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EASL 2017
Post-Congress Data Summary and Analysis

Global Medical Affairs, Hepatology

Congress Overview

- EASL 2017 data provides further evidence for the emerging treatment paradigm to establish 8 weeks of treatment for TN NC, across all genotypes
  - G/P: integrated analyses have demonstrated high efficacy across different patient types, regardless of baseline patient or viral characteristics
  - LDV/SOF: RWE data continues to support the potential expanded use in GT1 patients irrespective of HCV RNA baseline viral load
  - SOF/VEL/VOX: integrated analyses have identified multiple baseline predictors associated with lower SVR rates in GT1a patients
- From the data presented at EASL 2017, two regimens are expected to dominate the retreatment landscape: 16 weeks of G/P (MAGELLAN-1 Part 2) and 12 weeks of SOF/VEL/VOX (POLARIS integrated analyses)
- EASL 2017 saw the release of data for many patient groups considered once difficult to treat, including patients with CKD, PWID, HIV/HCV coinfection and post-liver/renal transplant; these data bring into question whether special patient populations still exist with highly efficacious next-generation DAAs
- EASL 2017 saw the release of a wealth of RWE data, including first reports of the use of SOF/VEL and EBR/GZR I real-life clinical practice; RWE continues to confirm the results of clinical trials across the currently approved regimens (OBV/PTV/r $\pm$ DSV, LDV/SOF, SOF/VEL, EBR/GZR)

TN NC, treatment-naive, non-cirrhotic; RWE, real-world evidence; CKD, chronic kidney disease; PWID, persons who inject drugs.

Outline: EASL 2017 Highlights

DAA-Naive ± Compensated Cirrhosis

DAA-Experienced

Patients with Chronic Kidney Disease

Other Populations

DDI & PK

Real-World Evidence

New Molecules

OBV/PTV/r + DSV

Extrahepatic Manifestations

HEOR

Diagnosis and Linkage to Care

HBV Reactivation

DAA-Naive ± Cirrhosis

Executive Summary

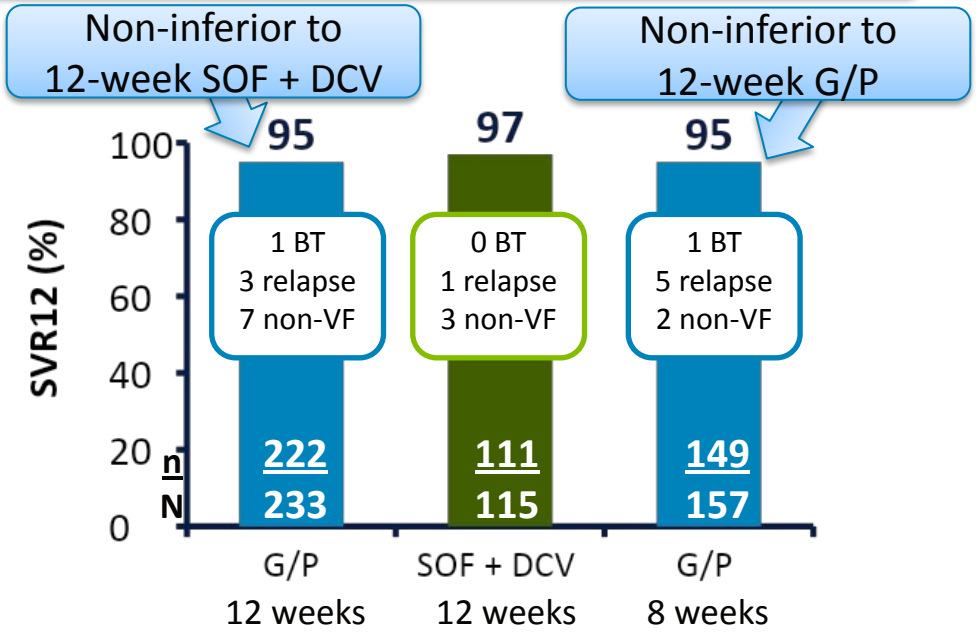
- Emerging treatment paradigm to establish 8 weeks of treatment for TN NC, across all genotypes, including GT3 patients
  - G/P demonstrates consistently high efficacy across different patient types regardless of baseline patient or viral characteristics
  - Limited RW data suggests that LDV/SOF use for GT1 patients may be expanded based on RWE data suggesting a HCV RNA baseline viral load >6 million IU/mL has no impact on SVR
  - Multiple baseline predictors were associated with lower SVR rates in GT1a patients treated for 8 weeks with SOF/VEL/VOX
  - Studies continue to pursue mix and match regimens (DCV + SOF, EBR/GZR + SOF) for 8 weeks in TN NC patients; this could be a feasible option for select markets

GS-007, Foster: ENDURANCE-3: Safety and Efficacy of G/P Compared to SOF + DCV in Treatment-Naive HCV GT3-Infected Patients without Cirrhosis

Treatment-naive, GT3-infected patients without cirrhosis were randomized 2:1 to receive 12 weeks of either G/P or SOF + DCV, or were assigned to an 8-week G/P arm

Baseline characteristics	G/P 12 weeks N = 233	SOF + DCV 12 weeks N = 115	G/P 8 weeks N = 157
Median age, years (range)	48 (22–71)	49 (20–70)	47 (20–76)
History of IDU, n (%)	149 (64)	73 (63)	104 (66)
Baseline fibrosis, n (%)			
F0 – F1	201 (86)	97 (84)	122 (78)
F2	12 (5)	8 (7)	8 (5)
F3	20 (9)	10 (9)	27 (17)

Safety, n (%)	G/P 12 weeks N = 233	SOF + DCV 12 weeks N = 115	G/P 8 weeks N = 157
SAE	5 (2)	2 (2)	3 (2)
AE possibly related to DAA	112 (48)	50 (43)	63 (40)
AE leading to study drug d/c	3 (1)	1 (1)	0



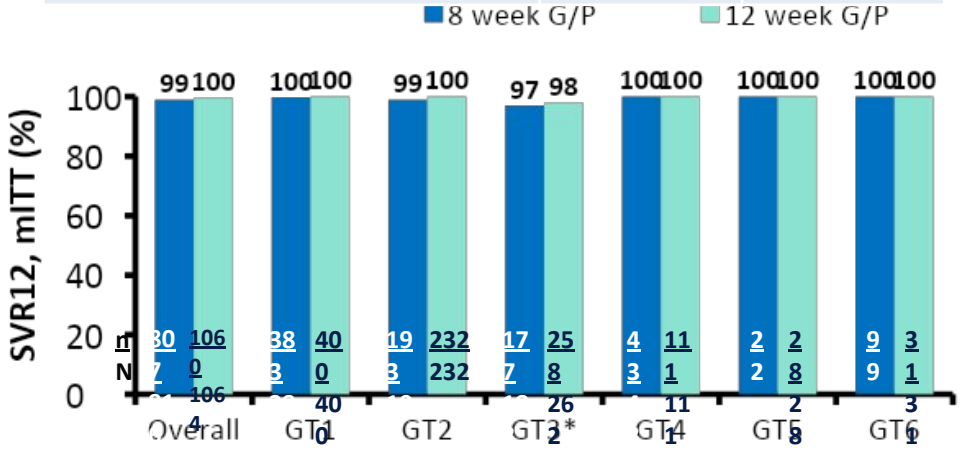
SVR12, n/N (%)	G/P 12 weeks N = 233	SOF + DCV* 12 weeks N = 115	G/P 8 weeks N = 157
NS3 only	26/26 (100)	–	14/15 (93)
NS5A only	35/36 (97)	20/21 (95)	34/36 (94)
NS3 + NS5A	6/7 (86)	–	5/7† (71)
None	151/153 (99)	89/89 (100)	94/95 (99)

BT, breakthrough; d/c, discontinuation; IDU, injection drug use; ND, not determined; non-VF, non-virologic failure; RAS, resistance-associated substitution.
* NS3 sequences not determined; † One patient with VF had poor adherence and both NS3 + NS5A baseline RASs.

SAT-233, Puoti: High SVR Rates with 8 and 12 Weeks of Pangenotypic G/P: Integrated Efficacy Analysis of Genotype 1–6 Patients without Cirrhosis (1)

Integrated efficacy analysis of 8 or 12 weeks' G/P treatment in non-cirrhotic patients with GT1–6 infection across seven phase 2 or 3 clinical trials

Baseline characteristics	8 weeks G/P N = 828	**12 weeks G/P N = 1076**
Median age, years (range)	53 (19–84)	53 (20–83)
White race, n (%)	688 (83)	825 (77)
Treatment-naive, n (%)	657 (79)	801 (74)
Baseline HCV RNA ≥6M IU/mL, n (%)	205 (25)	226 (21)



mITT, excludes patients with non-virologic failure.
* All GT3 patients were treatment-naive;
† GT1: n = 1; GT3: n = 1; ‡ GT3: n = 1; § GT2: n = 2; GT3: n = 5; ‖ GT3: n = 3;
¶ N adjusted for patients with missing data and excludes non-virologic failure.

Reasons for non-response, n (%)	8 weeks G/P N = 828	**12 weeks G/P N = 1076**
Breakthrough	2 (<1)†	1 (<1)‡
Relapse	7 (<1)§	3 (<1)‖
Non-virologic failure		
Discontinuation	5 (<1)	6 (<1)
Missing data	7 (<1)	6 (<1)

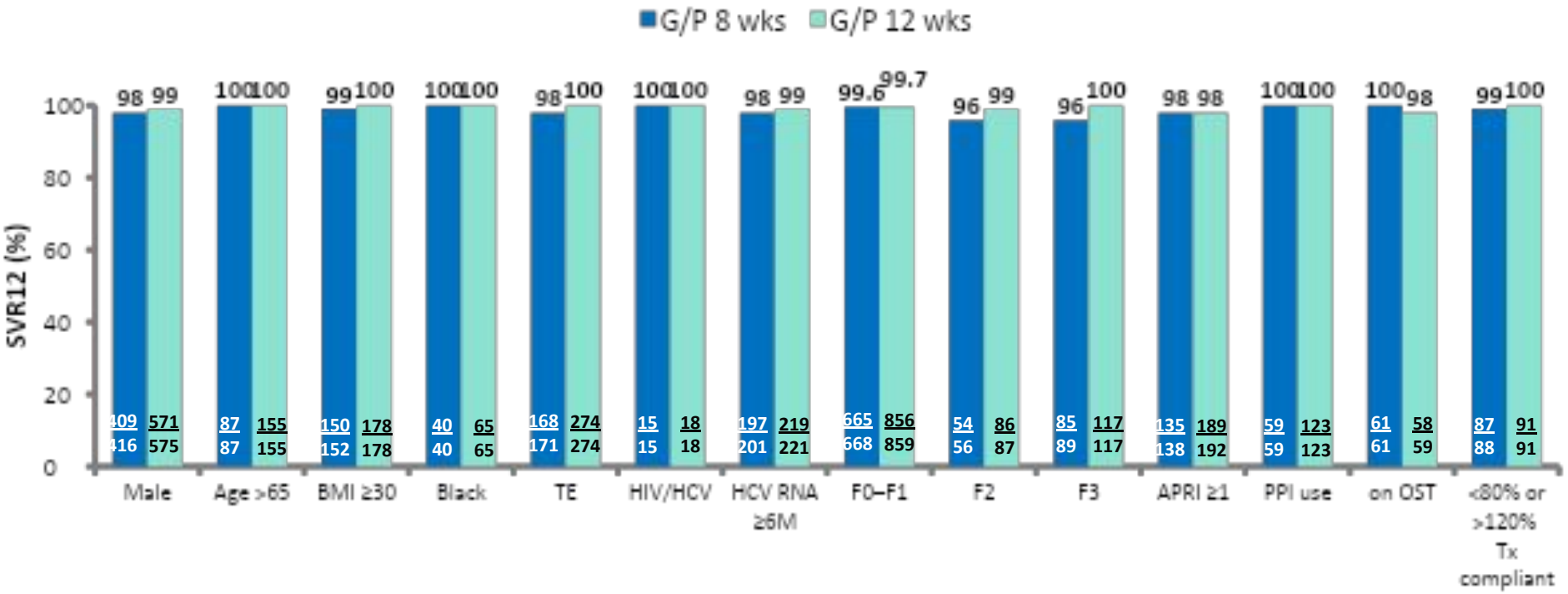
mITT SVR12 in patients with RASs, n/N (%)	8 weeks N = 772¶	**12 weeks N = 1001¶**
NS3 alone	6/6 (100)	14/14 (100)
NS5A alone	119/122 (98)	182/183 (99)
Both NS3 and NS5A	2/3 (67)	5/6 (83)
None	636/641 (99)	796/798 (99.7)

Logistic regression analysis showed presence of baseline NS3 155, 156, or 168 RASs combined with NS5A RASs had a statistically significant impact on SVR12 (P<0.0001) in this analysis

- <1% of patients had the combination of RASs and most achieved SVR12 (78%; 7/9)

SAT-233, Puoti: High SVR Rates with 8 and 12 Weeks of Pangenotypic G/P: Integrated Efficacy Analysis of Genotype 1–6 Patients without Cirrhosis (2)

Integrated efficacy analysis of 8 or 12 weeks' G/P treatment in non-cirrhotic patients with GT1–6 infection across seven phase 2 or 3 clinical trials



Logistic regression analysis showed presence of baseline NS3 155, 156, or 168 RASs combined with NS5A RASs had a statistically significant impact on SVR12 (*P*<0.0001) in this analysis

<1% of patients had the combination of RASs and most achieved SVR12 (78%; 7/9)

TE, treatment-experienced; Tx, treatment compliant; OST, opioid substitute therapy.

FRI-238, Dufour: Safety of G/P in Adults with Chronic GT1–6 HCV Infection: An Integrated Analysis

Patients received G/P for 8 weeks (non-cirrhotic; n = 828), 12 weeks (n = 1317; 225 [17%] with compensated cirrhosis) or 16 weeks (n = 120; 63 [53%] with compensated cirrhosis)

Baseline characteristics, n (%)	Non-cirrhotic N = 1977	Compensated cirrhosis N = 288	Total N = 2265
HCV genotype			
1	821 (42)	112 (39)	933 (41)
2	426 (22)	34 (12)	460 (20)
3	517 (26)	115 (40)	632 (28)
4–6	213 (11)	27 (9)	240 (11)
Treatment-experienced	571 (29)	114 (40)	685 (30)
PRS experienced	485 (25)	87 (30)	572 (25)
NS5A/PI-experienced*	86 (4)	27 (9)	113 (5)
Baseline fibrosis stage			
F0–F1	1593 (81)	0	1593 (71)
F2	154 (8)	0	154 (7)
F3	226 (12)	2 (<1)	228 (10)
F4	0	286 (99)	286 (13)
Missing	4	0	4

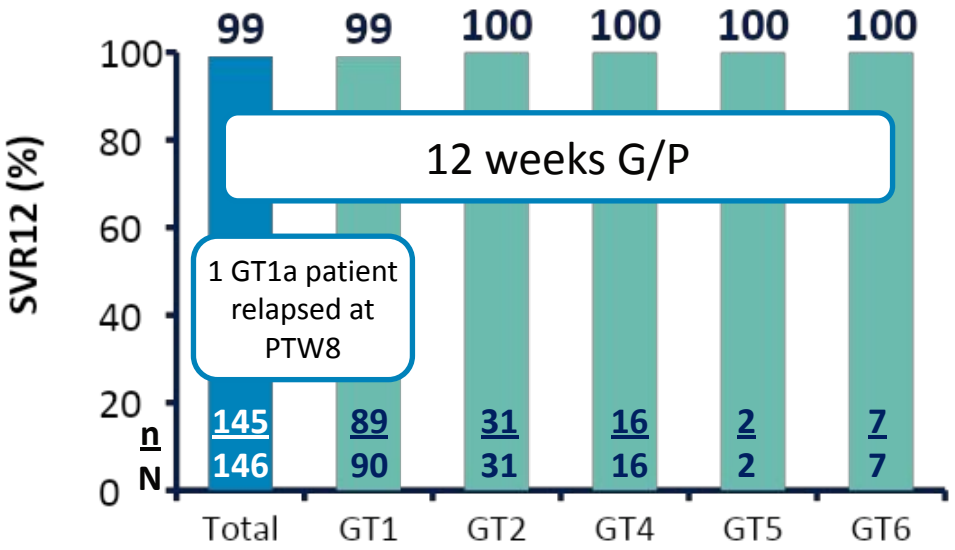
Event, n (%)	Non-cirrhotic N = 1977	Compensated cirrhosis N = 288	Total N = 2265
SAE	31 (2)	17 (6)	48 (2)
AE leading to d/c†	8 (<1)	0	8 (<1)
DAA-related SAE	1 (<1)	0	1 (<1)
DAA-related AE ≥ grade 3‡	4 (<1)	0	4 (<1)
Death§	5 (<1)	1 (<1)	6 (<1)
Laboratory abnormalities			
ALT ≥ grade 3 (>5 × ULN)¶	2/1975 (<1)	0	2/2263 (<1)#
Total bilirubin ≥ grade 3 (>3 × ULN) ¶	6/1975 (<1)	2/288 (<1)	8/2263 (<1)$

The frequency and severity of AEs were similar between non-cirrhotic patients and cirrhotic patients

d/c, discontinuation; GGT, gamma-glutamyl transferase; PI, protease inhibitor; PRS, pegIFN/RBV or SOF + RBV ± pegIFN.
* NS5A- and/or PI experienced; † Of the total eight patients, three experienced a total of nine DAA-related AEs leading to study drug d/c, including abdominal pain, diarrhoea, dyspepsia, nausea, fatigue, malaise, dizziness, headache, and transient ischaemic attack;
‡ Four (0.2%) patients experienced any DAA related AE with ≥ grade 3, including upper abdominal pain, asthenia, migraine, and increased ALT, AST, and GGT;
§ Causes of death were pneumonia, accidental overdose, adenocarcinoma, hepatic cancer metastatic, cerebral haemorrhage, alcohol poisoning and toxicity to various agents (none were considered to be related to treatment); ¶ Increased grade from baseline result;
# One patient experienced grade 3 and above ALT (>5 × ULN) elevations concomitant with total bilirubin (>2 × ULN) elevations 1 day post-treatment. Lab abnormalities were consistent with an obstructive pattern, most likely due to transient passage of a biliary stone;
$ Most elevations were predominantly indirect bilirubin without associated ALT increase in patients with indirect Gilbert's syndrome.

GS-006, Forns: EXPEDITION-I: Efficacy and Safety of G/P for Treatment of Chronic HCV GT1, 2, 4, 5 or 6 Infection in Adults with Compensated Cirrhosis

Baseline characteristics	N = 146
Male, n (%)	90 (62)
Median age, years (range)	60 (26–88)
HCV genotype, n (%)	
GT1a	48 (33)
GT1b	39 (27)
GT2	34 (23)
GT4	16 (11)
GT5	2 (1)
GT6	7 (5)
Treatment-experienced, n (%)	36 (25)
IFN-based, n/N (%)	25/36 (69)
SOF-based*, n/N (%)	11/36 (31)
Child-Pugh score, n (%)	
5	133 (91)
6	13 (9)



Safety, n (%)	N = 146
SAE	11 (8)
SAE related to DAA	0
Study drug d/c due to AE	0
Death	1 (1)

Patient with history of hemophilia died due to cerebral hemorrhage (not related to study drug)

Baseline RAS prevalence
NS3, 2/133 (2%); NS5A, 53/133 (40%); NS3 + NS5A, 2/133 (2%)

d/c, discontinuation; PTW, post-treatment Week; RAS, resistance-associated substitution.
* SOF + RBV ± pegIFN.

THU-263, Gane: Pharmacokinetics and Safety of G/P in Adults with chronic GT1–6 HCV Infection and Compensated Cirrhosis: An Integrated Analysis

An integrated safety and PK analysis of HCV GT1–6-infected patients with compensated cirrhosis treated with G/P for 12 or 16 weeks from four phase 2 and 3 clinical trials (EXPEDITION-1 and 4, SURVEYOR-II, and MAGELLAN-1)

Patients received G/P for 12 weeks (n = 245, including 20 patients with severe renal impairment [baseline eGFR of < 30 mL/min/1.73 m^2]) or 16 weeks (n = 63)

Baseline characteristics, n (%)	Patients with CC N = 288	Patients with severe RI N = 20
HCV genotype		
1	112 (39)	11 (55)
2	34 (12)	4 (20)
3	115 (40)	1 (5)
4–6	27 (9)	4 (20)
Treatment-experienced	114 (40)	12 (60)
Baseline fibrosis stage*		
F0–F1	0	0
F2	0	2 (11)
F3	2 (< 1)	0
F4	286 (99)	17 (90)
Missing	0	1
Baseline Child-Pugh Score		
5	249 (87)	15 (75)
≥ 6†	38 (13)	5 (25)
Missing	1	0

Event, n (%)	Patients with CC N = 288	Patients with CC (CP5) N = 261	Patients with CC (CP6) N = 27	Patients with severe RI N = 20
SAE	17 (6)	14 (5)	3 (11)	11 (55)
DAA-related SAE	0	0	0	0
AE leading to d/c	0	0	0	2 (10)
Death	1 (<1)‡	1 (<1)	0	1 (5)‡
AE consistent with hepatic decompensation	1 (<1)	0	1 (4)	0

Patient with a history of esophageal varices experienced an AE (esophageal variceal bleeding) with a sign of hepatic decompensation; event was not deemed related to study drug

GLE exposures in patients with compensated cirrhosis were 2.2-fold higher than in non-cirrhotics; PIB exposures were similar

There were no grade 3 ALT increases and no cases consistent with DILI

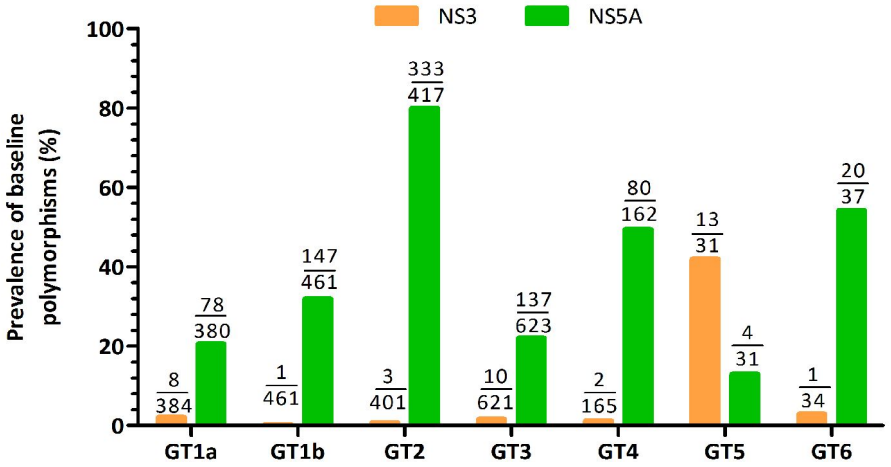
CC, compensated cirrhosis; CP, Child-Pugh; DILI, drug-induced liver injury; d/c, discontinuation; RI, renal impairment; PK, pharmacokinetics.
* Baseline fibrosis stage was defined for subjects with non-missing liver biopsy scores, FibroScan scores, or FibroTest scores; cirrhosis status was determined as collected in EDC; † 1 patient had a CP score of 7; ‡ Both deaths due to AE (cerebral hemorrhage) and not deemed related to treatment.

FRI-205, Krishnan: Pooled Resistance Analysis in HCV GT1–6-Infected Patients Treated with G/P in Phase 2 and 3 Clinical Trials

A pooled resistance analysis* was conducted in HCV GT1–6-infected patients with or without compensated cirrhosis (N = 2256) treated with G/P for 8, 12, or 16 weeks from eight phase 2 and 3 clinical trials

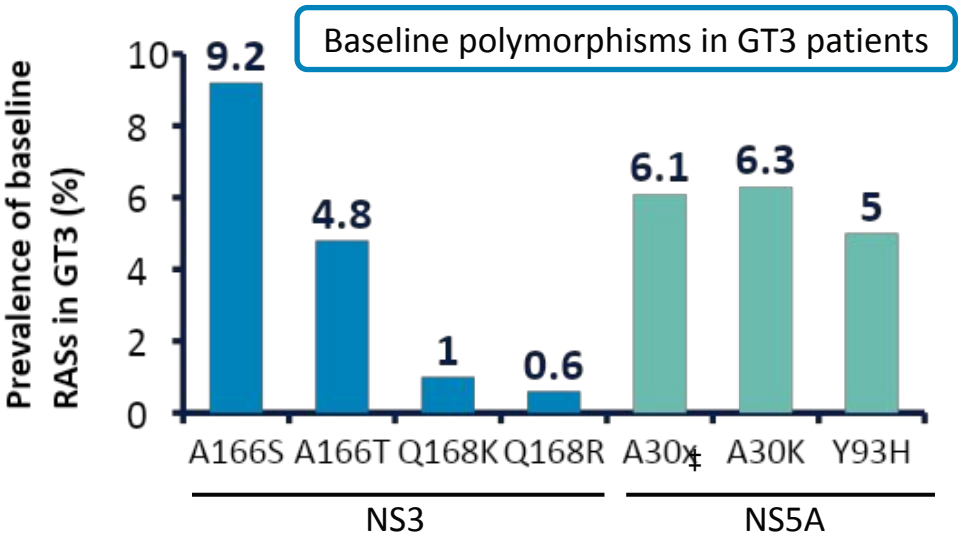
Baseline RASs did not impact SVR in GT1 and GT2 patients and there were no virologic failures in GT4–6 patients

There were 22 virologic failures (1%) (GT1a [n = 2], GT2a [n = 2], GT3a [n = 17], GT3b [n = 1])



High incidence of baseline NS5A RASs in GT2, GT4 and GT6 was driven by detection of:

- L/M31 (in GT2a and GT2b) and R30K (GT2c)
- position 58 (GT4a, 4d, and 4f)
- position 28 (GT6)



Baseline NS3 RASs did not impact SVR12 rates in GT3 patients

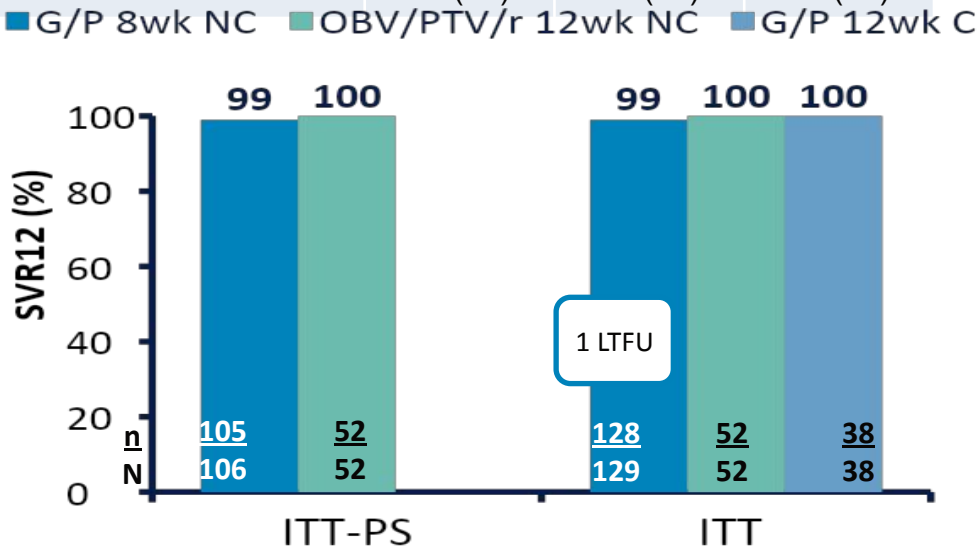
Baseline NS5A A30K and Y93H had minimal impact on efficacy, except in TE patients treated 12 weeks

RAS, resistance-associated substitution; TE, treatment-experienced; VF, virologic failure.
* Using next-generation sequencing (2% and 15% thresholds);
† Includes polymorphisms at amino acid positions 155, 156, 168 in NS3, and 24, 28, 30, 31, 58, 92, 93 in NS5A relative to the subtype specific reference sequence:
‡ A30x is A30L/M/R/S/T/V.

