EE326

Health Care Resource Utilization and Costs Among Patients With Paroxysmal Nocturnal Hemoglobinuria Initiating Eculizumab and Ravulizumab: A U.S. Claims Analysis

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SUMMARY

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired hematologic disease with high health care resource utilization (HCRU) and medical costs in all patients, but especially in patients with bone marrow disorder, such as aplastic anemia (AA) or myelodysplastic syndrome (MDS)

US Food and Drug Administration (FDA)-approved intravenous (IV) C5 inhibitors, eculizumab and ravulizumab, are the current standard of care for PNH treatment

Results from this analysis highlight the substantial HCRU and cost of initiating IV C5 inhibitors for PNH, with an even higher burden in patients with AA or MDS. C5 inhibitor drug cost was the primary driver of the total cost of care and was the highest in the hospital outpatient setting

This US claims analysis assessed the real-world HCRU and cost of care in patients with PNH who initiated eculizumab or ravulizumab, including those with an AA or MDS diagnosis at baseline

BACKGROUND

- PNH is a rare, acquired hematologic disease characterized by chronic hemolysis[1] with high HCRU and medical costs[2]
- PNH frequently manifests in association with bone marrow disorder, such as AA or MDS, with the majority of patients with PNH likely to have an underlying aplastic process in their bone marrow, resulting in higher transfusion needs[3-5]
- FDA-approved IV C5 inhibitors, eculizumab and ravulizumab, have greatly transformed disease outcomes and are considered as the standard of care by clinical experts in the US for symptomatic PNH[6-9]
- With more treatment options, such as proximal inhibitors, becoming available for PNH, it is important to continue generating economic evidence using real-world data for eculizumab and ravulizumab

OBJECTIVES

- The objectives of this US claims analysis are
  - To describe the real-world HCRU and cost of care in patients with PNH who initiated eculizumab or ravulizumab
  - To explore the differences in HCRU and costs between patients with a concurrent AA or MDS diagnosis at baseline and those without

METHODS

- This is a retrospective cohort study using IQVIA PharMetrics® Plus claims data on patients with PNH from June 21, 2018 to March 31, 2023
  - This time period was selected to reflect the FDA approval of ravulizumab on December 21, 2018 with a 6-month pre-index period
  - Index date was defined as the date of the first observed claims for eculizumab, ravulizumab, or pegcetacoplan
  - Pegcetacoplan, a proximal inhibitor, was approved by the FDA during the study period, but was not included in this analysis due to the small sample size
- Adult patients with PNH (≥18 years old on index date) were included in this analysis if they received eculizumab or ravulizumab during the treatment identification period (December 21, 2018 to March 31, 2022), did not receive these treatments during the pre-index period, and were continuously enrolled in medical and pharmacy benefits from 6 months pre-index through 12 months post-index
- Patients were excluded if they received eculizumab, ravulizumab, or pegcetacoplan for the treatment of atypical hemolytic uremic syndrome (aHUS), generalized myasthenia gravis (gMG), or neuromyelitis optica spectrum disorder (NMOSD), or if they were ever enrolled in clinical trials
- Study outcomes include patient baseline characteristics, HCRU (number of visits and percentage of patients who received any services by site [inpatient, emergency department, hospital outpatient, physician office, and home] and length of stay for a hospitalization), cost of care (medical [including by site], pharmacy, C5 inhibitor drug, and IV administration) for the first 12 months after treatment initiation, and C5 inhibitor drug costs per infusion during maintenance phase (overall and in the hospital outpatient, office, or home setting)
  - The maintenance phase was assumed to be starting from Day 29 and Day 15 post-index date for eculizumab and ravulizumab, respectively
  - All costs reported were adjusted to US dollars (USD) in 2022
- Outcomes were summarized using descriptive statistics and a subgroup analysis was performed to compare patients with an AA or MDS diagnosis at baseline versus those without
  - Standardized mean differences (SMD) were reported, where an SMD of 0.2, 0.5, and 0.8 represents a small, medium, and large effect, respectively[10]

RESULTS

- 75 patients who initiated IV eculizumab (n=27) or ravulizumab (n=48) were included in this analysis (**Figure 1**); patients who initiated pegcetacoplan were not included due to the small sample size

Figure 1. Patient cohort selection

Patient characteristics between both groups were generally well balanced, with the exception of a higher comorbidity burden in patients who initiated eculizumab versus ravulizumab (Table 1)

- Rheumatic disease, diabetes with chronic complication, renal disease, and malignancy (including lymphoma and leukemia) were more prevalent in the eculizumab group than ravulizumab group

