Patient-reported outcomes and daily activity assessed with a digital wearable device (Fitbit™) in patients with paroxysmal nocturnal hemoglobinuria treated with ravulizumab: the REVEAL study

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INTRODUCTION

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, chronic and potentially life-threatening blood disorder.[1,2]
  - Symptoms of PNH have a significant impact on patient quality of life (QoL).[2]
- The complement component 5 (C5) inhibitors ravulizumab and eculizumab are approved for patients with PNH.[3,4]
- Patient-reported outcomes (PROs) capturing QoL or fatigue in PNH have been described in clinical trials.[5,6]
  - Data on sleep patterns, physical and mental health, daily activity and work productivity are currently limited.
- There is a paucity of data regarding the relationship between PROs and activities of daily living.

OBJECTIVE

- To characterize patient experiences during treatment with C5 inhibitors for PNH using real-world data collected from a digital wearable device (Fitbit™, San Francisco, CA, USA) and electronically collected PROs (ePROs).

CONCLUSIONS

- Patients with PNH treated with ravulizumab had levels of physical and mental health, fatigue and daily activity similar to the general US population.
- Based on the data collected to date, improvements in daily step counts, resting heart rate and sleep while on ravulizumab treatment were positively correlated with increased QoL for patients with PNH.

LIMITATIONS

- Data collected regarding baseline demographics and clinical characteristics were self-reported by the participants.
- Data may not be representative of the general PNH population, owing to the small sample size.
- Owing to the lack of age- and sex-matched data, conclusions relating to comparisons against US population normative values may be limited.

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METHODS

- REVEAL was a 32-week, prospective, non-interventional, observational cohort study in adult patients (≥ 18 years) with PNH receiving C5 inhibitors in the USA.
- Patient demographics and clinical characteristics were self-reported at baseline.
- Continuous activity data were passively collected via Fitbit™ and included:
  - physical activity
  - sleep pattern
  - heart rate.
- The minimum number of consecutive hours of device wearing required to qualify as passive data collection was 10 hours/day.
- ePRO data were collected weekly by survey and included:
  - Functional Assessment of Chronic Illness Therapy (FACIT) – Fatigue
  - Patient-Reported Outcomes Measurement Information System (PROMIS)
    - PROMIS – Sleep-Related Impairment
    - PROMIS – Sleep Disturbance
    - PROMIS – Global Physical Health
    - PROMIS – Global Mental Health
  - Work Productivity and Activity Impairment Questionnaire – Specific Health Problem (WPAI-SHP).
- Exploratory analyses were performed to correlate activity data with ePROs and to descriptively evaluate results against general US population normative values.

RESULTS

Baseline demographics and clinical characteristics

- In total, 33 adult patients were enrolled in the study (**Table 1**).
- Owing to the limited number of eculizumab-treated patients, analyses were only performed for ravulizumab-treated patients.

Summary of PRO data

- Over the study period, ePRO survey completion rate was 82% and Fitbit™ data collection rate was 81%.
- Passively collected data and ePROs reported by patients treated with ravulizumab were within the general US population normal range (**Figures 1** and **2**).

Summary of passively collected data

- Passively collected data in ravulizumab-treated patients are described in **Figure 3**.

Summary of correlations between passively collected data and PROs

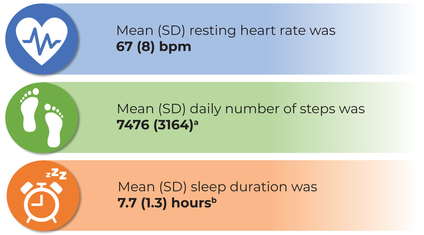
- In patients receiving ravulizumab:
  - higher daily steps were positively correlated with PROMIS – Global Physical Health and PROMIS – Global Mental Health scores (correlation coefficient [R] = 0.12; minimum false discovery rate [*q*] < 0.05)
  - lower resting heart rate was positively correlated with PROMIS – Global Physical Health score (R = 0.12; *q* < 0.05)
  - increased sleep duration was positively correlated with improvements in WPAI-SHP score (R = 0.13; *q* < 0.05).

Table 1. Baseline demographics and clinical characteristics of patients enrolled in the REVEAL study[a]

	Ravulizumab (n = 28)	Eculizumab (n = 5)	Total (N = 33)
Age, years, median (IQR)	34 (28–38)	36 (34–37)	34 (29–38)
Female gender, n (%)	15 (54)	2 (40)	17 (52)
Ethnicity, n (%)			
Hispanic or Latino	3 (11)	1 (20)	4 (12)
Non-Hispanic or Latino	25 (89)	4 (80)	29 (88)
Caucasian race, n (%)	24 (86)	4 (80)	28 (85)
Age at PNH symptom onset, years, median (IQR)	27 (21–30)	26 (25–28)	27 (21–30)
Age at PNH diagnosis, years, median (IQR)	28 (21–34)	28 (27–30)	28 (21–32)
Aplastic anemia comorbidity, n (%)	9 (32)	2 (40)	11 (33)
Clone size, %, median (IQR)	69 (35–94)	20 (1–82)	67 (20–93)

