Is there still a role for personalized treatment?

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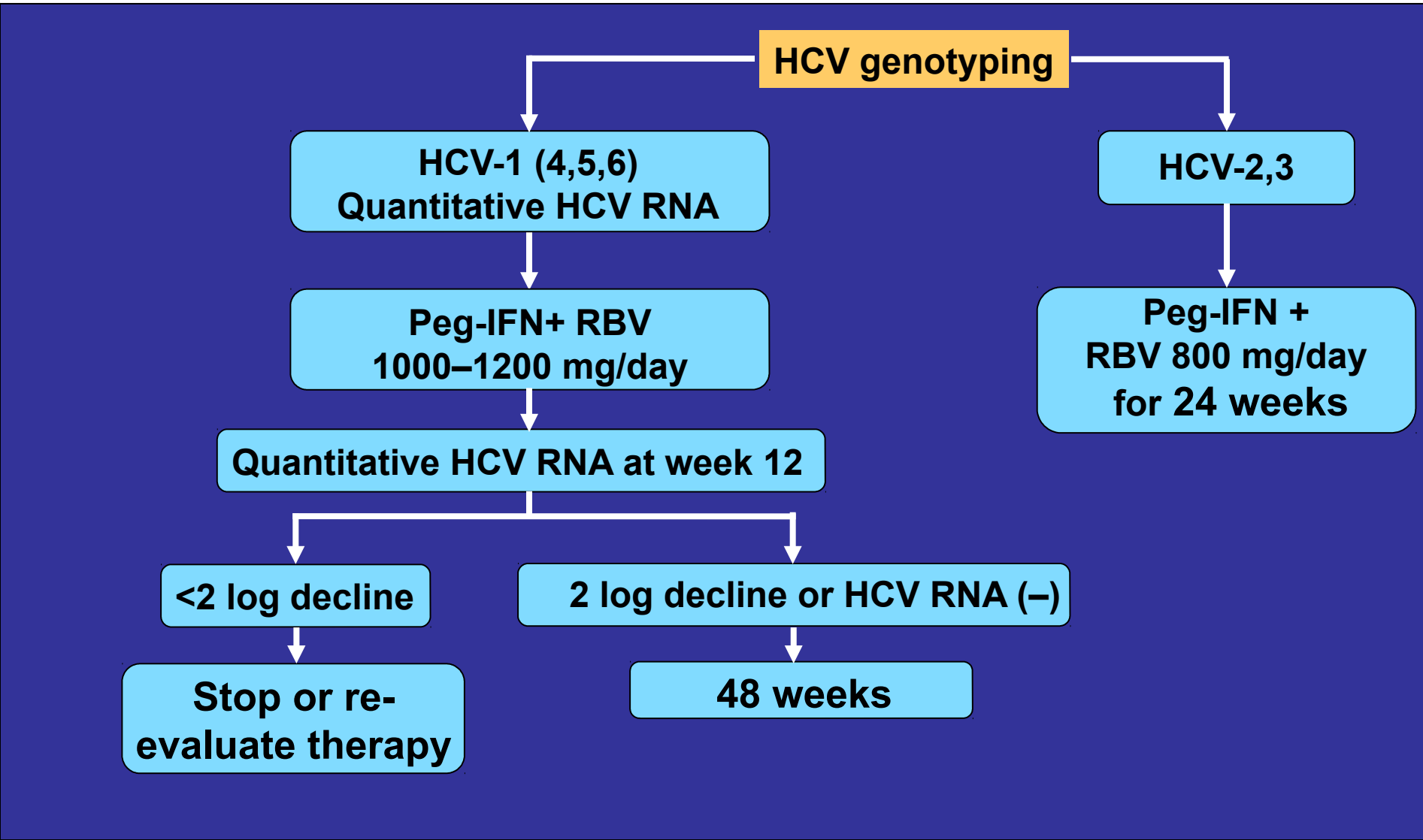
Conflicts of interest

- I have received speaker and consultancy fees from Abbvie, BMS, Gilead, MSD, GSK, Springbank

The ‘Bad Old Days’



The Good New Days
Just take the tablets

Is it really that easy?

- Benefits of pre-treatment assessments
- Benefits of avoiding pre-treatment assessment

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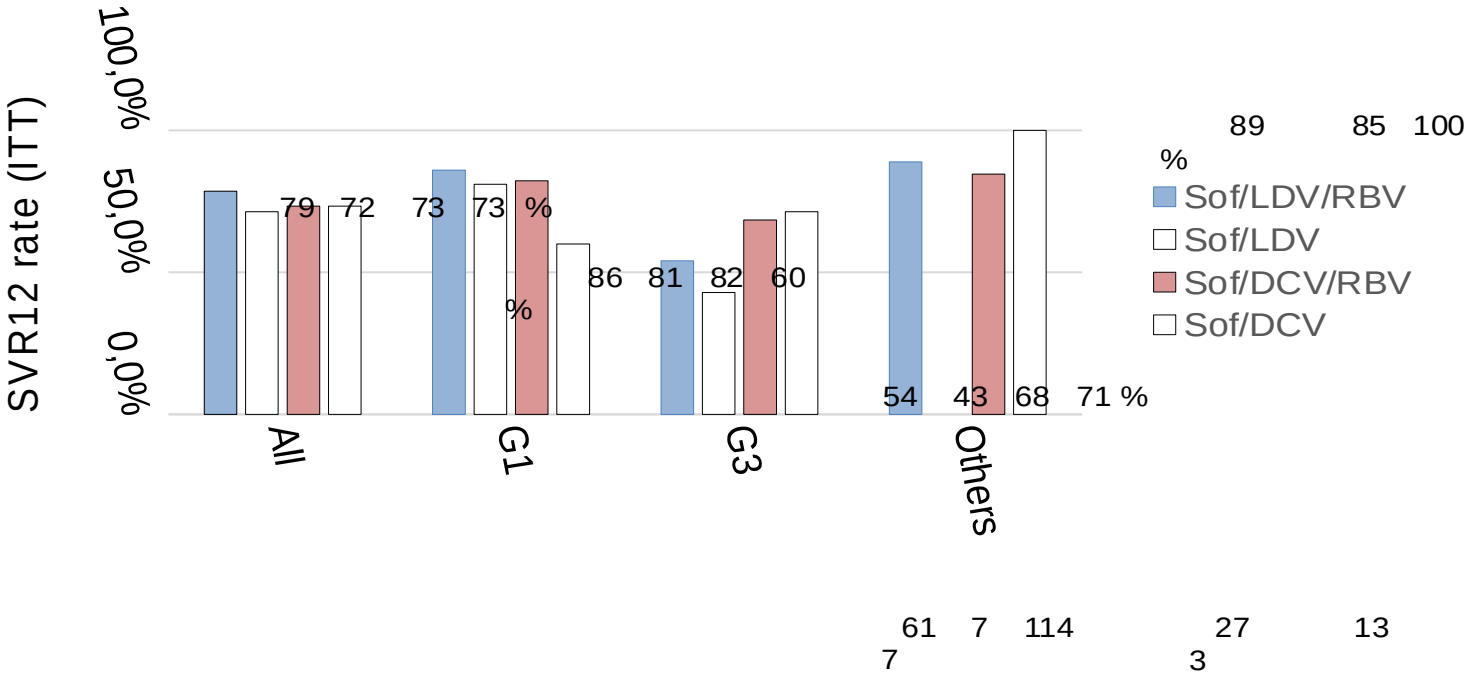
Compensated or decompensated?

