New Options for Retreating DAA Failure

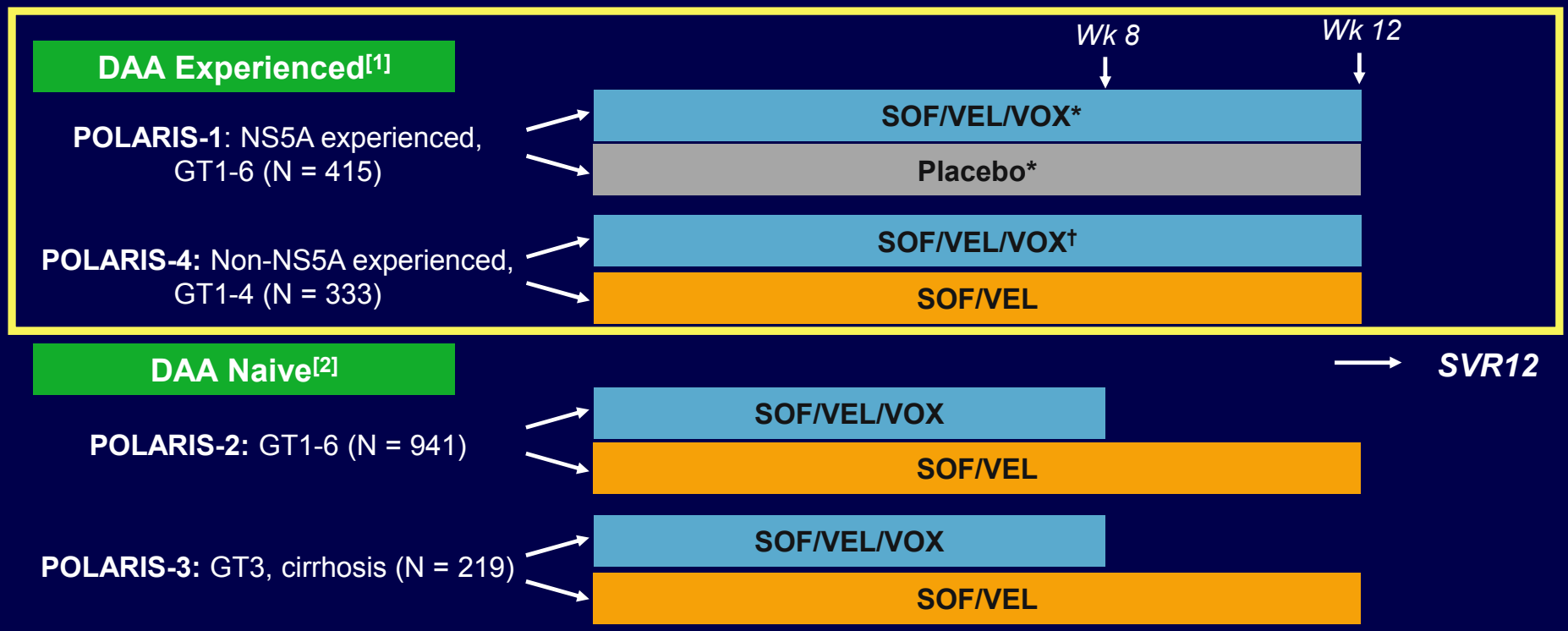
Sofosbuvir/Velpatasvir/Voxilaprevir

- SOF: potent pangenotypic nucleoside polymerase inhibitor
- VEL: potent pangenotypic NS5A inhibitor
- VOX: potent pangenotypic NS3/4A protease inhibitor
- **SOF/VEL/VOX:** once daily, oral, fixed-dose combination (400/100/100 mg) for GTs 1-6

FDA SOF/VEL/VOX. 2017.

