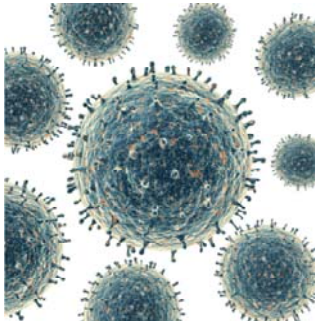
JORNADAS 2014

DE ACTUALIZACIÓN
EN ATENCIÓN FARMACÉUTICA
AL PACIENTE
CON PATOLOGÍAS VÍRICAS

24-25 de abril, 2014
Madrid



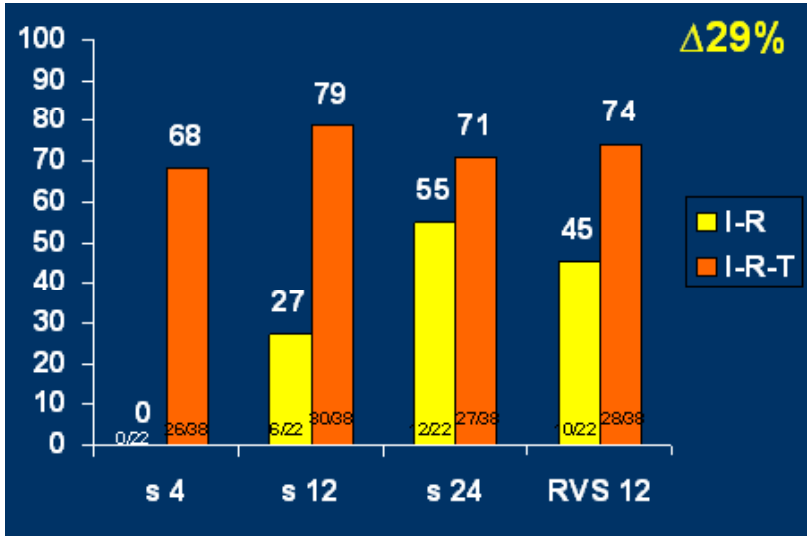
Resultados de la práctica clínica en la coinfección VIH/VHC

Miguel A von Wichmann

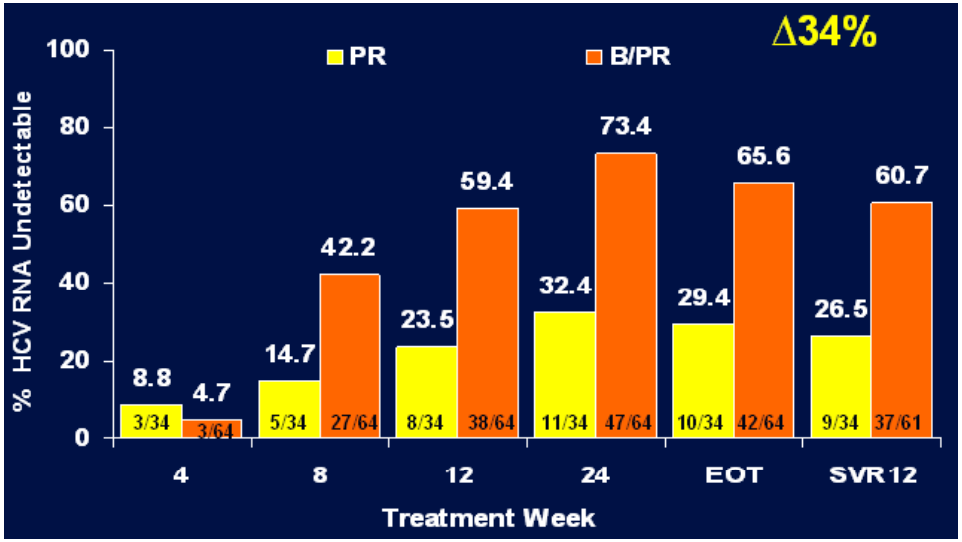
Hosp Univ Donostia, San Sebastián

RVS con AAD en pacientes coinfectados Gt-1 sin tratamiento previo (EC)

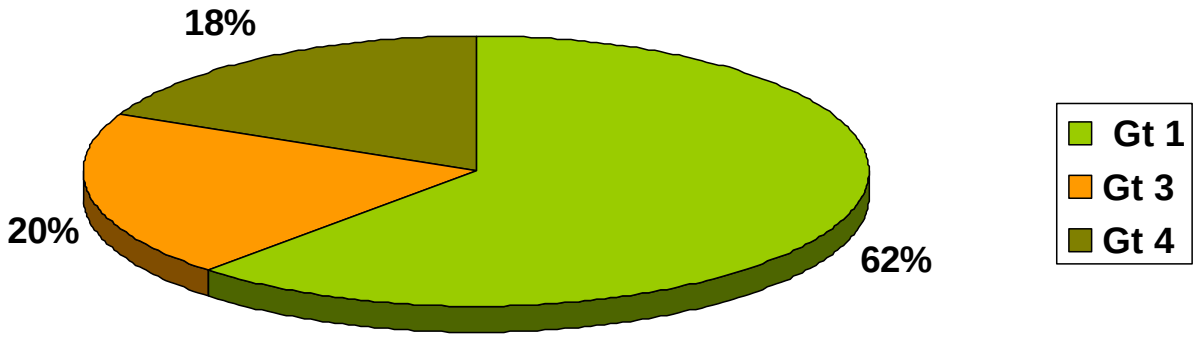
TVR



BOC



Distribución de genotipos y RVS en pacientes coinfectados



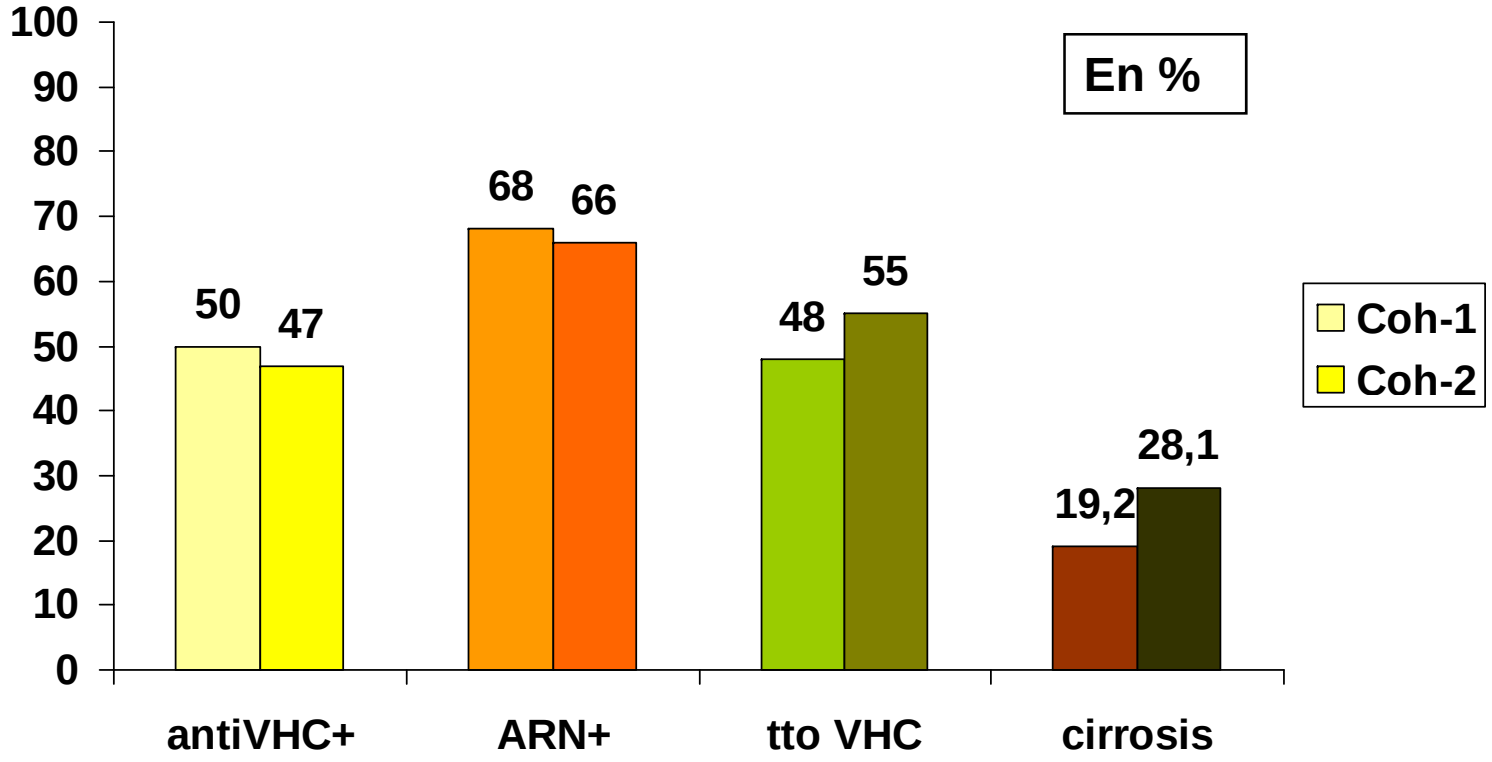
N=1701 pacientes tratados IFNp+RBV (RVS)	
Gt 1-4	25%
Gt 2-3	61%

Cifuentes C, et al. Enf Infecc Microbiol Clin 2012.

Berenguer J, et al, J Antimicrob Chemother 2011

Situación de los pacientes coinfectados VHC/VIH en España (Cohorte GESIDA)

Estudio 5707, datos de 43 hospitales con 1458 pacientes (Coh-1) y 3 hospitales de Madrid con 1549 pacientes (Coh-2) (años 2009-2010)



#PO41, J Gonzalez-García. IV Congreso de Gesida 2012.

