Poster# **PF671**

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Effectiveness and Safety of Iptacopan in Paroxysmal Nocturnal Hemoglobinuria (PNH) Patients with Persistent Anemia After C5 inhibition: The Real-World Experience of the French Early Access Program

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INTRODUCTION

- PNH is **a rare disorder** characterized by hemolytical anemia and thrombosis, and is associated with bone marrow failure.
- Iptacopan, a **first-in-class oral proximal complement inhibitor**, targets **Factor B** in the alternative pathway and thus controls both intra- and extravascular hemolysis.
- In the **Phase III APPLY-PNH trial** (1), iptacopan achieved **meaningful increases** in hemoglobin (Hb) levels compared to anti-C5 therapy and reduced transfusion needs.
- In France, iptacopan is available through an **Early Access Program** (EAP) to treat adults with PNH who remain anemic despite C5 inhibition (C5i) treatment for at least 6 months.

The aim of this study is to describe effectiveness and safety data in **real-world clinical practice in France**.

METHODS

- The program effectively launched on **19 June 2024** with **2 profiles of patients**:
  - Previously treated via compassionate access (CA) : **CA patients***
  - Initiating treatment: **EAP patients**
- Posology: **200 mg twice daily**.
- Data collection time points: at treatment request (baseline), after 15 days (D15) and 2 months (M2) of treatment, and every 2 months thereafter.

Key inclusion criteria

- **Adult patient** (≥18 years) with confirmed PNH and PNH clone size ≥ 10%.
- Patient with **persistent hemolytical anemia** (hemoglobin level **<10 g/dL**) despite C5i treatment for at least 6 month.
- Vaccination against neisseria meningitidis and streptococcus pneumoniae at least 2 weeks prior to treatment initiation.

Key exclusion criteria

- Hypersensitivity to iptacopan or excipients.
- Active encapsulated bacterial infections.

RESULTS

EAP: Latest Progress Update

As of June 2nd, 2025, 47 patients were included in the EAP across 17 sites in France (**Figure 1**).

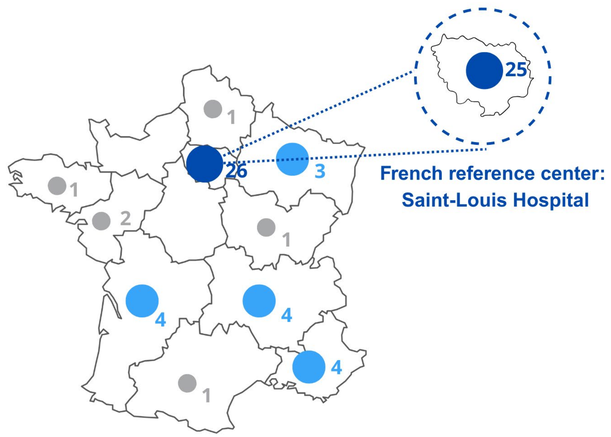

Figure 1. Included patients (N=47) by region

Preliminary Findings

Disposition and exposure to iptacopan

Between June 19th, 2024, and November 8th, 2024 (1st regulatory report cutoff date):

- **29** patients were included in the program:
  - 4 CA patients*
  - 25 EAP patients (**Table 1).**
- Mean treatment exposure **was:**
  - **5,3 ± 2,8 months for CA patients***
  - **0,9 ± 0,8 months for EAP patients.**

Baseline characteristics	EAP patients N=25
Age, mean (SD)	49.3 ± 19.4
Female, n (%)	16 (64.0%)
History of thrombotic event, n (%)	7 (28.0%)
Transfusion dependence in previous 12 m, n(%)	13 (52.0%)
↳ Number of transfusions, mean (SD)	10.2 ± 11.5

Table 1. Patients' characteristics at baseline

CA patients*: 3 females, 1 male; mean age 37.5 ± 2.6 years. Two patients had prior thrombotic events; one patient had 12 transfusions in the previous 12 months.

