New Hepatitis C Regimens

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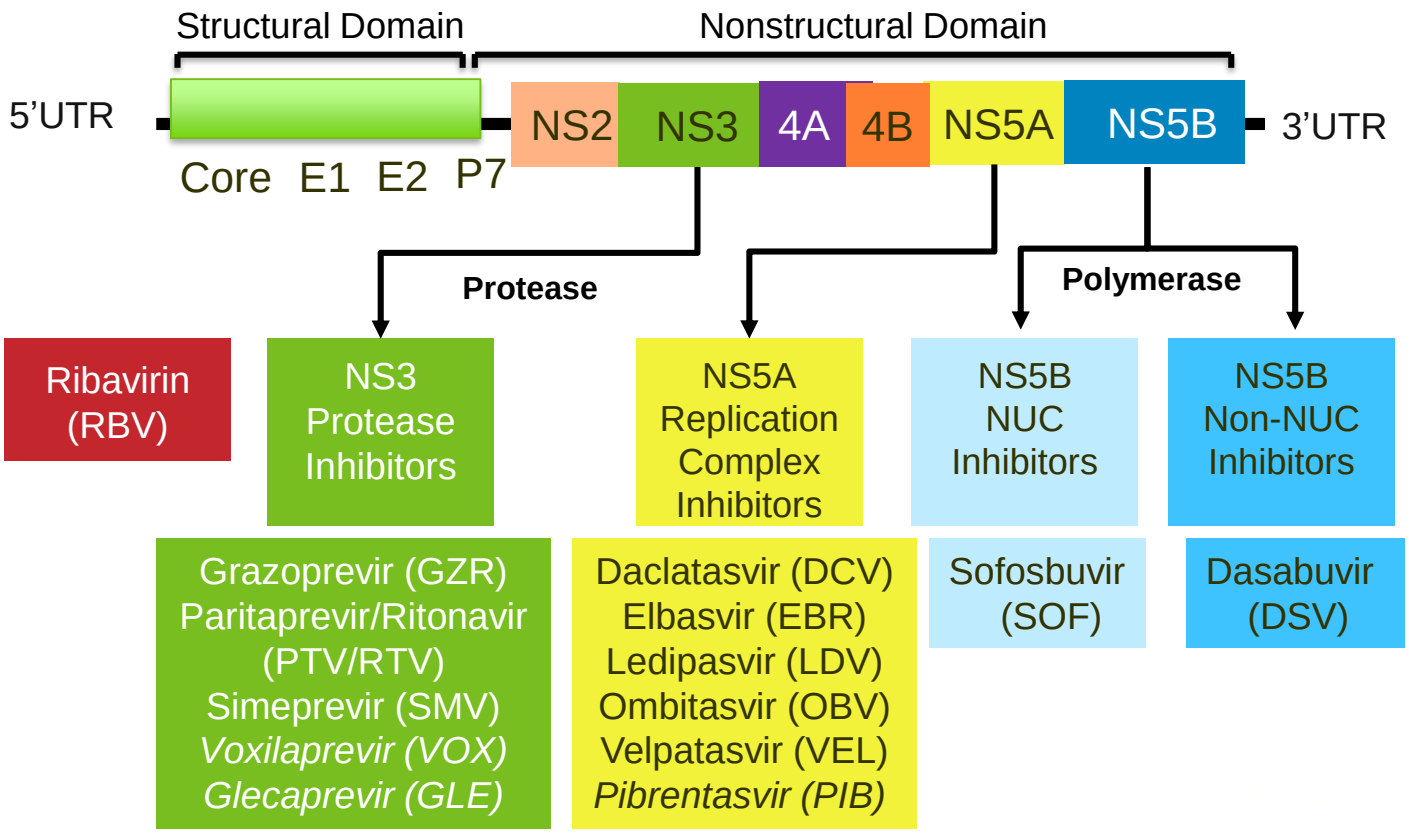
Slides adapted from Dr. Monto SF VA

VA HEALTH CARE Defining EXCELLENCE in the 21st Century

Approved DAAs From Multiple Classes: Basis of 2018 Combination HCV Regimens



Mechanisms of Combination DAA regimens

NS3 Protease Inhibitor	NS5A Replication Complex Inhibitors	NS5B Nucleoside Inhibitors	NS5B Nonnucleoside Inhibitors	*Brand Name*
		Sofosbuvir		*Sovaldi*®
Simeprevir				*Olysio*®
	Ledipasvir	Sofosbuvir		*Harvoni*®
Paritaprevir/ritonavir	Ombitasvir		Dasabuvir	*Viekira* ®
Paritaprevir/ritonavir	Ombitasvir			*Technivie*®
	Daclatasvir			*Daklinza*®
Grazoprevir	Elbasvir			*Zepatier*®
	Velpatasvir	Sofosbuvir		*Epclusa*®
Voxilaprevir	Velpatasvir	Sofosbuvir		*Vosevi*™
Glecaprevir	Pibrentasvir			*Mavyret*™

HCV GT	Treatment History	Cirrhosis Status	Treatment Option(s) (in alphabetical order)	Alternative Option(s) (in alphabetical order)
GT1	Naïve, HCV RNA <6 million IU/mL, HCV-monoinfected	Non-cirrhotic	• **LDV/SOF** x 8 weeks[a,b]	
GT1	Naïve or Experienced *(NS3/4A-naïve and/or NS5A-naïve)*	Non-cirrhotic **OR** cirrhotic, CTP A	• **EBR/GZR** ○ If GT1a, test for NS5A RASs prior to treatment. ▪ *GT1a **<u>without</u>** baseline NS5A RAS:* 12 weeks; add RBV if treatment-experienced ▪ *GT1a **<u>with</u>** baseline NS5A RAS:* Add RBV; 16 weeks[c] ▪ *GT1b:* 12 weeks; add RBV if treatment-experienced • **LDV/SOF** x 12 weeks ○ Add RBV for treatment-experienced cirrhotic patients; consider adding RBV in other situations • **PrOD** x 12 weeks if DAA-naïve ○ GT1a: add RBV (may consider 24 weeks in cirrhotics or prior null responders) ○ GT1b: RBV not required	**If RBV intolerant/ contraindicated[d]:** • SOF/VEL x 12 weeks
GT1	Naïve or Experienced *(NS3/4A-naïve and/or NS5A-naïve)*	Cirrhotic, CTP B, C	• **LDV/SOF + RBV** (600 mg/day and increase by 200 mg/day every 2 weeks only as tolerated) x 12 weeks If RBV intolerant/contraindicated: **LDV/SOF** x 24 weeks	• **SOF/VEL + RBV** x 12 weeks; start at lower RBV doses as clinically indicated (e.g., baseline Hgb)[e]
GT1	Experienced *(Prior NS3/4A-containing regimen only)*	Non-cirrhotic **OR** Cirrhotic, CTP A	• **SOF/VEL** x 12 weeks	

GT2	**Naïve or Experienced *(Prior SOF + RBV ± PEG-IFN)***	**Non-cirrhotic OR Cirrhotic, CTP A**	• **SOF/VEL x 12 weeks** ○ **If SOF experienced: Add RBV**	• **DCV + SOF x 12 weeks or 12-16 weeks if CTP A; add RBV if SOF experienced; *Not FDA approved***
GT2	Naïve or Experienced *(Prior SOF + RBV ± PEG-IFN)*	Cirrhotic, CTP B, C	• **SOF/VEL + RBV** x 12 weeks; start at lower RBV doses as clinically indicated (e.g., baseline Hgb)	• **DCV + SOF + RBV** (600 mg/day and increase as tolerated) x 12 weeks or 12-16 weeks if treatment-experienced; *Not FDA approved*

GT3	**Naïve**	**Non-cirrhotic**	• **SOF/VEL x 12 weeks**	• **DCV + SOF x 12 weeks**
GT3	Naïve	Cirrhotic	• **SOF/VEL** x 12 weeks ○ CTP A: Test for NS5A RAS and add RBV if Y93H RAS is present ○ CTP B or C: Add RBV; start at lower RBV doses as clinically indicated (e.g., baseline Hgb)	• **DCV + SOF + RBV** x 12-16 weeks in CTP A, or 12-24 weeks in CTP B and C patients
GT3	Experienced *(Prior PEG-IFN/RBV ± SOF)*	Non-cirrhotic	• **SOF/VEL** x 12 weeks ○ If PEG-IFN/RBV experienced only: Test for NS5A RAS and add RBV if Y93H RAS is present ○ If SOF experienced: Add RBV	• **DCV + SOF** x 12 weeks • If SOF experienced: Add RBV and treat for 12-16 weeks
GT3	Experienced *(Prior PEG-IFN/RBV ± SOF)*	Cirrhotic	• **SOF/VEL** x 12 weeks ○ CTP A: Test for NS5A RAS and add RBV if Y93H RAS is present ○ If SOF experienced: Add RBV ○ CTP B or C: Add RBV; start at lower RBV doses as clinically indicated (e.g., baseline Hgb)	• **DCV + SOF + RBV** x 12-16 weeks in CTP A, or 12-24 weeks in CTP B and C patients or if SOF experienced