BOC/TVR 6 meses de seguimiento en centros españoles

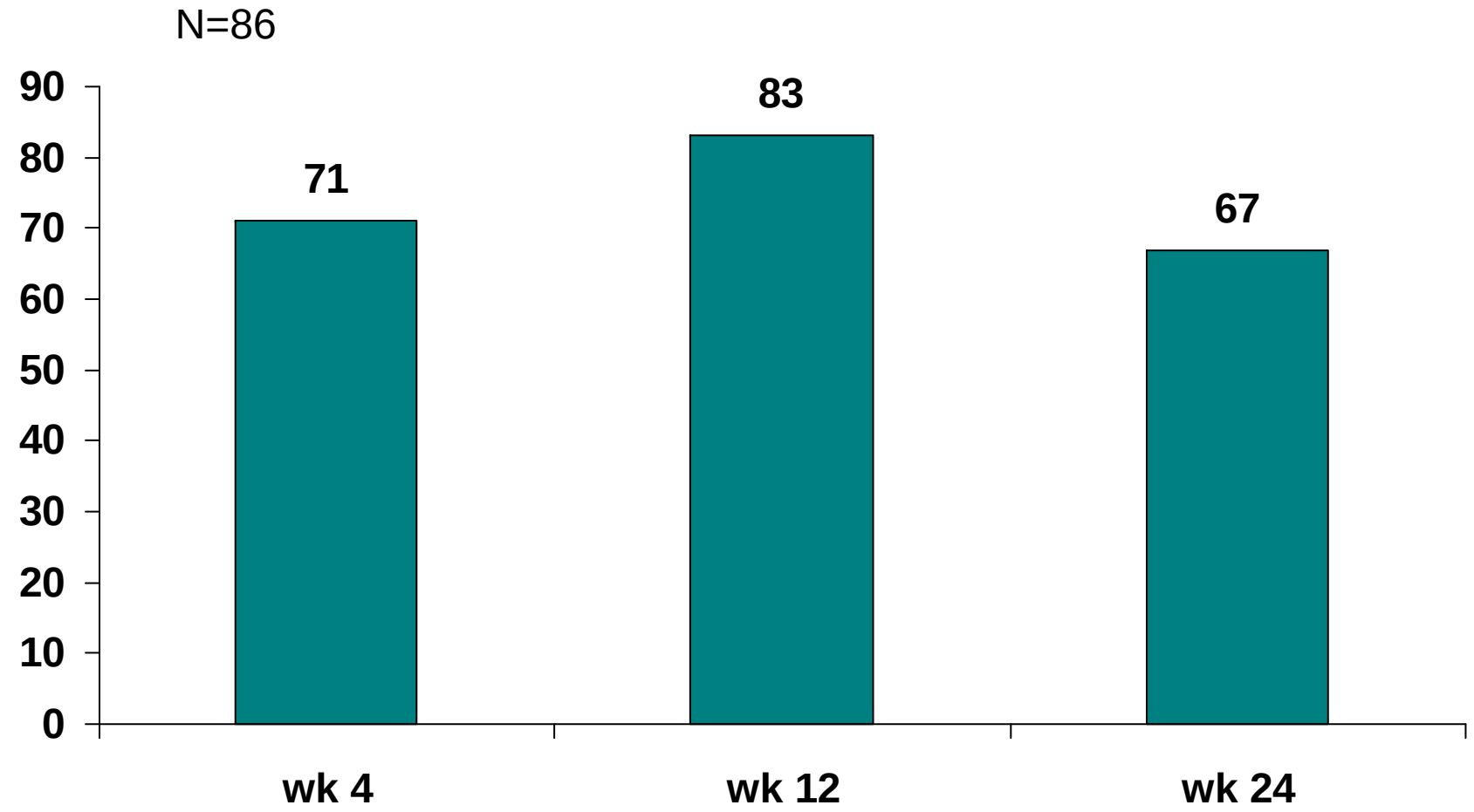
- En los centros participantes, se incluyeron todos los pacientes con fibrosis avanzada que comenzaron tratamiento con BOC/TVR y al menos, 6 meses de seguimiento.
- El estadiaje de la fibrosis hepática se hizo mediante biopsia en dos casos y por elastografía los otros (F3>9,5 kPa y F4>12.5 KPa).
- Todos fueron tratados con triple terapia con, IFN pegilado alpha2a/2b, ribavirina ajustada a peso y boceprevir. El 76% inició la terapia con una fase de lead-in.
- La toxicidad se cuantificó con la escala ACTG.

Von Wichmann MA, et al #1874. AASLD 2013
Von Wichmann et al #P016. V Congreso GESIDA 2013

Baseline characteristics TVR

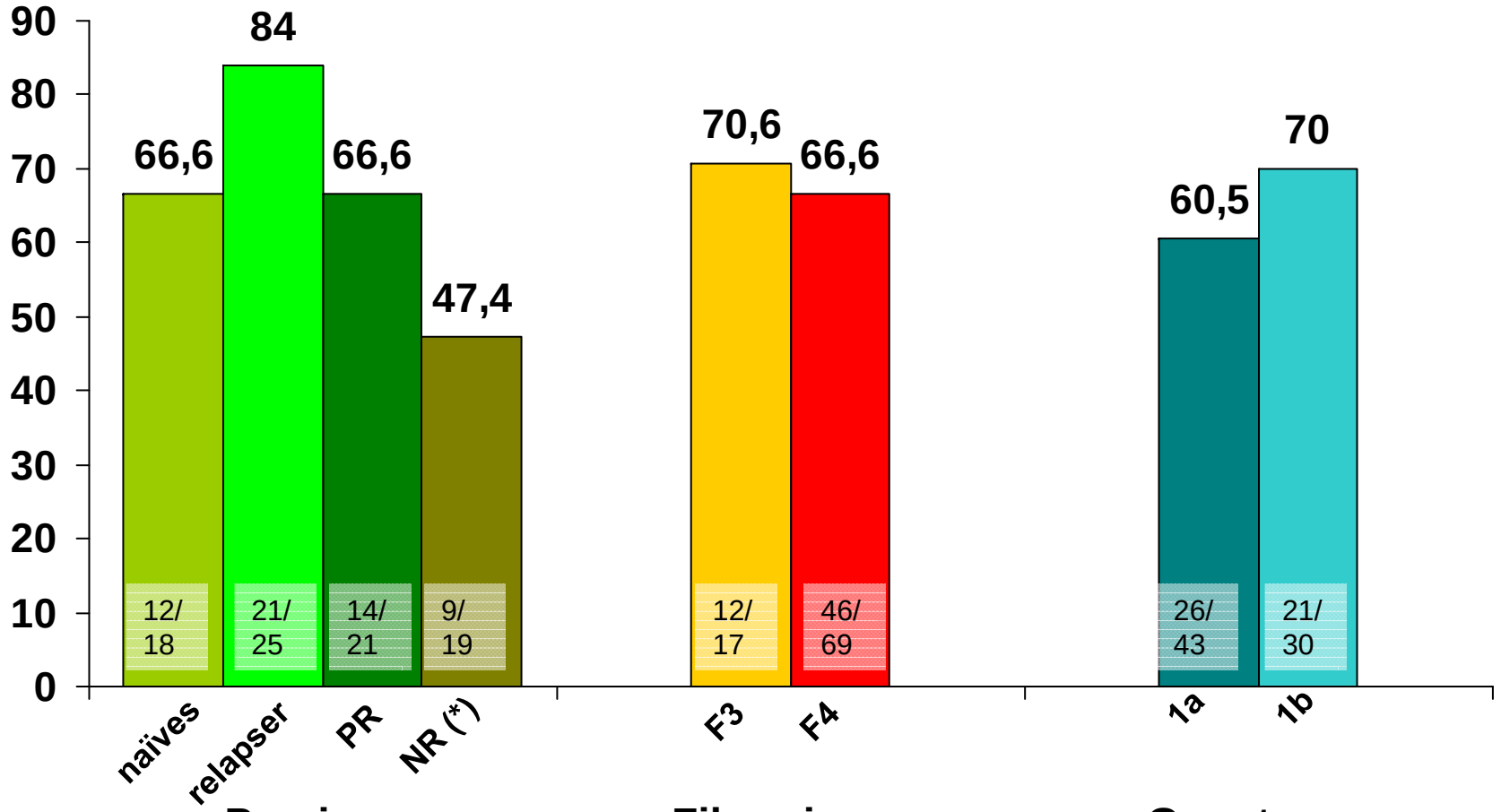
	N=86
Age (mean, SD)	48,7 ± 5,1
Males	85 %
Weight (kg)	73 ± 13
CD4 (mean, range)	716 (144.1555)
HIV viral load < 20 copies	87,2 %
ARTV (number)	83 / 86
-1-2 nucs/nuct	77
-RAL	47
-ATVr	28
-ETV	20
-EFV	3
-MVC	2
Genotype 1a / 1b / 1nt / mixed	43 / 30 / 11 / 2
F3 / F4 number (%)	17 / 69 (20 / 80 %)
HCV-VL >800K IU	72 %
IL28B genotype CC number (%)	22 / 72 (30,6%)
Naïves	18 (21%)
Relapsers	25 (29%)
Breakthrough	2 (2%)
Partial responders	21 (24%)
Null responders	19 (22%)

HCV-VL undetectable ITT (%)
TVR



Under 15-17 copies

Viral response at 24 weeks
TVR



(*) all were F4

Response by antirretroviral (TVR)

ARVT (other than nucleosides)	number	(%)
RAL	21 / 34	61,8%
RAL+2nd drug	6 / 9	66,6%
ATVr	16 / 24	66,6%
ETV	7 / 9	77,8%
EFV	3 / 3	100%
Others	3 / 4	75%
No therapy	2 / 3	66,6%

Discontinuation (TVR)

Treatment discontinuation	**29 (33,7%)**
Patient decision	3
Adverse events	3
Exitus	3 (1 liver related)
Breakthrough	12
Failure on treatment	8

Breakthrough 10/12 in patients with genotype 1a

Safety (TVR)

Decompensation (n)	2
Bacterial infection	
abscess	5
urinary tract infection	3
pneumonia	1
gastroenteritis	1
sepsis	1

