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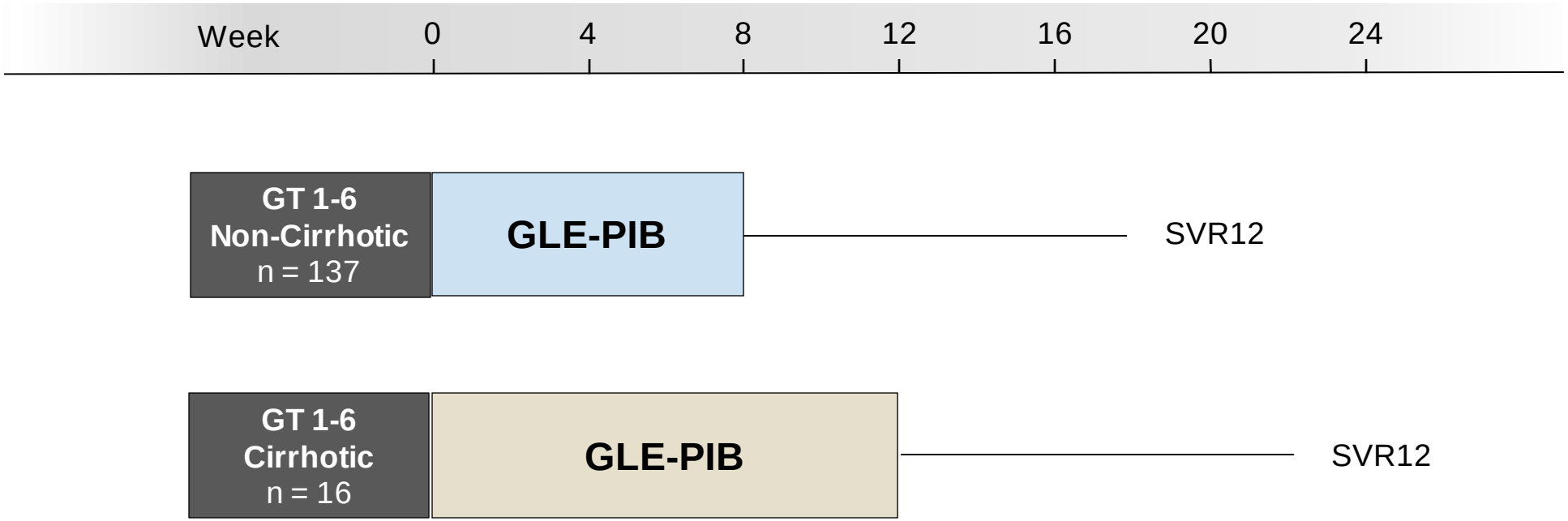
# Glecaprevir-Pibrentasvir in HIV-HCV Coinfected Patients
# EXPEDITION-2: Study Design




