Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired clonal stem-cell disorder arising on the background of bone marrow failure. PNH can result in hemolytic anemia, thrombocytopenia (TC), pulmonary hypertension (PHT) and chronic kidney disease (CKD) through uncontrolled complement activation. Despite transfusion and anticoagulation, approximately half of PNH patients die as a result of their PNH within 10 years.

- The terminal complement inhibitor eculizumab has previously been shown to rapidly and significantly reduce intravascular hemolysis leading to a reduction in TE and PHT and improvements in CKD, quality of life and survival. Long-term eculizumab therapy has been well tolerated by PNH patients.

**OBJECTIVE**

- To describe the long-term safety, efficacy and outcomes in all patients with PNH who received eculizumab from May 2002 to April 2012.

**METHODS**

- The UK has a nationally commissioned PNH service, led by the Leeds and Kings' centers.
- All UK PNH patients were assessed for long-term safety and efficacy.
- PNH patients were treated with eculizumab if they had:
  - Transfusion-dependent hemolysis or any of the following (independent of transfusions):
    - TE or
    - CKD or
    - PHT or
    - Pregnancy or
    - Lactate dehydrogenase (LDH) >1.5 times the upper limit of normal (ULN) with anemia and symptoms such as fatigue, dyspnea, dysphagia, or abdominal pain due to PNH

**RESULTS**

**Baseline Demographics**

- Between May 2002 and April 2012, 153 patients were treated for eculizumab in the UK.

**Survival with Long-term Eculizumab Treatment**

- The survival of UK PNH patients on eculizumab was compared with age- and sex-matched controls (Figure 2).
- Survival of PNH patients after 10 years of eculizumab treatment was slightly inferior to controls, and a cause of death was unrelated to hematologic conditions or related to the underlying bone marrow failure and not due to eculizumab therapy associated with the underlying PNH.
- No causes of death were related to PNH.
- UI-PNH patients on eculizumab had improved survival as compared with historical controls in previously published accounts.

**CONCLUSIONS**

- The UK PNH service now has more than 10 years of experience managing PNH with eculizumab.
- The results from this UK PNH patient cohort demonstrate that the significant clinical benefits and long-term safety of eculizumab were sustained over 10 years of treatment.
- Long-term eculizumab treatment led to:
  - Significant improvement in survival.
  - A significant reduction in the incidence of TE.

**DISCLOSURES**

- The authors have no financial interest in the products or companies referred to in this presentation.

**Figure 1** Kaplan-Meier Survival Plot for UK PNH Patients on Eculizumab Compared with Age- and Sex-Matched Controls

**Figure 2** Kaplan-Meier Survival Plot for UK PNH Patients on Eculizumab Compared with Age- and Sex-Matched Controls

**Figure 3** Kaplan-Meier Survival Plot for UK PNH Patients on Eculizumab Compared with Age- and Sex-Matched Controls

**Figure 4** Reduction in Transfusion Requirements with Long-term Eculizumab Therapy

- The 153 patients treated throughout the 10 year period (137 patients on drug) at TE during the most recent 12 months of eculizumab therapy were reported (0.6 cases per 100 patient-years on therapy).
- All cases were managed promptly and effectively, and all patients remained on eculizumab therapy and are doing well.
- 137 patients were still on treatment as of April 2012.
- 7 of the surviving 144 patients died on eculizumab therapy.
- 1 patient discontinued due to predominant aplastic anemia.
- 2 patients had spontaneous remissions of PNH clots during eculizumab treatment.
- 3 patients were treated for the indication of pregnancy alone with 1 patient subsequently restarting therapy.
- 1 patient underwent successful transplant for very severe aplastic anemia.

- Eculizumab-Treated PNH Population
- Age- and Sex-Matched Normal Population
- Hazard Ratio=2.24 (P<0.001)