Management of HCV and HIV Coinfection

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Disclosures

None

Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

Data Considerations

Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities

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. an approximately 5% of persons with chronic HCV have HIV coinfection.

Epidemiol Infect 2018 May;146(7):920-930; Lancet Infect Dis 2016 Jul;16(7):797-808; J Acquir Immune Defic Syndr 2015 Apr 1;68(4):425-31; J Infect Dis 2013 Mar;207 Suppl 1(Suppl 1):S1-6.

- 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

Lancet Gastroenterol Hepatol 2021 Jan;6(1):39-56.

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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.

Sources: PMID 23440167; 11732009; 24723077; 11462196; 21459211; 25522874;

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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
  - HCV genotype in patients with cirrhosis
  - HBV serologic testing
- Medication and drug-drug interaction review

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/hepatitis-c-virus?view=full

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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 ≥95% for treatment naïve individuals with and without compensated cirrhosis

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Glecaprevir-Pibrentasvir in HIV-HCV Coinfected Patients
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 ≥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/mm^3 or CD4 percentage ≥29%
- **Primary End Point**: SVR12

Source: Rockstroh JK, et al. Clin Infect Dis. 2018;67:1010-7.

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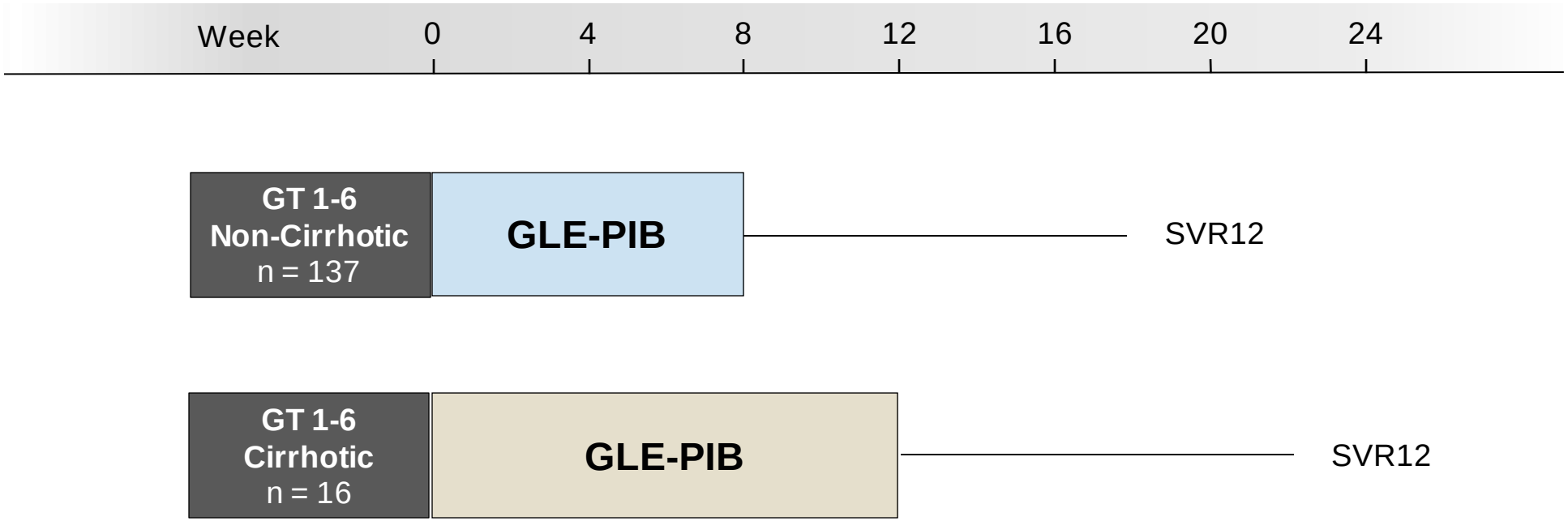
Glecaprevir-Pibrentasvir in HIV-HCV Coinfected Patients
EXPEDITION-2: Study Design



Abbreviations: GLE-PIB = Glecaprevir-pibrentasvir

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

Source: Rockstroh JK, et al. Clin Infect Dis. 2018;67:1010-7.

