Viral Hepatitis Abstracts

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No disclosures

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Liver Failure and Mortality After Discontinuation of Nucleos(t)ide Analogues in Patients with Chronic Hepatitis B: A Real World Analysis

Yao-Chun Hsu et al. Abstract #404

Background

- Chronic HBV can lead to cirrhosis, hepatic decompensation and HCC
- Nucleos(t)ide analogue therapy **suppresses- Cannot eradicate**
- Improves biochemical and histology
- Controversial if NAs can be stopped before HbsAg clearance
- Stopped prematurely risk of relapse and liver failure

Background

- Prevalence of HBV in Taiwan is 15-20% [1]
- Taiwan National Health Insurance Administration does not indefinitely reimburse HBV treatment
- Recommends 3 years treatment. Treatment cessation is routine.

1. Chien, Yin. Epidemiologic Reviews. 2006

Background

- What are the risks following NA cessation?
- Data for practice and policy development
- Real World Risk Analysis

Study Design

Retrospective Cohort Study from the E-Da Healthcare System in Taiwan

- Inclusion
  - Adults >18 years
  - HBV (Hbsag + > 6 months)
  - Treated with NAs for at least 1 year
  - Discontinued treatment for at least 1 month

- Exclusion
  - Any malignancy before treatment
  - Any organ transplant before treatment
  - Un-interrupted treatment duration shorter than one year
  - Followup duration < 1 month

Results-Outcomes After Cessation

- 722 patients enrolled
- Followed median duration 38 months (IQR, 18.8-59.1)
- 225 (31%) had to resume treatment

[Most for jaundice or coagulopathy]

- Over time 52% percent had to restart treatment (10 year outlook)

Results

- Catastrophic Events

	Number of patients
Severe flare ALT>400 u/L	98 patients (8 had cirrhosis)
Severe Jaundice Bilirubin >20 mg/dl	16 patients (9 had cirrhosis)
Hospitalization	25 patients
Deaths	9 patients
Transplant	1 patient

Patient Deaths: **3 (0.4%) directly related to HBV flare up**, 5 from HCC progression, 1 with alcoholism

Summary

- Half of the patients would require retreatment for clinical events
- Severe flare (ALT>10 ULN) occurred in 13.4%
- 3 (0.4%) died directly from HBV reactivation

Data argued for change in policy restricting treatment duration

Elevated HCC Risk Persists for Up to 10 Years After Hepatitis C Eradication in Patients with Cirrhosis and Elevated FIB-4

George Ioannou et al, Abstract #680

Background

- Patients with pre-existing cirrhosis-substantial risk after SVR may persist

- Does the risk decline in time?

- Can HCC surveillance be safely discontinued?

Describe changes in HCC annual incidence over time after SVR in cirrhotic patients

FIB-4 (Fibrosis 4)

