Post EASL 2012
HCV/Koinfektionen

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Cost-Effectiveness of HCV Treatment Impact of treatment and disease severity on health care costs

- Analysis of Private Health Insurance Claims Database:
  - Inclusion criteria: > 2 year follow-up (between 2001-2010)
  - Patients stratified according to stage of the disease
  - Mean all cause, follow-up direct health care costs per-patient-per-month (PPPM 2010 US$) for treated vs. non-treated

Gordon SC et al. EASL 2012; #1115 (S439)

Cost-Effectiveness of HCV Treatment
Impact of treatment on health care costs

Characteristics	Treated (N=4.116)	Non-treated (N=29.334)
Male	64%	61%
Mean age in years	50	50

82% of US patients with health care insurance did not receive any antiviral treatment

Gordon SC et al. EASL 2012; #1115 (S439)

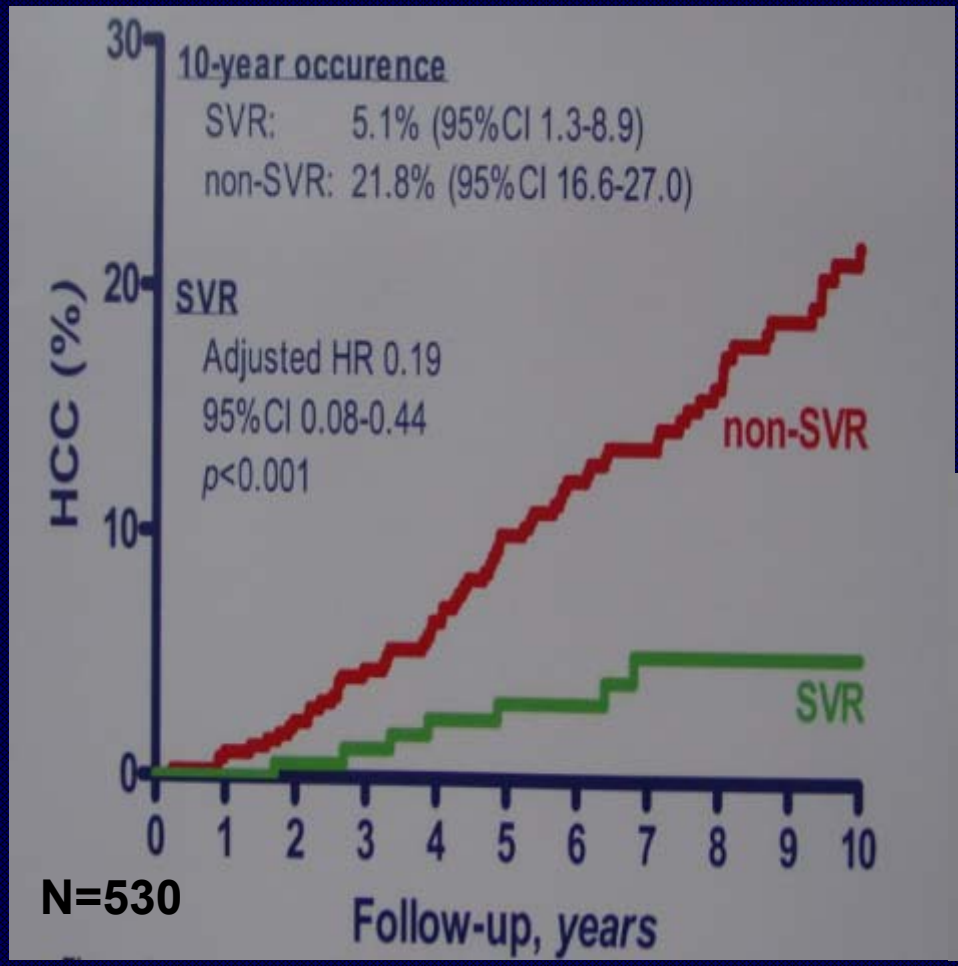
Cost-Effectiveness of HCV Treatment
Impact of treatment on health care costs

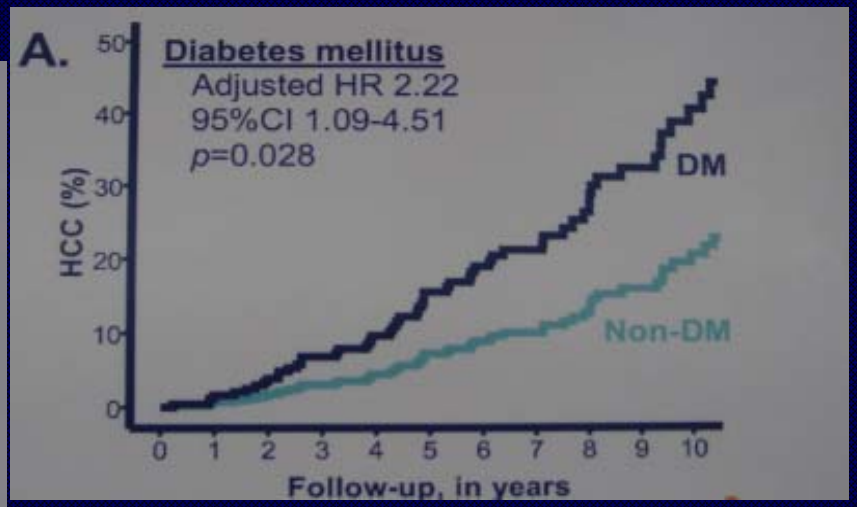
Mean follow-up PPPM health care costs (2010 US$)	Treated (N=4.116)	Non-treated (N=29.334)	P-value
All patients	1.509	1.943	<0.001
Non-cirrhotic	918	1.375	<0.001
Cirrhotic	1.400	1.793	0.068
End-stage liver disease (ESLD)	3.634	5.077	<0.001

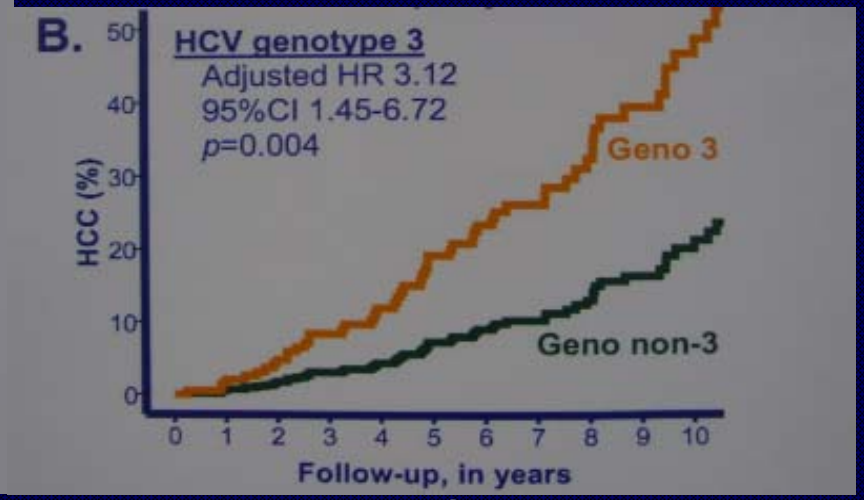
All cause health care costs appr. 4 fold higher in treated patients with ESLD vs. non-cirrhotic disease

Gordon SC et al. EASL 2012; #1115 (S439)

HCC Inzidenz für Patienten mit fortgeschrittener Leberfibrose (Ishak Stadium 4-6)







Non-SVR

Van der Meer EASL 2012 abstract 932

Deutsche Leberstiftung

Early versus delayed treatment of acute hepatitis C:

The German HEP – NET Acute HCV – III Study

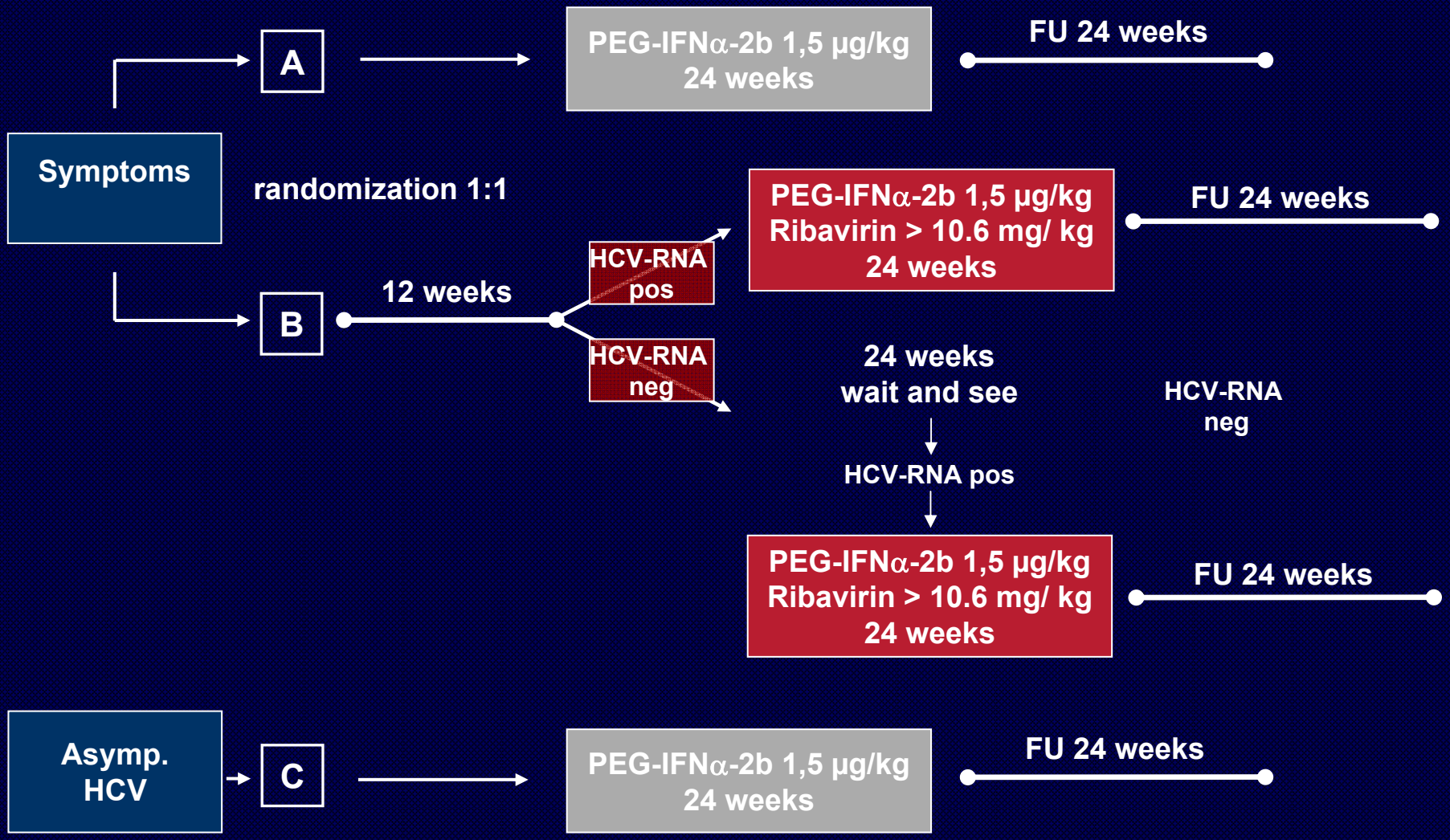
- a randomized controlled trial -

Katja Deterding, Norbert Grüner, Peter Buggisch, Johannes Wiegand,
Peter Galle, Ulrich Spengler, Holger Hinrichsen, Thomas Berg,
Andrej Potthoff, Nisar Malek, Helmut Diepolder, Sandra Feyerabend, Ansgar Lohse,
Markus Cornberg, Maria Christina Jung, Michael P. Manns, Heiner Wedemeyer

for The German Hep-Het Acute HCV - III Study Group

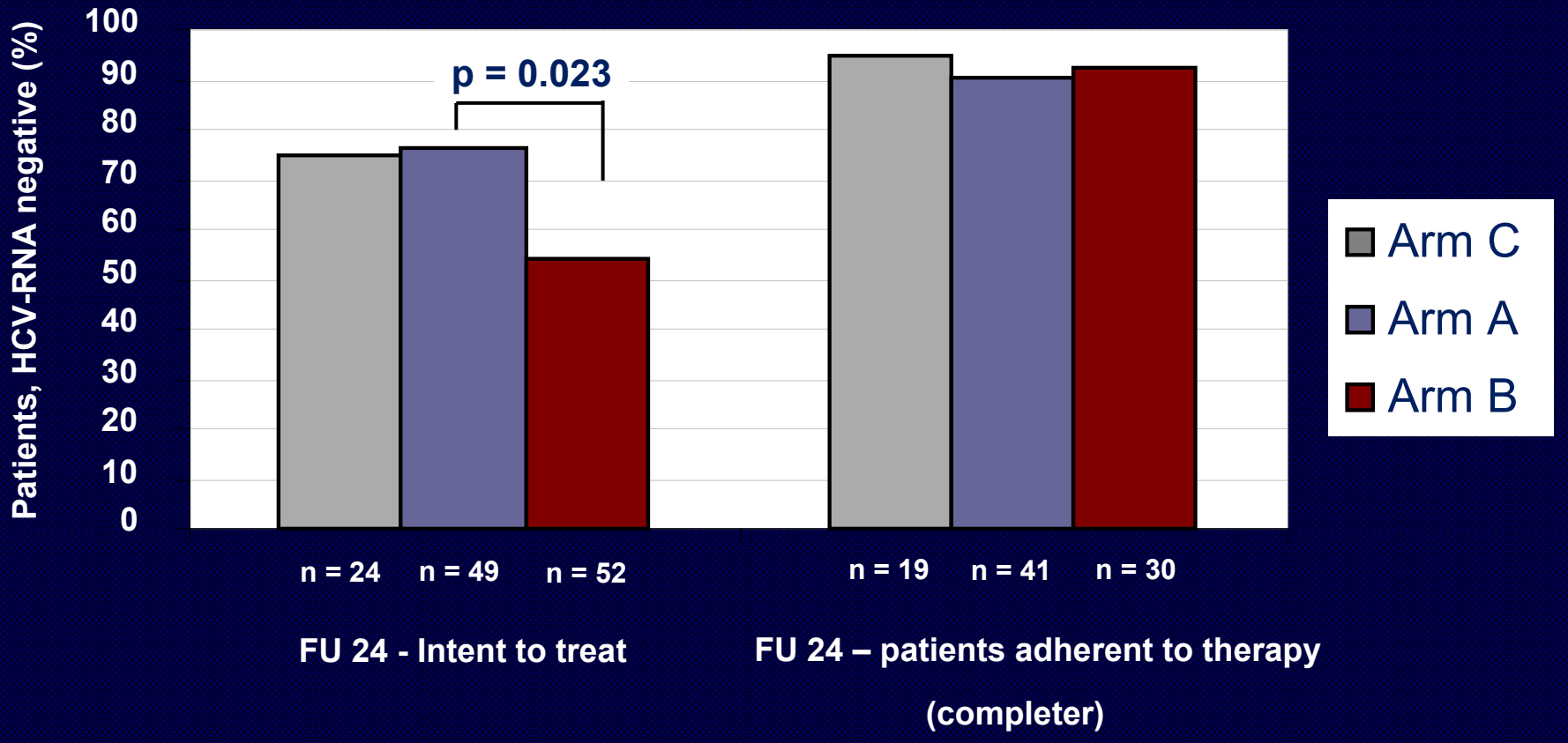
MHH Hannover Medical School

Study design – acute HCV – III Study



Deterding Acute HCV – III Study, EASL 2012

Acute Hepatitis C III Study: SVR Rates – Arm A, Arm B, Arm C



Deterding Acute HCV – III Study, EASL 2012

SELECTION OF HCV GENOTYPE 1 PATIENTS FOR DUALTHERAPY WITH PEGINTERFERON ALFA-2A/RIBAVIRIN WITHA HIGH PROBABILITY OF SUSTAINED VIROLOGIC RESPONSEACCORDING TO BASELINE CHARACTERISTICS ALONE

P. Ferenci1*, R. Aires2, I. Ancuta3, A. Arohnson4, H. Cheinquer5, D. Delic6, M. Gschwantler7, D. Larrey8, L. Tallarico9, M. Schmitz10, F. Tatsch11,D. Ouzan

Ferenci et al, EASL 2012, poster 1108

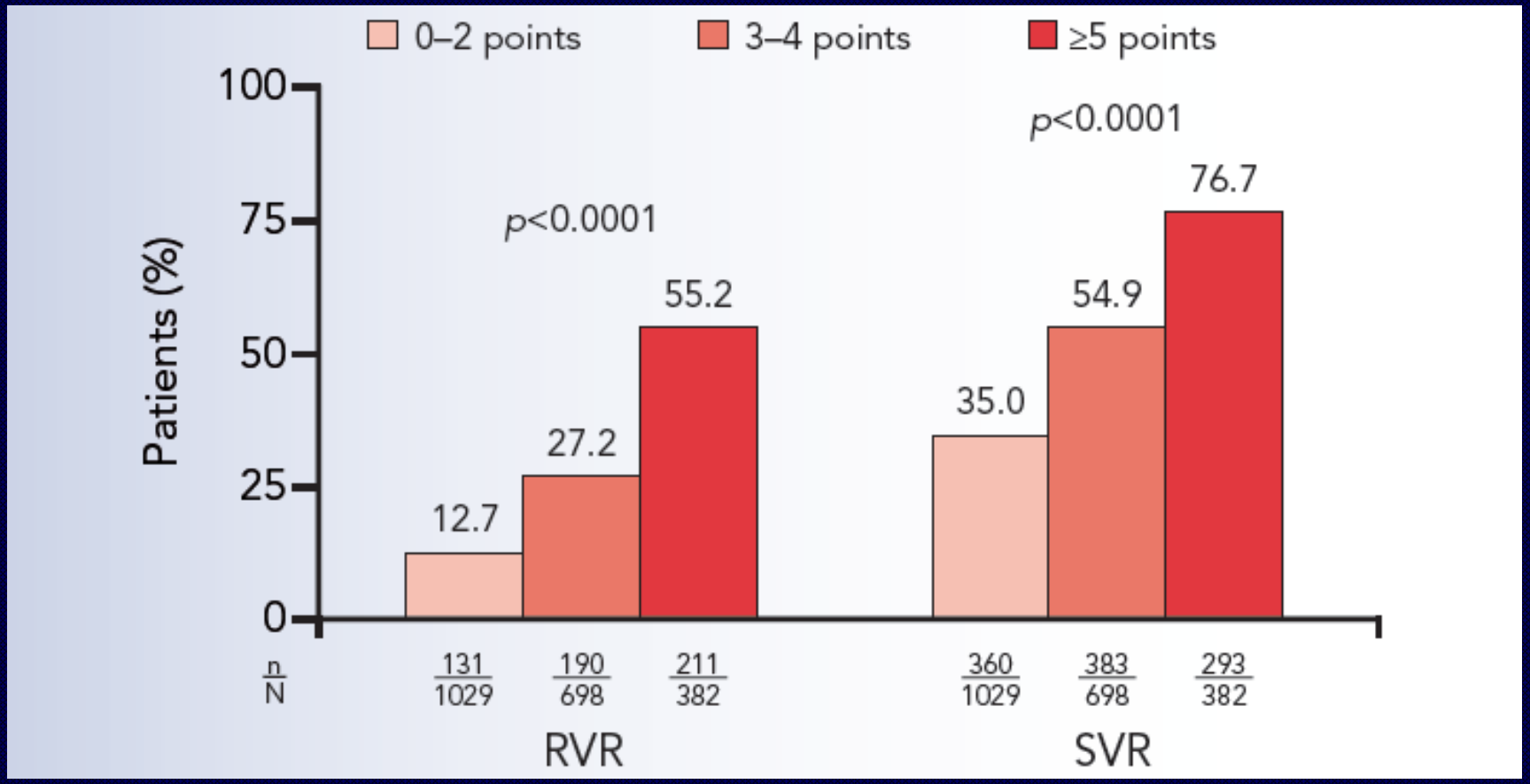
Scoring system (HCV Type 1)