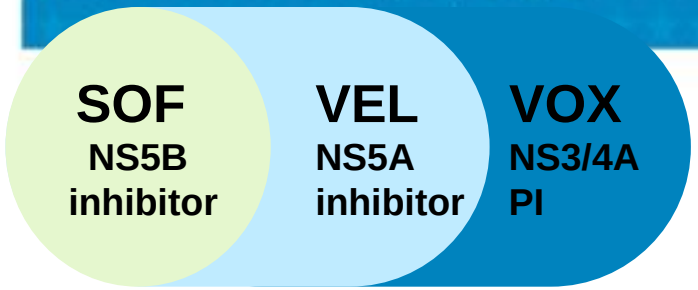
All-Oral Regimens for HCV Infection

Regimen	Component Classes	Genotypes
Grazoprevir/elbasvir	Protease inhibitor + NS5A inhibitor	1, 4
Ombitasvir/paritaprevir/ritonavir	Protease inhibitor + NS5A inhibitor	4
Ombitasvir/paritaprevir/ritonavir + dasabuvir	Protease inhibitor + NS5A inhibitor + polymerase inhibitor	1
Sofosbuvir + daclatasvir	Nucleotide polymerase inhibitor + NS5A inhibitor	1, 3
Sofosbuvir/ledipasvir	Nucleotide polymerase inhibitor + NS5A inhibitor	1, 4, 5, 6
Simeprevir + sofosbuvir	Nucleotide polymerase inhibitor + protease inhibitor	1
Sofosbuvir/velpatasvir	Nucleotide polymerase inhibitor + NS5A inhibitor	1, 2, 3, 4, 5, 6
Glecaprevir/pibrentasvir (Abbvie, Aug 2017)	Protease inhibitor + NS5A inhibitor	1, 2, 3, 4, 5, 6
Sofosbuvir/velpatasvir/voxilaprevir (Gilead, July 2017)	Nucleotide polymerase inhibitor + NS5A inhibitor+ Protease inhibitor	1, 2, 3, 4, 5, 6
Grazoprevir/ruzasvir /uprifosbuvir (Merck, early 2018)	Protease inhibitor + NS5A inhibitor+ Nucleotide polymerase inhibitor	1,2,3

8–12 week regimens
96%–100% SVR rates (even in NS5A treatment failures)

Slide:
P Belperio

New Regimens in 2018



Sofosbuvir/Velpatasvir/Voxilaprevir (VOX)

- Pan-genotypic against GT 1–6, including most RASs
- Once-daily, oral, fixed-dose combination (400/100/100 mg)
- Diarrhea (18%- 20%), PPI interaction

Glecaprevir/Pibrentasvir (G/P)

- Pan-genotypic activity against GT 1–6
- High barrier to resistance; potent against common NS3 RAS (80, 155, and 168) and NS5A RAS (28, 30, 31, and 93)
- Three 100mg/40 mg pills once daily with food
- No dose adjustment for CKD

Uprifosbuvir/Grazoprevir/Ruzasvir

- Activity against GT 1–3
- Two 225 mg/50 mg/30 mg tablets once daily
- High barrier to resistance; potent against NS5A DAA failures

CKD = chronic kidney disease.

New DAA Clinical Studies

SOF/VEL/VOX	Study Population	SVR
POLARIS-1	12 weeks for NS5A -experienced GT 1–6 ± cirrhosis (46%)	96% (91%–100%)
POLARIS-2	8 weeks for DAA-naive GT 1–6 (18% cirrhosis, 24% Peg-exp)	95% (92%–95%)
POLARIS-3	8 weeks for naïve GT 3 + cirrhosis	96% (91%–100%)
POLARIS-4	12 weeks for DAA-experienced (no NS5A inhibitors) GT 1–6 ± cirrhosis	97% (94%–100%)
GLE/PIB		
ENDURANCE-1	8 or 12 weeks for noncirrhotic GT 1 (naïve or PEG-exp)	99%
ENDURANCE-2	8 or 12 weeks for noncirrhotic SOF-naïve patients with GT 2	99%
ENDURANCE-3	8 or 12 weeks in naïve non-cirrhotic GT3	95%
ENDURANCE-4	12 weeks for noncirrhotic GT 4–6 (naïve or PEG-exp)	99%
SURVEYOR-II Part 3	12 or 16 week for patients with GT 3 ± prior PEG or SOF ± cirrhosis	91%–98%
EXPEDITION-I	12 weeks for patients with GT 1,2,4–6 ± prior PEG or SOF + cirrhosis	99%-100%
EXPEDITION-IV	12 weeks for patients with GT 1–6 and stage 4/5 CKD	98%
Magellan-1 Part 2	12 or 16 weeks for noncirrhotic patients with GT 1 or 4 and prior DAA failure	NS5A naïve: 100% NS5A only: 94% (16w) NS5A and PI: 81% (16w)

Bourlière M et al. AASLD 2016. Abstract 194; Jacobson IM et al. AASLD 2016. Abstract LB12; Foster GR et al. AASLD 2016. Abstract 258; Zeuzem S et al. AASLD 2016. Abstract 109; Zeuzem S et al. AASLD 2016. Abstract 253; Kowdley KV et al. AASLD 2016. Abstract 73; Asselah T et al. AASLD 2016. Abstract 114; Wyles DL et al. AASLD 2016. Abstract 113; Gane EJ et al. AASLD 2016. Abstract LB11; Lawitz E et al. AASLD 2016. Abstract 110; Serfaty L et al. AASLD 2016. Abstract 112; Wyles DL et al. AASLD 2016. Abstract 193. Poordad EASL 2017

ENDURANCE-1, -2, -4: GLE/PIB for Treatment of GT1, 2, 4, 5, 6 HCV

ENDURANCE-1: randomized, open-label phase III trial[1]

Noncirrhotic pts, GT1 +/- IFN experience +/- HIV
(N = 703; 38% tx-experienced†)

Wk 8 *Wk 12*

- GLE/PIB (n = 351)
- GLE/PIB (n = 352)

ENDURANCE-2: randomized, double-blind, placebo-controlled phase III trial[2]

Noncirrhotic pts, GT2 +/- IFN experience
(N = 302; 29% to 30% tx-exp†)

- GLE/PIB (n = 202)
- Placebo (n = 100)

ENDURANCE-4: open-label, single-arm phase III trial[3]

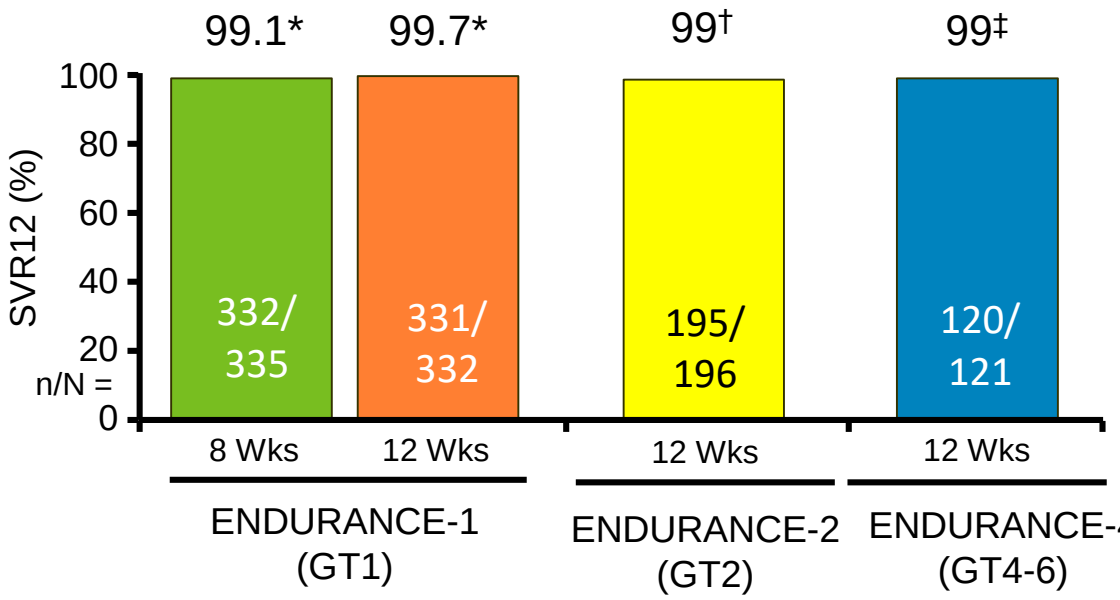
Noncirrhotic pts, GT4-6 HCV, +/- IFN experience
(N = 121; 32% tx-experienced†)

- GLE/PIB (N = 121)

*Dosing: GLE/PIB given as 3 coformulated 100/40-mg tablets QD
†Treatment experienced: IFN or pegIFN ± RBV or SOF + RBV ± pegIFN.

1.Zeuzem S, et al. AASLD 2016. Ab 253
2.Kowdley KV, et al. AASLD 2016. Ab 73
3. Asselah T, et al. AASLD 2016. Ab 114

ENDURANCE-1, -2, -4 Studies: Efficacy of GLE/PIB for Treating GT1, 2, 4, 5, 6 HCV

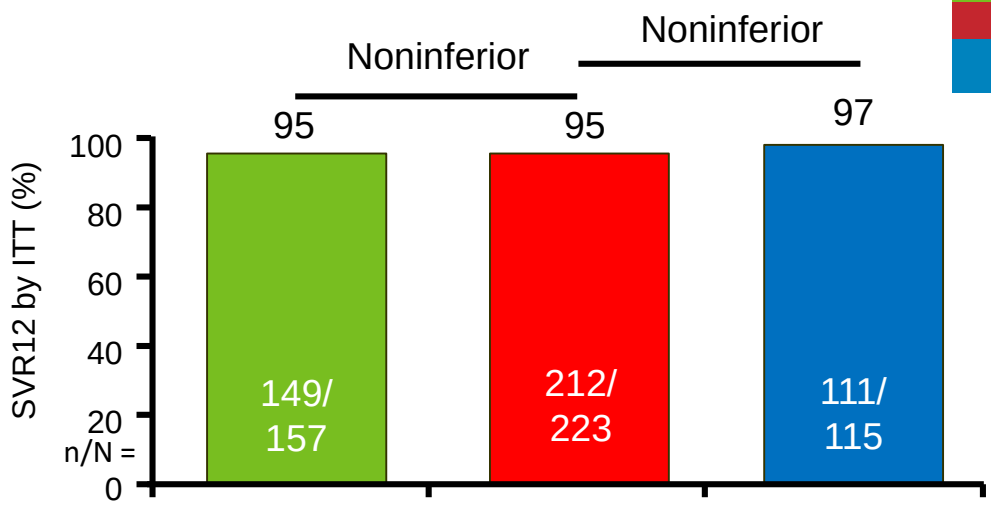


1 case of on-treatment virologic failure at Day 29 in pt with GT1a HCV infection

*ITT-PS analysis: included all pts receiving ≥ 1 dose of study drug; excluded pts with HIV coinfection or SOF experience. †ITT analysis: excluded pts with SOF experience. ‡ITT analysis.

