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Q80K testing prior to treatment with simeprevir-containing regimens for HCV infection

In 2011, boceprevir and telaprevir became the first direct-acting antiviral agents approved for treatment of HCV infection (in patients infected with genotype 1 only). Both of these drugs target the HCV NS3A protease and both can significantly boost response to treatment although they are poorly tolerated and treatment discontinuation rates are high. Following the success of this approach, a number of new drugs have been developed, targeting a range of viral enzymes.

Simeprevir is a NS3/4A protease inhibitor (PI) that has recently been licensed in Europe. Patients with genotype 1 or 4 infection who are intolerant to or ineligible for interferon (IFN) treatment may be treated with simeprevir and sofosbuvir (with or without ribavirin (RBV)) for 12 weeks. Patients infected with genotype 1 or 4 who are able to tolerate IFN may be treated with simeprevir and PEG-IFN/RBV. Course duration is determined by the past treatment status and current disease status of the patient.

Simeprevir/PEG-IFN/RBV induces significantly improved rates of sustained virological response (SVR) when compared with PEG-IFN/RBV alone (79.2% vs 45.6%) and has an improved side effect profile when compared to the first generation PIs boceprevir and telaprevir. HCV RNA levels should be monitored throughout therapy and treatment discontinued if viral load rises above 25 IU/ml at 4, 12 or 24 weeks.

Q80K is a naturally occurring polymorphism found in 0.4% of HCV genotype 1b strains and ~30% of genotype 1a strains. Q80K is associated with a reduced response to treatment with simeprevir. In persons infected with genotype 1a/Q80K, SVR rates following treatment with simeprevir/PEG-IFN/RBV were found to be the same as for treatment with PEG-IFN/RBV alone. It is therefore recommended that patients infected with genotype 1a are screened for Q80K prior to treatment and, if found to be Q80K positive, are not treated with simeprevir and PEG-IFN/RBV. High rates of SVR may still be seen in patients with genotype 1a/Q80K who are treated with simeprevir and sofosbuvir.

Micropathology Ltd have developed a Q80K testing protocol for patients known to be genotype 1a positive. Our assay is based on PCR-amplification and Sanger sequencing of the NS3A region in order to ascertain the Q80K genotype. We are also able to offer a more detailed analysis of resistance mutations pertaining to a wider range HCV PIs in genotype 1a and 1b strains where appropriate.