Post 2017 AASLD Update

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Disclosures

- Industry
  - Investigator: Merck, GS, ABV
  - Consultant/Advisor: Merck, GS, ABV
  - Speaker: Merck, ABV, GS

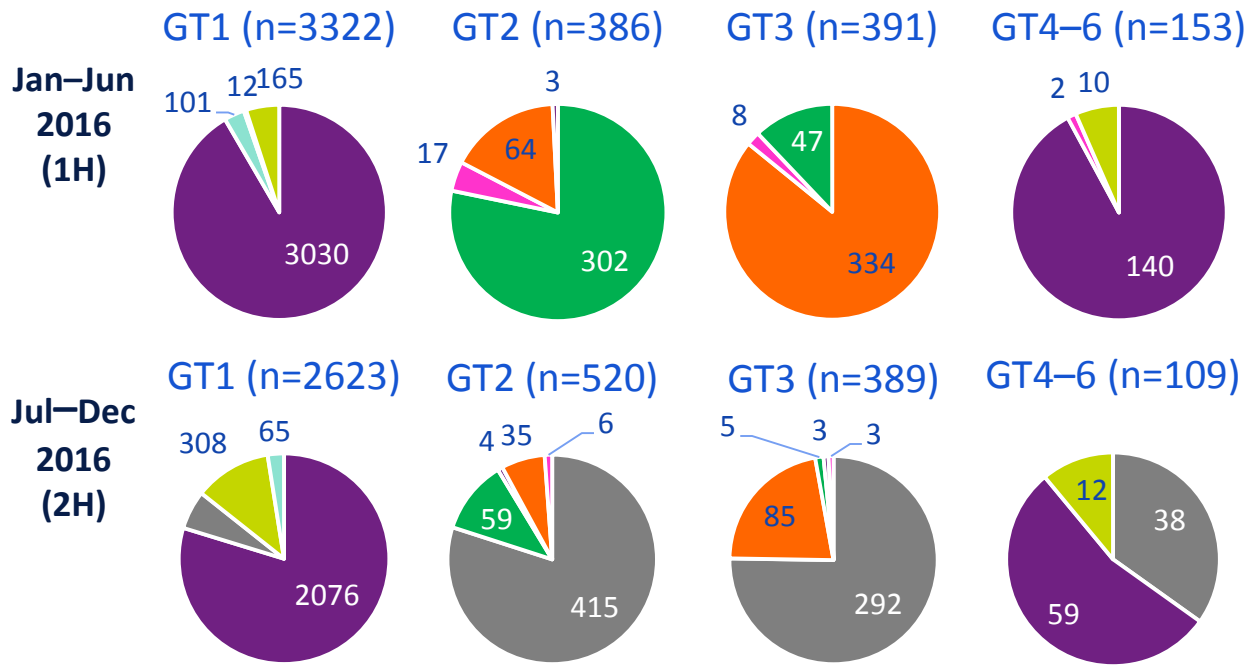
- Government
  - OHTN
  - CIHR
  - Health Canada
  - Ontario MOH
  - Ministerial Council

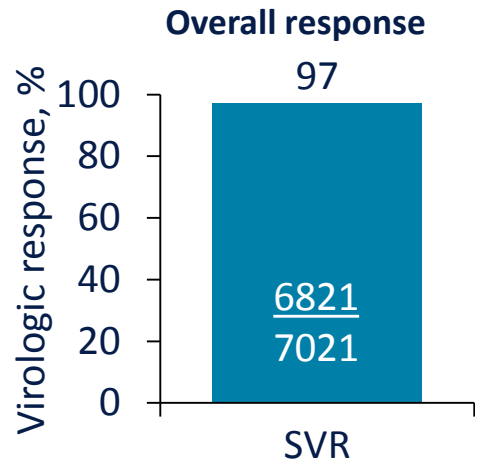
Standard of Care

#1093, Flamm:
Real-World Patterns of Therapy Utilization and Outcomes in 8049 HCV GT1–6: TRIO Network

- 8049 patients initiating therapy Jan–Dec 2016; 7651 patients completed therapy, 630 lost to follow-up
- Data from providers and specialty pharmacies through Trio Health's disease management program, assessing changes in treatment preferences and outcomes

Treatment preferences (Regimen starts by GT and date)





PPSVR remained the same or slightly increased (non-sig.) between 1H and 2H 2016 for nearly all subpopulations

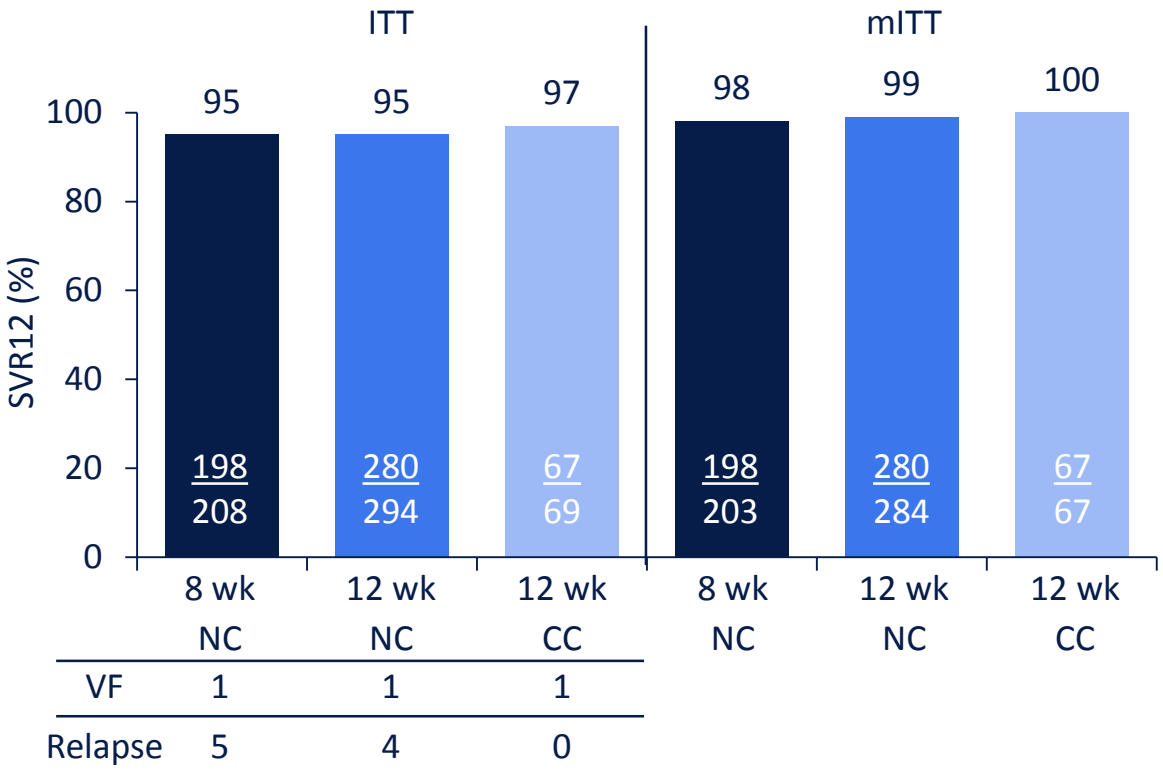
- Large shifts in treatment preferences from 1H to 2H 2016
- Little impact on SVR

- Patient characteristics were largely similar for regimens initiated in 1H and 2H for all GTs (cirrhosis, TE, CKD stage, HIV, prior transplant)
- Changes in composition of populations between 1H and 2H:
  - GT1: Cirrhosis decreased from 32% (1057/3295) to 26% (667/2596)
  - GT3 Cirrhosis decreased from 34% (132/388) to 26% (102/387) and TE decreased from 23% (88/391) to 16% (61/388)

#62, Flamm:
GLE/PIB for 8 or 12 Weeks in Tx-naïve GT3a: Integrated Phase 2/3 Analysis

7 Phase 2/3 clinical trials of 8 weeks and 12 weeks GLE/PIB in tx-naive
GT3 (N=571; ENDURANCE-3, EXPEDITION-1 & -4, SURVEYOR-2 (parts 1–3), MAGELLAN-2)

