ATHN 5 Hepatitis C Treatment Outcomes Study

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Hepatitis C Virus (HCV) Outcomes after Treatment with Direct Acting Agents (DAA) in Patients with Bleeding Disorders
Hepatitis C (Ab+) Patients by Age Group
Hemophilia Patients Carried the Virus 20+ Years!

Source: ATHN dataset June 30, 2016
HCV: A Leading Cause of Mortality in Males with Severe Hemophilia A  
1998-2011 - 432 Deaths Among 7,386 males

<table>
<thead>
<tr>
<th>Cause of Death Category</th>
<th>With Inhibitors N</th>
<th>(%)</th>
<th>Without Inhibitors N</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemophilia related</td>
<td>20</td>
<td>41.7</td>
<td>46</td>
<td>12.0</td>
</tr>
<tr>
<td>HIV related</td>
<td>5</td>
<td>10.4</td>
<td>71</td>
<td>18.5</td>
</tr>
<tr>
<td>Liver Disease related</td>
<td>8</td>
<td>16.7</td>
<td>123</td>
<td>32.0</td>
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<tr>
<td>Suicide</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>1.3</td>
</tr>
<tr>
<td>Other</td>
<td>10</td>
<td>20.8</td>
<td>104</td>
<td>27.1</td>
</tr>
<tr>
<td>Unknown</td>
<td>5</td>
<td>10.4</td>
<td>35</td>
<td>9.1</td>
</tr>
</tbody>
</table>

New Direct Acting Agents are Breakthrough

Sustained Virologic Response Achieved (SVR12- Harvoni study)

- 1 patient with HCV GT 1 was lost to follow-up following Week 4 visit
- 1/6 (17%) with GT 3 relapsed (patient had cirrhosis)

![Graph showing virologic response rates for LDV/SOF and SOF + RBV treatments.]

Source: Walsh C, AASLD, 2015, #1034
ATHN 5 Background and Rationale

• Prevalence of HCV in patients with bleeding disorders
  – The leading cause of mortality in the US Hemophilia population is due to HCV infection

• Recent Availability of Direct Acting Agents (DAA)
  – Epclusa® (sofosbuvir/velpatasvir); Daklinza ® (daclatasvir); Exviera ® (dasabuvir); Harvoni ® (sofosbuvir/ledipasvir); Olysio ® (simeprevir); Sovaldi ® (sofosbuvir); Viekirax ® (ombitasvir/paritaprevir/ritonavir)

• Recent MASAC recommendations
ATHN 5 Background and Rationale

• No systematic method to analyze HCV infection outcomes in patients with bleeding disorders
  – May be different from general population studied in DAA pivotal trials
• This study will focus on the gaps in evidence regarding treatment of HCV in bleeding disorders patients and generate data leading to more informed treatment decisions
ATHN 5 Study Design

This is a multi-center, longitudinal, observational, retrospective study to assess sustained virologic response (>95%) for 2 years post-DAA therapy (SVR-2 years) in bleeding disorders patients with HCV
ATHN 5 Primary Objective

• To determine the rate of sustained virologic response (SVR) 2 years post-treatment with new oral DAA regimens given as daily oral therapy in patients with bleeding disorders.
  – To measure SVR (reinfection) for 2 years post initiation of therapy for HCV infection in each treatment group, with SVR defined as undetectable viral load by PCR to under 50 IU/mL
  – To explore differences in SVR-2year based on genotype, stage of liver disease at start of therapy, treatment regimen, age, race, ethnicity, bleeding order severity, and presence of inhibitor
ATHN 5 Secondary Objectives

• To measure mortality, liver disease progression and requirement for liver transplantation
• To determine the number of patients that discontinue treatment due to side effects
• To determine the number of patients that discontinue treatment due to side effects
• To describe factors that may influence long-term treatment outcomes
ATHN 5 Study Population

The study will study approximately 300 male and female patients with hemophilia or other bleeding disorders who meet the eligibility criteria and are receiving care from one of the participating HTC centers.

— Opt-in to ATHNdataset key for retrospective design
ATHN 5 Inclusion Criteria

• Started a DAA regimen for treatment of active HCV infection.
  – Completed DAA with HCV Viral Load results available from 12 weeks after the last dose
• Diagnosed with a congenital bleeding disorder
  – Including Hemophilia A or B (F-VIII or F-IX Deficiency), Von Willebrand Disease, rare bleeding disorder, or platelet disorder
• Age > 19 years
• Opted in to the ATHN dataset
ATHN 5 Exclusion Criteria

• Patients diagnosed with liver cancer (i.e., Hepatocellular carcinoma, HCC or liver cell carcinoma of any type)
• History of liver transplant
• Lack of access to complete medical records for treatment for HCV infection and related co-morbidities
ATHN 5: Study Flow Chart

**DAA Treatment**
- **Start of Treatment**
  - Drug, Dose, Frequency
  - HCV Antibody
  - Viral Load
  - Liver Function
  - Liver Fibrosis Score
- **End of Treatment**
  - Treatment Duration and compliance
  - Side Effects
  - Reason for early discontinuation
  - Viral Load
  - Concomitant medications

**Study entry will occur after SVR12 results are available (> 3 mo. post-treatment)**

**Screening**
- ATHN dataset
  - Opt-in

**Continue Data Abstraction (at 6 month intervals)**
- Viral Load
- New Diagnoses (e.g., HBV, hepatocellular carcinoma)
- Liver Function
- Liver Fibrosis Score
- Changes in Bleeding
- Death

**Medical Record Data Abstraction (Post DAA Treatment)**
- Study Day 0
- 6 Months
- 12 Months
- 18 Months
- 2 Years

**Study Completed**
- Submit Final Data
ATHN 5 Project Status

• Steering Committee convened September 12, 2016
• Site Selection underway
  – 15 sites expressed interest via electronic survey
  – Contractual agreement template available
• Draft Protocol being finalized for SC approval (by end of October)
  – Data elements have been identified
• eCRF/Forms development to begin once protocol is approved
• First Patient In scheduled by January 1, 2017
ATHN 5 Funding

Hemophilia of Georgia (HOG)

• Thank You HOG!
• Grant supports study being conducted through ATHN
  • 15 sites
  • 4 years
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Contact Information

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