ENDURANCE-3: Glecaprevir/Pibrentasvir in GT 3 HCV Without Cirrhosis

- Most pts had history of IDU (63% to 66%)



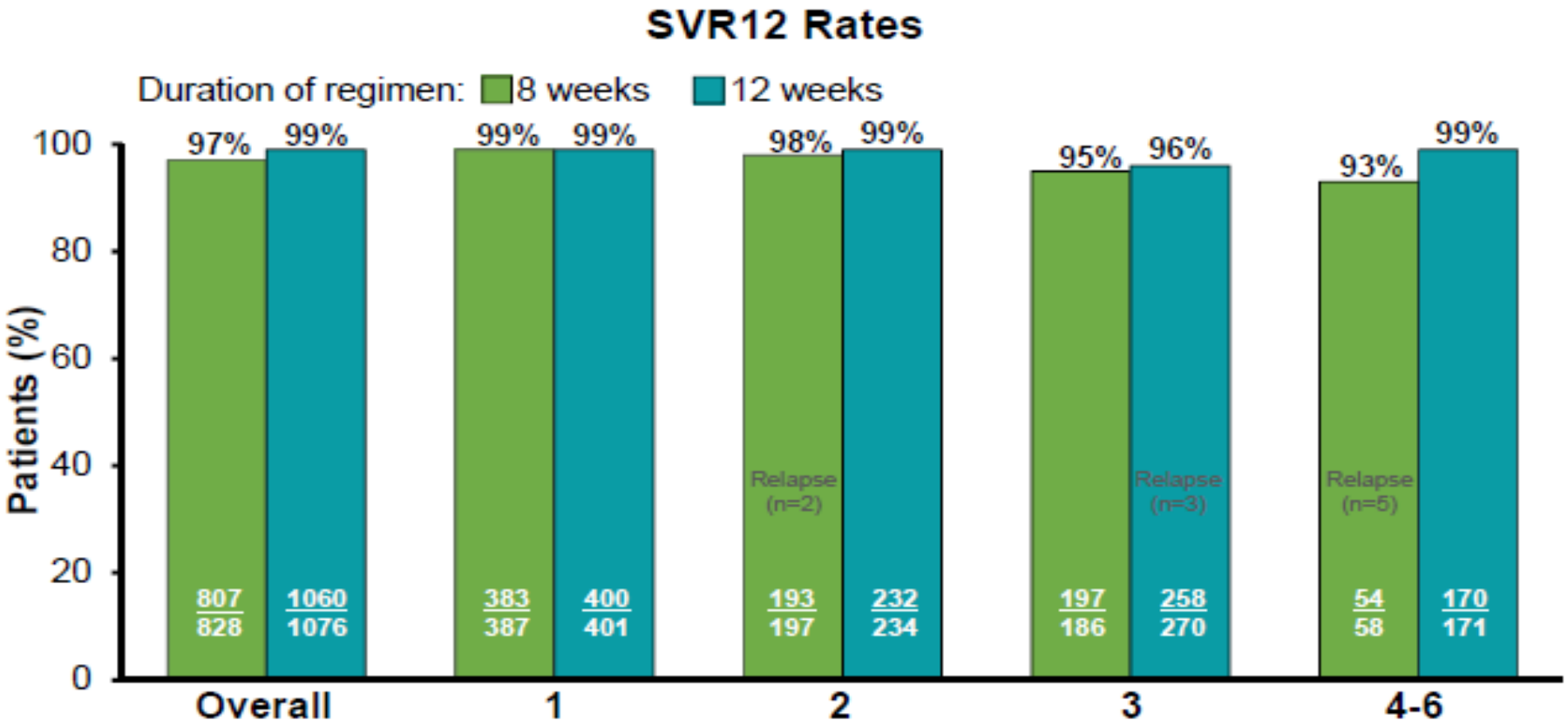
n/N =	149/157	212/223	111/115
Failure, n (%)	1 (1)	1 (< 1)	0
Breakthrough	5 (3)	3 (1)	1 (1)
Relapse	0	1 (< 1)	1 (1)
AE-related d/c	2 (1)	4 (2)*	2 (2)
LTFU			

- No SAEs deemed related to study drug
- 1 isolated bilirubin increase (G/P 8 wks), 1 isolated neutrophil count decrease (G/P 12 wks)

*2 other failures due to consent withdrawal and noncompliance.