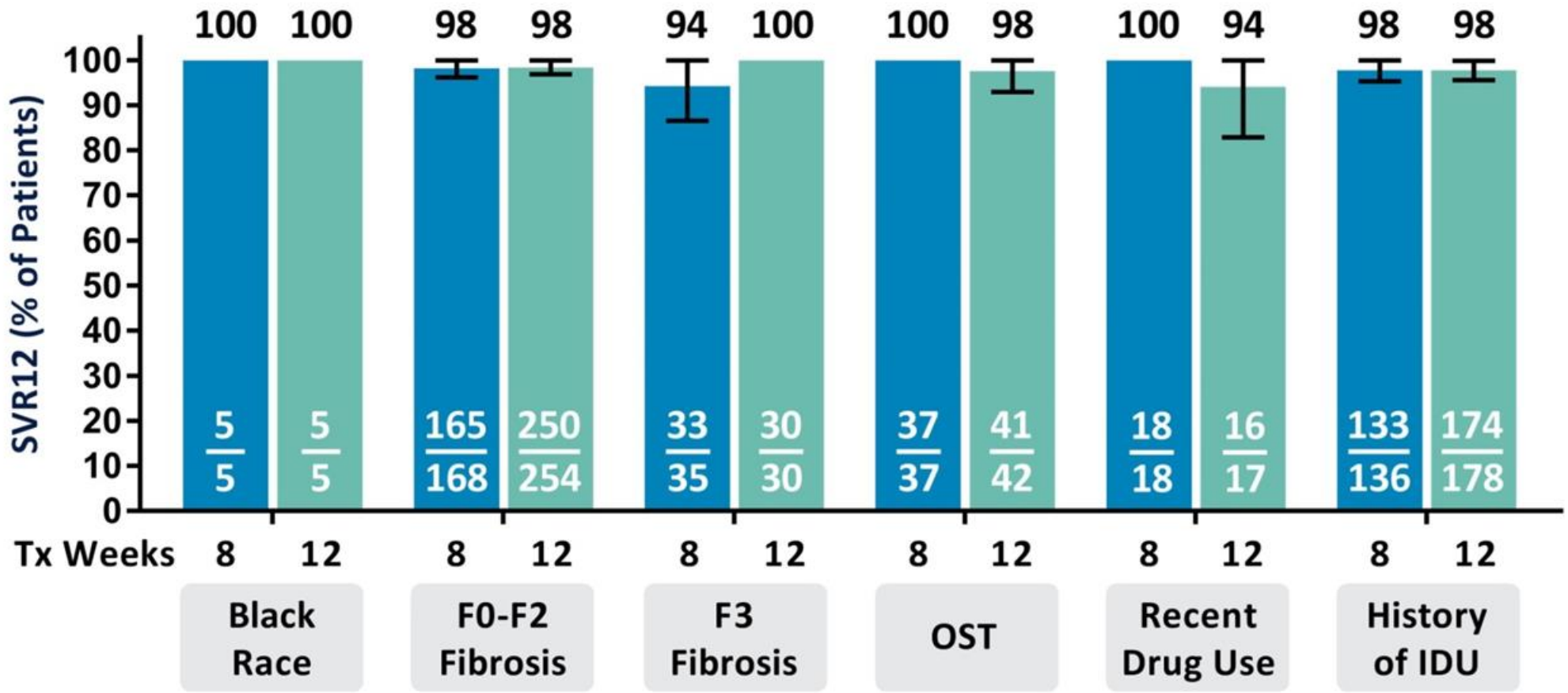
	No cirrhosis 8 wk (n=208)	No cirrhosis 12 wk (n=294)	With cirrhosis 12 wk (n=69)
Male, n (%)	123 (59)	167 (57)	41 (59)
White, n (%)	180 (87)	258 (88)	64 (93)
Age [yr], median (range)	46 (20–76)	49 (22–71)	56 (35–70)
F0-2	82%	89%	-
HCV RNA [log_{10} IU/mL], median (range)	6.1 (1.2–7.5)	6.2 (3.4–7.6)	6.2 (4.2–7.2)
HIV coinfection, n (%)	22 (11)	0	4 (6)
CKD stage 4–5, n (%)	0	11 (4)	1 (2)
Post transplant, n (%)	0	24 (8)	0
NS5a RAS	28%	17%	19%



SVR12 not significantly affected by black race, fibrosis status, OST, recent drug use, or history of IDU, viral load, or RAS

Results support FDA-approved indications for GLE/PIB for treatment-naive patients with GT3 infections

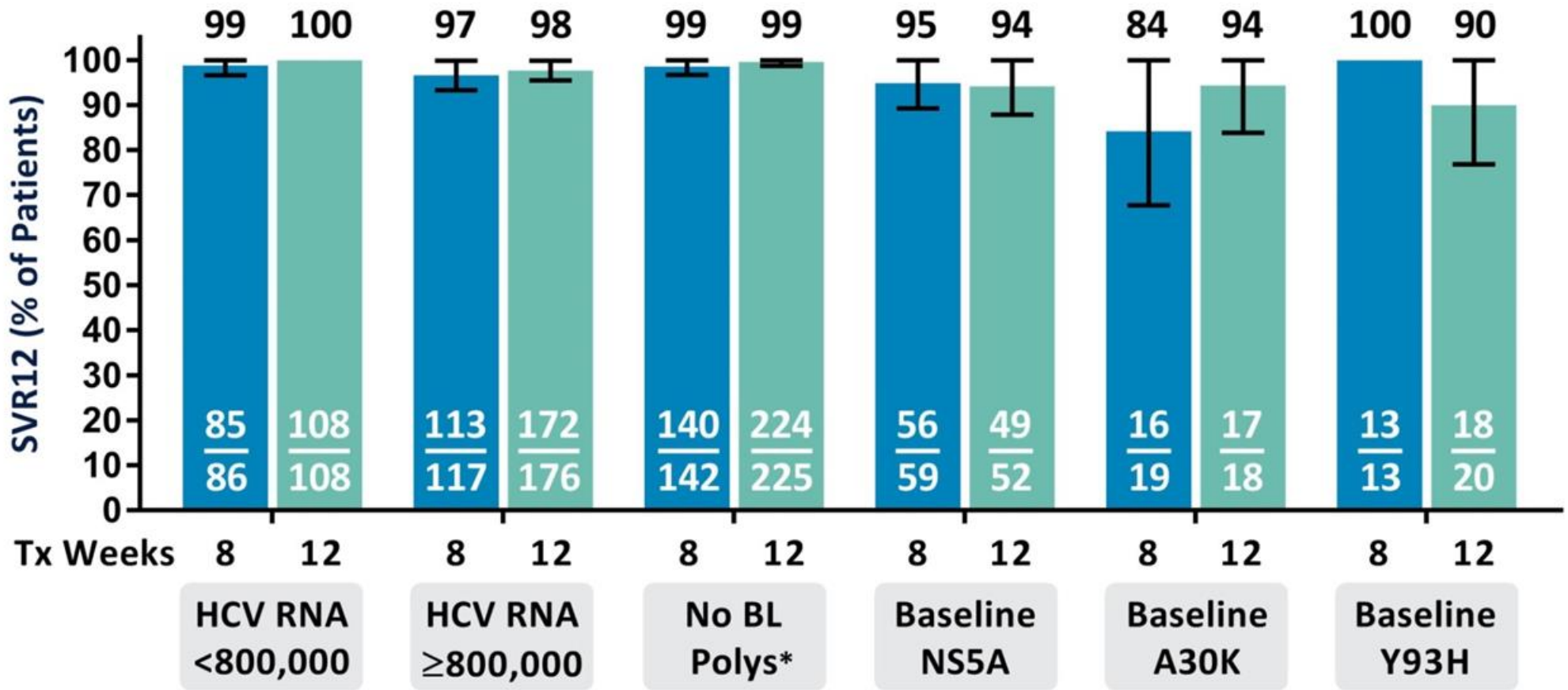
mITT SVR12 by Patient Characteristics Subgroups: Treatment-naïve patients without cirrhosis, 8 vs 12 weeks



No statistically significant difference in SVR12 rates (8 vs 12 weeks) for any subgroup

Recent drug use was defined as injection drug use reported within 12 months prior to screening and/or positive UDS not accounted for by prescribed concomitant medications
OST, opioid substitution therapy; IDU, injection drug use; UDS, urine drug screen

mITT SVR12 by Viral Characteristics Subgroups: Treatment-naïve patients without cirrhosis, 8 vs 12 weeks

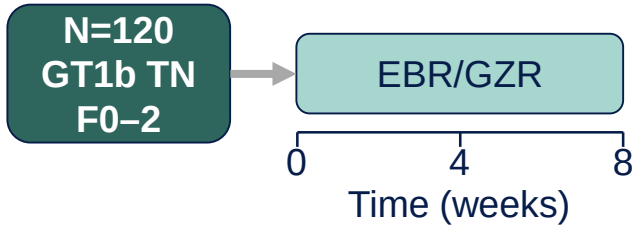


No statistically significant difference in SVR12 rates (8 vs 12 weeks) for any subgroup

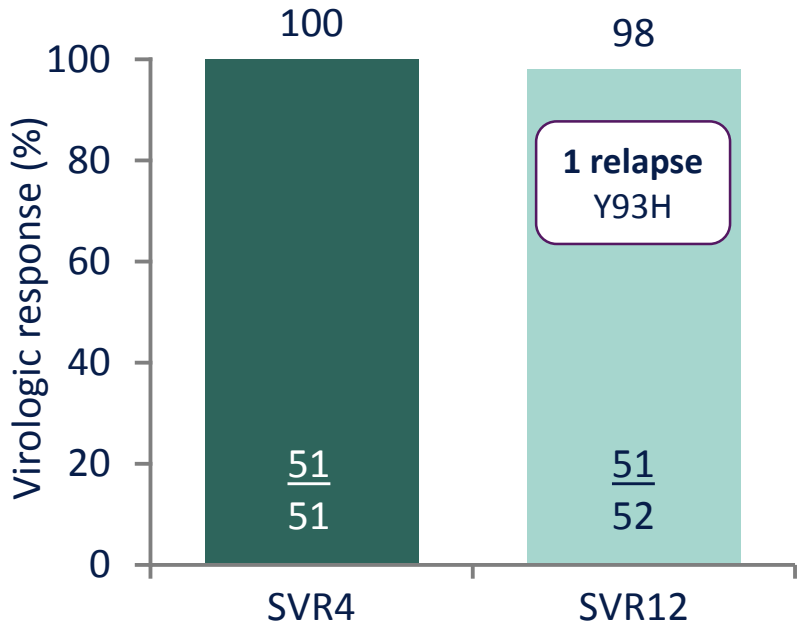
* Baseline polymorphisms (BL Polys) at amino acid positions: **NS3**: 155, 156, 168; **NS5A**: 24, 28, 30, 31, 58, 92, 93

#LB-5, Abergel:
EBR/GZR for 8/52 in Tx-naïve GT1b with Non-severe Fibrosis: Interim Results of the STREAGER Study

Interim analysis of GZR/EBR for 8 weeks in 53 HCV GT1b patients without severe fibrosis (Fibroscan <9.5 kPa and Fibrotest <0.59/Fibrometer <0.63) and w/o advanced kidney disease



Demographic	N=53
Female, n (%)	32 (60)
Mean age (SD), years	53 (12)
Mean BMI (SD), kg/m^2	24.5 (3.7)
BL viral load ≤800,000 IU/mL, n (%)	21 (40)
Fibroscan® (F0–F1), n (%)	46 (87)