- Decomensated cirrhosis responds differently



Foster et al J Hepatology 2016

The real-world Israeli experience of treating chronic hepatitis C, G1 patients with advanced fibrosis with OBV/PTV/r/ + DSV ± RBV: A large multi-center cohort

AE discontinuation, n (%)	3D ± RBV (N=661)
Serious AE	12 (1.8)
Liver decompensation	8 (1.2)

Predictors of hepatic decompensation?	Patients, n (%) (N=661)	P
Age >75 years	3 (37.5) vs 63 (9.6)	**0.005**
MELD score >10	3 (37.5) vs 39 (6)	**0.01**
Previous decompensation	3 (37.5) vs 0 (0)	**<0.001**

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Decompensated cirrhosis

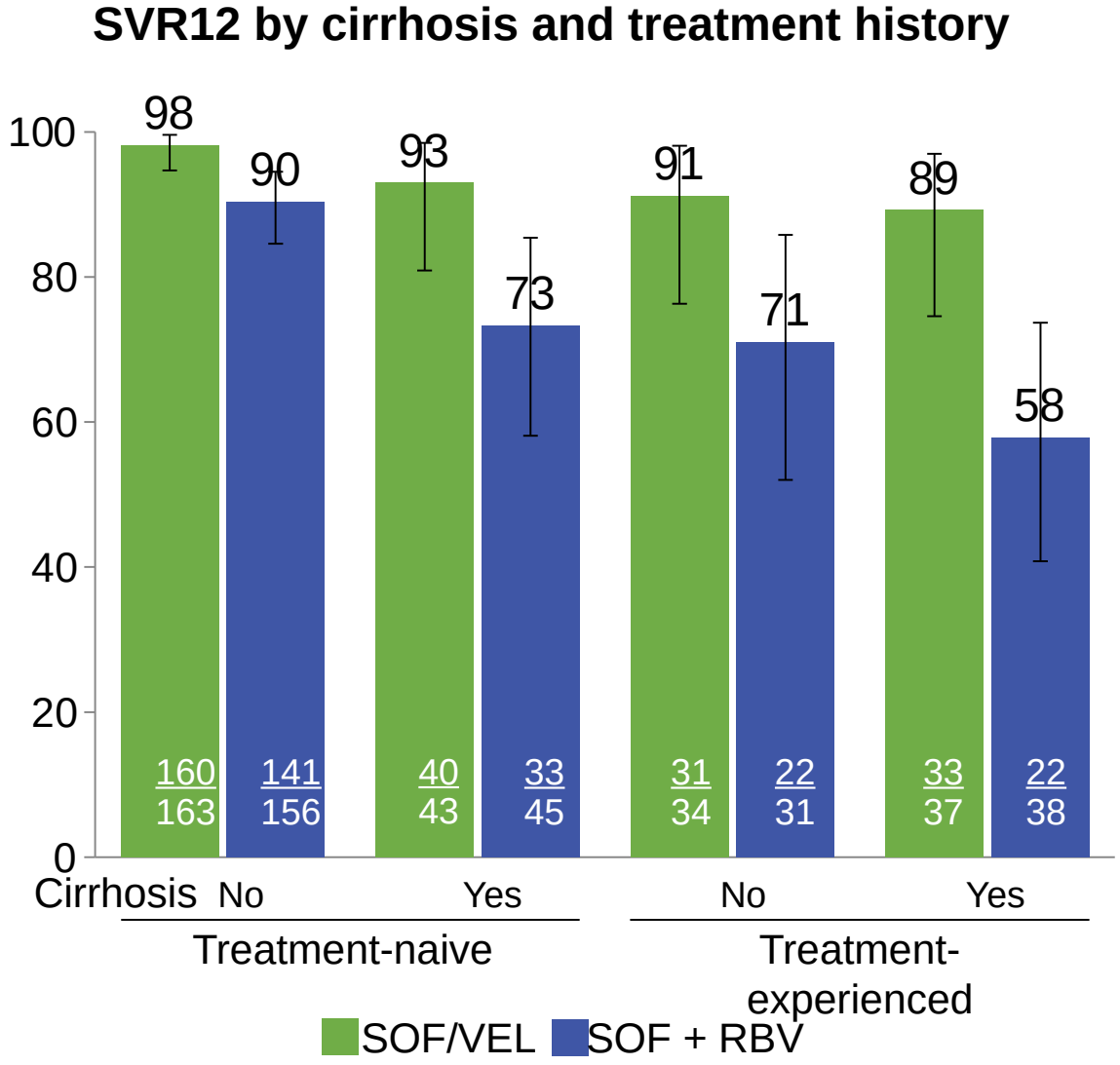
- Protease inhibitors may be toxic in patients with current or past decompensation

- NO protease inhibitor is licensed for decompensated cirrhosis

Cirrhosis

- Patients with cirrhosis may require different regimens (12 weeks vs 8)
- Patients with cirrhosis may respond less well
- Patients with cirrhosis may still develop cancer

ASTRAL-3 Phase 3 Study: SOF/VEL FDC for 12 weeks compared to SOF + RBV for 24 weeks in G3 HCV infected patients



Foster GR, et al. NEJM 2015

Renal Impairment

- Metabolites of sofosbuvir may be renally metabolised

- Sofosbuvir is not recommended if GFR <30ml/min

Pre-treatment assessment

- Mandatory to exclude decompensated cirrhosis if you want to use a protease inhibitor
- Important to exclude cirrhosis
- Renal function needs to be assessed if you want to use sofosbuvir

