PF670

Talha Munir | tmunir@nhs.net

Real-world outcomes and clinical burden of patients with paroxysmal nocturnal hemoglobinuria

Talha Munir[1], Eloise Beggiato[2], Maria-Magdalena Balp[3], Anggie Wiyani[4], Silvia Sanz[5], Yasmin Taylor[6], Alexander Röth[7]

[1]St James Hospital, Leeds, United Kingdom; [2]Città della Salute e della Scienza, Oncology and Hematology, Turin, Italy; [3]Novartis Pharma AG, Basel, Switzerland; [4]Novartis Pharmaceuticals UK Ltd, London, United Kingdom; [5]Novartis, Barcelona, Spain; [6]Adelphi Real World, Bollington, United Kingdom; [7]University Hospital Essen, Essen, Germany

KEY FINDINGS & CONCLUSIONS

- In this real-world study, despite receiving Ci, 63% of patients had suboptimal Hb (<12 g/dL).
  - Among C5i-treated patients, 18% and 45% still had Hb (g/dL) <10 and ≥10 to <12, respectively.
  - Among C3i-treated, 8% had Hb (g/dL) <10 while 46% had Hb (g/dL) ≥10 to <12.
- Besides anemia, many patients continue to experience symptoms, with fatigue being the most frequent, and some still require blood transfusions.
- These results highlight the clinical burden despite treatment with Ci and unmet need for treatments which sustain Hb levels and provide improved symptom control for majority of patients.

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INTRODUCTION

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare disorder characterized by complement-mediated hemolysis. Common manifestations of PNH, such as anemia and fatigue have a negative impact on patients' lives.[1]
- Current treatments include complement inhibitors (Ci) targeting complement 5 (C5),[2,3] complement 3 (C3),[4] and inhibitors of factor B[5] or D[6] of the alternative complement pathway.
- Treatment with Ci has led to improved clinical outcomes,[7] however, patients with PNH continue to experience significant clinical burden.
- The objective of this non-interventional study was to understand the real-world clinical profile and burden of patients with PNH.

METHODS

- Data were drawn from the Adelphi PNH Disease Specific Programme™ (DSP) Wave II, a real-world, cross-sectional survey of physicians and their PNH patients.
- DSP methodology has been validated and proved consistent over time.[8-11]
- This survey was conducted from December 2023 - May 2024, across France, Germany, Italy, Spain and the United Kingdom.
- Hematologists and hematologist-oncologists who managed and made treatment decisions for adult patients with PNH completed a questionnaire for up to their next 10 consecutively consulting patients using information from the consultation, clinical history, and their own clinical judgement.
- Physician-reported patient questionnaires included data on:
  - Patient demographics,
  - Clinical signs and symptoms,
  - Treatments, and blood transfusions,
  - Laboratory parameters (hemoglobin [Hb; g/dL], lactate dehydrogenase [LDH; U/L])
- Data were pooled and analyzed by country, using descriptive statistics with no imputation for missing values. Data were presented as median and interquartile range (IQR), mean and standard deviation (SD) or frequency distributions.
- Data were presented overall and stratified according to the type of Ci received (C5i and C3i) for the past 12 months.

RESULTS

- A total of 65 physicians provided data on 343 patients with 58% male. Median (IQR) age at the time of survey was 48.0 (35.0, 60.0), age at diagnosis 42.4 (31.7, 56.3), and time since diagnosis was 2.0 (0.9, 4.8) years **(Table 1)**.
- PNH subtype among all patients was 72% classical, 15% subclinical, and 12% PNH with concurrent bone marrow failure.
- Overall, 48% of patients had at least one comorbidity at survey.
  - PNH related comorbidities (aplastic anemia [23%], myelodysplastic syndrome [10%] and myelofibrosis [1%]) were reported among 33% of patients.
  - Non-PNH related comorbidities (e.g. diabetes, anxiety, depression etc.) were reported among 80% of cases.
- At the time of survey, a majority (77% [n=265]) of patients were prescribed Ci (C5i [91%] and C3i [9%]) (**Table 1**). Of those patients with treatment duration data, 60% had received Ci for >12 months.
- Among patients prescribed treatment, 18% required ≥1 transfusion within the 12 months prior to survey, with a mean (SD) of 3.6 (4.3) transfusions.

