Hepatitis C elimination needs involvement of all – turn the page

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Conflicts of Interest

- Speaker and consultancy fees received from
- AbbVie, BI, BMS, Gilead, Janssen, Roche, Merck, Novartis, Springbank, Achillion, Idenix

HCV

- The disease and its impact
- Viro-babble
- The politics

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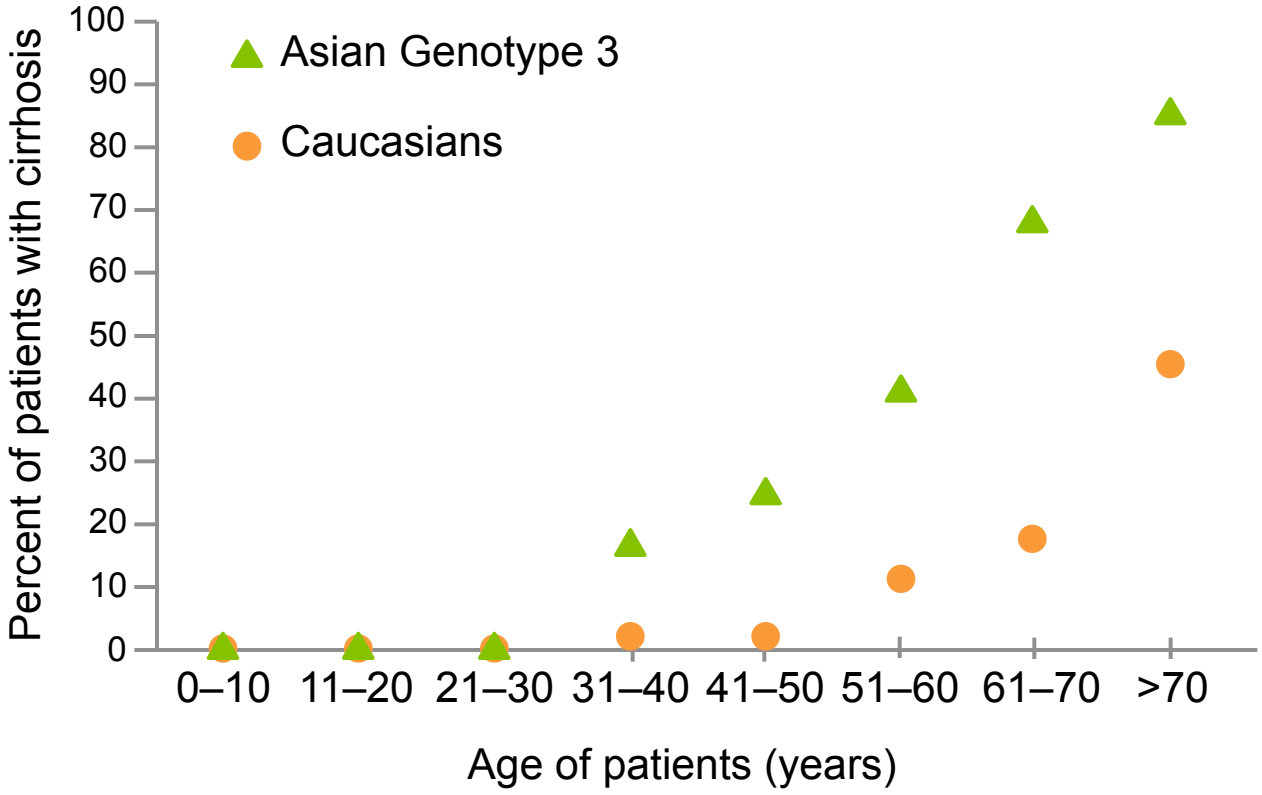
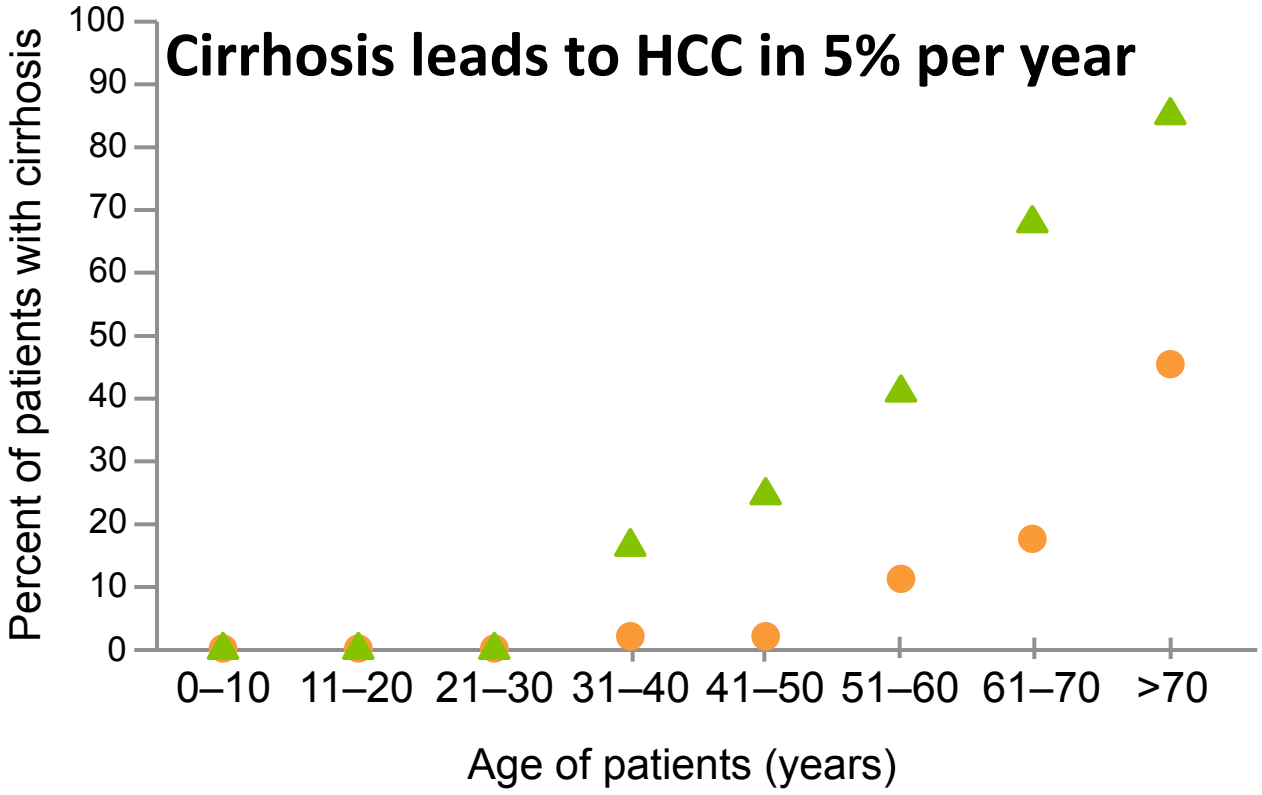
HCV causes slowly progressive liver fibrosis



