

Management of HCV and HIV Coinfection

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Disclosures

- None

Epidemiology

- Coinfection with hepatitis C virus (HCV) and HIV is common, owing to shared risk factors.
 - All persons with HIV should be screened for HCV.
- Among persons living with HIV in the U.S., an estimated 15 to 30% have HCV coinfection.
- In the U.S., approximately 5% of persons with chronic HCV have HIV coinfection.

Prevalence and Incidence of HCV Infection in MSM: Systematic Review and Meta-Analysis

- Systematic review and meta-analysis evaluating HCV prevalence and incidence in MSM.
- Pooled HCV prevalence in MSM was 3.4%
 - 1.5% in HIV-negative MSM
 - 6.3% in HIV-positive MSM
- In HIV-negative MSM, pooled HCV incidence was:
 - 0.12/1000 PY in individuals not on PrEP
 - 14.80/1000 PY in individuals on PrEP

HCV and HIV: Natural History

- Coinfection with HIV accelerates the progression of hepatic fibrosis in patients with HCV, and patient w/ HIV are less likely to spontaneously clear HCV.
- Cirrhosis has been observed to occur 12 to 16 years earlier in persons with HCV + HIV vs. HCV alone.
- Up to 80-90% of liver-related deaths in persons living with HIV are attributable to HCV infection.

Pre-Treatment Assessment

- Assess fibrosis
 - Non-invasive tests (e.g., FIB-4)
 - Transient elastography (e.g., FibroScan)
 - Liver biopsy is the gold standard but not routinely recommended
- Laboratory evaluation
 - CBC, CMP
 - HCV RNA
 - HBV serologic testing
 - +/- HCV genotype in patients with cirrhosis
- Medication and drug-drug interaction review

HCV Treatment Outcomes in Patients with HIV

SVR Rates with GT 1 HCV-HIV Coinfection and HCV Monoinfection				
Regimen (12 weeks)	Genotype 1			
	HCV-HIV Coinfection		HCV Monoinfection	
	Study	SVR	Study	SVR
Elbasvir-Grazoprevir	C-EDGE Coinfection	95%	C-EDGE TN	95%
Glecaprevir-Pibrentasvir	EXPEDITION-2	98%	ENDURANCE-1	99%
Ledipasvir-Sofosbuvir	ION-4	96%	ION-1	99%
Sofosbuvir-Velpatasvir	ASTRAL-5	95%	ASTRAL-1	98%

Glecaprevir-Pibrentasvir

- First pangenotypic NS3/4A protease inhibitor-NS5A inhibitor combination to be approved
- Not an option for patients with decompensated cirrhosis due to the presence of a protease inhibitor.
- SVR-12 rates $\geq 95\%$ for treatment naïve individuals with and without compensated cirrhosis

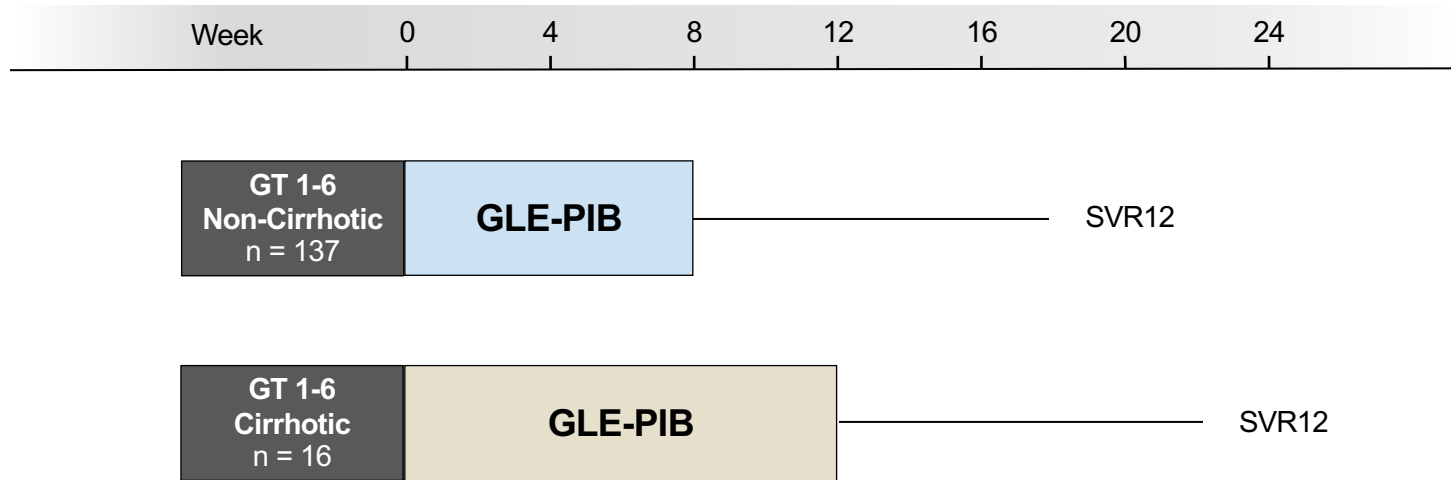
Glecaprevir-Pibrentasvir in Patients with HIV-HCV Coinfection