Excludes 1 patient with GT1e who relapsed

- Well tolerated with no grade 3 or 4 AEs reported
- AEs >10%:
  - Asthenia (28%)
  - Headache (23%)
  - Digestive disorders (13%)

EBR/GZR for 8 weeks has similar efficacy and safety compared with the 12-week regimen in treatment-naïve patients with GT1b

#1537, Babatin:
8/52 of LDV/SOF in GT4

Cohort prospective study in Saudi Arabia evaluating the safety and efficacy of an 8-week LDV/SOF in GT4

- 52 HCV GT4 subjects comprised the ITT population
- 45 TN NC patients were included in the PP analysis

Baseline demographics	N=45
Mean age (years)	43.98
Male, n (%)	26 (57.78)
BMI, mean (SD)	26.44 (5.82)
Genotype, n (%)	
4	43 (95.6)
4e	1 (2.2)
4acd	1 (2.2)
Fibrosis score, n	
F0	7
F1	33
F2	5
HCV characteristics	
RNA, log_{10} IU/ml (SD)	6.25 (6.32)
RNA ≥ $6x10^6$ IU/ml, n (%)	3 (6.67)

	N=45
HCV RNA <LLOQ, n/N (%)	43/44
At week 4 during treatment	(97.7%)
EOT, n (%)	
At week 8	45 (100%)
Post-treatment, n (%)	
SVR12 (week 20)	44 (**97.8%**)
[95% CI]	[88.2—99.9]
Overall virologic failure n (%)	
On treatment breakthrough	0 (0%)
Post-treatment relapse	1 (2.2%)

- Male (age 66) diagnosed with diabetes and hypertension taking esomeprazole had post-treatment relapse
- Patient's HCV values were within normal range throughout the study

	N=45
Comorbidities, n (%)	
Diabetes mellitus	9 (20)
Hypertension	9 (20)
Sickle cell disease	3 (6.67)
Hypothyroidism	1 (2.22)
Concomitant medication, n (%)	18 (40)
Average per patient	3.9
Proton pump inhibitor*	2 (4.44)
*esomeprazole, omeprazole	

- AEs reported in 18/52 subjects (34.6%)
- Most common Aes include:
  - Headache (26.3%)
  - Fatigue (18.4%)
  - Asthenia (13.2%)
  - Nausea (10.5%)
  - Pruritus (10.5%

8-week LDV/SOF treatment of HCV GT4 patients achieved SVR12 of 98% and was well tolerated with no serious AEs

#1096, Landis:
VEL-SOF-based Regimens in GT1–6: HCV-TARGET Study

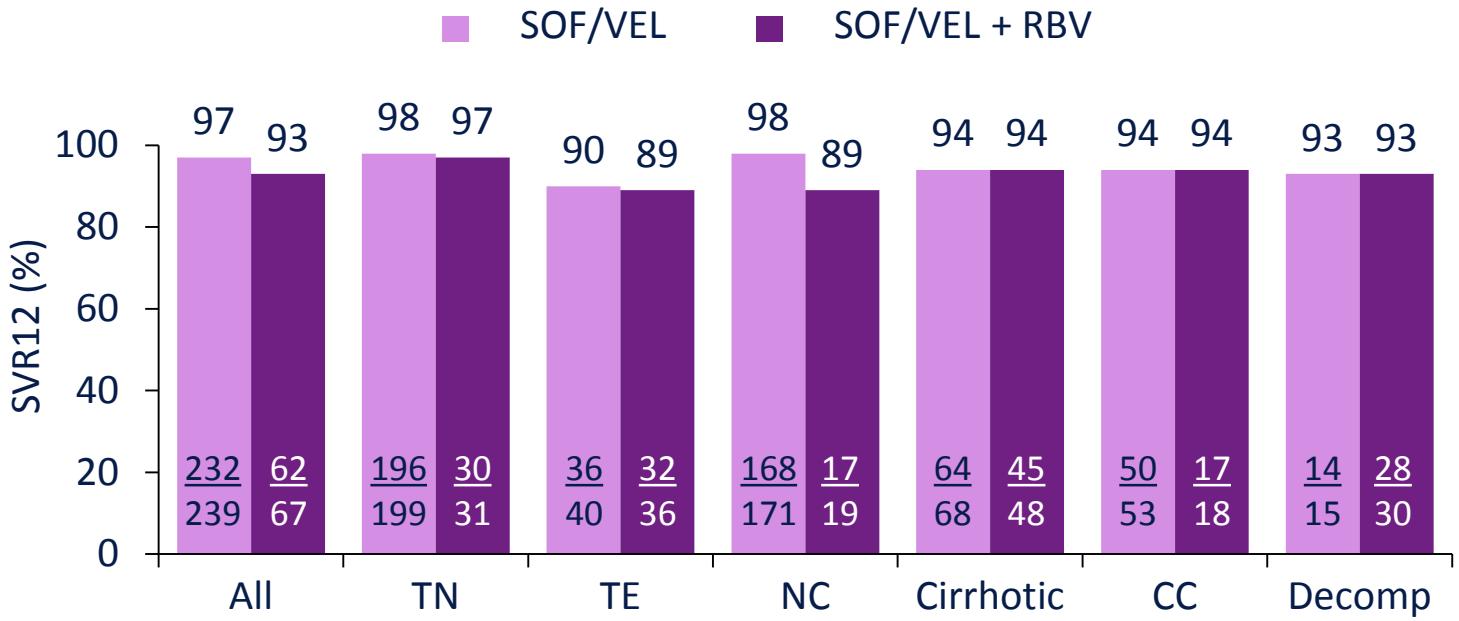
HCV-TARGET: Real-world safety and efficacy of SOF/VEL ± RBV 12 wk in 520 patients with HCV GT1–6 in North America and Europe

Baseline demographics, n (%)	SOF/VEL N=407	SOF/VEL + RBV N=119
Male	228 (56)	88 (74)
Age ≥60 yr	164 (40)	49 (43)
HCV genotype GT1 GT2 GT3 Other	 68 (17) 159 (39) 156 (38) 24 (6)	 38 (34) 16 (14) 52 (46) 7 (6)
Treatment-experienced	67 (17)	66 (58)
Cirrhosis	113 (28)	81 (72)
History of hepatic decompensation	30 (7)	57 (50)
CKD Stage 4/5	9 (2)	—
Dialysis	6 (1)	
HCV RNA (log_{10} IU/mL)	6.2 (1.8–8.2)	6.0 (2.1–8.0)

#1096, Landis

VEL-SOF-based Regimens in GT1–6: HCV-TARGET Study

HCV-TARGET: Real-world safety and efficacy of SOF/VEL ± RBV 12 wk in 520 patients with HCV GT1–6 in North America and Europe



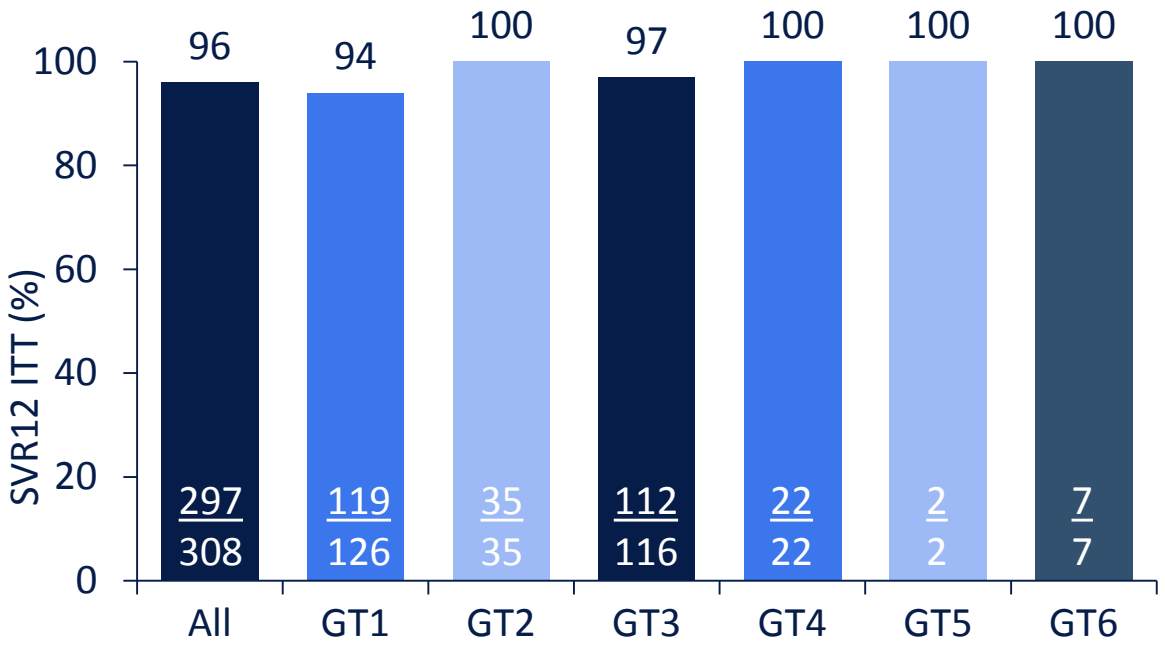
Safety, n (%)	SOF/VEL	SOF/VEL + RBV
AEs	208 (51)	87 (77)
SAEs	15 (4)	14 (14)
Fatigue	55 (14)	30 (27)
Headache	58 (14)	17 (15)
Nausea	28 (7)	16 (14)
Anemia†	3 (1)	22 (19)
Deaths	0	1