Slide credit: clinicaloptions.com

POLARIS Phase III: 4 Trials of SOF/VEL/VOX

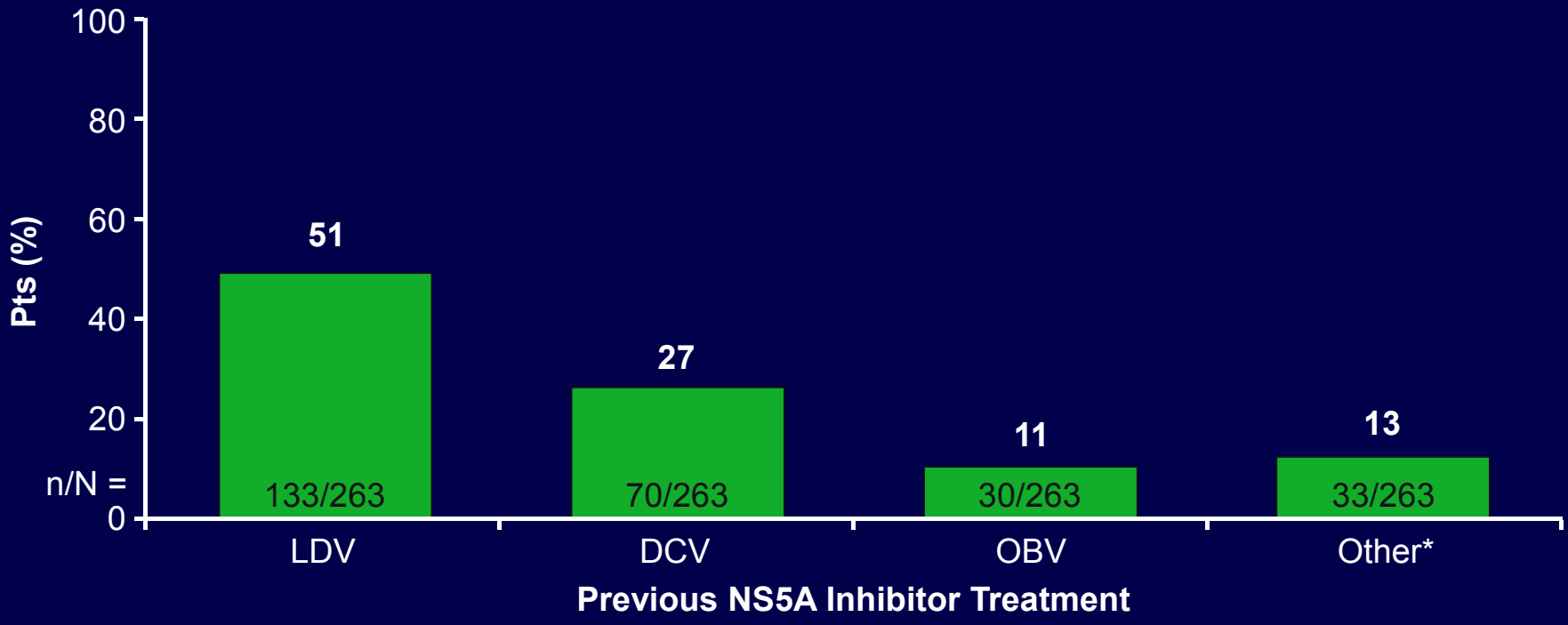


*Only pts with GT1 infection randomized to SOF/VEL/VOX vs placebo. All others received SOF/VEL/VOX.
†All pts with GT4 infection received SOF/VEL/VOX.

1. Bourlière M, et al. N Engl J Med. 2017;376:2134-2146.
2. Jacobson IM, et al. Gastroenterology. 2017;153:113-122.

Slide credit: clinicaloptions.com

POLARIS-1: SOF/VEL/VOX for 12 Wks in NS5A Inhibitor–Experienced GT1-6 HCV



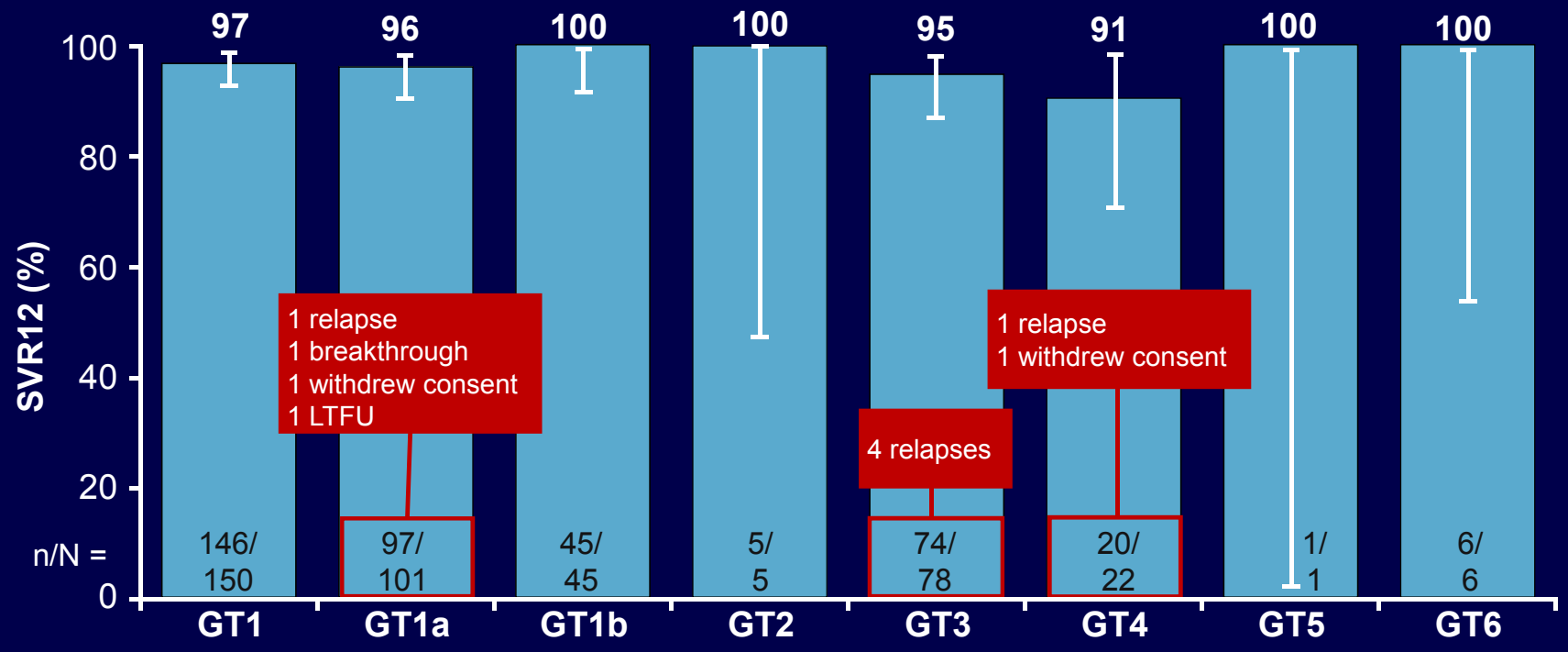
*Included SOF/VEL, EBR/GZR, and other investigational combinations and/or medications from discontinued programs. Three pts received both LDV and DCV.

