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# Real-world hemoglobin profiles and transfusion burden in patients with paroxysmal nocturnal hemoglobinuria receiving complement inhibitors: A US claims analysis

Carlos de Castro[1]; Peter Blandino[2], Fiston Vuvu[2]; Enrico Zanardo[3]; Lynn Huynh[3]; Robert Schell[3]; Nathaniel Downes[3]; Yixin Yang[3]; Mei Sheng Duh[3]; Peter Hillmen[2]
[1]Duke University, Durham, NC, USA; [2]Apellis Pharmaceuticals, Inc, Boston, MA, USA; [3]Analysis Group Inc, Boston, MA, USA

## INTRODUCTION

- Anemia and transfusion dependence are common in patients with PNH[1,2]
- Current standard of care in PNH includes complement inhibitors, classified as terminal and proximal agents
- Terminal inhibitors target IVH,[3–5] but residual IVH and the development of extravascular hemolysis can contribute to ongoing anemia[6]
- Clinical trials show that proximal complement inhibitors can improve Hb concentrations and reduce transfusion dependence. However, real-world evidence on Hb concentrations and transfusion burden among patients with PNH treated with terminal or proximal inhibitors is limited[7,8]

## OBJECTIVE

- To evaluate real-world Hb concentrations and transfusion burden among patients with PNH treated with terminal or proximal complement inhibitors

## METHODS

- We conducted a retrospective cohort study using the Komodo Research Database (January 1, 2016 to April 30, 2025), a large, nationally representative US claims database with linked Hb laboratory data
- Adults with PNH initiating terminal (eculizumab, ravulizumab) or proximal (pegcetacoplan, iptacopan) complement inhibitors were categorized into 3 cohorts: terminal inhibitor only (patients initiating terminal inhibitors who do not switch to proximal); terminal-to-proximal switchers (patients initiating terminal inhibitors as their first treatment and subsequently switching to proximal); and proximal inhibitor at index (patients initiating a proximal inhibitor as their first complement inhibitor)
- Index date was defined as the first observed complement inhibitor claim. Hb concentrations and transfusion burden were assessed at baseline (3 months prior to index) and follow-up (index to the end of continuous clinical activity, ≥1 month). For the terminal-to-proximal switch cohort, follow-up was divided into pre- and post-switch periods.
- Hb profiles, including mean (SD) Hb concentrations and proportion of patients with Hb ≥12 g/dL, were assessed only among patients with available Hb values during the period of interest
- Transfusion burden included transfusion rates (PPPY) and proportion of patients with transfusion dependence (defined as ≥4 transfusions per year)
- This analysis was descriptive in nature and no statistical testing was conducted

## RESULTS

- We identified 972 patients (**Table 1**): 783 (80.6%) terminal inhibitor only, 147 (15.1%) terminal-to-proximal switchers, and 42 (4.3%) proximal inhibitor at index
- Patients who switched to a proximal inhibitor had an average Hb concentration of 9.5 pre-switch and 11.0 post-switch; 13.0% of patients had Hb ≥12 g/dL pre-switch and 41.7% had Hb ≥12 g/dL post-switch (**Figure 1**)
- Patients who switched to a proximal inhibitor had a mean of 4.63 transfusions pre-switch and 2.77 post-switch; 22.4% of patients had transfusion dependence pre-switch and 10.9% had transfusion dependence post-switch (**Figure 2**)

**Table 1. Baseline characteristics of patients with PNH initiating complement inhibitors**

| Patient characteristics | Terminal inhibitor at index, no switch to proximal (N = 783) | Terminal inhibitor at index, switch to proximal (N = 147) | | Proximal inhibitor at index (N = 42) |
|---|---|---|---|---|
| Age at index, years, mean (SD) | 46.4 (18.3) | 45.2 (18.3) | | 52.4 (17.4) |
| Female, n (%) | 423 (54.0) | 76 (51.7) | | 25 (59.5) |
| Complement inhibitor agent,[a] n (%) | | *Terminal inhibitor (pre-switch)* | *Proximal inhibitor (post-switch)* | |
| Eculizumab | 459 (58.6) | 63 (42.9) | – | – |
| Ravulizumab | 325 (41.5) | 84 (57.1) | – | – |
| Pegcetacoplan | – | – | 88 (59.9) | 25 (59.5) |
| Iptacopan | – | – | 59 (40.1) | 17 (40.5) |

[a]One patient in the terminal inhibitor, no switch cohort initiated on eculizumab and ravulizumab simultaneously.
Crovalimab was included in the original search criteria, but no patients were identified as having initiated crovalimab during the study period.

