EVALUATION OF COST AND EFFICACY OF ECUORIZUMAB IN COMPLEMENT MEDIATED THROMBOTIC MICROANGIOPATHY IN THE CLINICAL SETTING

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BACKGROUND AND IMPORTANCE
Complement-mediated thrombotic microangiopathy (C-TMA) is caused by complement disruption that leads to hemolysis and thrombocytopenia.

Eculizumab inhibits the C5b-9 complex formation by binding protein C5. It has been approved for C-TMA; nevertheless, studies on the effectiveness of Eculizumab in real-world conditions are scarce, even considering its high cost.

AIM AND OBJECTIVES
To evaluate the real-world efficacy and cost of Eculizumab for C-TMA after 26 weeks of treatment.

MATERIALS AND METHODS
- Patients diagnosed with C-TMA whose treatment with Eculizumab had been approved and lasted >26 weeks (W) were included.
- Treatment: Eculizumab 900mg weekly for 4 weeks, followed by Eculizumab 1,200 mg weekly.
- Clinical variables were obtained from electronic-health-records. Lab test were evaluated at and weeks 0, 12, 26 and 38 after initiation.
- C-TMA remission definition: lactate dehydrogenase (LDH) < upper limit of normal, platelets >150x10⁹/L and <25% creatinine increase from baseline.

RESULTS
- Six patients were included
  - 1 woman and 5 men
  - Median age 43 years (range 23-59)
  - Any patient had genetics related with complement alteration
  - One patient had a pulmonary transplant and one a renal transplant
  - Two patients were in remission after 26W.
    - Hemoglobin and platelet count increased, LDH decreased.
    - LDH decreased in all patients, 3 patients had LDH> upper limit of normal after 38W
    - CH50 decreased in all patients and was undetectable for most patients within 12W (p=0.001).
    - Renal function was maintained or improved in 4/6 patients.
    - Two patients were in dialysis, one stopped.

<table>
<thead>
<tr>
<th>Weeks of treatment</th>
<th>0</th>
<th>12</th>
<th>26</th>
<th>38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11</td>
<td>12</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>(mg/dL)</td>
<td>10.2</td>
<td>10.7</td>
<td>10.2</td>
<td>9.8</td>
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<tr>
<td>Platelets (10⁹/µL)</td>
<td>206</td>
<td>189</td>
<td>233</td>
<td>291</td>
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<tr>
<td>LDH (U/L)</td>
<td>511</td>
<td>487</td>
<td>493</td>
<td>430</td>
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<tr>
<td>Creatinine (mg/dL)</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Reticulocytes (10⁶/µL)</td>
<td>112</td>
<td>69</td>
<td>65</td>
<td>37</td>
</tr>
<tr>
<td>C3 (mg/dL)</td>
<td>106</td>
<td>133</td>
<td>137</td>
<td>146</td>
</tr>
<tr>
<td>C4 (mg/dL)</td>
<td>31</td>
<td>35</td>
<td>31</td>
<td>42</td>
</tr>
<tr>
<td>CH50 (UI/mL)</td>
<td>59</td>
<td>&lt;13</td>
<td>&lt;13</td>
<td>&lt;13</td>
</tr>
<tr>
<td>sC5b9 (ng/mL)</td>
<td>440</td>
<td>1052</td>
<td>493</td>
<td>1251</td>
</tr>
</tbody>
</table>

- Eculizumab treatment
  - Duration 10(6.8-45.5) months
  - Two patients stopped because of resolution C-TMA
  - Estimated cost of 26 weeks treatment is 337,300 €
  - Median cost estimated/treatment was 160,458 € (118,055-640,870)

CONCLUSIONS AND RELEVANCE
- Eculizumab was effective in C-TMA according to cellular and biochemical markers (platelets, LDH, creatinine); change in some parameters might not be detected because the small sample.
- Two patients out of 6 were in remission after 26W; the estimated cost for an additional C-TMA-remission was 1,011,900€.