

Clinical Impact of New Data From the 2017 Washington, DC, Hepatology Meeting

CCO Independent Conference Coverage*

*of the 2017 American Association for the Study of Liver Diseases,
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Faculty Disclosures

Stephen A. Harrison, MD, COL (Ret.), FAASLD, has disclosed that he has received consulting fees from Axcella, Capulus, the Chronic Liver Disease Foundation, Cirius, Genfit, Echosens, Histoindex, Intercept, Madrigal, NGM Bio, Novartis, Novo Nordisk, Perspectum, and Prometheus; has received fees for non-CME/CE services received directly from a commercial interest or their agents (eg, speaker bureaus) from AbbVie, Alexion, and Gilead Sciences; and has an ownership interest in Cirius.

Paul Y. Kwo, MD, has disclosed that he has received consulting fees from AbbVie, Bristol-Myers Squibb, Gilead Sciences, and Merck and funds for research support from AbbVie and Gilead Sciences.

Norah Terrault, MD, MPH, FAASLD has disclosed that she has received consulting fees from Gilead Sciences and Merck and funds for research support from AbbVie, Gilead Sciences, and Merck.

Current HCV Therapy



AASLD/IDSA Recommendations for First-line HCV Treatment

HCV GT	Regimen	Duration, Wks	
		No Cirrhosis	Compensated Cirrhosis
1	GLE/PIB	8	12
	GZR/EBR*	12	12
	SOF/LDV	8 or 12 [†]	12
	SOF/VEL	12	12
2 or 3	GLE/PIB	8	12
	SOF/VEL	12	12 [‡]
4	GLE/PIB	8	12
	SOF/VEL	12	12
	GZR/EBR	12	12
	SOF/LDV	12	12
5 or 6	GLE/PIB	8	12
	SOF/LDV	12	12
	SOF/VEL	12	12

*If GT1a, use only if no baseline NS5A elbasvir RASs detected.

†If nonblack, no HIV, and HCV RNA < 6 million IU/mL, 8-wk duration recommended.

‡For GT3, if Y93H RAS detected, add RBV or consider SOF/VEL/VOX.

AASLD/IDSA Recommendations for DAA-Experienced Pts

HCV GT	Duration, Wks	Previous Experience		
		NS3/4A	NS5B	NS5A
1	12	GLE/PIB SOF/LDV (no cirrhosis) SOF/VEL	GLE/PIB SOF/VEL (1b) SOF/VEL/VOX (1a)	SOF/VEL/VOX
2*	12	NA	GLE/PIB SOF/VEL	NA
3	12	SOF/VEL/VOX	SOF/VEL/VOX	SOF/VEL/VOX ± RBV [†]
4, 5, 6	12	SOF/VEL/VOX	SOF/VEL/VOX	SOF/VEL/VOX

*Recommendations for any SOF + RBV experienced pt. †RBV if NS5A inhibitor failure and cirrhosis.

