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

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

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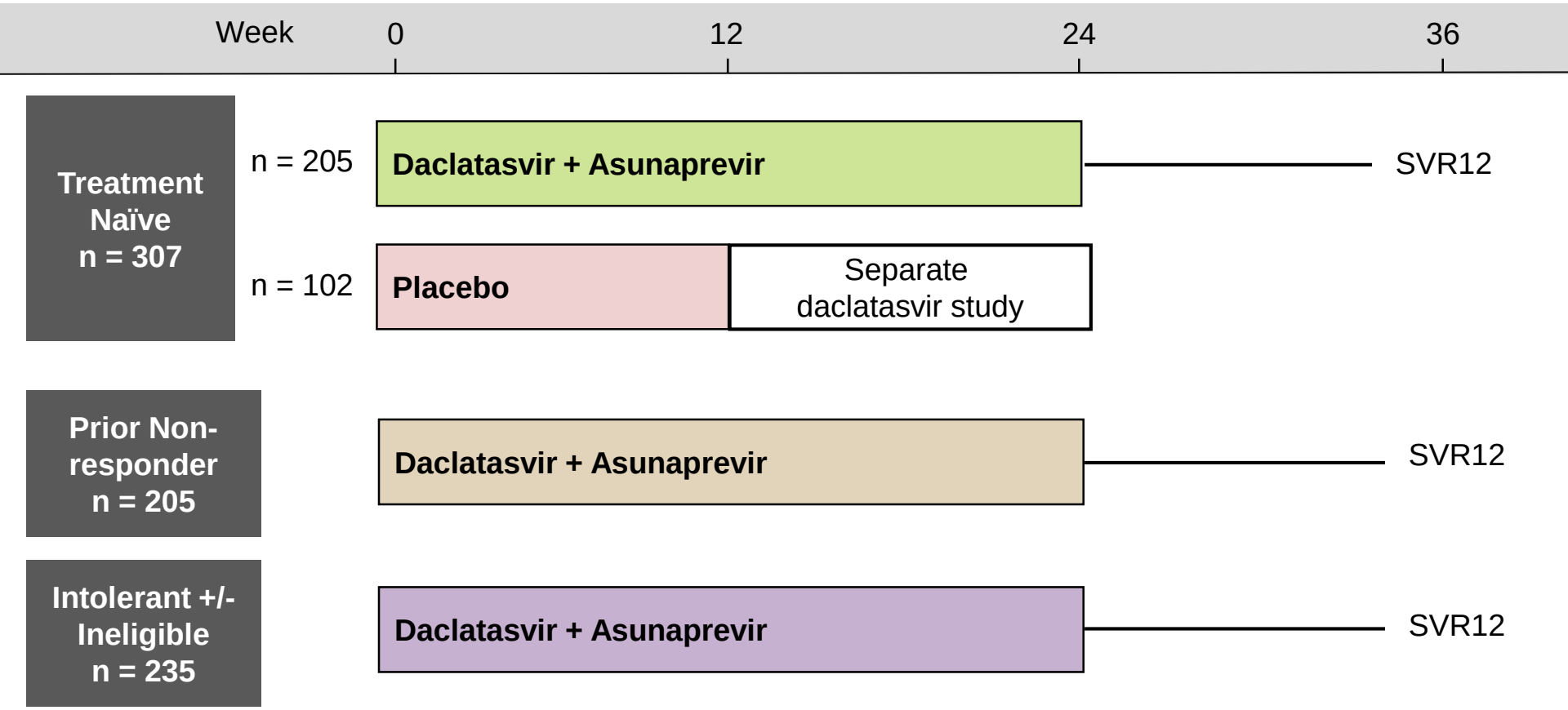
HALLMARK-DUAL: Study Design



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 Black Asian	 135 (66%) 14 (7%) 52 (25%)	 59 (58%) 8 (8%) 45 (22%)	 148 (72%) 10 (5%) 45 (22%)	 169 (72%) 10 (4%) 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 Partial	N/A	N/A	 119 (58%) 84 (41%)	N/A
Ineligible/intolerant reason Depression Anemia/neutropenia Advanced F3 or F4[a]	N/A	N/A	N/A	 71 (30%) 87 (37%) 77 (33%)

DCV=daclatasvir; ASV=asunaprevir. [a]Compensated (Child A) if cirrhotic but with thrombocytopenia.