Bourlière M, et al. AASLD 2016. Abstract 194.

Slide credit: clinicaloptions.com

POLARIS-1: SVR12 by Genotype With 12-Wk SOF/VEL/VOX in NS5A Inhibitor–Experienced Pts

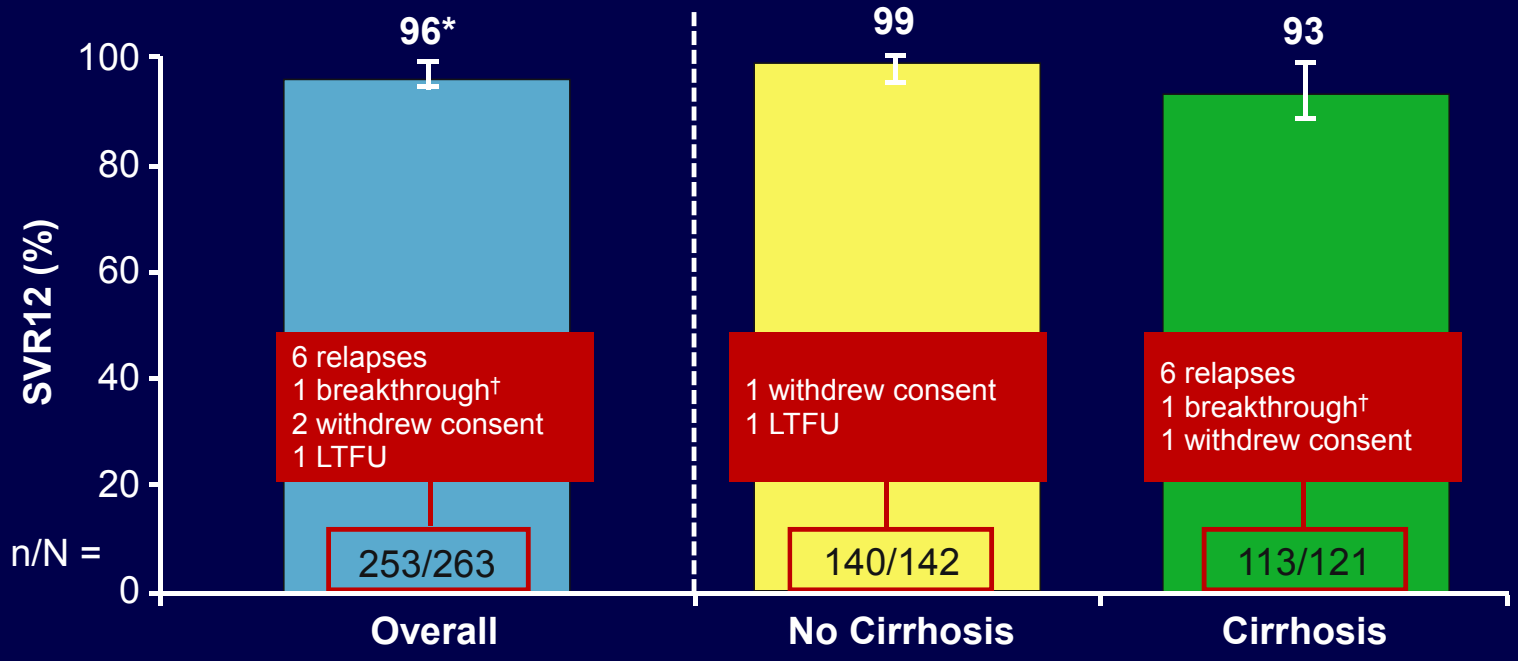
§ Only 1 GT4 pt developed a treatment-emergent RAS (NS5A Y93H)



