National Surveillance for Hemophilia Inhibitors in the United States

Mike Soucie, PhD
Associate Director for Science
Division of Blood Disorders, CDC

WFH Global Forum
October 22, 2015
### DISCLOSURES FOR: MIKE SOUCIE

<table>
<thead>
<tr>
<th>Conflict</th>
<th>Disclosure - if conflict of interest exists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Support</td>
<td>None</td>
</tr>
<tr>
<td>Director, Officer, Employee</td>
<td>None</td>
</tr>
<tr>
<td>Shareholder</td>
<td>None</td>
</tr>
<tr>
<td>Honoraria</td>
<td>None</td>
</tr>
<tr>
<td>Advisory Committee</td>
<td>None</td>
</tr>
<tr>
<td>Consultant</td>
<td>None</td>
</tr>
</tbody>
</table>
The Problem

• **Inhibitors are the number one complication facing people with hemophilia today**

• **Inhibitors are associated with:**
  – Increased morbidity
  – Greatly increased financial burden
  – Increased mortality

• **Everyone with hemophilia is at risk**

• **Inhibitors are potentially preventable**
Inhibitor Challenges

• Characterization and risk assessment of rare adverse events is methodologically difficult
• Evaluation of treatment product risk using a probabilistic model is imperfect
• Clinical trial methodology is problematic
  – Sample size not adequate to fully assess risk
  – Incomplete assessment of risk factors
  – Randomization to larger population is problematic
Product Issues

• FDA and EMA held workshops on inhibitors in 2003 and 2005
  – Clinical trials inadequate to assess risk
  – Long-term surveillance (registry)
  – Detailed prospective data on all exposures
  – Data on genetic factors (genotype, family hx)
  – Regular testing plus prior to product switch
  – Testing performed in lab(s) using standard method with high degree of quality control
Inhibitor Surveillance in the US

- Inhibitors were not the focus of UDC
  - Collects data on results of local testing
  - Ability to assess prevalence is limited
- FDA MedWatch is a passive system that:
  - Relies on voluntary reporting
  - Does not collect denominator data
  - Inhibitors “expected” adverse event
- Inhibitor rates and trends unknown in U.S.
- Need a system to detect “outbreaks”
Hemophilia Inhibitor Research Study (HIRS)

- Designed as a pilot project for national inhibitor surveillance to comply with FDA and EMA recommendations, initiated in 2006
- Funded by Pfizer and Baxter through grants to the CDC Foundation
- Goals:
  - Determine feasibility of methods (test & exposure data)
  - Identify the population at risk
  - Characterize the risk factors for inhibitors (genetic, treatment-related, and interactions)

HIRS Key Findings

• Centralized testing is feasible and reliable
• Laboratory research
  – Validation of testing methodologies
  – Creation of a mutation database resource
• Characteristics of patients with new inhibitors
  – All patients are at risk
  – Inhibitors in mild patients and low risk mutations
  – Inhibitors in patients with >150 exposure days
  – 61% had no clinical indication of inhibitor
Inhibitor Screening Rates Among Patients with Severe Hemophilia

Mean % tested = 46.2%

Source: UDC data on 6,665 severe hemophilia patients, 2006 - 2010
National Inhibitor Meeting

• Held March 2012 with key stakeholders
• Presented the results of the HIRS
• Inhibitors are a serious public health problem
• There are barriers to screening
  – Cost not covered by insurance
  – Testing methodologic issues
• No standard inhibitor definition or reporting practices
• No measures of the inhibitor burden in the US

National Inhibitor Surveillance

• Standardized protocol specifying patients to be tested and testing interval
• Standardized, centralized testing
• Confirmatory testing very important
• Provide data on national incidence and prevalence of inhibitors
• Incident inhibitor case surveillance
  – Similar to viral testing (HIV, Hep B, Hep C)
  – Collect additional information on new cases
Road to Inhibitor Prevention

- National surveillance
- Assessment of barriers to screening
- Education needs assessment
- Clinical and laboratory research
- Increase understanding of inhibitors
- Development of prevention strategies
- Evaluation of prevention strategies

Why Surveillance Matters

• Supports a broad public health program
• Powerful health outcomes data collection network
• Enables large numbers of observations on people with rare diseases
• Supports improvement in standards of care for bleeding disorder populations
• Builds the capacity to support research on risk factors and prevention strategies
Questions?