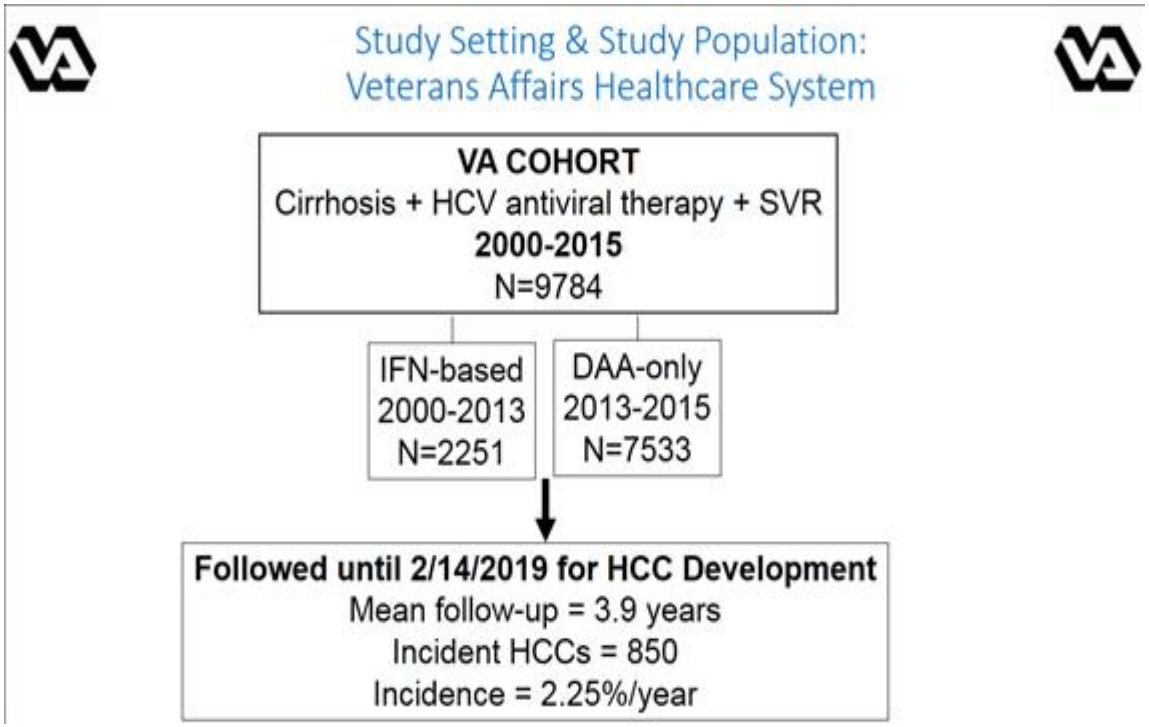
$$\frac{\text{Age x AST}}{\text{Platelets x } \sqrt{\text{ALT}}}$$