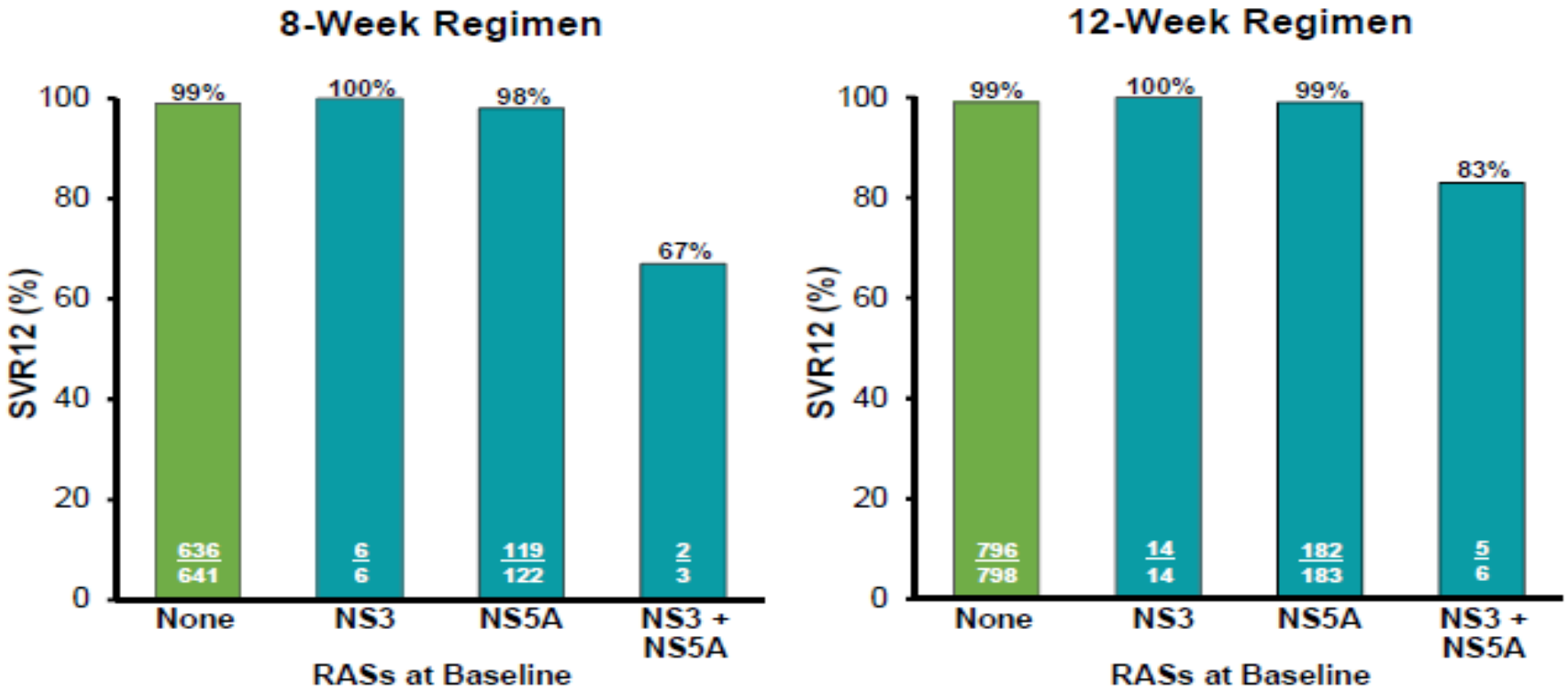
Foster GR, et al. EASL 2017. Ab GS-007

8 or 12 weeks of G/P in **Non-cirrhotic** HCV GT 1-6



Puoiti EASL 2017 abstract 429

8 or 12 weeks of G/P in **Non-cirrhotic** HCV GT 1-6: Impact of Baseline RAS

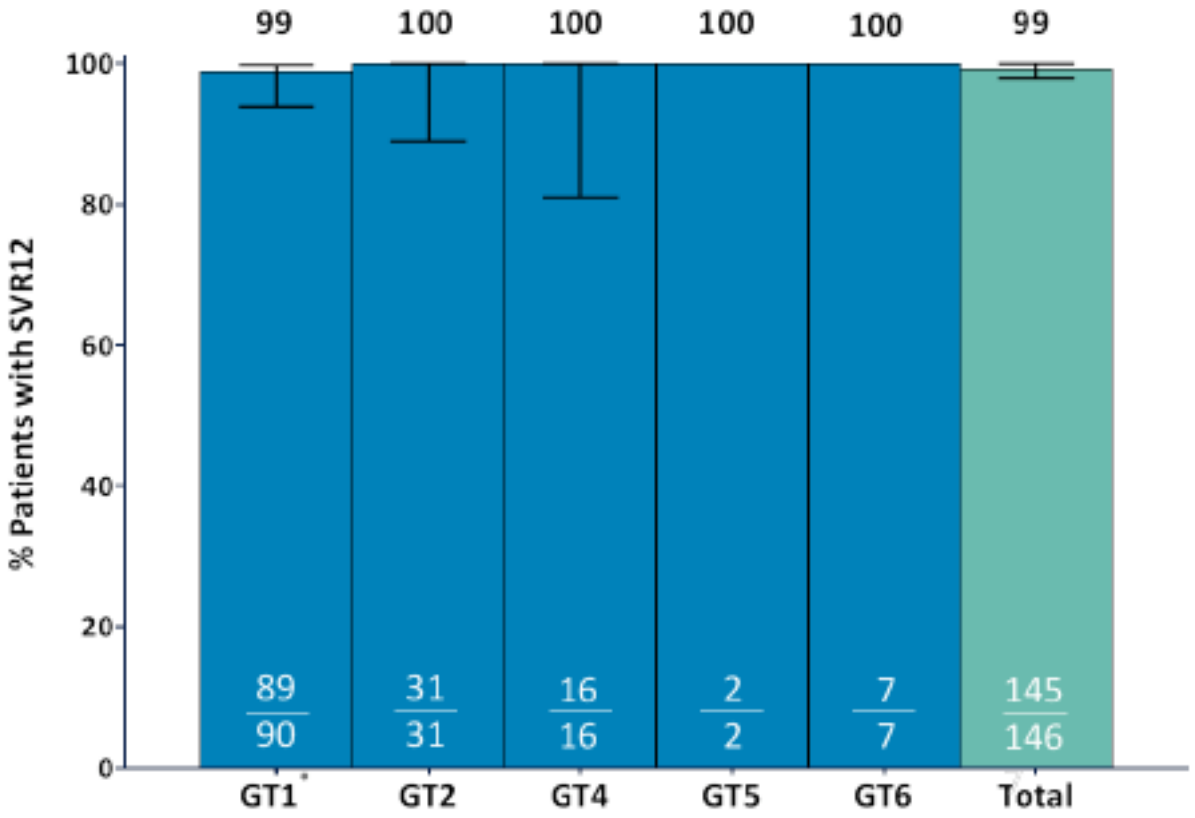


Presence of NS3+NS5A RAS reduced likelihood of SVR (p=0.017);
Avoid use in prior NS3/4A +NS5A failures unless RAS testing performed

Puoiti EASL 2017 abstract 429

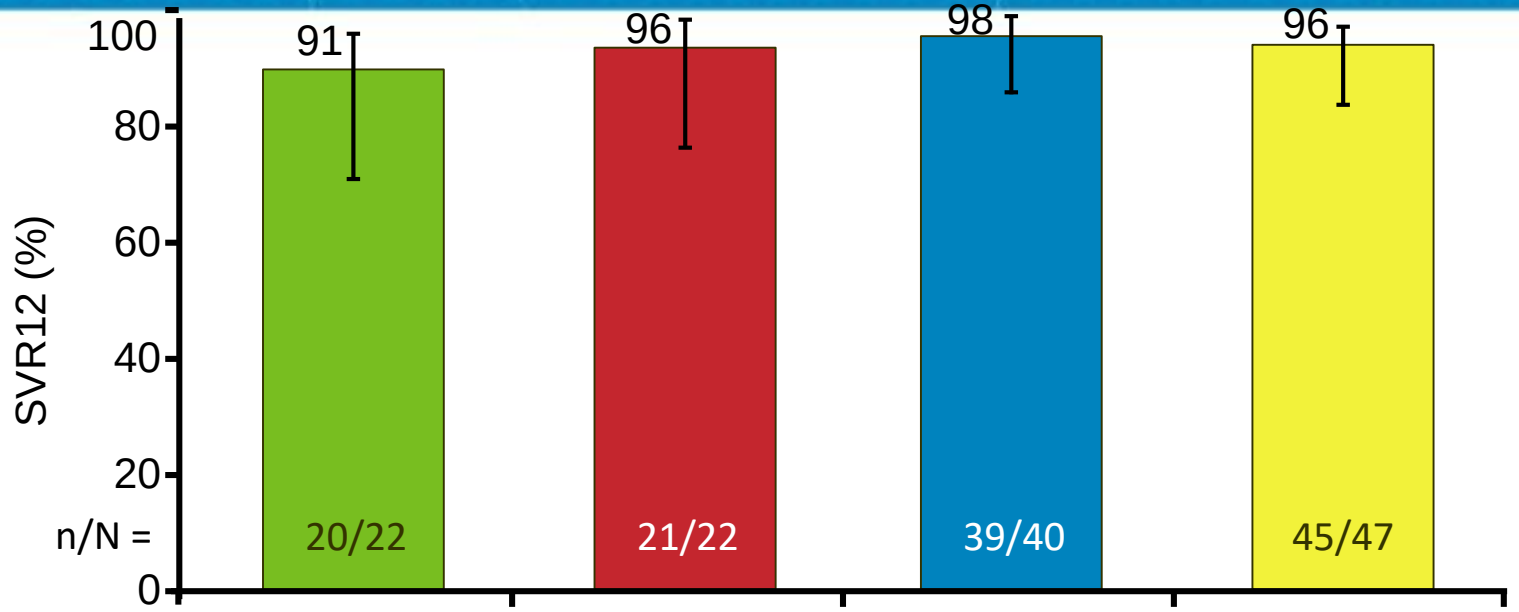
Expedition-1: G/P x 12 weeks in GT1,2,4-6 patients with **Cirrhosis** ± prior PEG or SOF

SVR12 by Intent-to-Treat (ITT) Analysis



- Treatment naïve (75%)
- PEG (17%) +/- SOF (8%) experience

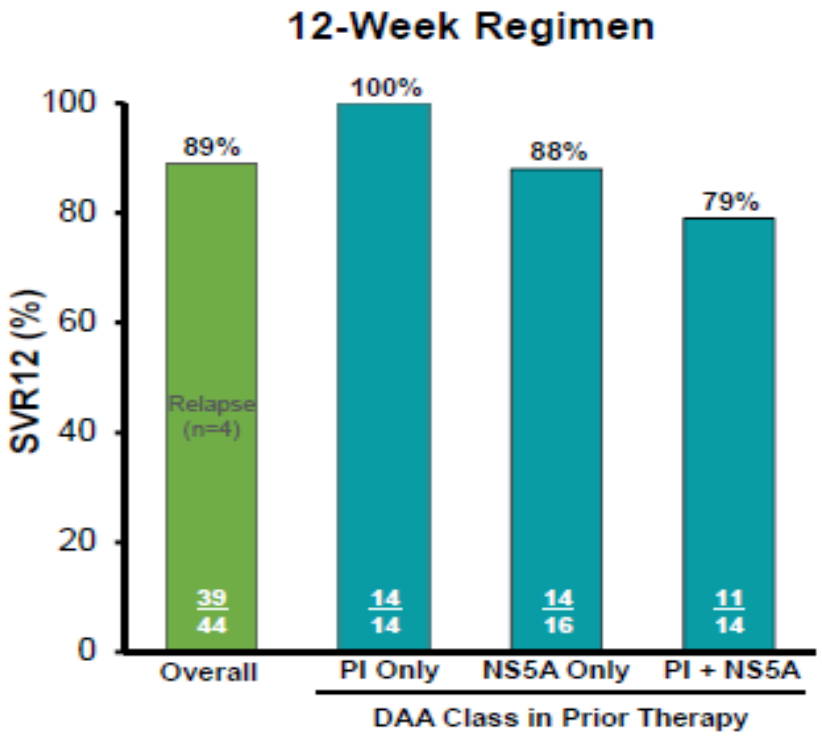
SURVEYOR-II, Part 3: GLE/PIB for Pts With GT3 ± Cirrhosis

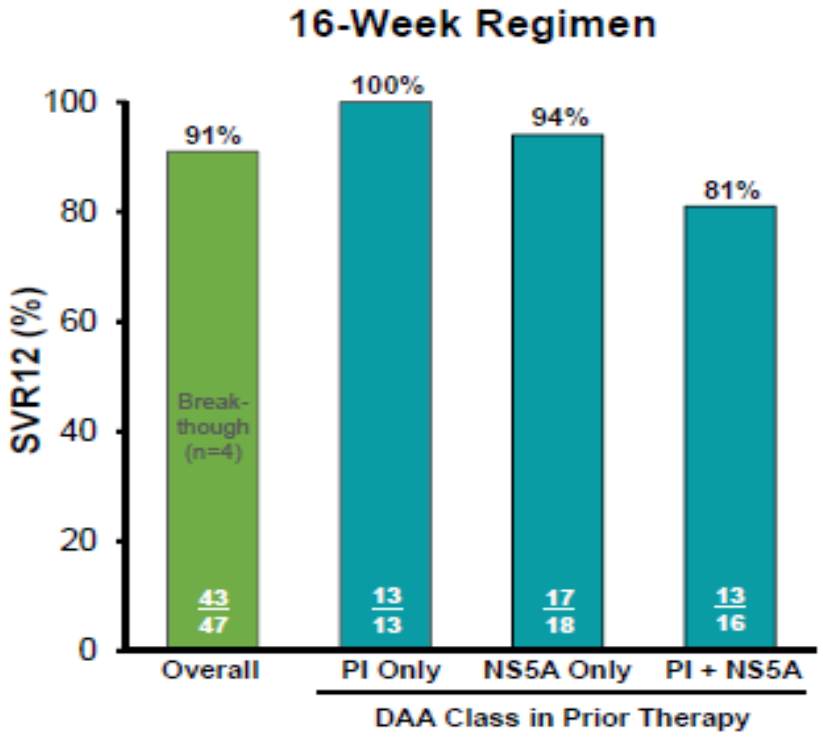


Tx Wks	12	16	12	16
Cirrhosis	-	-	+	+
Tx Experienced	+	+	-	+
Breakthrough	0	0	0	1
Relapse	2	1	0	1
LTFU	0	0	1	0

Wyles DL, et al. AASLD 2016. Abstract 113.

