TÜRK KARACİĞER VAKFI

3 Türkiye – Azerbaycan ortak hepatoloji kursu
29 - 30 Eylül 2017, Istanbul

AZERBAYCAN TIP ÜNİVERSİTESİ

IL-28B dimorphism variants, early viral kinetics and clinical outcomes in HCV(G1+G3) patients.

PegIFN + RIB vs. SOF + PegIFN + RIB -containing combinations regimens.

"EuroMed" single medical centre experience.

EuroMed
ÖZƏL TİBB MƏRKƏZİ

Yusif Alkhazov, MD
"EuroMed" Private Medical Center,
Baku, Azerbaijan

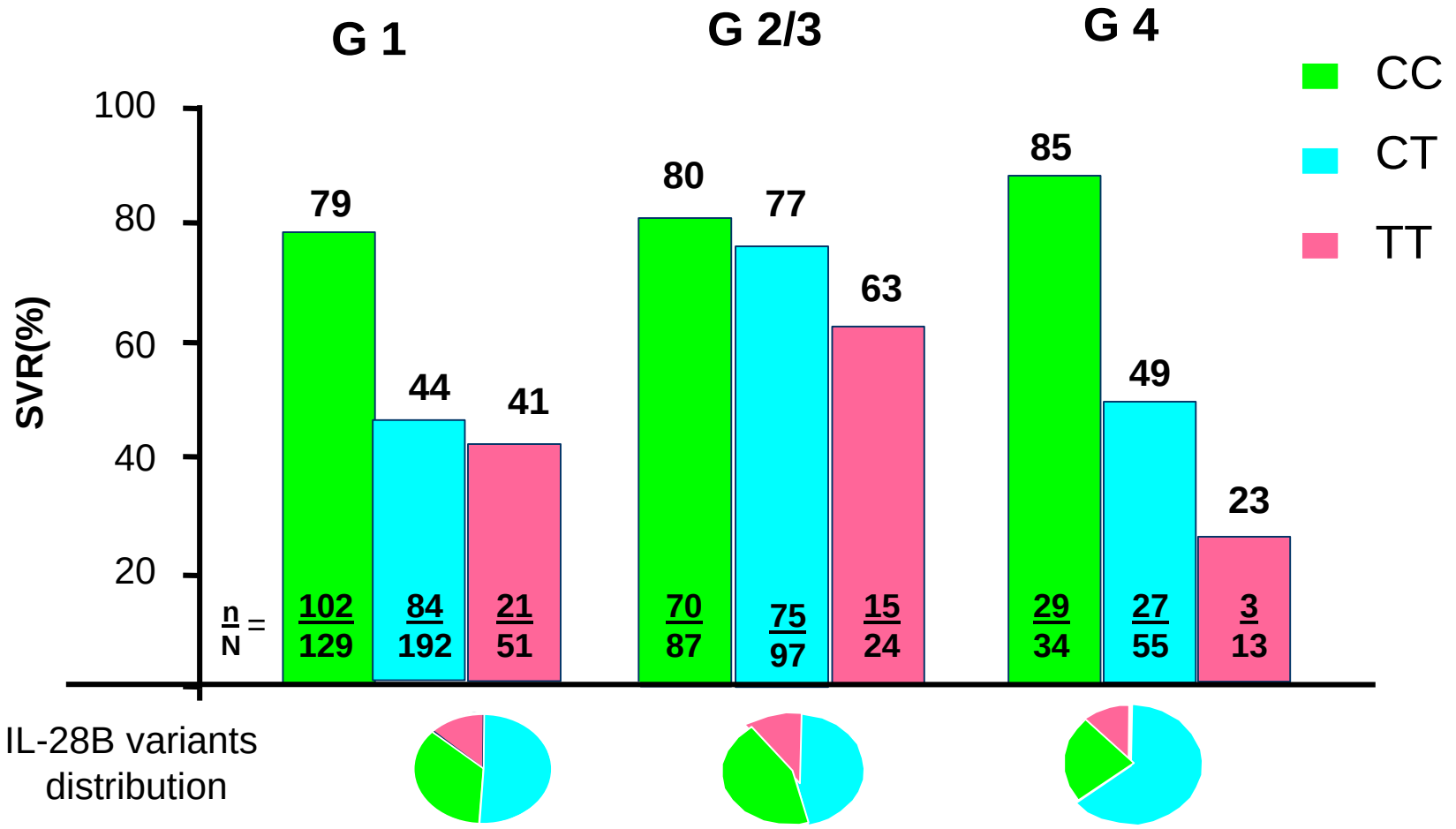
"Genotyping for *IL28B* broke onto the scene in 2009 with the discovery that a single nucleotide polymorphism in this gene was a predictor of sustained viral response in patients with dual therapy..."

A. Wu, M. Khalili:
"The birth and potential death of *IL28B* genotyping for hepatitis C therapy",
Personalized Medicine; (2015) 12(2)

The birth: "Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance".

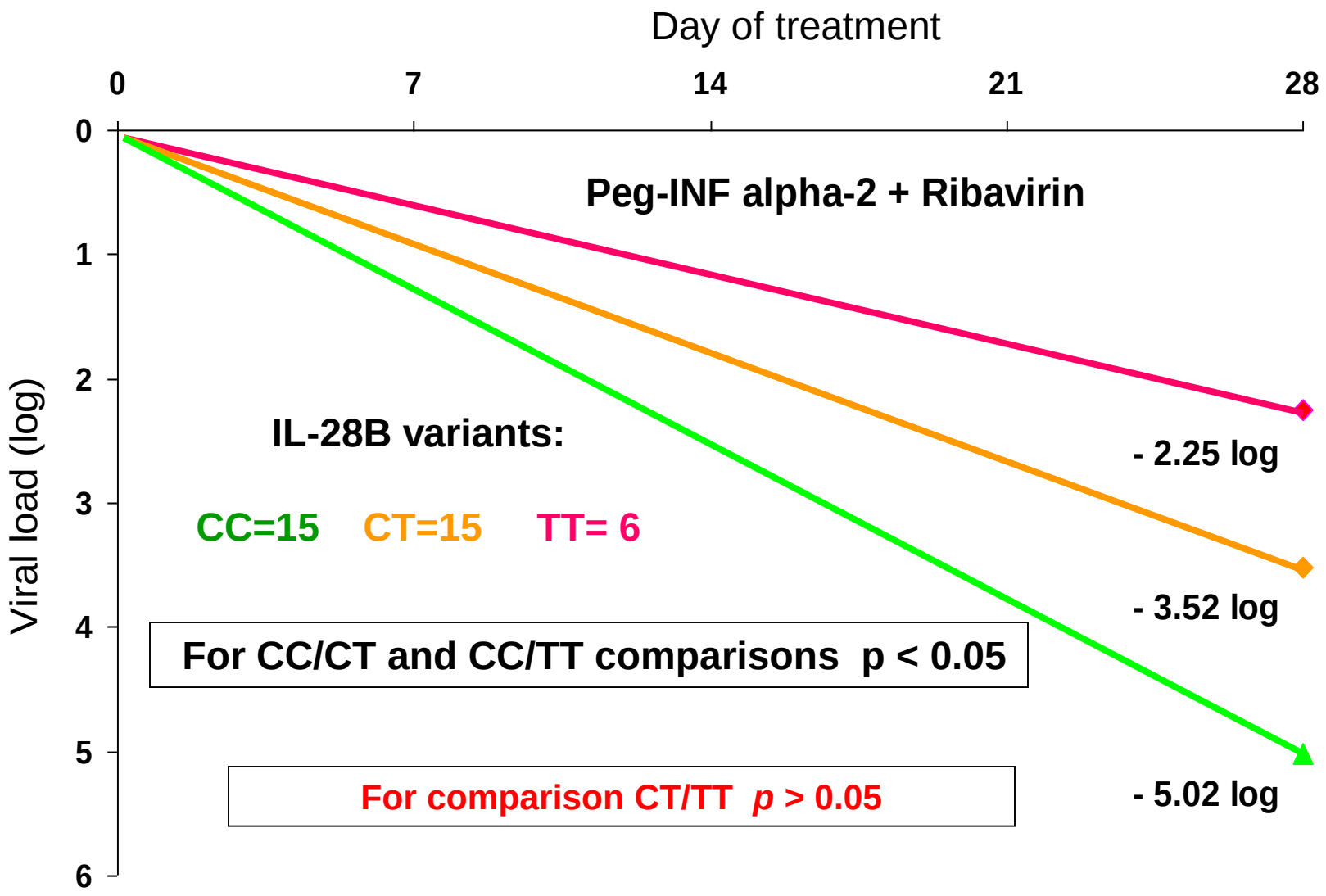
Dongliang Ge, et al.; Nature 2009; 461(7262): 399-401