Bourlière M, et al. N Engl J Med. 2017;376:2134-2146. Bourlière M, et al. AASLD 2016. Abstract 194.

Slide credit: clinicaloptions.com

POLARIS-1: SVR12 With SOF/VEL/VOX for 12 Wks Overall and by Cirrhosis Status

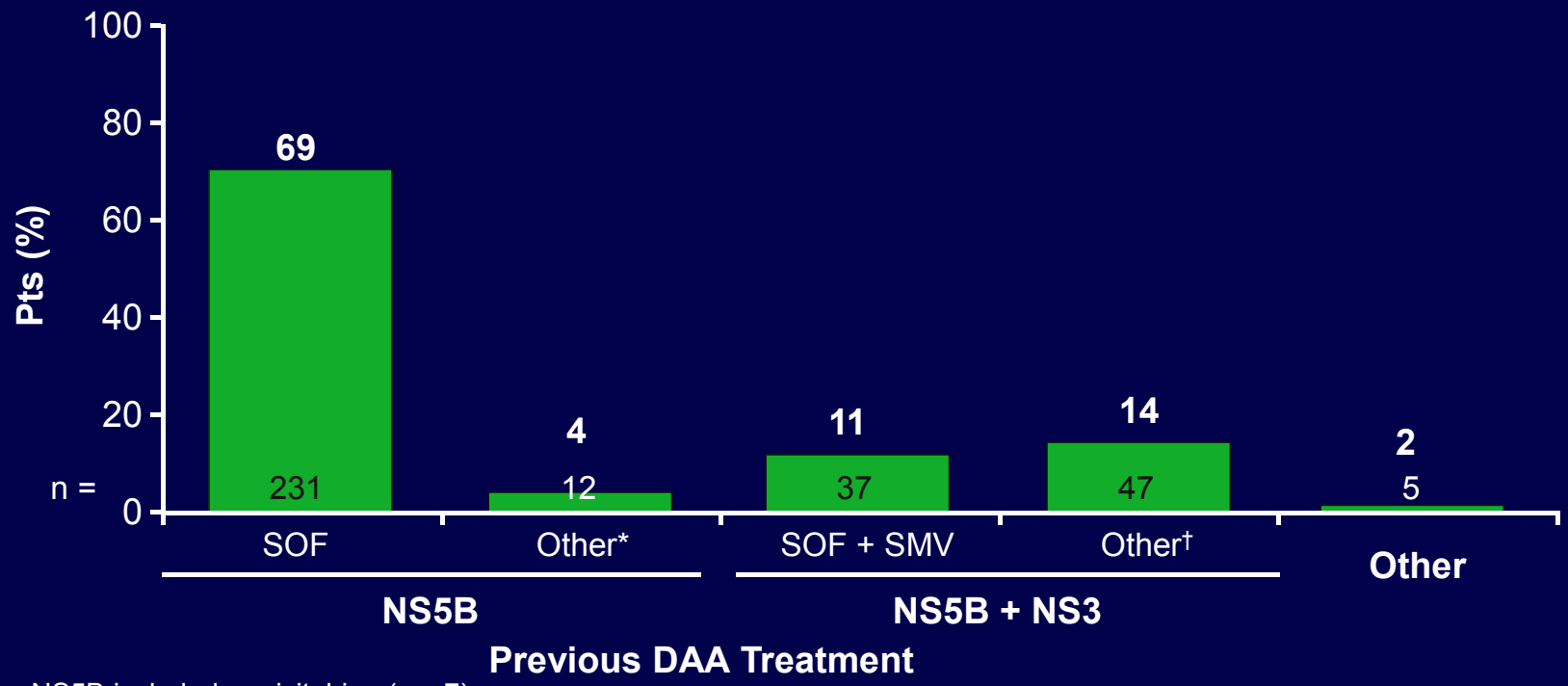


*P < .001 for superiority vs prespecified 85% performance goal for SOF/VEL/VOX.
†Exposure was consistent with nonadherence.

