Ledipasvir-Sofosbuvir in GT1 or GT4 and HIV Coinfection

ION-4

National HIV Curriculum

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Features

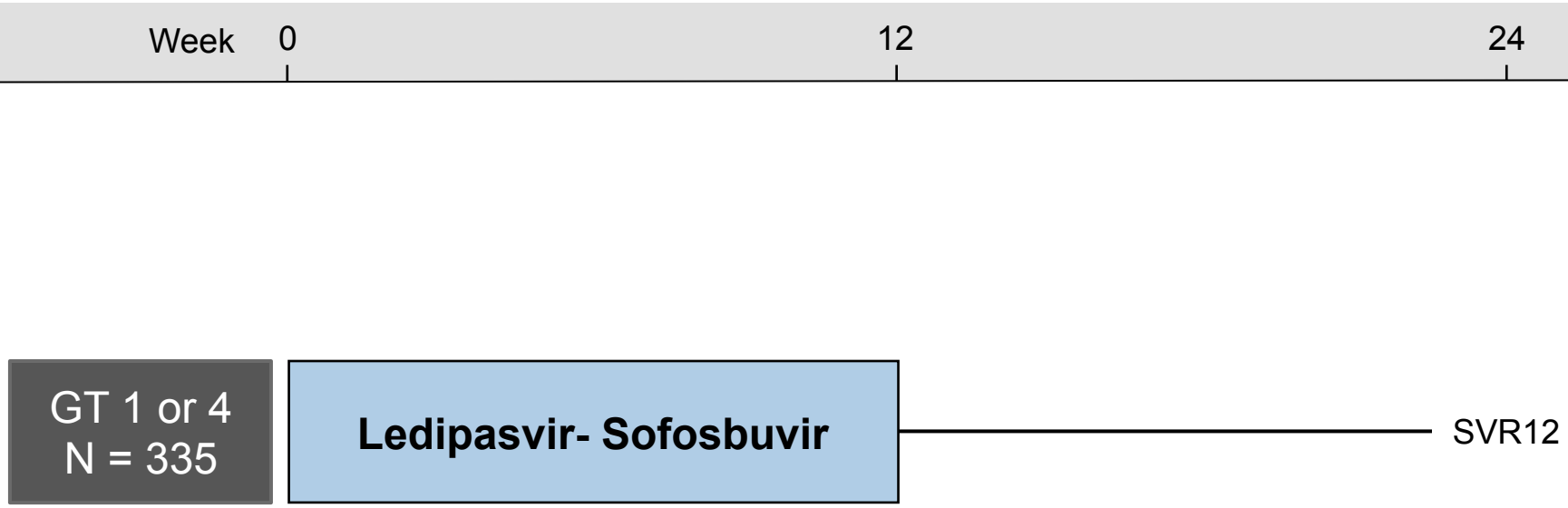
ION-4 Trial

- **Design**: Open-label, single group, phase 3 trial, using ledipasvir-sofosbuvir for 12 weeks in treatment-naïve or treatment-experienced patients with GT 1 or 4 and HIV coinfection
- **Setting**: multicenter in United States, Canada, New Zealand
- **Entry Criteria**
  - Chronic HCV Genotype 1 or 4
  - Treatment-naïve or treatment experienced
  - Noncirrhotic or compensated cirrhosis
  - Platelet count > 50,000/mm^3, hemoglobin ≥10 mg/dL, CrCl≥60 mL/min
  - Stable ARV with HIV RNA < 50 copies/ml and CD4 count > 100 cells/mm^3
  - ARV regimens: tenofovir-emtricitabine plus either efavirenz, rilpivirine, or raltegravir
- **End-Points**: Primary = SVR12; safety and tolerability

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

National HIV Curriculum

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Study Design



Drug Dosing: Ledipasvir-sofosbuvir (90/400 mg): fixed dose combination; one pill once daily

Antiretrovirals allowed: tenofovir-emtricitabine plus either efavirenz, rilpivirine, or raltegravir

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

National HIV Curriculum

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Baseline Characteristics

Baseline Characteristic	Ledipasvir-Sofosbuvir (n = 335)
Mean age, years	52
Male, n (%)	276 (82)
African American, n (%)	115 (34)
Hispanic or Latino, n (%)	56 (17)
Mean BMI, kg/m^2	26
IL28B CC, n (%)	81 (24)
GT 1 (%)	327 (98)
HCV treatment experienced, n (%)	185 (55)
Cirrhosis, n (%)	67 (20)
Mean HCV RNA, log_{10} IU/mL	6.7 ± 0.6
Median CD4 Count, $cells/mm^3$ (range)	628 (100-2069)