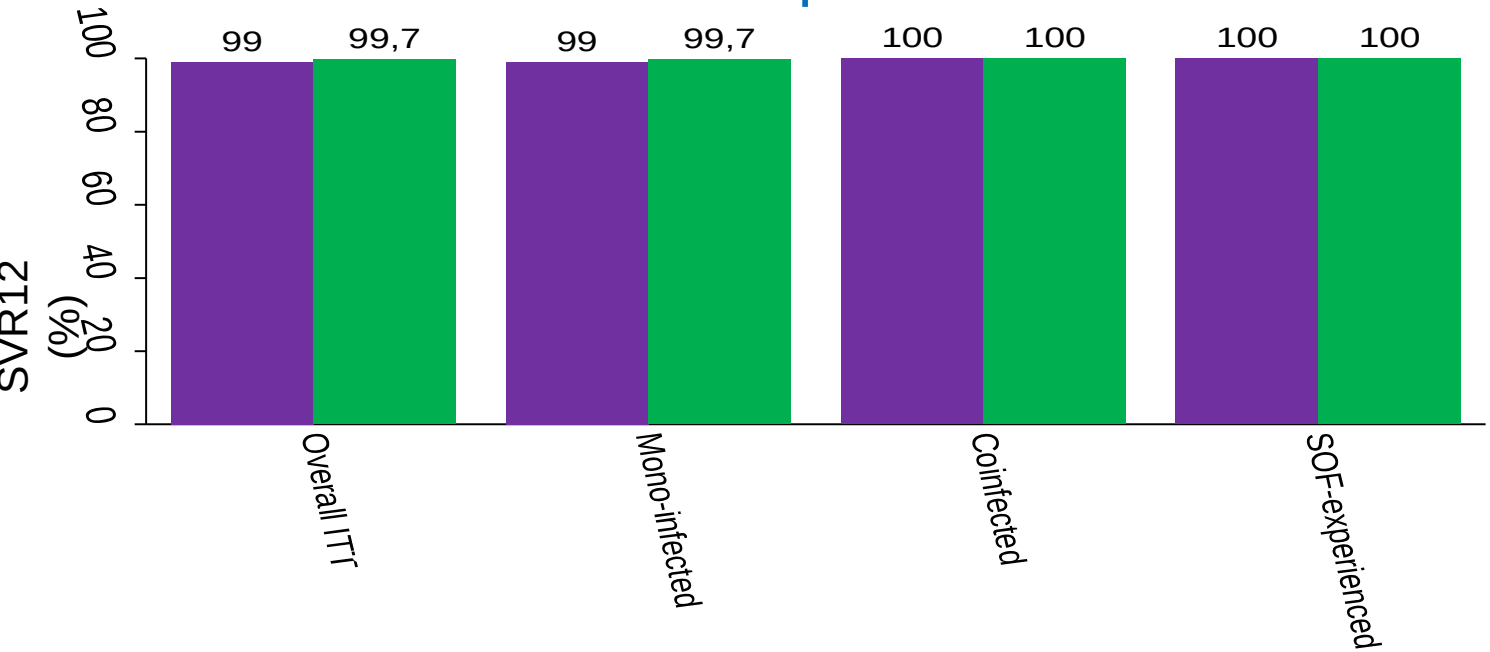
Genotype
Should we separate G1/4 from others?

- Often slow turn around time for genotype testing

- Can not be point of care

Do we still need it?

ENDURANCE-1: Efficacy and safety of 8- vs 12-week treatment with Glecaprevir/Pibrentasvir in G1 patients



ITT population: All pts receiving study drug; none excluded

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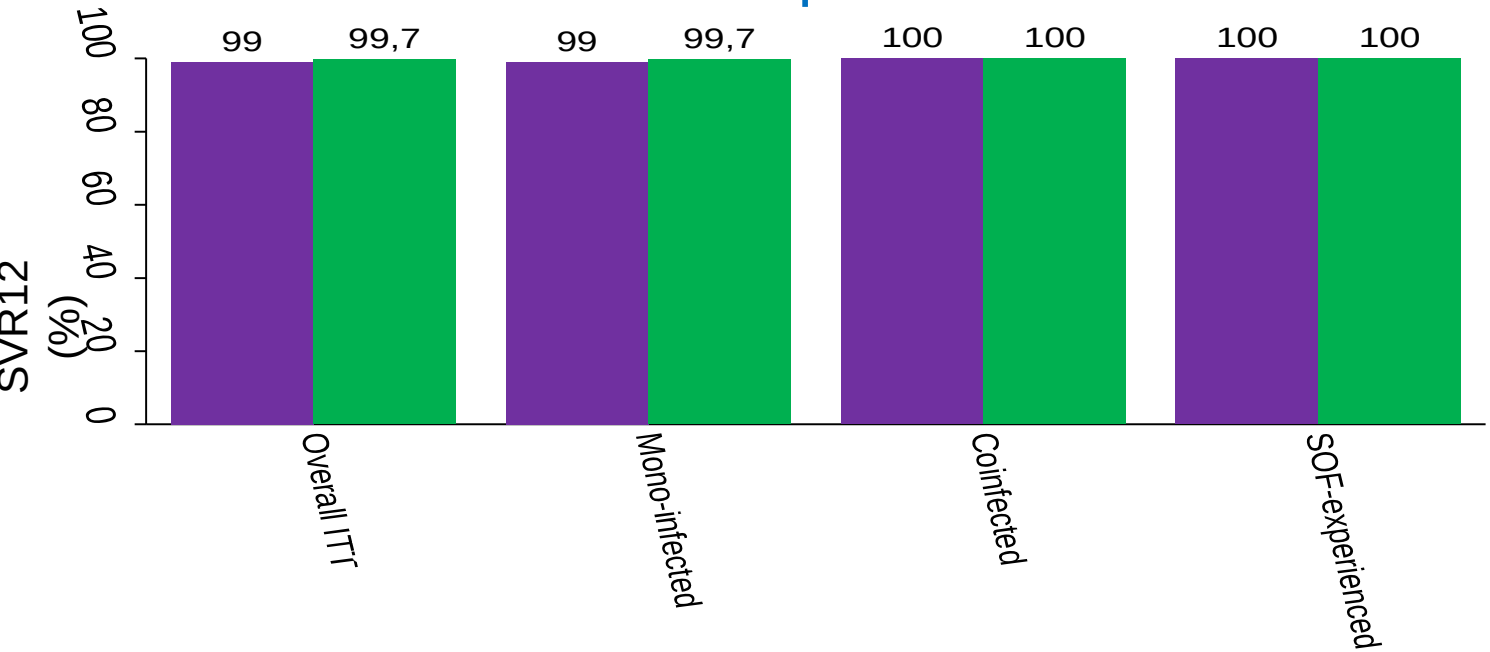
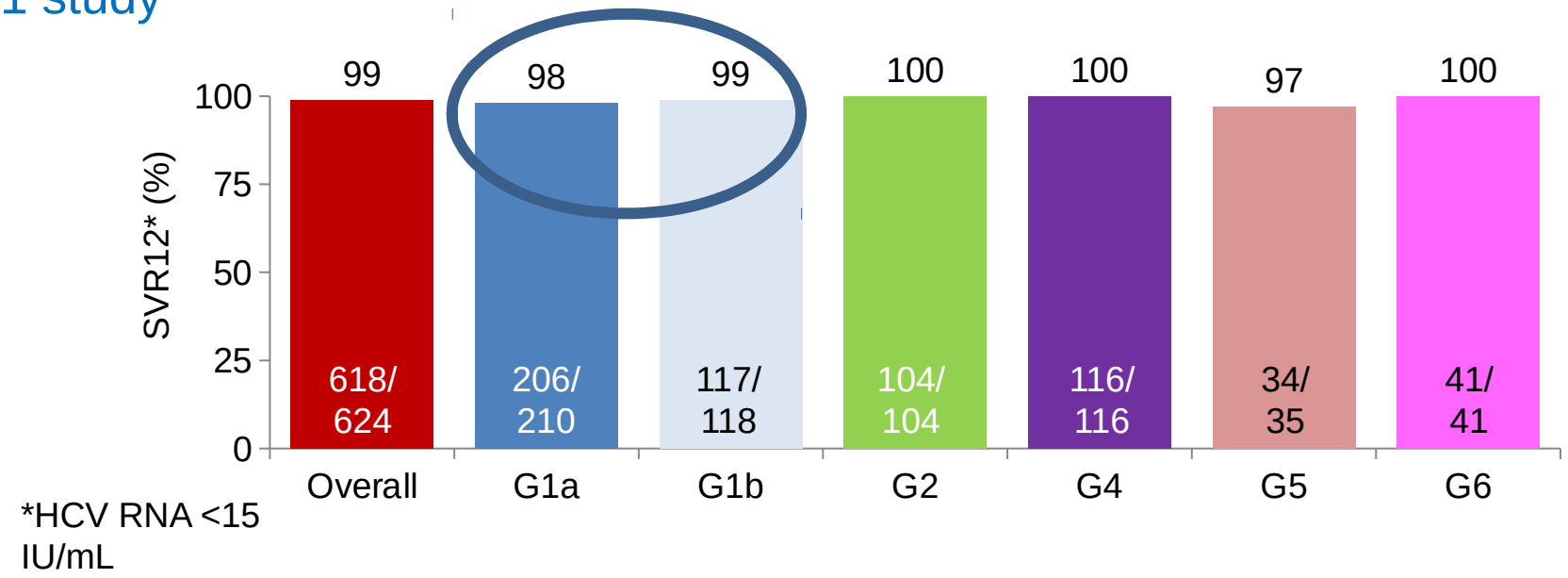


