

**Assessment of serum HCV-RNA at week 12 post-treatment is as relevant as week 24 to predict SVR in HCV patients receiving Peginterferon plus ribavirin**

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**Hepatology: in Press**

# Background

- **The goal of treating patients with chronic hepatitis C is to obtain a sustained virological response (SVR).**
- **When achieved sustained virological response is durable.**

Marcellin et al. Liver 1994

Marcellin et al. Ann Inter Med 1997

Lau et al. Hepatology 1998

McHutchinson et al. Hepatology 2002

Maylin et al. Gastroenterology 2008

# Background

- **The current standard for the identification of patients with SVR is undetectable serum HCV RNA at the end of the 24 weeks post-treatment follow-up\*.**
- **A previous study, in patients receiving IFN or PEG-IFN  $\alpha$  2a monotherapy, suggested that 12 weeks post-treatment follow-up is appropriate to determine SVR \*\*.**

\* Ghany et al. Hepatology 2009

\*\* Zeuzem et al. J Hepatol 2003

# Background

- **Timing of relapse during the 24 weeks post-treatment follow-up, in patients receiving PEG-IFN and ribavirin combination therapy, has never been investigated.**
  - **Early viral load outcome in patients with relapse has never been explored.**
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# Aims

- **Evaluate if the detection of serum HCV RNA 12 weeks after treatment cessation is as accurate as 24 weeks to identify SVR in patients receiving PEG-IFN and RBV combination therapy.**
  - **Assess early viral load outcome in patients with relapse.**
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# Patients

**781 patients, with chronic hepatitis C without HIV or HBV co-infection, treated with combination therapy**

- **439 patients: PEG-IFN  $\alpha$  2b (PegIntron<sup>®</sup>) 1.5  $\mu$ g / kg / week and RBV (Rebetol<sup>®</sup>) 800-1200 mg / day according to body weight.**
- **342 patients: PEG-IFN  $\alpha$  2a (Pegasys<sup>®</sup>) 180  $\mu$ g/week and RBV (Copegus<sup>®</sup>) 1000-1200 mg / day according to body weight.**

# Treatment Schedules

- **24 weeks**  
in naive patients genotype 2 or 3
  - **48 weeks**  
in naive patients genotype 1, 4-6  
in all experienced patients
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# Inclusion criteria

## **Patients were eligible**

- **Completed a full course of therapy**
  - **Had an end of treatment virological response**
  - **Complied with the 12 and 24 weeks post-treatment follow-up visit**
  - **Assessment at 4 weeks was optional**
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# Definitions

- **End of Treatment (EOT) Virological Response:**  
**Undetectable serum HCV RNA**
  - **Sustained Virological Response:**  
**Undetectable serum HCV RNA at the end of the 24 weeks post-treatment follow-up**
  - **Response with Relapse:**  
**Undetectable serum HCV RNA at EOT with detectable serum HCV RNA at the end of the 24 weeks post-treatment follow-up**
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# Methods

- **Serum HCV RNA qualitative detection was prospectively performed at:**
    - **end of therapy,**
    - **4, 12, 24 weeks after treatment cessation.**
  - **Serum HCV RNA quantitative measurements were retrospectively performed on available frozen serum samples at:**
    - **4, 12, 24 weeks after treatment cessation.**
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# Methods

## Serum HCV RNA testing

### *Qualitative detection*

**VERSANT HCV Qualitative assay (TMA)  
(sensitivity 9.6 IU/ml).**

### *Quantitative detection*

**VERSANT HCV 3.0 assay (bDNA)  
(sensitivity 615 IU/ml).  
(Siemens Healthcare Diagnostics)**

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# Results

## End of treatment

**573/781 (73%) patients had an end of treatment virological response and were included in the study**

- ✓ 319/439 (73%) received PEG-IFN  $\alpha$  2b**
- ✓ 254/342 (74%) received PEG-IFN  $\alpha$  2a**

