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Prevalence, Real-World Healthcare Resource Utilization, and Costs of Patients with Paroxysmal Nocturnal Hemoglobinuria in the US: A Retrospective Claims Database Analysis

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KEY FINDINGS & CONCLUSIONS

- Findings of this study indicated the 5-year prevalence of PNH to be 2.4 per 100,000 persons in commercial claims
- Despite treatment with C5 inhibitors associated with high annual PNH-related costs, patients with PNH still exhibited BTH and required blood transfusions, potentially indicating an unmet clinical need for more effective treatments

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BACKGROUND

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare blood disorder characterized by complement-mediated hemolytic anemia[1]
  - In the United States (US), ~6 per 1 million people are diagnosed with PNH each year, accounting for 400 to 500 new cases[1]
- Treatments for PNH include complement inhibitors such as C5 inhibitors (intravenous [IV] eculizumab and ravulizumab) which prevent formation of membrane attack complex and consequently intravascular hemolysis[2]
  - However, C5 inhibitors do not address extravascular hemolysis, which may result in incomplete response in some patients[3]
  - Despite C5 inhibitor treatment, breakthrough hemolysis (BTH), characterized by the return of intravascular hemolysis and reappearance of classical PNH symptoms, may also occur and may necessitate blood transfusions or additional doses of C5 inhibitor to re-establish disease control[4]
- More recently, an oral complement factor B inhibitor iptacopan, an add on therapy for C5 inhibitors danicopan, and a C3 inhibitor subcutaneous pegcetacoplan were approved for the treatment of PNH
- At the time the study was conducted, health plan claims did not include iptacopan and danicopan; availability of pegcetacoplan was limited[5,6]

OBJECTIVE

- To estimate the contemporary 5-year prevalence of PNH in commercial claims, given that the ICD-10-CM diagnosis code for PNH was not established until October 2015
- To describe the HRU and direct healthcare costs associated with C5 inhibitors (eculizumab or ravulizumab) among commercially insured patients in the US

METHODS

Data Source

- Health plan claims from the IQVIA PharMetrics® Plus database (01/01/2011 to 09/30/2022) was used
- Data contains comprehensive, integrated fully adjudicated medical and pharmacy claims. Data contributors to the database are largely commercial health plans, with commercial insurance being the most common plan type (~95% of enrollees). The data is representative of the commercially insured US national population for patients under 65 years of age
- Data are de-identified and compliant with the Health Insurance Portability and Accountability Act (HIPAA)

Study Design / Sample Selection

- A retrospective cohort study design was used for assessment of HRU and costs
- Adult (age ≥18 years) patients with PNH (ICD-10-CM diagnosis code: D59.5) treated with C5 inhibitors (eculizumab or ravulizumab) were included
  - **Index date** was defined as the first claim for the C5 inhibitor
- Patients were required to have ≥3 months of continuous health plan enrollment post-index date
- Patients were excluded if: (1) had another condition treated with C5 inhibitors (neuromyelitis optica spectrum disorder, generalized myasthenia gravis, and/or atypical hemolytic uremic syndrome), (2) had codes indicating a clinical trial, or (3) had haematopoietic stem cell transplantation (HSCT)
- **Follow-up period** started from the index date until the earliest of treatment discontinuation (treatment gap of >42 days for eculizumab, >112 days for ravulizumab), end of continuous health plan enrollment, or end of data availability (**end of follow-up period**)
  - Among patients with at ≥6 months of continuous health plan enrollment pre-index date, the **induction phase** was defined as the first 28 days and 14 days following the index date for eculizumab and ravulizumab, respectively[7,8]
  - The **maintenance phase** started from day 29 and day 15 post-index date for eculizumab and ravulizumab,[7,8] respectively, until the end of follow-up period

