“Does ADAMTS13 Inhibitor Titer Correlate with Response to Therapeutic Plasma Exchange in Thrombotic Thrombocytopenic Purpura?”

Jessica L. Scott, MD

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Introduction

- **Thrombotic thrombocytopenic purpura (TTP)**
  - Mortality rate 90% without plasma exchange or transfusion\(^1\)
  - 6-month survival ~ 80% with plasma exchange\(^2\)

- **Clinical Question**
  - Does inhibitor level correlate with number of therapeutic plasma exchanges (TPE) required to achieve a normal platelet count?

Methods

- Retrospective review of institutional records
- Admitted 2003-2012
- TTP definition
  - Thrombocytopenia
  - Microangiopathic hemolytic anemia
  - ADAMTS13 activity < 5%
  - Presence of inhibitor
Methods

Clinical and laboratory data

- Age, Race, Gender
- Admission Hemoglobin, Platelet count, Creatinine, LDH
- ADAMTS13 activity and inhibitor
- TPEs required to achieve normal platelet count (response)
- Rituximab use

Statistics

- Mean ± SD
- Student’s t test
- Spearman’s rank correlation
Results

- 61 patients
  - 54 patients included
  - 70 total episodes

Response: Normal platelet count and no hemolysis

- 54 Responders
  - 34 Non-relapsers
  - 20 Relapsers

- 7 Non-survivors

Relapse: Drop in platelet count with repeat ADAMTS13 <5% more than 30 days after response
# Episodes

<table>
<thead>
<tr>
<th></th>
<th>Initial (n=42)</th>
<th>Relapses (n=28*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (± SD)</td>
<td>Mean (± SD)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Gender</td>
<td>26 Females</td>
<td>12 Females</td>
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<tr>
<td></td>
<td>16 Males</td>
<td>8 Males</td>
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<tr>
<td><strong>Age (years)</strong></td>
<td>41 (± 16)</td>
<td>43 (± 16)</td>
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<tr>
<td><strong>Race</strong></td>
<td>33 African Americans</td>
<td>16 African Americans</td>
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<tr>
<td></td>
<td>7 Caucasians</td>
<td>4 Caucasians</td>
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<tr>
<td></td>
<td>1 Asian, 1 Other</td>
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<tr>
<td><strong>ADAMTS13 Inhibitor (units)</strong></td>
<td>3 (± 3)</td>
<td>2 (± 2)</td>
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<tr>
<td><strong>TPEs to reach normal platelet count</strong></td>
<td>6 (± 4)</td>
<td>5 (± 4)</td>
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*20 patients had one or more relapses

\[ p = 0.78 \]

\[ p = 0.12 \]
No correlation between inhibitor and number of TPEs to reach response (initial episodes)

$r_s = -0.06$
No correlation between inhibitor and number of TPEs to reach response (relapse episodes)

\[ r_s = 0.42 \]
No correlation between inhibitor and number of TPEs to reach response (all episodes)

$r_s = 0.18$
Rituximab results

- 42 patients with initial presentation at UAB
  - 15 received Rituximab
  - 27 with no Rituximab

Rituximab: Monoclonal antibody targeting B cells sometimes used to augment response to treatment in refractory cases of TTP
Evaluation of initial episodes

<table>
<thead>
<tr>
<th></th>
<th>Rituximab (n=15)</th>
<th>No rituximab (n=27)</th>
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<tbody>
<tr>
<td></td>
<td>Mean (±SD)</td>
<td>Mean (±SD)</td>
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<tr>
<td>Gender</td>
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<tr>
<td></td>
<td>9 Females</td>
<td>17 Females</td>
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<tr>
<td></td>
<td>6 Males</td>
<td>10 Males</td>
</tr>
<tr>
<td>Age (years)</td>
<td>40 (±17)</td>
<td>40 (±17)</td>
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<tr>
<td>Race</td>
<td>13 African Americans</td>
<td>20 African Americans</td>
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<tr>
<td></td>
<td>1 Caucasians</td>
<td>6 Caucasians</td>
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<tr>
<td></td>
<td>1 Asian</td>
<td>1 Other</td>
</tr>
<tr>
<td>ADAMTS13 Inhibitor</td>
<td>3 (±3)</td>
<td>3 (±2)</td>
</tr>
<tr>
<td>(Units)</td>
<td></td>
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</tr>
<tr>
<td>TPEs to reach normal</td>
<td>8 (±6)</td>
<td>5 (±3)</td>
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<td>platelet count</td>
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</tbody>
</table>
No correlation between inhibitor and number of TPEs to reach response (rituximab)

\[ r_s = 0.11 \]
No correlation between inhibitor and number of TPEs to reach response (non-rituximab)

\[ r_s = -0.07 \]
Conclusions

- No correlation between inhibitor level and TPEs to achieve response
  - Why?
    - Could *in vitro* inhibitor assay not directly correlate with *in vivo* inhibitor effect?
    - Unknown variables affect response to TPE