IL-28B dimorphism variants and SVR in different HCV genotypes



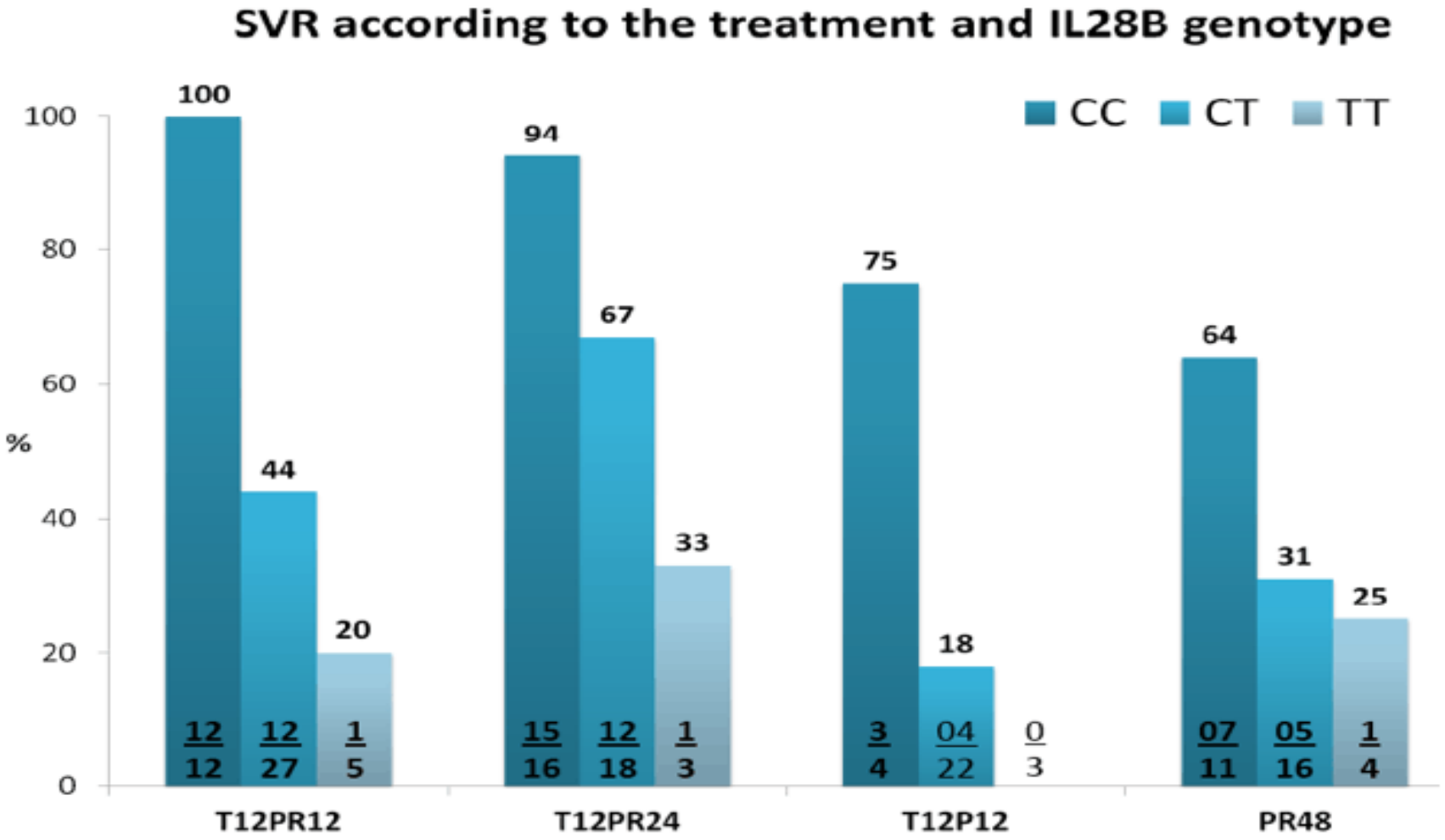
Stättermayer AF, et al. Clin Gastroenterol Hepatol 2011; 9: 344–50

Early viral kinetics as a function of IL-28B dimorphism



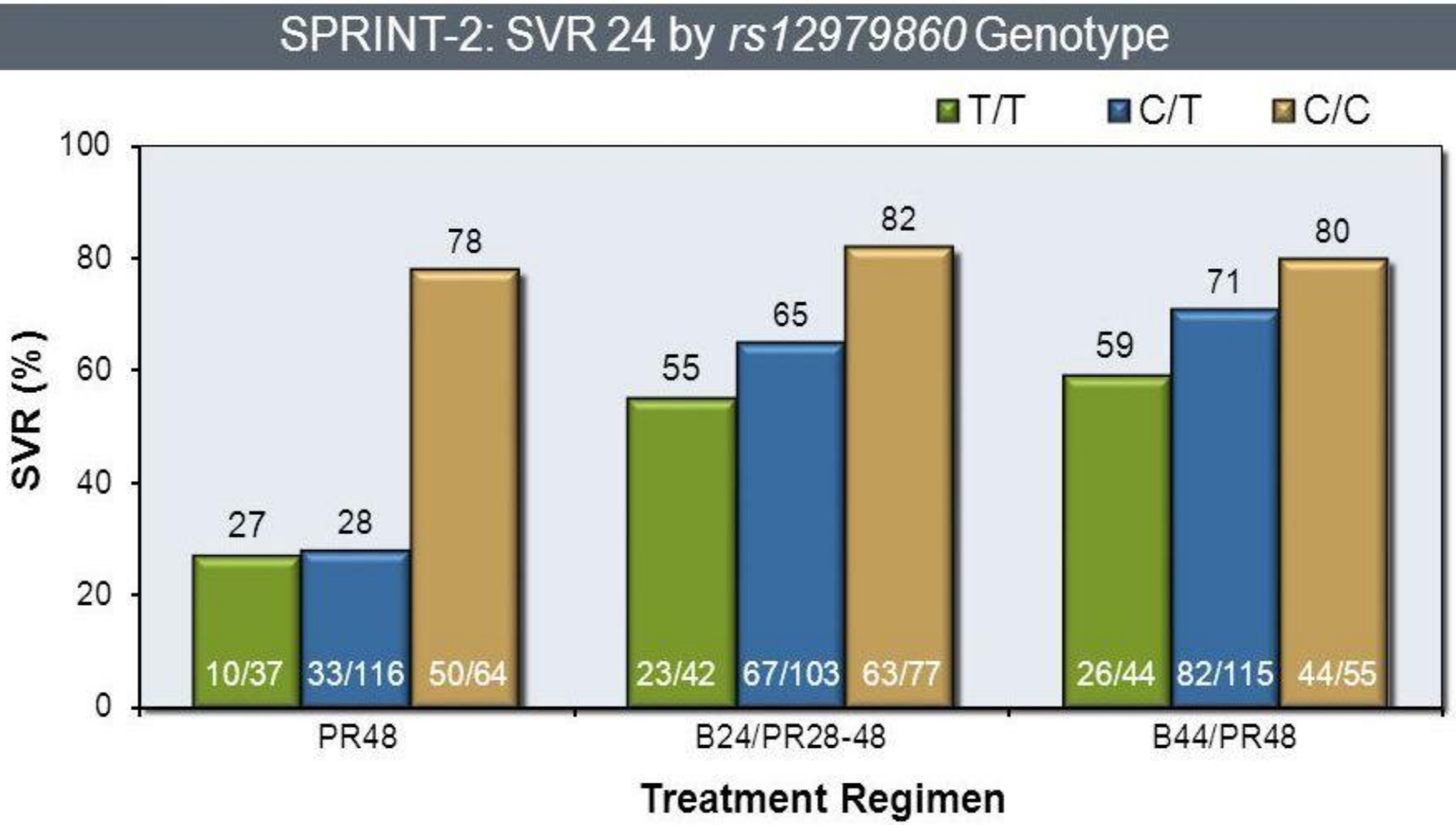
N.Abdullayeva, Y. Alkhazov et al.: Bulletin of the Pancreatologist`s Club, 1(14), 2012, 50-51