Table 2. PROPHESYS scoring system

Predictor		Score
Age, years	≤35	2
	>35 but ≤45	1
	>45	0
BMI, kg/m2	≤20	2
	>20 but ≤22	1
	>22	0
HCV RNA, IU/mL	≤100 000	3
	>100 000 but ≤400 000	2
	>400 000 but ≤800 000	1
	>800 000	0
Platelet count, $\times 10^9$/L	>150	1
	≤150	0
ALT/ULN*	>3	1
	≤3	0
AST/ULN*	≤1	1
	>1	0

Ferenci et al, EASL 2012, poster 1108

SVR according to scoring categories



Ferenci et al, EASL 2012, poster 1108 – to be presented orally April, 21st, poster area

Treatment options for naïve genotype 1 patients

TRIPLE THERAPY	CONSIDER DUAL THERAPY IN
Primary treatment option in CT/TT or F3–F4	France: ≤F2 with CC and LI RVR+ if CC + ≤F2 with LI RVR–, add PI Italy: ≤F2 with CC
Primary treatment option	No advanced fibrosis with CC, VL <600-800K IU/ml and LI RVR+
Primary treatment option in F2 with CT/TT or F3-F4	F0–F1 or F2 with CC regardless of RVR
Primary treatment option (TVR recommended over BOC)	Peg-IFN 2a/RBV if CC, mild fibrosis, VL<600K IU/mL, <40 years, absence of metabolic syndrome, IP10 <150pg/mL If LI RVR–, add PI or watchful waiting
Primary treatment option	≤F2 with viral load <400K IU/mL and RVR+
Primary treatment option	<F4 with VL<400-800K IU/mL and LI RVR+

Heilungschancen bei HCV Typ 1: Duale vs. Triple Therapie A Systematic Review

- Unvorbehandelt
  - Duale Therapie: N=1545
  - Triple-Therapie: N=1634
- Relapse/partial Response
  - Dual: N=539; Triple: N=719 Triple
- Nonresponse
  - Dual: N=255; Triple: N=386

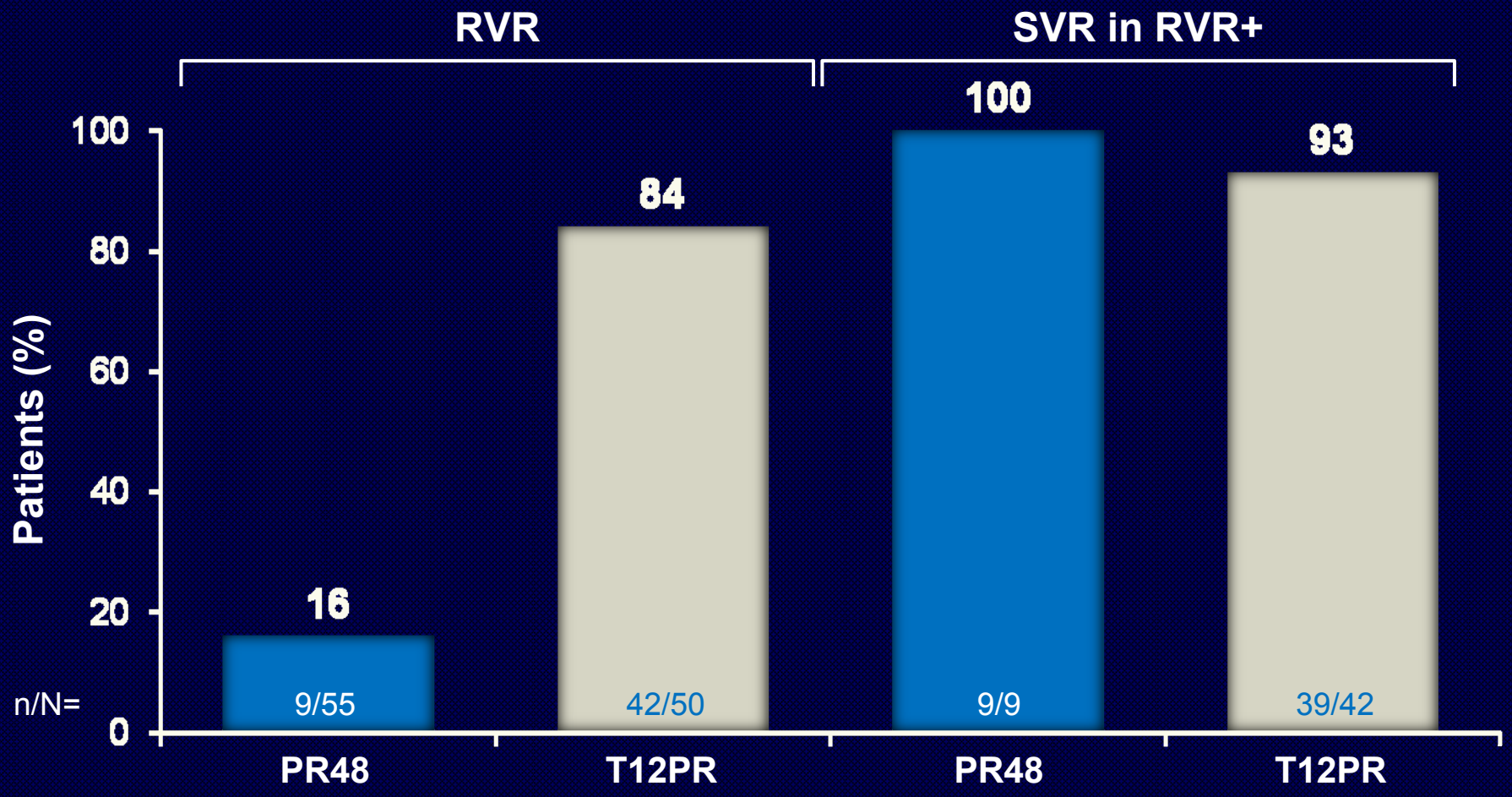
Jurchis AR et al. EASL 2012, Poster 1123 (S442)

Heilungschancen bei HCV Typ 1: Duale vs. Triple Therapie A Systematic Review

Group	SVR DUAL	SVR Triple	Diff.
Naive	39%	68.5%	2-fach
Relapse/ Partial Resp.	26%	73%	3-fach
Nonresponse	7.5%	44%	6-fach

Jurchis AR et al. EASL 2012, Poster 1123 (S442)

Telaprevir (ADVANCE): RVR and SVR in patients with *IL28B* CC genotype

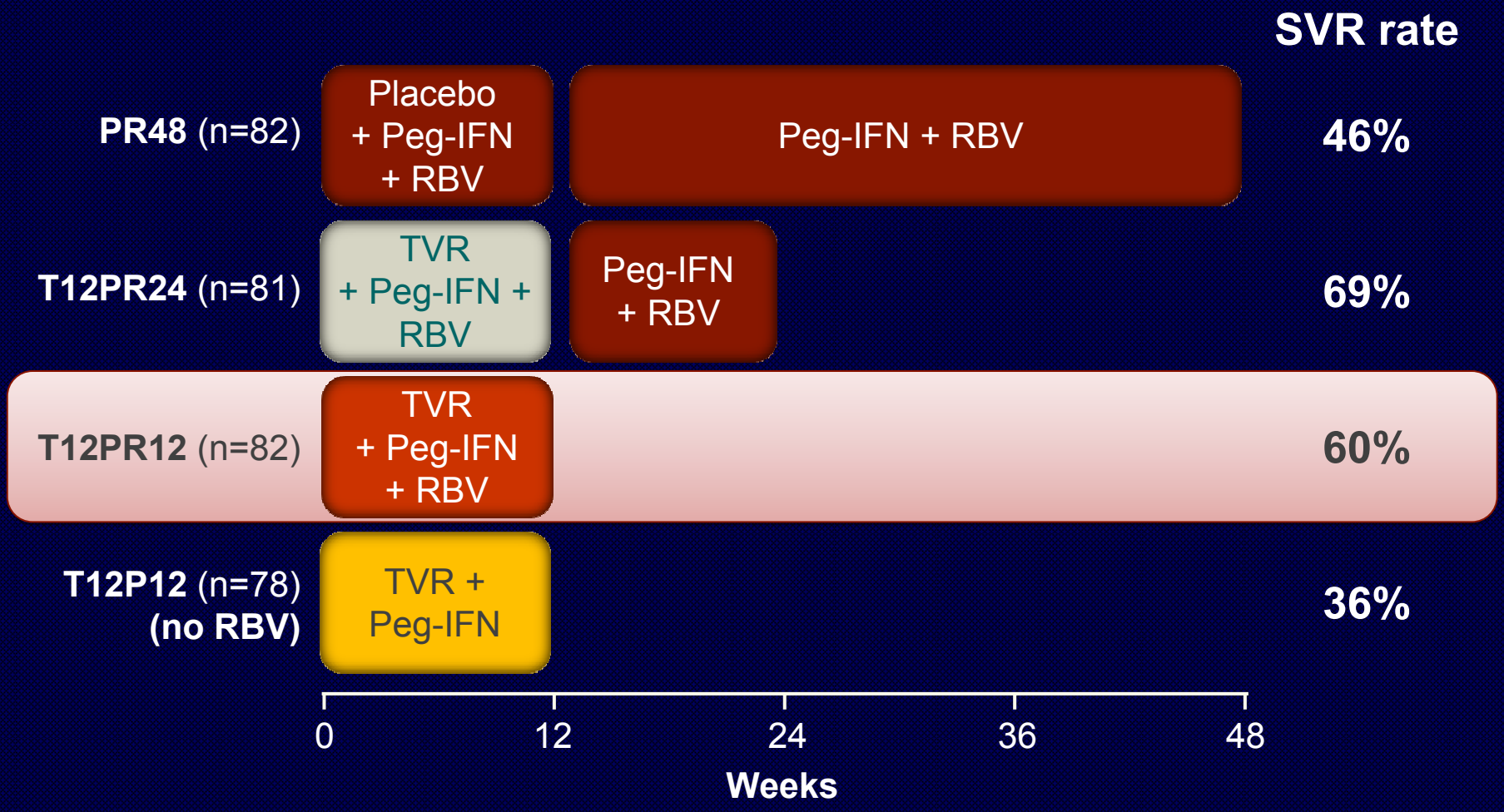


78% of CC patients in the T12PR arm were treated with 24 weeks of treatment

RVR: rapid viral response (undetectable HCV RNA at Week 4)

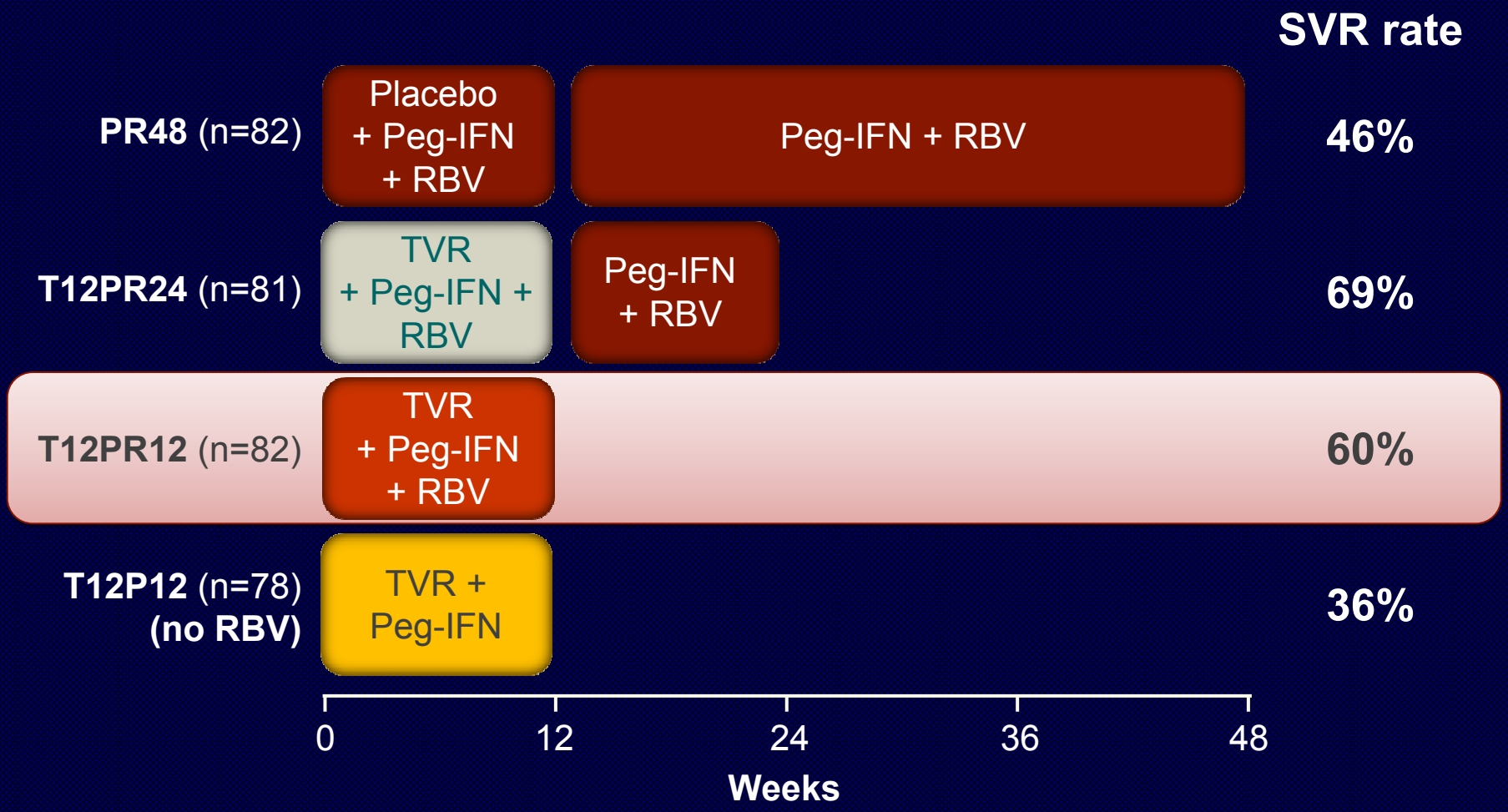
Jacobson IM, et al. J Hepatol 2011;54(Suppl. 1):S542

PROVE2: SVR Rates



Hézode C, et al. N Engl J Med 2009;360:1839–50

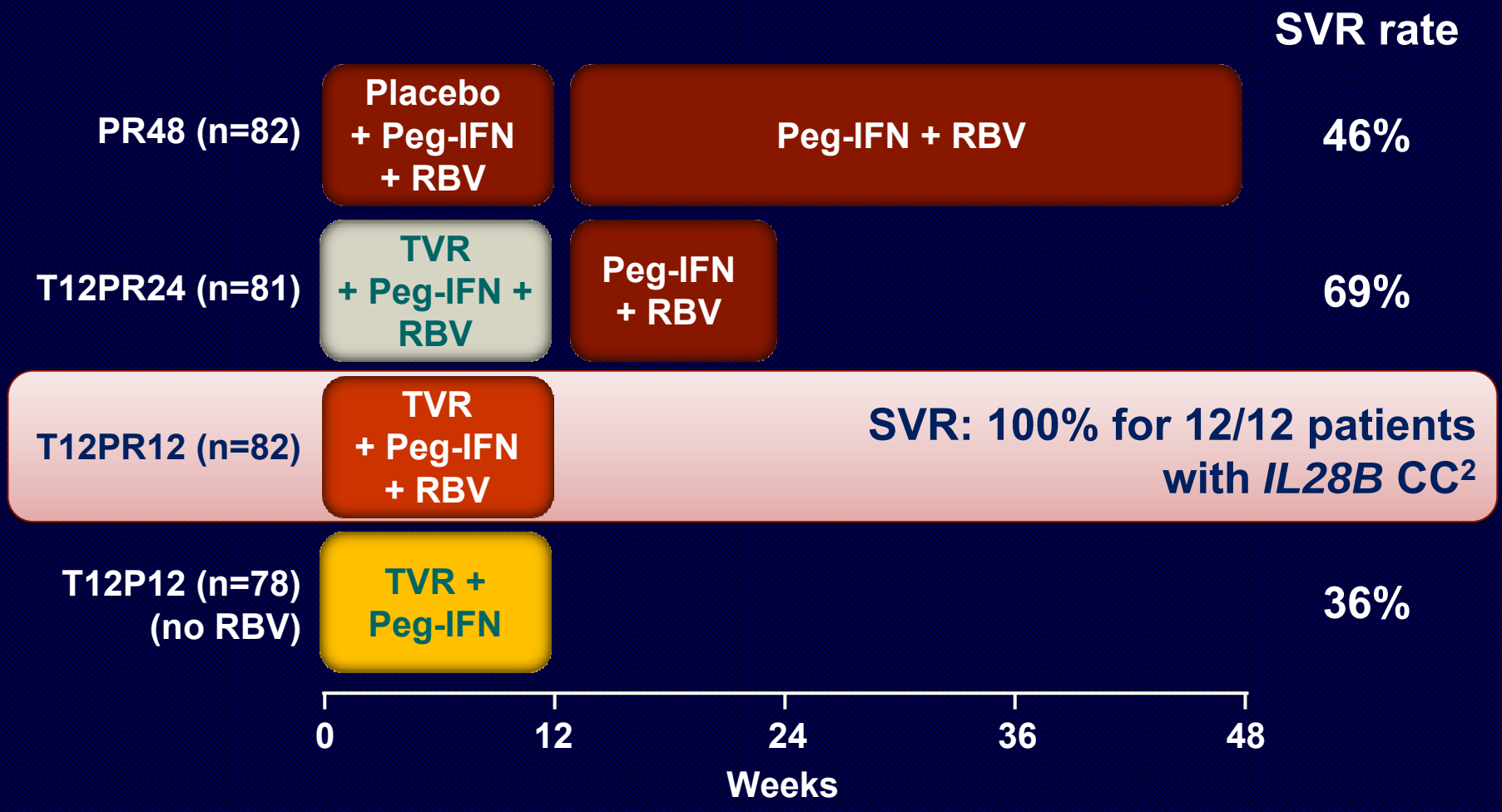
PROVE2: SVR Rates



- **The *IL28B* genotype at polymorphic site rs12979860 was determined in specimens at the PROVE2 French sites**

