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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. 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 3130xl genetic analyzer. The resultant sequence data is then analysed both manually and by software comparison to wild-type sequence. A resistance profile can then be derived using data in the table below.

Mutation site (amino acid change)	Drug affected	Resistance prediction
V173L	Lamivudine	compensatory
L180C/M	Lamivudine	Limited susceptibility
M204I/S/V	Lamivudine/Telbivudine/ Entecavir*	Resistant (Lamivudine/Telbivudine)/partly resistant (Entecavir, on its own)
A181T/V	Lamivudine/Adefovir/ Telbivudine	Resistant
L80V/I	Lamivudine/Telbivudine	Compensatory mutation
N236T	Adefovir/Tenofovir DF	Resistant (Adefovir)/limited susceptibility (Tenofovir)
I169T	Entecavir*	Compensatory (resistant with 204I/V)
T184A/G/I/S	Entecavir*	Compensatory (resistant with 204I/V)
S202G/I	Entecavir*	Compensatory (resistant with 204I/V)
M250V	Entecavir*	Compensatory (resistant with 204I/V)

Please note: L80V/I, V84M, S85A Adefovir associated mutations are not encompassed by our assay. *Adefovir - resistance only occurs if mutations at M204I/V and any of I169T, T184AGIS, 2S02GI, or M250V are present together.