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

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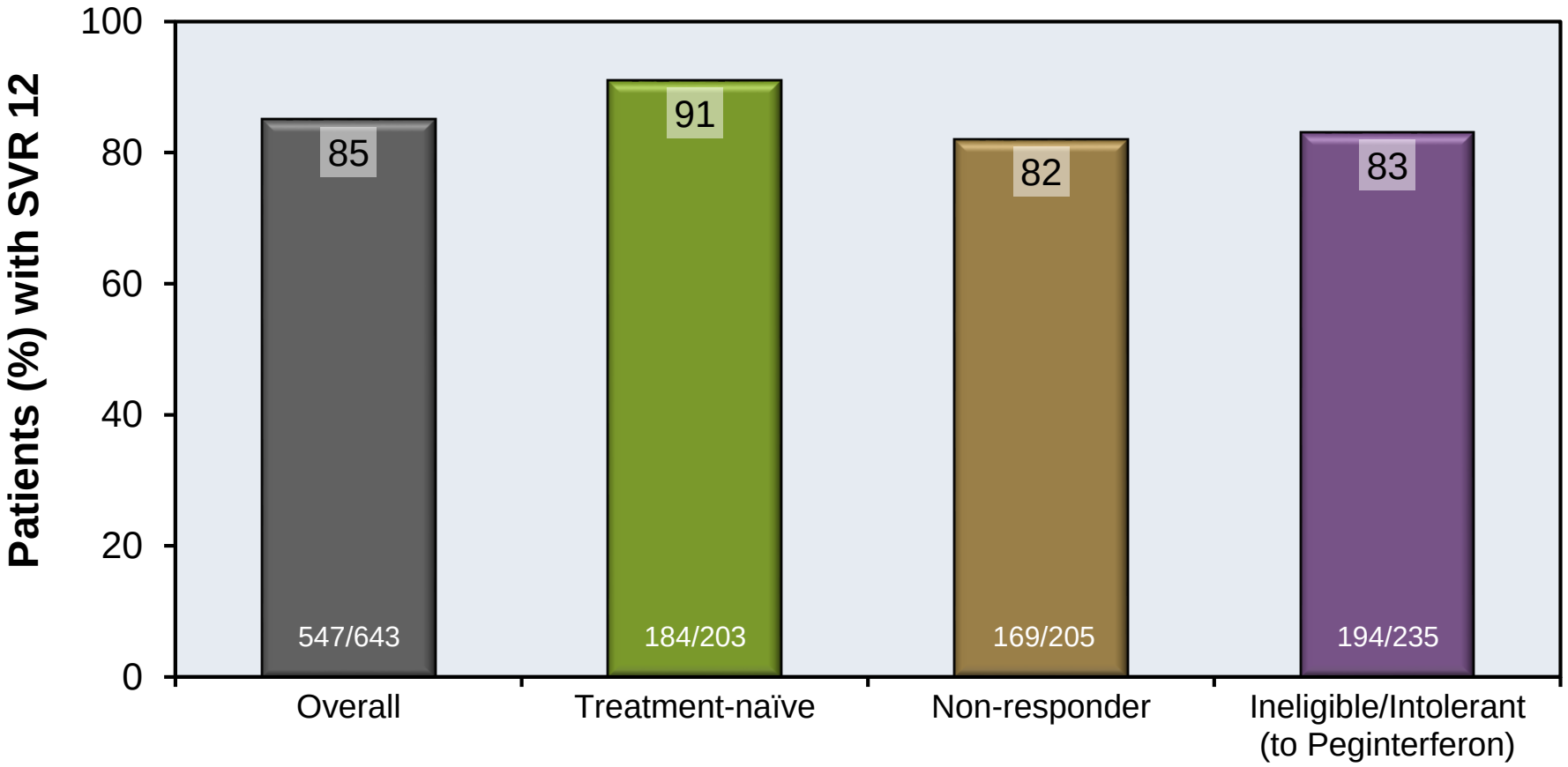
HALLMARK-DUAL Study