Outcomes and Statistical Analysis

- The 5-year prevalence of PNH from 2018-2022 was calculated as the number of adult (age ≥18 years) patients with PNH (≥1 medical claims with a diagnosis of PNH) with health plan enrollment during that period divided by the number of adult enrollees with health plan enrollment during that period
- Descriptive analyses of PNH-related (diagnosis of PNH or procedure codes for C5 inhibitor) HRU and associated direct healthcare costs measured during the follow-up period using data from 2011-2022
  - Annual incidence rate [IR] of PNH-related HRU per patient per year (PPPY), including the number of inpatient admissions, emergency department visits, days with outpatient services, days with blood transfusion (any setting),[9] and days with BTH event (any setting)
  - Total, medical, and pharmacy PNH-related costs, in induction phase and per patient per month (PPPM) in the maintenance phase
  - Costs of blood transfusion and BTH at the event level
  - Annualized total PNH-related costs PPPY for the first and subsequent years
    - First year: mean total PNH-related costs in induction phase + 11* mean total PNH-related costs PPPM in maintenance phase
    - Subsequent years: 12* mean total PNH-related costs PPPM during the maintenance phase
  - Costs from the payers' perspective, adjusted for inflation using the Consumer Price Index (CPI) and reported in 2022 USD
    - Exception: no adjustment for inflation for C5 inhibitor treatment costs
  - PNH-related HRU and costs reported for the C5 inhibitors as well as for eculizumab and ravulizumab separately

RESULTS

Prevalence of PNH

- From 2018-2022, the 5-year prevalence of PNH was 2.4 per 100,000 persons and the average annual compound growth rate was 3.24%
- During that period, 30.0% were treated with ≥1 complement inhibitors (eculizumab: 16.4%, ravulizumab: 21.9%, or pegcetacoplan: 2.2%)

Sample Selection

- From 2011-2022, a total of 371 patients met the study eligibility criteria and received C5 inhibitors (induction phase, n=175; maintenance phase, n=362)
  - 288 patients were treated with eculizumab (induction phase, n=83; maintenance phase, n=278)
  - 171 patients were treated with ravulizumab (induction phase, n=117; maintenance phase, n=171)

Patient Characteristics

- Among patients treated with C5 inhibitors, the mean age at PNH diagnosis was 41 years and 55.3% were females (**Table 1**)
  - Among patients treated with eculizumab, the mean age at PNH diagnosis was 41.9 years and 60.4% were females
  - Among patients treated with ravulizumab, the mean age at PNH diagnosis was 39.1 years and 42.7% were females
- The mean ± SD [median] follow-up was 19.3 ± 16.9 [14.7], 23.2 ± 22.4 [15.0], and 17.0 ± 10.8 [14.5] months for the patients treated with C5 inhibitors, eculizumab, and ravulizumab, respectively

PNH-related Healthcare Resource Utilization

- Annual IRs of PNH-related HRU are presented in **Table 2**
- Among patients treated with C5 inhibitors, the annual IR of PNH-related blood transfusion was 1.2 PPPY and BTH in any setting ranged from 3.2-4.5 PPPY
  - Among patients treated with eculizumab, the annual IR of PNH-related blood transfusion was 1.3 PPPY and BTH in any setting ranged from 4.8-5.2 PPPY
  - Among patients treated with ravulizumab, the annual IR of PNH-related blood transfusion was 1.0 PPPY and BTH in any setting ranged from 1.2-3.3 PPPY