- SOF/VEL was used predominantly among GT2/3 TN patients
- SOF/VEL + RBV was mostly used in cirrhotics with prior decompensation, DAA failures, and GT3 TE patients
- SOF/VEL ± RBV demonstrated high efficacy (SVR12 97.1% for SOF/VEL and 92.5% for SOF/VEL + RBV) and good tolerability in this real-world cohort, with 1% D/C due to AEs

#74, Gane:
GLE/PIB in Adults with GT1–6 and Compensated Cirrhosis: An Integrated Analysis

4 Phase 2/3 clinical trials of 12 weeks and 16 weeks GLE/PIB
(N=308; EXPEDITION-1 & -4, SURVEYOR-2, MAGELLAN-1)

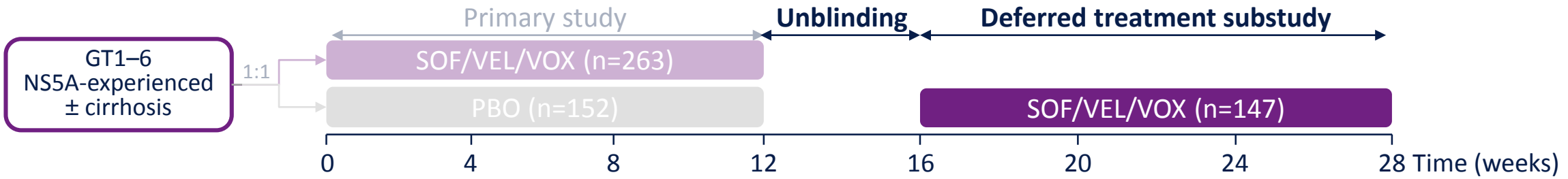
	N=308
Male, n (%)	199 (65)
White, n (%)	261 (85)
Age [yr], median (range)	58.5 (26–88)
BMI [kg/m^2], median (range)	28.2 (18.0–55.4)
HCV GT1 / 2 / 3 / 4–6, n (%)	123 (40) / 38 (12) / 116 (38) / 31 (10)
HCV RNA [$\log_{10}$ IU/mL], median (range)	6.2 (3–7)
Treatment experienced, n (%)	126 (41)
Baseline C-P score, 5 / 6 / 7, n (%)	264 (86) / 41 (13) / 2 (<1)
Platelet count <100 x 10^9/L	70 (23)
Albumin <3.5 g/dL, n (%)	23 (7)



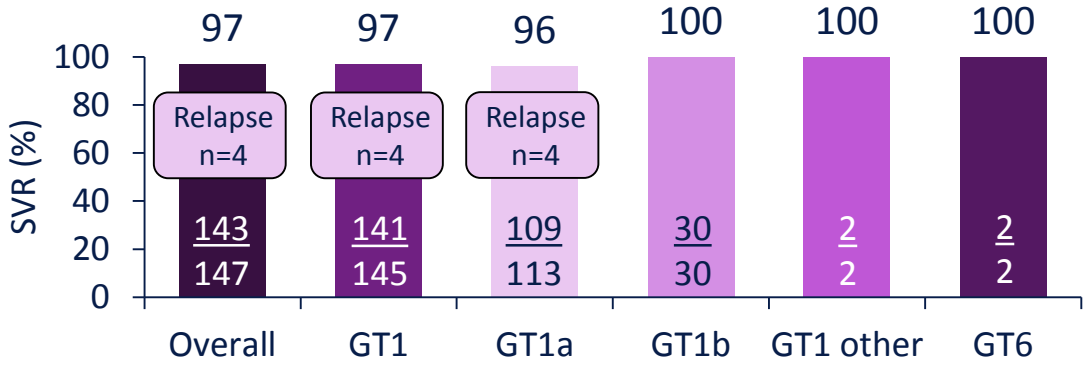
5 patients had breakthrough infections and 3 patients relapsed

Results support FDA-approved indications for GLE/PIB patients with compensated cirrhosis

#1178, Bourlière:
SOF/VEL/VOX for 12 Weeks in NS5A Inhibitor-experienced Patients: POLARIS-1 Study



Baseline demographics	N=147
Age (years), mean (range)	59 (29–80)
Male, n (%)	116 (79)
White, n (%)	121 (82)
GT1 GT1a / GT1b GT6	145 (99) 113 (77) / 30 (20) 2 (1)
Cirrhosis, n (%)	49 (33)
HCV RNA (log_{10} IU/mL), mean (range)	6.3 (4.5–7.6)
Treatment-experienced, n (%) NS5A + NS5B NS5A + NS3 ± NS5B NS5A ± others Others	 76 (52) 61 (41) 9 (6) 1 (<1)
Any RAS, n (%)	131/145 (90)



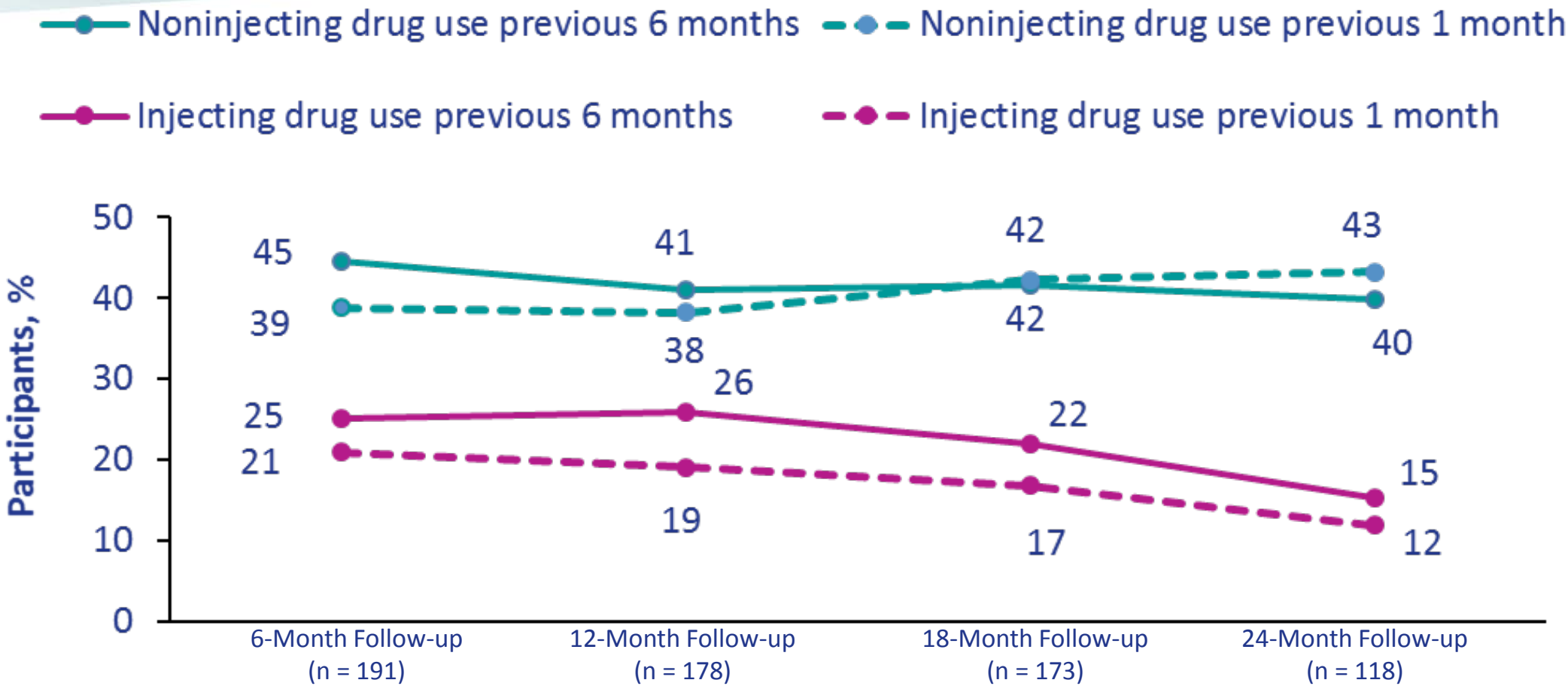
- Of the 4 patients with VF, 2 developed treatment-emergent RASs:
  - 1 had NS3 Y56H and D168A/V, and NS5A L31L/M
  - 1 had NS3 V36V/A

- High SVR12 rates were observed in NS5A inhibitor-experienced patients treated with SOF/VEL/VOX for 12 weeks
  - 96% in NS5A+NS5B-exposed patients
  - 98% in NS5A+NS3±NS5B-exposed patients
- Baseline RASs were common but did not impact SVR12 rates

AEs, n (%)	N=147
Any AE	112 (76)
AE in >10% of patients Fatigue Headache Diarrhea Nausea	 31 (21) 29 (20) 28 (19) 21 (14)
Grade 3–4 AE	7 (5)
SAE	6 (4)
Treatment-related SAE	0
D/C due to AE	0
Death	0
Grade 3–4 lab abnormalities	16 (11)

Substance Abuse

ONGOING RISK BEHAVIOR—REPORTED DRUG USE[a]



[a]Participants may have reported both injection and noninjection drug use.

Dore G. et al. AASLD 2017 Washington, DC. Oct. 20-24, 2017. #195.

