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Hepatitis B Virus Resistance Testing

Hepatitis B Virus (HBV) is a member of the hepadnavirus family. It is a partially double-stranded DNA enveloped virus that replicates via covalently closed circular DNA (cccDNA). Many infections appear asymptomatic and both acute and chronic infections are recognised. Chronic infection can lead to cirrhosis and liver failure. People living with HIV and HBV are at increased risk of severe hepatic damage, despite appropriate therapy for both viruses.

Understanding the genotype of the infecting virus can aid in the most appropriate treatment choice in infected individuals, particularly as there is some evidence that there is a lower barrier to resistance against lamivudine in patients infected with genotype A and that patients infected with genotype C are less likely to maintain a sustained virological response. Antiviral resistance analysis to agents such as lamivudine, tenofovir, adefovir, telbivudine and entecavir can guide clinicians to adjust therapy.

Nucleoside/Nucleotide analogues are routinely used in the management of Hepatitis B positive patients. They act by inhibiting the reverse transcriptase activity of HBV's endogenous polymerase, resulting in decreased viral replication within infected cells.

They are administered orally and mostly have an excellent tolerance and safety profile. However, a major consideration with the long-term use of these antiviral products is the selection of antiviral-resistant mutations. Resistance should be identified as early as possible, before clinical breakthrough (increased ALT), by monitoring HBV DNA levels and identifying the pattern of resistance mutations.

We use a well-established in-house method to detect sequence changes associated with antiviral drug resistance. Accepted sample types for these tests are EDTA plasma and serum. Briefly, this comprises semi-nested amplification of part of the polymerase gene, followed by direct sequencing using ABI BigDye-3 dye terminator technology on an ABI 3500xl genetic analyser, or NGS sequencing using the Illumina MiSeq platform with a custom HBV resistance drug resistance associated mutation pipeline. The resultant sequence data is then analysed both manually and by software comparison to wild-type sequence. A resistance profile of the drug resistance associated mutation can then be derived.