100% SVR in IL28B SNP rs12979860 C/C patients treated with 12 weeks of TPR, PegIFN and RIB in the PROVE2 trial



Bronowicki J-P et al., ILC-2012, April18-22, Barcelona, Spain

Boceprevir for treatment-naïve HCV G-1 patients
SPRINT-2: SVR rates by IL-28B rs12979860 Genotype



SVR = Sustained Virologic Response; RGT = Response Guided Therapy
PR = Peginterferon + Ribavirin; PRB = Peginterferon + Ribavirin + Boceprevir;

Source: Poordad F, et al. Gastroenterology. 2012:143:608-18.

IL-28B dimorphism variants distribution in HCV patients (G1+G3) treated PegIFN + RIB (2010 - 2015) - group A

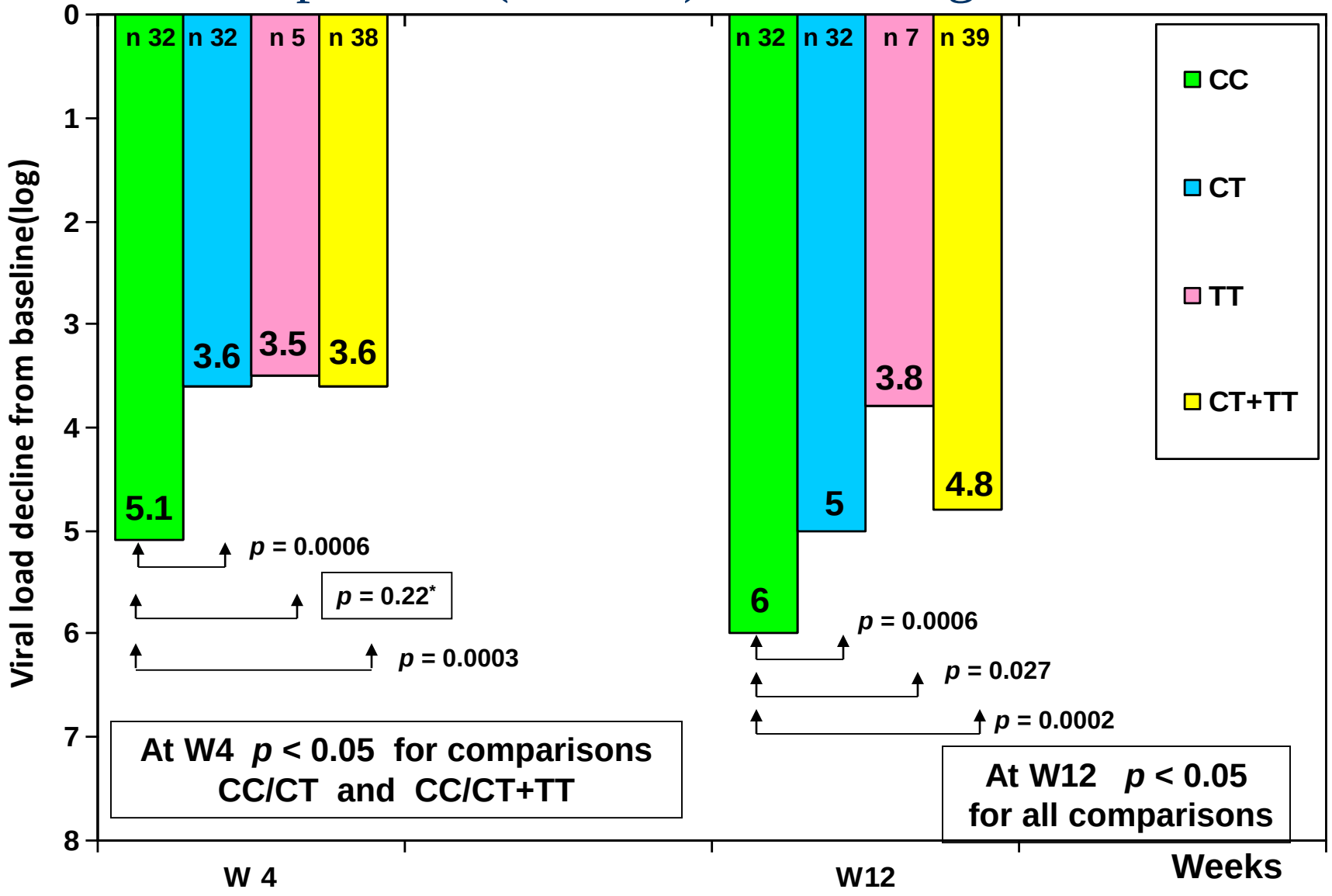
IL-28B dimorphism variant	HCV Genotypes					
	G 1 N=46 (64.8%)		G 3 N=25 (35.2%)		G 1 + G 3 N=71 (100%)	
CC	16 (34,8%)		16 (64%)		32 (45%)	
CT	23 (72%)	30 (65,2%)	9 (28%)	9 (36%)	32 (45%)	39 (55%)
TT	7 (100%)		0 (0%)		7 (10%)	
CC+ CT+ TT	46 (100%)		25 (100%)		71 (100%)	

♂ Male 42 (59,2%)

♀ Female 29 (40,8%)

MC «EuroMed», 2010 - 2015, internal data.

