HIV/HCV-Koinfektion: „Good news?“

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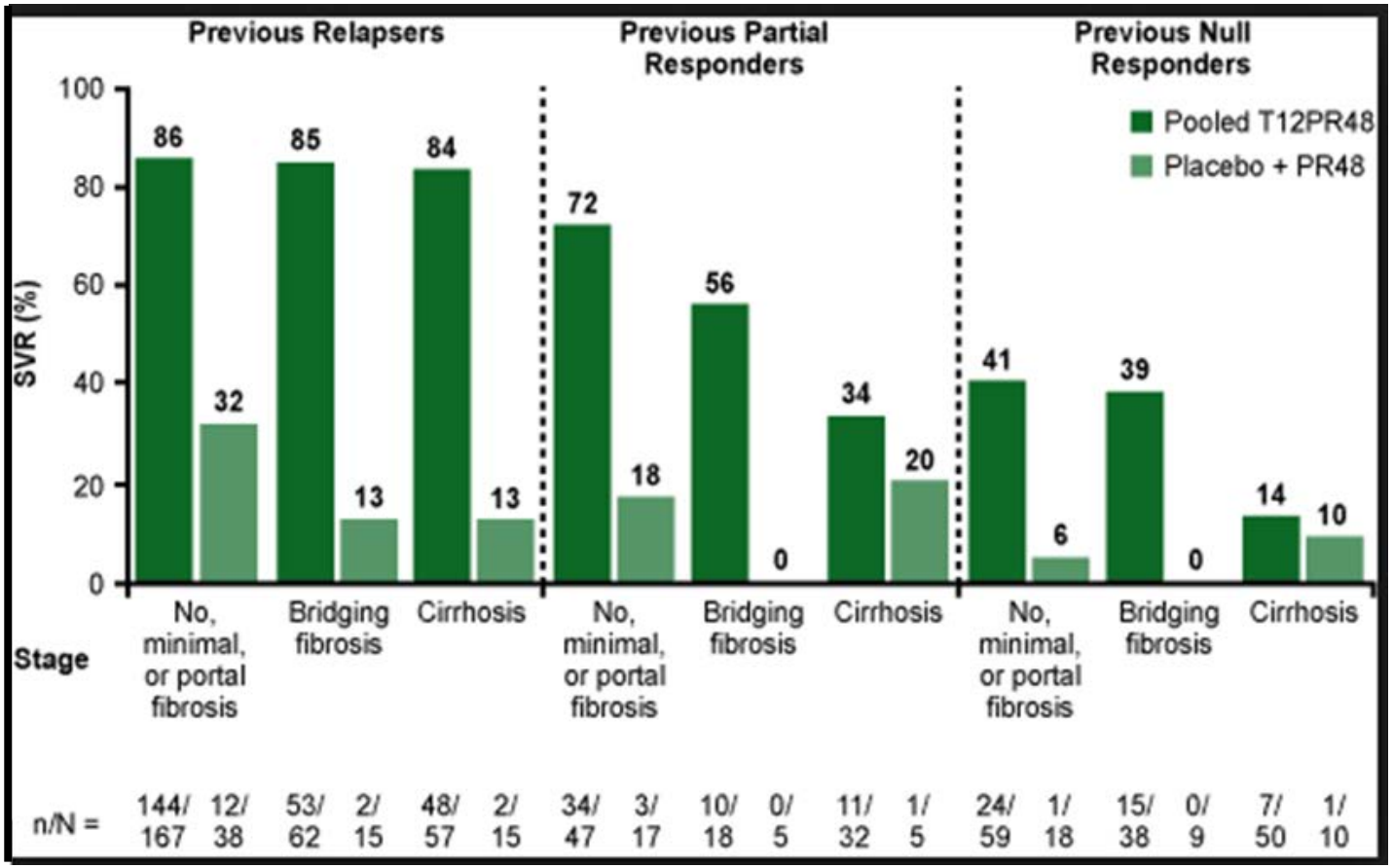
Telaprevir und Boceprevir bei vorbehandelten Patienten

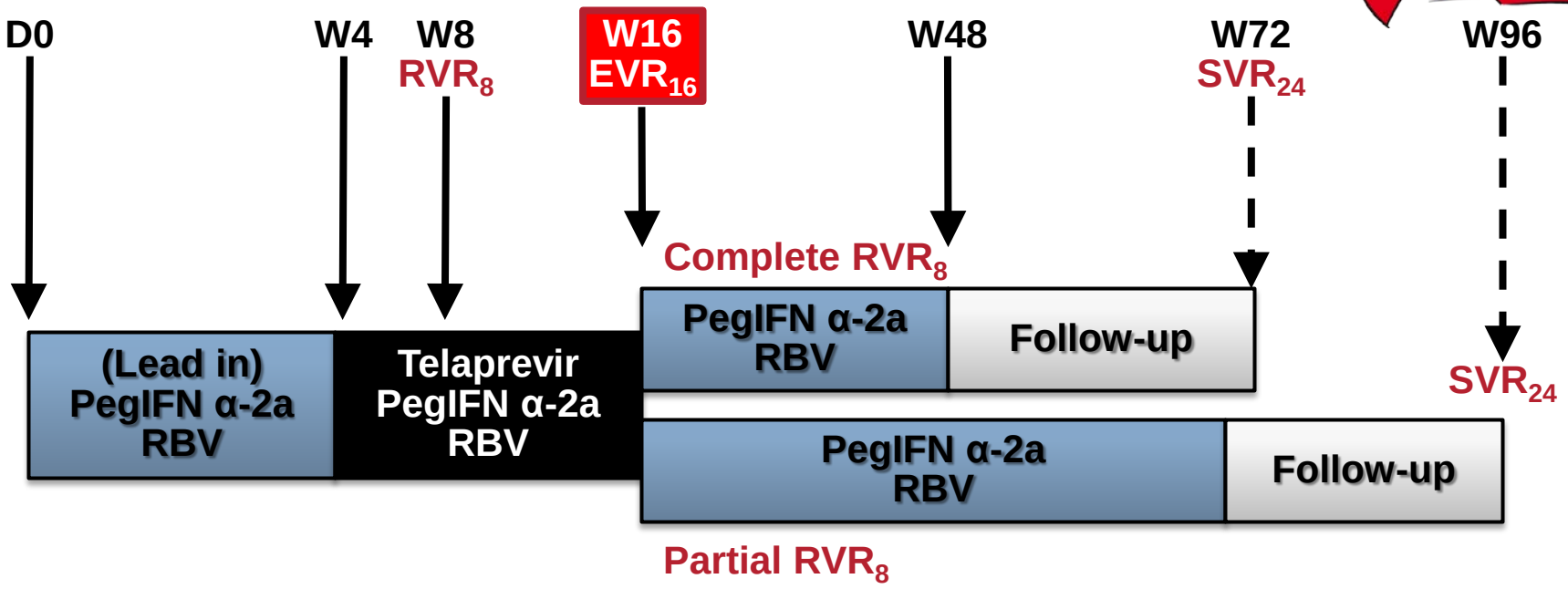
2 ANRS Studien bei ‘difficult-to-treat’ Patienten

Pooled data on telaprevir in treatment-experienced patients



Telaprevir + PegIFN + RBV in HIV/HCV Co-infected Patients with Virologic Failure on IFN + RBV

Single Arm, Phase 2 Clinical Trial



- Complete RVR_8 (HCV-RNA <15 IU/mL): 32 weeks PR phase (Total treatment: 48 weeks)
- Partial RVR_8 (15 IU/mL <HCV-RNA <1,000 IU/mL) 56 weeks PR phase (Total treatment: 72 weeks)

Cotte L, et al. 20th CROI; Atlanta, GA; March 3-6, 2013. Abst. 36.