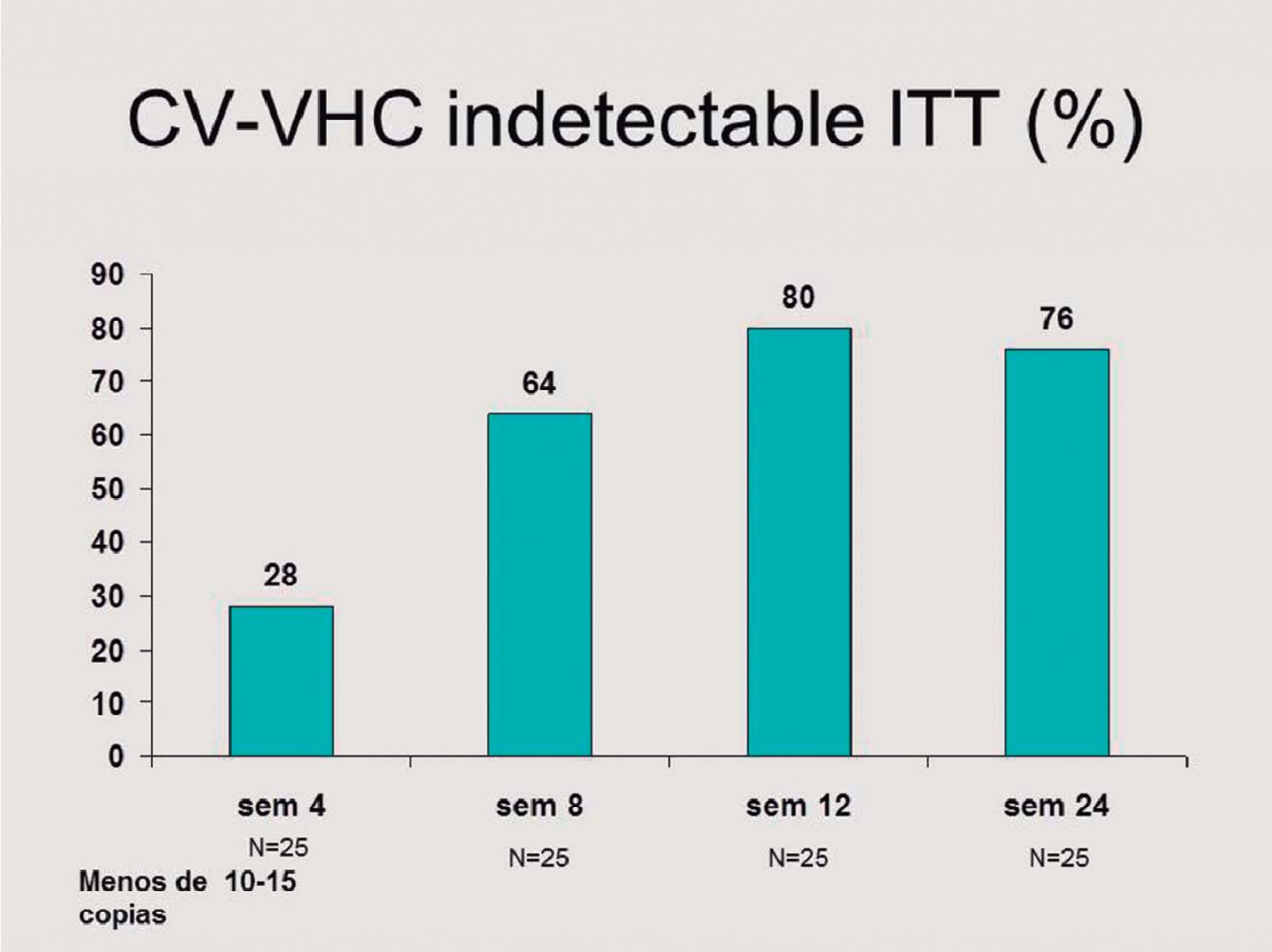
Severe adverse events (death, liver decompensation or admission) happened in 4/66 patients with more than 100.000 platelets/mm3 and 1/20 under 100.000 platelets/ mm3.

Características basales BOC

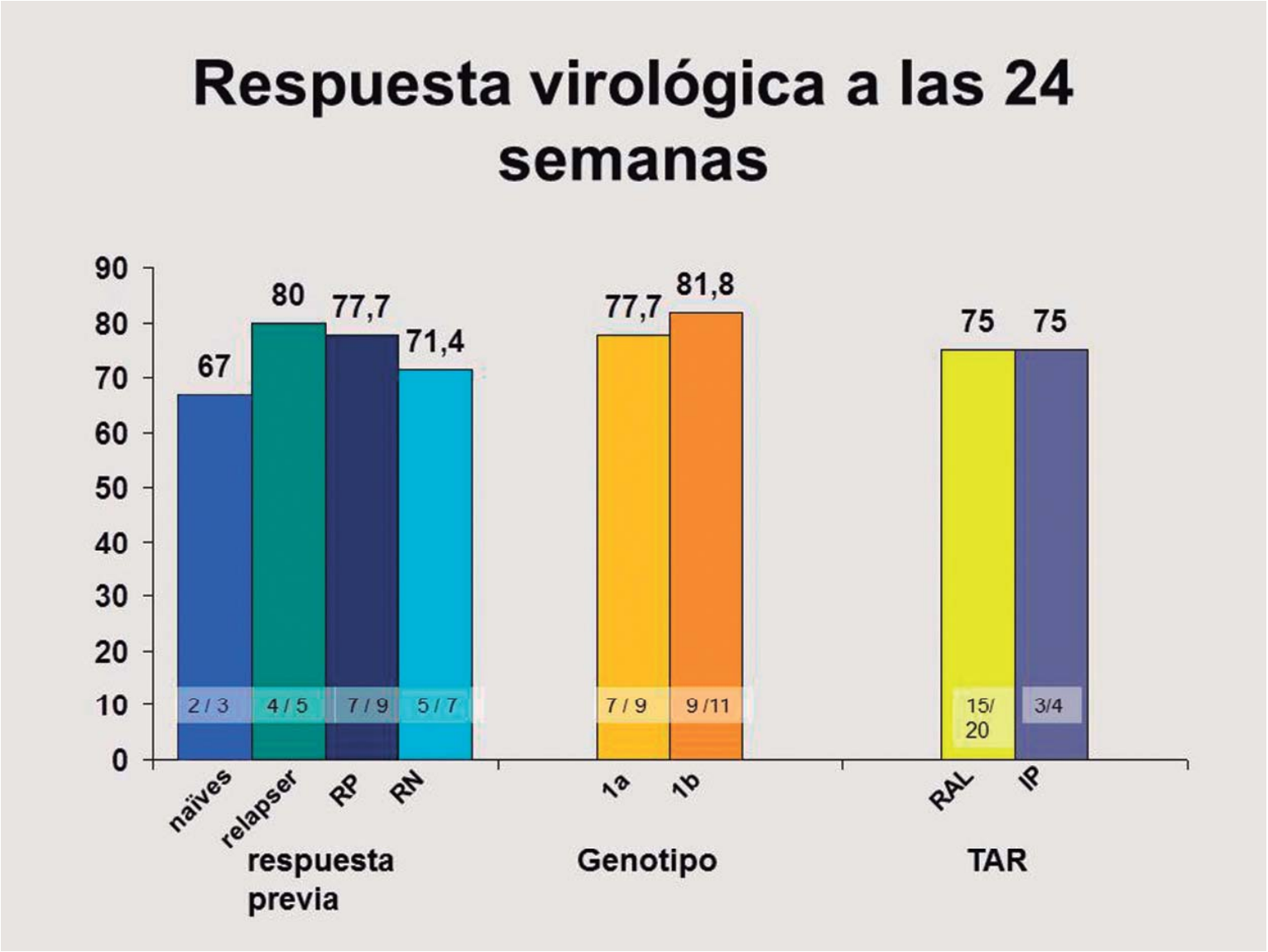
Características basales

	N=25
Edad (media, DS)	48 ± 4
Varones	84 %
Peso (kg)	70 ± 9.5
CD4 (meadia, rango)	527 (216,962)
CV-VIH < 20 copias	80 %
ARTV (numero)	25/25
- 1-2 nucs/nuct	22
- RAL	24
- ATVr	2
- FOSr	1
- LPVr	1
- MVC	1
Genotipo 1a / 1b / 1nt / mixto	9 / 11 / 2 / 3
F4 (numero (%))	24 / 25 (96 %)
CV-VHC >800K IU	76 %
IL28B genotipo CC numero (%)	12 / 23 (52 %)
Naïves	3 (12 %)
Recaedores	5 (20 %)
Respondedores parciales	9 (36%)
Respondedores nulos	7 (28%)
Toxicidad	1 (4%)

Boceprevir en pacientes coinfectados



BOC


Respuesta virológica a las 24 semanas
90
80
70
60
50
40
30
20
10
0
67
80
77,7
71,4
77,7
81,8
75
75
2 / 3
4 / 5
7 / 9
5 / 7
7 / 9
9 /11
15/ 20
3/4
naïves
relapser
RP
RN
1a
1b
RAL
IP
respuesta previa
Genotipo
TAR

BOC

Interrupción

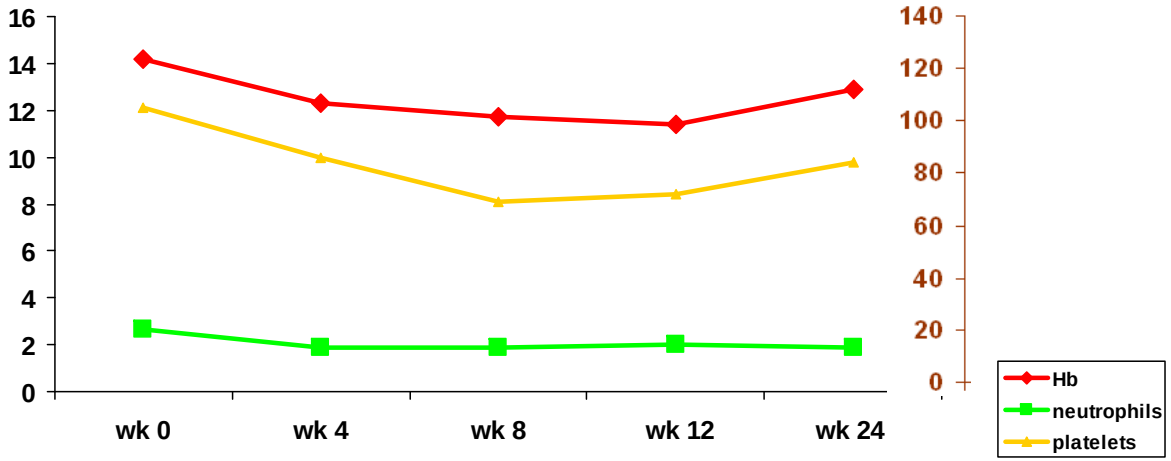
Interrupción del tratamiento	6 (24%)
Fracaso	3
Efectos adversos	3
Exitus	0
Breakthrough	0