C-EDGE CO-STAR

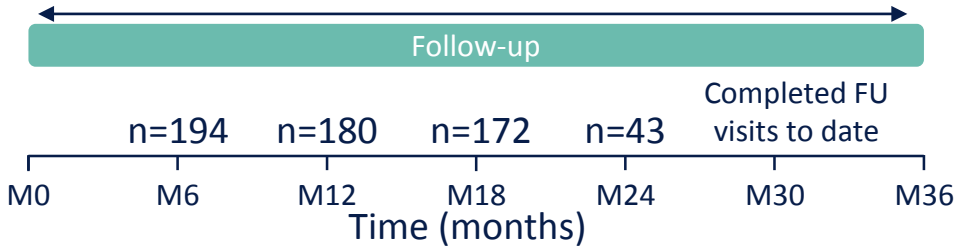
#195, Dore:
HCV Reinfection Following EBR/GZR: CO-STAR Part B

CO-STAR Part B: Ongoing 3-year observational follow-up
Patients were followed-up every 6 months to assess reinfection, urine drug screen, and patient-reported behaviors

GT1, GT4, and GT6
TN, receiving opiate agonist therapy ± cirrhosis (N=199)

- 76% male (n=151)
- 79% white (n=158)
- 59% +ve drug screen (n=117)
- 92% GT1a/1b (n=183)
- 8% HIV (n=16)
- 22% cirrhotic (n=44)

Part B

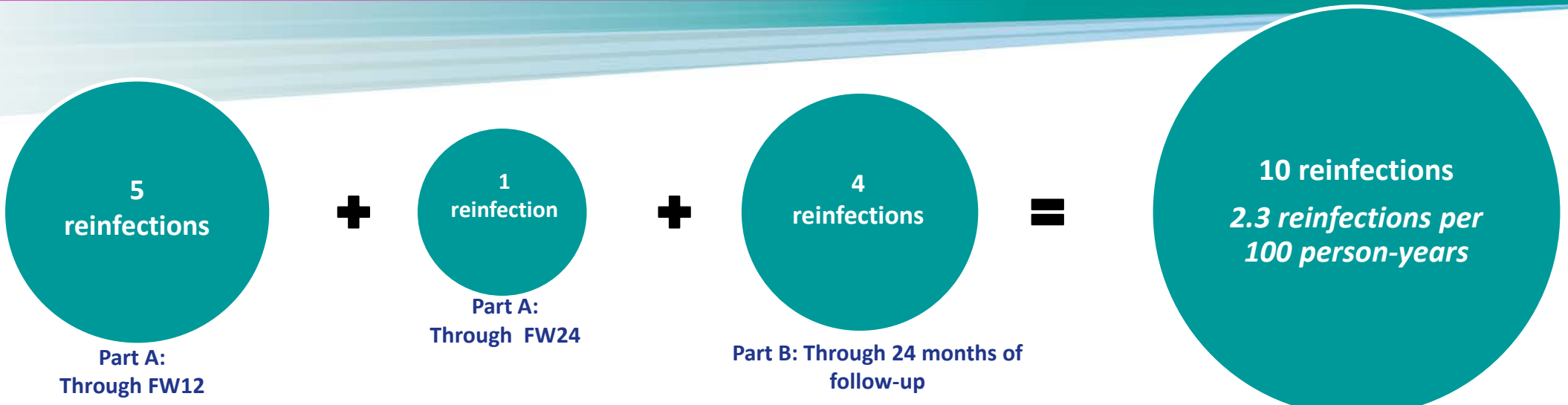


Increased risk of reinfection based on patient-reported injection drug use

74 patients (37%) reported injection drug use	125 patients (63%) reported no injection drug use
Rate of reinfection 4.2/100 person-yr 95% 1.5–9.2	**Rate of reinfection** 0.4/100 person-yr 95% CI 0.0–2.3

- HCV reinfection among participants on OAT following EBR/GZR therapy is uncommon, despite ongoing drug use
- Rates of reinfection are greater for patients with recent injection drug use

INCIDENCE OF REINFECTION



All Reinfections: From End of Treatment Through 24 Months of Follow-up		
• 10 reinfections	• 426 person-years	• 2.3 reinfections per 100 person-years (95% CI: 1.1, 4.3)
Persistent Reinfections: From End of Treatment Through 24 Months of Follow-up (includes only those participants with persistent HCV RNA)		
• 7 reinfections	• 429 person-years	• 1.6 reinfections per 100 person-years (95% CI: 0.7, 3.4)
Clearance of reinfection was observed in 3/10 (30%) reinfection cases		

CI, confidence interval; FW, follow-up week

Dore G. et al. AASLD 2017 Washington, DC. Oct. 20-24, 2017. #195.

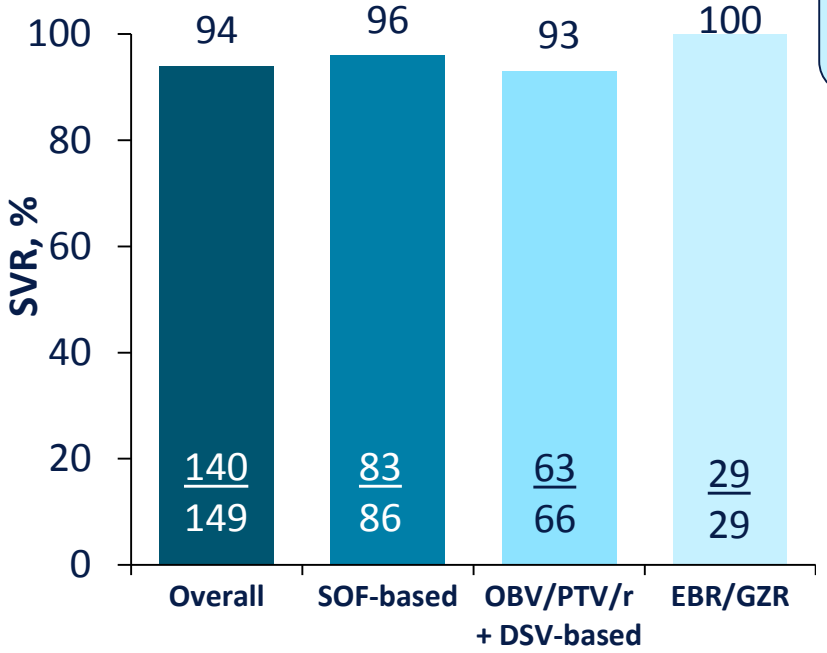
#1136, Alimohammadi:
Tx of HCV-infected Vulnerable Populations with All-Oral Regimens; Updated Real-world Data

- Retrospective analysis: 195 HCV-infected patients with current/recent drug use (PWUD) (documented by urine drug screen) who initiated all-oral HCV therapy at Vancouver Infectious Diseases Centre since June 2015

Characteristic	N=195
Age (mean), years	53.5
Male, n (%)	152 (78)
History of Opioid overdose, n (%)	16 (8)
Heroin use, n (%)	132 (68)
Cocaine use, n (%)	115 (59)
GT1, n (%)	133 (68)
GT3, n (%)	37 (19)

HCV treatment regimens:
86 with SOF (59 with LDV, 23 with RBV)
66 with OBV/PTV/r + DSV (56 with RBV)
29 with EBR/GZR

Virologic response overall and by treatment regimen



155 (79%) patients completed Tx
6 (3%) patients lost to follow-up
3 (1.5%) D/C

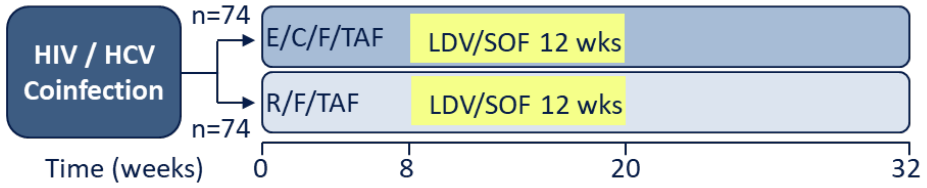
Safety

- 1 death, unrelated to HCV or its treatment
- 9 cases of virologic failure, all post-treatment relapses
- No cases of recurrent viremia (follow-up 6–21 months post-treatment)

- Within a multidisciplinary model of care, treatment of HCV-infected PWUD with all-oral regimens is safe and highly effective
- These data support feasibility of designating PWUD as a priority population to receive HCV treatment in real-world setting

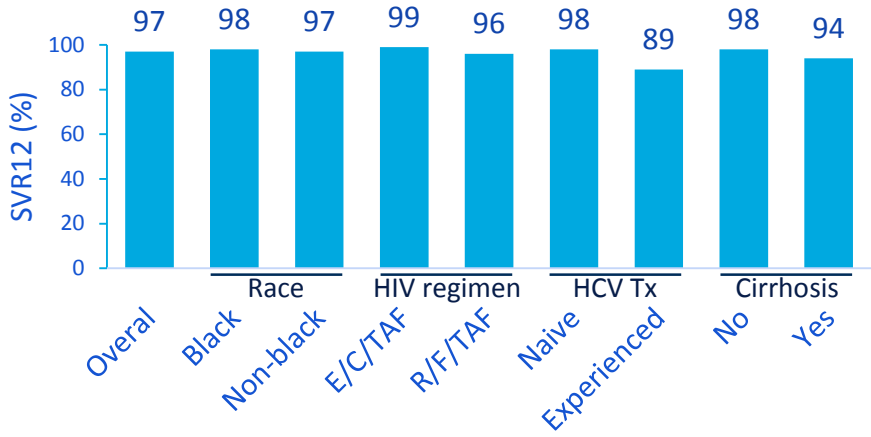
Special Populations

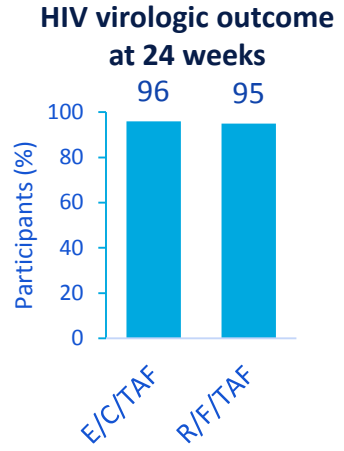
#LB-12, Ramgopal:
HIV-HCV
12/52 LDV/SOF after Randomized Switch to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) or Rilpivirine/F/TAF (R/F/TAF)



