Treatment-Naïve and Treatment-Experienced

Daclatasvir-Asunaprevir-Beclabuvir in GT1 Patients without Cirrhosis

UNITY-1 Study

Poordad F, et al. JAMA 2015;313:1728-35.

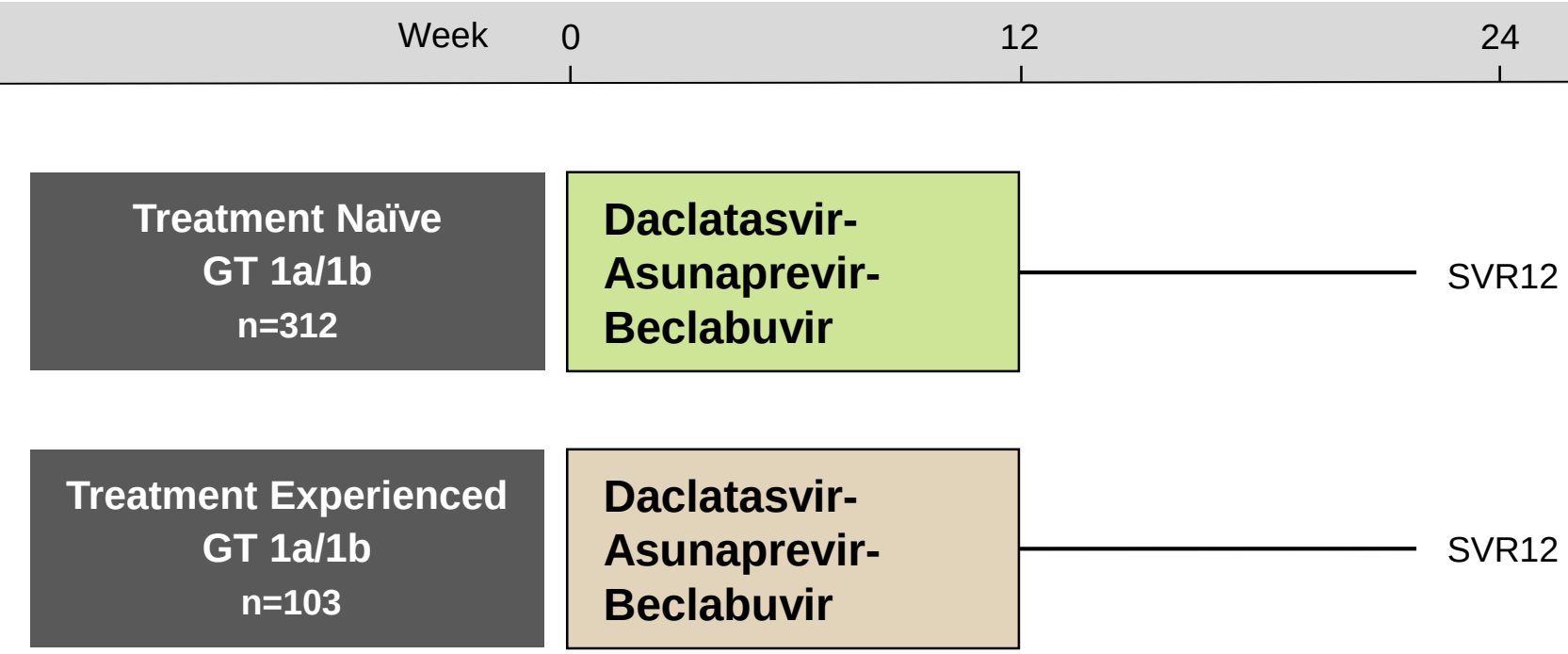
Daclatasvir-Asunaprevir-Beclabuvir for HCV GT 1
UNITY-1 Trial: Study Features

Daclatasvir-Asunaprevir-Beclabuvir Trial: Features

- **Design**: Multicenter, open-label single-arm phase 3 trial of daclatasvir-asunaprevir-beclabuvir (fixed-dose combination) +/- ribavirin in treatment-naïve or experienced, chronic HCV GT 1 patients without cirrhosis
- **Setting**: Multiple centers in the United States, Canada, Australia, France
- **Entry Criteria**
  - Chronic HCV Genotype 1
  - No cirrhosis
  - Treatment-naïve or treatment-experienced
  - HCV RNA ≥10,000 IU/ml
- **End-Points**: Primary = SVR12

Source: Poordad F, et al. JAMA 2015;313:1728-35.