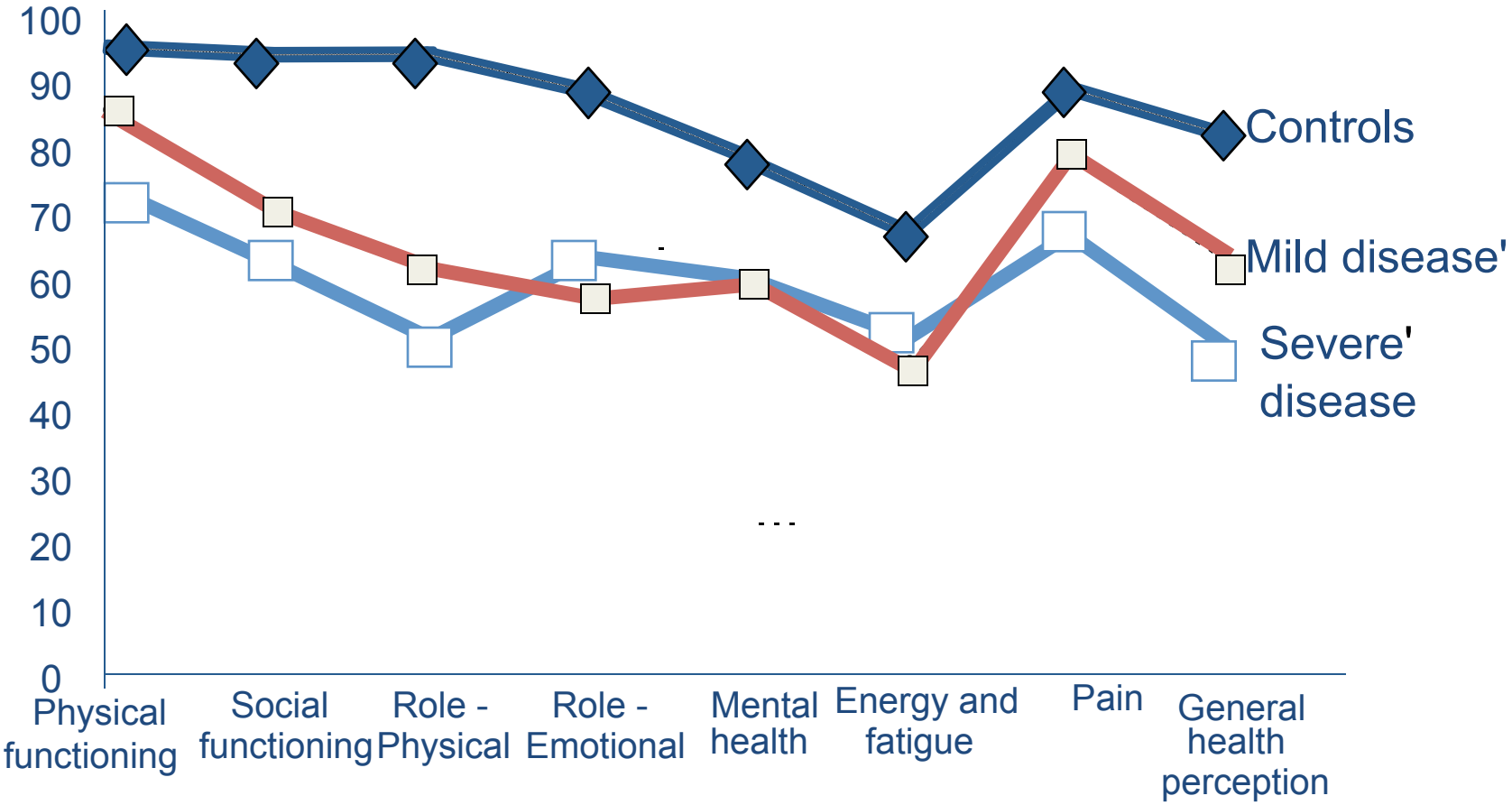
Adapted from D'Souza. Clin Gastroenterol Hepatol 2005;3:910–17

HCV causes slowly progressive liver fibrosis



Adapted from D'Souza. Clin Gastroenterol Hepatol 2005;3:910–17

Patients with chronic HCV feel unwell



Foster et al Hepatology 1998

HCV

- Makes people sick
- Then it kills them

Where we started

- Have HCV – get a liver biopsy (not very nice)
- If very severe disease – die quietly (not very nice)
- If moderate disease – get up to 18 months injections and tablets for a 70% chance of a cure (not very nice)

Where we are today

- Get a scan
- Take some tablets for a few weeks
- Get cured

(All very nice)

HCV

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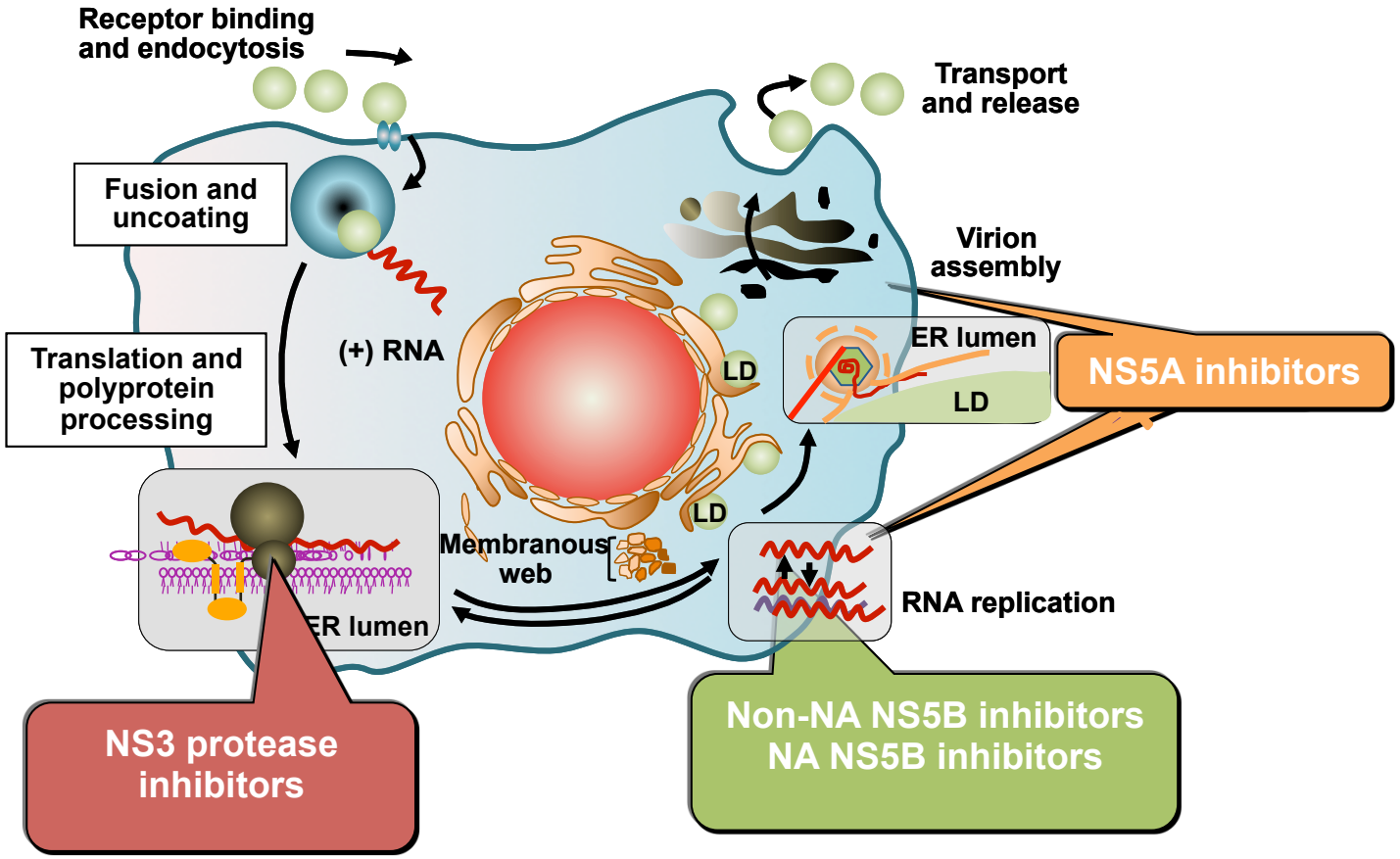
We now have highly efficacious DAAs that target different stages in the HCV lifecycle

