Treatment-Naïve and Treatment-Experienced

# Daclatasvir-Asunaprevir-Beclabuvir in Genotype 1 Cirrhotics

# UNITY-2 Study

Muir A, et al. JAMA 2015;313:1736-44.

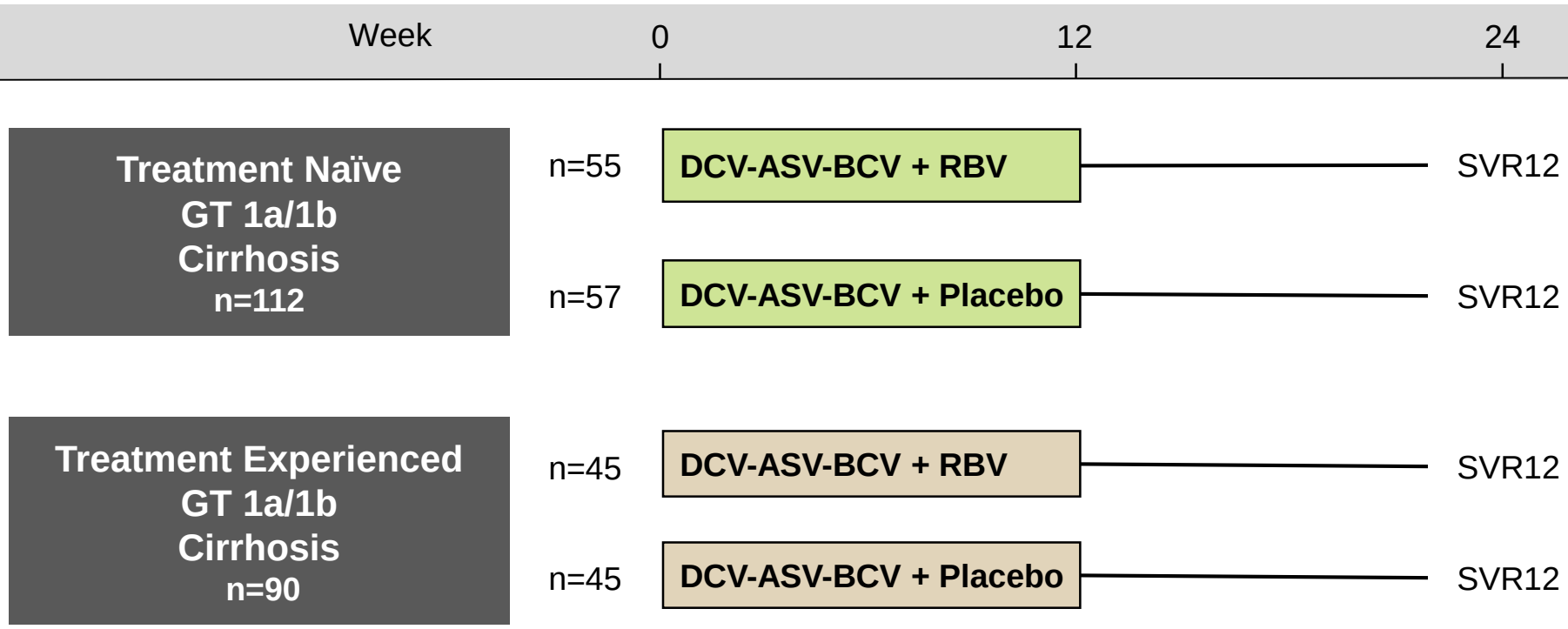
# Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1 UNITY-2 Trial: Study Features

## Daclatasvir-Asunaprevir-Beclabuvir Trial: Features

- **Design**: Multicenter, randomized, double-blind phase 3 trial of daclatasvir-asunaprevir-beclabuvir (fixed-dose combination) +/- ribavirin in treatment-naïve or experienced, chronic HCV GT 1 patients with compensated cirrhosis
- **Setting**: Multiple centers in the United States, Canada, Australia, France
- **Entry Criteria**
  - Chronic HCV Genotype 1
  - Compensated cirrhosis (METAVIR F4 or equivalent by biopsy, *FibroScan* >14.6 kPa or *FibroTest*/*FibroSURE* ≥0.75 or APRI >2)
  - Platelets >50,000 cells/$mm^3$
  - Albumin > 3.5 g/dL and INR < 1.7
  - Treatment-naïve or treatment-experienced
  - HCV RNA ≥10,000 IU/ml
- **End-Points**: Primary = SVR12