FRI-262, Chayama: CERTAIN-1: Efficacy and Safety of G/P in Japanese Patients with Chronic Genotype 1 Hepatitis C Virus Infection with and without Cirrhosis

Phase 3 study evaluating the safety and efficacy of G/P for 8 or 12 weeks or OBV/PTV/r for 12 weeks in Japanese patients with HCV GT1-infection without cirrhosis (Arms A and B) or with compensated cirrhosis (Arm C)

Baseline characteristics, n (%)	8 weeks G/P NC N = 129	12 weeks OBV/PTV/r NC N = 52	12 weeks G/P C N = 38
GT1b	125 (97)	52 (100)	38 (100)
NS5A Y93H present*	23 (18)	0	9 (24)
Treatment-naive	94 (73)	37 (71)	26 (68)



Safety, n (%)	8 weeks G/P NC N = 129	12 weeks OBV/PTV/r NC N = 52	12 weeks G/P C N = 38
DAA-related AE	30 (23)	14 (27)	7 (18)
DAA-related SAE	0	1 (2)	0
AE leading to d/c	0	1 (2)	1 (3)
Laboratory abnormalities, n (%)			
Hemoglobin, grade ≥3 (<8 g/dL)	0	0	0
ALT, grade ≥3 (>5 x ULN)	0	1 (2)	0
AST, grade ≥3 (>5 x ULN)	0	0	0
Total bilirubin, grade ≥3 (>3 x ULN)	0	0	0

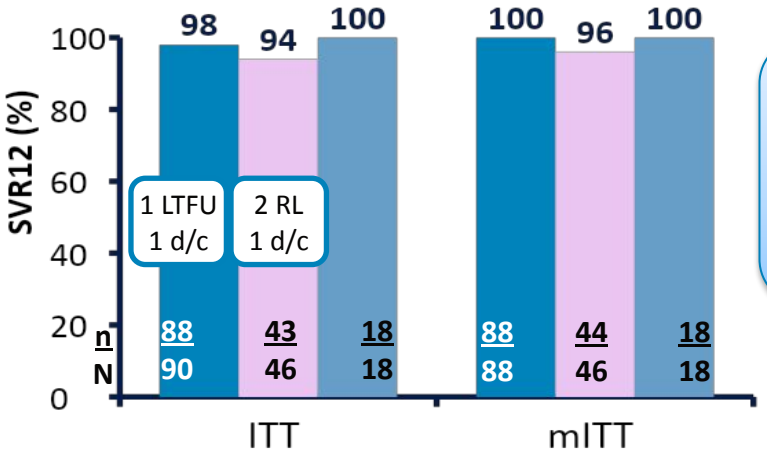
Among non-cirrhotic patients treated with G/P for 8 wks, all patients with BL Y93H RAS (n = 23) achieved SVR

BL, baseline; C, cirrhosis; d/c, discontinuation; ITT, intent-to-treat;
ITT-PS, ITT population excluding patients with the HCV Y93H polymorphism; LTFU, lost to follow-up; NC, no cirrhosis. * 15% cut off.

FRI-263, Chayama: Efficacy and Safety of G/P in Japanese Patients with Chronic Genotype 2 Hepatitis C Virus Infection with and without Cirrhosis

Phase 3 study of the safety and efficacy of G/P for 8 (CERTAIN-2) or 12 (CERTAIN-1) weeks in Japanese patients with HCV GT2-infection without cirrhosis (Arms A and B) or with compensated cirrhosis (Arm C)

Baseline characteristics	8 weeks G/P NC N = 90	12 weeks SOF + RBV NC N = 46	12 weeks G/P C N = 18
GT2a, n (%)	65 (72)	30 (65)	10 (56)
GT2b, n (%)	25 (28)	16 (35)	8 (44)
Treatment-experienced, n (%)	15 (17)	8 (17)	7 (39)



8 weeks G/P achieved non-inferiority compared with 12 weeks SOF + RBV

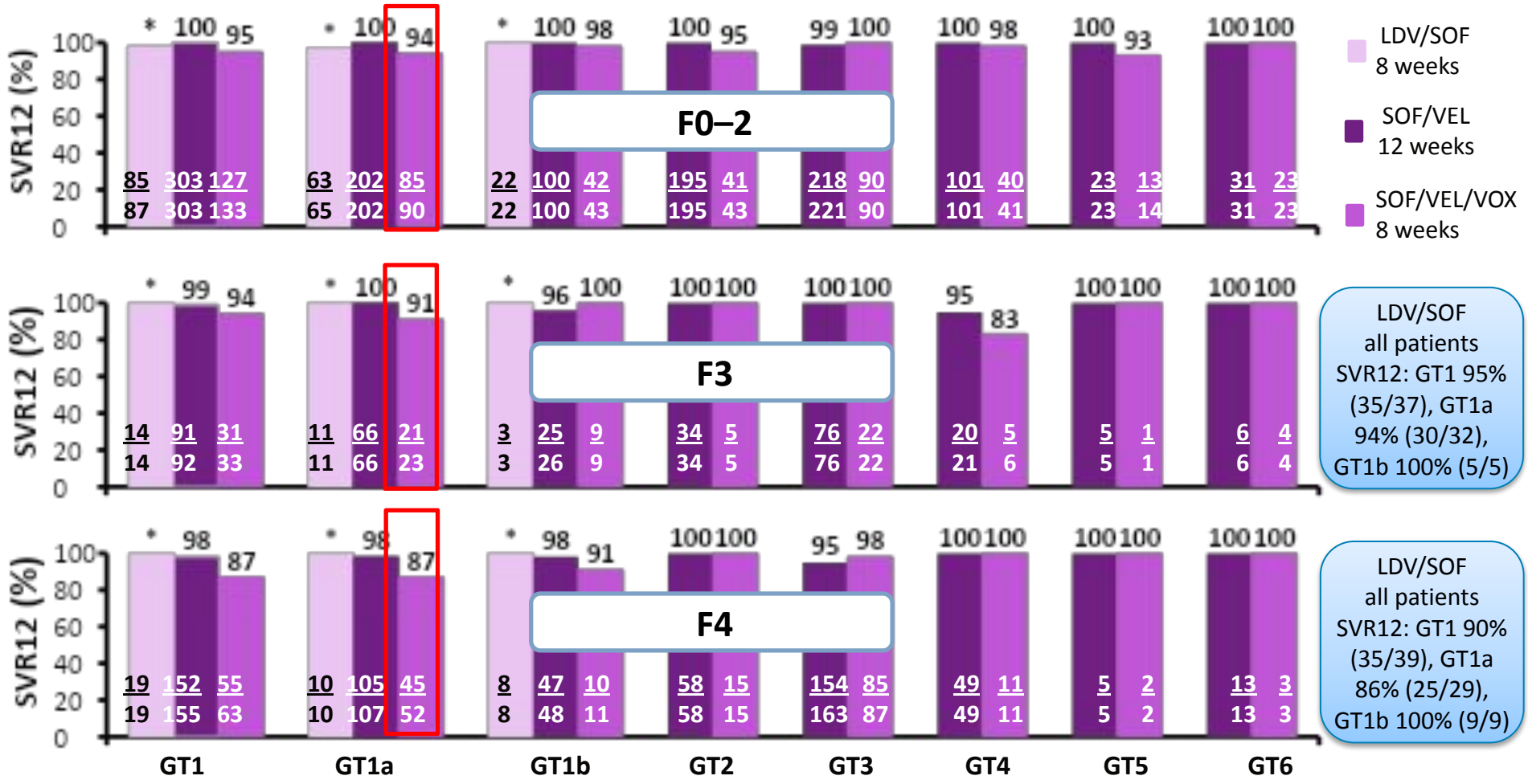
Safety, n (%)	8 weeks G/P NC N = 90	12 weeks SOF + RBV NC N = 46	12 weeks G/P C N = 18
Drug-related AE	16 (18)	23 (50)	7 (39)
Drug-related SAE	0	1 (2)	0
AEs leading to d/c	1 (1)*	1 (2)†	1 (6)‡
Laboratory abnormalities, n (%)			
Hemoglobin, grade ≥3 (<8 g/dL)	0	1 (2)	0
ALT, grade ≥3 (>5 x ULN)	0	0	0
AST, grade ≥3 (>5 x ULN)	0	0	0
Total bilirubin, grade ≥3 (>3 x ULN)	0	1 (2)	1 (6)

DAA-related AEs were significantly different between Arm A and Arm B (P<0.001)

C, cirrhosis; d/c, discontinuation; LTFU, lost to follow-up;
mITT, excludes non-virologic failures; NC, no cirrhosis; RL, relapse.
* Nausea and vomiting; † Malaise; ‡ Drug eruption, characterised as purpuric rash and eczema.

THU-273, Lawitz: Treatment with SOF/VEL or SOF/VEL/VOX is Well Tolerated and Results in High SVR12 in Genotype 1–6 HCV-Infected Patients with Minimal Fibrosis: A Retrospective Analysis of the ASTRAL and POLARIS Clinical Studies

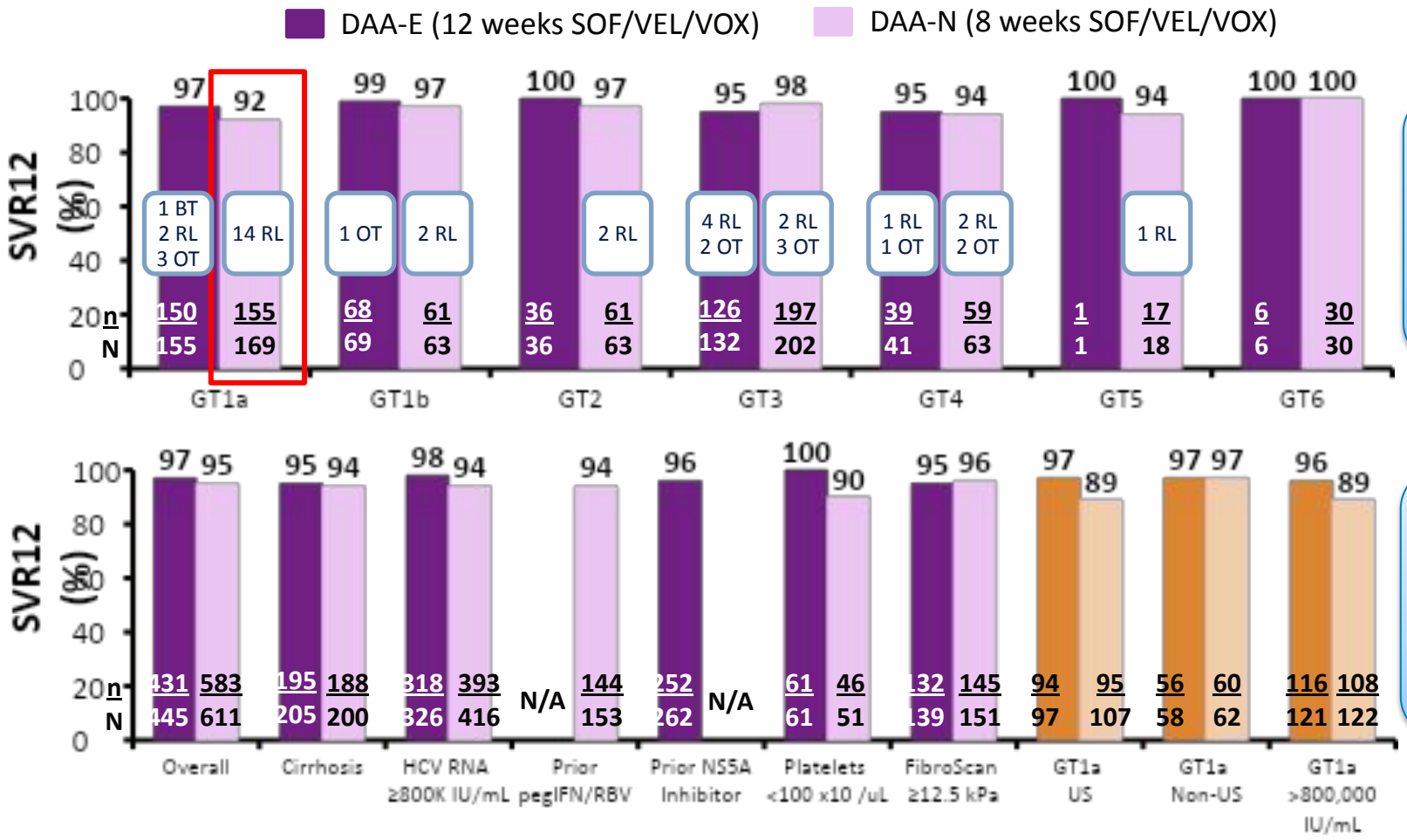
Trials analysed: ION-3; ASTRAL-1, -2, and -3; POLARIS-2 and -3; POLARIS-2 and -3
Data presented is the completer population: All patients who completed treatment, and had HCV RNA data at post-treatment week 12 or a later time point



* HCV RNA < 6 million IU/mL.

SAT-280, Roberts: SOF/VEL/VOX Results in High SVR12 Rates When Administered for 12 Weeks in DAA-experienced Patients or for 8 weeks in DAA-Naive Patients: An Integrated Analysis of the POLARIS-1, POLARIS-2, POLARIS-3 and POLARIS-4 Studies

Retrospective analysis of HCV GT1–6 infected patients treated with SOF/VEL/VOX for 8 weeks (DAA-naive) or 12 weeks (DAA-experienced) in the phase 3 POLARIS studies



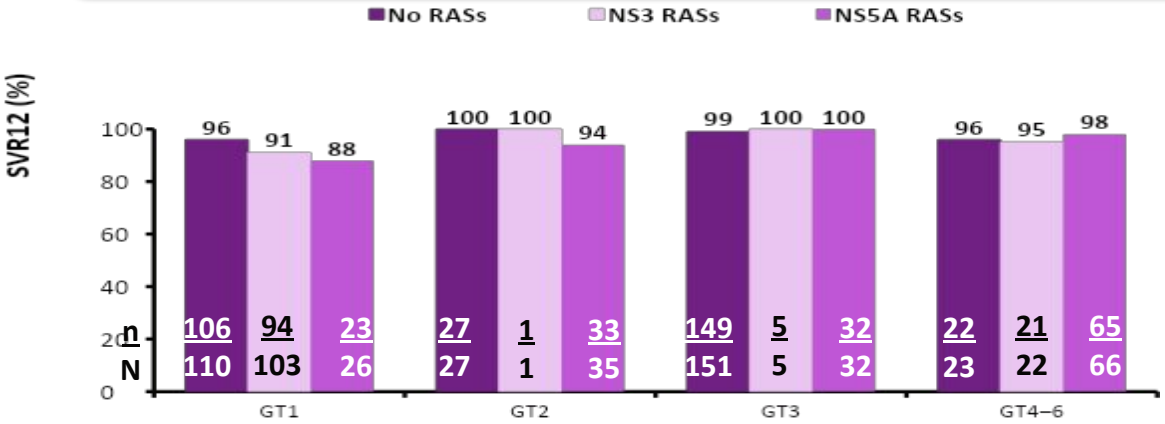
SVR12 was lower in DAA-naive GT1a patients

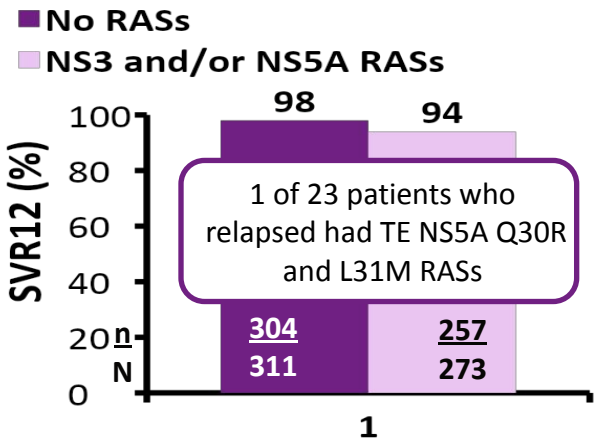
SVR12 rates were generally lower across subgroups in GT1a patients

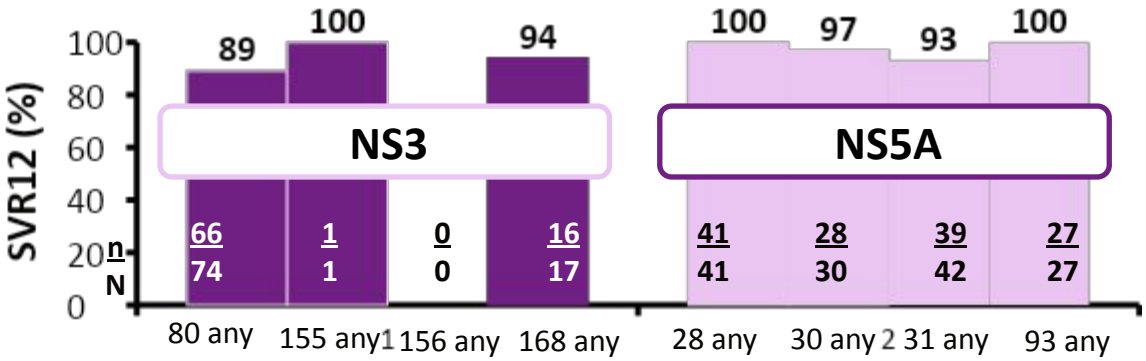
BT, breakthrough; DAA-E, direct-acting antiviral treatment-experienced; DAA-N, direct-acting antiviral treatment-naïve; OT, other; RL, relapse.

THU-257, Wyles: No Impact of RASs on the High Efficacy of SOF/VEL/VOX for 8 Weeks in DAA-Naive Patients: An Integrated Resistance Analysis of the POLARIS-2 and POLARIS-3 Studies

Integrated resistance analysis of baseline* and treatment emergent NS3, NS5A and NS5B RASs in DAA-naive HCV GT1-6 patients treated with SOF/VEL/VOX for 8 weeks in the phase 3 POLARIS-2 and -3 studies (RASs detected at 15% cut-off)







SVR12 was 88% (51/58) in GT1a patients with BL NS3 Q80K RAS

SVR12 was 100% (24/24) in GT3 patients with BL Y93H RAS

SVR12 was 98% (41/42) in patients with BL NS5B RASs

BL, baseline; NS3 and NS5A RASs, substitutions that confer >2.5 fold reduced susceptibility to any NS3 or NS5A inhibitor; RASs, resistance associated substitutions; TE, treatment emergent. * 15% cut-off.

SAT-236, Manns: The Safety and Tolerability of SOF/VEL/VOX for 8 or 12 Weeks in >1,000 Patients Treated in the POLARIS-1, POLARIS-2, POLARIS-3, and POLARIS-4 Studies: An Integrated Analysis

Retrospective safety analysis of 1056 HCV GT1–6 infected DAA-experienced (POLARIS-1 and -4) or DAA-naive (POLARIS-2 and -3) patients with or without compensated cirrhosis

DAA-experienced

POLARIS-1: SOF/VEL/VOX vs placebo (12 weeks)

POLARIS-4: SOF/VEL/VOX vs SOF/VEL (12 weeks)

DAA-naive

POLARIS-2 and -3: SOF/VEL/VOX (8 weeks) vs SOF/VEL (12 weeks)

Safety, n (%)	SOF/VEL/VOX 8 Weeks (N = 611)	SOF/VEL/VOX 12 Weeks (N = 445)	SOF/VEL 12 Weeks (N = 700)	Placebo 12 Weeks (N = 152)
Grade 3/4 AE	14 (2)	7 (2)	12 (2)	4 (2)
Treatment-related SAE	0	0	0	0
AE leading to D/C	0	1 (<1)*	4 (<1)*	3 (2)*
Death	1 (<1)*	1 (<1)*	0	0
AEs in ≥10% patients				
Headache	161 (26)	116 (26)	174 (25)	26 (17)
Fatigue	134 (22)	99 (22)	164 (23)	30 (20)
Diarrhea	105 (17)	83 (19)	44 (6)	19 (13)
Nausea	103 (17)	59 (13)	62 (9)	12 (8)

D/C, discontinuation; PTD, post-treatment Day; SAEs; serious adverse event. * Assessed as unrelated to treatment.

Most cases of diarrhea and nausea in the SOF/VEL/VOX group were grade 1; no grade 3/4 events

Older age, Asian race, cirrhosis and mild renal impairment did not impact incidence or severity of AEs in the SOF/VEL/VOX group

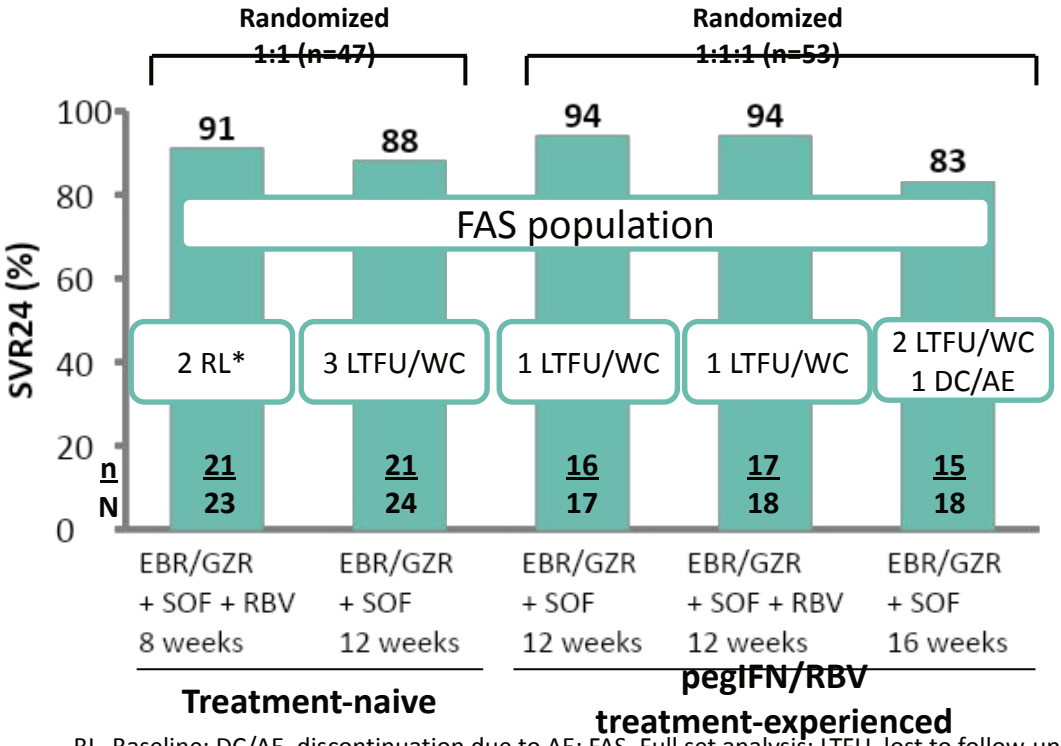
1 patient in the SOF/VEL/VOX group had a grade 3 elevation of ALT, while 1 patient had a grade 3 bilirubin elevation

FRI-213, Foster: EBR/GZR + SOF ± RBV in Treatment-Naive and Treatment-Experienced Cirrhotic People with HCV GT3 Infection and Compensated Cirrhosis: SVR24 Results of the C-ISLE Study

C-ISLE: UK study of patients with HCV GT3 infection and compensated cirrhosis treated with EBR/GZR + SOF ± RBV for 8–16 weeks (N = 100)

29% Asian

47% treatment-naive



52% (50/97) of patients had baseline NS5A RASs; 9 patients had Y93H RASs (1% level of detection)

Baseline NS5A RASs

- 98% SVR12 (49/50) in patients with baseline NS5A RASs
- 98% SVR12 (46/47) in patients without baseline NS5A RASs
- 89% SVR12 (8/9) in patients with Y93H RAS at BL†

Safety, n (%)	EBR/GZR + SOF + RBV 8 weeks n = 23	EBR/GZR + SOF 12 weeks n = 41	EBR/GZR + SOF + RBV 12 weeks n = 18	EBR/GZR + SOF 16 weeks n = 18
SAEs‡	0	1 (2)	3 (17)	1 (6)
DC due to AE§	0	0	0	1(6)
Hemoglobin <10 g/dL‖	0	1 (2)	2 (11)	0

BL, Baseline; DC/AE, discontinuation due to AE; FAS, Full set analysis; LTFU, lost to follow-up; RAS, resistance-associated substitution; RL, relapse; VF, virologic failure; WC, withdrew consent.

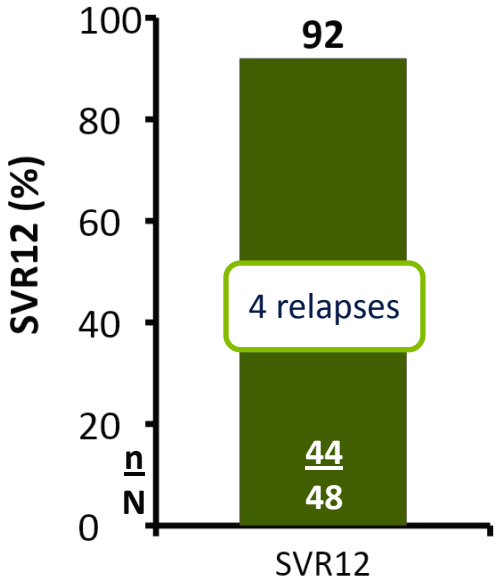
*1 patient has Y93H, P58S & S62T RASs present at BL and P58S & S62T present at treatment-failure; 1 patient has no RAS present; † Y93H RAS was not present at treatment failure in patient who did not achieve SVR; ‡ 1 case of each (lung infection, creatinine increased, chest pain, opiate overdose, and cellulitis); § 1 patient had a drug-related SAE of vomiting on Day 4 and subsequently d/c treatment on Day 7 due to cellulitis; ‖ Lowest level was 8.9 g/dL.

THU-249, Hezode: Efficacy and Safety of SOF and DCV for 8 Weeks in Treatment-Naive Non-Cirrhotic Patients with Chronic HCV GT3 Infection

Ongoing, multicenter, open-label, single-arm pilot study evaluating the safety and efficacy of DCV + SOF for 8 weeks in treatment-naive patients with HCV GT3 infection without cirrhosis

Baseline characteristics	N = 56
Male, n (%)	42 (75)
Mean age, years (±SD)	48 (11)
Median FS, kPa	7.3
FS <7 kPA, n (%)	23 (41)
FS>7 – ≤9.5 kPa, n (%)	28 (50)
FS>9.5 – <12.5 kPa, n (%)	5 (9)
Mean HCV RNA, log_{10} IU/mL	5.65
NS5A RASs, n (%)	
None	26 (93)
Present	2 (7)*

No safety signal reported



Resistance analysis

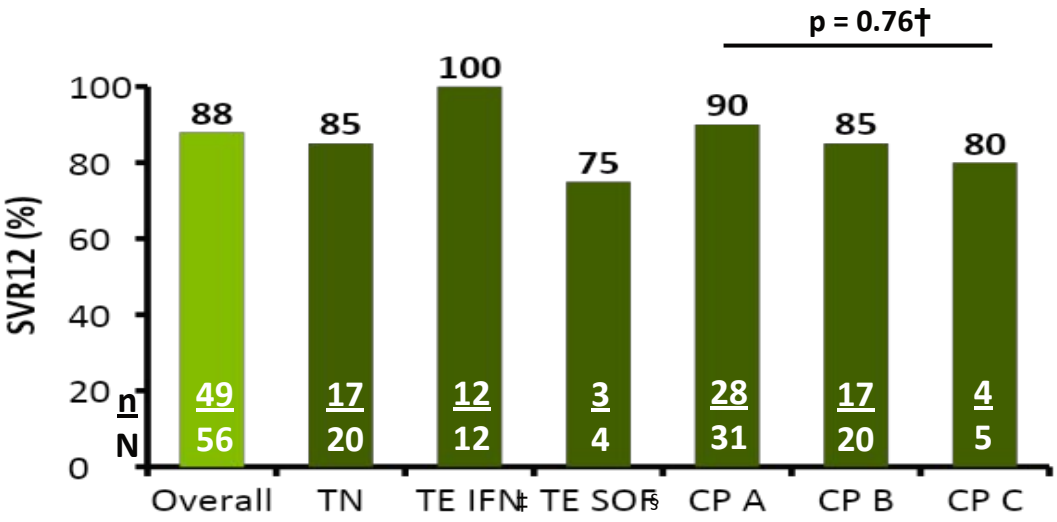
BL S62L/Y93H NS5A RAS (n = 1); TE A30K/Y93H (n = 1); poor compliance (n = 1); data not available (n = 1)

BL, baseline; FS, FibroScan Score; TE, treatment-emergent.
* A30V (n = 1); S62L/Y93H (n = 1).

