XXV CONGRESO SETH
Málaga 2015
Sociedad Española de Trasplante Hepático
7-9 OCTUBRE

Trasplante hepático y hepatitis C:
Estrategias de prevención pretrasplante y tratamiento postrasplante

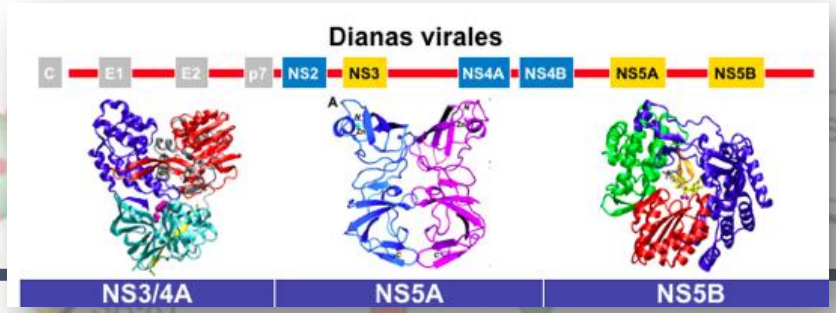
Datos de los estudios de Simeprevir

Dra Sánchez Antolín
Hospital U. Río Hortega

Conflictos de interés

- Ponencias
  - Novartis
  - Astellas
  - Janssen
  - Gilead


I+D+i



Virion del VHC

Endocitosis mediada

Nuevos viriones

INHIBIDORES DE LA ENTRADA

Maduración

INHIBIDORES DE LA CICLOFILINA

Simeprevir

Ledipasvir
Daclatasvir
Ombitasvir

Sofosb
Dasabu

Simeprevir
Agosto 2014

Sofosbuvir
Noviembre 2014

Daclatasvir
Febrero 2015

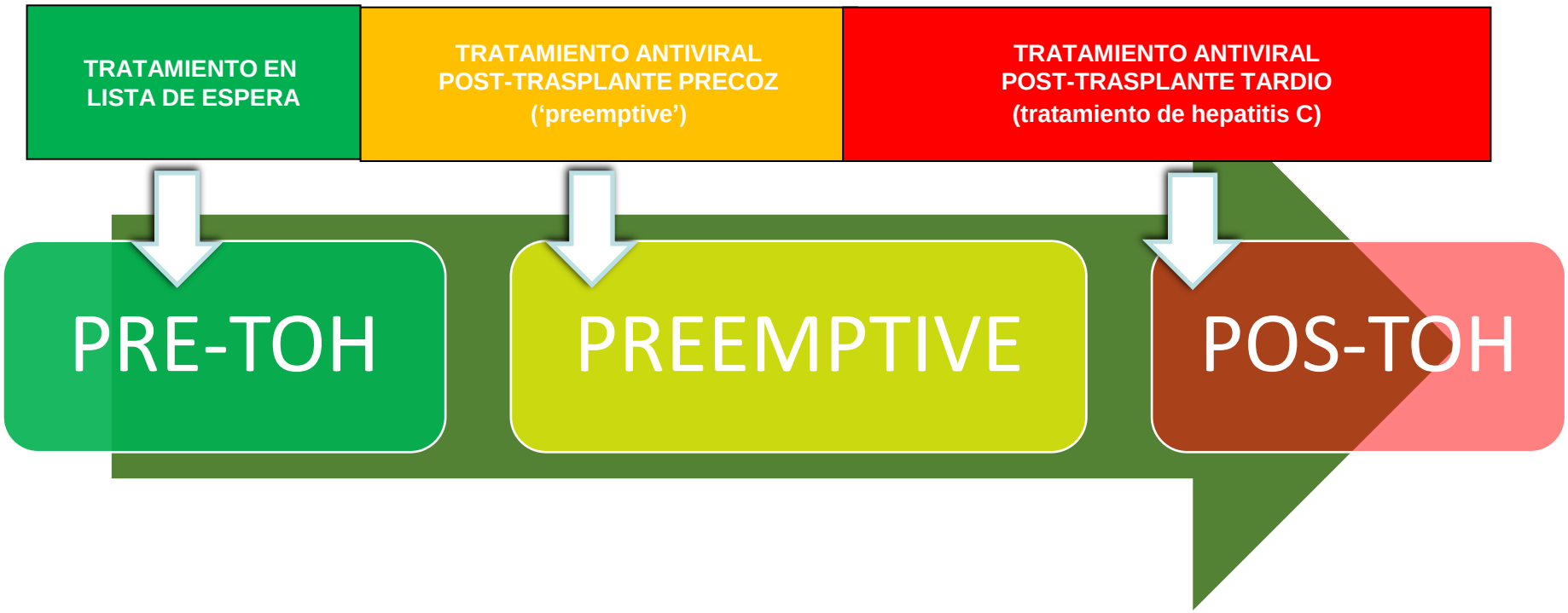
Sofosbuvir/ Ledipasvir
Abril 2015

Paritaprevir/r Ombitasvir/ Dasabuvir
Abril 2015

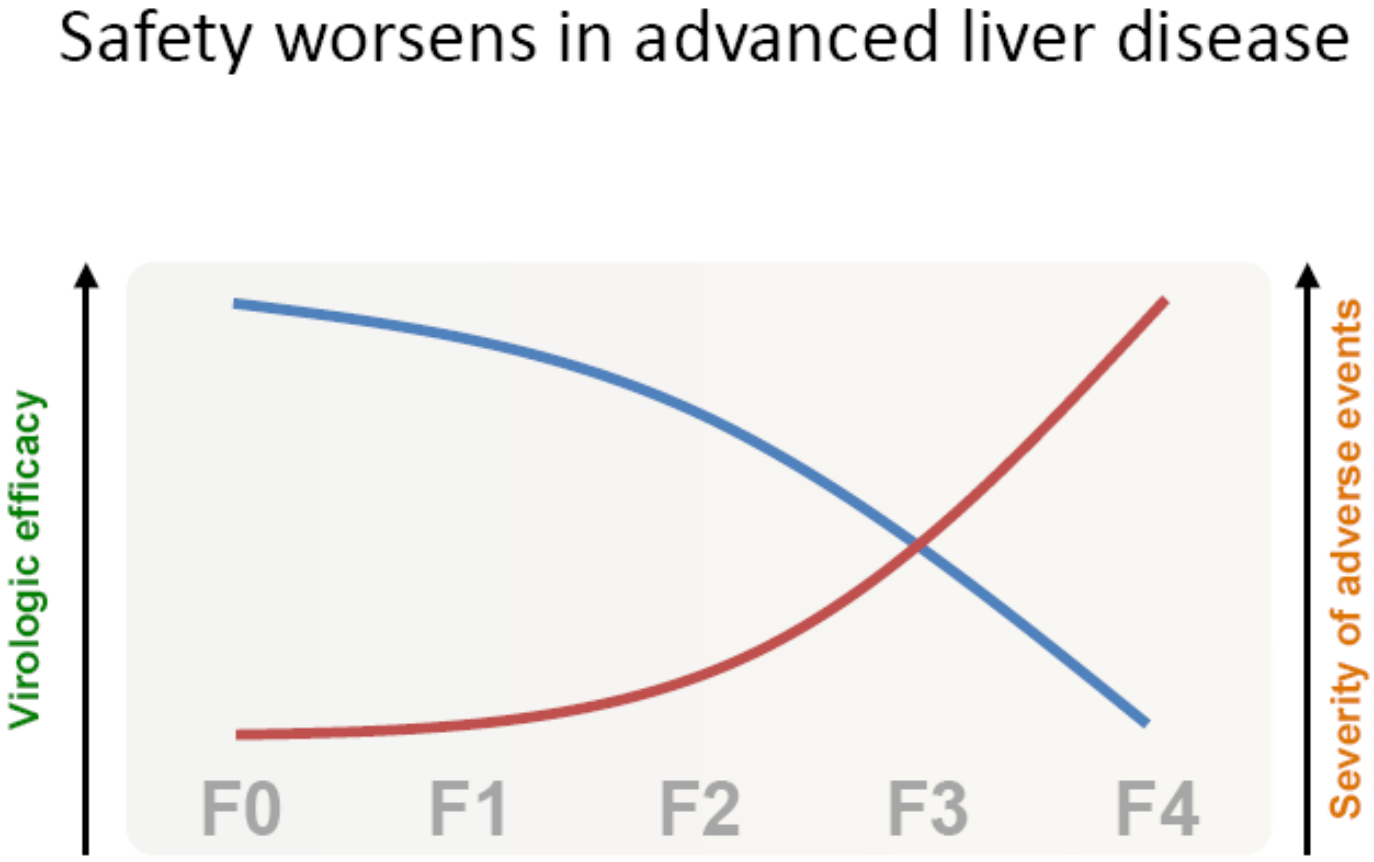
2014

2015

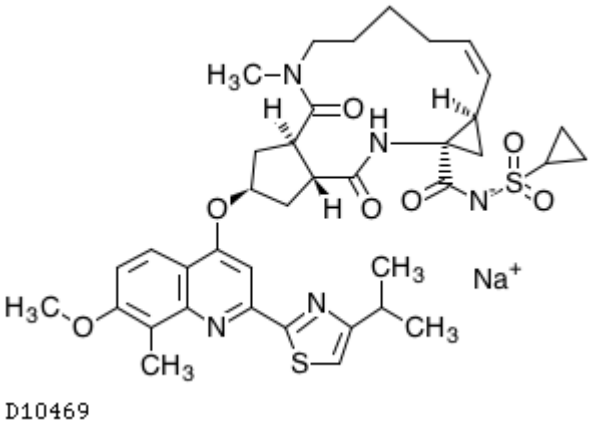
TRATAMIENTO DE LA HEPATITIS C PERI-TOH



NO ERA SEGURO CONSEGUIR RVS

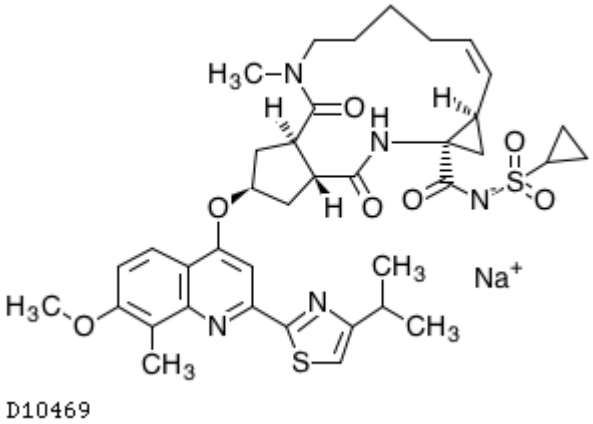


DATOS DE SIMEPREVIR



SIMEPREVIR: ENSAYOS CLINICOS

- COSMOS
  - FO-F2 NULL RESPONDERS
  - F3-F4 NAIVE O NULL
- OPTIMIST 1
  - <F3
    - Naïve/pretratados
    - 8/12 semana
    - NO RBV
- OPTIMIST 2
  - F4
    - SIM+SOF NO RBV



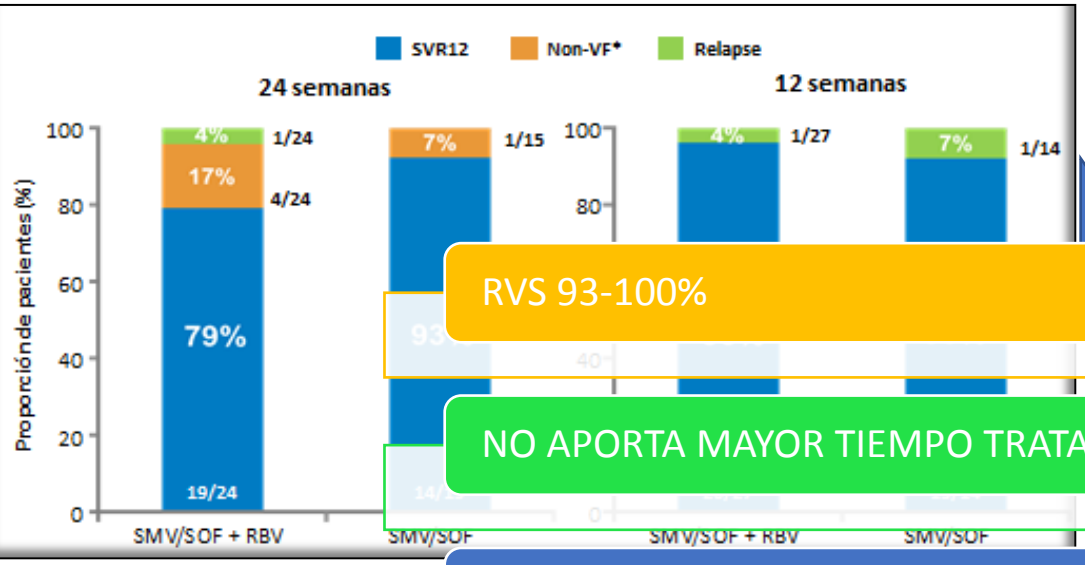
SIMEPREVIR

SIMEPREVIR:

DATOS EN VIDA REAL

- TARGET
- MAYO
- UCLA
- seth

COSMOS: F0F2



RVS 93-100%

NO APORTA MAYOR TIEMPO TRATAMIENTO

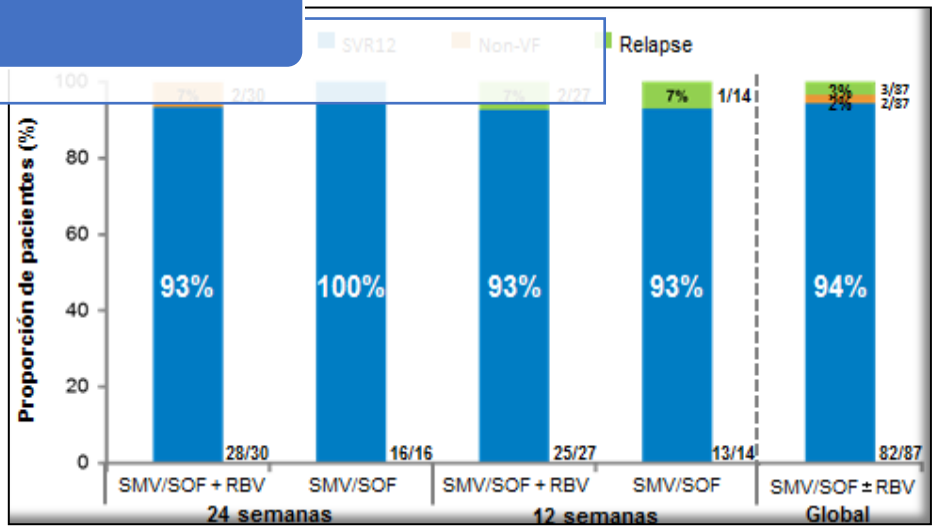
NO APORTA USO RBV

Eficacia Cohorte 1

- Pacientes con respuesta nula y fibrosis F0-F2
- Posibilidad de añadir o no RBV
- No impacto en la duración de 12 o 24 semanas
- Tasas de eficacia del 93 – 96%

Eficacia Cohorte 2

- Pacientes naïve o con respuesta nula previa y fibrosis F3-F4
- No impacto en la duración de 12 o 24 semanas
- Posibilidad de añadir o no RBV
- Tasas de eficacia del 93%