HCV Disease Characteristics	E/C/F/TAF n=74	R/F/TAF n=74	Total n=148
HCV RNA, log_{10} IU/mL, median (range)	6.4 (1.2-7.3)	6.5 (4.3-7.5)	6.4 (1.1-7.5)
HCV treatment experience	8%	4%	6%
Cirrhosis	11%	13%	12%

HIV Disease Characteristics	E/C/F/TAF n=74	R/F/TAF n=74	Total n=148
Age, median (range)	52 (26-70)	55 (25-69)	53 (25-70)
Male	78%	70%	74%
Black	41%	42%	41%
CD4 count, median cells/µl	671	640	651
Duration of prior AV use, median years	12	16	13





	ARVs only Day 1 – W8 n=148	ARVs + LDV/SOF W8—W20 n=144	Whole Study Day 1--End n=148
Any grade AEs	77 (52%)	95 (66%)	121 (82%)
Grade 3 or 4 AEs	5 (3%)	10 (7%)	17 (12%)
Serious AEs	3 (2%)	12 (8%)	19 (13%)
D/C of HIV drugs due to AEs	1 (<1%)	0	1 (<1%)
D/C of LDV/SOF drugs due to AEs	N/A	0	0
Death	0	0	1 (0.7%)

Switching HIV regimen to E/C/F/TAF or R/F/TAF and subsequent treatment of HCV with LDV/SOF was safe and effective

#1140, Qi:
SVR12 12-week HCV DAAs in Black - GT1 Infection

Meta-analysis of 26 clinical trials submitted to the FDA between 2013 and 2017 of 12-week IFN-free DAA regimens ± RBV in 2916 HCV GT1 monoinfected and 746 HCV GT1/HIV coinfected patients

Difference in SVR12 rates between black and non-black
HCV GT1 monoinfected subjects

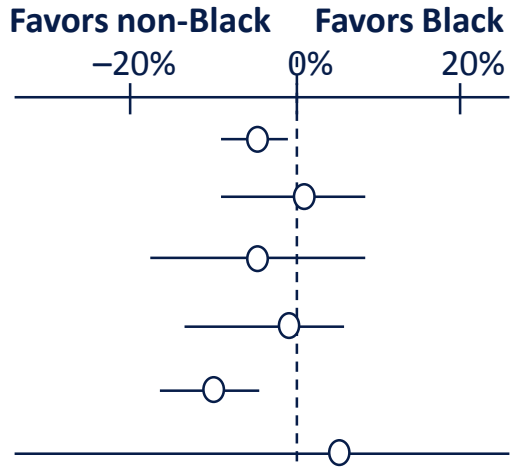
- There were no statistically significant differences in SVR12 rates for blacks vs non-blacks in clinical trials of HCV GT1 monoinfected patients
- Baseline characteristics did not affect SVR12 rates in black vs non-black HCV GT1 monoinfected patients

Difference in SVR12 rates between black and non-black
HCV GT1/HIV coinfected subjects

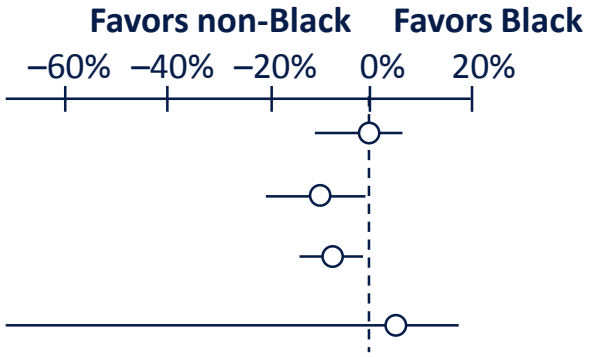
- SVR12 rates were significantly different for blacks vs non-blacks in clinical trials of HCV GT1/HIV co-infected patients (driven by ION-4 data)
- Significant differences in SVR12 rates for black vs non-black HCV GT1/HIV coinfected subjects were seen in subjects aged ≥55 years and in US subjects

Difference in SVR12 rates between black and non-black
HCV GT1/HIV coinfected subjects

HCV + HIV	Difference (95% CI) SVR12
Overall	–4.4% (–8.7%, –1.1%)
ALLY-2	1.5% (–8.8%, 8.8%)
ASTRAL-5	–4.4% (–17.5%, 9.0%)
C-EDGE	–0.5% (–14.0%, 6.1%)
ION-4	–9.6% (–16.7%, –4.7%)
TURQUOISE-I	5.6% (–33.9%, 26.2%)



HCV + HIV	Difference (95% CI) SVR12
Age: <55 years	–0.2% (–10.8%, 5.4%)
Age: ≥55 years	–8.6% (–19.2%, –0.4%)
US patients	–5.3% (–12.4%, –0.2%)
Non-US	4.8% (–71.0%, 16.8%)

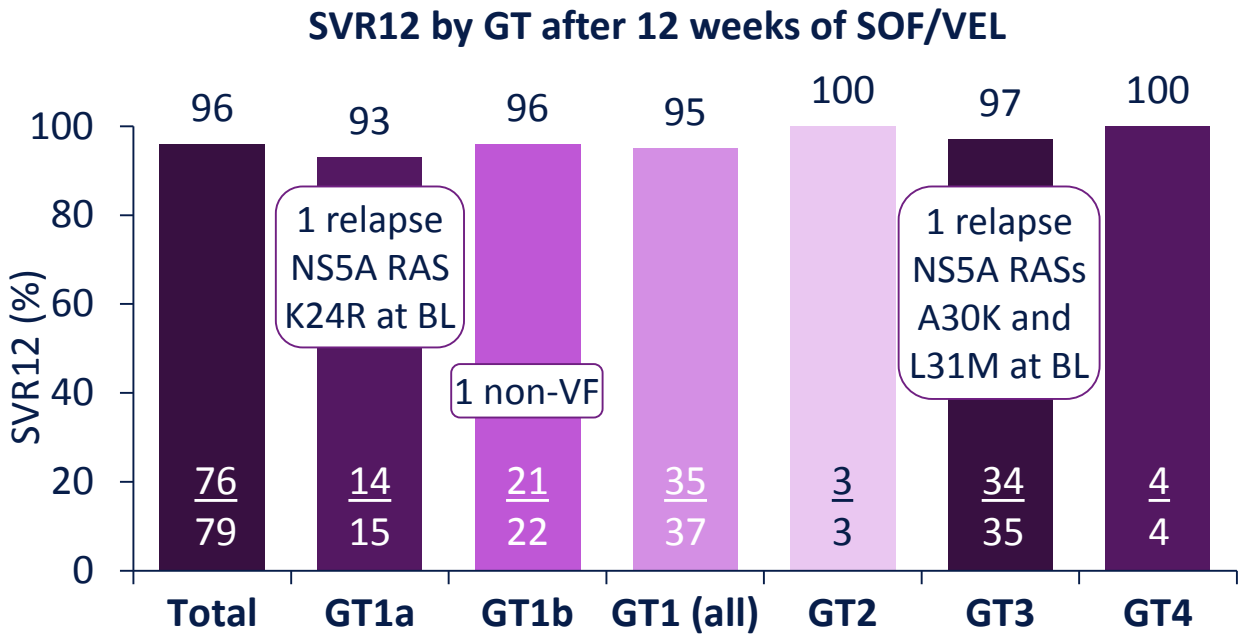


#1069, Agarwal:
SOF/VEL for 12/52 in GT1–4 Liver Transplant Recipients

- Phase 2, single-arm, open-label study
- Safety and efficacy of 12 wk SOF/VEL 400/100mg QD in liver transplant recipients with recurrent chronic GT1–6 HCV

- Liver transplant patients from Spain, UK, and Switzerland
- TE or TN; without cirrhosis or with CC
- ≥3 months post transplant

Demographics	Enrolled and treated (n=79)
Male, n (%)	64 (81)
White, n (%)	65 (82)
Compensated cirrhosis, n (%)	7 (9)
Treatment experienced, n (%)	47 (60)
Time from liver transplantation (years), mean (range)	8.7 (0.3–23.9)



SVR12 86% (6/7) for patients with protocol-defined CC (no VF)

Safety
- 62 (78%) patients with AEs (mostly headache/fatigue/cough)
- 1 patient discontinued SOF/VEL due to grade 1 AE
- No deaths, graft loss or acute rejection

Treatment with SOF/ VEL x 12/52 was highly efficacious and well tolerated in GT1–4 HCV-infected liver transplant recipients with and without cirrhosis

#875, Tran: CKD and HCV Mutually Advance Liver and Renal Disease Progression: Real-world Evidence from the United States

Real-world cohort of patients from the Optum Clinformatics® Data Mart claims database to assess how CKD affects liver disease progression in patients with HCV and how HCV affects renal disease progression in patients with CKD

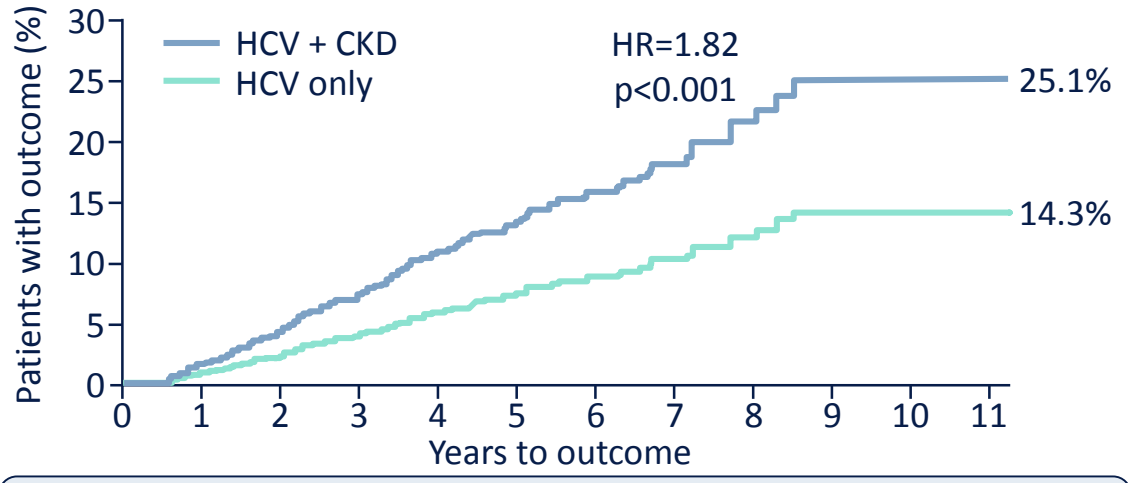
All patients included in the analysis required 6 months of continuous enrollment pre-index and ≥2 measures of fibrosis or CKD ≥6 months apart