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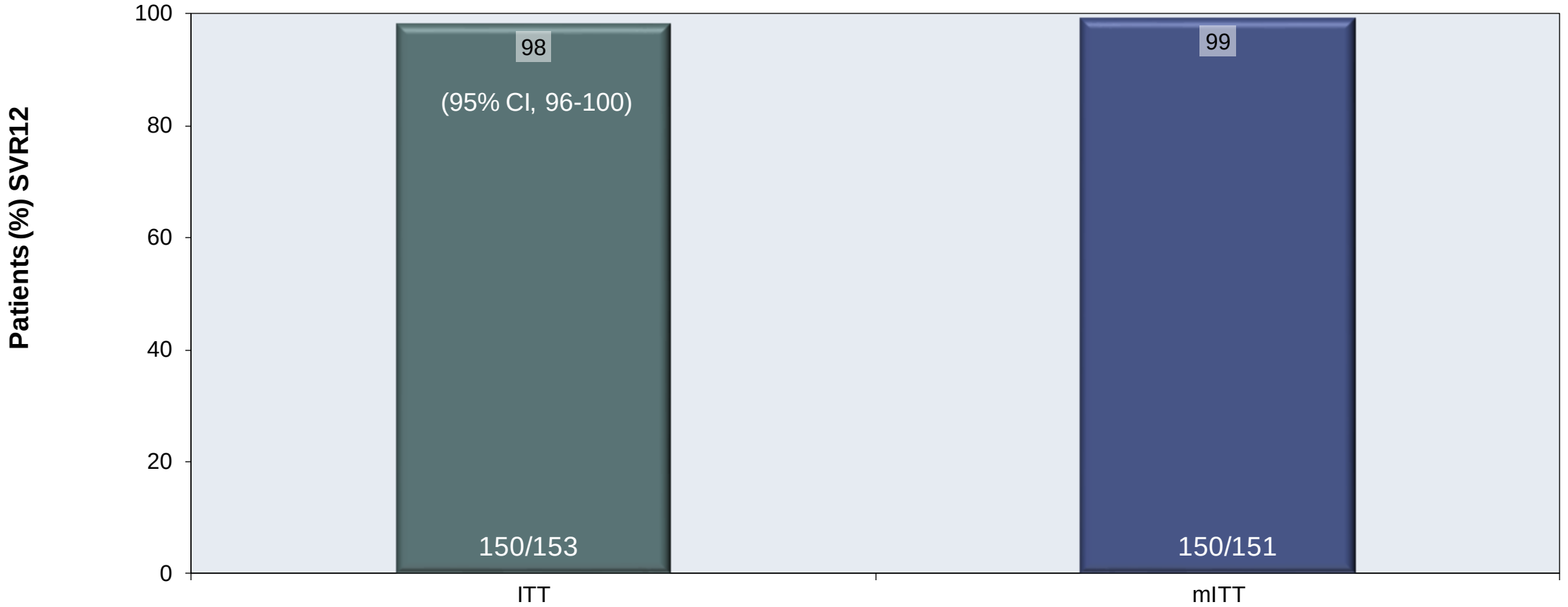
Glecaprevir-Pibrentasvir in HIV-HCV Coinfected Patients EXPEDITION-2: Results



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

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

Source: Rockstroh JK, et al. Clin Infect Dis. 2018;67:1010-7.