ITT population: All pts receiving study drug; none excluded

85% of patients were F0/F1

How will this work in F2-F3?

Phase 3 evaluation of SOF/VEL FDC for 12 weeks in Tx-naive and -experienced G1, 2, 4, 5, and 6 patients with and without cirrhosis: ASTRAL-1 study



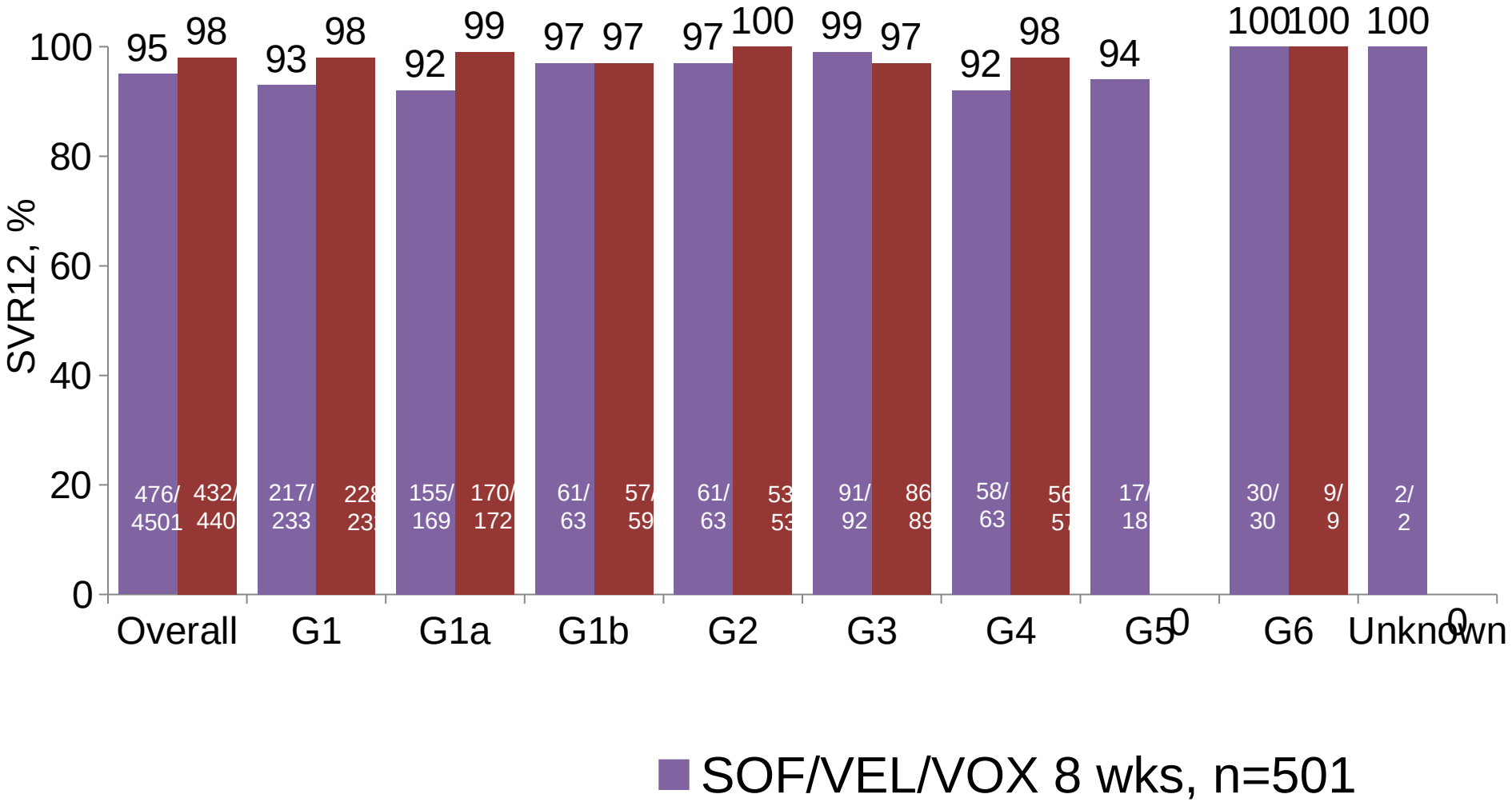
*HCV RNA <15 IU/mL

- 12 weeks rather than 8 weeks for G1

BUT

- 1 tablet NOT 3

SOF/VEL/VOX for 8 weeks compared to SOF/VEL for 12 weeks in DAA-naive G1–6 patients: The POLARIS-2 study