Telaprevir + PegIFN + RBV in HIV/HCV Co-infected Patients with Virologic Failure on IFN + RBV

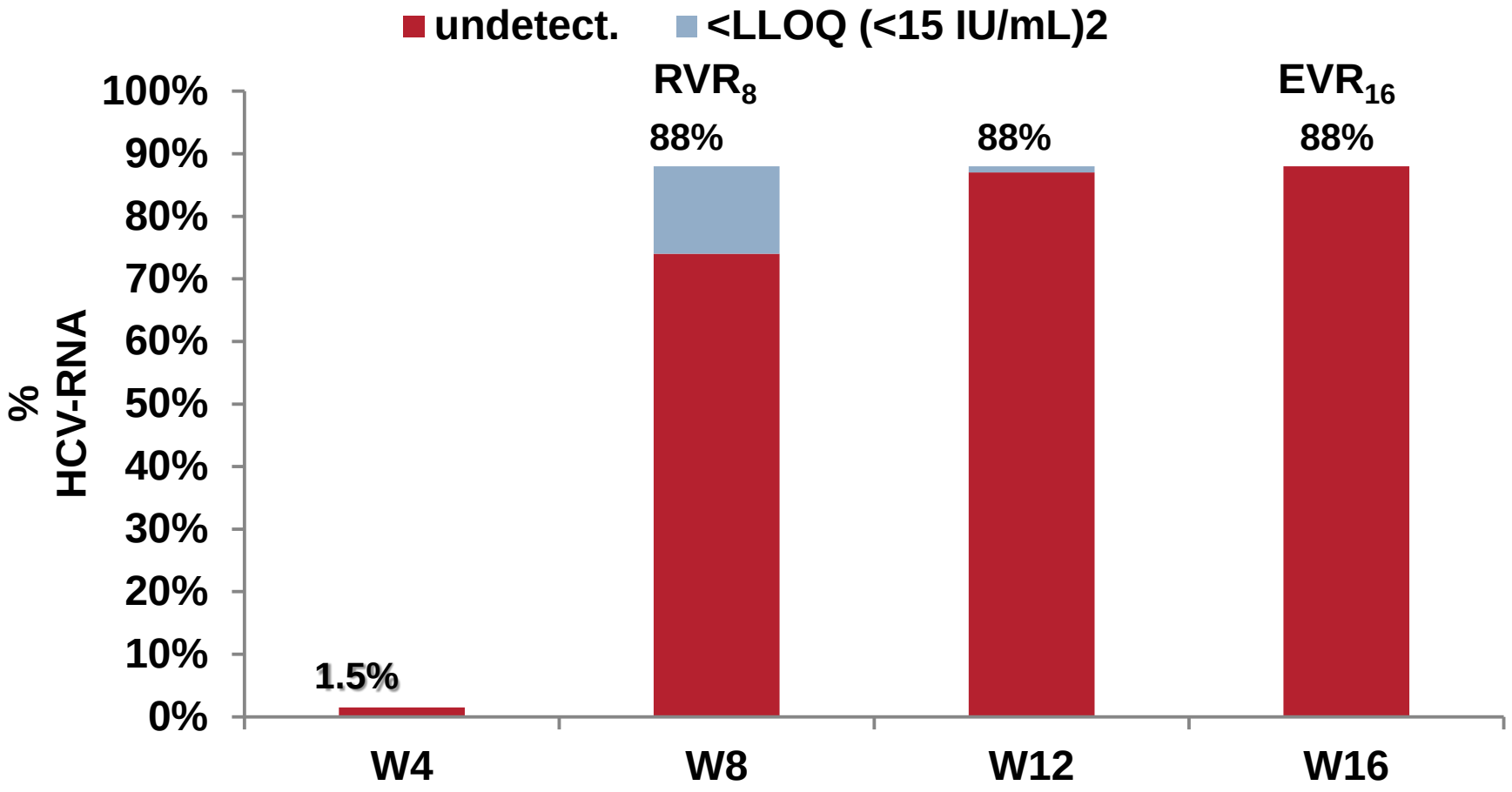
- Main Inclusion Criteria
  - HCV genotype 1 infection and HIV-1 infection
  - ***Previous virological failure*** *after ≥12 weeks PegIFN + RBV*
  - Stable ART for ≥3 months
  - Authorized antiretrovirals: **ATV, ATVr, EFV, RAL, TDF, FTC, 3TC**
  - CD4 ≥200 cells/mm^{3,} plasma HIV-RNA levels <50 cp/mL
  - Liver biopsy <3 years or cirrhosis on any previous biopsy
- Main Exclusion Criteria
  - HVB coinfection, HIV-2 infection
  - **Previous null response with cirrhosis**
- Important patient characteristics
  - **Relapser 39%, previous breakthrough 9%, partial responder 22%, Null-responder 30%**
  - F3 16%, F4 23%; HCV GT1a 70%

Cotte L, et al. 20th CROI; Atlanta, GA; March 3-6, 2013. Abst. 36.

Grade 3-4 AEs and treatment discontinuations up to W16

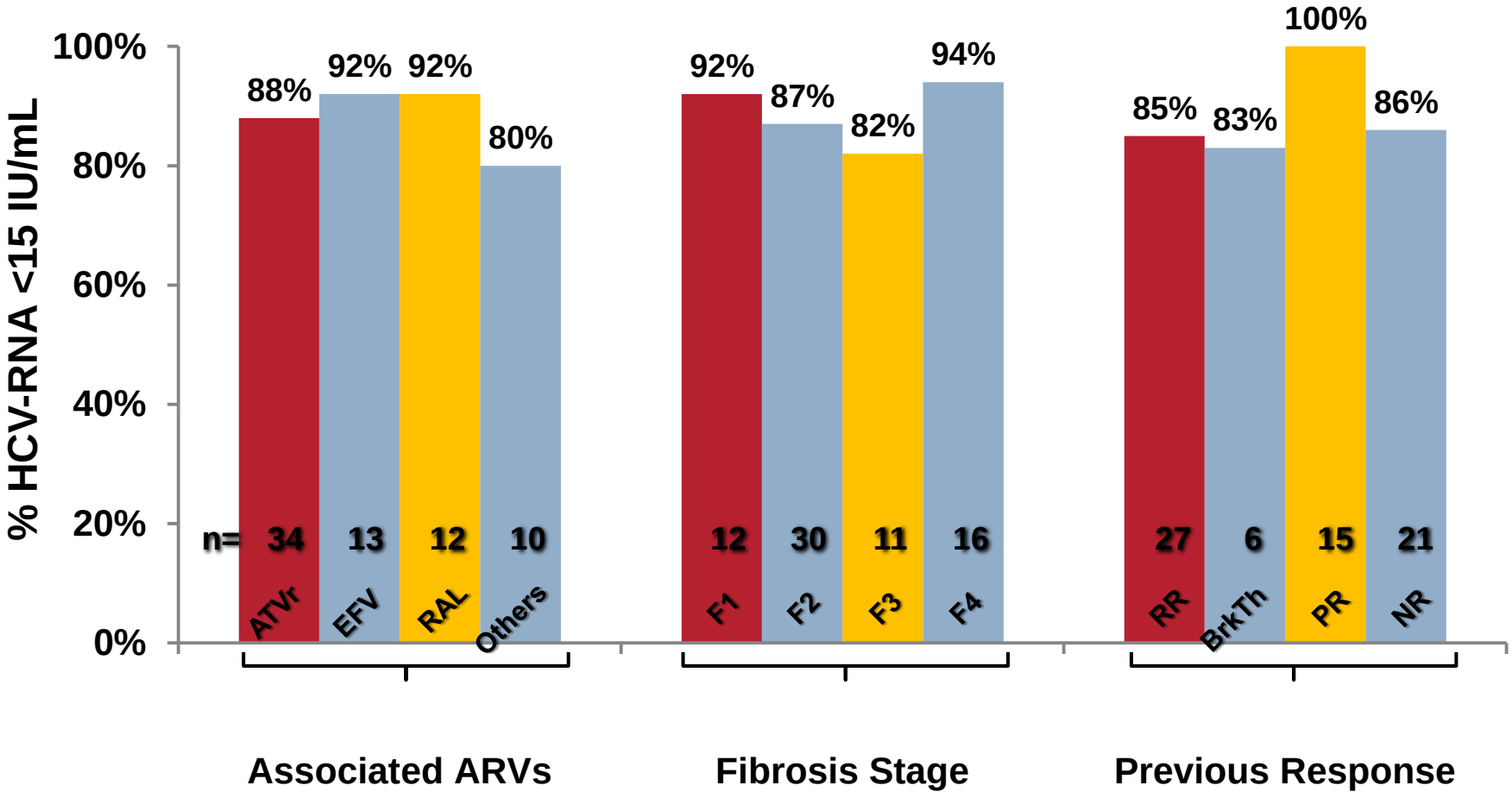
	N (%), n=69
Grade 3 AEs	18 (26%)
Blood	6 (9%)
General	5 (7%)
GI	2 (3%)
Cutaneous	3 (4%)
Neurological	2 (3%)
Psychiatric	1 (1%)
Others	2 (3%)
Grade 4 AEs	5 (7%)
Blood	4 (6%)
Psychiatric	1 (1%)
Reasons for treatment discontinuations	
Psychiatric AEs	3 (4%)
Cutaneous AEs	3 (4%)
Others AEs	1 (1%)
Virological failure	1 (1%)

Telaprevir + PegIFN + RBV in HIV/HCV Co-infected Patients with Virologic Failure on IFN + RBV: Virologic Response



Cotte L, et al. 20th CROI; Atlanta, GA; March 3-6, 2013. Abst. 36.