EXPEDITION-2: Study Features

- **Design:** Open-label, phase 3 trial to evaluate the safety and efficacy of the fixed-dose combination of glecaprevir-pibrentasvir for 8 or 12 weeks in persons with HIV-HCV coinfection, without or with compensated cirrhosis
- **Setting:** Australia, Europe, Russian Federation, UK, US
- **Key Eligibility Criteria**
 - Adults with chronic HCV GT 1, 2, 3, 4, 5, or 6
 - HCV RNA $\geq 1,000$ IU/mL at screening
 - Naïve or treated with peginterferon +/- ribavirin (PR) or PR +/- sofosbuvir
 - Compensated cirrhosis allowed
 - On ART or ART-naïve with CD4 ≥ 500 cells/mm³ or CD4 percentage $\geq 29\%$
- **Primary End Point:** SVR12

Glecaprevir-Pibrentasvir in Patients with HIV-HCV Coinfection

EXPEDITION-2: Study Design

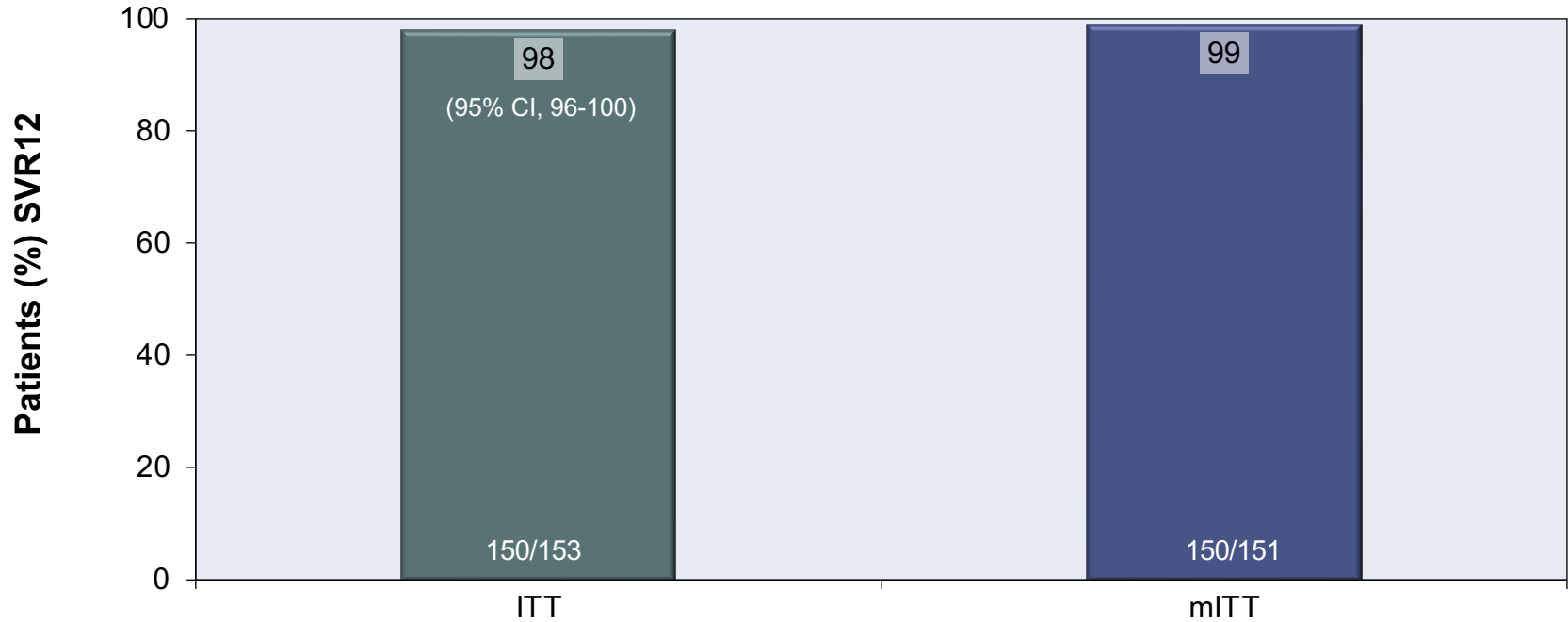


Abbreviations: GLE-PIB = Glecaprevir-pibrentasvir

Drug Dosing: Glecaprevir-pibrentasvir (100/40 mg) fixed-dose combination; three pills (300/120 mg) once daily

