HCV RNA Testing in HALT-C Sustained Virologic Responders

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Background/Rationale:
The Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C) study is a randomized multi-center clinical trial to assess the effects of long-term interferon-alfa 2a therapy on the progression of liver fibrosis and development of decompensated liver disease in patients who have advanced hepatitis C and were non-responders to prior interferon therapy. Subjects were enrolled and treated with a combination of pegylated interferon-alfa 2a (180 μg/week) and ribavirin (1000-1200 mg/day), and assessed for the presence of serum HCV RNA at week 20 of therapy. Subjects who were persistently viremic were randomized to no treatment or to treatment with pegylated interferon alone for 3.5 years. Those who had undetectable serum HCV RNA at week 20, however, completed 48 weeks of combination therapy and were followed for an additional 24 weeks of therapy.

All serum HCV RNA results used for the management of patients were obtained using the Roche COBAS Amplicor™ HCV Test, v. 2.0 assay (lower limit of detection (LOD) 100 IU/mL in serum). Patients who had undetectable serum HCV RNA by this test at the week 72 follow-up time point were considered to have achieved sustained virologic response (SVR), which in past studies has corresponded to a long-term durable clearance of HCV in the vast majority of patients.

As part of an ancillary study, the Bayer VERSANT® HCV RNA Qualitative (TMA) Assay (LOD ~10 IU/mL) was used to test serum samples from the same HALT-C subjects. The increased sensitivity of this assay for HCV RNA led to the identification of patients who had undetectable HCV RNA by the Roche Amplicor test, but were positive by the more sensitive TMA assay at various time points throughout the study. In particular, a small number of patients (11) had very low levels of HCV RNA in their week 72 samples by the TMA assay. One potential explanation or implication of this finding is that these patients never completely eliminated HCV from their circulation, and could still be actively infected. Alternatively, these results could represent false positives or laboratory errors. Additional testing is necessary to determine which of these possibilities best describes the situation.

Purpose of the study: To evaluate whether HALT-C patients with very low levels of HCV RNA detected in serum at week 72 have completely eliminated the virus at subsequent timepoint(s) using a highly sensitive test for HCV RNA.

Planned procedures:

1. Invitation to participate:
    - Patients will be contacted by the HALT-C clinical center where they received care during the study, and invited to return for a follow-up visit(s) and additional blood draw(s).
2. Informed consent:
    - The results obtained with the TMA test from their week 72 sample will be explained to the patients, and they will sign an informed consent for these follow-up visit(s). Patients will be informed that they may be asked to return

in the future for additional testing which is similar in nature to that described here, if necessary.
    - Patients will sign an informed consent to obtain any HCV test results that the patient has had after Week 72 in the HALT-C Trial, but before this follow-up visit.
3. A physical examination will be performed and blood will be drawn.
    - Laboratory tests done by the local laboratory will include a liver panel and AFP.
    - Approximately 5 mL of blood serum will be coded, processed and shipped to the Central Virology Laboratory at the University of Washington, Seattle, WA, for hepatitis C virus testing.
    - Results of HCV testing will be reported to the HALT-C clinical investigator.
    - The clinical investigator will inform the patient of the result, and will discuss the medical implications of the result with the patient.
    - The results will become part of the HALT-C database.
4. Additional visits or blood draws:
    - Confirmatory testing of the hepatitis C virus (if detected) may be performed by the Virology Laboratory, and may include quantification, genotyping, nucleotide sequencing or similar procedures performed with the virus from the serum sample.
    - Additional follow-up visits are at the discretion of the Principal Investigator for the purpose of clarifying the significance of the virus findings.
5. Data obtained from these studies may be published, but participating patients will not be identified in any publication.