**Figure 1. Changes in (A) mean hemoglobin concentrations and (B) distribution of hemoglobin concentrations**

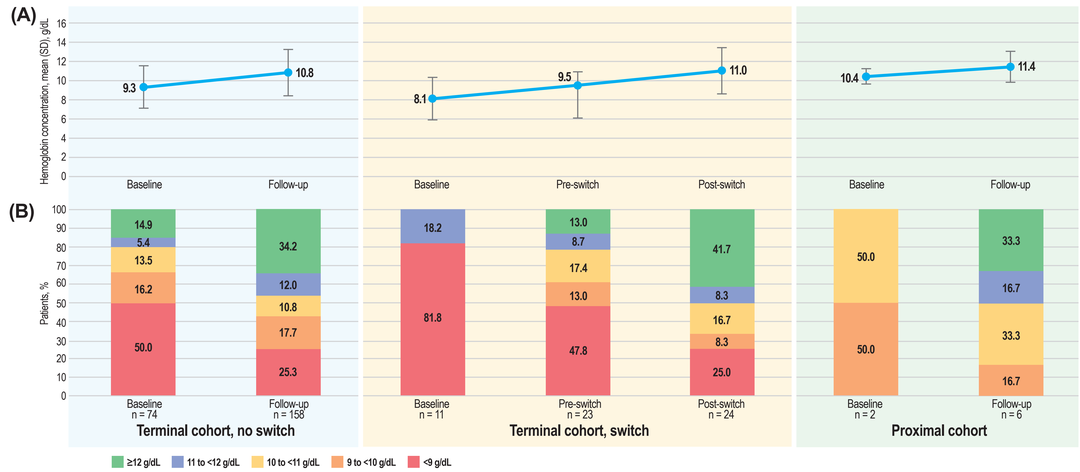
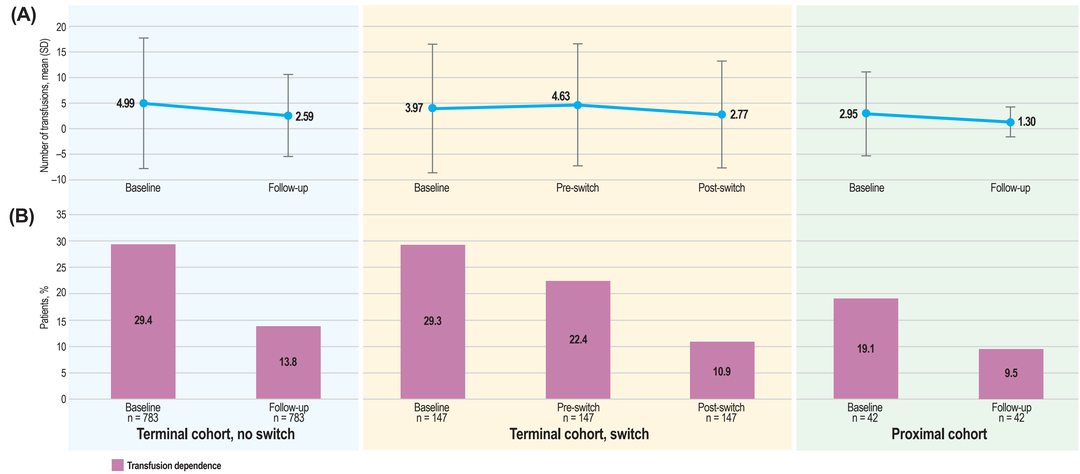



**Figure 2. Changes in (A) mean transfusion burden and (B) patients with transfusion dependence**




## LIMITATIONS

- Hb laboratory data availability was limited in the Komodo Research Database, and as such, Hb measurements were limited in both the proximal and terminal-to-proximal switch cohorts.
- Patients receiving danicopan were not included in this analysis due to the confounding nature of dual therapy and an insufficient number of patients to provide meaningful interpretation
- Additional limitations typical of claims analyses limit interpretation of results: data may be subject to miscoding or inaccurate data entry, and events occurring outside of insurance coverage captured in Komodo data may not be represented.

## CONCLUSIONS

- Patients with PNH treated with terminal inhibitors may experience persistent anemia and transfusion burden. Hb-based metrics provide clinically meaningful insight into disease control beyond IVH alone.
- In this study, patients switching from terminal to proximal inhibitors had mean Hb concentrations of 9.5 g/dL before and 11.0 g/dL after switching, and the proportion with transfusion dependence was 22.4% before and 10.9% after switching
- These findings highlight an ongoing unmet need in PNH and support treatment strategies addressing the full spectrum of complement-mediated hemolysis

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**ABBREVIATIONS:** Hb, hemoglobin; IVH, intravascular hemolysis; PNH paroxysmal nocturnal hemoglobinuria; PPPY, per person per year.

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