Sofosbuvir - Daclatasvir

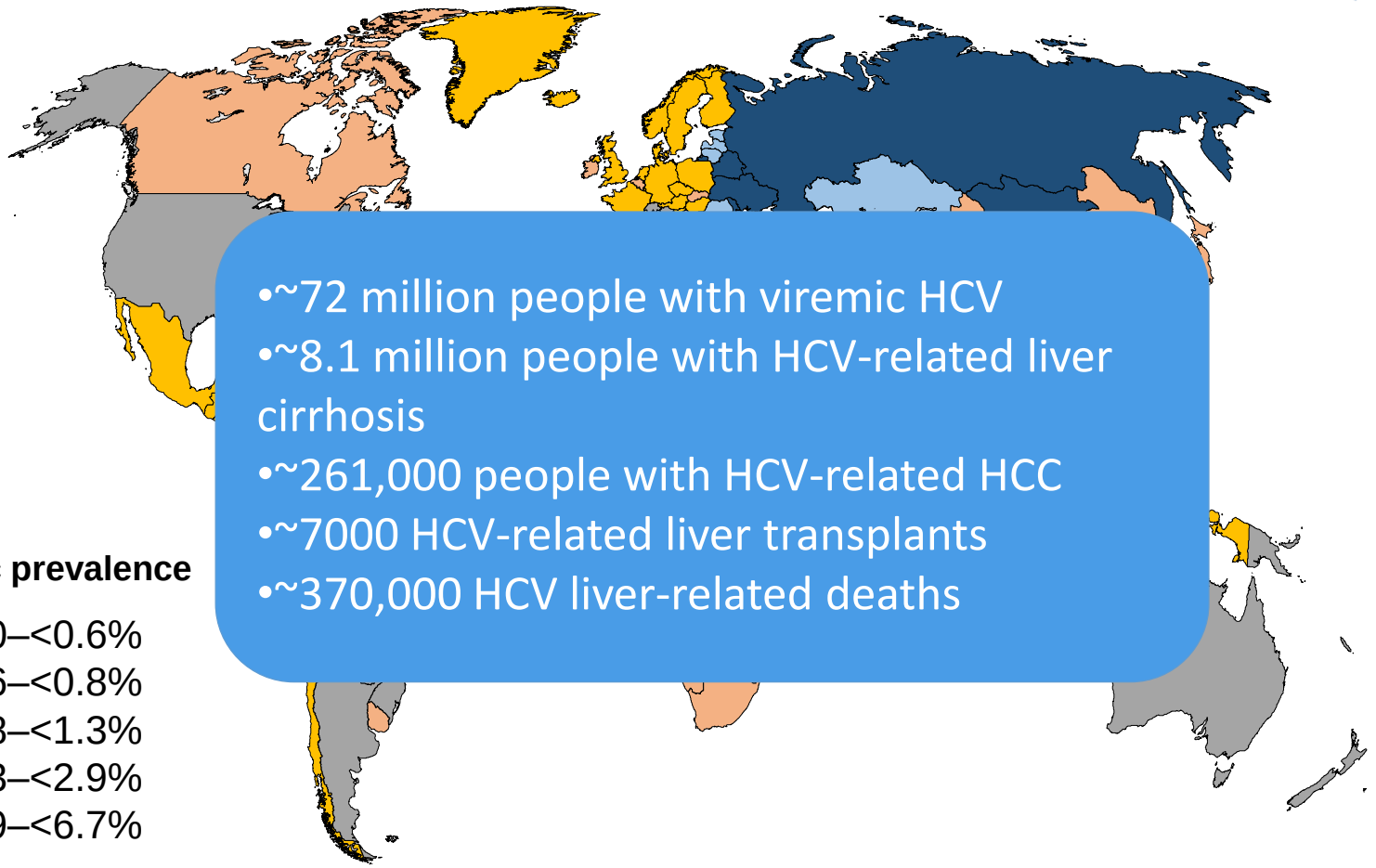
“Un esquema familiar”

Fernando Cairo

fercairo@yahoo.com

Hepatitis C – Epidemia Global Silenciosa

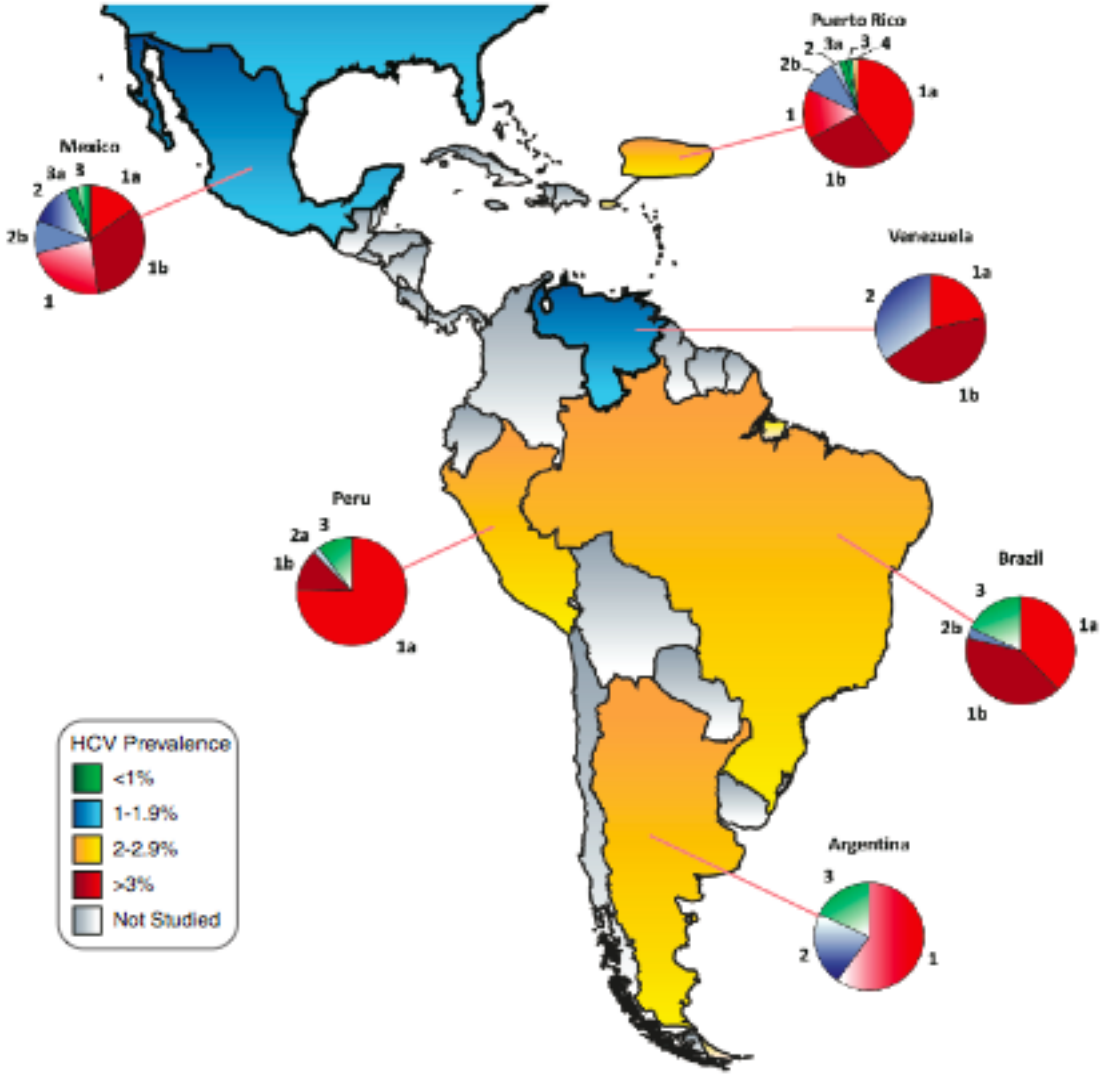
Observatory POLARIS



- ~72 million people with viremic HCV
- ~8.1 million people with HCV-related liver cirrhosis
- ~261,000 people with HCV-related HCC
- ~7000 HCV-related liver transplants
- ~370,000 HCV liver-related deaths

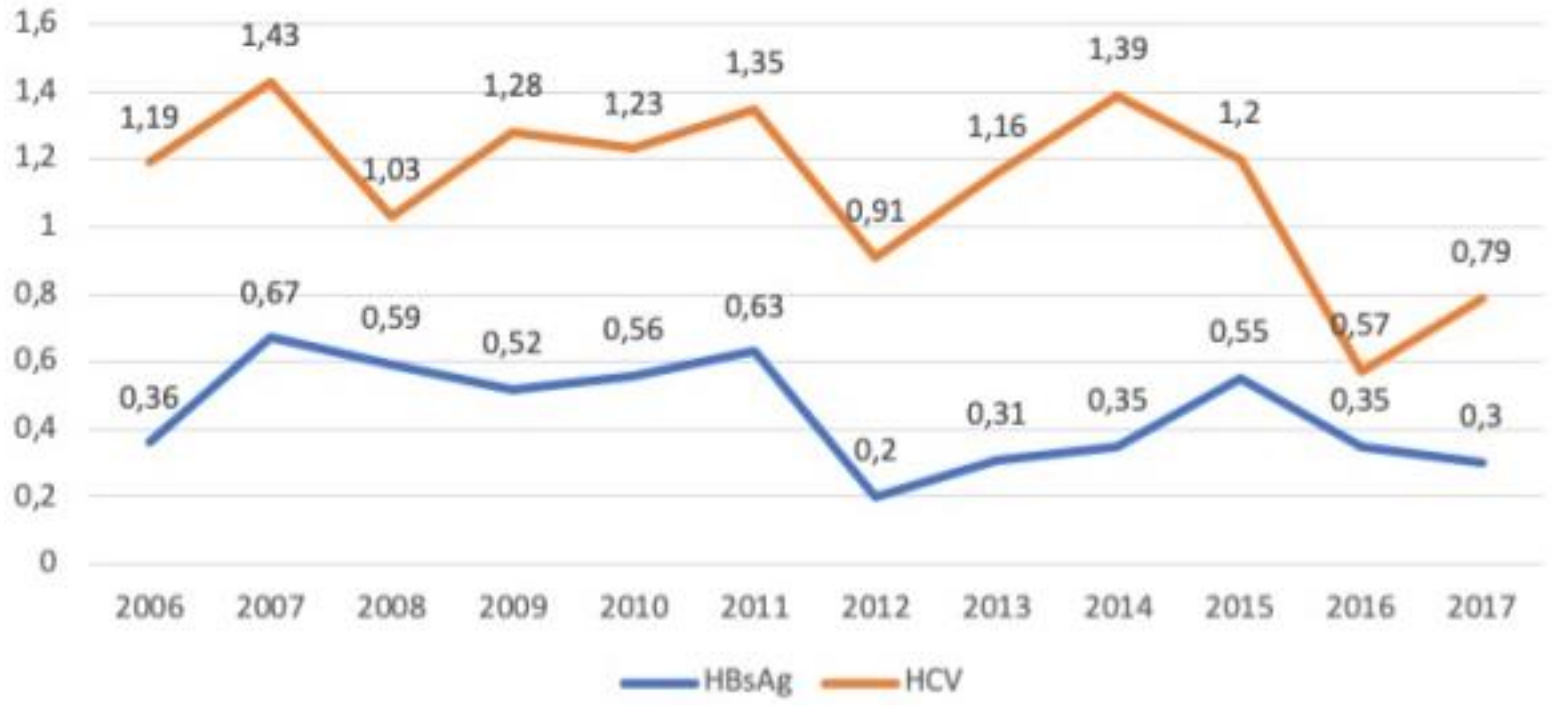
Blach S, et al. Lancet Gastroenterol Hepatol 2017;2:161–76;
The Polaris Observatory. Hepatitis C. Available at:
http://polarisobservatory.org/polaris/hepC.htm (accessed March 2017)