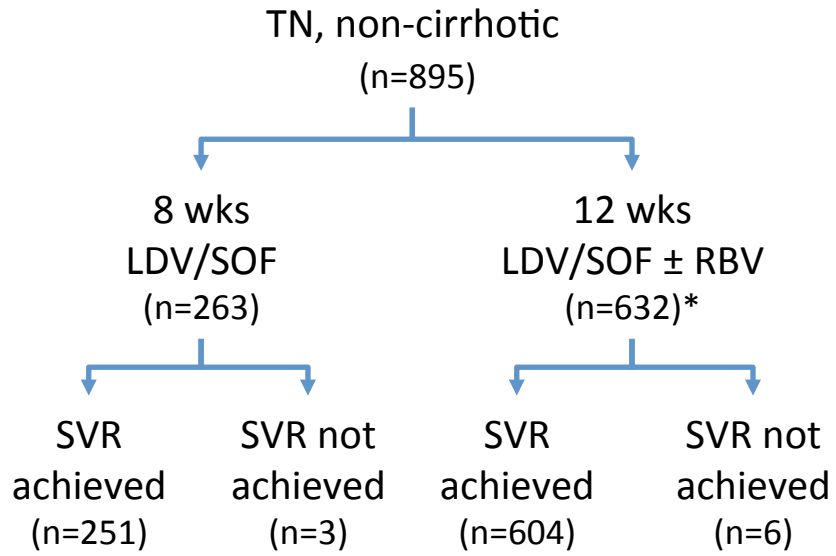


Lindenbach BD, Rice CM. Nature 2005;436(Suppl):933–8;
Liang J, Ghany MG. N Engl J Med 2014;370:2043–7.

DAA: direct-acting antiviral agent; ER: endoplasmic reticulum; GT: genotype; IFN: interferon; LD: luminal domain; NA: nucleos(t)ide analogue; NS: non-structural protein; SVR: sustained virological response

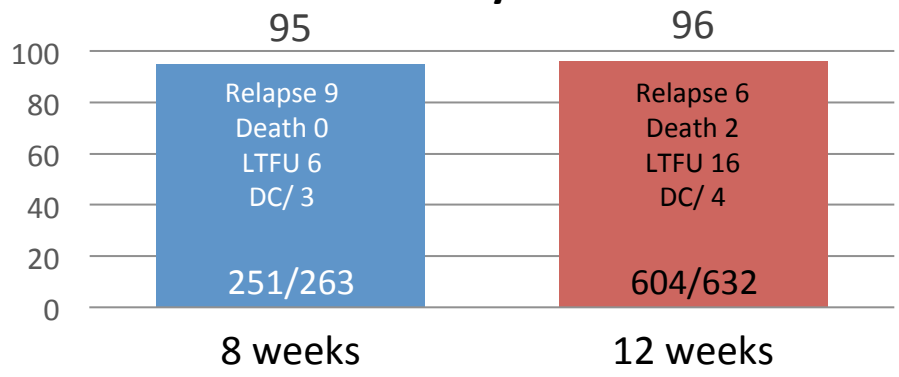
Real-world experience from the TRIO Network:
Effectiveness of 8 or 12 week LDV/SOF in treatment-naive patients with non-cirrhotic, G1 HCV

