Treatment of Hepatitis C in 2017

Special Populations: Every one is special

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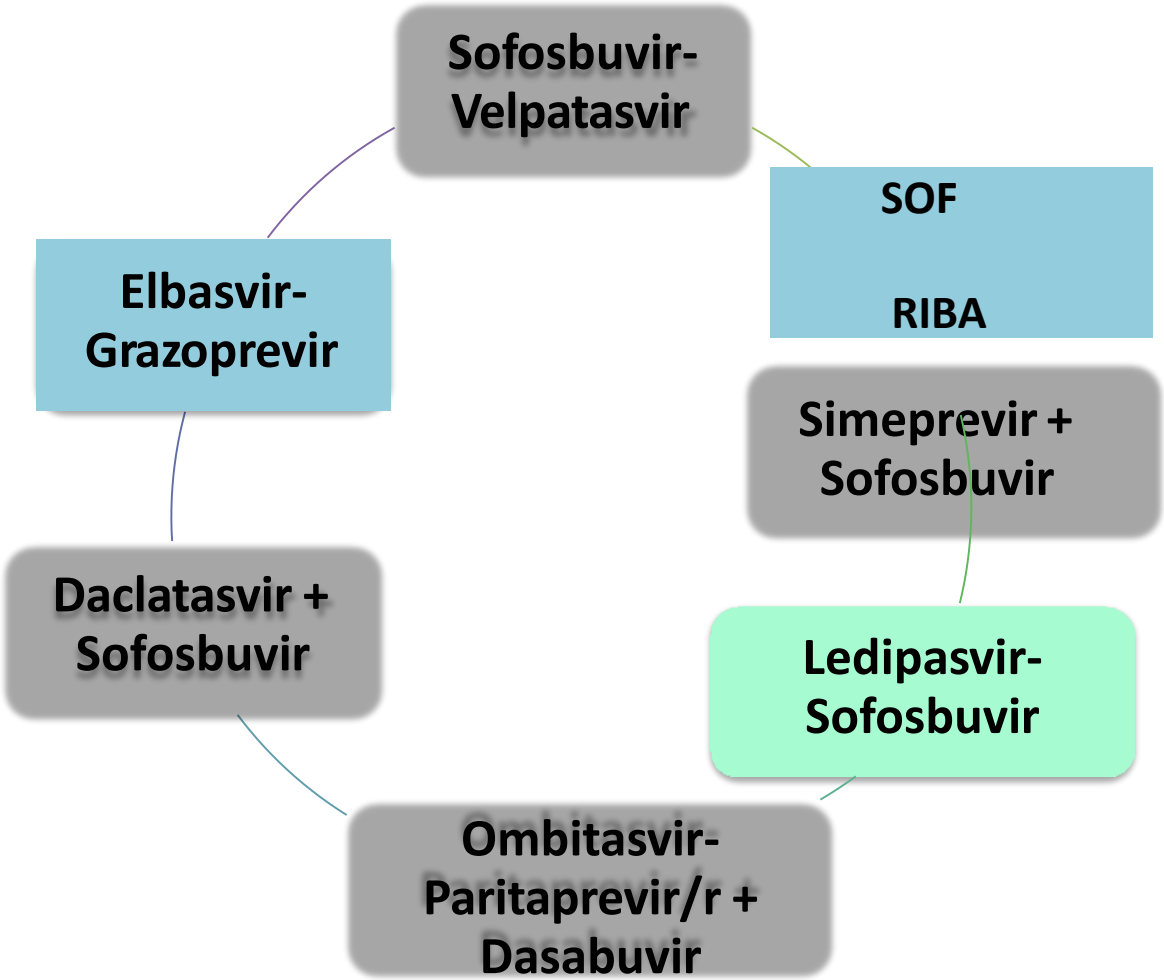
HASLD July 2017 Meeting HCMC VietNam

HCV Therapies in 2017
Many Tools in the Toolbox

Primary factors influencing choice:

1. HCV genotype
2. Prior HCV treatment
3. Cirrhosis, especially if decompensated
4. Renal disease
5. Insurer preference
6. Liver transplant
7. Cost
8. RAS/RAVs for GT1a and GT3
9. DDIs

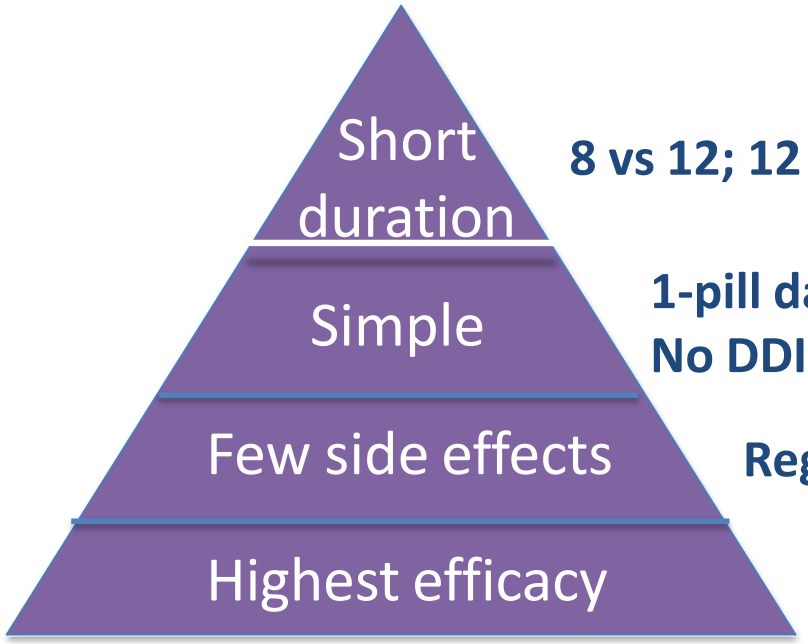


± Ribavirin

SVR rate ≥90-99%

Choosing Among DAA Regimens

- **Provider/patient preferences:**



8 vs 12; 12 vs 16 wks

1-pill daily (vs. 3-4 or BID dosing)
No DDIs or special timing required

Regimens without RBV

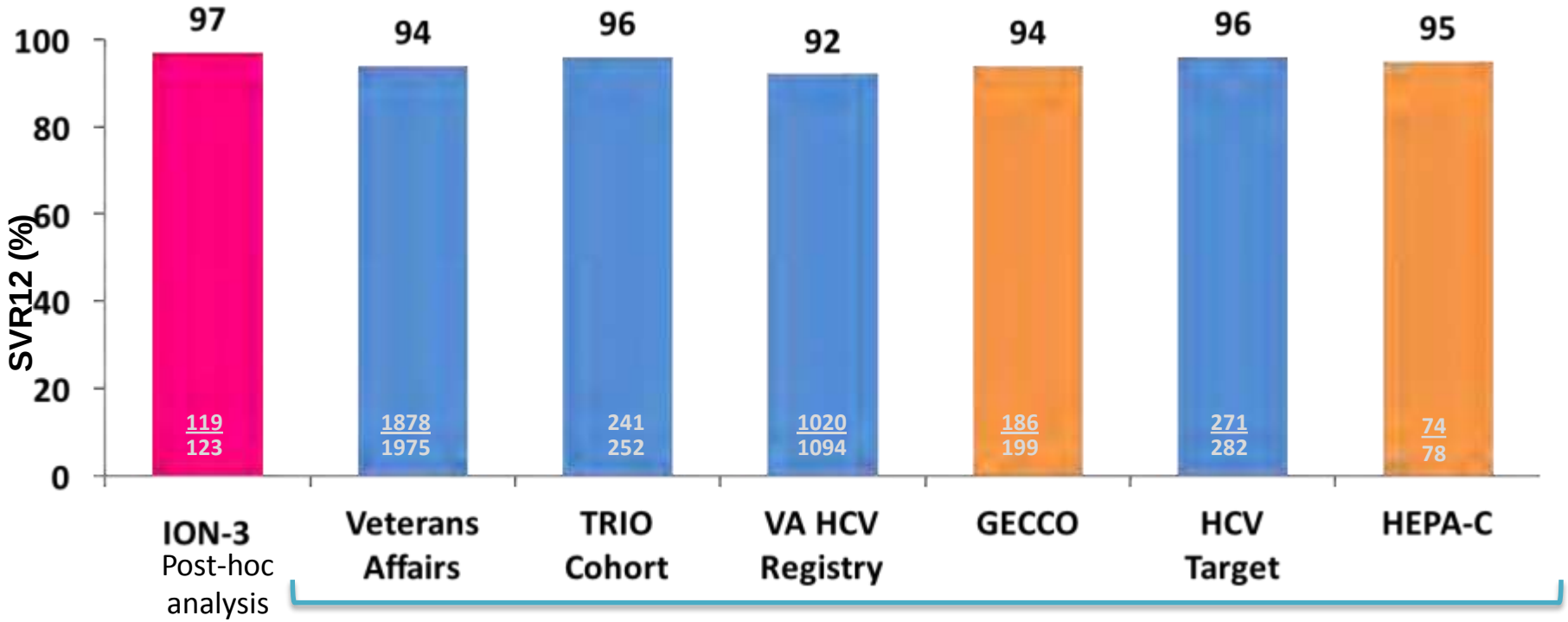
≥90%

- **External factors:**
  - **Approved drugs and their "label"**
  - **Access and ease of getting DAA approved**

Low Viral Load

8-weeks of LDV-SOF is Treatment of Choice

for GT-1 with VL <6M IU/mL and *no cirrhosis*



Real-world data suggests high SVR rates with 8-wks regimen in appropriate patients

Kowdley K, N Engl J Med 2015 ; O'Brien T, Hepatology 2016; Ioannou G, Gastroenterology 2016; Younossi Y, AJMC, 2016; Backus L, Hepatology 2016; Ingiliiz P, Clin Infect Dis, 2016; Terrault N, HCV-TARGET. Gastroenterology 2016

Zepatier

No RAS testing needed if VL < 800 000

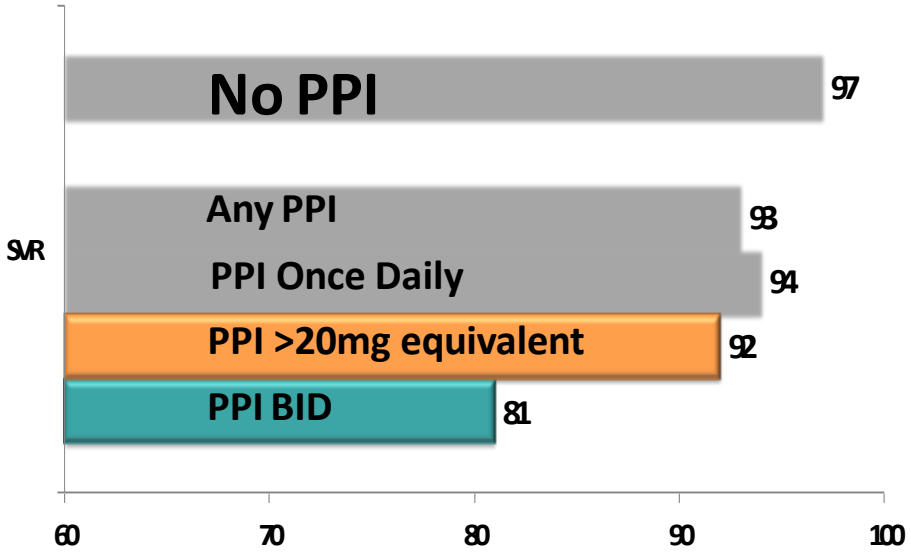
Treatment 12 weeks no ribavirin

Acid suppression therapy

High Dose PPI Use Significantly Impacts Efficacy of LDV-SOF Therapy

HCV-Target

- PPI use at baseline was independent predictor of SVR
- OR=0.41 (95% CI: 0.25-0.67)



Terrault N, Gastroenterology 2016

TRIO

Propensity-Matched Cohorts

Group	All N=887	Cirrhosis N=337
No PPI	97%	96%
High dose PPI	98%	96%
BID PPI	91%	77%*
Any PPI	98%	96%