THU-258, Troland: 12 Weeks of SOF, DCV and RBV for GT3 Patients with Cirrhosis

Real-world study of DCV + SOF + RBV for 12 weeks in HCV GT3-infected patients with cirrhosis in Scotland

Baseline characteristics	N = 57
Mean age, years (±SD)	49 (7)
Child Pugh, n (%) A B C	 31 (54) 21 (37) 5 (9)
Median LSM* (IQR)	28 (16–46)
Median platelet count (IQR)	90 (67–126)
Median baseline HCV RNA, $\log_{10}$ IU/mL (IQR)	5.2 (4.3–5.8)
HIV co-infected, n (%)	3 (5)
Treatment-experienced, n (%) IFN/RBV SOF/IFN/RBV	16 (28) 12 (21) 4 (7)



Quantifiable RNA at Week 4 was associated with numerically lower SVR12 vs unquantifiable RNA at Week 4 (75% [12/16] vs. 94% [33/35]; p=0.069)

No D/C due to drug-related AEs

SVR12 rates were similar to those in clinical trials

CP, Child Pugh; D/C, discontinuation; IQR, interquartile range; LSM, liver stiffness measurement; TE, treatment-experienced; TN, treatment-naive.
* LSM data available for 43 patients; † CP A vs CP B/C; ‡ IFN/RBV-experienced; § IFN/RBV/SOF-experienced.

DAA-Experienced

Executive Summary

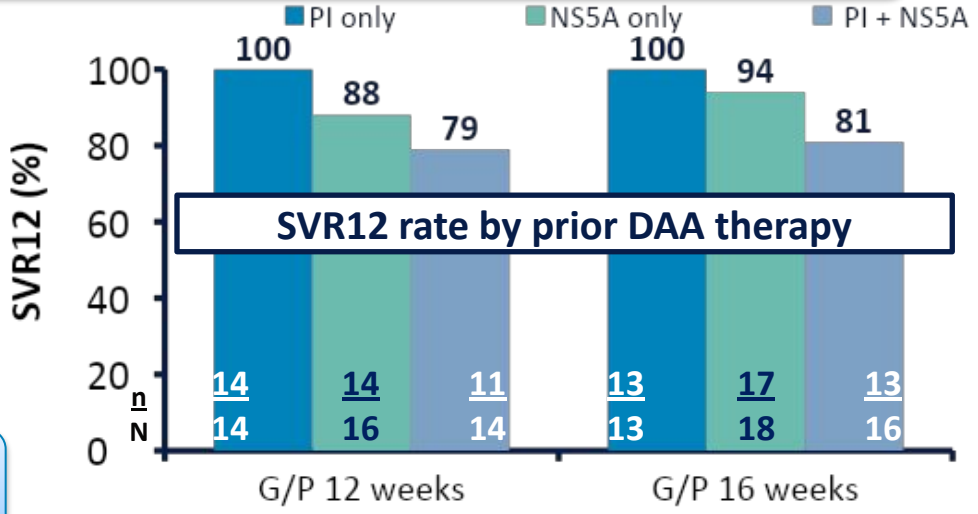
- Patients who have failed a DAA-containing regimen are a minority population (~5–10%), however there continues to be data generated
- The data reported for G/P established the 16 week regimen as a efficacious and safe retreatment option for the majority of GT1 DAA failures in 2018 and beyond
  - 16 weeks of G/P in GT1 NS5A failures resulted in a 94% SVR12 rate
  - 17/19 LDV/SOF failures achieved SVR12. LDV/SOF failures will represent the majority of DAA failures in the near future
  - 12 weeks of G/P in GT1 NS3 failures resulted in a 100% SVR12 rate
- Additional analyses reported for 12 weeks of SOF/VEL/VOX further support its use in the DAA failure population across all genotypes
  - The efficacy was ≥95% SVR12 irrespective of baseline characteristics
- Two regimens are expected to dominate the retreatment landscape: 16 weeks of G/P and 12 weeks of SOF/VEL/VOX
  - G/P has a longer treatment duration, is restricted to GT1 but appears to have a cleaner safety profile

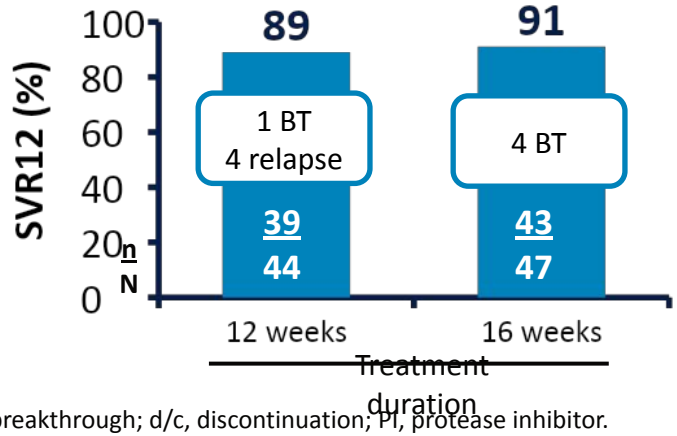
PS-156, Poordad: MAGELLAN-1, PART 2: G/P for 12 or 16 Weeks in Patients with Chronic HCV GT1 OR 4 and Prior Direct-Acting Antiviral Treatment Failure

Randomized trial of G/P for 12 or 16 weeks in HCV GT1- or GT4-infected patients with prior DAA failure, without cirrhosis or with compensated cirrhosis

Baseline characteristics, n (%)	G/P 12 weeks N = 44	**G/P 16 weeks N = 47**
HCV subtype		
GT1a	35 (80)	32 (68)
GT1b	8 (18)	11 (23)
GT1c	0	1 (2)
GT4	1 (2)	3 (6)
Compensated cirrhosis	15 (34)	12 (26)

- N = 19 patients had previously failed LDV/SOF
- N = 10 had previously failed ≥2 DAA-containing regimens





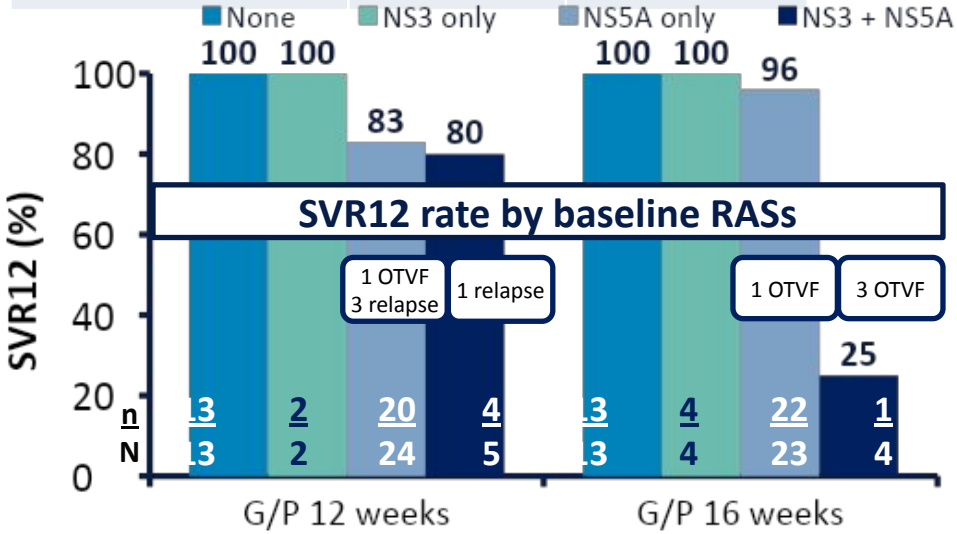
Safety, n (%)	G/P 12 weeks N = 44	**G/P 16 weeks N = 47**
SAE	1 (2)	2 (4)
SAE possibly related to DAA	0	0
AE leading to study drug d/	0	0

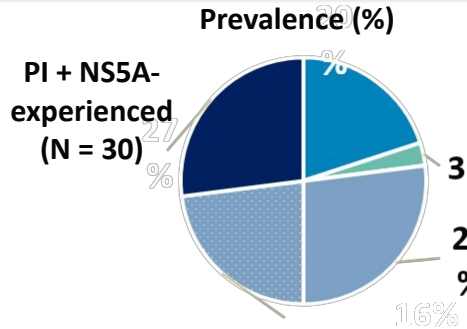
BT, breakthrough; d/c, discontinuation; PI, protease inhibitor.

SAT-204, Pilot-Matias: Resistance Analysis in the MAGELLAN-1 Study (Part 2): G/P Therapy in HCV-Infected Patients Who Had Failed Prior DAA Regimens Containing NS3/4A Protease and/or NS5A Inhibitors

NGS (detection threshold of 15%) was used to perform resistance analysis of HCV from DAA-experienced patients treated with 12- or 16-week G/P from the MAGELLAN-1 (Part 2) study

Baseline characteristics, n (%)	G/P 12 weeks N = 44	G/P 16 weeks N = 47
HCV subtype		
GT1a	35 (80)	32 (68)
GT1b	8 (18)	10 (21)
GT1e	0	1 (2)
GT4r	1 (2)	2 (4)
Missing	0	2 (4)
Compensated cirrhosis	15 (34)	12 (26)





SVR12 % (n/N)	
G/P 12 wks	G/P 16 wks
100 (3/3)	100 (3/3)
–	100 (1/1)
60 (3/5)	100 (3/3)
100 (2/2)	100 (5/5)
75 (3/4)	25 (1/4)
G/P 12 wks	G/P 16 wks
100 (1/1)	100 (4/4)
100 (4/4)	100 (6/6)
82 (9/11)	83 (5/6)
G/P 12 wks	G/P 16 wks
100 (9/9)	100 (6/6)
100 (2/2)	100 (3/3)
100 (1/1)	100 (2/2)
100 (1/1)	100 (1/1)
100 (1/1)	–

NGS, next-generation sequencing; OTVF, on-treatment virologic failure; PI, protease inhibitor; RAS, resistance-associated substitution; wks, weeks.

THU-305, Ng: Resistance Selection Using GLE and PIB in Replicons of Major HCV Genotypes

The *in vitro* resistance profiles of GLE or PIB in major HCV genotypes were determined using drug-resistant replicon colony selection

- GLE predominantly selected NS3 A156 substitutions in GTs 1–4 and D168 substitutions in GT6 *in vitro*
- PIB selected few NS5A substitutions *in vitro*

Activity of GLE against common GT1–4 and 6 RASs

HCV subtype	NS3 RAS	Fold change in GLE EC_{50}*
GT1a	V36M, F43L, T54S, V55I, Y56H, Q80K, R155K, D168A/E/V, I170T	0.2–4.4
GT1b	T54A, V55A, R155K, D168A/E/V, V170A	0.4–3.2
GT2a	D168A/E/V	1.9–3.3
GT2b	D168A/E/V	1.3–2.9
GT3a	R155K Q168R	0.5 54
GT4a	R155C D168V	2.6 9.7
GT4d	D168V	1.9
GT6a	D168Y	109

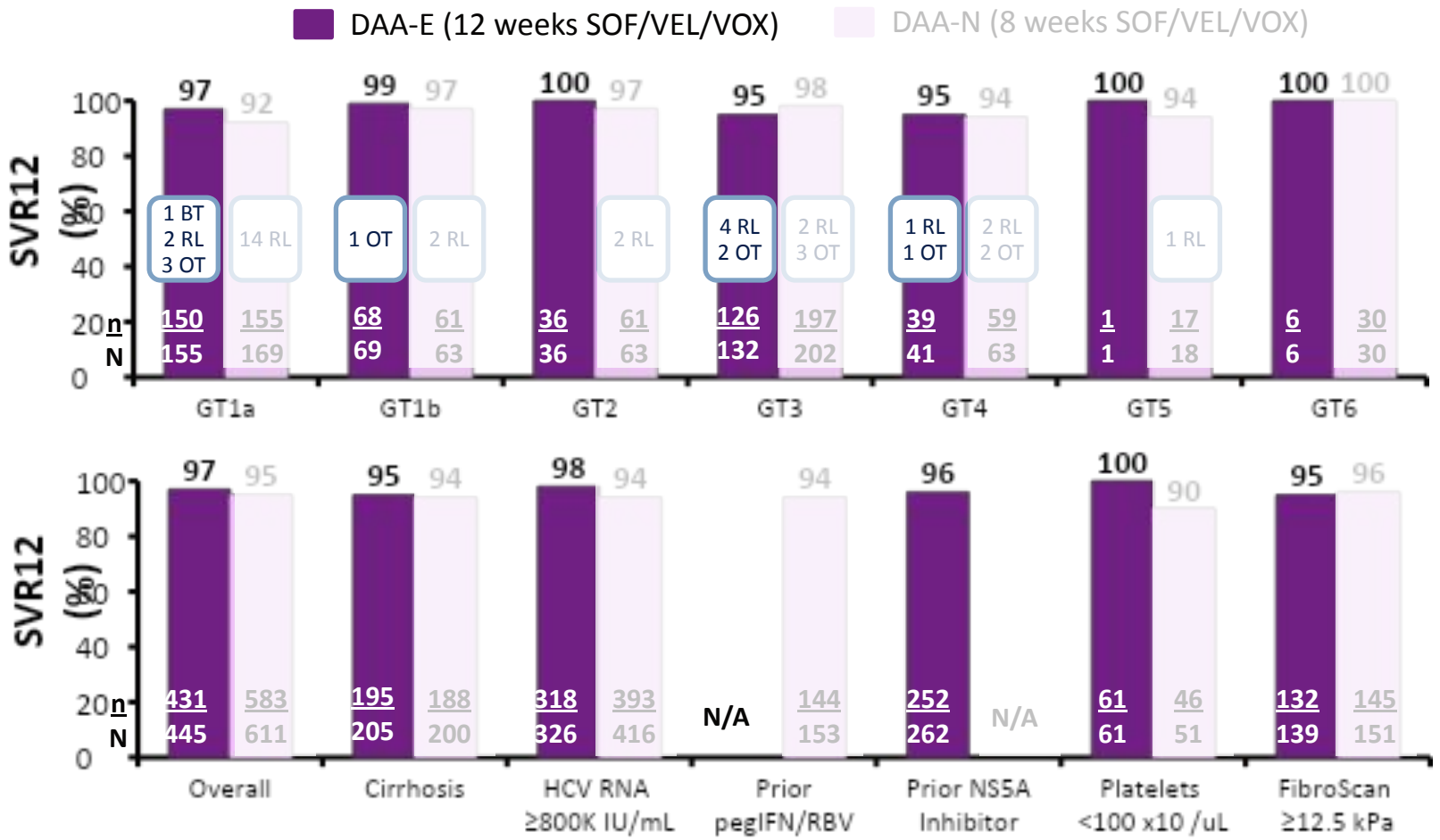
Activity of PIB against common GT1–6 RASs

HCV subtype	NS5A RAS	Fold change in PIB EC_{50}†
GT1a	M28T/V, Q30E/H/R, L31M/V, P32L, H58D Y93C Y93H Y93N	1.0–2.4 1.7 6.7 7.1
GT1b	L28T, Y93H/N	0.6–0.9
GT2a	T24A, F28S	1.2–1.3
GT2b	L28F, L31M/V	0.5–1.2
GT3a	M28T Y93H	1.7 2.3
GT4a	L28V, L30H	1.1–1.3
GT5a	L28I, L31F/V	0.8–2.1
GT6a	L31V, T58A/N	1.0–1.8

Relative to GLE EC_{50} for the respective wild type replicons in transient transfe
GT3a: 0.55 nM; GT4a: 0.67 nM; GT4d: 0.15 nM; GT6a: 0.15 nM; † Relative to GI
GT1a: 0.72 pM; GT1b: 1.9 pM; GT2a: 0.99 pM; GT2b: 1.2 pM; GT3a: 0.65 pM; GT4a: 0.78 pM; GT5a: 0.93 pM; GT6a: 1.0 pM.

SAT-280, Roberts: SOF/VEL/VOX Results in High SVR12 Rates When Administered for 12 Weeks in DAA-experienced Patients or for 8 weeks in DAA-Naive Patients: An Integrated Analysis of the POLARIS-1, POLARIS-2, POLARIS-3 and POLARIS-4 Studies

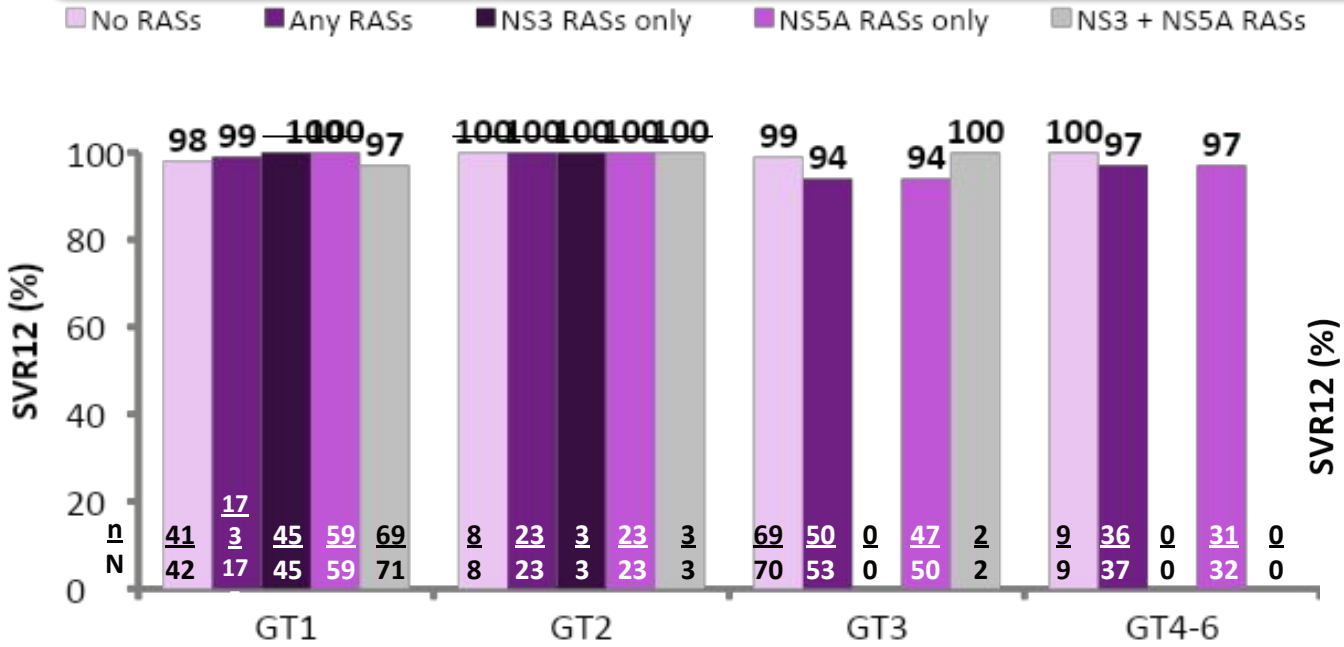
Retrospective analysis of HCV GT1–6 infected patients treated with SOF/VEL/VOX for 8 weeks (DAA-naive) or 12 weeks (DAA-experienced) in the phase 3 POLARIS studies



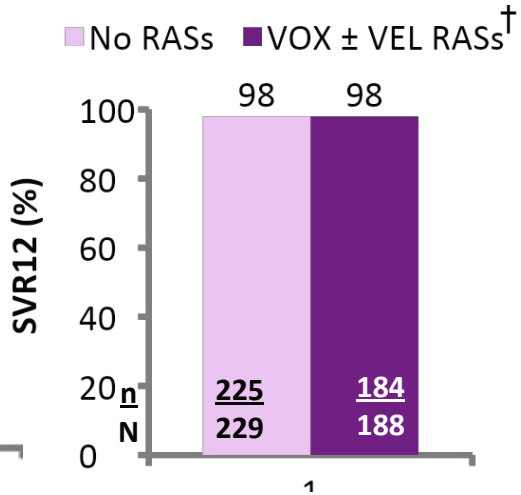
BT, breakthrough; DAA-E, direct-acting antiviral treatment-experienced; DAA-N, direct-acting antiviral treatment-naïve; OT, other; RL, relapse.

THU-248, Sarrazin: No Impact of RASs on the High Efficacy of SOF/VEL/VOX for 12 Weeks in DAA-Experienced Patients: An Integrated Resistance Analysis of the POLARIS-1 and POLARIS-4 Studies

Integrated resistance analysis of baseline* and treatment-emergent NS3, NS5A and NS5B RASs in DAA-experienced HCV GT1–6 patients treated with SOF/VEL/VOX for 12 weeks in the phase 3 POLARIS-1 (NS5A inhibitor-experienced) and -4 (DAA-experienced) studies



VOX- or VEL-specific RASs did not impact SVR12



GT3-infected patients:
93% (25/27) with Y93H NS5A RAS achieved SVR12

97% (32/33) of patients with NS5B RASs achieved SVR12

Of the 7 patients who relapsed (POLARIS-1, n = 6; POLARIS-4, n = 1), 1 (GT4d) had treatment-emergent NS5A Y93H RAS

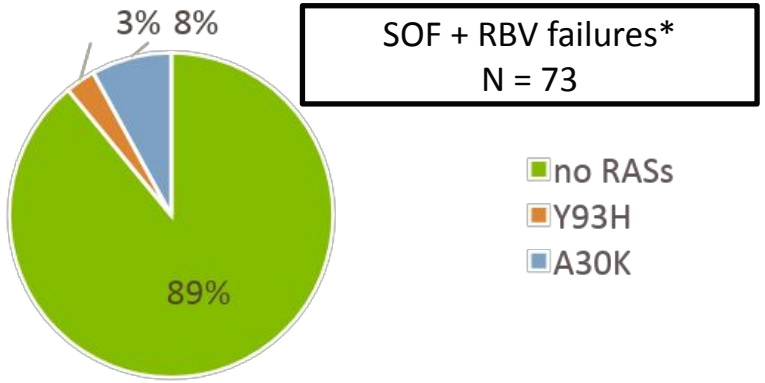
RASs, resistance associated substitutions * 15% cut-off; † VOX- or VEL-specific RASs that confer >2.5-fold change compared with GT-specific reference.

PS-155, Vermehren; High SVR Rates in HCV GT3 Patients ± Cirrhosis Treated with DCV + SOF or SOF/VEL ± Ribavirin According to Baseline Resistance Analysis

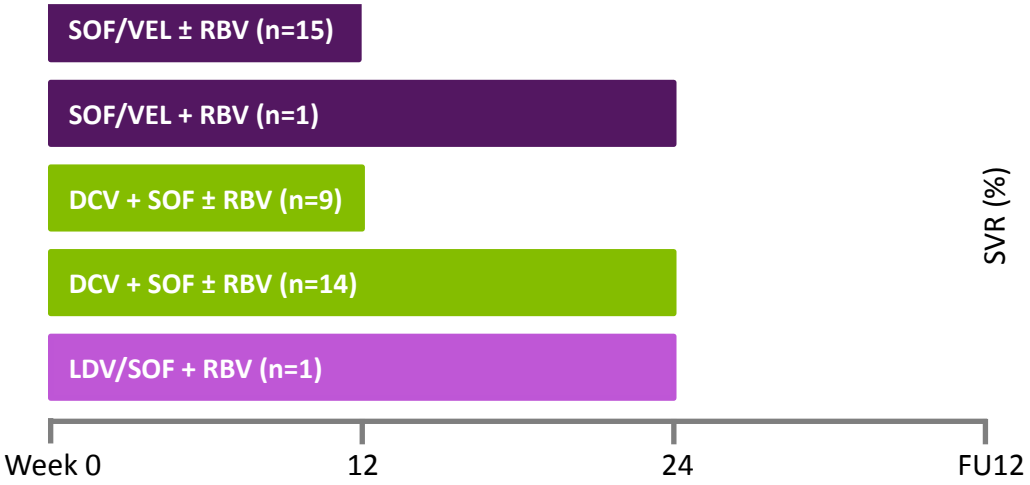
Real-world data from treatment-experienced patients with HCV GT3 infection treated with DCV + SOF ± RBV for 12–24 weeks or SOF ± VEL/LDV ± RBV for 12–24 weeks

Resistance Analysis after SOF + RBV failure

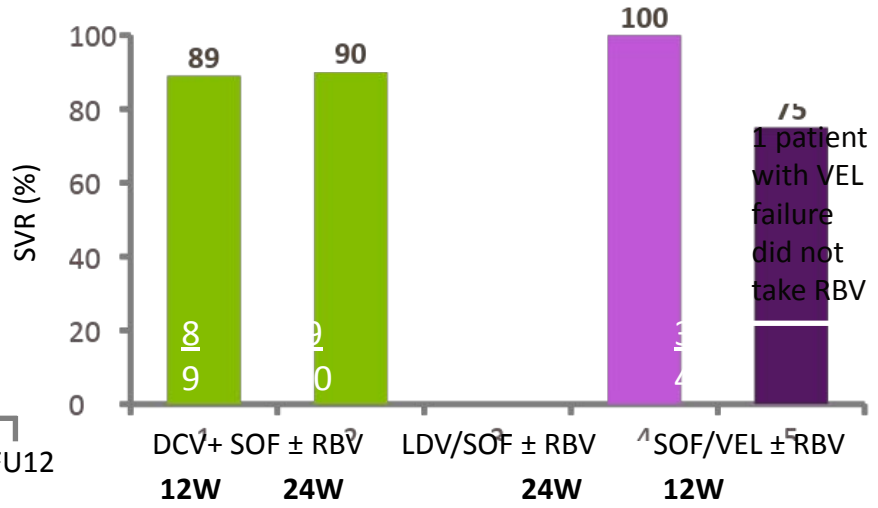
SOF + RBV Failures
n = 86



Retreatment with an NS5A-inhibitor (n=40)



Interim analysis: SVR 88% (n=21/24)



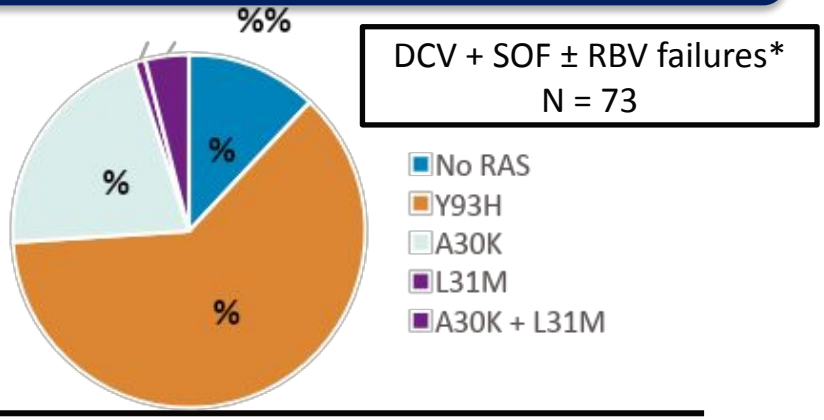
* Patients with BL RAS testing results.

PS-155, Vermehren; High SVR Rates in HCV GT3 Patients ± Cirrhosis Treated with DCV + SOF or SOF/VEL ± Ribavirin According to Baseline Resistance Analysis

Real-world data from treatment-experienced patients with HCV GT3 infection treated with DCV + SOF ± RBV for 12–24 weeks or SOF ± VEL/LDV ± RBV for 12–24 weeks

Resistance Analysis after DCV + SOF ± RBV failure

DCV + SOF ± RBV Failures n = 80



Retreatment of GT3 patients who failed a first course of DCV + SOF therapy

	Gender	Cirrhosis	Prior PEG/R experience	Y93H	Retreatment	Outcome
DCV + SOF, 24 wks	male	yes	yes	yes	DCV + SOF + RBV, 24 wks	REL
DCV + SOF, 12 wks	male	no	yes	yes	DCV + SOF + RBV, 24 wks	SVR12
DCV + SOF, 24 wks	male	yes	yes	yes	LDV/SOF, 24 wks	REL
DCV + SOF, 12 wks	male	yes	yes	yes	SOF/VEL + RBV, 24 wks	Pending
DCV + SOF, 12 wks	male	no	yes	yes	SOF/VEL + RBV, 24 wks	SVR4
DCV + SOF, 12 wks	male	no	yes	yes	SOF/VEL, 12 wks	REL

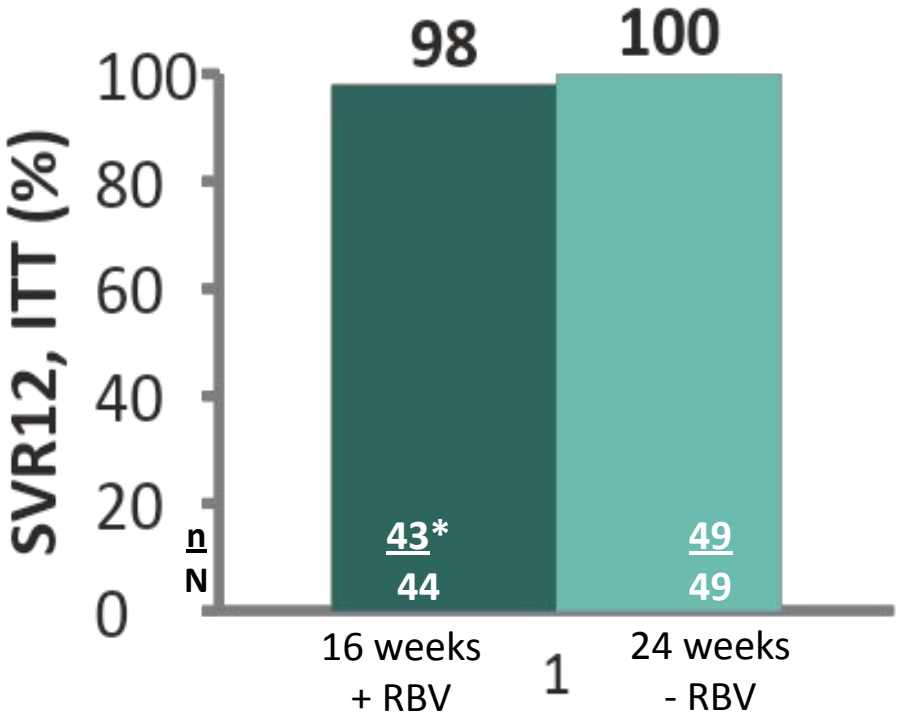
1 patient with VEL failure did not take RBV

* Patients with BL RAS testing results; NS5A RASs not available in n = 22 patients due to missing serum or failed sequence analysis.