Bourlière M, et al. N Engl J Med. 2017;376:2134-2146. Bourlière M, et al. AASLD 2016. Abstract 194.

Slide credit: clinicaloptions.com

POLARIS-4: SOF/VEL/VOX for 12 Wks in Non-NS5A Inhibitor, DAA-Experienced GT1-4 HCV



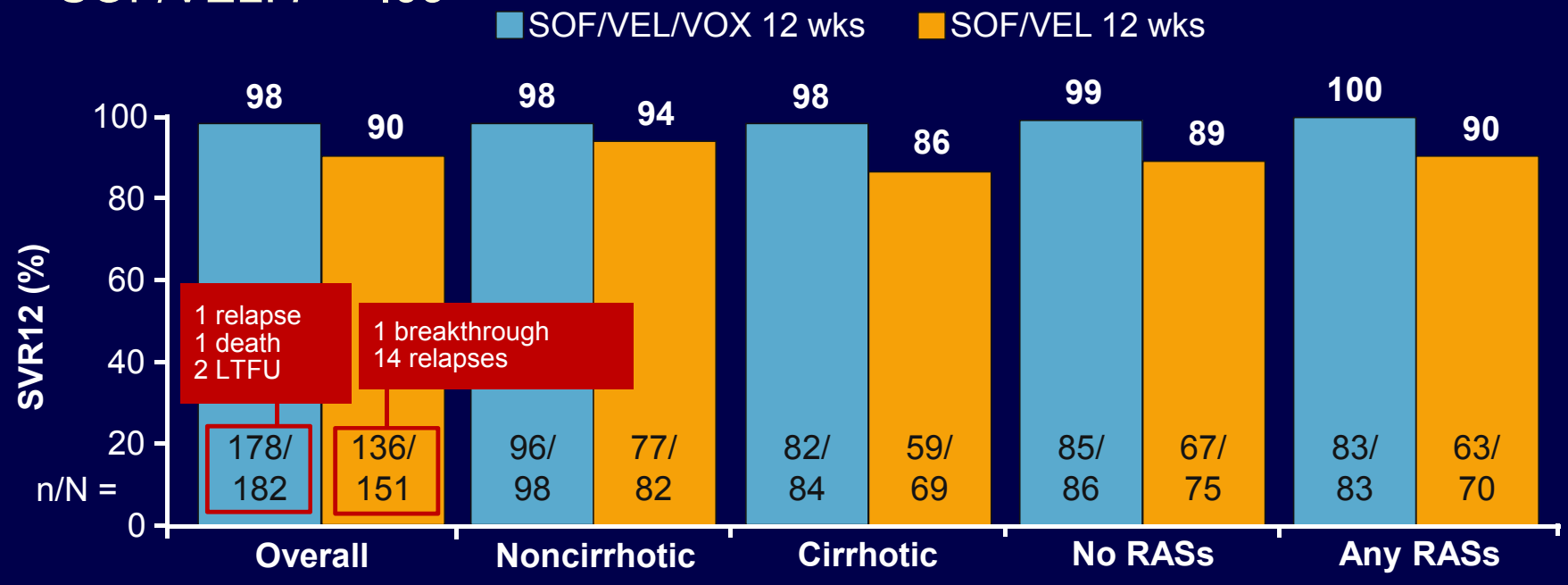
*Other NS5B included mericitabine (n = 7).
†Other NS5B + NS3 included deleobuvir + faldaprevir (n = 14), mericitabine + danoprevir (n = 8), and SOF + telaprevir (n = 6).
One pt without previous DAA exposure excluded.

Zeuzem S, et al. AASLD 2016. Abstract 109.

Slide credit: clinicaloptions.com

POLARIS-4: SVR12 With SOF/VEL/VOX for 12 Wks in Non-NS5A Inhibitor, DAA-Exp'd Pts

