Eculizumab Protects Against Thromboembolism and Prolongs Survival in Patients with Paroxysmal Nocturnal Hemoglobinuria: An International PNH Registry Study

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BACKGROUND
- Paroxysmal nocturnal hemoglobinuria (PNH) is a chronic and life-threatening hematopoietic stem cell disorder characterized by uncontrolled complement-mediated intravascular hemolysis.
- Compromised renal function (CFR) and idiopathic thrombocytopenic purpura (ITP) can lead to thrombosis (TTE). The leading cause of mortality in PNH is TTE.
- The incidence of TTE is about 6% per year, and it is estimated that 50% of TTE-related deaths occur within 6 months of enrollment.
- Median survival in untreated patients range from 10 to 15 years.
- Prior TTE, even in isolation at age 50 years of disease duration has been associated with over 50% of mortality.
- Eculizumab, a monoclonal antibody that inhibits terminal complement activation, may be effective in reducing the risk of TTE and improving survival, with current and recent RBC transfusion(s) in the 6 months before enrollment.

OBJECTIVE
Patients are eligible for the registry if they have a detectable PNH clone, regardless of disease severity, comorbidities, or treatments (past, current, or planned).

METHODS
Patients eligible for the registry if they have a detectable PNH clone, regardless of disease severity, comorbidities, or treatments (past, current, or planned).

RESULTS
Patient Characteristics
- Of June 12, 2013, a total of 1047 patients from 25 countries on 6 continents had been enrolled in the PNH Registry.
- Of these patients, 646 patients (21%) were treated with eculizumab during follow-up; 51 patients (18%) were untreated.
- A total of 579 patients (55%) had one or more prior TTEs.

Table 1: Demographic and Clinical Characteristics at Enrollment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Eligible Patients (N=1047)</th>
<th>Eculizumab-Treated Patients (N=646)</th>
<th>Untreated Patients (N=399)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>44.3 (17.3)</td>
<td>41.3 (16.5)</td>
<td>50.9 (19.1)</td>
</tr>
<tr>
<td>History of impaired hepatic function</td>
<td>126 (12.1)</td>
<td>75 (11.6)</td>
<td>51 (13.1)</td>
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<tr>
<td>Lactate dehydrogenase (LDH) concentration ≥ 2.9 ULN</td>
<td>284 (27.0)</td>
<td>172 (26.6)</td>
<td>112 (28.1)</td>
</tr>
<tr>
<td>Presence of headache and dyspnea at enrollment.</td>
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| Symptoms, n (%) | | | |
|-----------------|----------------|----------------|
| Fatigue | 786 (75.7) | 470 (72.7) | 316 (79.2) |
| Dyspnea | 581 (55.7) | 369 (57.1) | 212 (53.1) |
| Headache | 536 (51.5) | 321 (49.6) | 215 (54.0) |
| Eculizumab use during follow-up | 536 (51.5) | 321 (49.6) | 215 (54.0) |

Outcomes for all eligible patients are reported in Table 2.

Table 2: Patient Outcomes During Mean Follow-up of 23 Months

- The cumulative incidence of TE at 1 year and 2 years was 1.74% and 2.61%, respectively.
- The cumulative incidence of death at 1 year and 2 years was 12.4% and 24.8%, respectively.
- Mortality risks were assessed using a multivariate model (Figure 4).

CONCLUSIONS
- Eculizumab-treated patients had a statistically significant reduction in the cumulative incidence of TE at 1 year and 2 years compared to untreated patients (Figure 3).
- Mortality risk factors were assessed using a Cox proportional hazards model, the greatest associations with TE were RBC transfusions in the 6 months prior to enrollment (hazard ratio [HR] 9.61), and history of impaired hepatic function (HR=5.33), BMT during follow-up (HR=2.36).

REFERENCES
- Khursigs G, Bedrosian C, Schneebeli H, et al. Mortality risks were assessed using a multivariate model (Figure 4).
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