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508.BONE MARROW FAILURE: ACQUIRED

Disease Management and Outcomes in Patients with Paroxysmal Nocturnal Hemoglobinuria: A Retrospective Analysis of Observational Data from the United States

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Background: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hemolytic disease characterized by complement-mediated hemolysis, thrombophilia, bone marrow failure (BMF), and renal disease. PNH is clinically heterogeneous, and hospitalization and regular blood transfusions may be needed. Treatment with currently approved C5 inhibitors (C5i), eculizumab and ravulizumab, have shown efficacy in intravascular hemolysis control and reduction in thrombosis risk. Yet, in routine clinical practice, a limited number of patients receive C5i in the United States. Moreover, less than 70% of patients treated with eculizumab continue to receive treatment 1 year following PNH diagnosis. If the disease is managed inadequately, patients may experience prolonged morbidity, increased frequency and severity of symptoms, and early mortality. There is limited real-world evidence available on PNH disease management.
Aim: To better understand the disease management and consequences of PNH.
Methods: In this retrospective observational study, we analyzed 1227 patients aged ≥18 years in the TriNetX network who were diagnosed with PNH on or after 1 January 2007 and had ≥180 days of post-diagnosis follow-up data (97% were based in the United States). Patients were followed from 1 January 2007 to 6 May 2023. Disease management and outcomes were analyzed for all patients, including those with chronic anemia who were complement-inhibitor naïve. Chronic anemia was defined as hemoglobin <10 g/dL without any hemoglobin measure of ≥10 g/dL between 3 months prior to PNH diagnosis (index date) and 6 months after diagnosis. PNH-related hospitalization was defined by specific International Classification of Diseases codes. The baseline period was defined as 1 year prior to PNH diagnosis. Event rates were estimated for hospitalization (recurrent), transfusions (recurrent), BMF, and death. Rates are adjusted for exposure time (time between diagnosis and end of follow-up) and reported as per person-year with 95% confidence intervals (CIs).
Results: In the overall cohort, 58% of patients were female, and the median (interquartile range) age was 56 (38-68) years. During a median 35 (19-62) months of follow-up, 322 (26%) patients received blood transfusions and 172 (14%) patients received C5i. Median time to C5i initiation since diagnosis was 1 (0-10) month with a median treatment duration of 14 (0-49) months. Out of 1227 patients, 50 (4%) had chronic anemia and were complement-inhibitor naïve. The median length of follow-up in this subgroup was 14 (7-43) months. Most of these patients (96%) had PNH with bone marrow disorder subtype. Median hemoglobin and lactate dehydrogenase levels at baseline were 8 (7-8) g/dL and 313 (218-489) U/L, respectively. Out of these 50 patients, first-line treatment was initiated a median of 1 (1-6) month after diagnosis, with anticoagulants and corticosteroids being the most frequently prescribed. During follow-up, 32 (64%) of these patients experienced ≥1 hospitalization (rate 0.78, 95% CI 0.62-0.95) with a median of 3 (2-9) days stay for the first hospitalization. Anemia (42%), abdominal pain (36%), and infections (9%) were the leading causes of admission. In addition, 26 (52%) patients were transfusion dependent (rate 1.52, 95% CI 1.30-1.77) and 30 (60%) experienced BMF (rate 0.71, 95% CI 0.48-0.99). Moreover, 21 (42%) of these patients died during follow-up (rate 0.19, 95% CI 0.12-0.28).
Discussion: These findings indicate that complement-inhibitor naïve patients with chronic anemia have substantial disease burden, including frequent hospitalization, high transfusion dependency, and early mortality. In addition, the results show that only a minority of patients in this cohort received C5i. Study limitations include that mortality is likely to be underestimated, as only in-hospital deaths are captured in these data. The small sample size limits the drawing of robust conclusions. However, overall, these findings support the need to address PNH disease burden and improve disease management.

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