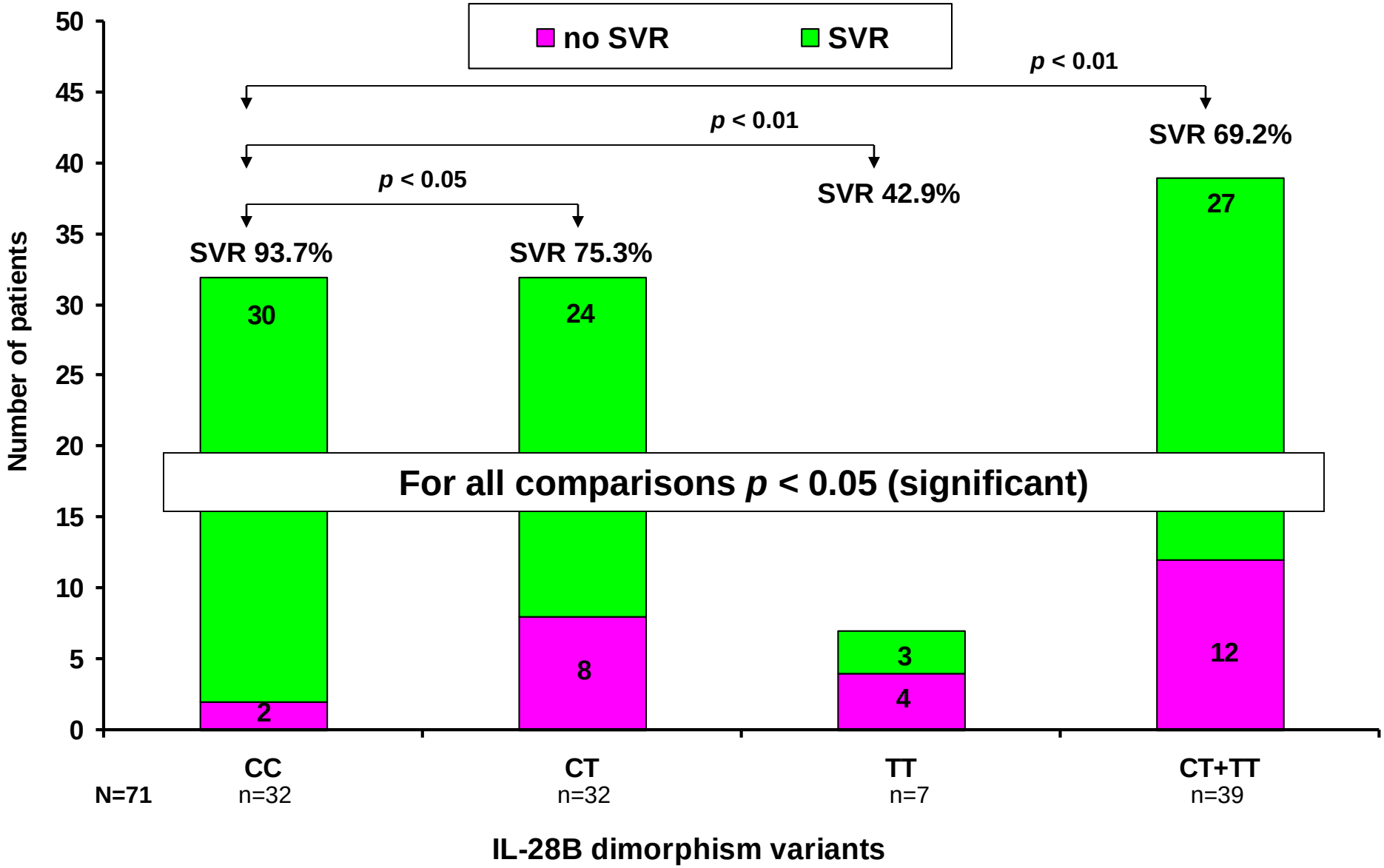
IL-28B dimorphism variants and early viral kinetics in HCV patients (G1+G3) treated PegIFN + RIB



• $p > 0.05$ for comparison CC/TT due to low TT-patients number

MC «EuroMed», 2010 - 2015, internal data.

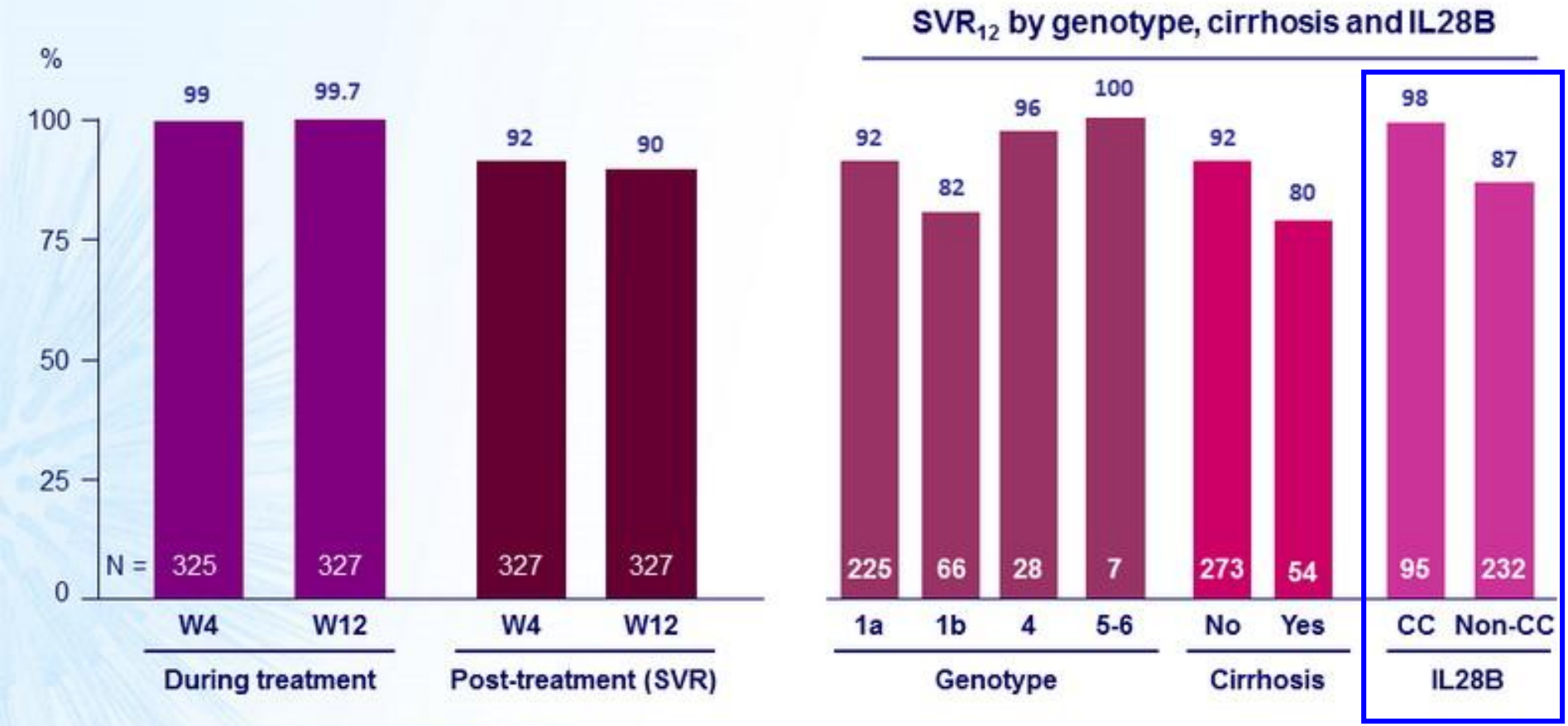
IL-28B dimorphism variants and treatment outcomes in HCV patients (G1+G3) treated PegIFN + RIB



MC «EuroMed», 2010 - 2015, internal data.

NEUTRINO Study: SOF + PEG-IFNα-2a + RBV

HCV RNA < 25 IU/ml



SVR_{12} = 90% (95% CI : 87 -93) :
superiority to adjusted historal SVR_{12} of 60% (two-sided exact test, p < 0.001)

Lawitz E. NEJM 2013;368:1878-87

"The rumors of my death have been greatly exaggerated[1]."

