Abstract: P833

Title: REAL-WORLD CLINICAL OUTCOMES IN PATIENTS WITH PAROXYSMAL NOCTURNAL HEMOGLOBINURIA TREATED WITH ECULIZUMAB OR RAVULIZUMAB IN THE US - A RETROSPECTIVE CLAIMS DATABASE ANALYSIS

Abstract Type: Poster Presentation

Topic: Bone marrow failure syndromes incl. PNH - Clinical

Background:

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare and potentially life-threatening disorder with ongoing hemolysis that may cause thrombosis and bone marrow failure. Current treatments for PNH include complement inhibitors such as C5 inhibitors, eculizumab (ECU, FDA-approved in March 2007) and ravulizumab (RAVU, FDA-approved in December 2018), a C3 inhibitor pegcetacoplan (FDA-approved in May 2021), with most recent option iptacopan, an oral complement factor B inhibitor (FDA-approved in December 2023).

Aims:

This study aimed to assess the clinical outcomes among patients with PNH treated with ECU or RAVU in the US clinical practice.

Methods:

This was a retrospective cohort study using data from the IQVIA PharMetrics® Plus (01/01/2011 to 09/30/2022). Adult (age ≥18 years) patients with PNH (ICD-10-CM code D59.5) treated with ECU or RAVU with ≥6 months of continuous health plan coverage prior to and ≥3 months following the first claim for ECU or RAVU (index date) were included. Patients with a diagnosis of neuromyelitis optica spectrum disorder, generalized myasthenia gravis, or atypical hemolytic uremic syndrome were excluded. The follow-up period started from the index date until the first occurrence of treatment discontinuation/end of data/end of continuous health plan coverage. Transfusion avoidance (TA) was defined as no blood transfusions from the index date to end of follow-up period among patients with ≥6 months of follow-up. PNH-related thrombosis was 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. Time to first PNH-related thrombosis event post-index was estimated by Kaplan-Meier analyses.

Results:

A total of 83 patients treated with ECU (at index date: mean ± SD age, 42.7 ± 14.7 years; 60.2% female; during 6-month baseline: mean± SD Charlson Comorbidity Index [CCI]: 0.7 ± 1.7; 9.6% PNH-related thrombosis; 47.0% blood transfusion; 98.8% complement-inhibitor-naïve) and 117 patients treated with RAVU (at index date: mean ± SD age, 40.5 ± 12.1 years; 45.3% female; during 6-month baseline: mean ± SD CCI: 0.6 ± 1.3; 6.8% PNH-related thrombosis; 21.4% blood transfusion; 28.2% complement-inhibitor-naïve) were included.

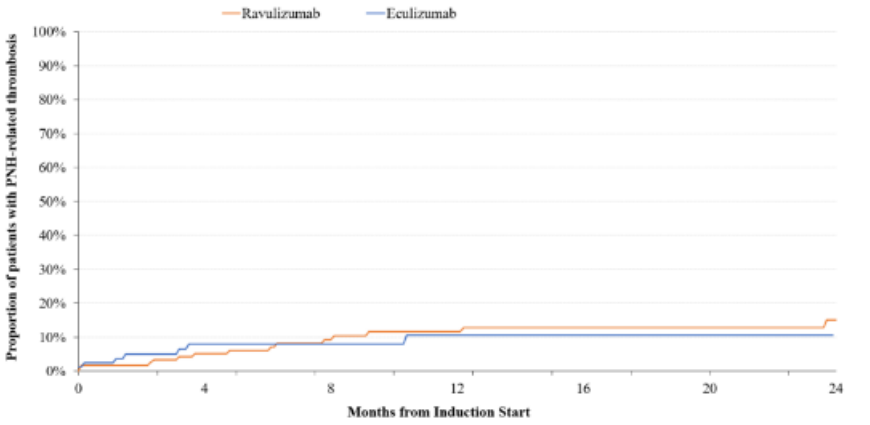
Among those with ≥6 months of follow-up, 46.2% and 11.9% of patients required blood transfusions in the first 6 months post-index in the ECU and RAVU cohorts, respectively. During a mean ± SD follow-up of 25.5 ± 20.6 and 20.7 ± 10.3 months, TA was observed in 46.2% and 78.2% of patients in the ECU and RAVU cohorts, respectively. During a mean follow-up of 17.1 ± 19.6 and 18.4 ± 11.1 months, 12.0% of patients experienced PNH-related thrombosis in each of the ECU and RAVU cohorts, of which, 20.0% and 28.6% were observed in an inpatient setting, respectively. The 6- and 12-month rates of PNH-related thrombosis post-index were 8.0% and 10.6% for ECU and 6.1% and 11.6% for RAVU, respectively (**Figure 1**).

Summary/Conclusion:

Despite treatment with C5 inhibitors, patients with PNH required blood transfusions and experienced PNH-related thrombosis which may potentially indicate a critical unmet need, suggesting that patients might benefit

from more effective treatment.

Figure 1. Time to First PNH-related Thrombosis Event Following Eculizumab and Ravulizumab Initiation



PNH-related Thrombosis event in any setting		1-Month	3-Month	6-Month	9-Month	12-Month	18-Month	24-Month
Eculizumab	N at risk	75	67	50	41	33	26	21
	Kaplan-Meier probability, %	2.4%	5.1%	8.0%	8.0%	10.6%	10.6%	10.6%
Ravulizumab	N at risk	115	111	94	75	67	44	39
	Kaplan-Meier probability, %	1.7%	3.4%	6.1%	10.4%	11.6%	12.9%	15.1%

Keywords: Paroxysmal nocturnal hemoglobinuria (PNH), Thrombosis, Blood transfusion