OPTIMIST 1: SMV/SOF SIN RBV

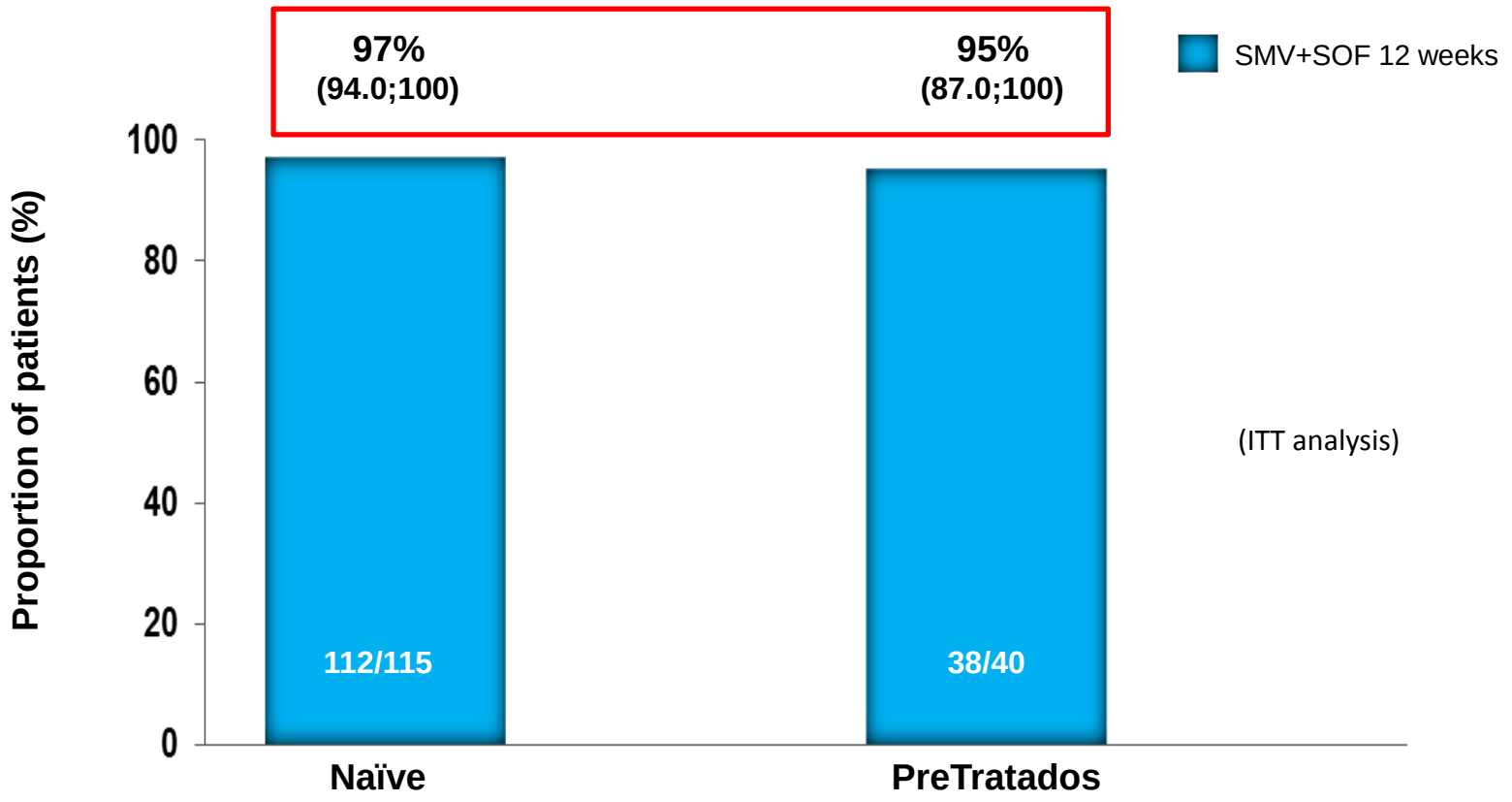
	SMV + SOF 12 weeks (N=155)	SMV + SOF 8 weeks (N=155)
Age (years; median [range])	56 (19–70)	56 (21–70)
Male, n (%)	82 (53)	87 (56)
BMI (kg/m^2; median [range])	28.0 (16.5–54.5)	26.9 (16.9–56.4)
Race, n (%) White / Black or African American	120 (77) / 31 (20)	125 (81) / 24 (15)
Ethnicity, n (%) Hispanic or Latino	24 (15)	24 (15)
HCV geno/subtype, n (%) 1a 1a with baseline Q80Ka 1a without baseline Q80Ka 1b	 116 (75) 46 (40) 70 (60) 39 (25)	 116 (75) 49 (42) 67 (58) 39 (25)
Baseline HCV RNA (log_{10} IU/mL; median [range])	6.83 (3.9–7.9)	6.85 (4.8–7.8)
IL28B genotype, n (%) CC / CT / TT	43 (28) / 86 (55) / 26 (17)	41 (26) / 86 (55) / 28 (18)
Prior treatment history, n (%) Treatment-naïve Treatment-experienced	 115 (74) 40 (26)*	 103 (66) 52 (34)**

*12 week arm: prior relapsers (n=8), prior non-responders (n=14), IFN-intolerant (n=2) and other patients (n=16);
** 8 week arm: prior relapsers (n=13), prior non-responders (n=10), IFN-intolerant (n=11) and other patients (n=18);

Kwo P. et al. EASL 2015, LB-Poster14

OPTIMIST 1: SMV/SOF SIN RBV

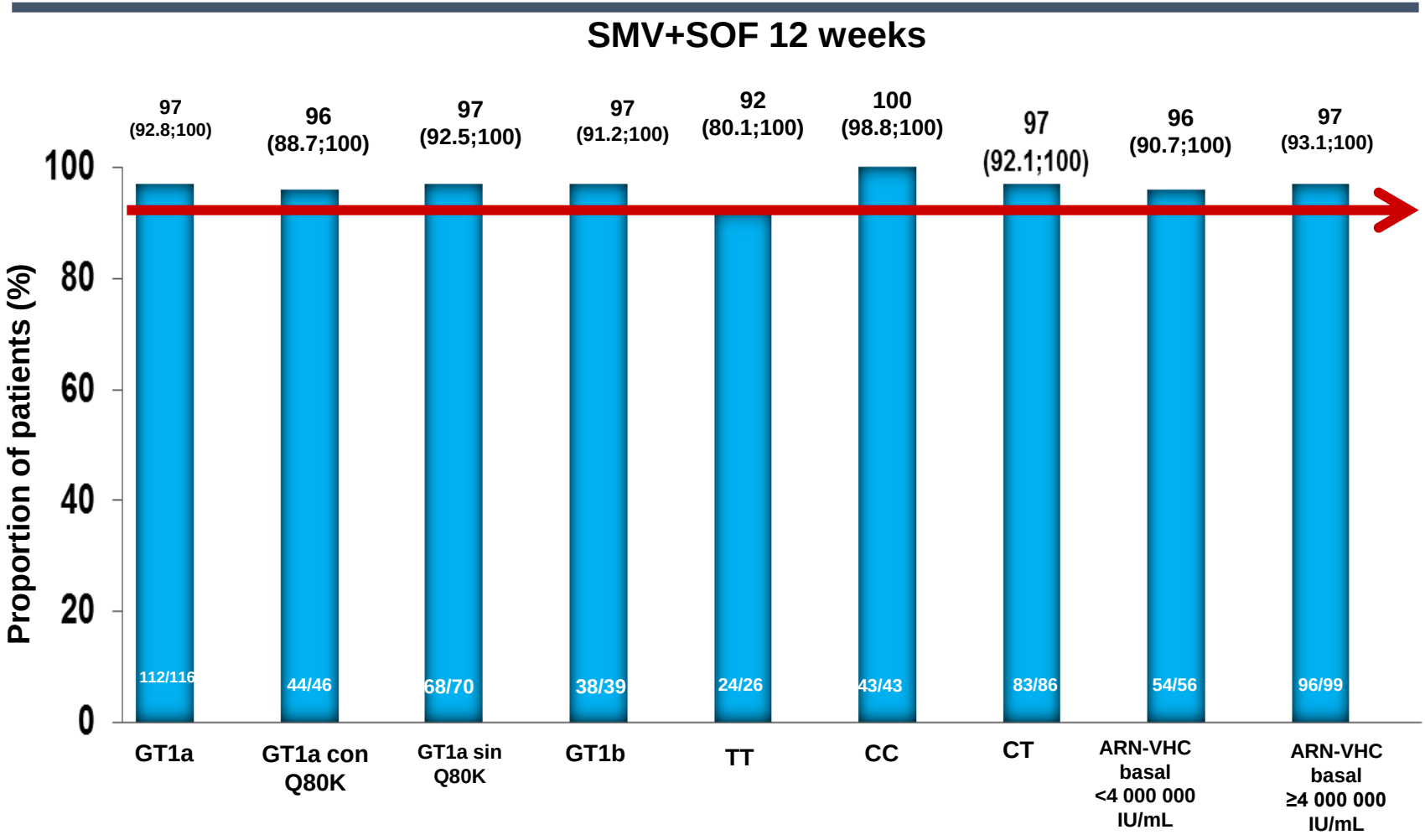
RVS 95 – 97% SIN RBV, independiente de la respuesta previa



Kwo P. et al. EASL 2015, LB-Poster14

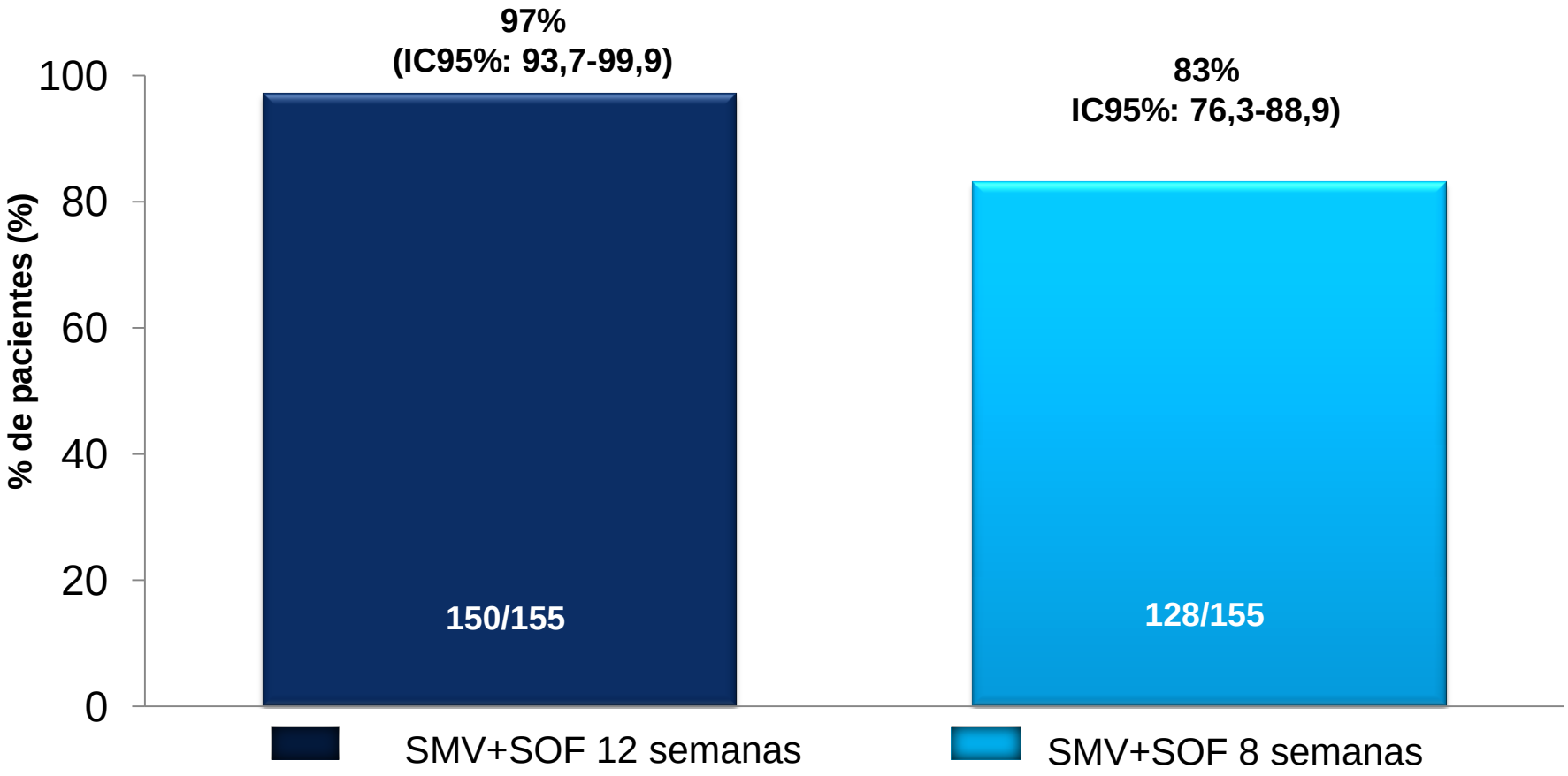
OPTIMIST 1: SMV/SOF 12 semanas sin RBV

Perfiles de pacientes: 1a/b, Ile 28b, PCR VHC



Kwo P. et al. EASL 2015, LB-Poster14

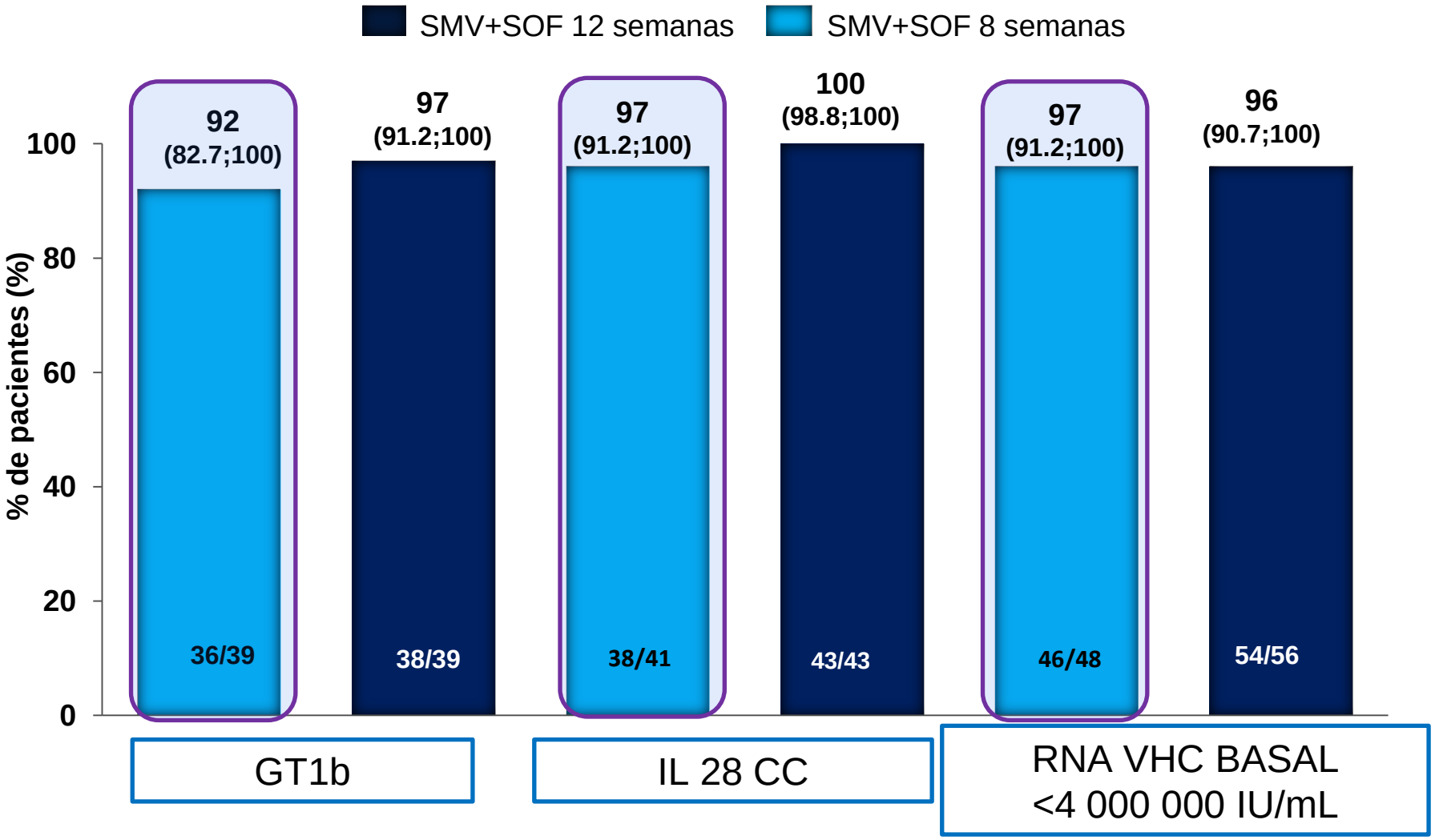
OPTIMIST 1: SMV/SOF SIN RBV
12 semanas versus 8 semanas



Kwo P. et al. EASL 2015, LB-Poster14

OPTIMIST 1: SMV/SOF SIN RBV

12 semanas versus 8 semanas: Perfiles



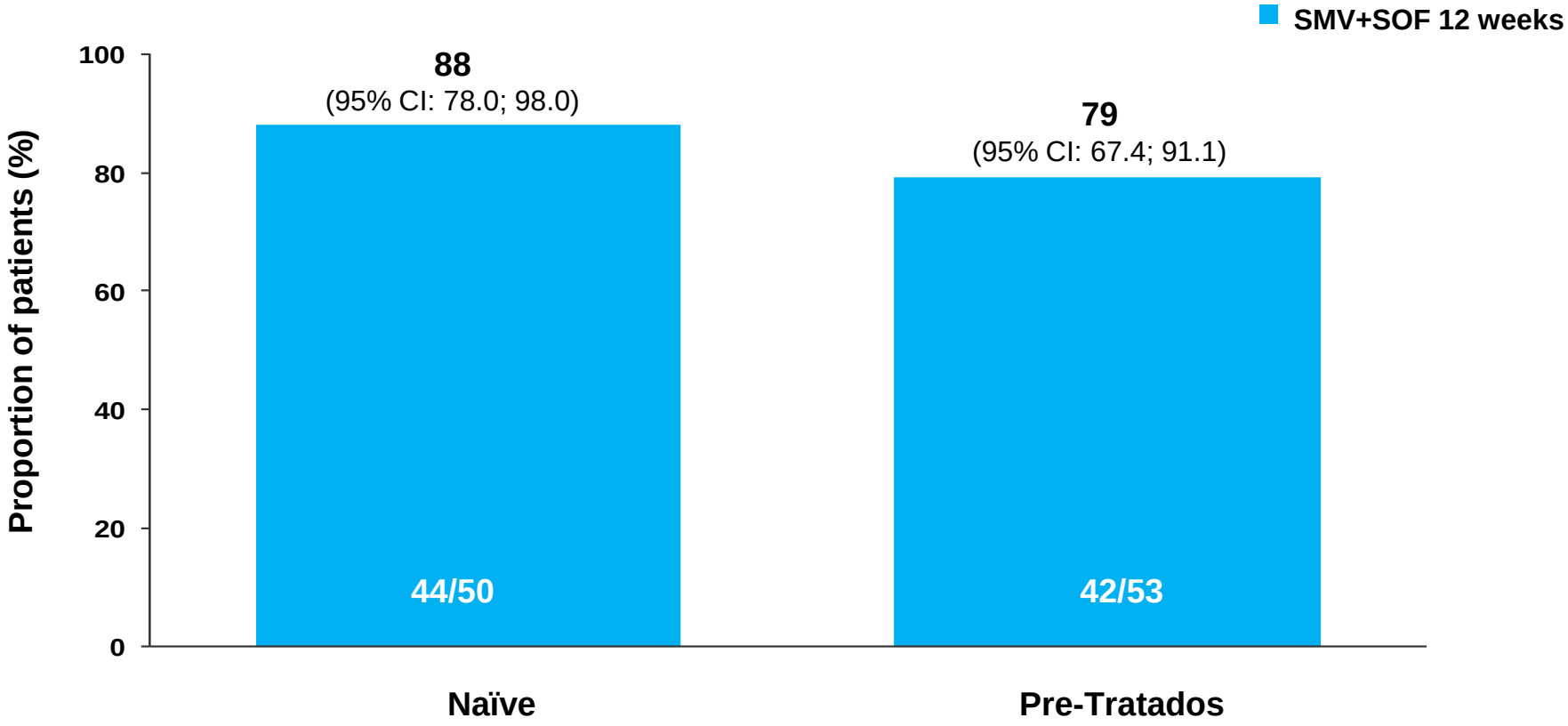
Kwo P. et al. EASL 2015, LB-Poster14

OPTIMIST-2: SMV/SOF 12 semanas No RBV Cirróticos

	SMV+SOF N=103
Age (years; median [range])	58 (29–69)
Male, n (%)	83 (81)
BMI (kg/m^2; median [range]) ≥ 30, n (%)	28.8 (18.7–42.8) 41 (40)
Race, n (%) White / Black or African American	82 (80) / 19 (18)
Ethnicity, n (%) Hispanic or Latino	16 (16)
HCV geno/subtype, n (%) 1a 1a with baseline Q80Ka 1a without baseline Q80Ka 1b	 72 (70) 34 (47) 38 (53) 31 (30)
Baseline HCV RNA ($\log_{10}$ IU/mL; median [range])	6.8 (5.0–7.7)
IL28B genotype, n (%) CC / CT / TT	29/102 (28) / 54/102 (53) / 19/102 (19)
Prior treatment history, n (%) Treatment-naïve Treatment-experienced*	 50 (49) 53 (51)
Platelets <90 000/mm^3, n (%)	19 (18)
Albumin <4g/dL, n (%)	53 (51)
Fibroscan score >20 kPa, n (%)**	15 (58)

