Naturally occurring substitutions conferring resistance to hepatitis C virus polymerase inhibitors in treatment-naive patients infected with genotypes 1-5

BACKGROUND: The hepatitis C virus (HCV) RNA-dependent RNA polymerase, NS5B, is essential for virus RNA replication. It is thus an attractive therapeutic target. Several compound nucleoside analogues, non-nucleoside inhibitors and cyclosporine analogues are being developed to inhibit NS5B activity. However, nucleotide changes in the NS5B gene can confer resistance to them.

METHODS: We investigated the prevalence of known substitutions conferring resistance in HCV polymerase in 124 treatment-naive French patients infected with HCV genotypes 1, 2, 3, 4 or 5 by sequencing the NS5B gene. RESULTS: None of the 124 HCV NS5B sequences analysed contained substitutions conferring resistance to nucleoside analogues; however, NS5B polymerases containing substitutions conferring resistance to non-nucleoside inhibitors were frequent within genotype 1 strains (17%) and very common in non-genotype 1 strains. Similarly, substitutions conferring resistance to cyclosporine analogues were more prevalent within the various genotypes. CONCLUSIONS: Naturally occurring substitutions conferring resistance to NS5B inhibitors are common in treatment-naive patients infected with HCV genotype 1, 2, 3, 4 or 5. Their influence on treatment outcome should be assessed.

URL de la notice http://okina.univ-angers.fr/publications/ua3543 [21]
Liens

Publié sur Okina (http://okina.univ-angers.fr)