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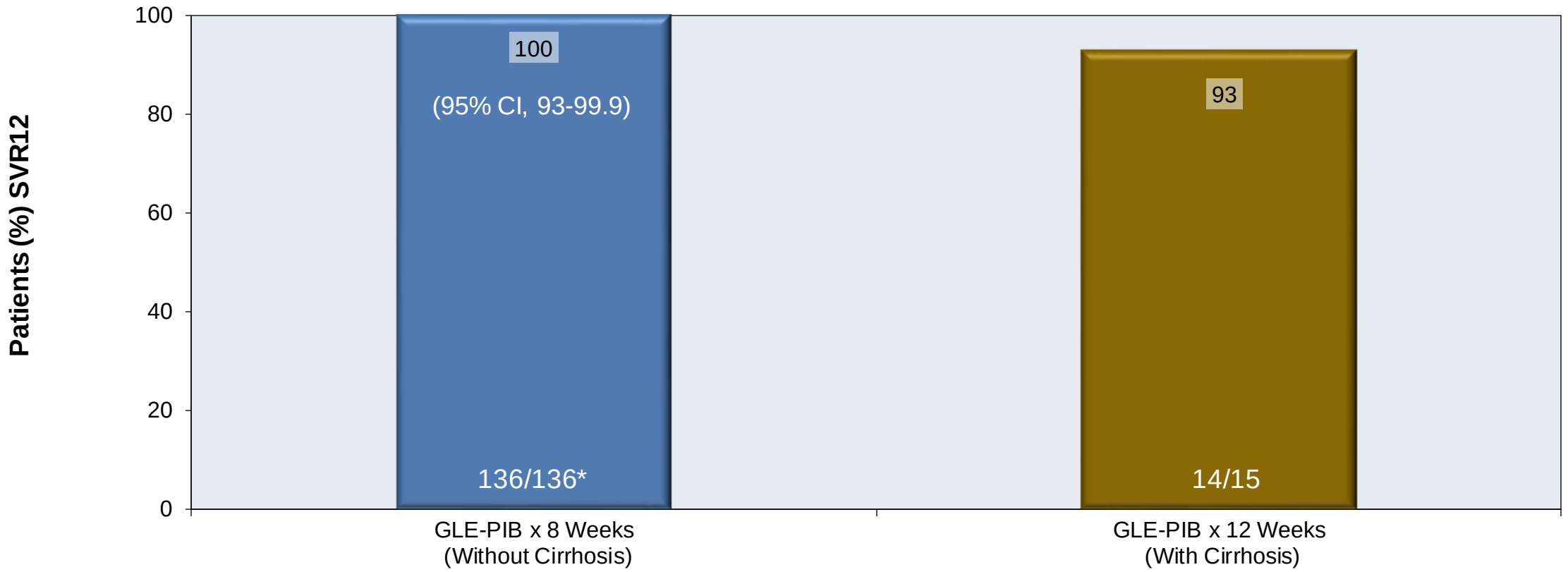
Glecaprevir-Pibrentasvir in HIV-HCV Coinfected Patients
EXPEDITION-2: Results



*Excludes one patient with missing data who achieved SVR24

Source: Rockstroh JK, et al. Clin Infect Dis. 2018;67:1010-7.

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Sofosbuvir-Velpatasvir

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

Sofosbuvir-Velpatasvir in HIV-HCV Coinfected Patients
ASTRAL-5: Study Features

- **Design**: Single-arm, open-label, multicenter, phase 3 trial of sofosbuvir-velpatasvir in HIV-HCV coinfected 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/mm^3 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

Source: Wyles D, et al. Clin Infect Dis. 2017;65:6-12.