Bronowicki et al, EASL 2012, poster (1094)

What to expect if treatment is discontinued? Lessons from PROVE2[1]



Bronowicki et al, EASL 2012, poster (1094)

Personalisierte Medizin
Biomarker und Prädiktoren……

- **Zuverlässigkeit der Diagnostik**

- **(V. Gonzalez: Evaluation of accuracy of HCV Typing (Innogenentics vs. Abbott Assay, EASL 2012; #1114 (S439))**

Quantifying and Detecting HCV RNA Levels in Phase 3 Trials

Telaprevir[2,3]

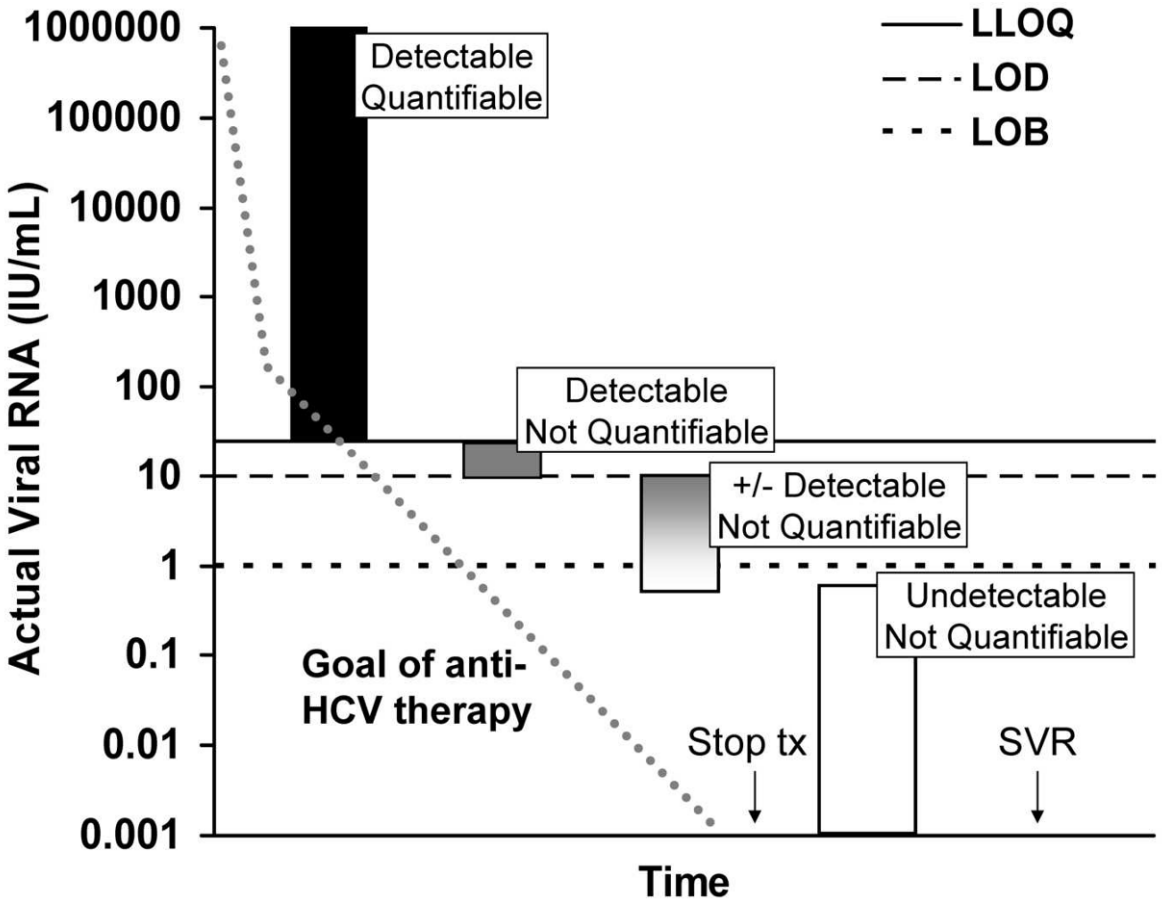
- LLOQ: 25 IU/mL
- HCV RNA values <25 IU/mL were reported as <25 IU/mL detectable or <25 IU/mL undetectable

Boceprevir[4]

- LLOQ: 25 IU/mL
- LLOD: 9.3 IU/mL claimed

1. http://molecular.roche.com/diagnostics/virology/products_virology_17.html; 2. Jacobson IM, et al. Hepatology 2010;52(Suppl.):427A
3. Sherman KE, et al. Hepatology 2010;52(Suppl.):401A; 4. Poordad F, et al. Hepatology 2010;52(Suppl.):402A

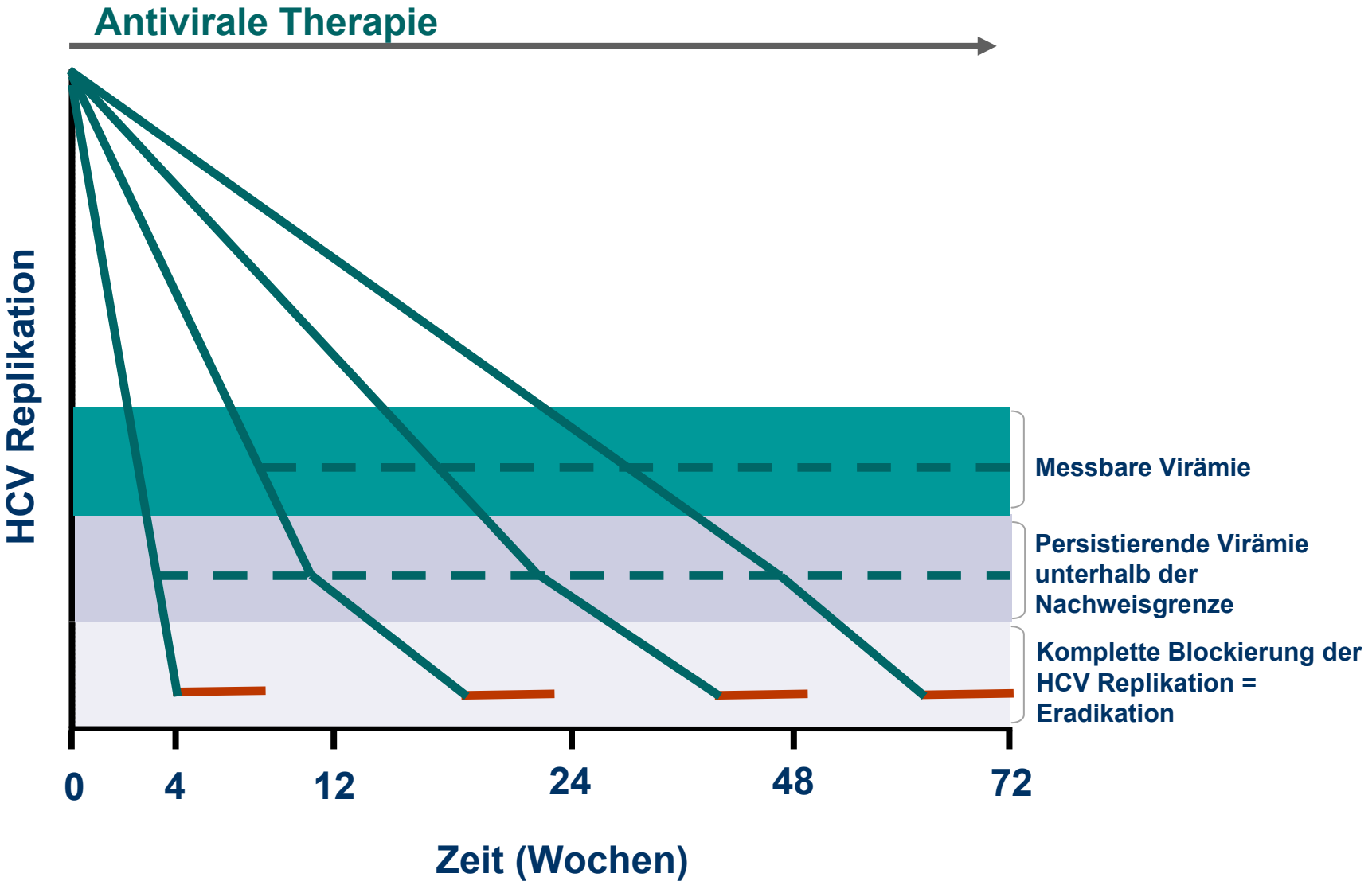
HCV RNA Quantification 2012 LLOQ - „the tip of the iceberg“?



LLOQ = lower limit of quantification (< 25 /ml)
LOD = lower limit of detection

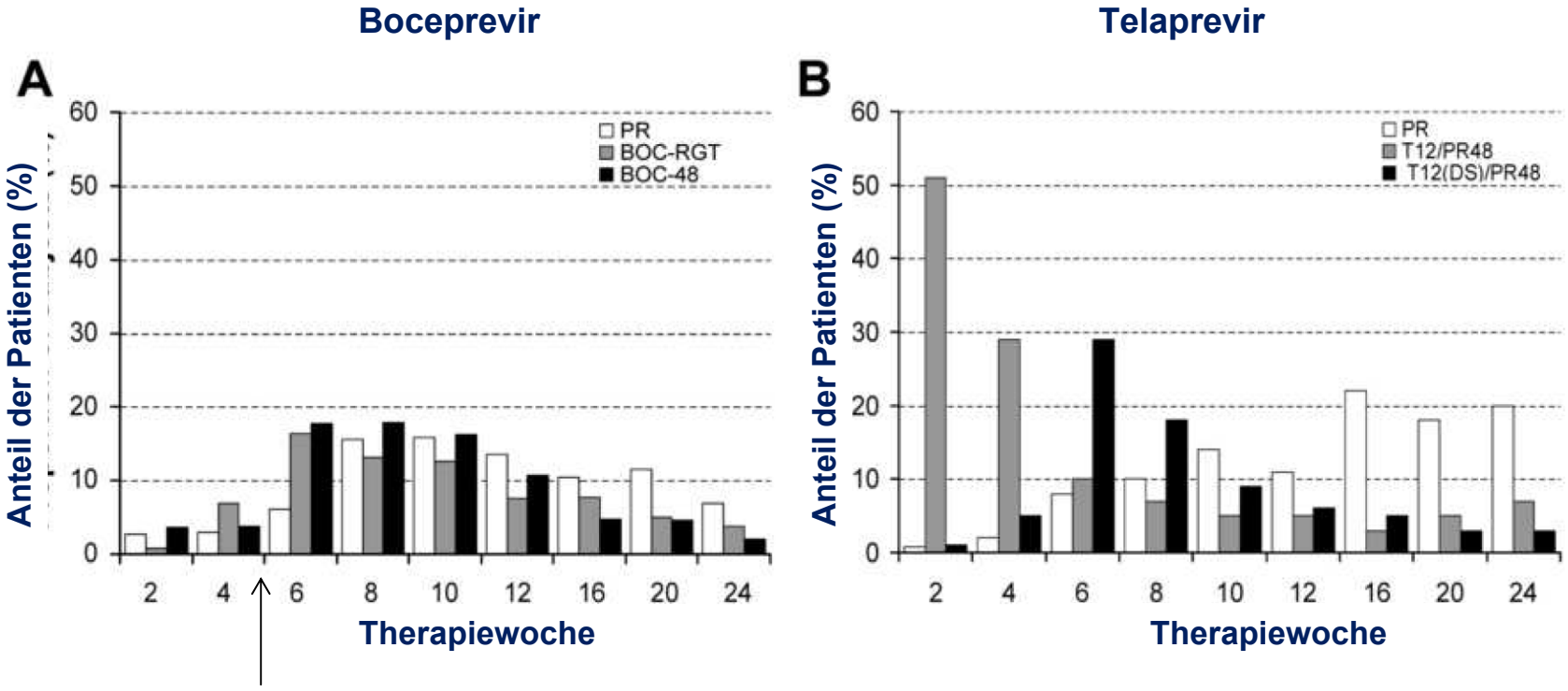
Harrington PR et al. Hepatology 2012

New concept of response-guided therapy?



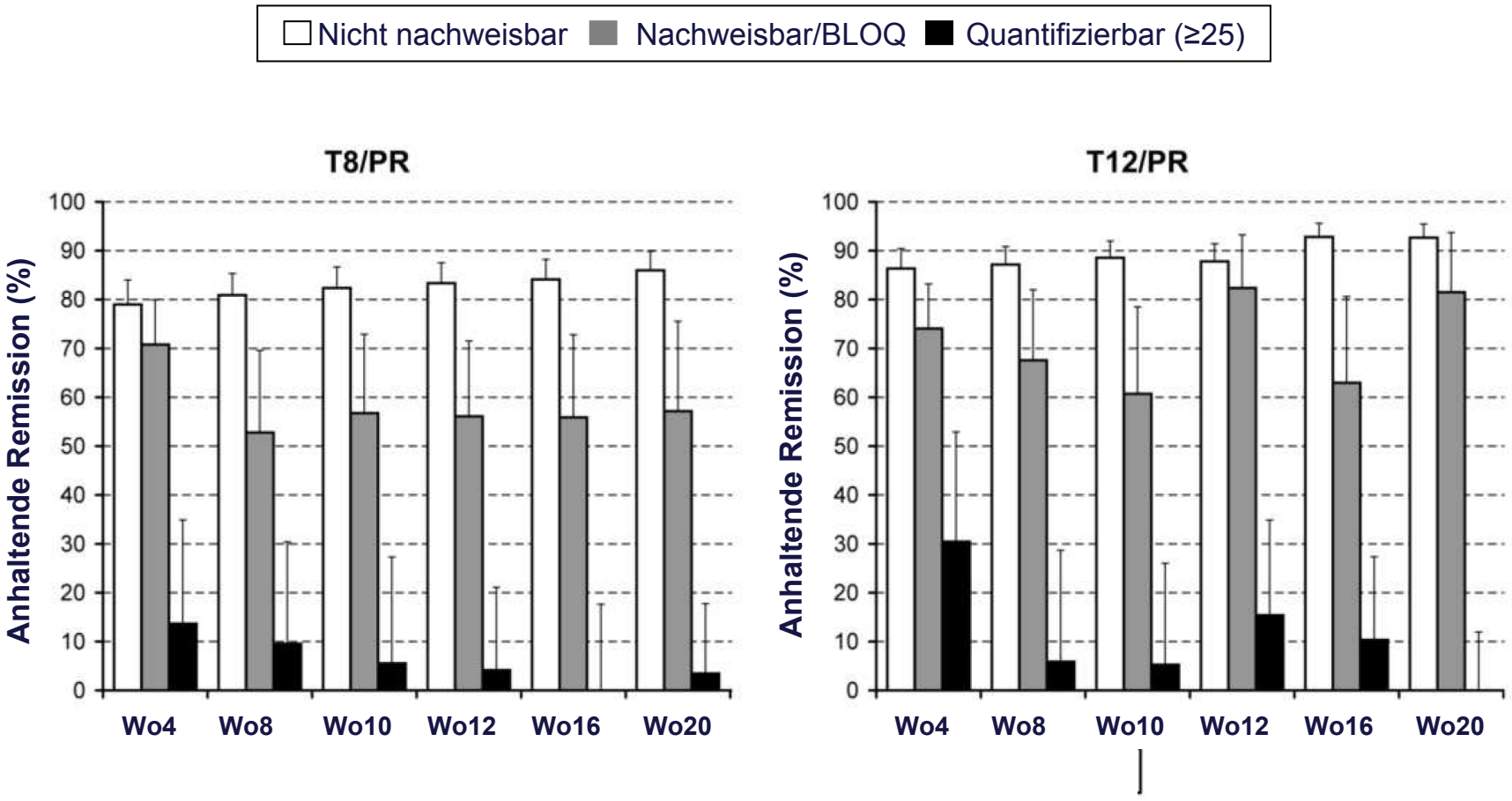
Berg T. Hepatitis&more 2/2011

Minimale Restvirämie unter Tripletherapie (< 25 IU/ml, aber HCV RNA +)



Harrington PR et al. Hepatology 2011; epub

Bedeutung der minimalen Restvirämie für die SVR-Rate - Telaprevir-Triple



Harrington PR et al. Hepatology 2011; epub

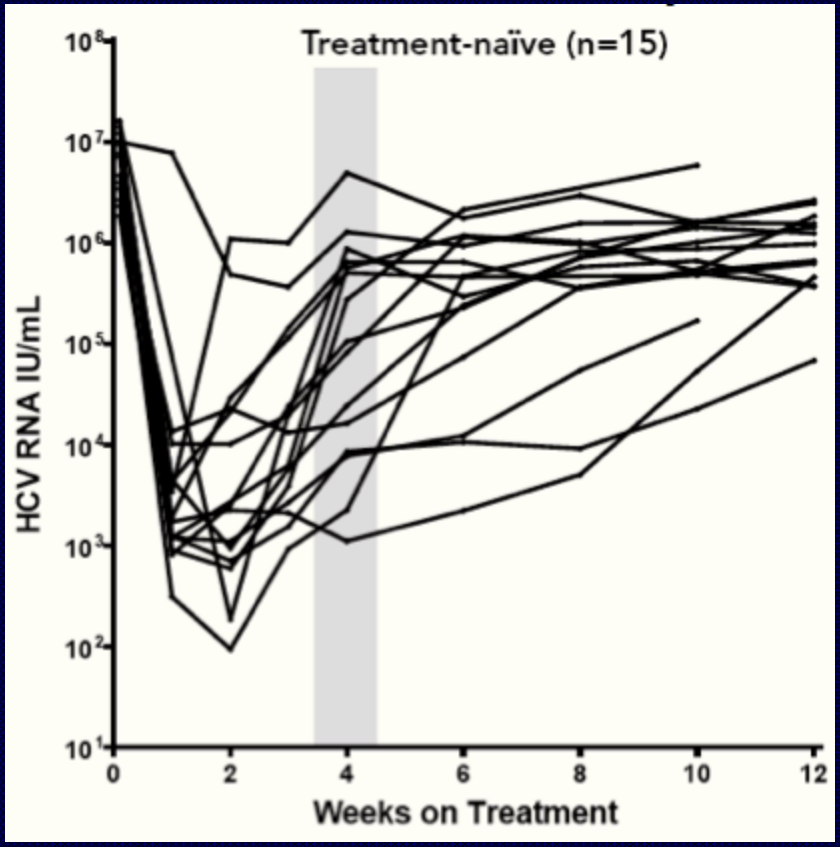
Re-Evaluation der Stopping Rules zu Woche 4 bei Telaprevir-Triple Therapie

