Effect of Early Intervention with Combination Ledipasvir/Sofosbuvir (Harvoni®) in Patients with Chronic Hepatitis C Virus Infection

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Introduction

In the United States, hepatitis C virus (HCV) is the most common bloodborne infection with an estimated prevalence of 3.2 million people. Although new cases of HCV are declining since the 1980s there are still approximately 17,000 new cases diagnosed each year. There are multiple risk factors, however, in the United States the most common mode of transmission is intravenous drug use. Among infected individuals, approximately 55-85% will develop a chronic HCV infection. In this population, the risk of cirrhosis of the liver is 15-30% within 20 years and morbidity can be significant. HCV infection has become the most frequent reason for hepatologic consultation and the single leading indication for hepatic transplantation, accounting for 30% of such procedures in the United States.

Until late 2013, the treatment of choice for chronic HCV was pegylated interferon-α plus ribavirin, which achieved a cure rate of 54%-63%. Recently, novel antiviral drugs that specifically target HCV have provided better options in HCV treatment. Use of ledipasvir, an HCV NS5A replication complex inhibitor in combination with sofosbuvir, a nucleotide analog HCV NS5B inhibitor, is approved for treatment of chronic HCV genotypes 1, 4, and 6. Although extremely successful, the use of this medication is inhibited by high costs, upwards of $90,000 for each 12-week treatment.

Research Objectives

1. Evaluate the efficacy of ledipasvir-sofosbuvir (90 mg/400 mg) therapy for treatment of genotype 1 Hepatitis C infection by monitoring sustained viral response and changes in liver function values.
2. Apply this information to current indications and qualifications for drug treatment.

Methods

Table 1. Inclusion and exclusion criterion for proposed study

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects identified according to inclusion and exclusion criteria.</td>
<td>Pregnant or nursing</td>
</tr>
</tbody>
</table>

Subjects were assigned a patient identification number for use by research and treatment regimen. Subjects were assigned a patient identification number for use by research and treatment regimen. Subjects assigned according to inclusion and exclusion criteria.

Researchers obtained demographic information and laboratory data outlined in table 2.

Data was compiled and preliminary statistics were run using Excel. Final statistics will be analyzed using SigmaPlot®.

Table 2. Laboratory data utilized in this study.

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Range</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST</td>
<td>15-57 U/L</td>
<td>AST and ALT levels may be normal in 10-40% of patients with chronic HCV infection, AST/ALT ratio &gt; 2 suggests cirrhosis</td>
</tr>
<tr>
<td>ALT</td>
<td>0-50 U/L</td>
<td>AST and ALT levels may be normal in 10-40% of patients with chronic HCV infection, AST/ALT ratio &gt; 2 suggests cirrhosis</td>
</tr>
<tr>
<td>HCV-RNA</td>
<td>&lt;1.18 log IU/mL</td>
<td>amount of HCV viral RNA in the blood. “Gold standard” for detection. Sensitivity and specificity: representing 100%</td>
</tr>
<tr>
<td>APRI Ratio Index</td>
<td>&lt;1.5</td>
<td>Moderate elevation (7%) and specific (29%) marker of liver fibrosis. Ratio &gt; 1.5 is a predictor of cirrhosis</td>
</tr>
</tbody>
</table>

Inclusion Criteria

- Compliant with dosing instructions and treatment regimen
- Patient of the Harrisonburg-Rockingham Free Clinic

Exclusion Criteria

- Pregnant or nursing

Future Research

- Continue to recruit additional eligible subjects to research study with a final goal of 50 study subjects.
- Continue to follow study subjects for at least 6 months after completion of HCV treatment with ledipasvir-sofosbuvir (90mg/400mg) to evaluate SVR.
- Consider utility of resistance genotyping prior ledipasvir-sofosbuvir (90mg/400mg) initiation.
- Evaluate the functionality of the APRI and its usefulness in monitoring patients with chronic HCV.
- Use data gathered from this study to establish a testing protocol for patients being treated with ledipasvir-sofosbuvir (90mg/400mg).
- Expand scope of research to include quality of life assessment before and after use of ledipasvir-sofosbuvir (90mg/400mg) using the Chronic Liver Disease Questionnaire (CLDQ) which includes 29 items in the following domains: fatigue, activity, emotional function, abdominal symptoms, systemic symptoms, and worry.

Acknowledgements

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References