Telaprevir + PegIFN + RBV in HIV/HCV Co-infected Patients with Virologic Failure on IFN + RBV: Early Virologic Response by Patient Group



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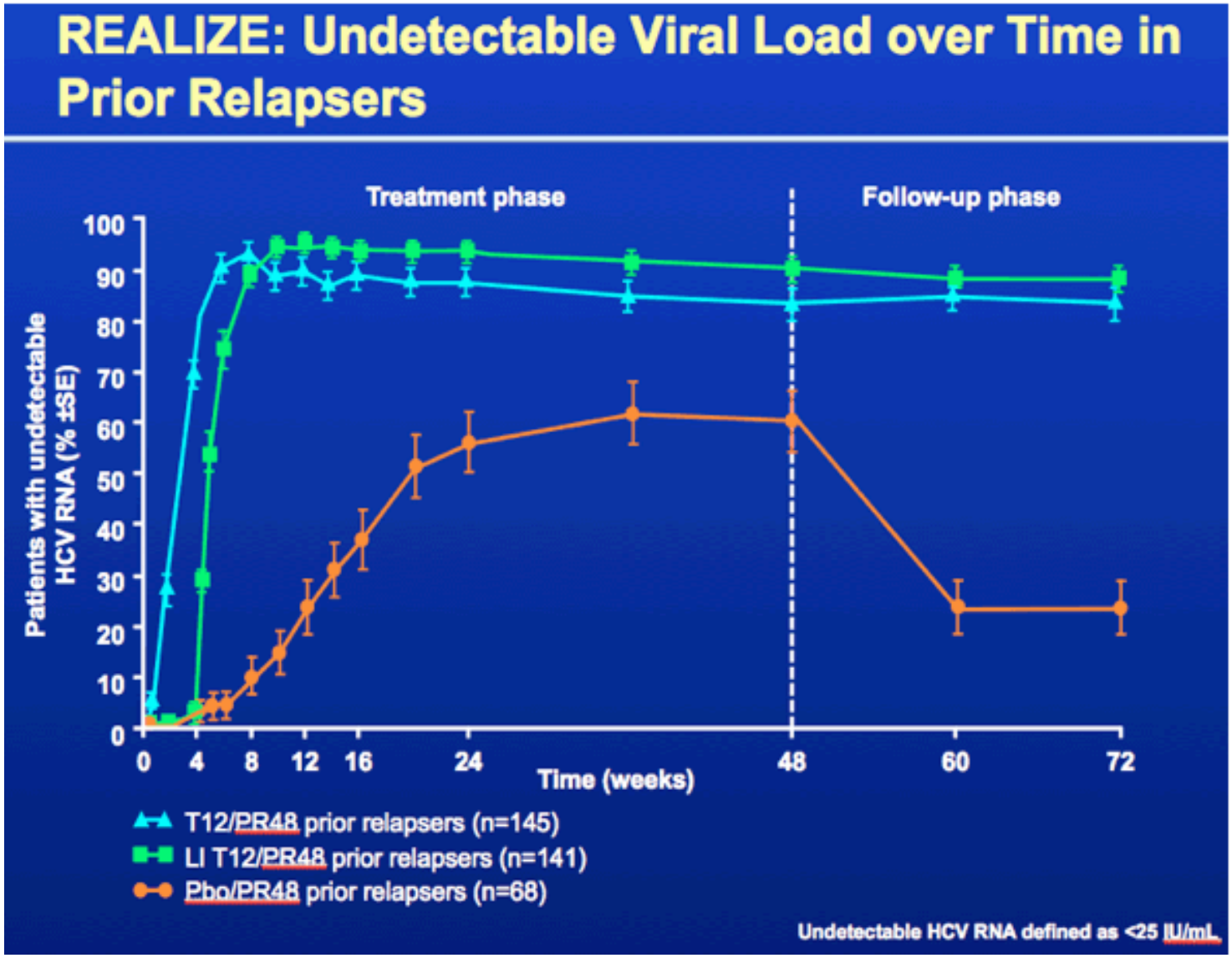
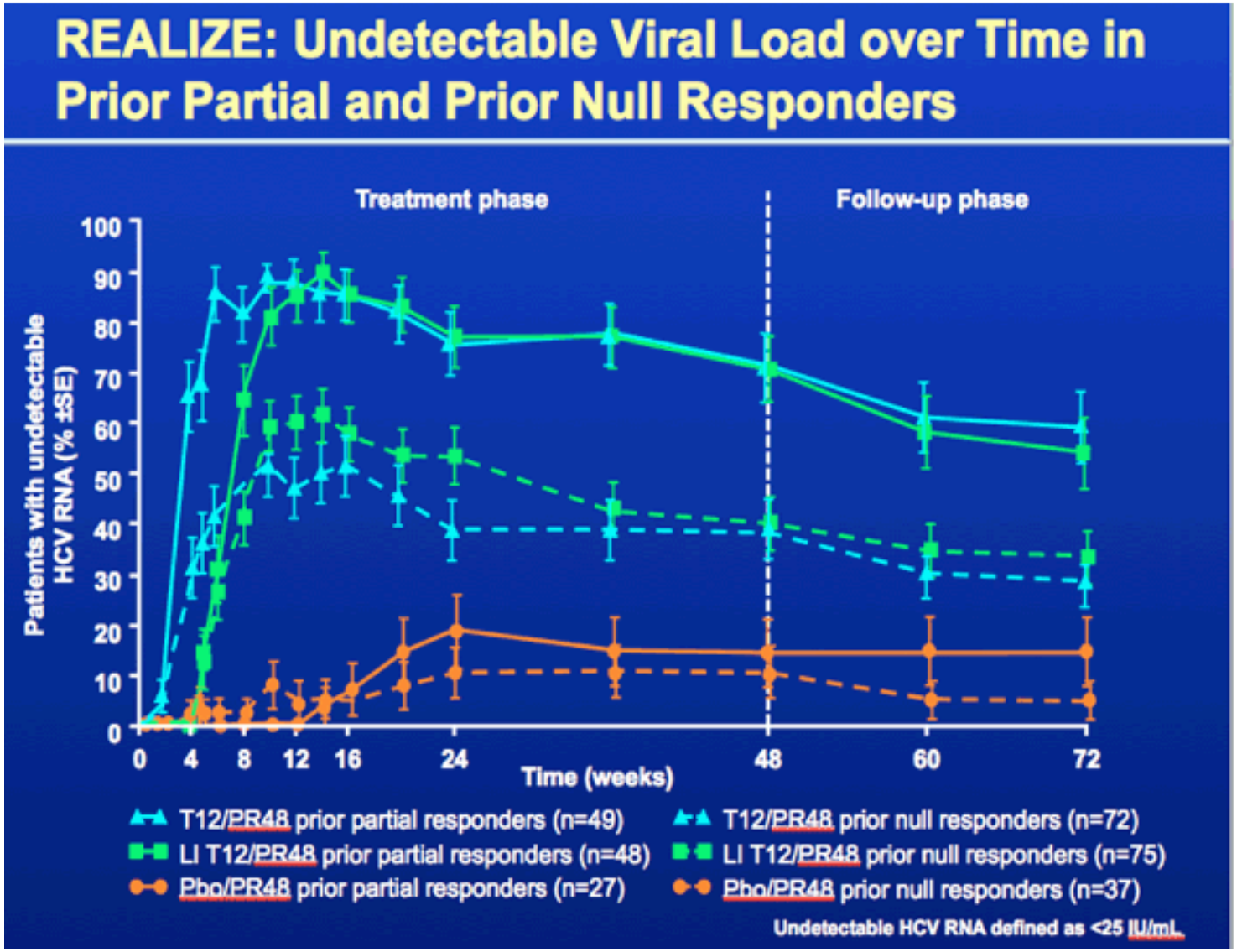
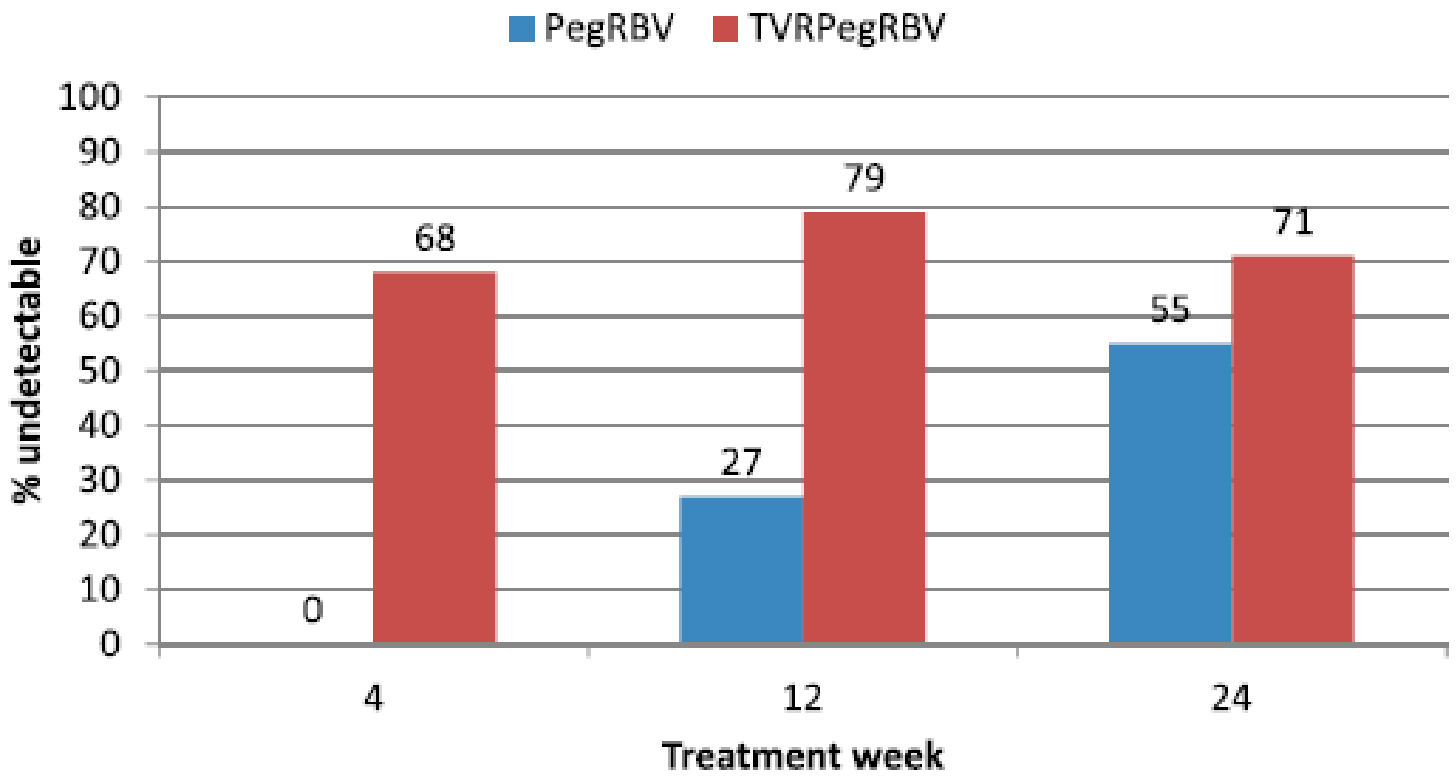
Besser als bei HCV-Monoinfizierten?