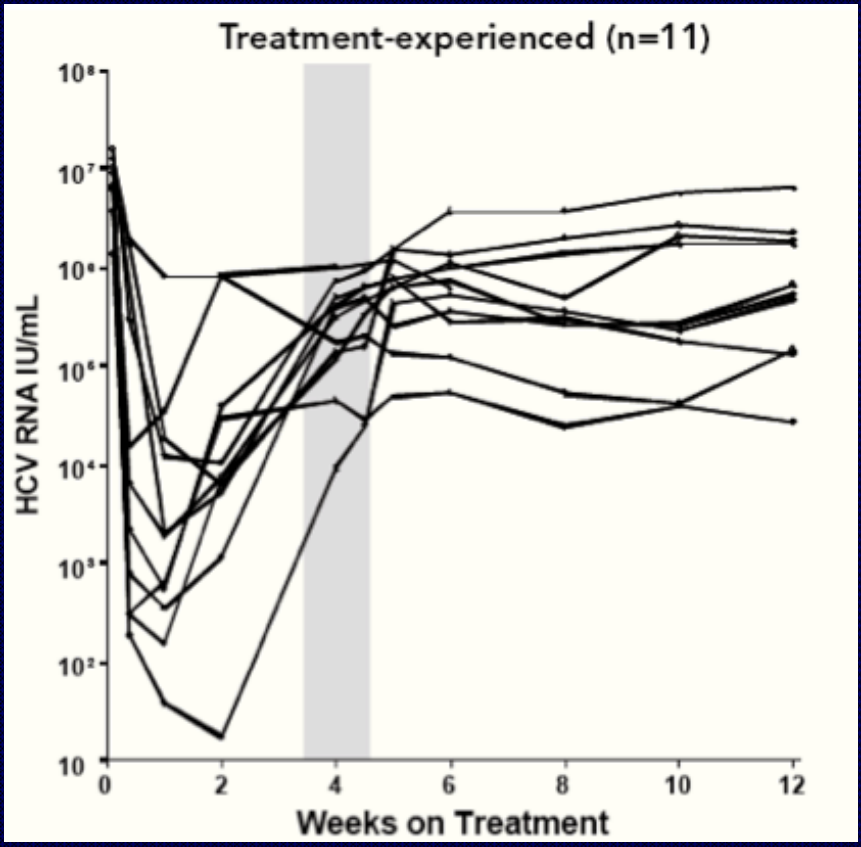
W4 HCV-RNA	Frequenz*	SVR
100 - <1000 IU/ml	1.9%	25% (4/16)
> 1000 IU/ml	1.7%	0%

*Unvorbehandelte Patienten

Jacobsen I et al, EASL 2012, #55(

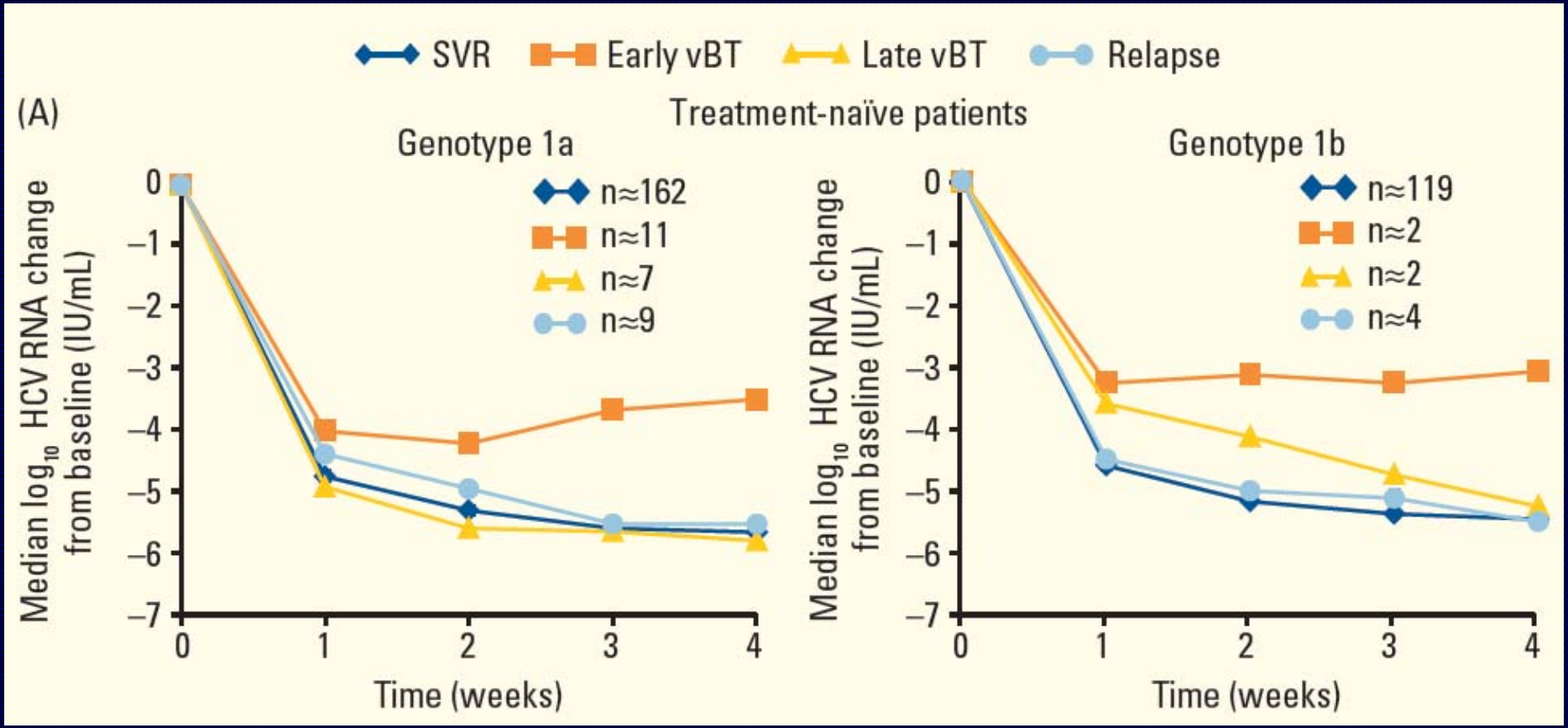
Viral kinetics in patientes fulfilling early stopping rules on telaprevir





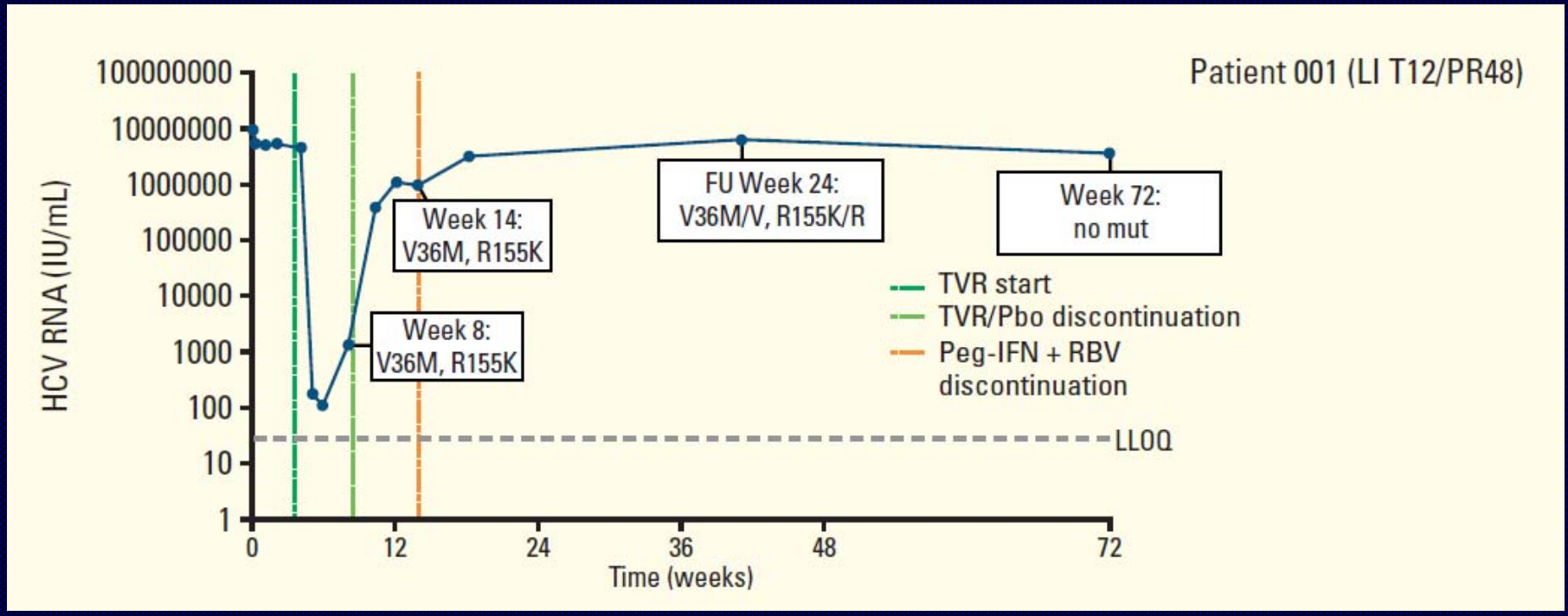
Adda et al., HepDart 2011

HCV-RNA Profile unter Telaprevir-Triple Therapie



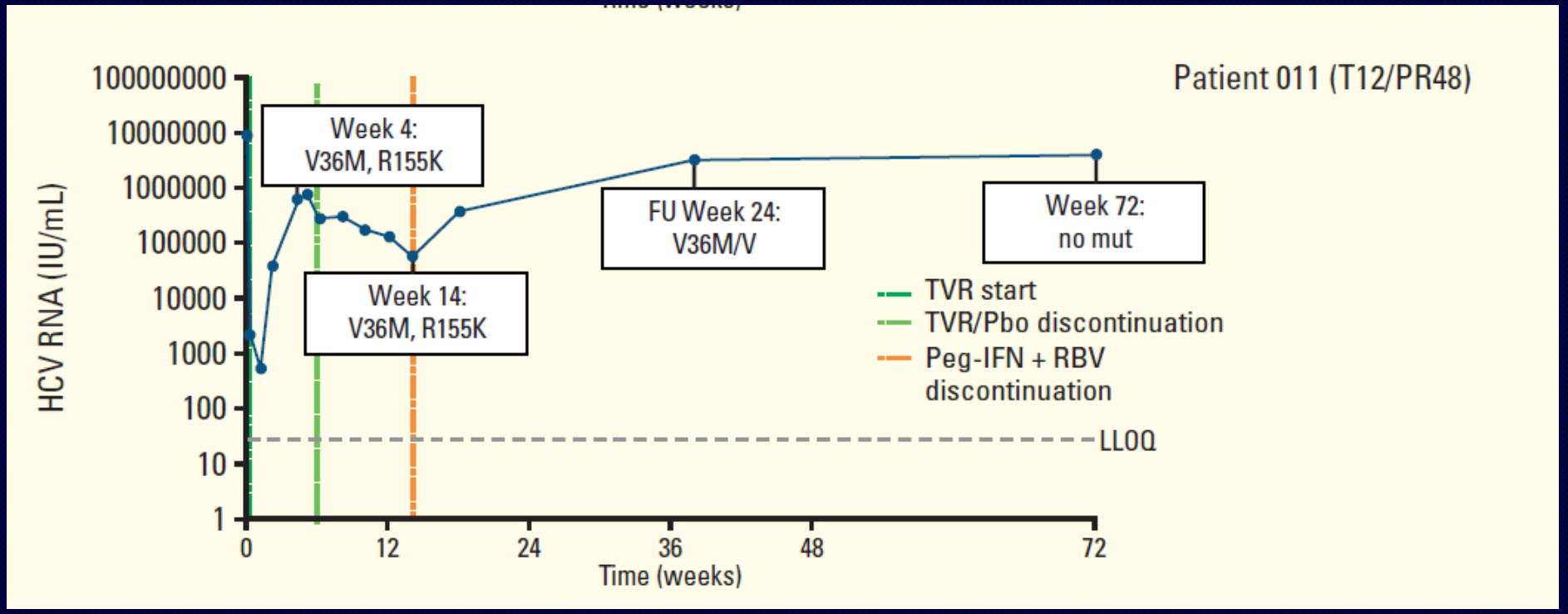
Picchio G et al, EASL 2012, #1150

HCV Deep Sequencing in treatment failure patients from REALIZE



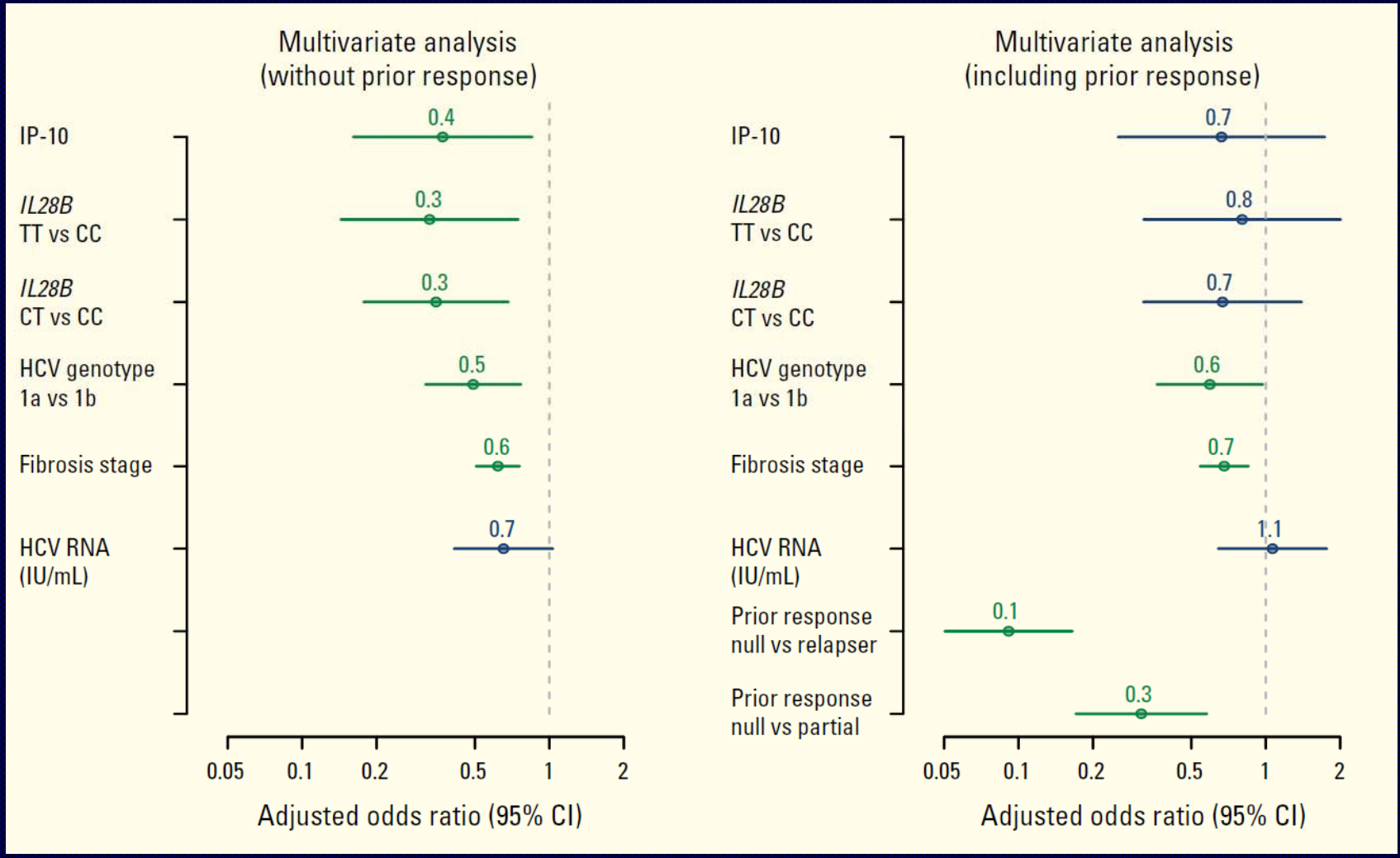
De Meyer S et al, EASL 2012, #1174

HCV Deep Sequencing in treatment failure patients from REALIZE



De Meyer S et al, EASL 2012, #1174

SVR Prädiktion bei Telaprevir-Triple Therapie (REALIZE): Relevanz von IL28B und IP10



Vijgen L et al, EASL 2012, #1167

SVR12 vs. SVR24: wie sicher ist die Vorhersage?