Patient disposition

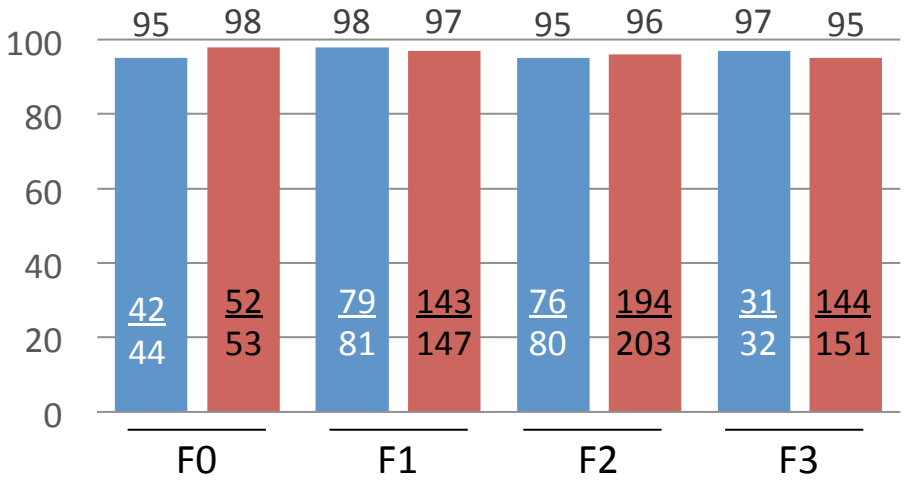


*21 Patients were on 12 weeks of LDV/SOF+RBV

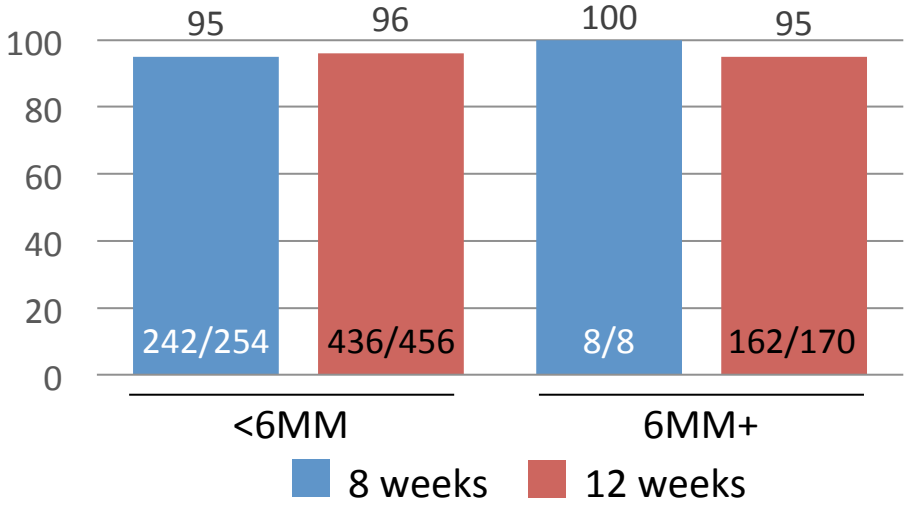
SVR12 by duration



SVR12 by fibrosis

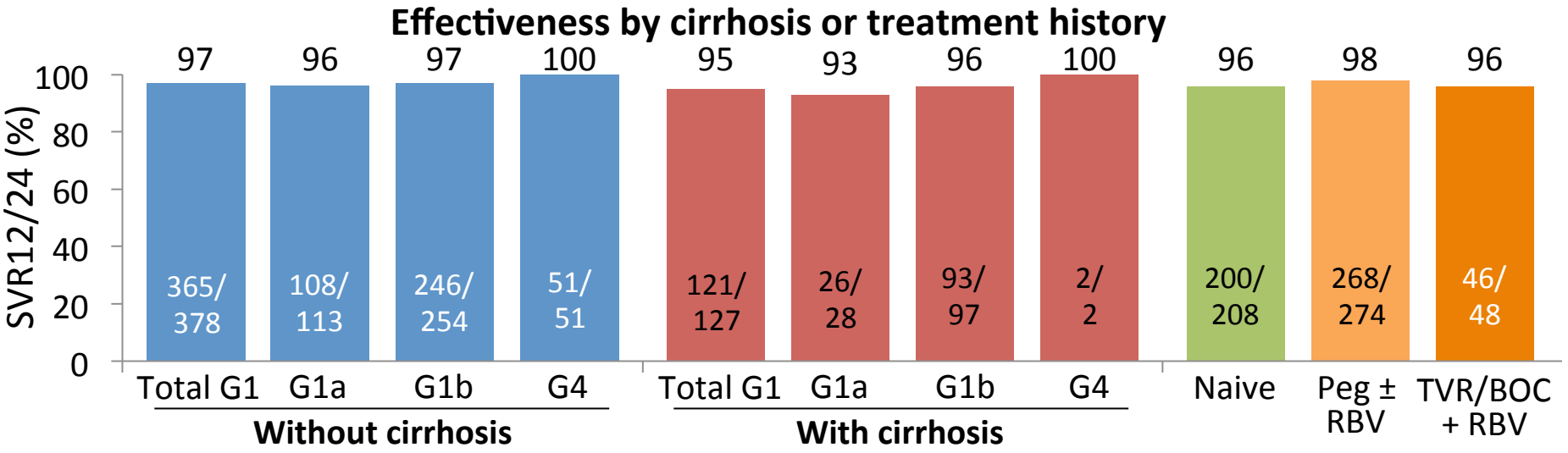


SVR12 rates by baseline viral load



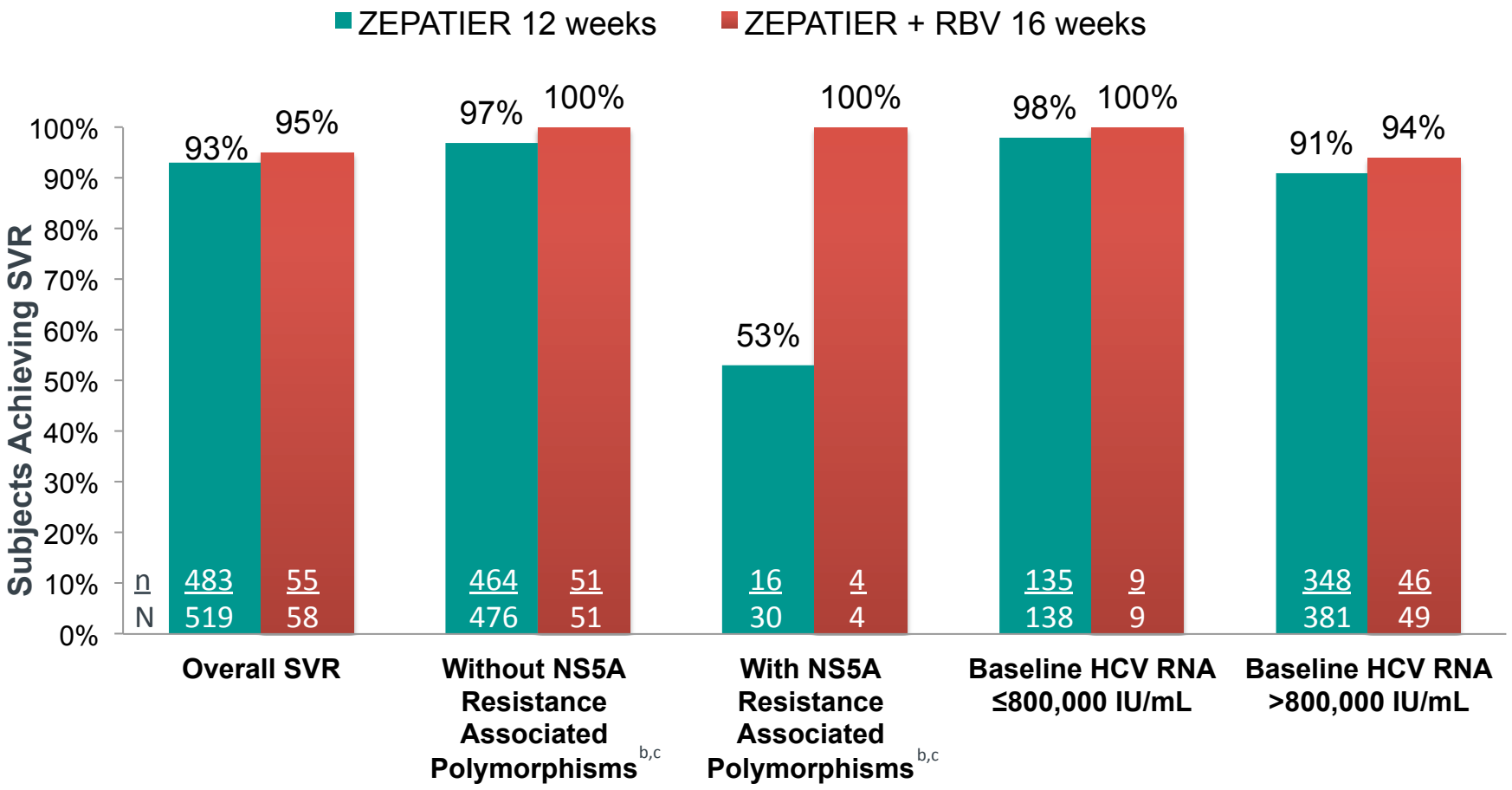
Curry M, et al. AASLD 2015, San Francisco. #1046

