

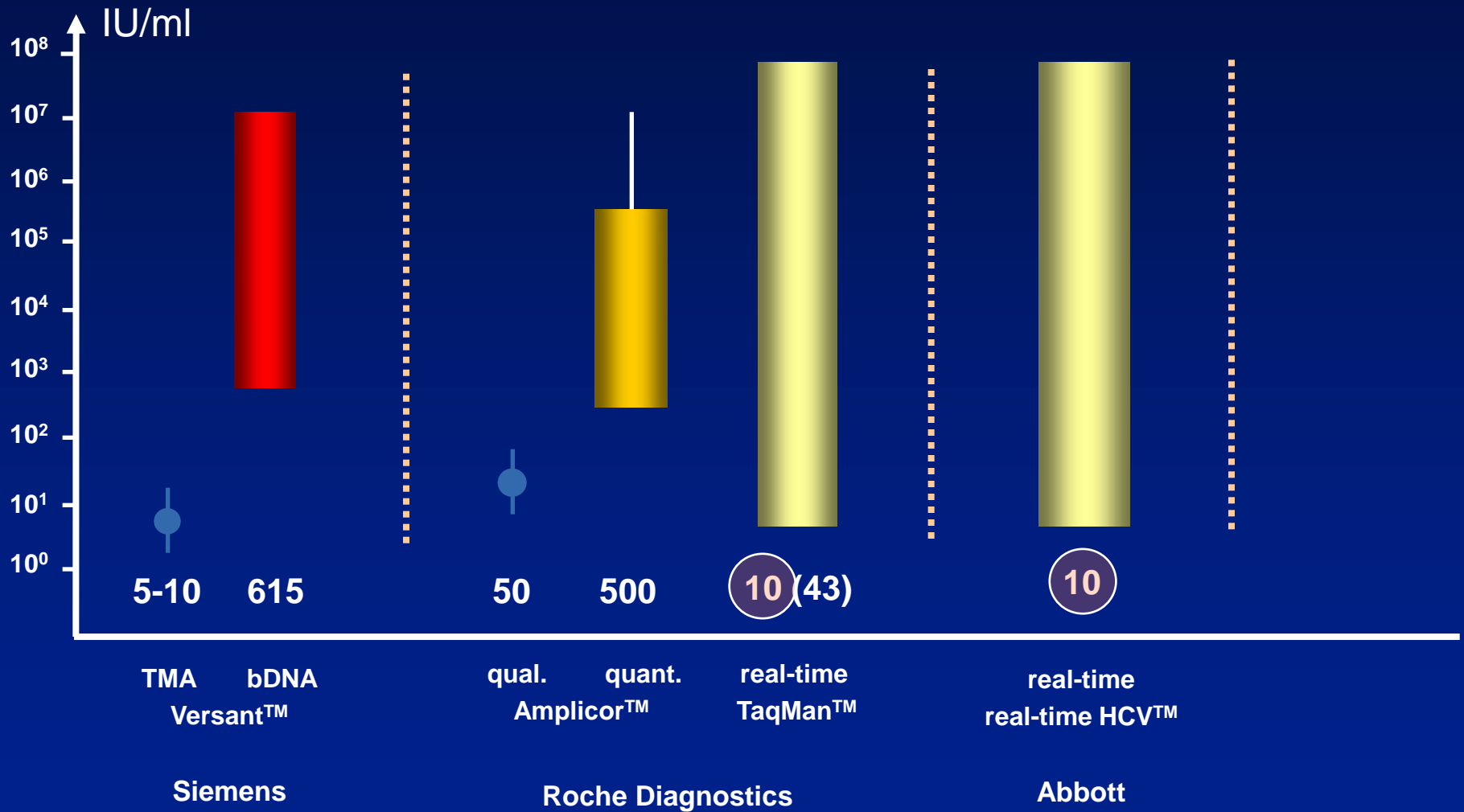
# HCV RNA viral load assays

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# International commercially available HCV RNA assays



