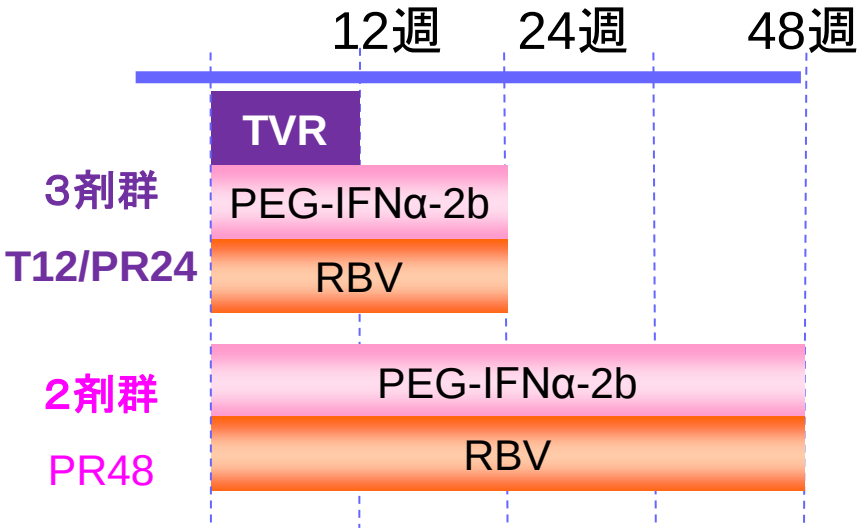
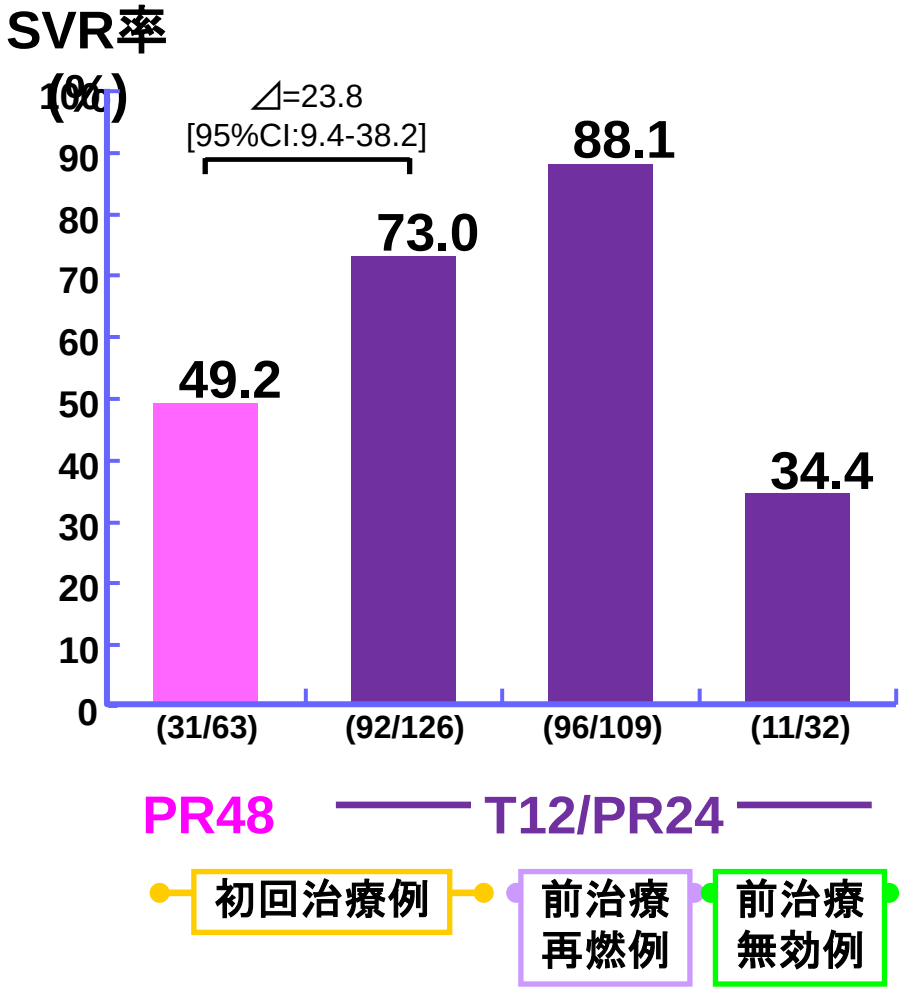
テラプレビルによる3剤治療
（1型高ウイルス量）



65歳以下、Hb>13g･dl



MP-424 (Telaprevir 国内第3相試験)