Real-world safety and effectiveness of OBV/PTV/r with DSV and/or RBV in the **German hepatitis C Registry**

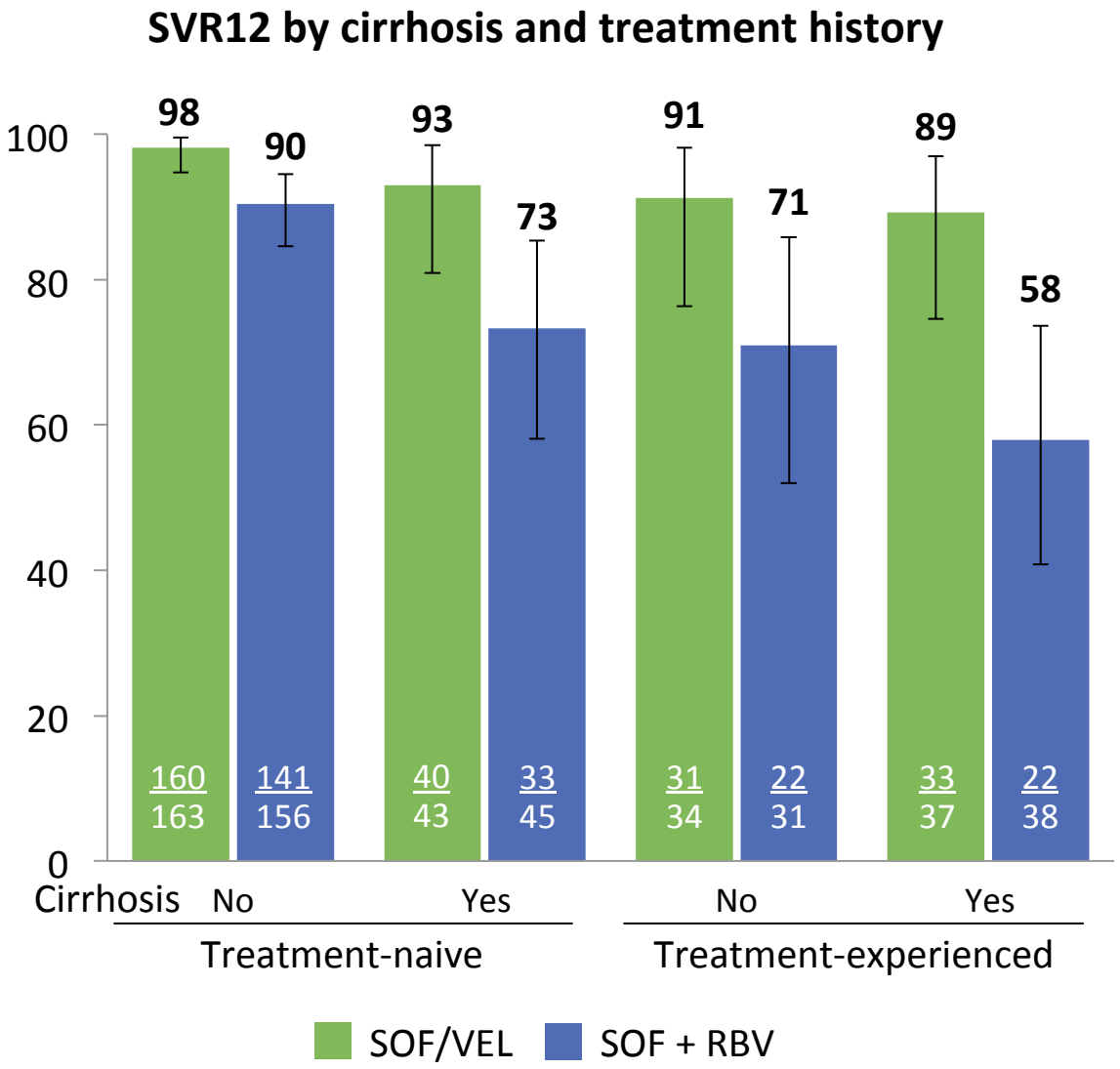


Safety, n (%)		2D/3D -RBV (n=436)	2D/3D + RBV (n=353)	2D/3D -RBV (n=44)	2D/3D + RBV (n=184)
Any AE		185 (42)	201 (57)	20 (45)	119 (65)
Any SAE		5 (1)	8 (2)	0	8 (4)
RBV dose mod.		-	26 (7)	-	18 (10)
Death		2 (0.5)	0	0	0
D/C due to AE		2 (0.5)	4 (1)	0	9 (5)
AEs in ≥5%of patients	Fatigue	80 (18)	97 (27)	8 (18)	58 (32)
	Pruritus	33 (8)	40 (11)	2 (5)	26 (14)
	Headache	35 (8)	35 (10)	5 (11)	16 (9)
	Insomnia	17 (4)	29 (8)	0	18 (10)
	Nausea	16 (4)	20 (6)	3 (7)	12 (7)
	Anemia	1 (0.2)	15 (4)	0	20 (11)

Elbasvir and grazoprevir: Pooled Efficacy in HCV GT1a Infected Patients

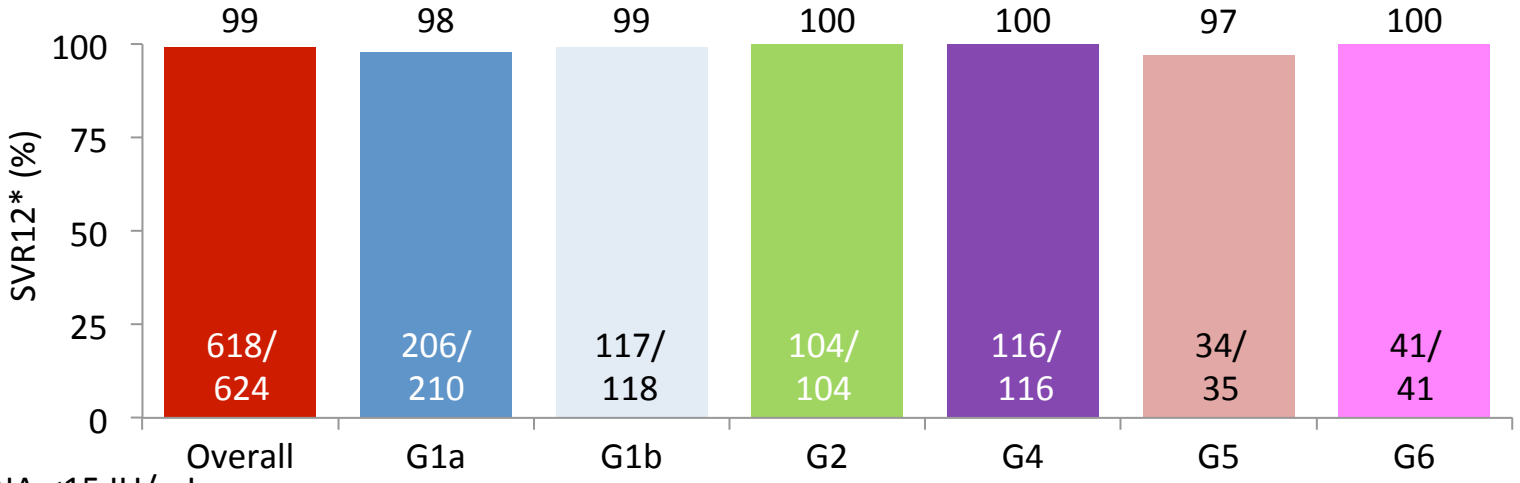


ASTRAL-3 Phase 3 Study: SOF/VEL FDC for 12 weeks compared to SOF + RBV for 24 weeks in G3 HCV infected patients