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

National HIV Curriculum

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Antiretroviral Regimens

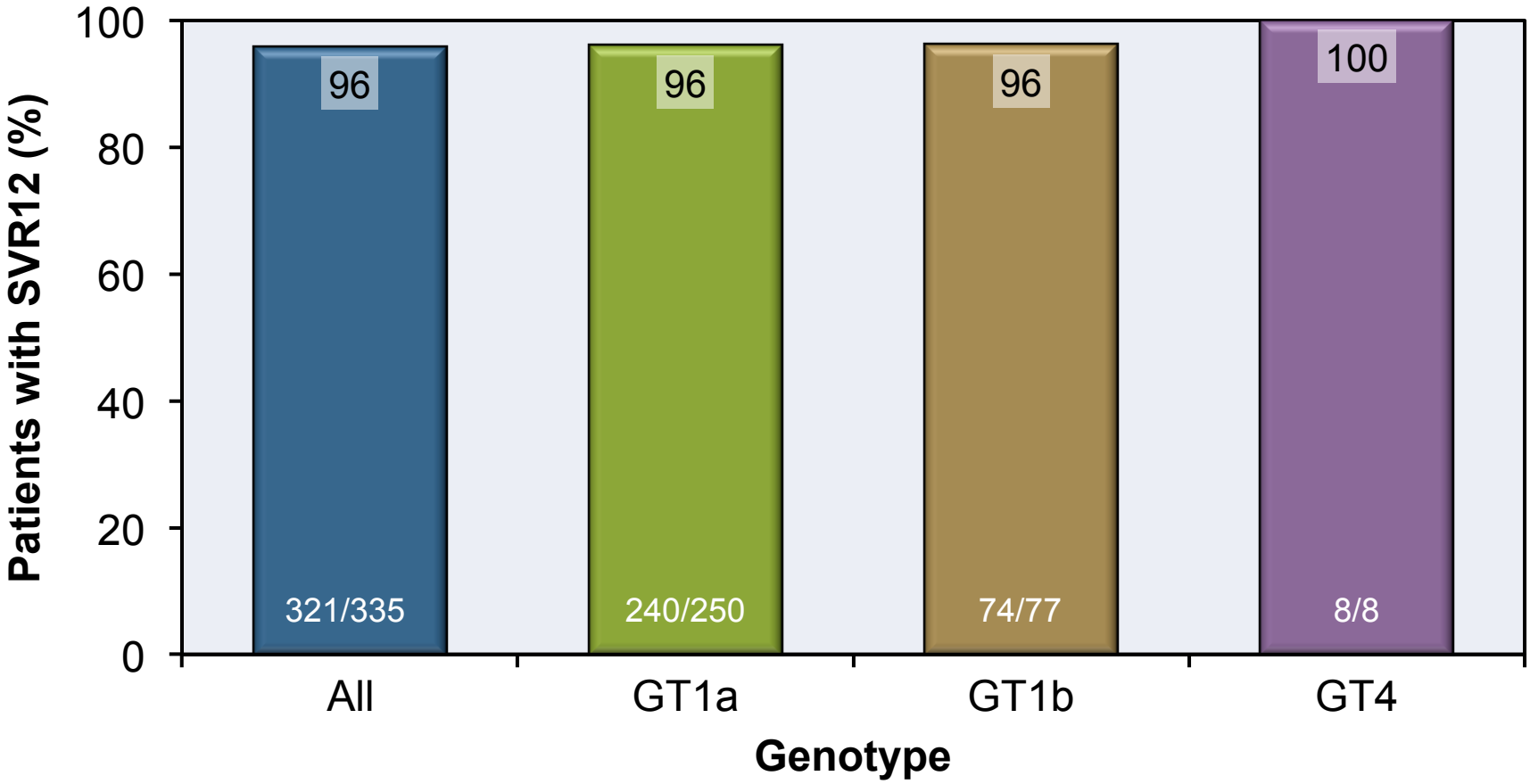
ION-4: HIV Antiretroviral Regimen	
Antiretroviral Agent	**Antiretroviral Received** (n = 335)
Tenofovir-emtricitabine-efavirenz	160 (48)
Tenofovir-emtricitabine-rilpivirine	29 (9)
Tenofovir-emtricitabine + Raltegravir	146 (44)