Daclatasvir-Asunaprevir-Beclabuvir for HCV GT 1
UNITY-1 Trial: Study Design



Drug Dosing

Daclatasvir-Asunaprevir-Beclabuvir (30/200/75 mg): fixed dose combination BID

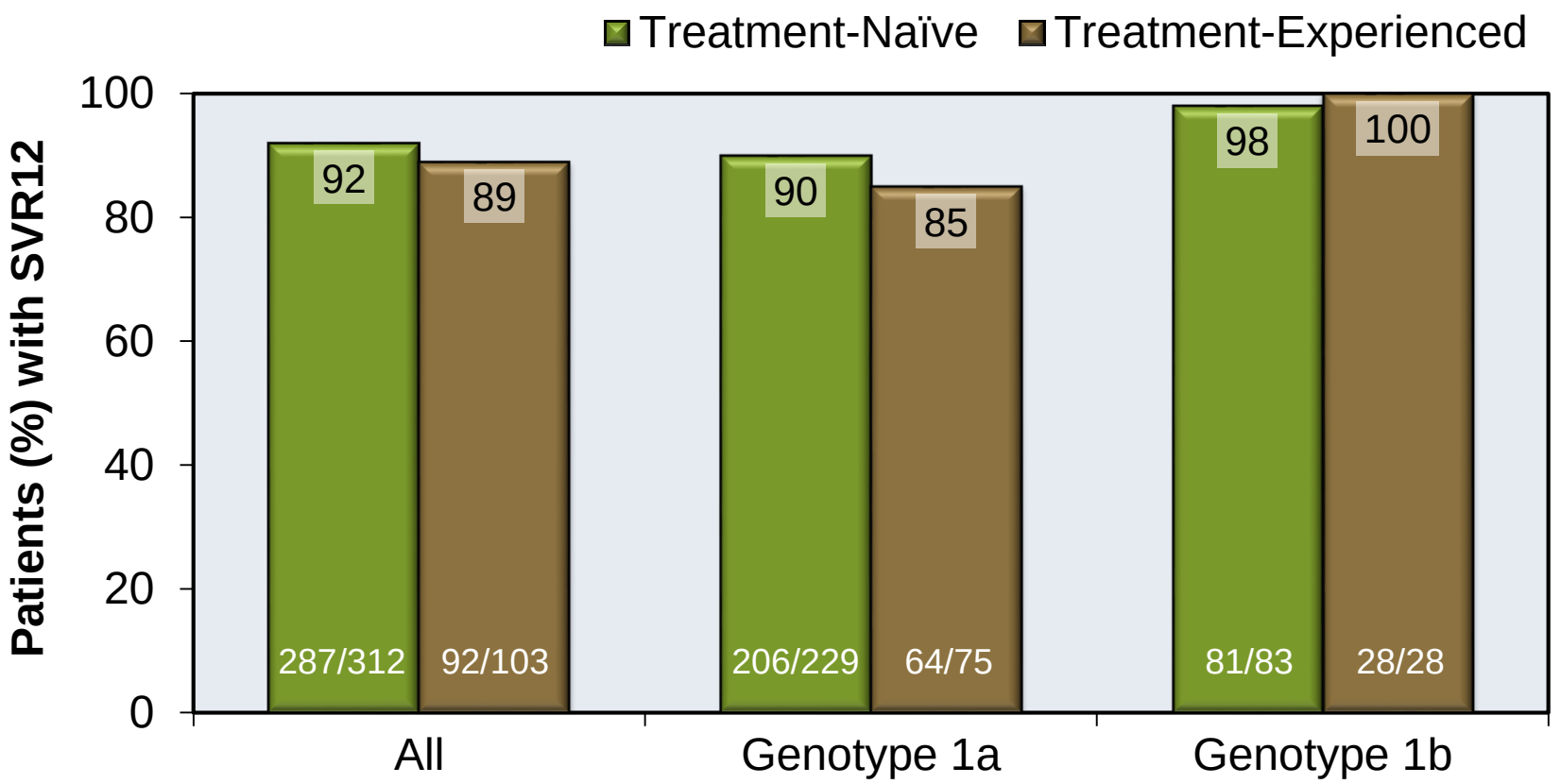
Source: Poordad F, et al. JAMA 2015;313:1728-35.