# Patients Characteristics

	All	PEG-IFN	
	(n=573)	$\alpha$ 2a (n=254)	$\alpha$ 2b (n=319)
Male	68 %	66 %	70%
Age*	49±10	50±10	47±10
ALT (IU/ml)*	124±76	126±91	121±91
Viral load** (log IU/ml)*	5.52±0.76	5.55±0.76	5.49±0.75
Pretreatment status			
Naive	57 %	59 %	57 %

\* Mean ± SD \*\*log<sub>10</sub>

# Patients Characteristics

	All	PEG-IFN	
	(n=573)	$\alpha$ 2a (n=254)	$\alpha$ 2b (n=319)
<b>HCV Genotype</b>			
1	45%	47%	44%
2-3	42%	37%	46%
4-5	13%	16%	10%
<b>Fibrosis stage*</b>			
1-2	66%	63%	69%
3	19%	21%	17%
4	15%	16%	14%

\* Metavir scoring system

# Results

**At the end of the 24 weeks post-treatment follow up**

- **408/573 (71.2%) patients achieved a SVR**
    - ✓ **227/319 (71.1%) received PEG-IFN  $\alpha$  2b**
    - ✓ **181/254 (71.2%) received PEG-IFN  $\alpha$  2a**
  - **165 (28.8%) experienced a relapse**
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# 4 weeks after treatment cessation

**337 patients underwent a follow-up visit**

**252 HCV RNA undetectable  
242 demonstrated a SVR**

**PPV 96.0%**

**(95%CI: 93.9-98.1)**

- ✓ PEG  $\alpha$  2a: 95.4% (95%CI: 92-98.8)
- ✓ PEG  $\alpha$  2b: 96.4% (95%CI: 93.7-99)

**95 demonstrated a relapse  
85 detectable HCV RNA**

**Sensitivity 89.4%**

**(95%CI: 83.2-95.6)**

- ✓ PEG  $\alpha$  2a: 82.7% (95%CI: 70-95.4)
- ✓ PEG  $\alpha$  2a: 86.1% (95%CI: 76-96.6)