Seguridad

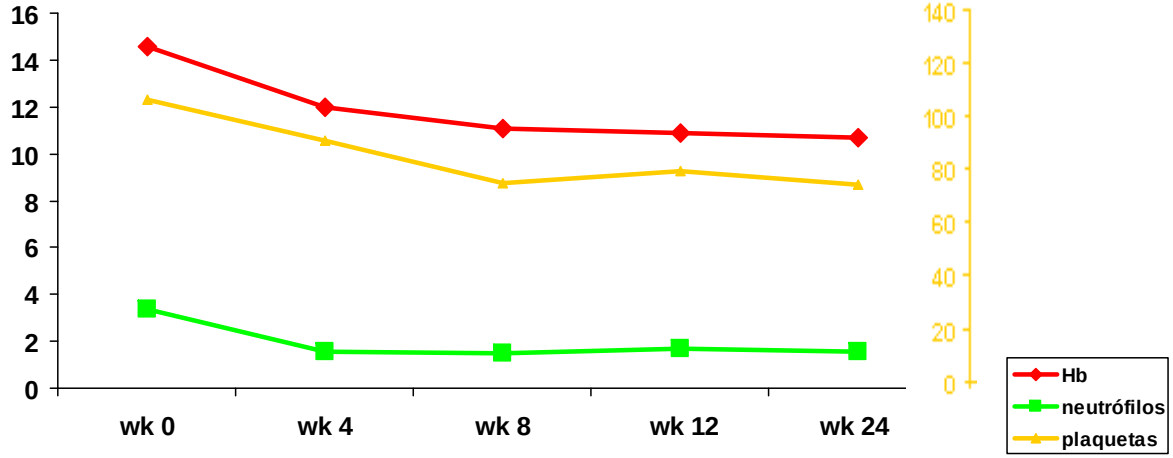
Descompensación (n)	3
Infecciones	
respiratorias	4
colecistitis	1
sepsis	1

Toxicidad hematológica

TVR



BOC



Toxicidad hematológica

TVR

Toxicity (ACTG scale)	grade 3	grade4
Hb	19,8%	7%
neutrophils	30,2%	1,2%
platelets	66%	4,6%
EPO	18,6%	
transfusion	10,5%	
G-CSF	11,6%	
platelets growth factors	1,2%	

BOC

Toxicidad (escala ACTG)	grade 3	grade4
Hb	32%	8%
neutrofilos	52%	0%
plaquetas	47,4%	0%
EPO	44%	
transfusóon	20%	
G-CSF	20%	
Factores crecimiento plaquetario	4%	

Reflexiones

- Los datos disponibles muestran la factibilidad de tratar a esta población vulnerable de pacientes cirróticos.
- Tras 24 semanas de terapia muestran una tasa de respuesta similar a los pacientes VIH-.
- Los resultados provisionales muestran una toxicidad significativa.

Predictores de rebrote viral en pacientes con fibrosis severa

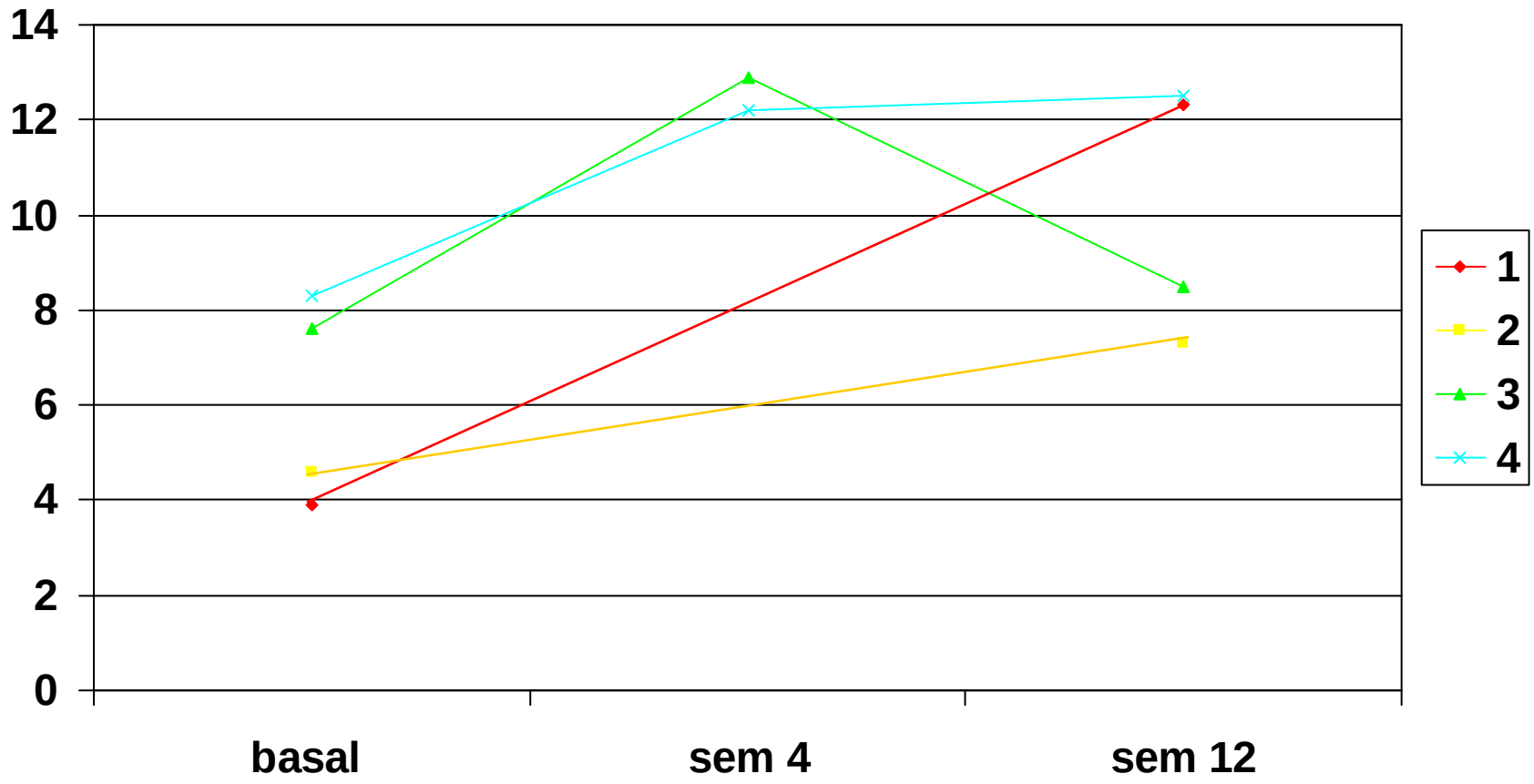
- TPV 66% (n=62), BOC 34% (n=32). HIV/HCV-coinfected (n=37).
- Cirrhotic (86%, n=81),
- Viral rebound 25% (n=19).

multivariate analysis:

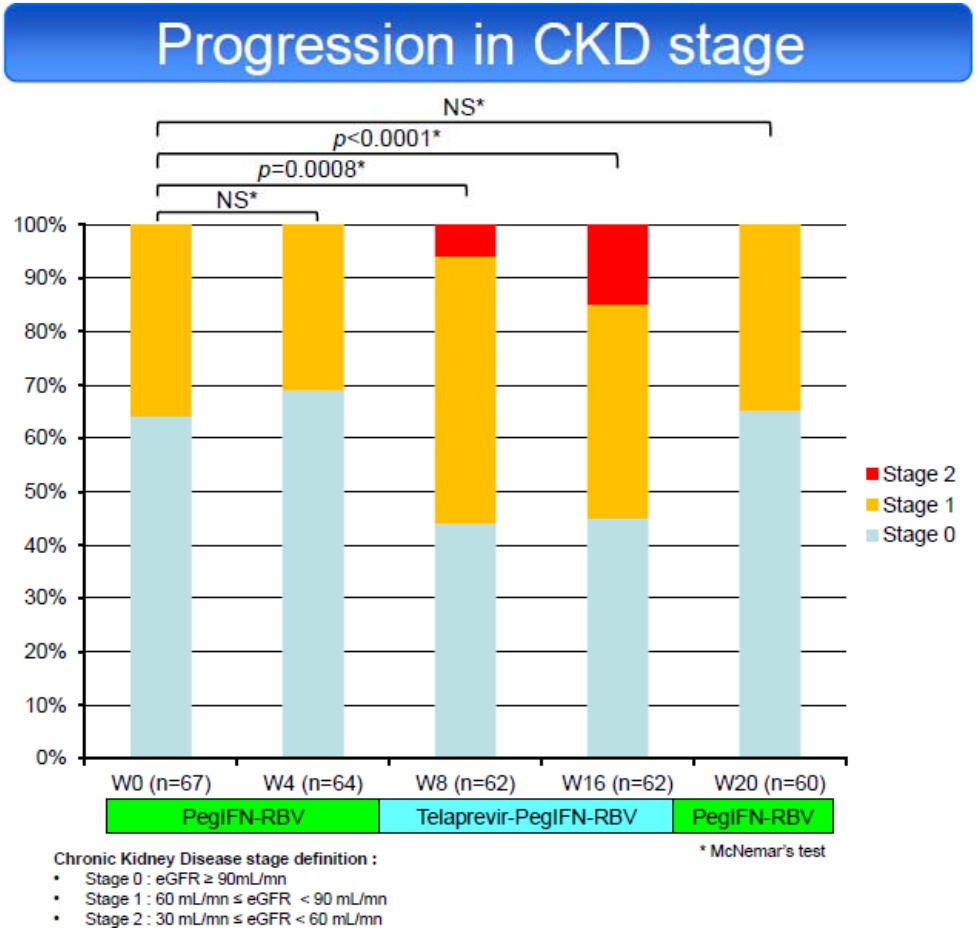
negative HCV-RNA at week 4 (protector)	HR 8.802, 95%CI 1.527-50.749	p=0.015
prior relapse after peg-IFN/RBV(protector)	HR 18.222, 95%CI 1.612-206.011	p=0.019
IL28B TT		p=0.13