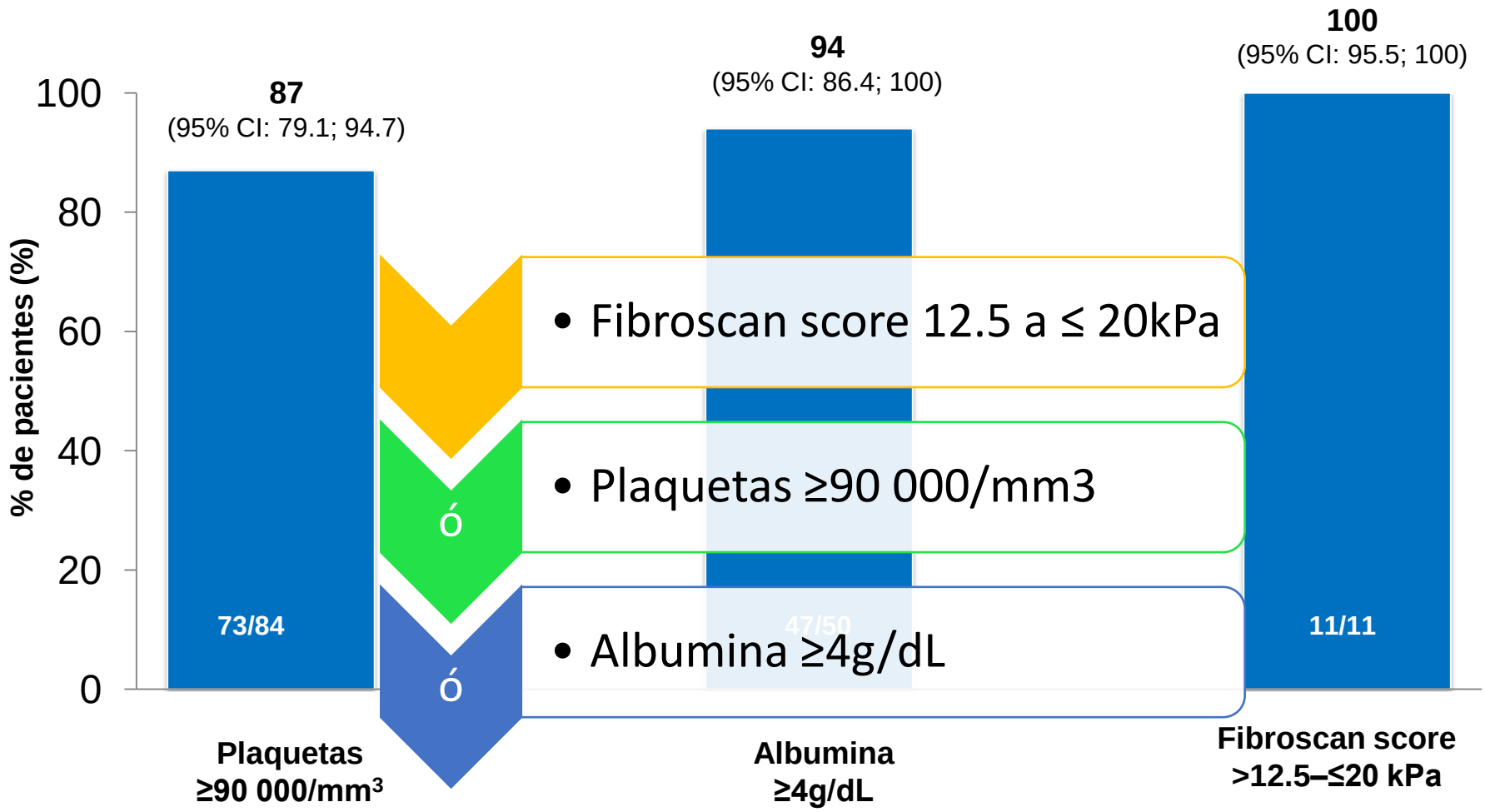
*prior relapsers (n=2), prior non-responders (n=17), IFN-intolerant (n=9) and other patients (n=25);
**Among the 26 patients who had Fibroscans, 15 had a score >20 kPa.

OPTIMIST-2: SMV/SOF 12 semanas No RBV Cirróticos



CI, confidence interval;
[a]Treatment-experienced patients included prior relapses, prior non-responders, IFN-intolerant and other patients

OPTIMIST-2: SMV/SOF 12 semanas No RBV Cirróticos Perfiles de pacientes



Lawitz E. et al. EASL 2015, LB-Poster 04

PERFIL DE SEGURIDAD OPTIMIST 1 Y 2

OPTIMIST 1 Pacientes, n (%)	SMV + SOF 12 weeks (N=155)	SMV + SOF 8 weeks (N=155)
Any AE	103 (66)	97 (63)
Grade 1/2 AE	99 (64)	94 (61)
Grade 3 AE	3 (2)	3 (2)
Grade 4 AE	1 (1)[a]	0
Serious AE	1 (1)	3 (2)
AE with fatal outcome	0	0
AE leading to permanent discontinuation[b]	0	0
Most common AEs[c]		
Nausea	23 (15)	14 (9)
Headache	22 (14)	26 (17)
Fatigue	19 (12)	23 (15)
AEs of interest		
Increased bilirubin	1 (1)	1 (1)
Rash (any type)	10 (6)	12 (8)
Pruritus (any type)	7 (5)	9 (6)
Photosensitivity	2 (1)	5 (3)
Dyspnea	3 (2)	1 (1)

OPTIMIST 2 Patients, n (%)	SMV + SOF 12 sem (N=103)
Any AE	72 (70)
Grade 1/2 AE	66 (64)
Grade 3 AE	5 (5)
Grade 4 AE	1 (1)
Serious AE	5 (5)
AE with fatal outcome [a]	1 (1)
AE leading to permanent discontinuation	3 (3)
Most common AE	
Headache	21 (20)
Fatigue	21 (20)
Nausea	11 (11)
AEs of interest	
Rash	16 (16)
Pruritus	14 (14)
Photosensibility	5 (5)
Dyspnea	3 (3)
Increased de bilirubin	2 (2)

[a]Elevated gamma-glutamyl transpeptidase levels not related to SMV/SOF treatment; [b]Permanent stop of at least one study drug; [c]In ≥10% of patients in at least one of the two arms during the treatment phase

Increased bilirubin was reported as an AE in only 2 (1%) patients, with no Grade 3/4 AEs, SAEs or discontinuation of treatment.

Kwo P. et al. EASL 2015, LB-Poster14

PERFIL DE SEGURIDAD OPTIMIST 1 Y 2

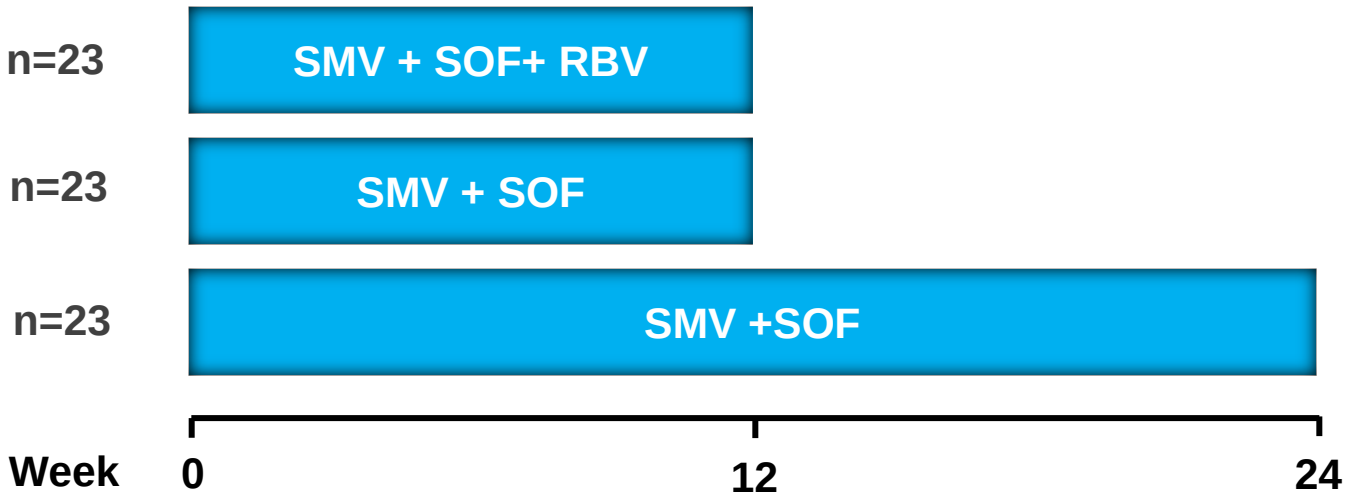
OPTIMIST 1 Pacientes, n (%)	SMV + SOF 12 semanas (N=155)	SMV + SOF 8 semanas (N=155)
Elevacion bilirrubina		
Grado 1/2	21 (14)	21 (14)
Grado 3	0	0
Grado 4	0	0
Descenso Hb		
Grado 1/2	0	1 (1)
Grado 3	0	0
Grado 4	0	0
Elevacion amilasa		
Grado 1/2	19 (12)	19 (12)
Grado 3	7 (5)	2 (1)
Grado 4	0	0
Elevacion lipasa		
Grado 1/2	14 (9)	12 (8)
Grado 3	1 (1)	2 (1)
Grado 4	0	0

OPTIMIST 2 Pacientes, n (%)	SMV + SOF 12 semanas (N=103)
Elevacion bilirrubina	
Grado 1/2	19 (18)
Grado 3	1 (1)
Grado 4	0
Elevacion amilasa	
Grado 1/2	23 (22)
Grado 3	6 (6)
Grado 4	0
Elevacion lipasa	
Grado 1/2	17 (17)
Grado 3	0
Grado 4	1 (1)

GALAXY: SOF + SMV ± RBV en TRASPLANT HEPATICO

- Randomised, open-label, Phase II study to evaluate efficacy and safety of SMV + SOF ± RBV in post-transplant patients

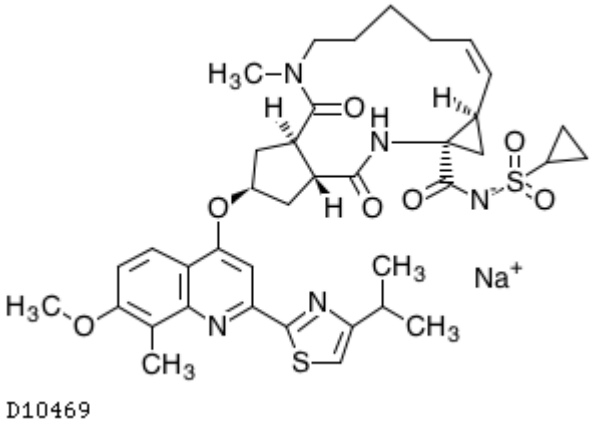
- Including patients with compensated cirrhosis



SMV 150 mg qd, SOF 400 mg qd

Clinicaltrials.gov NCT02165189

RESULTADOS EN VIDA REAL



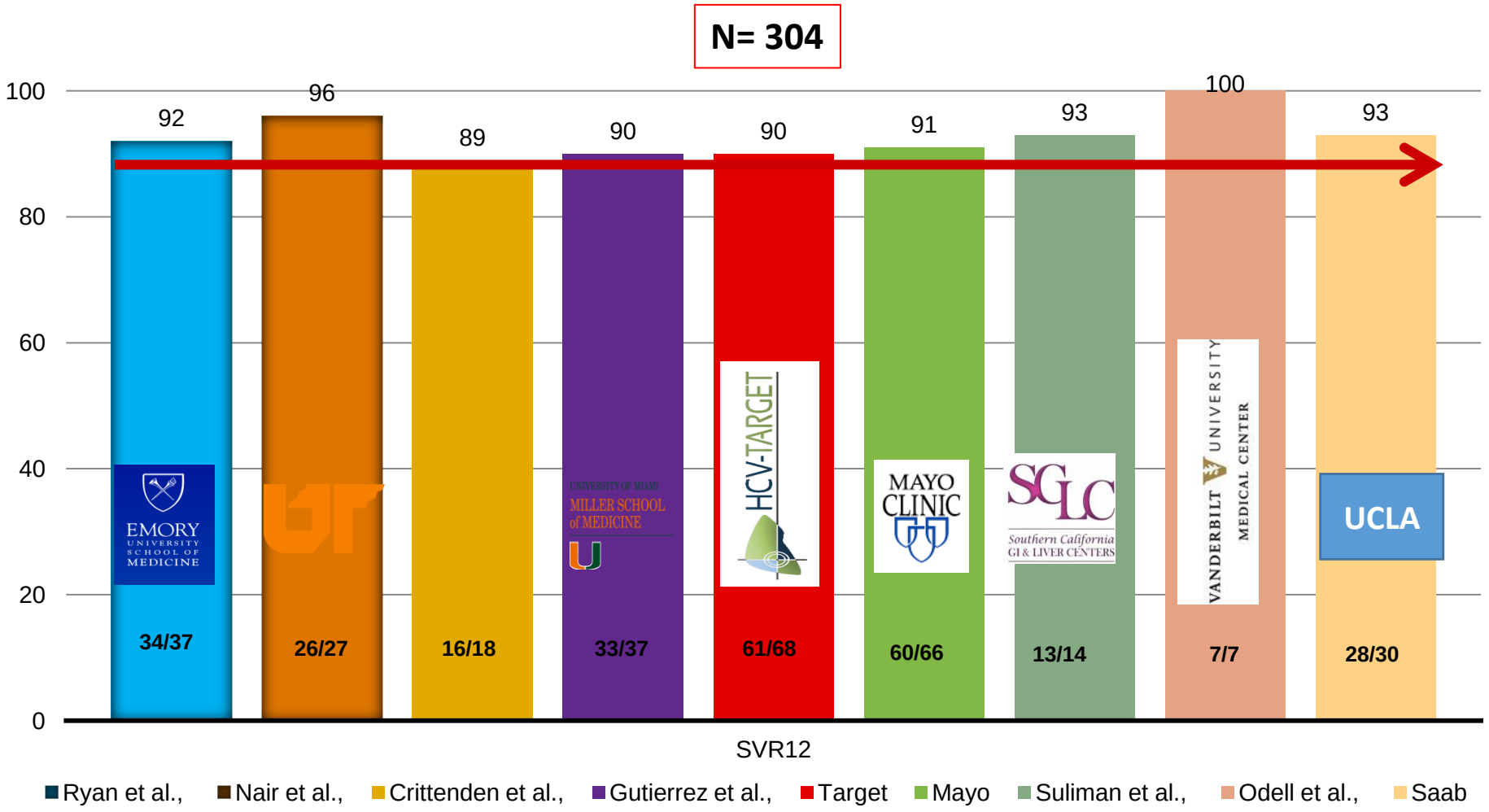
DATOS DE SIMEPREVIR

SIMEPREVIR:

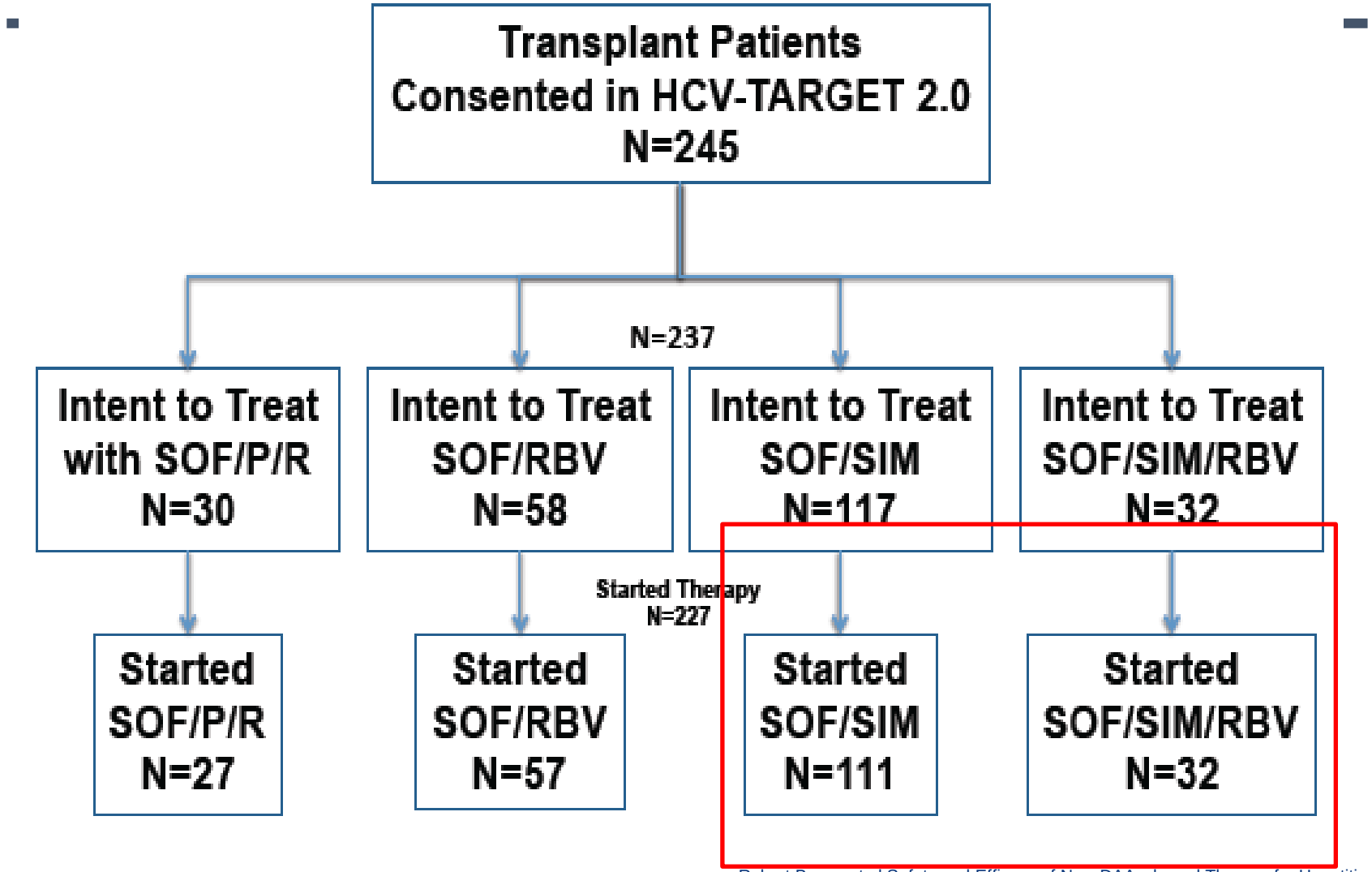
DATOS EN VIDA REAL

- TARGET
- MAYO
- UCLA
- seth

Cohortes de SIM+SOF en vida real



TARGET Cohort

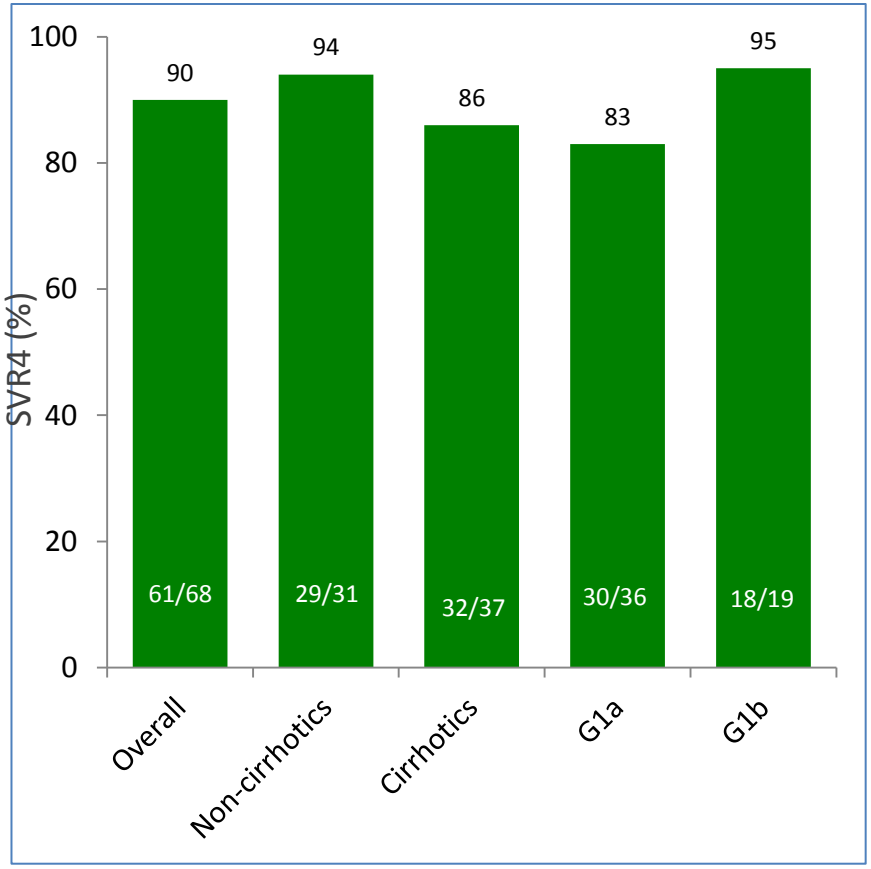


N=5 will not start treatment
N=3 Data transfer pending

Robert Brown et al Safety and Efficacy of New DAA---based Therapy for Hepatitis C Post--
-Transplant: Interval Results from the HCV---TARGET Longitudinal, Observational Study
AASLD Boston 2014

TARGET Cohort

	SOF+SMV (n=111)	SOF+SMV+RBV (n=32)
Male gender	77 (69%)	27 (84%)
Age	61 (49-78)	59 (46-71)
Previous Treatment No Yes PI failure	 51 (46%) 60 (54%) 7 (12%)	 10 (31) 22 (68%) 4 (18%)
Cirrhosis MELD >10	67 (60%) 14 (21%)	19 (59%) 6 (32%)
Immunosuppression TAC CsA mTOR MMF	 90 (81%) 13 (12%) 13 (12%) 48 (43%)	 22 (69%) 2 (6%) 10 (31%) 20 (62%)



Robert Brown et al Safety and Efficacy of New DAA---based Therapy for Hepatitis C Post---Transplant: Interval Results from the HCV---TARGET Longitudinal, Observational Study
AASLD Boston 2014

TARGET Cohort

Adverse Event	SOF+SMV	SOF+SMV+RBV
Total	64 (77%)	22 (92%)
Fatigue	21 (25%)	5 (21%)
Anemia	1 (1%)	9 (38%)
Headache	16 (19%)	7 (29%)
Flu-like	8 (10%)	5 (21%)
Infections	16 (19%)	1 (4%)
Diarrhea	6 (7%)	3 (13%)

NO EPISODIOS DE RECHAZO AGUDO

Robert Brown et al Safety and Efficacy of New DAA---based Therapy for Hepatitis C Post---Transplant: Interval Results from the HCV---TARGET Longitudinal, Observational Study AASLD Boston 2014

Mayo Clinic Cohort

	N=119
Male gender	93 (76%)
Age	61 ± 6
Time since LT	32 (2-317)
Genotype	
1a	74 (60%)
1b	43 (35%)
Previous Treatment	
No	22 (18%)
Yes	85 (69%)
PI failure	15 (12%)
SOF failure	1 (1%)
Fibrosis	
F0-F2	85 (70%)
F3-F4	37 (30%)
Cholestatic recurrence	13 (11%)
Decompensation	5 (4%)

HEPATOLOGY
Official Journal of the American Association for the Study of Liver Diseases
AASLD
VIRAL HEPATITIS

Experience Using Simeprevir and
ith or Without Ribavirin to Treat
notype 1 in Patients With Cirrhosis

gpapong,[1] Michael Leise,[3] K. Tuesday Werner,[1] Amy E. Chervenak[1]
Murphy,[2] Kriste
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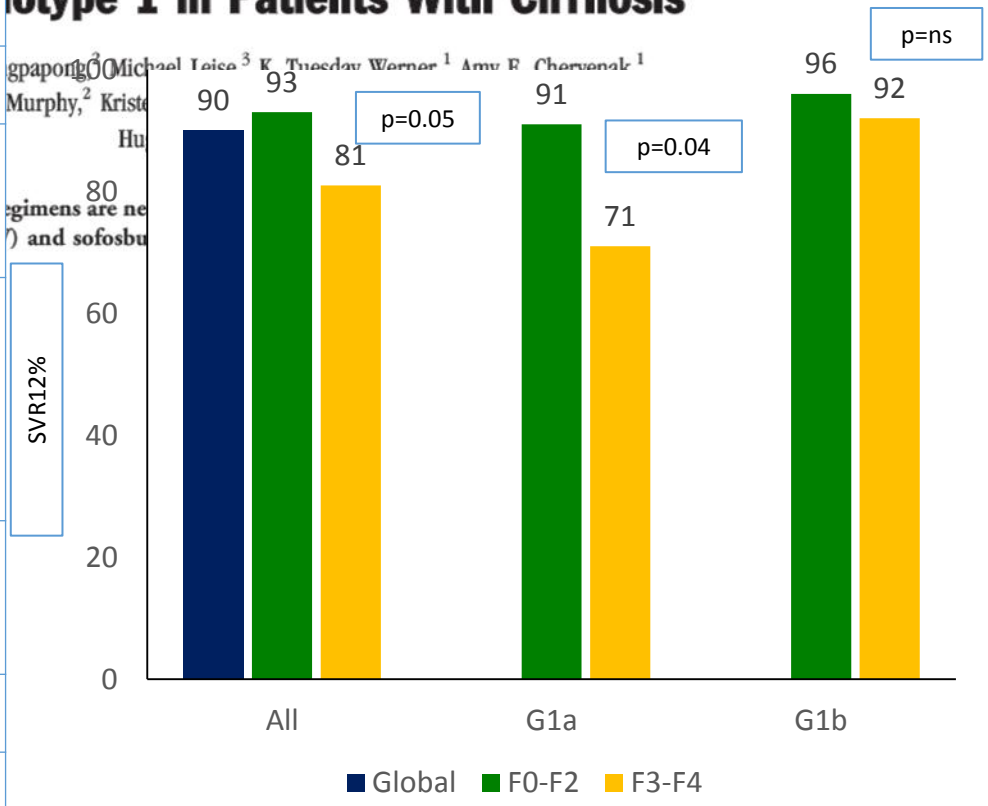
) and sofosbu



1. Pungpapong S. et al . 65th Annual Meeting of the AASLD . Boston, MA Nov 7-11 2014 Hepatology 2015 Oct;62(4):1004-12
http://www.natap.org/

Mayo Clinic Cohort

Event	Patients With Event, no. (%)
Any adverse event	59 (48%)
Any adverse event leading to discontinuation*	3 (2%)
Serious adverse events	
Death (pneumonitis)	1 (1%)
Acute pancreatitis*	1 (1%)
Acute kidney injury (obstructive ureteral stone)	1 (1%)
Common adverse events	
Fatigue	16 (13%)
Skin complaints (rash, pruritus, or photosensitivity)	7 (6%)
Headache	6 (5%)
Gastrointestinal complaints (nausea or diarrhea)	6 (5%)
Dyspnea	5 (4%)
Insomnia	2 (2%)
Fluid retention	2 (2%)
Anemia (RBV group)	18/25 (72%)
Anemia (non-RBV group)	5/98 (5%)
Grade 3 chemical or hematological abnormalities	
Hemoglobin <8 g/dL (RBV group)	2/25 (8%)
Hemoglobin <8g/dL (non-RBV group)	0
Total bilirubin >3 mg/dL†	2/110 (2%)
Creatinine >3 mg/dL	1 (1%)
Amylase and/or lipase >3 × ULN	1 (1%)
Alanine aminotransferase	0
Aspartate aminotransferase	0
Alkaline phosphatase	0

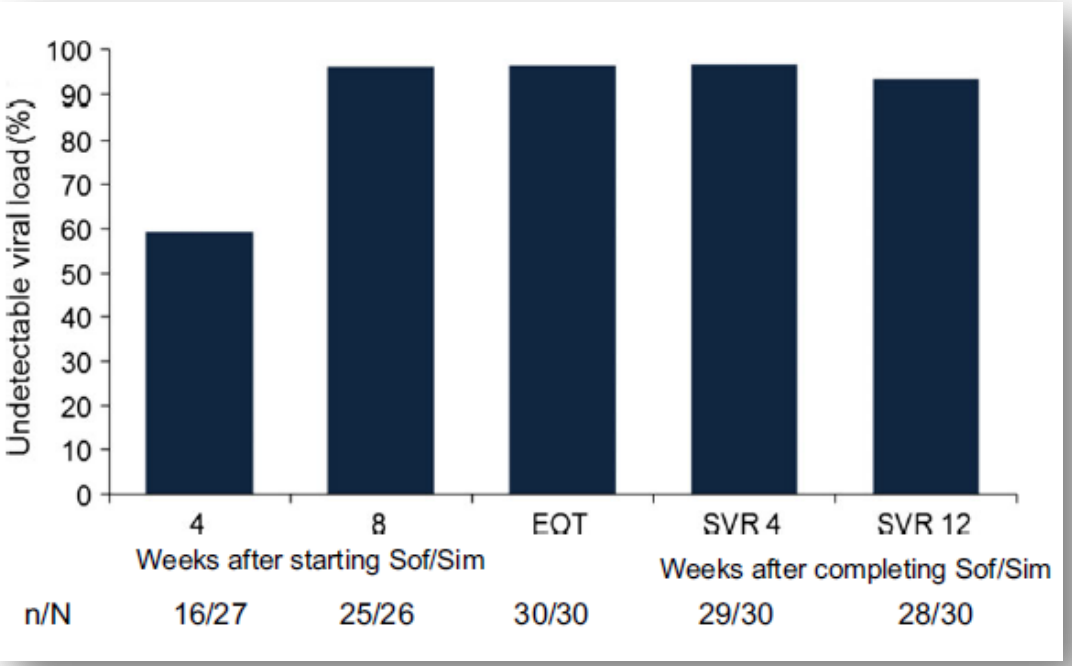
Pungpapong et al. Hepatology 2015

Single center experience: UCLA Liver Transplant database

SMV/SOF sin RBV	N=30
Age	61 ± 6
Male gender	23 (76%)
Time since LT (months)	72 ± 77
Treatment experience	13 (43%)
FCH	1 (3%)
Immunosuppression	
TAC	22 (73%)
CsA	8 (27%)
Fibrosis stage	
F0-F2	17 (58%)
F3-F4	11 (42%)

N= 30
12 weeks without RBV

SVR12
93%



. Saab et al., Sofosbuvir and simeprevir in liver transplant recipients, Liver International April 2015, DOI:10.1111/liv.12856

Single center experience: UCLA Liver Transplant database SAFETY

- *Ningun paciente necesito transfusions ni factores de crecimiento durante el tratamiento.*
- *Ningun paciente desarrollo rash cutaneo o aumento de la bilirrubina durante el tratamiento.*
- *Ningun paciente discontinuo el tratamiento*

Table 2. Laboratory data and mixed model regression output

Mean	White blood cells (×1000 cells/μL)	Hemoglobin (g/dL)	Platelets (× 1000 cells/μL)	Creatinine (mg/dL)	Alanine aminotransferase (U/L)	Total bilirubin (mg/dL)
Baseline (SD)	4.3 (1.5)	12.4 (1.8)	121 (57.3)	1.1 (0.27)	70.4 (39.5)	1.2 (1.2)
Week 4 (SD)	4.7 (2.0)	12.5 (1.4)	136 (75.7)	1.1 (0.34)	25.9 (15.6)	1.1 (0.98)
EOT (SD)	4.5 (1.3)	12.6 (1.4)	130.0 (52.4)	1.1 (0.32)	24.3 (13.0)	0.91 (0.52)
SVR (SD)	4.9 (1.6)	12.6 (1.4)	136.2 (54.6)	1.1 (0.32)	26.4 (21.7)	0.75 (1.6)
Mixed model *P*-value	0.0939	0.0001	0.0996	0.5017	<0.0001	0.0012
Coefficient (SE)	0.0167 (0.001)	0.0304 (0.008)	0.356 (0.216)	0.001 (0.002)	−1.197 (0.28)	−0.017 (0.005)
95% CI	−0.0028, 0.0362	0.0148, 0.0461	−0.6764, 0.7789	−0.0025, 0.0051	−1.7469, −0.6485	−0.028, −0.0069
Intercept variance	1.6344	1.6526	3392.59	0.0604	154.39	0.5076
Residual variance	0.9937	0.6228	442.52	0.0381	786.45	0.2900

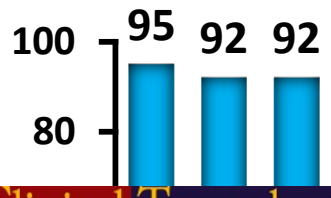
CI, confidence interval; EOT, end of treatment; SVR, sustained viral response; SD, standard deviation; SE, standard error.