[1] From the telegram of the American writer Mark Twain (Samuel L. Clemens, 1835 - 1910) to the "Associated Press" agency, which he sent in connection with the reports that appeared in the newspapers about his death.

IL-28B dimorphism variants distribution in HCV patients (G1+G3) treated SOF+PegIFN+RIB (2015 - 2016) - group B

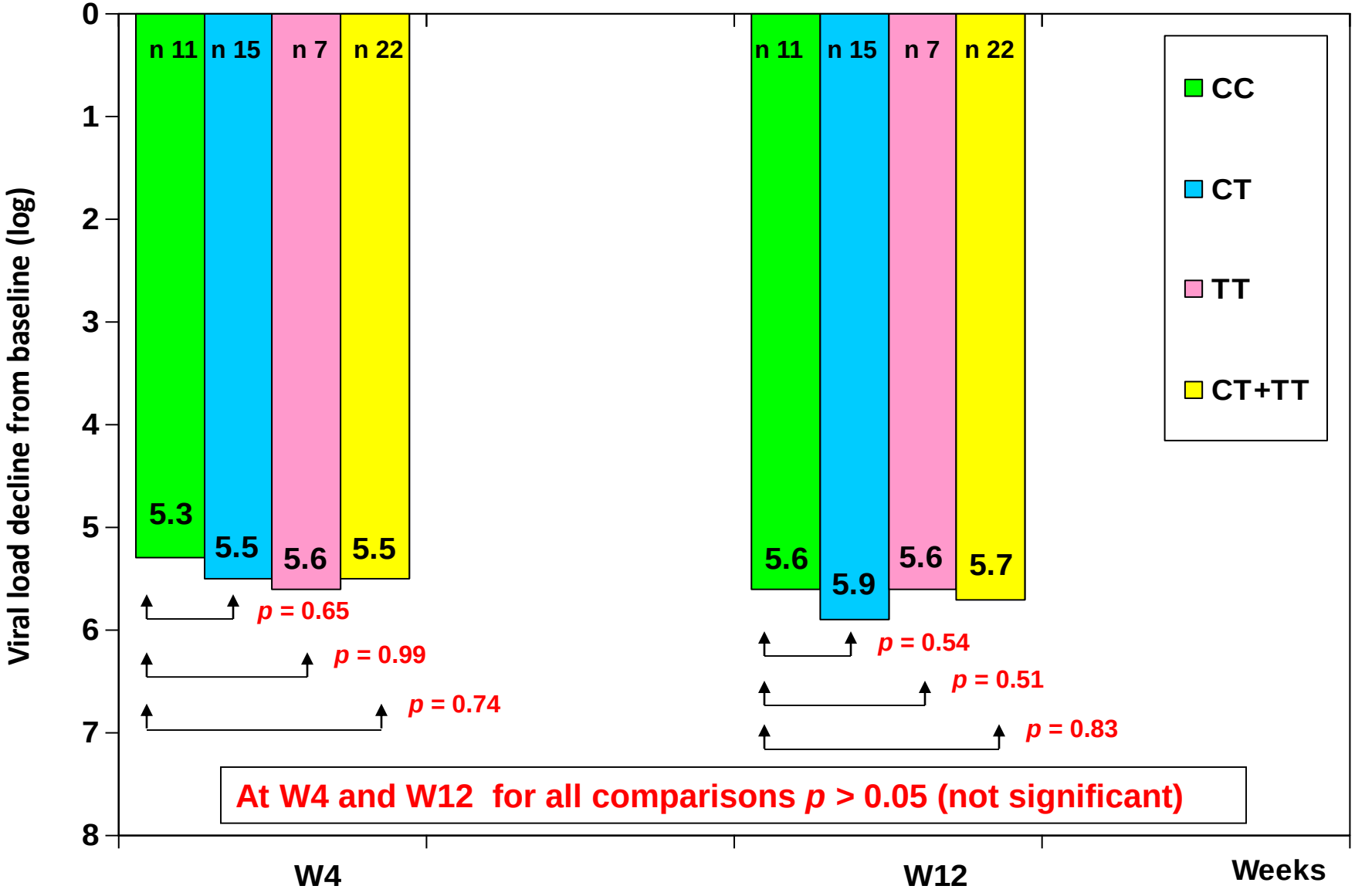
IL-28B dimorphism variant	HCV Genotypes					
	G 1 N=27 (77.1%)		G 3 N=8 (22.9%)		G 1+ G 3 N=35 (100%)	
CC	10 (37%)		3 (37,5%)		13 (37%)	
CT	11 (40,8%)	17 (63%)	3 (37,5%)	5 (62,5%)	14 (40%)	22 (63%)
TT	6 (22,2%)		2(25%)		8 (23%)	
CC+CT+TT	27 (100%)		8 (100%)		35 (100%)	

Male 25 (71,4%)

Female 10 (28,6%)

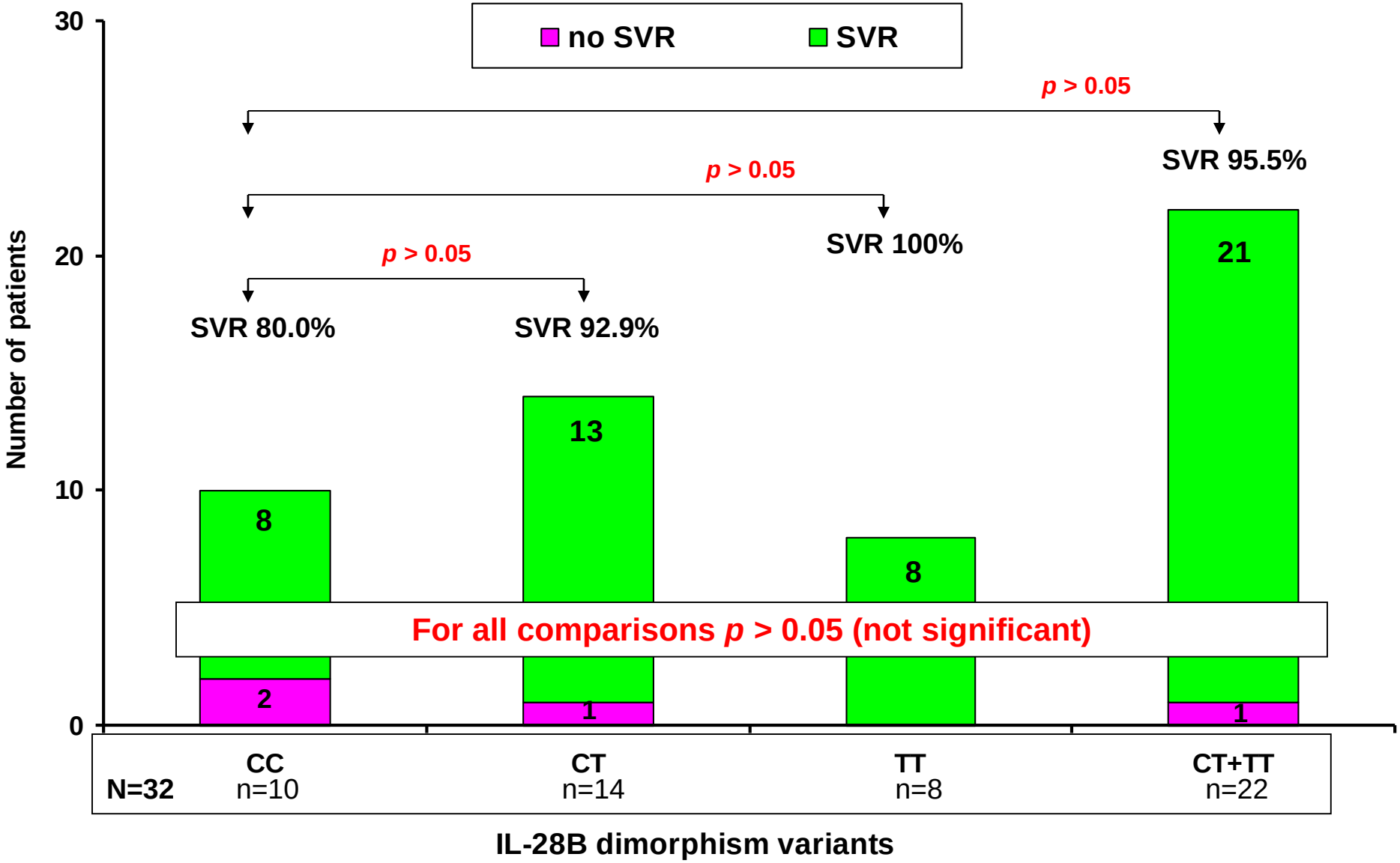
MC «EuroMed», 2015 - 2016, internal data.