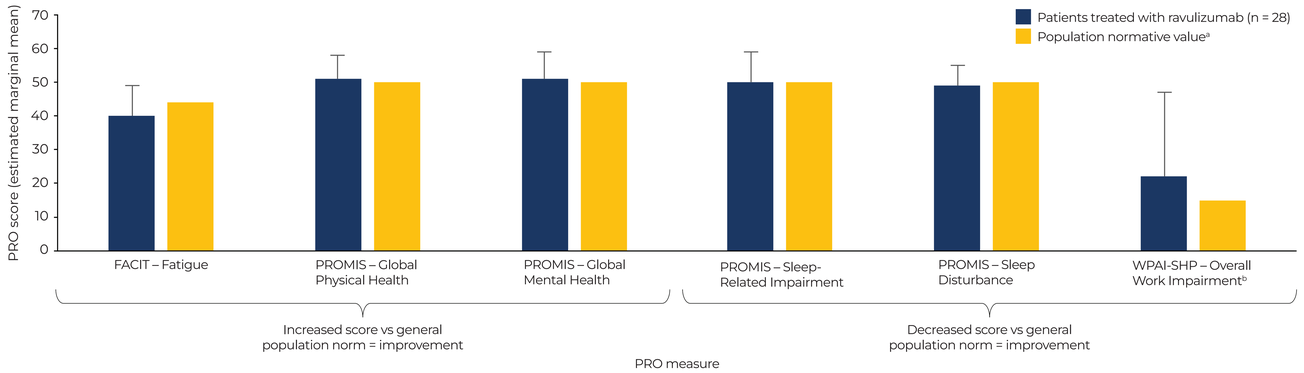
[a]Note: 3 patients who switched from eculizumab to ravulizumab during the study were excluded from the analysis.
IQR, interquartile range; PNH, paroxysmal nocturnal hemoglobinuria; SD, standard deviation.

Figure 3. Summary of passively collected data



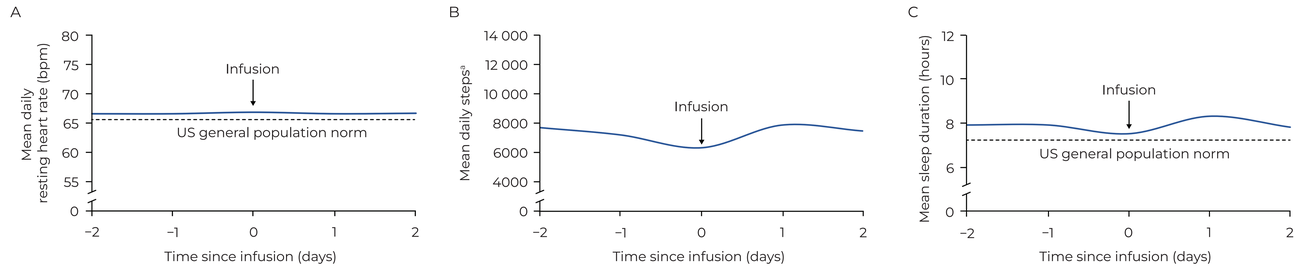
[a]A decrease to 6313 (4183) steps was observed on the day of infusion.
[b]A decrease to 7.5 (1.6) hours of sleep was observed on the day of infusion, followed by an increase to 8.3 (1.9) hours at 1 day after infusion.
bpm, beats per minute; SD, standard deviation.

Figure 1. Summary of PRO measures in patients with PNH treated with ravulizumab compared with the US general population



Values were collected longitudinally for each participant, and estimated marginal means across multiple observations per participant are shown. Whiskers represent standard deviation.
[a]Population normative values are 43.6[7] for FACIT – Fatigue, 50.0[8] for PROMIS measures and 15.0 for WPAI-SHP.[9]
[b]Five patients in the ravulizumab group were not working.
FACIT, Functional Assessment of Chronic Illness Therapy; PRO, patient-reported outcome; PROMIS, Patient-Reported Outcomes Measurement Information System; WPAI-SHP, Work Productivity and Activity Impairment Questionnaire – Specific Health Problem.

Figure 2. (A) Resting heart rate, (B) daily step count and (C) sleep duration from –2 to +2 days since infusion in patients with PNH treated with ravulizumab (n = 28)



[a]Population normative values are not presented owing to the wide range in step count (5003–18 425 steps/day).[11]
Data presented as locally estimated scatter plot smoother. Four patients were excluded from the analysis: two patients who withdrew and two who were considered to be outliers (daily number of steps > 2 SD from the mean). General population normative values for resting heart rate range from 50 bpm to 80 bpm with the mean value at 65.5 bpm.[10] General population normative values for daily steps range from 5003 steps/day to 18 425 steps/day.[11] General population normative value for mean (SD) sleep duration is 7.2 (1.0) hours.[12] Dashed lines represent US general population normative values.
bpm, beats per minute; PNH, paroxysmal nocturnal hemoglobinuria; SD, standard deviation.

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