Jacobson IM, et al. AASLD 2016, Boston. #LB-12

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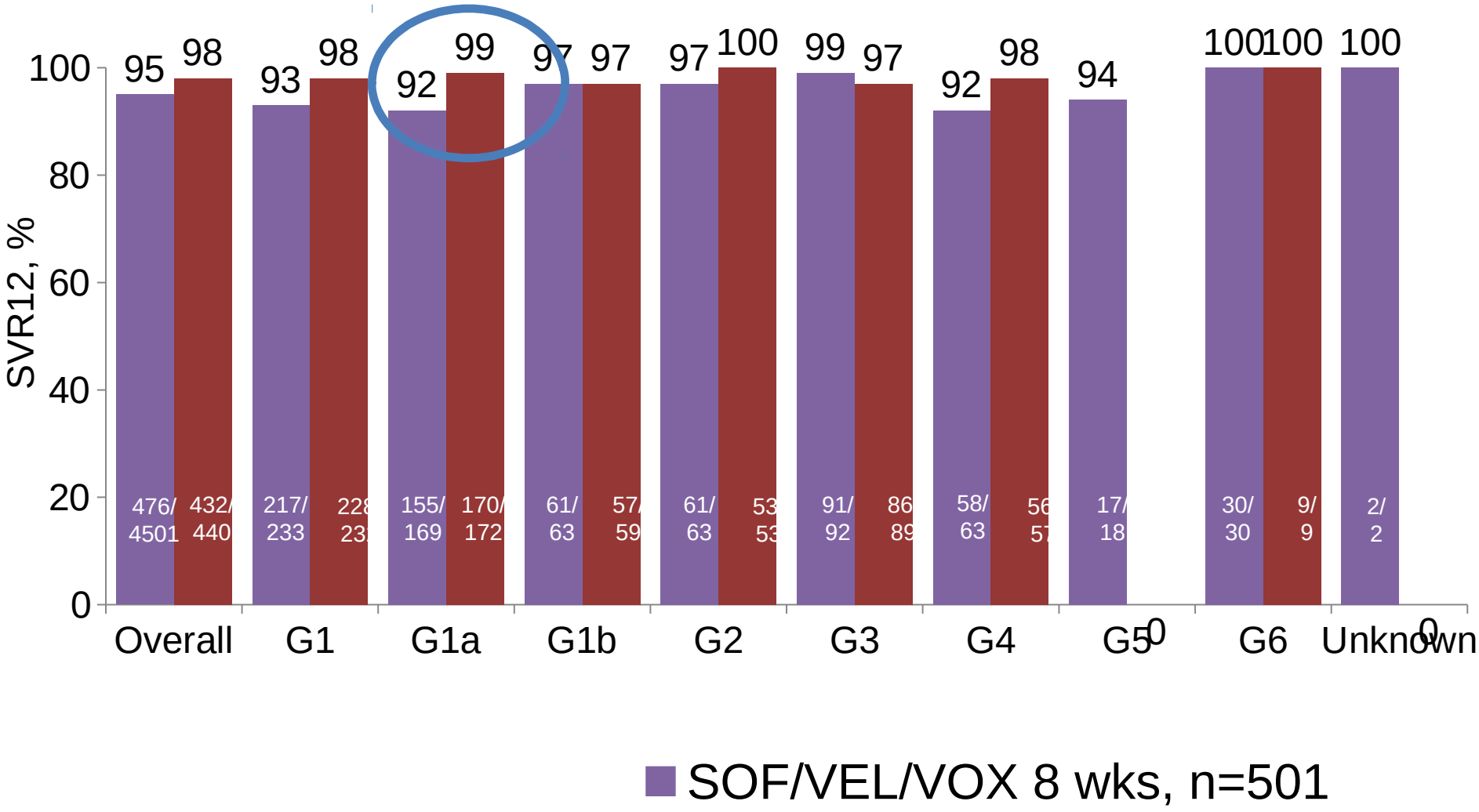


Jacobson IM, et al. AASLD 2016, Boston. #LB-12

Pan-genotypics for G1

- A few nuances that reduce efficacy or increase pill burden

- What about genotype specific therapy?

One pill – 8 weeks

LDV/SOF in treatment-naive patients with non-cirrhotic, G1 HCV

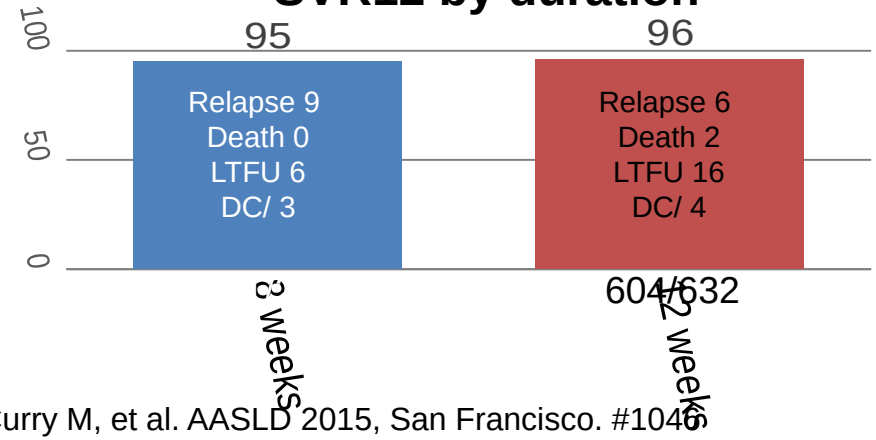
Patient disposition

TN, non-cirrhotic
(n=895)

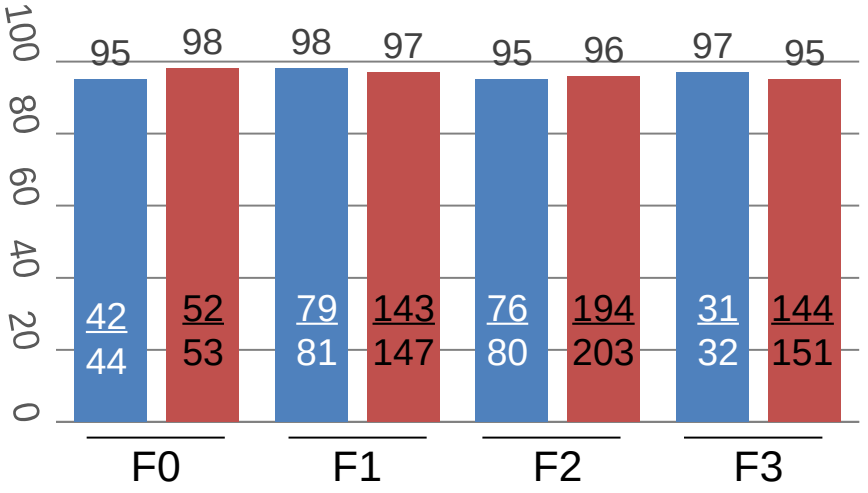
- 8 wks LDV/SOF (n=263)
  - SVR achieved (n=251)
  - SVR not achieved (n=3)
- 12 wks LDV/SOF ± RBV (n=632)*
  - SVR achieved (n=604)
  - SVR not achieved (n=6)