IL-28B dimorphism variants and early viral kinetics in HCV patients (G1+G3) treated SOF + PegIFN + RIB



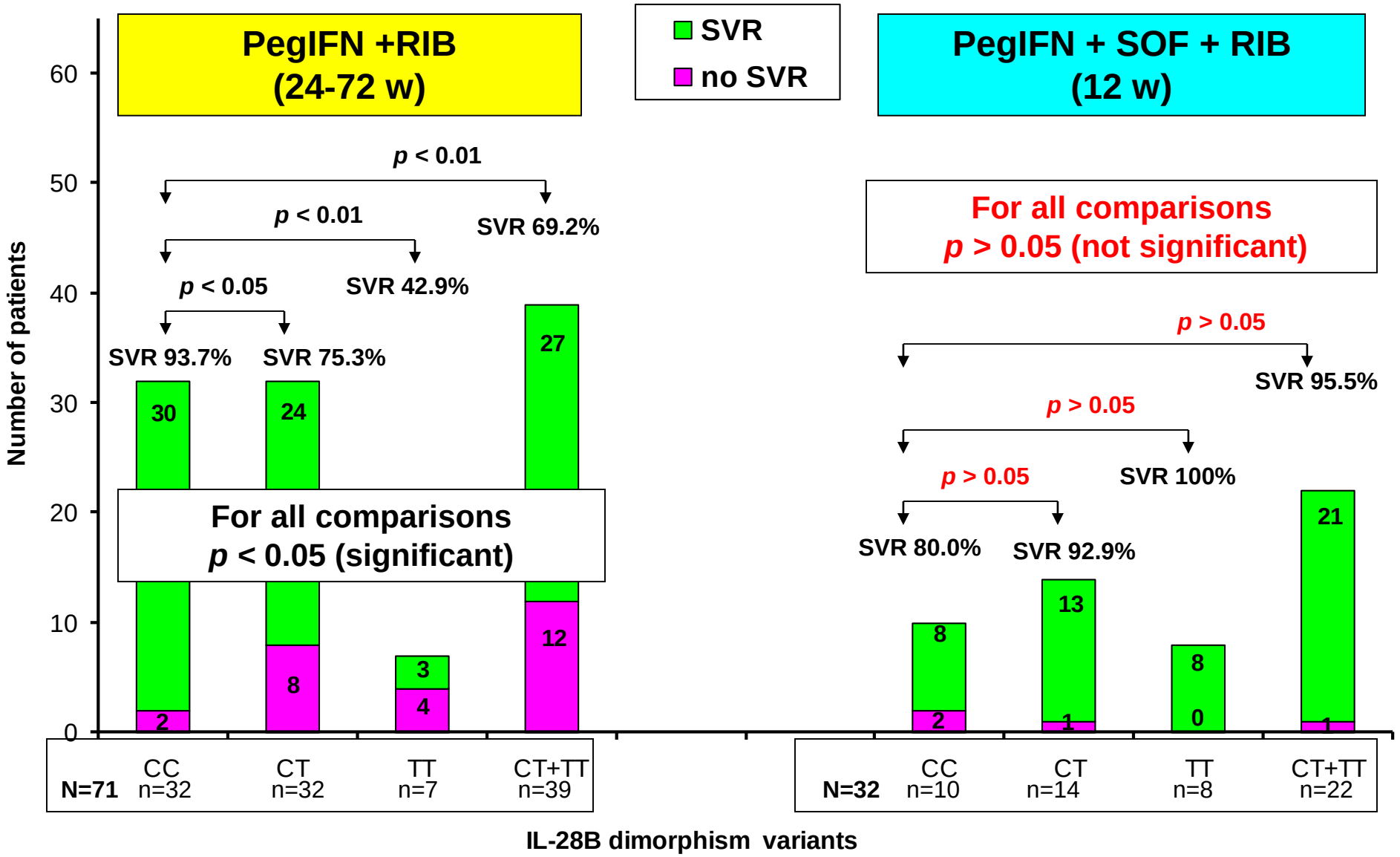
MC «EuroMed», 2015 - 2016, internal data.

IL-28B dimorphism variants and treatment outcomes in HCV patients (G1+G3) treated SOF + PegIFN + RIB



MC «EuroMed», 2015 - 2016, internal data.

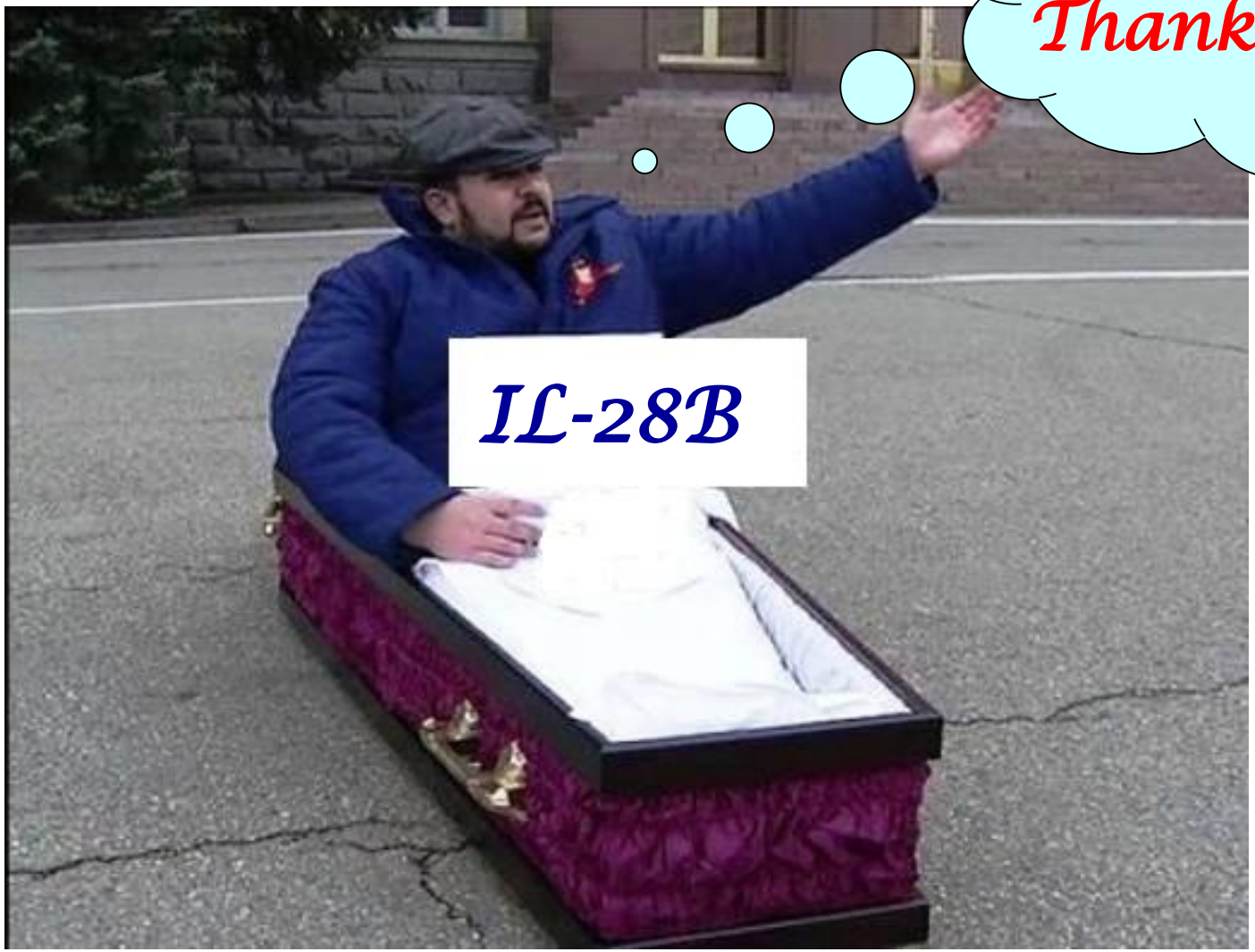
IL-28B dimorphism variants and treatment outcomes in HCV patients (G1+G3) treated PegIFN+RIB vs. PegIFN+SOF+RIB