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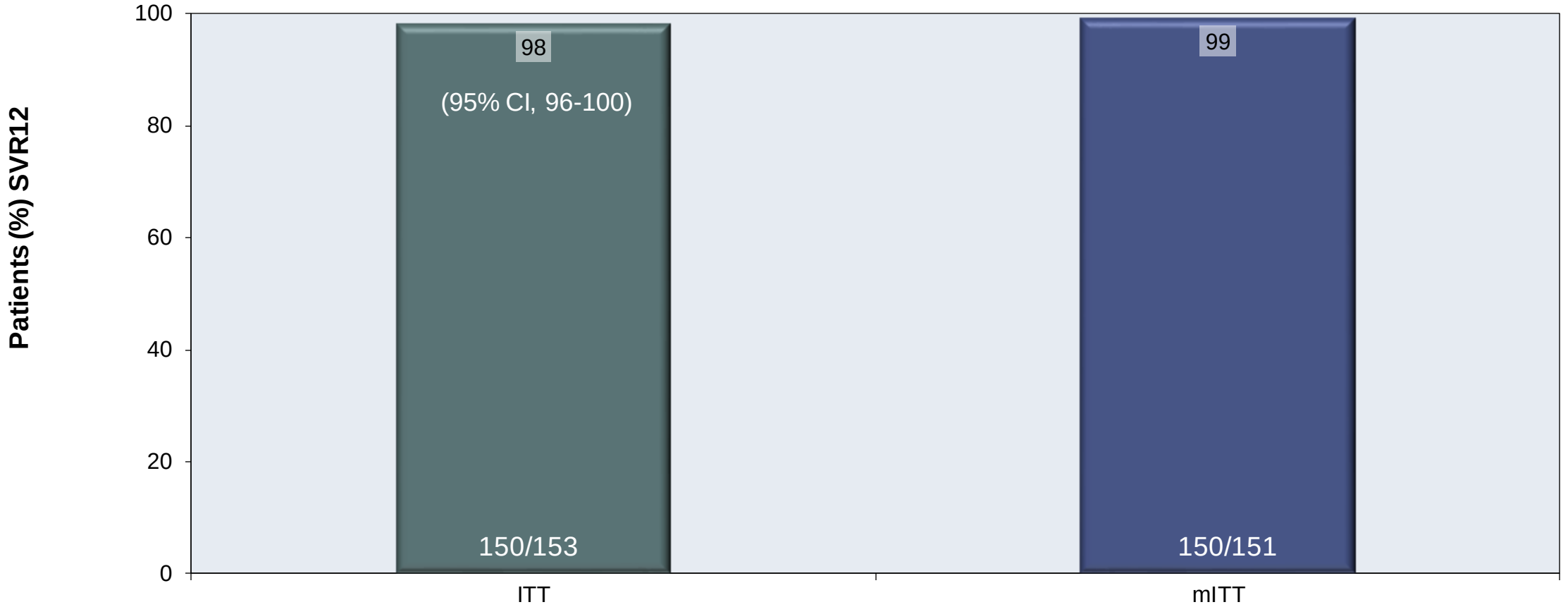
# Glecaprevir-Pibrentasvir in HIV-HCV Coinfected Patients EXPEDITION-2: Results




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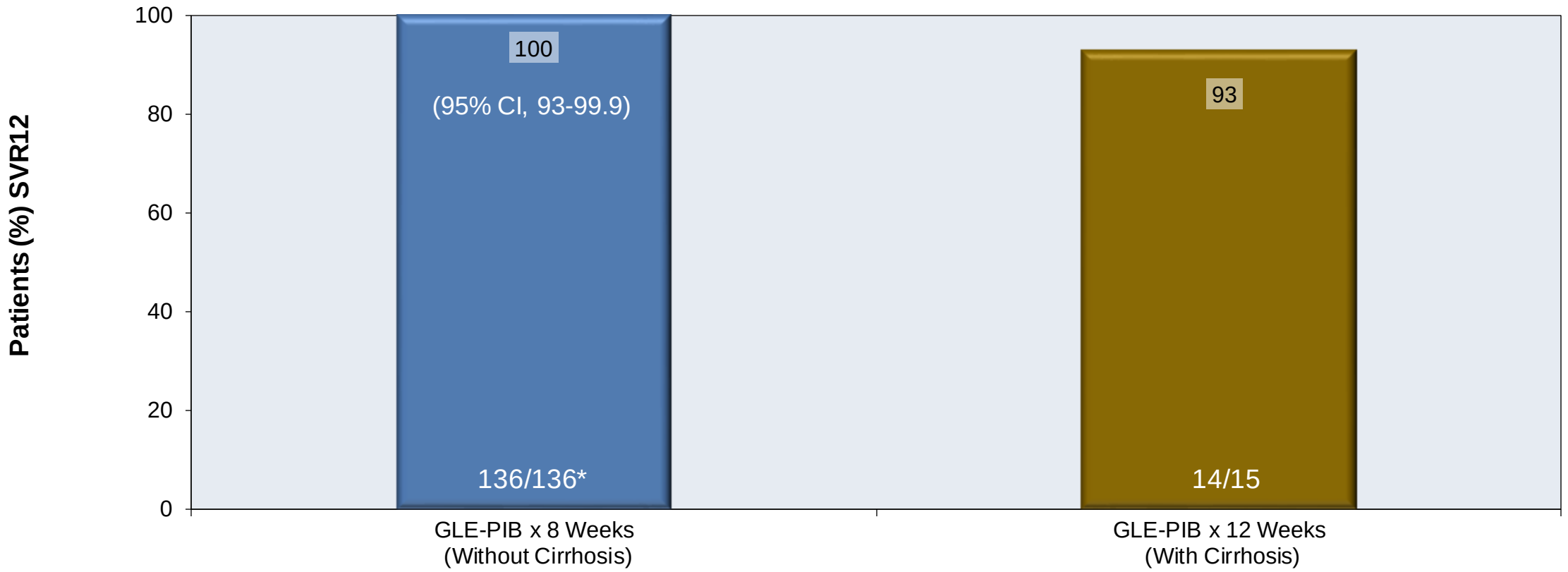
# Glecaprevir-Pibrentasvir in HIV-HCV Coinfected Patients
## EXPEDITION-2: Results