STREAGER: 8-Wk GZR/EBR for Treatment-Naive, Noncirrhotic Pts With GT1b HCV

§ Interim analysis of single-arm study



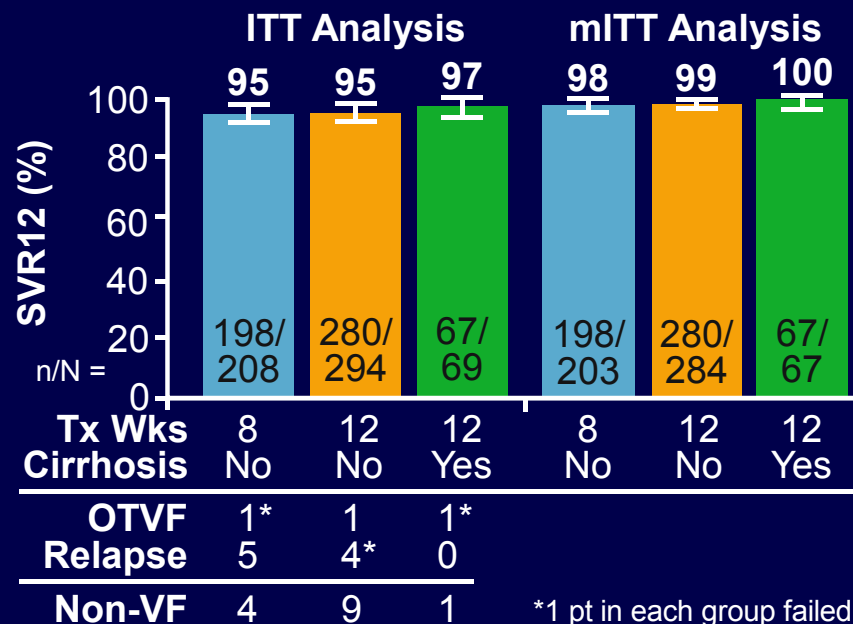
§ n = 2 relapses

- Pt 1: HCV RNA 14 million IU/mL, F0-F1 fibrosis, Y93H mutation
- Pt 2: HCV RNA 453,899 IU/mL; F2 fibrosis; **GT1e HCV**; L28M, R30Q, A92T, Y93H mutations

*Interim analysis; planned N = 120.

Efficacy and Safety of GLE/PIB for Treatment-Naive Pts With GT3 HCV

§ Integrated analysis of phase II/III trials of **GLE/PIB** for 8 wks (noncirrhotic pts, n = 208) or 12 wks (noncirrhotic pts, n = 294; cirrhotic pts, n = 69) in treatment-naive pts with GT3 HCV



§ No statistically significant differences in SVR12 for 8-wk vs 12-wk treatment across subgroups, including:

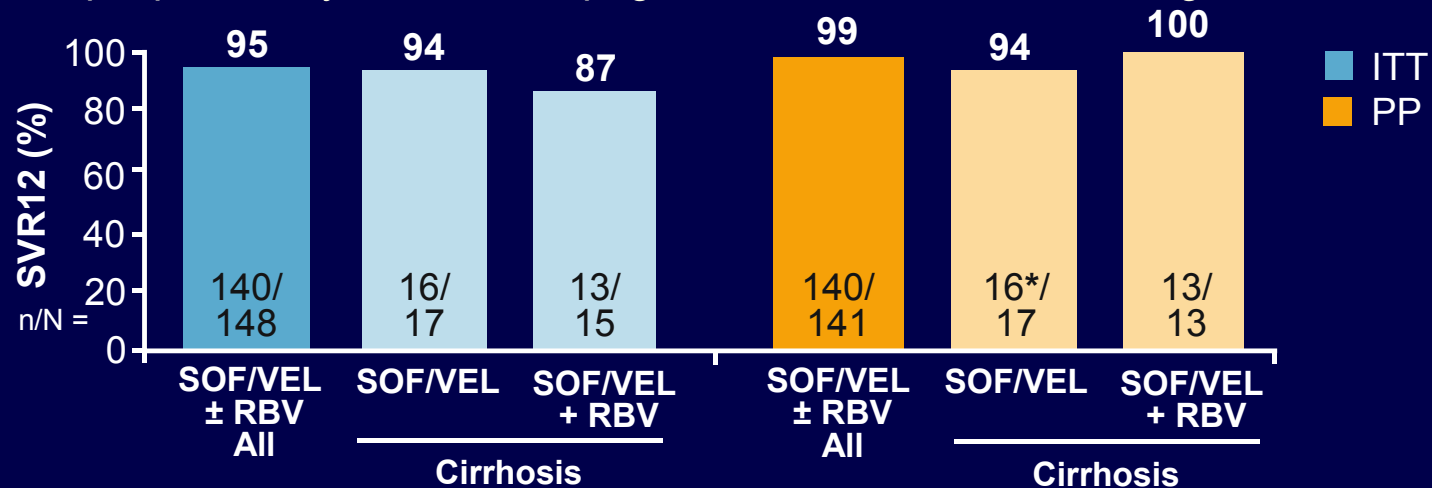
- Black race (n = 10)
- OST (n = 79)
- Recent or history of drug use (n = 35)
- Baseline RAS (n = 181)

§ Only n = 3 discontinued for AE

GECCO: Real-World Efficacy of SOF/VEL in Pts With GT3 HCV

§ Prospective German cohort study assessing efficacy of **SOF/VEL ± RBV** for 12 wks in pts with GT3 HCV (N = 232 [n = 148 analyzed]; 14% treated with RBV)

– 26% of pts previously treated with pegIFN + RBV or SOF-based regimen



§ *n = 1 relapse (prior SOF + RBV for 6 mos, no BL RAS, emergent Y93H)