7 a 9 millones de pacientes con HCV en América Latina



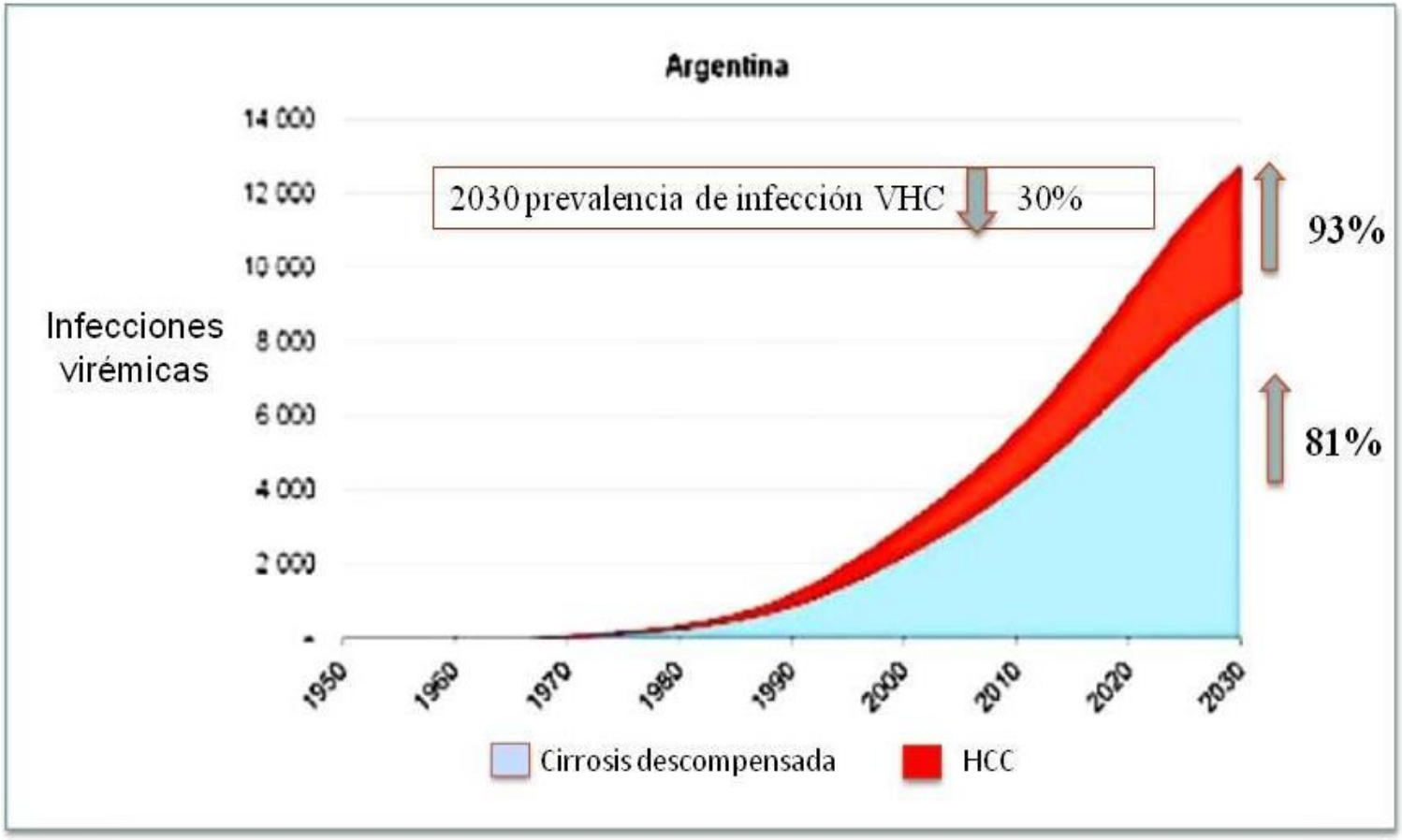
Kershenobich, et al, Liver Int 2011

Prevalencia de serologia HCV y HBV en Potenciales Donantes de Organos



Anders M, et al. XX Congreso AAEEH 2019

Estimación de Nº casos de cirrosis descompensada y HCC en el tiempo



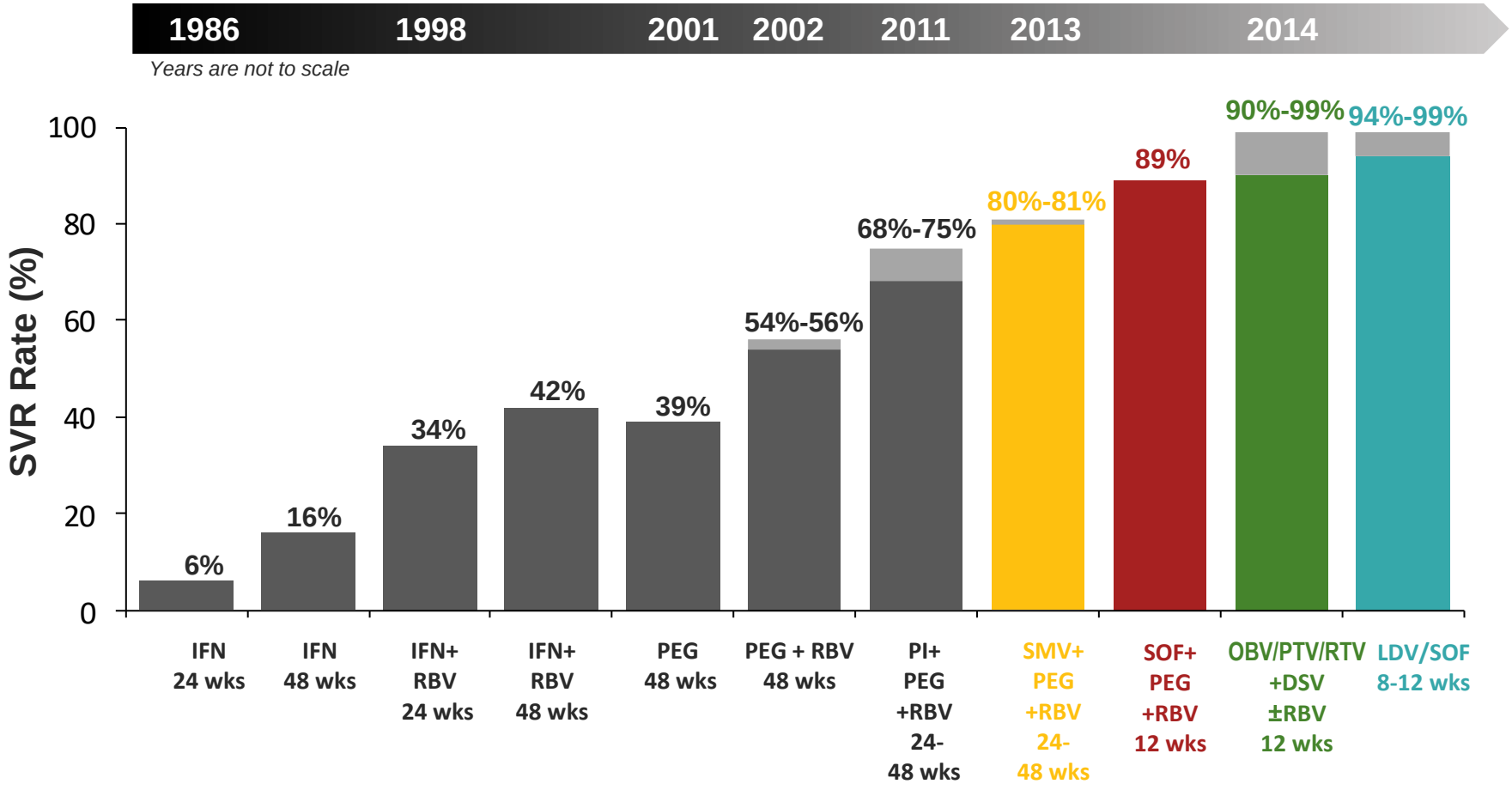
Hatzakis A, J Viral Hepatitis 2015

Ridruejo E, O 03 XVIII Congreso de Hepatología 2015

Elección de candidatos a recibir tratamiento: AAEEH 2018

- **Todos los pacientes con hepatitis crónica por HCV, naïve de tratamiento o no respondedores a un tratamiento previo, que quieran ser tratados y no tengan contraindicaciones, DEBEN ser considerados candidatos a recibir tratamiento.**

SVR Rates for Approved Therapies in HCV Genotype 1 Treatment-Naïve Patients



Efficacy rates are not directly comparable, due to differing study designs

Adapted from Strader DB, et al. Hepatology 2004;39:1147-71. INCIVEK [PI]. Cambridge, MA: Vertex Pharmaceuticals; 2013. VICTRELIS [PI]. Whitehouse Station, NJ: Merck & Co; 2014. Jacobson I, et al. EASL 2013. Amsterdam. The Netherlands. Poster #1425. Manns M, et al. EASL 2013. Amsterdam. The Netherlands. Oral #1413. Lawitz E, et al. APASL 2013. Singapore. Oral #LB-02; Afdhal N, et al. *N Engl J Med* 2014; 370: 1889-98; Kowdley K, et al. *N Engl J Med* 2014; 370: 1879-88. Feld JJ, et al. *N Engl J Med* 2014;370:1594-603. Ferenci et al. *N Engl J Med* 2014; 370:1983-92.

