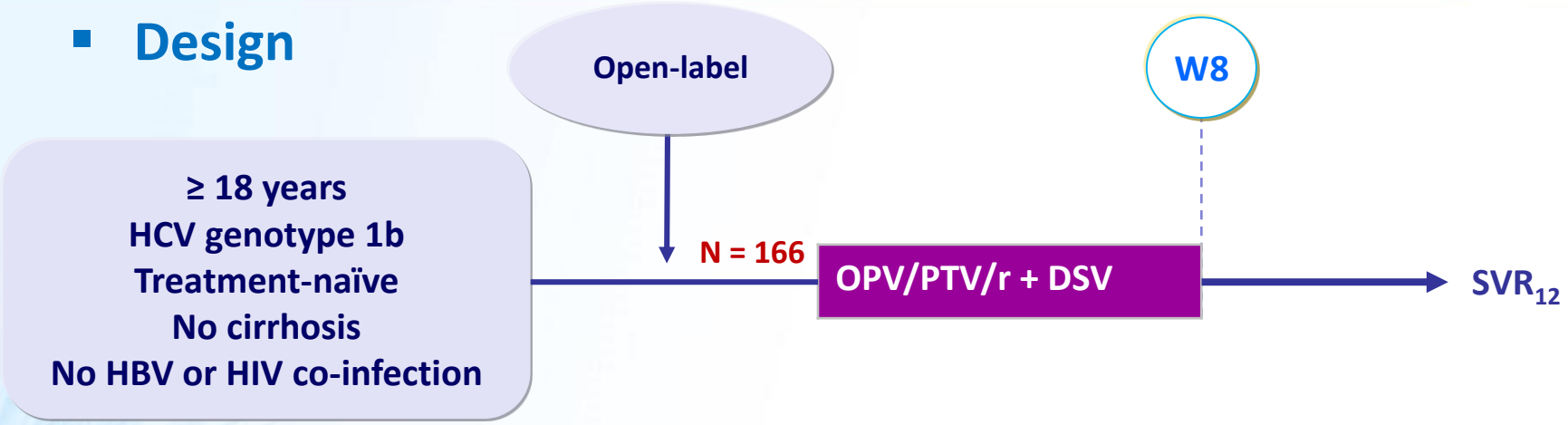
GARNET Study: OBV/PTV/r + DSV 8 weeks in genotype 1b

- **Design**



- **Treatment regimens**
  - Co-formulated ombitasvir (OBV)/paritaprevir (PTV)/ritonavir (r): 25/150/100 mg QD = 2 tablets
  - Dasabuvir (DSV) : 250 mg bid
- **Objectives**
  - SVR_{12} (HCV RNA < 15 IU/ml)
  - Virologic failures and relapses
  - SVR_{12} in patients with baseline HCV RNA < 6 000 000 IU/mL

GARNET

Welzel TM. Lancet Gastroenterol Hepatol. 2017; 2:494-500

GARNET Study: OBV/PTV/r + DSV 8 weeks in genotype 1b

Baseline characteristics and outcome

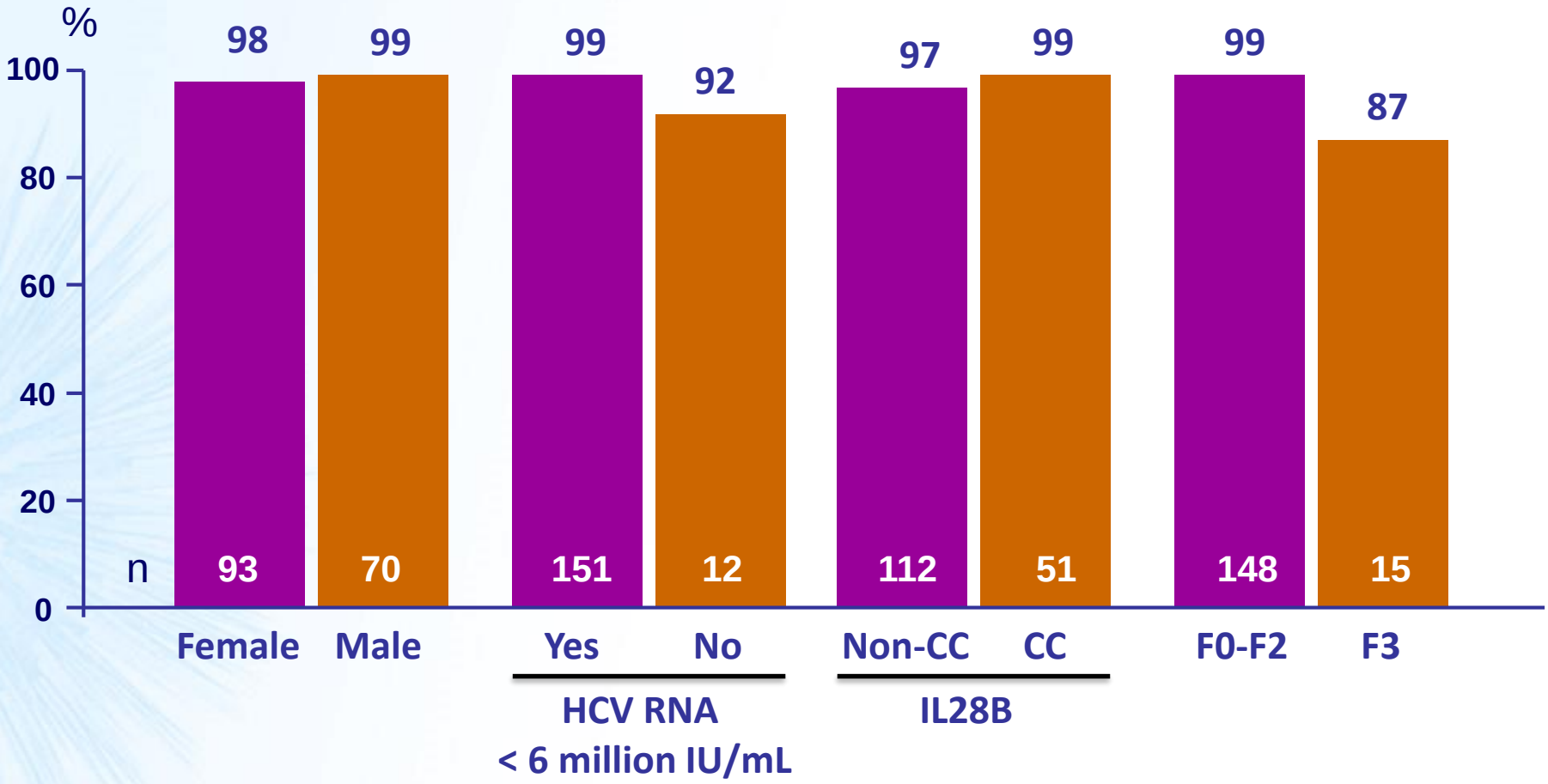
	OBV/PTV/r + DSV 8W , n = 166
Median age, years	53
Female, %	57
White, %	96
Median BMI, kg/m^2	25.3
HCV RNA	
log_{10} IU/mL, median	6.0
< 6 000 000 IU/mL, %	93
Fibrosis stage : F0-F2 / F3, %	91 / 9
RASs at baseline, %	55
NS5A only	14
NS5B only	28
NS5A + NS5B	12
NS3A (± NS5A)	2
SVR_{12}, n/N (%)	
ITT	162/166 (98%)
mITT-GF *	160/163 (98%)
mITT-VF	160/162 (99%)

