

Treatment-Naïve and Treatment-Experienced

Daclatasvir + Asunaprevir in Genotype 1b HALLMARK-DUAL Study

Manns M, et al. Lancet. 2014;384:1597-605.

Daclatasvir + Asunaprevir for HCV GT 1b

HALLMARK-DUAL: Study Features

Daclatasvir + Sofosbuvir Trial: Features

- **Design:** Phase 3 open-label multi-cohort study of daclatasvir (DCV) plus asunaprevir in treatment-naïve or experienced, chronic HCV GT 1b
- **Setting:** 18 countries in North & South America, Europe and Asia
- **Entry Criteria**
 - Chronic HCV Genotype 1b
 - Treatment-naïve or treatment-experienced (prior null or partial responder to peginterferon + ribavirin)
 - Ineligible or intolerant (or both) to peginterferon + ribavirin
 - Compensated cirrhosis allowed
- **Patient Groups**
 - N = 307 treatment-naïve randomized to DCV + asunaprevir x 24 weeks versus placebo (latter then enrolled in separate DCV study)
 - N = 205 treatment-experienced: DCV + asunaprevir x 24 weeks
 - N = 235 Peg/RBV intolerant +/- ineligible: DCV + asunaprevir x 24 weeks
- **End-Points:** Primary = SVR12

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HALLMARK-DUAL: Study Design

Week 0 12 24 36

