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Clinical, Humanistic, and Economic Burden in Patients with PNH receiving C5 Inhibition Treatment Across UK, Germany, and France. Insights from the COMMODORE Burden of Illness Study

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Summary

PNH is a rare, life-threatening blood disorder. The current standard of care are C5 complement inhibitors such as eculizumab and ravulizumab which are intravenously (IV) infused

The COMMODORE Burden of Illness study aims to quantify the real-life socioeconomic burden of PNH

This poster presents the results from the first phase of the study for participants from the UK, Germany and France focusing on those receiving IV C5 inhibition treatment

The results presented suggest that patients with PNH continue to experience substantial burden of disease, which translates into considerable costs and diminished QoL

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Introduction

- Paroxysmal nocturnal haemoglobinuria (PNH) is a rare life-threatening disease[1,2].
- In several European countries (including the United Kingdom, France and Germany), the standard of care for PNH are C5 complement inhibitors, such as eculizumab and ravulizumab, both of which are typically intravenously (IV) infused[3,4].
- A study from the United States of America shows that people with PNH, treated with IV C5 complement inhibitors, have been associated with a significant burden of disease, including a diminished quality of life (QoL).[5]

Objectives

- The objective of the COMMODORE BOI study was to quantify the real-life burden of illness (BOI) associated with PNH, in the UK, France and Germany.
- The COMMODORE BOI study aimed to measure the socioeconomic burden of PNH across two phases, in order to form a longitudinal analysis.
- For the purposes of the present analyses, the focus was specifically on patients with PNH currently receiving IV C5 inhibition treatment. This poster includes the results of the first phase of this study, which measured outcomes in the 12 months prior to enrolment. The results of the second phase, which will follow patients for 6 months post-study initiation, will be disseminated at a later point.

Methods

- Physicians were asked to complete Case Report Forms (CRFs), collecting information on patient sociodemographic characteristics, as well as the clinical characteristics of their disease, over the 12 months prior to enrolment.
- Subsequently, the physicians invited the same patients, and their caregivers, to complete additional questionnaires (the Patient and Caregiver Questionnaires, respectively), that collected information on patient- and caregiver-reported outcomes (**Box 1**).
- The economic burden (measured for the 12 months prior to enrolment) was categorised as costs to the healthcare system, costs to patients, and costs to the caregivers.
- Adult participants diagnosed ≥12 months prior to study initiation were enrolled in the study between November 2021 and April 2022.
- All analyses were descriptive, and results are presented as n (%), and mean (standard deviation [SD]).

Box 1. Patient- and Caregiver-reported Outcomes

Patient-reported outcomes	Abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9)	The TSQM-9 is a tool for evaluating patient satisfaction with medication, including ratings on three scales: effectiveness, convenience, and overall satisfaction.[6]
	Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-Fatigue)	The FACIT-Fatigue is a 13-item measure that assesses self-reported fatigue and its impact upon daily activities and function.[7]
	Patient Global Impression of Severity (PGI-S)	The PGI-S is a one-item questionnaire that is used to measure a patient's perception of the severity of their sickness.[8]
	Quality-of-Life Tool for Patients with Aplastic Anaemia and/or PNH (QLQ-AA/PNH-54)	The QLQ-AA/PNH-54 measure is based off the EORTC guidelines and contains 54 items, out of which 12 dimensions can be constructed.[9]
	5 level EuroQoL 5-dimension (EQ-5D-5L)	The EQ-5D-5L consists of a set of questions covering five dimensions, each with five levels of impairment. A utility value can be calculated based on pre-defined value sets*. Additionally, the EQ-5D-5L includes a visual analogue scale (VAS), allowing patients to report their perceived health.[10]
Caregiver-reported outcomes	Carer Experience Scale (CES)	The CES is a measure of caregiver experience. The scale covers aspects related to activities, support, assistance, fulfilment, control, and getting-on with the care recipient.[11]
	Short Form 6 Dimension (SF-6Dv2)	The SF-6Dv2 is a six-dimension QoL classification, from which a continuous index for health can be generated.[12]

*As the highest proportion of participants was from France, the EQ-5D-5L utility scores were calculated based on the French value set.[13]

Patient Demographic Characteristics

- In total, 150 participants across all three countries treated with IV C5 inhibition were analysed (n=83 for France, n=26 for Germany, and n=41 for the UK), comprising 150 CRFs, 58 Patient Questionnaires, and 33 Caregiver Questionnaires.
- The mean age at enrolment was 41.0 (SD, 12.8) years and 68.7% of the participants were males.

Clinical Characteristics of the Disease

- The vast majority of the participants were diagnosed with classic PNH (92.6%), and most patients received IV eculizumab (72.7%) (**Table 1**).
- The most common clinical events in the 12 months prior to enrolment (irrespective of the time of C5 inhibition treatment initiation) are listed in **Table 1**.

Table 1. Clinical Characteristics of the Disease

Clinical Characteristic	Study Sample, n=150 participants
PNH type, n (%)	
Classic PNH	139 (92.6%)
PNH associated with another bone marrow disease	11 (7.3%)
C5 inhibition treatment, n (%)	
Eculizumab	109 (72.7%)
Ravulizumab	36 (24.0%)
Switched between eculizumab and ravulizumab	5 (3.3%)
Most common clinical events in the 12 months prior to enrolment, n (%)*	
Haemolysis	76 (50.7%)
Fatigue	63 (42.0%)
At least one thrombotic event	62 (41.3%)
Haemoglobinuria	45 (30.0%)

*Patients may be included more than once if they had multiple clinical events.