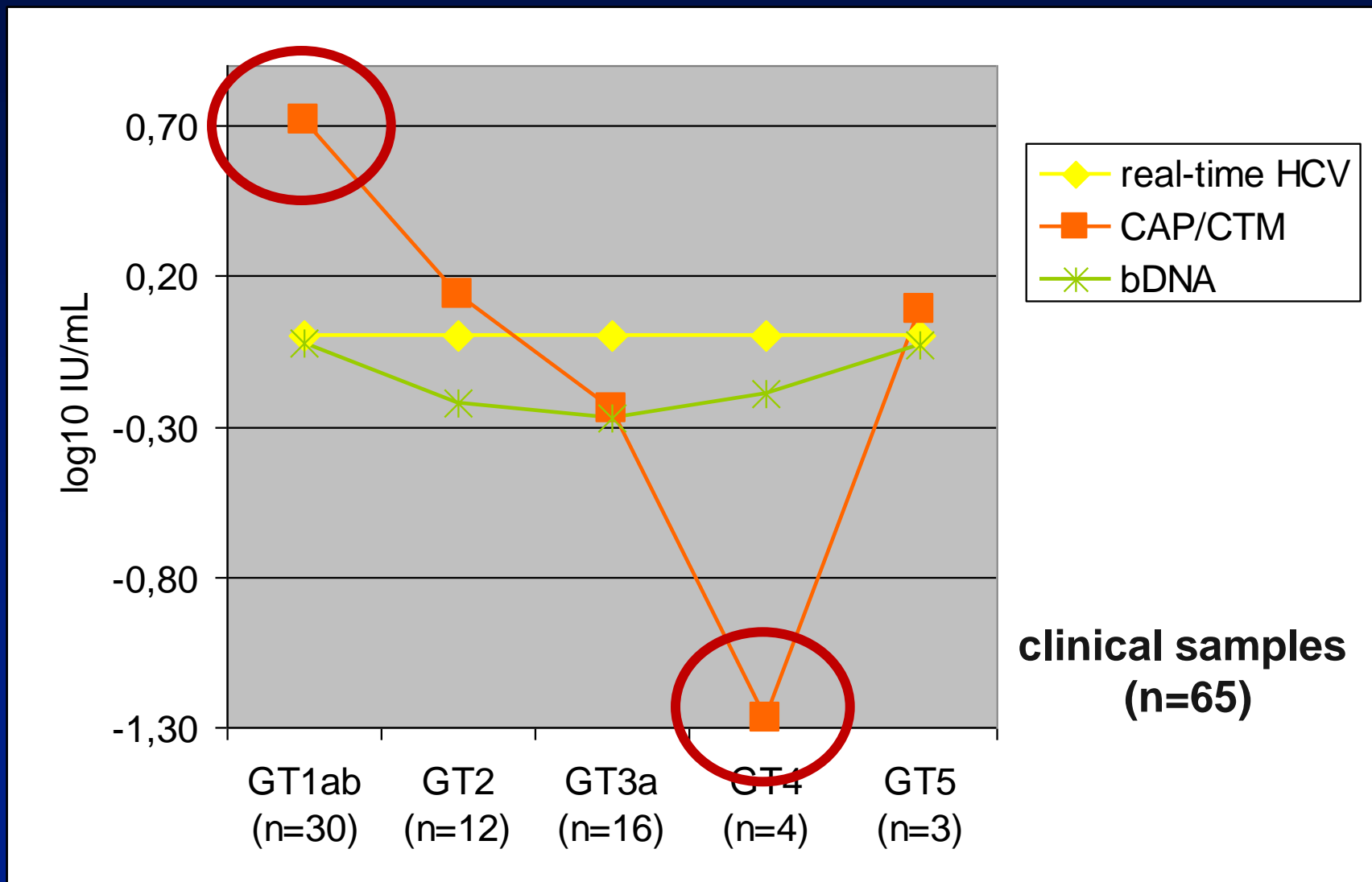
# Reported results of HCV RNA assays

## *Residual viremia and country specific cut-offs*

	limit of detection (95% hit rate)	residual viremia / not quantifiable	quantifiable viremia (linear range)
	negative / undetectable	positive / detectable	positive / detectable
Versant Qual. TMA	neg. (<5 IU/ml)		pos. (>5 IU/ml)
Cobas Amplicor	neg. (<50 IU/ml)		pos. (>50 IU/ml)
Cobas TaqMan (Ampliprep, EU)	neg. (<10 IU/ml)	pos. (<15 IU/ml)	≥15 IU/ml (43 IU/ml)
Cobas TaqMan (Ampliprep, US)	neg. (<10 IU/ml)	pos. (<43 IU/ml)	≥43 IU/ml (43 IU/ml)
Cobas TaqMan (HPS, EU/US)	neg. (<10 IU/ml)	pos. (<25 IU/ml)	≥25 IU/ml (25 IU/ml)