プロテアーゼ阻害剤に対するHCV変異

	V36A/M	T54A	V55A	Q80R/K	R155K/T/Q	A156S	A156V/T	D168A/V/T/H	V170A
Telaprevir (linear)			*			*			*
Boceprevir (linear)							*		
SCH900518 (linear)									
BILN-2061 (macrocyclic)									
ITMN191 (macrocyclic)						*	*		
MK7009 (macrocyclic)						*			
TMC435350 (macrocyclic)									
BI-201335 (linear)									
MK5172 (macrocyclic)									
GS-9256 (macrocyclic)									
ABT 450 (macrocyclic)									
BMS-791325 (macrocyclic)									

Table . Amino acid positions within the NS3/4A protease associated with resistance mutations to different NS3 protease inhibitors and a cross-resistance table of different NS3 protease inhibitors based on mutations selected in patients from clinical studies and/or from in vitro studies./Mutations associated with resistance in vitro. Resistance mutations of NS3 protease inhibitors with a P4-fold increase in EC50 are shown in red (Resistant) and resistance mutations described 64-fold change in EC50; are shown in white (S = susceptible) EC50 = 50% effective concentration (replicon HCV-1b).

Philippe Halfon. Journal of Hepatology 2011 in press

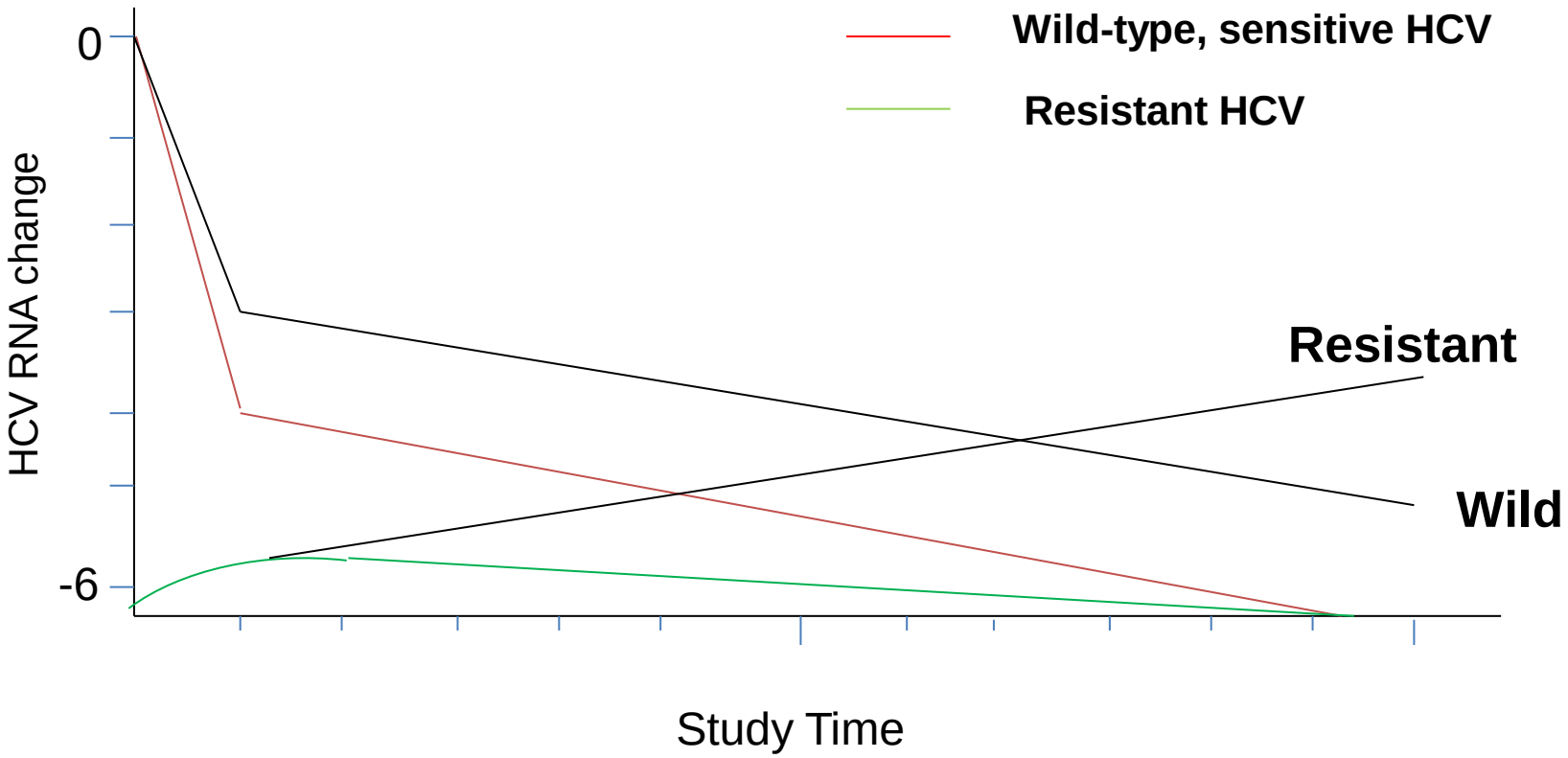
テラプレビル臨床試験におけるHCV変異

Variant	% of sequenced patients	
	Subtype 1a	Subtype 1b
WT	16%	46%
V36M	10%	3%
R155K	20%	0%
V36M+R155K	46%	0%
V36A	3%	16%
T54A	<1%	22%
A156S/T	3%	13%