FIB-4 ≥ 3.25: High Probability of Cirrhosis

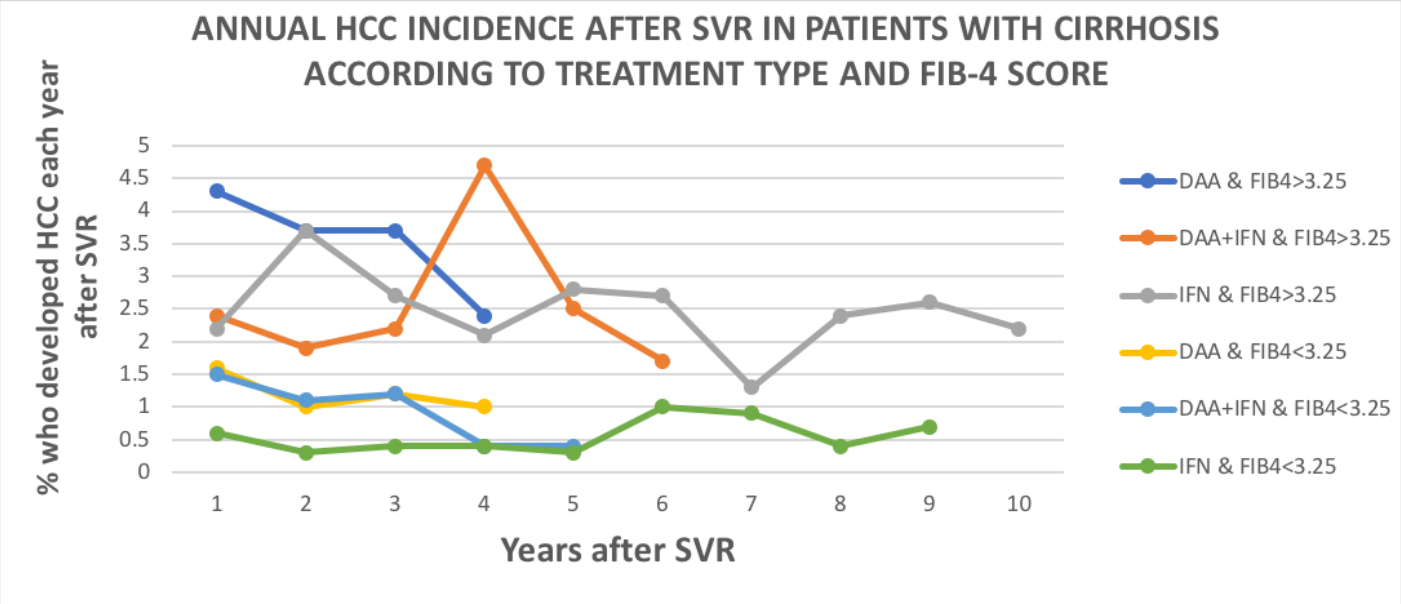
Aim

Describe changes in HCC annual incidence over time after SVR in cirrhotic patients

Study Design



Results


ANNUAL HCC INCIDENCE AFTER SVR IN PATIENTS WITH CIRRHOSIS ACCORDING TO TREATMENT TYPE AND FIB-4 SCORE
% who developed HCC each year after SVR
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
10
Years after SVR
DAA & FIB4>3.25
DAA+IFN & FIB4>3.25
IFN & FIB4>3.25
DAA & FIB4<3.25
DAA+IFN & FIB4<3.25
IFN & FIB4<3.25

Results

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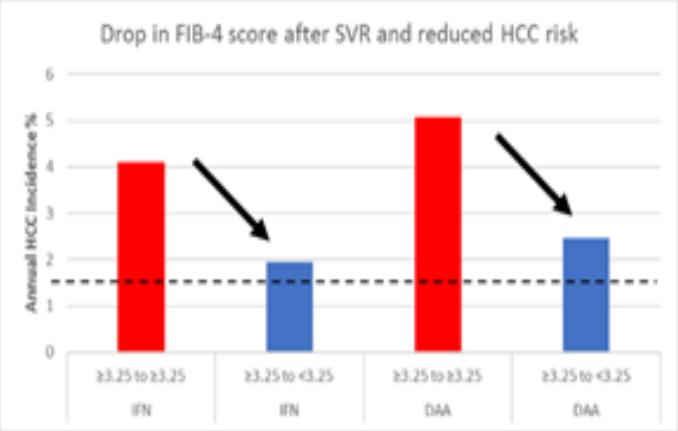
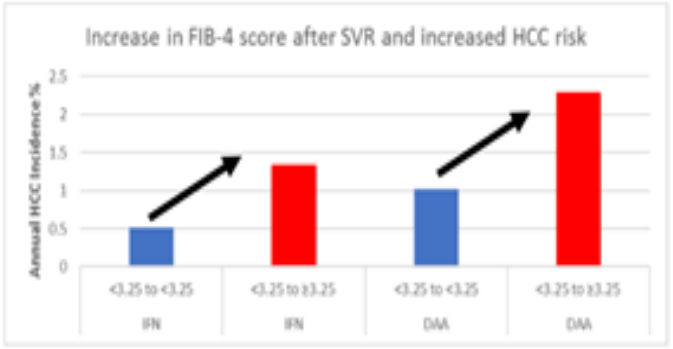
Drop in FIB-4 after SVR → Reduced risk of HCC



FIB-4 Score Pre-treatment	FIB-4 Score Post-treatment	Number of patients	Patient-years	Number who developed HCC (%)	HCC per 100 patient-years	Crude hazard ratio (95% CI)	Adjusted* hazard ratio (95% CI)
≥3.25	≥3.25	2,232(49.3)	6,255	317(14.2)	5.07	1	1
≥3.25	<3.25	2,297(50.7)	6,889	170(7.4)	2.47	0.49 (0.40-0.58)	0.59 (0.48-0.73)