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

National HIV Curriculum

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Results

ION-4: SVR12 Results by Genotype

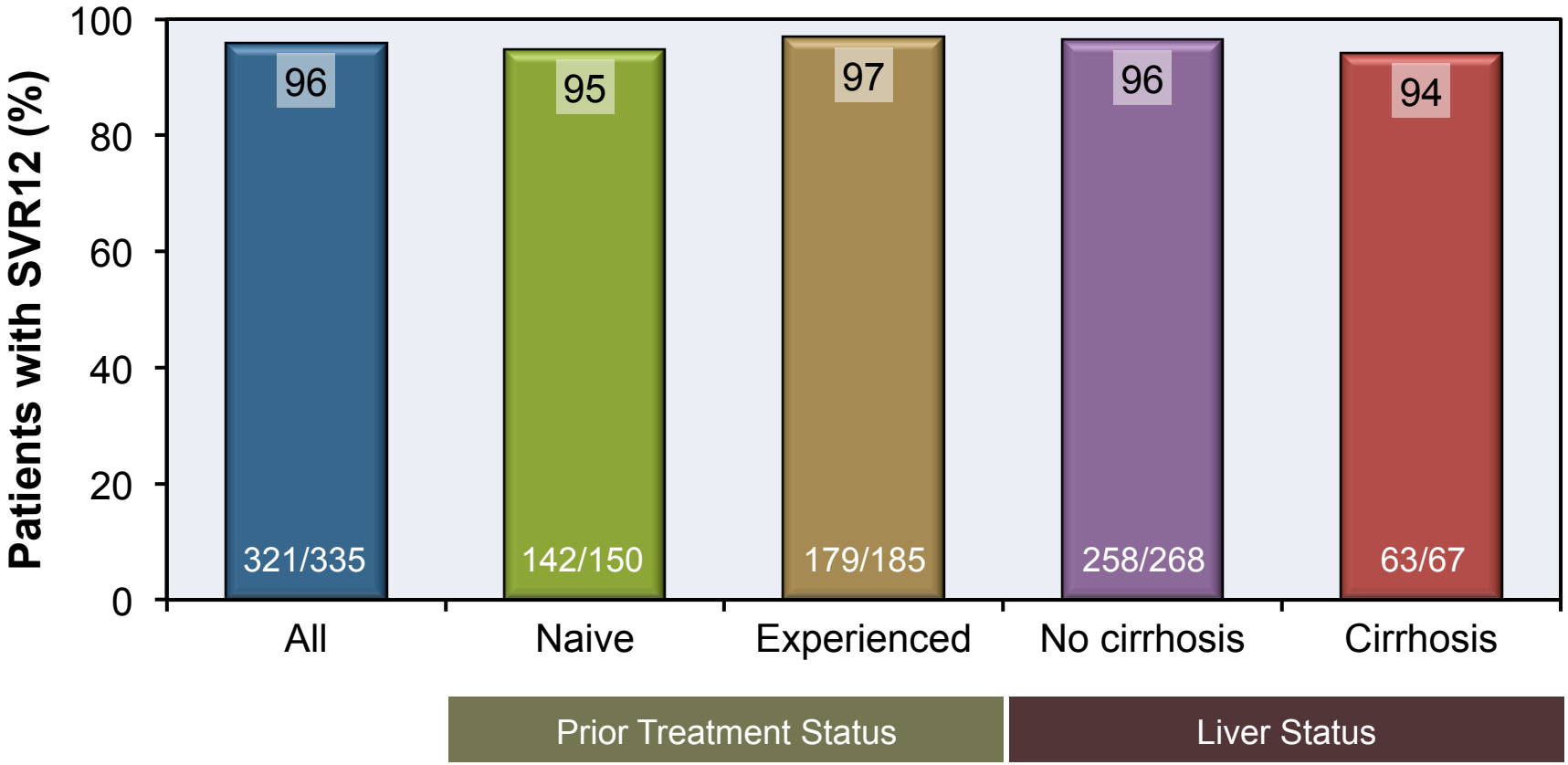


Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

National HIV Curriculum

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Results

ION-4: SVR12 Results by Prior Treatment Status and Liver Status



Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

National HIV Curriculum

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Adverse Effects

Event	Ledipasvir-Sofosbuvir (n = 335)
Discontinuation due to adverse event	0
Grade 3-4 Adverse Event	14 (4%)
Serious Adverse Event	8 (2%)
Headache	83 (25%)
Fatigue	71 (21%)
Diarrhea	36 (11%)
Nausea	33 (10%)
Arthralgia	22 (7%)
Upper respiratory tract infection	18 (5%)
Vomiting	14 (4%)
Muscle spasms	11 (3%)

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

National HIV Curriculum

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Conclusions

Conclusions: “Ledipasvir and sofosbuvir for 12 weeks provided high rates of sustained virologic response in patients coinfected with HIV-1 and HCV genotype 1 or 4.”

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Acknowledgment

The **National HIV Curriculum** is an AIDS Education and Training Center (AETC) Program resource funded by the United States Health Resources and Services Administration. The project is led by the University of Washington and the AETC National Coordinating Resource Center.

The content in this slide set does not represent the official views of the U.S. Department of Health and Human Services, Health Resources & Services Administration.

National HIV Curriculum

AETC AIDS Education & Training Center Program
National Coordinating Resource Center