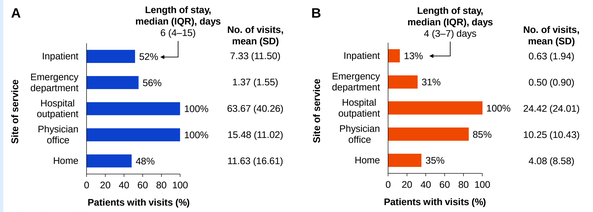
Table 1. Patient characteristics

	Eculizumab (n=27)	Ravulizumab (n=48)
Age at index date, mean (SD)	43 (17)	44 (14)
Sex, male, n (%)	13 (48)	25 (52)
Region, n (%)		
Northeast	4 (15)	6 (12)
Midwest	6 (22)	14 (29)
South	10 (37)	18 (38)
West	7 (26)	10 (21)
Concurrent diagnosis of bone marrow disorder, n (%)		
AA	12 (44)	20 (42)
MDS	1 (4)	3 (6)
CCI score, mean (SD)	1.89 (2.42)	0.65 (1.41)
Payer types, n (%)		
Commercial	17 (63)	35 (73)
Medicare Advantage	2 (7)	4 (8)
Medicare Supplemental	0	1 (2)
Self-insured	8 (30)	8 (17)
Year of index, n (%)		
2019	12 (44)	22 (46)
2020	8 (30)	13 (27)
2021	6 (22)	10 (21)
2022	1 (4)	3 (6)

CCI, Charlson Comorbidity index; SD, standard deviation.

HCRU during the 12 months post-treatment initiation was substantial in terms of inpatient hospitalization and emergency department visits for both the eculizumab and ravulizumab groups (Figure 2)

Figure 2. HCRU at 12 months post-index by site of service in the (A) eculizumab (n=27) and (B) ravulizumab (n=48) groups

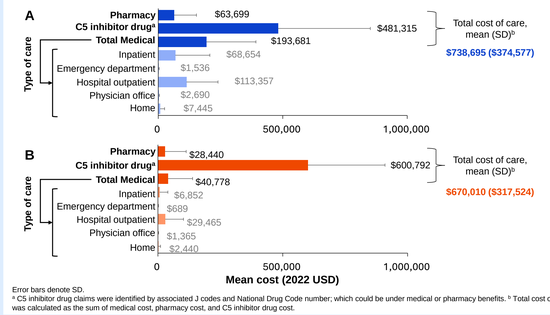


IQR, interquartile range.

C5 inhibitor drug cost during the 12 months post-initiation accounted for 65% and 90% of the total cost of care for patients who received eculizumab and ravulizumab, respectively (Figure 3)

- Within 12 months post-initiation, patients in the eculizumab group had an average of 16 infusions and those in the ravulizumab group had an average of 6.7 infusions
- Mean (SD) C5 inhibitor IV administration cost was $5,749 ($4,391) for patients who initiated eculizumab and $2,307 ($2,123) for those who initiated ravulizumab
- Hospital outpatient cost was the cost driver of medical cost for both the eculizumab and ravulizumab groups

Figure 3. Cost of care at 12 months post-index in the (A) eculizumab (n=27) and (B) ravulizumab (n=48) groups

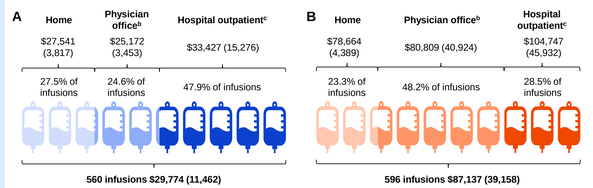


Error bars denote SD.
[a] C5 inhibitor drug claims were identified by associated J codes and National Drug Code number; which could be under medical or pharmacy benefits. [b] Total cost of care was calculated as the sum of medical cost, pharmacy cost, and C5 inhibitor drug cost.

Cost of the C5 inhibitor drug per infusion in maintenance phase was the highest in the hospital outpatient setting for both groups (Figure 4)

- In maintenance phase, the majority of eculizumab and ravulizumab infusions were administered in the hospital outpatient and physician office settings, respectively
- The average cost of the C5 inhibitor drug per infusion in the hospital outpatient setting was about $8K more for eculizumab and $26K more for ravulizumab when compared with the setting with the lowest drug cost per infusion (physician office for eculizumab and home for ravulizumab), suggesting significant markups by hospitals

Figure 4. Mean (SD) cost of C5 inhibitor per infusion[a] in the maintenance phase in the (A) eculizumab and (B) ravulizumab groups

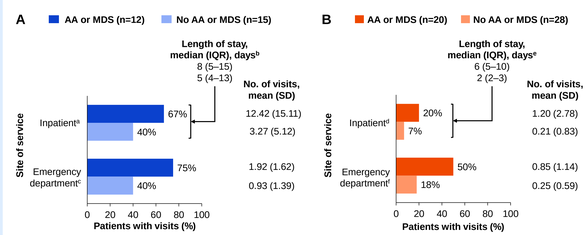


[a] C5 inhibitor drug claims were identified by associated J codes and National Drug Code number; which could be under medical or pharmacy benefits. Does not include drug IV administration costs. [b] Physician Office is defined as a location, other than the hospital, which provides care and services on an ambulatory basis. [c] Hospital outpatient is defined as a portion of a hospital campus which provides care and services for patients who do not require hospitalization or institutionalization.