Cobas TaqMan vs2 (Ampliprep, EU, 2012)	neg. (<10 IU/ml)	pos. (<15 IU/ml)	≥15 IU/ml (15 IU/ml)
RealTime HCV	neg. (<10 IU/ml)	pos. (<12 IU/ml)	≥12 IU/ml (12 IU/ml)

# Differences between assays

*CobasTaqMan (CAP) / RealTimeHCV / Versant bDNA*

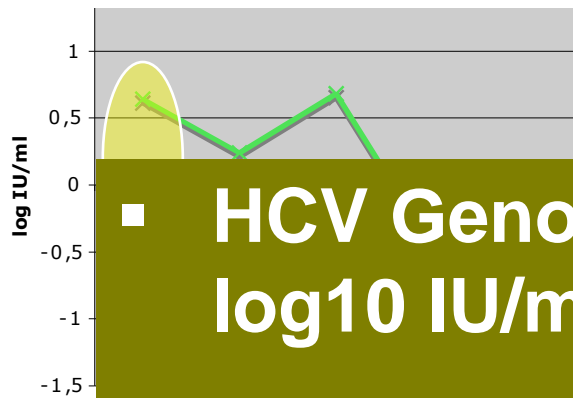


# HCV RNA viral load assessment

*Despite International Units (IU) differences between assays*

Cobas TaqMan Roche vs bDNA Siemens

Sarrazin et al., J Clin Microbiol 2006



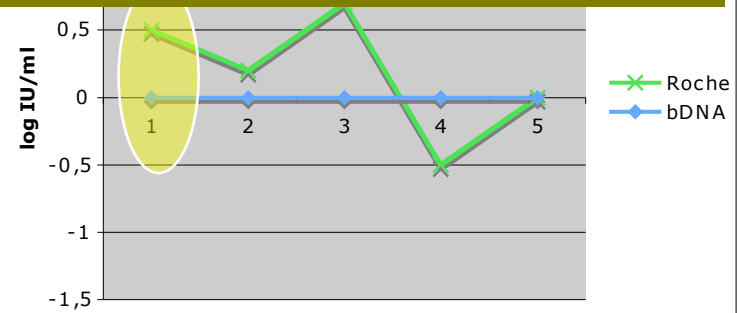
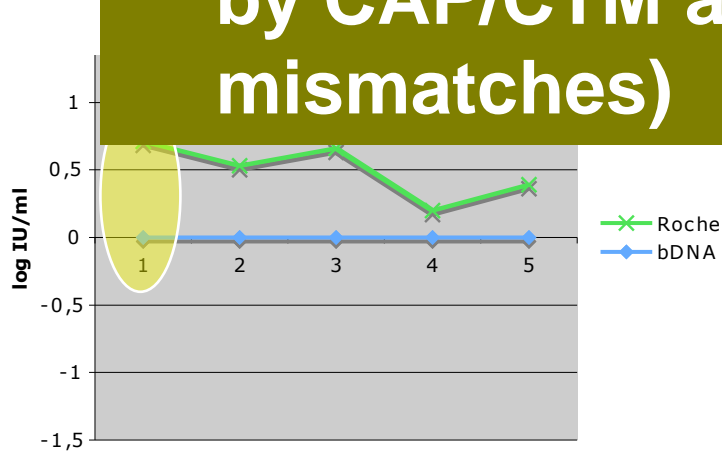
Cobas TaqMan Roche vs bDNA Siemens