Treatment Naïve
n = 307

n = 205

Daclatasvir + Asunaprevir

SVR12

n = 102

Placebo

Separate
daclatasvir study

Prior Non-responder
n = 205

Daclatasvir + Asunaprevir

SVR12

Intolerant +/-
Ineligible
n = 235

Daclatasvir + Asunaprevir

SVR12

Drug Dosing

Daclatasvir: 60 mg once daily

Asunaprevir: 100 mg twice daily

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HALLMARK-DUAL: Patient Characteristics

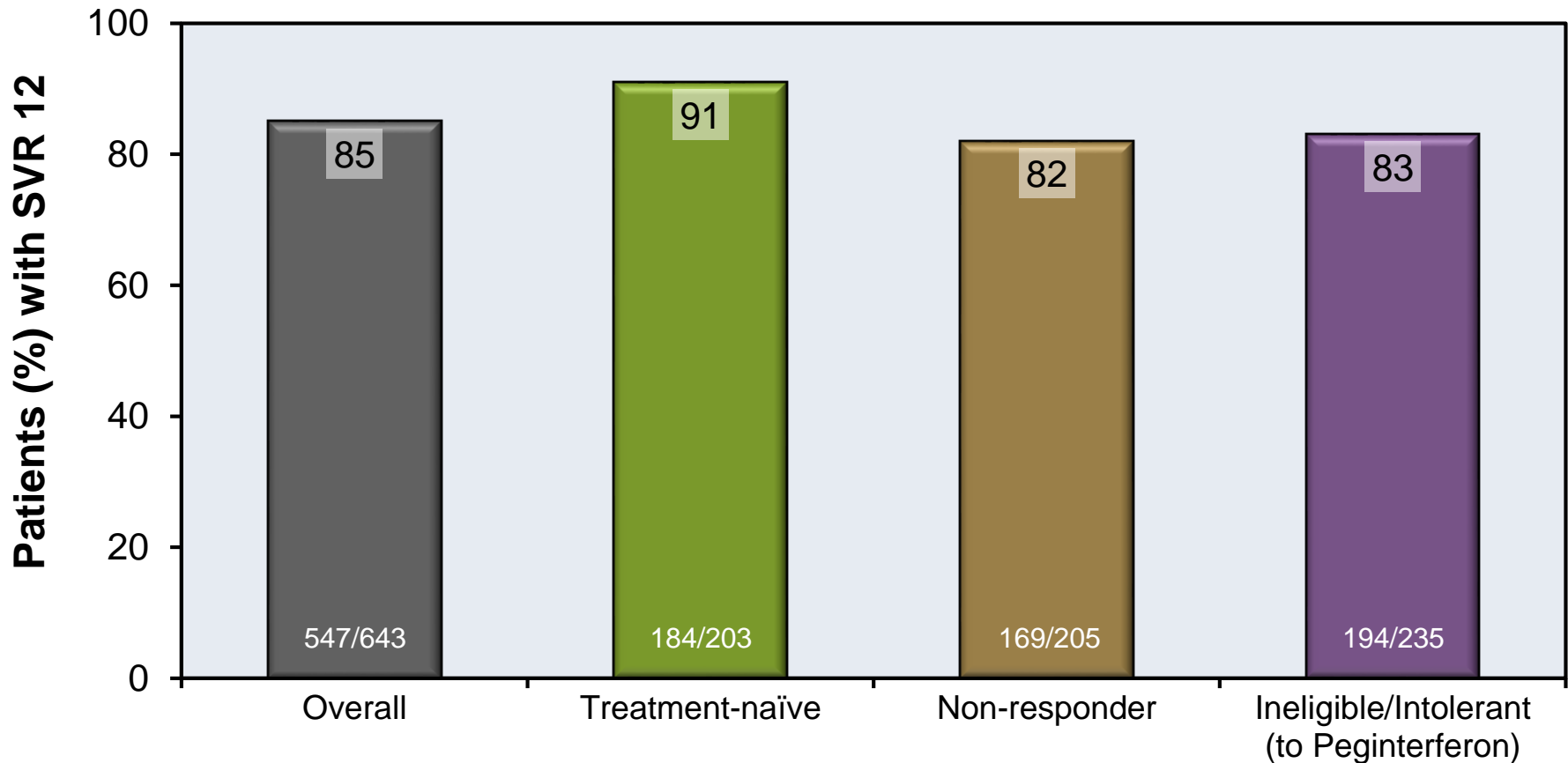
Characteristic	Treatment-naïve on DCV + ASV (n=205)	Treatment-naïve on Placebo (n=102)	Prior Non-responder (n=205)	Intolerant/Ineligible (n=235)
Age (years)	55 (20-79)	54 (22-83)	58 (23-77)	60 (24-77)
Men	101 (49%)	54 (53%)	111 (54%)	98 (42%)
Race				
White	135 (66%)	59 (58%)	148 (72%)	169 (72%)
Black	14 (7%)	8 (8%)	10 (5%)	10 (4%)
Asian	52 (25%)	45 (22%)	45 (22%)	56 (24%)
HCV RNA ≥800,000 IU/ml	152 (74%)	76 (75%)	178 (87%)	187 (80%)
Cirrhosis	33 (16%)	16 (16%)	63 (31%)	111 (47%)
Prior response to P/R				
Null	N/A	N/A	119 (58%)	N/A
Partial			84 (41%)	
Ineligible/intolerant reason				
Depression				71 (30%)
Anemia/neutropenia	N/A	N/A	N/A	87 (37%)
Advanced F3 or F4 ^a				77 (33%)