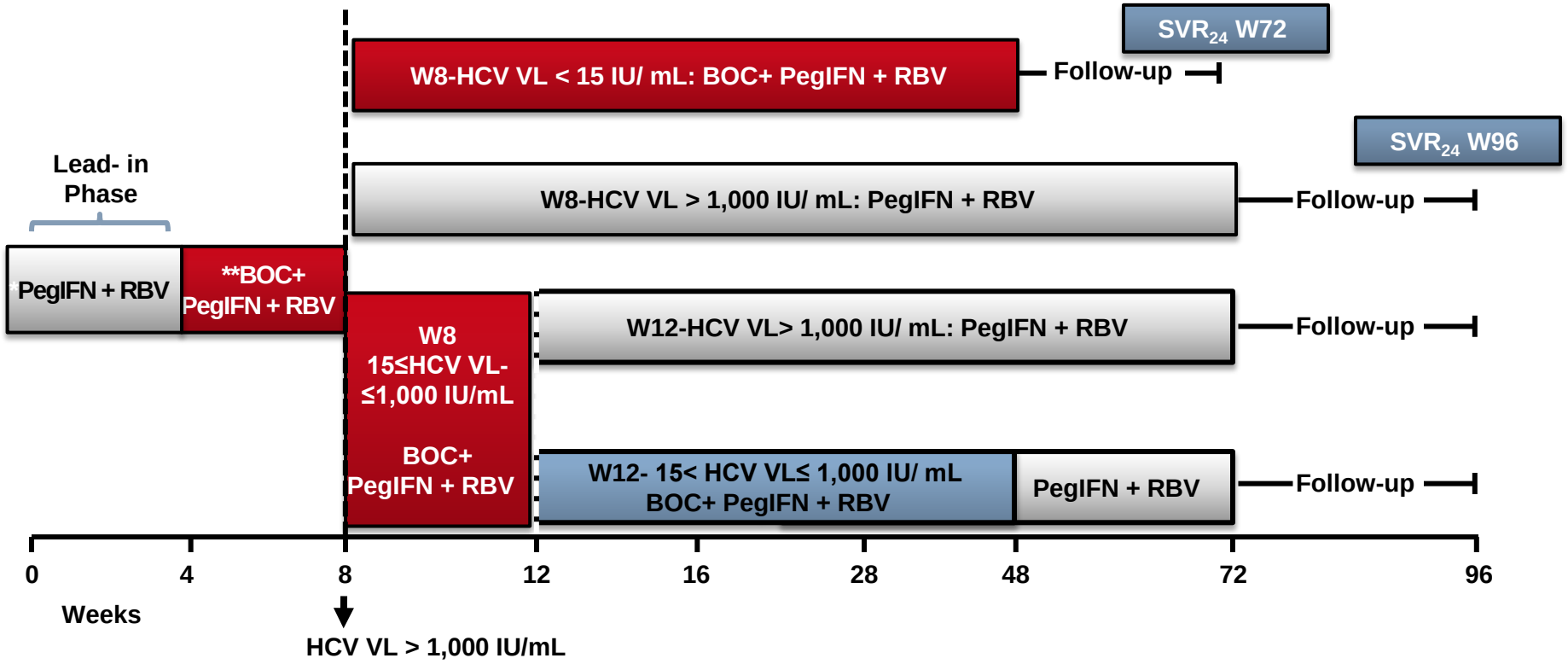
Besser als bei HCV-Monoinfizierten?



Besser als bei therapie-naiven?



Boceprevir + PegIFN + RBV for HIV-HCV Co-Infected Patients with Previous Virologic Failure on PegIFN + RBV



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Inclusion/Exclusion Criteria

- Inclusion
  - Chronic HCV genotype 1
  - Previous virologic failure on PegIFN + RBV
  - Stable antiretroviral therapy with 3 or more ARV agents among TDF, ABC, FTC, 3TC, **ATV** (boosted or not), and RAL
  - CD4+ count ≥200 cells/mm^3 and VL <50 c/mL for ≥6 months
  - Any fibrosis level on liver bx within past 3 years or cirrhosis
- Exclusion
  - HBV co-infection, Childs B or C; decompensated cirrhosis
  - Previous null response with cirrhosis
- Important patient characteristics
  - F4 17%
  - GT1a 78%
  - Previous null responders 33%

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Grade 3-4 AEs and SAEs

		Grade 3-4	SAEs
G3/4 N=26	General Disorders (**asthenia**)	8	**3**
	Gastrointestinal Disorders (**cholecystitis**)	4	**1**
	Cardiac Disorders (**cardiac insufficiency**)	3	**2**
	Infections (**cellulitis, pneumonia**)	3	**2**
	Psychiatric	2	
	Musculoskeletal (**arthritis**)	2	**1**
	Respiratory	2	
	Skin (**pruritus**)	1	**1**
	Anorexia	1	**1**
G3/4 N=39	Blood and lymphatic system	28	**7**
	Hyperbilirubinemia	6	
	ASAT/ALAT	5	**1**