Esquemas recomendados por las guias internacionales

◎ 1 comprimido por día

Ledipasvir - Sofosbuvir

Velpatasvir - Sofosbuvir

Velpatasvir – Sofosbuvir - Voxilaprevir

Elbasvir- Grazoprevir

◎ múltiples comprimidos por día

Paritaprevir/r - Ombitasvir + Dasabuvir

Glecaprevir- Pibrentasvir

Daclatasvir - Sofosbuvir

Esquemas Disponibles en Argentina

◎ 1 comprimido por día

Ledipasvir - Sofosbuvir

Velpatasvir - Sofosbuvir

Elbasvir- Grazoprevir

Sofosbuvir + Velpatasvir + Voxilaprevir

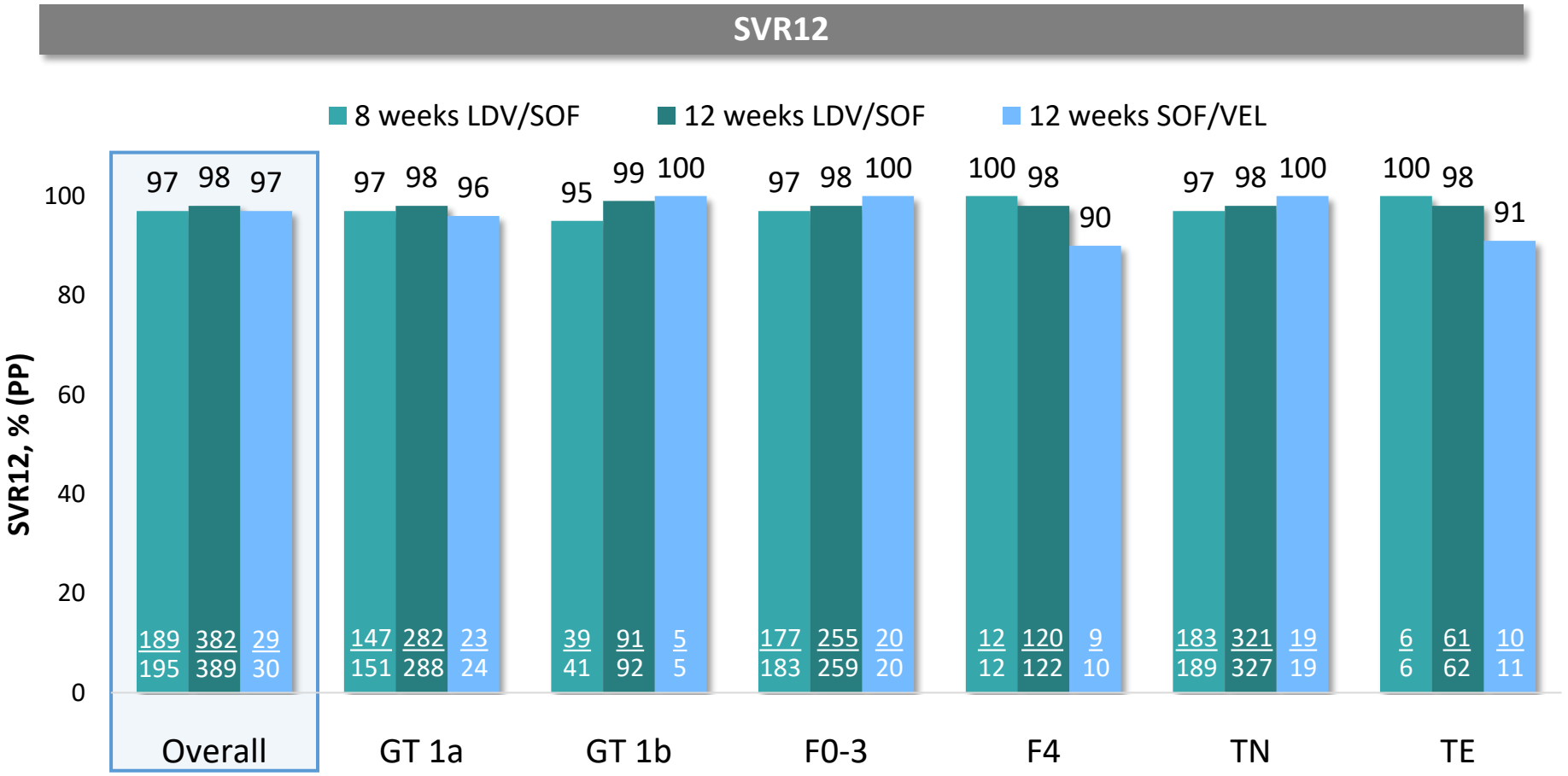
◎ múltiples comprimidos por día

Sofosbuvir + Daclatasvir

Glecaprevir + Pibrentasvir

TRIO Real-World Cohort

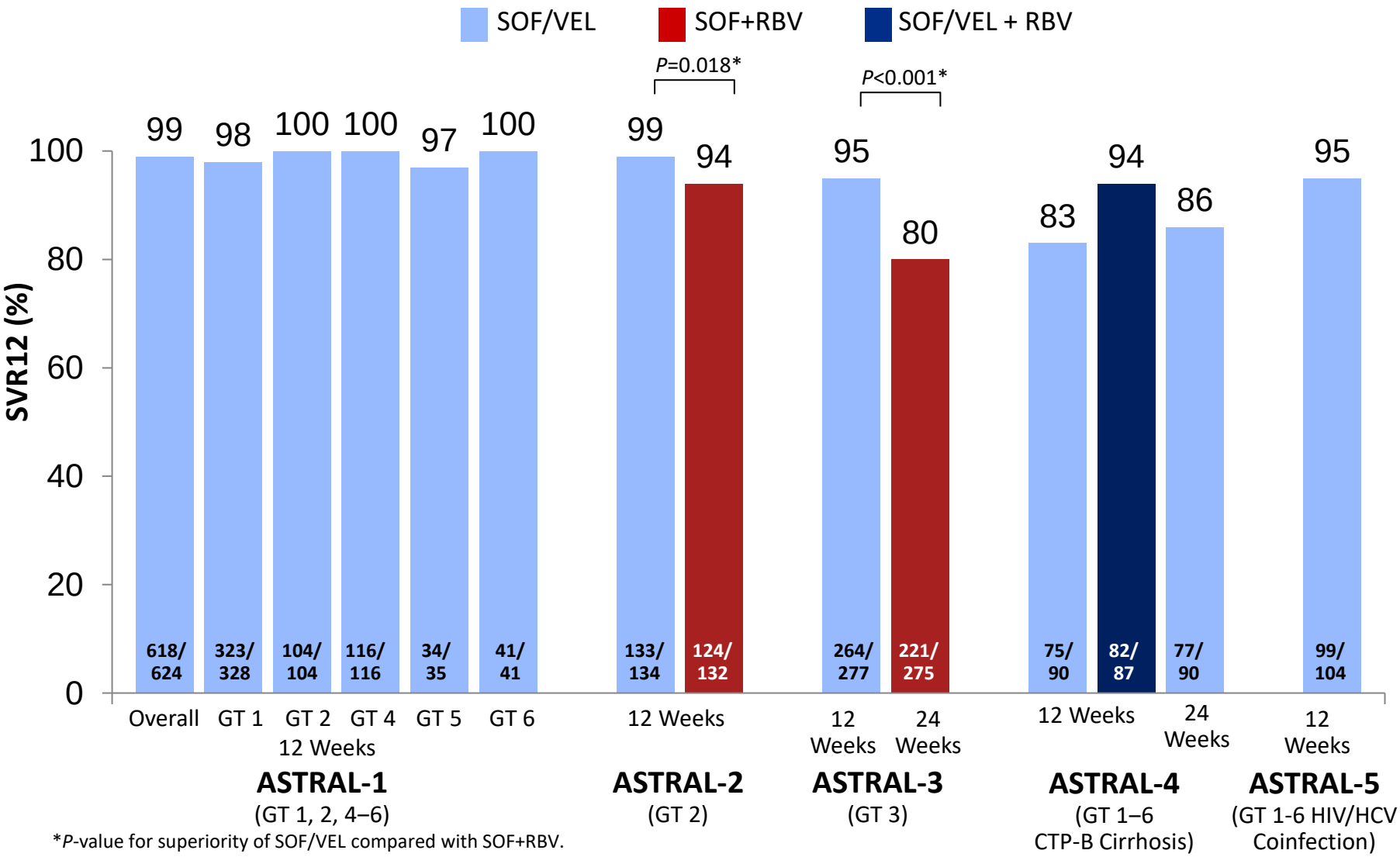
Real-World Experience of LDV/SOF and SOF/VEL in GT1 patients



In real-world cohort, high SVR12 was achieved with 8 and 12 weeks LDV/SOF and 12 weeks SOF/VEL, regardless of genotype subtype, fibrosis or prior treatment status

Tsai, EASL 2017, SAT-244

Efficacy Summary (ITT Analysis)

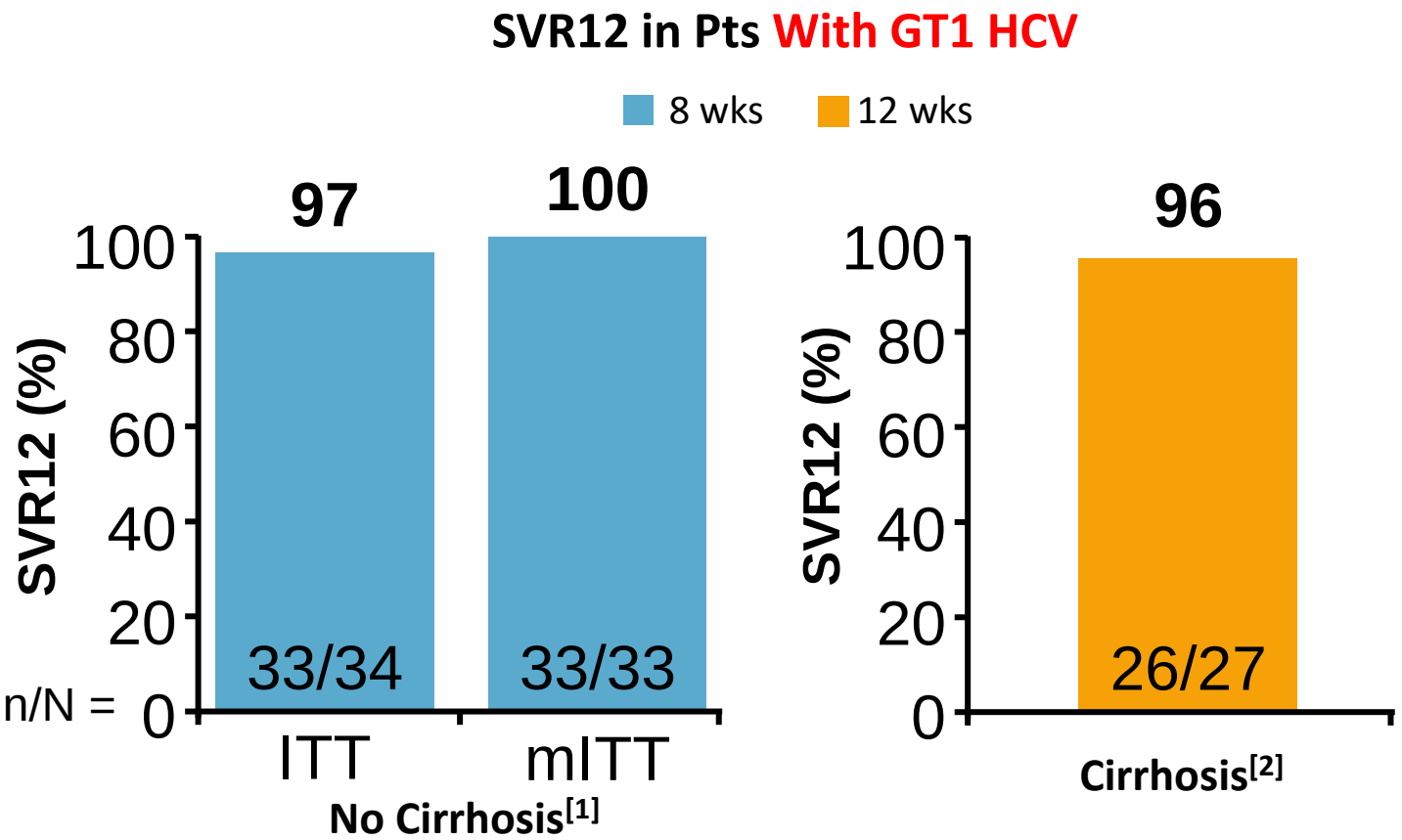


*P-value for superiority of SOF/VEL compared with SOF+RBV.