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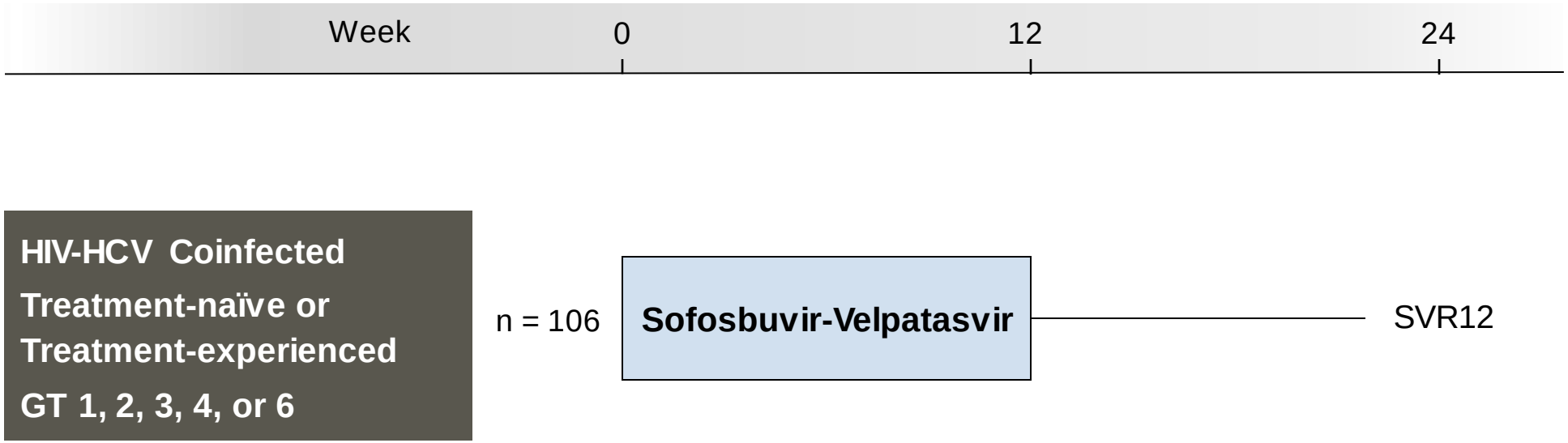
# Sofosbuvir-Velpatasvir in HIV-HCV Coinfected Patients
# ASTRAL-5: Study Design