Magellan-1: G/P x 12 or 16 weeks in **Non-Cirrhotic** GT 1 or 4 **Prior DAA Failures**



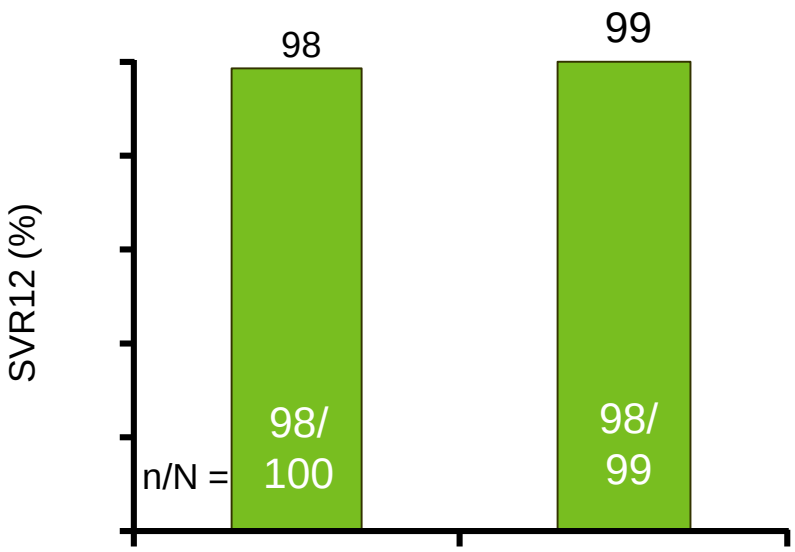


Lower SVR in prior NS3/4A +NS5A failures

Poordad EASL 2017 Abstract PS-156

MAGELLAN-2: Glecaprevir/Pibrentasvir for 12 Wks in GT1-6 HCV With Liver or Renal Transplant

- Liver/kidney transplant: 80%/20%
- 1 relapse: GT3a HCV; 1 pt LTFU



Outcome, %	GLE/PIB (N = 100)
Any AE	85
Serious AE	8
▪DAA related	2
D/c for AE	1
▪DAA related	0
AEs in ≥ 10% of pts	
▪Headache	22
▪Fatigue	22
▪Nausea	12
▪Pruritus	12
Grade ≥ 3 abnormality	
▪AST	0
▪ALT	1
▪Total bilirubin	1
▪CrCl	2

Reau N, et al. EASL 2017. Abstract LBO-03

- No deaths during study, 1 pt with transplant rejection (unrelated to DAA)

Potential Use of G/P

- 8 weeks for naïve, non-cirrhotic GT 1 (99%), GT 2 (98%) or GT 3 (95%)
- 12 weeks for naïve cirrhotic (GT 1-6) **OR** any PEG or SOF experience ±cirrhosis (GT1, 2, 4-6)
- 16 weeks GT 3 treatment PEG or SOF-experienced with cirrhosis (96%)
- 16 weeks for NS5A-only experience; RAS testing; consider ribavirin?
- For prior NS3/4A and NS5A experience: RAS testing (for NS3 and NS5A)
  - If no RAS: 16 weeks (consider adding RBV?)
  - If RAS present: consider alternative regimen

New DAA Clinical Studies

SOF/VEL/VOX	Study Population	SVR
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Bourlière M et al. AASLD 2016. Abstract 194; Jacobson IM et al. AASLD 2016. Abstract LB12; Foster GR et al. AASLD 2016. Abstract 258; Zeuzem S et al. AASLD 2016. Abstract 109; Zeuzem S et al. AASLD 2016. Abstract 253; Kowdley KV et al. AASLD 2016. Abstract 73; Asselah T et al. AASLD 2016. Abstract 114; Wyles DL et al. AASLD 2016. Abstract 113; Gane EJ et al. AASLD 2016. Abstract LB11; Lawitz E et al. AASLD 2016. Abstract 110; Serfaty L et al. AASLD 2016. Abstract 112; Wyles DL et al. AASLD 2016. Abstract 193. Poordad EASL 2017

Overview of Sof/Vel/Vox

- A spectacular regimen with great efficacy, but received FDA approval for retreatment of prior NS5a and/or sofosbuvir failures, so it will be primarily used in that setting
- 12 weeks (e.g. GT 1a, cirrhotic, experienced – including NS5A)
    - Lower SVR in NS5A-experienced cirrhotic (93%) vs noncirrhotic (99%)
    - Minimal impact of RAS
    - Higher SVR in DAA experienced patients when compared to Sof/Vel, particularly in GT 1a, GT 3 and cirrhotics
    - Role of RBV in NS5A-experienced cirrhotics? not studied
- If one were using it in treatment-naïve, good efficacy for 8 weeks for naïve GT 1b, GT 2, GT 3; maybe GT 2 and GT 3 naïve cirrhotics

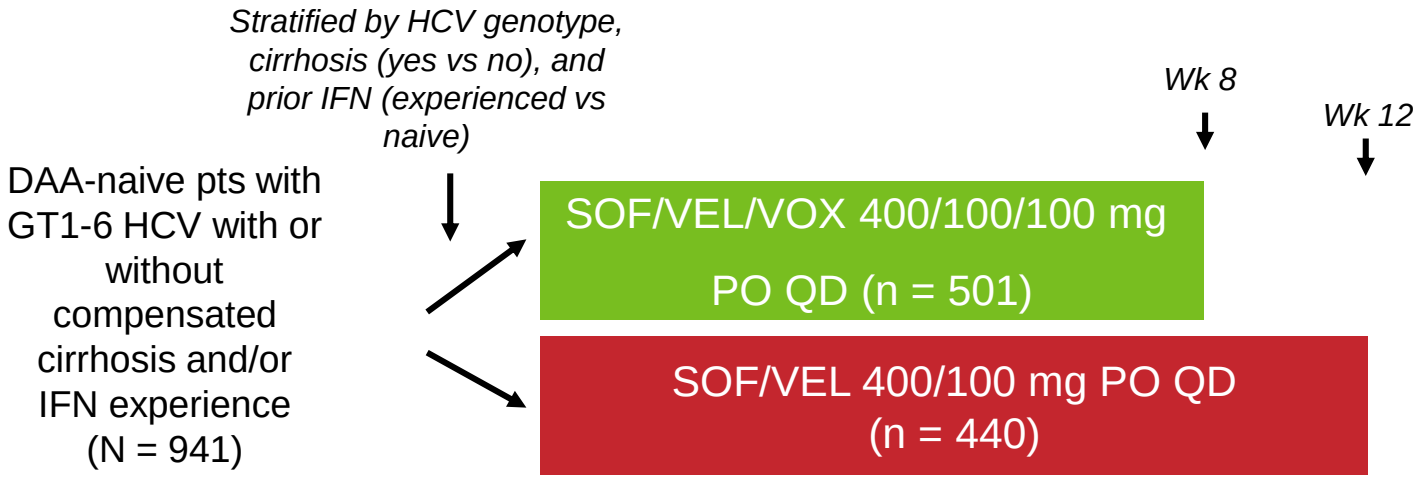
Polaris-1: Retreatment of Prior NS5a failures with SOF/VEL/VOX x 12 weeks

- Randomized, double-blind, placebo-controlled: evaluated efficacy of SOF/VEL/VOX
- 263 NS5a inhibitor-experienced pts (n= 150 GT 1), 46% with cirrhosis
- Previous failure: LDV/SOF (51%), DCV-containing regimen (27%), PrOD (11%), other (13%) including SOF/VEL or EBR/GZR
- SVR: 96% (97/101, 95% CI 90-99) in GT 1a and 100% (45/45, 95% CI 92-99) with GT 1b
- Across genotypes, SVR rates similar in patients with RAS: 97% (199/205), or without RAS: 98% (42/43)
- These results demonstrate that baseline RAS testing may not be needed prior to using SOF/VEL/VOX. Because SOF/VEL/VOX contains an NS3/4a protease inhibitor: not recommended in patients with decompensated cirrhosis

Bourliere M, et al, NEJM 2017;376:2134

POLARIS-2: 8-Wk SOF/VEL/VOX vs 12-Wk SOF/VEL for DAA-Naive GT1-6 Pts

- Randomized, open-label, active-controlled phase III trial

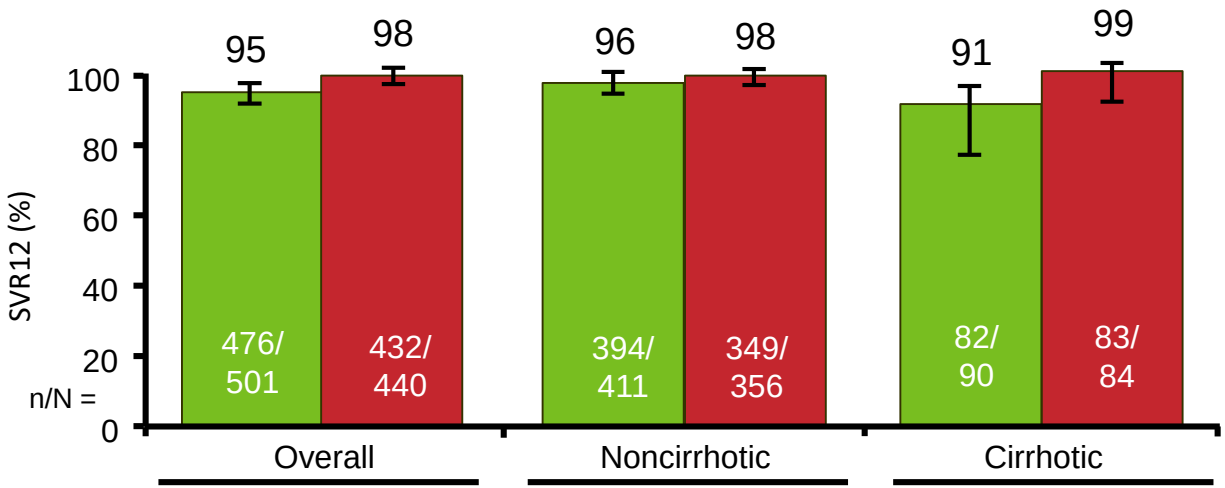


* Pts with GT1-4 HCV randmized; pts with GT5/6 HCV allocated to SOF/VEL/VOX arm; cirrhotic pts with GT3 HCV infection enrolled in POLARIS-3