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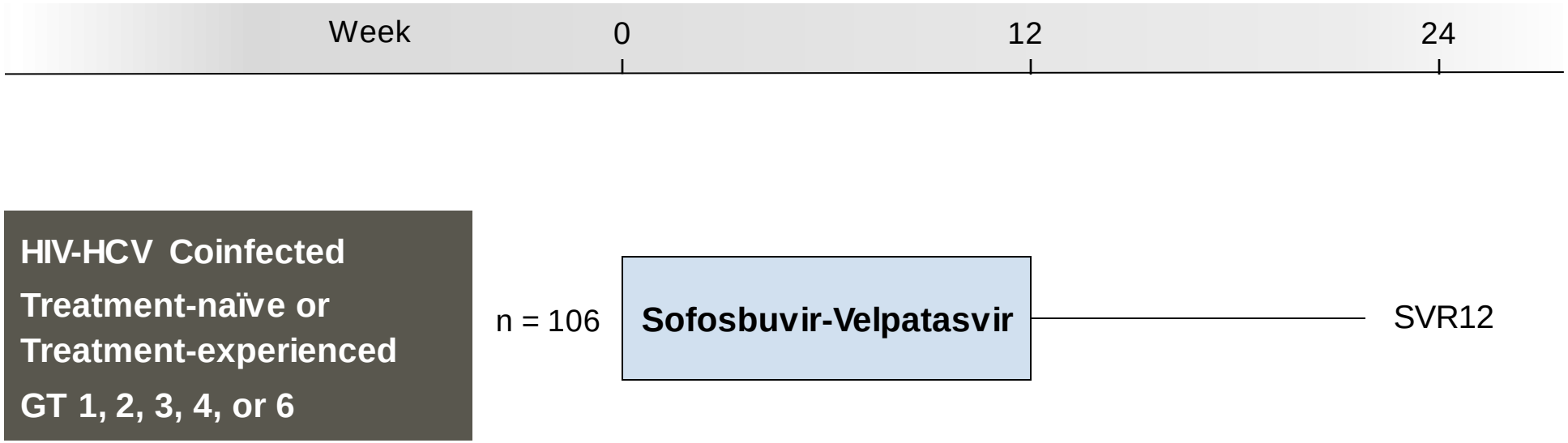
Sofosbuvir-Velpatasvir in HIV-HCV Coinfected Patients
ASTRAL-5: Study Design

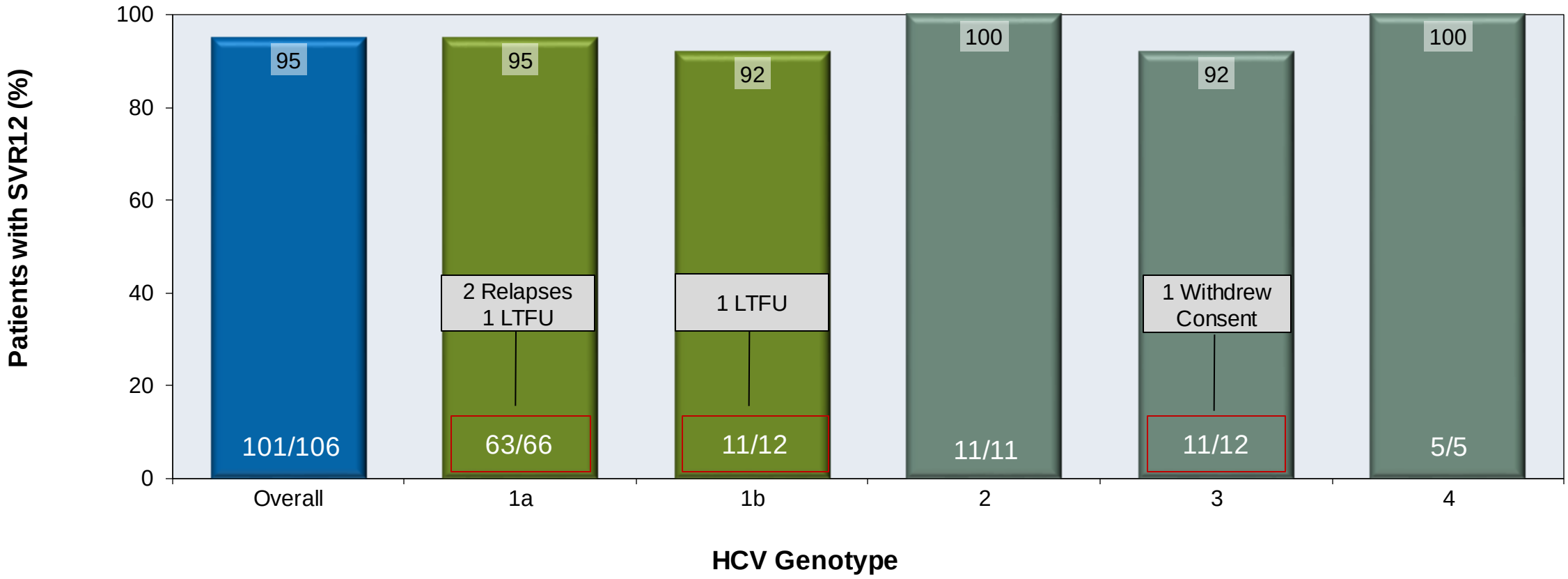


Drug Dosing: Sofosbuvir-velpatasvir (400/100 mg): fixed-dose combination; one pill once daily

Source: Wyles D, et al. Clin Infect Dis. 2017;65:6-12.