#1939, A. Moreno et al. AASLD 2013

Elevaciones asintomáticas del urato con telaprevir



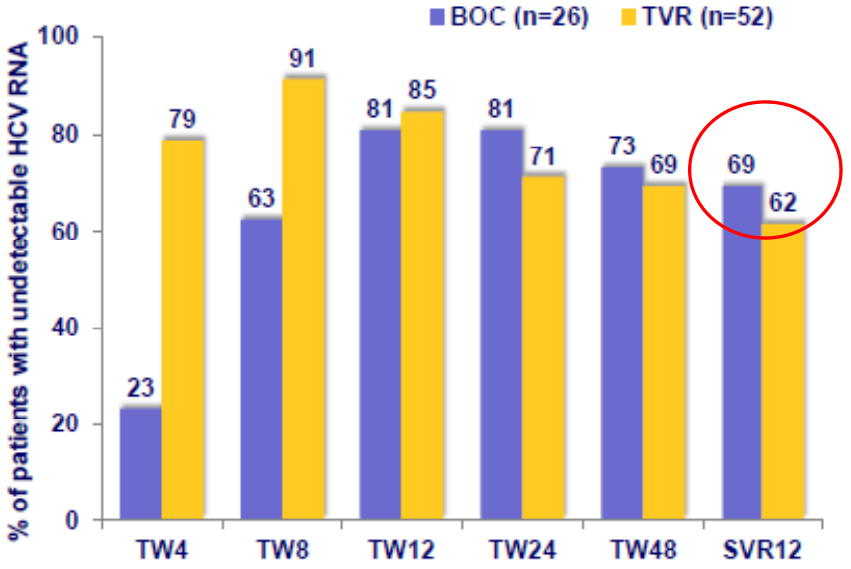
Toxicidad renal en Telaprevih



Cotte L, et al. #664LB.CROI 2014

Estudio cohorte hispano-alemana pacientes coinfectados

Parameter	BOC (n=32)	TVR (n=151)
Age (years)*	46 (43-51)	48 (45-51)
Male gender, no. (%)	26 (81)	128 (85)
IL28B rs12979860 CT/TT, no. (%)±	19 (68)	99 (72)
HCV subtype 1a, no. (%)#	15 (58)	88 (69)
Plasma HCV RNA >600 IU/µL, no. (%)	27 (84)	118 (78)
Cirrhosis, no. (%)¶	21 (75)	74 (53)
Liver stiffness	19.5 (11.7-25.7)	14.8 (10.2-26.5)
Platelets (cells/µL)	136 (90-217)	159 (102-205)
Albumin (g/dL)	4 (3.6-4.15)	4.1 (3.9-4.4)
Alanine aminotransferase, IU/mL*	56 (39-90)	63 (40-97)
Previous response to anti-HCV therapy		
Naives, no. (%)	14 (54)	44 (39)
Null responders, no. (%)	5 (16)	45 (29)
Partial responders, no. (%)	0	21 (14)
Relapsers, no. (%)	7 (22)	25 (17)
Other, no. (%)	6 (19)	16 (11)
Discontinuation due to adverse events	2 (6.3)	17 (11)



Overall SVR12: 50/78 (64.1%)

Neukam K, et al. #660. CROI 2014.

Virological response and tolerance of triple therapy including Telaprevir or Boceprevir in HIV-HCV co-infected cirrhotic patients: real-life early findings from the prospective ANRS CO13 HEPAVIH cohort

Patrick Miailhes[1], Eric Rosenthal[2], Stéphanie Dominguez[3], Philippe Morlat[4], Michel Dupon[5], Marc-Antoine Valantin[6], Camille Gilbert[7], Maria Winnock[7], Dominique Salmon[6], Philippe Sogni[8] and HEPAVIH-ANRS CO13 study group.

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THE LIVER MEETING 2013

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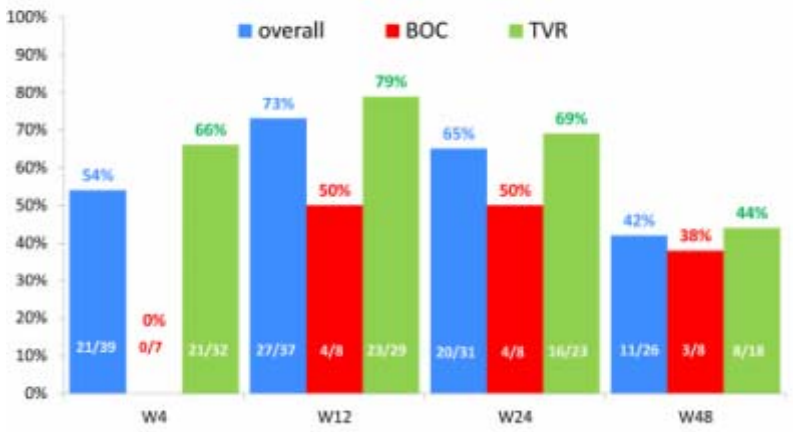
Baseline characteristics of patients

Variables [1]	Overall (n=42)	Boceprevir (n= 8)	Telaprevir (n=34)	p [2]
Age (years)	52 (49-53)	52 (49-58)	52 (48-53)	0.59
Male	33 (79%)	6 (75%)	27 (79%)	1
HCV RNA (log_{10} UI/ml)	6.1 (5.5-6.5)	6.0 (5.4-6.3)	6.1 (5.5-6.6)	0.41
HCV genotype				1
1a	33 (79%)	6 (75%)	27 (79%)	
1b	9 (21%)	2 (25%)	7 (21%)	
Previous anti-HCV treatment status				0.72
Naive	4 (9%)	0 (-)	4 (12%)	
Relapser	2 (5%)	0 (-)	2 (6%)	
Non responder	36 (86%)	8 (100%)	28 (82%)	
Child score				0.47
Child A	39 (93%)	7 (88%)	32 (94%)	
Child B [3]	3 (7%)	1 (12%)	2 (6%)	
HCC before triple therapy	1 (2%)	1 (12%)	0 (-)	0.19
Type of ARV [4]				0.5
Raltegravir	20 (48%)	5 (63%)	15 (44%)	
Atazanavir	15 (36%)	3 (37%)	12 (35%)	
other ARV [5]	7 (17%)	0 (-)	7 (21%)	
CD4 (/mm³)	483 (295-782)	555 (412-802)	466 (293-595)	0.57
HIV viral load < 50 copies/ml	40 (95%)	8 (100%)	32 (94%)	1
Transient elastometry (kPa) (n=37) [6]	19.2 (13.0-30.0)	13.2 (10.6-34.3)	21.1 (14.0-27.4)	0.55
Lead-in phase	11 (26%)	7 (88%)	4 (12%)	<0.0001
Hemoglobin (g/dl) (n=41)	13.9 (12.6-15.7)	12.9 (12.3-13.9)	13.9 (12.6-15.8)	0.14
Albumin (g/l) (n=25)	40 (36.6-42.0)	41.3 (35.5-43.8)	40 (36.6-42.0)	0.91
Albumin < 35 g/l (n=25)	1 (4%)	1 (25%)	0 (-)	0.16
Platelets (Giga/l) (n=41)	123 (77-168)	123 (68-149)	124 (77-169)	0.70
Platelets < 100 Giga/l (n=41)	15 (37%)	2 (29%)	13 (38%)	0.69

Figure 1: Virological response from W4 to W48



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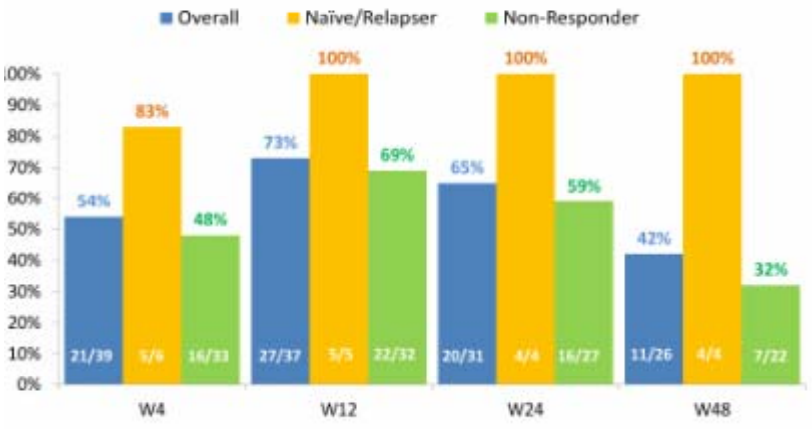
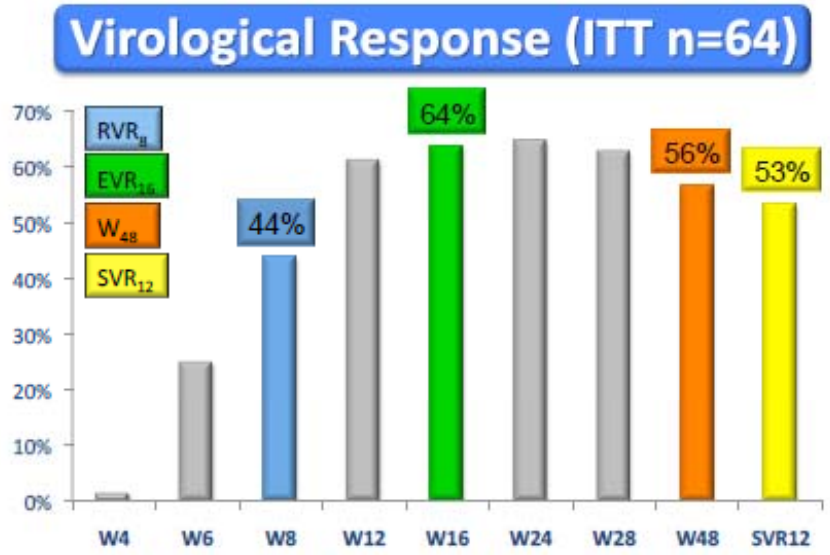


	Overall (N=42)	BOC (n=8)	TVR (n=34)	p
Early discontinuation of HCV therapy.[1]	15 (36%)	5 (63%)	10 (29%)	0.11
Discontinuation reasons (n=15)				0.38
Virological failure	8 (53%)	4 (80%)	4 (40%) [3]	
Breakthrough	3 (20%)	0 (-)	3 (30%)	
Adverse events [2]	4 (27%)	1 (20%)	3 (30%)	
Rash [2]	7 (17%)	1 (13%)	6 (18%)	1
Severe anemia (< 9 g/dl or decrease >4.5 g/dl).	14 (33%)	2 (25%)	12 (35%)	0.70
EPO use	25 (60%)	5 (63%)	20 (59%)	1
Blood transfusion	8 (19%)	1 (13%)	7 (21%)	1

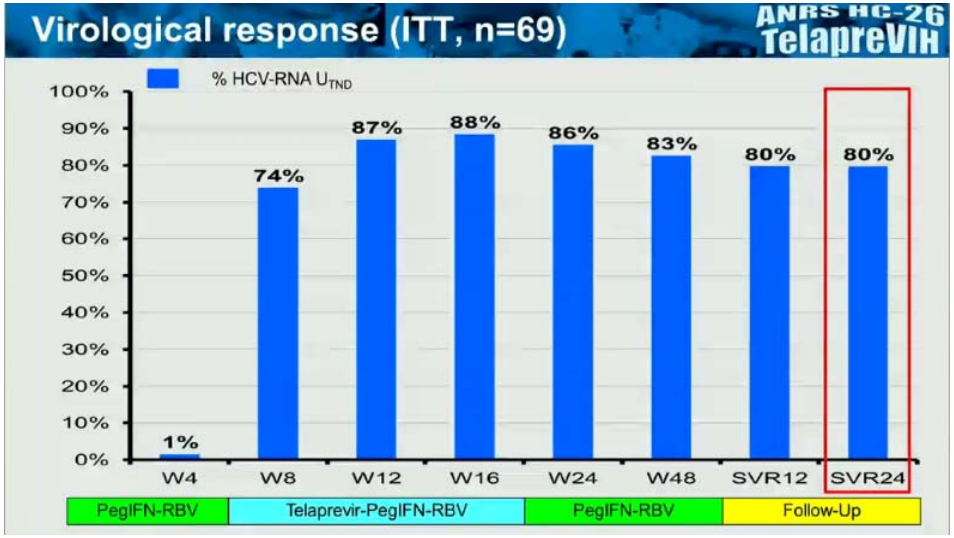
BocepreVIH



- **20 patients presented at least one grade 4 AE.**
- **10 patients stopped HCV treatment for AEs:**

infections in 3(5%), general disorders in 4(6%), acute pancreatitis in 1, neutropenia in 1 and thrombopenia in 1.