*21 Patients were on 12 weeks of LDV/SOF+RBV

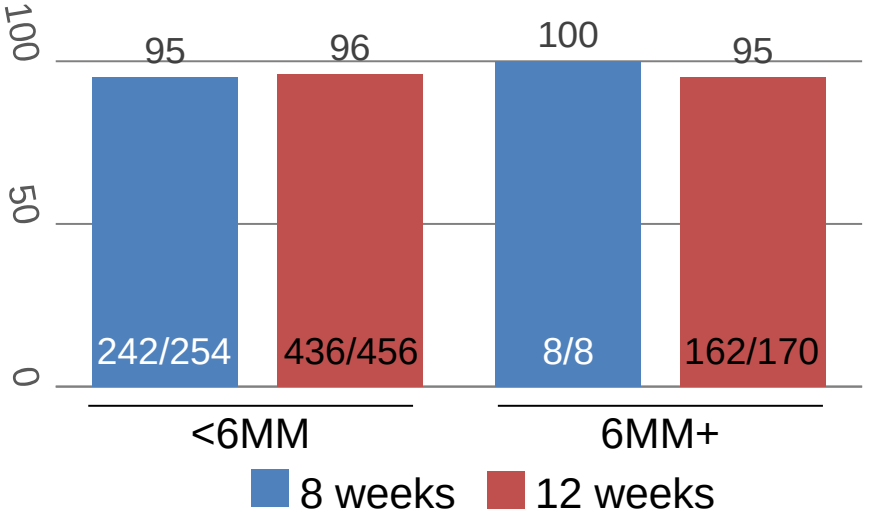
SVR12 by duration



SVR12 by fibrosis

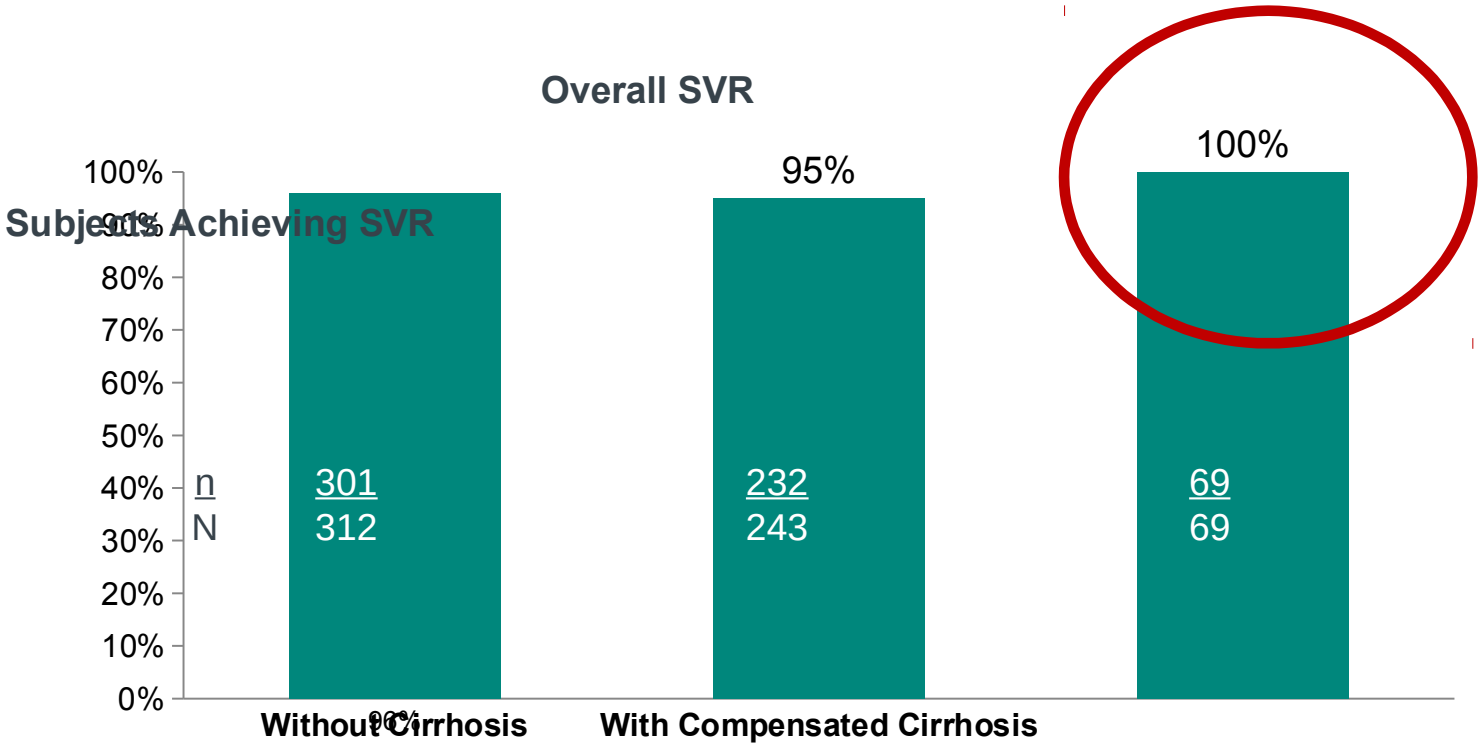


SVR12 rates by baseline viral load

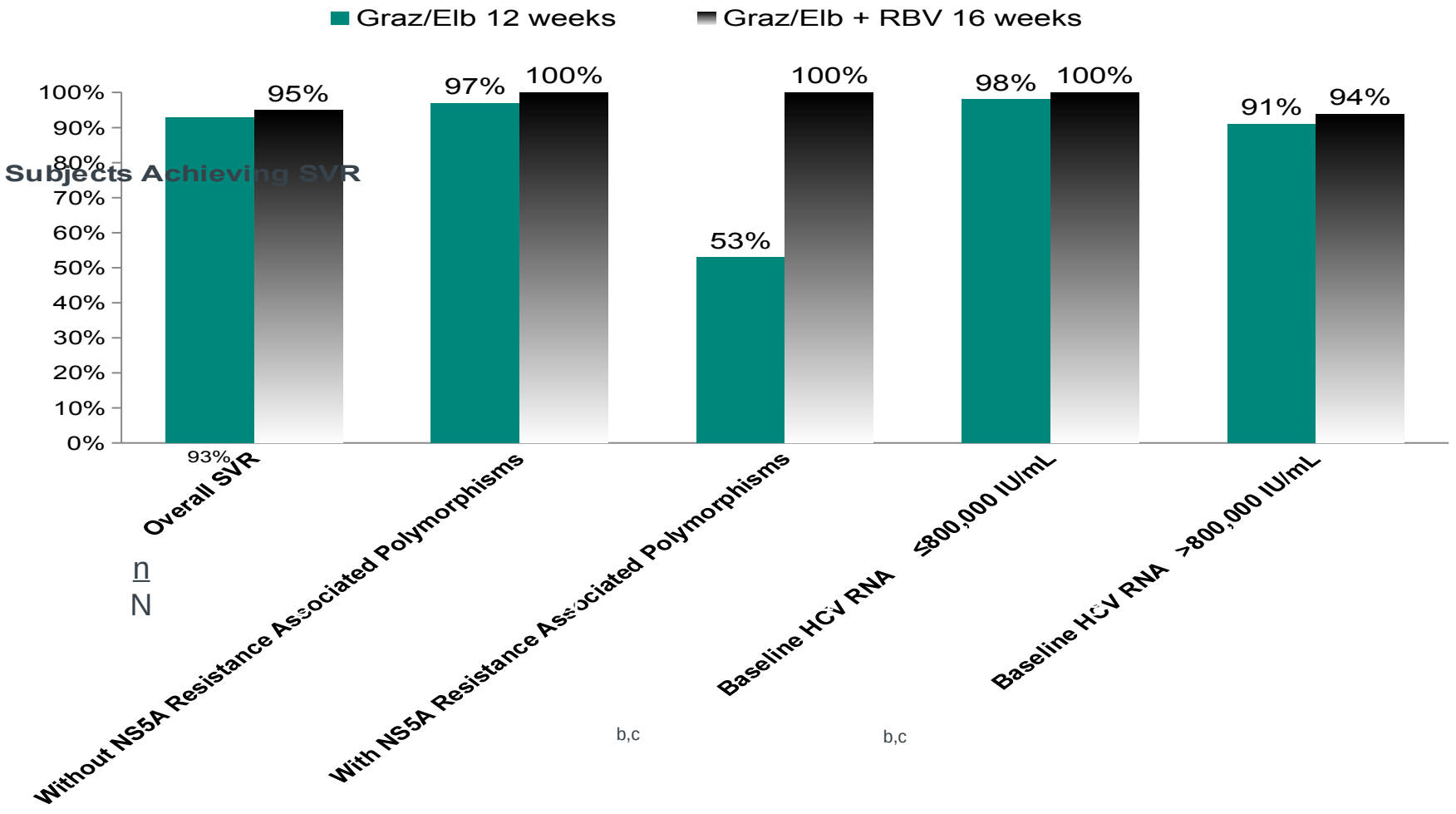


Curry M, et al. AASLD 2015, San Francisco. #1045

Elbasvir and grazoprevir- one pill Efficacy in HCV GT1b Infected Patients



Elbasvir and grazoprevir: Pooled Efficacy in HCV GT1a Infected Patients



Pan-genotypics for G1