Sofosbuvir-Velpatasvir in HIV-HCV Coinfected Patients
ASTRAL-5: Results

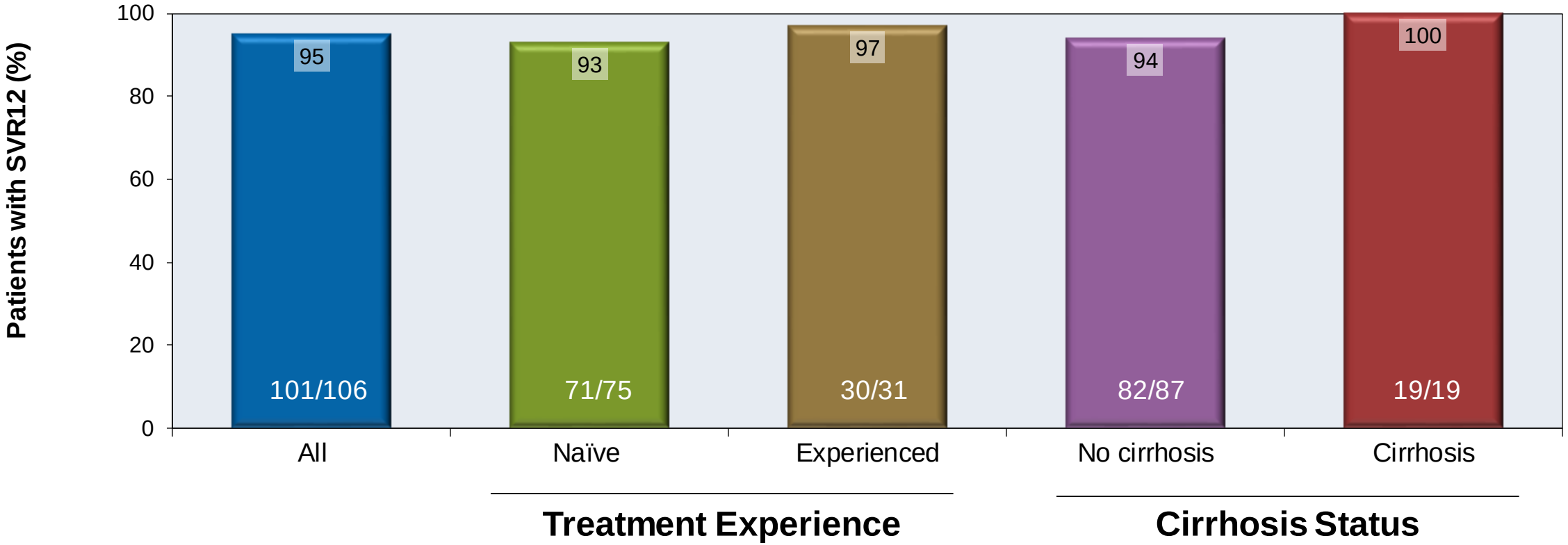
SVR12 Results by Genotype



Source: Wyles D, et al. Clin Infect Dis. 2017;65:6-12.

Sofosbuvir-Velpatasvir in HIV-HCV Coinfected Patients
ASTRAL-5: Results

SVR12 Results by Treatment Experience and Cirrhosis Status



Source: Wyles D, et al. Clin Infect Dis. 2017;65:6-12.