Feld, AASLD, 2015, LB-2. Feld JJ, et al. *N Engl J Med*. 2015. DOI: 10.1056/NEJMoa1512610; Sulkowski, AASLD, 2015, 205. Foster GR, et al. *New Engl J Med*. 2015. DOI: 10.1056/NEJMoa1512612; Mangia, AASLD, 2015, 249; Charlton, AASLD, 2015, LB-13. Curry MP, et al. *New Engl J Med*.2015. DOI: 10.1056/NEJMoa1512614

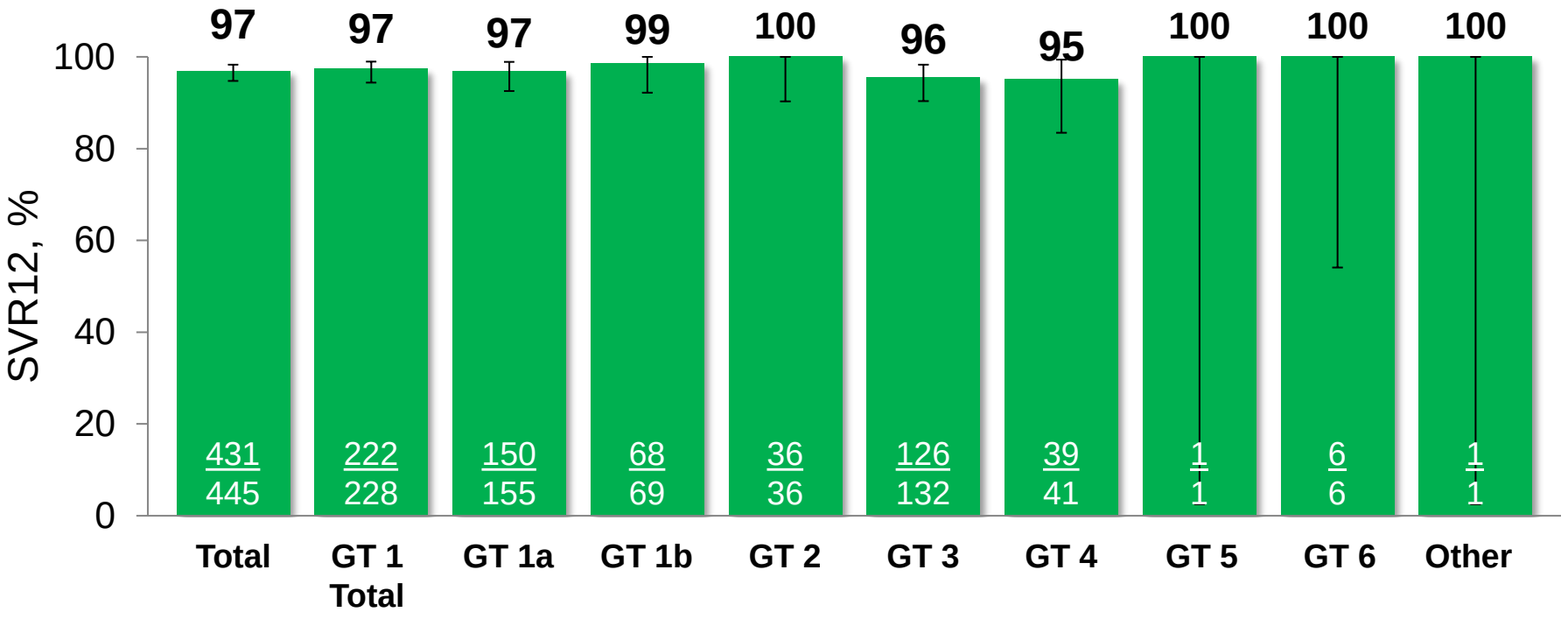
SURVEYOR-I/II: Glecaprevir+ Pibrentasvir for 8 or 12 Wks in Pts With GT1

- Open-label, treatment naive or pegIFN/RBV experienced



1. Poordad F, et al. EASL 2016. Abstract SAT-157.
2. Gane EJ, et al. EASL 2016. Abstract SAT-135.

Efficacy of SOF/VEL/VOX for 12 Weeks in DAA-Experienced Patients



Breakthrough	1*	1	1	0	0	0	0	0	0	0
Relapse	7	2	2	0	0	4	1	0	0	0
Other	6	3	2	1	0	2	1	0	0	0

The SVR12 rate was 97% (431/445) in DAA-experienced patients treated with SOF/VEL/VOX for 12 weeks; Rates were similar regardless of genotype

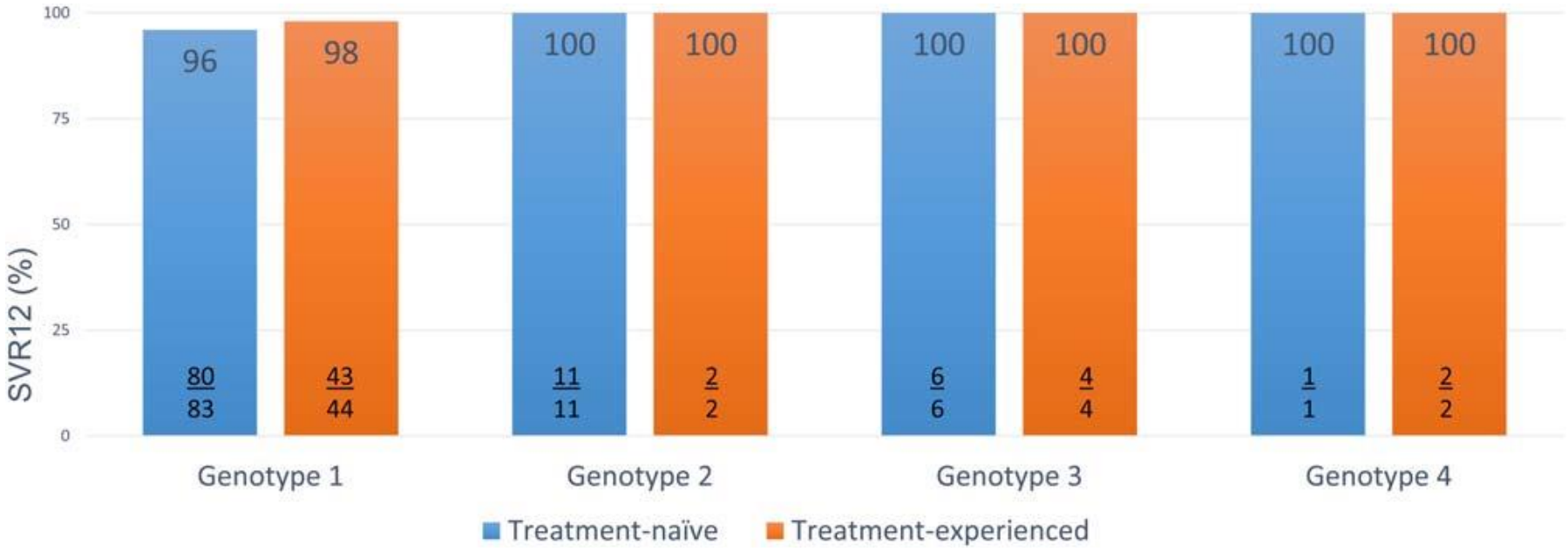
*Patient had drug levels consistent with nonadherence.

Roberts, EASL 2017, SAT-280

Daclatasvir en tratamiento de HCV

Genotype and Treatment History	Daclatasvir + Sofosbuvir
Genotype 1, naive or PEG/PI failure	
No cirrhosis	Recommended, 12 weeks
Cirrhosis	Recommended, 24 weeks ± RBV
Genotype 2	
Naive	Recommended, 12 weeks
PEG/RBV failure	Limited data
Sofosbuvir failure	Recommended if interferon ineligible, 24 weeks ± RBV

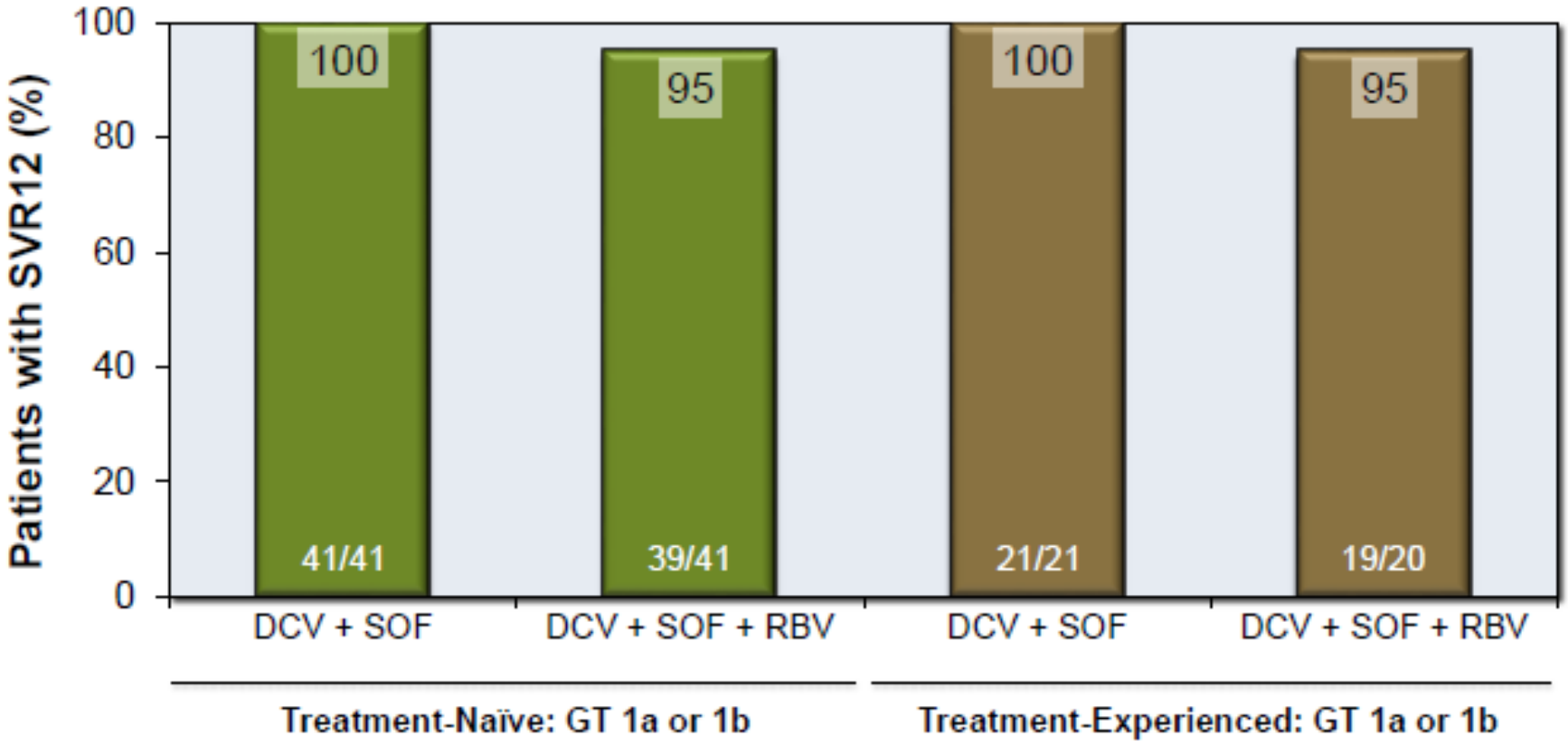
Abbreviations: PEG, peginterferon; RBV, ribavirin; PI, protease inhibitor.