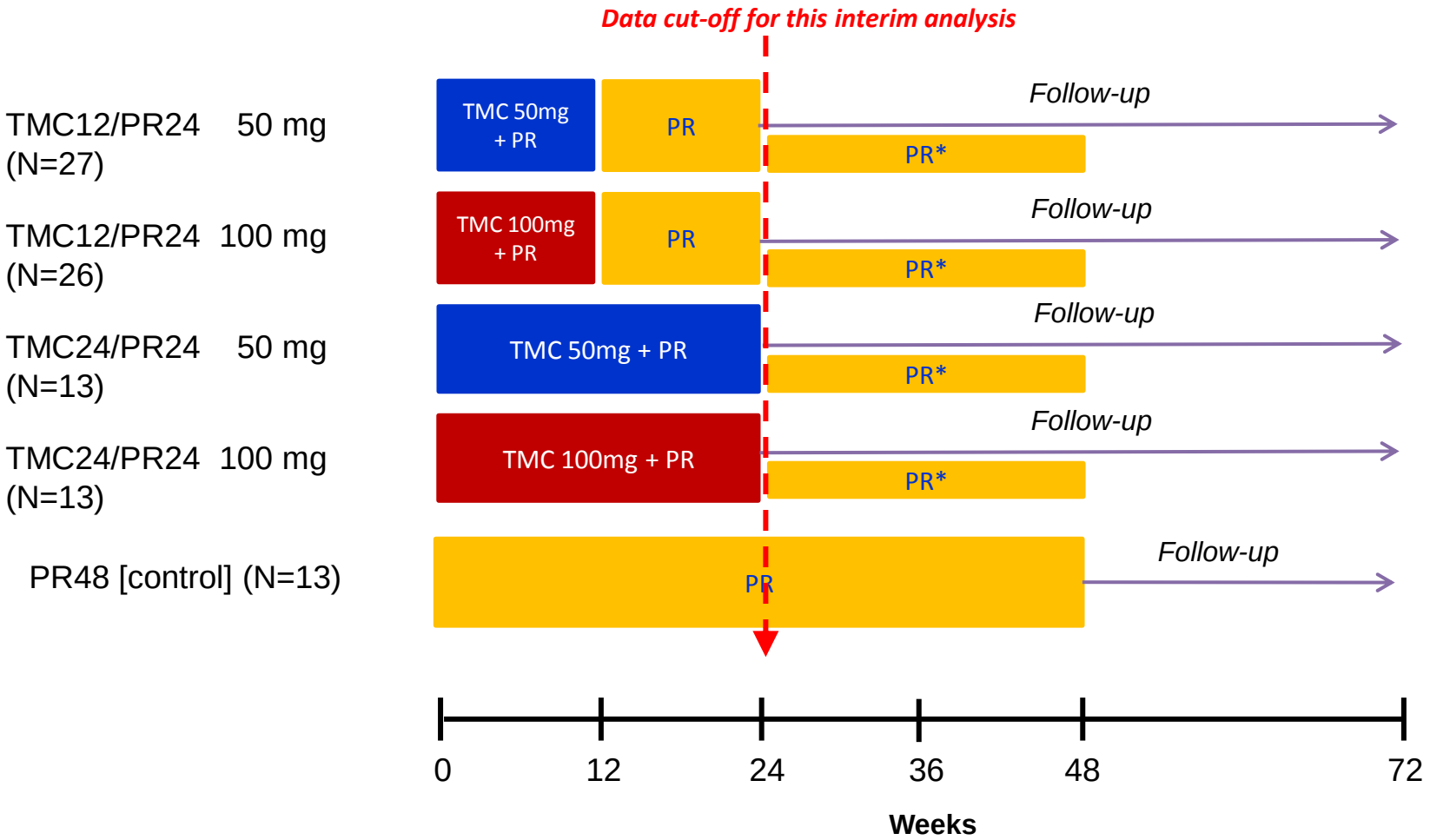
J.C Sullivan. EASL 2011 oral #8

3剤併用療法におけるHCVダイナミックス