§ Baseline RAS did not impact ability to achieve SVR12

SOF/LDV for Pts With Severe Renal Impairment

§ Single-arm, open-label phase II study

Pts with GT1/4 HCV and
severe renal impairment
($\text{CrCl}_{\text{CG}} \leq 30 \text{ mL/min}$)
not undergoing dialysis
(N = 18)



SOF/LDV QD
(N = 18)

Wk 12



SVR12

100%

§ Pharmacokinetics

- Mean SOF, GS-331007, LDV exposures 103%, 501%, 57% higher in study population vs those in the phase II/III SOF/LDV trial populations

§ Safety

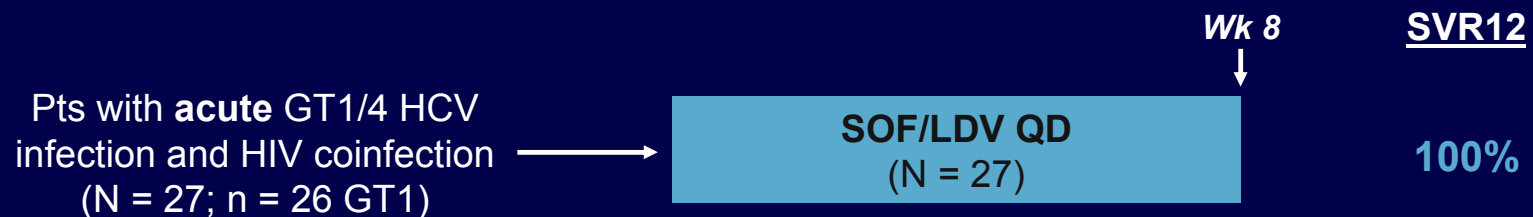
- No treatment-related serious AEs or cardiac AEs, discontinuations for AEs, clinically meaningful eGFR change

SWIFT-C: 8-Wk SOF/LDV for Pts With HIV and Acute GT1/4 HCV Coinfection

§ Optimal duration of SOF/LDV for acute HCV infection in HIV-coinfected pts not known; previous study showed SVR12 rate of 77% with 6 wks of therapy^[1]

§ SWIFT-C: single-arm study^[2]

- Baseline HIV regimens: boosted PI, 26%; NNRTI, 30%; INSTI, 52%; TDF/FTC, 85%; ABC/3TC, 15%



1. Rockstroh JK, et al. Lancet Gastroenterol Hepatol. 2017;2:347-353.
2. Naggie S, et al. AASLD 2017. Abstract 196.



Co-STAR Part B: Assessment of Reinfection Risk in Pts on OAT Who Received GZR/EBR

§ Observational study in which pts on OAT* with GT1/4/6 HCV who received GZR/EBR in Co-STAR Part A were assessed for HCV reinfection and drug use for 3 yrs (N = 199)^[2]

- Part A: SVR12 rate of 91% with 12-wk GZR/EBR; 97% of pts had > 95% adherence

§ **10 reinfections occurred during 24 mos following end of HCV treatment**

Parameter at Post-Tx Mo 24	Reported IDU*	No Reported IDU*
IDU, % (n)	37 (74)	63 (125)
Reinfection rate/100 PY (95% CI)	4.2 (1.5-9.2)	0.4 (0-2.3)

*In the previous 6 mos.

HCV Therapy and Risk of Mortality and HCC



ANRS HEPATHER: HCV DAA Therapy and Risk of Mortality, HCC, and Decompensated Cirrhosis

§ Multicenter observational cohort study assessing short-term effects of DAAs on mortality, HCC, and DC risk in pts with HCV (N = 9295)

– Median follow-up: 24 mos

§ **DAA treatment associated with decreased risk of death vs no DAA treatment**

Event, n (%)	DAA Treatment (n = 6460)*	No DAA Treatment (n = 2835)†	aHR (95% CI)
All-cause death	90 (1.4)	78 (2.8)	0.65 (0.45-0.95); P = .0258
§ Liver related	NR	NR	0.68 (0.36-1.29)
§ Nonliver related	NR	NR	0.75 (0.43-1.31)
HCC	164 (2.5)	57 (2.0)	1.19 (0.85-1.66); P = .3178
DC	77 (1.2)	35 (1.2)	0.90 (0.58-1.41); P = .6533

Effect of DAAs quantified with weighted Cox proportional hazards models adjusted for confounding via IPTW. IPTW scores derived from covariates associated with DAA, including age, sex, cirrhosis, and treatment experience.