. Saab et al., Sofosbuvir and simeprevir in liver transplant recipients, Liver International April 2015, DOI:10.1111/liv.12856

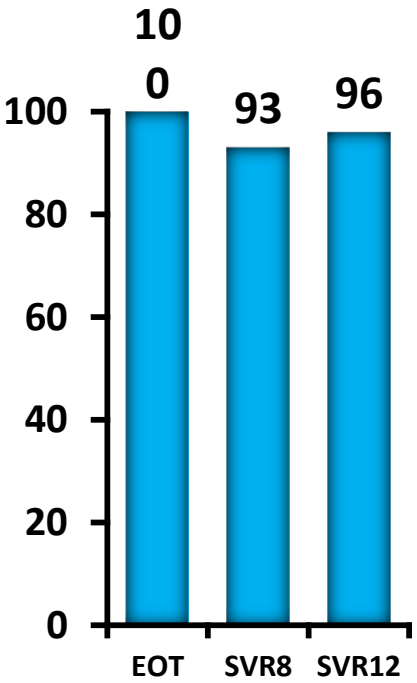
SIME+SOF±RBV EN EMORY, ATLANTA
SIME+SOF±RBV EN University of Tennessy, Memphys
University of Massachusetts Medical Center, Worcester, MA
.....

N=37. SIM/SOF±RBV 12 SEMANAS

Genotype 1A	25 (68%)
Genotype 1B	8 (22%)
Genotype 1 (undifferentiated)	4 (11%)
Average age	57 (32-69 range
Male	27 (73%)
African-American	14 (38%)
Treatment-experienced	20 (54%)
Cirrhosis post-OLT	8 (22%)
Treated with ribavirin	16 (43%)
Tacrolimus monotherapy	23 (62%)
mTOR inhibitor monotherapy	5 (14%)
High viral load (>800,000 IU/mL) at baseline	30 (81%)
Serum Cr > 1.5 mg/dL	13 (35%)
BMI >30	14 (38%)



Pacient Characteristics (n=37)	
Age (years)	56±5
Gender M/F	28/18
Race C/AA	32/14
HCV RNA million (IU/ml)	4,5±3,5



Clinical Transplantation

Clin Transplant 2015: 29: 813–819 DOI: 10.1111/ctr.12584

Clinical Transplantation

Treating fibrosing cholestatic hepatitis C with sofosbuvir and ribavirin: a matched analysis

Saab S, Jimenez M, Bau S, Goo T, Zhao D, Durazo F, Han S, El Kabany M, Kaldas F, Tong MJ, Busuttil RW. Treating fibrosing cholestatic hepatitis C with sofosbuvir and ribavirin: a matched analysis.

Abstract: Background: Fibrosing cholestatic hepatitis (FCH) is an uncommon but potentially fatal complication of recurrent hepatitis C (HCV) in liver transplant recipients.
Methods: We matched the treatment outcomes of 10 liver transplant recipients who developed FCH with those of 10 recipients with recurrent HCV without FCH treated with sofosbuvir and ribavirin.
Results: Baseline mean alanine transaminase, aspartate transaminase, alkaline phosphatase, and total bilirubin were 186 U/L, 197 U/L, 243 U/L, and 6.7 mg/dL, respectively, in the FCH recipients and 82 U/L, 60 U/

Sammy Saab[a,b], Melissa Jimenez[b], Sherona Bau[b], Tyralee Goo[a], Difan Zhao[c], Francisco Durazo[a,b], Steven Han[a,b], Mohammed El Kabany[a,b], Fady Kaldas[b], Myron J. Tong[b,d] and Ronald W. Busuttil[b]

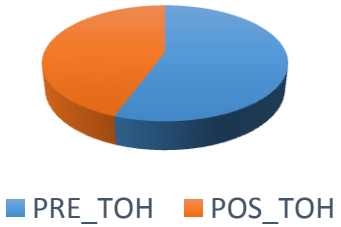
[a]Department of Medicine, University of California at Los Angeles, [b]Department of Surgery, University of California at Los Angeles, [c]Department of Biostatistics, University of California at Los Angeles, Los Angeles, CA, and [d]Liver Center, Huntington

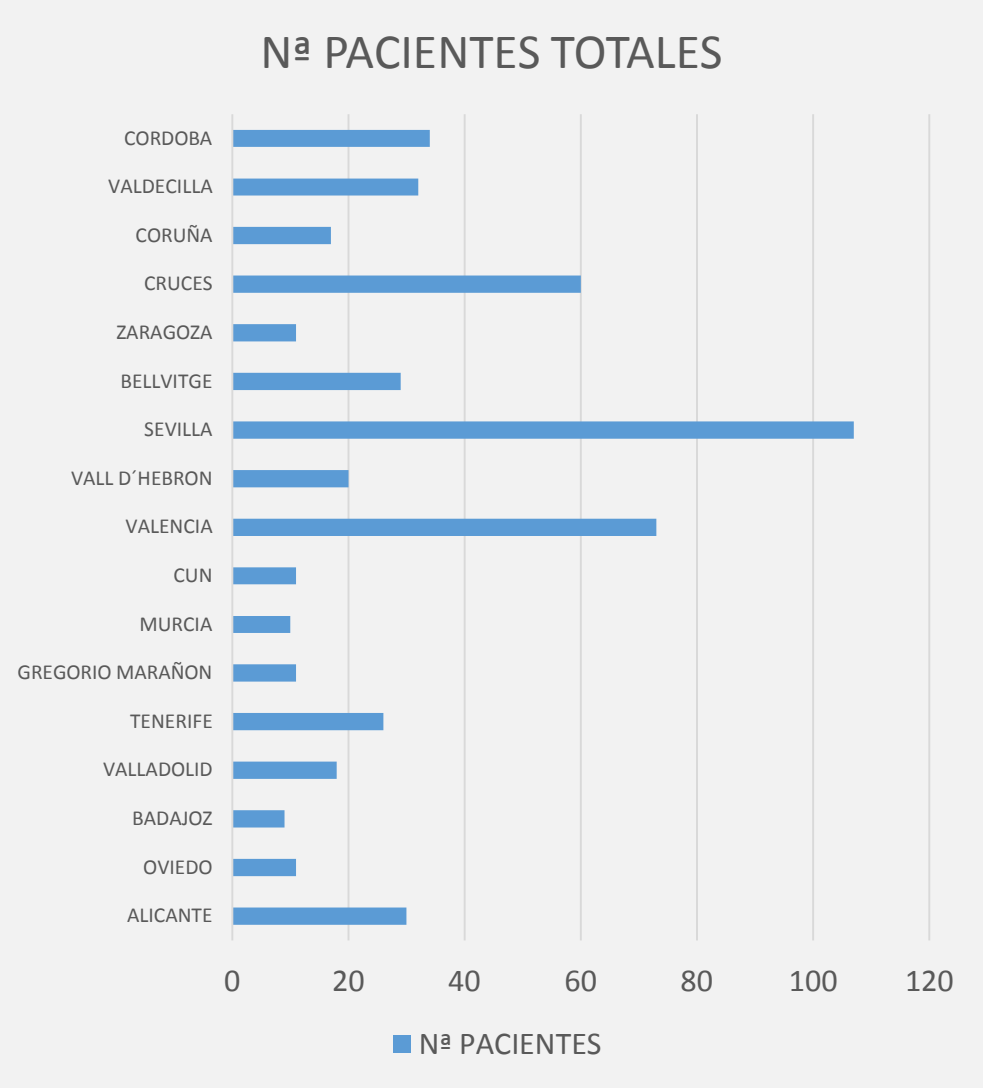
Ryan M Ford, et al. AASLD 2014.
Emory Transplant Center, Atlanta

COHORTE SETH: SIM+SOF EN TOH

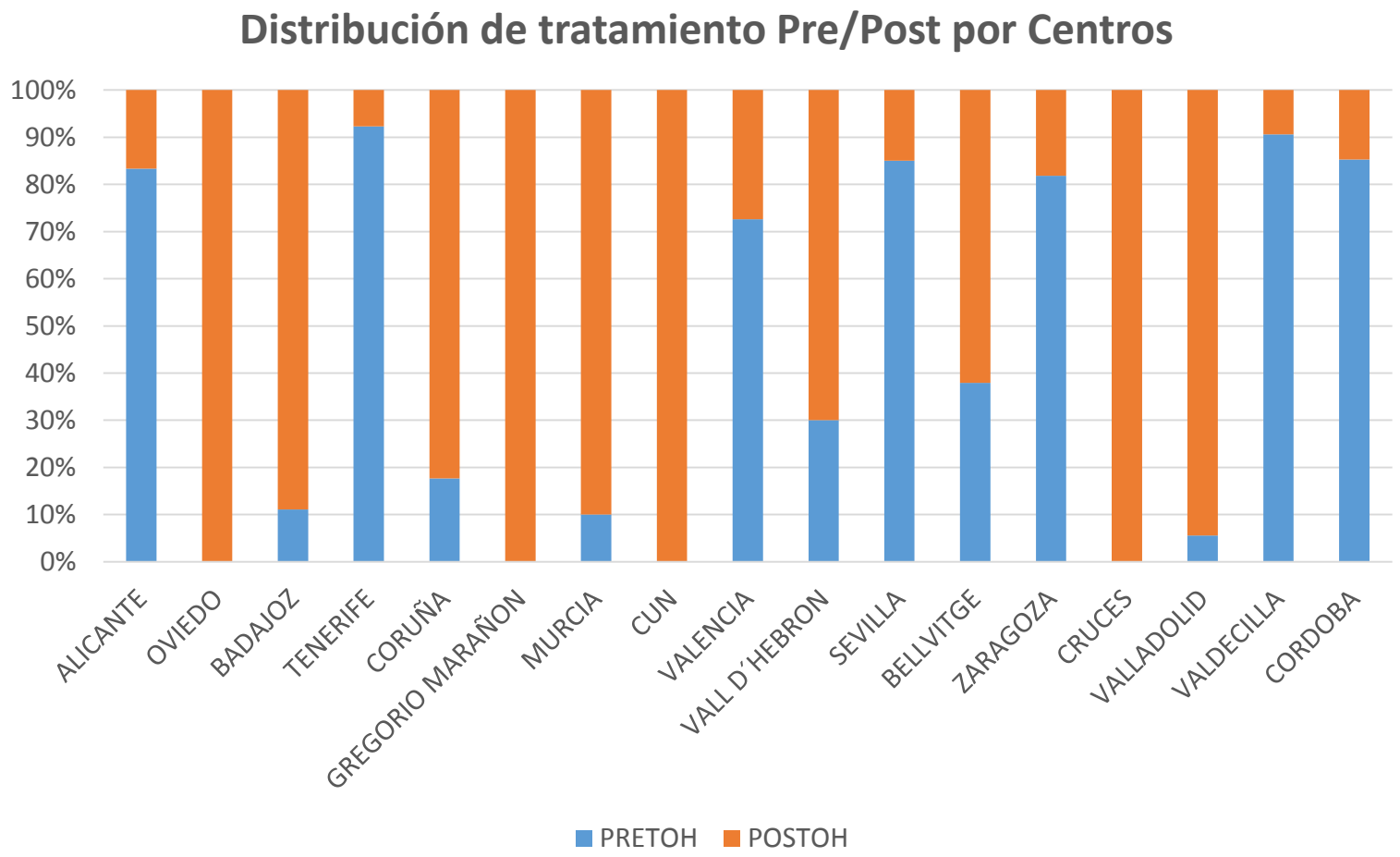
- ❑17 HOSPITALES
- ❑509 PACIENTES
  - ✓283 PRETOH
  - ✓226 POSTOH

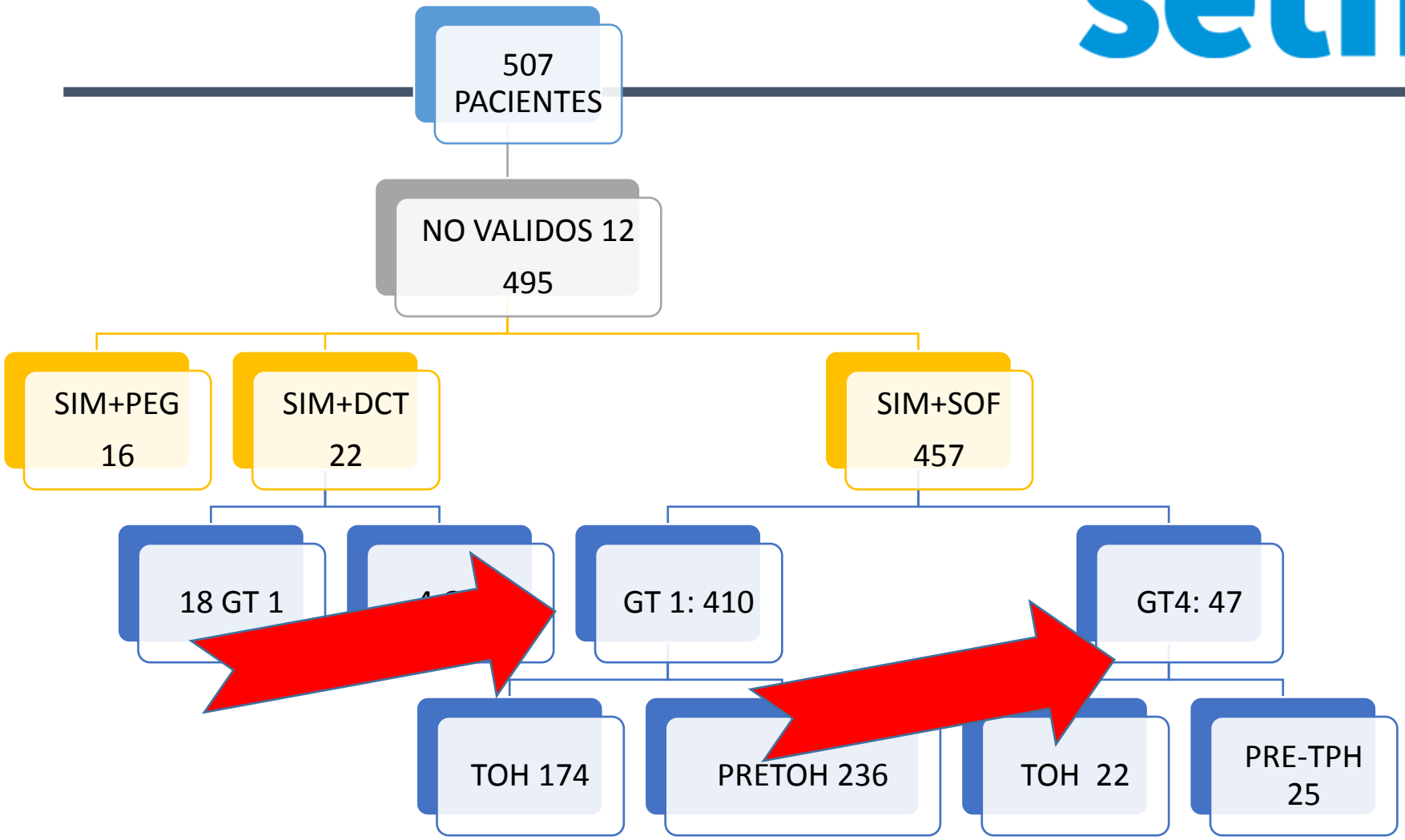
Pacientes tratados





COHORTE SETH: SIM+SOF EN TOH



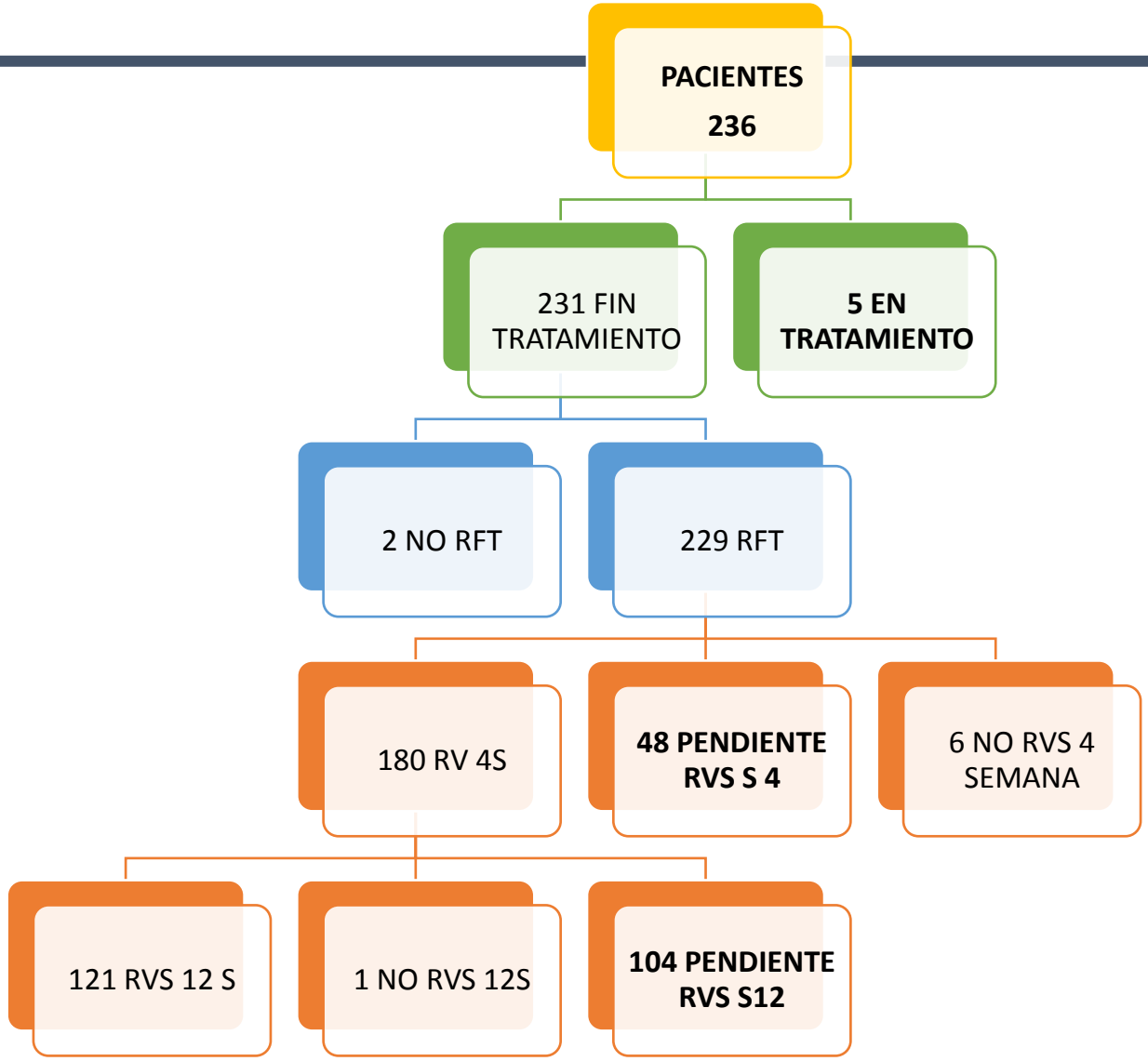

507 PACIENTES
NO VALIDOS 12
495
SIM+PEG 16
SIM+DCT 22
SIM+SOF 457
18 GT 1
GT 1: 410
GT4: 47
TOH 174
PRETOH 236
TOH 22
PRE-TPH 25

