Impact of Hemophilia A Inhibitor on Joint Health and Health-Related Quality of Life from the Hemophilia Utilization Group Studies Part VIII in the U.S.

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Introduction

- The significant economic burden on persons with hemophilia A (PwHA) and active inhibitors is associated with:
  - High treatment costs
  - Compromised physical health
  - Compromised psychosocial health

- Few studies have compared burden of illness for PwHA with active inhibitors to those with tolerized or no inhibitors

- The study objective is to describe joint health and health-related quality of life (HRQoL) in PwHA with and without inhibitors using the Hemophilia Utilization Group Studies Part VIII (HUGS VIII) baseline cross-sectional data
Methods

- Enrolled PwHA (FVIII activity level <5%) aged ≥ 2 years with and without inhibitors at a 1:2 ratio

- Participants were classified into three groups
  - Active inhibitors: FVIII inhibitor titer > 1.0 BU prior to six months enrollment
  - Presumably tolerized inhibitors: history of Immune Tolerance Induction (ITI), and using factor VIII for prophylaxis
  - No inhibitors

- Parents/adult participants completed a standardized interview at enrollment to collect sociodemographic and clinical data, self-reported pain, joint health, and HRQoL measured by the EQ-5D-3L

- Clinical chart review documented hemophilic severity, inhibitor titer level and treatment regimen
# Results: Participants Characteristics by Inhibitor Status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (N=73)</th>
<th>Tolerized inhibitor (n=23, 31.5%)</th>
<th>Active inhibitor (n=8, 11.0%)</th>
<th>No inhibitor (n=42, 57.5%)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age</td>
<td>24.8 (14.1)</td>
<td>17.3 (9.3)</td>
<td>22.6 (20.4)</td>
<td>29.3 (13.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Age group: Adults</td>
<td>48 (65.8)</td>
<td>10 (43.5)</td>
<td>5 (62.5)</td>
<td>33 (78.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Employment†§</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Full-time</td>
<td>39 (55.7)</td>
<td>12 (54.5)</td>
<td>3 (42.9)</td>
<td>24 (58.5)</td>
<td></td>
</tr>
<tr>
<td>Part-time</td>
<td>14 (20.0)</td>
<td>3 (13.6)</td>
<td>3 (42.9)</td>
<td>8 (19.5)</td>
<td></td>
</tr>
<tr>
<td>Not Employed/Retired</td>
<td>17 (24.3)</td>
<td>7 (31.8)</td>
<td>1 (14.3)</td>
<td>9 (22.0)</td>
<td></td>
</tr>
<tr>
<td>Hemophilic severity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td>Moderate</td>
<td>9 (12.3)</td>
<td>1 (4.3)</td>
<td>0 (0.0)</td>
<td>8 (19.0)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>64 (87.7)</td>
<td>22 (95.7)</td>
<td>8 (100.0)</td>
<td>34 (81.0)</td>
<td></td>
</tr>
<tr>
<td>Self-reported Prophylaxis§</td>
<td>61 (87.1)</td>
<td>18 (81.8)</td>
<td>7 (100.0)</td>
<td>36 (87.8)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Note: Data are presented as number (column percentage) for categorical variables, or mean (SD) for continuous variables. *P values were calculated from chi-square tests for categorical variables and analysis of variances for continuous variables. † Employment was for adult participants or parents of age<18 years. Abbreviation: SD, standard deviation.
Results: Self-reported Joint Health by Inhibitor Status

- **Self-reported Joint Pain**
  - Very stiff joint upon arising:
    - No Inhibitor: 75.6%
    - Tolerized inhibitor: 59.1%
    - Active Inhibitor: 85.7%
    - **P = 0.26**
  - Very stiff joint during the day:
    - No Inhibitor: 73.2%
    - Tolerized inhibitor: 27.3%
    - Active Inhibitor: 71.4%
    - **P = 0.002**
  - Very stiff joint during the day:
    - No Inhibitor: 63.4%
    - Tolerized inhibitor: 27.3%
    - Active Inhibitor: 71.4%
    - **P = 0.01**
Results: Quality of Life by Inhibitor Status

EQ VAS, EuroQoL Visual Analogue Scale ranges from 0-100, has been converted to 0-1 to be presented in the figure. Higher score represents better health. EQ-5D index score ranges from 0-1, 0, 1 values corresponding to death and full health, respectively. Score difference of 0.07 was considered clinically significant in the literature. *Covariates included age, employment, and hemophilic severity.
Conclusions

- The study is limited to a small sample with a skew to younger age in persons with tolerized inhibitor

- Individuals with active inhibitors experienced greater negative impacts on full-time employment and HRQoL than PwHA without inhibitors or tolerized inhibitors

- These data suggest that younger persons with tolerized inhibitors showed better joint health (less pain, stiffness) than older persons with active inhibitors or without inhibitors

- Future research using longitudinal data on these participants will examine whether individuals in the tolerized inhibitor group with successful ITI continue with long-term prophylaxis and achieve positive joint health outcomes
Acknowledgments

The study is supported by Investigator-Initiated Research collaboration provided by Genentech, Inc. Authors thank all study participating centers (ranked by study center ID): University of Southern California: Michael B. Nichol, PhD, Principal Investigator (PI), Joanne Wu, MD, MS, Steven Carrasco, MPH. Gulf States Hemophilia & Thrombophilia Center, University of Texas Health Science Center at Houston, TX: Megan M. Ullman, MA, MPH, Site PI; Bleeding & Clotting Disorders Institute, Peoria, IL: Jonathan C. Roberts, MD, Site PI, Sarah Gonzales; University of Colorado Denver Hemophilia and Thrombosis Center: Marilyn Manco-Johnson, MD, Site PI, Jason Thomas; The Center for Comprehensive Care And Diagnosis of Inherited Blood Disorders: Amit Soni, MD, Site PI, Nicole Crook, RN.
Conflict of Interest Disclosure

The current project is supported by Genentech, Inc. through a research agreement between Genentech Inc. and the University of Southern California. Michael B. Nichol is a principal investigator for the HUGS studies and received grant funding from multiple sources including Genentech Inc., Sanofi (formerly Biogen Idec), Pfizer, Shire (formerly Takeda/Baxter), Octapharma, CSL Behring, and Global Blood Therapeutics. Rahul Khairnar is an employee of Genentech Inc. Joanne Wu and Steven Carrasco received financial support through the project funding provided by Genentech Inc. Randall Curtis received consultant fee from USC through the project funding provided by Genentech Inc. He also received consultant fees from Bayer and Novo Nordisk. Judith Baker, Megan Ullman have no significant conflicts of interest to declare. Duc Quang Tran Jr. received consultant fee from Bayer, Bioverativ, Novo Nordisk, and Takeda. Marilyn Manco-Johnson, Jonathan C. Roberts, MD, Nicole Crook, RN, have no conflicts of interest to declare.