Group	SVR12	SVR24	Diff.
ADVANCE	73%	72%	1.2% (9/727)
ILLUMINATE	92%	90%	1.9% (6/322)
REALIZE	86% (Rel) 60% (Partial) 33% (Null)	86% 57% 31%	1.3% (7/530)

Luo D et al. EASL 2012, Poster 1132 (S446)

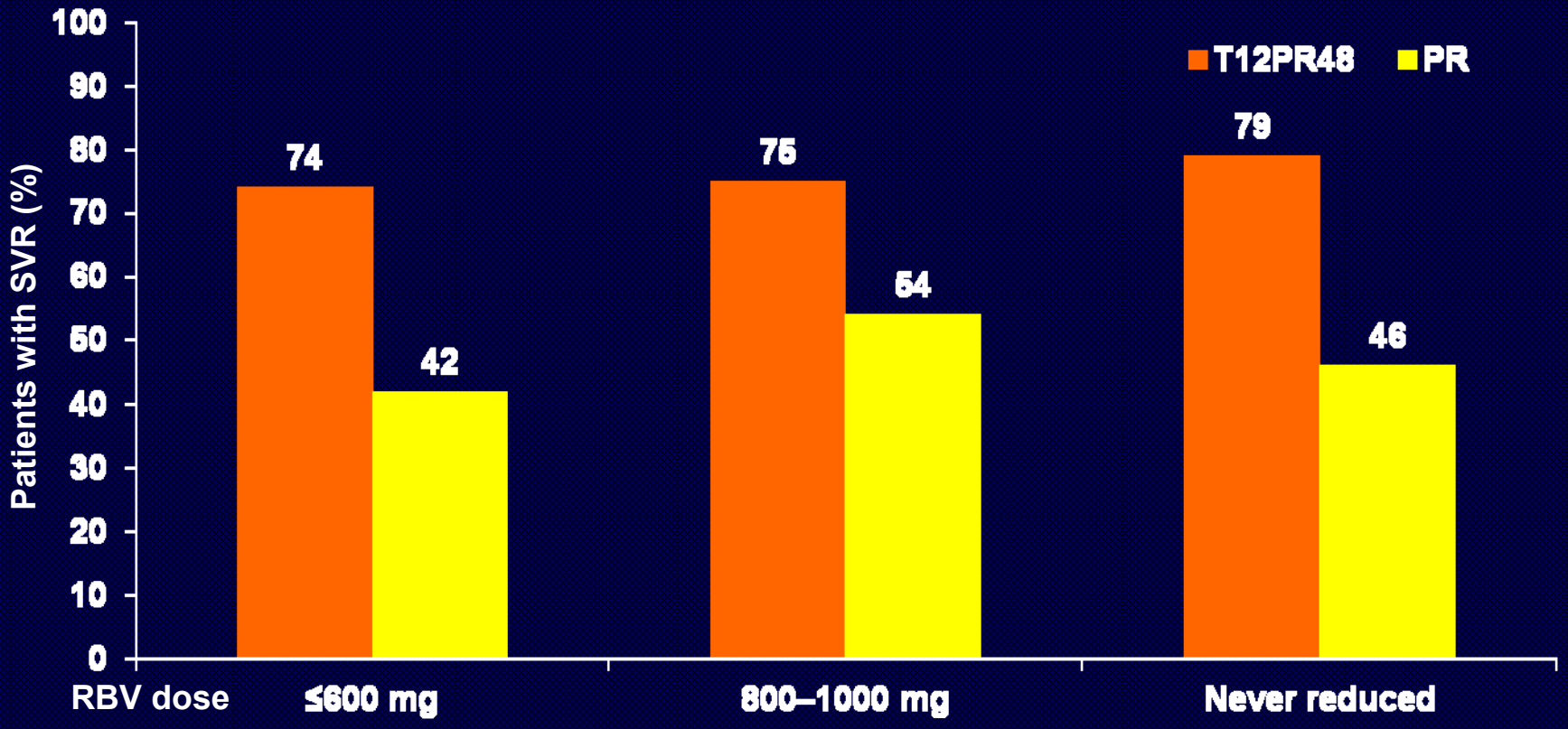
Ribavirin dose modification in treatment-naive and previously treated patients who received telaprevir combination treatment: No impact on sustained virologic response in Phase 3 Studies

M.S. Sulkowski, S. Roberts, N. Afdhal, P. Andreone, M. Diago, S. Pol, F. Poordad, S. Zeuzem, L. Bengtsson, D. Luo, J. Witek, N. Adda

Sulkowski et al, EASL 2012, poster (1162)

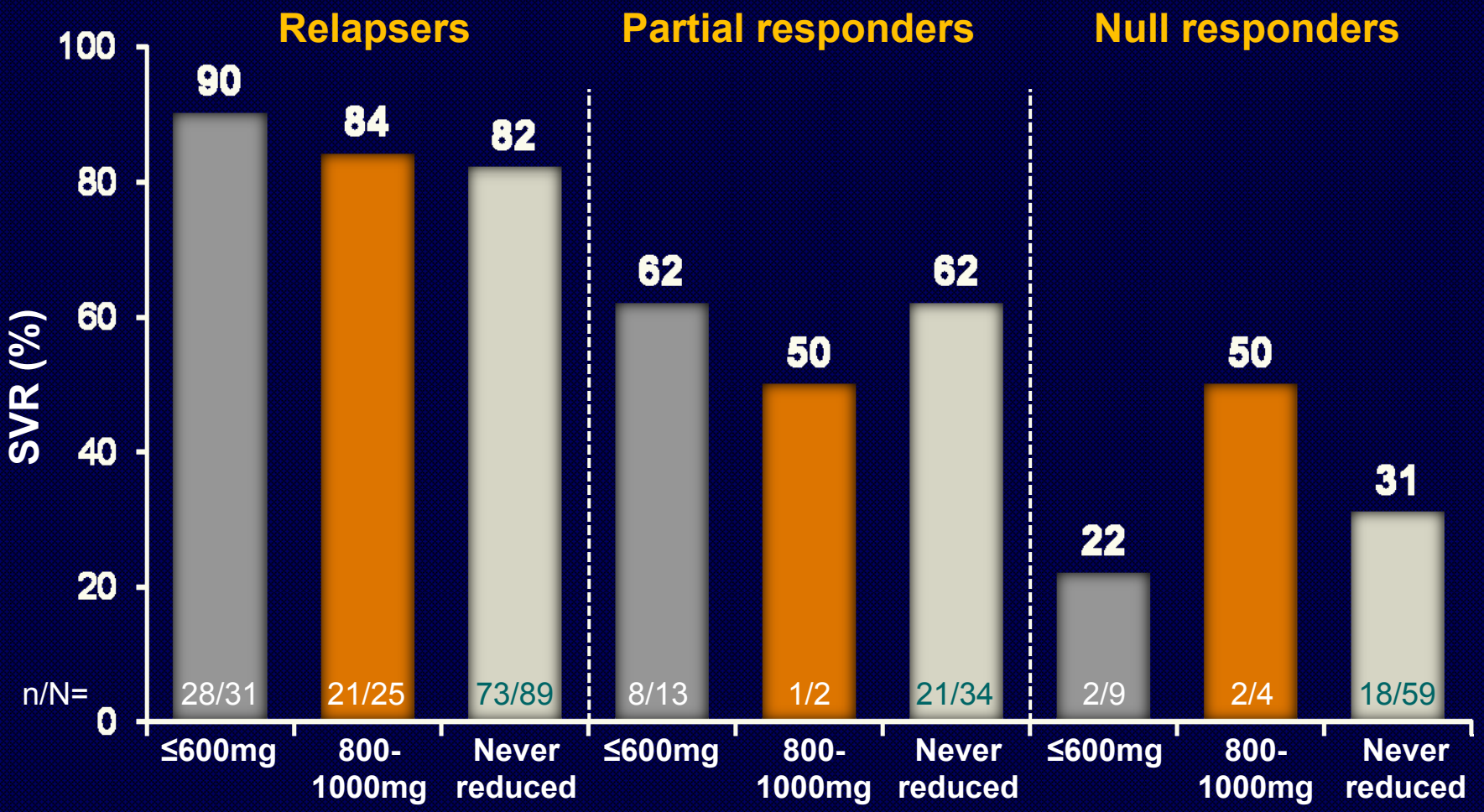
No impact of RBV dose modifications on SVR in treatment-naive pts in telaprevir phase III studies

Treatment-naive pts from ADVANCE and ILLUMINATE



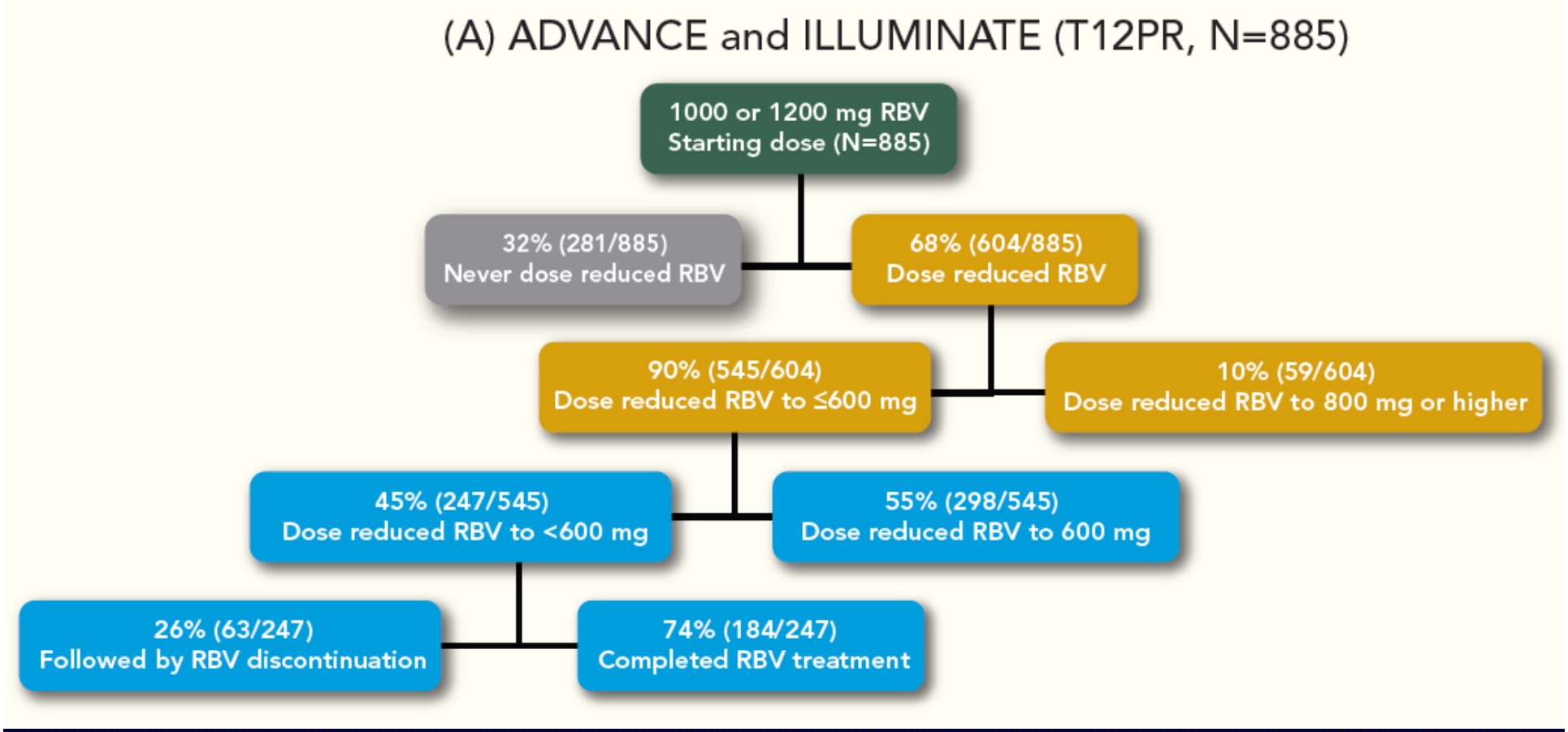
Sulkowski et al, EASL 2012, poster (1162)

No impact of RBV dose reduction on SVR with telaprevir (REALIZE: T12PR48)



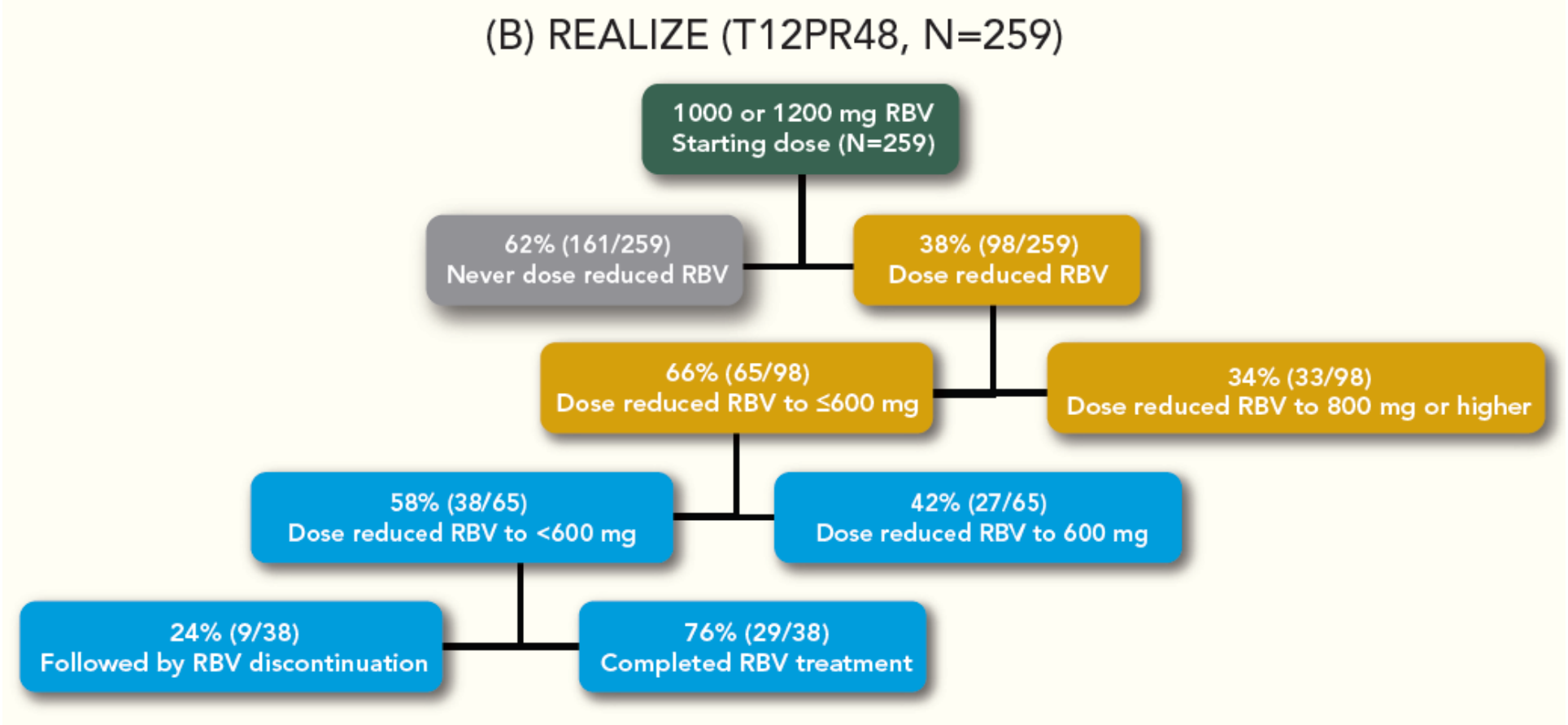
Sulkowski MS, et al. EASL 2012. Abstract 1162.
Poster to be presented on Saturday 21st April

Ribavirin Dosisreduktion unter Telaprevir-Triple Therapie bei *unvor*behandelten Patienten



Sulkowski SM et al, EASL 2012, #1162

Ribavirin Dosisreduktion unter Telaprevir-Triple Therapie bei *vor*behandelten Patienten



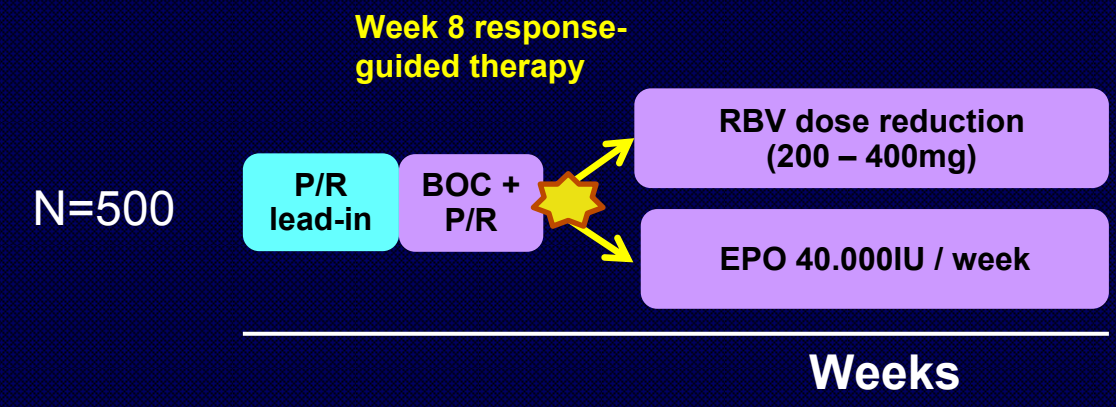
Sulkowski SM et al, EASL 2012, #1162

A randomized trial comparing ribavirin dose reduction versus erythropoietin for anemia management in previously untreated patients with chronic hepatitis c receiving boceprevir plus peginterferon/ribavirin

F.F. Poordad, E.J. Lawitz, K.R. Reddy, N.H. Afdhal,
C. Hézode, S. Zeuzem, S.S. Lee, J.L. Calleja,
R.S. Brown, Jr, A. Craxi, H. Wedemeyer, W. Deng,
K. Koury, N. Boparai, L.D. Pedicone, M. Burroughs,
J. Wahl, C.A. Brass, J.K. Albrecht, M.S. Sulkowski

Study design

- Design: Multinational, open-label trial
- Population (N=687):
  - Treatment-naive GT1 pts
  - Baseline Hb: 12–15 g/dL (female) and 13–15 g/dL (male)
- Treatment:

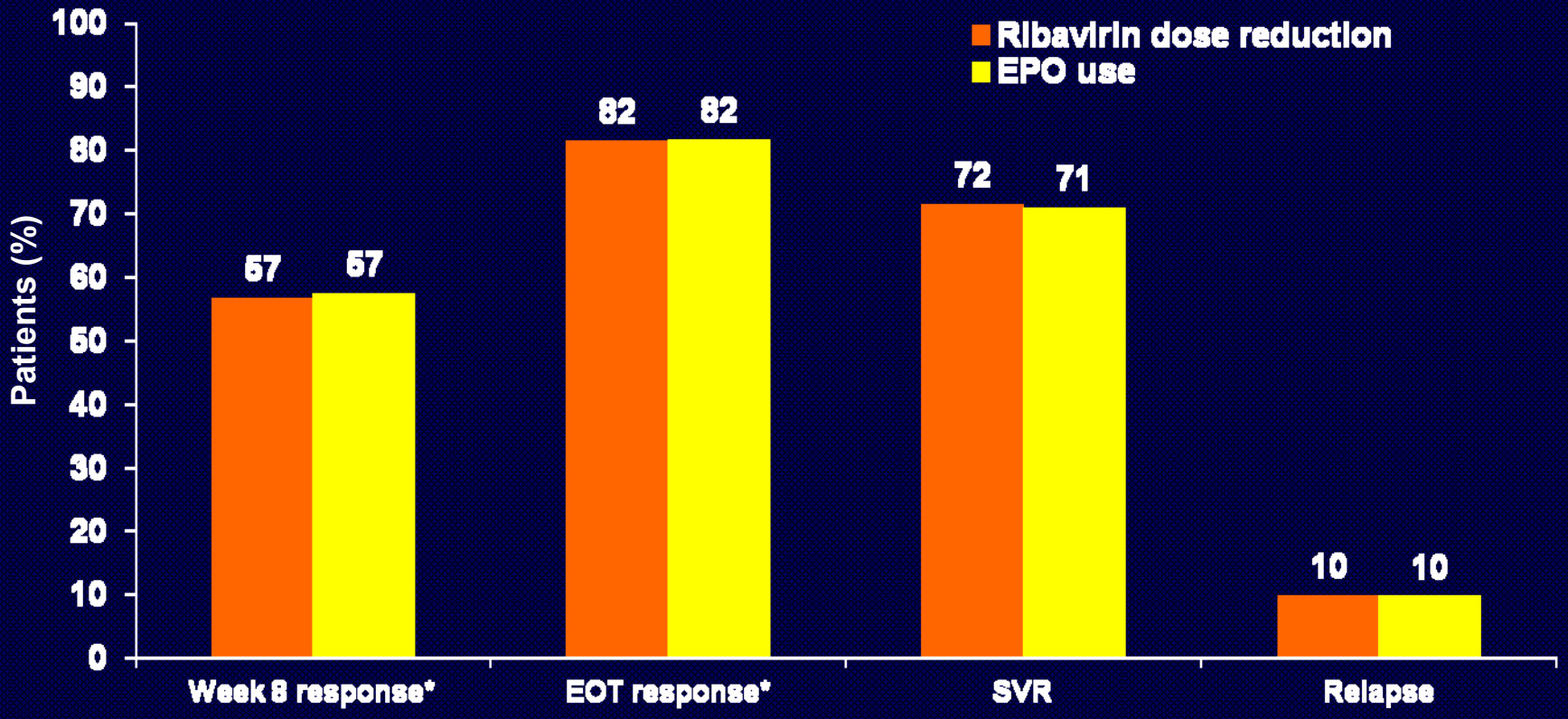


Randomization of patients with Hb<10g/dl

Poordad et al, EASL 2012, poster (1419, late-breaker)