IFNα+ribavirin effect

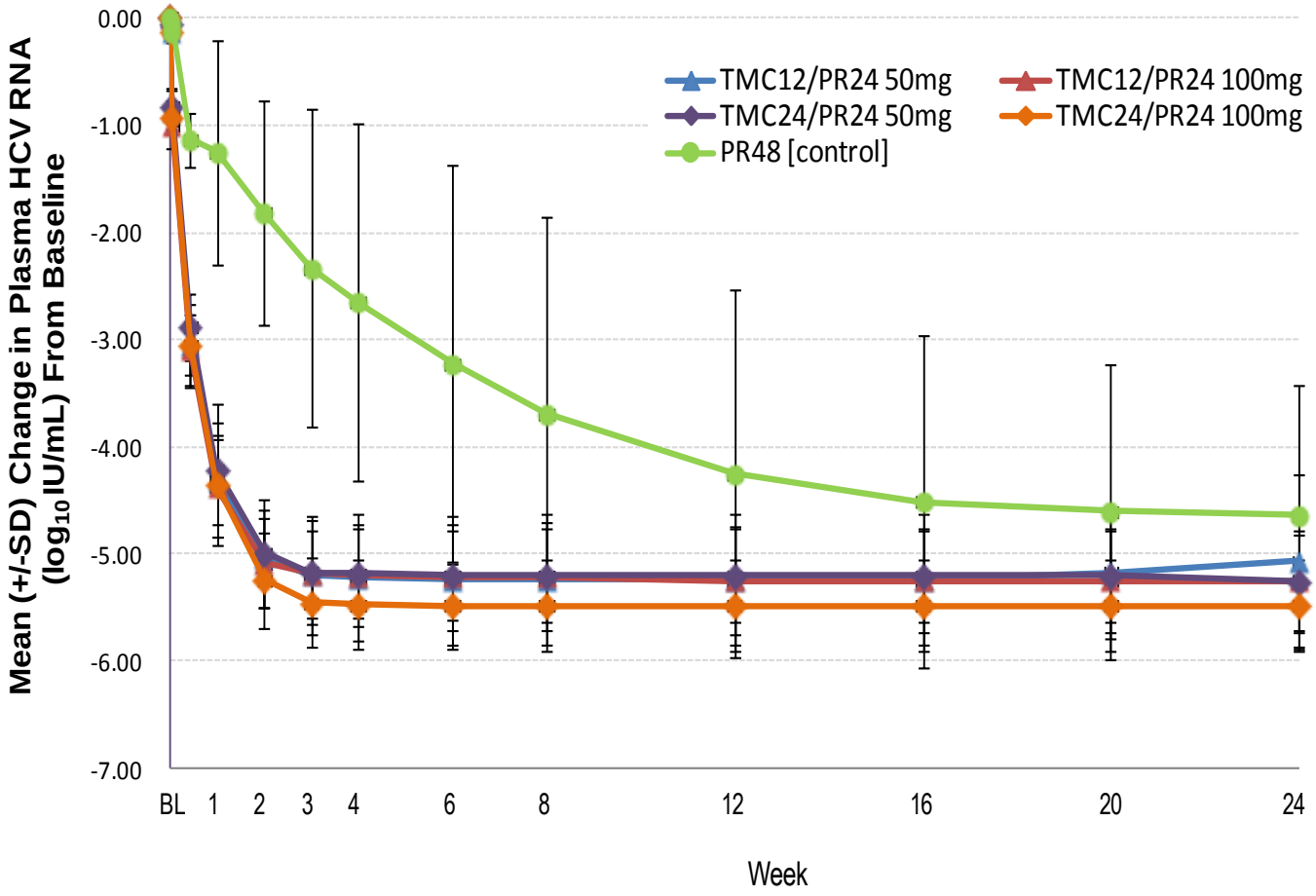


TMC435の第Ⅱ相臨床試験 (DRAGON)