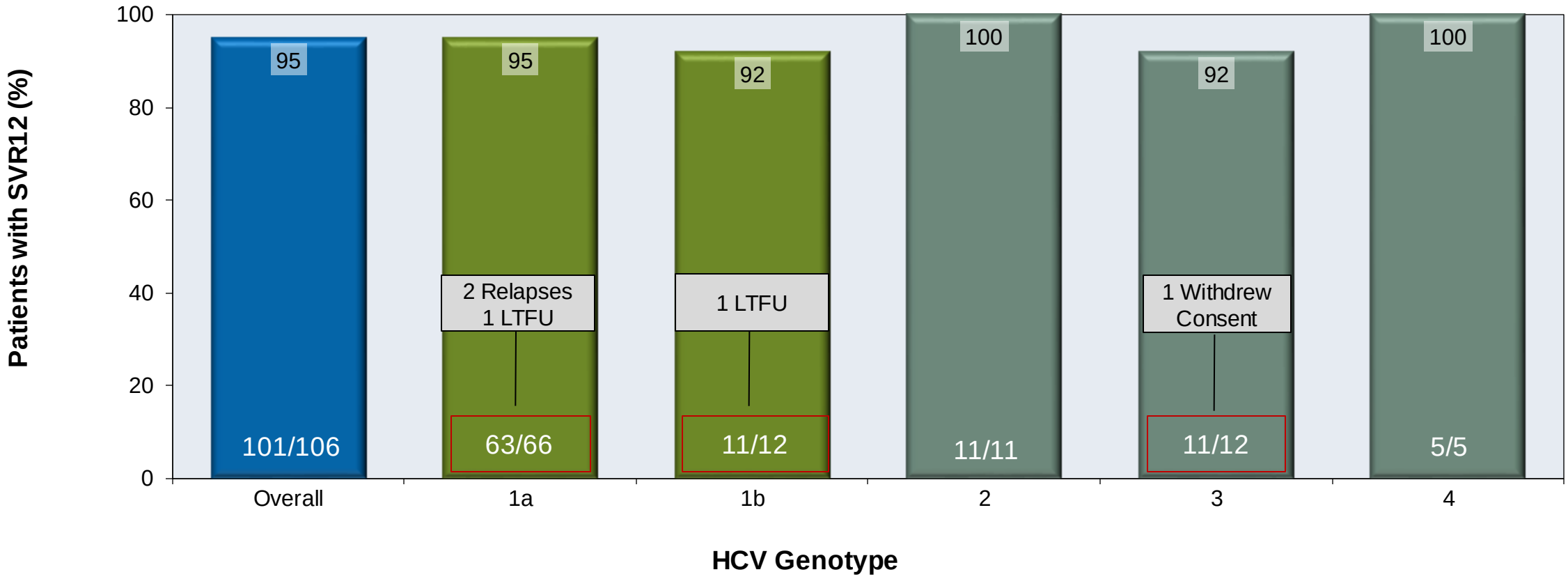



**Drug Dosing**: Sofosbuvir-velpatasvir (400/100 mg): fixed-dose combination; one pill once daily

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

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

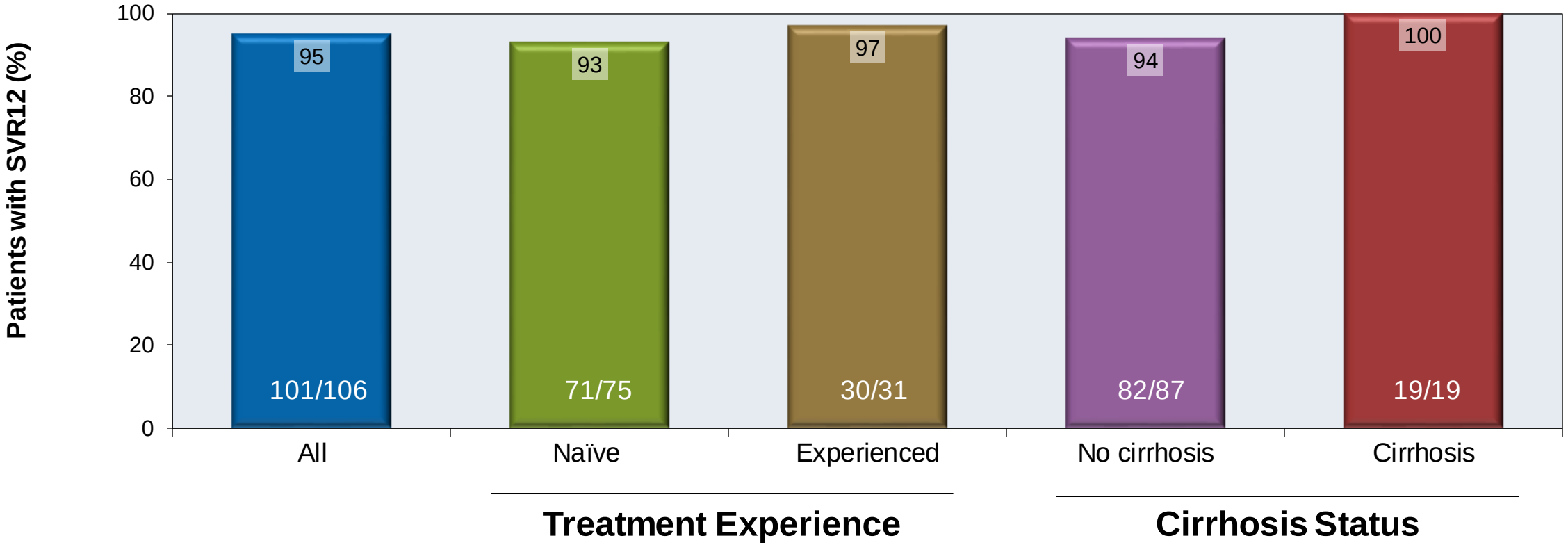