MC «EuroMed», 2010 - 2016, internal data.

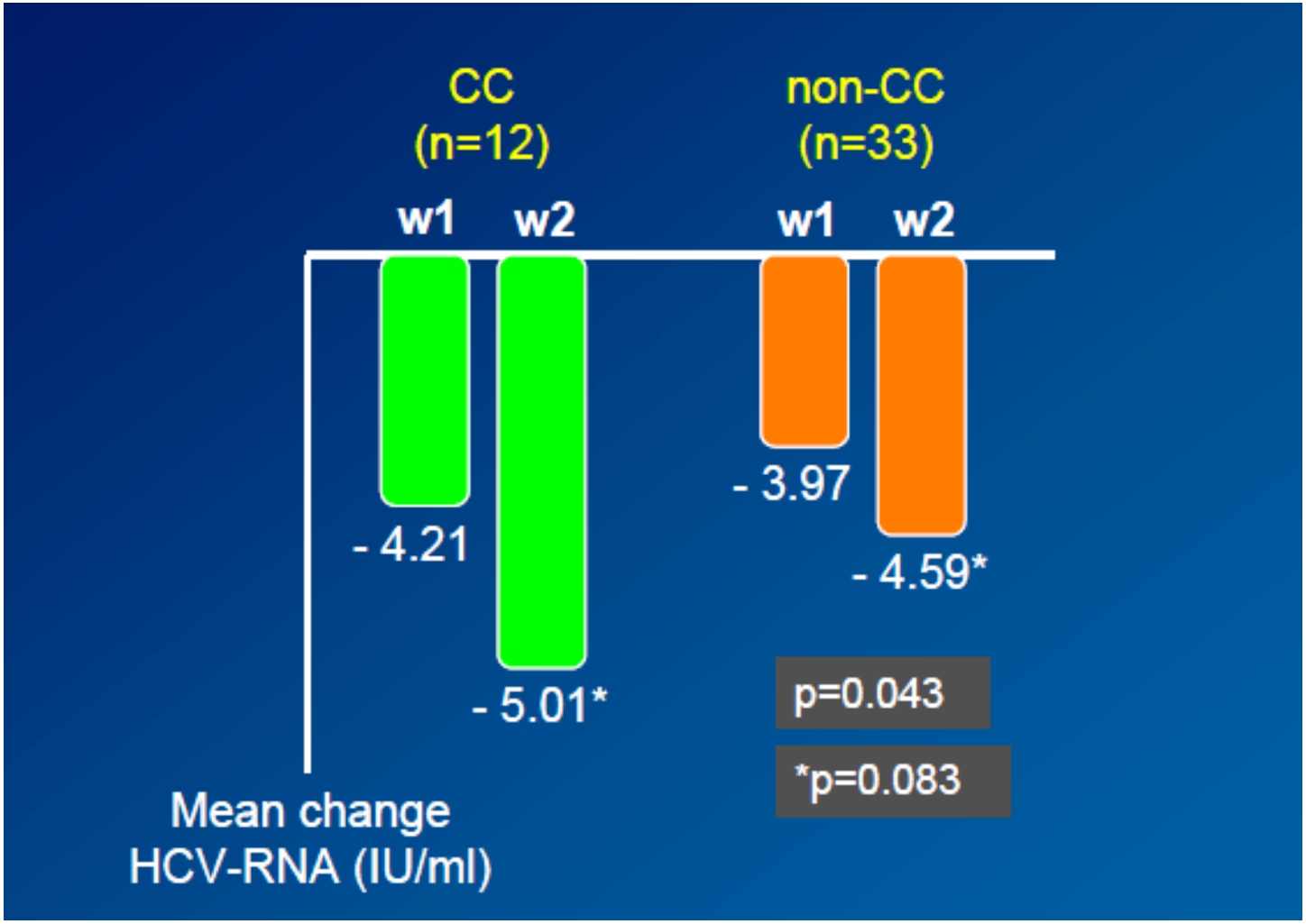
What role can IL28B play in the era of DAA therapy without interferon?

IL 28B: time to die too ???



Don't forget to say Thank You !