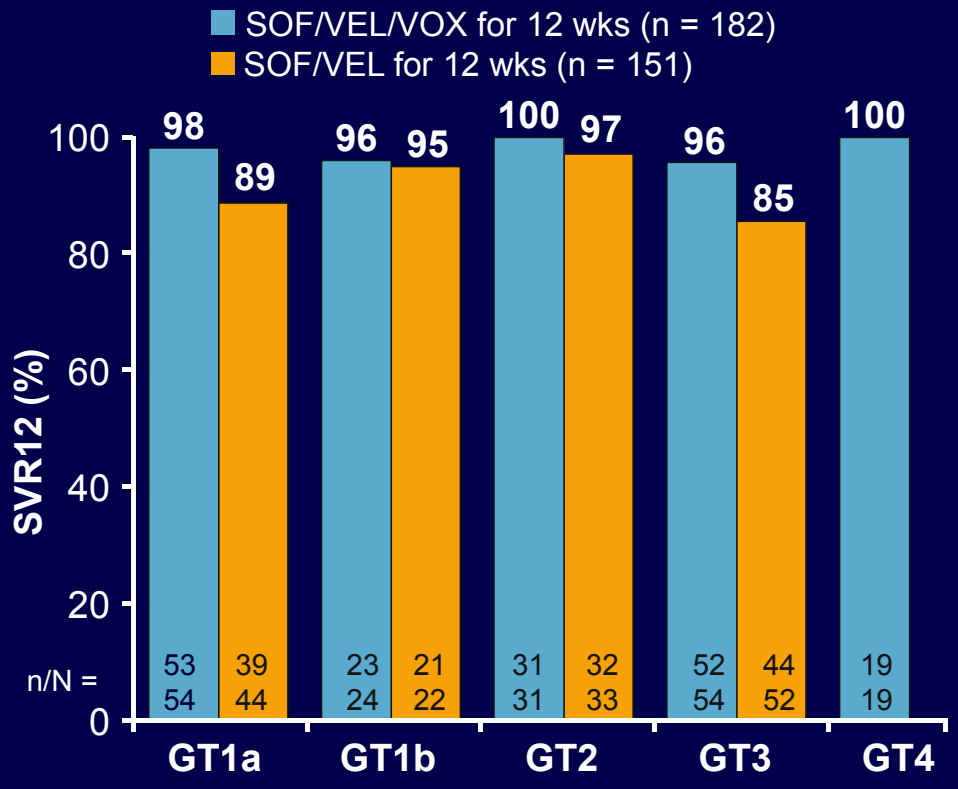
§ SOF/VEL/VOX: *P* < .001 for superiority vs prespecified 85% goal; SOF/VEL: *P* = .09



Bourlière M, et al. N Engl J Med. 2017;376:2134-2146. Zeuzem S, et al. AASLD 2016. Abstract 109.

Slide credit: clinicaloptions.com

POLARIS-4: SVR12 by Genotype and Other Outcomes



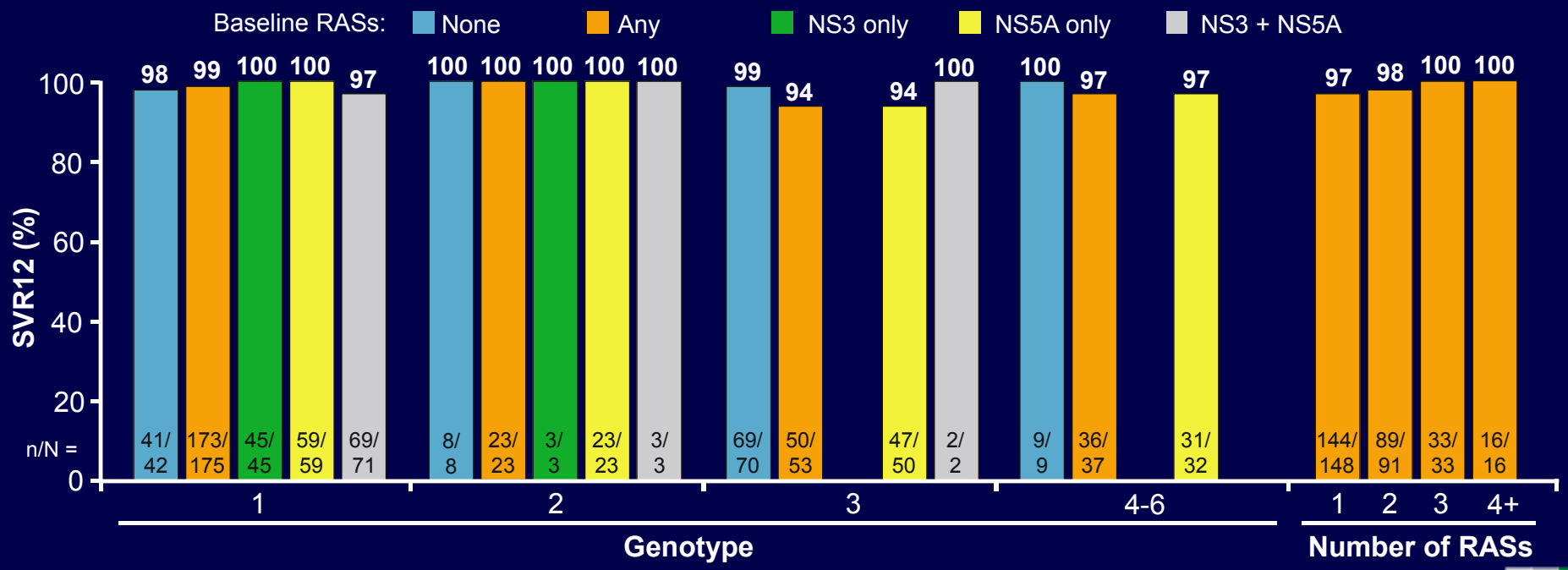
- Treatment emergent RASs
  - SOF/VEL/VOX: none
  - SOF/VEL: 11 of 15 with Y93H
- 4 serious AEs in each arm; no discontinuation for AE with SOF/VEL/VOX
- VOX associated with increase in diarrhea (20%) vs SOF/VEL alone (5%) and trend toward more nausea
  - All mild and no discontinuations