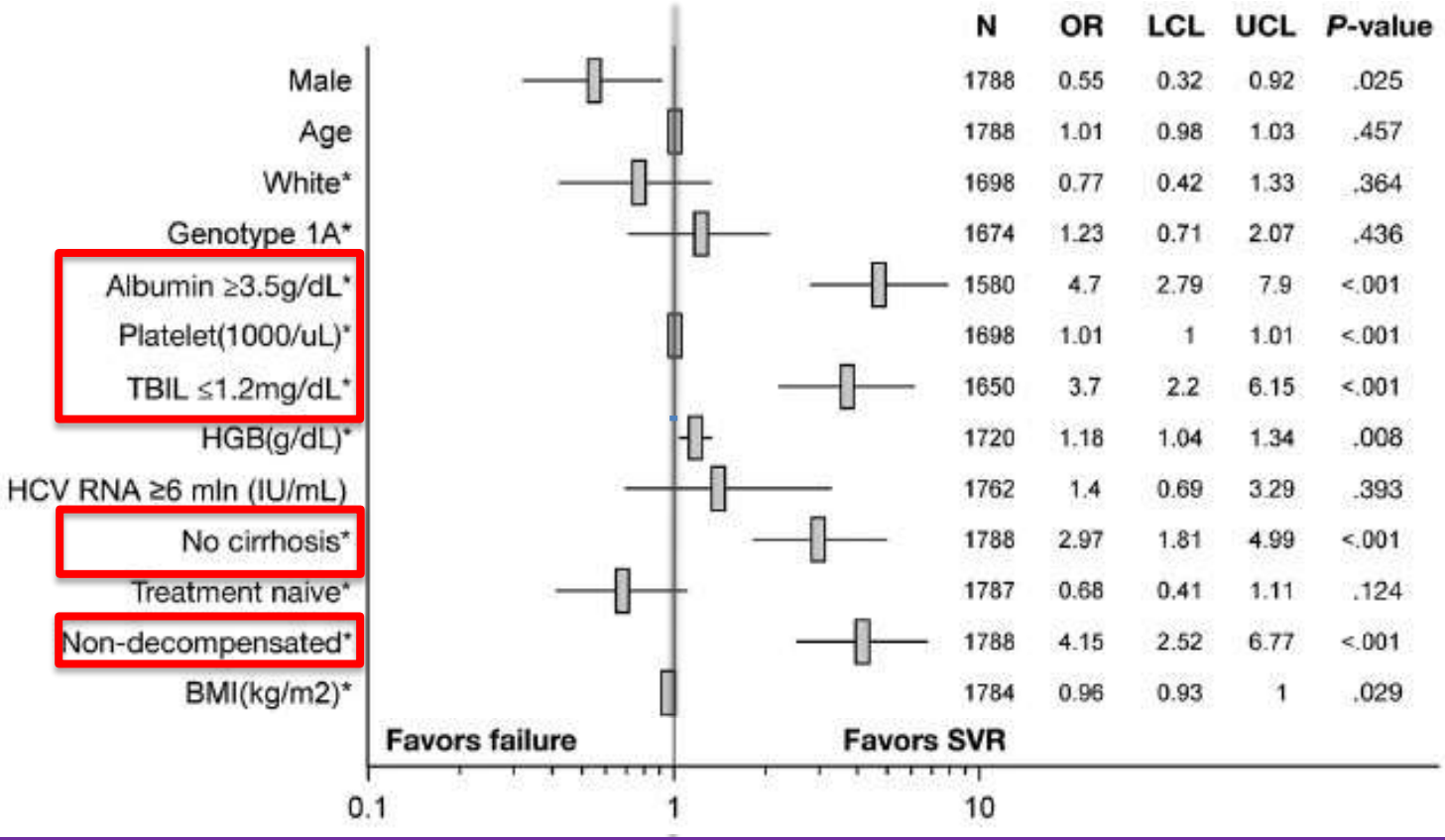
*P=0.05

- Only twice daily PPI at baseline associated with lower SVR
- Effect most marked in cirrhotics

Tapper E, Hepatology 2016

Cirrhosis, Especially if Decompensated, Reduced SVR Rates

Predictors of SVR in patients treated with SOF/LDV for 12 wks

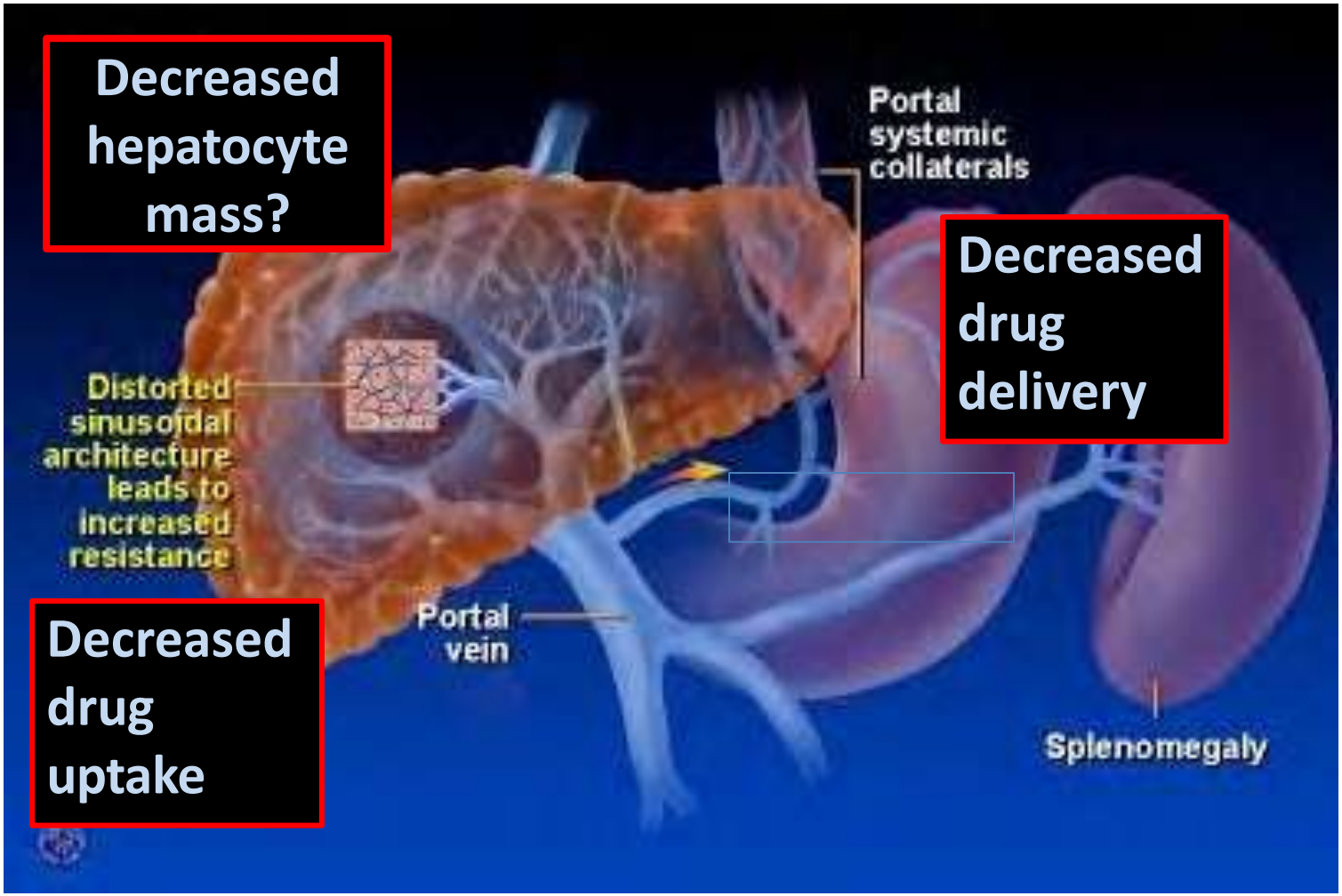


3 fold higher odds of SVR if no cirrhosis (vs. cirrhosis)
4 fold higher odds of SVR if compensated cirrhosis (vs decompensated)

SVR12: SVR at 12 (±1) weeks post treatment

Terrault N, et al Gastroenterology 2016

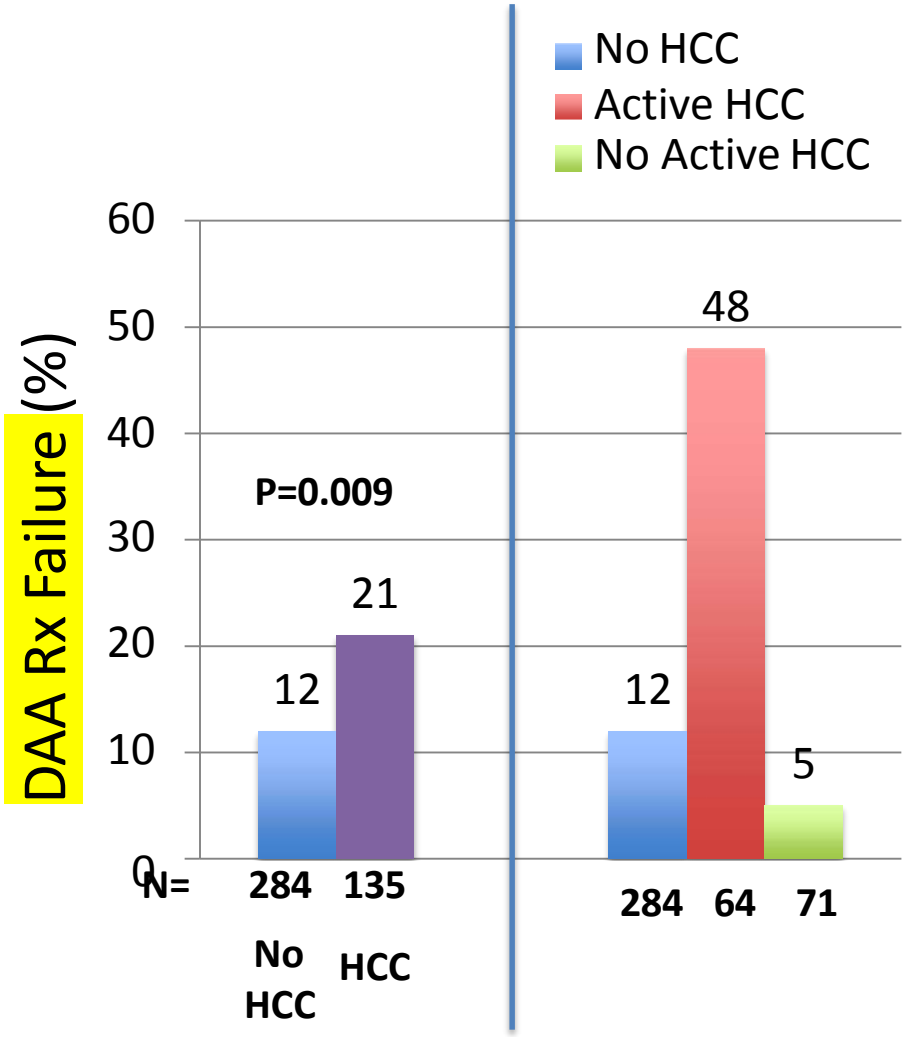
Why Higher Rates of Virologic Failure with Advanced Cirrhosis?



HCC

Does liver cancer sequester virus?

SVR12 Rates Reduced in Patients with HCV and "Active" HCC



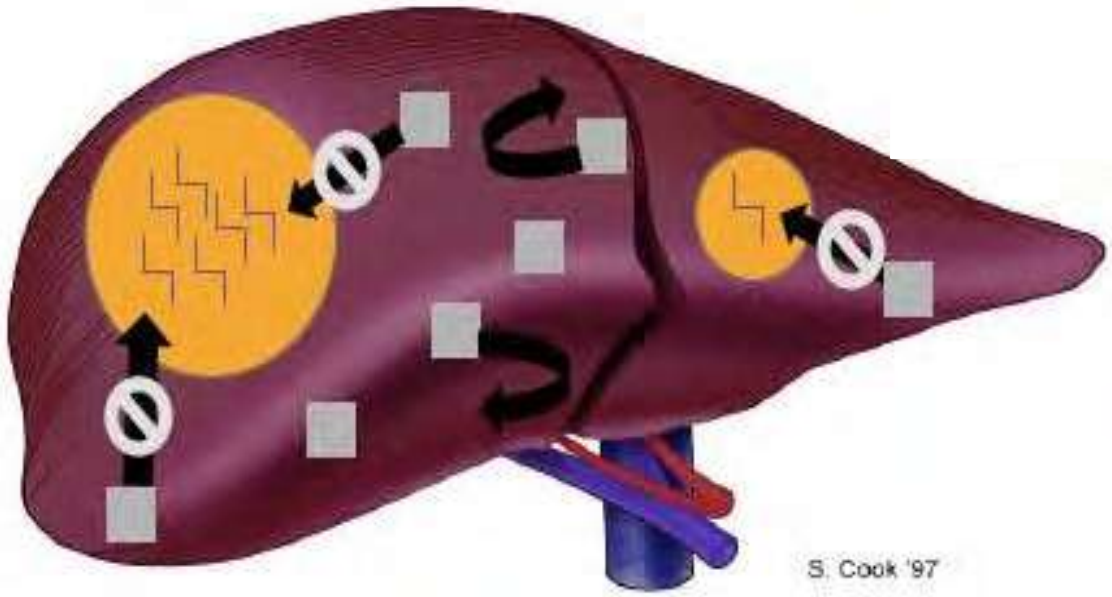
Predictors of DAA Treatment Failure

Covariates	OR	95% CI	P Value
Inadequate regimen	2.85	1.32-6.16	0.008
Active tumor	**8.49**	**3.90-18.49**	**<0.001**
Platelet count	0.99	0.99-1.0	0.09

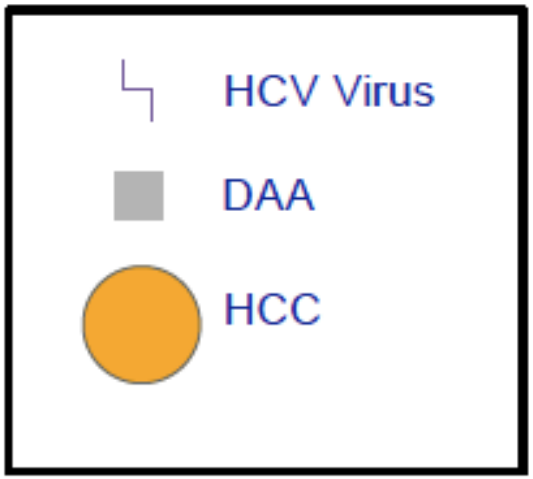
Adjusted for age, sex, race, CPT class, genotype and anti-HBc

Prenner S et al, J Hepatology, 2017

Why Higher Rates of Virologic Failure if HCC is Present?