TelapreVIH

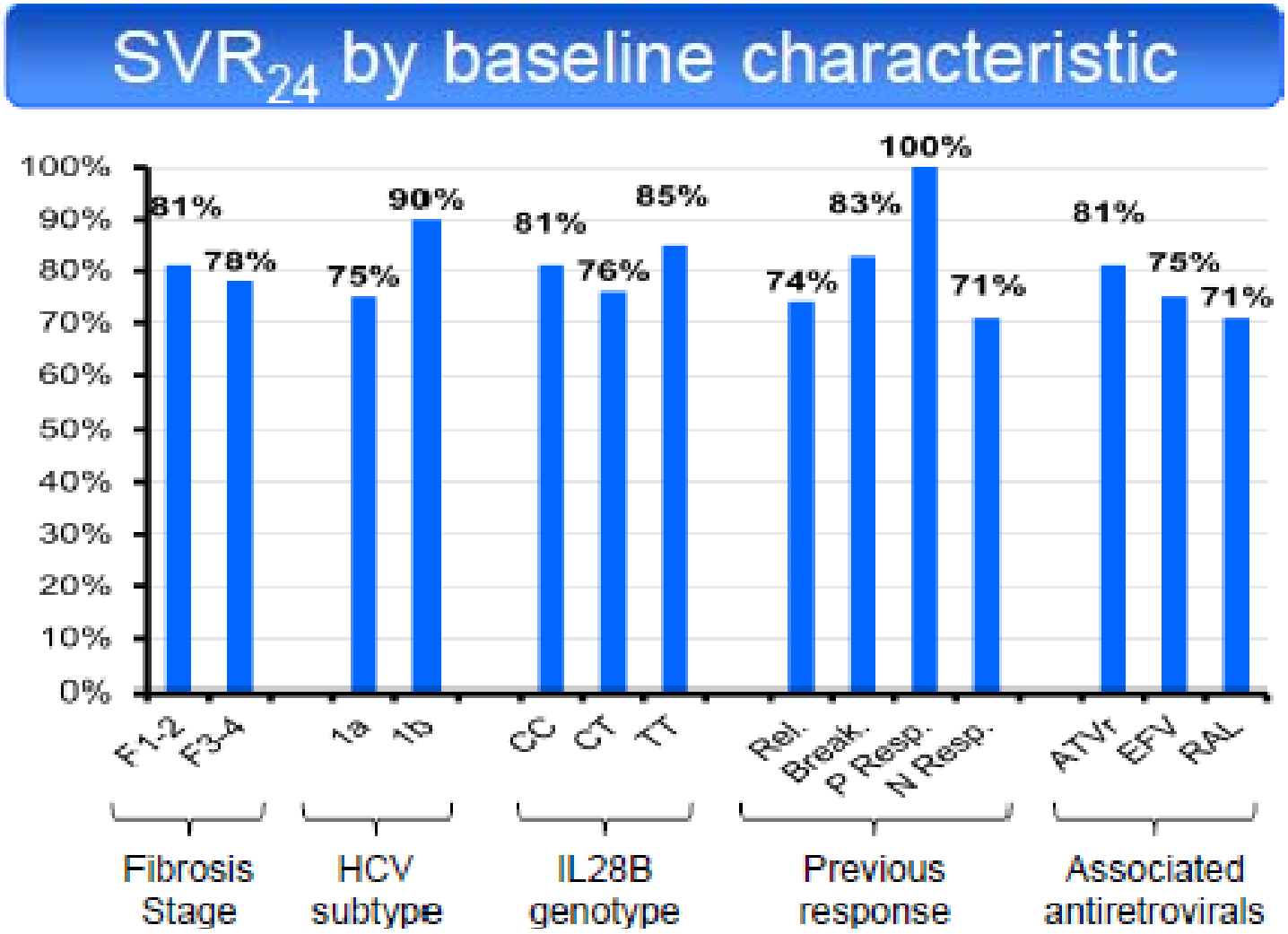


Treatment interruption	Failure	AE
W0-W16	1 (1.4%)	7 (10%)
> W16	3 (4%)	7 (10%)