# 12 weeks after treatment cessation

All the 573 patients underwent a follow-up visit

409 HCV RNA undetectable  
408 demonstrated a SVR

**PPV:99.7%**

**(95%CI: 99.1-100)**

- ✓ PEG  $\alpha$  2a PPV 99.5% (95%CI: 98.5-100)
- ✓ PEG  $\alpha$  2b PPV 100%

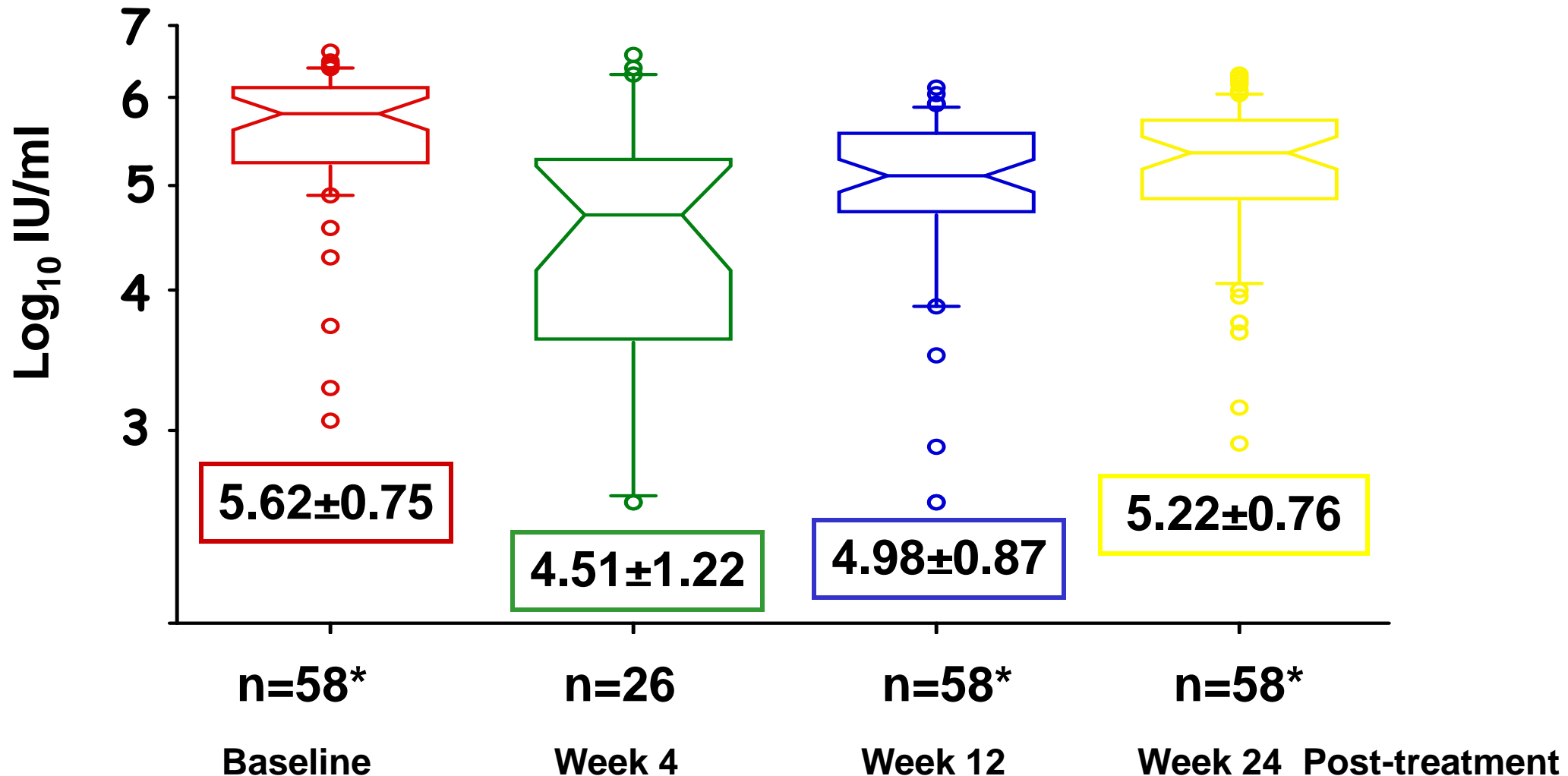
165 demonstrated a relapse  
164 detectable HCV RNA