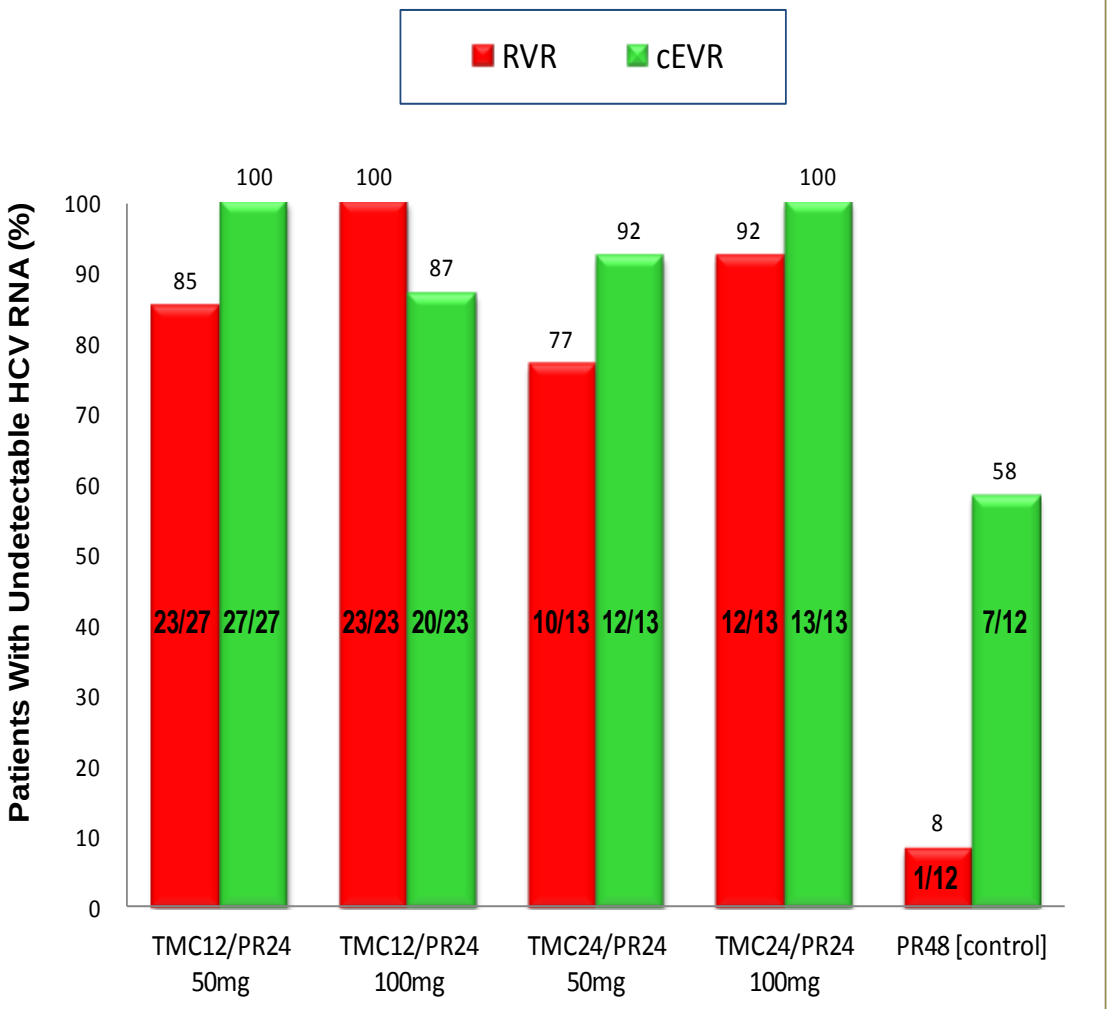


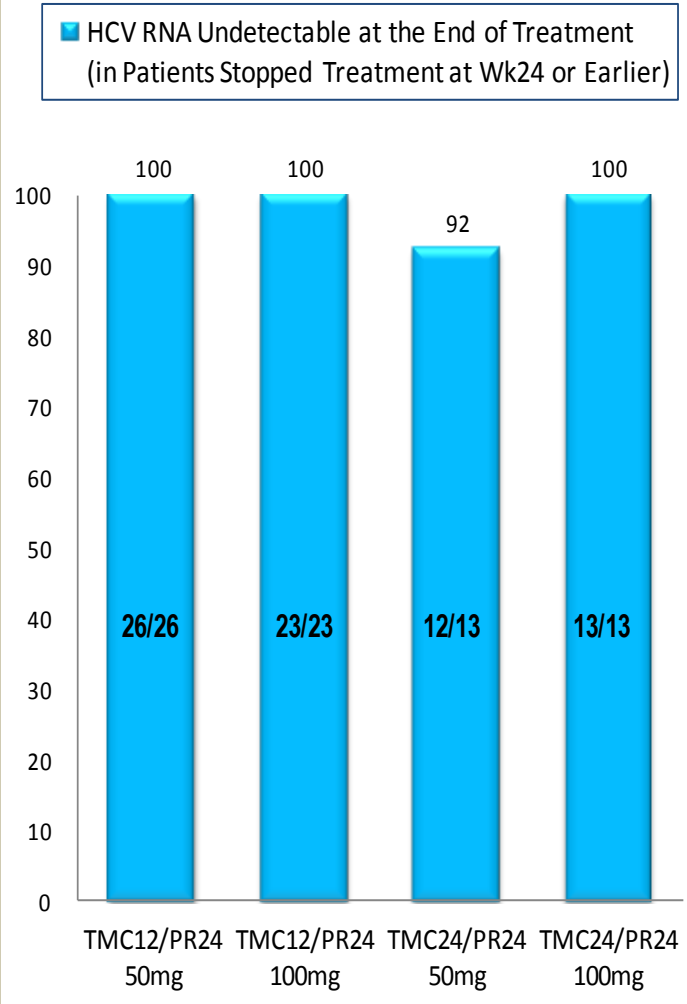
*: Patients who did not achieve HCV RNA < 15IU/mL and undetectable HCV RNA (< 15IU/mL undetectable) at week 4, 12,16 and 20 continue PR until week 48; (P) Peg-IFN = pegylated interferon alfa-2a 180 µg/wk; (R) RBV = ribavirin weight based 600 to 1,000 mg/day

HCV RNAの減少率


Mean (+/-SD) Change in Plasma HCV RNA (log10 IU/mL) From Baseline
0.00
-1.00
-2.00
-3.00
-4.00
-5.00
-6.00
-7.00
BL
1
2
3
4
6
8
12
16
20
24
Week
TMC12/PR24 50mg
TMC12/PR24 100mg
TMC24/PR24 50mg
TMC24/PR24 100mg
PR48 [control]