Rapid hemoglobin increase and normalization with iptacopan

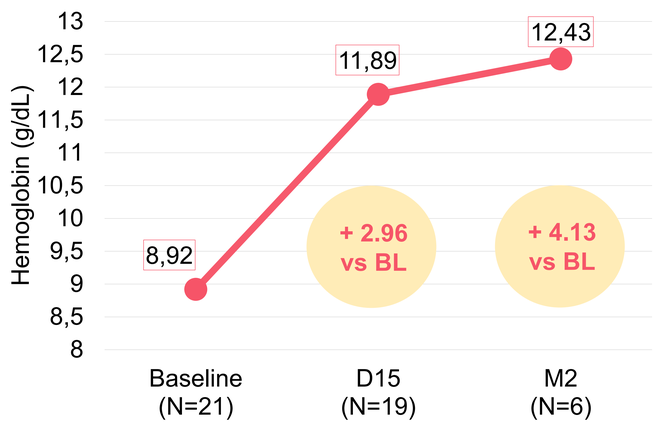

Figure 2. Mean Hb level over time of EAP patients

For the 4 CA patients*, Hb levels (12.47 g/dL ± 0.90 at baseline) remained stable (-0,07 ± 0,59 g/dL at M4).

Transfusion independence with iptacopan

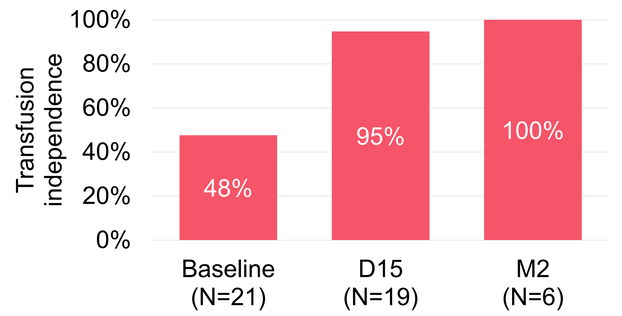

Figure 3. EAP patients with transfusion independence

For CA patients*: At baseline: 75% (3/4) - At D15, M2 and M4: 100 % (4/4) were transfusion independent.

Safety profile with iptacopan

- No treatment interruptions or permanent discontinuations were reported.
- No thromboembolic event or hemolytic crisis occurred.
- One non serious bacterial infection (a cystitis due to Klebsiella) was documented; it did not lead to treatment modification or discontinuation.

*switched from another proximal inhibitor to iptacopan due to medical need, not responding to 1L anti-C5 treatment, & issue with previous proximal inhibitor.

KEY FINDINGS & CONCLUSIONS

Initial results of the French EAP show :

- **Rapid hemoglobin increase**: iptacopan led to a clinically meaningful rise in hemoglobin levels within 15 days.
- **Reduced transfusion needs**: iptacopan markedly improved transfusion independence.
- **Excellent tolerability**: no treatment discontinuations occurred, and no new safety signals were identified.

References

1. Peffault de Latour R, Roeth A, Kulasekararaj A, Scheinberg P, Ueda Y, de Castro CM, et al. Oral Monotherapy with Iptacopan, a Proximal Complement Inhibitor of Factor B, Has Superior Efficacy to Intravenous Terminal Complement Inhibition with Standard of Care Eculizumab or Ravulizumab and Favorable Safety in Patients with Paroxysmal Nocturnal Hemoglobinuria and Residual Anemia: Results from the Randomized, Active-Comparator-Controlled, Open-Label, Multicenter, Phase III Apply-PNH Study. Blood. 2022;140(Supplement 2):LBA-2-LBA-.

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* All Other centers that included patients in the EAP : Besançon, Brest, Castres, Clermont-Ferrand, Colmar, Grenoble, Metz, Rochefort and Saint-Antoine Hospital (Paris).

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