PS-159, Wedemeyer: Safety and Efficacy of the Fixed-dose Combination Regimen of Uprifosbuvir (MK-3682)/Grazoprevir/Ruzasvir in Cirrhotic or Non-cirrhotic Patients with HCV GT1 Infection Who Previously Failed a DAA regimen: C-SURGE

A multicentre, open-label, randomized (1:1) study in n = 94 HCV GT1-infected patients who relapsed after receiving LDV/SOF or EBR/GZR

Baseline characteristics, n (%)	N=93*
GT1a	80 (86)
Cirrhosis†	40 (43)
Presence of BL RAS‡ NS5A NS3	 78 (84) 60 (65)
BL HCV RNA >2,000,000 IU/mL	62 (67)
Prior treatment LDV/SOF (12–24 weeks) LDV/SOF (8 weeks) EBR/GZR (12 weeks)	 57 (61) 14 (15) 22 (24)



BL NS5A or NS3 RASs† had no impact on SVR12 and all patients with BL NS5A Y93 RAS achieved SVR

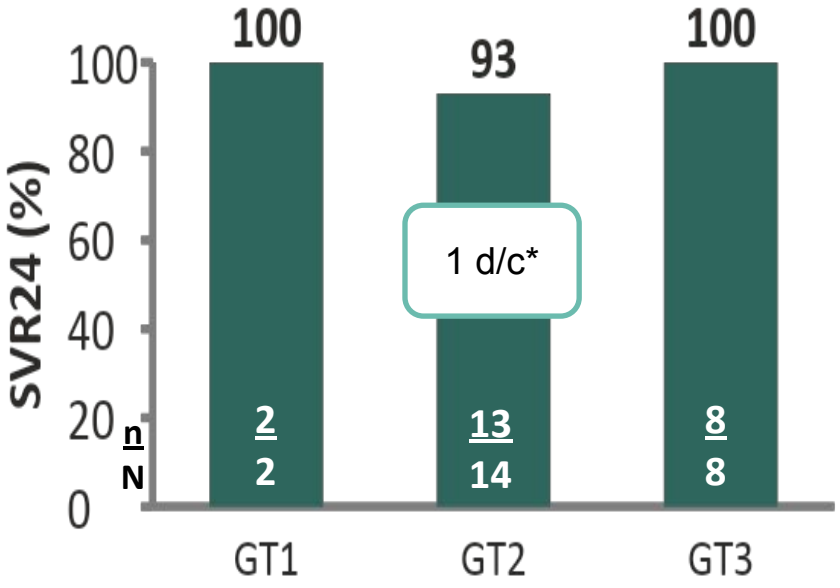
No DAA-related SAEs or d/c due to AEs

at position 28, 30, 31 or 93; NS3 RASs = any change from wild-type at positions 36, 54, 55, 56, 80, 107, 122, 132, 155, 156, 158, 168, 170 or 175);;

THU-264, Serfaty: High SVR24 Rates in Participants with Chronic HCV GT1, 2, 3 Infection Following 16 Weeks of GZR/RZR/Uprifosbuvir (MK-3682) + RBV After Having Failed 8 Weeks of a Triple Drug Regimen (Part C of C-CREST-1 & -2)

Retreatment with GZR + RZR + UPR + RBV for 16 weeks in HCV GT1, 2, 3 non-cirrhotic patients that experienced relapse following 8 weeks of a 3-DAA regimen in Part A of C-CREST

Baseline characteristics	N = 24
Male, n (%)	12 (50)
Metavir F0–F2, n (%)	23 (96)
HCV GT (subtype), n	2 GT1 (1 GT1a, 1 GT1b) 14 GT2 (8 GT2a, 4 GT2b, 2 GT2c) 8 GT3 (7 GT3a, 1 GT3b)
NS5A inhibitor in Part A regimen, GT (n) EBR RZR	 GT2 (9), GT3 (5) GT1 (2), GT2 (5), GT3 (3)
RASs at retreatment baseline, n (%) NS3 NS5A NS5B	 20 (96) 20 (83) 1 (4)



83% (19/23) had RASs in both NS3 and NS5A

High-impact RASs† were detected in:
77% (10/13) GT2 (L31M, F28C)
88% (7/8) GT3 (Y93H, A30K, L31M, S62L)

susceptibility to RZR *in vitro*.

FRI-233, Chhatwal: Projection of Patients Who Fail Treatment in the Era of Direct-Acting Antivirals

Modelling

- Natural history and disease progression were modelled using published meta-analyses and observational models
- DAA treatment was modelled in different waves:
  - TVR, BOC launched in 2011
  - SOF/SMV, SOF+RBV±IFN in 2014
  - Multiple NS5A-inhibitors from 2015
- F3–F4 patients assigned priority
- SVR rates taken from published EU/US RW data
- Non-cirrhotic NS5A treatment failures were not re-treated until 2018, after which they were eligible for re-treatment with new NS5As

Majority of treatment failures will occur in patients treated with NS5A inhibitors, or who are cirrhotic, or infected with HCV GT1a

Expected treatment failures					
Pts receiving treatment 2014–2020	**France N = 102,555**	**Germany N = 92,166**	**Italy N = 207,917**	**Spain N = 156,980**	**UK N = 94,971**
Treatment failure, n (%)	13,226 (13)	9,291 (10)	23,224 (11)	15,193 (10)	9,999 (11)
Among treatment failures, n (%)					
PR	8,015 (61)	1,369 (15)	5,759 (25)	4,864 (32)	3,990 (40)
NS5A	4,322 (33)	4,126 (44)	9,381 (40)	7,900 (52)	3,861 (39)
Non-NS5A	889 (7)	3,796 (41)	8,084 (35)	2,429 (16)	2,148 (22)
Cirrhotic	6,408 (49)	4,426 (48)	14,722 (63)	7,586 (50)	3,201 (32)
GT1	9,281 (70)	4,641 (50)	16,353 (70)	11,150 (73)	4,578 (46)
GT2	716 (5)	649 (7)	5,161 (22)	436 (3)	466 (5)
GT3	2,087 (16)	3,672 (40)	864 (4)	2,988 (20)	4,582 (46)
GT4–6	1,142 (9)	329 (4)	843 (4)	619 (4)	373 (4)

Patients with Chronic Kidney Disease

Executive Summary

- G/P demonstrates high SVR12 and favorable safety across all genotypes and all CKD stages – irrespective of baseline characteristics
  - Only option for GT2–3 patients with severe CKD, including those on hemodialysis
- Real world data are emerging for the use of SOF-based regimens in patients with severe CKD with attempts to establish safety and effectiveness
  - Conflicting data presented on impact of SOF on eGFR
- First real-world data confirmed the effectiveness of EBR/GZR in patients across all stages of CKD
- One analysis demonstrated the difficulty in capturing true renal function changes; no correlation was found between MDRD, cystatin-C and NGAL biomarkers with traditional biomarkers eGFR or Creatinine

SAT-273, Pol: Safety and Efficacy of G/P in Adults with Chronic HCV Infection GT1–6 as a Function of Chronic Kidney Disease Stage

An integrated efficacy, safety, and PK analysis of HCV GT1–6-infected patients treated with G/P for 8 (n = 822), 12 (n = 1347), or 16 (n = 69) weeks from eight phase 2 and 3 clinical trials, as a function of CKD stage

Patients were stratified by CKD stage (eGFR [mL/min/1.73 m2] by MDRD)
Stage 1, eGFR ≥90; stage 2, eGFR 60 to <90; stage 3, eGFR 30 to <60; stage 4, eGFR 15 to <30; stage 5 eGFR<15

Baseline characteristics, n (%)	CKD 1 n=1054	CKD 2 n=1045	CKD 3 n=36	CKD 4–5 n=103
HCV genotype				
1	399 (38)	421 (40)	15 (42)	54 (52)
2	195 (19)	239 (23)	12 (33)	16 (16)
3	329 (31)	285 (27)	7 (19)	11 (11)
4–6	131 (12)	100 (10)	2 (6)	22 (21)
Treatment-naive	786 (75)	757 (72)	25 (69)	60 (58)
Compensated cirrhosis	129 (12)	115 (11)	8 (22)	20 (19)

SVR12 (ITT) rate was 98% overall, and high irrespective of CKD stage

Event, n (%)	CKD 1 n=1054	CKD 2 n=1045	CKD 3 n=36	CKD 4–5 n=103
Any SAE	25 (2)	17 (2)	3 (8)	25 (24)
DAA-related SAE*	0	1 (<1)	0	0
AE leading to d/c	4 (<1)	3 (<1)	1 (3)	4 (4)
Death†	3 (<1)	1 (<1)	1 (3)	1 (1)

Laboratory abnormalities, n/N (%)	CKD 1	CKD 2	CKD 3	CKD 4–5
ALT ≥ grade 3	0/1052	2/1045 (<1)	0/36	0/103
Total bilirubin ≥ grade 3	5/1052 (<1)	3/1045 (<1)	0/36	1/103 (1)

Most total bilirubin elevations were primarily driven by indirect bilirubin and were not associated with ALT increase

Overall, the mean change in eGFR (mL/min/1.73 m^2) from baseline to final post-treatment visit was –2.5 ± 12.7

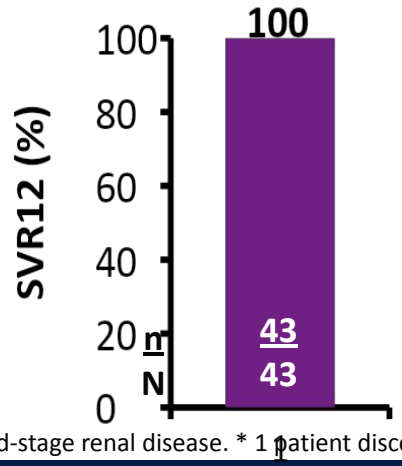
Exposures of GLE and PIB were higher in patients with more advanced CKD, however PK changes were not clinically relevant

CKD, chronic kidney disease; d/c, discontinuation; ITT, intent-to-treat; PK, pharmacokinetic.
* DAA-related SAE was transient ischemic attack (patient d/c treatment and did not achieve SVR12); †Causes of death (all not related to study drug): CKD stage 1 (n=3) pneumonia, accidental overdose, alcohol poisoning and toxicity to various agents; CKD stage 2 (n=1) cerebral haemorrhage; CKD stage 3 (n=1) adenocarcinoma; CKD stage 4–5 (n=1) cerebral haemorrhage.

FRI-219, Nazario: Full Dose, Daily SOF Treatment in End-Stage Renal Disease: Tolerability and Safety of Largest ESRD Patient Cohort

Analysis of chronic HCV GT1–3 infected patients with ESRD on dialysis or GFR <30 mL/min treated with full-dose (400 mg) SOF-based regimens (SOF + SMV, LDV/SOF, SOF + DCV, SOF/VEL) for 12 or 24 weeks

Baseline characteristics	N = 45
Median age, years (range)	57 (42–70)
Male, n (%)	31 (69)
GT1a, n (%)	29 (64)
HCV RNA >800,000 IU/mL, n (%)	27 (60)
On dialysis, n (%)	42 (93)
Cirrhosis, n (%)	22 (49)
Treatment-naive, n (%)	35 (78)



7% (3/45) of patients were not on dialysis

Safety, n (%)	SOF + SMV N = 33	LDV/SOF N = 9	SOF + DCV N = 2	SOF/VEL N = 1
AE	9 (27)	2 (22)	0	0
Discontinued	2 (6)*	0	0	0

No hepatic decompensation events

No dose adjustments

Most frequent AEs were:
nausea (n = 4 [9%]), insomnia (n = 4 [9%], headache (n = 3 [7%]), pruritus (n = 1 [2%]), and anemia (n = 1 [2%])

The AE profile and rate of discontinuation were similar to those in the general HCV population

ESRD, end-stage renal disease. * 1 patient discontinued due to severe nausea; 1 patient discontinued due to sepsis from pneumonia unrelated to treatment.

FRI-229, Kuo: No Adverse Renal Side Effects in Patients with Mild to Moderate Renal Dysfunction Treated with SOF

Real-world retrospective study of the effect of SOF on renal function in patients with baseline eGFR <60 mL/min/1.73 m^2 and chronic HCV infection in Hawaii

Baseline characteristics, n (%)	N = 221
Male	143 (65)
Age ≥65 years	76 (34)
Baseline eGFR (mL/min/1.73 m^2)	
>60	207 (94)
50–59	10 (5)
40–49	3 (1)
30–39	0
20–29	1 (<1)

Serum creatinine

Overall average increase in SCr of 0.04 from baseline to EOT (p <0.01); there was no significant different in SCr between EOT and PTW12 (p = 0.26)

In patients ≥65 years old, SCr increased on average by 0.05 during therapy (p< 0.01); no significant difference was found between EOT and PTW12 (p = 0.45)

No significant difference in SCr between baseline, EOT, and PTW12 in patients with renal impairment (p = 0.61)

GFR: baseline to EOT

Laboratory GFR: no significant difference in any eGFR subgroup

Cockcroft–Gault formula: average decrease of 4.72 (p <0.01) among patients with GFR >60

MDRD formula: average decrease of 5.18 (p <0.01) among patients with GFR >60

CKD-EPI formula: average decrease of 5.18 (p <0.01) among patients with GFR >60

GFR: EOT to PTW12

No significant difference when GFR was calculated by any of the GFR equations

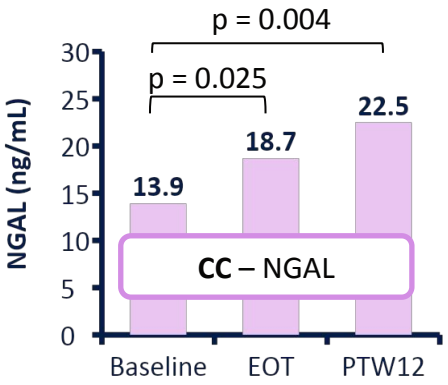
CKD-EPI, chronic kidney disease epidemiology collaboration; eGFR, estimated glomerular filtration rate;
EOT, end of treatment; MDRD, modification of diet in renal disease; PTW12, post-treatment Week 12; SCr, serum creatinine.

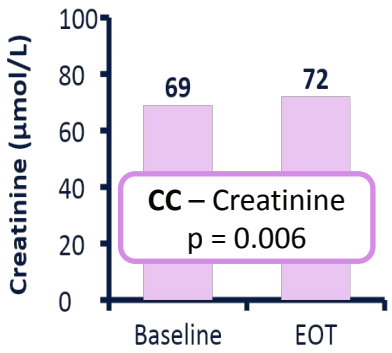
THU-269, Theocharidou: Changes in Renal Function in Patients with Hepatitis C-Related Cirrhosis Treated with DAA Agents

Assessing changes in renal function during DAA (mostly SOF) therapy in HCV-infected patients with compensated or decompensated cirrhosis using conventional markers (creatinine and eGFR using MDRD) and serum biomarkers (NGAL and cystatin C)

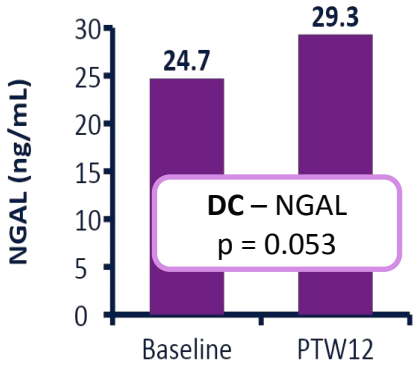
Baseline characteristics	CC N = 40	DC N = 47	p-value
Age, years (range)	60 (34–77)	57 (28–78)	0.24
MELD score (range)	8 (6–12)	11 (5–18)	<0.0005
Renal risk factor,* n (%)	20 (50)	35 (75)	0.033
NGAL, ng/mL (range)	14 (3–79)	25 (12–46)	0.002
Cystatin C, mg/L (SD)	1.18 (0.44)	1.43 (0.18)	0.001

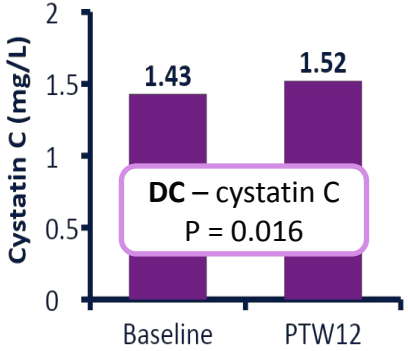
No difference in baseline creatinine or eGFR between CC and DC patients





No difference in eGFR between baseline and EOT





No significant changes in creatinine or eGFR

A poor correlation between NGAL or cystatin c and eGFR or creatinine existed

Impairment of renal function (detected by serum biomarkers) occurred during treatment in both groups and persisted beyond EOT

CC, compensated cirrhosis; DC, decompensated cirrhosis; eGFR, estimated glomerular filtration rate;
EOT, end of treatment; MDRD, modification of diet in renal disease equation; NGAL, neutrophil gelatinase-associated lipocalin; PTW12, post treatment week 12.
* Renal risk factors include pre-existing renal impairment, diabetes mellitus, hypertension, and diuretics.

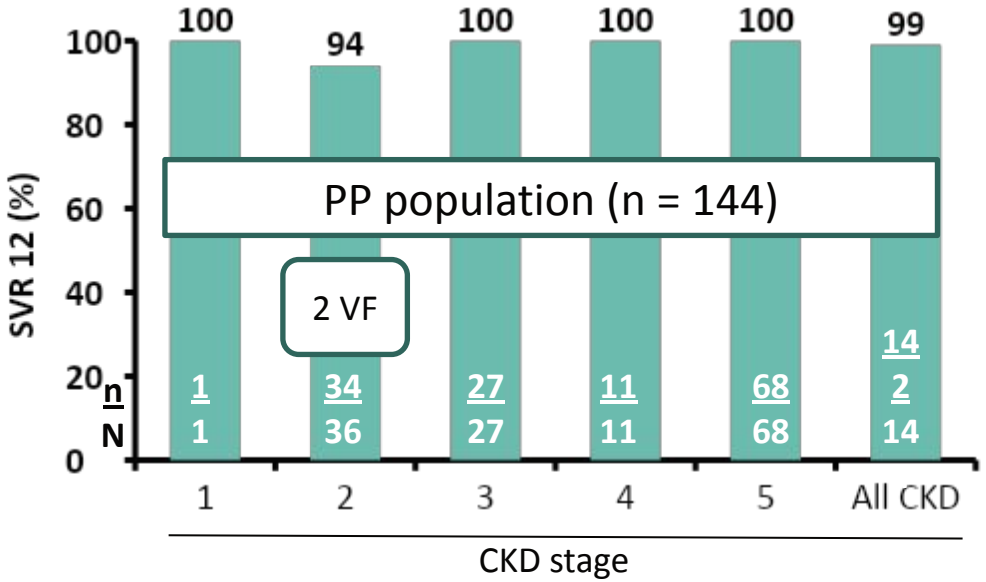
SAT-297, Younossi: EBR/GZR Effectiveness in Patients with Chronic HCV and Chronic Kidney Disease: Real-World Experience from the TRIO Network

Data from the TRIO Network were used to evaluate the real-world effectiveness of EBR/GZR in patients with CKD* (baseline eGFR <90 mL/min/1.73 m^2) in the United States

440 patients treated with EBR/GZR; 261 with CKD (24% stage 2, 20% stage 3, and 53% stage 4–5

Baseline characteristics	EBR/GZR N = 440
Male, n (%)	277 (63)
HCV RNA > 6MM IU/mL, n/N (%)	63/428 (15)
HCV genotype, n/N (%)	
GT1a	254/440 (58)
NS5A RAS tested	160/254 (63)
NS5A RAS present	12/160 (8)
GT1b	147/440 (33)
GT4	28/440 (6)
Other†	11/440 (3)
Fibrosis stage, n/N (%)	
F3	63/437 (14)
F4	131/437 (30)
Treatment-naive, n (%)	355 (81)

EBR/GZR was used in 93% of patients with 7% receiving RBV. Most patients were treated for 12 wks.



CKD, chronic kidney disease; PP, per-protocol (defined as patients that completed intended therapy and received SVR testing at 12 weeks); VF, virologic failure.
* eGFR values were calculated using the CKD-EPI Creatinine equation; † Includes GT1 unknown, GT2, GT3, and GT unknown.

Other Populations

Executive Summary

Summary:

- It appears to be a question as to whether special patient populations still exist with highly efficacious next-generation DAAs
- High SVR rates (>98%) were observed in special populations (HIV/HCV coinfected, post-transplant) treated with G/P with minimal drug-drug interactions anticipated to require additional patient monitoring requirements. No new safety signals were observed and the SVR rates were high regardless of patient or viral characteristics
- HIV/HCV coinfected and patients post-transplant treated with G/P are not expected to require treatment durations that differ from TN NC or TN C patients
- A pangenotypic regimen like G/P that can deliver high SVR rates with the shortest treatment durations available should provide additional benefits, especially for difficult to treat patient populations (i.e. GT3)
- PWIDs achieved high SVR rates with DAAs despite challenges to adherence. These patients may benefit from shorter courses of treatment, as adherence was noted to decline with extended therapy duration

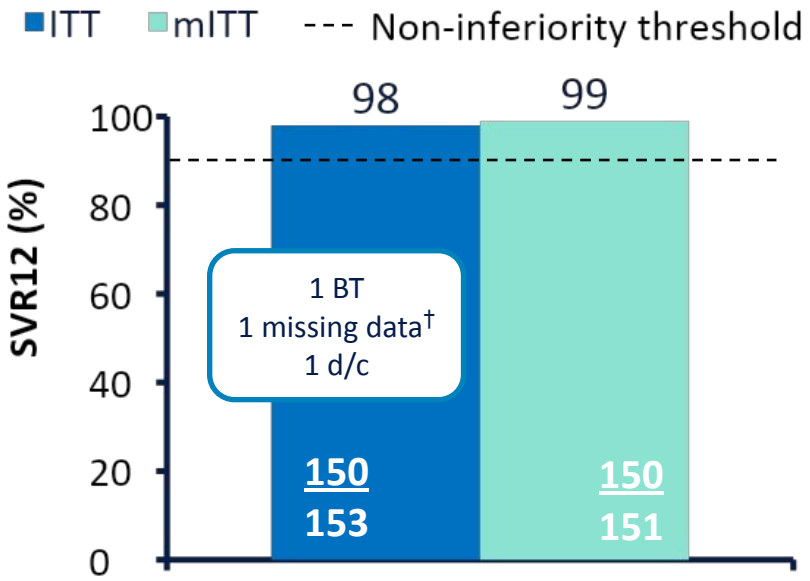
TN NC, treatment-naïve, non-cirrhotic; TN C, treatment-naïve with compensated cirrhosis.

LBP-522, Rockstroh: Efficacy and Safety of G/P in Patients Co-infected with Hepatitis C and Human Immunodeficiency Virus-1: The EXPEDITION-2 Study

Phase 3, multicenter study evaluating G/P treatment in HCV/HIV-1 co-infected patients for 8 weeks (non-cirrhotic) or 12 weeks (cirrhotic) in HCV/HIV co-infected patients with HCV GT1–6 infection

Baseline characteristics	8 weeks No cirrhosis N = 137	**12 weeks Cirrhosis N = 16**
Median age, years (range)	45 (23–74)	50 (35–62)
No ART, n (%)	9 (7)	0
Genotype,* n (%)		
1a	66 (48)	5 (31)
1b	18 (13)	5 (31)
2	12 (9)	1 (6)
3	22 (16)	4 (25)
4	16 (12)	1 (6)
6	3 (2)	0
Treatment-naive, n (%)	111 (81)	14 (87)
Safety, n (%)		
DAA-related SAE, n (%)	0	0
AE leading to d/c, n (%)	0	1 (6)‡
ALT, grade ≥3 (>5 x ULN)	0	0
AST, grade ≥3 (>5 x ULN)	0	0
Total bilirubin, grade ≥3 (>3 x ULN)	1 (0.7)	0

BT, breakthrough; d/c, discontinuation; mITT, excludes non-virologic failure.
* No GT5 were enrolled; † Patient achieved SVR4, but was lost to follow-up;
‡ Cerebrovascular accident and cerebral haemorrhage; both unrelated to G/P.



