Treatment-Naïve and Treatment-Experienced

Daclatasvir-Asunaprevir-Beclabuvir in Genotype 1 Cirrhotics

UNITY-2 Study

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

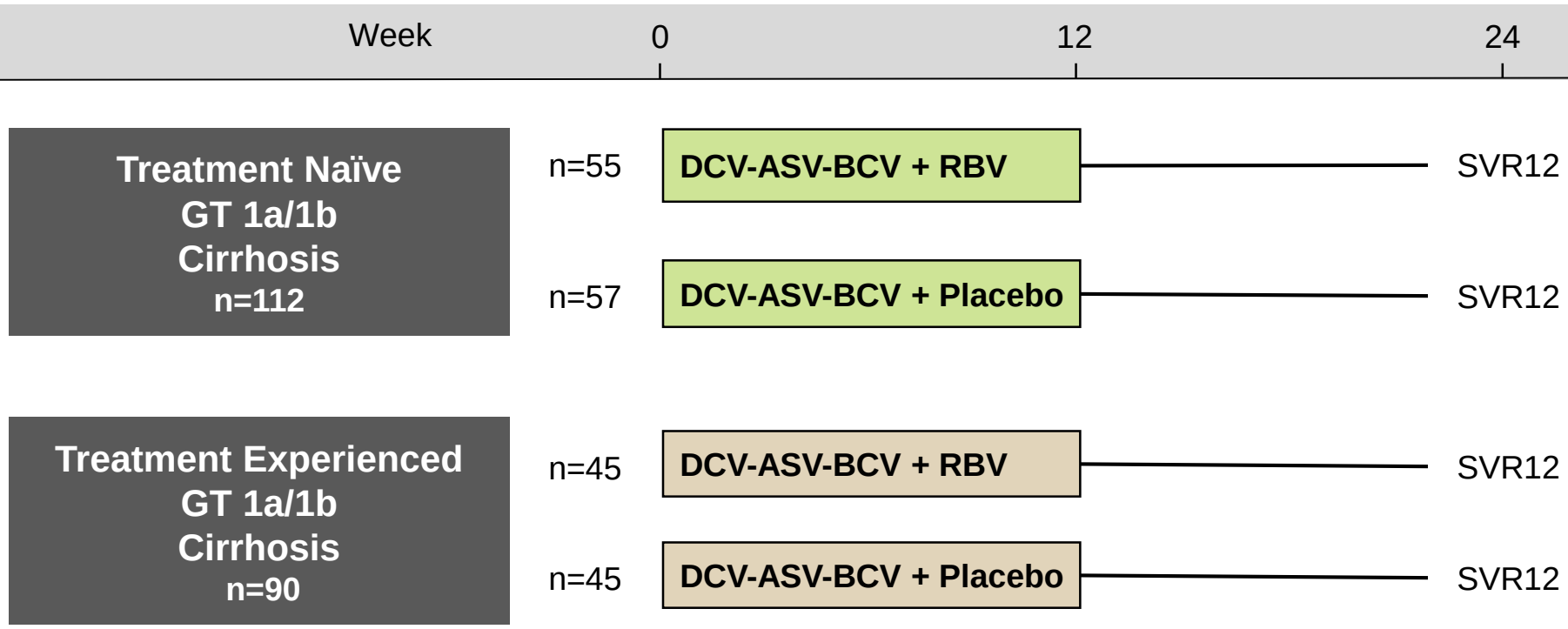
Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1 UNITY-2 Trial: Study Features

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)

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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 White Black/African American Asian	 46 (84%) 6 (11%) 1 (2%)	 49 (86%) 6 (11%) 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 ≥125 100-<125 50-<100 25-<50	 28 (51%) 10 (18%) 16 (29%) 1 (2%)	 35 (63%) 13 (23%) 8 (14%) 0

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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%)