Vermehren et al., J Clin Microbiol 2008



- HCV Genotype 1: Differences of 0.5-0.7 log<sub>10</sub> IU/ml (approx. 4-fold)
- HCV Genotype 4: Under-quantification by CAP/CTM assay (Chevaliez: primer mismatches)

Cob



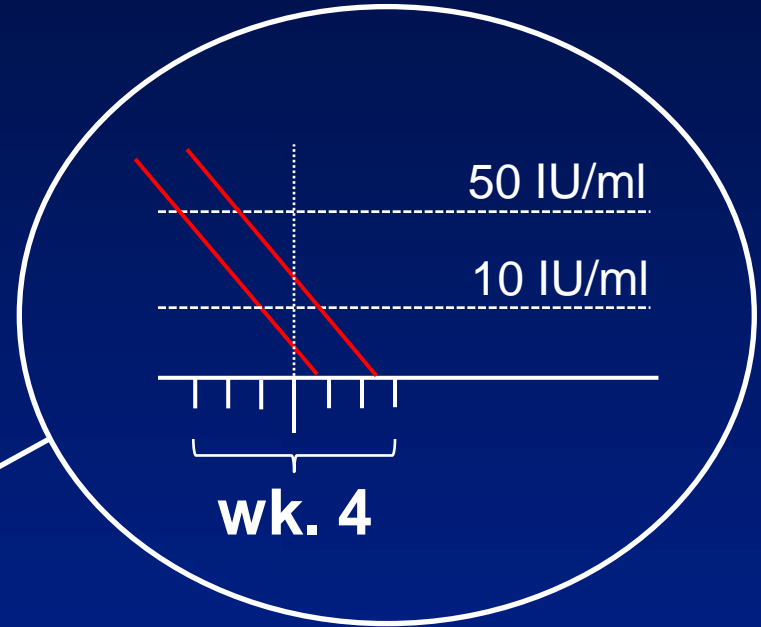
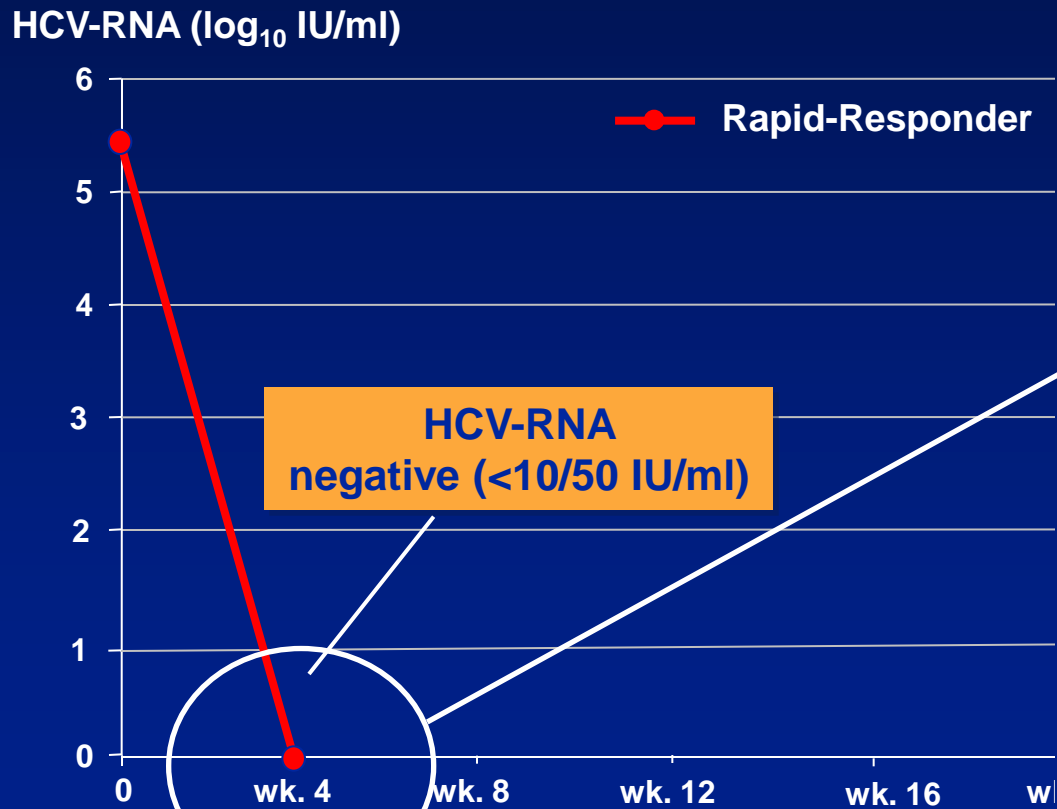
# Definition of RVR