Daclatasvir-Asunaprevir-Beclabuvir for HCV GT 1
UNITY-1 Trial: Patient Characteristics

Characteristic	Treatment-Naïve (n=312)	Treatment-Experienced (n=103)
Male	175 (56%)	64 (62%)
Median age, years (range)	54 (19-77)	57 (22-69)
Race White Black Asian	 270 (87%) 34 (11%) 9 (2%)	 91 (88%) 7 (7%) 2 (2%)
HCV RNA ≥800,000 IU/ml	244 (78%)	93 (90%)
HCV subtype 1A	229 (73%)	75 (73%)
IL28B non-CC genotype	221 (71%)	87 (85%)
Prior treatment failure Relapse Partial response Null response Interferon intolerant	 N/A N/A N/A N/A	 39 (38%) 12 (12%) 25 (24%) 7 (7%)

Source: Poordad F, et al. JAMA 2015;313:1728-35.

Daclatasvir-Asunaprevir-Beclabuvir for HCV GT 1
UNITY-1 Trial: Results



DCV = daclatasvir; ASV = asunaprevir; BCV = beclabuvir

Source: Poordad F, et al. JAMA 2015;313:1728-35.

Daclatasvir-Asunaprevir-Beclabuvir for HCV GT 1
UNITY-1 Trial: Virologic Failure

- Virologic failure occurred in 34 patients (8%): 32 of whom had genotype 1A infection.
- Among GT1A patients who failed, NS5A resistance-associated variants (RAVs) emerged in 30/31 (97%) patients
  - Q30 most common substitution
- NS3 protease RAVs emerged in 29/31 (94%) genotype 1A patients
  - R155 most common substitution
- NS5B RAVs emerged in 12 of 31 (39%) genotype 1A patients
  - P495 most common substitution

Source: Poordad F, et al. JAMA 2015;313:1728-35.

Daclatasvir-Asunaprevir-Beclabuvir for HCV GT 1
UNITY-1 Trial: Adverse Events

Event	Total Patients (n=415)
Serious Adverse Events (AEs)	7 (2%)
AEs leading to discontinuation	3 (1%)
Adverse Events, ≥10% incidence	
Headache	107 (26%)
Fatigue	69 (17%)
Diarrhea	58 (14%)
Nausea	56 (14%)
Grade 3 or 4 Lab Abnormalities	
Hemoglobin < 9 g/dl	0
Neutrophils < 0.75 x 10^9/L	2 (0.5%)
ALT >5 x ULN	19 (5%)
AST >5 x ULN	9 (2%)
Bilirubin, total > 2.5 x ULN	0
Lipase, total > 3 x ULN	16 (4%)

ULN = upper limit of normal

Source: Poordad F, et al. JAMA 2015;313:1728-35.

Daclatasvir-Asunaprevir-Beclabuvir for HCV GT 1
UNITY-1 Trial: Conclusion

Conclusions and Relevance: “In this open-label, non-randomized, uncontrolled study, a high rate of SVR12 was achieved in treatment-naive and treatment-experienced noncirrhotic patients with chronic HCV genotype 1 infection who received 12 weeks of treatment with the oral fixed-dose regimen of daclatasvir, asunaprevir, and beclabuvir.”

Source: Poordad F, et al. JAMA 2015;313:1728-35.

This slide deck is from the University of Washington's *Hepatitis C Online* and *Hepatitis Web Study* projects.

Hepatitis C Online

www.hepatitisc.uw.edu

Hepatitis Web Study

http://depts.washington.edu/hepstudy/

Funded by a grant from the Centers for Disease Control and Prevention.

Hepatitis
web study