RVR率とcEVR率

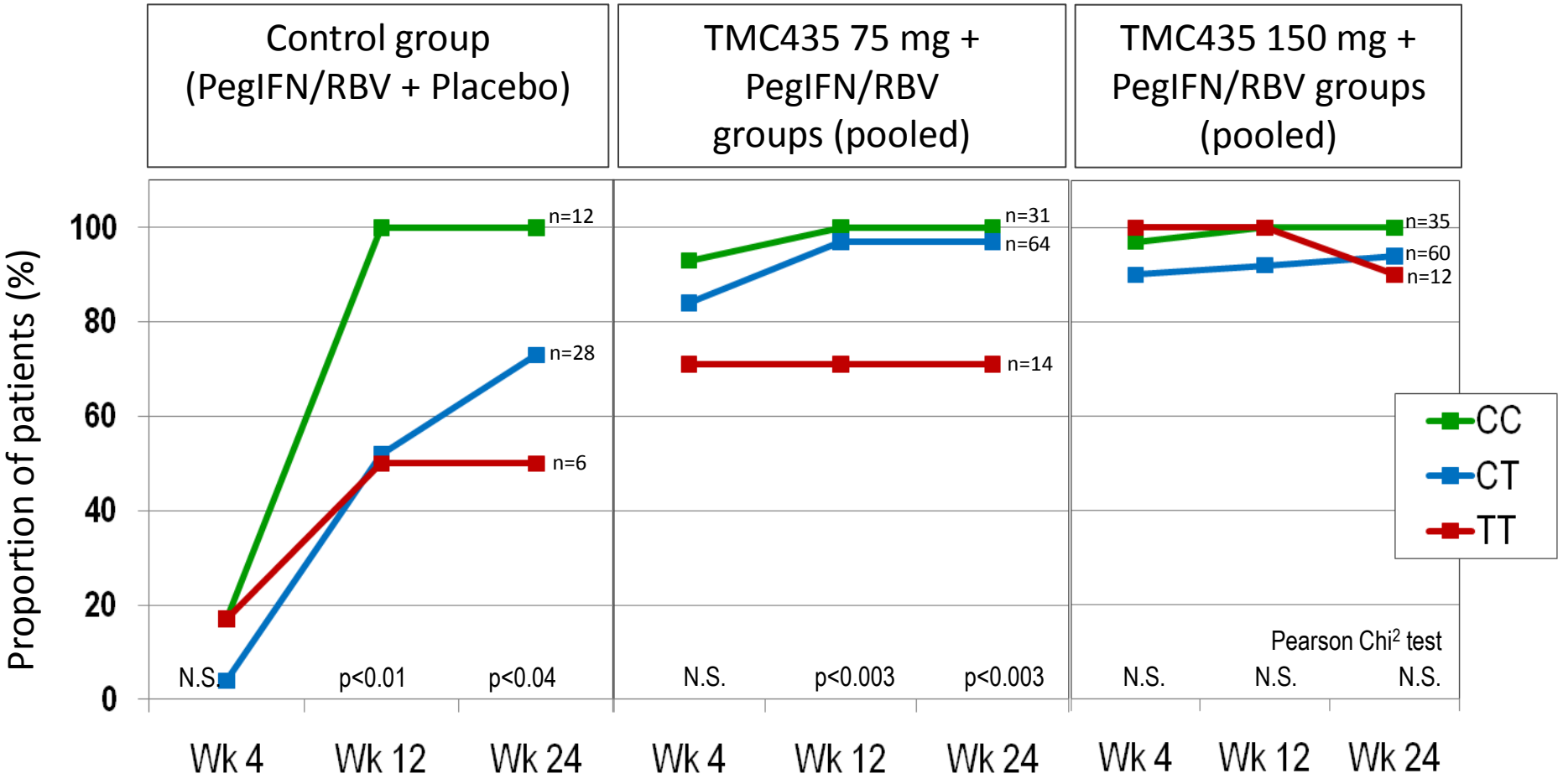




RVR: HCV RNA undetectable at Week 4　cEVR: HCV RNA undetectable at Week 12
The subjects who stopped all medications are handled as those not achieved HCV RNA undetectable