HCC Liver

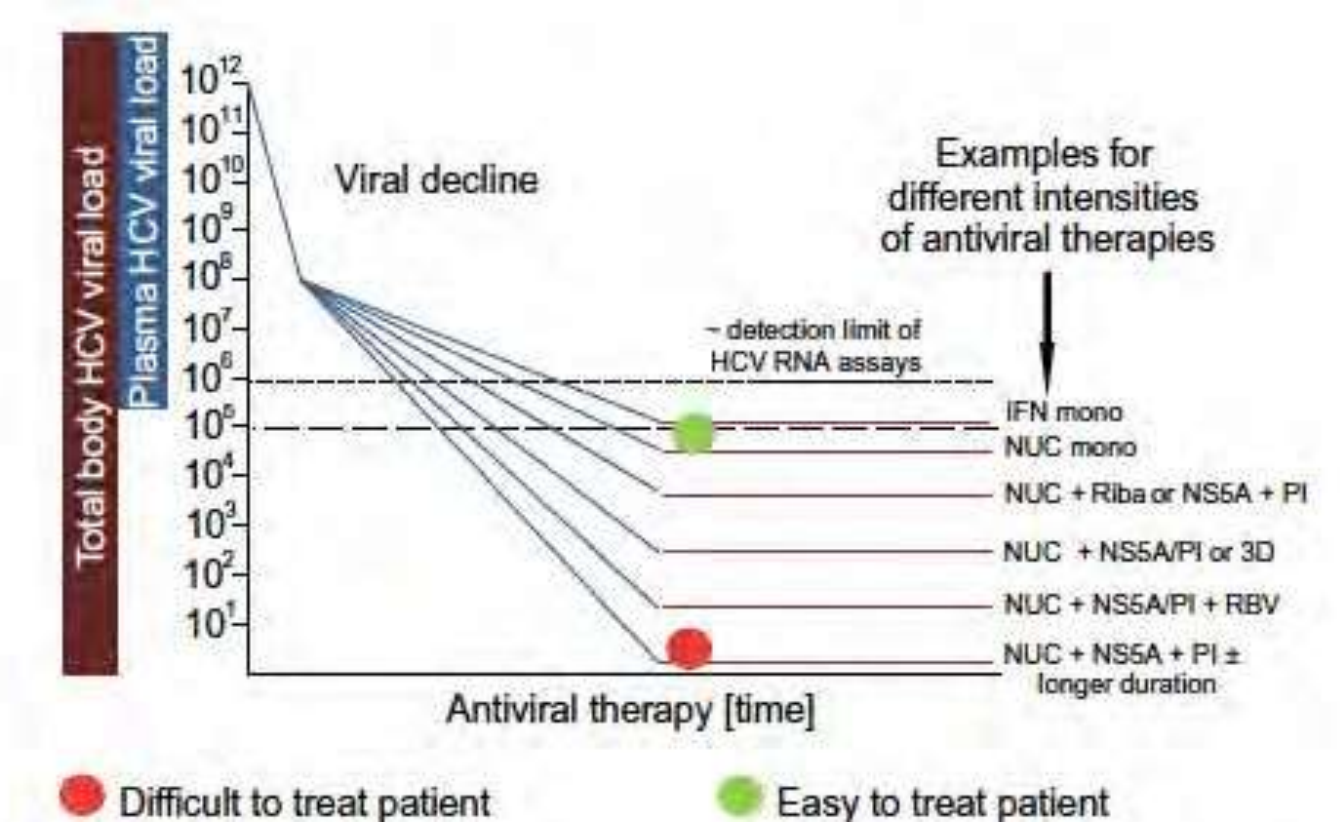


Prenner S et al, J Hepatology, 2017, in press

Composite of special populations

Conceptual Framework for Special Populations

- High VL
  HIV Renal dx
- Cirrhosis
- Child-Pugh Score
- Prior Treatment
- Genotype 3
- IL28B non-CC
- Baseline RAVs
- PPI Use Adherence
- HCC



Multiplicity of negative factors increases chances of treatment failure

Sarrazin C, J Hepatol 2016;64:486–504

We are choosing the best medications:

With low side effect profiles

1 pill per day

Pan-genotypic

Use in liver failure

Use in renal failure

Few DDI

What Was Special About These Additions?

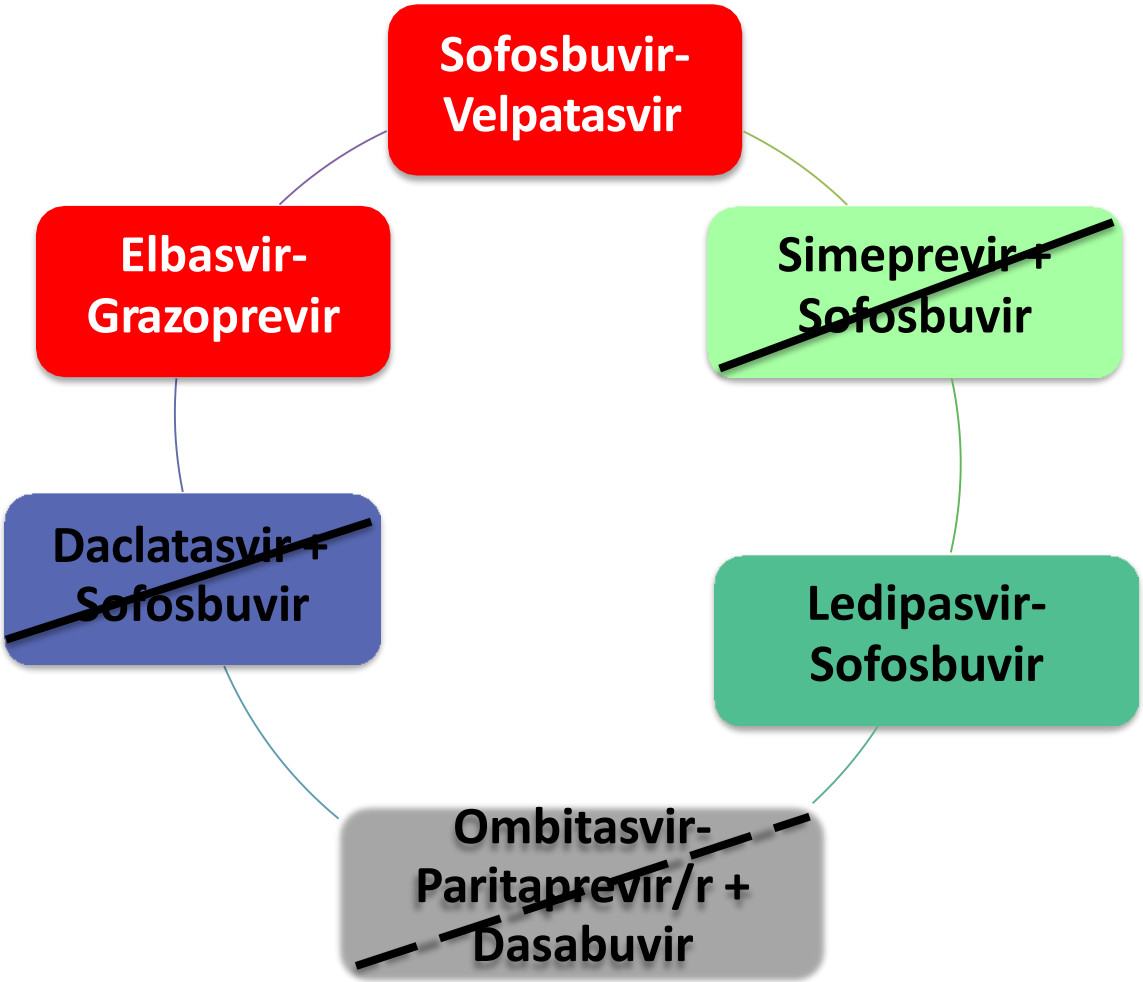
One-pill daily for 12 weeks for majority of patients

SOF-VEL

- Pangenotypic
- First RBV-free therapy for G2/3

EBR-GZP: G1, 4

- Ideal for ESRD patients
- RBV-free option for those on PPIs
  - High response in Compensated cirrhosis



± Ribavirin

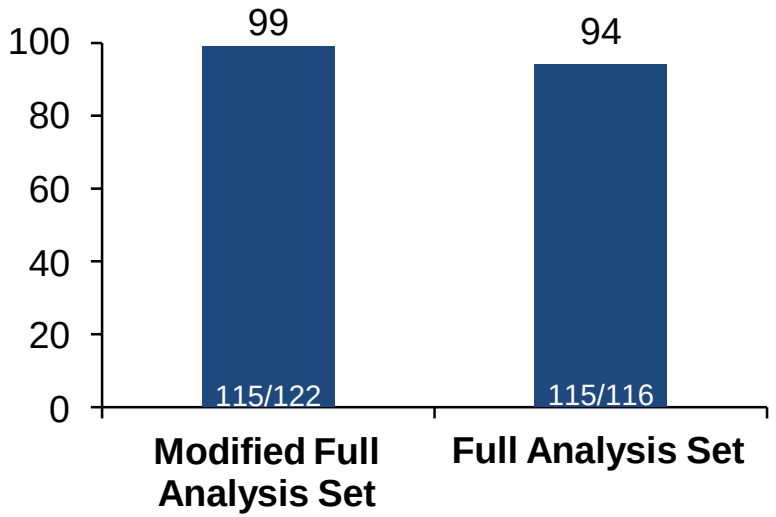
Renal failure

A major population in need of treatment

Elbasvir/Grazoprevir in HCV Genotype 1 and Chronic Kidney Disease (C-SURFER)

- **RCT of Elbasvir-Grazoprevir (50/100) for 12 wks vs placebo**

Characteristic	N=235 (%)
AA race	6%
Prior Treatment	20%
Cirrhosis	6%
G1A G1B	52% 47%
CKD Stage 4 Stage 5 Dialysis	 18% 82% 76%



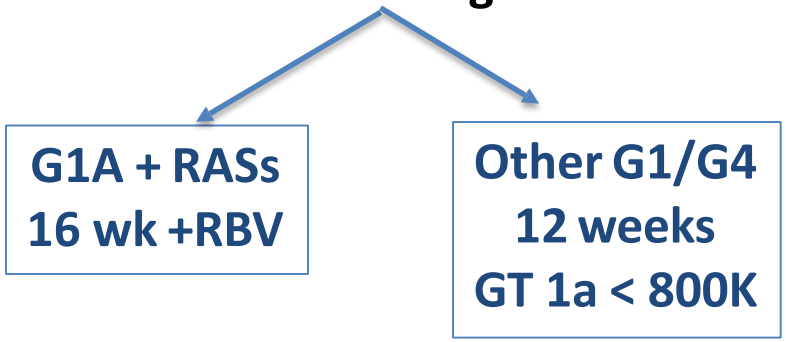
Relapse	1	1
D/C early	6	0

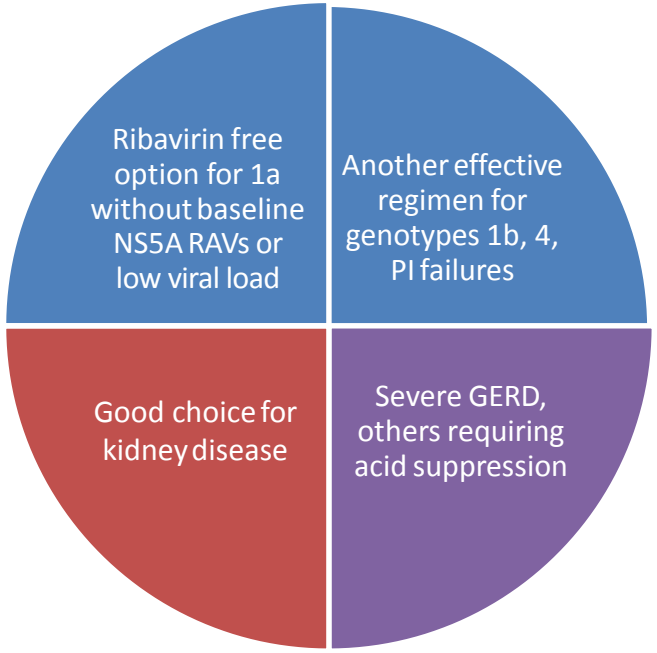
- **Adverse effects similar to placebo group, including anemia**

Roth D, et al. *Lancet.* 2015 Oct 17;386(10003):1537-45.