Genotipo 1. CIRROSIS

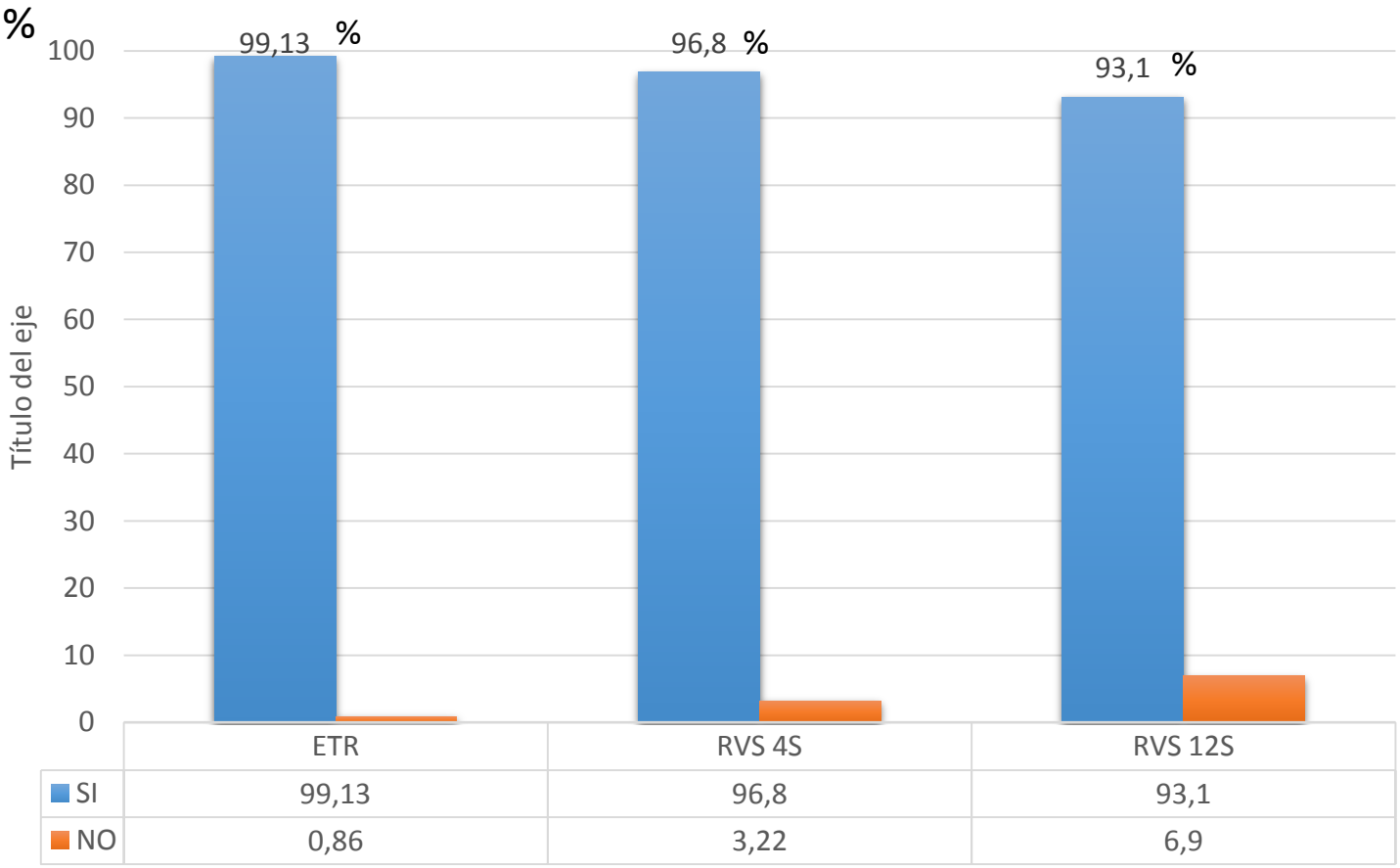
CIRROTICOS GT 1	N=236
Sexo varon	141(59,7%)
Edad	60,64 ±8,04
Genotipo	
1a	47 (19,9%)
1b	174 (61,9%)
1	15(10,2%)
ILE28B: 147 (62,3)	
CC	28(19,04%)
CT	91(61,9%)
TT	28(19,04%)
Fibrosis	
F1-F2	2(0,8)
F3	9(3,8)
F4	204(86,4%)
CIRROSIS DESCOMPENSADA	18(7,6)
FIBROSCAN	26,15±14,55
MELD (RANGO)	9,04±3,22 5-26

CIRROTICOS GT 1	N=236
Previous Treatment	
No	107 (45,3%)
Yes	126 (53,4%)
Desconocido	3(1,2%)
TIPO DE TRATAMIENTO	
IFN pautas	94(75,2)
IP fallo	29(23,2)
Otros	2(1,6)
RESPUESTA TRATAMIENTO PREVIO	
NULL RESPONDER	66(52,38)
RESPONDEDOR LENTO	11(8,73)
RECAEDOR	29(23,01)
DESCONOCIDO	20(15,87)

Pacientes Cirroticos Genotipo 1 PreTOH

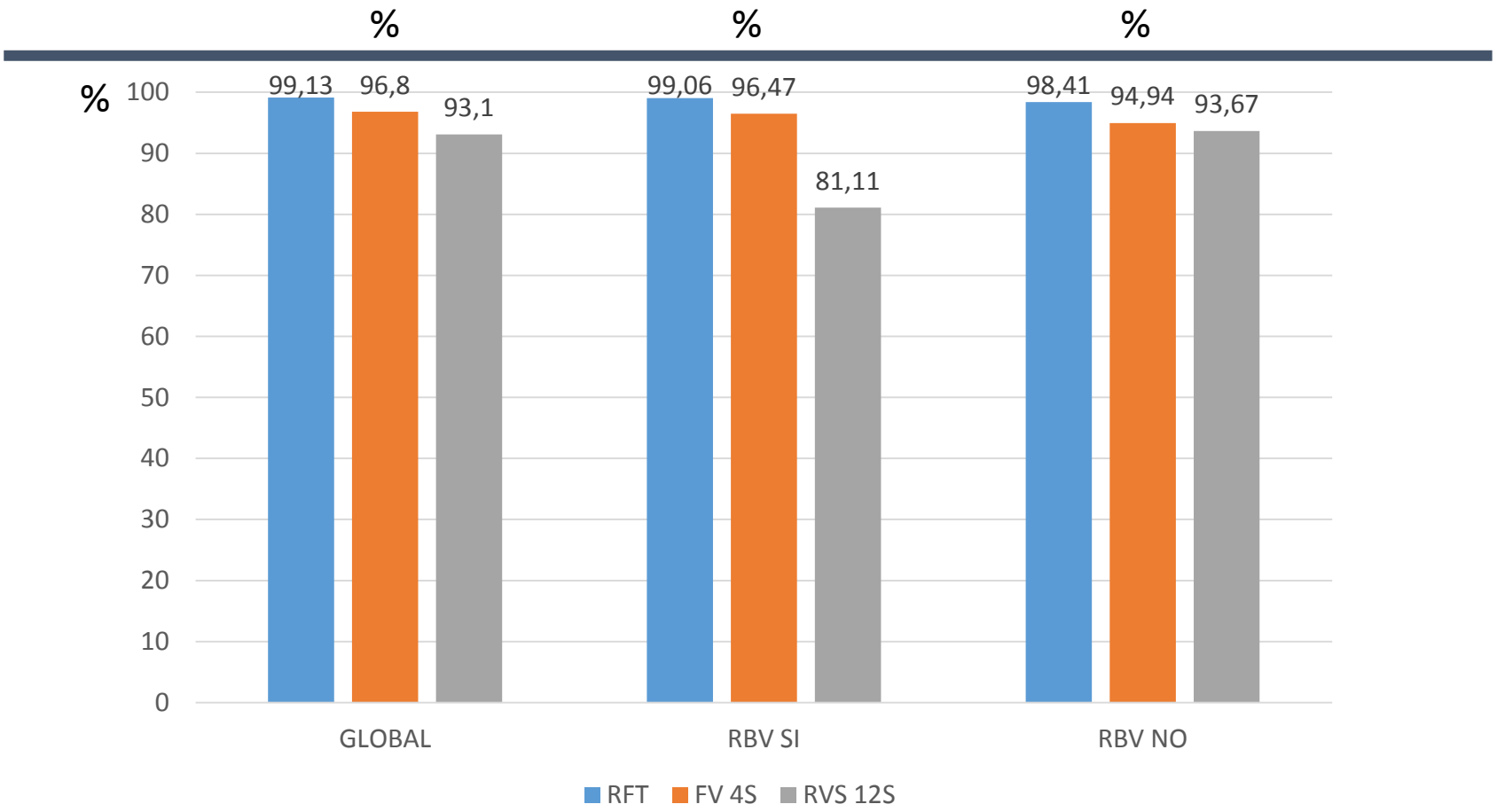


SIM+SOF. RESPUESTA VIRAL SOSTENIDA
PACIENTES CIRROTICOS GENOTIPO 1



	TOTAL	RV	NO	PENDIENTE
FIN TRATAMIENTO	231	229	2	5
4 SEMANA	186	180	6	48
12 SEMANAS	130	121	9	104

RVS SEGÚN USO DE RBV EN CIRROTICOS



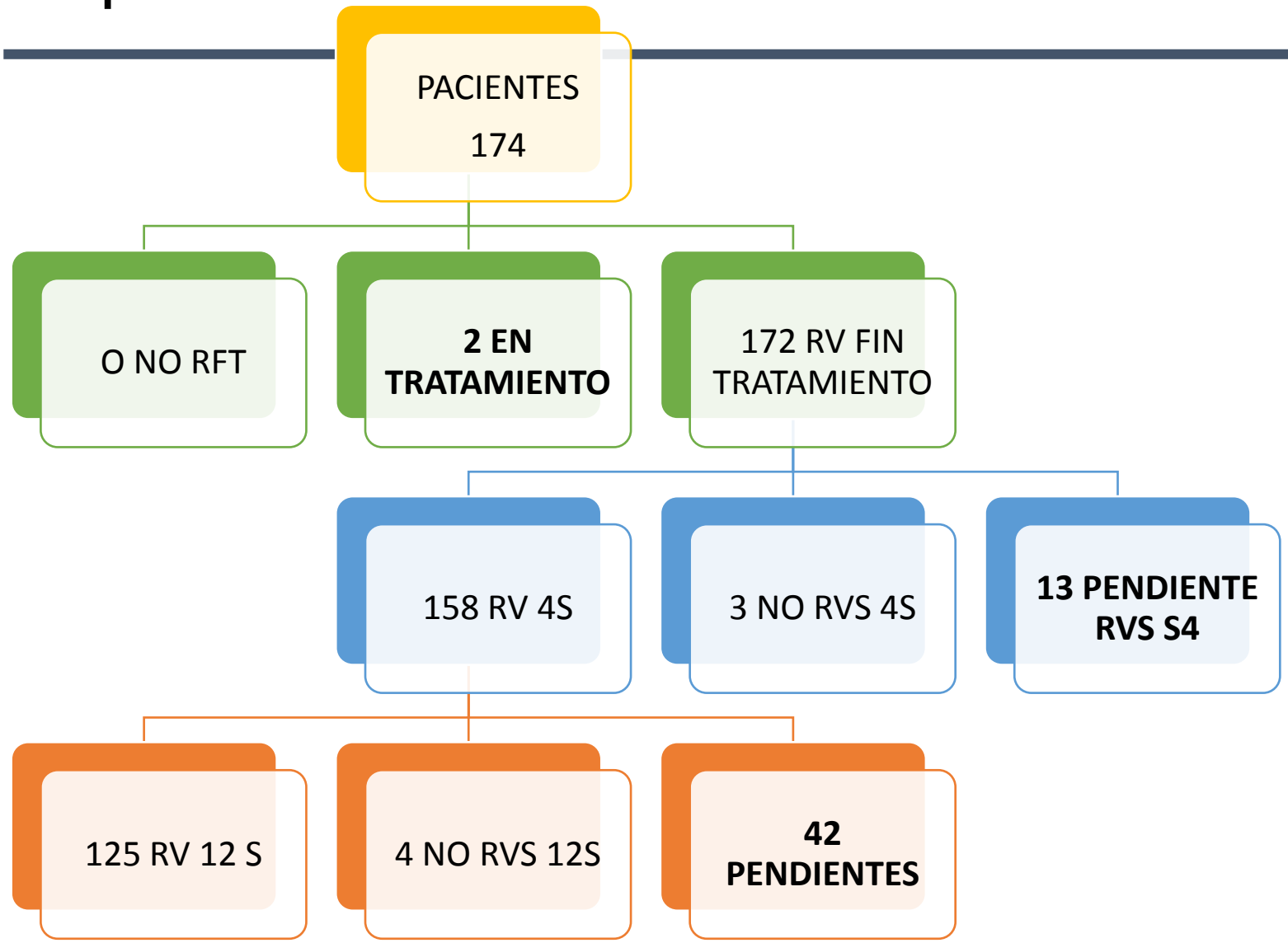
	RFT	RV 4S	RVS 12S
GLOBAL	229/231	180/186	121/130
RBV SI CIRROSIS	106/107	82/85	43/53
RBV NO CIRROSIS	124/126	94/99	74/79