*8482 person-yrs. †10040 person-yrs.

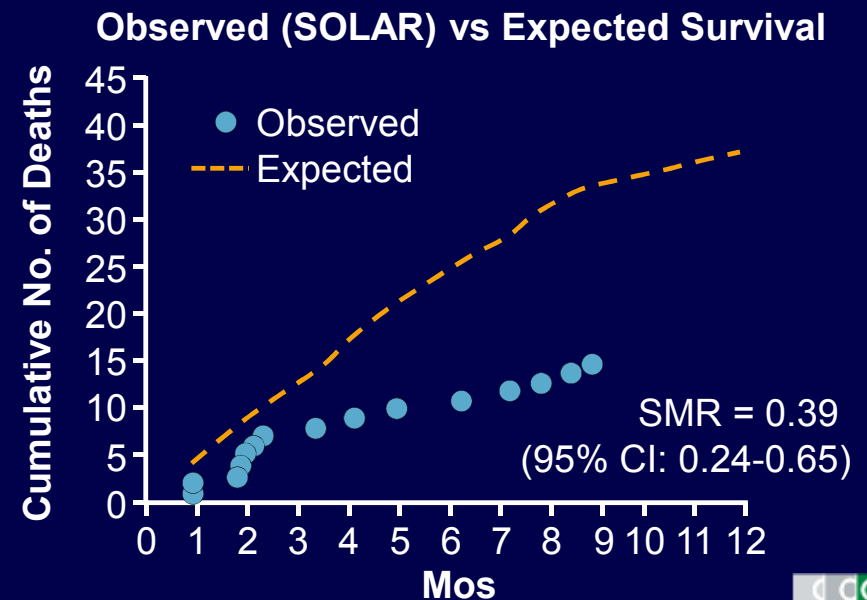
HCV DAA Therapy and Survival in Pts With Decompensated Cirrhosis

§ Comparison of incidence of death in pts with hepatic decompensation in the SOLAR studies of SOF/LDV + RBV (n = 212) and pre-DAA era pts in OPTN meeting SOLAR criteria (model creation set, n = 2071; validation set, n = 899)

- Survival prediction model created using OPTN data to determine expected mortality for 1 yr in pts not receiving DAA therapy; model included age, albumin, HE grades 1/2 and 3/4, MELD, sodium

§ 15 deaths in 1 yr in SOLAR study

§ DAA therapy lowered risk of death by 60%



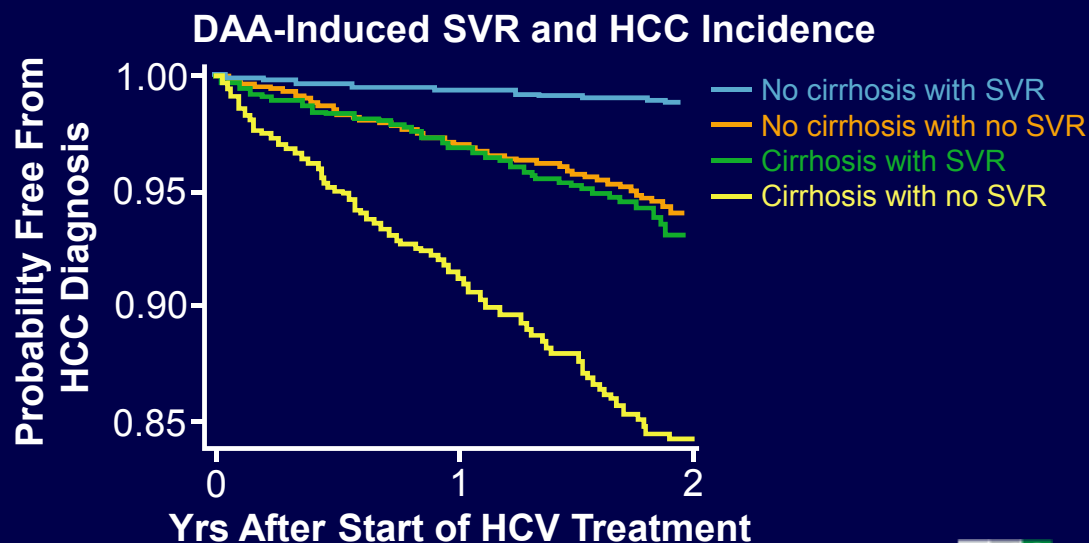
DAA Therapy and HCC Risk in Large VA Cohort