*Difference between undetectable / <15 IU/ml and importance for SVR?*

	Amplicor <50 IU/mL
RVR <b>Genotype1</b>	32%
SVR in RVR	
24 wks Tx	95%
48 wks Tx	100%
$\Delta$ 24 vs 48 wks	5%
RVR <b>Genotype2/3</b>	50%
SVR in RVR	
16 wks Tx	82%
24 wks Tx	91%
$\Delta$ 16 vs 24 wks	9%

# Rapid virologic response ?

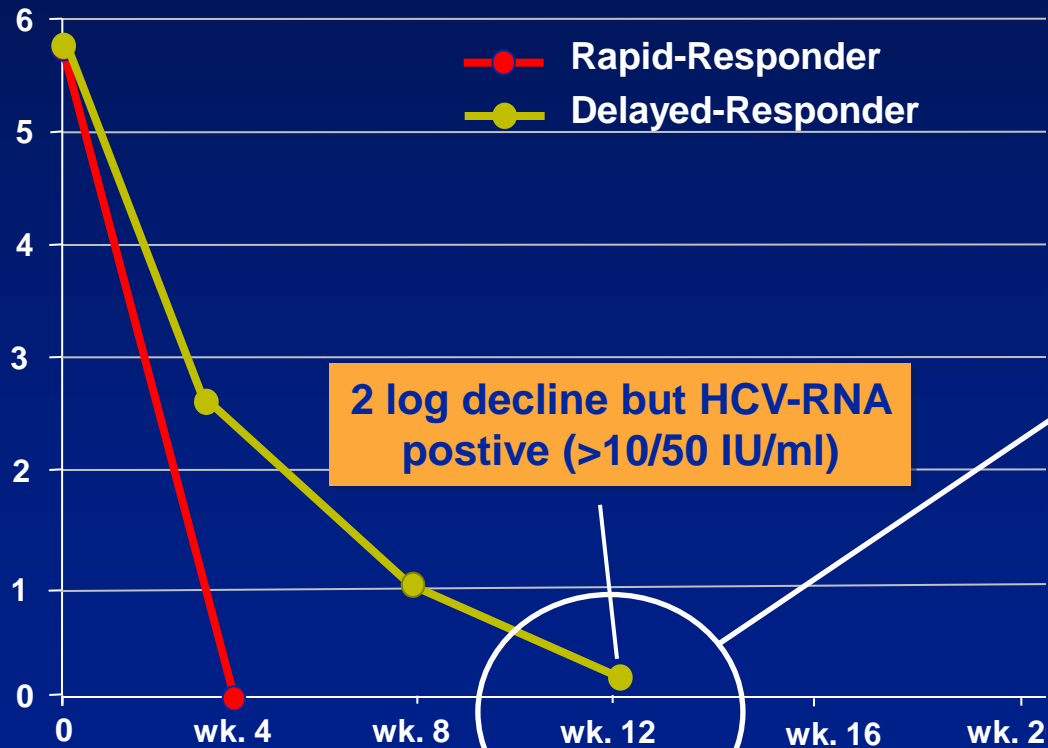
## Rapid Responder



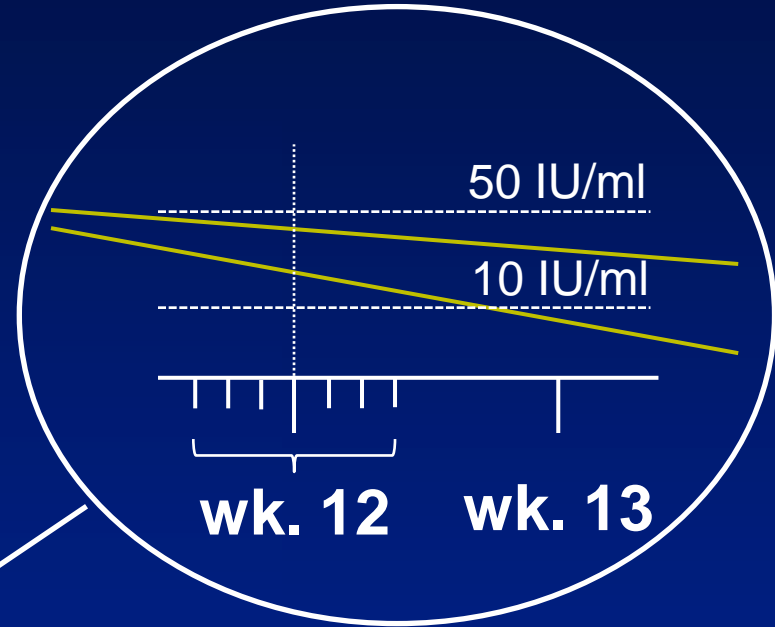
# Delayed virologic response?

## Delayed Responder

HCV-RNA( $\log_{10}$  IU/ml)



2 log decline but HCV-RNA positive (>10/50 IU/ml)





# Differences of 0.5 log (up to factor 3-4)!

## *Which Assay is correct?*

Quantification in IU results from Standardization to the WHO Standard

⇒ WHO Standard vs. Cobas TaqMan and RealTime HCV

WHO Standard	RealTime HCV		
Nominal input IU/mL ( $\log_{10}$ )	Mean (range) IU/mL	Mean (range) $\log_{10}$	Mean difference to WHO Standard
1,500 (3.2)	920 (674-1102)	3.0 (2.8-3.0)	-0.2
25,000 (4.4)	13,558 (8,997-16,102)	4.1 (4.0-4.2)	-0.3

*Mean, mean concentrations or mean  $\log_{10}$ -transformed concentrations*