SVR12 was 100% (136/136) in patients without cirrhosis treated for 8 weeks

SVR12 (mITT) was 93% (14/15) in patients with cirrhosis

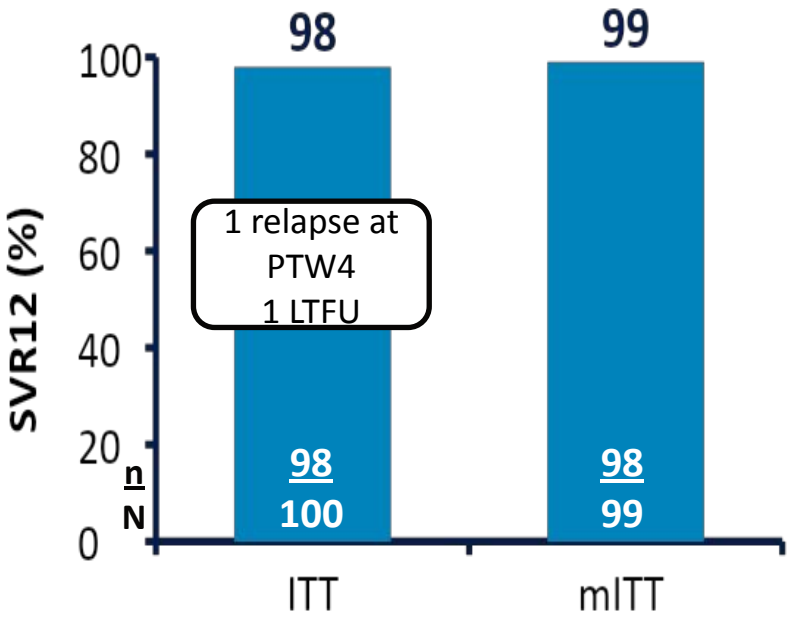
- 1 patient with GT3a infection and cirrhosis had on-treatment failure at Week 8
  - No NS3 RASs at baseline; Y56H at failure
  - NS5A A30V at baseline; S24F, M28K at failure

LBO-03, Reau: MAGELLAN-2: Safety and Efficacy of G/P in Liver or Renal Transplant Adults with Chronic Hepatitis C Genotype 1–6 Infection

Phase 3 study to evaluate the efficacy and safety of G/P for 12 weeks in adults with chronic HCV GT1–6 infection without cirrhosis who have had liver (n = 80) or renal (n = 20) transplant

GT: 1 (57%), 2 (13%), 3 (24%), 4–6 (6%)
Fibrosis: F0–1 (80%), F2 (6%), F3 (14%)

BL immunosuppressant medication:
tacrolimus (68%), mycophenolic acid (30%), cyclosporine (13%), prednisone (13%), prednisolone (11%), everolimus (8%), azathioprine (6%), and sirolimus (7%)



Safety, n/%	G/P, 12 weeks N = 100
SAE	8
DAA-related SAEs	2
AE leading to study drug d/c	1
DAA-related AE leading to study drug d/c	0
Death	0
Transplant rejection	1

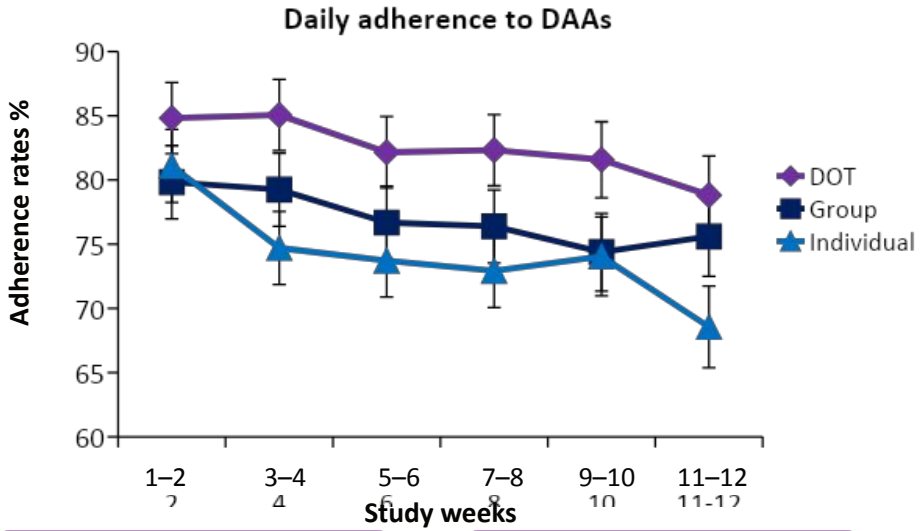
Patient with mild liver transplant rejection unrelated to DDIs and did not lead to treatment interruption

Grade 3 laboratory abnormalities were rare

PS-130, Litwin: PREVAIL: Intensive Models of HCV Care for People Who Inject Drugs

PWIDs with HCV GT1 were randomized to one of three models of HCV care delivered on-site in an OAT program. Adherence measured by electronic blister pack

Total screened	N = 190		
Total enrolled	n = 166		
Eligible	n = 158		
Randomisation	**Individual (n = 53)**	**Group (n = 52)**	**DOT (n = 53)**
Withdrawn*	2	4	2
Treated	51	48	51
Male, %	63	67	65
Age (years)	51	51	51
Genotype 1a, %	86	85	84
Cirrhosis, %	20	33	29
Drug use, %†	55	50	49
Methadone, %	96	98	100
DAA regimen, %			
SOF/LDV	69	79	61
SOF/SMV	8	4	10
SOF/RBV	10	6	18
SOF/RBV/pegIFN	14	6	10
TVR/RBV/pegIFN	0	4	2



Overall adherence:
Individual: 74%
Group: 78%
DOT: 83%

Overall SVR12 rate was 94%‡
Individual: 90% (46/51)
Group: 94% (48/51)
DOT: 98% (50/51)

On-site DAA treatment as highly effective among PWIDs receiving OAT despite active drug use and comorbidities

Intensive care models led to higher rates of adherence

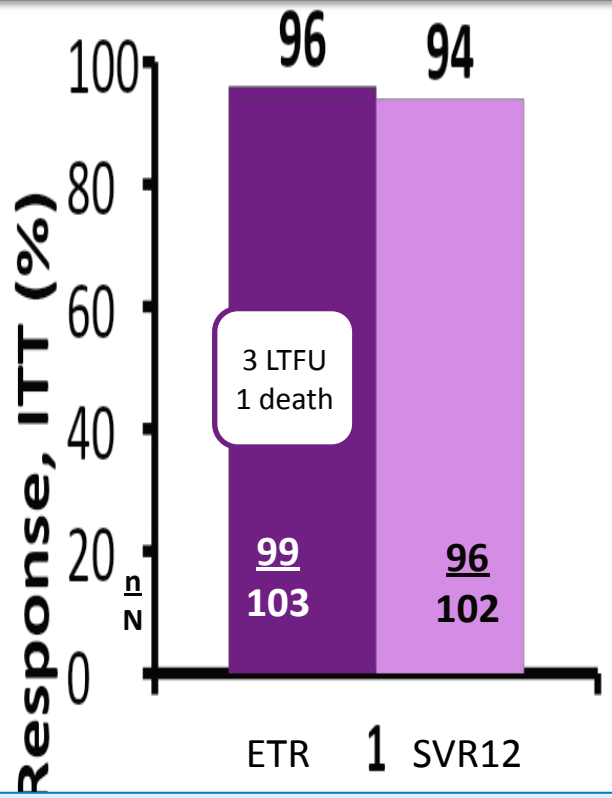
OAT = Outcomes, Adherence, Treatment; TAU = Individual self-administered treatment; DOT = directly observed treatment; * Reasons for treatment withdrawal include not interested in HCV treatment, and no longer in OAT; † Any drug use includes use of any drugs in 6 months, including opiates, cocaine and benzodiazepines; ‡ 3 patients did not achieve undetectable HCV RNA, 2 patients died, 4 patients with HCV RNA not detected at EOT.

FRI-234, Grebely; The SIMPLIFY Study: Efficacy and Safety of SOF/VEL in People with Chronic HCV Infection and Recent Injecting Drug Use

A phase 4, open-label, single arm, multicenter, international trial of SOF/VEL for 12 weeks in n = 103 patients with HCV infection and recent injection drug use.

Baseline characteristics, n (%)	SOF/VEL 12 Weeks N = 103
HCV genotype	
1	36 (35)
2	5 (5)
3	60 (58)
4	2 (2)
OST and injecting drug use (in the last month)*	
No OST, no injecting	12 (12)
No OST, injecting	33 (32)
OST, no injecting	15 (15)
OST, injecting	43 (42)
Fibrosis stage (METAVIR)†	
F0-F1	59 (62)
F2-F3	27 (28)
F4	9 (9)

* At study screening; † Missing data in n = 8 patients.



No cases of virologic failure, n = 1 virologic relapse/re-infection to date

DDIs and PK

Executive Summary

- Data presented at EASL allowed for a better understanding of the comparison of DDIs for SOF/VEL/VOX. The addition of VOX to the regimen leads to increased drug-drug interactions
- For certain classes of medications, G/P will have a more competitive DDI profile than SOF/VEL/VOX. In statins, for example, SOF/VEL/VOX may have a more challenging DDI profile
- The actual number of DDIs will be confirmed in the pending label; the main classes of interactions are similar to GLE

FRI-187, Garrison: Drug-Drug Interaction Profile of SOF/VEL/VOX Fixed-Dose Combination

The DDI profile of SOF/VEL/VOX with drug transporter and CYP probes, and commonly used concomitant medications was characterized using Phase 1 clinical data

SOF/VEL/VOX 400/100/100 mg (+ VOX 100 mg when evaluating perpetrator interactions to approximate systemic VOX exposures observed in HCV-infected patients) was administered to healthy volunteers

Drug	Effect on AUC, %
SOF/VEL/VOX as perpetrator	
Pravastatin (OATP)	↑ 116
Rosuvastatin (OATP/BRCP)	↑ 639
Dabigatran etexilate (P-gp)	↑ 161
SOF/VEL/VOX as victim	
Voriconazole 200 mg (CYP3A)	VOX ↑ 84
Ketaconazole 200 mg (CYP3A)	VEL ↑ 71
Gemfibrozil 600 mg (CYP2C8)	↔ VOX
Multiple dose RIF 600 mg (OATP)	SOF ↓ 72; VEL ↓ 82; VOX ↓ 73
Single dose RIF 600 mg (OATP)	VOX ↑ 691; VEL ↑ 46
Cyclosporine 600 mg (P-gp/BRCP/OATP)	VOX ↑ 839; SOF ↑ 353; VEL ↑ 103
EFV/FTC/TDF	VEL ↓ 53
ATV/r (single dose)	VOX ↑ 331; VEL ↑ 93; SOF ↑ 40

Drugs without clinically significant interactions

Inhibitors of P-gp, BCRP, and/or CYPs

HIV ARVs
Bictegravir, cobicistat, darunavir, dolutegravir, elvitegravir, emtricitabine, raltegravir, rilpivirine, ritonavir, tenofovir alafenamide, and boosted regimens

Oral Contraceptives
Ethinyl estradiol, norgestrel, or norelgestromin

Strong OATP inhibitors increased VOX exposures

Inducers of P-gp, BCRP, and/or CYPs decreased SOF, VEL, and/or VOX exposures

Sensitive substrates of P-gp, BCRP, or OATP1B1/1B3 may require dose adjustment or use with caution and/or monitoring

Clinically significant interactions with HIV ARVs limited to EFV, ATV and lopinavir

ARVs, antiretrovirals; ATV, atazanavir; EFV, efavirenz; FTC, emtricitabine; r, ritonavir; RIF, rifampin; TDF, tenofovir disoproxil fumarate.

Real World Evidence

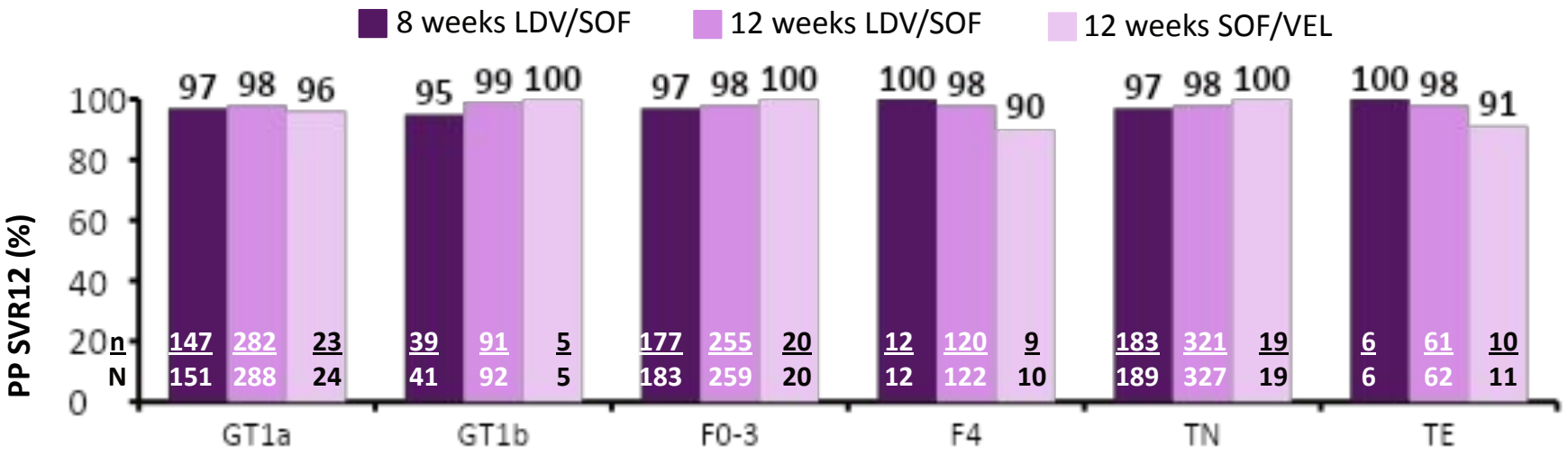
Executive Summary

- RWE continues to confirm the results of clinical trials across the currently approved regimens (OBV/PTV/r ± DSV, LDV/SOF, SOF/VEL, EBR/GZR)
- First real-world data confirms the effectiveness of EBR/GZR in patients with and without chronic kidney disease
- Advanced fibrosis and presence of cirrhosis continue to be a predictor of lower SVR rates
- LDV/SOF use may be expanded based on RWE data suggesting HCV RNA BL VL >6 million has no impact on SVR
- It will be important to show that the presence of baseline characteristics (especially patients with advanced liver fibrosis) have no impact on SVR rates in patients treated with G/P in the real world

SAT-244, Tsai: Utilization of DAA therapies LDV/SOF and SOF/VEL in Patients with GT1 HCV: Real-world experience from the TRIO Network

Real-world study to evaluate utilization of LDV/SOF (n = 1327) and SOF/VEL (n = 89) in HCV GT1-infected patients. Data were collected through Trio Health's Innervation Platform in the US in 36 states and predominantly in community practices

Baseline characteristics of patients were similar between 12 week LDV/SOF and 12 week SOF/VEL groups, with the exception of prior TE (17% [159/949] 12 weeks LDV/SOF vs. 31% [28/89] SOF/VEL, p <0.001) and platelets <100,000/mL (9% [72/803] 12 weeks LDV/SOF vs. 18% [14/78] SOF/VEL, p = 0.011)



Overall SVR12 (PP)
LDV/SOF (8 weeks): **97%** (189/195)
LDV/SOF (12 weeks): **98%** (382/389)
SOF/VEL (12 weeks): **97%** (29/30)

Among patients treated with LDV/SOF for 8 weeks, those treated in community settings were more likely to achieve SVR than those treated in academic settings (p = 0.026; 98% vs 88%)

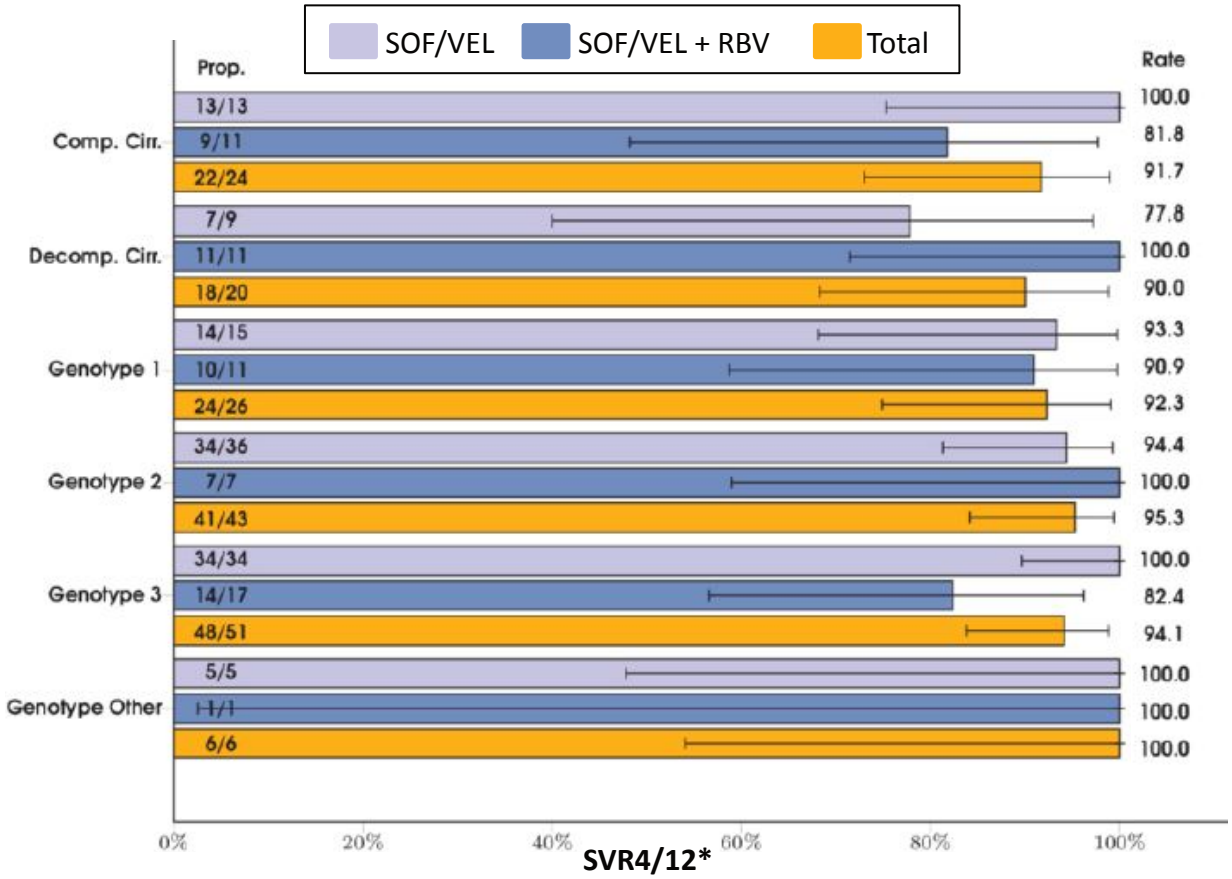
PP, Per protocol; TE, treatment experienced; TN, Treatment-naive.

SAT-222, Khalili: Safety and Efficacy of SOF/VEL ± RBV for the Treatment of HCV GT1–6: Results of the HCV-TARGET Study

Real-world efficacy and safety of SOF/VEL +/- RBV for 12 weeks in treatment-naive or -experienced HCV GT1-6 patients in the HCV-TARGET registry

Baseline characteristics, n (%)	SOF/VEL N = 387	SOF/VEL + RBV N = 108
Male	224 (58)	82 (76)
HCV genotype		
1	60 (16)	33 (31)
2	151 (39)	15 (14)
3	153 (40)	53 (49)
Other	23 (6)	7 (7)
Cirrhosis	89 (23)	74 (69)
Treatment experienced	58 (15)	62 (57)
Prior hepatic decompensation	24 (6)	46 (43)

Safety	SOF/VEL N = 217	SOF/VEL + RBV N = 66
Any AE, n (%)	120 (55)	53 (80)
SAE, n	8	10
Death, n (%)	1 (<1)	0 (0)



Patients who did not achieve SVR were mainly treatment experienced and/or had advanced liver disease

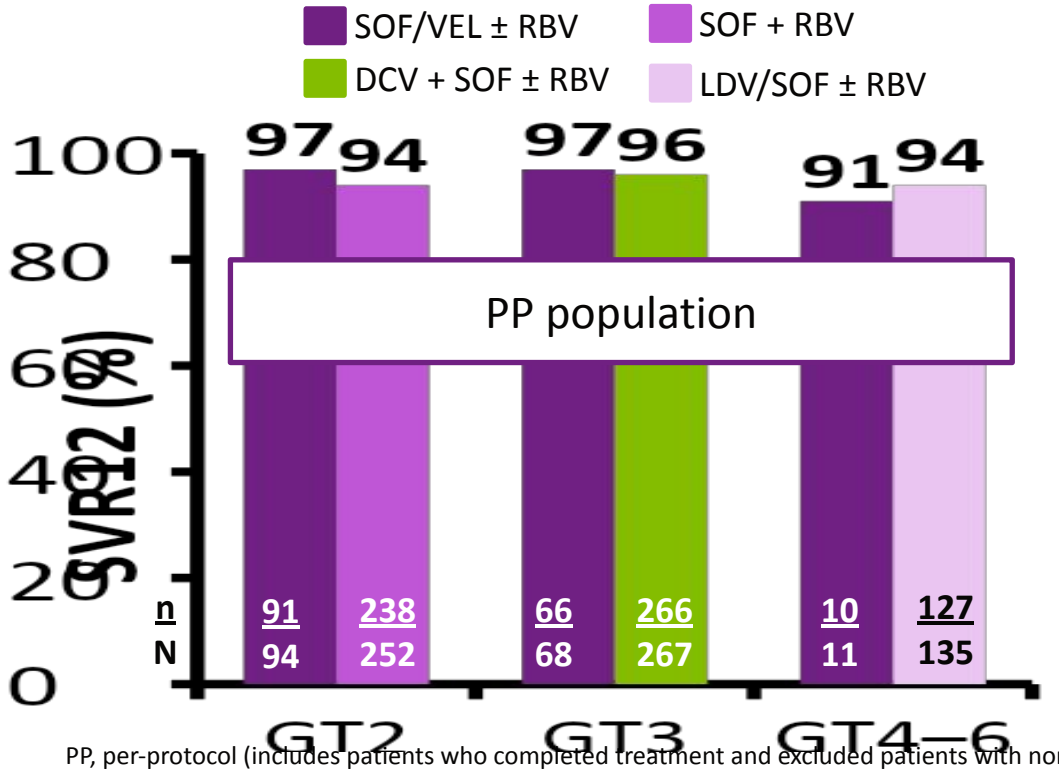
*SVR presented for patients with available virological outcomes, excluding patients who d/c early except for whom lack of efficacy was recorded.

PS-102, Curry: Utilization of SOF/VEL in GT2–6 HCV: Real-World Experience from the TRIO Network

Real-world study of 1827 patients in the US HCV TRIO network to evaluate treatment utilization and compare outcomes between SOV/VEL ± RBV and existing DAA therapies in patients with GT2–6 chronic HCV

Prior to SOF/VEL approval in June 2016, the most commonly used regimens were SOF + RBV (77% in GT2), DCV + SOF ± RBV (86% for GT3), and LDV/SOF ± RBV (90% in GT4–6)

After approval, SOF/VEL ± RBV was used in 81% of GT2 patients, 74% of GT3 patients, and 36% of GT4–6 patients



SOF/VEL ± RBV SVR12, % (n/N)	GT2	GT3
Treatment-naive	97 (70/72)	98 (55/56)
Treatment-experienced	95 (21/22)	92 (11/12)
F0–3	97 (70/72)	100 (52/52)
F4	95 (21/22)	93 (14/15)

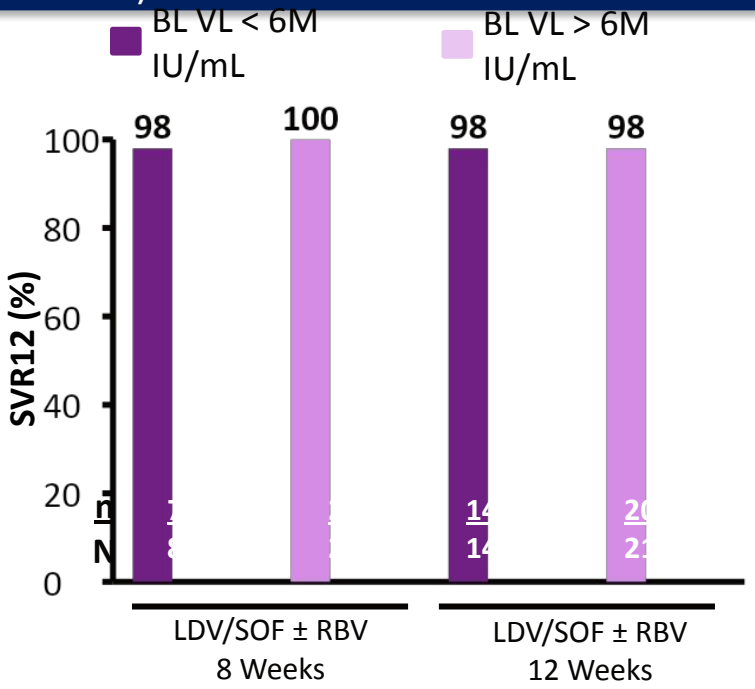
SVR rates were similar to those observed in clinical trials

PP, per-protocol (includes patients who completed treatment and excluded patients with non-virologic failure).

FRI-247, Vermehren: Use of the 6 Million Viral Load Cut-off to Guide Treatment Duration with LDV/SOF in Patients With Chronic HCV GT1 Infection: Results from the German Hepatitis C-Registry (DHC-R)

DHC-R: A prospective, multicentre, real-world cohort study comprising ~10,000 HCV infected patients. This analysis includes HCV GT1-infected patients who received LDV/SOF ± RBV for 8 (N = 981) or 12 (N = 1939) weeks

Baseline characteristics	LDV/SOF 8 Weeks N = 981	LDV/SOF 12 Weeks N = 1939
TN, NC, BL VL < 6M IU/mL, n (%)*	848 (86)	430 (23)
BL VL > 6 M IU/mL, n/N (%)	23/830 (3)	214/1677 (13)



42 relapsers

- 4/42 (10%) had a BL VL >6M IU/mL (all were treated for 12 weeks)
- 12/42 (29%) had been treated for 8 weeks and all had BLVL <6M IU/mL

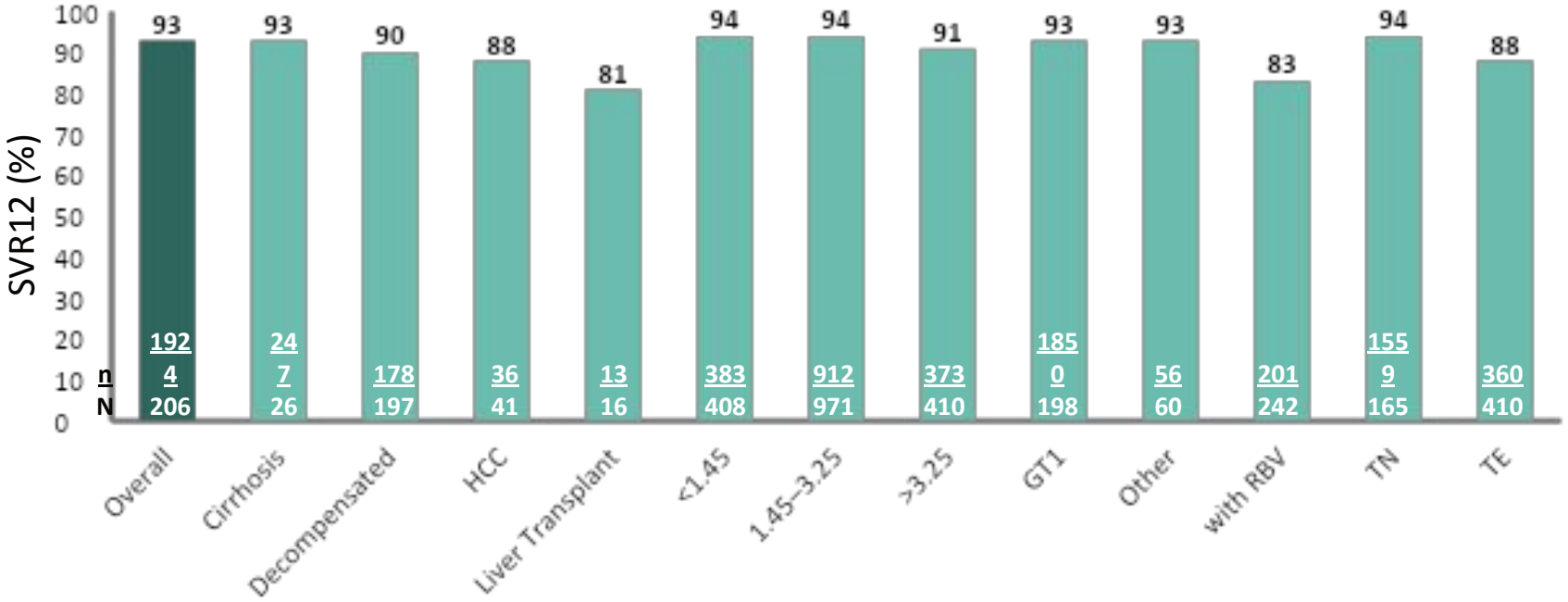
All patients with BL VL > 6M treated for 8 weeks achieved SVR

TN, treatment naive; NC, non-cirrhotic; BL VL, baseline viral load.
* Criteria for 8-week LDV/SOF ± RBV treatment.

*

FRI-239, McCombs: Analysis of the Real-World Treatment Effectiveness of EBR/GZR

A real-world, retrospective, cohort study to evaluate the effectiveness of EBR/GZR in HCV-infected patients within the Veterans Health Administration



Patients who received RBV (OR 0.31 (95% CI, 0.20–0.49); $p < 0.0001$) and treatment-experienced patients* (OR 0.61 (95% CI, 0.40–0.92); $p = 0.02$) were less likely to achieve SVR12

FIB4 > 3.25 (OR 0.73 (95% CI, 0.41–1.29); $p = 0.28$) demonstrated a trend towards being a negative predictor of SVR12

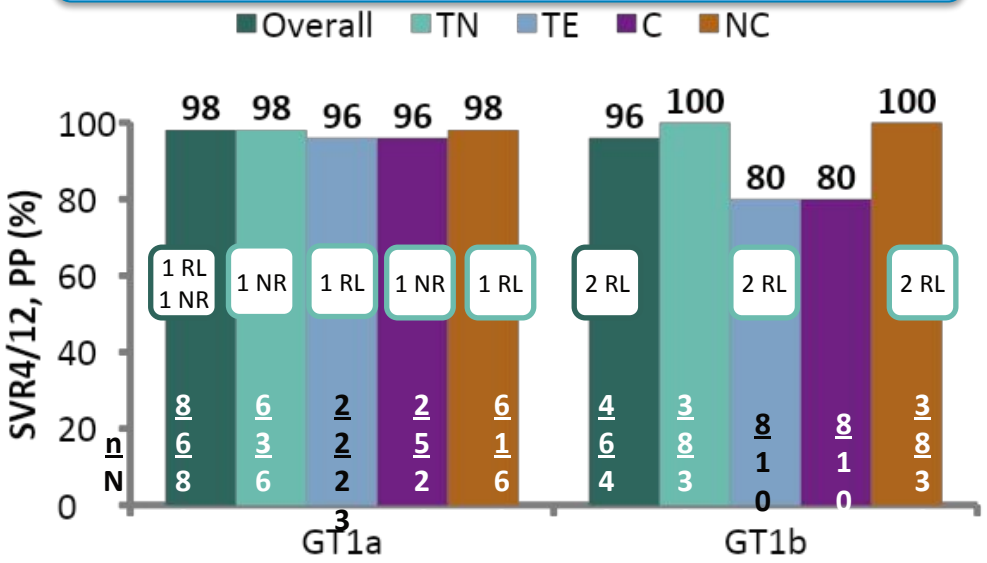
HCC, hepatocellular carcinoma; TE, treatment-experienced; TN, treatment-naive.
* Reference group = treatment-naive patients

THU-237, Pearlman: Safety and Efficacy of EBR/GZR ± RBV for the Treatment of HCV GT1: Results of the HCV-TARGET Study

Analysis of HCV GT1-infected patients treated with EBR/GZR ± RBV in the real-world HCV-TARGET study at academic and community medical centres in Europe and North America

Baseline characteristics, n (%)	EBR/GZR N = 297	EBR/GZR + RBV N = 22	Total N = 319
Male	182 (61)	16 (73)	198 (62)
Genotype			
GT1a	173 (58)	17 (77)	190 (60)
GT1b	119 (40)	4 (18)	123 (39)
GT1 nos	5 (2)	1 (5)	6 (2)
GT1a NS5A RAS tested	147 (85)	17 (100)	164 (86)
NS5A RASs present	2 (1)	12 (71)	14 (7)
TE	60 (20)	7 (32)	67 (21)
Cirrhotic	61 (21)	4 (18)	65 (20)
Treatment duration			
12 weeks	191 (96)	9 (56)	200 (93)
16 weeks	3 (2)	7 (44)	10 (5)
Prior decompensation	14 (5)	1 (5)	15 (5)
CKD Stage			
1–3	196 (66)	18 (82)	214 (67)
4	15 (5)	2 (9)	17 (5)
5	70 (24)	1 (5)	71 (22)
Dialysis	48 (16)	1 (5)	49 (15)

RBV added in <10% of patients, and mainly limited to those with baseline RASs and those who are TE or cirrhotic



Safety, n (%)	EBR/GZR N = 297	EBR/GZR + RBV N = 22	Total N = 319
AEs	102 (34)	11 (50)	113 (35)
SAEs	15 (5)	0	15 (5)

AEs leading to d/c:
Depression n = 1; Drug intolerance n = 1

Anemia was reported in 2/200 treated with EBR/GZR alone and 1/16 treated with EBR/GZR + RBV

BL, baseline; C, cirrhosis; GT1 nos, not defined in abstract;
NR, non-responder; PP, per protocol (excludes non-virologic failures); RL, relapse; TE, treatment-experienced; TN, treatment-naive.