Foster GR, et al. NEJM 2015

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

- No pts in the PBO group had HCV RNA <15 IU/mL at any timepoint

Virologic failure, n (%)	
On-treatment failure	0
Post-treatment relapse	2 (<1)
Other reasons for classification as failure to achieve SVR 12, n (%)	
Lost to follow-up	2 (<1)
Withdrew consent	1 (<1)
Death	1 (<1)

Feld JJ, et al. AASLD 2015, San Francisco. #LB-2
Feld JJ, et al. N Engl J Med. 2015 Nov 16. [Epub ahead of print]

What is coming next?

- We have great options available
- What can we expect in the future?

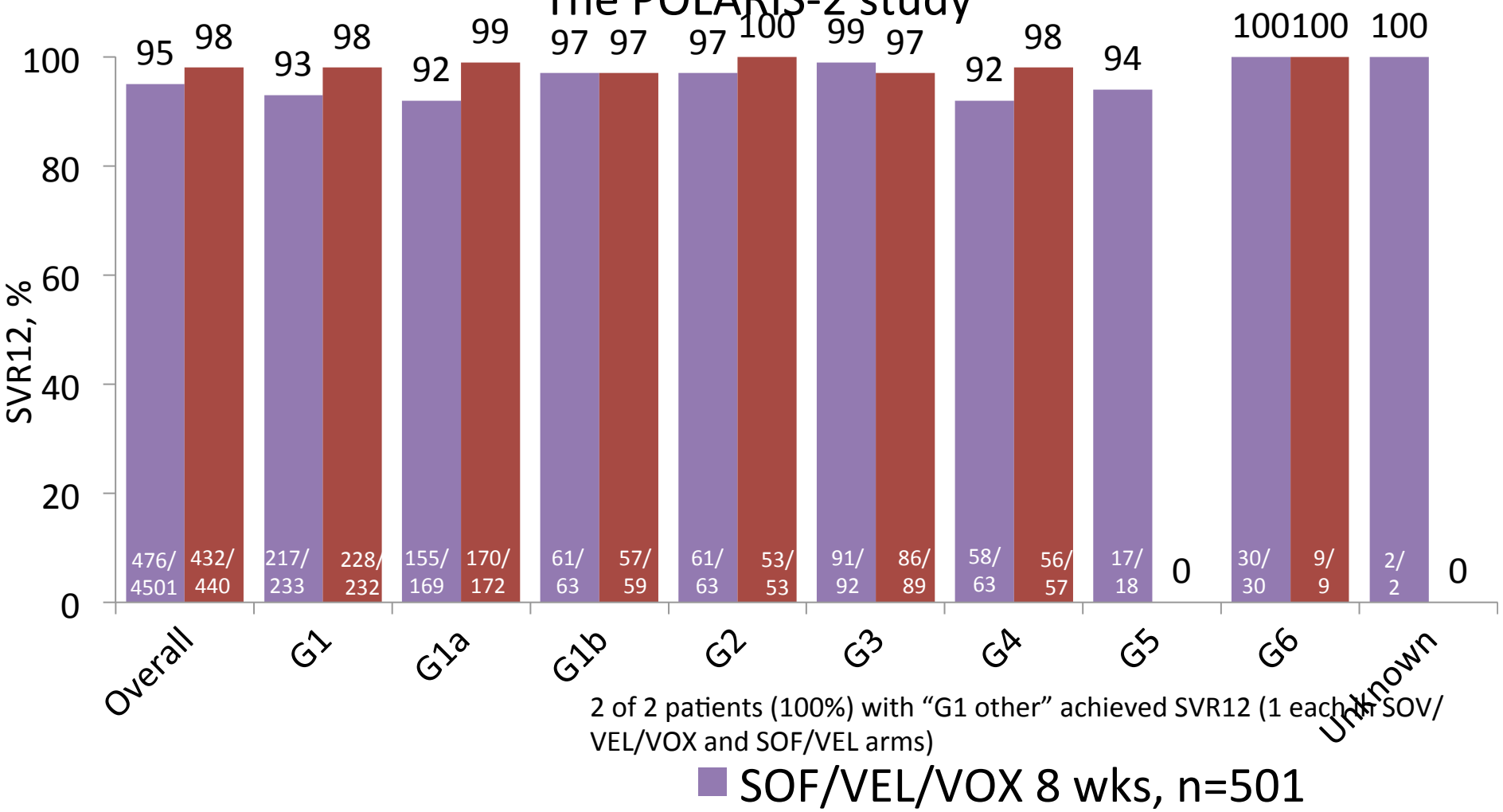
Two drugs good, three drugs better
Sofosbuvir based regimens

- Triple therapy with:-

- Nucleotide
- NS5A inhibitor
- Protease inhibitor

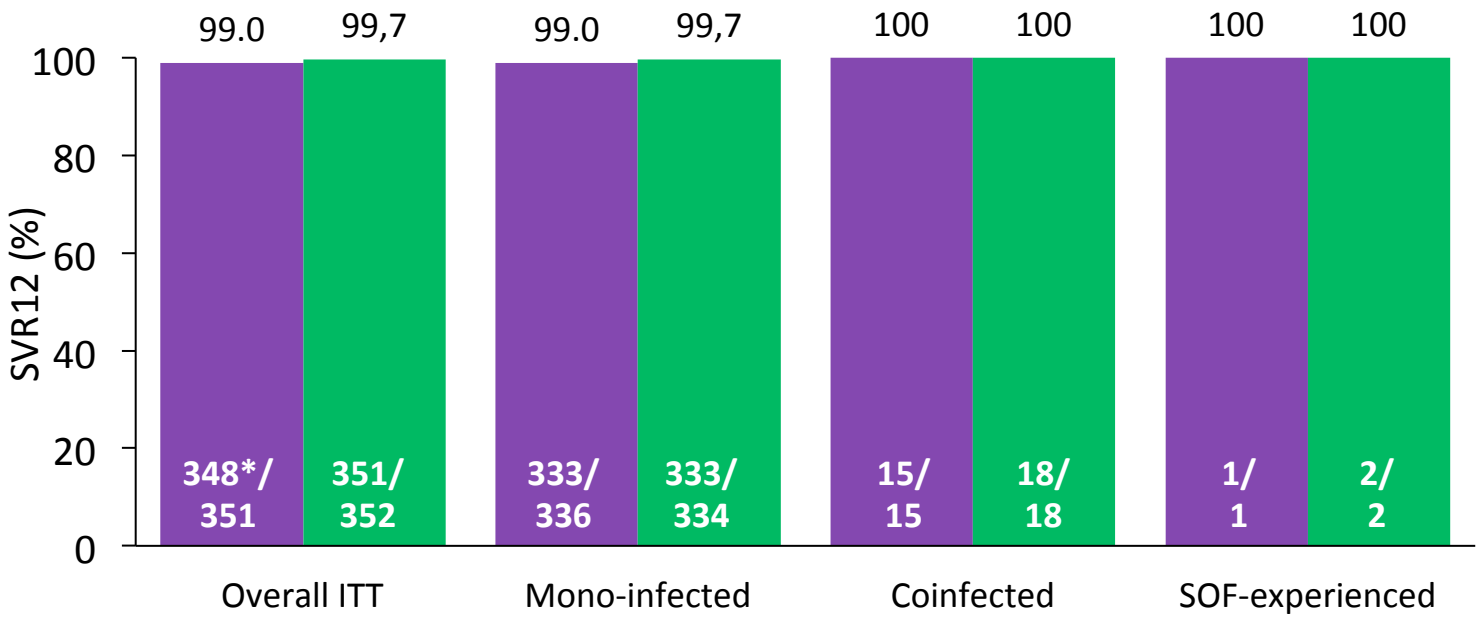
A randomized Phase 3 trial of SOF/VEL/VOX for 8 weeks compared to SOF/VEL for 12 weeks in DAA-naive G1–6 patients:

The POLARIS-2 study



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

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

■ 8-wk

*1 pt in the 8-wk Tx arm experienced on-treatment virologic failure; 1 pt in the 8-wk tx arm d/c in Week 2 due to non-compliance; 2 pts, 1 in each tx arm, are missing SVR12 data

- All-oral, RBV-free G/P regimen can yield high SVR12 rates in 8 weeks for non-cirrhotic G1 patients, including those with HIV-1 coinfection

Zeuzem S, et al. AASLD 2016, Boston. #253

Next generation regimes

- Expected soon
- 2 or 3 drug 8 week regimens for all genotypes
- Sof/led OR G/P for G1
- Sof/vel/vox OR G/P for all others

HCV – a dead virus

- We can cure ALL patients with HCV with simple tablet based, side effect free regimens

HCV

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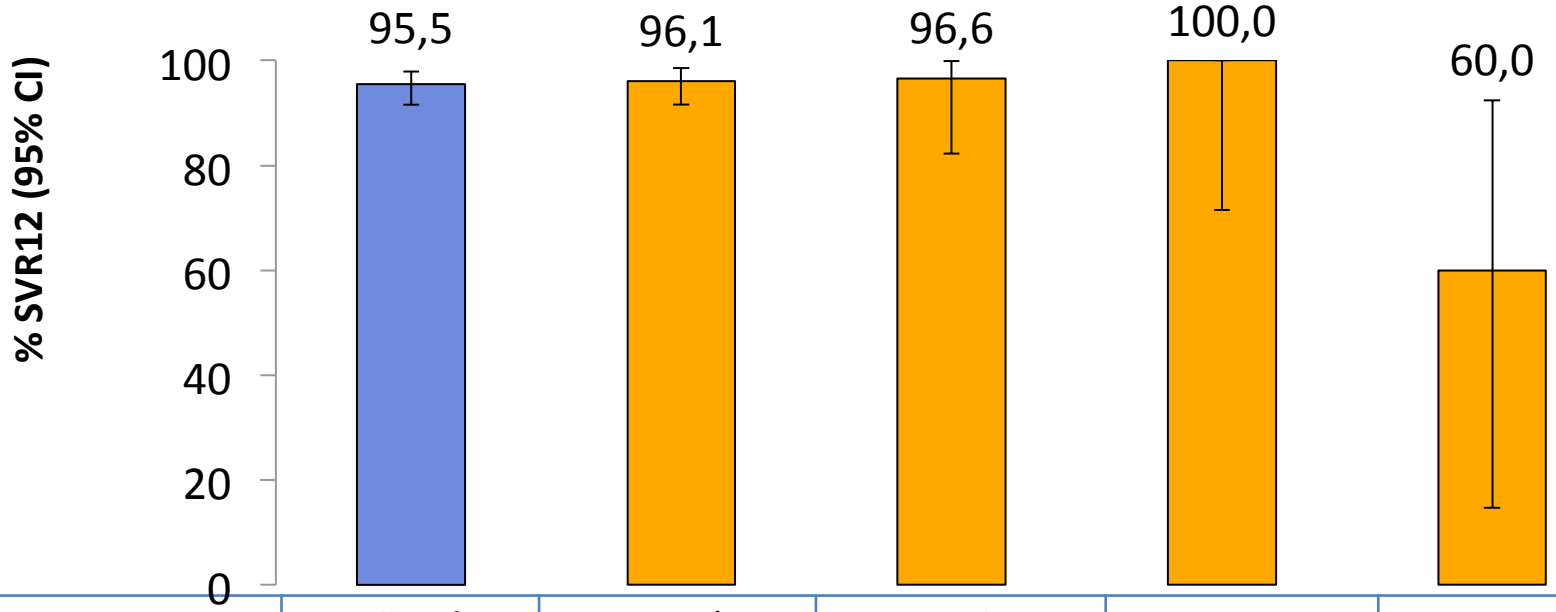
HCV - Politics

- The drugs are expensive (but getting cheaper)
- Some people are ‘more difficult’ to treat than others

HCV - Politics

- The drugs are expensive (but getting cheaper)
- Some people are ‘more difficult’ to treat than others
- Where do active injectors sit on the treatment list?