Muir M. Clin Liv Dis, 2016

DCV+SOF en HCV G-1

<u>Similar RVS</u> DCV+SOF 12 Sem ➡ ± RBV o Naïve /Exper



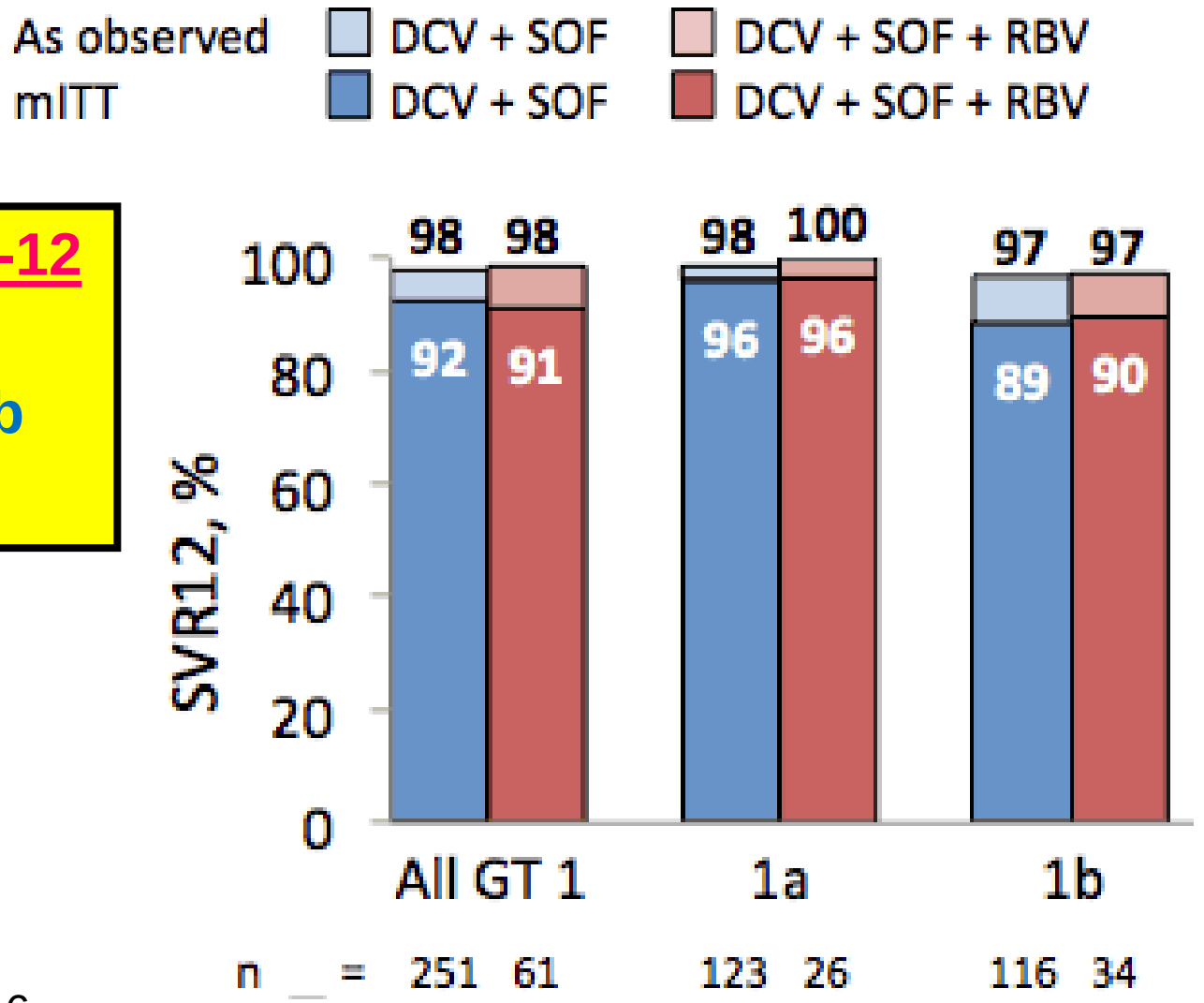
Sulkowski MS, N Engl J Med 2014 (ALLY-1)

DCV+SOF ±RBV 24 Sem: Cirrosis HCV G-1

Similar RVS-12

⬇

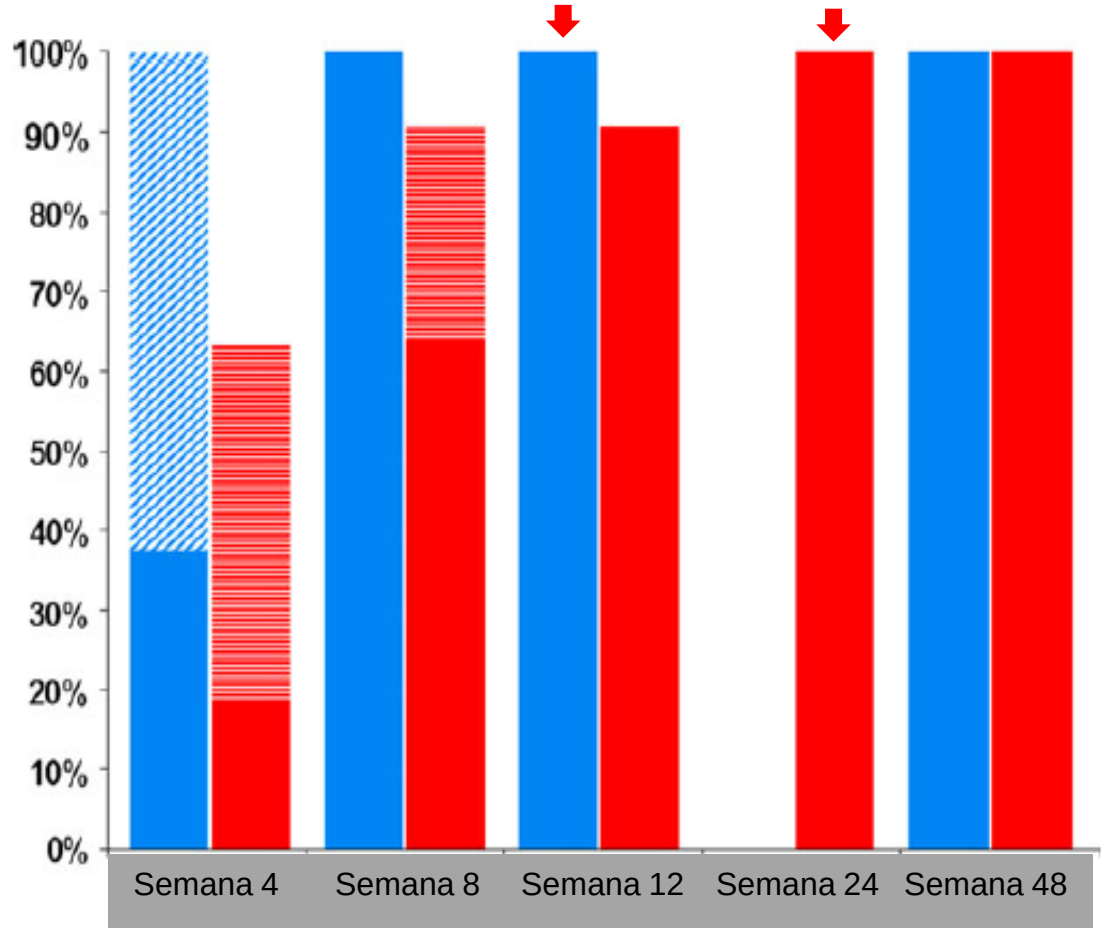
G-1a Vs 1b (Cirrosis)



Welzel TM, EASL 2016

SOF-DAC,G2 exp, naive, sin-con cirrosis (19p)

12 Sem sin cirro/24 Sem cirro (CPT A-B)



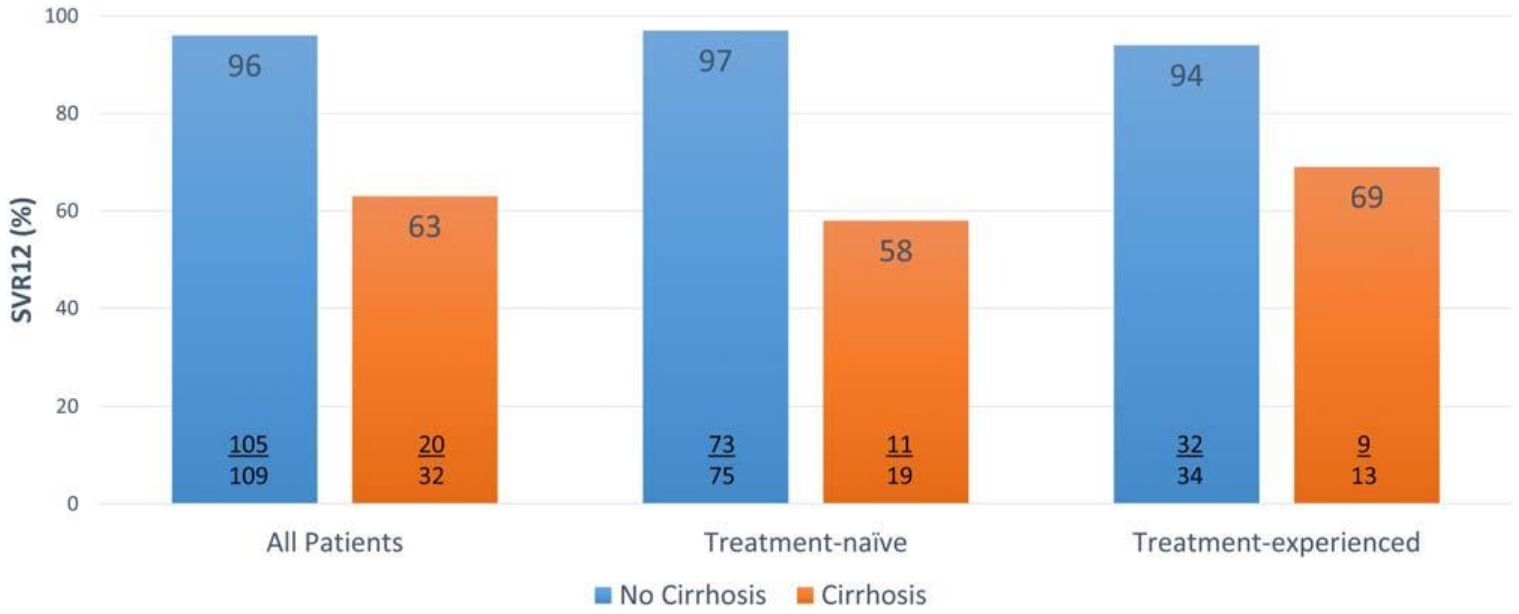
- SVR 100% ambos grupos
- Grupo Cirro 2 pac HDA variceal, no susp.
- EA 85% (fatiga)

Mangia A, Liv Int 2016

Daclatasvir en tratamiento de HCV(G3)

Genotype and Treatment History	Peginterferon + Sofosbuvir + Ribavirin	Sofosbuvir + Ribavirin	Daclatasvir + Sofosbuvir
Naive	Recommended 12 weeks	Alternative 24 weeks	Recommended, 12 weeks Cirrhosis: 24 weeks ± ribavirin
Peginterferon/Ribavirin failure	Recommended 12 weeks		Recommended if IFN ineligible, 12 weeks Cirrhosis: 24 weeks + ribavirin
Sofosbuvir failure	Recommended 12 weeks		Recommended if IFN ineligible, 24 weeks + ribavirin