The end of treatment (at Wk48) for group 5 (PR48): data not available yet

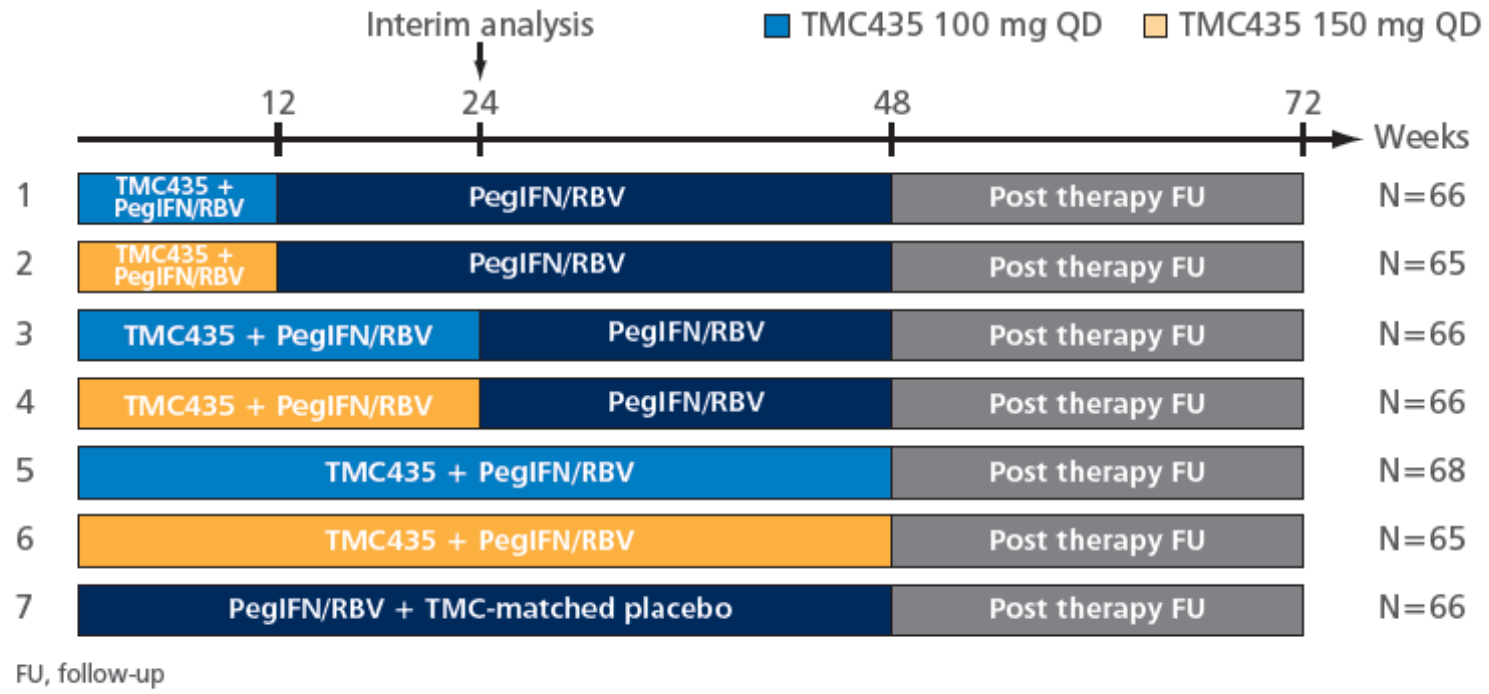
IL28B別のウイルス陰性化率

Virologic response: HCV RNA <25 IU/ml (detectable or undetectable)