Where Does Elbasvir/Grazoprevir Fit In?

- Excellent rates of SVR
- Easy to use –
- < 800 000 IU no riba 12 weeks
- but requires RAS testing if 1A
  but not in renal failure patients
- Treatment algorithm, is otherwise straightforward





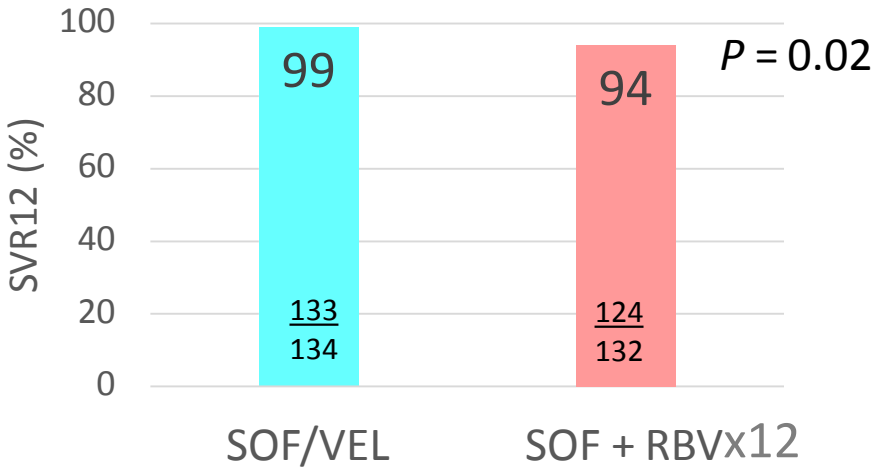
Same if:

- Cirrhosis (compensated)/no cirrhosis
- Treatment naïve or experienced
- HIV positive or negative
- Renal failure or not

Sofosbuvir/Velpatasvir vs SOF/RBV

ASTRAL-2

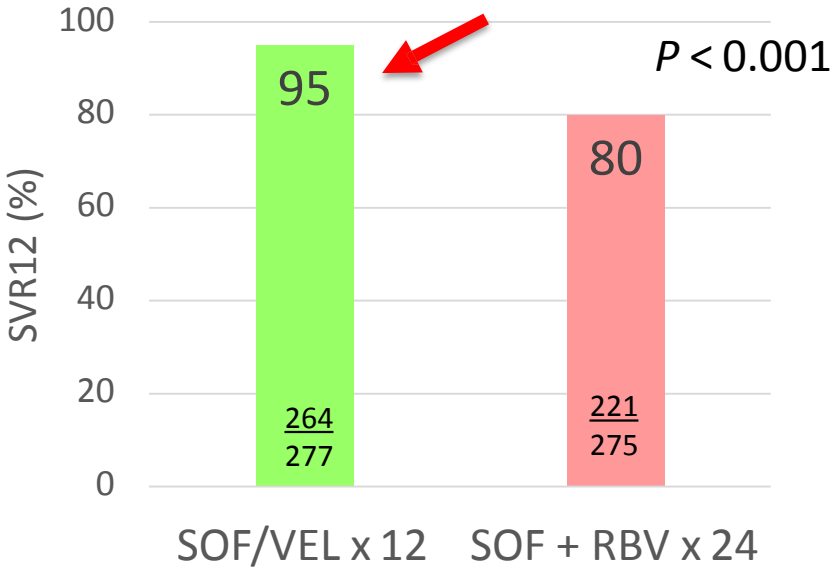
- HCV genotype 2
- Naïve and previously treated
  Compensated cirrhosis included



Endpoint, n (%)	SOF/VEL	SOF + RBV
Relapse	0	6 (5)
Discontinuations due to AE	1 (1)	0

ASTRAL-3

- HCV genotype 3
- Naïve and previously treated
  Compensated cirrhosis included



Endpoint, n (%)	SOF/VEL	SOF + RBV
Relapse	11 (4)	38 (4)
Breakthrough	0	1 (<1)

Foster GR. N Engl J Med 2015:373(27):2608-17

Genotype 2: not covered well by

Zepatier
Viekira
SOF LED

AASLD/IDSA Guidance: is this best for VN?

Genotype 2

Population	SOF/RBV	DAC/SOF	SOF/VEL
G2, naïve, no cirrhosis	Not recommended	Alternative, 12 weeks	✓ 12 weeks
G2, naive , compensated cirrhosis	Not recommended	Alternative, 16-24 weeks	✓ 12 weeks
G2, PEG/RBV, no cirrhosis	Not recommended	Alternative, 12 weeks	✓ 12 weeks
G2, PEG/RBV, compensated cirrhosis	Not recommended	Alternative, 16-24 weeks	✓ 12 weeks
G2, SOF/RBV	Not recommended	✓ 24 wks, + RBV	✓ 12 weeks + RBV

hcvguidelines.org

General Approach to Patient Who Has Failed DAA Therapy

- Compliance
- Virologic evaluation
  - Exclude genotype shift
  - Exclude HCV reinfection
  - Assess for RASs
- Approach guided by urgency of retreatment
  - Most patients can await next generation DAAs
- If must treat NOW
  - Tailor regimen according to results of RAS testing; use drugs without cross-resistance
  - If no RAS: Extend duration to 24 weeks
  - Add weight-based ribavirin, if not contraindicated

What's Available Now/soon?

- Retreatment with SOF/LED +- Riba 24 weeks
  - GT 1, 3, 4, 5, 6
- Sofosbuvir/velpatasvir + RBV
  - All genotypes, extensive data for GT 1 - 3
  - Also OK to use in decompensated patients (CTP B/C)
  - 24 weeks
- Sofosbuvir + elbasvir/grazoprevir + RBV
  - Data for GT 1 and 4
  - Contraindicated in decompensated patients
  - 12-24 weeks
- Also: SMV/SOF + RBV x 24, PROD + SOF + RBV x 24

REVENGE Retreatment: EBR/GZR + SOF + RBV X 16 vs 24 weeks

- GT 1 and 4 with documented NS5A or NS3 RASs
- Included patients with compensated cirrhosis
- SOF + EBR/GZR + RBV for 16 vs 24 weeks in DAA failures (SIM, LDV, DCV) +/- RBV

PATIENTS & METHODS

Randomized, double arm, multicenter, open-labeled, Phase II pilot study conducted in France.

Main inclusion criteria

- Adult ≥18 years
- Infection with HCV genotype 1 or 4, confirmed by detectable HCV RNA at pre-inclusion
- Failure to a prior therapy with Sofosbuvir +/- Ribavirin associated with Simeprevir or Daclatasvir or Ledipasvir, with documented presence of NS5A or NS3 RASs (Resistance-Associated Substitutions) at the time of failure (presence of RASs on at least one sample since the time of failure).
- Fibrosis at any stage

Main non-inclusion criteria

- Child B or C cirrhosis (or Child A patients with history of Child B)
- Patients with documented presence of RASs conferring resistance to sofosbuvir
- Positive HBs Antigen
- Confirmed HIV-1 or HIV-2 infection
- Transplant recipients

- Prior DAAs used: SOF/LDV, SOF/DCV, SMV/SOF
- GT 1: 77% (20/26); GT 4 23% (6/26)
- > 50% of patients had cirrhosis
- 24/26 patients had NS5A RASs, 17/24 had Y93

SVR4= 100%

De Ledinghen V et al.: AASLD 2016; abstract LB-18

AASLD Guidelines

Recommended for All Patients with HCV Infection Who Have Decompensated Cirrhosis

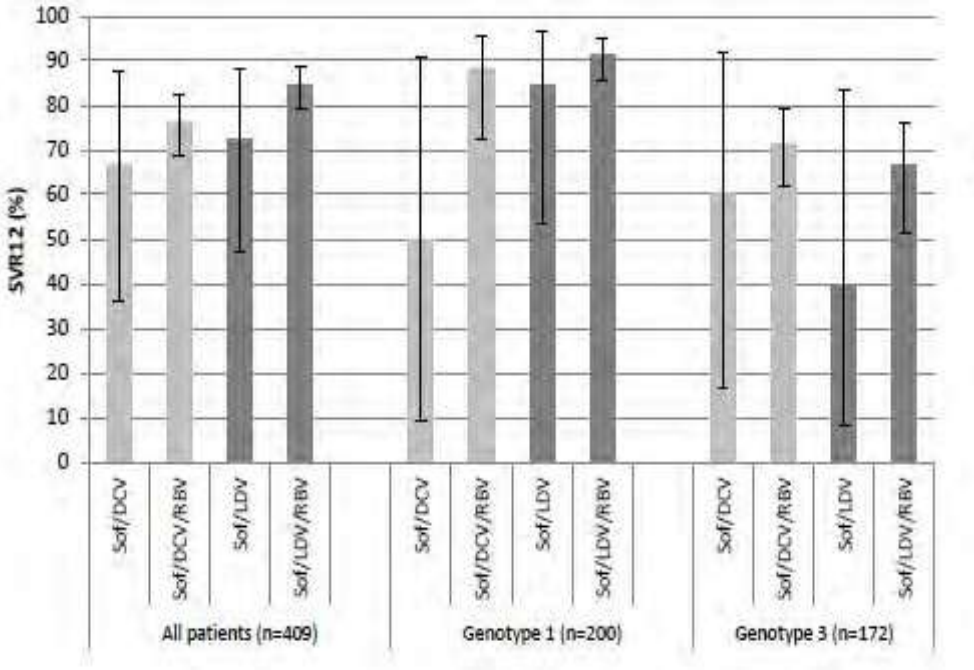
- Patients with HCV infection who have decompensated cirrhosis (moderate or severe hepatic impairment; Child Turcotte Pugh [CTP] class B or C) should be referred to a medical practitioner with expertise in that condition (ideally in a liver transplant center).

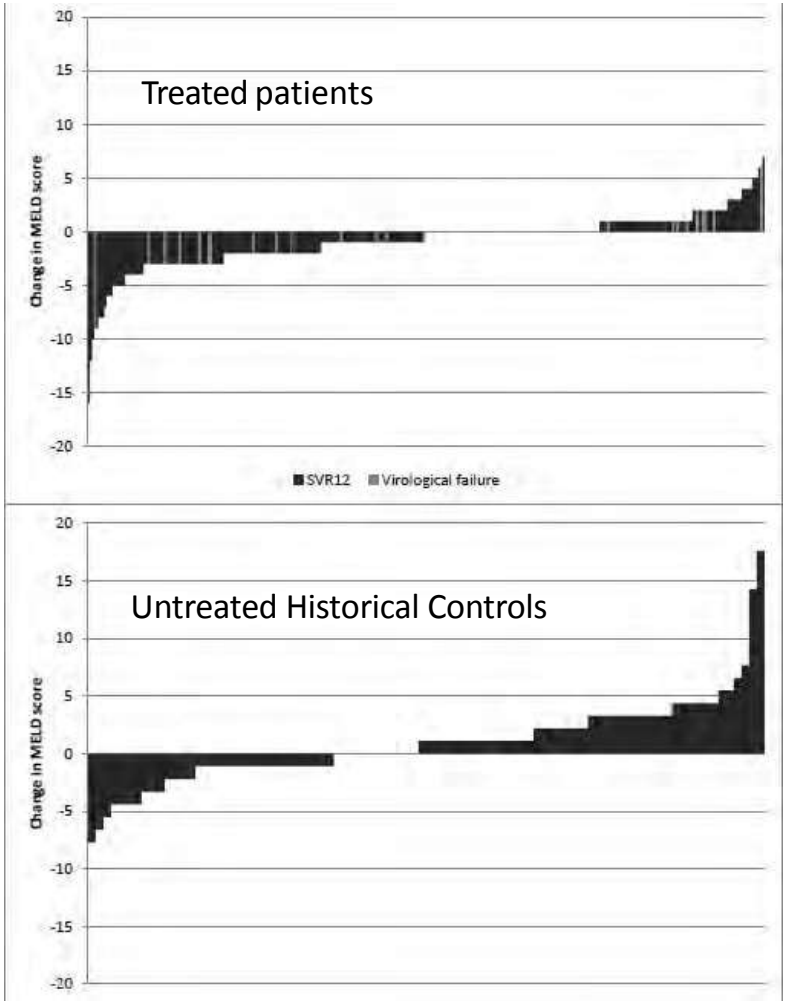
  Rating: Class I, Level C

AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org.