RBV dose reduction vs. epo use in naive G1 pts receiving BOC + peginterferon alfa-2b + RBV

- A total of 500 patients developed anemia and were randomised to receive RBV dose reduction (by 200–400 mg/d) or EPO (40,000 units/wk sc)



*Undetectable HCV RNA

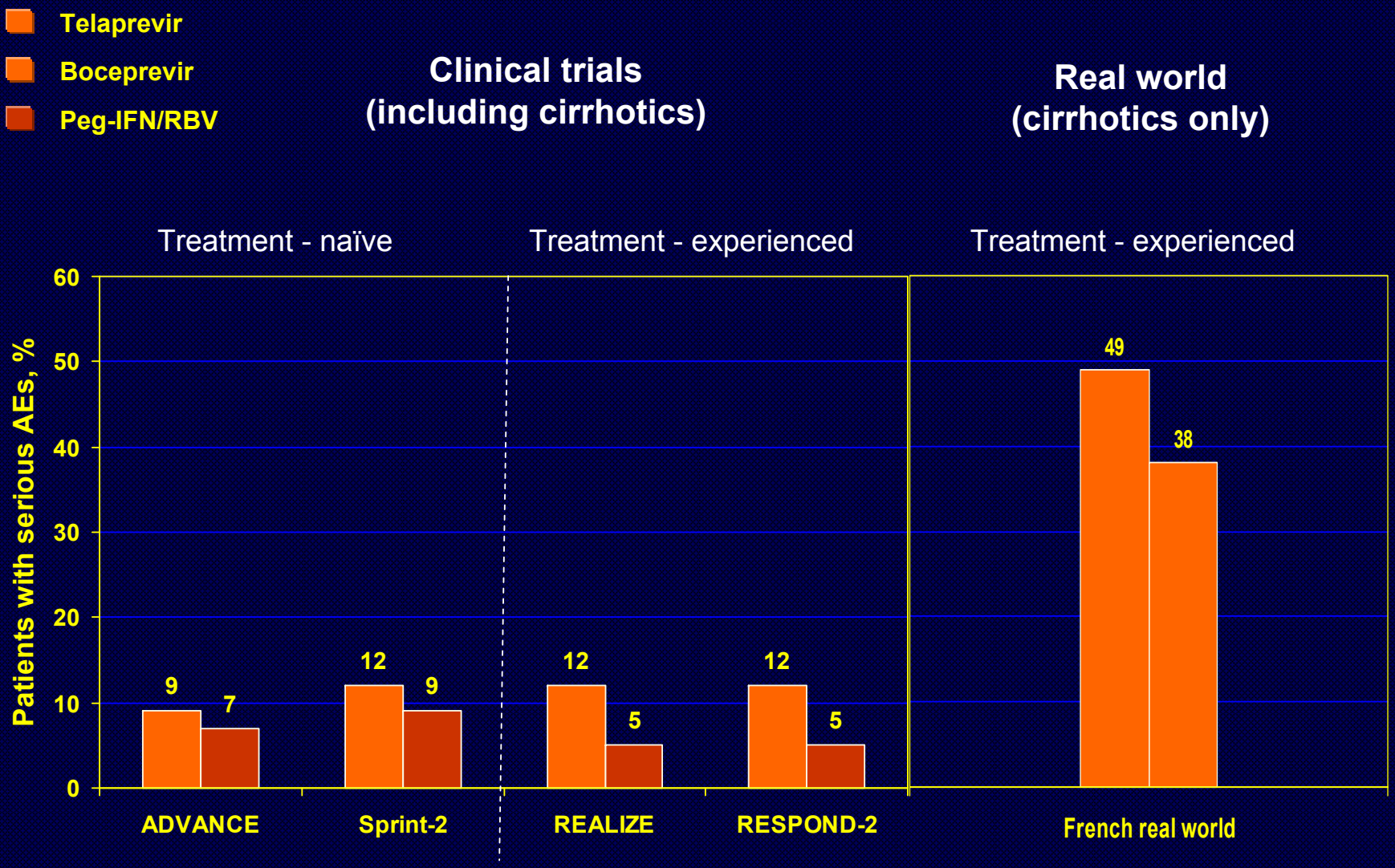
Poordad et al, EASL 2012, poster (1419, late-breaker)

Safety in Cirrhotics (CUPIC)

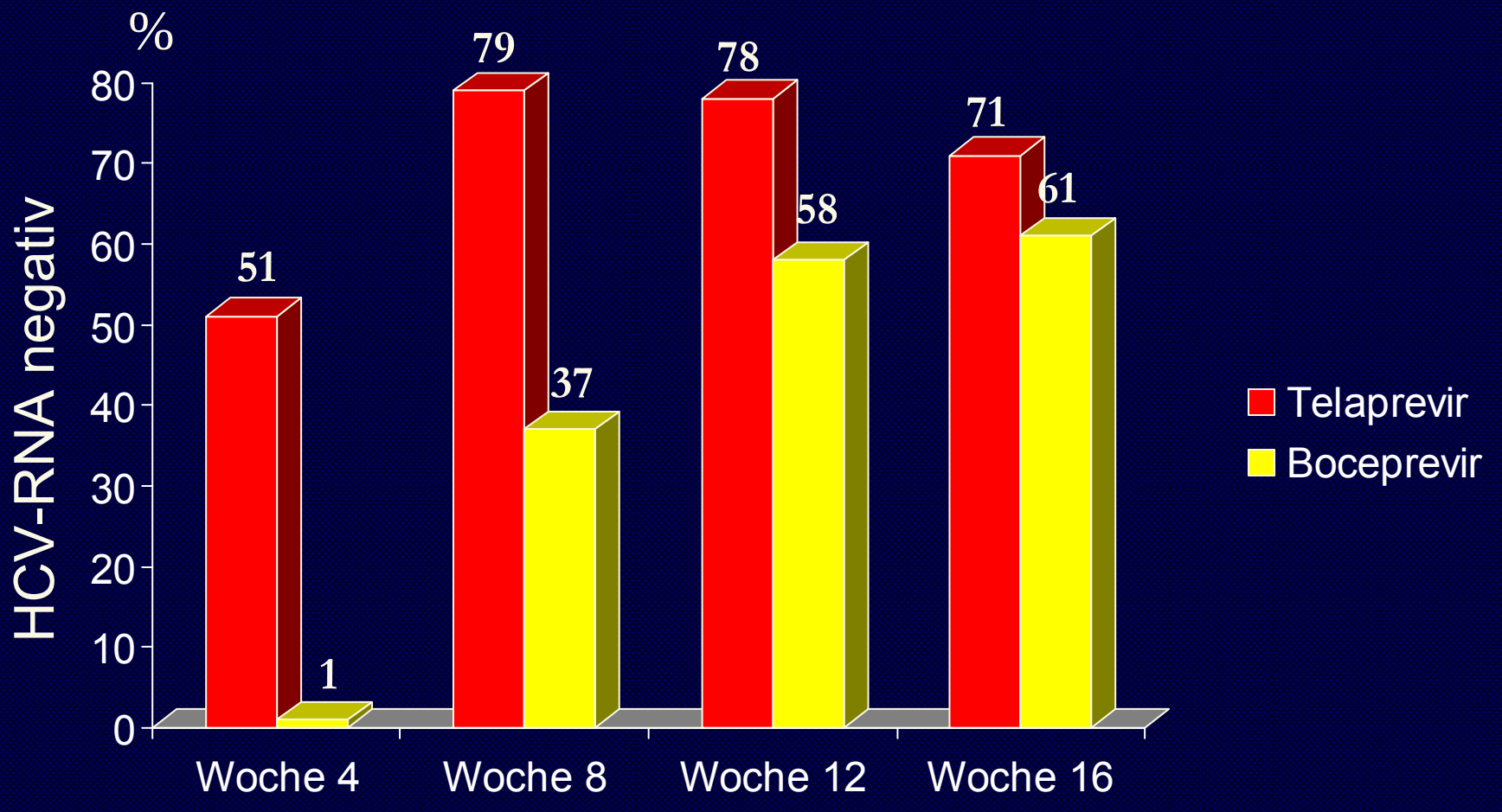
Patients (at week 16)	Telaprevir (n = 296) [%]
Serious adverse events (SAEs)	48.6
Premature discontinuation Premature discontinuation due to SAEs	26.0 14.5
Death Septicemia, septic shock, pneumopathy, variceal bleeding, encephalopathy, lung carcinoma	2.0 (6 cases)
Anemia Grade 2 (8.0 - <10.0 g/dl) Grade 3-4 (<0.8 g/dl) EPO use Blood transfusion	 19.6 10.1 56.8 15.2

Hezode C et al. EASL 2012

Clinical Trials vs Real World

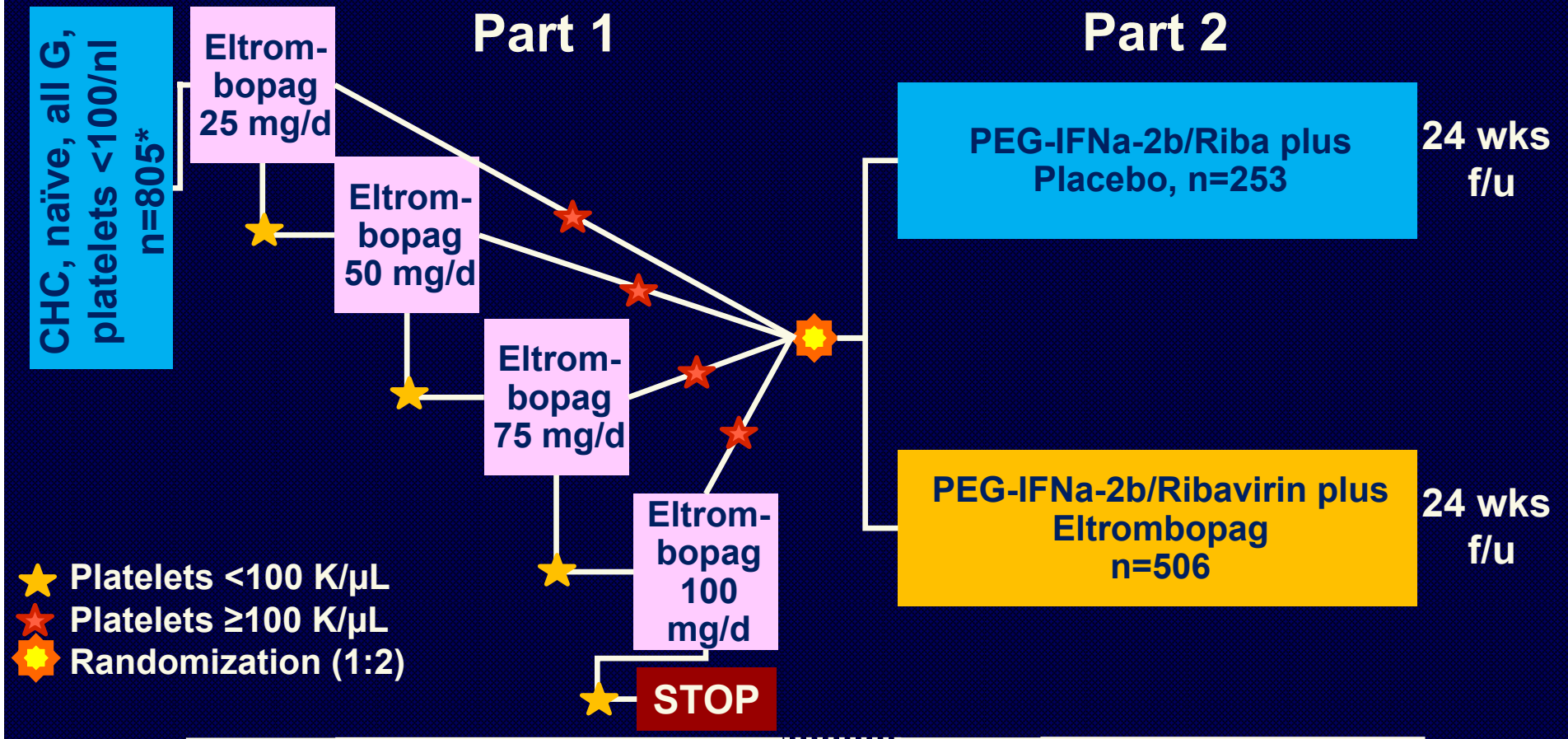


Virologisches Ansprechen
ITT-Analyse



Hezode EASL 2012 abstract 8

ENABLE 2 – Eltrombopag in Thrombocytopenic Subjects with HCV – Phase III Study



§ Discontinuation if no EVR (>2 $\log_{10}$ drop)

$ RBV dose and tx duration depending on genotype

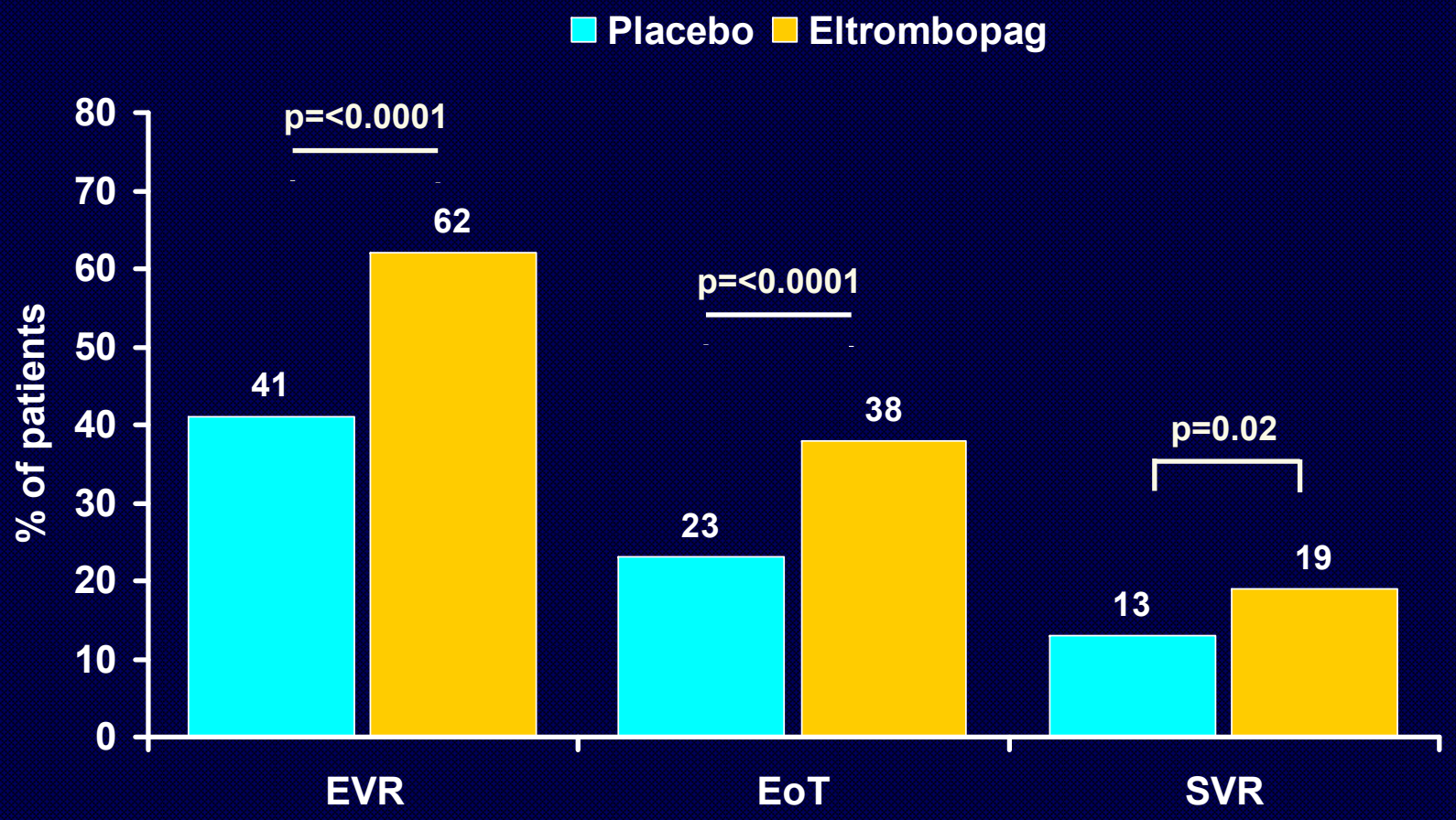
Dusheiko G et al, EASL 2012; #60

ENABLE-2 Phase III Study: Eltrombopag and Peg-IFNa-2b in HCV patients with thropmbocytopenia

- N=805
- Thrombozyten < 75/nl (mittel 59/nl)
- 94% erreichten unter Eltrombopag > 100/nl und erhielten einen antivirale Therapie
- 2:1 Randomisierung
  - N=506 Eltrombopag
  - N=253 Placebo

Dusheiko G et al, EASL 2012, #60 (S27)

ENABLE 2 – Final Results (all Genotypes)



Dusheiko G et al, EASL 2012, #60 (S27)

