Combined effects of different interleukin-28B gene variants on the outcome of dual combination therapy in chronic hepatitis C virus type 1 infection.

In patients with chronic hepatitis C virus (HCV) infection, several variants of the interleukin-28B (IL28B) gene have been shown to correlate significantly with a sustained virologic response (SVR). Recent evidence shows that determination of one single IL28B polymorphism, rs12979860, is sufficient for predicting treatment outcome. We examined whether the combined determination of the IL28B single-nucleotide polymorphisms (SNPs), rs12979860, rs8099917, rs12980275, and rs8103142, might improve the prediction of SVR in patients with HCV. In the study cohort, 54% of 942 patients with chronic HCV type 1 infection had SVR. The IL28B SNPs, rs12979860CC and rs8099917TT, correlated significantly with SVR (68% and 62%). The SNPs, rs12980275 and rs8103142, were in strong linkage disequilibrium with rs12979860 and were not included in further analysis. In homozygous carriers of the rs12979860 responder allele C, additional genotyping of the rs8099917 SNP had no effect on response prediction, whereas in carriers of the rs12979860 nonresponder allele, the rs8099917 SNP improved the response prediction. In heterozygous carriers of the rs12979860 nonresponder T allele, SVR rates were 55% in the
presence of the rs8099917TT genotype and 40% in patients carrying the rs8099917 TG or GG genotype. Analysis of an independent confirmation cohort of 377 HCV type 1-infected patients verified the significant difference in SVR rates between the combined genotypes, rs12979860CT/rs8099917TT and rs12979860CT/rs8099917TG (38% versus 21%; P = 0.018).

Conclusion: Treatment outcome prediction could not be improved in homozygous carriers of the IL28B rs12979860 C responder allele by the additional determination of the rs8099917 SNP. There is evidence that a significant proportion of heterozygous carriers of the rs12979860 T nonresponder allele can profit with respect to SVR prediction by further determination of the rs8099917 SNP.