## SVR12 Results by Genotype




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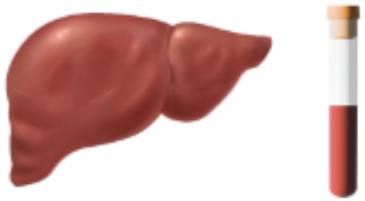
# Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection ACTG A5360 (MINMON):

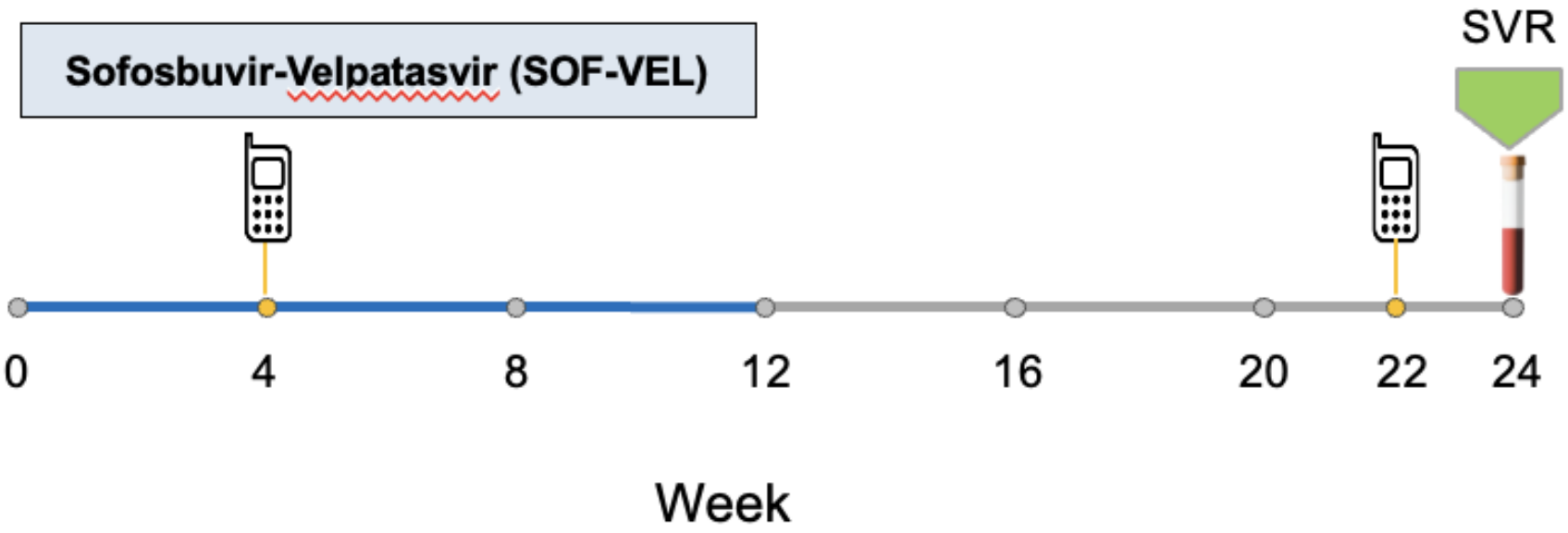
No Genotype

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.