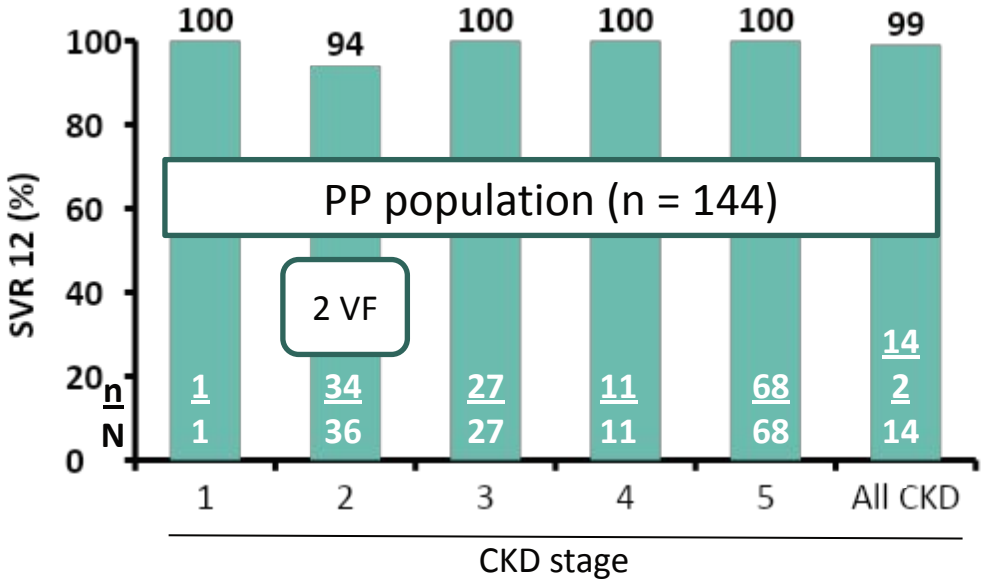
SAT-297, Younossi: EBR/GZR Effectiveness in Patients with Chronic HCV and Chronic Kidney Disease: Real-World Experience from the TRIO Network

Data from the TRIO Network were used to evaluate the real-world effectiveness of EBR/GZR in patients with CKD* (baseline eGFR <90 mL/min/1.73 m^2) in the United States

440 patients treated with EBR/GZR; 261 with CKD (24% stage 2, 20% stage 3, and 53% stage 4–5

Baseline characteristics	EBR/GZR N = 440
Male, n (%)	277 (63)
HCV RNA > 6MM IU/mL, n/N (%)	63/428 (15)
HCV genotype, n/N (%)	
GT1a	254/440 (58)
NS5A RAS tested	160/254 (63)
NS5A RAS present	12/160 (8)
GT1b	147/440 (33)
GT4	28/440 (6)
Other†	11/440 (3)
Fibrosis stage, n/N (%)	
F3	63/437 (14)
F4	131/437 (30)
Treatment-naive, n (%)	355 (81)

EBR/GZR was used in 93% of patients with 7% receiving RBV. Most patients were treated for 12 wks.

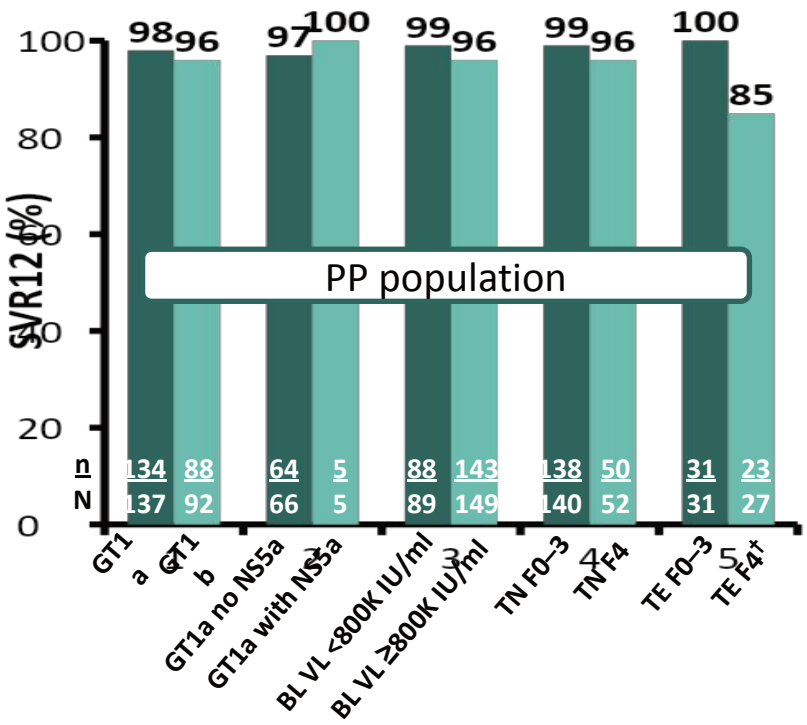


CKD, chronic kidney disease; PP, per-protocol (defined as patients that completed intended therapy and received SVR testing at 12 weeks); VF, virologic failure.
* eGFR values were calculated using the CKD-EPI Creatinine equation; † Includes GT1 unknown, GT2, GT3, and GT unknown.

THU-239, Bacon: Real-World Use of EBR/GZR and Outcomes in Patients with Chronic Hepatitis C: Retrospective Data Analyses From the TRIO Network

Retrospective analysis of HCV-infected patients treated with EBR/GZR and a HCV GT1-infected comparator group treated with non-EBR/GZR regimens in the real-world TRIO Health Network

Baseline characteristics	All EBR/GZR regimens N = 462	GT1 only EBR/GZR regimens N = 410	GT1 only Non-EBR/GZR regimens N = 6165
Mean age, years (range)	59 (25–88)	60 (25–88)	59 (19–92)
Male n, (%)	290 (63)	262 (64)	3593 (58)
Baseline HCV RNA >6 M IU/ml, n/N (%)	64/430 (15)	63/396 (16)	1098/5970 (18)
Genotype, n/N (%)			
1a	259/462 (56)	259/410 (63)	4309 (70)
1a NS5A RAS tested	162/259 (63)	162/259 (63)	70/4309 (2)
1b	150/462 (32)	150/410 (37)	1593 (26)
4	28/462 (6)	–	–
Other*	24/462 (5)	–	–
Fibrosis, n/N (%)			
F0–2	181/445 (41)	167/408 (41)	2572/6038 (43)
F3	65/445 (15)	61/408 (15)	899/6038 (15)
F4	134/445 (30)	123/408 (30)	1817/6038 (30)
Treatment naive, n (%)	359 (78)	330 (80)	4983 (81)
Comorbidities, n/N (%)			
CKD (stage 3-5?)	261/440 (60)	243/402 (60)	2258/6015 (38)
Diabetes	134/433 (31)	126/397 (32)	1047/5923 (18)



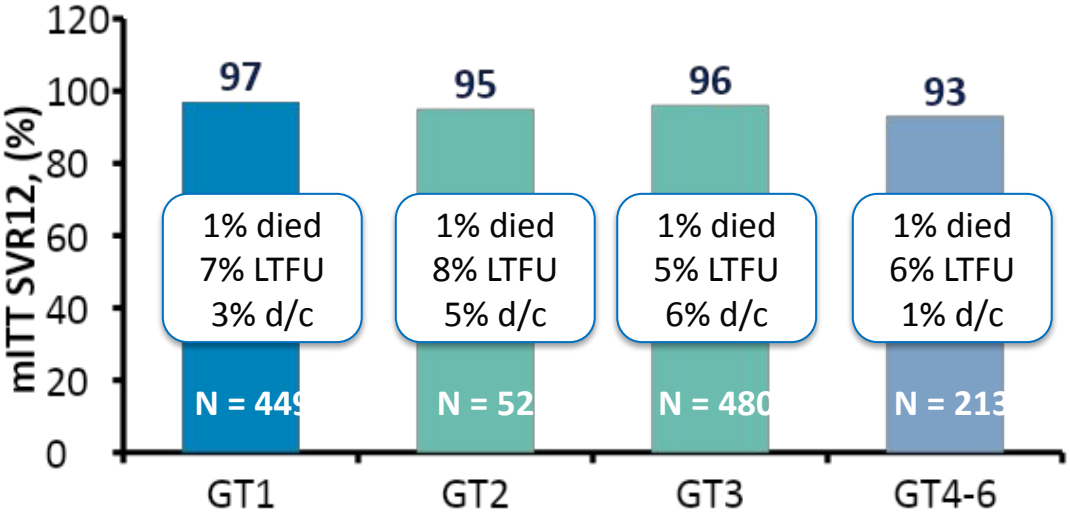
90% of the observed EBR/GZR use was for 12 weeks without RBV and mostly in GT1-infected patients

BL VL, baseline viral load; CKD, chronic kidney disease; LTFU, lost to follow-up; PP, per protocol; RAS, resistance associated substitution; TE, treatment experienced; TN, treatment naive.
*GT2 n=2, GT3 n=1, GT unknown n=21; † Of the 4 TE F4 patients who did not achieve SVR, prior treatments were LDV/SOF, SMV + SOF, pegIFN + RBV and unknown.

Sat-279, Flamm: Real-World Treatment Utilisation and Results in the Renaissance of HCV Care: Analyses of Treatment for 8,955 Patients From the TRIO Network

Retrospective analysis of HCV-infected patients in the real-world TRIO Health Network treated with DAA regimens October 2015–October 2016 (N = 8955)

Baseline characteristics n/N (%)	GT1 (n = 6598)	GT2 (n = 875)	GT3 (n = 732)	GT4-6 (n = 311)	Total (N = 8955)
LDV/SOF ± RBV	5764 (87)	6 (1)	5 (1)	241 (77)	6267 (70)
DCV + SOF ± RBV	20 (0)	110 (13)	480 (66)	0	660 (7)
SOF/VEL ± RBV	108 (2)	294 (34)	166 (23)	31 (10)	634 (7)
SOF + RBV	7 (0)	436 (50)	67 (9)	2 (1)	553 (6)
EBR/GZR ± RBV	407 (6)	2 (0)	1 (0)	28 (9)	459 (5)
OBV/PTV/r + DSV ± RBV	262 (4)	0	0	0	276 (3)



SVR12 failures and d/c rates were higher with use of non-preferred therapies, for TE patients and patients with cirrhosis

CKD, chronic kidney disease; ITT, intent to treat.; d/c, discontinuation; TE, treatment experienced; LTFU, lost to follow-up.

THU-284, Maunoury: Cost-Effectiveness of EBR/GZR Regimen for Treating HCV GT1 Infection in Stage 4–5 Chronic Kidney Disease Patients in France

A decision-analytic model using both medical and economic criteria was used to estimate the cost-effectiveness of EBR/GZR vs no treatment (standard of care) in patients with HCV GT1 infection and CKD stage 4–5 (creatinine clearance <30 mL/min/1.73 m^2, including hemodialysis patients)

The model was designed to identify the best strategy from an 'all payers' perspective

Strategy	Total cost (€2015)	Life years (LY)	QALYs	Cost/LY (€2015)	Cost/QALY (€2015)
Standard of care	€259,125	5.1	3.7	–	–
EBR/GZR	€296,672	6.2	6.2	€31.51	€15,212

Sensitivity analysis shows that key drivers are:

- Risk of CKD progression
- Average annual cost of kidney transplant
- Risk of death from HCV

100% of incremental cost-utility ratio simulations were < €31,500

Probabilistic sensitivity analysis suggests that EBR/GZR is increasingly more effective than standard of care in CKD patients, but also more expensive

CKD, chronic kidney disease; LY, life years; QALY, quality-adjusted life years.

PS-096, Deterding: Long-Term Follow-Up After IFN-Free Therapy of Advanced HCV-Associated Liver Cirrhosis: Continued Improvement of Liver Function Parameters – Results From the German Hepatic C-Registry (DHC-R)

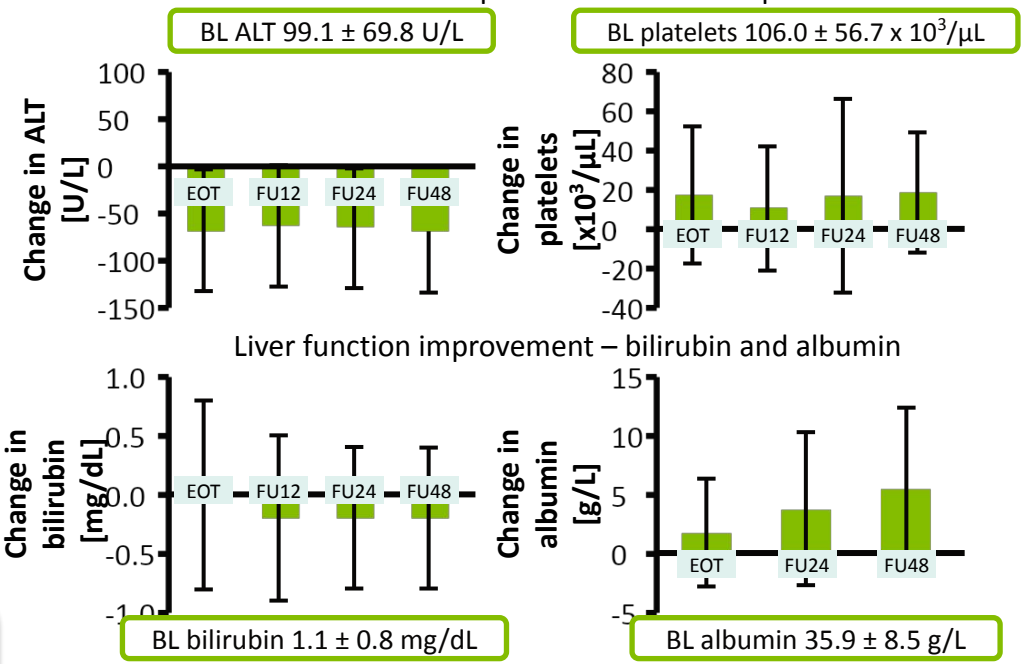
Analysis of DAA treatment in HCV-infected patients with advanced liver cirrhosis in the DHC-R – a large, multicenter, real-world cohort in Germany

Criteria for advanced liver cirrhosis included at least one of the following:
FibroScan >20 kPa, platelets <90,000/µL, albumin <35 g/L or clinical signs of liver decompensation

Baseline characteristics, n (%)	N = 1108
Child-Pugh, n (%) A B C	 771 (70) 151 (14) 21 (2)
ALT (U/l), mean (SD)	99 (70)
Mean bilirubin, mg/dL (SD)	1.1 (1)
Mean albumin, g/L (SD)	35.9 (9)
Mean platelets per nL (SD)	106 (57)

- 121 (11%) patients reported SAEs
- 63 SAEs were liver-related; HCC (n = 17), variceal bleeding (n = 19), and ascites (n = 4)
- 14 deaths; 10 were liver-related

Liver function improvement – ALT and platelets



Liver function improvement – bilirubin and albumin

Liver function improved in the majority of patients during and after treatment

Child-Pugh B or C were associated with clinical events*

Neither use of HCV PIs nor RBV were associated clinical events*

HCCs, hepatocellular carcinoma; PIs, protease inhibitors.
*Clinical events defined as defined by increase in MELD by ≥3 points, variceal bleeding, ascites, encephalopathy, liver transplantation, *de novo* HCC, or death.

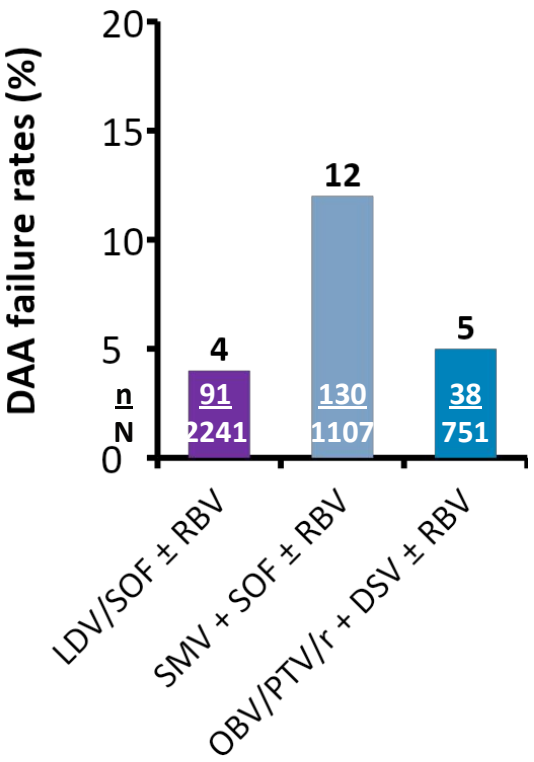
SAT-229, Sulkowski: Incidence of and Predictors for DAA Treatment Failure Among 4099 HCV GT1 Infected Adults: Real World Outcomes From HCV TARGET

Analysis of the incidence and predictors of virologic failure as well as re-treatment outcomes in HCV GT1-infected patients treated with ≥2 DAAs in the real-world HCV TARGET cohort

Of 4099 GT1-infected patients treated with ≥ 2 DAAs, 259 (6%) experienced treatment failure (primarily as relapse)

Factors associated with virologic failure (univariate analysis)	Patients with failure (%) N = 259	Patients with SVR (%) N = 3840
Male	73	59
Cirrhosis	65	42
Prior decompensation	40	18
MELD score >15	8	4
Liver cancer	16	7
D/C treatment due to AE	7	1

Cirrhosis, low albumin/platelet, high total bilirubin, and male sex were associated with treatment failure at the $p < 0.001$ level



IPW analysis

Compared to SMV + SOF ± RBV patients, LDV/SOF ± RBV (OR 2.63; p < 0.01) and OBV/PTV/r + DSV ± RBV (OR 1.92; p < 0.01) patients were more likely to achieve SVR

To date, 19/22 (86%) DAA failures retreated with LDV/SOF ± RBV or OBV/PTV/r + DSV ± RBV achieved SVR

42 d/c due to AEs

d/c, discontinuation; IPW, inverse probability weighting.

FRI-280, Kondili: Clinical Characterization and Economic Impact Evaluation of Anti-HCV DAA Treatment Failure: Real-Life Data From the Italian Platform for the Study of Viral Hepatitis Therapies (PITER)

An analysis of DAA treatment failure and its clinical and economic burden using data from HCV-infected patients in the PITER study cohort

Of 3926 patients who underwent DAA treatment, 4% (n = 140) failed to achieve SVR12

DAA regimen	Treatment failures, n/N (%)
SOF + RBV	69/747 (9)
SMV + SOF ± RBV	38/713 (5)
LDV/SOF ± RBV	16/1031 (2)
OBV/PTV/r + DSV ± RBV	9/894 (1)
OBV/PTV/r + RBV	2/64 (3)
DCV + SOF ± RBV	6/471 (1)
DCV + SMV	0/6 (0)

Reason for treatment failure, n (%)	Treatment failures (n = 140)
Non-response	4 (3)
Breakthrough	3 (2)
Relapse	133 (95)

Failure rate increased with higher degree of fibrosis at baseline

Clinical burden of DAA failure

- HCC occurred in 6 (5%) patients at end of treatment and in 10 patients (8%) after 6-months' follow-up
- 5 patients with cirrhosis underwent transplant
- CP class changed from A to B in 15 (12%) patients and from B to C in 1 (1%) patient
- 24 patients experienced hepatic decompensation

Economic burden of DAA failure

- Mean cost among non-hospitalized patients was €694/patient (main cost driver was laboratory tests)
- Mean cost among hospitalized patients was €18607/patient (main cost driver was number of diagnostic procedures, after hospital admission costs)

HCC, hepatocellular carcinoma.

PS-097, Freeman: 94% SVR with Parallel Imported Generic DAA Treatment for HCV

Real-world evaluation of the efficacy and safety of legally imported generic DAAs (including SOF, LDV, DCV) across five treatment access programs in 88 countries worldwide

Cohorts include the Australian access program REDEMPTION-1, and a large cohort from London (Cohort 1)

Baseline characteristics	REDEMPTION-1 N = 448	Cohort 1 N = 1160
Treatment, n (%)		
SOF	–	24 (2)
SOF + RBV	4 (1)	66 (6)
LDV/SOF	205 (46)	452 (39)
LDV/SOF + RBV	21 (5)	56 (5)
DCV + SOF	191 (43)	475 (41)
DCV + SOF + RBV	27 (6)	87 (8)
Male, %	57	61
Mean age, years	55	49
Genotype 1, %	67	55
Mean HCV RNA, log IU/mL	6.5	6.6
Cirrhosis, %	28	18

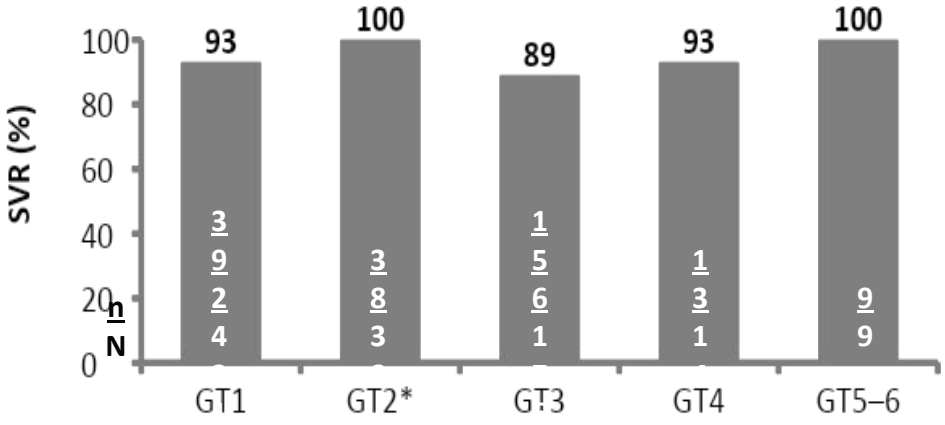
Cohort 2: N = 226; GT1, 2, 3, 4, 5
Cohort 3: N = 263; GT1, 2, 3, 4, 6
Cohort 4: N = 224; GT1b, 2, 3

* GT2 results almost entirely DCV + SOF; – Not applicable.

REDEMPTION-1
The negative predictors significantly associated with SVR were cirrhosis (p = 0.01) and HCV RNA detectable after Day 24 (p = 0.02)

No new AEs reported

Aggregated results for the 4 cohorts.
Cohort 1 final results & Cohorts 2–4 interim results

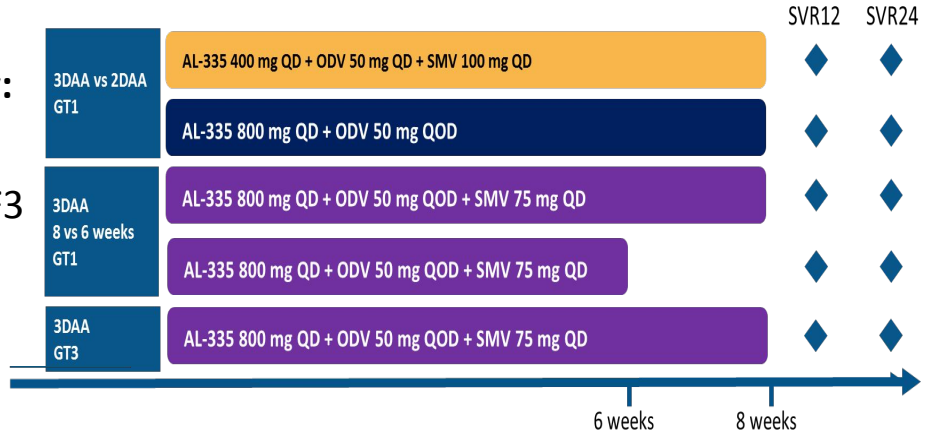


New Molecules

PS-153, Gane: Short duration treatment with AL-335 and odalasvir (ODV) ± SMV, in treatment naive patients with HCV infection with or without cirrhosis

Dose finding study:

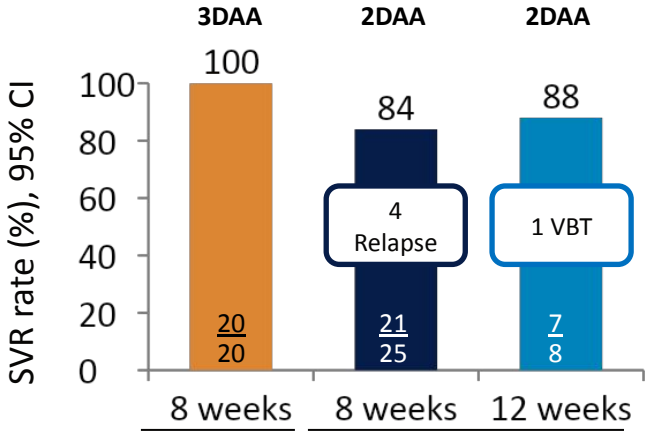
- Inclusion criteria:
- Fibrosis stage F0–F3
- GT1 or 3 infection
- Treatment naive