SIM+SOF EN PACIENTES TRASPLANTADOS GENOTIPO 1 POSTOH

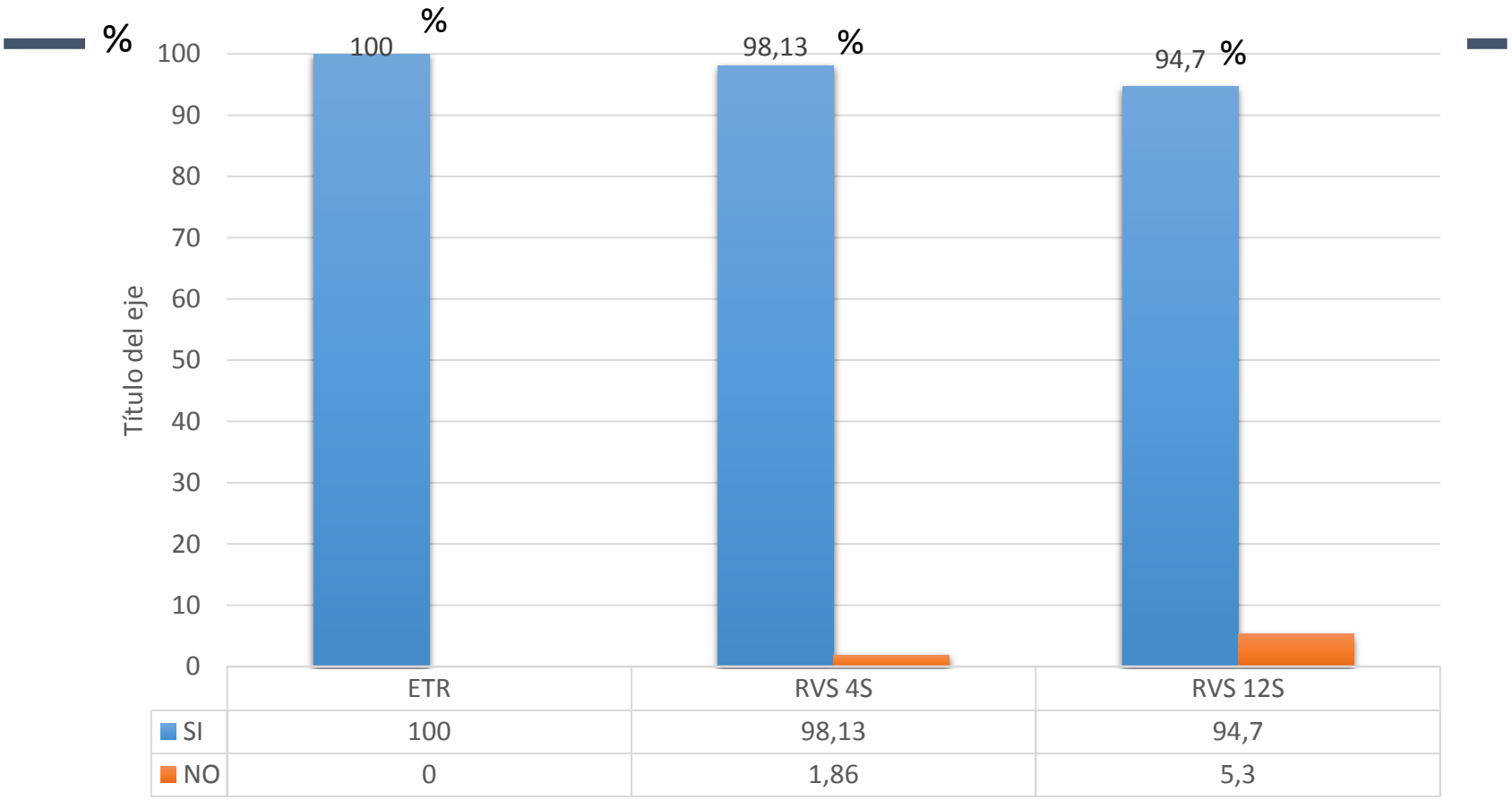
POSTOH GT 1	N=174
Sexo varon	138(79,3%)
Edad	60,93 ±9,28
Genotipo 1a 1b 1 ILE28B: 82 (47,1) CC CT TT	 29 (16,6%) 135 (77,6%) 10(5,7%) 10(12,1) 55(67,1) 17(20,7)
Fibrosis F0-F2 F3 F4 CIRROSIS DESCOMPENSADA FIBROSCAN	 38(21,8) 46(26,4) 82(47,1%) 7(4,1) 16,54±11,91
MELD (RANGO)	8,6±2,5 6-24

POSTOH GT 1	N=174
Tratamiento No Si TIPO DE TRATAMIENTO IFN PI fallo Otros RBV	 75 (45,3%) 99(56,9%) 89(89,9) 8(8,1) 3(3,1) 107(61,5)
RESPUESTA TRATAMIENTO PREVIO **NULL RESPONDER** **RESPONDEDOR LENTO** **RECAEDOR** **DESCONOCIDO**	 **48(48,5)** **16(16,2)** **29(29,3)** **6(6,1)**

Pacientes Genotipo 1 Trasplantados Hepaticos

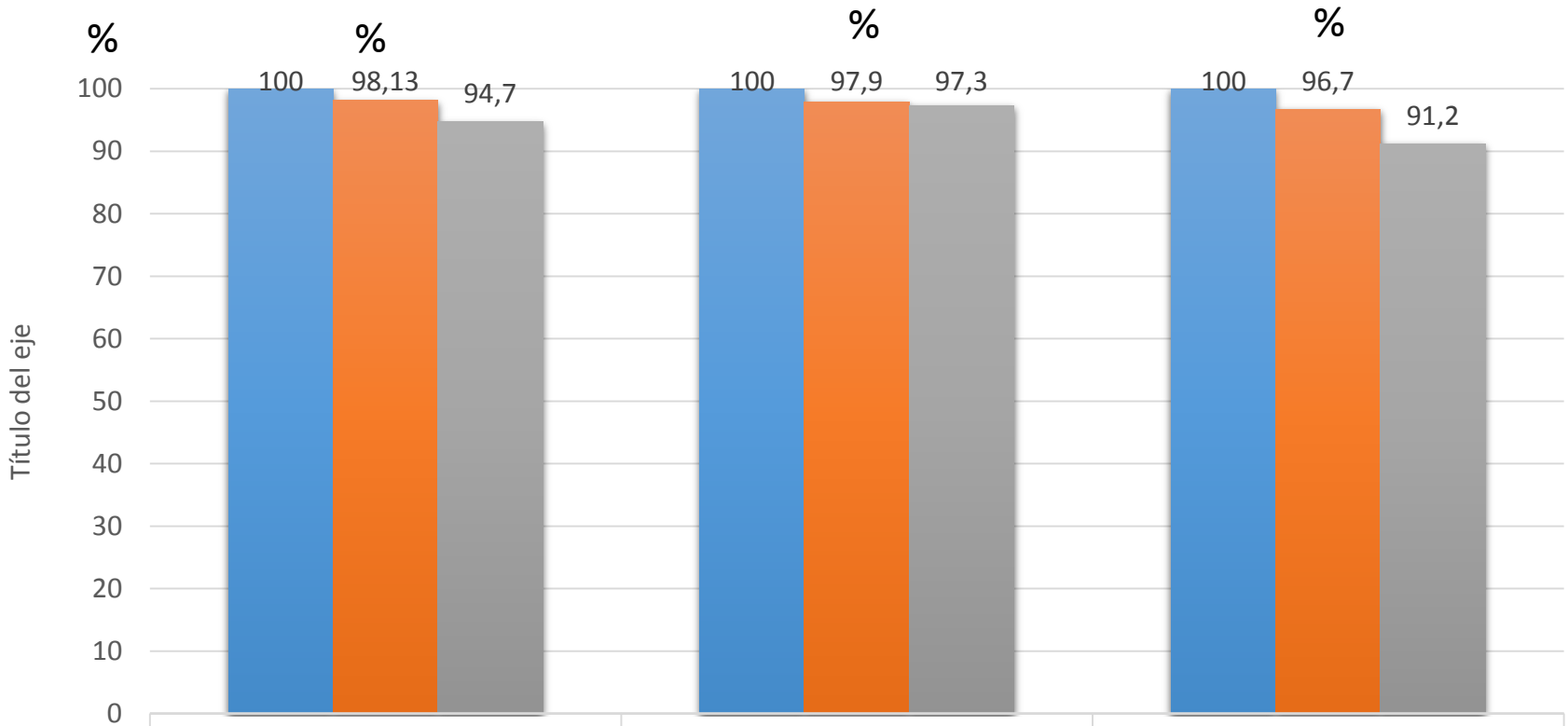


RESPUESTA VIRAL SOSTENIDA EN PACIENTES POSTOH GENOTIPO 1 SOF+SIME



	TOTAL	RV	NO	PENDIENTE
FIN TRATAMIENTO	172	172	0	2
4 SEMANA	161	158	3	13
12 SEMANAS	132	125	7	42

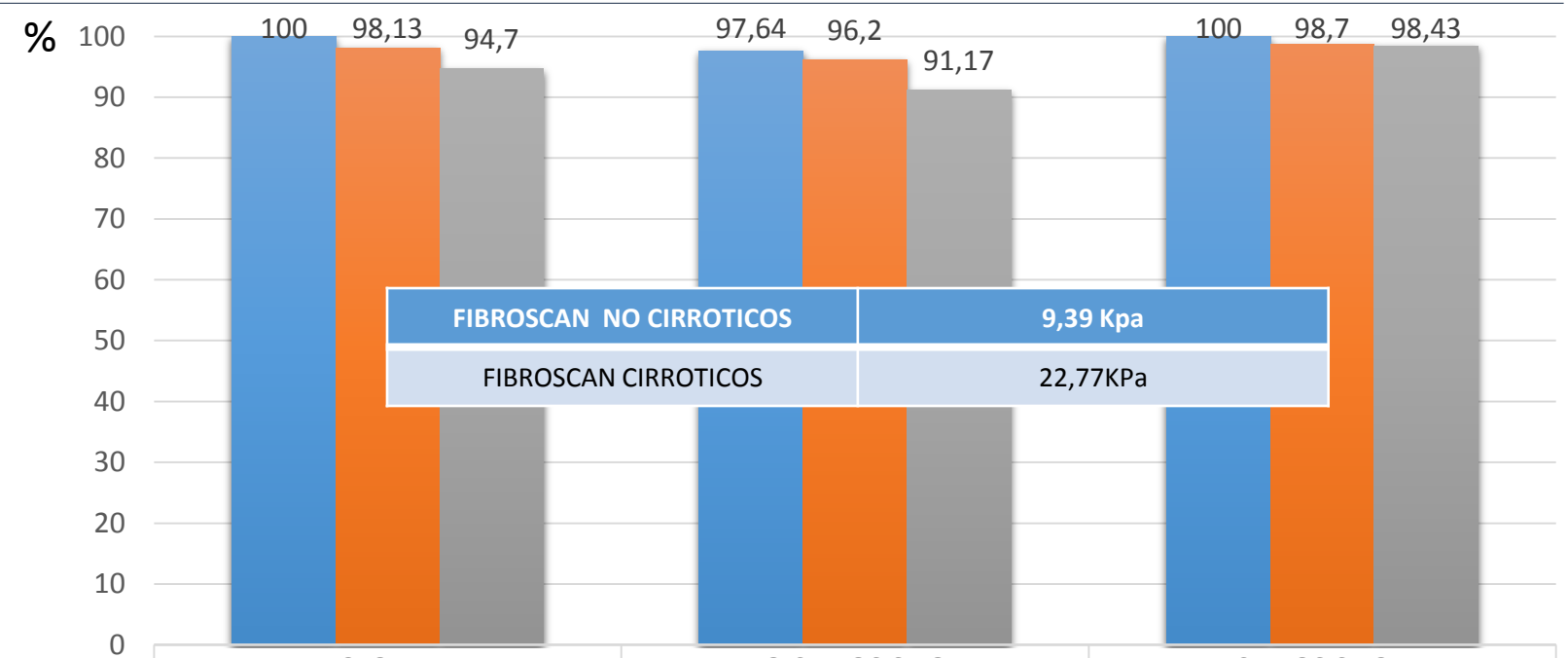
RESPUESTA VIRAL SOSTENIDA EN PACIENTES POSTOH GENOTIPO 1
RIBAVIRINA vs NO RIBAVIRINA



	GLOBAL	RBV SI TOH	RBV NO TOH
RFT	100	100	100
RV 4S	98,13	97,9	96,7
RVS 12S	94,7	97,3	91,2

	RFT	RV 4S	RVS 12S
GLOBAL	172/172	158/161	125/132
RBV SI TOH	107/107	93/95	73/75
RBV NO TOH	65/65	58/60	52/57

RESPUESTA VIRAL SOSTENIDA EN PACIENTES POS-TOH GENOTIPO 1 CIRROSIS vs NO CIRROSIS



	GLOBAL	NO CIRROSIS TOH	CIRROSIS TOH
RFT	100	97,64	100
RV 4S	98,13	96,2	98,7
RVS 12S	94,7	91,17	98,43

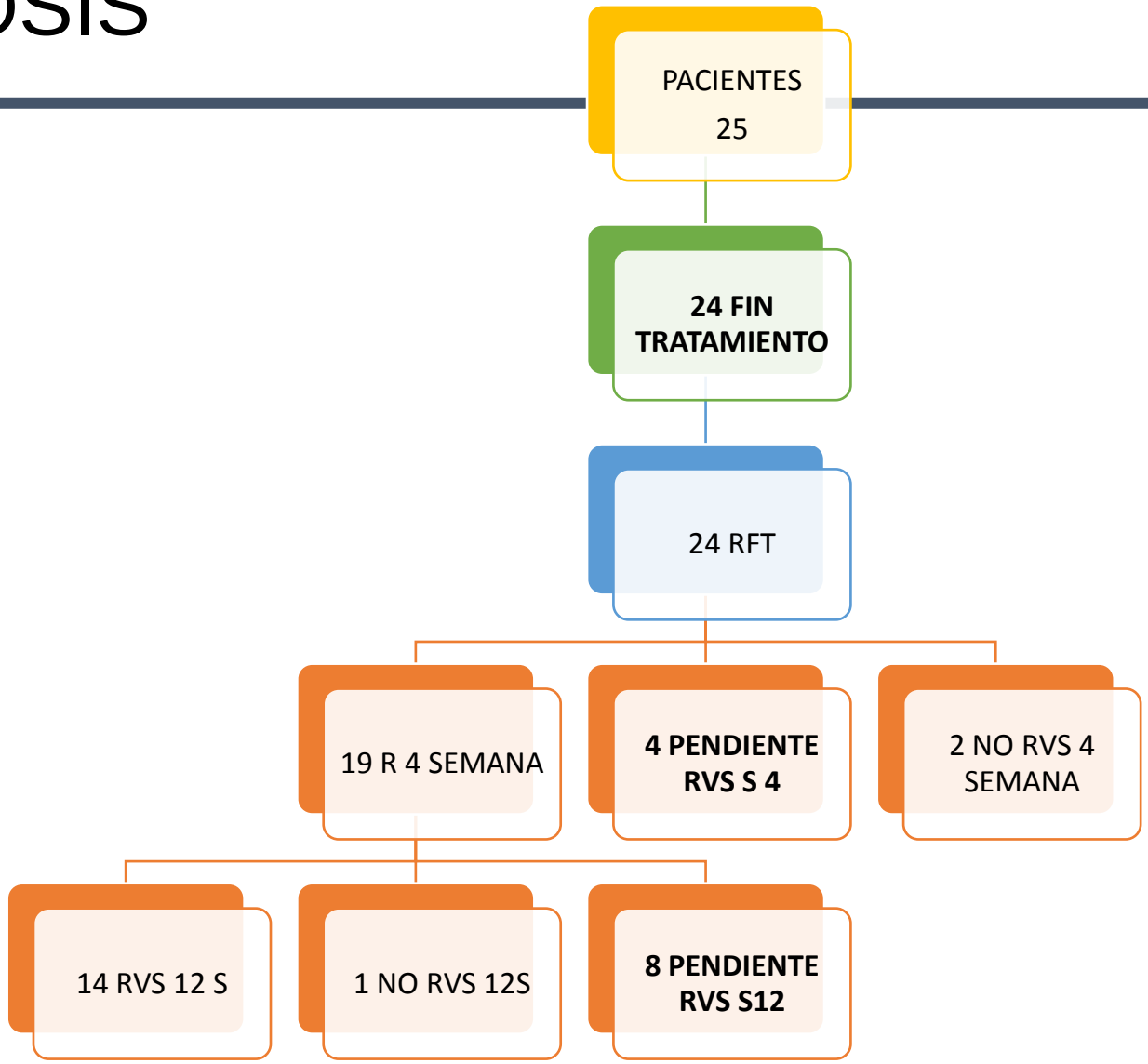
	RFT	RV 4S	RVS 12S
GLOBAL	172/172	158/161	125/132
NO CIRROSIS TOH	83/85	76/79	62/68
CIRROSIS TOH	89/89	82/83	6364

SIM+SOF EN TRATAMIENTO Genotipo 4 CIRROSIS

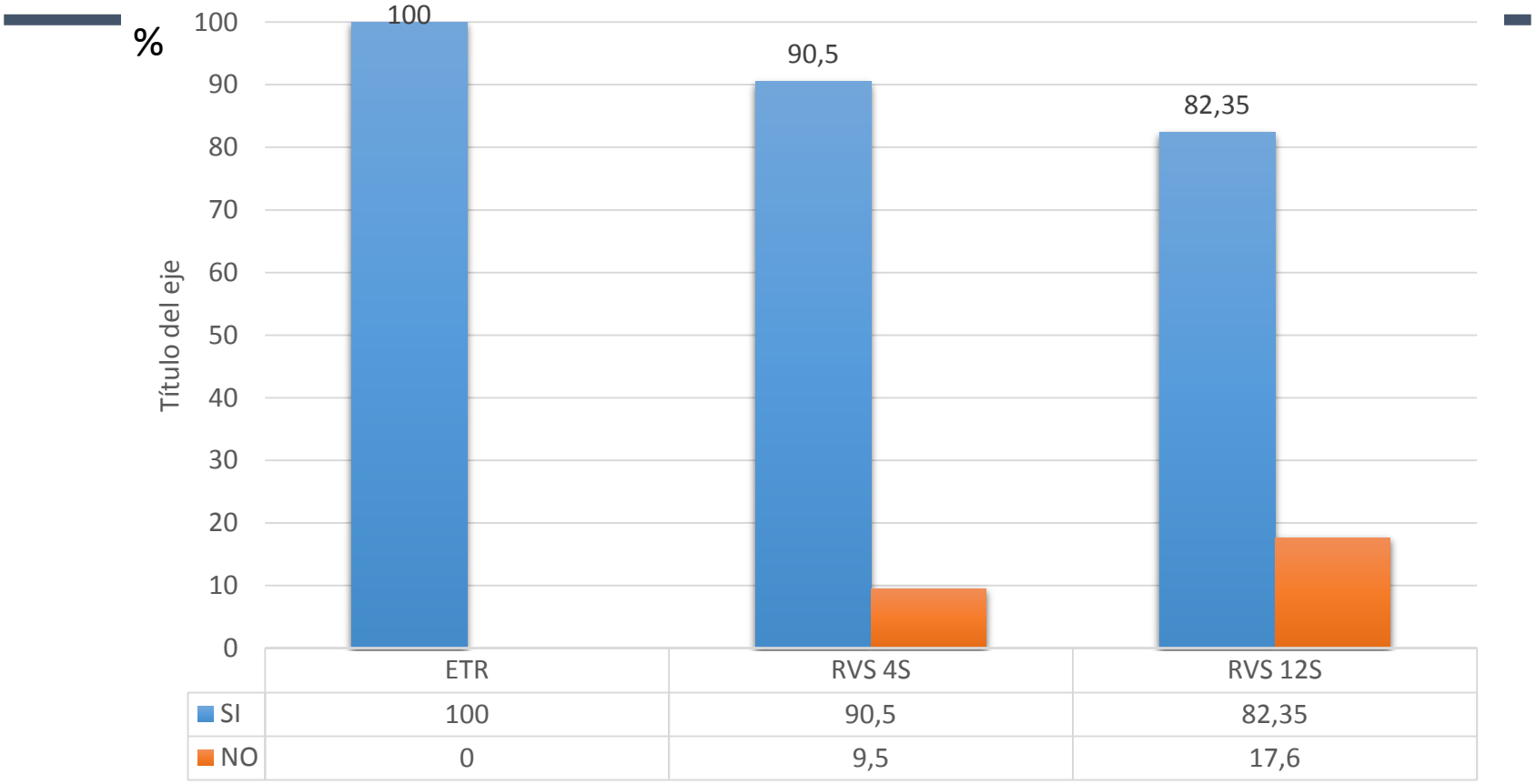
CIRROTICOS GT 4	N=25
Sexo varon	25(100%)
Edad	54,6 ±6,47
ILE 28	CC 1(9,09%) CT 6(54,54%) TT 4(36,36)
Fibrosis F1-F2 F3 F4 CIRROSIS DESCOMP DESCONOCIDA	 0 0 19(83,3%) 3(13,3%) 3
MELD	10,38±5,18