Jacobson IM, et al Gastroenterology 2017;153:113

POLARIS-2: SVR12 Rates With 8-Wk SOF/VEL/VOX vs 12-Wk SOF/VEL

- 8-wk SOF/VEL/VOX did not meet criteria for noninferiority vs 12-wk SOF/VEL
  - Treatment difference: -3.4% (95% CI: -6.2% to -0.6%)
  - 14/21 pts with relapse to SOF/VEL/VOX 8 wks had GT1a



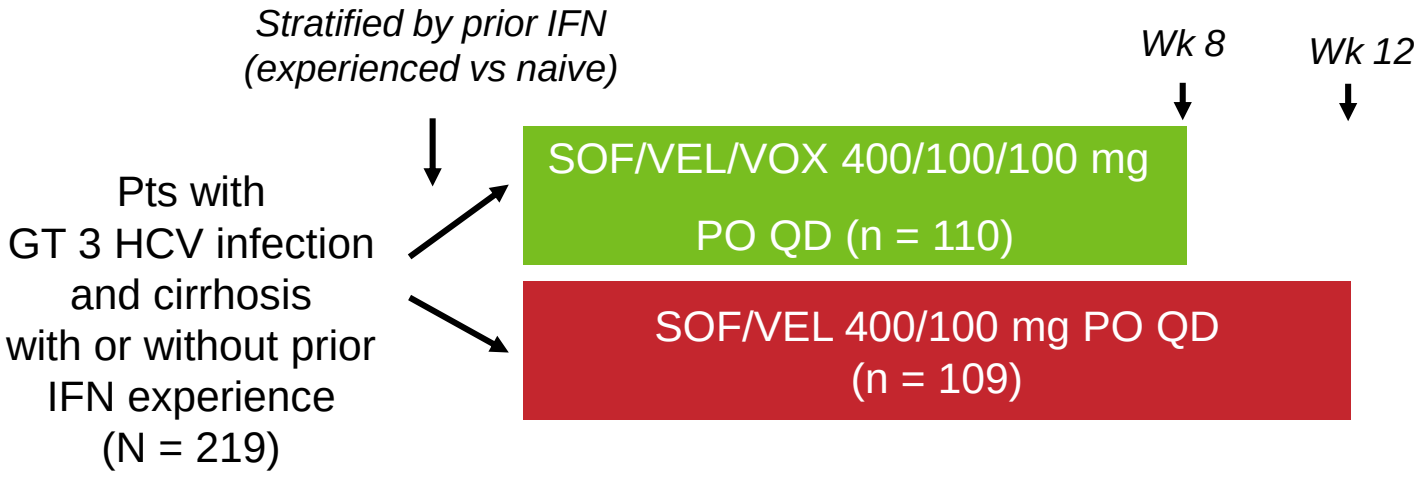
	Overall		Noncirrhotic		Cirrhotic	
Relapse, n	21	3	14	2	7	1
LTFU, n	4	4	3	4	1	0
D/c for AE, n	0	1	0	1	0	0

-More relapses in 1a (14 vs 1, SVR 92% vs 99%)
-Lower SVR with baseline NS3 (PI) or NS5A RAS (91-94% vs 98-100%)

Jacobson IM, et al Gastroenterology 2017;153:113

POLARIS-3: 8-Wk SOF/VEL/VOX vs 12-Wk SOF/VEL for Cirrhotic, DAA Naive GT 3

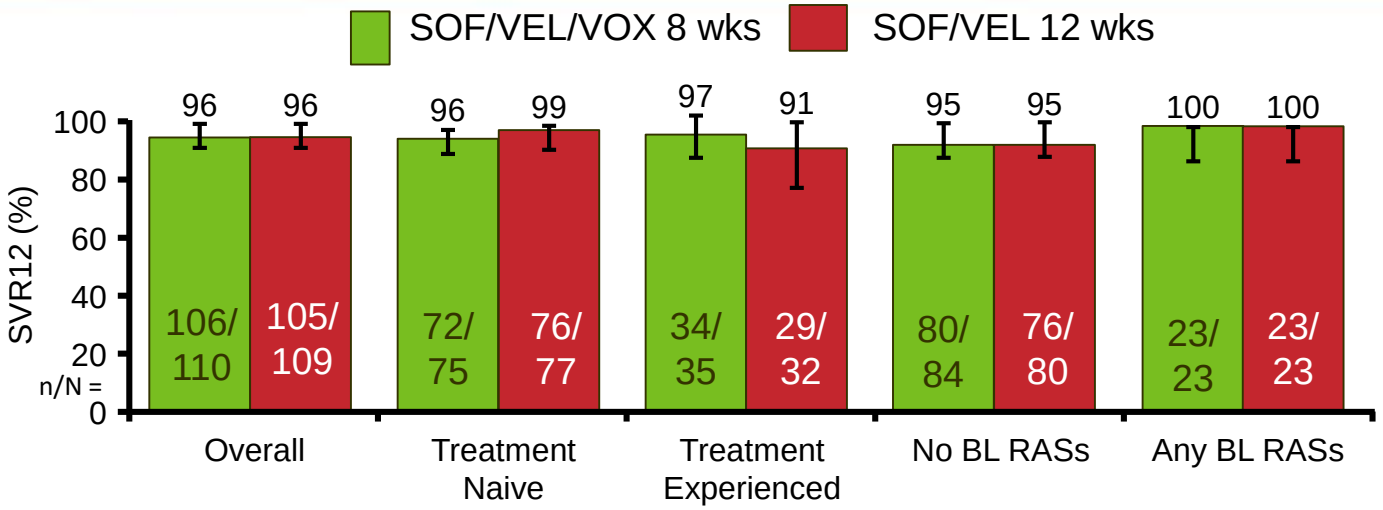
- Randomized, open-label, active-controlled phase III trial



- IFN experience in 29% to 32% of pts

Jacobson IM, et al Gastroenterology 2017;153:113

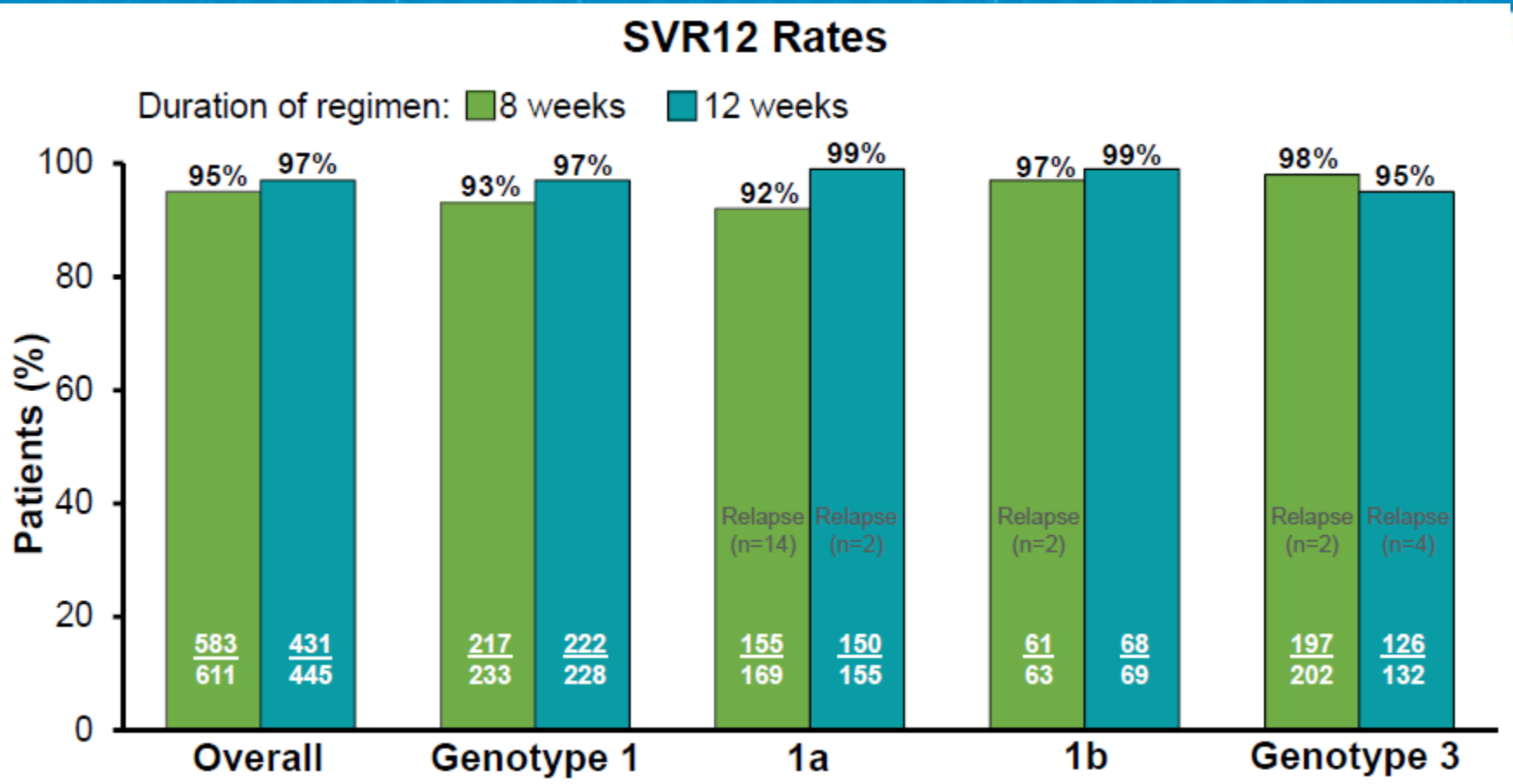
POLARIS-3: SVR12 Rates With 8-Wk SOF/VEL/VOX for Cirrhotic GT 3 Pts