AL-335 + ODV ± SMV 6 or 8 weeks achieved high SVR in non-cirrhotic GT1 patients

- AEs were mild and unspecific
- 1 d/c due to AE

3DAA vs 2DAA in GT1-infected patients

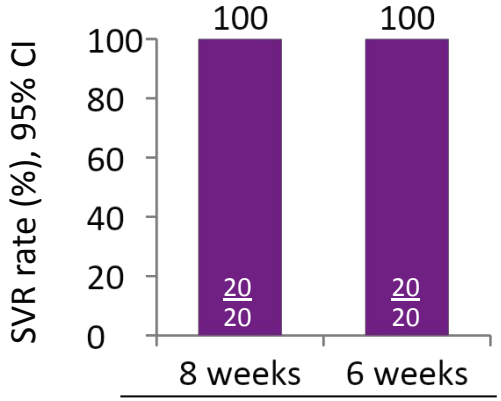


AL-335 400 mg QD + ODV 50 mg QD + SMV 100 mg QD

AL-335 800 mg QD + ODV 50 mg QOD

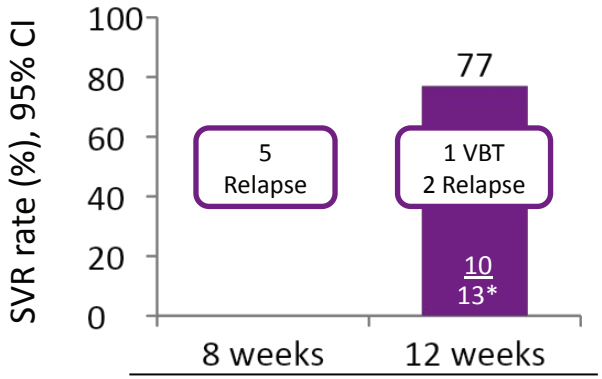
VBT = Viral Breakthrough

3DAA 8 vs 6 weeks in GT1-infected patients



AL-335 800 mg QD + ODV 50 mg QOD + SMV 75 mg QD

3DAA in GT3-infected patients



AL-335 800 mg QD + ODV 50 mg QOD + SMV 75 mg QD

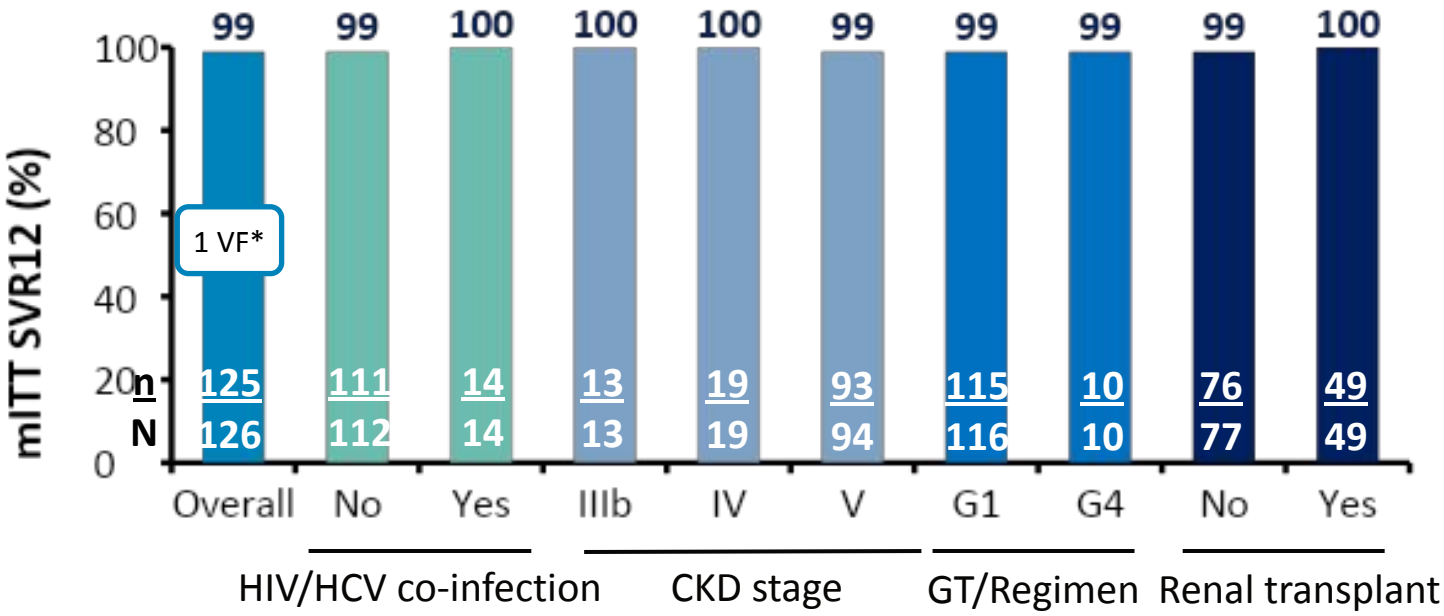
OBV/PTV/r + DSV

Executive Summary

- Real world results
  - confirm safety and effectiveness of 2D and 3D – including patients with CKD 3b/4/5, HIV/HCV co-infection with & without compensated cirrhosis, and renal transplant
  - demonstrate improvement in perceived burden of disease and work productivity/activity
  - Reiterate that rates of hepatic decompensation and HCC in patients with advanced liver disease are similar to those seen in the literature
- Treatment with 2D/3D demonstrates high SVR in patients with liver and renal transplant – with and without compensated cirrhosis
  - One death due to tacrolimus overdose [contraindicated in the USPI as of March 2017, and 'not recommended' in the EU label]
- 100% SVR12 [mITT] seen in first available pediatric data with 2D/3D ± RBV. The regimen was well tolerated by adolescents [12–17 yrs old] with no grade 3 or 4 laboratory abnormalities or treatment-emergent SAEs
- Real world evidence of SOF-based regimens used in patients with severe CKD attempt to establish safety and effectiveness
  - Conflicting data presented on impact of SOF on eGFR

SAT-226, Londoño: Effectiveness, Safety/Tolerability of OBV/PTV/r ± DSV in Patients with HCV GT1 or 4 with/without HIV-1 Co-Infection, Chronic Kidney Disease Stage IIIb/V and Dialysis in Spanish Clinical Practice – Vie-KinD Study

A non-interventional, retrospective, multi-center, real-world study of OBV/PTV/r ± DSV ± RBV in n = 135 HCV GT1- or 4-infected (14/135 [10%] HIV/HCV co-infected patients) with CKD stages IIIb–V in 31 centers in Spain



- 26% of GT1-infected patients received OBV/PTV/r + DSV **+ RBV**
- 80% of GT4-infected patients received OBV/PTV/r **+ RBV**

11 (8%) patients had severe AEs
Most AEs were mild or moderate in severity
5 (4%) patients withdrew treatment

Most patients (94% [33/35]) did not have a clinically significant decrease in CKD Stage IIIb and IV baseline eGFR levels at EOT or PTW12 in any CKD stage group

CKD, chronic kidney disease; EOT, end of treatment; PTW, post-treatment Week; VF, virologic failure. * Male patient with GT1b HCV infection and CKD Stage 5 experienced VF with 12 weeks of treatment with OBV/PTV/r + DSV + RBV. Patient did not reach SVR12.

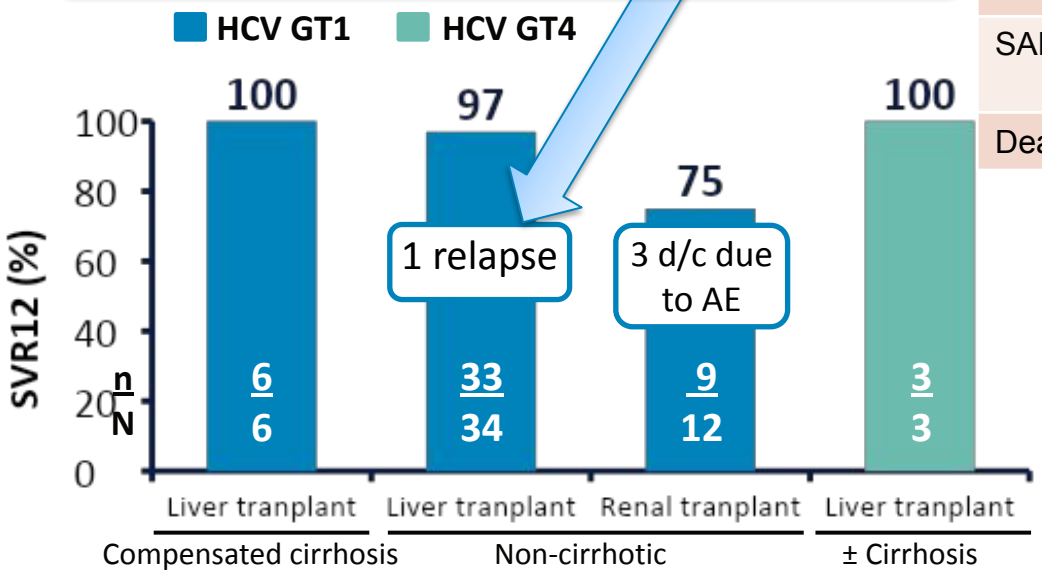
FRI-267, Agarwal: CORAL-I (Cohorts 3–6): Safety and Efficacy of OBV/PTV/R ± DSV ± RBV in Adult Renal or Liver Transplant Recipients with HCV Infection

An ongoing, phase 2, open-label study evaluated OBV/PTV/R ± DSV ± RBV in HCV GT1-infected patients with liver or kidney transplant and HCV GT4-infected patients with liver transplant

Patients were treatment-naive or IFN-experienced receiving tacrolimus or cyclosporine

Baseline characteristics, n (%)	N = 55
Male	46 (84)
White race	47 (85)

Relapse patient had treatment-emergent RASs D168V in NS3 and Q30R in NS5A



Safety, n/N (%)	Cohort 3 GT1 LT + C	Cohort 4 GT1 LT, NC	Cohort 5 GT1 RT, NC	Cohort 6 GT4 LT ± C
AE leading to D/C of study drugs	0	1/34 (3)	2/12 (17)	0
SAE	0	3/34 (9)	4/12 (33)	0
Death				

There were 3 study drug related SAEs (nausea and vomiting, acute respiratory failure, and tacrolimus overdose), and led to d/c of study drug

Death was due to tacrolimus overdose

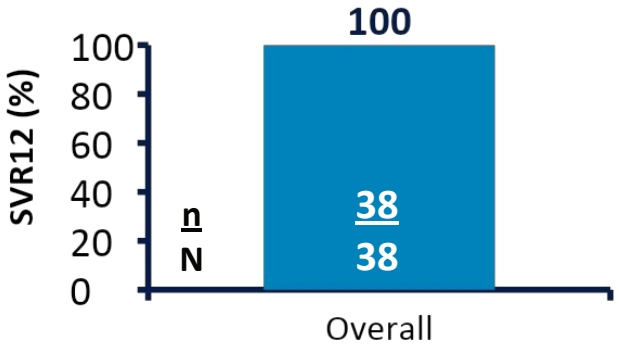
Grade 3 laboratory abnormalities were rare, and there were no grade 4 events

C, cirrhosis; d/c, discontinuation; LT, liver transplant; RAS, resistance-associated substitution; RT, renal transplant.

THU-251, Leung: ZIRCON: Pharmacokinetics, Safety, and Efficacy of OBV/PTV/r ± DSV ± RBV in Adolescents with GT1 or 4 HCV Infection

An two-part, ongoing, open-label, phase 2/3 study assessed the PK of OBV/PTV/r + DSV ± RBV in GT1-infected adolescents without cirrhosis (Part 1) and the efficacy and safety of OBV/PTV/r ± DSV ± RBV in GT1- or GT4-infected adolescents with or without cirrhosis (Part 1 and 2)

Baseline characteristics	N = 38
Median age, years (range)	15 (12–17)
Male, n (%)	13 (34)
White race, n (%)	29 (76)
HCV genotype, n (%) GT1a GT1b GT4	 16 (42) 15 (40) 7 (18)
Treatment experienced, n (%)	13 (34)
Non-cirrhotic, n (%)	37 (97)



CV, coefficient of variation; d/c, discontinuation; EOT, end of treatment; PK, pharmacokinetics.* N = 11 for AUC and C_{trough} of OBV and PTV; † $AUC_{0–24\ hours}$ for OBV and PTV, $AUC_{0–12\ hours}$ for DSV; ‡ as assessed by investigator.

Preliminary PK results: Geometric means from Part 1 (N = 12)*

	C_{max} (ng/mL)	AUC† (ng/mL)	C_{trough} (ng/mL)
OBV (CV%)	75.4 (31)	918 (23)	19.0 (18)
PTV (CV%)	738 (70)	4880 (52)	19.4 (64)
DSV (CV%)	646 (49)	4460 (45)	158 (43)

DAA exposures were comparable to historical results seen in adults

Safety, n (%)	N = 38
Any AE	32 (84)
AE possibly related to DAAs‡	15 (39)
AE possibly related to RBV‡	14 (37)
AE leading to d/c of study drug	0
SAE	0

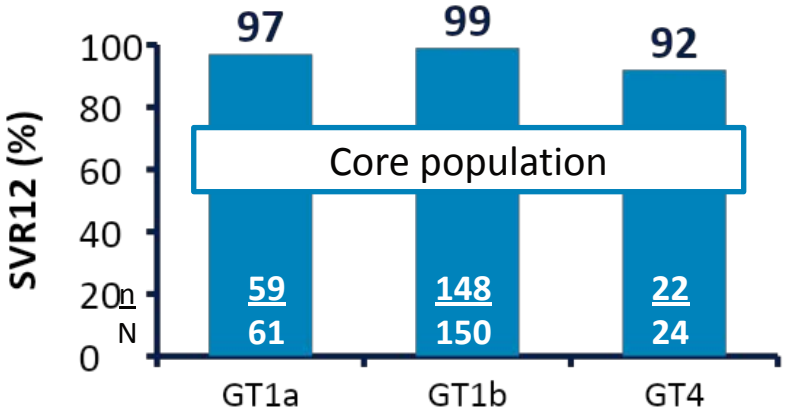
No confirmed grade 3 or 4 laboratory abnormalities were reported

FRI-269, Buggisch: Effectiveness, Safety and Quality of Life in Patients Treated with OBV/PTV/r ± DSV ± RBV Under Real-Life Conditions – Data from the German Observational Study LIFE-C

LIFE-C: German observational study assessing effectiveness, safety, and health-related QoL in patients treated with OBV/PTV/r ± DSV ± RBV according to local label, using several health-related QoL questionnaires (N = 472)

Study populations were: Core (excluded patients who had not begun treatment and those without confirmed on-label treatment) and Subgroup (excluded those who received 24-week therapy or began treatment after the cut-off date)

Baseline characteristics, n (%)	Core N = 470	**Subgroup N = 252**
HCV genotype		
GT1a	145 (31)	70 (28)
GT1b	278 (59)	156 (62)
GT4	47 (10)	26 (10)
Cirrhotic	48 (10)	19 (8)
Treatment-experienced	158 (34)	84 (33)
≥ 1 comorbidity	324 (69)	179 (71)



Questionnaire used in core population	Mean score at baseline	**Mean score change at SVR12 visit**
PRISM	11.8 (n = 251)	+ 6.4 (n = 206)
FACIT	36.0 (n = 241)	+ 4.7 (n = 166)
WPAI (work productivity impairment)	17.3 (n = 96)	– 5.4 (n = 67)
WPAI (total activity impairment)	26.8 (n = 236)	– 11.7 (n = 158)

96% (215/225) of treated patients in the subgroup population achieved adherence rates ≥ 95%

Safety, n (%)	**Subgroup (N = 252)**
Patients with ≥1 AE	66 (26)
Patients with ≥1 SAE	5 (2)

113 AEs occurred in 66 patients

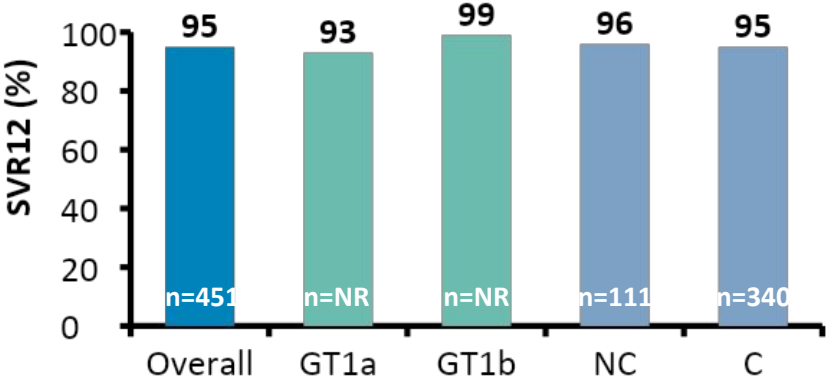
Fatigue, pruritus, and rash were the most common AEs

QoL, quality of life.

FRI-250, Lubel: Very High Real-World Efficacy of OBV/PTV/r + DSV ± RBV in HCV GT1 in Patients with Advanced Fibrosis – Final Results of the REV1TAL Study

Real-world study of OBV/PTV/r + DSV ± RBV in HCV GT1-infected patients at 20 centers in Australia (N = 451)

Baseline characteristics, n (%)	Non-cirrhotic N = 111	Cirrhotic N = 340
Treatment-naive	72 (65)	172 (51)
HCV subtype		
1a	60 (54)	231 (68)
1b	44 (40)	86 (25)
Child-Pugh class		
A	–	306 (90)
B	–	34 (10)
C	–	0



Safety, n (%)	Non-cirrhotic N = 111	Cirrhotic N = 340
SAEs	5 (5)	44 (13)
Hepatic decompensation*	0	12 (3.5)
HCC	0	8 (2)†
Hospital admission	5 (5)	32 (9)‡

SAEs occurred in 35% (12/34) of CPB patients and 12% (36/306) of CPA patients (p = 0.0005)

In multivariate analysis, CPB was a significant predictor of SAEs (OR 7.2 [95% CI, 1.5–33.9]; p = 0.012)

In multivariate analysis, baseline bilirubin (OR 0.96, p = 0.015) and early cessation (OR 0.04, p < 0.0001) were significant factors related to SVR

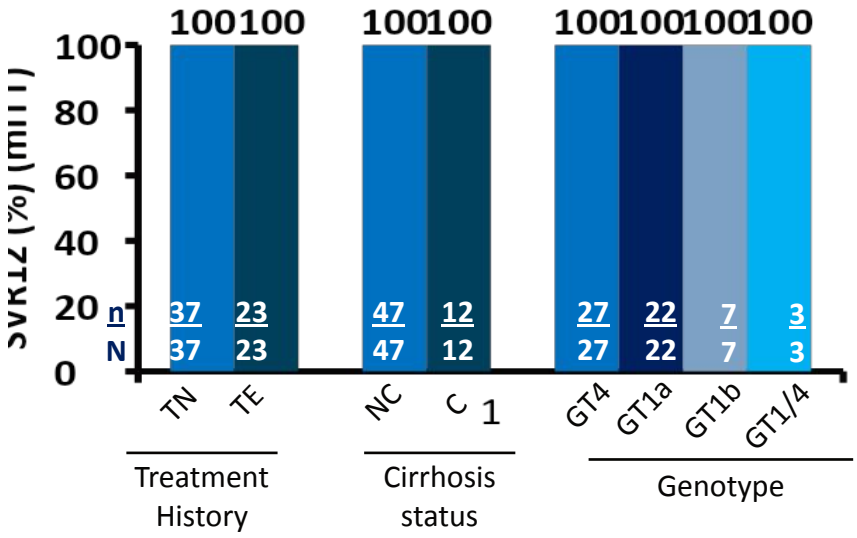
C, cirrhotic; CPA/B, Child-Pugh A/B; HCC hepatocellular carcinoma; NC, non-cirrhotic; NR, not reported.
* Variceal hemorrhage n = 4; hepatic encephalopathy n = 5; ascites n = 1; spontaneous bacterial peritonitis n = 1; unspecified cause n = 1;
† 7 patients had CPA cirrhosis and 1 patient had CPB cirrhosis; 5 were *de novo* HCC; ‡ Hospital admission due to hepatic decompensation n = 7.

THU-277, Sanai: 100% Efficacy to OBV/PTV/r ± DSV ± RBV in HCV GT1 and 4-Infected Hemodialysis Patients

SOLID registry: an ongoing observational, cohort study, evaluating real-world safety and efficacy of OBV/PTV/r ± DSV ± RBV for 12 or 24 weeks in HCV GT1- or 4-infected patients with severe CKD* on hemodialysis

Baseline characteristics	N = 62
Age, years, (SD)	46 (13)
HCV genotype (regimen), n (%) GT1 (OBV/PTV/r + DSV ± RBV) GT4 (OBV/PTV/r ± RBV) Mixed GT1/4	 31 (50) 28 (45) 3 (5)
Female, n (%)	33 (53)
Treatment-experienced, n (%)	24 (39)
RBV included in regimen, n (%)	49 (79)
Fibrosis, n (%) F0–2 F3 F4	 40 (65) 8 (13) 13 (21)
HCV RNA <15 IU/mL, n/N (%)	54/56 (96)

Patients receiving RBV were more likely to have higher hemoglobin levels, GT1a and be TE



Safety	
RBV dose modification or d/c, n/N (%)	15/49 (31)
Study drug d/c, n	1‡
Death, n	2§

CKD, chronic kidney disease; d/c. discontinuation; TN, treatment naive, TE, treatment experienced; NC, non cirrhotic; C, cirrhotic .
* <15 mL/min/1.73 m^2 by MDRD; ‡ Patient d/c study drugs at Week 4 and went on to achieve SVR12; § Deaths were due to myocardial infarction (n = 1) and sepsis-related complications (n = 1); both were considered unrelated to study drugs.

SAT-239, Alkadi: Decline in eGFR in HCV-Infected Patients While on Treatment with LDV/SOF or OBV/PTV/r + DSV Regimens Is Not Dependent on Baseline eGFR

The ERCHIVES cohort of HCV-infected US veterans was used to evaluate declines in eGFR during treatment with LDV/SOF ± RBV or OBV/PTV/r + DSV ± RBV by baseline kidney function

Patients with ≥ 2 eGFR values 3 months apart prior to baseline and ≥ 1 eGFR value ≥ 12 weeks after baseline were included in the analysis

Baseline characteristics	LDV/SOF N = 9837	LDV/SOF + RBV N = 3826	OBV/PTV/r + DSV N = 1017	OBV/PTV/r + DSV + RBV N = 2944
Cirrhosis*, %	29	11	47	23
Median eGFR, mL/min/1.73 m^2 (IQR)	82 (67–96)	84 (69–99)	82 (67–96)	83 (71–97)

		Percentage of patients with decline in eGFR of > 10 mL/min/1.73 m^2				
Baseline eGFR (mL/min/1.73 m^2)	N	LDV/SOF	LDV/SOF + RBV	OBV/PTV/r + DSV	OBV/PTV/r + DSV + RBV	*P* value
eGFR ≥60	15,086	33	38	30	33	0.03
eGFR 30–59 (CKD 3)	2281	17	16	18	14	0.58
eGFR <30 (CKD 4–5)	257	7	3	2	0	0.03

Small number of CKD 4–5 patients

CKD, chi
* Cirrho

Extrahepatic Manifestations

Executive Summary

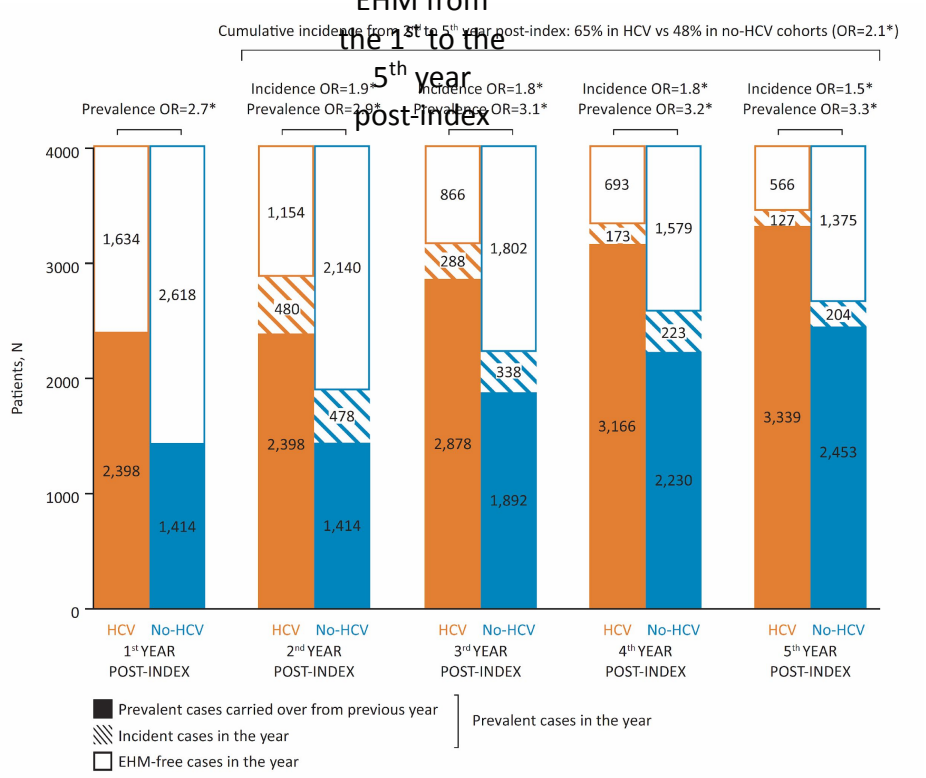
- Accumulating evidence for cyroglobulinemia, cardiovascular events and infertility/pregnancy outcomes provide additional argument for initiating DAA therapy as early as possible

SAT-216, Sanchez-Gonzalez: The Cumulative Prevalence and Incidence of Extra-Hepatic Manifestations in Patients with HCV Infection: Real-World Evidence from the United States

Optum™ Claims Data - Clinformatics™ Data Mart dataset was used to evaluate the prevalence and incidence of 20 EHMs (including CKD, CVD, and metabolic- and immune-mediated diseases) in HCV-infected and non-HCV-infected patients in the United States

Two cohorts of adult patients with ≥5 years of post-index follow-up were matched 1:1 on age, sex, region, and years of follow-up: HCV and no-HCV (both N = 4032)

Cumulative prevalent and incident cases of any EHM from the 1st to the 5th year post-index



Cumulative incidence from 2nd to 5th year post-index for any EHM
HCV: 65%
Non-HCV: 48%
(OR = 2.1; p < 0.05)

Prevalence of CKD among HCV versus no-HCV cohorts in the 5th year post-index
HCV: 10.7%
Non-HCV: 4.4%
(OR = 2.6)

*P < 0.05

PS-099, Saadoun: VASCUVALDIC 2 study: SOF + DCV for HCV-cryoglobulinemia vasculitis (HCV-CryoVas)

Open label study of SOF (400 mg/day) + DCV (60 mg/day) for 12 or 24 weeks

Baseline characteristics	N=41
Age, mean (range)	56 (50–62)
Female gender (n, %)	22 (54)
HCV genotype: 1 2 3 4 5	25 (61) 2 (5) 9 (22) 3 (7) 2 (5)
Metavir score: F1 F2 F3 F4	12 (29) 3 (7) 8 (20) 18 (44)
HCV RNA (baseline, $\log_{10}$ IU/mL)	5.6 ± 0.3
Mixed cryoglobulinemia	
Cryoglobulin level (mean, g/L)	0.56 ± 0.18
C4 level (mean, g/L)	0.08 ± 0.02
Rheumatoid factor (IU/mL)	47 ± 18
Vasculitis, n (%)	
Arthralgia	26 (63)
Purpura	24 (59)
Polyneuropathy	21 (51)
Skin ulcer	7 (17)
Kidney involvement	5 (12)

Efficacy	SOF + DCV N=41
Complete clinical response At Week 12 At end of therapy (W24)	 90.2% 90.2%
Virologic response At Week 12 After end of therapy (W36)	 100% 100%
Safety, n (%)	**SOF + DCV N = 41**
SAE	0
Clearance of cryoglobulin (W24)	50%
Steroids and/or rituximab	4.8%

PS-099, Saadoun: VASCUVALDIC 2 study: SOF + DCV for HCV-cryoglobulinemia vasculitis (HCV-CryoVas)

Open label study of SOF (400 mg/day) + DCV (60 mg/day) for 12 or 24 weeks

Outcome of kidney parameters

Purpura, skin ulcers and arthralgia disappeared in all cases

- Kidney involvement improved in 5/5
- complete renal response in 4/5

Immunological response kinetics of cryoglobulinemia and C4

- Cryoglobulin level decreased from 0.56 ± 0.18 to 0.21 ± 0.14 g/L (W0 vs W36)
- Cryoglobulin disappeared in 50%
- C4 serum level increased from 0.08 ± 0.02 to 0.14 ± 0.02 g/L (W0 vs W36)

DAAs improve mixed cryoglobulinemia however longer follow up is needed

PS-032, Cacoub: The Cumulative Prevalence and Incidence of Extra-Hepatic Manifestations in Patients with HCV Infection: RWE from the US

Patients enrolled/prospectively followed up from 2006–2012 with: a) biopsy-proven HCV cirrhosis; b) CP A; c) +ve viremia; d) no prior liver complication. All patients received HCV treatment after inclusion

Predictors of MACE in patients with compensated HCV-related cirrhosis Multivariate Cox proportional hazards model

Features	HR	95% CI	P-value
Arterial hypertension	3.24	1.78–5.91	<0.001
Tobacco consumption			<0.001
Never	Ref		
Past	1.75	0.76–3.91	0.18
Ongoing	4.20	2.11–8.64	<0.001
Ethnic origin			<0.001
European	Ref		
African	1.14	0.36–2.80	0.80
Asian	9.20	2.46–24.95	0.003
Serum albumin ≤35 g/L	2.78	1.30–5.56	0.009
SVR	0.35	0.09–0.97	0.044

At endpoint, a SVR was noted in 4 (6.9%) who did vs 302 (37.8%) pts who did not present a MACE (HR = 0.39 [0.13; 0.95], p =0.036)