§ Retrospective cohort study assessing the relationship between SVR and HCC risk in pts with HCV in the VA healthcare system receiving antiviral therapy 1999-2015 (N = 62,354)

- 58% received IFN-only therapy, 35% received DAA-only therapy

§ **SVR with DAA regimen associated with 71% decrease in HCC risk**

Regimen	HCC/100 PY	aHR
IFN only		
§ SVR	0.28	0.32
§ No SVR	1.07	
DAA + IFN		
§ SVR	0.6	0.48
§ No SVR	1.73	
DAA only		
§ SVR	0.92	0.29
§ No SVR	5.2	

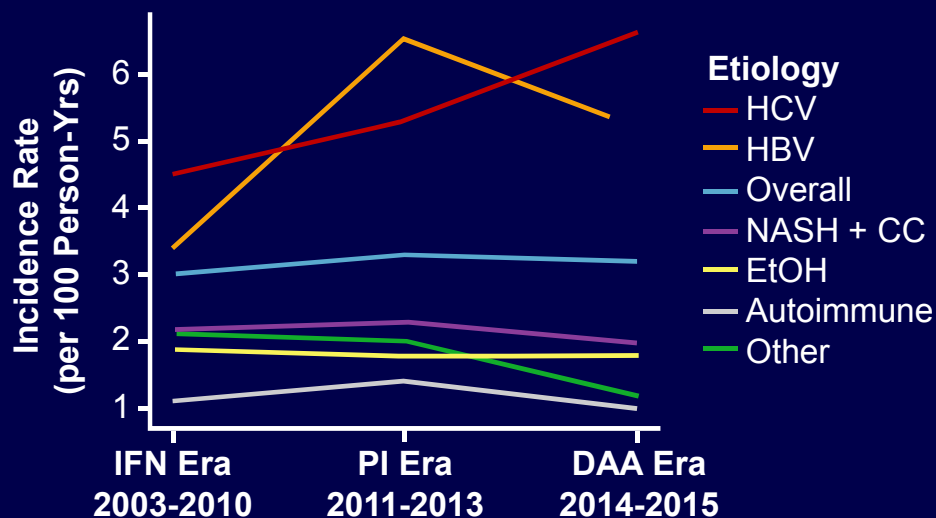


Incidence of HCC in Liver Transplant Registrants With HCV

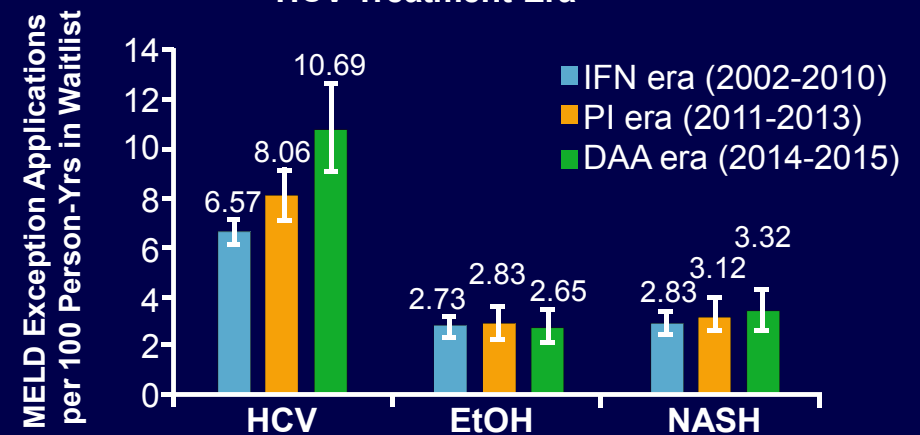
§ Analysis of HCC incidence in pts awaiting liver transplantation in SRTR database (N = 48,158; n = 20,039 with HCV)^[1]

§ Analysis of HCC-related MELD exceptions in pts awaiting liver transplantation in OPTN database (N = 55,416; n = 23,020 with HCV)^[2]

Incidence of HCC by Etiology and HCV Treatment Era



HCC-Related MELD Exceptions By Etiology and HCV Treatment Era



1. Kwong AJ, et al. AASLD 2017. Abstract 121. 2. Esteban JP, et al. AASLD 2017. Abstract 1040. Reproduced with permission.