**Source: Muir A, et al. JAMA 2015;313:1736-44.**

# Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1
# UNITY-2 Trial: Study Design




**Drug Dosing**

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

Ribavirin (RBV): weight-based and divided BID (1000 mg/day if < 75kg or 1200 mg/day if ≥ 75kg)

**Source: Muir A, et al. JAMA 2015;313:1736-44.**

# Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1
# UNITY-2 Trial: Patient Characteristics

| Characteristic | Treatment-Naive | |
|---|---|---|
| | DCV-ASV-BCV + RBV (n=55) | DCV-ASV-BCV (n=57) |
| Male | 35 (64%) | 39 (68%) |
| Median age, years (range) | 59 (35-73) | 58 (25-75) |
| Race<br>White<br>Black/African American<br>Asian | <br>46 (84%)<br>6 (11%)<br>1 (2%) | <br>49 (86%)<br>6 (11%)<br>0 |
| HCV RNA ≥800,000 IU/ml | 41 (75%) | 93 (90%) |
| HCV subtype 1A | 39 (71%) | 75 (73%) |
| *IL28B* non-CC genotype | 37 (67%) | 43 (75%) |
| Platelets x $10^3$/µl<br>≥125<br>100-<125<br>50-<100<br>25-<50 | <br>28 (51%)<br>10 (18%)<br>16 (29%)<br>1 (2%) | <br>35 (63%)<br>13 (23%)<br>8 (14%)<br>0 |

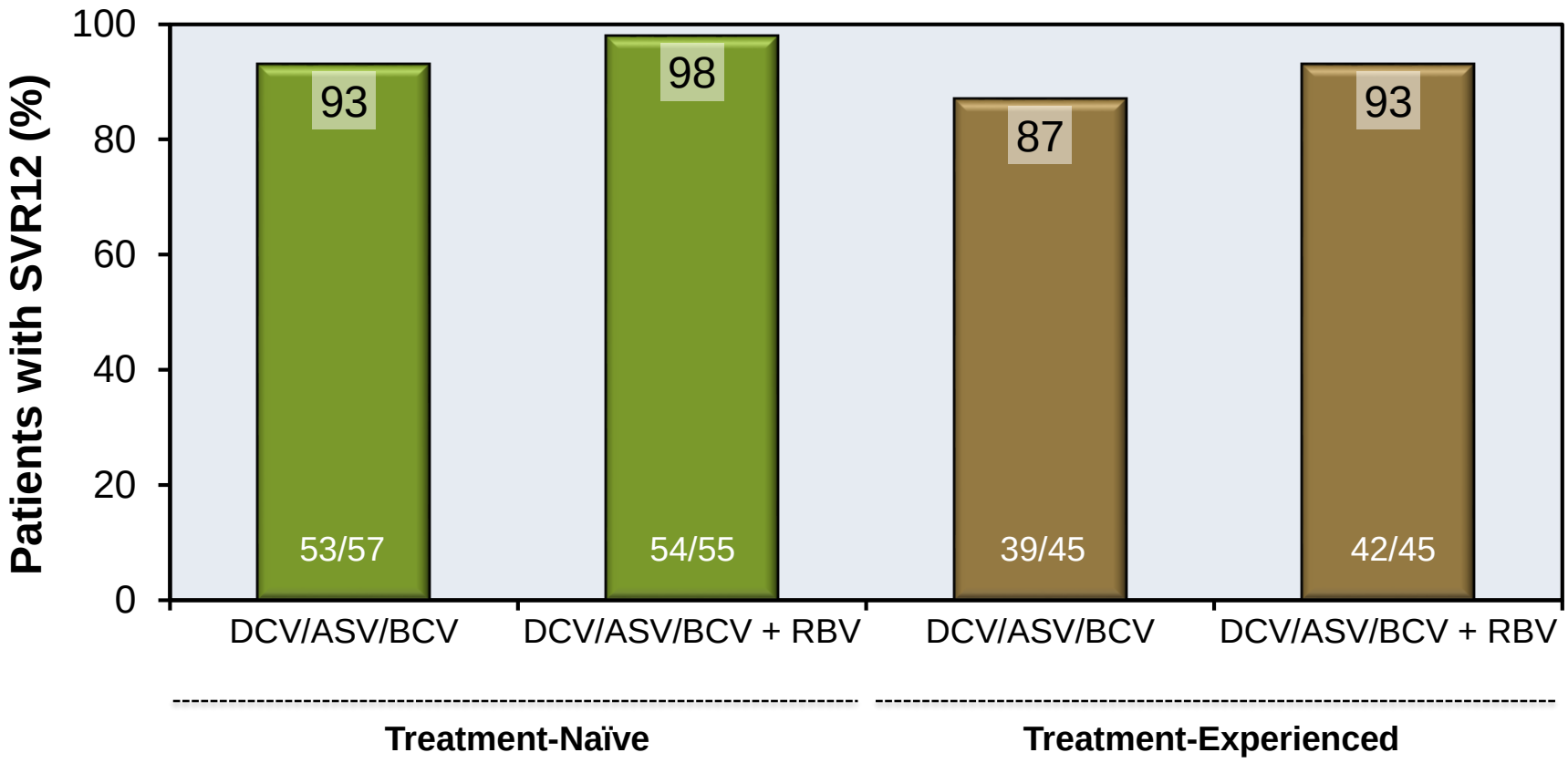
**Source: Muir A, et al. JAMA 2015;313:1736-44.**

# Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1
# UNITY-2 Trial: Patient Characteristics

| Characteristic | Treatment-Experienced | |
|---|---|---|
| | DCV-ASV-BCV + RBV (n=45) | DCV-ASV-BCV (n=45) |
| Male | 27 (60%) | 32 (71%) |
| Median age, years (range) | 60 (48-73) | 59 (19-76) |
| Race | | |
| White | 37 (82%) | 41 (91%) |
| Black/African American | 6 (13%) | 2 (4%) |
| Asian | 1 (2%) | 2 (4%) |
| HCV RNA ≥800,000 IU/ml | 41 (91%) | 43 (96%) |
| HCV subtype 1A | 35 (78%) | 35 (78%) |
| *IL28B* non-CC genotype | 35 (80%) | 30 (67%) |
| Prior Treatment Outcome | | |
| Relapse | 8 (18%) | 8 (18%) |
| Partial Response | 2 (4%) | 6 (13%) |
| Null Response | 16 (36%) | 19 (42%) |
| Interferon-intolerant | 10 (22%) | 6 (13%) |

**Source: Muir A, et al. JAMA 2015;313:1736-44.**

# Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1
# UNITY-2 Trial: Results

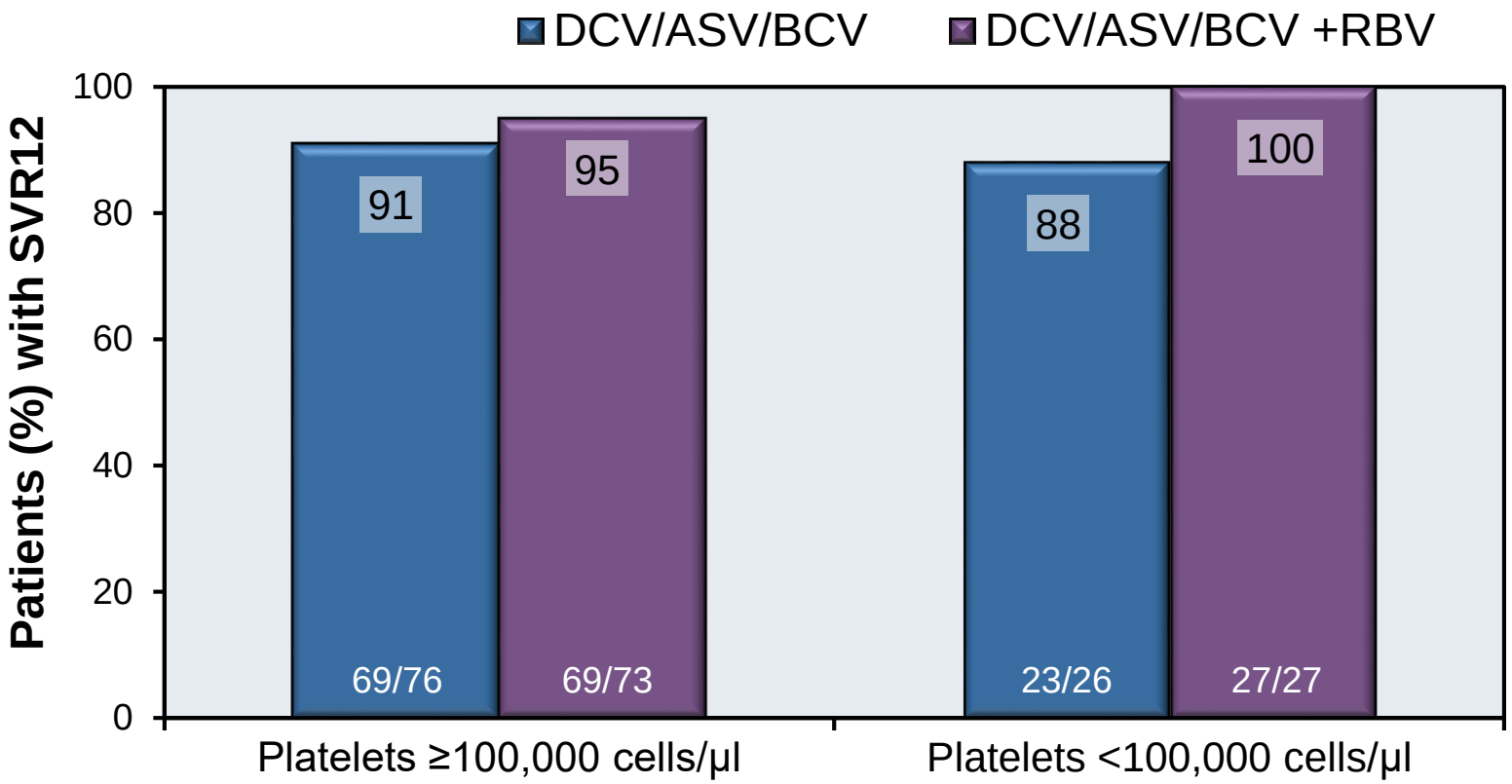



Abbreviations: DCV=daclatasvir; ASV=asunaprevir; BCV=beclabuvir; RBV=ribavirin

**Source: Muir A, et al. JAMA 2015;313:1736-44.**

# Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1
# UNITY-2 Trial: Results

## UNITY-2: SVR12 by Regimen and Platelet Count




Abbreviations: DCV=daclatasvir; ASV=asunaprevir; BCV=beclabuvir; RBV=ribavirin