HCV + CKD (n=1586)
CKD diagnosis at or prior to first HCV diagnosis (HCV index date, 2006–2016)

VS

HCV only (n=3172)

Proportion of patients with fibrosis stage increase (Dx 2006–2016)



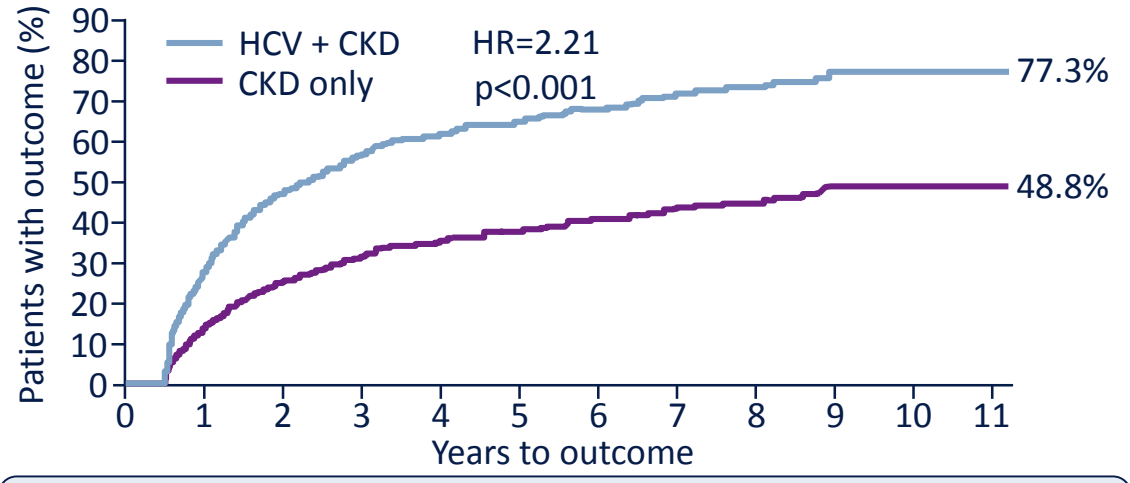
Mean time to fibrosis stage progression was lower in patients with CKD vs those without CKD (827 vs 987 days, p=0.330)

HCV + CKD (n=540)
HCV diagnosis at or prior to first CKD diagnosis (CKD index date, 2006–2016)

VS

CKD only (n=1080)

Proportion of patients with CKD stage increase (Dx 2006–2016)



Mean time to progression was lower in patients with HCV vs those without HCV (506 vs 676 days, p=0.032)

- Liver fibrosis and CKD are worsened when both are present as comorbidities compared with when only one condition is present
- Early identification and treatment of HCV could lead to mutual health benefits for liver and renal diseases

#1088, Alric:
Real-world Efficacy and Safety of EBR/GZR in GT1 or GT4 with Severe CKD (Stage 4/5) or Hemodialyzed

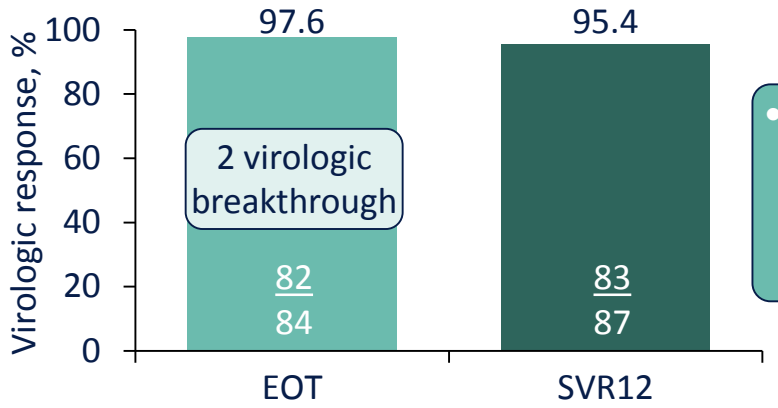
Non-randomized, multicenter, nationwide French observational study assessing safety and efficacy of EBR/GZR in HCV GT1 or 4 infected patients with stage 4 or 5 advanced CKD, including patients mainly on hemodialysis

87 HCV infected patients with CKD

- GZR+EBR 100/50 mg for 12 weeks (n=73), 16 weeks (n=13) or 24 weeks (n=1)
- 2 patients (2.2%) treated with RBV in combination with GZR+EBR

Demographics	Patients (n=87)
HCV GT, n (%)	
GT1a	19 (21.8)
GT1b	47 (54.0)
GT1 unclassified	3 (3.4)
GT4	17 (19.5)
GT6	1 (1.1)
eGFR	30.5± 34.5 ml/min
Patients hemodialyzed, n (%)	64 (73.5)
Metavir F3/F4, n (%)	30 (34.4)

Efficacy



- SVR12 similar for:
  - ± cirrhosis
  - HCV GT1 and GT4
  - ± hemodialysis

Co-medications and safety

- Most patients received many drugs (average 7 ± 4.4) related to comorbidities
- Serious AEs occurred in 7/87(8 %) patients: 3 deaths (3.4%) not related to GZR + EBR therapy, 2 SAEs not related to GZR+EBR, 1 SAE related to GZR + EBR
- No patient required GZR + EBR withdrawal

- Once-daily GZR + EBR is highly effective with a low rate of AEs in the very difficult to treat population with severe renal impairment and HCV GT1 or 4 infection

#1587, Lawitz: LDV/SOF (90/400 mg) x 12/52 in GT1 with Severe Renal Impairment

18 HCV GT1 treatment-naïve or -experienced patients, with or without compensated cirrhosis and **CrCL ≤30 mL/min**, not on dialysis, received LDV/SOF for 12 weeks

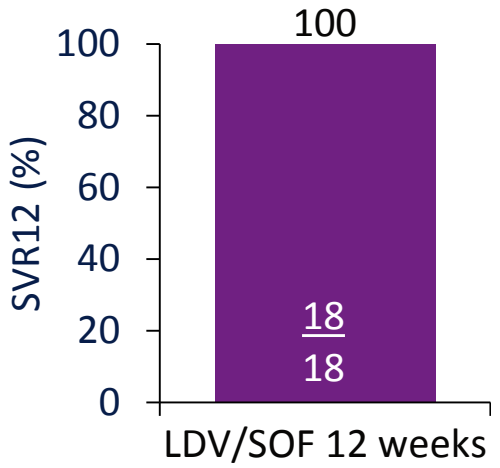
- **Male:** 67%
- **African American:** 56%
- **BMI, mean (range):** 30 (21–39) kg/m^2
- **eGFR, mean (range):** 24.9 (9.0–39.6) mL/min/1.73m^2
- **GT1a:** 78%
- **Treatment-naïve:** 78%
- **Cirrhosis:** 11%

Drug exposure vs subjects in LDV/SOF Phase 3 studies:

- **SOF:** ↑ ~2.6-fold
- **GS-331007:** ↑ ~5.1-fold
- **LDV:** ↔

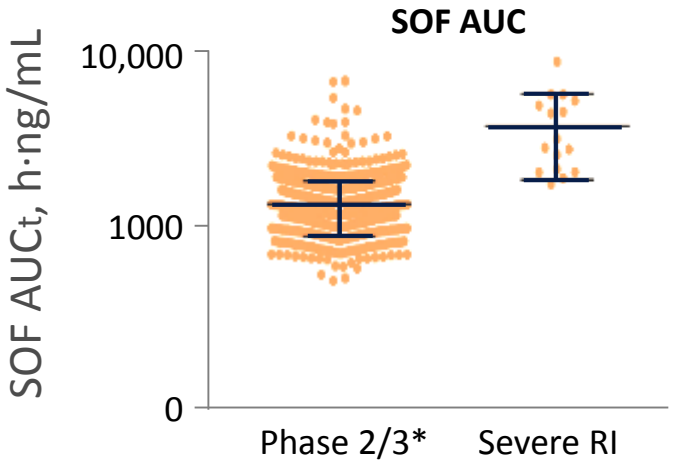
No clinically meaningful change in eGFR: a decrease of 1.2 mL/min/1.73 m^2 from baseline to EOT

- Treatment with LDV/SOF (90/400 mg) for 12 weeks in GT1 patients with and without cirrhosis and severe renal impairment resulted in 100% SVR4 rate
- The regimen was safe and well-tolerated with no treatment discontinuations and no treatment-related SAEs



Safety	N=18
Serious AEs	22%
Common AEs	
Fatigue	22%
Headache	22%
Hyperkalemia	22%

No SAEs were considered related to study drugs



*Includes patients with normal renal function (CrCl ≥90 mL/min.