# Differences of RVR rates

## *TMA versus Real-Time HCV*

INDIV-2 Study, treatment-naive HCV genotype 1, PEG/Riba 24-72 weeks

	<b>TMA neg. N</b>	<b>Real-Time HCV Positive N (%)</b>	<b>Off these pos. &lt;12 IU/ml</b>	<b>Real-time HCV pos. &amp; subsequent relapse</b>
RVR	31	17 (55%)	13/17 (76%)	0/17
EVR	77	13 (17%)	13/13 (100%)	3/13 (23%)
EOT	103	4 (4%)	4/4 (100%)	2/4 (50%)
FU24/SVR	91	2 (2%)	2/2 (100%)	

➤ Comparison TMA versus CAP/CTM and CAP/CTM versus RealTime HCV?

# Response guided Triple Therapy

## *Definitions of extended RVR*

### Boceprevir & Telaprevir studies used Cobas TaqMan Assay

#### Boceprevir

➤ eRVR            HCV RNA undetectable\* at week 8 and 24

\* Below the limit of detection (approx. 10 IU/ml) HPS/Cobas TaqMan

#### Telaprevir

➤ eRVR            HCV RNA undetectable\* at week 4 and 12

\* Below the limit of detection (approx. 10 IU/ml) HPS/Cobas TaqMan

- **How many patients had < 25/43 IU/ml but detectable HCV RNA at week 4/8?**
- **Importance of minimal viremia at week 4/8 for possible shortened treatment / resistance?**