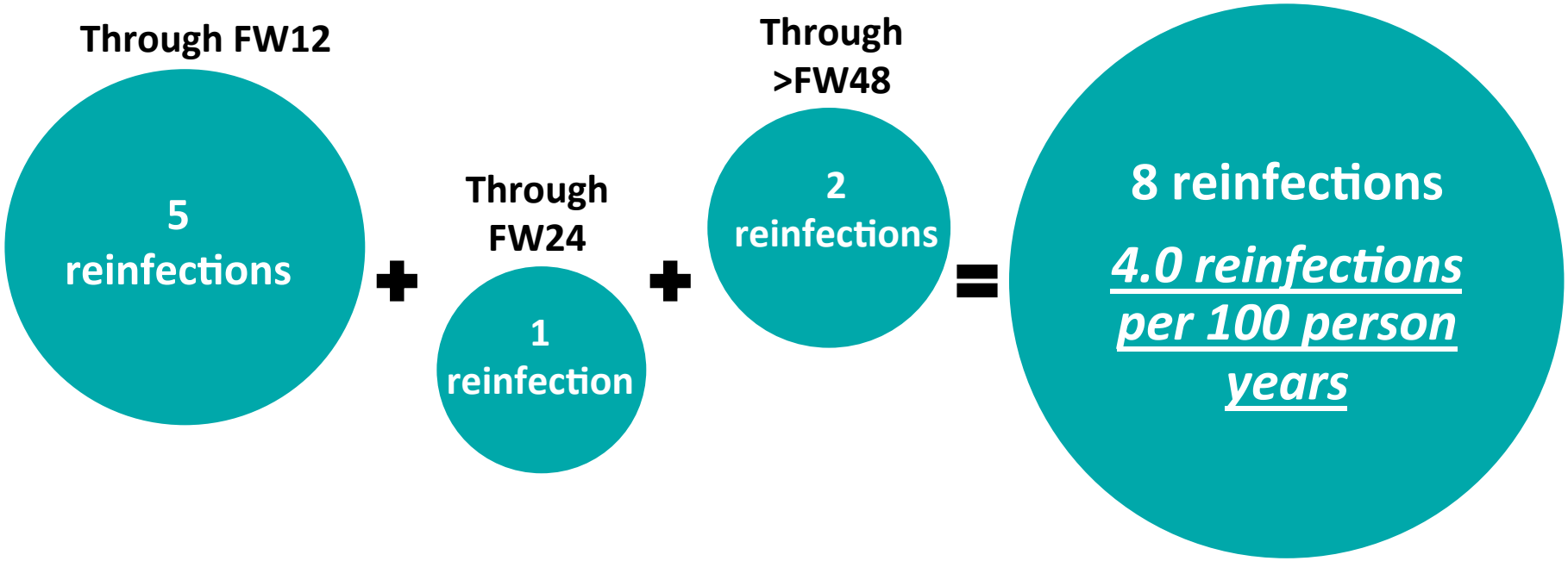
Trial of Grazoprevir/Elbasvir in Injecting drug users



	All GT†	GT1a*	GT1b	GT4	GT6
	189/198	147/153	28/29	11/11	3/5
Failures					
Relapse	7	4	1	0	2
Discontinuation	2	2	0	0	0
Reinfection – counted as success					
	5	3	0	0	2
LTFU or discontinued unrelated to Virologic Failure – excluded from mFAS analysis					
	3	1	1	1	0

*Includes one subject with mixed infection (GT1a and GT1b) who achieved SVR12

Incidence of reinfection



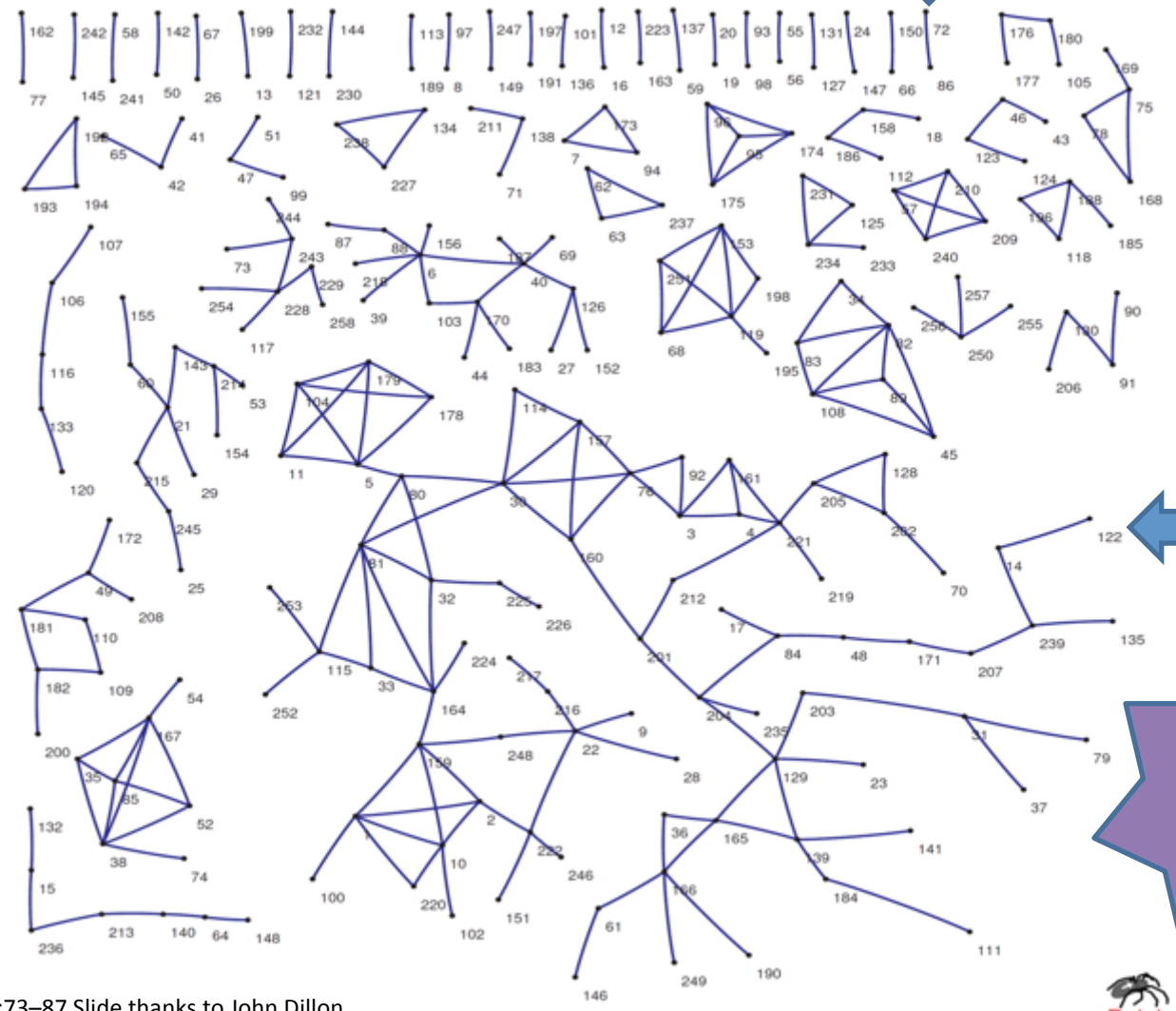
From End of Treatment Through Observation Visit 1		
• 8 reinfections	• 197.5 person years	• 4.0 reinfections per 100 person years (95% CI: 1.7, 8.0)
From End of Treatment Through Observation Visit 1 (Includes only those patients with persistent HCV RNA)		
• 5 reinfections	• 199.0 person years	• 2.5 reinfections per 100 person years (95% CI: 0.8, 5.9)

HCV in Drug Users

- HCV is common in those who use drugs
- Therapy is effective in drug users
- The benefits of treating drug users may be huge

Empirical social network of PV

200% SVR



8,100% SVR

Rolls DA, et al. J Theor Biol 2012;297:73–87 Slide thanks to John Dillon

Pajek

Hawthorne Effect

- Benefits of engaging with health care systems goes beyond the treated disease

Treating active drug users

- Drug users should be a priority for treatment

- Are they……

Transplant waiting lists in the USA

- If you have kidney failure
- You wait 7 years for a kidney
- (7 weeks if you will accept an HCV +ve kidney)

In summary

- We have fantastic curative therapies for HCV
- Treating drug users is the most effective way to use these wonderful drugs
- What is stopping us?