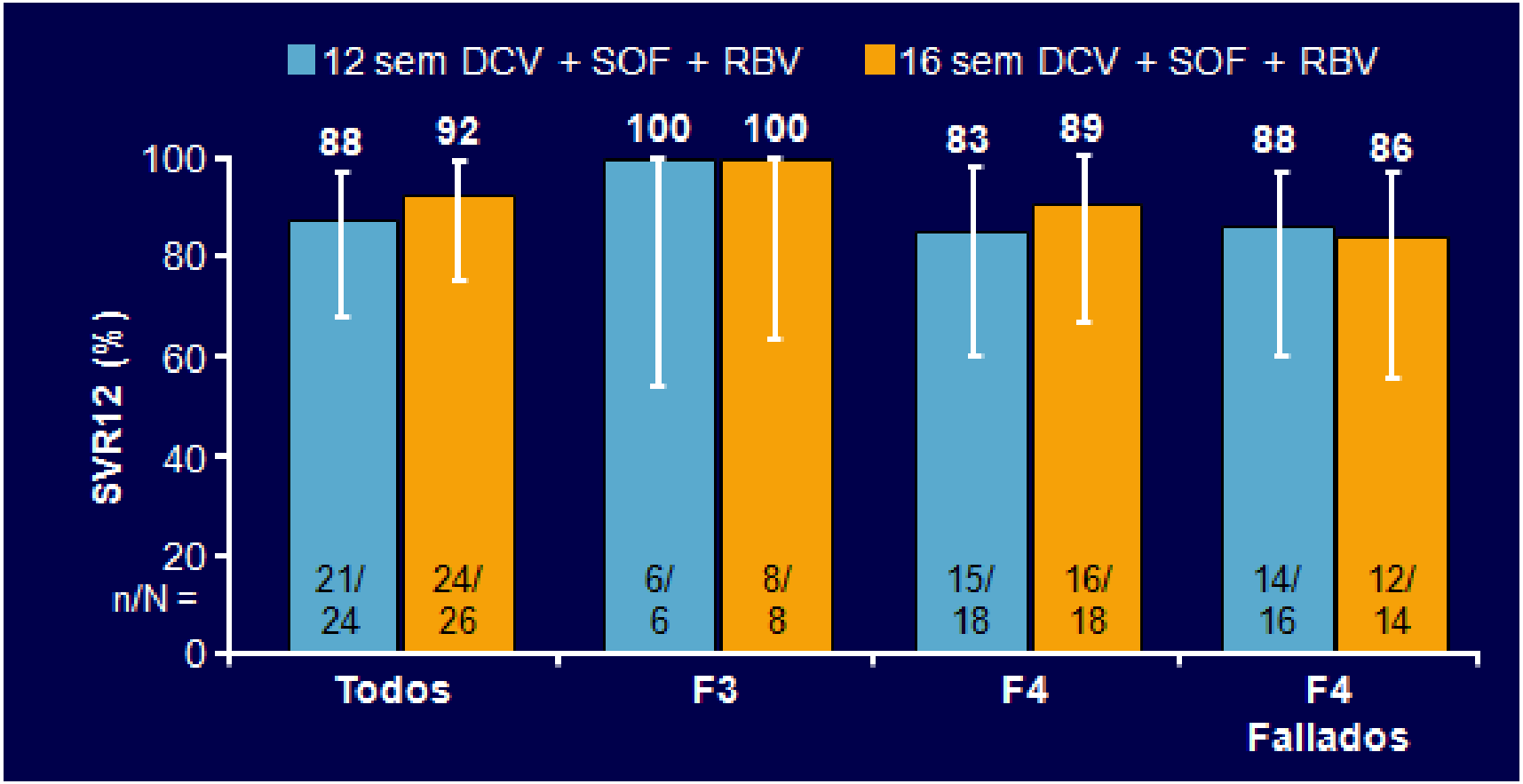
Abbreviation: IFN, interferon.



SOF + DCV 12 SEM SIN RBV (ALLY3)

Nelson, Hepatology, 2015

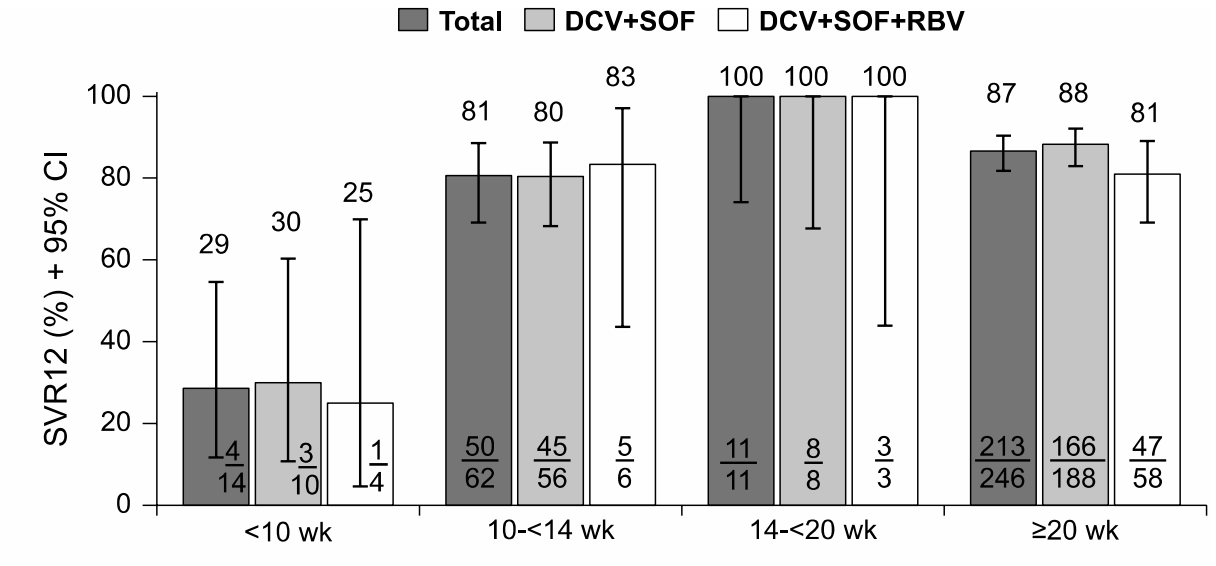
ESTUDIO ALLY – 3 +
SOF + DCV + RBV

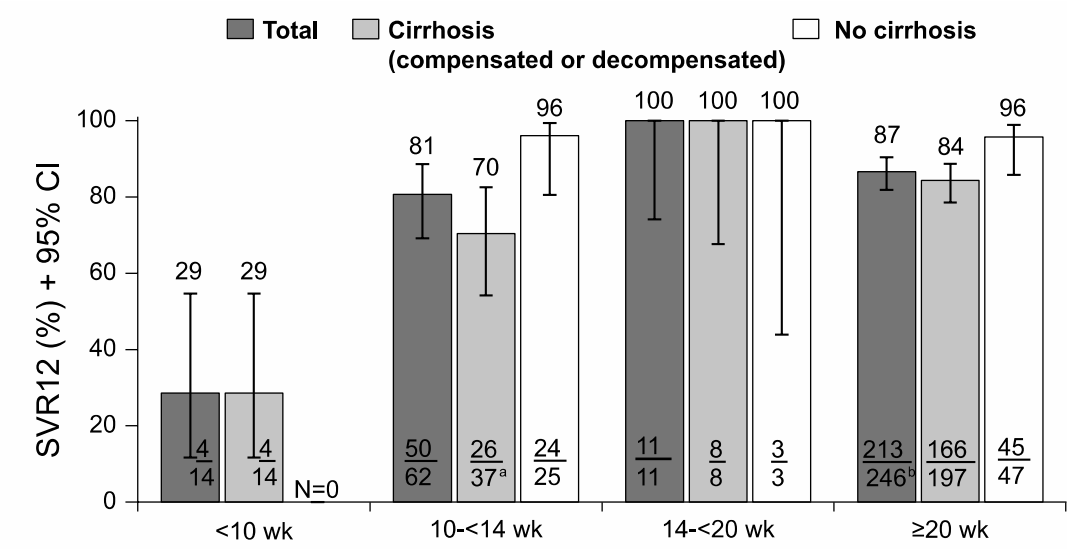


Similar eficacia entre 12 y 16 semanas

Leroy V, et al. AASLD 2015. Abstract LB-3.

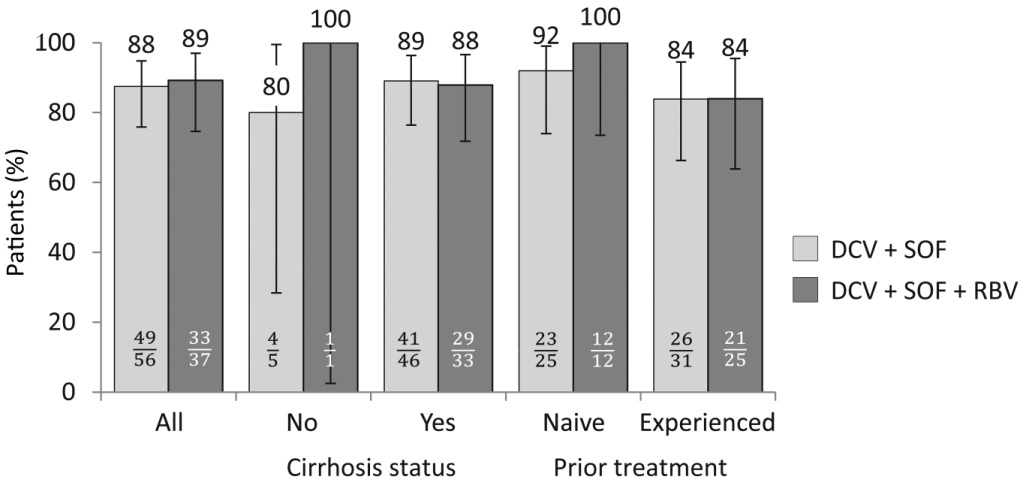
SOF-Daclatasvir en tratamiento de HCV(G3). Programa Francés