Glecaprevir-Pibrentasvir in Patients with HIV-HCV Coinfection

EXPEDITION-2: Results



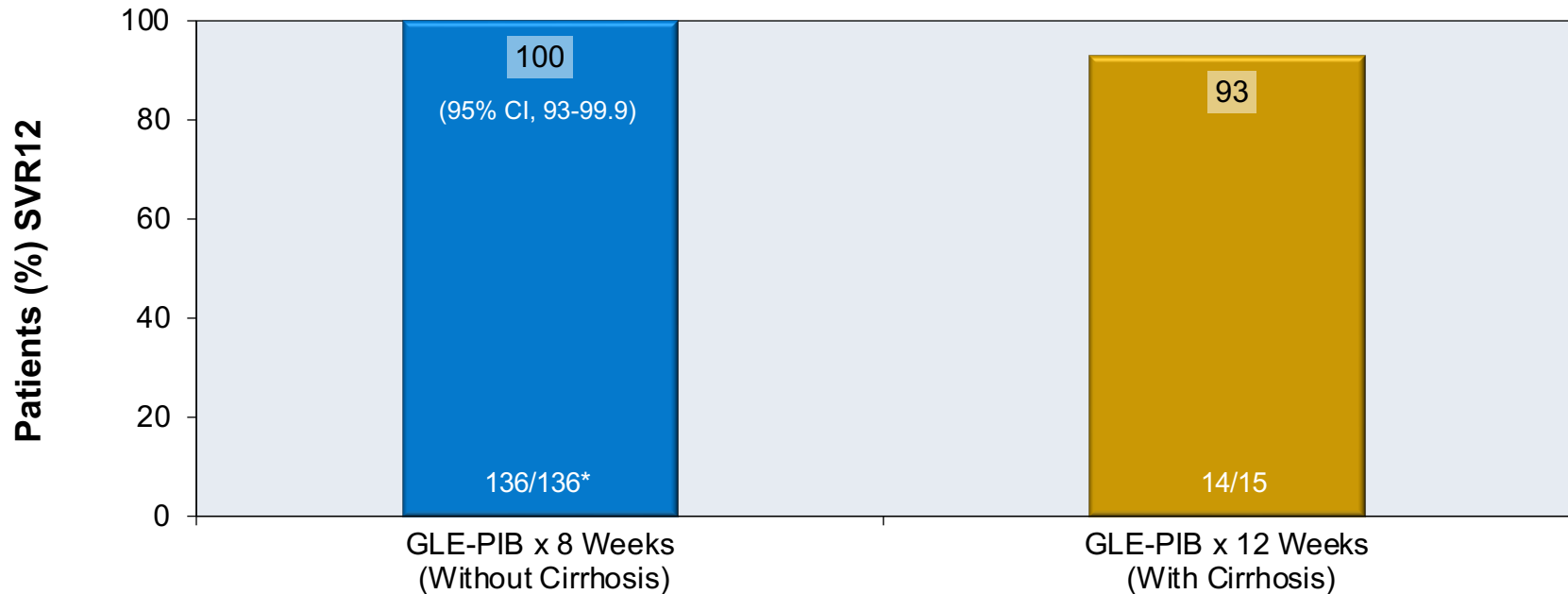
One GT3 patient with cirrhosis and 85% compliance had on-treatment virologic failure

Abbreviations: ITT = Intent-to-treat; mITT = modified intent-to-treat

Glecaprevir-Pibrentasvir in Patients with HIV-HCV Coinfection

EXPEDITION-2: Results

EXPEDITION-2: Overall SVR by Treatment Regimen



*Excludes one patient with missing data who achieved SVR24

Sofosbuvir-Velpatasvir

- Pangenotypic NS5A-NS5B inhibitor, given as a single pill combination.
- Safe for use in patients with decompensated cirrhosis.
- SVR-12 rates $\geq 95\%$ for treatment naïve individuals with and without compensated cirrhosis