Bourlière M, et al. N Engl J Med. 2017;376:2134-2146. Zeuzem S, et al. AASLD 2016. Abstract 109.

Slide credit: clinicaloptions.com

POLARIS-1 and -4: Impact of Baseline RASs on 12-Wk SOF/VEL/VOX in DAA-Experienced Pts

§ Integrated analysis of data from SOF/VEL/VOX arms of 2 phase III trials of DAA-experienced pts with (n = 263) and without (n = 182) previous NS5A inhibitors, 46% with cirrhosis



Sarrazin C, et al. EASL 2017. Abstract THU-248.

Slide credit: clinicaloptions.com

Glecaprevir/Pibrentasvir

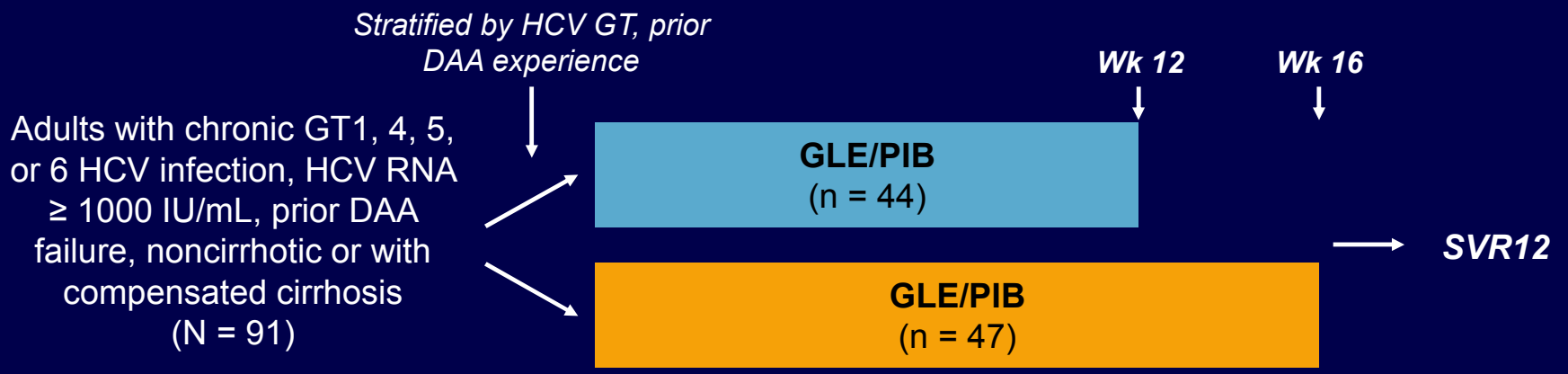
- GLE: potent pangenotypic NS3/4A protease inhibitor
- PIB: potent pangenotypic NS5A inhibitor
- **GLE/PIB**: once daily (taken as 3 tablets with food), oral, fixed-dose combination (100/40 mg) for GT1-6

FDA GLE/PIB. 2017.

Slide credit: clinicaloptions.com

MAGELLAN-1, Pt 2: GLE/PIB for 12 or 16 Wks in DAA-Experienced Pts With GT1 or 4 HCV

§ Randomized, open-label study



§ BL characteristics of 12-wk vs 16-wk arms well balanced by sex, race, BMI, previous DAA regimen and response, RASs