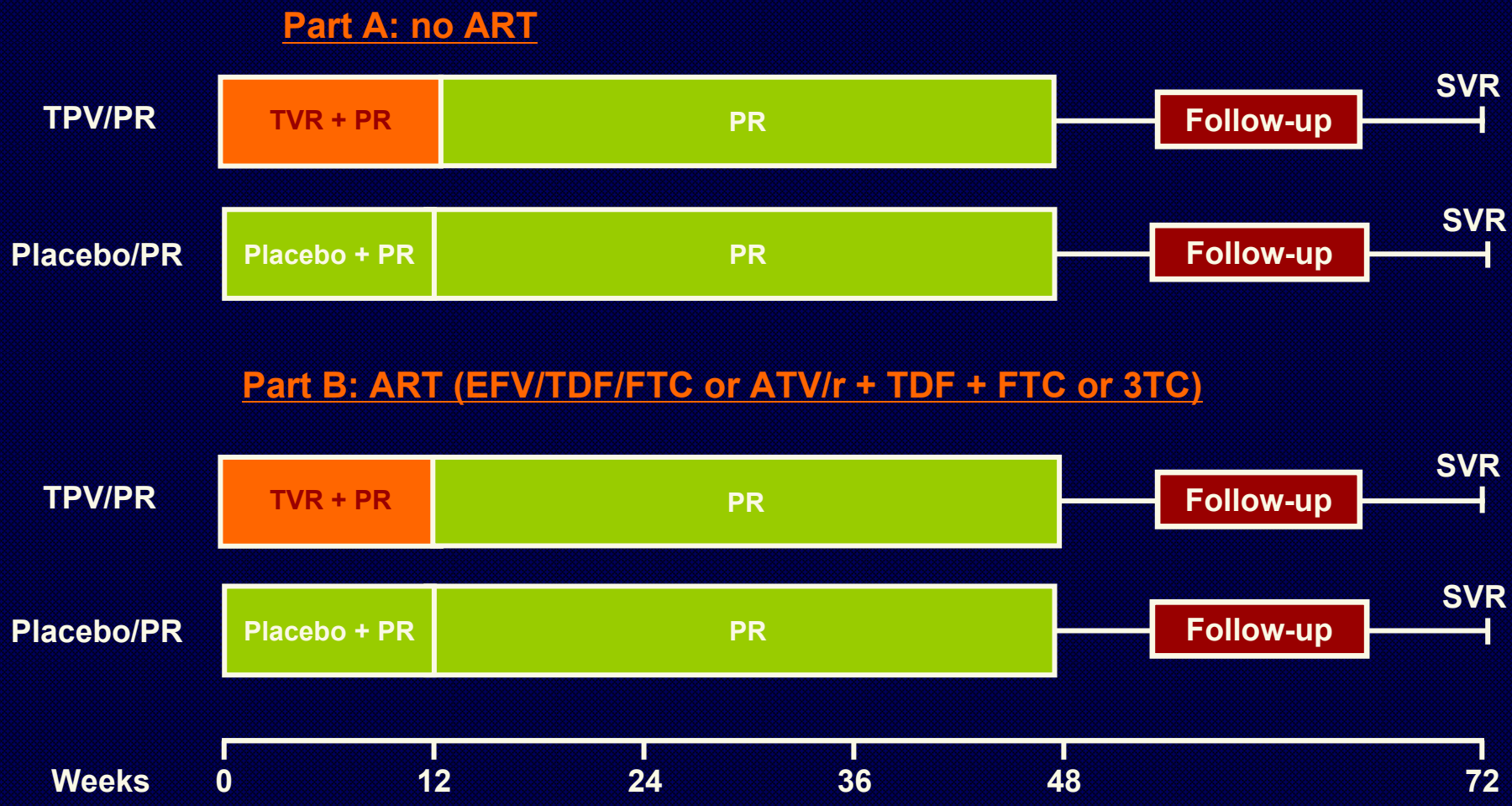
ENABLE-2 Phase III Study: Eltrombopag and Peg-IFNa-2b in HCV patients with thropmbocytopenia

AE	Placebo	Eltrombopag
Dekompensation	8%	15%
Thrombose	<1%	4%
Tod	2%	4%

Dusheiko G et al, EASL 2012, #60 (S27)

Triple Therapie bei HIV-HCV Koinfekiton

Telaprevir study 110
HIV/HCV koinfizierte Patienten - Studiendesign



EFV, efavirenz; TDF, tenofovir; FTC, emtricitabine; ATV/r, ritonavir-boosted atazanavir; 3TC, lamivudine; TVR, telaprevir 750 mg q8h or 1125 mg q8h (with EFV); PR, pegylated interferon alfa-2a (40 kDa) 180 µg/wk plus ribavirin 800 mg/day or weight-based (1000 mg/day if weight < 75 kg, 1200 mg/day if weight ≥ 75 kg; France, Germany) Roche COBAS® TaqMan® HCV test v2.0, LLOQ of 25 IU/mL (pts with values below 25IU/mL were reported as < 25 detectable or undetectable)

Sulkowski et al. CROI 2011, abstract 146LB.

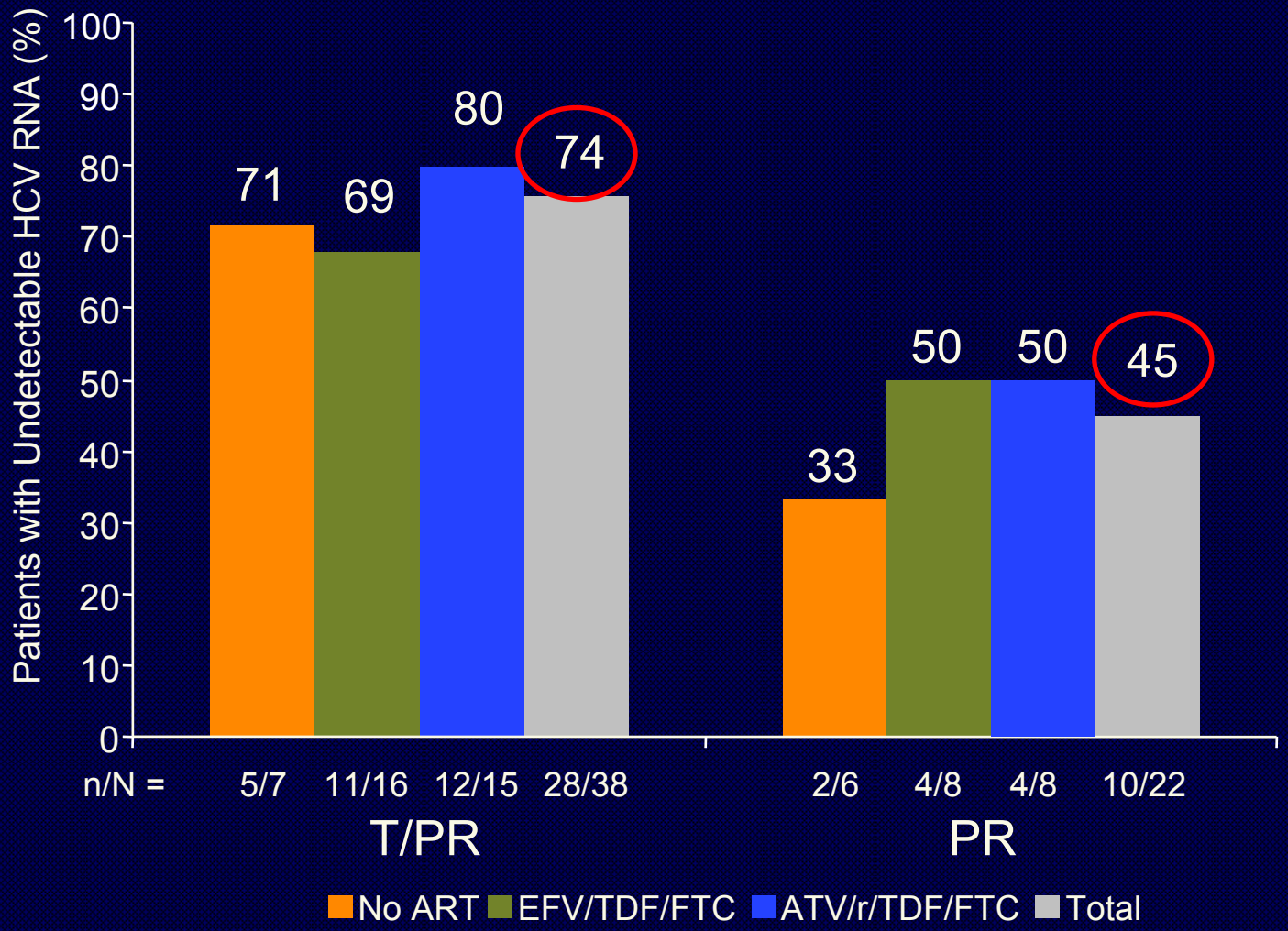
Telaprevir + PEG-IFNa-2a + Ribavirin in Naïve HIV HCV Co-Infected G1 – Week 24 Interim Results

n, %	Part A No ART		Part B EFV/TDF/FTC		Part B ATV/r + TDF + FTC		Total	
	T/PR N=7	Control N=6	T/PR N=16	Control N=8	T/PR N=15	Control N=8	TPR N=38	Control N =22
Undetectable HCV RNA* at wk 4 (RVR)	5 (71)	0 (0)	12 (75)	1 (12)	9 (60)	0 (0)	26 (68)	1 (4.5)
Undetectable HCV RNA* at wk 12 (cEVR)	6 (86)	2 (33)	14 (88)	2 (25)	11 (73)	3 (38)	31 (82)	7 (32)
Undetectable HCV RNA* at wk 24	6 (86)	2 (33)	12 (75)	4 (50)	10 (67)	6 (75)	28 (74)	12 (55)

* Roche Taqman® v2, LLOQ of 25 IU/mL, LOD of <10-15 IU/mL

Sherman et al, AASLD 2011, poster (LB-8)

Study 110
Therapieerfolg - SVR 12



*Patient was defined as SVR12 if HCV RNA was < LLOQ in the visit window

Dieterich D, et al. 19th CROI; Seattle, WA; March 5-8, 2012. #46

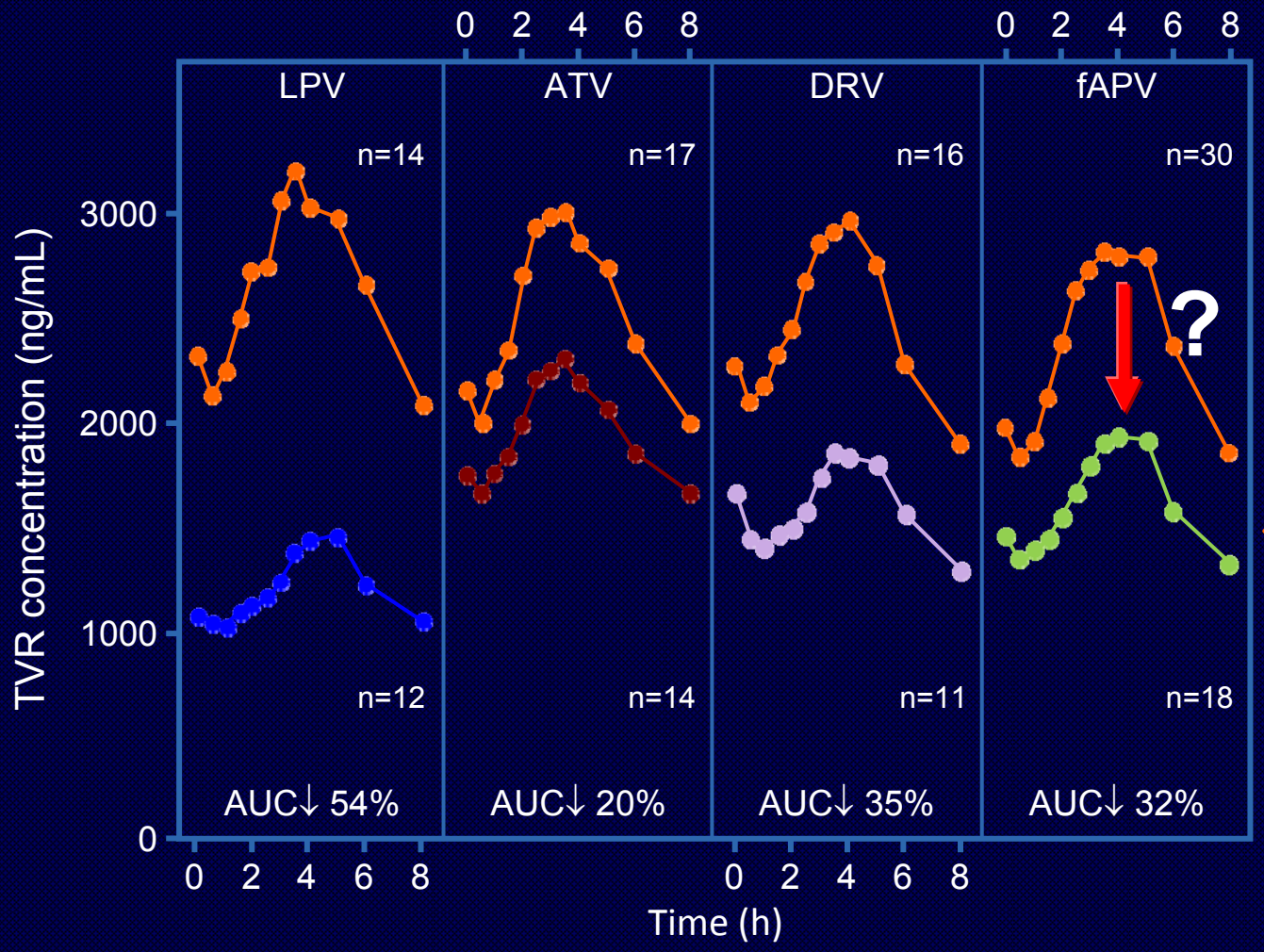
Telaprevirkonzentrationen

Parameter	ART Drug Regimens	In HIV/HCV Co-infected Patients	
		Ref Conc (no ART)	**Conc Ratio to Ref (%)**
		Mean (ng/mL)	**Mean (90% CI)**
C_{min}	**EFV**	1984	93 (56,156)
	ATV/r		131 (77, 222)
C_{avg}	**EFV**	2830	97 (64, 146)
	ATV/r		107 (70, 165)
C_{max}	**EFV**	3718	101 (72, 143)
	ATV/r		98 (69, 140)

EFV = efavirenz-based ART regimen; ATV = atazanavir/ritonavir-based ART regimen

Dieterich D, et al. 19th CROI; Seattle, WA; March 5-8, 2012. #46

Medikamenteninteraktionen Telaprevir und HIV-PIs



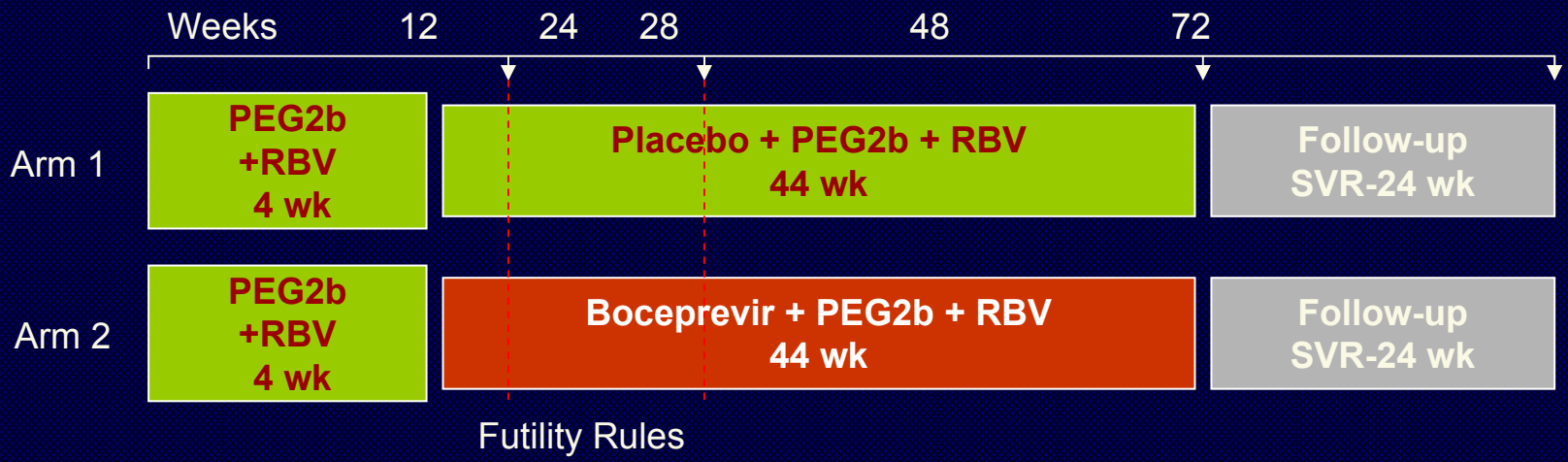
TVR alone

TVR + ARV

PK = pharmacokinetic
ART = antiretroviral therapy
TVR = telaprevir
LPV = lopinavir
ATV = atazanavir
DRV = darunavir
fAPV = fosamprenavir
AUC = area under the curve

Van Heeswijk et al. CROI 2011, abstract 119.