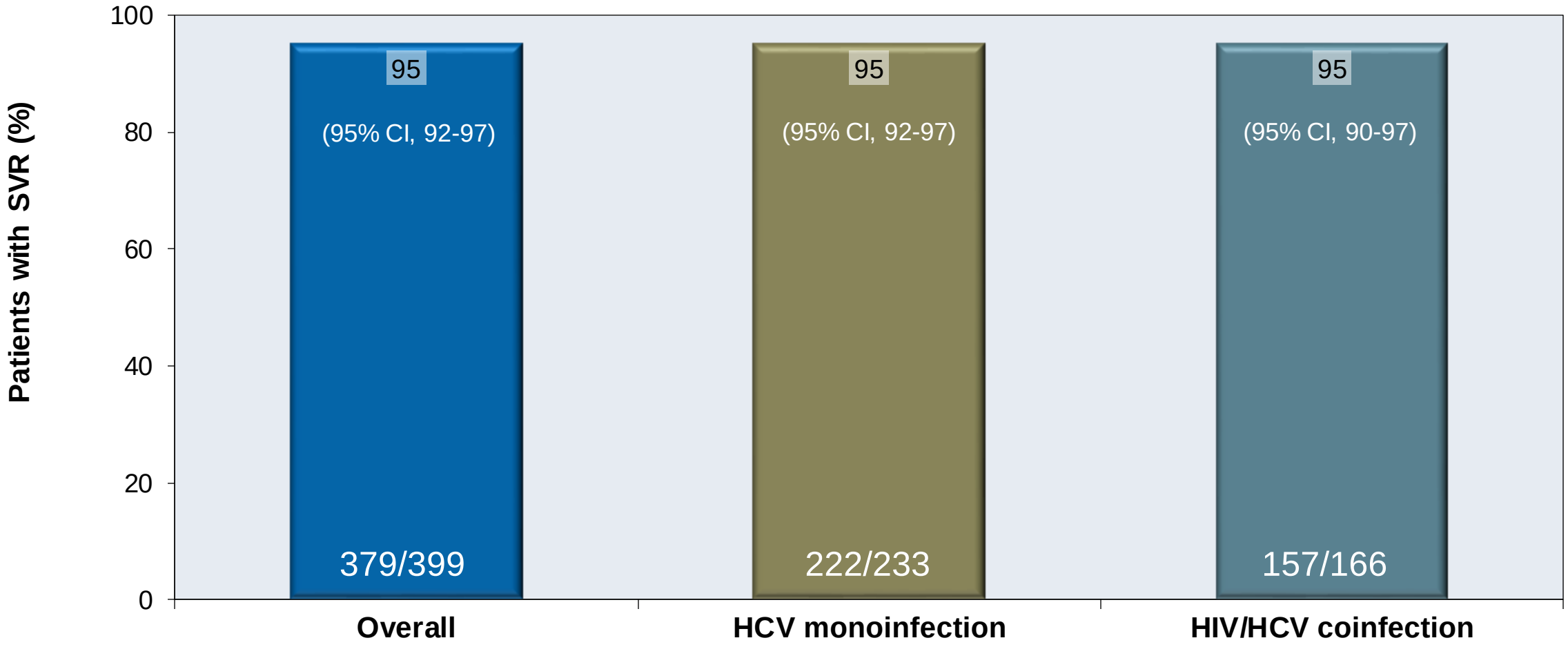
# Sofosbuvir-Velpatasvir with Minimal Monitoring +/- HIV Coinfection ACTG A5360 (MINMON): Study Population

| 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 (%)<br>White<br>Black<br>Asian | <br>166 (42)<br>72 (18)<br>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 (%)<br>Suppressed on antiretroviral therapy, n (% of HIV/HCV) | 166 (42)<br>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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