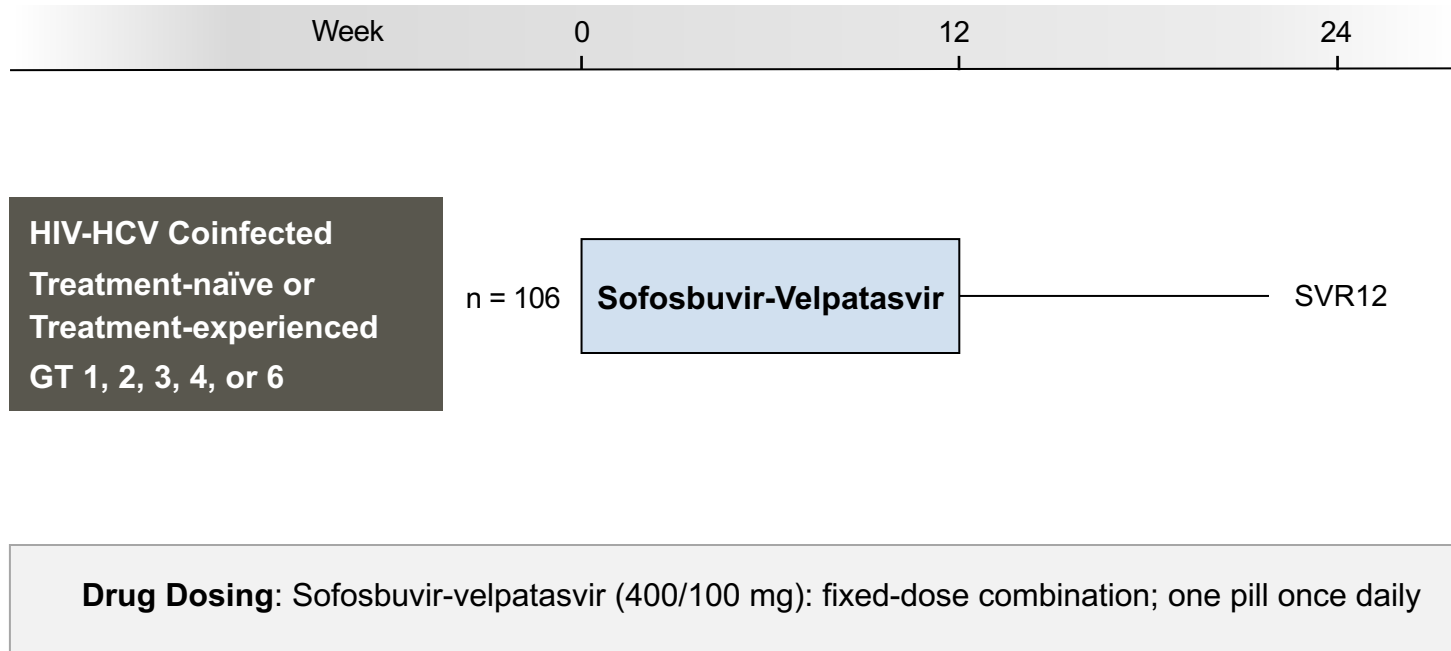
Sofosbuvir-Velpatasvir in Patients with HIV-HCV Coinfection

ASTRAL-5: Study Features

- **Design:** Single-arm, open-label, multicenter, phase 3 trial of sofosbuvir-velpatasvir in HIV-HCV coinfecting treatment-naïve and treatment-experienced patients with genotypes 1-6 HCV
- **Setting:** Multiple sites in US
- **Entry Criteria**
 - Chronic HCV GT 1-6
 - Age ≥ 18 years
 - HIV coinfection
 - CD4 count ≥ 100 cells/mm³ and HIV RNA ≤ 50 copies/mL
 - On stable ART for ≥ 8 weeks
 - Prior treatment failure allowed (but no prior NS5A or NS5B)
 - Patients with compensated cirrhosis allowed
- **Primary End Point:** SVR12