Results

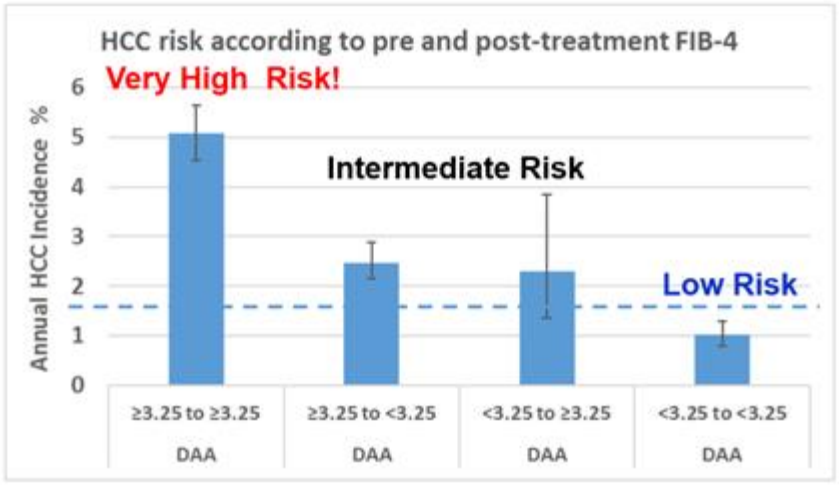
Increase in FIB-4 after SVR → Increased risk of HCC



FIB-4 Score Pre-treatment	FIB-4 Score Post-treatment	Number of patients	Patient-years	Number who developed HCC (%)	HCC per 100 patient-years	Crude hazard ratio (95% CI)	Adjusted* hazard ratio (95%CI)
<3.25	<3.25	2,069(90.5)	6,357	65(3.1)	1.02	1	1
<3.25	≥3.25	217(9.5)	612	14(6.5)	2.29	2.25 (1.26-4.00)	2.18 (1.16-4.09)

Results

FIB-4 before and after SVR stratifies patients



Summary

- High FIB-4 score identifies patients with cirrhosis who continue to have a high risk of HCC despite many years after SVR

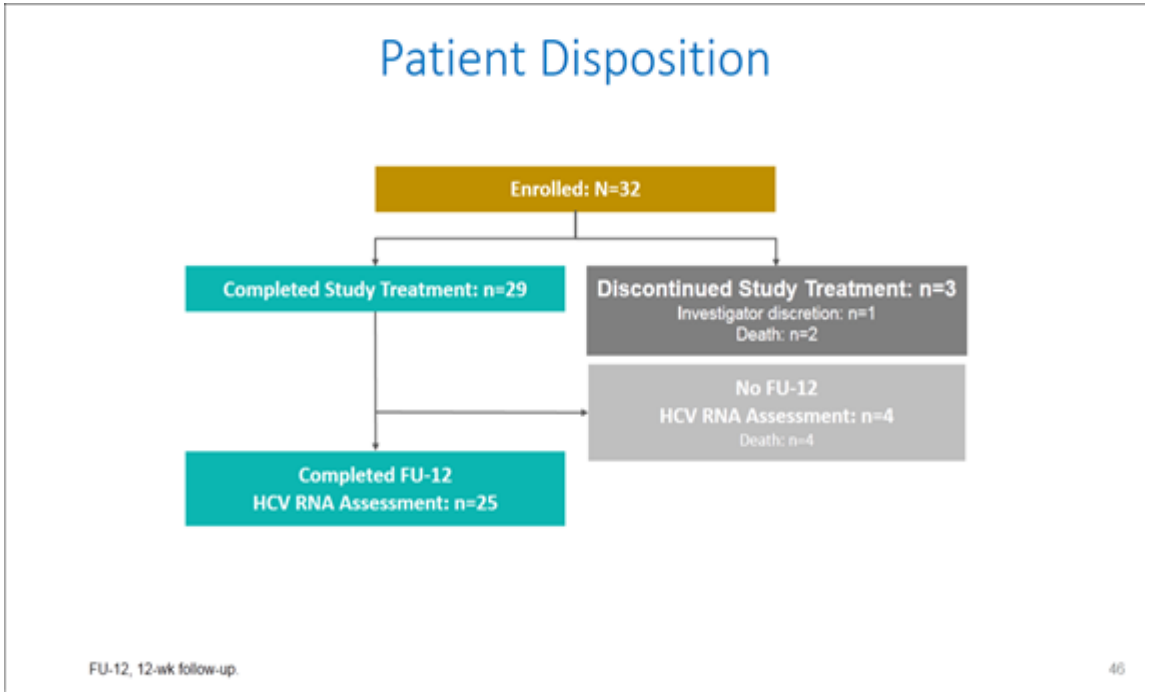
High Efficacy and Improvement in CPT Class With Sofosbuvir/Velpatasvir Plus Ribavirin in 12 Weeks with CPT C Decompensated Cirrhosis

