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Clinical Characteristics and Outcomes in Complement-Inhibitor Treated Patients with Paroxysmal Nocturnal Hemoglobinuria in the United States: A Retrospective Claims Database Analysis

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KEY FINDINGS & CONCLUSIONS

- Complement inhibitor-treated patients with paroxysmal nocturnal hemoglobinuria continue to experience adverse clinical outcomes, particularly major adverse vascular events. Additionally, a considerable proportion of these patients require red blood cell transfusions while on treatment.
- Findings from a large US claims database study show a substantial remaining disease burden among patients with paroxysmal nocturnal hemoglobinuria treated with complement inhibitors.

Limitations

- Due to the descriptive nature of this analysis, it is difficult to comment on the contribution from an underlying bone marrow failure state and other concomitant hypercoagulable states to transfusion needs and thrombotic events, respectively.
- Given the rarity of the disease, limitations of this study include the limited sample size and lack of generalizability.
- As only 13.3% of patients were treated with complement inhibitors, it may be that the majority had small paroxysmal nocturnal hemoglobinuria clones and hence were not treated.

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INTRODUCTION

- Paroxysmal nocturnal hemoglobinuria (PNH) is marked by complement-mediated hemolysis and propensity for thrombosis.[1-3]
- The advent of complement inhibitors (Cis) has improved patient survival,[4] however, real-world data among patients with PNH treated with Cis in routine clinical care is limited.
- While prior observational studies have assessed treatment patterns, healthcare resource utilization, and costs,[5-8] there currently exists a need for further studies evaluating patient characteristics and clinical outcomes that can help further understand the patient journey.[9-11]
- The aim of this study was to characterize Ci-treated patients with PNH in the United States (US) and describe their clinical outcomes following Ci-treatment initiation.

METHODS

- This retrospective cohort study analyzed closed claims (medical and pharmacy) and laboratory data of patients with PNH, sourced from HealthVerity.
- Within the study period (October 1, 2015, through July 21, 2023), the analysis included individuals ≥18 years of age with a claims-based PNH diagnosis (≥1 International Classification of Diseases, 10th Revision, Clinical Modification [ICD-10-CM] code D59.5).
- Patients were excluded if they had a diagnosis of Neuromyelitis Optica Spectrum Disorder (NMOSD) (ICD-10-CM G36.0), generalized myasthenia gravis (gMG) (ICD-10-CM G70.XX), or atypical hemolytic uremic syndrome (aHUS) (ICD-10-CM D59.3) any time in the study period.
- To be included in the Ci-treated cohort, patients must have had received ≥2 doses of eculizumab, ravulizumab, or pegcetacoplan within the study period. Index was defined as the date of first Ci treatment, and patients were required to have ≥12 months continuous enrollment before index (baseline period) and ≥3 months continuous enrollment after index (follow-up period).
- Demographics, comorbidities, PNH-related signs and symptoms, and history of clinical events were described for the baseline period.
- In the follow-up period after Ci-treatment initiation, the proportion of patients with a recorded clinical event of incident chronic kidney disease (CKD), pulmonary hypertension, acute kidney injury (AKI), major adverse vascular events (MAVE), infections requiring hospitalization, and hematopoietic stem cell transplant were reported among patients without a prior history of the event. For CKD and pulmonary hypertension, only patients without a prior history of the event were considered.
- Clinical events were defined according to ICD-10-CM diagnosis codes and Current Procedural Terminology (CPT)/Healthcare Common Procedure Coding System (HCPCS) and ICD-10-PCS procedure codes. MAVE was defined using ICD-10-CM codes as a composite of thromboembolic events (thrombosis in veins [deep and superficial], arterial thrombosis, or thromboembolism), non-traumatic, non-diabetic lower extremity gangrene or amputation, unstable angina, myocardial infarction, cerebral arterial occlusion, cerebrovascular accident (ischemic stroke), or transient ischemic attack.[12]
- The number of red blood cell (RBC) transfusions was reported among those with ≥1 RBC transfusion. The number of RBC transfusions was defined as the number of distinct episodes (unique days) with RBC transfusions.
- All analyses presented are descriptive and all results are unadjusted.

RESULTS

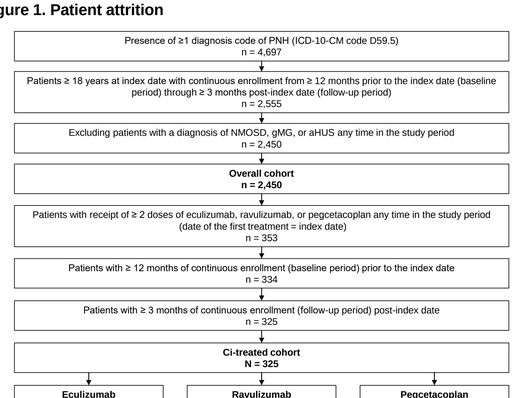
Patient attrition

- Of the 2450 identified patients with a presumed diagnosis of PNH, 325 (13.3%) were Ci-treated. Of those, 168 (51.7%) initiated eculizumab, 153 (47.1%) ravulizumab, and 4 (1.2%) pegcetacoplan (**Figure 1**).

Baseline demographics and clinical characteristics

- Median age (interquartile range [IQR]) was 44 years (31–57). Most patients were female (n=193, 59.4%) and had commercial insurance (n=238, 73.2%). During the 6 months prior to Ci treatment initiation, 40.6% (n=132) of patients received RBC transfusions (**Table 1**).
- At baseline, 50.5% (n=164) had a history of thrombocytopenia, 29.2% (n=95) had a history of aplastic anemia, 17.8% (n=58) had a history of MAVE and 13.8% (n=45) had a history of thromboembolic events (**Figure 2A**).
- The most common PNH-related signs and symptoms included abdominal pain (n=59, 18.2%), dyspnea (n=58, 17.8%), fatigue (n=49, 15.1%), and joint pain (n=36, 11.1%) (**Figure 2B**).
- Prior to Ci-treatment initiation, common supportive therapies included antibiotics (n=179, 55.1%), corticosteroids (n=119, 36.6%), and anti-thrombotics (n=79, 24.3%) (**Figure 2C**).