Sofosbuvir-Velpatasvir in Patients with HIV-HCV Coinfection

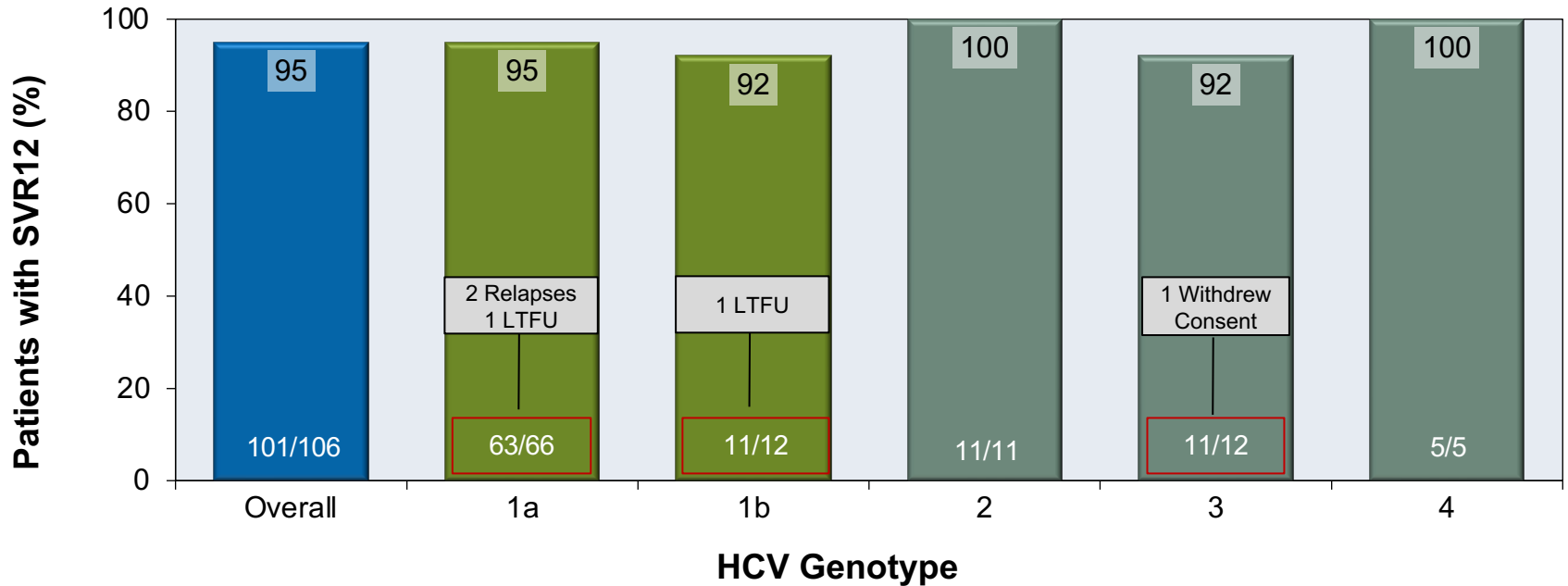
ASTRAL-5: Study Design



Sofosbuvir-Velpatasvir in Patients with HIV-HCV Coinfection

ASTRAL-5: Results

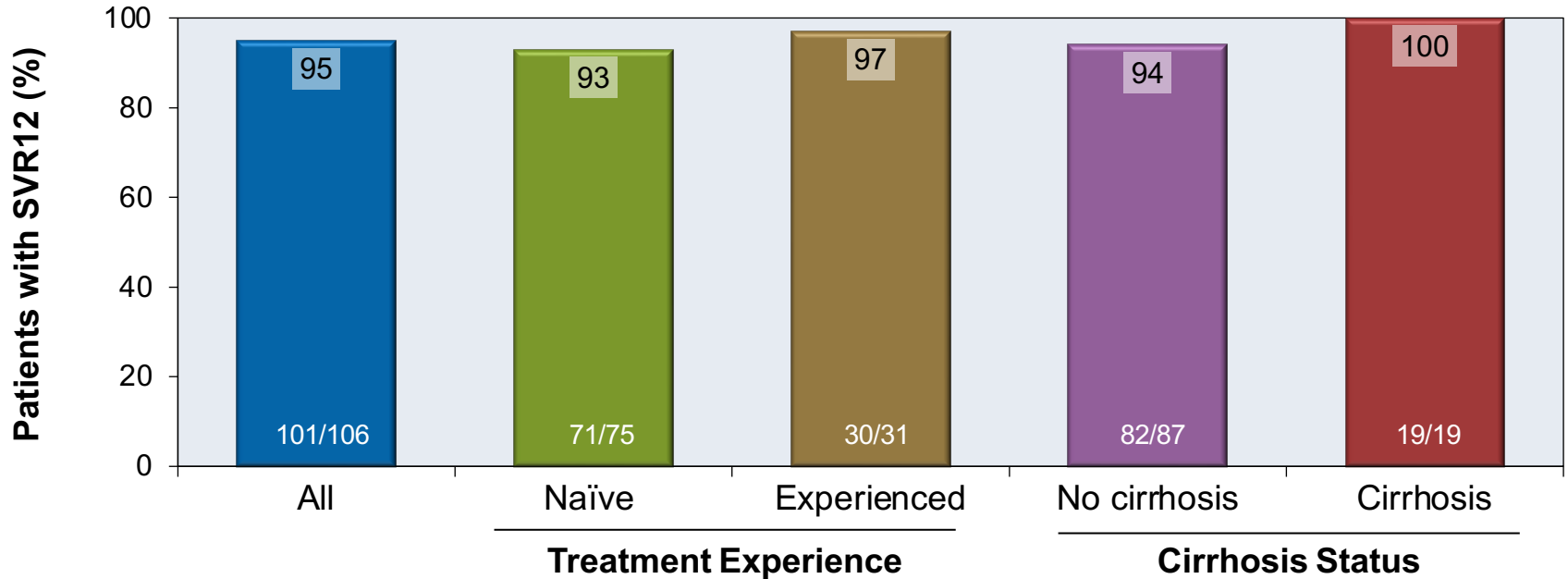
SVR12 Results by Genotype



Sofosbuvir-Velpatasvir in Patients with HIV-HCV Coinfection

ASTRAL-5: Results

SVR12 Results by Treatment Experience and Cirrhosis Status



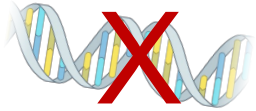
Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection

ACTG A5360 (MINMON): Study Overview

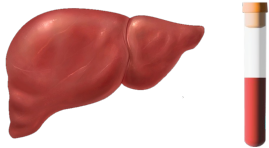
- **Design:** Phase 4 open-label single-arm trial to examine the safety and efficacy of a minimal monitoring approach to HCV care delivery using 12 weeks of sofosbuvir-velpatasvir in treatment-naïve patients