Impact of HCV Therapy on Decompensated Cirrhosis

- 409 patients with decompensated cirrhosis treated through expanded access program with SOF/LDV or SOF/DCV ±RBV for 12 weeks



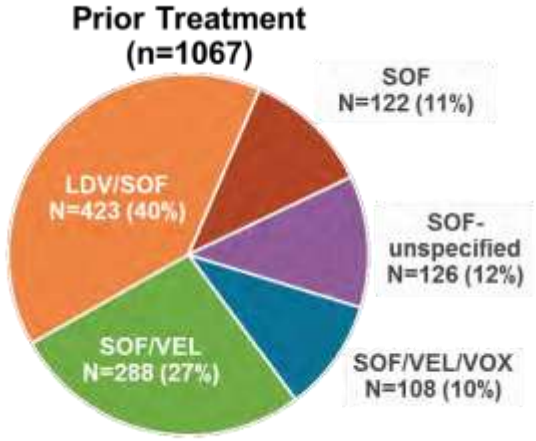


Foster et al, J Hep 2016

Long-term Follow-up of >1,000 HCV Patients With Compensated or Decompensated Cirrhosis Who Achieved SVR Following Treatment With Sofosbuvir-Based Regimens

Assessments

- Every 6 mo: HCV RNA; labs, CPT, MELD; any occurrence within preceding 6 mo of HCC, death, liver transplant, and hepatic events, and results of endoscopy or biopsy (if performed); health-related QoL questionnaires
- Baseline and yearly thereafter: transient elastography
- Baseline and Week 240: endoscopy
- End of study: liver biopsy (optional)



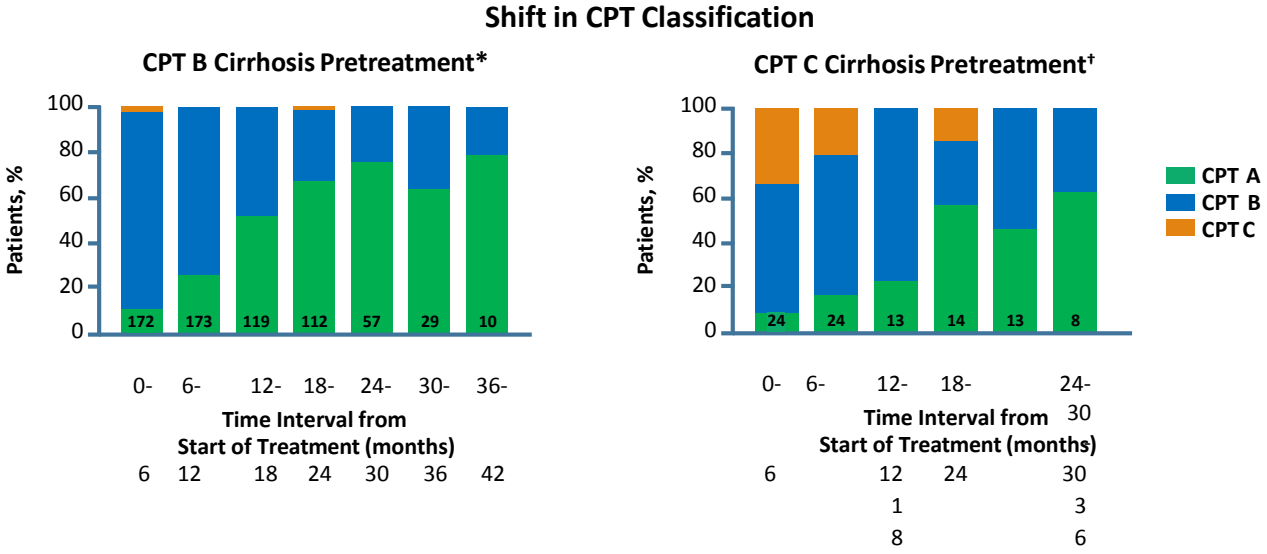
Muir A, AASLD, 2016, #880

Demographics and Disease Characteristics

			N=1067
Demographics	Mean age, y (range)		59 (33–83)
	Male, n (%)		712 (67)
	Race, n (%)	White	915 (86)
		Black	92 (9)
	Hispanic/Latino		145 (14)
	Region, n (%)	North America	840 (78)
		Europe	149 (14)
		Australia/New Zealand	71 (7)
	Patient source, n (%)	Clinical study	834 (78)
		Clinical practice	233 (22)
	Mean BMI, kg/m^2 (Q1, Q3)		30 (26, 33)
Disease characteristics	Mean time since HCV diagnosis, y (range)		14 (1–51)
	Cirrhosis, n (%)*		1064 (>99)
	Decompensated		201 (19)
	HCV GT, n (%)	1	592 (55)
		2	49 (5)
		3	148 (14)
		4–6	43 (4)
		Missing	235 (22)
	Median platelets, x10^3/µL (range)		133 (20–626)

*Cirrhosis status determined prior to treatment with SOF-based regimen resulting in SVR. BMI, body mass index;GT, genotype; IL28B, interleukin-28B; Q, quartile.

Long-term Follow-up of >1,000 HCV Patients With Compensated or Decompensated Cirrhosis Who Achieved SVR Following Treatment With Sofosbuvir-Based Regimens

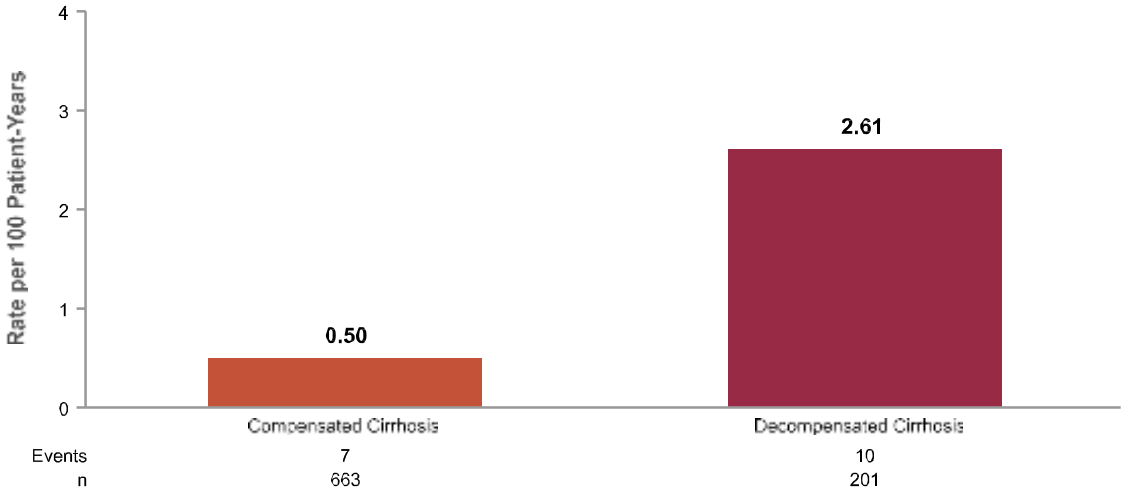


- The majority of patients maintained or improved their CPT category relative to pretreatment through up to 36 (CPT C) or 42 (CPT B) months relative to treatment start
- Overall improvements in key laboratory components such as mean bilirubin and mean albumin were observed

*Only 1 patient with CPT B cirrhosis prior to treatment has reached >42 mo since start of treatment; this patient had CPT A cirrhosis at last assessment.
†Only 1 patient with CPT C cirrhosis prior to treatment has reached >36 mo since start of treatment; this patient had CPT A cirrhosis at last assessment.

Muir A, AASLD, 2016, #880

HCC : Long-term Follow-up of >1,000 HCV Patients With Compensated or Decompensated Cirrhosis Who Achieved SVR Following Treatment With Sofosbuvir-Based Regimens

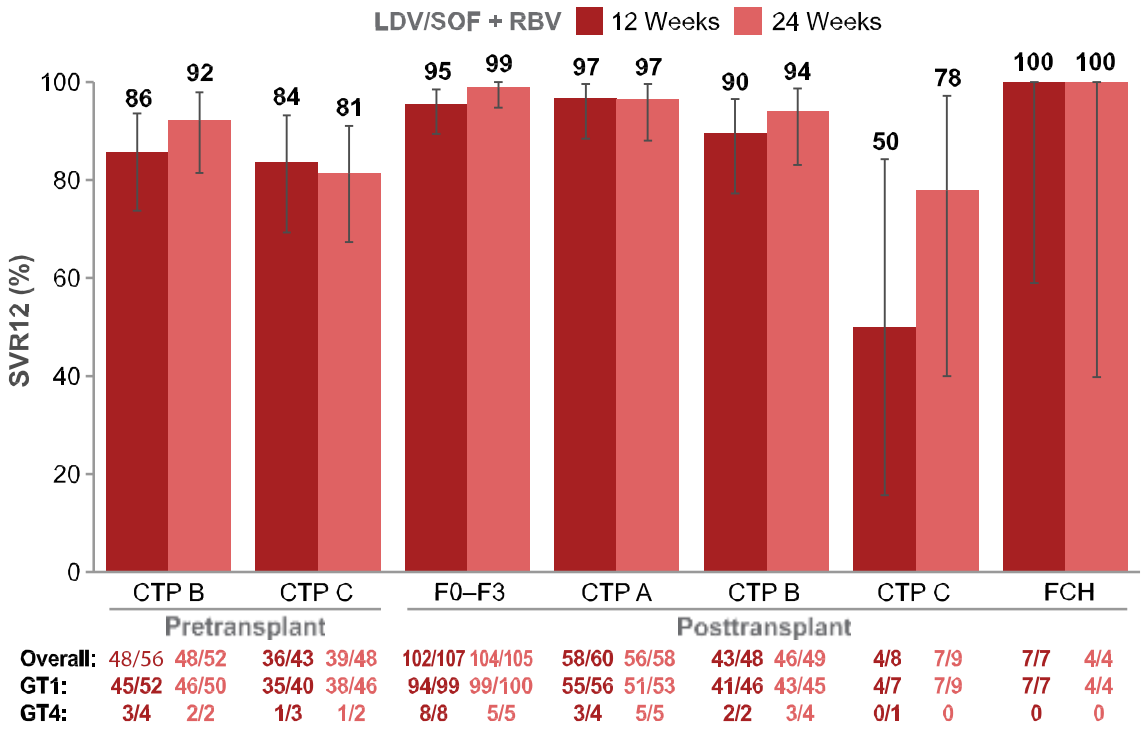


- >99% (1066/1067) have maintained SVR with a median (range) follow-up of 21 (2–44) months from end of treatment
- The incidence of de novo HCC among patients with compensated cirrhosis (0.50) was lower than the rates of 1.39 and 1.82 per 100 patient-years reported for IFN-treated patients with cirrhosis who achieved SVR[1,2]
- The incidence of de novo HCC was higher among patients with decompensated cirrhosis (2.61), most of whom would not have been treated in the past

1.El-Serag HB, et al. Hepatology 2016;64:130-7.
2.Hiramatsu N, et al. Hepatol Res 2015;45:152-61.