SAEs N= 11

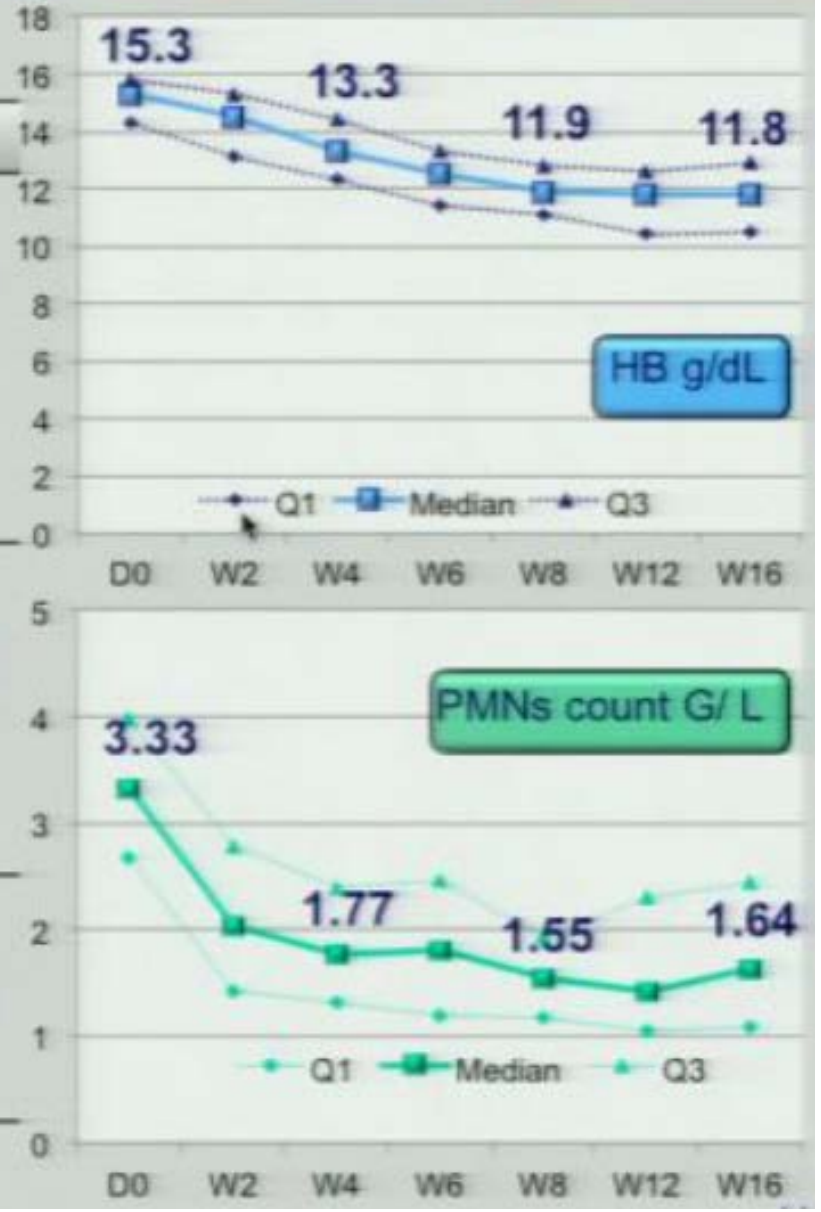
SAEs N= 8

AES lead Discontinuation: n= 4 Cardiac Insufficiency grade 3, Coronaropathy grade 3,Vomiting grade 2, Infection with anemia grade 2

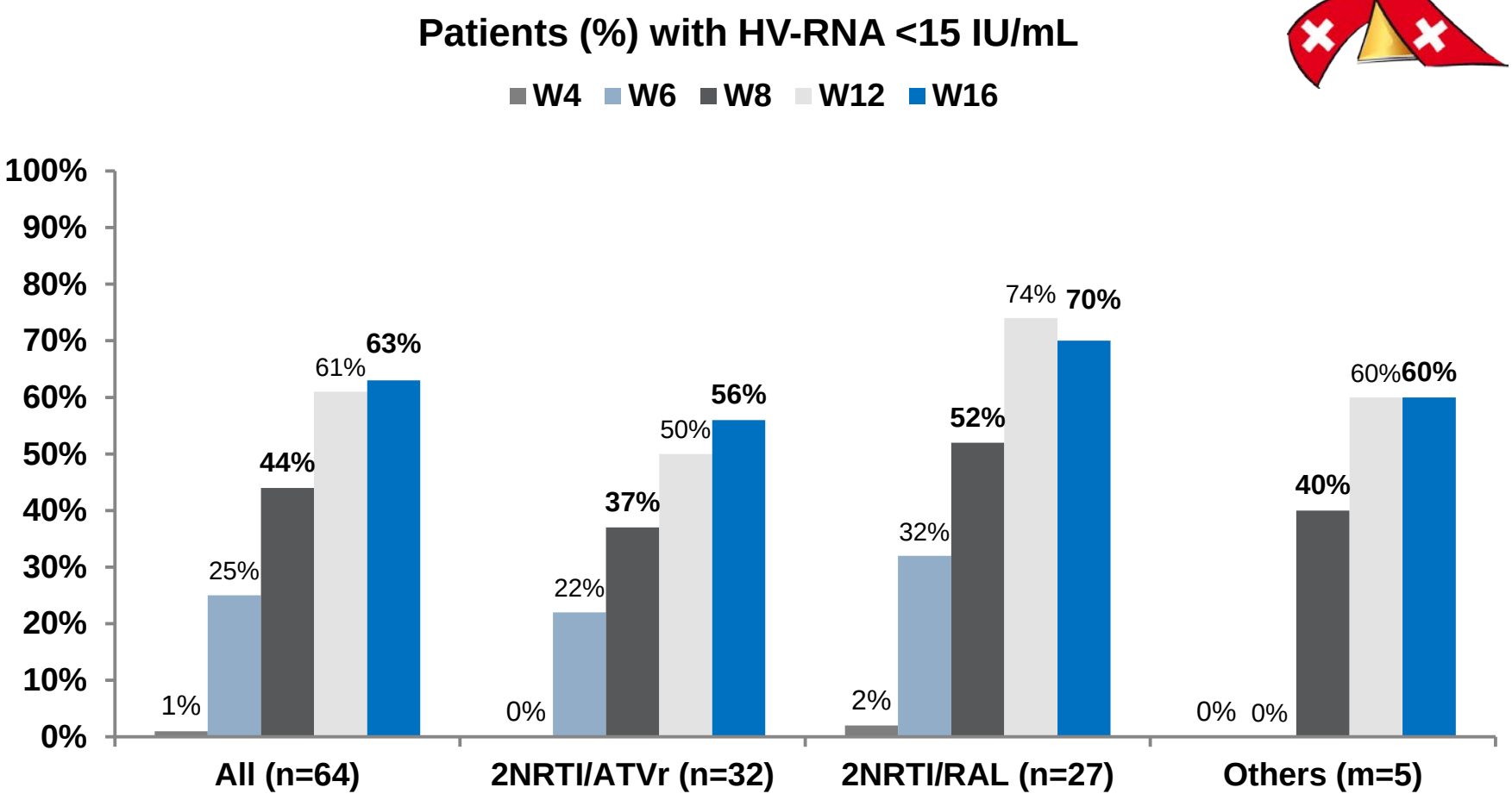
Hematological AEs

ANRS HC27

	N (%), (n=64)
Anemia	27 (42%)
Grade 3-4 (<7 g/dL)	3 (5%)
EPO use	27 (42%)
Transfusion	2 (3%)
RBV dose reduction	5 (8%)
Neutropenia	45 (70%)
Grade 3-4 (< 750 G/L)	11 (17%)
G-CSF use	3 (5%)
PegIFN dose reduction	2 (3%)
Thrombocytopenia	27 (42%)
Grade 3-4 (<50 G/L)	2 (3%)
PegIFN dose reduction	1 (2%)