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 or older
  - HIV coinfection permitted
  - Compensated cirrhosis permitted (FIB-4 ≥3.25, capped at ≤20% participants)
  - Absence of coinfection with HBV
- **Primary End-point**: SVR ≥22 weeks post-treatment initiation

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

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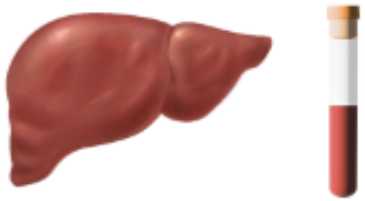
Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection ACTG A5360 (MINMON):

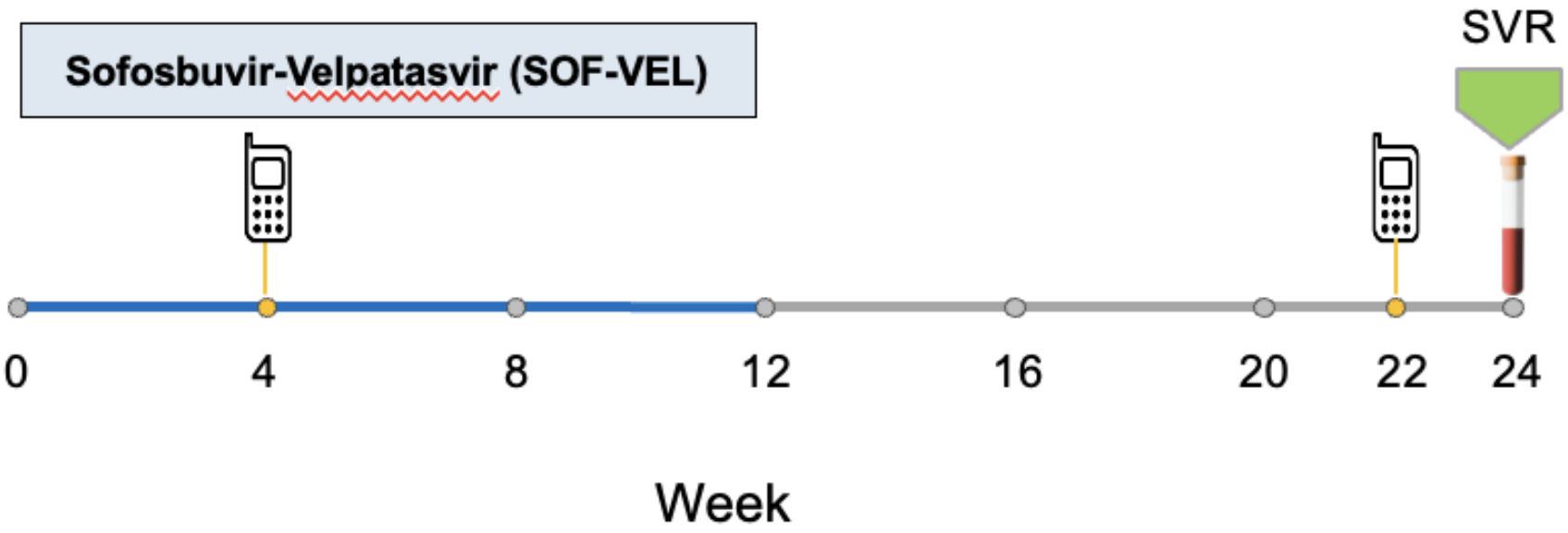
No Genotype

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



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

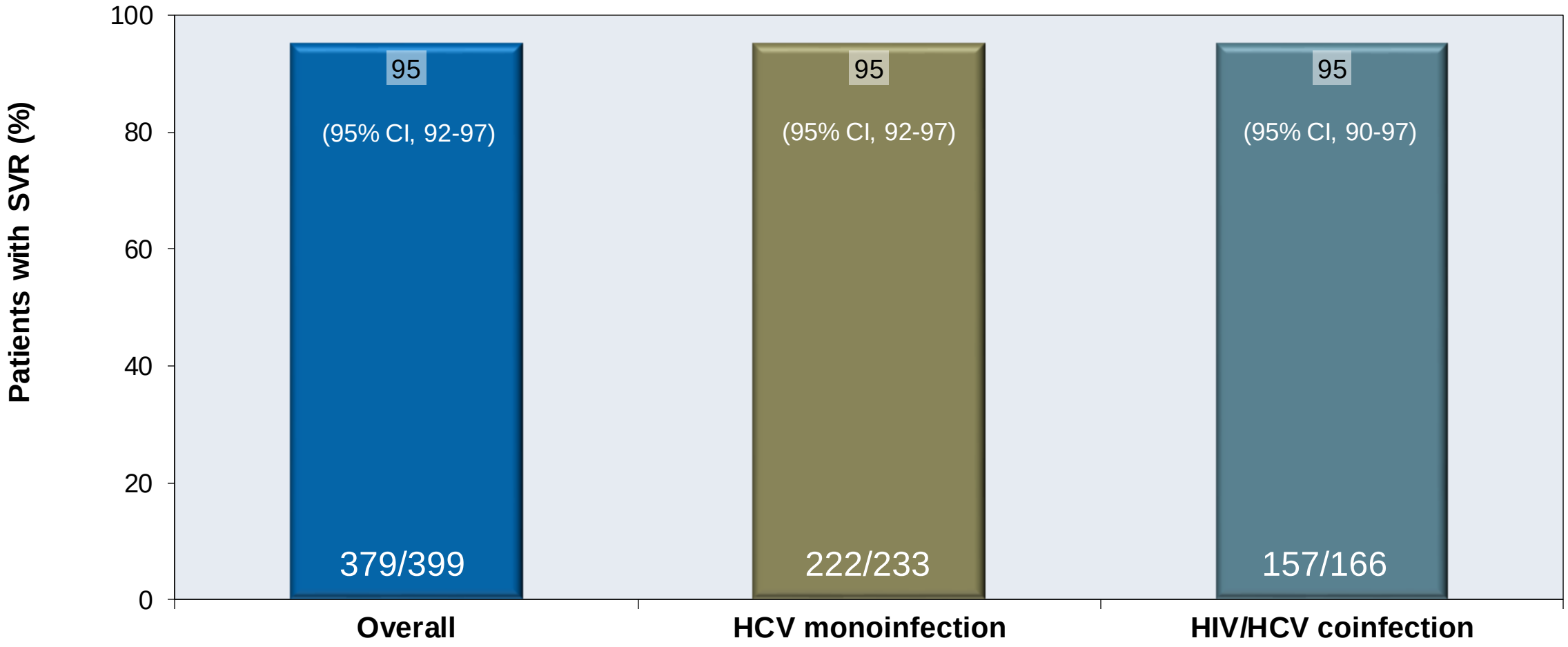
Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection ACTG A5360 (MINMON): Study Population

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 Black Asian	 166 (42) 72 (18) 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 (%) Suppressed on antiretroviral therapy, n (% of HIV/HCV)	166 (42) 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



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

Recommendations for HCV Treatment in PLWH

- Treatment-naïve without cirrhosis
  1. Glecaprevir/pibrentasvir for 8 weeks
  2. Sofosbuvir/velpatasvir for 12 weeks

- Treatment-naïve with compensated cirrhosis (GT 1,2,4-6)
  1. Glecaprevir/pibrentasvir for 8 weeks
     - Although 12-week duration is better studied, real world data suggest 8wk duration ok. 12wk duration listed as “alternative” in OI guidelines
  2. Sofosbuvir/velpatasvir for 12 weeks

- Treatment-naïve with compensated cirrhosis (GT 3)
  1. Glecaprevir/piprentasvir for 8 weeks (12wk course is an alternative)

*Sofosbuvir/velpatasvir requires pre-treatment NS5A RAS testing in pt’s w/ GT3 + cirrhosis
- if no resistance 12wks of sof/vel ok; if resistance, must add ribavirin

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/hepatitis-c-virus?view=full

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		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

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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.

Source: AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

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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 PWH.
- 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.
- G/P and sof/vel ”play well” with most first line ART but have several drug-drug interactions with PIs and NNRTIs.

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