- **Setting:** Multiple sites in Brazil, South Africa, Thailand, Uganda & United States
- **Entry criteria:**
 - Chronic HCV infection as determined by HCV RNA >1000 IU/mL
 - Treatment-naïve
 - Age 18 years or older
 - HIV coinfection permitted
 - Compensated cirrhosis permitted (FIB-4 ≥ 3.25 , capped at $\leq 20\%$ participants)
 - Absence of coinfection with HBV
- **Primary End-point:** SVR ≥ 22 weeks post-treatment initiation

Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection ACTG A5360 (MINMON):

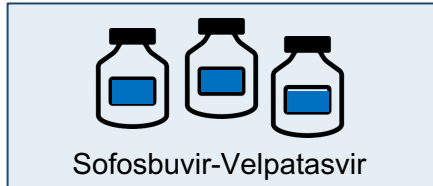
No Genotype



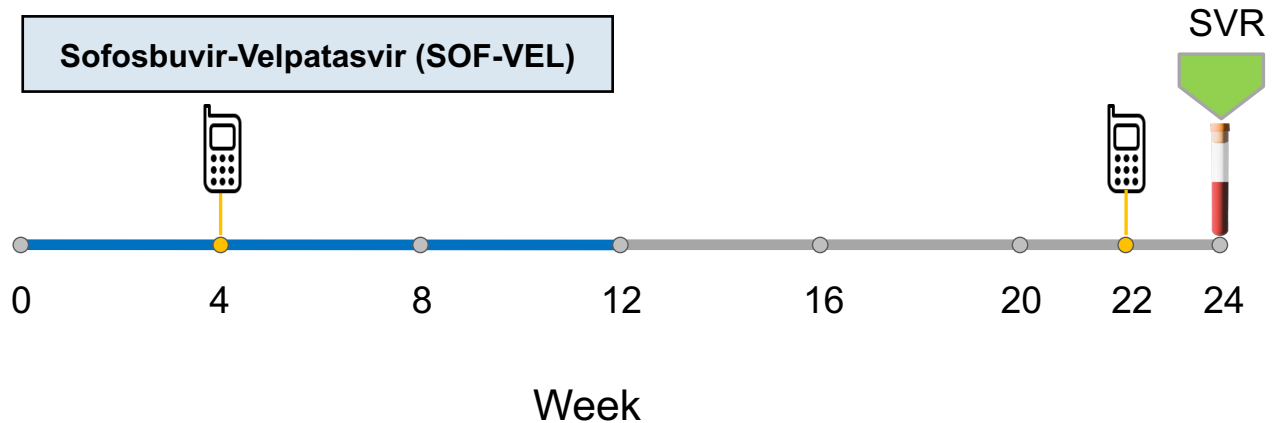
Cirrhosis Status by Fib-4



All pills provided at Entry



- No pre-treatment genotyping
- Cirrhosis determination based on Fib-4
- All treatment medication provided at entry
- No scheduled on treatment visits/labs
- Remote contact at weeks 4 and 22



Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection ACTG A5360 (MINMON): Study Population

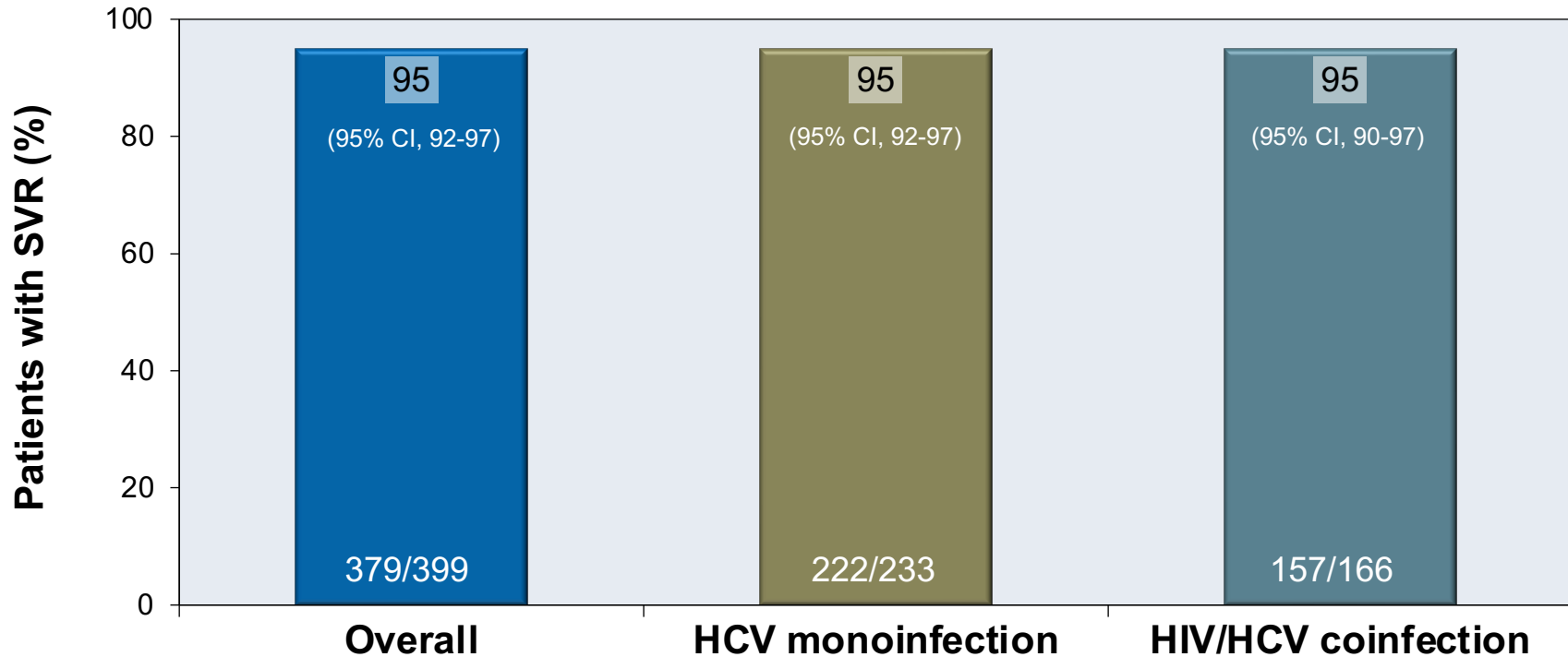
Baseline Characteristic	Sofosbuvir-Velpatasvir (n = 399)
Age, median (range)	47 (20-82)
Female sex at birth, n (%)	139 (35)
Identity across transgender spectrum, n (%)	22 (6)
Race, n (%)	
White	166 (42)
Black	72 (18)
Asian	113 (28)
HCV RNA log ₁₀ IU/mL, median (IQR)	6.1 (5.6 – 6.6)
Current injection drug use, n (%)	12 (3)
Current alcohol use, n (%)	161 (40%)
Cirrhosis (by FIB-4 ≥3.25), n (%)	34 (9)
HIV coinfection, n (%)	166 (42)
Suppressed on antiretroviral therapy, n (% of HIV/HCV)	164 (99)



IQR, interquartile range; FIB-4, Fibrosis-4 index

Source: Solomon SS, et al. *Lancet Gastroenterol Hepatol.* 2022;7:307-17.

Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection ACTG A5360 (MINMON): Results, Overall and by HIV Status



Recommendations for HCV Treatment in PLWH

- **Treatment-naïve without cirrhosis**
 - Glecaprevir/pibrentasvir for 8 weeks
 - Sofosbuvir/velpatasvir for 12 weeks
- **Treatment-naïve with compensated cirrhosis (GT 1,2,4-6)**
 - Glecaprevir/pibrentasvir for 8-12 weeks[^]
 - Sofosbuvir/velpatasvir for 12 weeks
- **Treatment-naïve with compensated cirrhosis (GT 3)***
 - Glecaprevir/pibrentasvir for 8 weeks (12 week course is an alternative)

[^]Although 12-week duration is better studied, real world data suggest 8wk duration is ok. 12wk duration listed as “alternative” in OI guidelines

*Sofosbuvir/velpatasvir requires pre-treatment NS5A RAS testing in patients w/ GT3 + cirrhosis
- if no resistance 12wks of sofosbuvir/velpatasvir is ok; if resistance, must add ribavirin

		Ledipasvir/ Sofosbuvir (LDV/SOF)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Elbasvir/ Grazoprevir (ELB/GRZ)	Glecaprevir/ Pibrentasvir (GLE/PIB)	Sofosbuvir/ Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)
Protease Inhibitors	Boosted Atazanavir	A	A			
	Boosted Darunavir	A	A			
	Boosted Lopinavir	ND, A	A			ND
NNRTIs	Doravirine		ND		ND	ND
	Efavirenz				ND	ND
	Rilpivirine					
	Etravirine	ND	ND	ND	ND	ND
Integrase Inhibitors	Bictegravir			ND	ND	
	Cabotegravir	ND	ND	ND	ND	ND
	Cobicistat-boosted elvitegravir	C	C			C
	Dolutegravir					ND
	Raltegravir					ND
Entry Inhibitors	Fostemsavir	ND	ND	ND	ND	ND
	Ibalizumab-uiyk	ND	ND	ND	ND	ND
	Maraviroc	ND	ND	ND	ND	ND
NRTIs	Abacavir		ND	ND		ND
	Emtricitabine					
	Lamivudine		ND	ND		ND
	Tenofovir disoproxil fumarate	B, C	B, C			C
	Tenofovir alafenamide	D	D	ND		D

Source: HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C, October 24.2022.

Laboratory Monitoring

- Most patients will not require any on-treatment laboratory monitoring.
- Patients taking diabetes medications should monitor for hypoglycemia.
- Patients on warfarin should have INR monitoring to evaluate for subtherapeutic anticoagulation.
- In patients with compensated cirrhosis, providers may order liver function testing to monitor for liver injury during treatment.
- All patients should undergo repeat HCV RNA and liver function testing 12 weeks post-treatment to assess for HCV cure and transaminase normalization.

Conclusions

- HIV and HCV coinfection is common, owing to shared risk factors.
- Coinfection with HIV accelerates the progression of hepatic fibrosis in patients with HCV, and HCV is the leading cause of liver-related deaths in PLWH.
- Glecaprevir/pibrentasvir and sofosbuvir/velpatasvir are the preferred regimens to treat HCV in patients w/ and w/o HIV due to their efficacy and pangenotypic activity.
- Many patients with HIV can be treated for HCV using a minimal monitoring approach, and most will need on-treatment monitoring.
- Preferred HCV treatment regimens have limited interactions with most first line ART, but important drug-drug interactions with PIs and NNRTIs exist.

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Funded by
Centers for Disease Control and Prevention (CDC)

HCV Medications

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HCV Course Modules

Screening and Diagnosis of Hepatitis C Infection

For any clinician who may encounter persons with hepatitis C virus infection and would like to establish core competence in testing for hepatitis C, counseling patients on preventing hepatitis C transmission, and diagnosing acute hepatitis C infection.

Overview / Quick Reference >

Rapidly access info about Screening and Diagnosis of Hepatitis C Infection

Clinical Challenges

Expert opinions for challenging and controversial cases

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