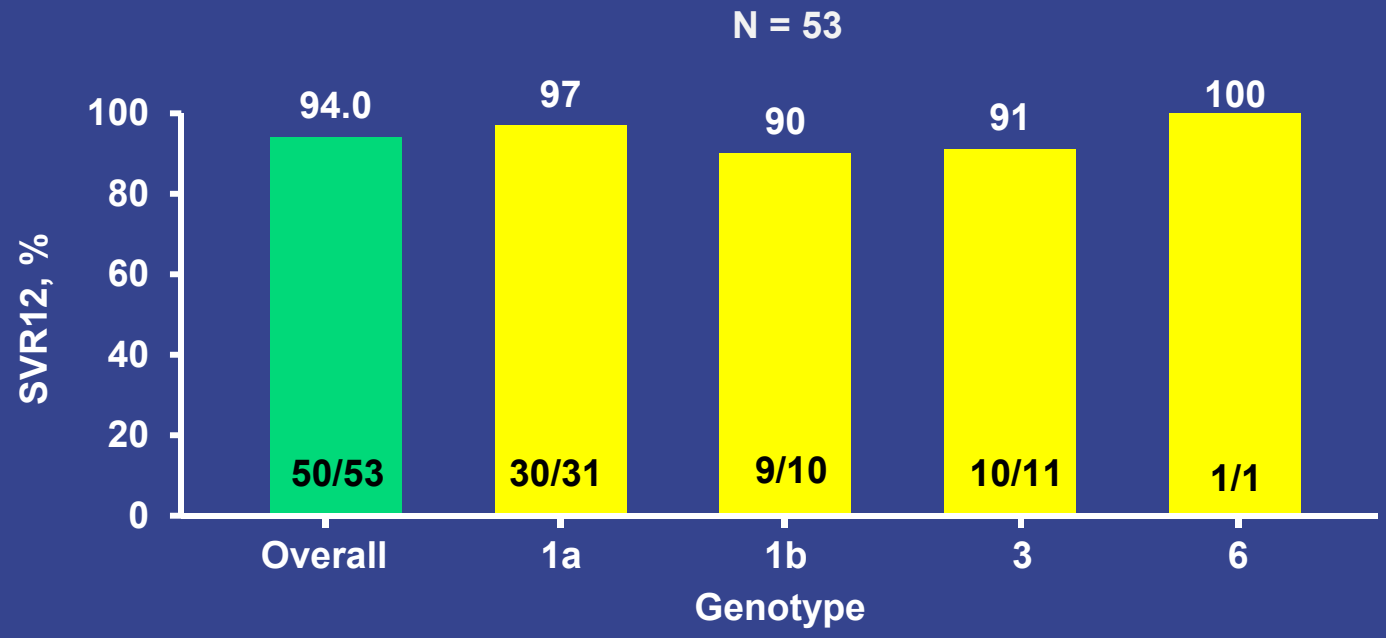
SOLAR-1: SVR12 Rates in Liver Transplant Patients Receiving LDV/SOF + RBV



- In the 24-week arm, 8 patients with CPT B and 1 patient with CPT C have not reached the follow-up week 12 visit
- MELD scores improved from baseline through follow-up week 4 in 15/48 patients with CPT A and 8/41 patients with CPT B disease
- Forty instances have been reported of investigators adjusting immunosuppression due to improved hepatic function after viral clearance
- No relapses have occurred in the 24-week arm with preexisting NS5A variants
- Most common AEs were infection, vomiting, and diarrhea

Charlton M, et al. *Gastroenterology*. 2015. [epub ahead of print].

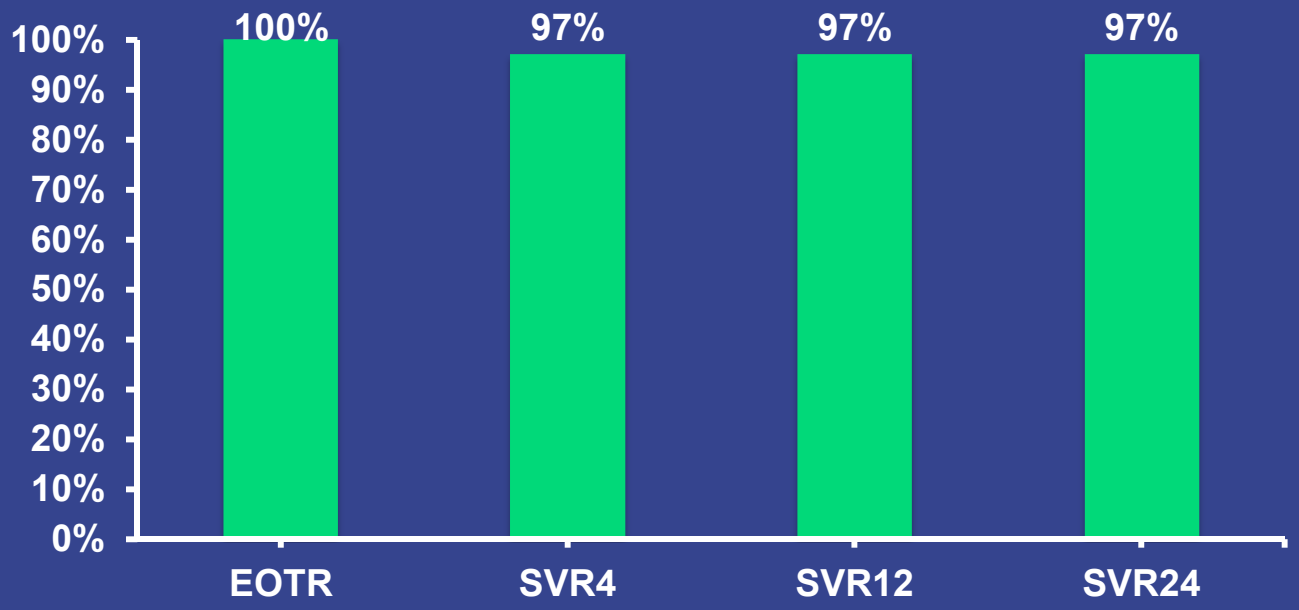
ALLY-1: SOF + DCV + RBV 600 mg Post–Liver Transplant SVR12 by HCV GT