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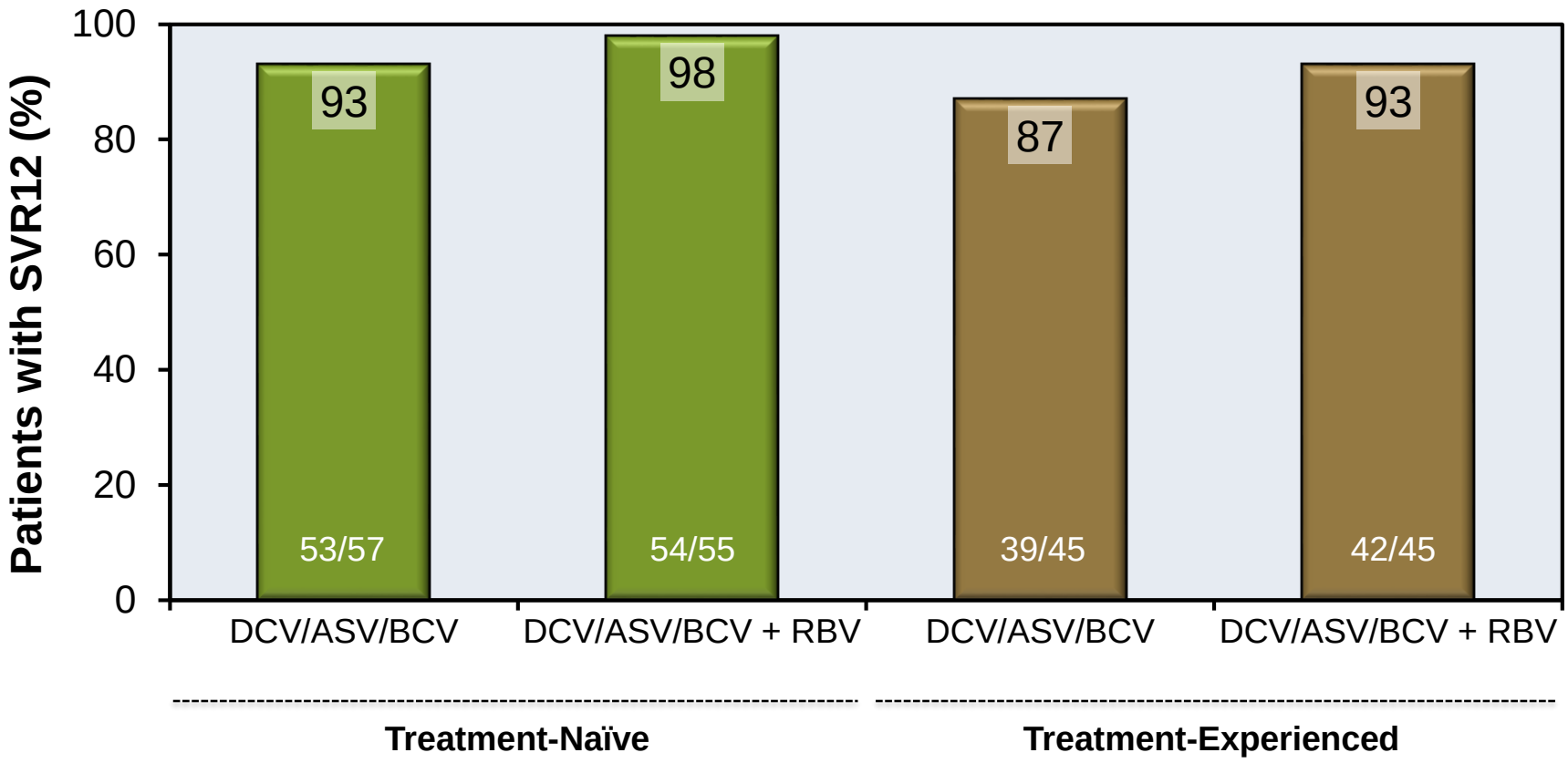
Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1
UNITY-2 Trial: Results



