The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

904.OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

Health-Related Quality of Life and Symptom-Specific Functional Impairment Among Patients Treated with Parenterally Administered Complement Inhibitors for Paroxysmal Nocturnal Hemoglobinuria

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Introduction: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, life-threatening, stem cell disorder that renders red blood cells vulnerable to complement-mediated hemolysis. This study describes the health-related quality of life (HRQoL) and symptom-specific functional impairment of patients with PNH in a real-world setting.

Methods: US-based adults with PNH treated with a parenterally administered complement inhibitor (PACI) for ≥ 6 months completed an online, cross-sectional, observational survey; a subset of patients also participated in individual semi-structured qualitative interviews after completing the survey. The survey included the PROMIS® 29+2 Profile v2.1 (PROMIS 29+2) to measure HRQoL. The FACIT Fatigue, Neuro-QoL Item Bank v2.0 Cognitive Function Short Form, and PROMIS Item Bank v1.0 Dyspnea Functional Limitations 10a Short Form measured functional impairment associated with specific symptoms of PNH. For each patient with PNH who completed the online survey, up to 3 age- (+/- 3 years) and sex-matched adults without PNH also completed the survey. The HRQoL and functional impairment of the PNH sample was compared to that of general population (GP) sample using independent samples t-tests or Mann-Whitney tests. To further explore the experiences of patients with PNH, the association between HRQoL/functional impairment and fatigue severity was investigated. Patients with PNH were grouped according to their self-reported fatigue severity over the past 7 days (very mild or mild vs moderate, severe, or very severe [no patients reported no fatigue]). Differences in scores across these 2 groups were tested. Data from the qualitative interviews were coded using thematic analysis to explore key concepts related to HRQoL and impairment due to PNH symptoms. Data collection began in March 2023; results are based on interim data.

Results: Demographic characteristics of the study samples (PNH survey sample: N=31, GP survey sample: N=62, PNH interview sample: N=10) are shown in Table 1. Patients were treated for PNH with eculizumab, pegcetacoplan, or ravulizumab, with an average duration of current PACI treatment of 3.4 years.

Compared to the age and sex-matched GP sample, patients with PNH had significantly higher median scores on the PROMIS 29+2 fatigue domain (GP: 48.70 vs PNH: 57.10, p=0.041) and PROMIS Dyspnea Functional Limitations short form (GP: 40.70 vs PNH: 48.60, p=0.036), indicating that patients with PNH experience more fatigue and dyspnea limitations than the GP sample. Patients with PNH also had significantly lower median scores on the PROMIS 29+2 ability to participate in social roles/activities domain (GP: 53.50 vs PNH: 44.20, p=0.013), indicating greater role/activity limitations among patients with PNH. Compared to the GP sample, patients with PNH had numerically lower (i.e., worse) median PROMIS 29+2 cognitive functioning domain scores (GP: 50.00 vs PNH: 46.30, p=0.058) and FACIT Fatigue scores (GP: 39.50 vs PNH: 30.00, p=0.057). Within the PNH sample, statistically significant associations (p<0.05) were observed between fatigue severity and HRQoL/functional impairment for all outcomes except for the PROMIS 29+2 sleep disturbance and cognitive functioning domains (Table 2). Patients with more severe fatigue had worse HRQoL and more functional impairment than patients with less severe fatigue.

Interview participants described fatigue-related functional impairments in their physical, social, and cognitive functioning. Fatigue made daily activities (e.g., cooking, cleaning, going for a walk) difficult and sometimes impossible. Planning social activities in advance was also challenging as patients could not predict how they would feel on any given day, and often found

they had to miss, postpone, or cancel social engagements. Finally, patients described experiencing "brain fog" including difficulty concentrating, forgetfulness, and delayed cognitive processing.

Conclusions: Despite receiving treatment for PNH, patients experienced deficits in areas of HRQoL related to fatigue, participation in social roles, cognitive function, and functional limitations due to dyspnea, relative to a sample of GP adults. During follow-up interviews, patients emphasized the deep and broad impacts that fatigue and cognitive functioning had, making daily activities and their social lives very difficult.

Disclosures Dingli: *Genentech:* Consultancy; *Sorrento:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy; *Apellis:* Consultancy; *Janssen:* Consultancy; *K-36 Therapeutics:* Research Funding; *Novartis:* Consultancy; *Sanofi:* Consultancy; *Alexion (AstraZeneca); Apellis Pharmaceuticals; BMS; GSK; Janssen; Novartis; Sanofi; Takeda:* Consultancy; *BioCryst:* Consultancy. **Rizio:** *Novartis Pharmaceutical Corporation:* Other: I am an employee of QualityMetric Incorporated, LLC, which received research funding from Novartis to conduct this research. **Broderick:** *Novartis Pharmaceutical Corporation:* Other: I am an employee of QualityMetric Incorporated, LLC, which received research funding from Novartis to conduct this research. **LaGasse:** *Novartis Pharmaceutical Corporation:* Other: I am an employee of QualityMetric Incorporated, LLC, which received research funding from Novartis to conduct this research. **Carty:** *Novartis Pharmaceutical Corporation:* Other: I am an employee of QualityMetric Incorporated, LLC, which received research funding from Novartis to conduct this research. **Burton:** *Novartis Pharmaceutical Corporation:* Consultancy. **Gordon:** *Novartis Pharmaceutical Corporation:* Consultancy, Honoraria. **Weigand:** *Novartis Pharmaceutical Corporation:* Consultancy. **Yen:** *Novartis Pharmaceuticals Corporation:* Current Employment, Current holder of *stock options* in a privately-held company. **Paulose:** *Novartis Pharmaceuticals Corporation:* Current Employment. **Geevarghese:** *Novartis Pharmaceutical Corporation:* Current Employment. **Lee:** *Novartis Pharmaceutical Corporation:* Current Employment.