Clinical profile of Ci-treated patients at the time of survey

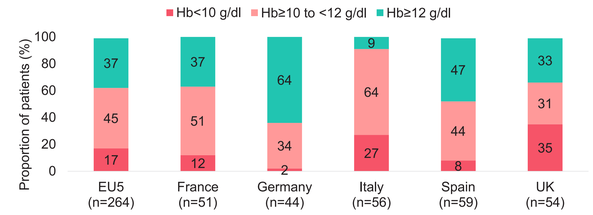
- Median (IQR) PNH granulocyte clone size (%) of patients on C5i and C3i was 20.0 (5.0, 60.0) and 55.0 (20.0, 63.0) respectively.
- Median (IQR) absolute reticulocyte count (x10^9/L) of patients on C5i and C3i was 151.0 (112.0, 245.5) and 107.5 (100.0, 142.5) respectively.
- Among Ci-treated patients, 17%, 45% and 37% of patients had Hb (g/dL) <10, 10 to <12 and ≥12 at survey (**Figure 1**).
  - Among C5i-treated patients, 18%, 45% and 36% had Hb (g/dL) <10, ≥10 to <12 and ≥12 respectively **(Figure 2).**
  - Among C3i-treated patients, 8%, 46% and 46% had Hb (g/dL) <10, ≥10 to <12 and ≥12 respectively **(Figure 3).**
- Median (IQR) LDH (U/L) of patients on C5i and C3i was 250.0 (203.0, 338.5) and 220.0 (190.0, 345.0) respectively.
- At time of survey, 73% of C5i- and 83% of C3i-treated patients experienced PNH symptoms with most common being anemia (C5i, 47%; C3i, 29%), and fatigue (C5i, 42%; C3i, 46%).
- Among patients treated with Ci for >12 months, 17% experienced a breakthrough haemolysis with a mean (SD) of 1.7 (1.0) events and 4% of patients had thrombotic events with a mean (SD) of 1 (0) event in the past 12 months.

Table 1. Demographics and clinical profile; overall and by country

	EU5 (N=343)	France (N=69)	Germany (N=77)	Italy (N=80)	Spain (N=63)	UK (N=54)
Male, n (%)	198 (58)	47 (68)	45 (58)	44 (55)	34 (54)	28 (52)
Age at survey, median (IQR), years	48.0 (35.0-60.0)	36.0 (28.5-50.0)	41.0 (34.5-54.0)	55.0 (44.0-60.8)	55.0 (41.0-66.0)	60.0 (45.3-71.3)
Age at diagnosis, median (IQR), years	42.4 (31.7-56.3)	33.7 (25.9-46.0)	38.7 (32.9-49.0)	52.3 (41.8-59.3)	47.2 (33.0-65.4)	43.7 (29.0-60.4)
Time since diagnosis, median (IQR), years	2.0 (0.9-4.8)	2.8 (1.2-5.2)	1.3 (0.6-3.3)	1.1 (0.5-2.9)	1.9 (1.2-4.0)	7.0 (3.5-15.4)
Patients on Ci, (n) Time receiving Ci, median (IQR),years	260 1.3 (0.6-2.5)	51 1.2 (0.7-1.9)	44 1.0 (0.5-1.9)	55 0.9 (0.2-2.0)	59 1.6 (0.8-2.8)	51 2.2 (1.1-3.3)
Patients on C5i, (n) Time receiving C5i, median (IQR), years	236 1.5 (0.6-2.7)	38 1.5 (0.9-2.8)	42 0.9 (0.5-1.9)	54 1.0 (0.3-2.1)	55 1.7 (0.8-2.9)	47 2.2 (1.3-5.7)
Patients on C3i, (n) Time receiving C3i, median (IQR), years	24 0.8 (0.4-1.0)	13 0.8 (0.5-0.9)	2 1.3 (1.1-1.4)	* 	4 0.7 (0.3-1.1)	4 1.0 (0.4-2.3)

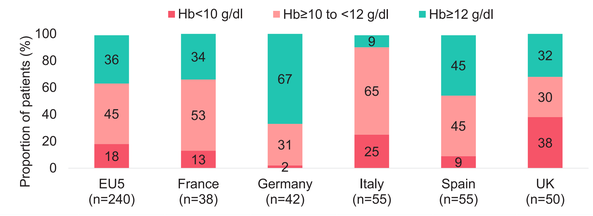
*Data at individual level (n=1) not shown to maintain patient anonymity. Ci: complement inhibitors; C5i: Complement 5 inhibitors; C3i: Complement 3 inhibitors

Figure 1. Proportion of Ci-treated patients stratified by Hb levels



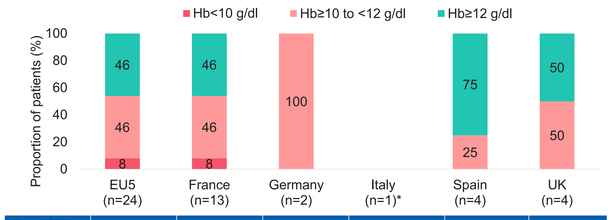
	EU5 (n=264)	France (n=51)	Germany (n=44)	Italy (n=56)	Spain (n=59)	UK (n=54)
Mean (SD), Hb g/dL	11.1 (1.5)	11.1 (1.1)	11.9 (1.2)	10.3 (1.2)	11.4 (1.2)	10.9 (2.0)

Figure 2. Proportion of C5i-treated patients stratified by Hb levels



	EU5 (n=240)	France (n=38)	Germany (n=42)	Italy (n=55)	Spain (n=55)	UK (n=50)
Mean (SD), Hb g/dL	11.1 (1.5)	11.1 (1.2)	12.0 (1.2)	10.3 (1.2)	11.3 (1.2)	10.8 (2.0)

Figure 3. Proportion of C3i-treated patients stratified by Hb levels



	EU5 (n=24)	France (n=13)	Germany (n=2)	Italy (n=1)*	Spain (n=4)	UK (n=4)
Mean (SD), Hb g/dL	11.4 (1.1)	11.4 (0.9)	10.5 (0.6)	*	12 (0.8)	11.9 (1.2)

*Data at individual level (n=1) not shown to maintain patient anonymity.

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Disclosures

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