- SVR rates similar between treatment arms, and both regimens superior to prespecified historic SVR rate of 83% (P < .001 for each arm)
- Overall VF: SOF/VEL/VOX, n = 2 relapses; SOF/VEL, n = 1 each for relapse and on-treatment failure
- No treatment-emergent RASs in SOF/VEL/VOX arm; Y93H in both VFs in SOF/VEL arm

Jacobson IM, et al Gastroenterology 2017;153:113

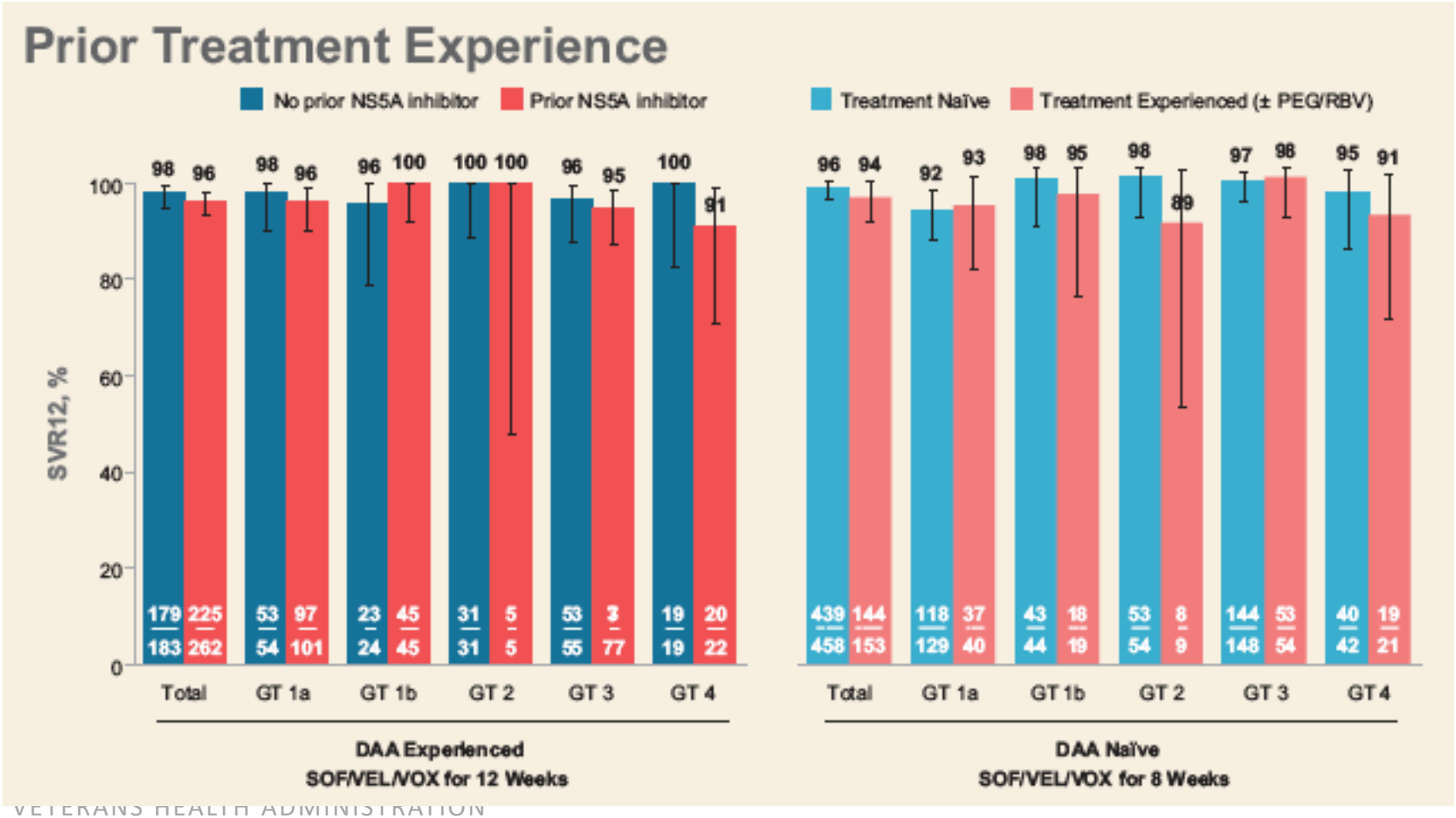
POLARIS Integrated Analysis: Sof/Vel/Vox for 8 or 12 weeks



SVR rate in cirrhotics: 8 weeks - 94%; 12 weeks – 95%
All 8 week patients were treatment-naïve or PEG/RBV experienced

Flamm SL, EASL 2017 Abstract 424

Polaris 1,2 (naïve, cirrhotic),3(TE no cirrhosis),4 (no NS5A experience) Integrated analysis



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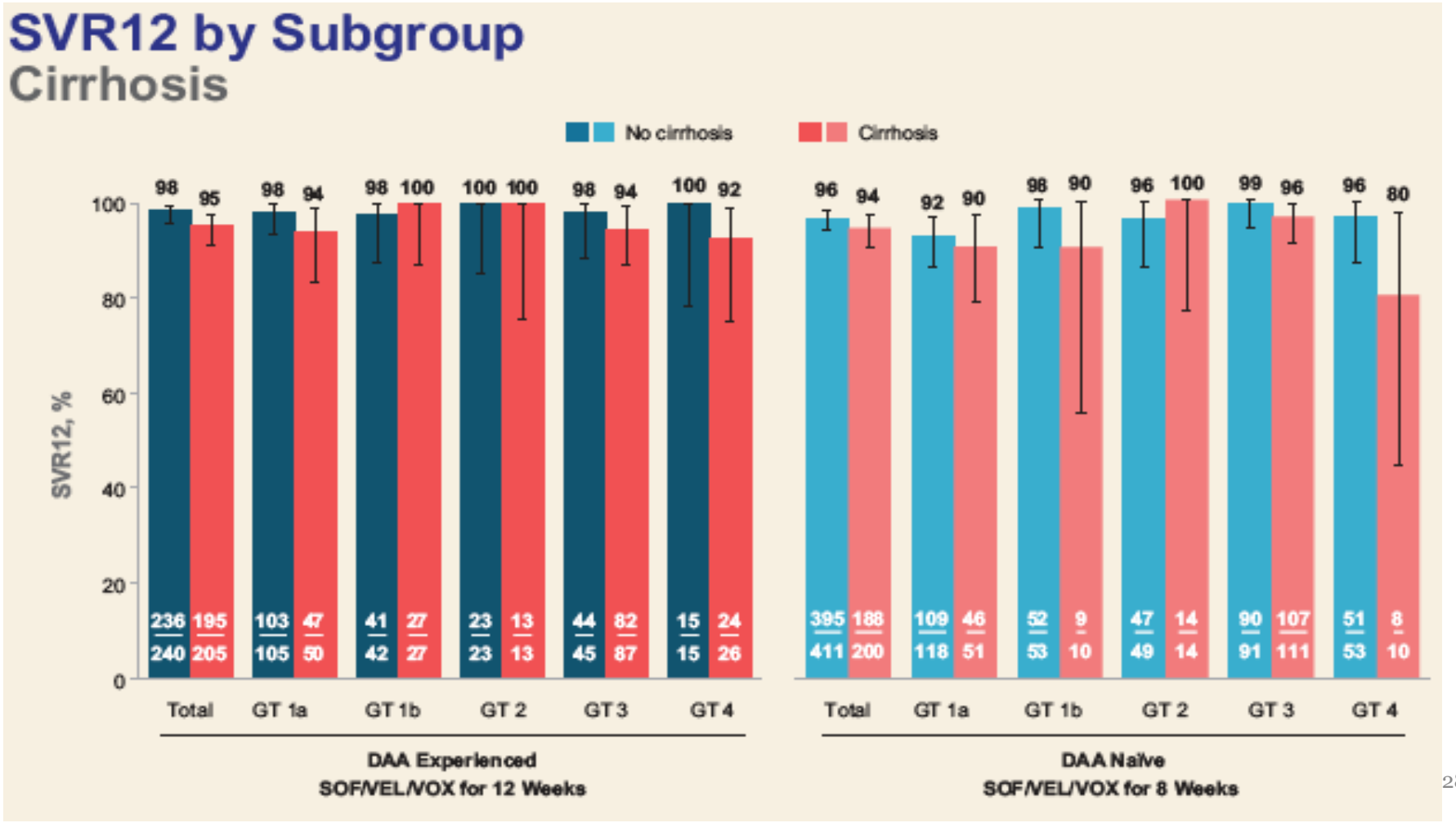