Increased HCRU in inpatient and emergency department utilization during the 12 months post-C5 inhibitor initiation was observed in patients who had AA or MDS versus those without (Figure 5)

- AA or MDS diagnosis at baseline was observed in 43% of the study cohort

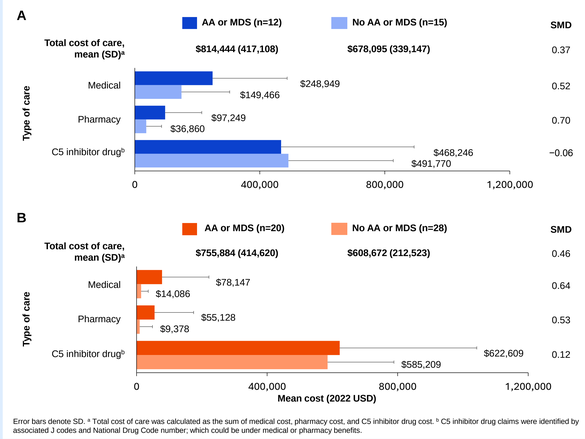
Figure 5. HCRU at 12 months post-index by site of service in the (A) eculizumab (n=27) and (B) ravulizumab (n=48) groups by AA or MDS diagnosis



[a] SMD was 0.55 for percentage of patients with inpatient visits and 0.85 for number of inpatient visits. [b] SMD was 0.19 for length of inpatient stay. [c] SMD was 0.76 for percentage of patients with emergency department visits and 0.68 for number of emergency department visits. [d] SMD was 0.38 for percentage of patients with inpatient visits and 0.49 for number of inpatient visits. [e] SMD was 1.60 for length of inpatient stay. [f] SMD was 0.72 for percentage of patients with emergency department visits and 0.68 for number of emergency department visits.

Patients with an AA or MDS diagnosis at baseline incurred 20% and 24% higher total cost of care for eculizumab and ravulizumab treatment, respectively, versus those without AA or MDS (Figure 6)

Figure 6. Cost of care at 12 months post-index in the (A) eculizumab (n=27) and (B) ravulizumab (n=48) groups by AA or MDS diagnosis



Error bars denote SD. [a] Total cost of care was calculated as the sum of medical cost, pharmacy cost, and C5 inhibitor drug cost. [b] C5 inhibitor drug claims were identified by associated J codes and National Drug Code number; which could be under medical or pharmacy benefits.

LIMITATIONS

- Patients who initiated eculizumab and switched to ravulizumab (n=5) and those who initiated ravulizumab and switched to pegcetacoplan (n=1) within 12 months were not included in this analysis since the aim was to provide estimates for eculizumab and ravulizumab
- The current analysis reported HCRU and cost of care in the first 12 months post-treatment initiation, during which the loading phase and maintenance phase were both included
  - The definition of maintenance phase for each drug was derived from the US prescribing information, which may not reflect real-world considerations, such as the availability of appointments at the infusion clinic
- The study period overlapped with the COVID-19 pandemic, which may have impacted the total cost of care and the preference for infusion setting (i.e. clinic versus home)
- Administrative claims database was subject to coding errors and data omissions
- Given the limitation in sample size, outcomes were not adjusted or controlled for confounding variables

CONCLUSIONS

- Patients with PNH who initiated IV treatment with eculizumab or ravulizumab experienced extensive HCRU burden with frequent hospital outpatient visits
  - Higher cost and HCRU burden were found specifically for patients with AA or MDS at baseline
- The mean total cost of care for patients with PNH was $739K for the eculizumab group and $670K for the ravulizumab group within 12 months post-initiation
- C5 inhibitor drug cost was the primary driver of the total cost of care, accounting for 65% and 90% of costs for patients who received eculizumab and ravulizumab, respectively
- Hospital outpatient cost represented approximately 44% of non-drug costs for patients who initiated eculizumab or ravulizumab
  - Cost per infusion was the highest in the hospital outpatient setting, with about $8K more for eculizumab and $26K more for ravulizumab than the lowest cost setting, indicating a sizable markup of treatment cost in hospitals

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Disclosures

All authors are employees of Genentech, Inc. and may own stocks of Roche.