Flamm et al. Abstract #953

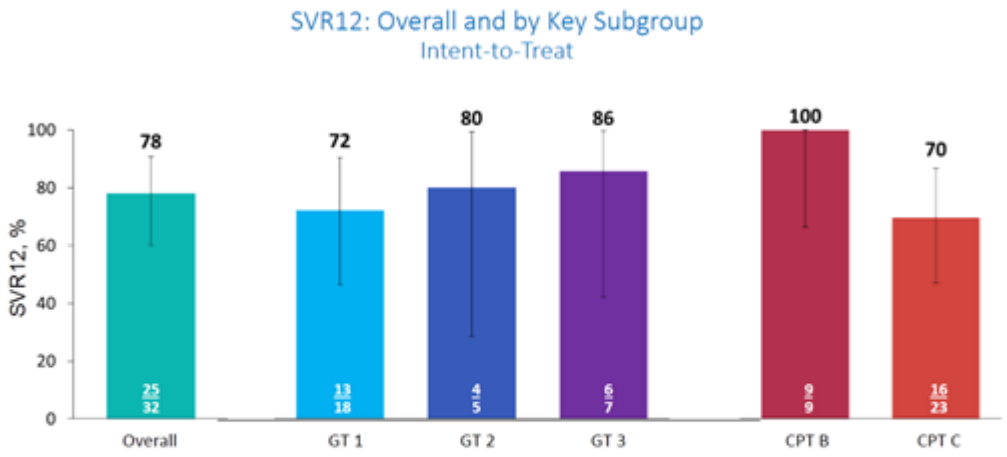
Background

- Evaluate Sofosbuvir/Velpatasvir plus Ribavirin for 12 weeks in CPT C decompensated cirrhosis

Study Design



Results



- No patients experienced virologic failure at FU-12
  - 7 had no FU-12 assessment due to investigator discretion (n=1) and death (n=6); all unrelated to study drugs
- 1 patient with SVR12 did not achieve SVR24
  - No baseline NS5A or NS5B resistance-associated substitutions (RASs) detected; NS5A RAS Y93H emerged at Week 24

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Results

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Changes in Liver Function at Posttreatment Week 24 in Patients Who Achieved SVR

Shift in CPT Class From Baseline

		Baseline CPT Class, n/n (%)*	
		B n=8	C n=16
Posttreatment Week-24 CPT Class	A (5–6)	1/6 (17)	0/13
	B (7–9)	5/6 (83)	7/13 (54)
	C (10–15)	0/6	6/13 (46)

Shift in MELD Score from Baseline

	SOF/VEL + RBV 12 wk , n/n (%)*
Decrease (improvement)	10/19 (53)
No Change	4/19 (21)
Increase (worsening)	5/19 (26)

- Of the 19 patients who achieved SVR24, did not have a liver transplant, and were assessed at posttreatment Week 24, there were improvements in CPT class in 8 (42%) and in MELD score in 10 (53%)
- Changes in liver function were primarily due to improvements in laboratory parameters

*Only patients with assessments at posttreatment Week 24 and without on-study liver transplant were included.

Summary

- SOF/VEL +RBV for 12 weeks was well tolerated resulted in high rates of SVR 12
- Improvement in CPT class and MELD post treatment 42% and 53%
- Treatment safe and well tolerated, with AEs consistent with expectations for a patient population with advanced liver disease

Thank you