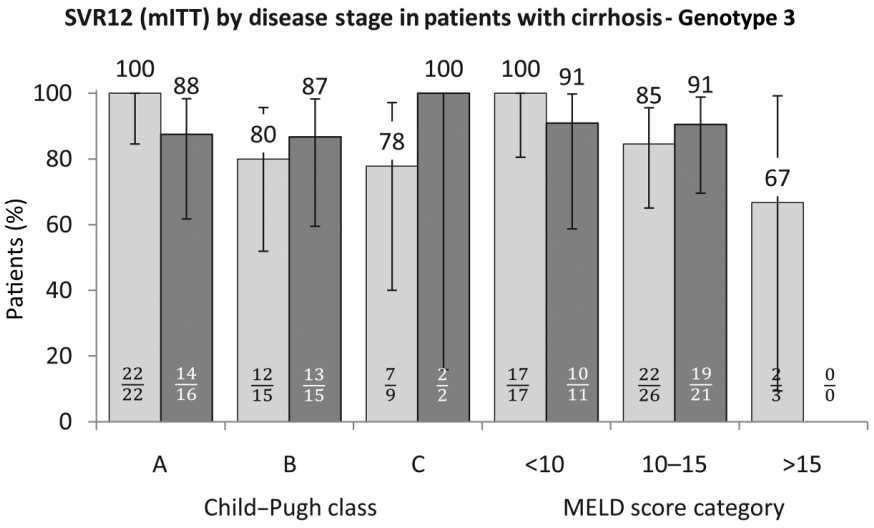


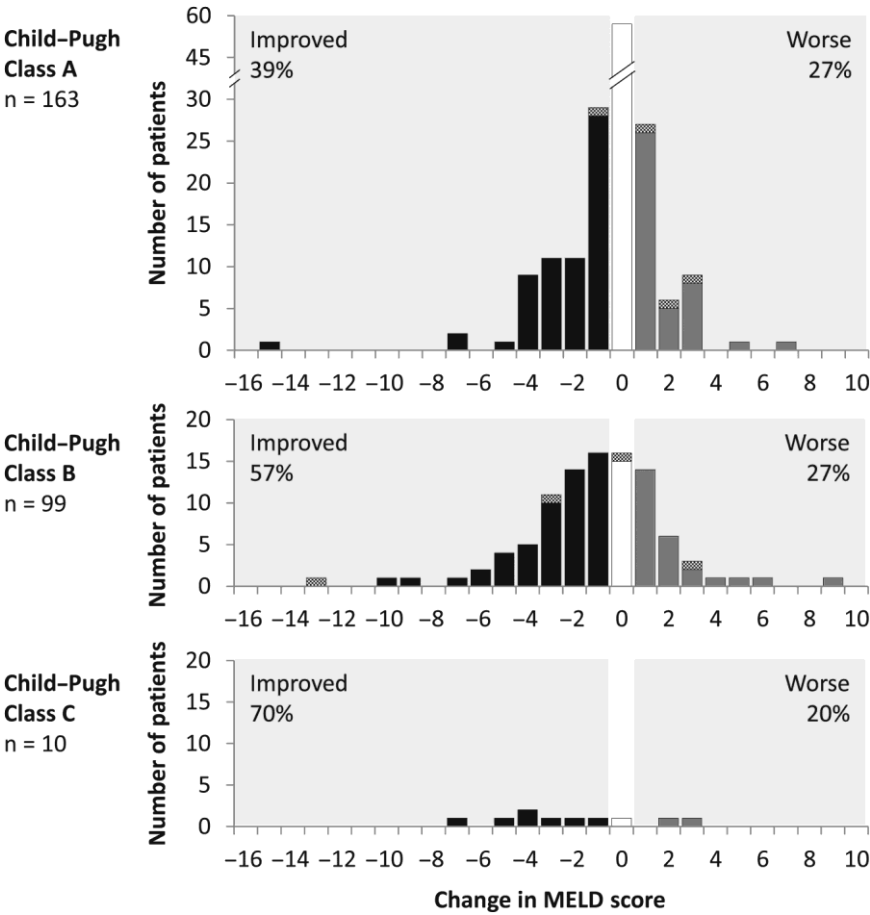


Hézode, C. Liv Int 2016

SOF-DAC ± RBV en G3. Experiencia Europea

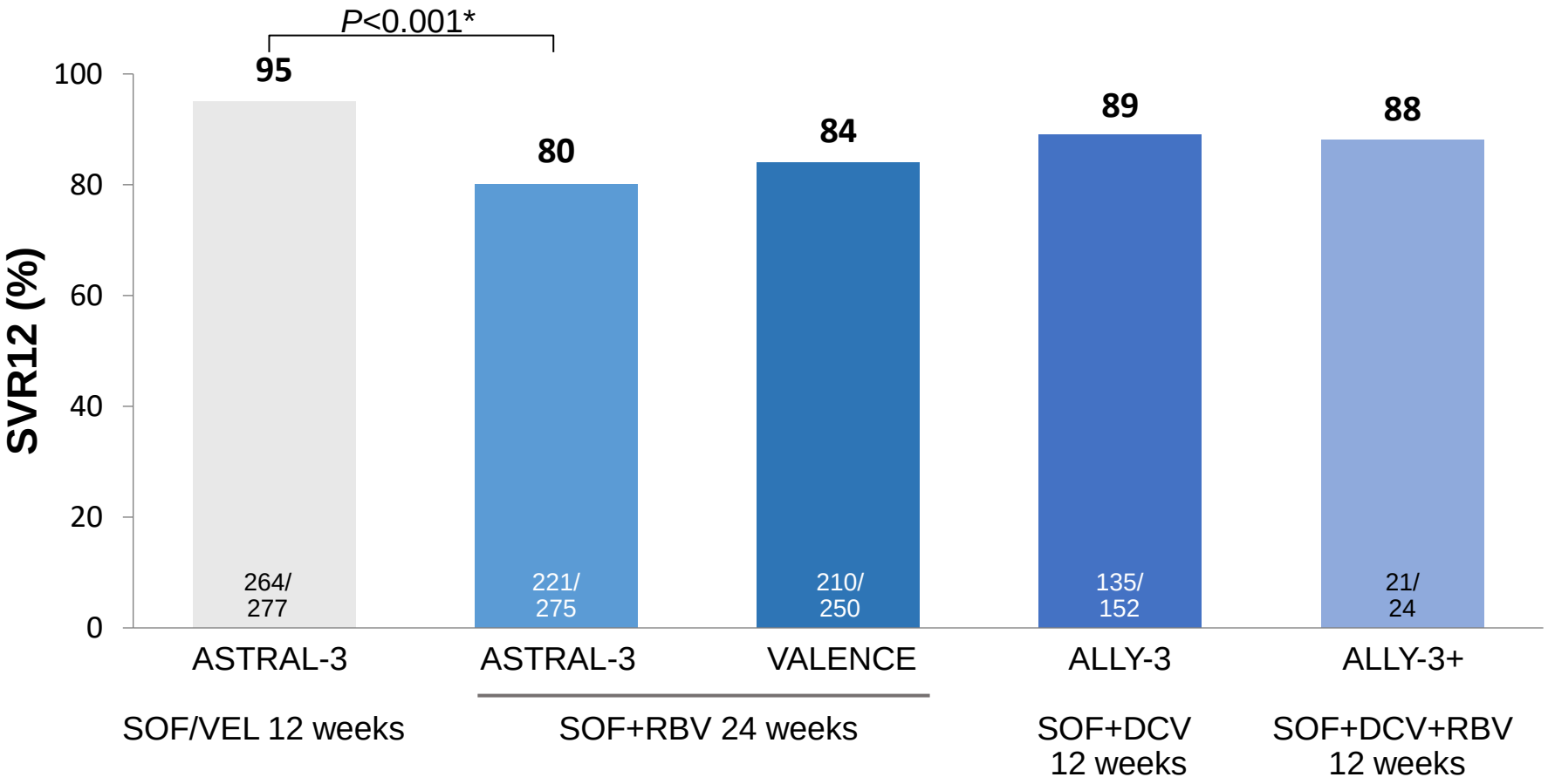






Zeuzen S. Gut 2016

Overall SVR of SOF-Based Regimens for HCV GT 3

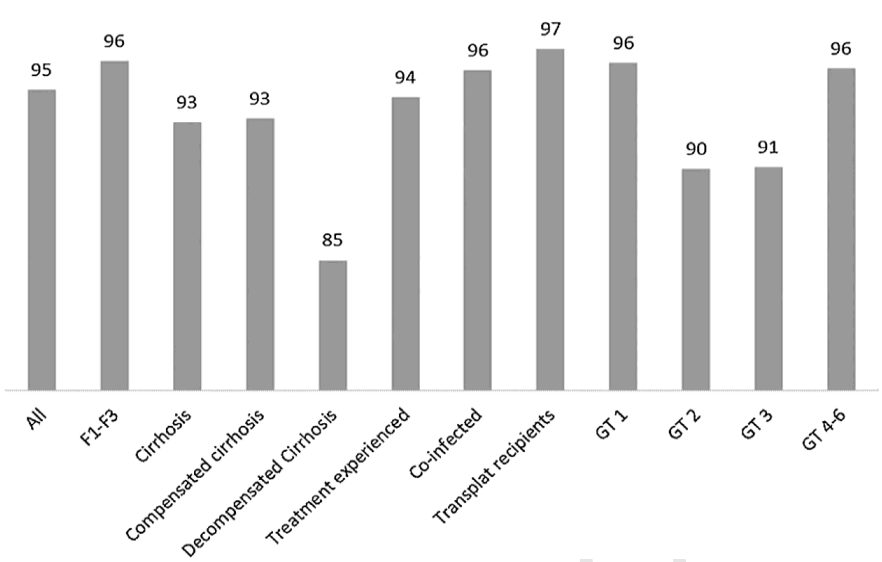


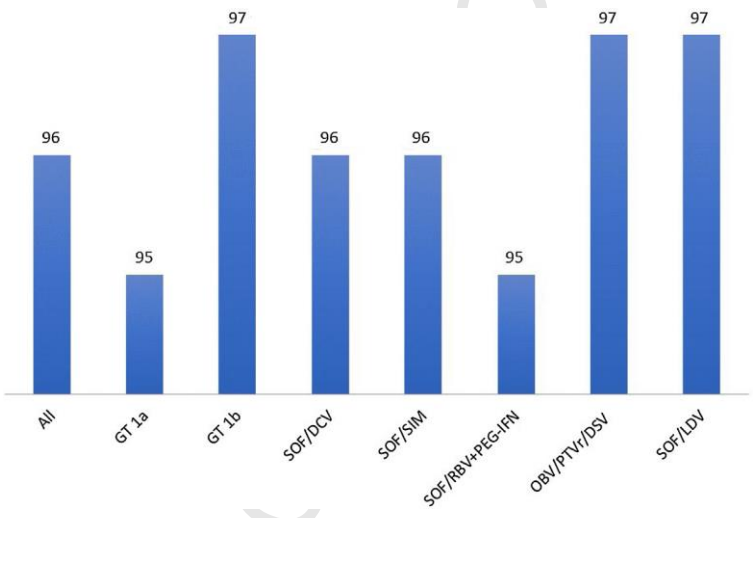
SOF/VEL for 12 weeks yielded high SVR12 rates without the need for RBV in HCV GT 3 subjects

**P*-value for superiority of SOF/VEL compared with SOF+RBV.

Foster GR, et al. *N Engl J Med* 2015;373(27):2608-2617; SOVALDI® [PI]. Gilead Sciences, Inc. Foster City, CA August 2015; Daklinza™US PI April 2016; Nelson, *Hepatology* 2015;61(4):1127-1135; Leroy V. et al. *Hepatology* 2016;63(5):1430-1441

Terapia AAD en HCV. Vida Real Brasil





Resultados de SOF-DAC+RBV

Oliveira, CM. Ann Hepatol 2019

SOF-DAC. Tratamiento vida real Experiencia Argentina

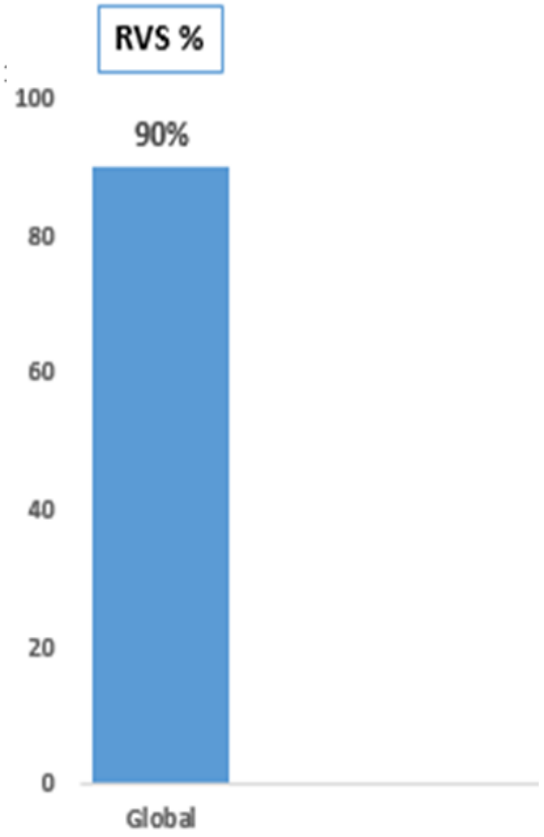
Objetivo Primario: Describir la efectividad y tolerancia del tratamiento de la hepatitis C con esquemas basados en sofosbuvir.