BOC/IFN/RBV Following Virologic Failure: Results by ARV Regimen



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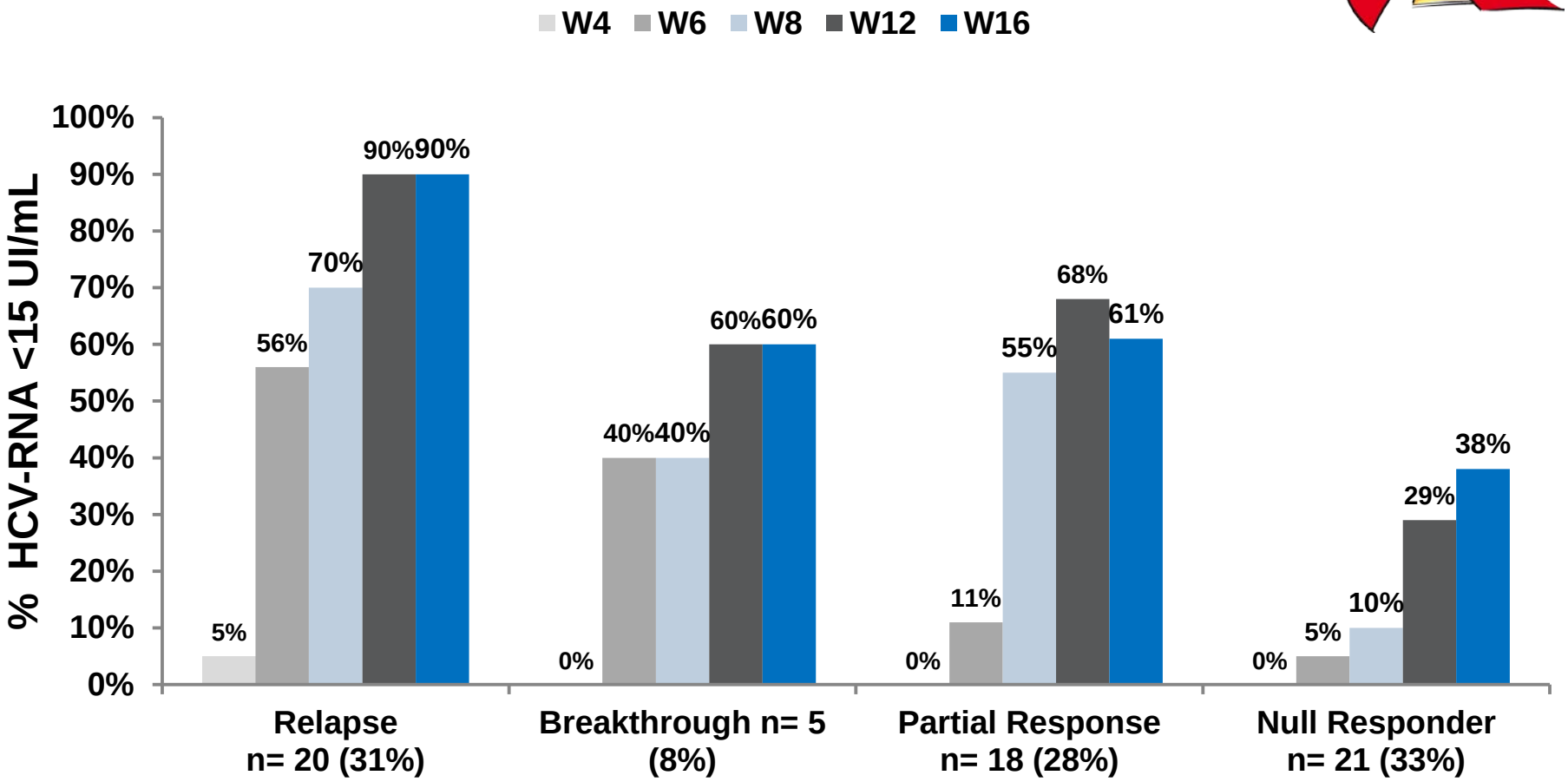
BOC/IFN/RBV Following Virologic Failure: Results by Previous Response to PegIFN + RBV



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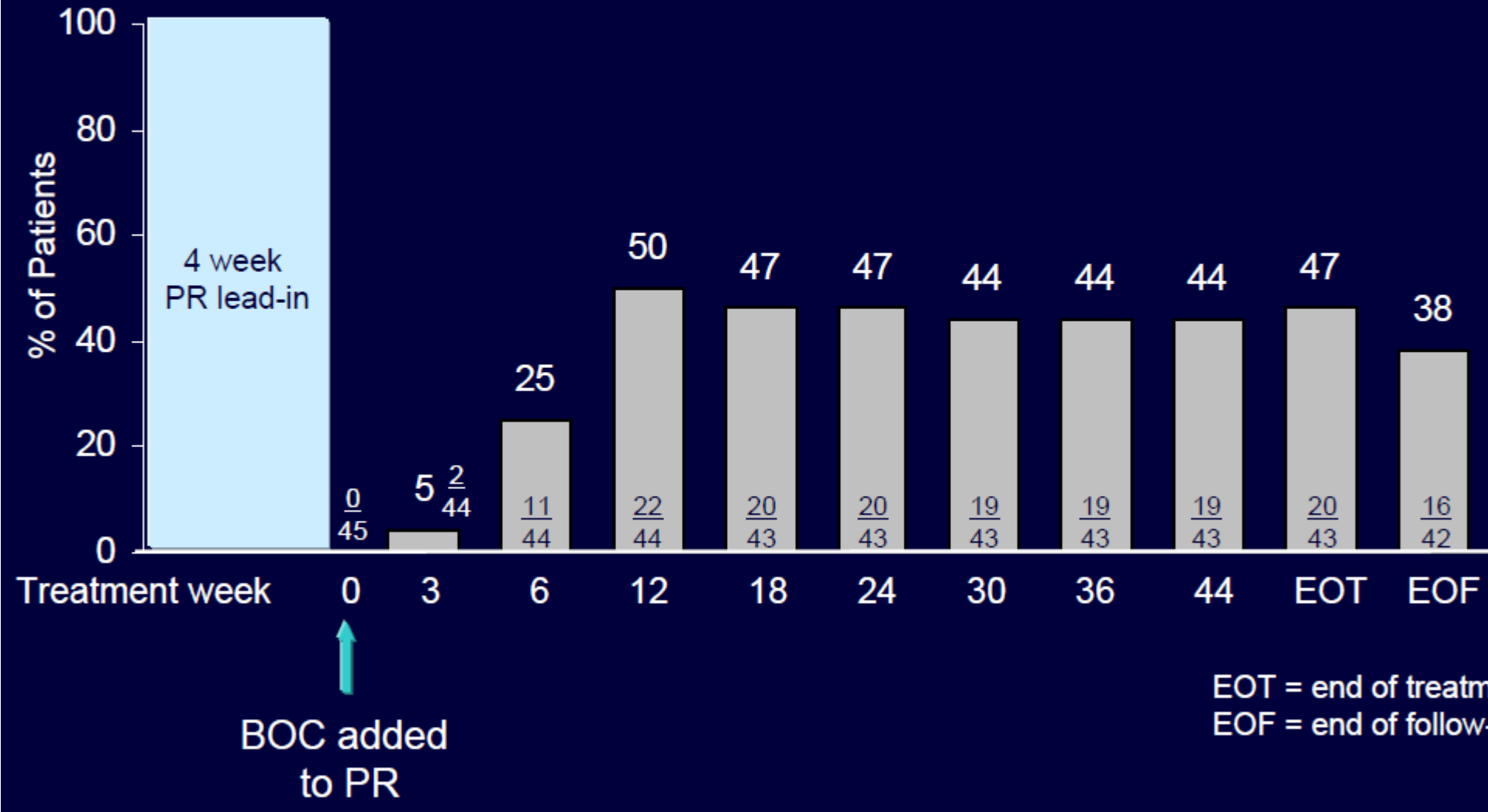
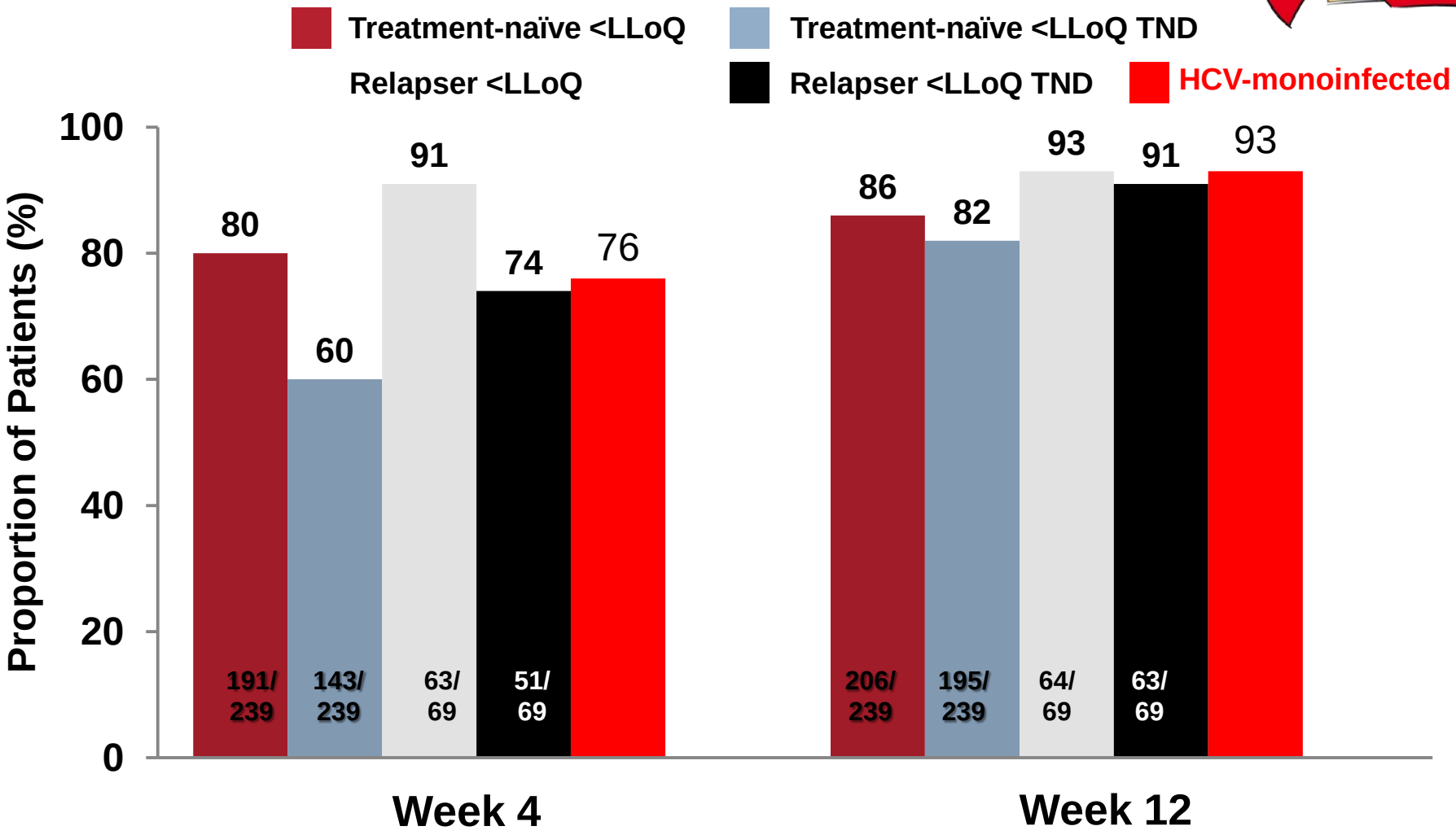
Cumulative Achievement of Undetectable HCV RNA in Prior Null Responders*



