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</th>
<th>Without Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>(%)</td>
</tr>
<tr>
<td>Hemophilia related</td>
<td>20</td>
<td>41.7</td>
</tr>
<tr>
<td>HIV related</td>
<td>5</td>
<td>10.4</td>
</tr>
<tr>
<td>Liver Disease related</td>
<td>8</td>
<td>16.7</td>
</tr>
<tr>
<td>Suicide</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>10</td>
<td>20.8</td>
</tr>
<tr>
<td>Unknown</td>
<td>5</td>
<td>10.4</td>
</tr>
</tbody>
</table>

Hepatitis C
A Pathogenic RNA Virus

• Preferentially infects liver hepatocytes causing
  – Liver fibrosis (20-30% of patients)
  – Hepatocellular carcinoma (1-5% of patients)

• The major risk of end-stage liver disease and hepatocellular carcinoma due to HCV are
  – Length of time of infection
  – Co-morbid infection with HIV

Source: Poynard T et al, Lancet 1997; 349:825-32
Westbrook RH, Dusheiko G, J Hepatol 2014; 61:S58-68
Hepatitis C (Ab+) Patients by Age
Hemophilia Patients Carried the Virus 20+ Years!

Source: ATHNdataset June 30, 2015; F-VIII Def. n=9026, F-IX Def.=2,699)
New class of oral non-interferon based drugs has become the standard of care.

- Sofosbuvir /Ledipasvir (Harvoni) + Ribavirin tested in 14 bleeding patients (hemophilia, vWD etc) with Genotype 1. After a 3 month course (daily pill)- all patients were had an undetectable HepC viral load at 4 and 12 weeks. Fatigue, headache and nausea where common side effects.

Ref- Stedman C et al, *Haemophilia*, 2015
Gilead Study of Harvoni in US bleeding disorders patients

13 HTCs in the US enrolled 123 patients with Genotypes 1-4

- Hemophilia, vWD, RBD patients entered study with a Hep C + viral load. 25% of patients had cirrhosis (Stage ¾ Metavir)
- Patients with genotype 2/3 received Sofosbuvir + Ribavirin
- Daily doses for 3 months with 6 month follow-up

Data embargoed until presentation at AALD Meeting in November but ... (if you don’t tell anyone).
MASAC Recommendation 234 (June 4, 2015)
For patients with Hemophilia and other bleeding disorders

• Patients who received plasma-derived products should be tested for HCV
  – HCV genotype, HCV RNA viral load and Fibrosure test
• If HCV+, refer to hepatologist or ID for evaluation
  – Extent of liver disease and indications for treatment
• Barriers to treatment should be identified/eliminated
• All evaluated by 12/31/2016; Treated by 12/31/2017