Figure 1. Patient attrition



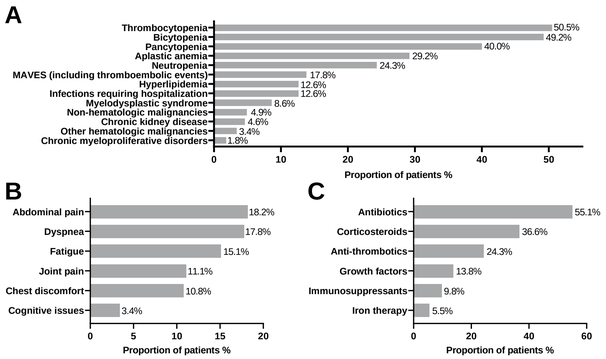
Abbreviations: aHUS, atypical hemolytic uremic syndrome; **Ci**, complement inhibitor; **gMG**, generalized myasthenia gravis; **ICD-10-CM**, International Classification of Diseases, 10th Revision, Clinical Modification; **NMOSD**, neuromyelitis optica spectrum disorder; **PNH**, paroxysmal nocturnal hemoglobinuria

Table 1. Baseline demographics and clinical characteristics

Characteristic	Ci-treated cohort (n=325)
Age at index, years	
Median (IQR)	44.0 (31.0-57.0)
Sex, n (%)	
Female	193 (59.4%)
Region, n (%)	
South	112 (34.5%)
Midwest	81 (24.9%)
Northeast	68 (20.9%)
West	57 (17.5%)
Unknown	5 (1.5%)
Other	2 (0.6%)
Primary insurance type, n (%)	
Commercial	238 (73.2%)
Medicaid/Medicare/Medicare Advantage[a]	85 (26.2%)
Unknown	2 (0.6%)
Patients with hemoglobin lab measurement during baseline (n=92) Hemoglobin (g/dL), median (IQR)	10.2 (8.5-11.3)
Patients with LDH lab measurement during baseline (n=64) LDH (U/L), median (IQR)	309.0 (198.0-732.0)
Patients with RBC transfusion during six months prior to treatment (n=132) Number of episodes of RBC transfusion, median (IQR)	3.0 (1.0-6.0)

[a]Includes patients with any combination of Medicaid, Medicare, or Medicare Advantage including patients with secondary commercial insurance.
Abbreviations: Ci, complement inhibitor; **g/dL**, grams per deciliter; **IQR**, interquartile range; **LDH**, lactate dehydrogenase; **PNH**, paroxysmal nocturnal hemoglobinuria; **RBC**, red blood cell; **U/L**, units per liter

Figure 2. Baseline comorbidities (A), signs and symptoms (B), and treatments (C)

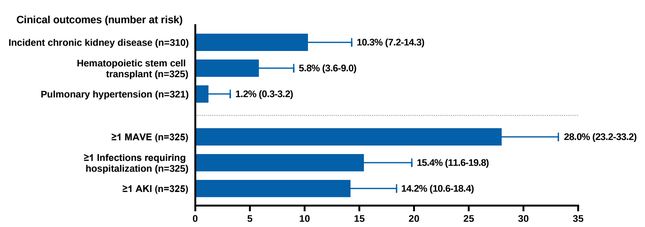


Abbreviations: MAVES, major adverse vascular events

Clinical outcomes after treatment initiation

- During a median follow-up of 27.7 months (IQR: 14.1–48.1), 10.3% (n=32) were diagnosed with incident CKD and 1.2% (n=4) with pulmonary hypertension among patients without a prior diagnosis of these conditions (**Figure 3**).
- 5.8% (n=19) of patients received hematopoietic stem cell transplant.
- 28.0% of patients (n=91) had ≥1 MAVE, 14.2% (n=46) had ≥1 AKI episode, and 15.4% (n=50) had ≥1 infection requiring hospitalization.
- Among patients with ≥1 event, the median (95% CI) number of events per-patient per-year were highest for MAVE (2.5 [2.3–2.7]), followed by AKI (0.8 [0.7–1.0]), and infections requiring hospitalization (0.5 [0.4–0.6]).

Figure 3. Clinical outcomes after treatment initiation



For CKD and pulmonary hypertension, patients without a history of the event and at risk for the outcome during the follow up were included.
Abbreviations: AKI, acute kidney injury; **CI**, confidence interval; **CKD**, chronic kidney disease; **MAVE**, major adverse vascular events

Number of days with RBC transfusions

- Additionally, 32.7% (99 of 303 with follow-up at 6 months post Ci-treatment initiation) had ≥1 RBC transfusion (mean [SD]: 6.1 [8.1] days with transfusion) (**Table 2**).

Table 2. Number of days with RBC transfusions

Number of days with RBC transfusions among all Ci-treated patients	Number at risk	Patients with ≥1 RBC transfusion	Median (IQR) of transfusion episodes among patients with ≥1 RBC transfusion
At 6 months	303	99 (32.7%)	2.0 (2.0-4.0)
At 12 months	260	90 (34.6%)	3.5 (2.0-6.0)
At 18 months	214	86 (40.2%)	4.0 (3.0-7.0)
At 24 months	187	78 (41.7%)	4.0 (3.0-7.0)

Abbreviations: Ci, complement inhibitor; **IQR**, interquartile range; **RBC**, red blood cell

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Disclosures

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