**Sensitivity:99.3%**

**(95%CI:98.0-100)**

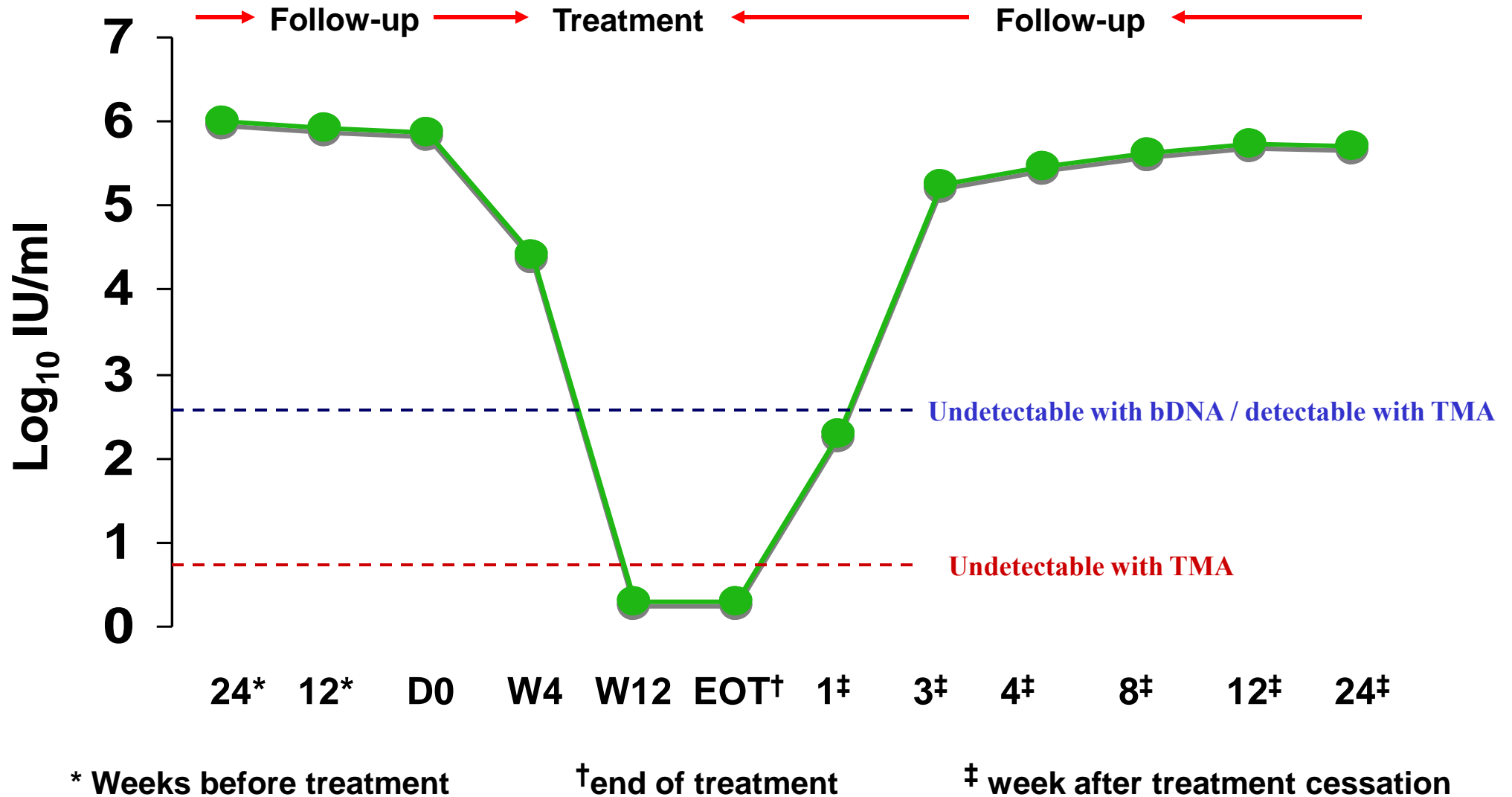
- ✓ PEG  $\alpha$  2a: 98.6% (95%CI: 97.2-100)
- ✓ PEG  $\alpha$  2b: 100%