Criterios de inclusión: > 17 años que iniciaron tratamiento para hepatitis C con esquemas basados en sofosbuvir (hiperurgentes)

321 pacientes incluidos:

- ✓ 91% cirrosis
- ✓ 24% cirrosis descompensada
- ✓ 75% Genotipo 1
- ✓ 42% expuestos a tratamiento

SOF-DCV +/- RBV



Asociación Argentina para el Estudio de las Enfermedades del Hígado

Marciano S, et al, JMV 2017

Uso AAD - Tratamiento vida real

TABLA 1. Tratamiento según genotipo

99 pac TOT 2016-2017	1b (=42)	1a (n=22)	1 (n=6)	2 (n=11)	3 (n=11)	4 (n=2)
SOF-DCV-RBV X 12	24	15	6	1	-	2
SOF-DCV X 12	12	5	-	7	1	-
SOF-DCV X 24	1	1	-	-	10	-
SOF-DCV-RBV X 24	1	1	-	-	-	-
3D X 12	2	-	-	-	-	-
SOF-SMV	2	-	-	-	-	-
SOF-DCV X 20	-	-	-	1	-	-
SOF-RBV X 12	-	-	-	1	-	-
SOF-RBV X 16	-	-	-	1	-	-

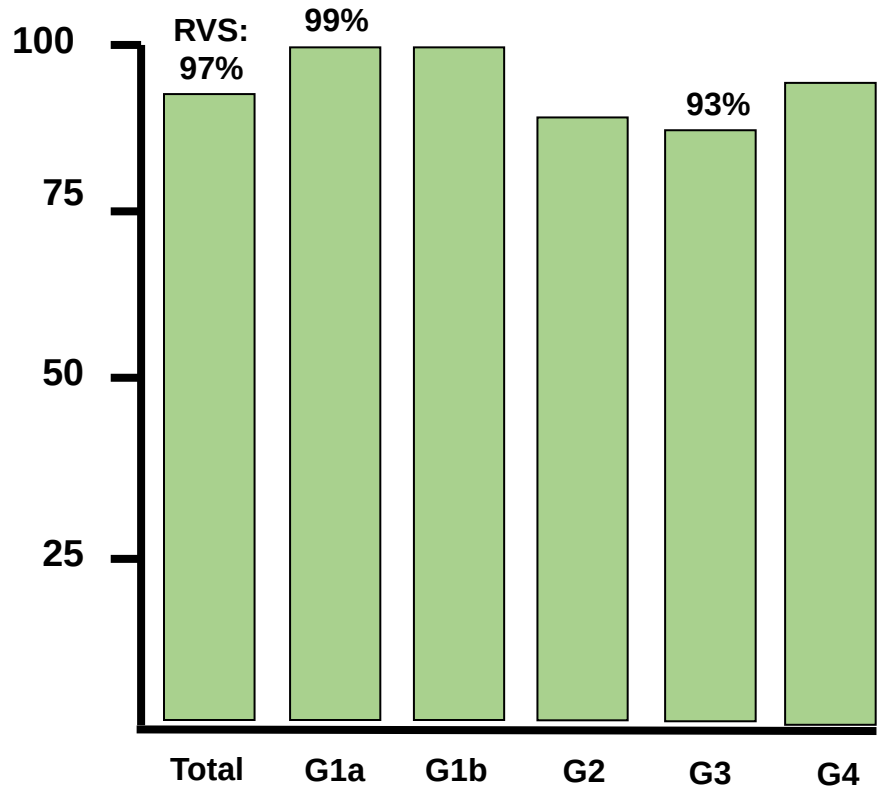
SOF: Sofosbuvir; DCV: Daclatasvir; RBV: Ribavirina; SMV: Simeprevir

RVS: 90% cirro desc; 98% no cirro/ c comp

Rojas P, AAEEH 2017

Uso AAD - Tratamiento vida real

Experiencia El Cruce 2016-2019 (94p)



Cirro comp: MELD: 9.3 a 8.6 (dif 0.7±3.1, ns); Child-Pugh: 6.4 a 5.7 (dif 0.7±1.4, p=0.002); APRI: 3.7 a 1.3 (dif 2.4±3.5, p<0.001); y FIB4: 7.0 a 4.1 (dif 2.9±4.0, p<0.001).
Cirrosis descomp: MELD: 11.3 a 10.2 (dif 1.1±3.2, ns); Child-Pugh: 8.1 a 6.6 (dif 1.5±1.8, p=0.013); APRI: 3.8 a 1.6 (dif 2.2±2.6, p<0.005); y FIB4: 8.1 a 5.1 (dif 3.0±3.8, p<0.008),

Czarnowski, Ana. AAEEH 2019

Uso AAD - Tratamiento vida real

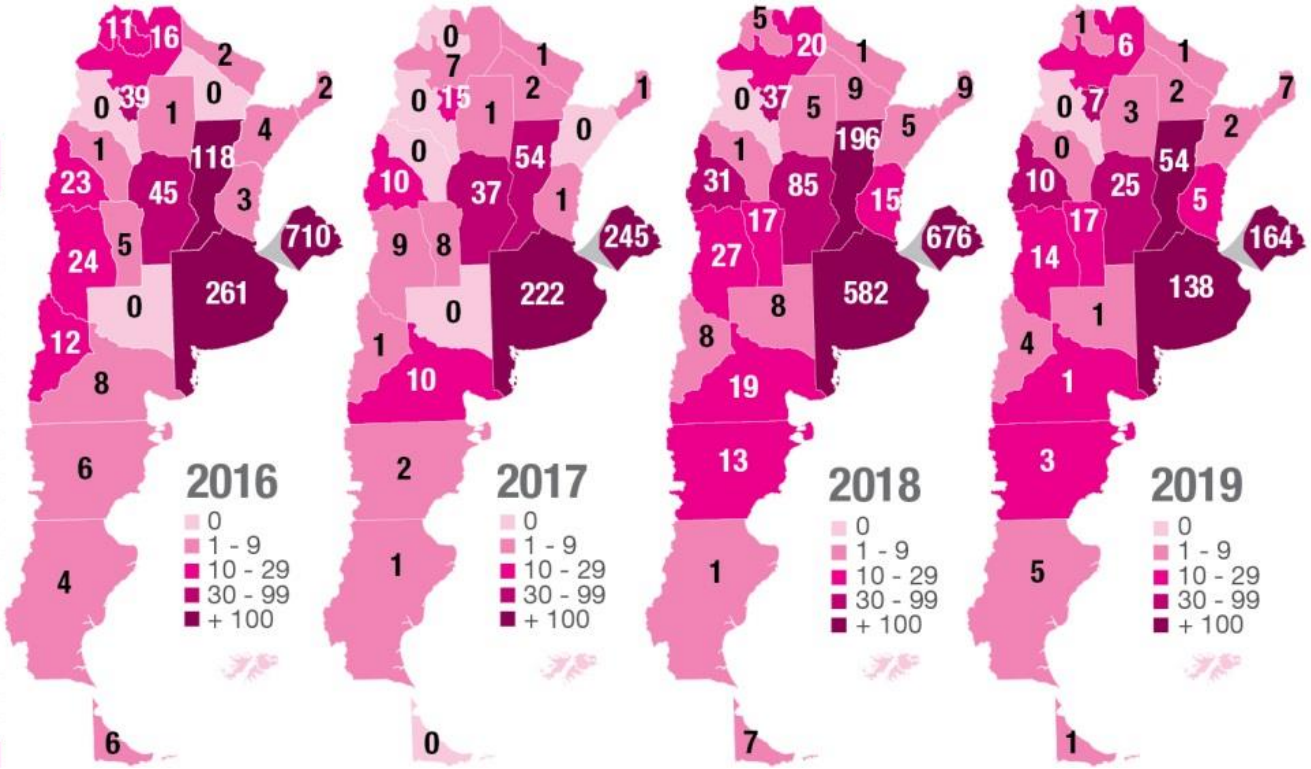
Programa Nacional de Hepatitis 2016-2019

Resultados:

- 4176 tratamientos

(1301 en 2016; 627 en 2017; 1777 en 2018; 471 hasta junio de 2019.)

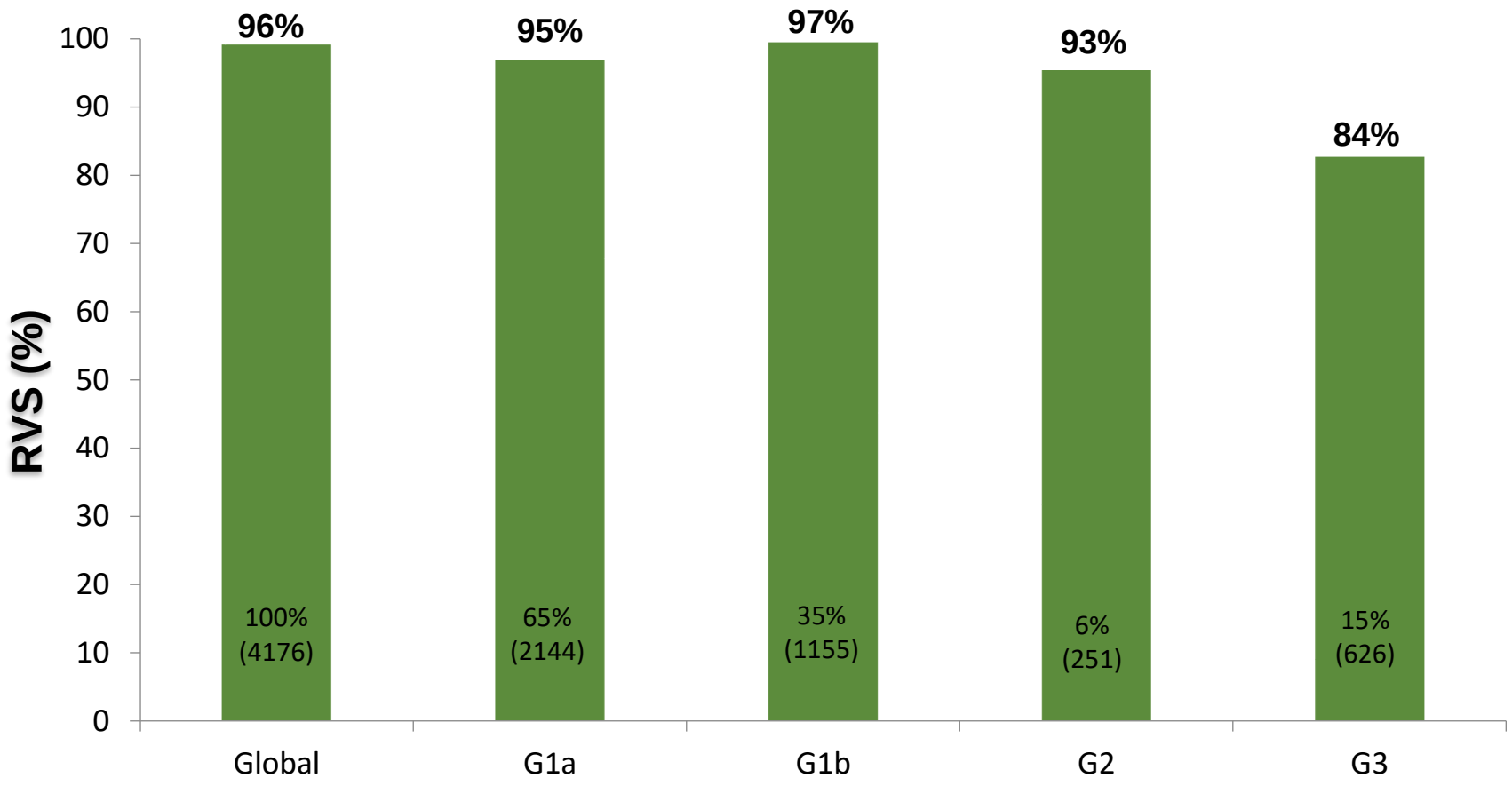
Provincia	Tratamientos			
	2016	2017	2018	2019
Buenos Aires	261	222	582	138
CABA	710	245	676	164
Chaco	-	2	9	2
Chubut	6	2	13	3
Córdoba	45	37	85	25
Corrientes	4	-	5	2
Entre Ríos	3	1	15	5
Formosa	2	1	1	1
Jujuy	11	-	5	1
La Pampa	-	-	8	1
La Rioja	1	-	1	-
Mendoza	24	9	27	14
Misiones	2	1	9	7
Neuquén	12	1	8	4
Río Negro	8	10	19	1
Salta	16	7	20	6
San Juan	23	10	31	10
San Luis	5	8	17	17
Santa Cruz	4	1	1	5
Santa Fe	118	54	196	54
Santiago del Estero	1	1	5	3
Tierra del Fuego	6	-	7	1
Tucumán	39	15	37	7
Total	**1301**	**627**	**1777**	**471**



Coronel E.PNHV 2019

Uso AAD - Tratamiento vida real

Programa Nacional de Hepatitis 2016-2019



86 pac con IRC (3D-(83%)/E-G (17%))

4096 pac TTO con SOF-DAC±RBV

Coronel E.PNHV 2019

Resumen final

1. La terapia SOF-DAC esta ampliamente evaluada en el mundo
2. Las tasas de RVS son adecuadas pero inferiores a las drogas de primera línea
3. Ante un plan estratégico de erradicación universal la combinación SOF-DAC/RBV puede ser una opción
4. La mejor droga para tratar el HCV es la que tiene mejor acceso

“En la cancha se ven los pingos”

Monumental 1-10, 21-30