Muir A, AASLD, 2016, #880

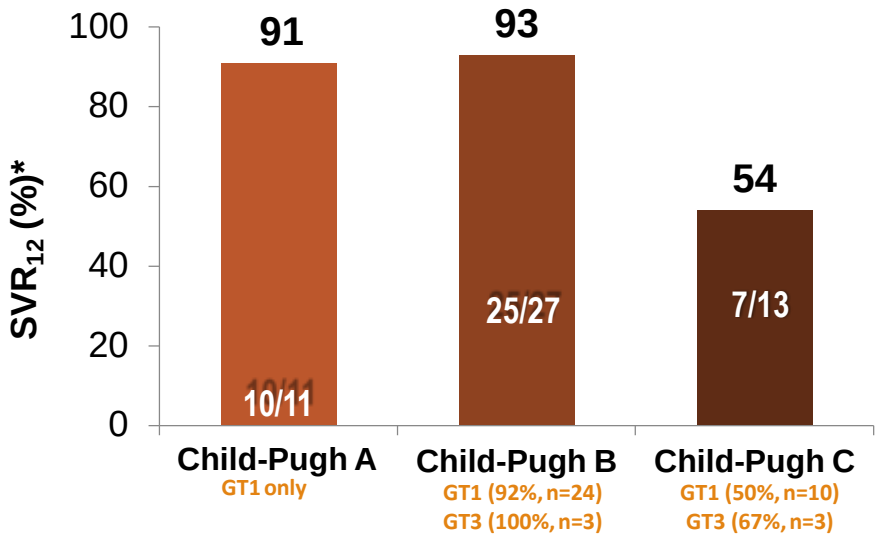
Efficacy



Gane, AASLD, 2015,1049

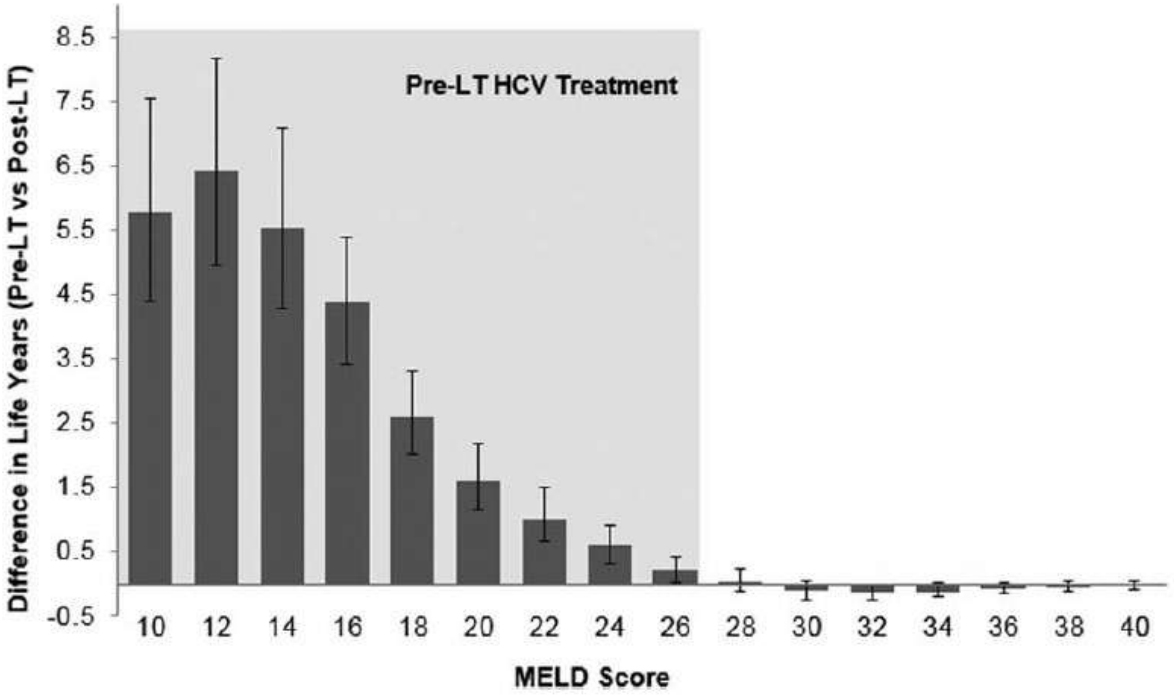
Analysis excluded 13 patients transplanted prior to posttreatment Week (FU) 12 with HCV RNA <LLOQ at last measurement prior to transplant, and 3 pretransplant patients who were CTP A at baseline. *Error bars* represent 95% confidence intervals (CIs).

GT1 and GT3 Decompensated Cirrhotics treated with SOF/DCV + RBV for 12 weeks



Daklinza™ (daclatasvir) Prescribing Information. Bristol-Myers Squibb Company, Princeton, NJ.

Life Expectancy with liver transplant a consideration for Timing of Treatment



**Based on modeling

Chhatwal et al, Hepatol 2017

So Treatment Before Transplant?

Pros

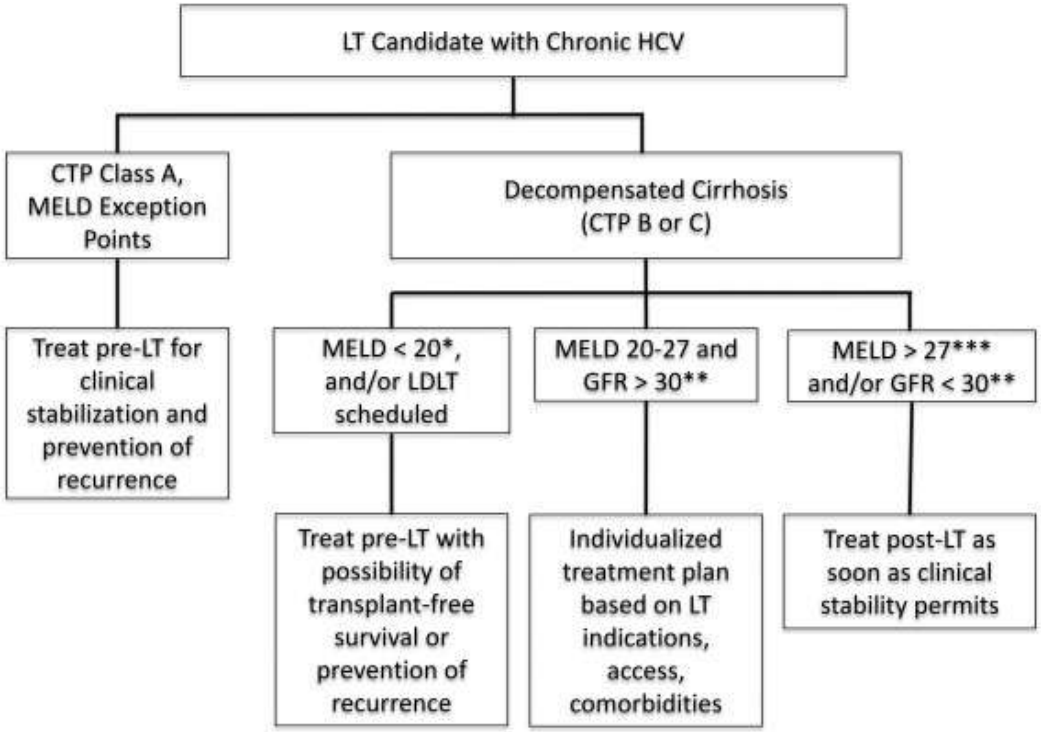
- Can remain active on waitlist during therapy
- Cure of HCV is likely:
  - May stabilize or improve liver disease
  - Decreased risk of progression/decompensation
  - Decreased risk of new onset diabetes after transplant
- Avoids drug interactions with IS
- Public health concern

Cons

- More ? Efficacious/safe in post transplant setting
- Cure eliminates HCV+ donor option
  - Longer wait times
  - May limit choice of deceased donor
  - May lose transplant opportunity
  - Inadvertantly shorten life expectancy
  - Increased graft discard rate
- Potential DDI necessitates close IS monitoring

Sawinski et al, Transplantation 2015

Proposed Algorithm for HCV treatment for Liver Transplant Candidates

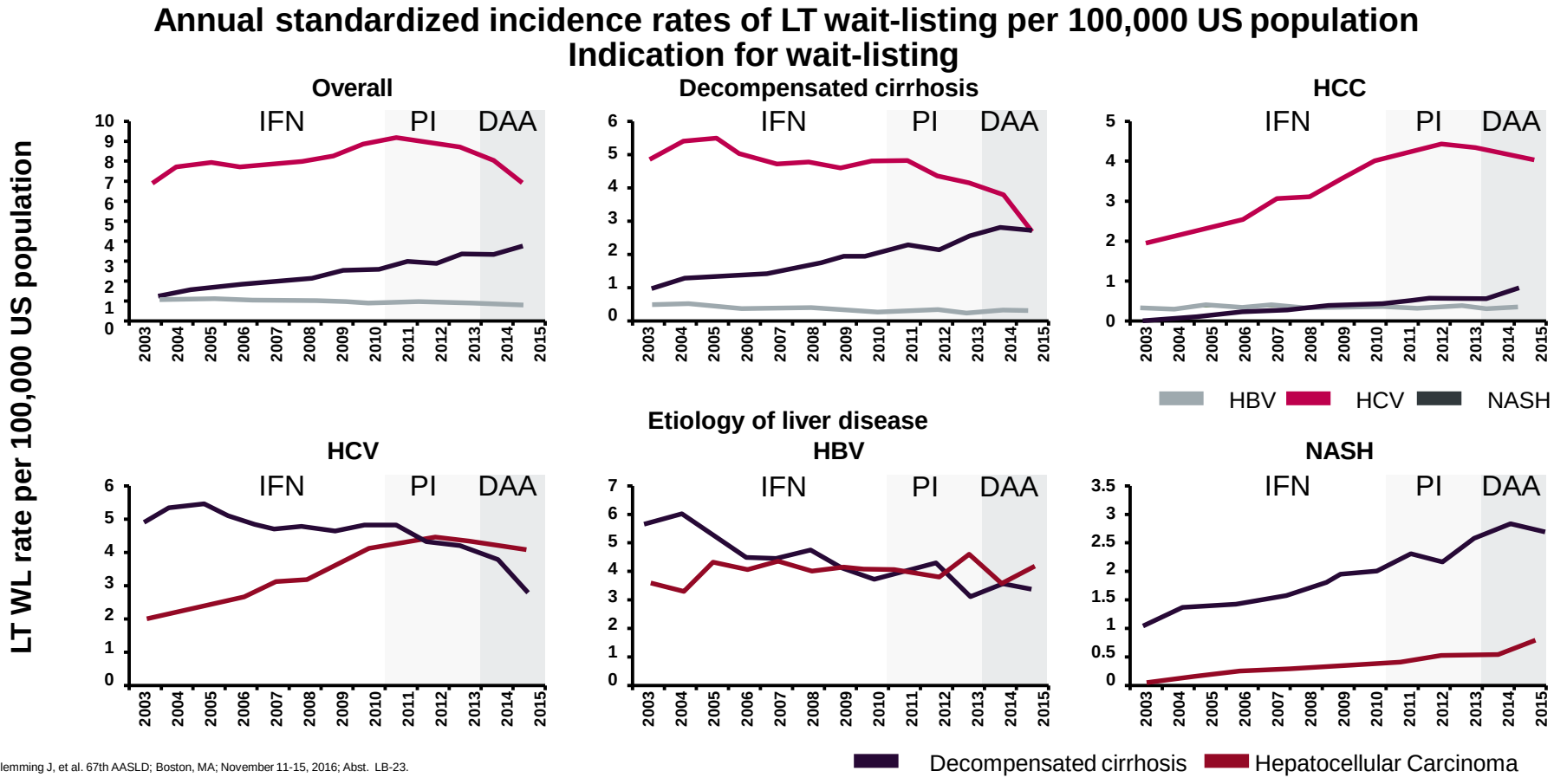


Verna E, Hepatol 2017

DAAs in Advanced Liver and/or Renal Disease

	CTP A	CTP B	CTP C	GFR<30 or dialysis
Simeprevir	✓	NO	NO	✓(but needs SOF so NO)
Sofosbuvir/Ledipasvir	✓	✓	✓	NO
Sofosbuvir/Velpatasvir	✓	✓	✓	NO
Daclatasvir	✓	✓	✓	✓(but needs SOF so NO)
Paritaprevir/r/ombitasvir /dasabuvir	✓	NO	NO	✓
Elbasvir/Grazoprevir	✓	NO	NO	✓

LB-23. Reduction in Liver Transplant Wait-Listing in the Era of Direct Acting Anti-Viral Therapy



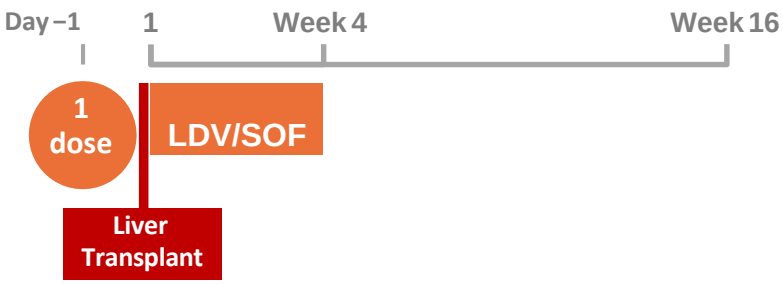
Flemming J, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. LB-23.