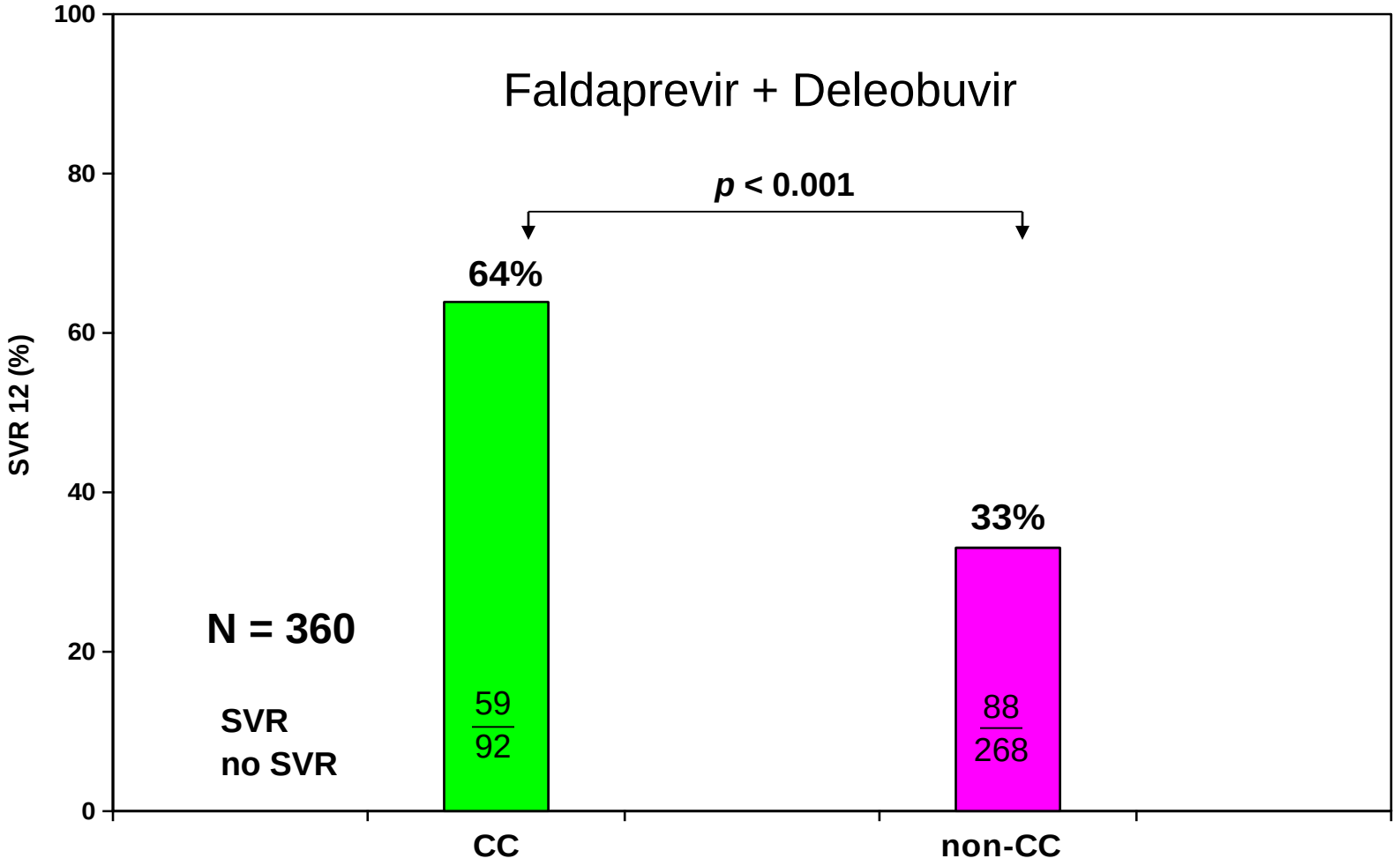
IL-28B dimorphism and early viral kinetics in G1 patients treated with mericitabine and danoprevir (INFORM-1)



Mericitabine (an NS5B polymerase inhibitor)
Danoprevir (an NS3/4A protease inhibitor)

Chu et al. Gastroentrology 2012; 142: 790-5.

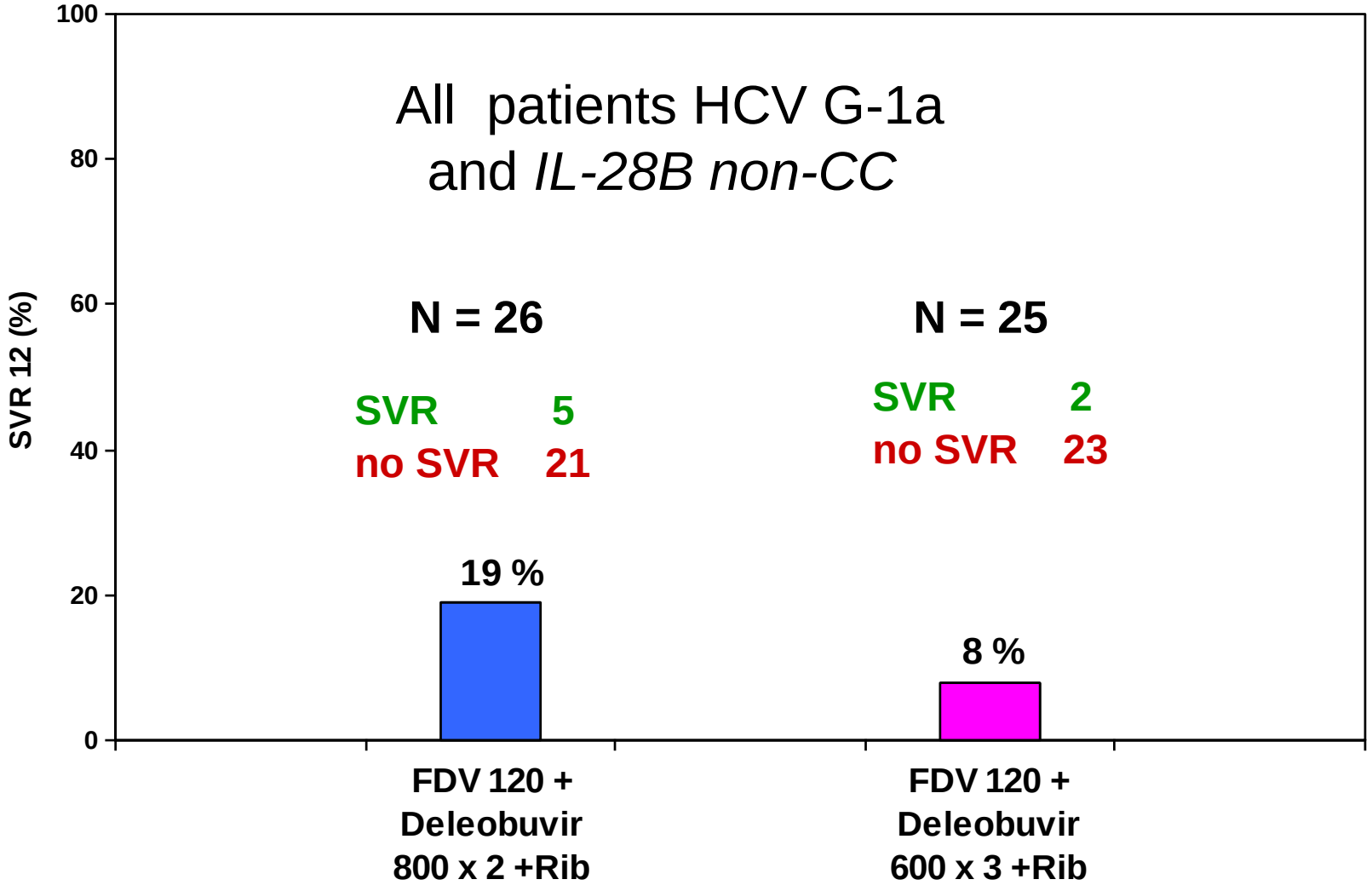
Faldaprevir and deleobuvir for HCV G1 infected patients included in the SOUND-C2 phase 2b study.



Faldaprevir (an NS3/4A protease inhibitor),
Deleobuvir (a non-nucleoside polymerase inhibitor)

Adopted by Zeuzem et al; N Engl J Med. 2013 Aug 15; 369(7):630-9.

Faldaprevir, deleobuvir and ribavirin in IL28B non-CC patients with HCV genotype-1a infection included in the SOUND-C3 phase 2b study.



Adopted to Zeuzem et al; Eur J Gastroenterol Hepatol. 2016 Aug; 28(8):923-6.

Conclusion

- IL28B genotype has a limited impact on SVR rates in patients treated with second generation DAA
- Some clinical evidence suggests that IL28B genotypes will likely continue to play some role in predicting SVR using interferon-free regimens
- IL28B genotyping can be useful for personalized CHC treatment possibly by predicting a shorter treatment duration
- IL28B SNPs plays a role in the study of the efficacy of new antiviral agents

Thank you for your attention!

Birlikte - güçlüyüz!