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

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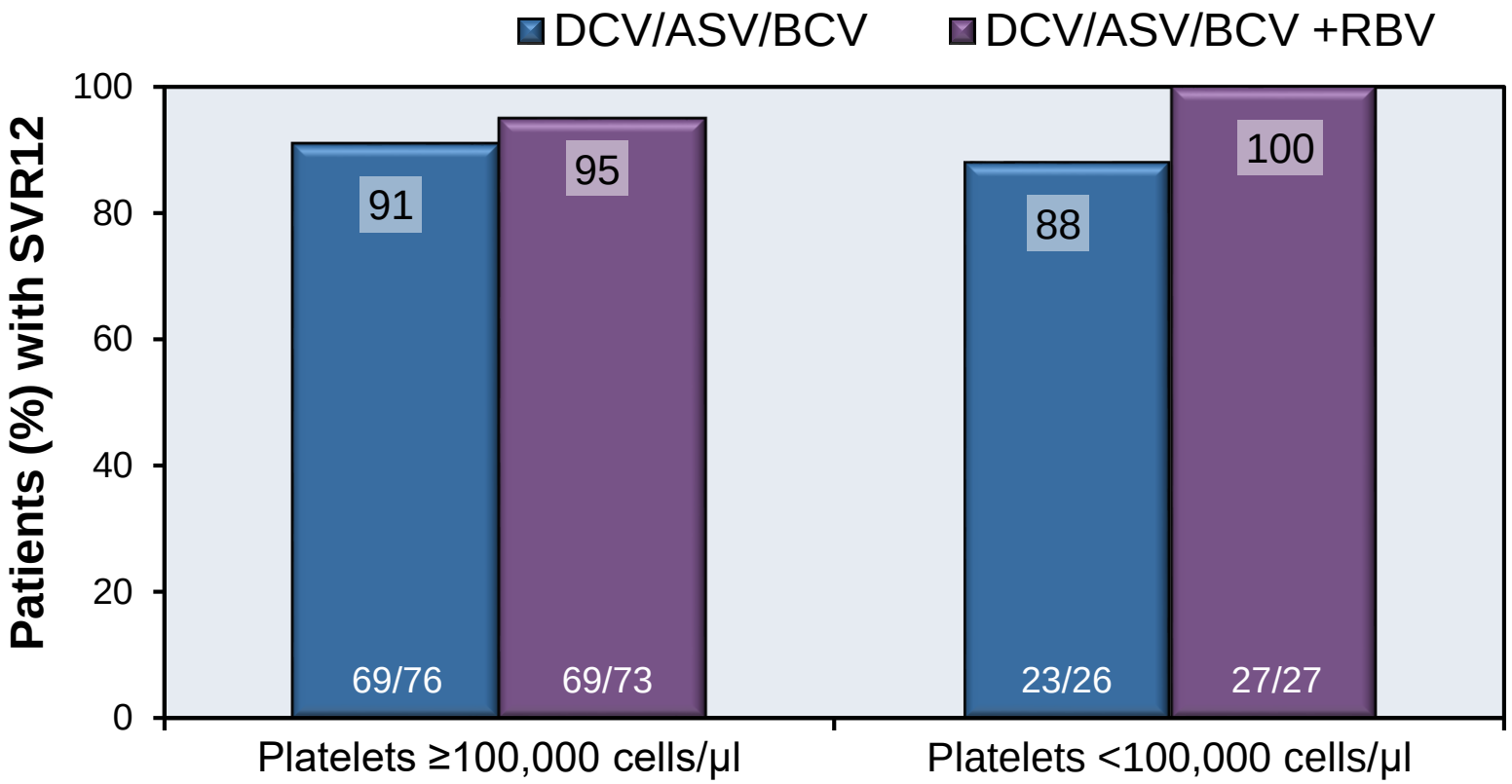
Daclatasvir-Asunaprevir-Beclabuvir +/- RBV for HCV GT 1
UNITY-2 Trial: Results

UNITY-2: SVR12 by Regimen and Platelet Count



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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/

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

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web study