*Of 48 prior Null Responders from SPRINT-2 and RESPOND-2, 3 discontinued during the lead-in phase

Early Virologic Response in HIV/HCV Co-infected Patients: HCV Treatment-naïve and Relapsers treated with Faldeprevir



Dieterich D, et al. 20th CROI; Atlanta, GA; March 3-6, 2013. Abst. 40LB.

HIV/HCV-Koinfektion: Good news?

Good news:

- Telaprevir und boceprevir effektiv bei previous non-response
- Severe rash <5%, Anämie ‘manageable’

Allerdings:

EVR ≠ SVR!

THISTLE

The HIV-HCV Silibinin Trial

SWISS HIV COHORT STUDY

SHCS #688

Flow-chart for HCV therapy in HIV-infected patients (Page 1)

SHCS-ID:	HCV-Genotype:	HCV Treatment history = Treatment naive = **Partial response**: >2 log IU/ml decrease in HCV RNA at wk 12 but detectable HCV RNA at wks 12 or 24 = **Breakthrough**: Reappearance of HCV RNA at any time during treatment after virological response = **Relapse:** Reappearance of HCV RNA after virological response at the end-of-treatment = **Premature discontinuation of Tx:** Insufficient duration or dosage of previous therapy due to side effects = Other:	*Reasons for stopping HCV therapy: 1. HCV virological failure/stopping rule 2. Anemia 3. Leukopenia 4. Thrombocytopenia 5. Depression 6. Rash 7. Other side effects (specify)	** Patients with lead-in: Additional visits with plasma storage 4 and 2 weeks before starting the HCV PI
	Fibrosis (Metavir):	RVR: Undetectable HCV RNA at wk 4 during previous therapy: = YES = NO = unknown		

Date of Tx start:	*Start or change of dosage = dose. Stop=↓; unchanged = →. Indicate treatment interruption of > 1 day. For a stop always indicate predominant reason for each drug, see legend).*																				
	Date and treatment week (mandatory visits with sample storage at weeks 0,1,2,4,8,12,24,48, 72 and at treatment failure for pts treated with an HCV PI)**																				
	Base-line																				
Interferon-alpha (indicate product name) ..... (µg/wk)																					
Ribavirin (indicate product name) ..... (mg/d)																					
HCV Protease inhib. (indicate product name) ..... (mg/d)																					
Other HCV drug (indicate product name) ..... (mg/d)																					
EPO, neupogen or transfusion																					
Reason for stopping drug (see legend*)																					
HCV RNA (log_{10} IU/ml)																					
Hemoglobin (g/L)																					
Neutrophile count (G/L)																					
Thrombocyte count (G/L)																					
Adherence: How often did you miss a dose of your HCV medication? Every day	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□
More than 1/week	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□
Less than 1/week	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□
Never	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□	□

Pharmakokinetiks, register time of sampling and drug intake; only weeks 0,1,4 for patients treated with an HCV-Protease- or Polymeraseinhibitor

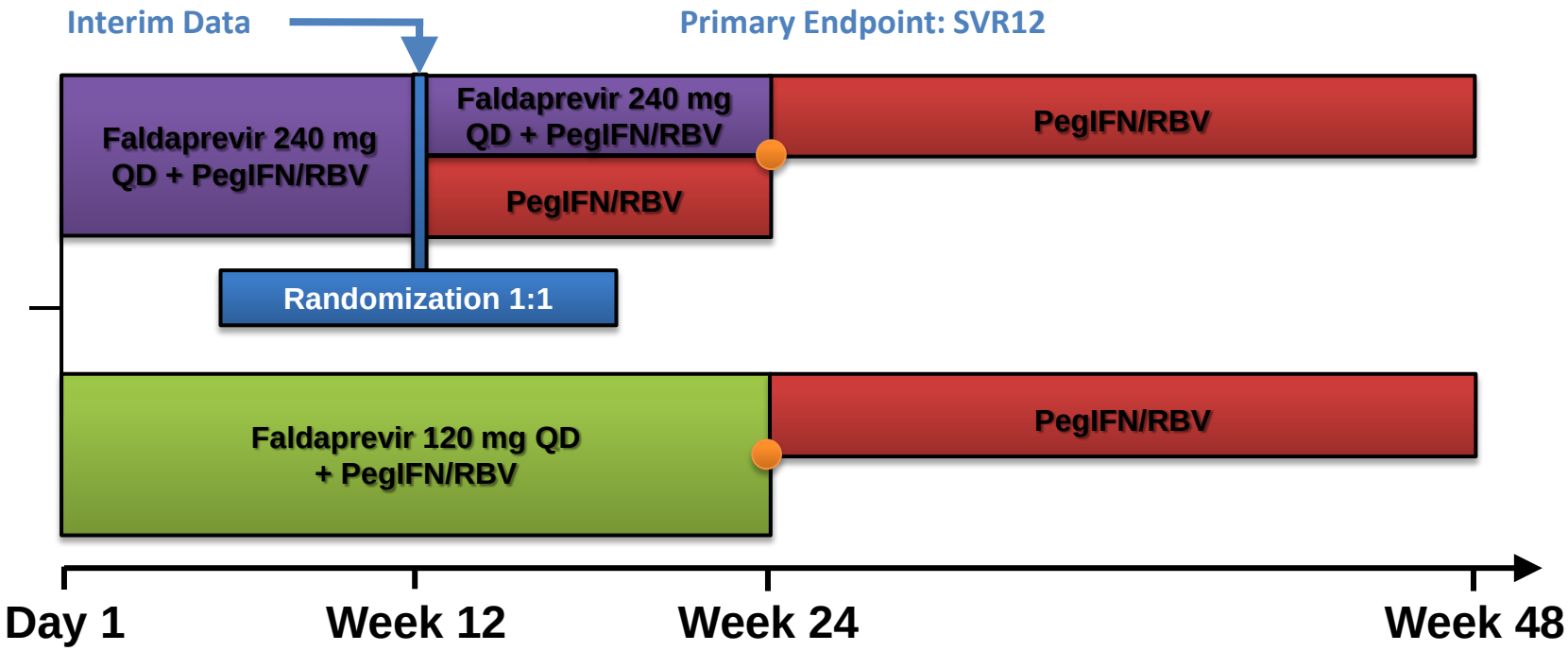
For instructions see page 2		HIV-PI, NNRTI or Int.inh. N°1 Product name:	HIV-PI, NNRTI or Int.inh. N°2 Product name:	HCV Protease or Polymerase Inhibitor	Ribavirin
	Sampling time: day/month hour/min	Last drug intake day/month hour/min	Last drug intake day/month hour/min	Last drug intake day/month hour/min	Last drug intake day/month hour/min
Baseline	__/__ __/__	__/__ __/__	__/__ __/__	Not applicable	Not applicable
Week 1	__/__ __/__	__/__ __/__	__/__ __/__	__/__ __/__	__/__ __/__
Week 4	__/__ __/__	__/__ __/__	__/__ __/__	__/__ __/__	__/__ __/__