DCV=daclatasvir; ASV=asunaprevir. ^aCompensated (Child A) if cirrhotic but with thrombocytopenia.

Source: Manns M, et al. *Lancet*. 2014;384:1597-605.

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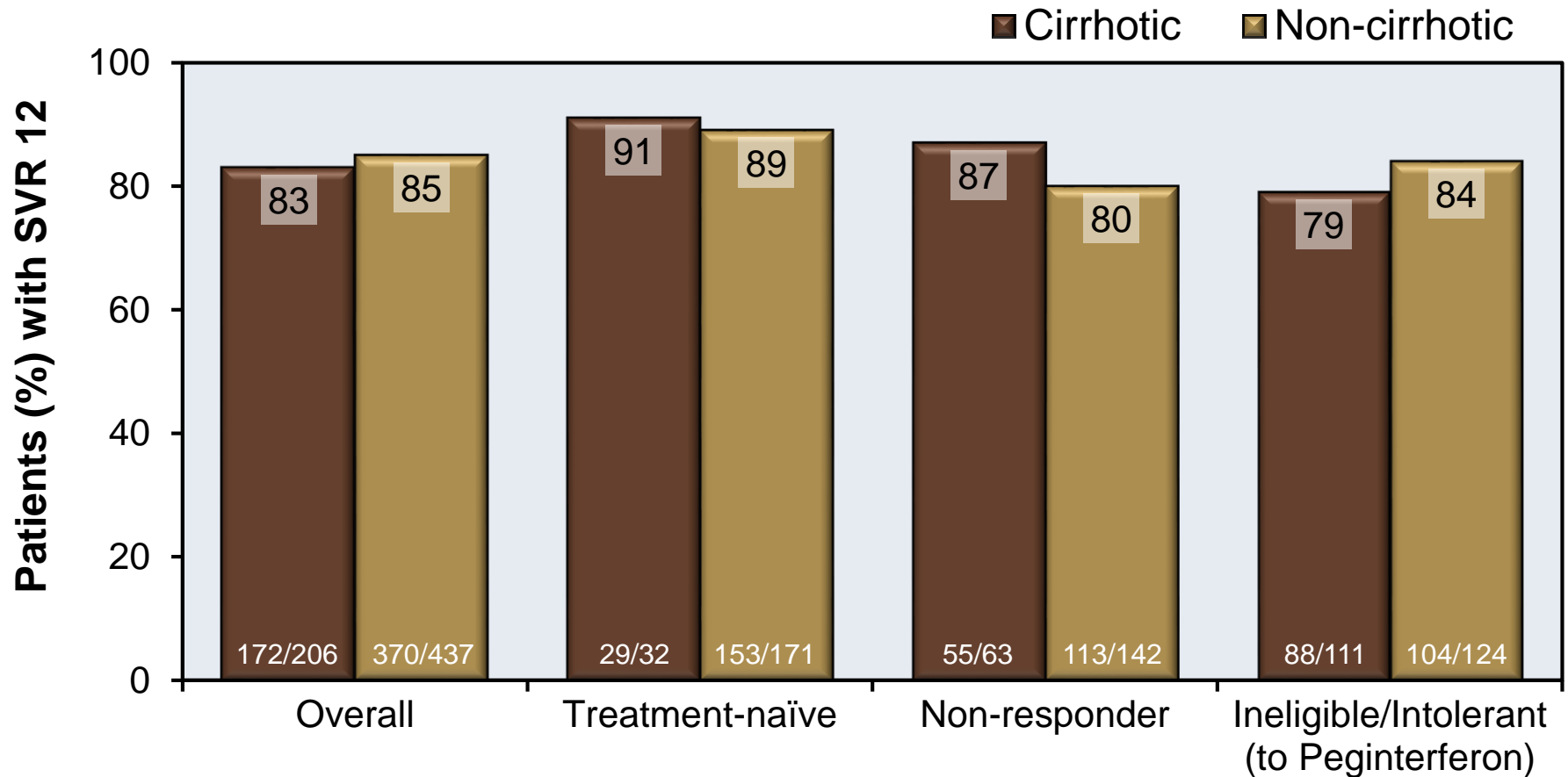
HALLMARK-DUAL: SVR12, by Treatment Experience



Source: Manns M, et al. Lancet. 2014;384:1597-605.

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HALLMARK-DUAL: SVR12, by Cirrhosis Status



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HALLMARK-DUAL: Adverse Events

Adverse Effects	Treatment-naïve on DCV + ASV (n=205)	Treatment-naïve on Placebo (n=102)	Prior Non-responder (n=205)	Intolerant/Ineligible (n=235)
Any adverse event	176 (86%)	74 (73%)	167 (81%)	204 (87%)
Serious adverse events	12 (6%)	1 (1%)	11 (5%)	16 (7%)
Adverse events leading to discontinuation	6 (3%)	0	2 (1%)	2 (1%)
Adverse events in ≥10% in any cohort				
Headache	50 (24%)	17 (17%)	50 (24%)	59 (25%)
Fatigue	43 (21%)	18 (18%)	45 (22%)	52 (22%)
Diarrhea	24 (12%)	10 (10%)	28 (14%)	51 (22%)
Nausea	25 (12%)	12 (12%)	22 (11%)	28 (12%)
Asthenia	4 (2%)	1 (1%)	12 (6%)	25 (11%)
Grade 3-4 lab events				
ALT 5.1-10 x ULN	1 (<1%)	2 (2%)	3 (1%)	3 (1%)
ALT >10 x ULN	6 (3%)	0	1 (<1%)	1 (<1%)
AST 5.1-10 x ULN	5 (2%)	1 (1%)	1 (<1%)	2 (1%)
AST >10 x ULN	2 (1%)	0	1 (<1%)	1 (<1%)

ULN, upper limit of normal

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Daclatasvir + Asunaprevir for HCV GT 1b HALLMARK-DUAL: Conclusions

Interpretation: “Daclatasvir plus asunaprevir provided high sustained virological response rates in treatment-naive, non-responder, and ineligible, intolerant, or ineligible and intolerant patients, and was well tolerated in patients with HCV genotype 1b infection. These results support the use of daclatasvir plus asunaprevir as an all-oral, interferon-free and ribavirin-free treatment option for patients with HCV genotype 1b infection, including those with cirrhosis.”

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/>

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