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Poster# **MDS-1048**

A single institution experience of iptacopan in paroxysmal nocturnal hemoglobinuria

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KEY FINDINGS & CONCLUSIONS

- Iptacopan was well tolerated in patients, with no breakthrough hemolysis occurring and no discontinuation secondary to side effects
- Iptacopan resulted in an improvement from baseline in hemoglobin (Hgb) in complement inhibitor (CI)-treated patients at 3 months
- Iptacopan resulted in an improvement in Hgb in CI-naive patients who had previously not been treated for paroxysmal nocturnal hemoglobinuria (PNH)
- These findings underscore that the most marked hematologic improvements occur by 3 months following iptacopan initiation, with persistent Hgb elevation
- Although longer follow-up is needed to confirm durability and safety, these results suggest that iptacopan can be an effective and convenient alternative for patients with PNH

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BACKGROUND

- Real-world experiences of prescribers and patients with new medications may differ from those of clinical investigators and selectively chosen trial participants
- The FDA recently approved iptacopan, an oral factor B inhibitor, for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) in December 2023

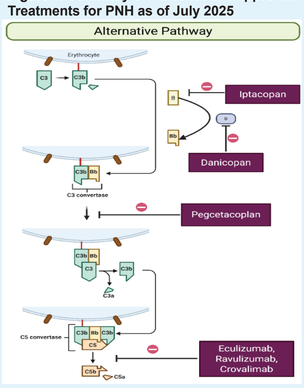
OBJECTIVE

- We report on the largest US cohort of patients with PNH who incorporated iptacopan into their standard-of-care treatment

METHODS

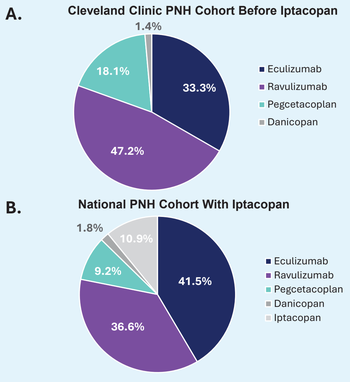
- We analyzed 43 patients (35 CI-experienced; 8 CI-naive) with hemolytic PNH requiring CIs or currently on CIs between iptacopan approval in December 2023 and January 2025 (**Figure 1**)
  - The 8 CI-naive patients all elected iptacopan as initial CI treatment, mainly due to it being an oral medication
  - Among the 35 CI-experienced patients who switched to iptacopan, 25 had a suboptimal response to ravulizumab (n=16), pegcetacoplan (n=6), or eculizumab (n=3)
  - Suboptimal response was defined as hemoglobin <11 g/dL or active hemolysis
- The study compared patients who decided to switch to iptacopan and those who preferred to stay on their current treatment
  - Their longitudinal baseline, 3-month, 6-month, and 12-month responses, as applicable, were analyzed
- This study included >200,000,000 patients in Cosmos for analysis, to compare adoption of iptacopan following FDA approval[1]
- A breakdown of CI use for PNH prior to approval of iptacopan in December 2023 at Cleveland Clinic is shown in **Figure 2**
- The use of Cosmos to compare utilization of therapeutics after FDA approval showed 10.9% adoption of iptacopan following approval

Figure 1. Summary of Current FDA-Approved Treatments for PNH as of July 2025



FDA, US Food and Drug Administration, PHN, paroxysmal nocturnal hemoglobinuria.

Figure 2. Iptacopan Use Before and After FDA Approval



FDA, US Food and Drug Administration, PHN, paroxysmal nocturnal hemoglobinuria.

RESULTS

- Demographic data for patients with PNH seen in the clinic are shown in **Table 1**
- Mean (SD) age at the time of PNH diagnosis was 44 (18) years, with mean (SD) disease duration of 10 (8) years

Table 1. Patient Baseline Demographic and Clinical Characteristics

	Eculizumab (n=5)	Ravulizumab (n=23)	Pegcetacoplan (n=13)	Danicopan + ravulizumab (n=1)	CI naive (n=10)
Race/ethnicity, n					
Asian	0	2	1	0	2
Black	2	3	1	0	1
Hispanic	0	0	1	0	2
White	3	18	10	1	5
Male sex, n	1	8	6	1	5
Age at iptacopan initiation (mean (SD), years	58 (15)	51 (17)	55 (17)	25 (0)	60 (19)
Erythrocyte clone size, mean (SD), %	47 (44)	39 (31)	69 (33)	85 (0)	23 (31)
Granulocyte clone size, mean (SD), %	61 (40)	63 (37)	81 (23)	100 (0)	32 (22)
White blood cell count, mean (SD), cells/μL	5.2 (0.9)	4.5 (1.8)	6.1 (5.2)	3.5 (0)	4.8 (2.0)
Hgb, mean (SD), g/dL	10.5 (2.4)	11.1 (2.3)	10.8 (2.1)	12.1 (0)	9.6 (1.8)
Platelets, mean (SD), ×10^6 cells/μL	174 (39)	138 (58)	178 (97)	190 (0)	100 (64)
Reticulocytes, mean (SD), per μL	0.17 (0.12)	0.16 (0.09)	0.13 (0.11)	0.18 (0)	0.10 (0.05)
Aplastic anemia, n/N	4/5	9/23	9/13	0/1	8/10
Thrombosis, n/N	1/5	10/23	4/13	0/1	1/10
No. of prior treatments	0-1	0-1	0-2	2	0

CI, complement inhibitor; Hgb, hemoglobin; SD, standard deviation.

