PathGroup HCV Viral Load Testing and VICTRELIS (boceprevir) and INCIVEK (telaprevir)

Overview July, 2011

The FDA has recently approved two new drugs to be used in combination with peginterferon alfa-2a and ribavirin for the treatment of chronic hepatitis C genotype 1 infection. As with all hepatitis C treatments, accurate viral load monitoring will play a significant role in the patient management.

PathGroup uses the Roche COBAS AmpliPrep/ COBAS TaqMan HCV test for viral load measurement. This is an FDA-cleared system. There are two important analytic parameters of this system in relation to these new drugs. First, the Limit of Detection (LOD) of this system, for HCV genotype 1 infections, is 7.1 IU/ml. This was established in the clinical trial performed for the approval of the system. The second parameter, the Lower Limit of Quantitation LLOQ), for this system is 43 IU/ml. The LLOQ is genotype independent.

The prescribing information for both VICTRELIS (boceprevir) and INCIVEK (telaprevir) recommend using HCV monitoring assays with a LOD of 10-15 IU/ml and LLOQ of 25 IU/ml. HCV viral load testing as performed at PathGroup exceeds the LOD recommendation. However, this assay does not quite meet the LLOQ recommendation. The difference of 18 IU/ml (0.23 log IU/ml) is likely to not be clinically significant but remains to be characterized. This recommendation is also only needed for the last viral load measurement at the end of either therapy. Roche is the manufacturer of the assay used in both drug approval trials, and that assay is very similar in design to the assay in use at PathGroup. Roche is pursuing FDA-clearance for a revised version of the current HCV viral load assay. PathGroup will remain in communication with Roche and will update you with any new information.

The PathGroup HCV viral load patient report includes the qualitative result of Detected / Det, <LOQ / Not Detected, and if appropriate, the quantitative viral load (in both IU/ml and log IU/ml). The result of Det, <LOQ, is used when a patient specimen has a result of Detected, but the quantitative value is determined to be less than 43 IU/ml (1.63 log IU/ml). The Det, <LOQ result should therefore not be misinterpreted as a Not Detected result. PathGroup is currently seeing the result of Det, <LOQ in approximately 1% of specimens.

Another important aspect of HCV viral load testing is providing enough patient material for analysis. The current minimum volume of serum or plasma for HCV viral load testing is 2 ml. For HCV viral load testing with reflex to HCV genotyping, the minimum volume is 3 ml.

Methodology: Roche COBAS AmpliPrep/ COBAS TaqMan HCV Viral Load Assay (reverse transcription real time PCR)

Test Codes: **HCVRL**

CPT Codes: **87902**

Specimen Collection: Serum or plasma are acceptable specimen types.

- Minimum serum or plasma volume is 2.0 ml. Recommended volume is 3.0 ml.
- Blood should be collected in SST® Serum Separation Tubes or in sterile tubes using EDTA (lavender top) as the anticoagulant.
- Store whole blood at 2-25^{o}C for no longer than 6 hours.
- Allow SST® Serum Separation Tubes to sit for 30 minutes before processing. EDTA tubes can be processed immediately.
- Separate serum or plasma from whole blood within 6 hours of collection by centrifugation at 800-1600 x g for 20 minutes at room temperature. Transfer serum or plasma to a sterile polypropylene tube.
- Store frozen.
- Do not allow a specimen to thaw once frozen.

Shipping and Handling: Transport frozen. Do not allow a specimen to thaw once frozen.

Reference Ranges: Not Detected

Turnaround Time: 3-4 days

References

- VICTRELIS (boceprevir) prescribing information, issued May 2011.
- INCIVEK (telaprevir) prescribing information, issued May 2011
- COBAS AmpliPrep/COBAS TaqMan HCV Test Package Insert, 10/2008, rev 1.0

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