Poizot-Martin I. CROI 2014

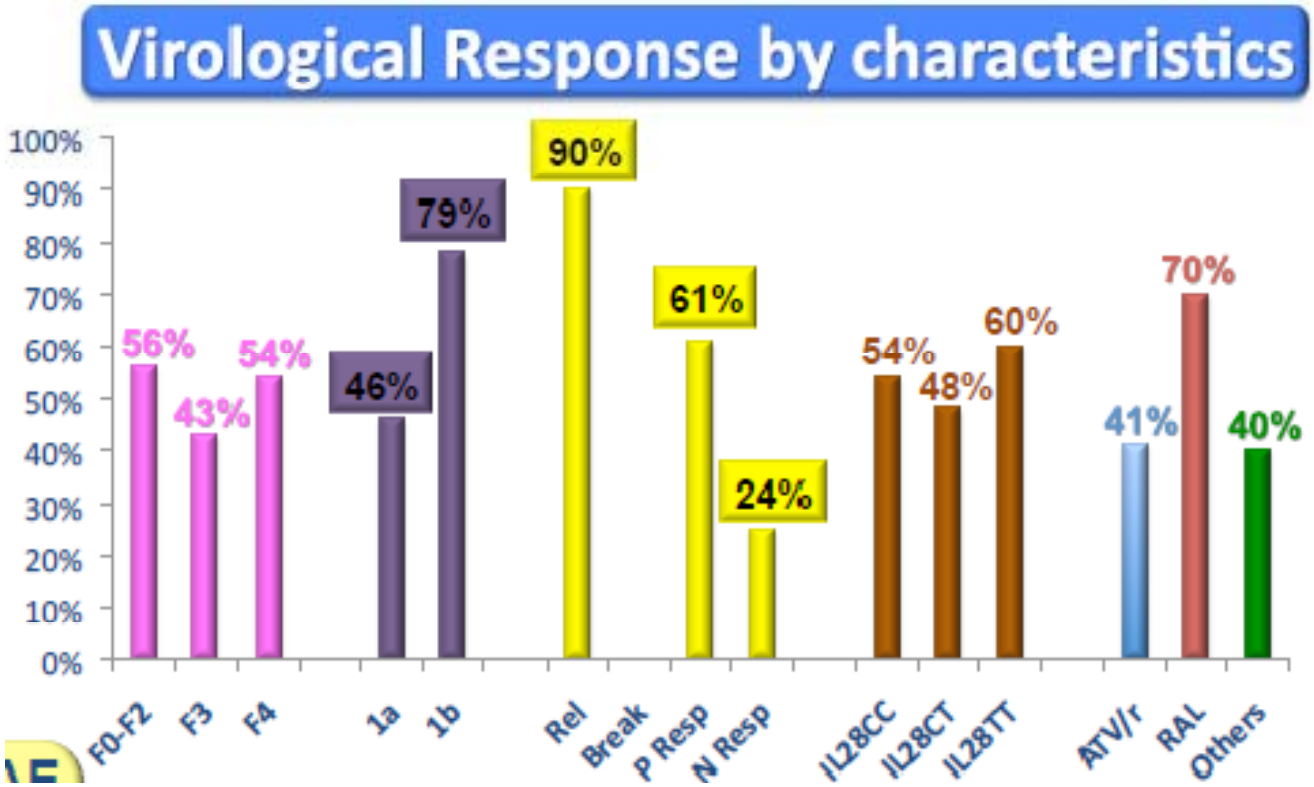
Cotte L, et al. CROI 2014

TelapreVIH



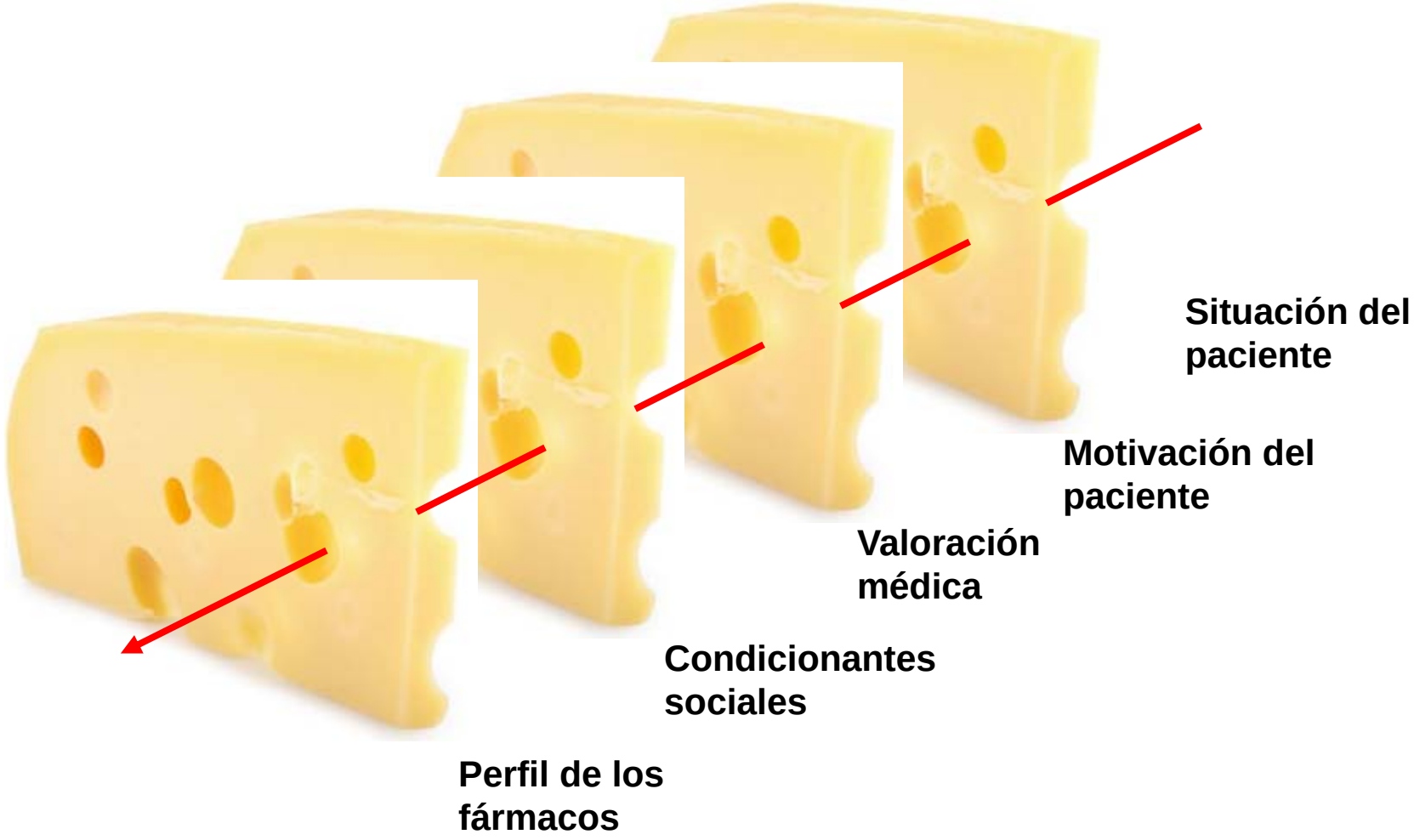
#668. CROI 2014

boceprevih

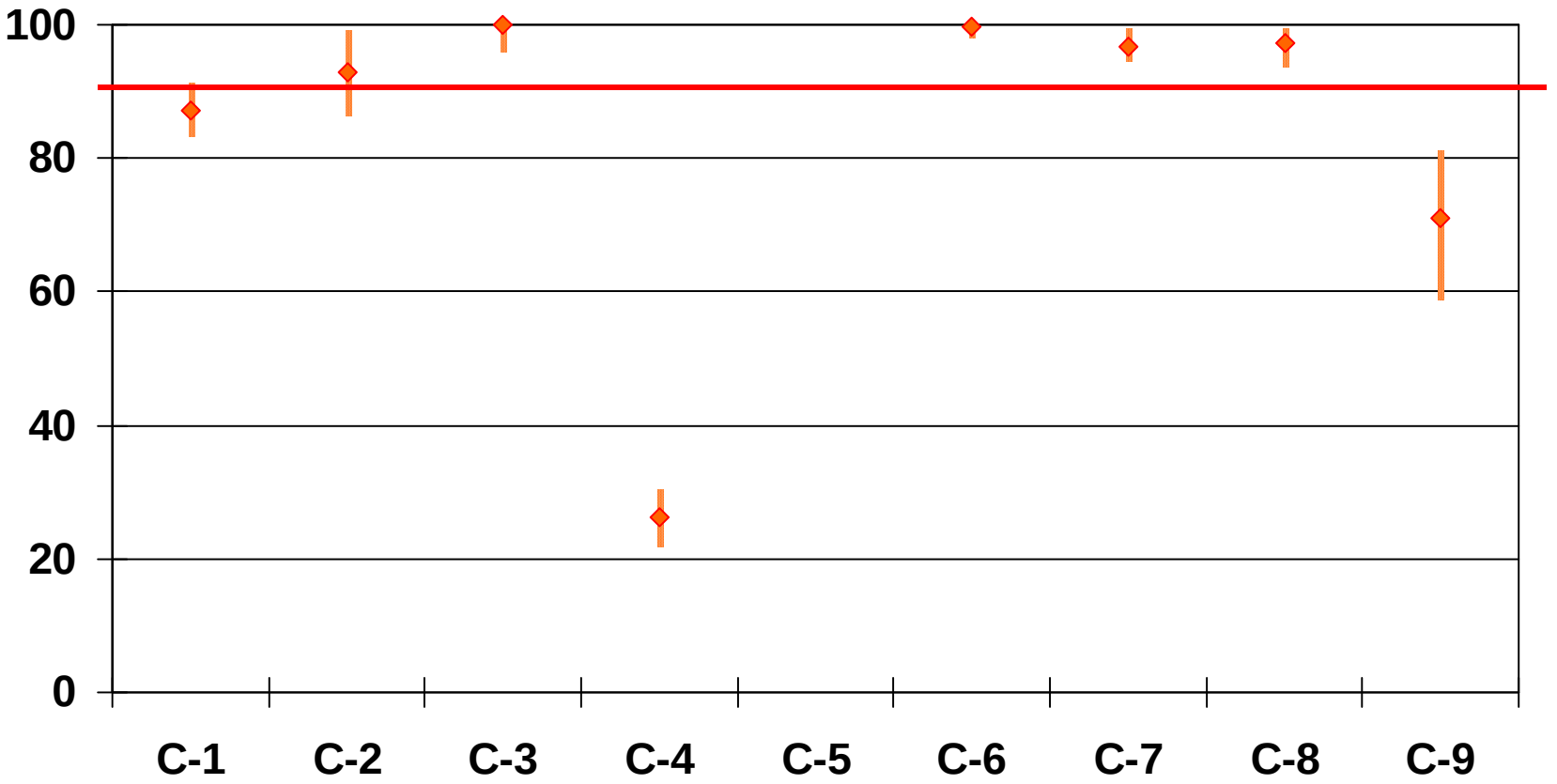


#659 Poizot-Martin I, CROI 2014

Tratamiento de hepatitis C no todo es el fármaco

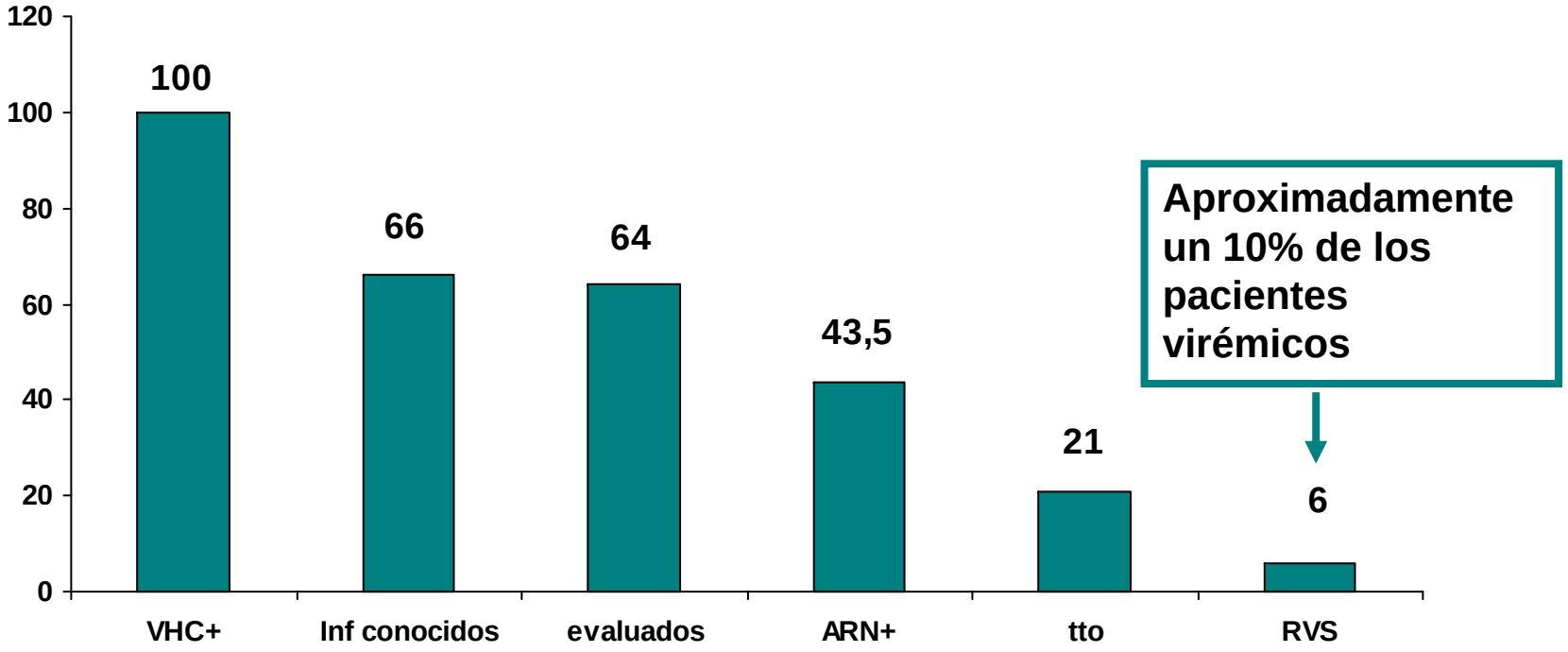


Evaluación del paciente coinfectado por VHC (ARN y estadío de fibrosis en VHC+)



Monitorización indicadores de calidad. IV Congreso GESIDA nov 2012.