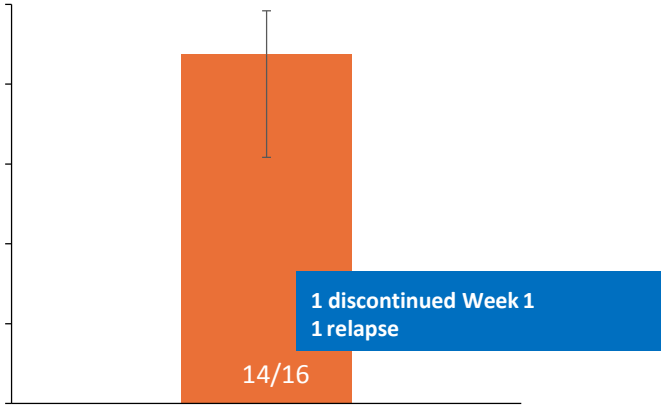
Post Liver Transplant

Natural History of HCV Pre vs Post Transplant

	Immunocompetent	Post-Transplant
Fibrosis Progression per year	0.1-0.2/year	0.4-0.6/year
Median Time to Cirrhosis	20-30 years	10-12 years
Decompensation after Cirrhosis	20% in 10 years	50% in 1 year
Survival after Decompensation	50% in 5 years	40% in 1 year

LDV/SOF peri-OLT for 4 weeks to prevent HCV recurrence





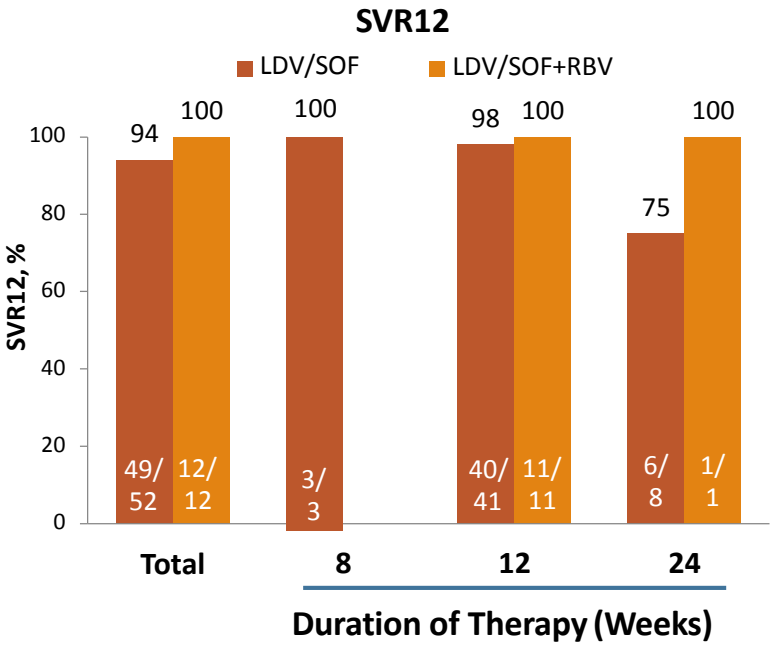
LDV/SOF±RBV for Recurrent HCV in Liver Transplant Recipients: Interim Analysis

Multicenter, retrospective analysis of LDV/SOF±RBV in 190 patients with HCV recurrence post-liver transplant

Baseline Demographics

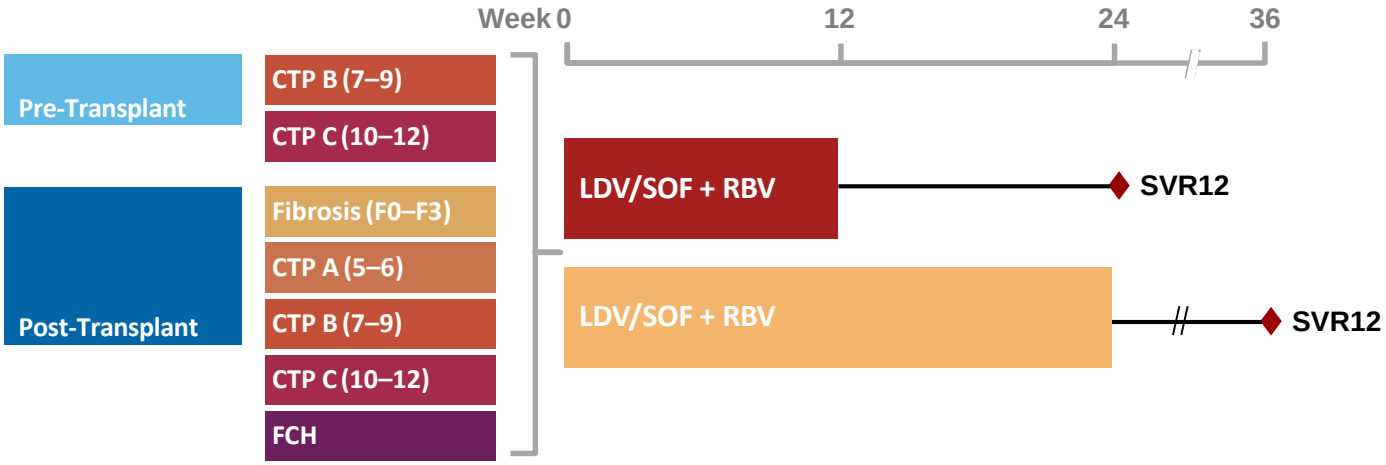
Patients	LDV/SOF±RBV n=190
Mean age, years ± SD	56 ± 6
Male, n (%)	136 (72)
Caucasian, n (%)	125 (66)
GT 1a, n (%)	128 (67)
GT 1b, n (%)	45 (24)
Treatment naïve, n (%)	98 (52)
F0-F2, n (%)	128 (67)
F3-F4, n (%)	40 (21)

- Common AEs: fatigue, headache, nausea
- 3 (2%) D/C due to AEs
- Immunosuppressant adjustment in 60 (32%)



Kwok, AASLD 2015,1101

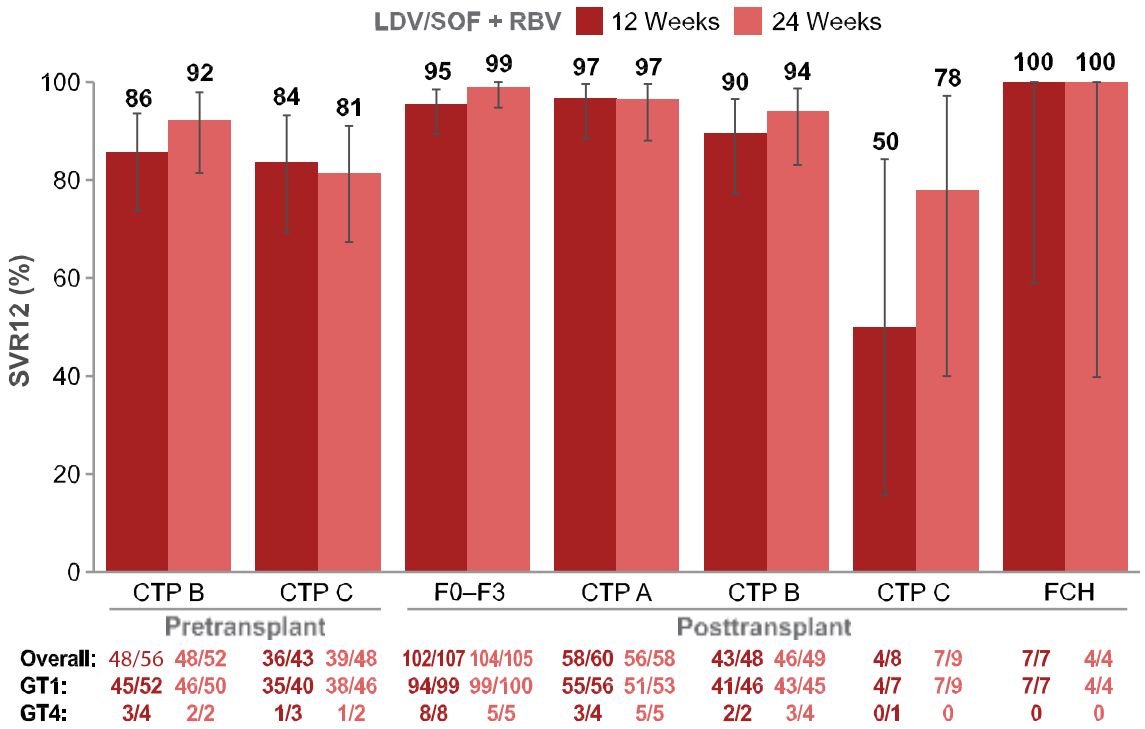
LDV/SOF+RBV for 12 or 24 Weeks in 667 Decompensated and Post-Liver Transplant HCV GT 1 and GT 4 Patients



- Broad inclusion criteria:
  - No hepatocellular carcinoma (HCC)
  - Total bilirubin ≤ 10 mg/dL, Hemoglobin ≥ 10 g/dL
  - CrCl ≥ 40 mL/min, Platelets > 30,000/mL
- RBV dosing
  - FCH, Metavir F0–F3 and CTP A cirrhosis: weight-based (1000 mg or 1200 mg)
  - CTP B and C cirrhosis (pre- and post-transplant: dose escalation, 600–1200 mg/d

Gane, AASLD, 2015, 1049

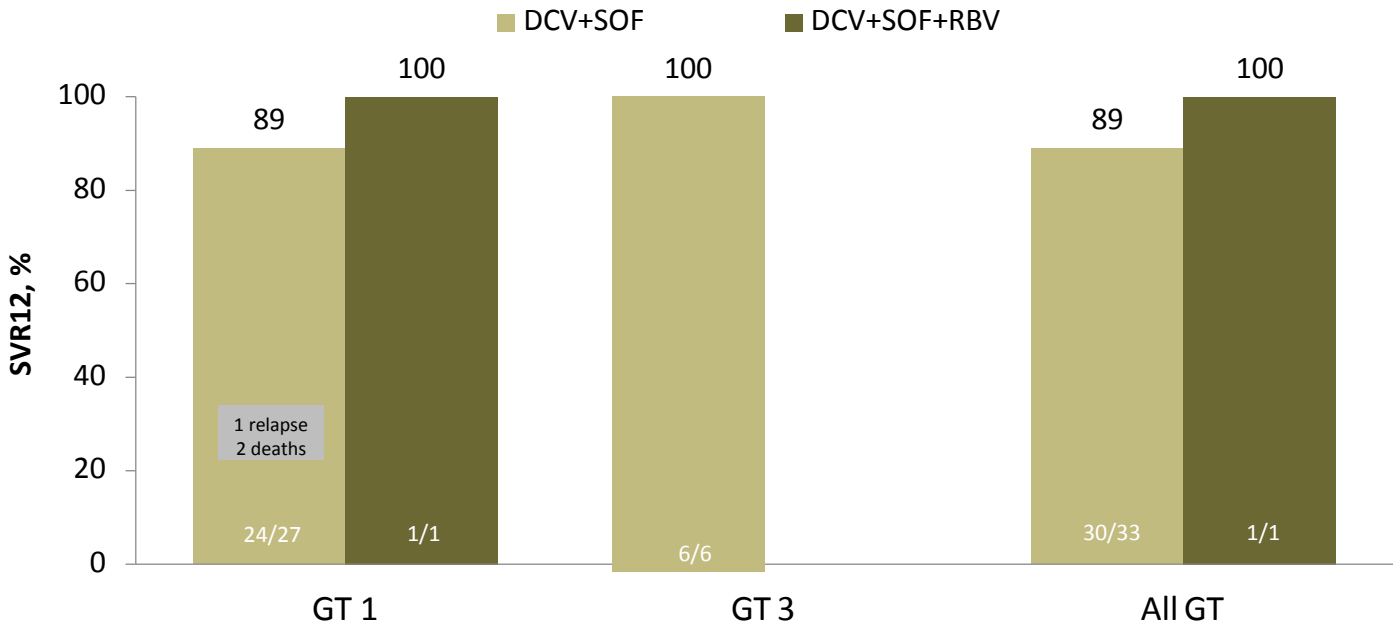
Efficacy



Gane, AASLD, 2015,1049

Analysis excluded 13 patients transplanted prior to posttreatment Week (FU) 12 with HCV RNA <LLOQ at last measurement prior to transplant, and 3 pretransplant patients who were CTP A at baseline. *Error bars* represent 95% confidence intervals (CIs).