Table 1. Characteristics of Patients with PNH Treated with C5 inhibitors

	C5 inhibitors[a] N = 371	Eculizumab N = 288	Ravulizumab N = 171
Age at PNH diagnosis, years			
Mean ± SD [Median]	41 ± 13.6 [40]	41.9 ± 13.6 [41]	39.1 ± 12.2 [39]
≥ 65 years, N (%)	17 (4.6%)	10 (3.6%)	8 (4.7%)
Female, n (%)	205 (55.3%)	168 (60.4%)	73 (42.7%)
U.S Census region at index date, n (%)			
Northeast	48 (12.9%)	37 (12.8%)	21 (12.3%)
South	178 (48.0%)	139 (48.3%)	80 (46.8%)
Midwest	96 (25.9%)	74 (25.7%)	53 (31.0%)
West	48 (12.9%)	37 (12.8%)	17 (9.9%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)
Commercial health plan type at index date, n (%)			
Consumer directed health care	6 (1.6%)	5 (1.7%)	1 (0.6%)
Health Maintenance Organization	54 (14.6%)	43 (14.9%)	21 (12.3%)
Indemnity/traditional	1 (0.3%)	1 (0.3%)	1 (0.6%)
Point of service	27 (7.3%)	20 (6.9%)	14 (8.2%)
Preferred provider organization	283 (76.3%)	219 (76.0%)	134 (78.4%)
Calendar year of index date			
≤2018	168 (45.3%)	233 (80.9%)	0 (0%)
2019-2020	129 (34.8%)	40 (13.9%)	108 (63.2%)
2021-2022	74 (19.9%)	15 (5.2%)	63 (36.8%)

Abbreviations: PNH: paroxysmal nocturnal hemoglobinuria, SD: standard deviation
Note:
[a] For patients with PNH treated with both C5 inhibitors (i.e., switch from eculizumab to ravulizumab), ravulizumab was prioritized and patients were included in the ravulizumab cohort.

Table 2. PNH-related HRU of Patients with PNH Treated with C5 inhibitors

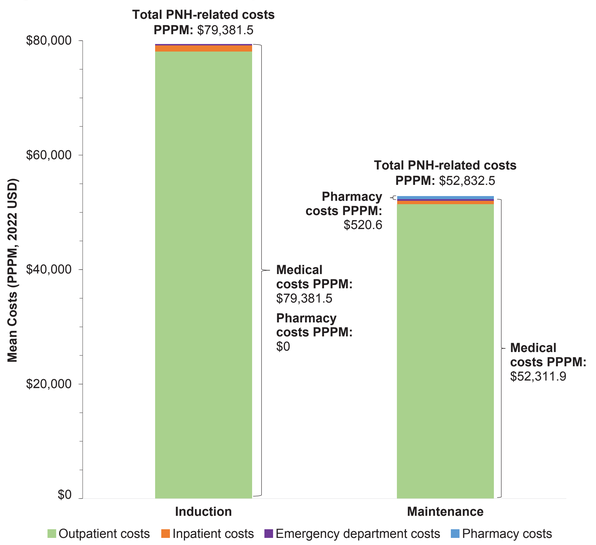
Annual incidence rate, PPPY	C5 inhibitors[a] N = 371	Eculizumab N = 288	Ravulizumab N = 171
Inpatient admissions	0.17	0.17	0.13
Emergency department visits	0.19	0.22	0.14
Days with outpatient services[a]	24.4	31.6	14.0
Days with blood transfusion (any setting)	1.2	1.3	1.0
Days with BTH-related events (any setting)			
Based on symptoms of BTH[b]	4.5	5.2	3.3
Based on treatments for BTH[c]	3.2	4.8	1.2

Abbreviations: BTH: Breakthrough hemolysis, HRU: Healthcare resource utilization, PNH: Paroxysmal nocturnal hemoglobinuria, PPPY: per patient per year
Note:
[a] Intravenous C5 inhibitors (eculizumab and ravulizumab) are administered by a healthcare professional mainly in an outpatient setting.[10] See label-recommended dosing schedule for more details.[7,8]
[b] Defined as ≥1 of the following conditions: venous thrombosis, pulmonary embolism, pulmonary hypertension, arterial thrombosis, or cerebral venous sinus thrombosis, along with a diagnosis of PNH.[11]
[c] Defined as PNH-related blood transfusion (medical service with diagnosis of PNH and a procedure for blood transfusion) or change in C5 inhibitor dosing schedule (e.g., shorter interval, i.e., dose escalation).[4]

