



UNIVERSITÀ DEGLI STUDI DI MILANO



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Sistema Socio Sanitario



Regione  
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ASST Fatebenefratelli Sacco

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HCV: il punto sulla resistenza ai DAA nel  
trattamento dei pazienti con pregresso fallimento ai  
DAA

# HCV resistance testing in treatment Experienced Patients with Prior Exposure to DAAs

*perché*

**Following the approval of SOF/VEL/VOX and GLE/ PIB, there is no clear role for NS3 RAS testing in DAA experienced patients**

**there is no major role for NS5B RAS testing in clinical practice**

# Quando

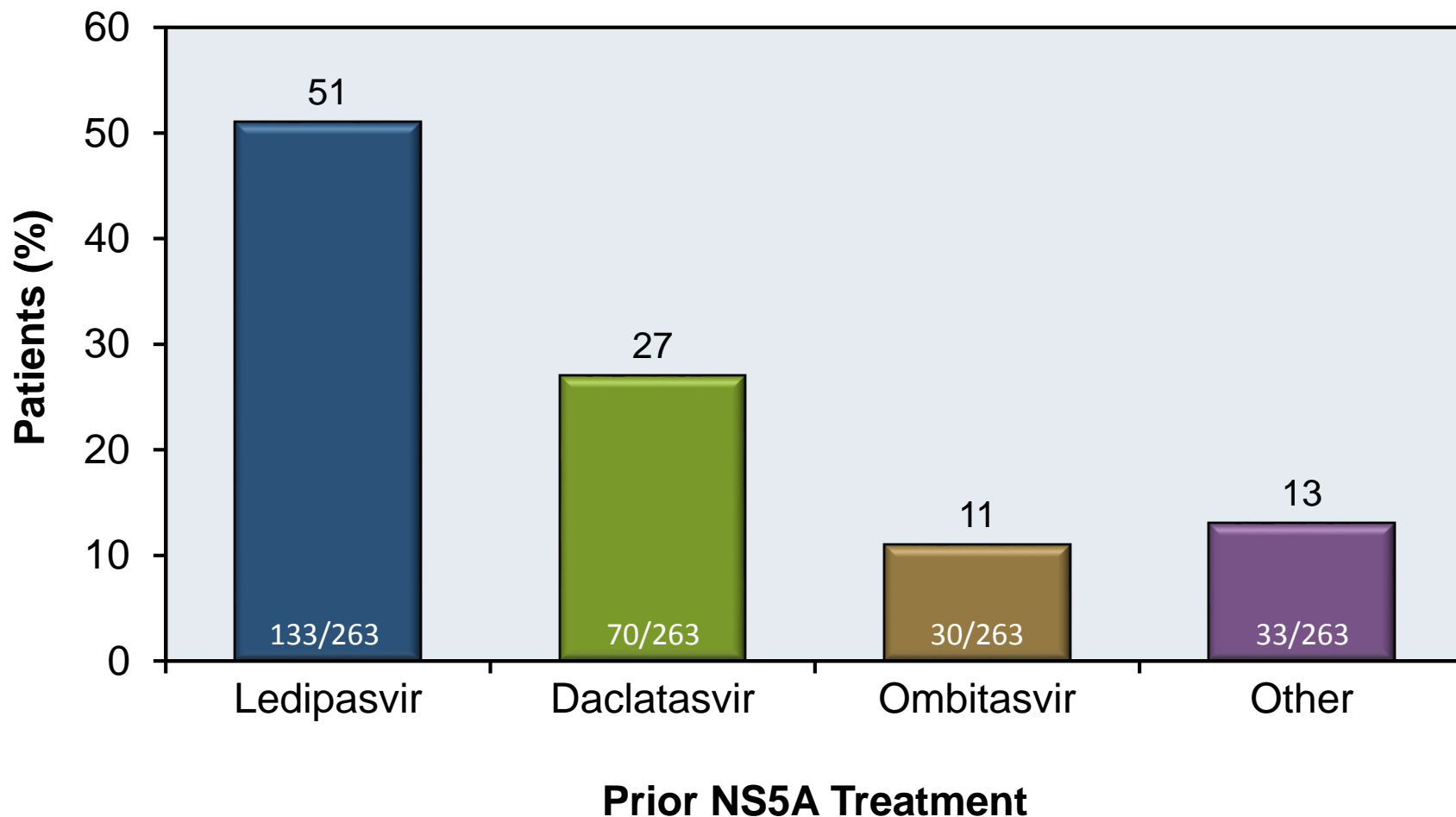
Prior the approvals of SOF/VEL/VOX and GLE/PIB: resistance testing was routinely recommended prior to retreatment for all patients who had previously failed an interferon-free DAA regimen containing an NS3 PI and/or an NS5A inhibitor

**Now:** However, impressive new data from phase 2 and 3 trials with these regimens in this difficult to treat population suggest that resistant variants present prior to treatment **have no impact** on retreatment responses—with the exception being DAA failures exposed to both NS3 PI and NS5A inhibitors retreated with GLE/PIB

**EASL 2018:** HCV resistance testing prior to retreatment in patients who failed after any of the DAA-containing treatment regimens is useful to guide retreatment by probabilities of response, according to the resistance profile observed in the context of a multidisciplinary team including experienced treaters and virologists (B2).

# Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6

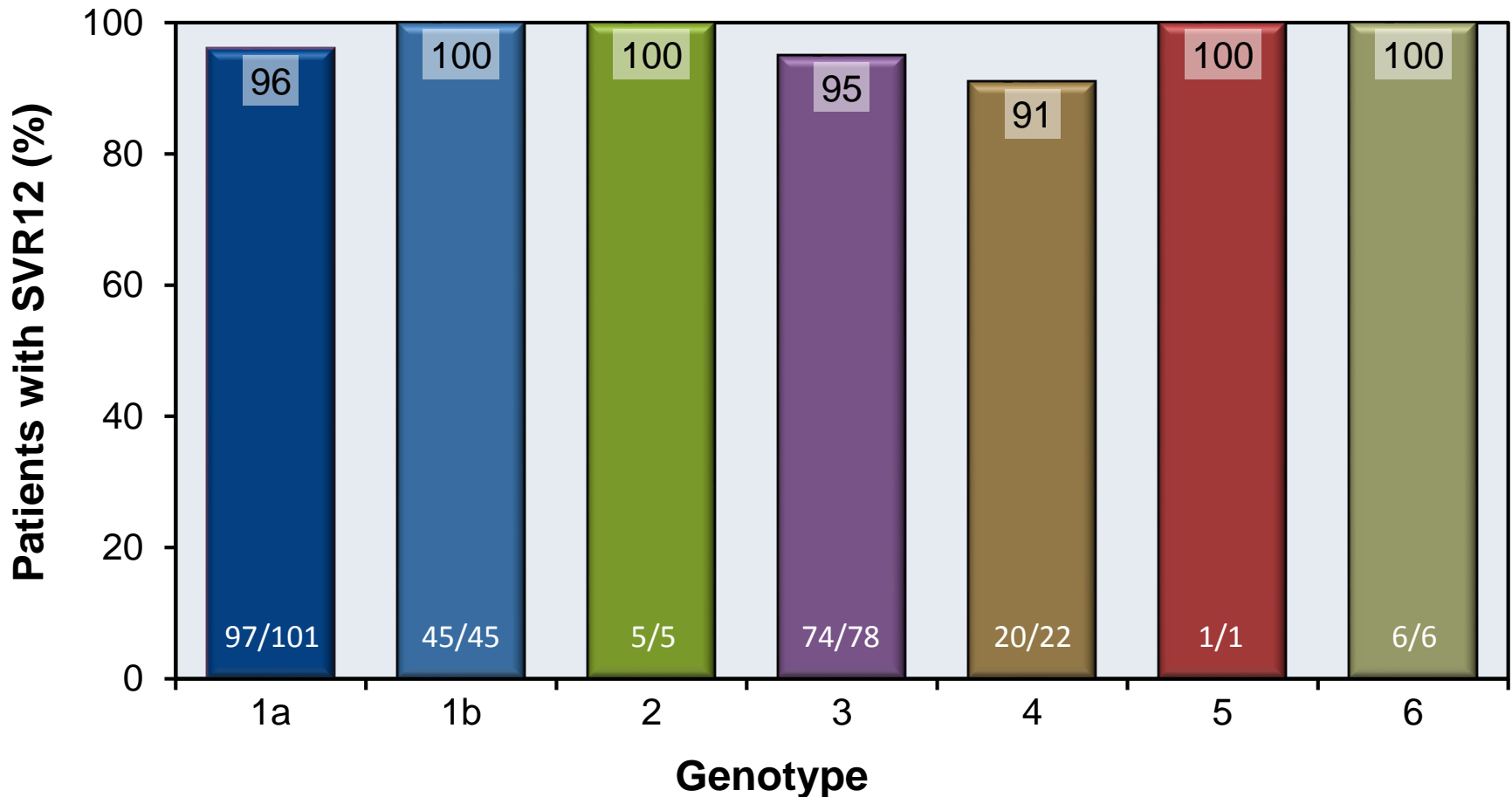
## POLARIS-1: Prior NS5A Treatment



# Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6

## POLARIS-1: Results

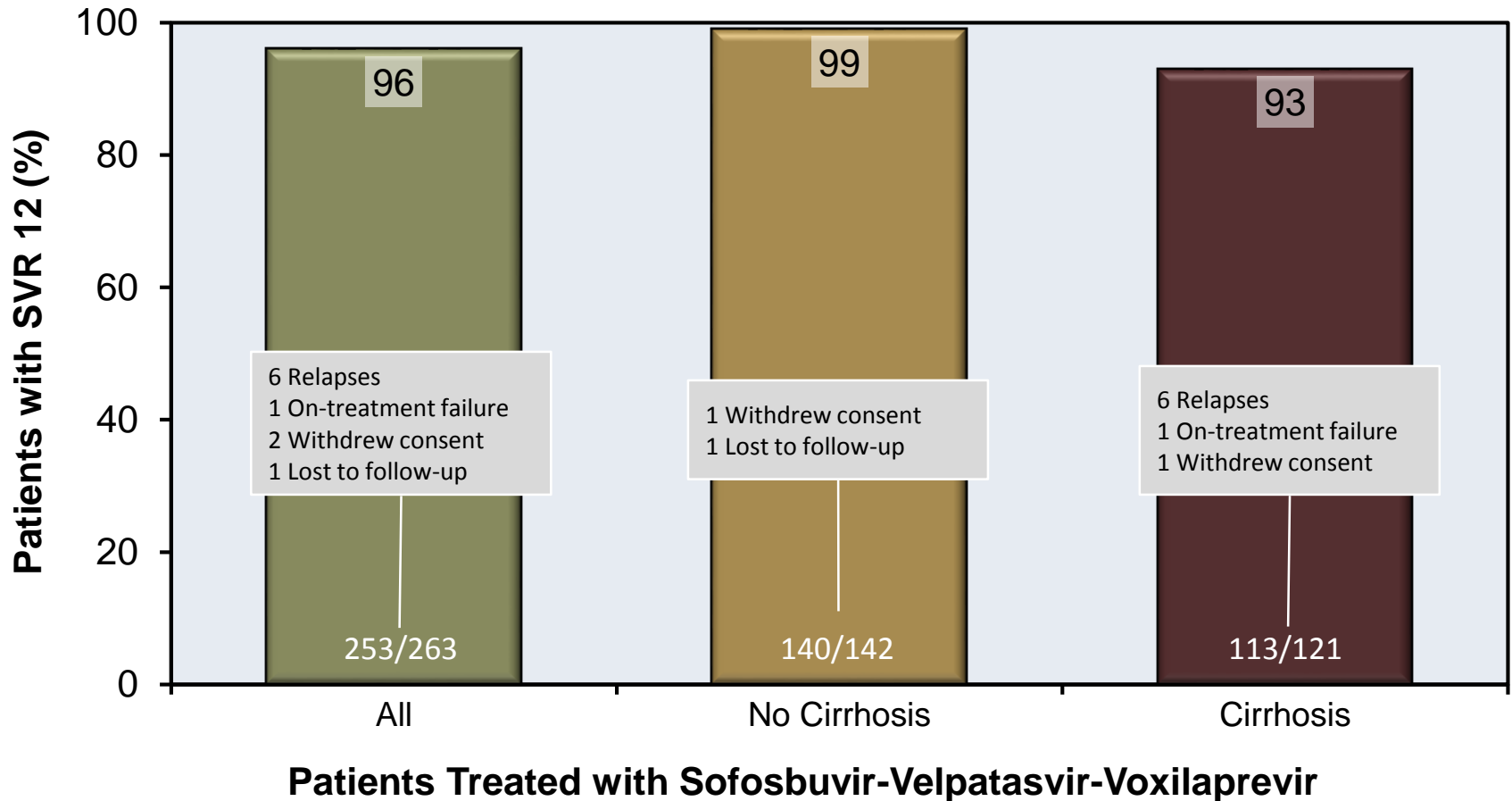
### POLARIS-1: SVR12 Results by Genotype



# Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6

## POLARIS-1: Results

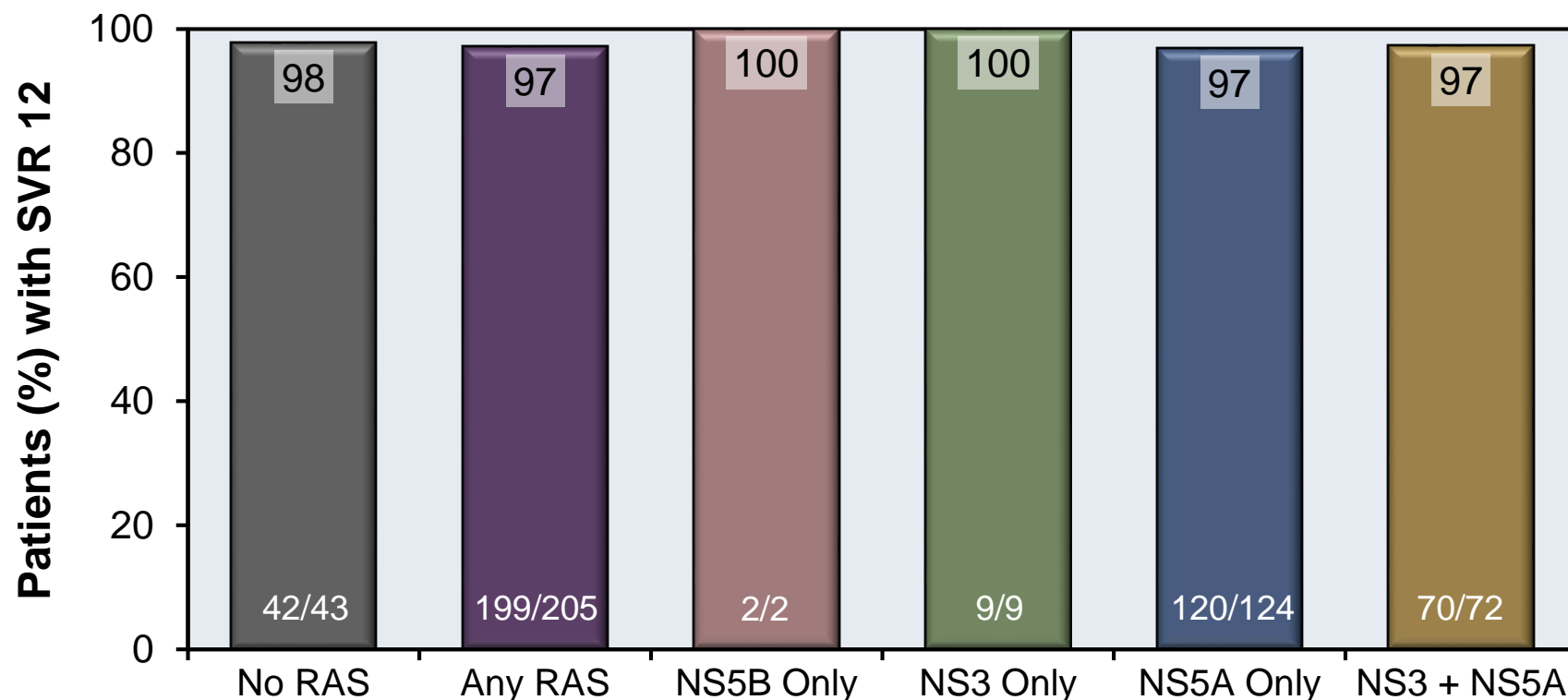
### POLARIS-1: SVR 12 by Cirrhosis Status



# Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6

## POLARIS-1: Results

POLARIS-1: SVR12 by Baseline Resistance-Associated Substitutions (RAS)



83% of patients had baseline resistance-associated substitutions (RASs); 79% had NS5A RASs. None who relapsed had treatment-emergent RASs.

**Source:** Bourlière M, et al. *N Engl J Med.* 2017;376:2134-46.

GS, 48 anni

Pretrattato con IFN+RBV; relapser

Genotipo 1a; F2

PTV+OMV+DSV+RBV

baseline: V36G + R155K su NS3 (ombitasvir)

M28V su NS5A (paritaprevir)

Failure (24 weeks post-tp): **no RAS**

*Che fare?*



In the absence of prior drug exposure, NS5A class RASs are relatively frequent in genotype 1 HCV being found in 13% of GT1a isolates and 18% of GT1b isolates at a 15% threshold [24]. Despite being more prevalent in GT1b, the majority of the clinical impact is in GT1a. NS5A RASs are also of clinical impact in GT3 where they are found in about 9–13% of viral sequences [50, 51].

When Should You Look for NS5A RASs?

Genotype 1a patients to be treated with EBR/GZR (elbasvir/grazoprevir)

Genotype 1a patients treatment experienced to be treated with LDV/SOF

Genotype 3 patients IFN-treated experienced or cirrhotic to be treated with SOF/VEL (for Y93H)

**EASL 2018:** systematic testing for HCV resistance prior to treatment in direct-acting antiviral (DAA) drug-naïve individuals is not recommended. The current EASL recommendations suggest treatment regimens that do not necessitate any resistance testing prior to first-line therapy.