- All 3 relapses with NS5A RAVs by population sequencing
- AEs included headache, fatigue, anemia, diarrhea, nausea, and arthralgia

Poordad F, et al. *Hepatology*. 2016;63:1493-505.

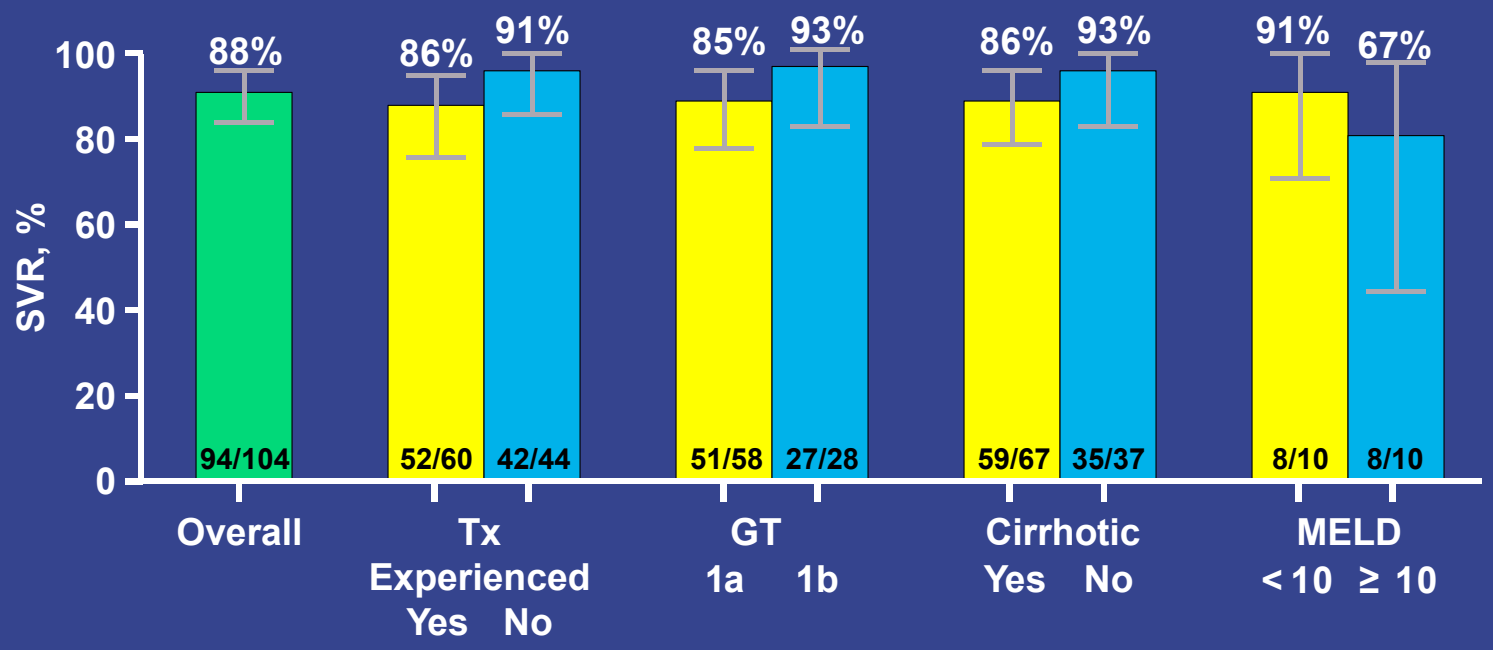
CORAL-1: SVR Rates in GT 1 Liver Transplant Patients Receiving PrOD + RBV for 24 Weeks



- No breakthroughs reported
- One patient had a relapse (post-treatment day 3)
  - At the time of relapse, this patient had R155K in NS3 protease, M28T + Q30R in NS5A, and G554S in NS5B, none of which were present at baseline
- Study now includes F3-F4, 12-week duration, no RBV for naïve GT 1b
- AEs included fatigue, headache, and cough

Kwo PY, et al. *N Engl J Med*. 2014;371:2375-82.

HCV-TARGET: Post-Transplant HCV RNA Outcomes for SOF + SMV ± RBV—GT 1 Interim Analysis



- AEs included fatigue, headache, infection, rash, influenza-like illness, nausea/vomiting, and anemia

Brown RS, et al. *Liver Transpl*. 2016;22:24-33.

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Contact Information

Call (toll-free) 866 858 7434
E-mail info@med-iq.com

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