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NS5A testing prior to treatment with Zepatier for HCV infection

In 2016, a new direct-acting anti-viral agent (DAA) was licenced in the UK as an alternative treatment option for HCV infection in individuals with genotype 1 or 4.

Zepatier is a fixed dose combination drug (elbasvir- grazoprevir). Elbasvir inhibits non-structural viral protein, NS5A, and grazoprevir inhibits NS3/4A protease. Zepatier can be taken as a stand-alone treatment whereas current DAAs are often used in combination with peginterferon alpha or ribavirin. Interferon free treatment is an important advantage to individuals with renal disease or those who are immunocompromised as it improves tolerability and reduces adverse reactions. However, there are certain NS5A polymorphisms that mean combination therapy may be necessary.

In genotype 1a infected individuals the presence of one or more polymorphisms at positions M28, Q30, L31, or Y93 of the NS5A coding region are associated with a reduced response to treatment. Sustained virological response was achieved in 98% of subjects without NS5A resistance associated polymorphisms following 12 weeks therapy compared with 70% of subjects with NS5A resistance associated polymorphisms.

It is recommended that patients infected with genotype 1a are screened for resistance associated polymorphisms prior to treatment initiation and if found to be positive should then be considered for combination therapy with ribavirin and an extended treatment duration of 16 weeks to minimise the risk of treatment failure.

Micropathology Ltd have developed a NS5A testing protocol for patients known to be genotype 1a positive. Our assay is based on PCR- amplification and Sanger sequencing of the NS5A region in order to ascertain the polymorphism genotype.

Regulatory Analysis of Effects of Hepatitis C Virus NS5A Polymorphisms on Efficacy of Elbasvir and Grazoprevir. Komatsu, Takashi E. et al. Gastroenterology , Volume 152 , Issue 3 , 586 - 597