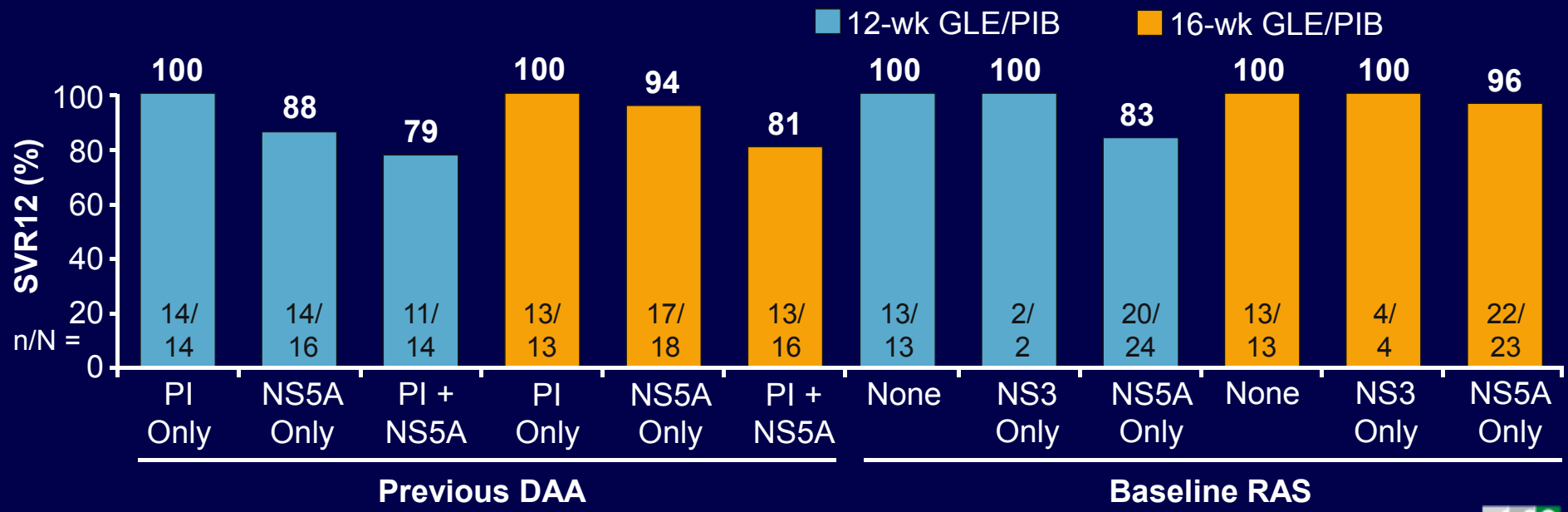
– GT1a, 80% vs 71%; compensated cirrhosis, 34% vs 26%

Poordad F, et al. EASL 2017. Abstract PS-156.

Slide credit: clinicaloptions.com

MAGELLAN-1, Pt 2: SVR12 With GLE/PIB in GT1 or 4 HCV With Previous DAA Failure

- Of pts with NS3 & NS5A RASs, 9/9 had previous failure with PI + NS5A, 5/9 had SVR12 on GLE/PIB
- Rare grade 3 lab abnormalities, no d/c for AEs, no DAA-related serious AEs



Poordad F, et al. EASL 2017. Abstract PS-156.

Slide credit: clinicaloptions.com

AASLD/IDSA Recommended Retreatment Regimens for DAA-Experienced GT1 HCV

- SOF experienced, but no previous NS5A inhibitor, ± compensated cirrhosis
  - SOF/VEL/VOX for 12 wks (GT1a)
  - SOF/VEL for 12 wks (GT1b)
  - GLE/PIB for 12 wks (GT1a or 1b)

FDA indications include GLE/PIB for 8 wks if no cirrhosis

- NS5A inhibitor experienced (regardless of NS3 inhibitor experience) ± compensated cirrhosis:
  - SOF/VEL/VOX for 12 wks

FDA indications include GLE/PIB for 16 wks if NS5A (without NS3) experienced

AASLD/IDSA. HCV guidance. September 2017. FDA GLE/PIB. 2017

Slide credit: clinicaloptions.com

AASLD/IDSA Recommended Retreatment Regimens for DAA-Experienced GT3 HCV

- DAA experienced (including NS5A inhibitors) ± compensated cirrhosis
  - SOF/VEL/VOX for 12 wks
  - Add RBV if previous NS5A inhibitor failure + compensated cirrhosis

AASLD/IDSA. HCV guidance. September 2017.

Slide credit: clinicaloptions.com

Key Take-home Points for Retreatment of DAA-Experienced GT1 or 3 HCV Infection

- GLE/PIB approved for GT1 with NS5A ***or*** NS3 inhibitor experience only, not both[1]
  - AALSD/IDSA only recommends for GT1 with SOF experience without NS5A inhibitor experience[2]
- SOF/VEL/VOX approved for GT1, 2, 3, 4, 5, or 6 with NS5A inhibitor experience (regardless of NS3 experience) and GT1a or GT3 with SOF experience without NS5A inhibitor experience (regardless of NS3 experience)[3]

SOF/VEL/VOX is now the go-to regimen for dual NS5A and NS3 inhibitor–experienced pts with GT1 or 3

1. FDA GLE/PIB. 2017. 2. AASLD/IDSA. HCV guidance. September 2017. 3. FDA SOF/VEL/VOX. 2017.

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