- All require some degree of pre-treatment assessment

- ‘Perfect’ therapy requires knowledge of the genotype
  - Genotyping allows duration, efficacy and tablet number optimisation

Is it really that easy?

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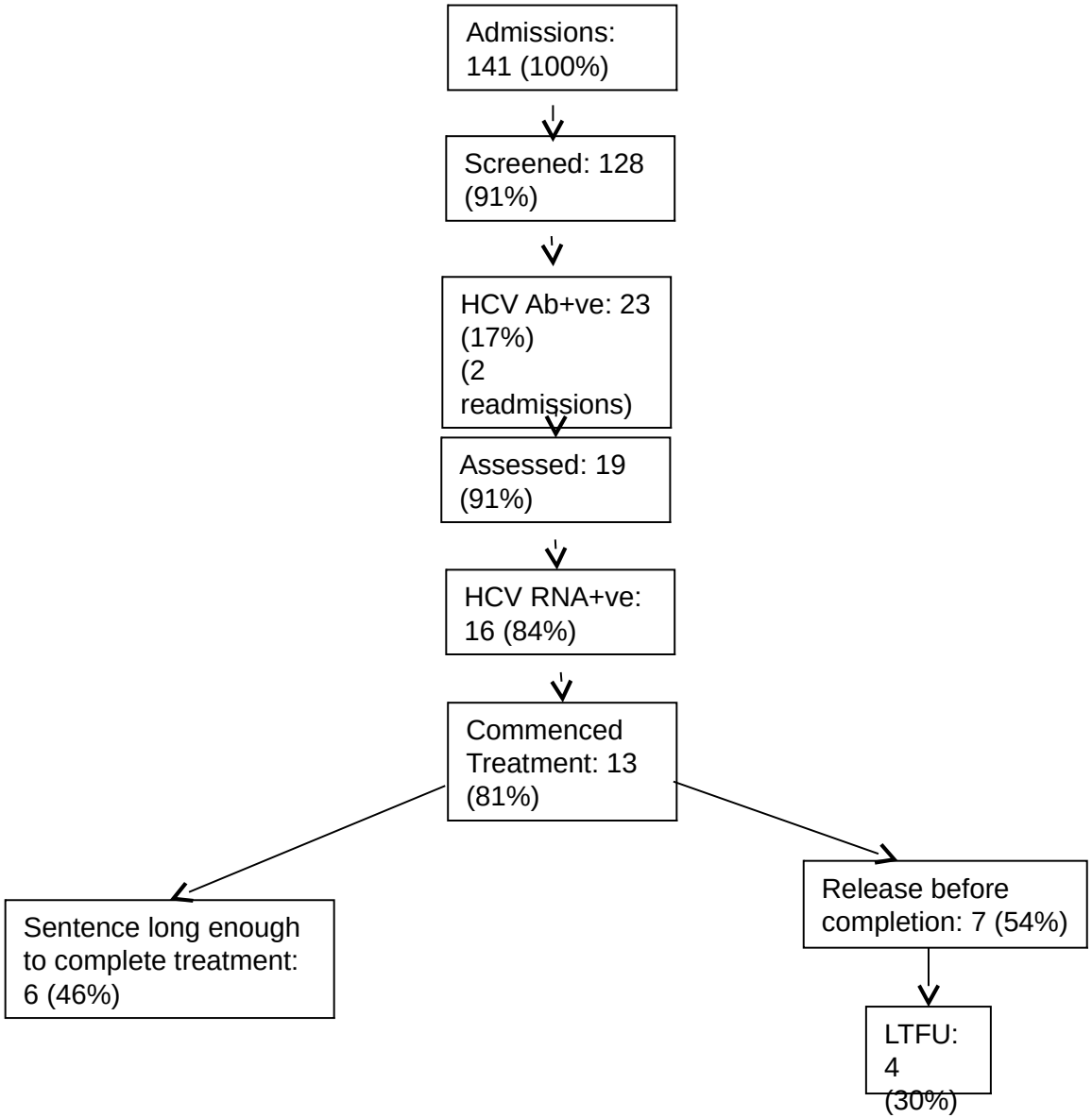
Test and treat

Test and treat

- Allows access to marginal patient groups
- May improve uptake of therapy
- ? Essential for an elimination campaign

Prison ‘test and treat’ model in West London (Prof A. Brown)