Other Issues in HCV Management

#1019, Mücke:
HBV reactivation in patients with active or resolved HBV infection treated with DAAs: systematic review and meta-analysis

PubMed, Ovid MEDLINE, Cochrane Central Register of Controlled Trials, and **Web of Science** through June 6, 2017

- Serologic HBV status known/assessed at BL
- Repeated HBV DNA and ALT monitoring during DAA therapy for patients with chronic HBV
- Repeated ALT monitoring with additional HBVDNA monitoring at EOT/during follow-up in patients with resolved HBV

15 studies, 1541 patients: 237 chronic, 1304 resolved, different DAAs

Patient population	Reactivation	HBV-related hepatitis
Chronic HBV (HBsAg-positive)	≥2log$_{10}$ increase in HBV DNA from BL **Or** detection of HBV DNA >100 IU/ml in patients with undetectable HBV DNA at BL	ALT levels >2-fold above the ULN in combination with molecular HBV-R
Resolved HBV (HBsAg-negative → HBsAg-positive)	reverse HBsAg seroconversion (HBsAg-negative becomes HBsAg-positive) **Or** any quantifiable HBV DNA (≥20 IU/ml) during study period	

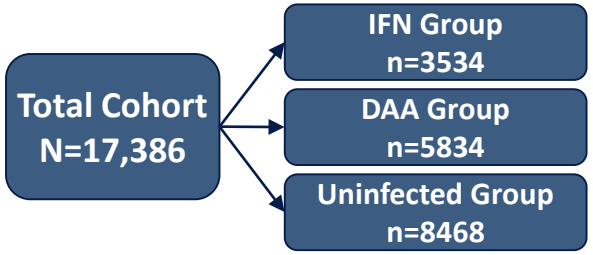
Pooled risk ratios for reactivation	
Chronic	**Resolved**
0.24 (95% CI: 0.19–0.36)	0.014 (95%CI : 0.00–0.0239)
Pooled risk ratios for HBV-related hepatitis	
Chronic	**Resolved**
0.09 (95% CI: 0.05–0.14)	0 (95%CI : 0–0.01)

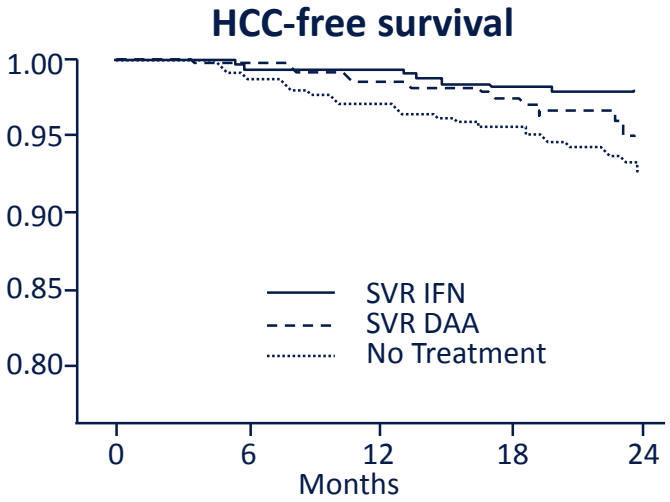
In patients with resolved HBV infection, no HBV-related hepatitis or major clinical event was reported. Some ALT flares were observed, but none could be associated with increased HBV DNA.

- Results support universal HBV screening prior to DAA treatment in HCV-infected patients
- In HBsAg negative/HBcAb-positive patients, risk of reactivation is low, therefore use of antiviral prophylaxis may not be justified

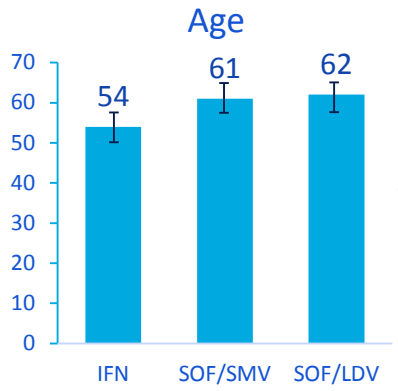
#226, Li: HCC
Incidence not Increased after SVR with IFN-free Tx compared with IFN-containing Tx: An ERCHIVES Study

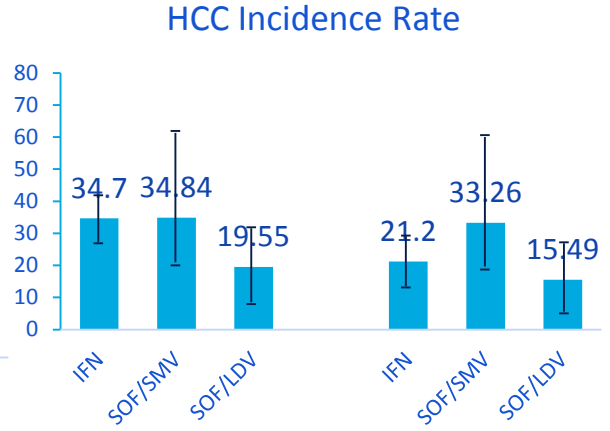
ERCHIVES, a large national cohort of HCV-infected and uninfected Veterans, used to assess the impact of DAA treatment compared to IFN treatment on the development of *de novo* HCC

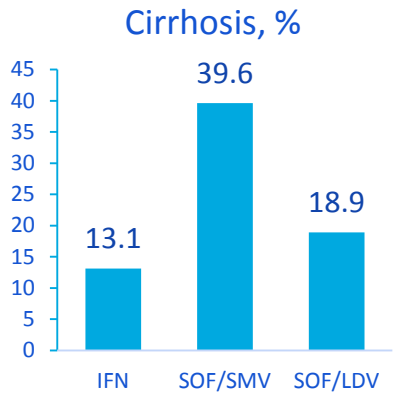




Multivariate Regression Model of HCC risk	Hazards ratio	95% CI
Age, per 10 yr increase	1.76	1.26, 2.46
Male sex	1.34	0.32, 5.62
Diabetes	1.01	0.67, 1.50
BMI, per 1 unit increase	0.98	0.95, 1.01
Alcohol abuse history	1.27	0.85, 1.89
Statin use	0.50	0.31, 0.80
AFP>20 (vs ≤ 20)	4.10	2.75, 6.10
Treatment Regimen		
PEF/RBV (comparator)	1	—
Any DAA	1.07	0.55, 2.08
Attainment of SVR	0.66	0.42, 0.98







Patients treated with early DAA regimens had higher baseline risk of HCC but not increased incidence

- DAA-treated patients had higher incidence of HCC risk factors (cirrhosis, diabetes, age) but no association between DAA exposure and increased de novo HCC incidence after controlling for these risk factors
- No difference in HCC-free survival between cirrhotics successfully treated with DAAs or IFN

#142, Ioannou: Eradication of HCV Induced by DAAs Is Associated with a 71% Reduction in HCC risk

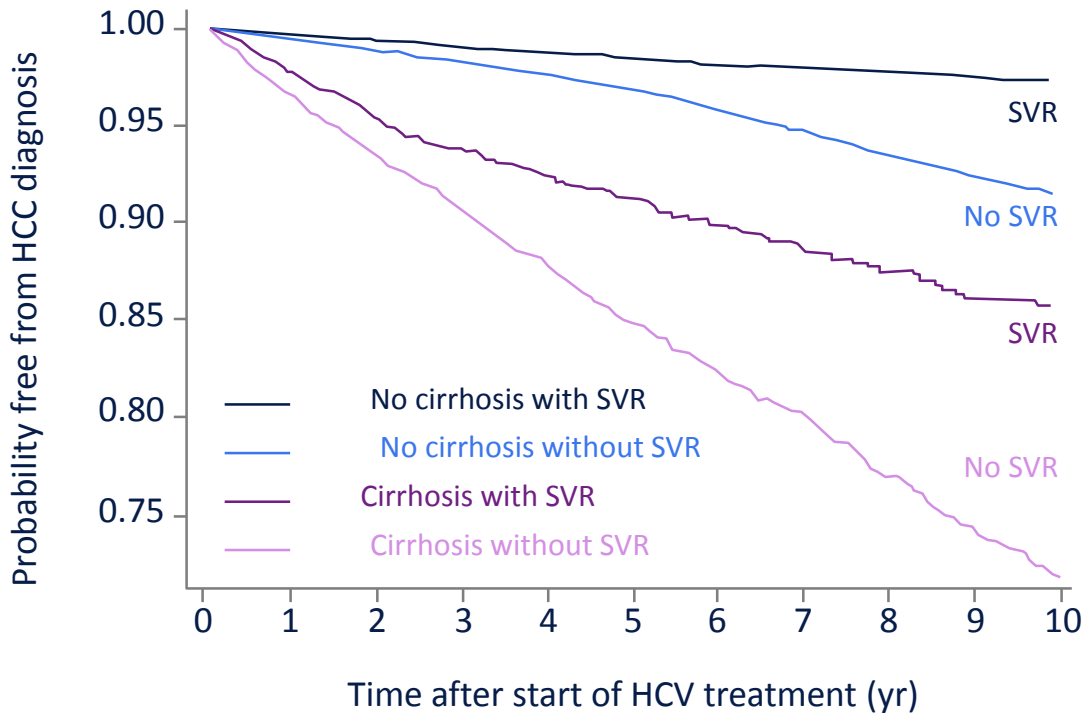
Retrospective analysis of 62,354 patients in the VA national healthcare system (1999–2015) to determine the association between SVR and *de novo* HCC risk

As of June 15, 2017:
Mean follow-up: 6.1 years
Incident HCCs: 3271

Regimen	Patients, n (%)
IFN-only	35,871 (58)
DAA ± IFN	4535 (7)
DAA only	21,948 (35)

Irrespective of cirrhosis status, SVR was associated with a **lower HCC risk**
Cirrhosis: AHR 0.50; 95% CI 0.43–0.59
No cirrhosis: AHR 0.32; 95% CI 0.28–0.37

SVR was associated with a **lower HCC risk:**
Interferon only **68% risk reduction**
DAA plus interferon **52% risk reduction**
DAA only **71% risk reduction**



DAA-induced SVR is associated with an 71% reduction in HCC risk