* Exclusion of 3 patients with non-1b genotype : 1 genotype 1a, 1 genotype 1d, 1 genotype 6
** Exclusion of non-virologic failures (1 early discontinuation for non-compliance)

Welzel TM. Lancet Gastroenterol Hepatol. 2017; 2:494-500

GARNET Study: OBV/PTV/r + DSV 8 weeks in genotype 1b

SRV_{12} rates by subgroups, mITT-GT, %



Welzel TM. Lancet Gastroenterol Hepatol. 2017; 2:494-500

GARNET Study: OBV/PTV/r + DSV 8 weeks in genotype 1b

- **Virologic failures, n = 2 (exclusion of a 3rd failure in a patient with genotype 6)**

Characteristics	Patient A	Patient B
Time of failure	Post-treatment W4	Post-treatment W12
Age / gender	40 / Male	56 / Female
Race	White	White
BMI, kg/m^2	30.2	26.9
Fibrosis stage	F3	F3
IL28B	CT	CT
Baseline HCV RNA (IU/mL)	> 6 million (7,162,669)	< 6 million (1,243,706)
Adherence	99%	100%
Resistance-associated substitutions at baseline / at failure		
NS3	None / None	None / None
NS5A	L31M / L31M, Y93C	None / None
NS5B	C316N, S556G / C316N, S556G	None / None

Welzel TM. Lancet Gastroenterol Hepatol. 2017; 2:494-500

GARNET Study: OBV/PTV/r + DSV 8 weeks in genotype 1b

Treatment-emergent adverse events

	OBV/PTV/r + DSV 8W N = 166
Any treatment-emergent adverse event	67%
Adverse event leading to discontinuation	1 (0.6%) *
Serious adverse event, N (%)	2 (1%) **
Adverse events occurring in ≥ 5%, % Headache Fatigue Nasopharyngitis Pruritus Nausea Asthenia	 21 17 8 8 6 5
Hemoglogin < 10 g/dL	0
ALT ≥ Grade 3 (> 5 x ULN) / AST ≥ Grade 3 (> 5 x ULN), N	1 ** / 0
Total bilirubin >3-10 x ULN / > 10 x ULN, N	1 ** / 0

* One 24-year-old female patient with F0–F1 fibrosis discontinued study drug on D45 due to grade 3 hyperbilirubinemia (direct and indirect) that was considered possibly related to study drugs. A grade 3 ALT elevation occurred following hyperbilirubinemia; both returned to normal. The patient achieved SVR_{12}

** syncope on D17, gastroenteritis on post-treatment D8; both were deemed unrelated to study drugs

Welzel TM. Lancet Gastroenterol Hepatol. 2017; 2:494-500

GARNET Study: OBV/PTV/r + DSV 8 weeks in genotype 1b

Summary

- The 3D regimen administered for 8 weeks achieved a 98% SVR_{12} in treatment-naïve genotype 1b patients without cirrhosis
- Both patients who experienced virologic failure had F3 fibrosis at baseline
- Fibrosis (F3 vs F0–F2) was the only significant predictor of SVR_{12}
- Baseline HCV RNA, sex, BMI, age, and former IV drug use were not predictive of treatment failure
- Presence of resistance-associated polymorphisms at baseline did not impact SVR
- The 8-week, RBV-free 3D regimen was well tolerated
  - Most adverse events were mild or moderate in severity
  - Serious adverse events and clinically significant laboratory abnormalities were rare (<1%)
- The 98% SVR_{12} rate demonstrates that treatment-naïve genotype 1b patients without cirrhosis can be effectively treated with 3D for 8 weeks

Welzel TM. Lancet Gastroenterol Hepatol. 2017; 2:494-500