¿Que impacto tiene nuestra práctica actual? Pacientes coinfectados

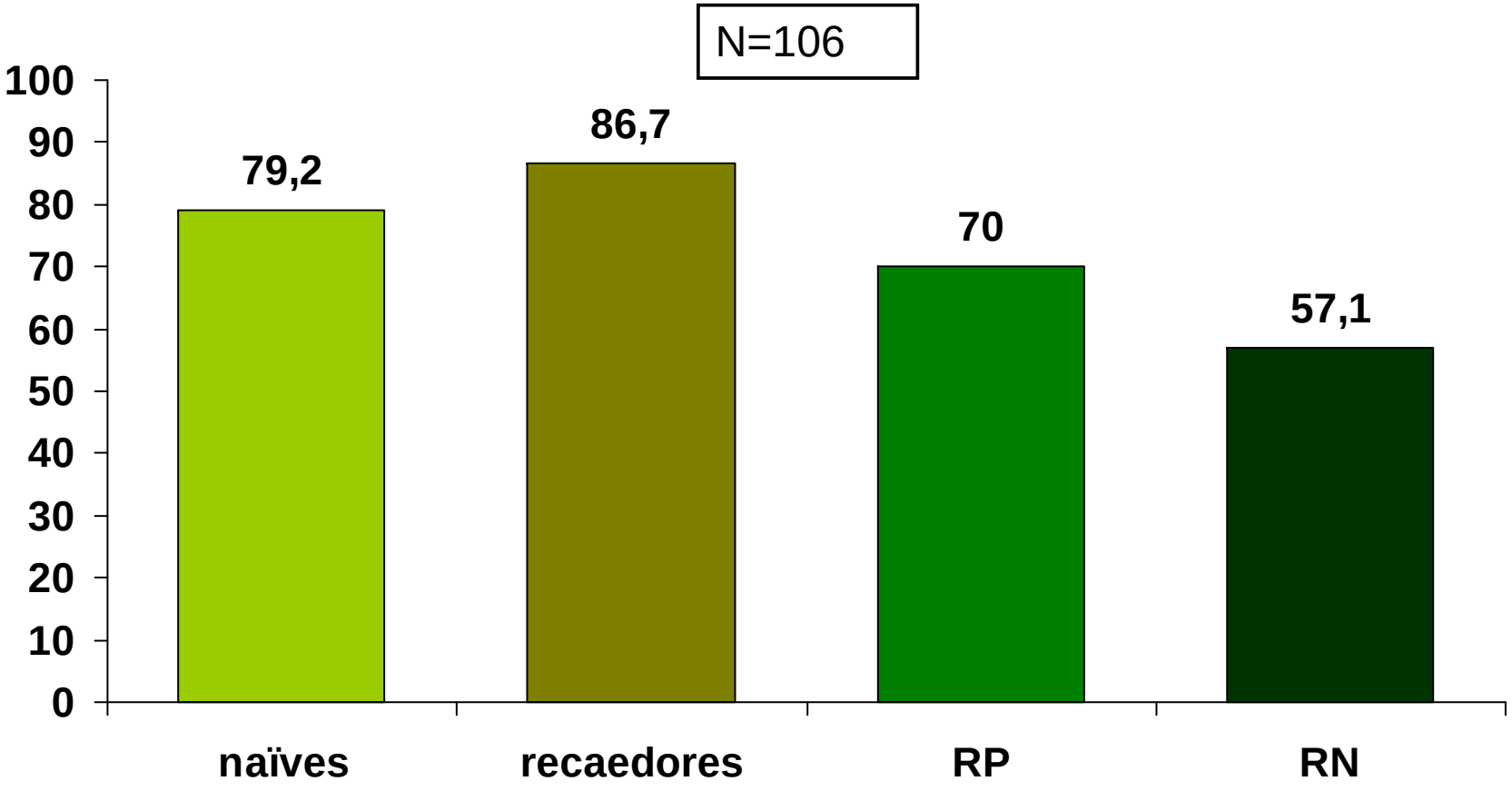


Estimando un tercio de infección VIH no conocida, con una proporcion similar de coinfección

Futuro cercano (¿?) en el tratamiento de la coinfección

- ✓ Optimización de los fármacos disponibles: tratamiento guiado por respuesta, retratamiento de fracaso a biterapia: Estudios INSIGHT, UNITE, BOC en fracaso
- ✓ Nuevos fármacos con I-R
- ✓ Nuevas fármacos sin I
- ✓ Nuevos fármacos sin I ni R

C212: Simeprevir + PegIFN/RBV en pacientes coinfectados GT1 RVS-12

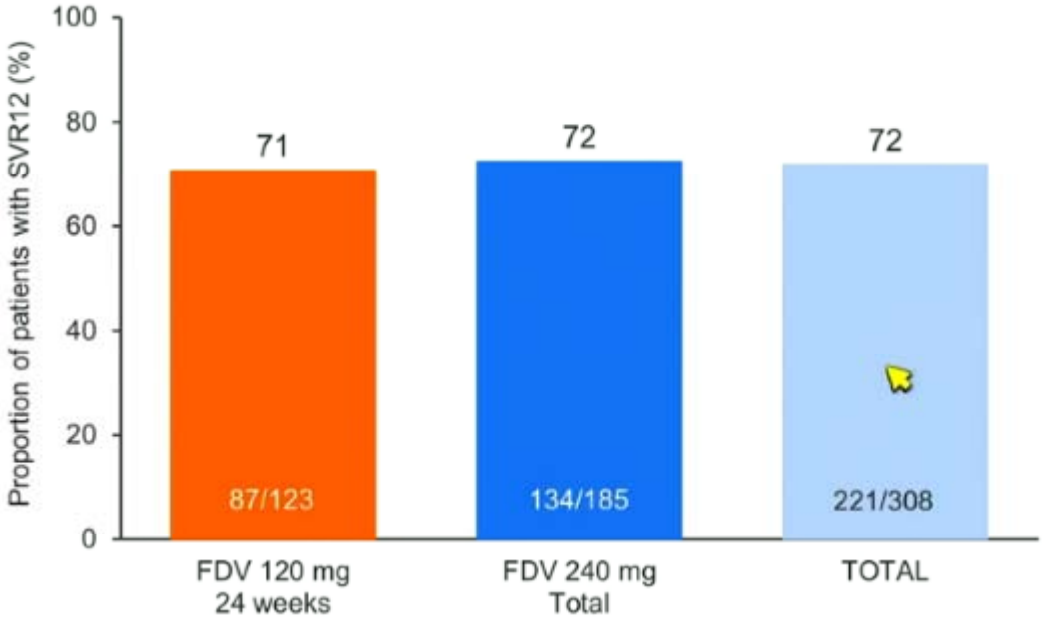


88,5% criterios para TGR

 # LBPS 9/5. Dieterich D. EACS 2013

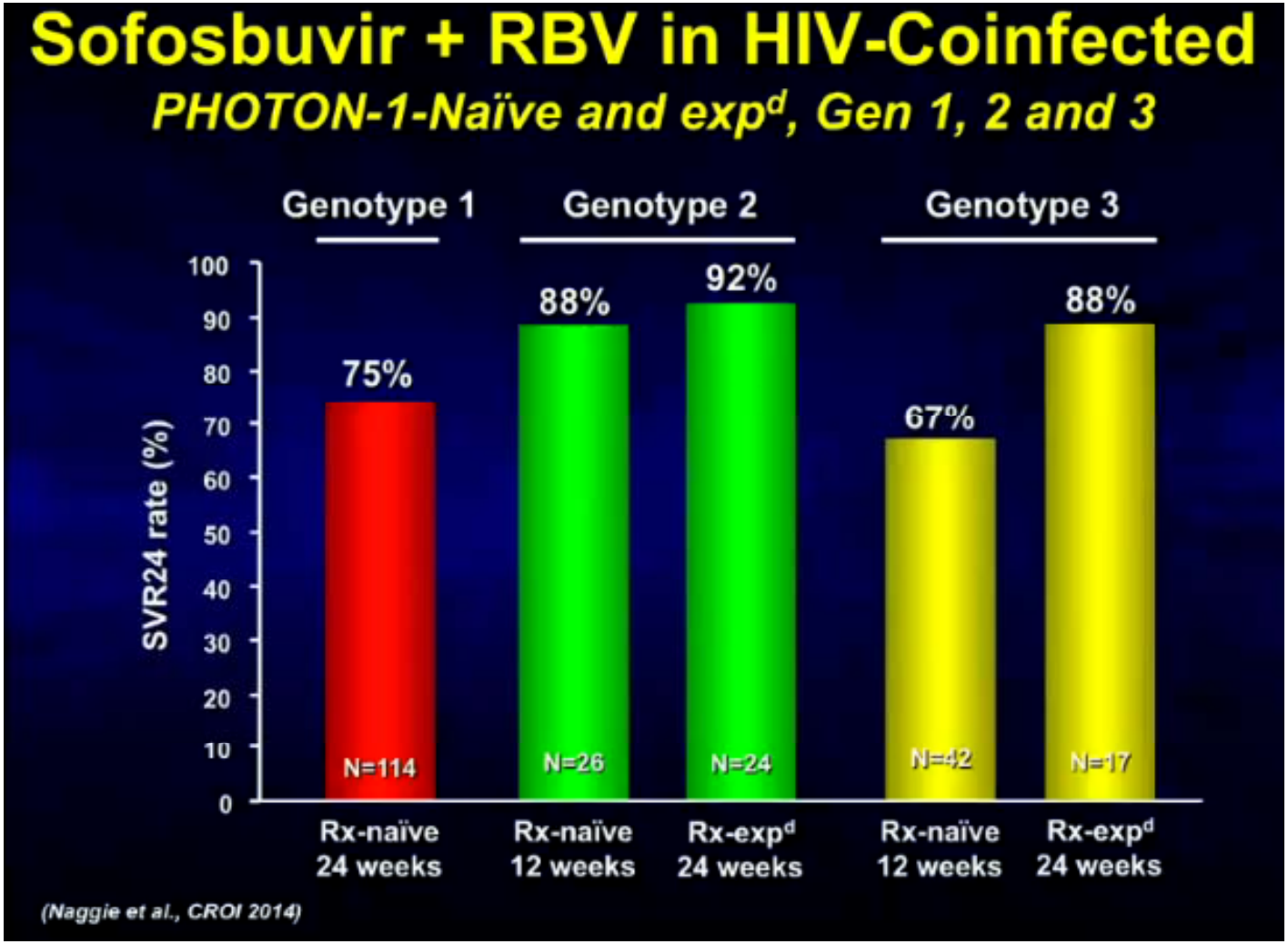
STARTVerso4 PHASE III TRIAL OF FALDAPREVIR PLUS PEGYLATED INTERFERON α-2a AND RIBAVIRIN IN PATIENTS WITH HIV AND HCV GENOTYPE-I CO-INFECTION

SVR12: overall population



 # 1099. Rockstroh JK et al. CROI 2014

PHOTON-1



Sulkowski M et al. #212, CROI 2014

- Treatment-naïve, non-cirrhotic patients with HCV/HIV co-infection, MK-5172/MK-8742 treated for 12 weeks - 90 percent (26/29) and MK-5172/MK-8742 plus RBV for 12 weeks 97 percent (28/29).
- These data were presented at the 49th Annual Meeting of the European Association for the Study of the Liver (EASL), also known as The International Liver Congress™ 2014 in London, UK.

- ERADICATE: Sofosbuvir/Ledipasvir Fixed-Dose Combination Results in 100% SVR Rates in HCV Treatment-Naive Patients Coinfected With Genotype 1 HCV and HIV in Phase II Trial
- Source: 2014 Annual Meeting of the European Association for the Study of the Liver*

Gracias