HALLMARK-DUAL: SVR12, by Treatment Experience



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

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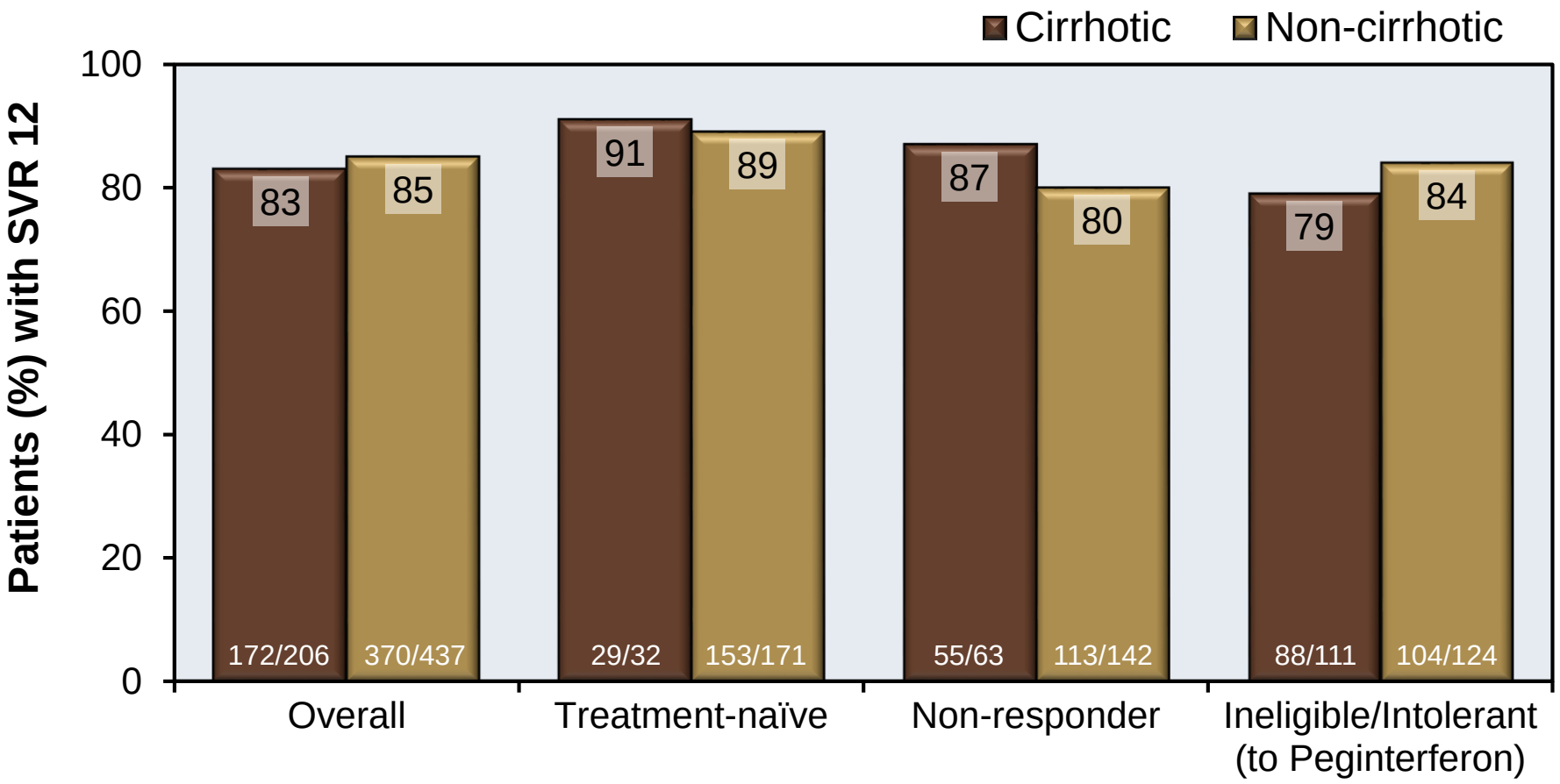
HALLMARK-DUAL Study

HALLMARK-DUAL: SVR12, by Cirrhosis Status



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Daclatasvir + Asunaprevir for HCV GT 1B
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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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.”

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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