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# Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1 UNITY-2 Trial: Adverse Events

| Event (%) | DCV-ASV-BCV (n=102) | DCV-ASV-BCV + RBV (n=100) |
|---|---|---|
| Serious Adverse Events (AEs) | 2 | 7 |
| AEs leading to discontinuation of all meds | 0 | 1 |
| Adverse Events, ≥10% incidence | | |
| Fatigue | 12 | 28 |
| Headache | 17 | 23 |
| Nausea | 14 | 17 |
| Diarrhea | 13 | 9 |
| Insomnia | 6 | 15 |
| Pruritus | 6 | 15 |
| Grade 3 or 4 Lab Abnormalities | | |
| Hemoglobin < 9 g/dl | 0 | 5 |
| ALT >5 x ULN | 3 | 1 |
| Lipase, total >3 x ULN | 5 | 1 |

Abbreviations: DCV=daclatasvir; ASV=asunaprevir; BCV=beclabuvir; RBV=ribavirin; ULN = upper limit of normal

**Source: Muir A, et al. JAMA 2015;313:1736-44.**

# Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1 UNITY-2 Trial: Conclusion

**Conclusions and Relevance**: “In this open-label, uncontrolled study, patients with chronic HCV genotype 1 infection and cirrhosis who received a 12-week oral fixed-dose regimen of daclatasvir, asunaprevir, and beclabuvir, with or without ribavirin, achieved high rates of SVR12.”

**Source: Muir A, et al. JAMA 2015;313:1736-44.**

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Hepatitis Web Study

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

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