- A summary of the clinical characteristics at 3 months follow-up for CI-naive patients, CI-experienced patients with suboptimal response, and CI-experienced patients who switched to iptacopan despite initial response is shown in **Table 2**

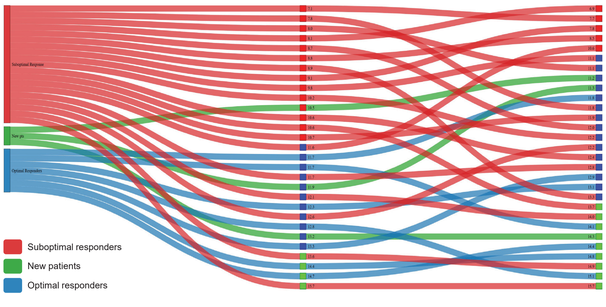
Table 2. Clinical Characteristics at 3 Months Follow-Up After Initiating or Switching to Iptacopan

	CI-naive (n=8)		CI-experienced suboptimal response[a] (n=25)			CI-experienced switch to iptacopan (n=10)	
	Baseline	3 months	Baseline	3 months	*P* value	Baseline	3 months
Hgb, mean (SD), g/dL	11.9 (1.35)	12.3 (1.76)	10.3 (2.21)	11.6 (2.43)	0.006	13.0 (1.21)	13.7 (1.18)
Reticulocytes, mean (SD), ×10^6 cells/μL	0.130 (0.08)	0.083 (0.02)	0.167 (0.100)	0.103 (0.06)	<0.001	0.106 (0.03)	0.08 (0.02)
LDH, mean (SD), IU/L	485 (541)	457 (129)	312 (189)	231 (80.2)	0.003	188 (33.9)	188 (34.4)
PNH clone size, % change							
Erythrocytes	—	+17.0	—	+17.4	—	—	+1.1
Granulocytes	—	+30.9	—	+7.6	—	—	+11.0

CI, complement inhibitor; Hgb, hemoglobin; LDH, lactate dehydrogenase; PNH, paroxysmal nocturnal hemoglobinuria; SD, standard deviation.
[a] Suboptimal response to ravulizumab (n=16), pegcetacoplan (n=6), and eculizumab (n=3). Suboptimal response was defined as hemoglobin <11 g/dL and elevated hemolytic markers (LDH >250 IU/L, D-dimer >500 ng/mL).

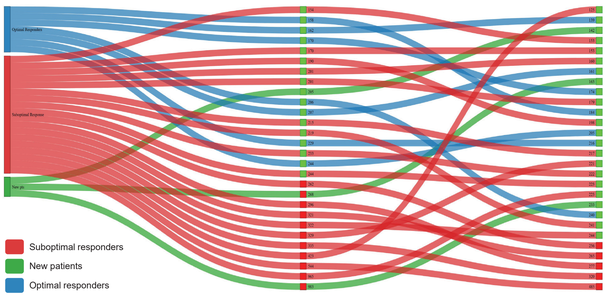
- Sankey plots shows individual Hgb (**Figure 3**) and LDH (**Figure 4**) trends from baseline to three months of suboptimal responders (red), new patients (green) and responders (blue)
  - Suboptimal responders were classified as those with active hemolysis or Hgb <11 g/dL
  - Red boxes indicate Hgb <11 g/dL, blue 11-13.5 g/dL, and green >13.5 g/dL
- A significant improvement in Hgb and a notable decrease in LDH from baseline to 3 months were observed
- No patients on iptacopan discontinued treatment or required a switch to another CI
  - Platelet counts improved in 8 of 29 patients and worsened in 6 of 29 patients
  - Absolute neutrophil counts improved in 15 of 28 patients and declined in 8 of 28 patients
- There were no grade 2 toxicities observed and no major adverse events such as thrombotic complications, or breakthrough hemolysis
- Two patients reported instances of missed iptacopan doses, without notable clinical consequences

Figure 3. Sankey Plot Showing Trend of Hgb From Baseline to 3 Months and Then to 6 Months



Hgb, hemoglobin.

Figure 4. Sankey Plot Showing Trend of LDH From Baseline to 3 Months Then to 6 Months



LDH, lactate dehydrogenase

References

1. Tarabichi Y, et al. ACI open. 2021;5(1):e36-e46.

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Disclosures

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