CIRROTICOS GT 4	N=25
TRATAMIENTO PREVIO NO SI DESCONOCIDO	 7(28%) 17(68%) 1(4%)
TIPO TRATAMIENTO IFN±RBV	 17(100%)
RESPUESTA TRATAMIENTO PREVIO NULL RESPONDER RESPONDEDOR LENTO RECAEDOR DESCONOCIDO	 8(47,0%) 3(17,6%) 5(29,41%) 1(5,8%)

TRATAMIENTO GENOTIPO 4 CIRROSIS



RESPUESTA VIRAL SOSTENIDA EN PACIENTES CIRROTICOS GENOTIPO 4



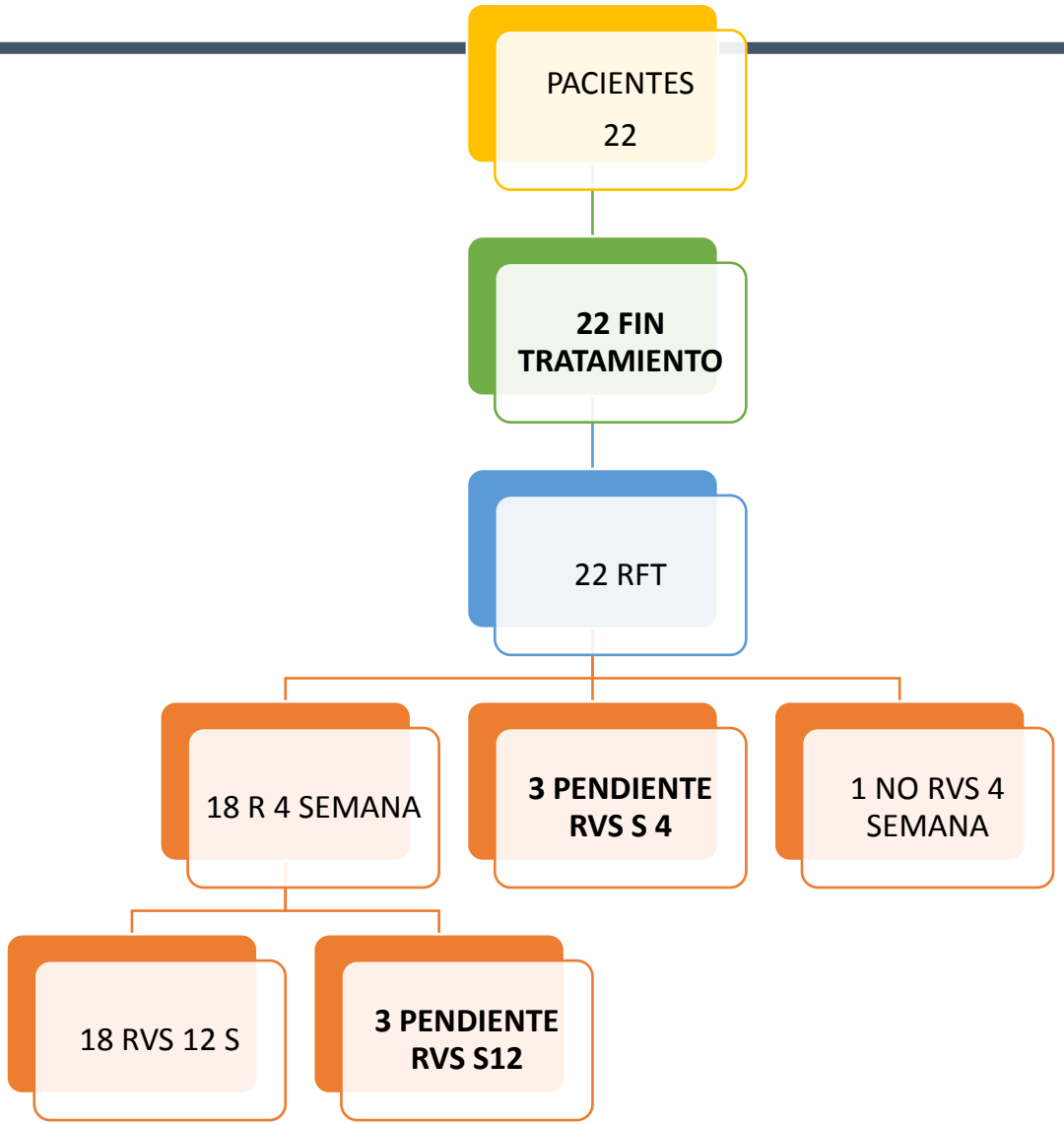
	TOTAL	RV	NO	PENDIENTE
FIN TRATAMIENTO	24	24	0	1
4 SEMANA	21	19	2	4
12 SEMANAS	17	14	3	8

SIM+SOF EN TRATAMIENTO Genotipo 4 POSTOH

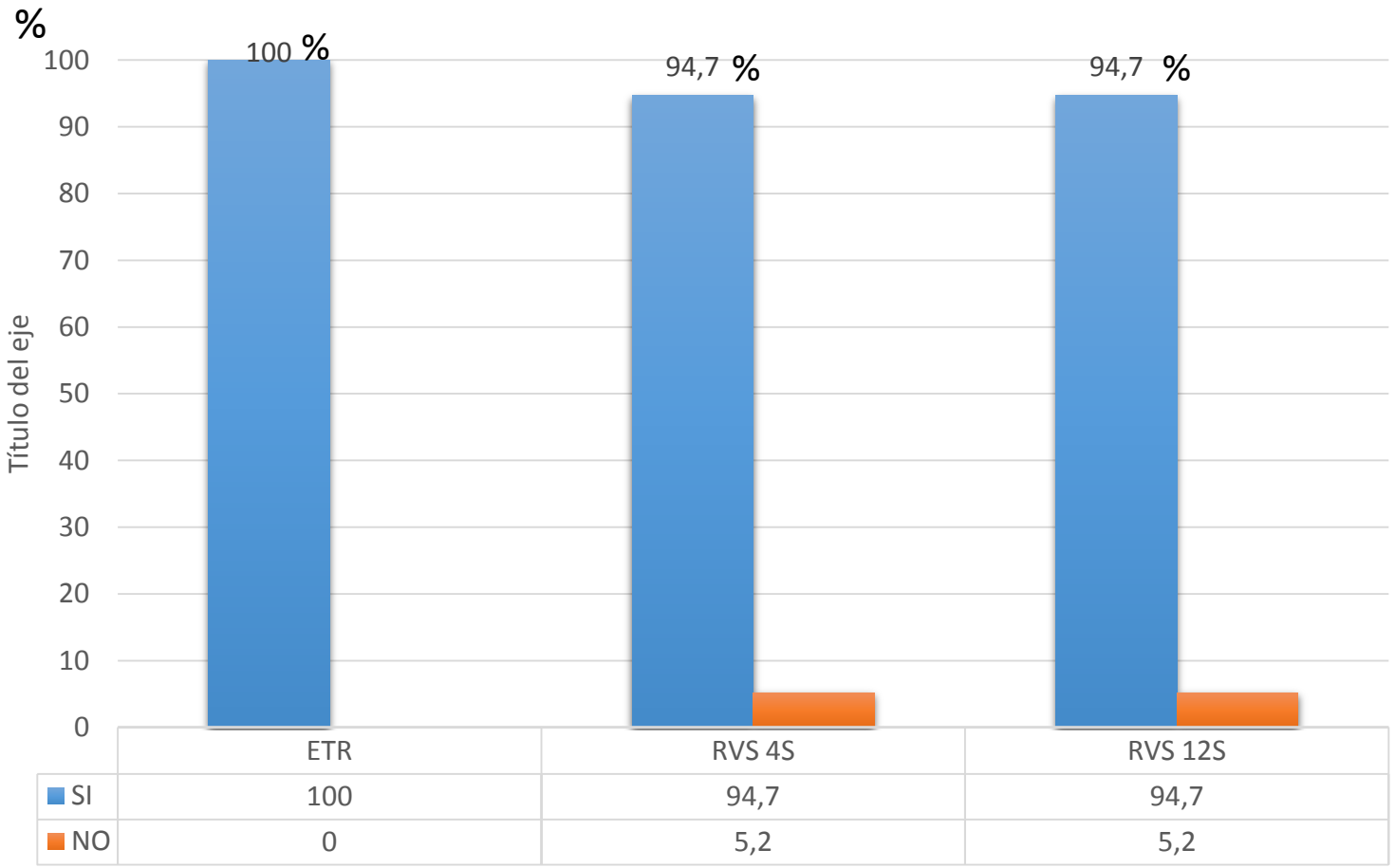
POSTOH	N=22	
Sexo varon	22(100%)	
Edad	52,6 ±8,98	
ILE 28	CC	0
	CT	3
	TT	3
Fibrosis		
F1-F2	6(27,3%)	
F3	9(40,9%)	
F4	7(31,8%)	
CIRROSIS DESCOMP	0	

POSTOH	N=22
TRATAMIENTO PREVIO	
NO	14(63,6%)
SI	8(36,3%)
TIPO TRATAMIENTO	
IFN±RBV	100%
RESPUESTA TRATAMIENTO PREVIO	
NULL RESPONDER	7(87,5%)
RESPONDEDOR LENTO	1(4,54%)
RECAEDOR	0

TRATAMIENTO SIM+SOF GENOTIPO 4 POSTRASPLANTE HEPATICO



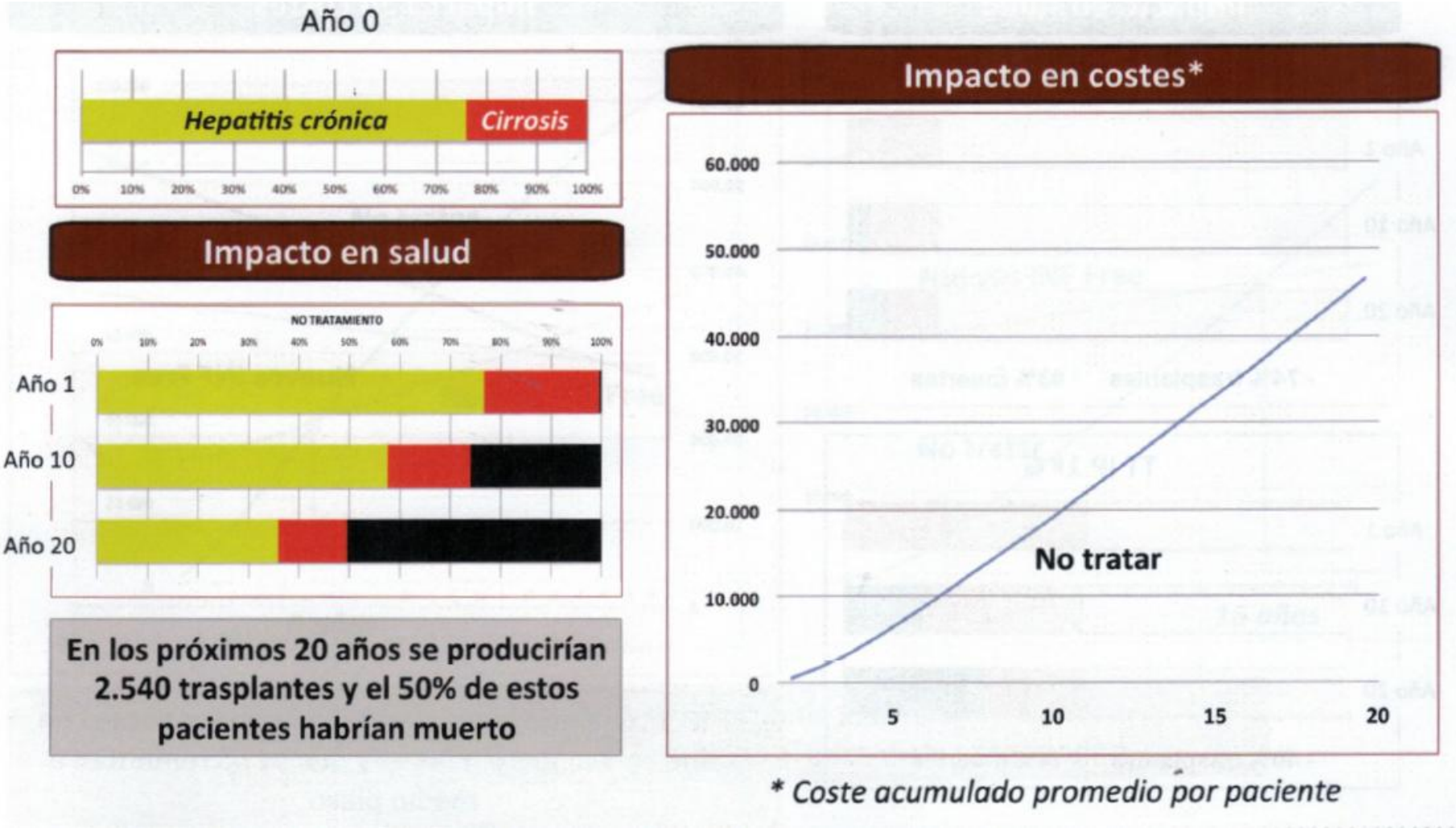
RESPUESTA VIRAL SOSTENIDA EN PACIENTES TRASPLANTADOS GENOTIPO 4 SIM+SOF



	TOTAL	RV	NO	PENDIENTE
FIN TRATAMIENTO	22	22	0	0
4 SEMANA	19	18	1	3
12 SEMANAS	19	18	1	3

EFICIENCIA

COSTES DE NO TRATAR



¿SON EFICIENTES LOS TRATAMIENTOS IFN-FREE?

Scottish Medicines Consortium

SIMEPREVIR+SOFOSBUVIR

12 semanas

Indicación	Régimen tto.	£/QALY
G1 naive	SMV + SOF x 12s vs. No Tto.	7.622
G1 pretratado	SMV + SOF x 12s vs. No Tto.	7.018

* Coste SMV + SOF x 12s: 57.369 £

https://www.scottishmedicines.org.uk/Home

Conclusiones

- Simeprevir ha sido evaluado en ensayos clinicos y más ampliamente en cohortes de la vida real, incluyendo los receptores de trasplante hepatico.
- Los resultados de los ensayos, pero tambien en las cohortes de vida real, han mostrado tasas de RVS superiores al 90% en la mayoría de los estudios.
- La seguridad de esta combinación es muy elevada, sobre todo cuando se usa sin Ribavirina
- En la cohorte de la SETH, la combinación ha sido utilizada en un numero elevado de pacientes y la RVS a las 4 y 12 semanas en cirróticos y en trasplantados hepáticos es superior al 90% en Genotipo 1 y ligeramente menor en Genotipo 4.

NUNCA

Una solución puede ser un problema

Hospital General Universitari d'Alacant

GENERALITAT VALENCIANA

Clínica Universitaria Universidad de Navarra

Clínico Universitario Lozano Blesa

Arrixaca Hospital Universitario "Virgen de la Arrixaca"

HOSPITAL UNIVERSITARIO CENTRAL de ASTURIAS

Vall d'Hebron Hospital

Servicio Andaluz de Salud CONSEJERÍA DE SALUD

Hospital Universitario Reina Sofía

HOSPITALES UNIVERSITARIOS Virgen del Rocío

Hospital Universitario Infanta Cristina

La Fe
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COMPLEXO HOSPITALARIO A Coruña

SERVICIO GALEGO DE SAÚDI

Gurutzeta Ospitalea Hospital Cruces

HOSPITAL UNIVERSITARIO RÍO HORTEGA

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Hospital Universitario Gregorio Marañón

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