# Viral load outcome in relapse patients

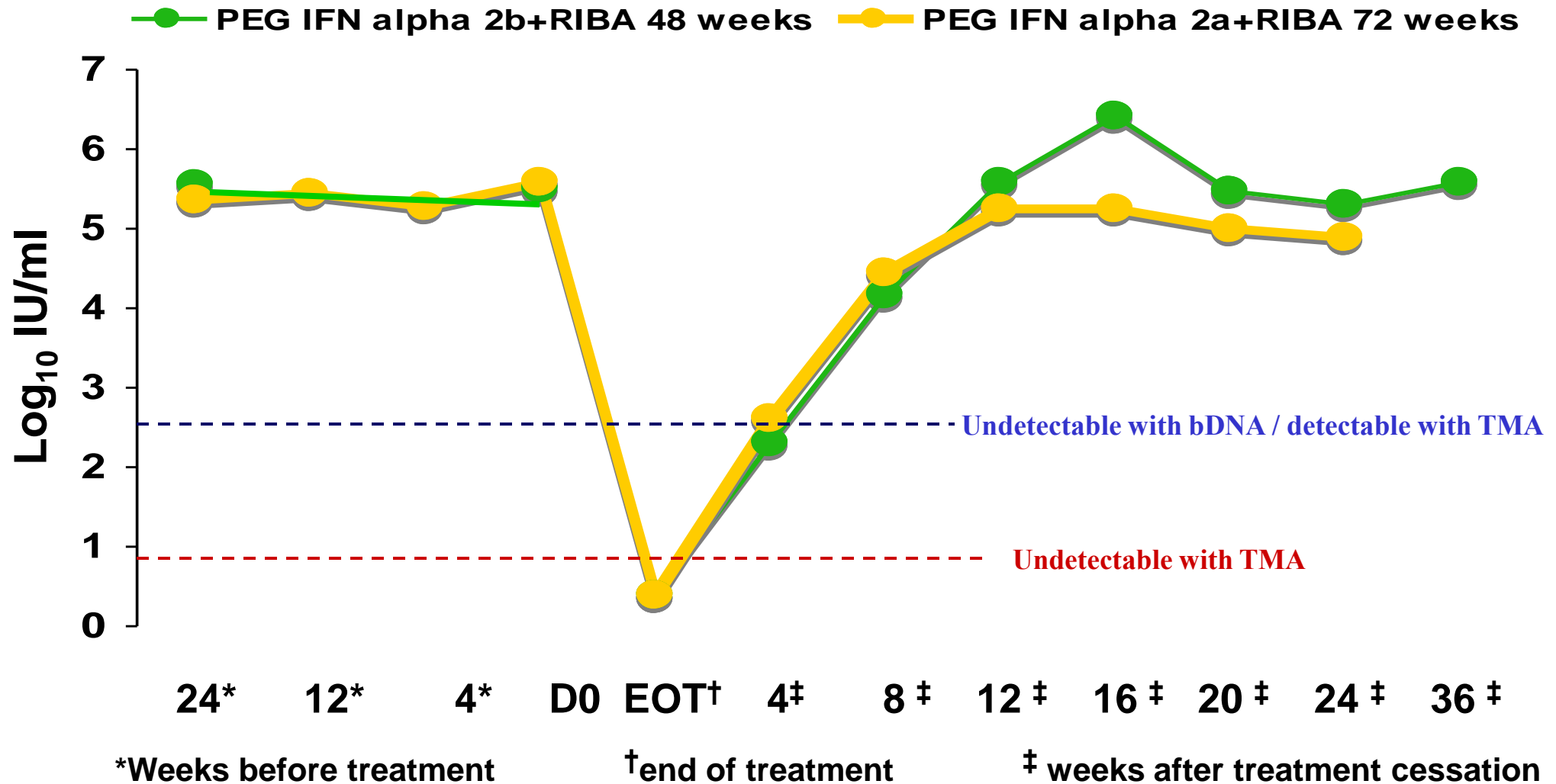


\* 26 had a week 4 post-treatment available serum sample

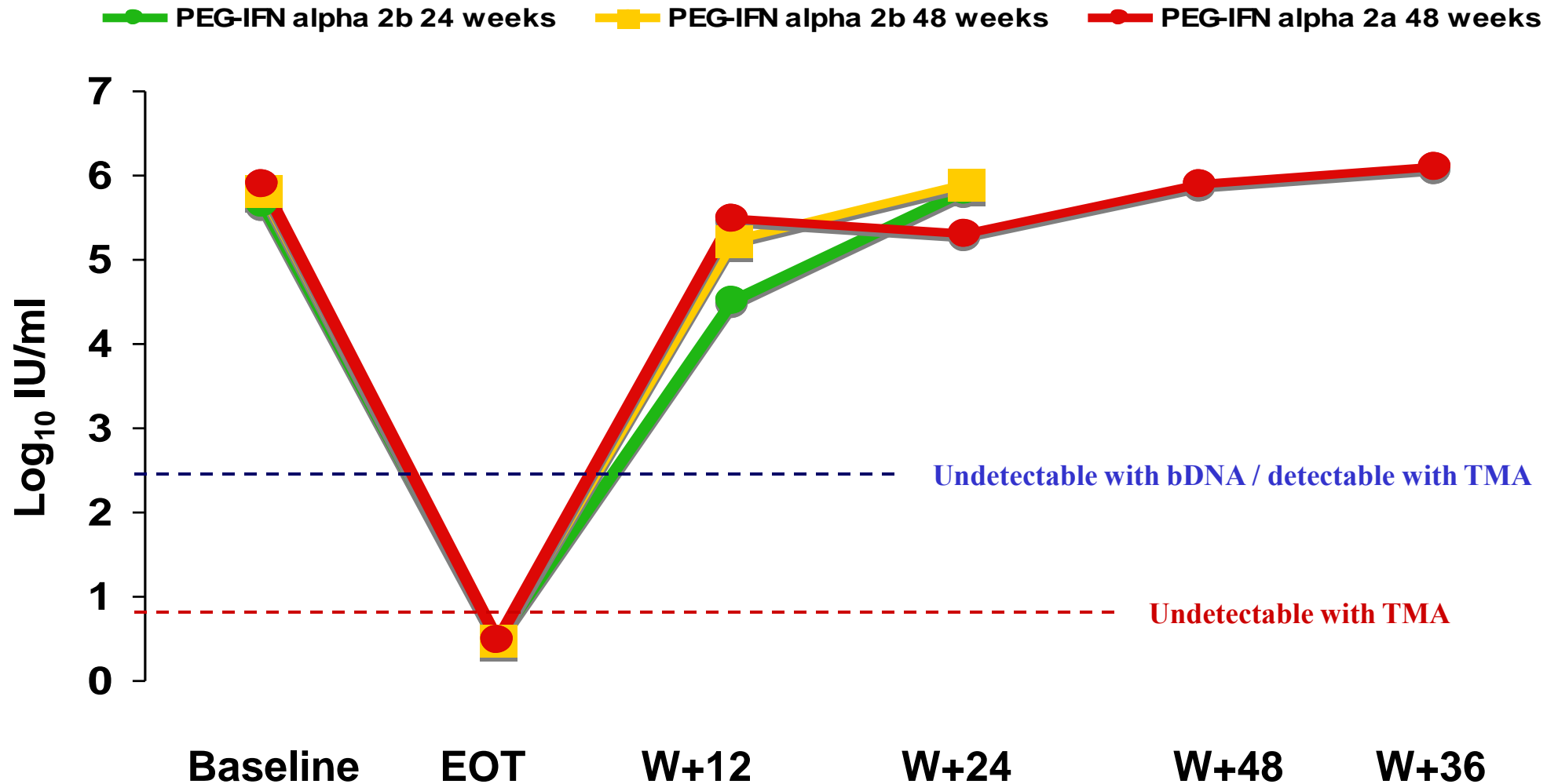
# Viral load outcome in a genotype 1 naive patient



# Viral load outcome in a Genotype 1 relapse patient receiving 2 courses of combination therapy



# Viral load outcome in one genotype 3 patient receiving 3 courses of combination therapy



# Conclusions

- Our results show that the assessment of serum HCV RNA **12 weeks** after treatment cessation (PPV 99.7%) is as accurate as **24 weeks** to predict SVR, in patients receiving combination therapy
  - In relapse patients, viral load shows a trend towards reverting to baseline level as early as 24 weeks after treatment cessation
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# Conclusions

**A shorter duration of post-treatment follow-up might:**

- ✓ **accelerate the assessment of the efficacy of new compounds and/or new treatment schedules such as triple therapy**
- ✓ **reduce the costs for both patients and society**