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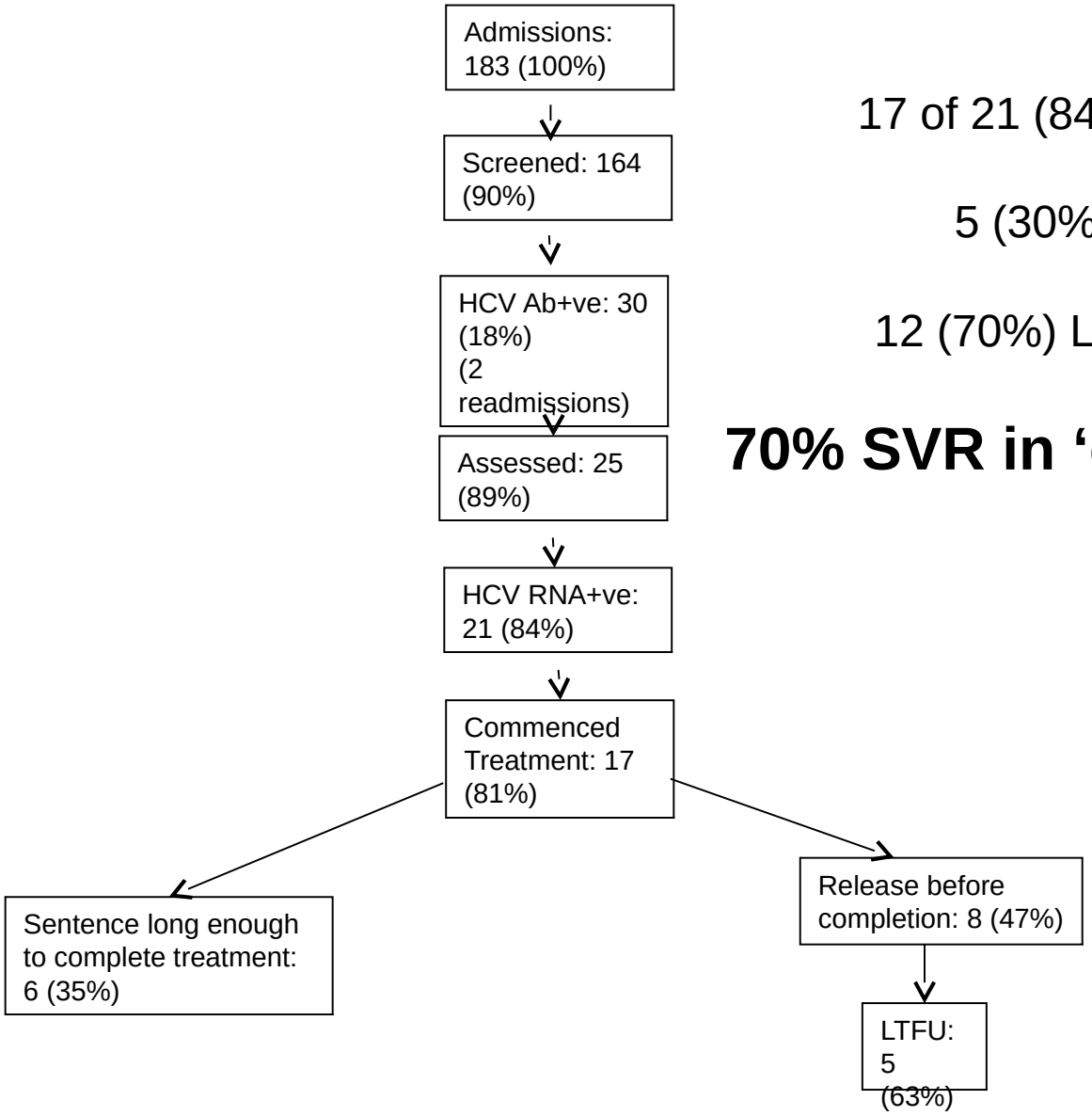


17 of 21 (84%) treated

5 (30% Lost)

12 (70%) Likely SVR

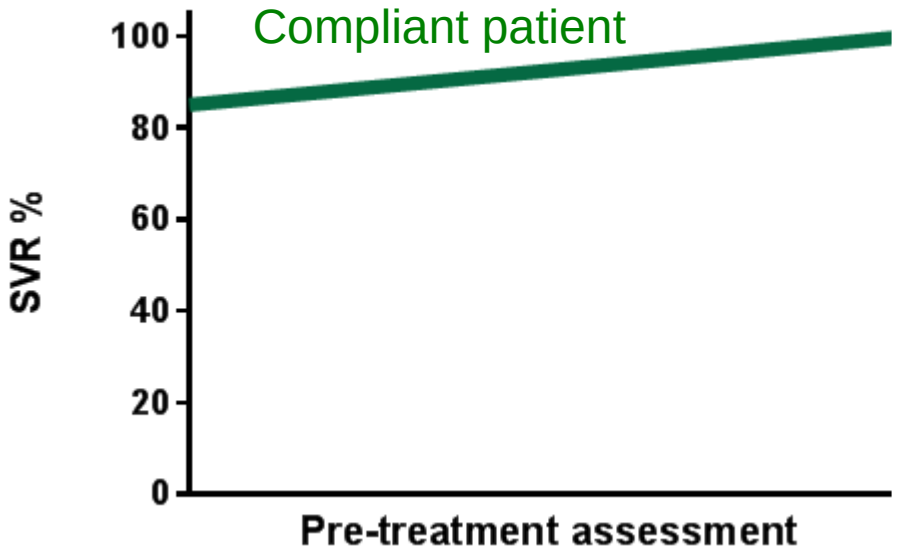
70% SVR in ‘disengaged’

Pan-genotypics in ‘Hard to reach’ Veterans Glecaprevir/Pibrentasvir data

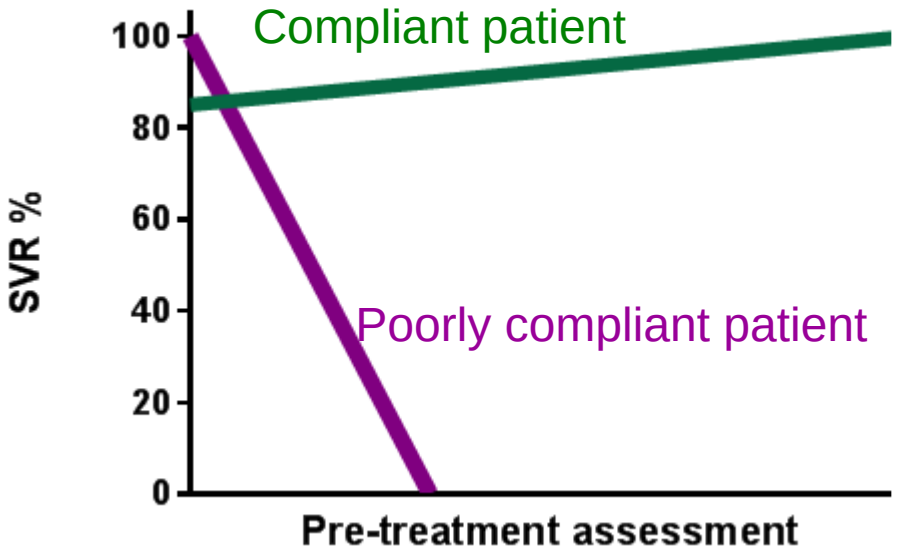
Antiviral experience	Cirrhosis status	SVR % (n/N) 8 weeks	SVR % (n/N) 12 weeks	SVR % (n/N) 16 weeks
Genotype 1				
Naïve	Non-cirrhotic	91.9 (610/664)	91.6 (141/154)	100 (14/14)
	Cirrhotic	92.3 (24/26)	94.4 (68/72)	100 (5/5)
Genotype 2				
Naive	Non-cirrhotic	93.8 (150/160)	88.1 (37/42)	100 (1/1)
	Cirrhotic	100 (3/3)	100 (20/20)	
Genotype 3				
Naive	Non-cirrhotic	84.8 (78/92)	91.7 (44/48)	100 (7/7)
	Cirrhotic	100 (3/3)	96.4 (27/28)	100 (3/3)

Belperio P, et al. AASLD 2018, San Francisco, USA. #703

Personalised medicine



Personalised Medicine



Personalised Medicine
Is there still a need?

- Good medicine is ALWAYS personal

- Detailed pre-treatment assessment allows optimal therapy

BUT

- Pre-treatment assessment reduces access

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Don’t let the perfect be the enemy of the good