Additional comments:

After completion of HCV therapy send flow chart to:
A. Rauch, PKT2B, Inselspital 3010 Bern

STARTVerso 4: Study Design

Phase III Open-label, Sponsor-blinded Study in Treatment-naïve and Relapser Patients with Chronic HCV GT-1 and HIV Infection

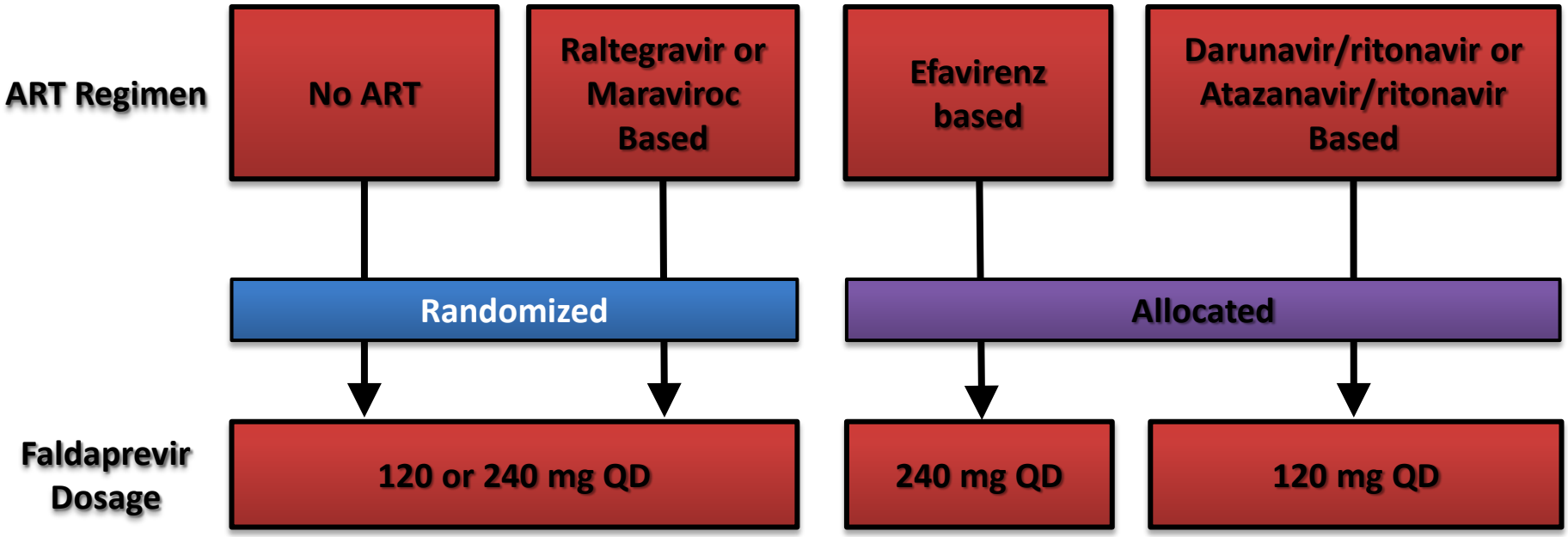


Patients with HCV RNA below LLoQ, at Week 4, and HCV RNA below LLoQ target not detected at Week 8 (=ETS) will be re-randomized 1:1 at week 24 to stop treatment or continue pegIFN/RBV through week 48
Patients who did not achieve ETS will continue pegIFN/RBV through week 48

Dieterich D, et al. 20th CROI; Atlanta, GA; March 3-6, 2013. Abst. 40LB.

STARTVerso 4: Study Design

- HCV GT-1 infection, including compensated cirrhosis
  - HCV treatment-naive or relapsers
  - Cirrhosis F4 or FibroScan >13 kPa 17%; GT1a 78%



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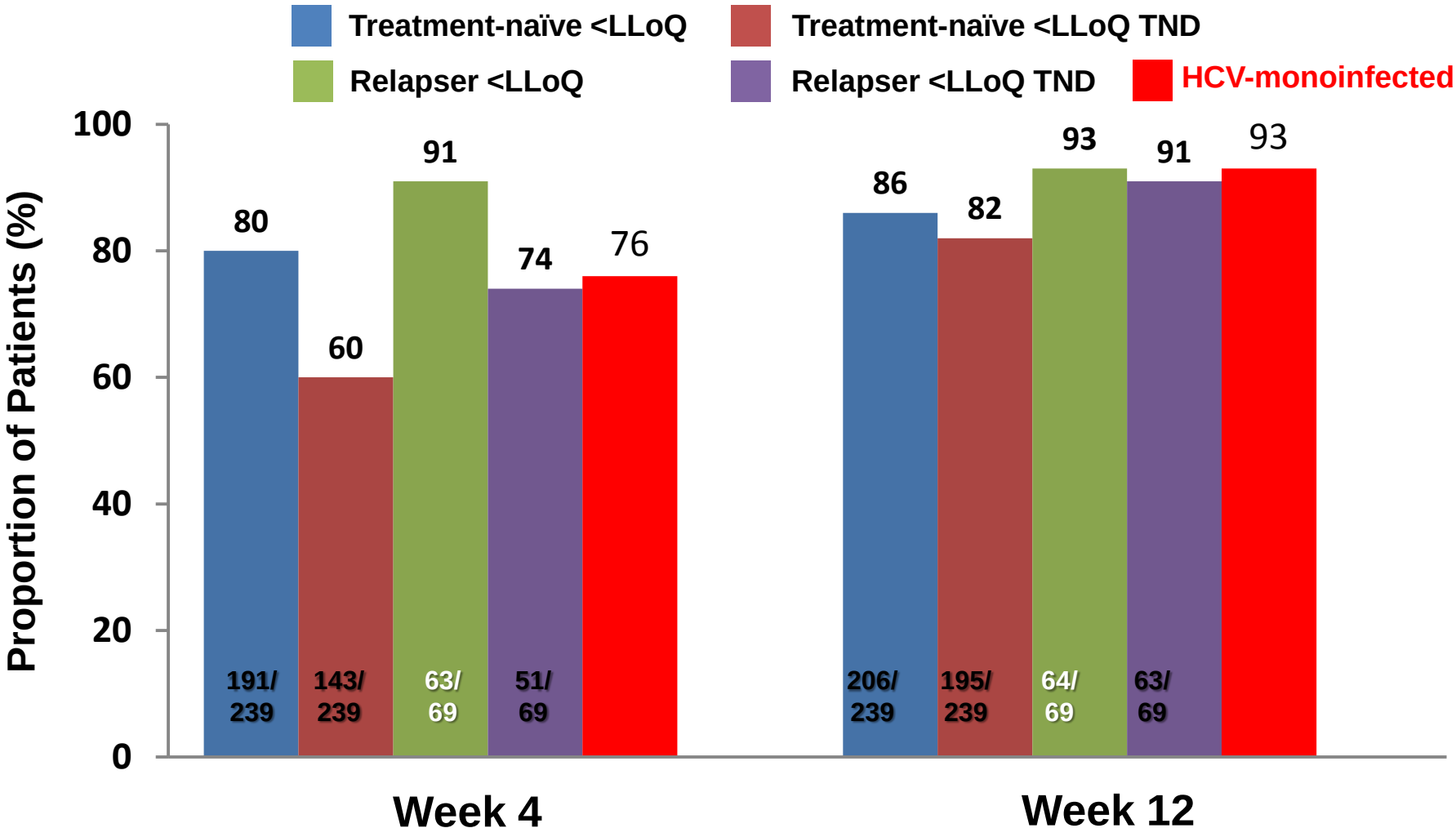
Early Virologic Response in HIV/HCV Co-infected Patients: HCV Treatment-naïve and Relapsers



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