- MACE included stroke, myocardial infarction, ischemic heart disease, heart failure, peripheral arterial disease, cardiac arrest, and CV death
- 7% (62/878) of patients had total of 79 MACE after a median f/u of 57.5 months
- Overall survival at 5 years was 60% vs 88% in those who did/did not have a MACE (p < 0.001)
- Causes of death in patients who had a MACE mainly related to cardio-vascular disease in 32% (7/22) cases, liver failure 23% (n = 5) and HCC 14% (n = 3)

SVR12 was considered a time-dependent covariate and associated with reduced rate of cardiovascular events
There is insufficient data from DAA era to compare differences between IFN-based and IFN-free therapy

SAT-217, Villa: Extra-hepatic manifestations from hepatitis C virus infection related to female infertility and adverse pregnancy outcomes: A real-world observation

US Insurance Claims Data from 2000-2015 was used to assess the relationship between HCV infection and female infertility and pregnancy outcomes in a large real-world population in the United States (US)

Rates of Adverse Pregnancy Outcomes

Outcome, n (%)	Pregnant HCV Cohort N = 1,225	Pregnant No HCV Cohort N = 12,250
Premature birth	91 (7)	696 (6)
Live birth without complications	537 (44)	6,732 (55)
Stillbirth	5 (0.4)	47 (0.4)
Gestational diabetes	131 (11)	1,102 (9)
Pre-eclampsia	74 (6)	640 (5)
Miscarriage	106 (8)	1,096 (9)

HEOR

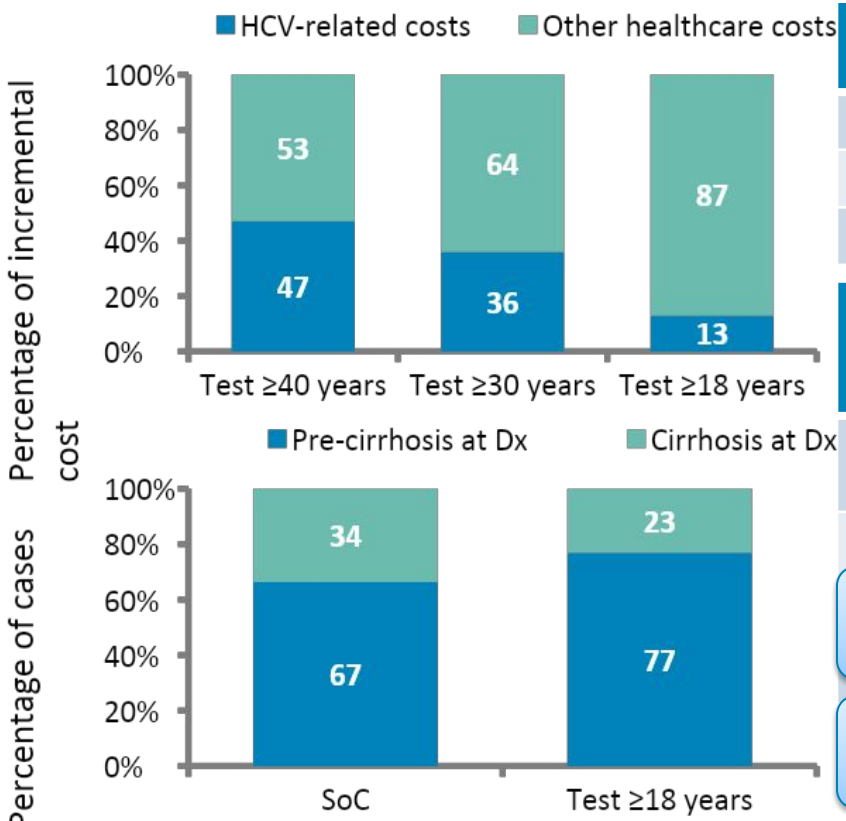
Executive Summary

- Screening younger age cohorts will increase overall costs but is cost-effective relative to the current screening recommendations (either cohort based or risk based)
- AbbVie needs to continue to reinforce the potential benefits of early screening and diagnosis and communicate the added costs associated with cohort or risked based screening approaches

FRI-183, Barocas: Population Level Outcomes and Cost-Effectiveness of Expanding Guidance for Age-Based Hepatitis C Testing in the United States

Monte Carlo simulation of HCV testing and treatment with SOF/VEL was used to assess population-level outcomes and cost-effectiveness of expanding guidance for age-based HCV testing in the US with 4 strategies

The 4 strategies* were: 1) current SoC; 2) one-time testing adults ≥40 years old; 3) one-time testing adults ≥30 years old; and 4) one-time testing adults ≥18 years old



Parameter	Estimate
Median time to cirrhosis, years	34
HCV antibody test cost, 2016 US$	19
HCV therapy cost, 2016 US$	71,000–89,000

Outcome	Current SOC	Test ≥40 years old	Test ≥30 years old	Test ≥18 years old
Incremental cost, $	–	62.39	8.36	3.75
Incremental	–	0.00214	0.00037	0.00014

Expanded HCV testing increased the number of HCV cases identified, linkage to care, treatment uptake and numbers cured

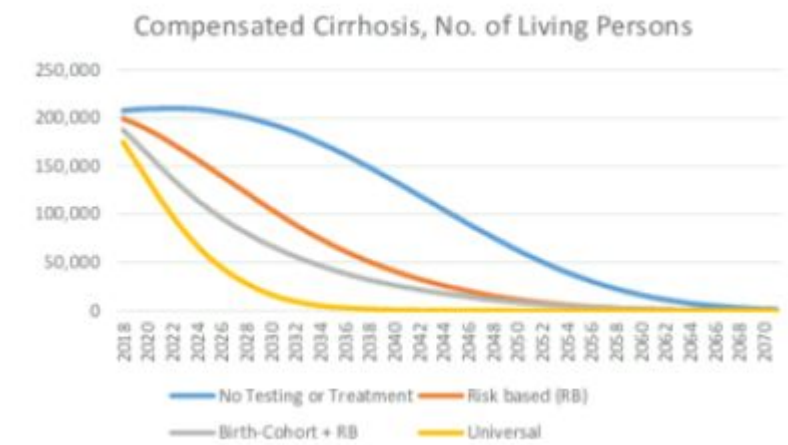
Findings were robust in sensitivity analysis that assessed the impact of treatment on cost, utility, and mortality

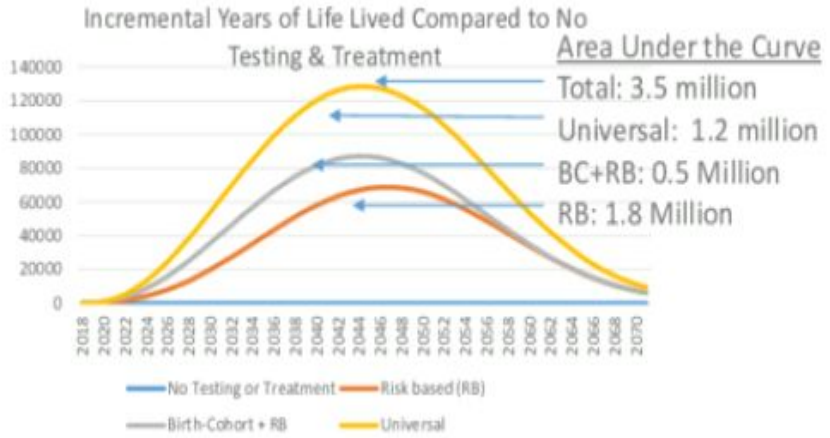
Dx, diagnosis; ICER, incremental cost-effectiveness ratio; QALYs, quality adjusted life years; SoC, standard of care (one-time testing of persons born 1945–1965).
* All strategies assumed continued targeted testing of people who inject drugs.

FRI-458, Rein: The Cost-Effectiveness of a One Time HCV Antibody Test Followed by Treatment for All Americans Ages 18 and Older as Compared to Current Testing Recommendations in the United States

Analysis of health outcomes and cost-effectiveness of no HCV testing or treatment, and 3 testing scenarios in the US: 1) risk-based (RB) testing; 2) birth-cohort (BC) testing (1945–1965) and RB testing; 3) universal testing of all adults aged ≥18 years in 2014

Simulation model*: health outcomes and costs for HCV RNA+ persons unaware of their infection status in 2018 and followed until death or age 100





Universal testing decreased liver-related morbidity and mortality

Universal testing would result in 1.2 million additional years lived compared with the current US testing strategy

Implementing a one-time universal screening strategy at 18 years of age would lead to the largest benefit in terms of discounted incremental HCV-related costs and impact on QALYs

BC, birth cohort 1945–1965; RB, risked-based; QALYs, quality-adjusted life years; Tx, treatment.
* Annual probabilities of HCV testing: 0.05 risk-based, 0.212 birth-cohort, and 0.212 universal; for HCV GT1–4, SVR rates were weighted averages based on clinical trial and market share data; treatment costs were weighted averages based on listed wholesale acquisition costs and market share data; 3% annual discount rate was used; † Compared with next most costly scenario; ‡ medical management costs; § Testing, treatment, and medical management costs.

SAT-225, Buti: Cost-Effectiveness of Screening for HCV in Population Born Between 1956 and 1970 in Spain

Study assessing the cost-effectiveness of HCV testing the Spanish population born 1956–1970 (birth cohort) versus screening only high-risk* individuals born 1956–1970 (current screening strategy)

A decision analysis model to establish the eligible population for screening and a Markov model to simulate disease progression from diagnosis were used; 82% of ≥F2 detected cases were assumed to be treated with DAAs†

The screening strategy was applied to 5,915,645 people, with 1.9% diagnosed with chronic HCV

Scenario	Birth cohort vs current screening strategy‡			
	Δ Costs§, €	Δ LYG	Δ LYG QALY	ICER/QALY, €
Base case: (82% ≥F2 treated)	13,767	1.75	2.14	6,423
Sensitivity analysis: (95% ≥F2 treated)	15,518	2.03	2.48	6,249

Outcome‡	Birth cohort screening	Current screening	Reduction in cases (%)
Decompensated cirrhosis	7581	21,457	65%
HCC	7953	16,907	53%
Liver transplantations	1204	3031	60%
Liver-related mortality	10,480	25,335	59%

At an efficiency threshold of €30,000 per QALY, screening of the Spanish population born 1956-1970 is cost effective vs current screening strategy

ICER, incremental cost-effectiveness ratio; LYG, life-years gained; QALY, quality-adjusted life years.
* Prisoners, people who inject drugs, HIV/HCV co-infected. A 3% discount was used; † SVR rates obtained from clinical trials; ‡ Lifetime horizon was considered and a 3% discount rate was applied to costs and outcomes; § direct costs (2016 €) only were considered.

Diagnosis and Linkage to Care

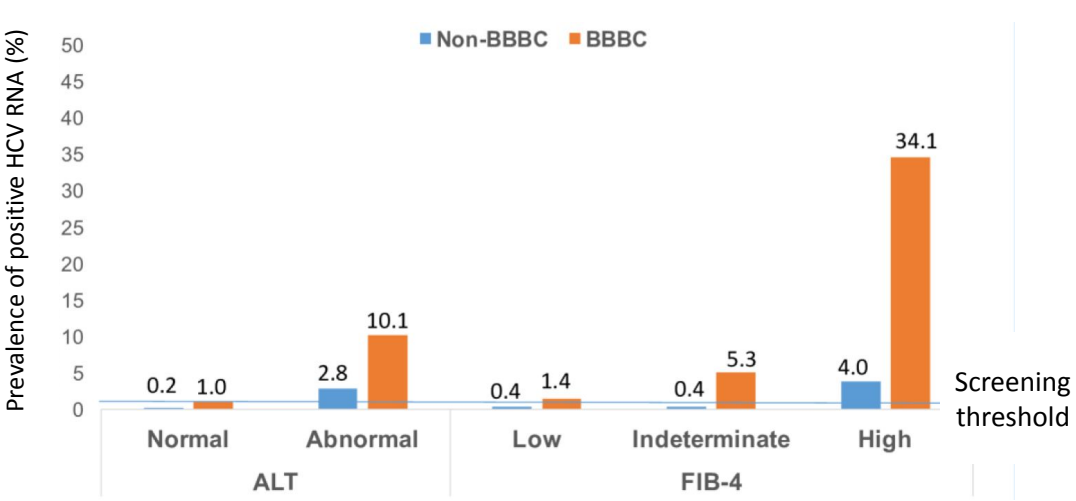
Executive Summary

- There remains significant challenges in terms of screening, diagnosis, and connection to care
- Alternative screening strategies may help to reduce some of these challenges and connect more patients to care; however, it is important to understand the dynamics and roadblocks of each individual health care system
- Regimens such as G/P that simplify treatment decisions may have a positive impact on the number of patients that can be successfully diagnosed and connected to care
- In order to successfully achieve SVR, we also need to address other points of the HCV care cascade

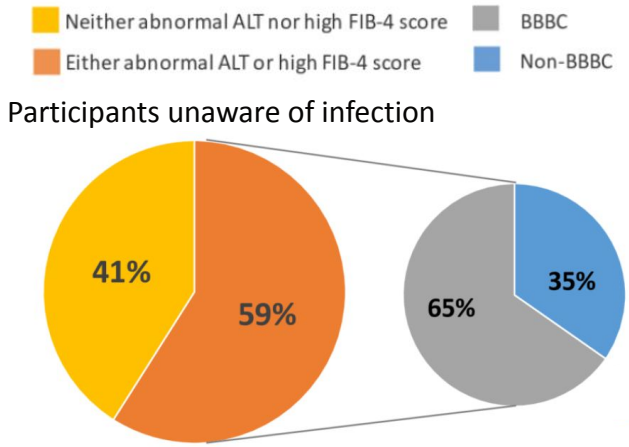
FRI-478, Udompap: An Alternative Screening Strategy for HCV Infection Among Americans Not Belonging in the Baby Boomer Birth Cohort

Evaluation of abnormal ALT and FIB-4 score as a trigger for HCV screening using data from the National Health and Nutrition Examination Survey (NHANES) 1999–2012

NHANES participants were stratified by FIB-4* score and ALT† levels and the prevalence of HCV calculated for each stratum;
33,476 participants had complete laboratory data for FIB-4 calculation; 33,468 were tested for HCV



Prevalence of HCV infection was higher among BBBC than non-BBBC participants (3.3% vs 0.7%)

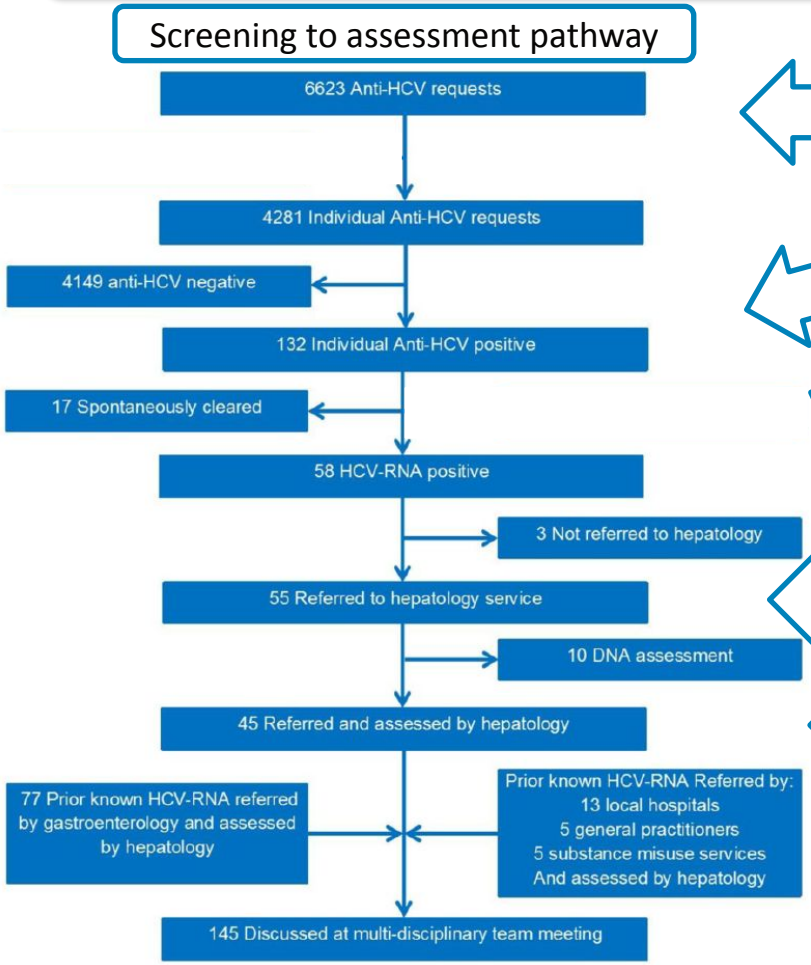


Among patients unaware of their HCV infection, 59% would be diagnosed if abnormal ALT or high FIB-4 scores were used as a trigger for screening; 35% of these individuals did not belong to the BBBC

BBBC, baby boomer birth cohort.
* FIB-4 scores defined as Low (<1.45), Indeterminant (1.45–3.25), High (>3.25); † Abnormal ALT >45 in men and >30 in women

THU-189, Pratt: An Audit of Hepatitis C Screening and Referral Patterns to a Specialist Hepatology Service in a Secondary Care Facility in the UK

Audit of HCV serology requests October 2015–September 2016 at York teaching hospital, UK, to determine if the launch of a specialist hepatology service improved screening, assessment, and treatment of HCV-infected patients



Of 6,223 requests for HCV serology identified, 2,342 (35%) were duplicates; a reduction of ~5% after the launch of specialist hepatology service

Of 4,281 HCV serology tests, 132 (3%) were positive

Of 132 positive serology tests, 57 (43%) were not subsequently tested for HCV RNA

45/55 (82%) of patient were assessed

Of 58 HCV RNA-positive patients, 55 (95%) were referred and assessed by the Hepatology service; the most common route of referral was via general practitioner (49%)

An additional 100 HCV RNA-positive patients were referred from different specialities

HCV treatment has been started in 105 patients compared with 4 patients in 2013; 76 patients reached PTW12 and 95% achieved an SVR12

PTW12, post-treatment Week 12.
* DNA, did not attend.

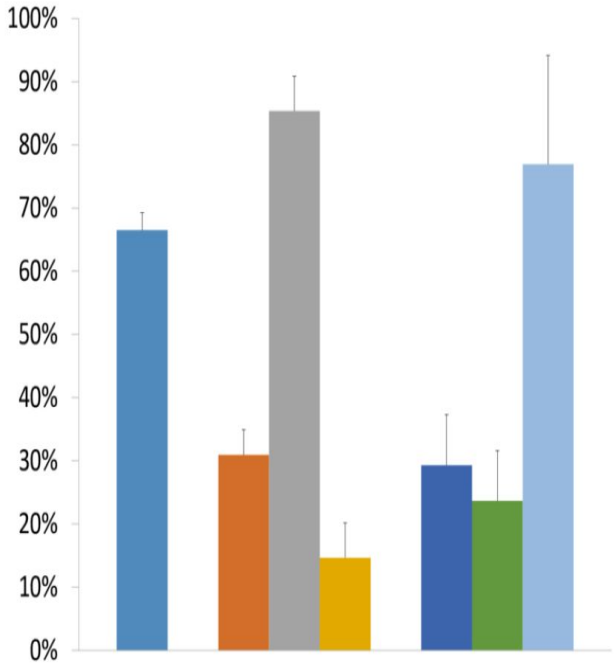
SAT-194, Wong: Low Rates of HCV Testing and HCV Awareness Among Individuals at High Risk for Chronic HCV Infection Among an Underserved Safety-Net Population

Prospective cohort study of HCV screening rates and awareness of prior HCV test results among high-risk individuals*

Baseline characteristics, n (%)	'High-risk' screening group (N = 748)
Male	375 (50)
Race/Etnnicity	
African American	182 (27)
Asian	128 (19)
Hispanic	241 (36)
White	89 (13)
Other	18 (3)
History of IV drug use	36 (6)
History of incarceration	116 (19)
HCV/HIV co-infection	19 (10)
Blood transfusion prior to 1992	42 (7)
1945–1965 birth cohort	672 (90)

Significant differences in acceptance of HCV testing by race ($p<0.001$), country of birth ($p<0.01$), BB cohort ($p<0.05$) and English speaking vs non-English speaking ($p<0.01$)

HCV Screening and Awareness



67% were high-risk for HCV (eligible for screening)

30% received prior HCV testing

30% were aware of prior testing

When offered HCV testing, > 80% of patients accepted, 64% of patients completed testing; All HCV positive patients were linked to care

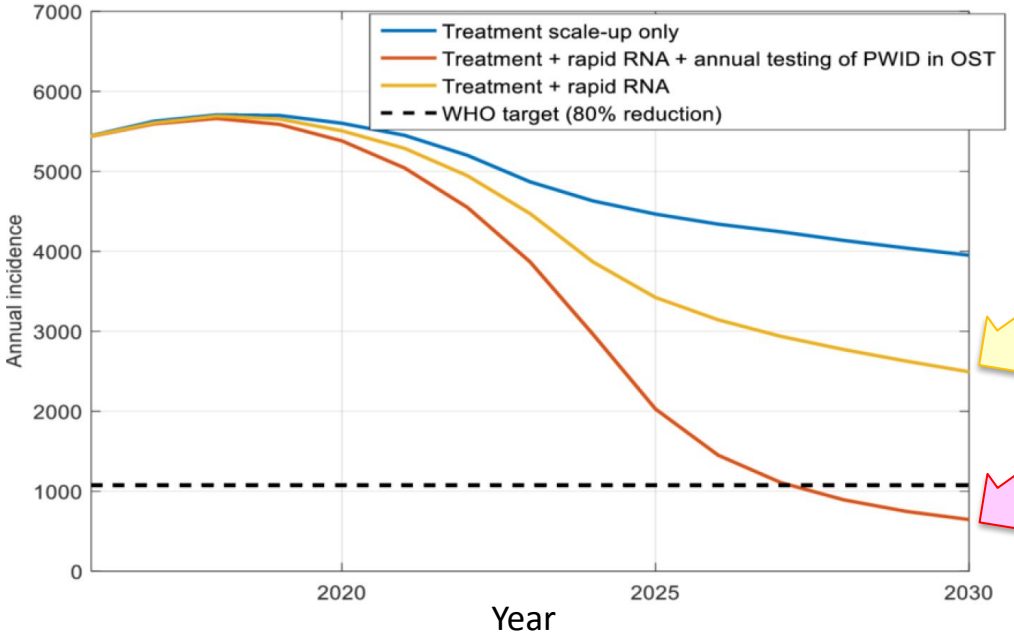
IV, inrtravenous. * Based on U.S. Preventative Services Task Force guidelines.

FRI-475, Scott: Reaching HCV Elimination Targets Requires Health System Interventions to Enhance the Care Cascade

Assessment of interventions required in Australia, a setting where all living persons with HCV have access to therapy, to reach WHO HCV elimination targets. A dynamic HCV transmission and liver disease progression model was used to test the following interventions:
1) scaling up primary care treatment delivery; 2) using biomarkers in place of liver stiffness measurement; 3) point-of-care HCV RNA testing; 4) testing of PWID on OST

Treatment scale-up alone was not enough to reach WHO elimination targets by 2030 as remaining infections were among PWID who were unaware of their infection, and could continue to transmit infection

Annual HCV incidence among PWID



Scaling up primary case treatment
+ using APRI to assess cirrhosis
+ point-of-care RNA testing
= $62 million in healthcare cost savings by 2030

Required to achieve WHO HCV elimination targets

- Increased testing of PWID
- Annual HCV RNA testing as part of OST

OST, opioid substitution therapy; PWID, persons who inject drugs.

HBV Reactivation

Executive Summary

- Data on HBV reactivation after HCV DAA therapy are unlikely to be clinically relevant
- HBV/HCV coinfected patients require monitoring once they initiate HCV treatment although clinically significant reactivation is seen rarely
- No need for prophylactic therapy
- HBsAg- and HBcAg+ risk of reactivation is negligible

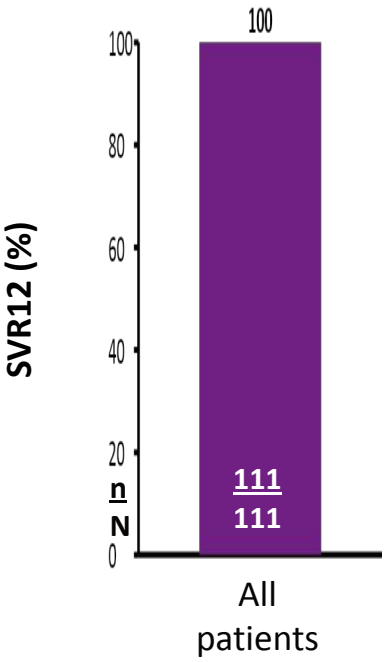
Liu, PS-098: 12 Weeks LDV/SOF is Safe and Effective in Patients with Chronic HCV/HBV Coinfection: A Phase 3 Study in Taiwan

Taiwanese, open-label study to evaluate the efficacy and safety of LDV/SOF for 12 weeks in HCV/HBV coinfected patients with or without compensated cirrhosis.
Patients were not receiving HBV treatment at enrolment

Baseline characteristics	LDV/SOF N = 111
Male, n (%)	42 (38)
Mean age, years (range)	55 (32–76)
Cirrhosis, n (%)	18 (16)
Treatment-experienced, n (%)	37 (33)
HCV genotype, n (%) 1 2	 68 (61) 43 (39)
Mean ALT, U/L (range)	68 (17–281)
HBsAg positive, n (%)	110* (99)
HBeAg positive, n (%)	1 (<1)
Baseline HBV DNA <LLOQ, n (%)	37 (33)

* n = 1 patient changed HBsAg status between screening and baseline.

Efficacy



HBV DNA kinetics

LDV/SOF 12 weeks associated with asymptomatic HBV reactivation in 63% (70/111) of patients

No patient experienced clinical signs or symptoms of HBV reactivation

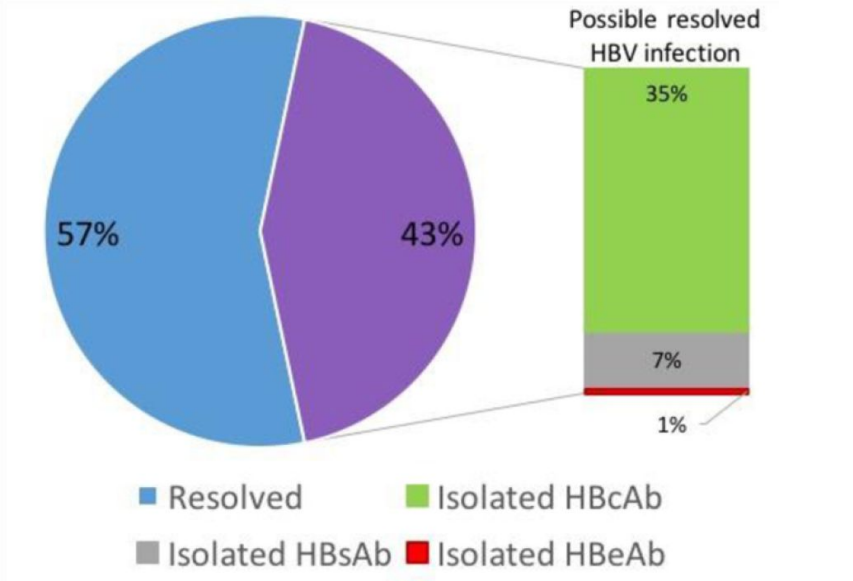
- 5% (5/111) of patients had concomitant increase in ALT
- 2% (2/111) of patients started HBV therapy

Higher baseline HBV DNA and ALT were associated with up to 1 $\log^{10}$ increase in HBV DNA

THU-144, Tang: Absence of Hepatitis B Reactivation Among Veterans with Serological Evidence of Previous Hepatitis B Infection Receiving Anti-HCV Direct Acting Antivirals

Retrospective analysis of HBV reactivation in 192 Veterans, receiving HCV DAA therapy at the Baltimore Veterans Affairs Medical Center, with evidence of previous HBV infection*

Baseline characteristics	N = 192
Mean age, years (± SD)	63 (± 5)
Male, n (%)	191 (99.5)
Black, n (%)	160 (83)
Fibrosis stage, n (%)	
F0–F2	89 (46)
F3	50 (26)
F4	52 (27)
Missing	1 (1)
HCV treatment, n (%)	
LDV/SOF ± RBV	156 (81)
OBV/PTV/r + DSV	7 (4)
SOF/VEL	1 (<1)
EBR/GZR ± RBV	28 (15)
Treatment-naive, n (%)	159 (83)
Achieved SVR, n (%)	177 (92)



No HBV reactivation events were observed

2 patients experienced ALT increase > ULN during treatment without HBV reactivation, both of which normalized without intervention

ALT, alanine aminotransferase; ULN, upper limit of normal.
* Patients with HIV coinfection or post solid organ transplant were excluded.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