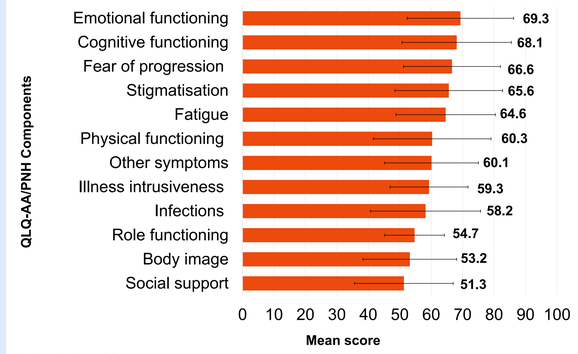
Patient and Caregiver-reported Outcomes

- Patients' treatment satisfaction was limited, as indicated by TSQM-9, with 'effectiveness' and 'convenience' scores below 65 (**Table 2**).
- The QLQ-AA/PNH-54 results are presented in Graph 1. All patients reported a diminished QoL (all dimensions scored at >50, indicating lower QoL).
- The patients' QoL, as reported via EQ-5D-5L, was also diminished (**Table 2**); while the dimension 'anxiety/depression' was the one affected the most, with several patients reporting moderate to extreme impact in this dimension of their life.
- The caregivers reported that their caring experience was relatively poor, as indicated by the CES score (**Table 2**), with the main factors affecting this score including: limited 'support from family and friends', limited 'assistance from organisations and government', and limited 'control over the caring'.
- The caregivers further reported a diminished QoL, as indicated by the SF-6Dv2 score (**Table 2**), with the main factors affecting this score including: the large amount of 'time the caregivers accomplished less than they would like at work or during other regular activities', the high level of 'bodily pain', and the high proportion of 'time they felt worn out'.

Table 2. Patient- and Caregiver-reported Outcomes

Patient-reported Outcomes, mean (SD)	n=58 Patient Questionnaires	Score Interpretation
TSQM-9 Effectiveness Convenience Overall Satisfaction	 63.2 (14.3) 64.1 (18.0) 57.4 (18.7)	Score range: 0-100; with higher scores representing higher satisfaction.
FACIT-Fatigue	28.2 (6.5)	Score range: 0-52; with higher scores indicating lower fatigue severity.
PGI-S	4.5 (2.3)	Score range: 0-10; with 10 reflecting the perception of severity of sickness 'as bad as you can imagine'.
EQ-5D-5L, Utility score	0.8 (0.2)	Utility score range: 0-1; with 1 indicating perfect health.
EQ-5D-5L, VAS score	62.0 (19.3)	VAS score range: 0-100; with higher values indicating higher perceived health.
Caregiver-reported Outcomes, mean (SD)	**n=33 Caregiver Questionnaires**	**Score Interpretation**
CES	68.9 (19.8)	Score range: 0-100; with higher scores indicating the higher caring experience.
SF-6Dv2	0.86 (0.1)	Score range: 0-1; with higher scores indicating higher utility.

Graph 1. QLQ-AA/PNH-54



Error bars indicate SD.

Economic Burden

- The total mean annual cost to the healthcare system was € 350,122.70 per patient (SD, 118,508.10), with the main cost driver being the IV C5 inhibition treatment costs (**Table 3**).
- The total mean annual cost to patients was € 3,557.70 (SD, 7,901.70), with the travel costs and costs related to loss of work comprising most of the relevant cost (**Table 3**).
- The total mean annual cost to caregivers was € 1,740.40 (SD, 3,788.70), with costs related to loss of work accounting for most of it (**Table 3**).

Table 3. Economic Burden

Mean Annual Cost to the Healthcare System, mean (SD)	n=150 CRFs
Treatment costs	€ 329,874.60 (109,002.70)
Consultation costs	€ 187.30 (236.60)
Procedures costs	€ 1,554.70 (1,272.50)
Tests costs	€ 111.40 (149.00)
Hospitalisation costs	€ 18,394.70 (39,002.10)
Mean annual total cost to the healthcare system	€ 350,122.70 (118,508.10)
Mean Annual Cost to Patients, mean (SD)	**n=58 Patient Questionnaires**
Alternative therapy cost	€ 11.40 (52.50)
Professional caregiver cost	€ 285.90 (1,036.40)
Travel costs	€ 1,649.70 (5,464.60)
Cost of work loss	€ 1,431.80 (5,809.80)
Medications cost (as paid by patient)	€ 179.00 (823.30)
Mean annual total cost to the patients	€ 3,557.70 (7,901.70)
Mean Annual Cost to Caregivers, mean (SD)	**n=33 Caregiver Questionnaires**
Cost of work loss	€ 1,345.50 (3,834.80)
Travel cost	€ 394.90 (651.40)
Total cost to the caregivers	€ 1,740.40 (3,788.70)

Conclusions

- Despite treatment with IV C5 inhibitors, the overall patient treatment satisfaction is low.
- The patient-reported QoL was lower than the normative values for several of the tools, such as the FACIT-Fatigue score (which has been reported to be 43.5) [14], and the EQ-5D-5L utility score (which has been reported to be up to 0.90)[15]; with anxiety/depression constituting a key factor.
- This study is one of the first to use and report on the results of the PNH-specific QLQ-AA/PNH-54 questionnaire. Via this tool, the patients enrolled in our study reported diminished QoL.
- In addition, the caregiver-reported outcomes indicated a relatively poor caring experience.
- The costs associated with the management of PNH patients in 12 months prior to enrolment were significant as well, and appear to be similar to those reported for other rare diseases (such as haemophilia and mucopolyssacharidosis)[16].
- The key strength of this present study was the inclusion of several patient- and caregiver-reported outcomes, which highlighted that there is remaining unmet need and disease burden in patients as well as caregivers.
- Alternative treatment options may benefit these patients.

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