Boceprevir Phase II (HIV/HCV-koinfiziert): Studiendesign



	PR	B/PR
Any*	34 (100)	64 (100)
HIV protease inhibitors†	31 (91)	54 (84)
ATV/r	13 (38)	20 (31)
Lopinavir/r	10(29)	16 (25)
Darunavir/r	7 (21)	12 (19)
NRTIs††	33 (97)	60 (94)
Integrase inhibitors	4 (12)	11 (17)
CCR5 antagonists	1 (3)	1 (2)

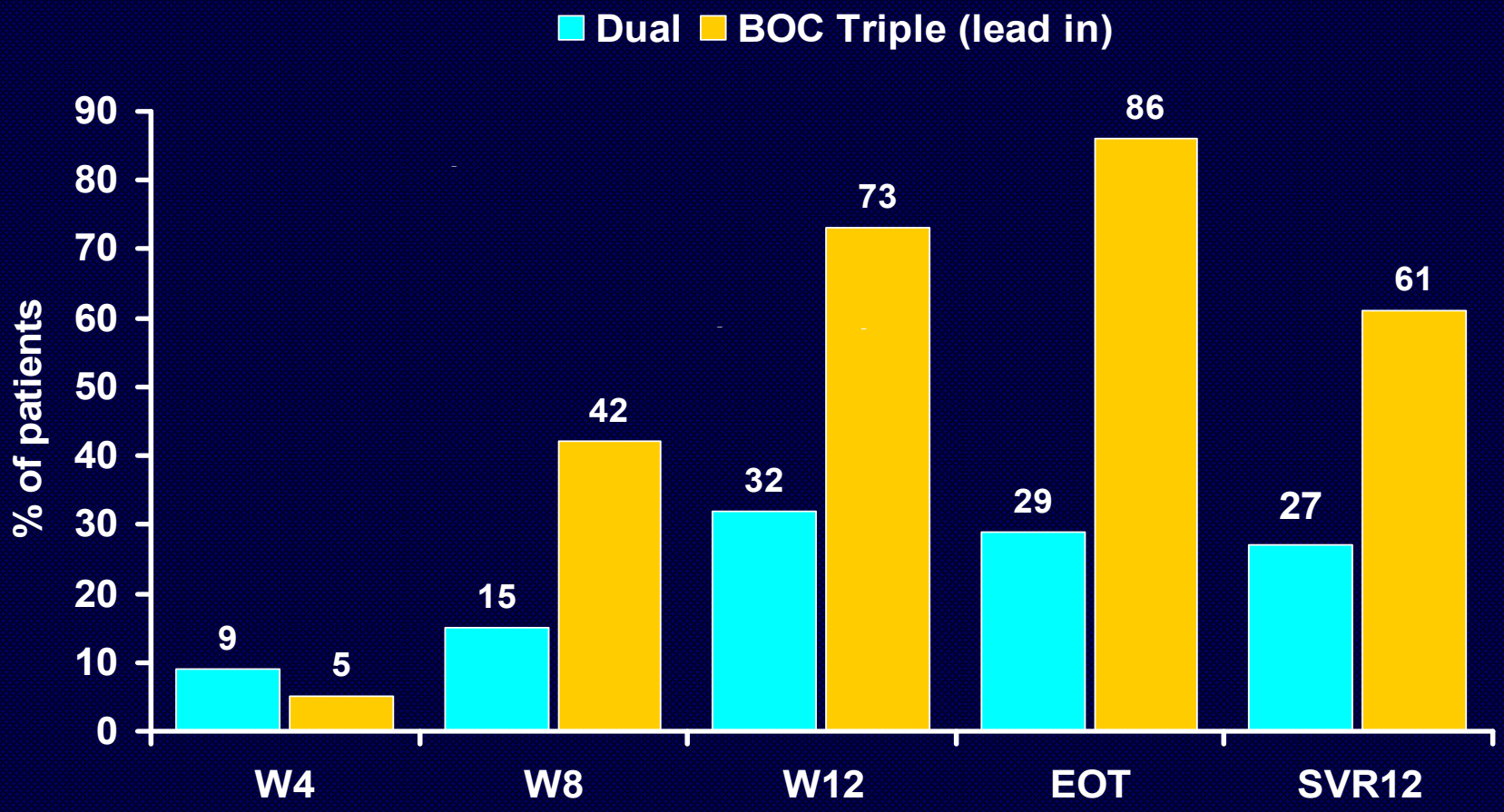
* To maintain blinding in this continuing study, data is only shown where at least 1 patient in each treatment group is represented.

† HIV PIs included ATVr, DRV/r, LPV/r, fAMP/r, SAQ/r

†† NRTIs included TDF, ABC, 3TC, FTC

Sulkowski et al. IDSA 2011, abstract LB-37.

Triple Therapie bei HCV HIV Koinfektion



Sulkowski M, et al.; 19th CROI; Seattle, WA, 2012. Abst. 47

Unerwünschte Ereignisse

	PR (N=34)	B/PR (N=64)
Any AE	34 (100)	63 (98)
Serious AEs	7 (21)	11 (17)
Death	0	0
Treatment-related treatment-emergent AEs	34 (100)	61 (95)
Study discontinuation due to an AE	3 (9)	13 (20)
Any drug modification due to an AE	8 (24)	18 (28)

All data shown as number (%) of patients.

Sulkowski M, et al.; 19th CROI; Seattle, WA, 2012. Abst. 47

Unerwünschte Ereignisse

	PR (N=34)	B/PR (N=64)
Anemia	26%	41%
Pyrexia	21%	36%
Asthenia	24%	34%
Decreased appetite	18%	34%
Diarrhea	18%	28%
Dysgeusia	15%	28%
Vomiting	15%	28%
Flu-like illness	38%	25%
Neutropenia	6%	19%

Sulkowski M, et al.; 19th CROI; Seattle, WA, 2012. Abst. 47

HIV Durchbrüche unter B/PR

- Overall, 7 patients had HIV breakthrough (>50 copies HIV RNA at 2 consecutive visits): 3/64 randomized to B/PR, and 4/34 to PR

Regimen	HIV RNA (copies/mL)						
	BL	TW4	TW12	TW24	TW36	EOT	FW4
ATV/r	<50	<50	---	659	---	53	2990
†LPV/r	<50	<50	<50	55	59	67	68
ATV/r	<50	<50	<50	<50	243	---	7870

ATV/r, atazanavir/ritonavir; LPV/r, lopinavir/ritonavir
†The only subject to change ART. LPV/r changed to ATV/r at TW42; ATV/r to DRV/r at FW24.

Sulkowski M, et al.; 19th CROI; Seattle, WA, 2012. Abst. 47

BOC Wechselwirkung mit ATV/RTV

Table 1. PK Interactions Among BOC, ATV, and RTV

PK Parameter	N	GM	N	GM	GMR	90% CI	rMSE†
ATV PK	**ATV/RTV MD**		**BOC MD + ATV/ RTV MD**		**(BOC + ATV/RTV)/ (ATV/RTV)**		
$AUC_{0\text{-last}}$‡ (ng•hr/mL)	12	39,900	11	26,000	0.65	(0.55, 0.78)	0.23
C_{max}‡ (ng/mL)	12	3,610	11	2,700	0.75	(0.64, 0.88)	0.21
C_{min}‡ (ng/mL)	12	693	11	357	0.51	(0.44, 0.61)	0.22
BOC PK	**BOC MD**		**BOC MD + ATV/ RTV MD**		**(BOC + ATV/RTV)/ (BOC)**		
AUC_{τ}‡ (ng•hr/mL)	13	4,840	11	4,610	0.95	(0.87, 1.05)	0.12
C_{max}‡ (ng/mL)	13	1,450	11	1,350	0.93	(0.80, 1.08)	0.20
C_{min}‡ (ng/mL)	13	106	11	86.6	0.82	(0.68, 0.98)	0.25
RTV PK	**ATV/RTV MD**		**BOC MD + ATV/ RTV MD**		**(BOC + ATV/RTV)/ (ATV/RTV)**		
AUC_{τ}‡ (ng•hr/mL)	12	9,270	11	5,980	0.64	(0.58, 0.72)	0.14
C_{max}‡ (ng/mL)	12	1,470	11	1,080	0.73	(0.64, 0.83)	0.17
C_{min}‡ (ng/mL)	12	35.8	8	19.8	0.55	(0.45, 0.67)	0.21

Hulskotte et al.; 19th CROI; Seattle, WA, 2012. Abst. 771LB

BOC Wechselwirkung mit LPV/RTV

Table 2. PK Interactions Among BOC, LVR, and RTV

PK Parameter	N	GM	N	GM	GMR	90% CI	rMSE[†]
LPV PK	**LPV/RTV MD**		**BOC MD + LPV/RTV MD**		**(BOC + LPV/RTV)/(LPV/RTV)**		
$AUC_{0\text{-last}}$[‡] (ng•hr/mL)	13	117,000	13	77,000	0.66	(0.60, 0.72)	0.13
C_{max}[‡] (ng/mL)	13	13,300	13	9,370	0.70	(0.65, 0.77)	0.12
C_{min}[‡] (ng/mL)	13	6,730	13	3,800	0.57	(0.49, 0.65)	0.19
BOC PK	**BOC MD**		**BOC MD + LPV/RTV MD**		**(BOC + LPV/RTV)/(BOC)**		
AUC_{τ}[‡] (ng•hr/mL)	13	6,040	13	3,310	0.55	(0.49, 0.61)	0.15
C_{max}[‡] (ng/mL)	13	1,770	13	878	0.50	(0.45, 0.55)	0.15
C_{min}[‡] (ng/mL)	13	91.9	12	39.8	0.43	(0.36, 0.53)	0.27
RTV PK	**LPV/RTV MD**		**BOC MD + LPV/RTV MD**		**(BOC + LPV/RTV)/(BOC)**		
AUC_{τ}[‡] (ng•hr/mL)	12	5,440	13	4,270	0.78	(0.71, 0.87)	0.15
C_{max}[‡] (ng/mL)	13	990	13	869	0.88	(0.72, 1.07)	0.28
C_{min}[‡] (ng/mL)	13	155	13	90.5	0.58	(0.52, 0.65)	0.16

Hulskotte et al.; 19th CROI; Seattle, WA, 2012. Abst. 771LB

BOC Wechselwirkung mit DRV/RTV

Table 3. PK Interactions Among BOC, DRV, and RTV

PK Parameter	N	GM	N	GM	GMR	90% CI	rMSE†
DRV PK	**DRV/RTV MD**		**BOC MD + DRV/ RTV MD**		**(BOC + DRV/RTV)/ (DRV/RTV)**		
$AUC_{0\text{-last}}$‡ (ng•hr/mL)	11	60,300	11	33,500	0.56	(0.51, 0.61)	0.12
C_{max}‡ (ng/mL)	11	8,090	11	5,190	0.64	(0.58, 0.71)	0.13
C_{min}‡ (ng/mL)	10	3,220	11	1,320	0.41	(0.38, 0.45)	0.11
BOC PK	**BOC MD**		**BOC MD + DRV/ RTV MD**		**(BOC + DRV/RTV)/ (BOC)**		
AUC_{τ}‡ (ng•hr/mL)	12	5,350	11	3,650	0.68	(0.65, 0.72)	0.072
C_{max}‡ (ng/mL)	12	1,560	11	1,180	0.75	(0.67, 0.85)	0.16
C_{min}‡ (ng/mL)	12	94.7	11	61.5	0.65	(0.56, 0.76)	0.20
RTV PK	**DRV/RTV MD**		**BOC MD + DRV/ RTV MD**		**(BOC + DRV/RTV)/ (BOC)**		
AUC_{τ}‡ (ng•hr/mL)	11	4,830	10	3,530	0.73	(0.68, 0.79)	0.092
C_{max}‡ (ng/mL)	11	776	11	677	0.87	(0.76, 1.00)	0.18
C_{min}‡ (ng/mL)	11	155	11	86.1	0.55	(0.52, 0.59)	0.077

BOC, boceprevir; CI, confidence interval; DRV, darunavir; GM, geometric least-squares mean; GMR,

Hulskotte et al.; 19th CROI; Seattle, WA, 2012. Abst. 771LB

SVR in Abhängigkeit von der ART

	PR	B/PR
Atazanavir/r	**8/13 (62%)**	**12/18† (67%)**
Lopinavir/r	**0/10 (0%)**	**10/15†† (67%)**
Darunavir/r	**0/5 (0%)**	**8/12 (67%)**
Other PI/r*	**0/3 (0%)**	**4/7 (57%)**
Raltegravir**	**1/3 (33%)**	**3/7 (43%)**
Other¶	**0**	**0/2 (0%)**

† Excludes 2 patients not yet at FW12 but undetectable at FW4.

†† Excludes 1 patient not yet at FW12 but undetectable at FW4.

*Includes saquinavir, fosamprenavir and tipranavir; **Raltegravir without concurrrent HIV PI/r

¶other ARV's were maraviroc and efavirenz

Sulkowski M, et al.; 19th CROI; Seattle, WA, 2012. Abst. 47

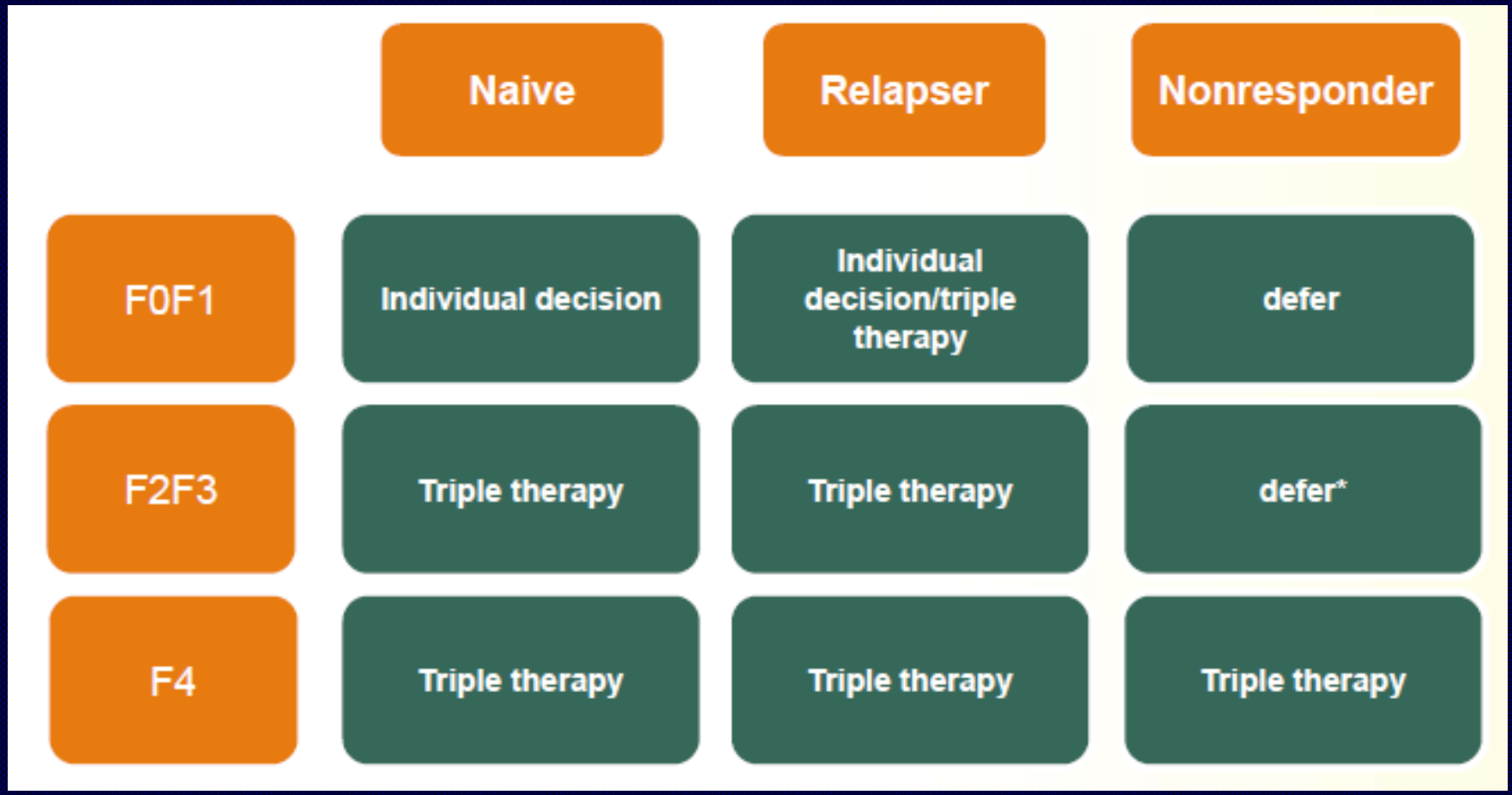
Mögliche ART simultan zur Therapie der HCV-Koinfektion

Limited choice of antiretrovirals

Telaprevir
- **NRTIs**
- **raltegravir**
- **atazanavir/r**
- **(efavirenz: dose increase of TPV to 1125 mg tid)**

Boceprevir
- **NRTIs**
- **raltegravir**
- **(atazanavir: ATV AUC – 35%, BCV +5%)**

Expert view: Management of HIV/HCV GT1-coinfected patients (chronic) according to prior treatment outcome



*monitor fibrosis stage annually, preferably with two established methods. Treat with triple therapy, if rapid progression.

Rockstroh J; 51st ICAAC,;Chicago IL; September 17-20, 2011. Symposium 155.

DHHS Guidelines: Use of ARVs in HIV/HCV coinfected patients

- Given the substantial heterogeneity in patient populations and drug regimens, comparison of hepatotoxicity rates for individual ARV agents across clinical trials is difficult.
- Initial combination regimens preferred for the ARV-naïve patient with HCV/HIV are the same as for persons without HCV infection (TDF/FTC + ATV/r, DRV/r, EFV or RAL)
- The highest incidence rates of Grade 3 or 4 elevations in liver enzyme levels have been observed during therapy with d4T, NVP, full-dose RTV or TPV/r. These drugs should be used with caution
- Cirrhotic patients should be carefully monitorized. Overall, PIs and RAL are not recommended in patients with severe hepatic impairment.

Soriano et al. Antiviral Res 2010;85:303

Antiretrovirals and efficacy of hcv therapy

Table 3. SVR after pegylated interferon plus ribavirin according to the different NRTI backbones including only patients with G1 or 4 and HCV RNA >500000 IU/mL

NRTI backbone	*n*	% SVR	AOR[a]	95% CI	*P*
TDF+3TC/FTC	172	20.9	reference	—	—
3TC+d4T	104	19.2	0.84	0.44–1.61	0.594
AZT+3TC overall	157	18.5	0.83	0.46–1.50	0.542
AZT+3TC without ABC	89	18.0	0.76	0.37–1.55	0.444
AZT+3TC with ABC	68	19.1	0.94	0.44–2.04	0.880
3TC+ABC without AZT	54	25.9	1.20	0.53–2.70	0.660
ddI+d4T	21	9.5	0.43	0.09–1.97	0.278
ddI+3TC/FTC	23	17.4	0.87	0.27–2.77	0.810

TDF, tenofovir; 3TC, lamivudine; FTC, emtricitabine; d4T, stavudine; AZT, zidovudine; ABC, abacavir; ddI, didanosine; AOR, adjusted odds ratio.
[a]Adjusted for CDC clinical category and ribavirin dose (mg/kg/day).

Table 4. SVR after pegylated interferon plus ribavirin according to the third drug used in the HAART regimen (NNRTI or protease inhibitor)

HAART regimens	*N*	% SVR	AOR[a]	95% CI	*P*
2 NRTIs+1 NNRTI	682	39.1	reference	—	—
2 NRTIs+1 unboosted PI	172	40.7	1.09	0.72–1.64	0.684
2 NRTIs+1 boosted PI	244	30.7	0.72	0.40–1.32	0.289
2 NRTIs+other	37	29.7	0.42	0.16–1.09	0.075
Other combinations	566	38.5	0.94	0.71–1.24	0.637

AOR, adjusted odds ratio; PI, protease inhibitor.
[a]Adjusted for HCV genotype, HCV RNA level, CDC clinical category, ribavirin dose (mg/kg/day) and use of zidovudine+lamivudine.

Berenguer J Antimicrob Chemother 2011, epub ahead of print

Factors associated with sustained virological response to HCV therapy in HIV patients

Host	Virus	Treatment
Genetic (white ethnicity) **IL28B (in GT1)**	**Genotypes 2/3**	**Adequate peginterferon dose**
Younger age	**Low baseline HCV RNA**	**Weight-based ribavirin dose**
Minimal liver fibrosis	**Undetectable HCV-RNA at week 4**	**Good adherence**
Lower BMI		**No concurrent didanosine or zidovudine**
Lack of insulin resistance		
Higher CD4 count		
No psychiatric disease		

Soriano et al. Antiviral Res 2010;85:303