Overview of Sof/Vel/Vox

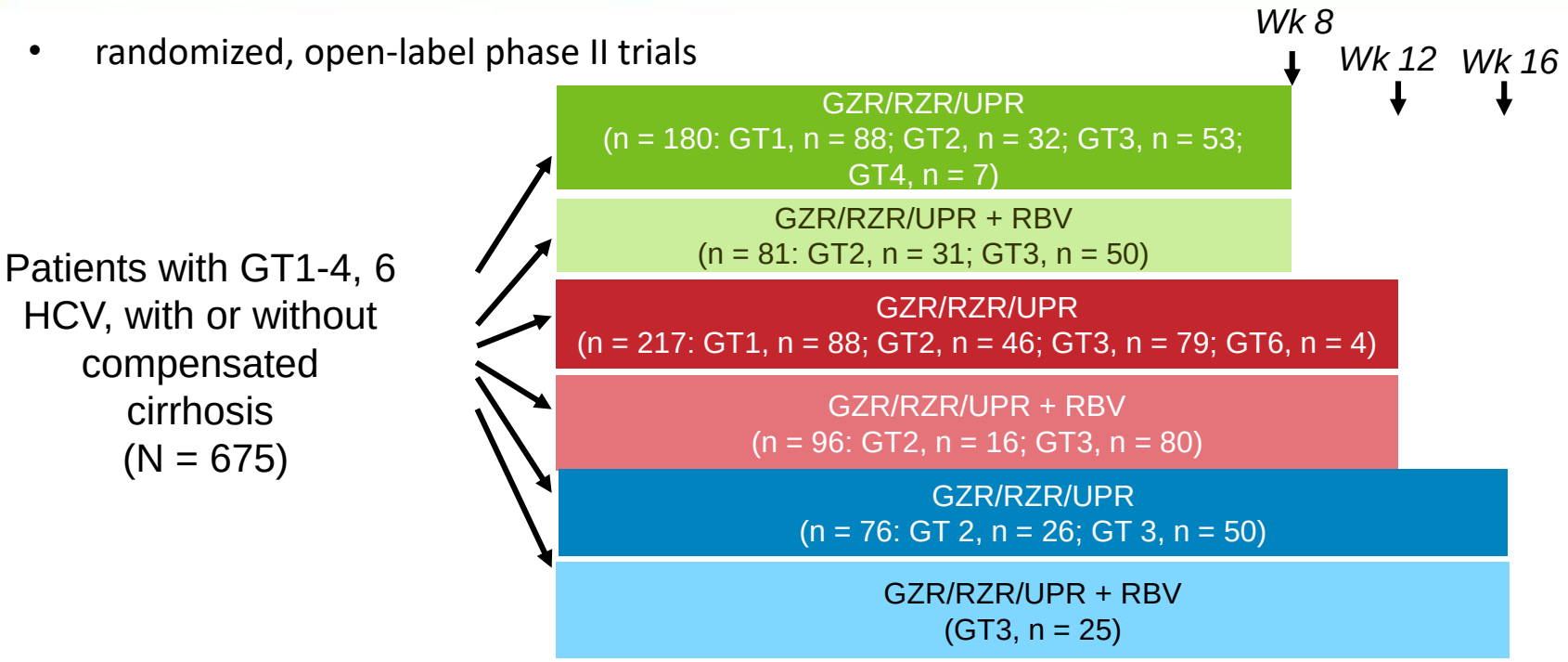
- A spectacular regimen with great efficacy, but received FDA approval for retreatment of prior NS5a and/or sofosbuvir failures, so it will be primarily used in that setting
- 12 weeks (e.g. GT 1a, cirrhotic, experienced – including NS5A)
    - Lower SVR in NS5A-experienced cirrhotic (93%) vs noncirrhotic (99%)
    - Minimal impact of RAS
    - Higher SVR in DAA experienced patients when compared to Sof/Vel, particularly in GT 1a, GT 3 and cirrhotics
    - Role of RBV in NS5A-experienced cirrhotics? not studied
- If one were using it in treatment-naïve, good efficacy for 8 weeks for naïve GT 1b, GT 2, GT 3; maybe GT 2 and GT 3 naïve cirrhotics

Summary Points for Current Regimens

- EBR/GZR, GLE/PIB or SOF/VEL/VOX should not be used in patients with moderate to severe hepatic impairment (CTP B and C)
- If LDV/SOF is used, treatment duration should be 12 weeks in pts with baseline HCV RNA >6M IU/ml, HIV/HCV-coinfected patients, African Americans and those with quantifiable (>LLOQ) HCV RNA at week 4 on treatment
- Baseline NS5A resistance testing is recommended in GT1a-infected patients prior to initiating EBR/GZR
- If the results would guide re-treatment options, NS3/4 and/or NS5A RAS testing can be performed by the VHA Public Health Reference Laboratory or a commercial laboratory

C-CREST 1 & 2: GZR/RZR/UPR ± RBV for Treating Pts With GT1-4, 6 HCV

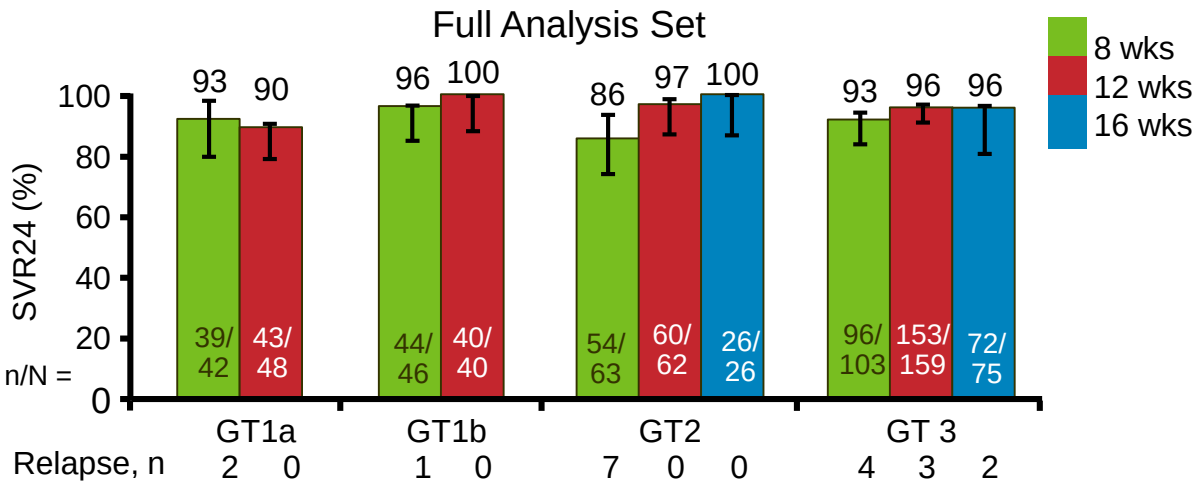
- randomized, open-label phase II trials



Dosing: GZR/RZR/UPR dosed as two 50/30/225-mg tablets QD. Pts with GT 3 HCV could be treatment naive or have failed on pegIFN/RBV; all others treatment naive

- Baseline: 35% to 43% cirrhotic; 44% of GT 3 pts had prior pegIFN/RBV

C-CREST 1 & 2: Efficacy of GZR/RZR/UPR ± RBV for Pts With GT1-4, 6 HCV



100% SVR12 rates in 7 pts with GT4 (treated for 8 wks) and 4 pts with GT 6 (treated for 12 wks)

- Presence of cirrhosis, use of ribavirin, prior tx experience did not impact SVR12 rates

SVR12 by Baseline RAS Presence, % (n/N)	GT 2 HCV		GT 3 HCV	
	No L31M	L31M	No Y93H	Y93H
8 wks	94 (31/33)	81 (21/26)	98 (95/97)	50 (2/4)
12 wks	100 (28/28)	100 (31/31)	99 (147/148)	71 (5/7)

Slide credit

Lawitz E, et al. EASL 2017. Abstract THU-285.

Mechanisms of Combination DAA regimens

NS3 Protease Inhibitor	NS5A Replication Complex Inhibitors	NS5B Nucleoside Inhibitors	NS5B Nonnucleoside Inhibitors	*Brand Name*
		Sofosbuvir		*Sovaldi*®
Simeprevir				*Olysio*®
	Ledipasvir	Sofosbuvir		*Harvoni*®
Paritaprevir/ritonavir	Ombitasvir		Dasabuvir	*Viekira*®
Paritaprevir/ritonavir	Ombitasvir			*Technivie*®
	Daclatasvir			*Daklinza*®
Grazoprevir	Elbasvir			*Zepatier*®
	Velpatasvir	Sofosbuvir		*Epclusa*®
Voxilaprevir	Velpatasvir	Sofosbuvir		*Vosevi*™
Glecaprevir	Pibrentasvir			*Mavyret*™

Hepatitis B serology interpretation

HBsAg **anti-HBc** **anti-HBs**	negative negative negative	Susceptible
HBsAg **anti-HBc** **anti-HBs**	negative positive positive	Immune due to natural infection
HBsAg **anti-HBc** **anti-HBs**	negative negative positive	Immune due to hepatitis B vaccination
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive positive negative	Acutely infected
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive negative negative	Chronically infected
HBsAg **anti-HBc** **anti-HBs**	negative positive negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

Question

A patient is 65 yo WM with a past medical history of CAH C, HTN, DM II, and hyperlipidemia. He presents for hepatitis C treatment and is found to be genotype 1a, Viral load is >25,000,000, naïve to treatment and is fibrosis score is 2.5 and his NS5A is negative. He gets a CT of the abdomen with and without contrast, Which demonstrates no hepatocellular carcinoma. He gets a fibroscan that shows F3 fibrosis (10 kpa). He is started on zepatier for 12 weeks and returnsAfter 1 month of therapy with yellow eyes and fatigue.

Temp: 98.0 F BP 121/70 HR 100 RR 19 PO2 99% on RA
AAO x 3 NAD WD, WN, WG age appropriate
HEENT: icterus of conjunctiva present
Lungs: both lung fields clear to auscultation
CVS: S1S2 normal RRR no R/G
Abdomen: organomegaly of RUQ, tenderness moderate RUQ, ND BS present
Ext: pulses intact, no edema noted
Skin: jaundice no rashes

Continuation of question

Labs: Na: 135
K: 3.9
Cl: 121
CO2: 24
BUN: 20
Cr: .8
T. bili 8

Hb: 14
WBC: 8
Plt: 121

HbsAg +
H A Ab +
HbcAb +
HCV Ab+

blood cultures - ve
urine cultures –ve
sputum cultures >25 epi, >25 WBC

AST: 800
ALT: 991

Continuation of the question

What accounts for the abnormalities found?

a. Severe sepsis
b. Drug adverse event
c. Alcoholic hepatitis
d. Ischemia
e. Hepatitis b
f. Ascending cholangitis
g. CBD stone obstruction

Thank you!!!

“You only live once, but if you do it right, once is enough.”
— Mae West