PNH-related Direct Healthcare Costs

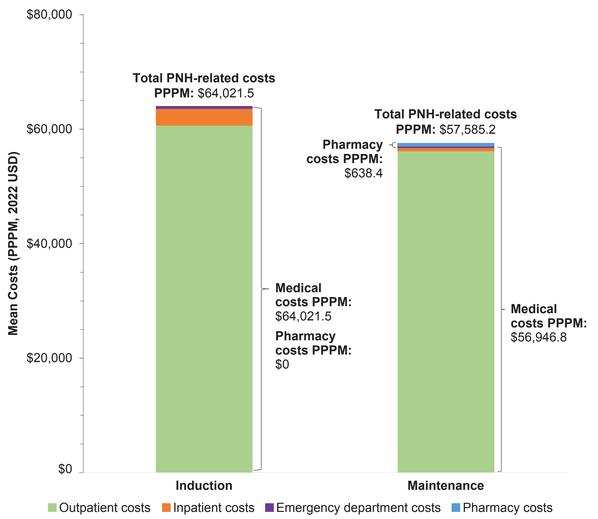
- Mean PNH-related costs during the induction and maintenance phases for patients treated with C5 inhibitors, eculizumab, and ravulizumab are presented in **Figure 1a, Figure 1b**, and **Figure 1c**, respectively
- Among patients treated with C5 inhibitors, the mean ± SD [median] costs of:
  - Blood transfusion was $1,483 ± $7,148 [$625] per event
  - BTH in any setting based on symptoms of BTH was $24,200 ± $35,413 [$19,383] per event
  - BTH in any setting based on treatments for BTH was $26,310 ± $23,815 [$26,274] per event
- Among patients treated with C5 inhibitors, the annual total PNH-related costs PPPY were estimated at $660,533 for the first year and $633,984 for subsequent years, of which treatment costs accounted for 94.3%-94.6%
  - Among patients treated with eculizumab, the annual total PNH-related costs PPPY were estimated at $697,459 for the first year and $691,022 for subsequent years, of which treatment costs accounted for 92.2%-92.2%
  - Among patients treated with ravulizumab, the annual total PNH-related costs PPPY were estimated at $612,522 for the first year and $570,832 for subsequent years, of which treatment costs accounted for 96.1%-96.4%

Figure 1a. PNH-related costs in patients with PNH treated with C5 inhibitors



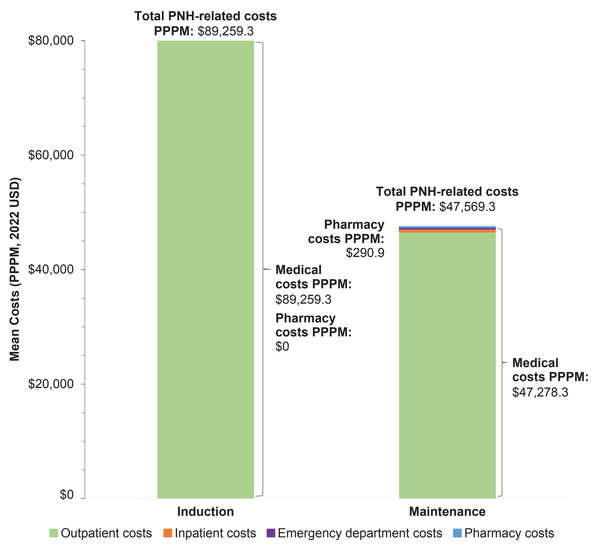
Abbreviations: PPPM: per patient per month, USD: United States Dollars

Figure 1b. PNH-related costs in patients with PNH treated with eculizumab



Abbreviations: PPPM: per patient per month, USD: United States Dollars

Figure 1c. PNH-related costs in patients with PNH treated with ravulizumab



Abbreviations: PPPM: per patient per month, USD: United States Dollars

Limitations

- Findings from this study should be interpreted in the context of the sample selection criteria
- Health plan claims only include diagnosis and procedure codes that are recorded for reimbursement purposes and are subject to coding errors or data omissions
- Laboratory data, patient weight, race, and reasons for diagnosis codes are not available

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