ＴＭＣ４３５の既治療に対する臨床試験
（ASPIRE 試験）

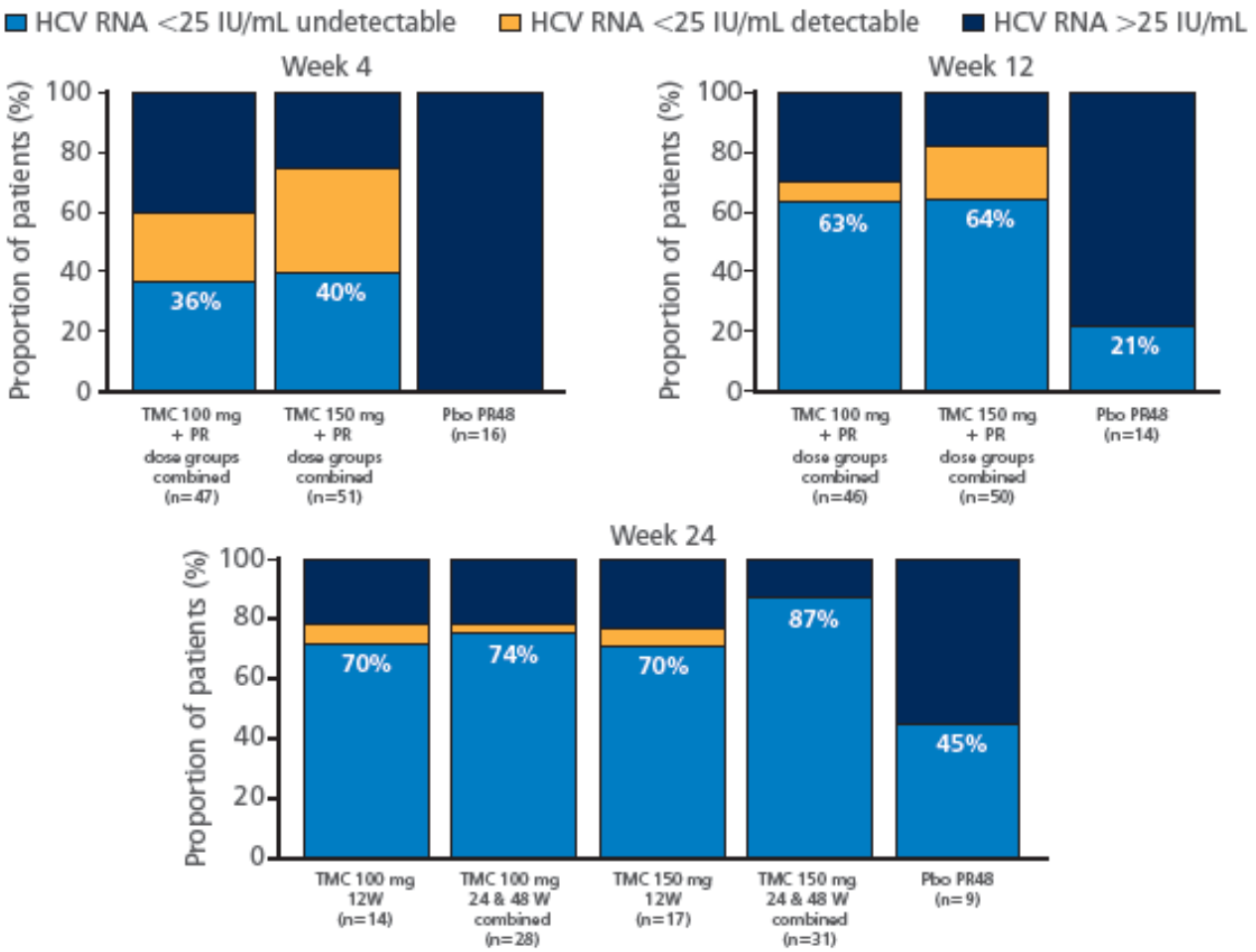
FIGURE 1: ASPIRE study design.



FU, follow-up

ＮＲ症例のウイルス陰性化率

FIGURE 3c: Observed virologic response rate at Weeks 4, 12, 24, by treatment group: Null responders.



Pbo PR48, Placebo in addition to PegIFN/RBV for 48 Weeks; PegIFN, peginterferon; RBV, ribavirin; TMC, TMC435