DCV+SOF in Patients with Recurrent HCV Following Liver Transplantation

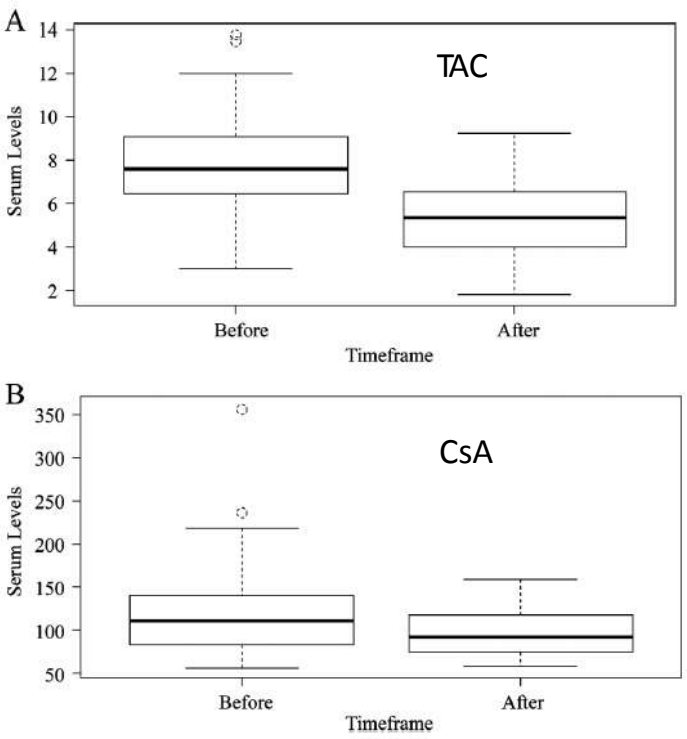


- 7/58 patients had FCH, of whom 4 had data at post-treatment Week 12
  - All 4 showed rapid viral decline and achieved SVR12

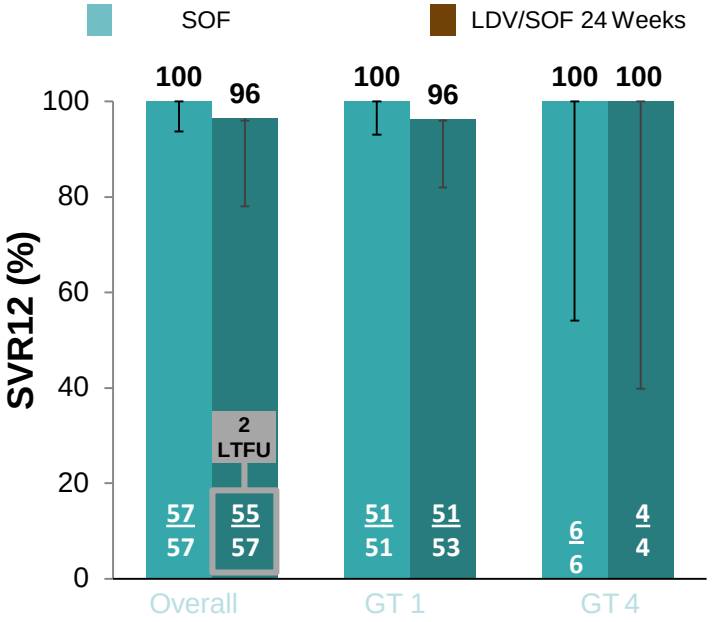
Kwo, AASLD, 2015,220

Changes in IS Drug Levels After SVR

- Curing HCV may result in increased immunosuppression dosing needs due to increased drug metabolism
- Caution to monitor drug levels carefully during and after treatment to minimize risk of ACR, especially with tacrolimus



LDV/SOF for 12 or 24 Weeks in Kidney Transplant Recipients with GT1 or 4 HCV



	LDV/SOF 12 or 24 weeks n=114
AE	78 (68)
Serious AE	13 (11)
Grade 3–4 laboratory abnormality	25 (22)

LDV/SOF for 12 weeks resulted in 100% SVR12 in HCV-infected kidney transplant irrespective of cirrhosis and treatment experience

Error bars represent 95% confidence intervals.

Colombo, EASL 2016, Oral GS-13

Summary: DAAs, Cirrhosis, Post Transplant

	Cirrhosis			Post Transplant Immunosuppression	
Regimen	CTP A	CTP B	CTP C	Tacrolimus	Cyclosporine
Ledipasvir/SOF	Yes	Yes	Yes	Yes	Yes some DDIs
Daclastavir/SOF	Yes	Yes	Yes	Yes	Yes
Grazoprevir/Elbasvir	Yes	NO	NO	Yes some DDIs	NO
Paritaprevir/Ritonovir/ Ombitasvir/Dasabuvir	Yes	NO	NO	Significant DDIs, only early stage fibrosis	Significant DDIs, only early stage fibrosis
Simeprevir/SOF	Yes	NO	NO	Yes some DDIs	NO

Other “New” Concerns

- **Drug toxicity**
- **HBV reactivation**

Drug Toxicities: Continued Vigilance

CORRESPONDENCE

Bradyarrhythmias Associated with Sofosbuvir Treatment

N Engl J Med 2015; 373:1886-1888 | November 5, 2015 | DOI: 10.1056/NEJMc1505967

- Prospective study from France, N=415
- 5 cases of severe arrhythmias (1.3%)
- All occurred within days of starting SOF
- 3 had pacemaker placed
- 1 recurred on re-challenge

Coadministration of sofosbuvir and amiodarone is not recommended
→reports of symptomatic bradycardia and a fatal cardiac arrest

October 22, 2015

FDA Drug Safety Communication: FDA warns of serious liver injury risk with hepatitis C treatments Viekira Pak and Technivie

- Ombitasvir-paritaprevir-ritonavir ± dasabuvir in cirrhotics → **hepatic decompensation, need for LT and death**
- Most cases occurred within one to four weeks of drug initiation
- Some of the cases occurred in patients for whom these medicines were contraindicated or not recommended

Are DAA's safe?

- Institute for Safe Medication Practices
  - "nation's only 501c (3) nonprofit organization devoted entirely to medication error prevention and safe medication use"
- Jan 25 2017 report
  - 12 months ending June 30, 2016
  - FDA Adverse Event Reporting System (FAERS) data
  - 524 cases of liver failure associated with drugs (worldwide)
    - ~50% with encephalopathy
    - 165 (31%) died
  - 1058 reports of severe liver injury
  - 761 cases with adverse event of virologic failure
  - 90% of reports by MD's
  - 34 cases from the literature

www.ismp.org/QuarterWatch/

Are DAA's safe? Yes: reporting of AE are biased by use in ill/ESLD patients

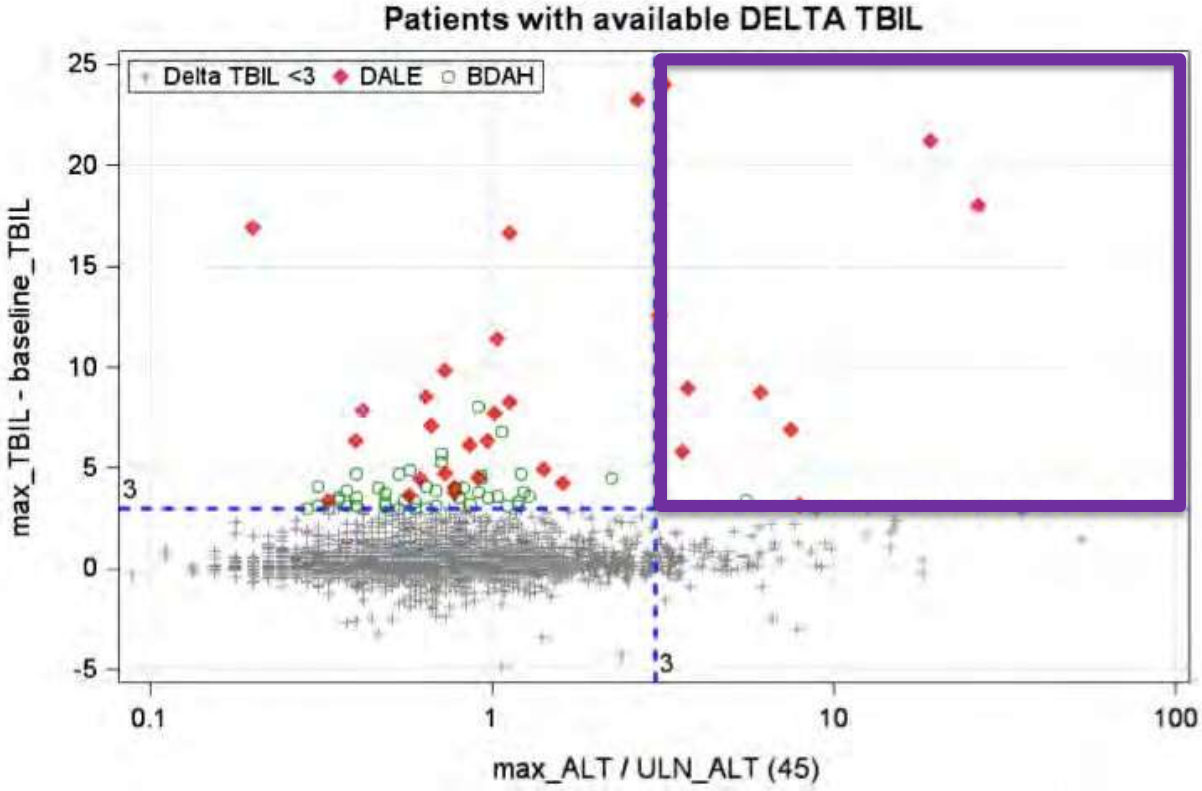
Primary and secondary drugs in liver injury cases				
Drug name	**Primary**	**Secondary**	**Total**	**Percent**
Daclatasvir	74	35	99	18.9%
Elbasvir-grazoprevir	1	0	1	0.2%
Ledipasvir-sofosbuvir	116	5	121	23.1%
Paritaprevir combos	120	61	181	34.5%
Simeprevir	16	21	37	7.1%
Sofosbuvir	91	80	171	32.6%

Limitations: incompleteness and bias of voluntary reporting

www.ismp.org/QuarterWatch/

Drug Associated Liver Events (DALE)

- Drug-induced liver injury (DILI) define by ALT as indicator of hepatocellular injury and total bilirubin (TBIL) as measure of impaired liver function alone and together
- Upper right quadrant = potential DILI cases, and normal cases are in the lower left quadrant (Guo T, et al., 2009).



N=10

3 completed treatment, no sequelae

2 LT on treatment

1 LT post-treatment

2 deaths, liver failure

2 Lost to f/u

Reference lines, 3xULN to account for RBV effects) for TBILxULN (ULN=1.2) and 3xULN for ALTxULN (ULN=45)

DAAs Safety in Real-World Cohorts

- **Real life cohorts, such as target indicate DAA therapy has an exemplary safety profile across a broad population of patients treated in usual clinical practice.**
  - **Fewer than 2% of patients discontinued therapy due to adverse events**
  - **Only 2.3% had hyperbilirubinemia and 0.2% met definition of drug-induced liver injury**
- **Differentiating potential DILI from progression of underlying disease remains challenging**
  - **Hyperbilirubinemia may be associated with acute co-morbid medical conditions, benign DAA +/- RBV effects, or treatment emergent drug-associated liver events.**
  - **Drug-associated liver events associated with features of cirrhosis and use of ribavirin-containing regimens**

HBV risk of reactivation

- **For HBsAg+ patients who are not already on HBV suppressive therapy, monitoring of HBV DNA levels during and immediately after DAA therapy for HCV is recommended and antiviral treatment for HBV should be given if treatment criteria for HBV are met.**
  Rating: Class IIa, Level B

Summary

HCV Treatment in 2017 for special populations

- Currently approved drugs achieve SVR rates in clinical practice similar to that of clinical trials
- Large real life cohorts help identify new factors associated with treatment failure: PPIs (VEL/LDV), HCC, some RAS/RAVs
- Baseline and treatment-emergent RASs may influence treatment options and anticipated SVR rates, use Riba, extend therapy ?
- Fewer "difficult to cure" or "special" patient groups
  - DAA failures represent small but challenging group currently
- Exceptional safety record when used in the appropriate patient population but continued vigilance necessary, especially in patients with cirrhosis, decompensation
- TB: evaluate for drug-drug interactions: if active TB treat TB first, if + skin test, but no active disease, treat HCV first
- HIV HCV co-infection: treat 12 weeks with SOC therapies
  - Watch for DDI
- Children: can treat down to age 12 with LED SOF and SOF based therapies

Thank you to

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Thank you to

BS Hoang

BS Thuy

and the HASLD team !