Table 1. Characteristics of the Study Samples

Continuous Variables (years)	General Population Participants without PNH (N=62)		Patients with PNH			
			Patients who completed the online survey (N=31)		Subgroup of patients who also completed an interview (N=10)	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Age	44.7 (12.8)	45.0 (37 - 57)	45.9 (13.5)	45.0 (37 - 57)	48.9 (16.4)	50.0 (33 - 62)
Time since PNH diagnosis	--	--	11.6 (9.3)	9.3 (4.3 - 15.6)	7.0 (4.7)	5.8 (3.0 - 9.3)
Time since start of treatment with current PACI[1]	--	--	3.4 (3.4)	2.1 (1.3 - 3.9)	2.3 (1.6)	1.8 (1.3 - 3.9)
Categorical Variables	**n (%)**		**n (%)**		**n (%)**	
Sex assigned at birth						
Female	47 (75.8%)		23 (74.2%)		8 (80.0%)	
Male	15 (24.2%)		8 (25.8%)		2 (20.0%)	
Race and/or ethnicity[2]						
American Indian or Alaska Native	1 (1.6%)		1 (3.2%)		0 (0.0%)	
Asian	14 (22.6%)		2 (6.5%)		0 (0.0%)	
Black	12 (19.4%)		4 (12.9%)		1 (10.0%)	
Caucasian or White	27 (43.5%)		24 (77.4%)		8 (80.0%)	
Hispanic or Latino	6 (9.7%)		3 (9.7%)		1 (10.0%)	
Native Hawaiian or Other Pacific Islander	1 (1.6%)		1 (3.2%)		1 (10.0%)	
Other / Do not wish to answer	4 (6.5%)		0 (0.0%)		0 (0.0%)	
Current PACI treatment						
Eculizumab	--		5 (16.1%)		1 (10.0%)	
Pegcetacoplan	--		8 (25.8%)		5 (50.0%)	
Ravulizumab	--		18 (58.1%)		4 (40.0%)	

[1] 17 survey patients (54.8%) and 8 interview patients (80%) had been treated with a different PACI prior to their current one.
[2] Patients could select more than one response: percentage sums to >100%.
Abbreviations: IQR, Interquartile range; PACI parenterally administered complement inhibitor; PNH, paroxysmal nocturnal hemoglobinuria; SD, standard deviation

Table 2. Comparison of Health-Related Quality of Life and Symptom-Specific Functional Limitations between Groups of Patients with PNH Defined by Level of Fatigue Severity

Instrument	Fatigue Severity						
	Very Mild, Mild			Moderate, Severe, Very Severe			
	n	Mean (SD)	Median (IQR)	n	Mean	Median (IQR)	P
PROMIS® 29+2 Profile v2.1							
Physical Functioning ↑	12	50.85 (8.37)	57.00 (44.20, 57.00)	19	44.65 (8.00)	41.40 (39.60, 57.00)	0.033
Anxiety	12	47.13 (7.47)	45.85 (40.30, 52.80)	19	57.67 (9.92)	59.60 (51.70, 65.20)	0.005
Depression	12	44.07 (4.73)	41.00 (41.00, 48.90)	19	55.18 (10.47)	55.90 (41.00, 62.20)	0.003
Fatigue	12	48.33 (5.78)	48.60 (46.00, 50.80)	19	62.56 (5.51)	64.30 (57.10, 64.70)	<.001
Sleep disturbance	12	48.27 (10.41)	51.55 (39.15, 55.10)	19	53.73 (7.80)	52.80 (51.10, 57.50)	0.135
Ability to participate in social roles and activities ↑	12	55.15 (8.82)	55.65 (48.90, 64.20)	19	43.55 (3.89)	44.20 (42.30, 44.20)	<.001
Pain interference	12	47.90 (8.16)	41.60 (41.60, 53.90)	19	54.72 (8.55)	58.40 (41.60, 61.30)	0.033
Cognitive functioning ↑	12	50.28 (11.44)	52.60 (40.75, 61.20)	19	45.53 (5.81)	43.50 (40.50, 50.00)	0.213
Pain intensity	12	1.42 (1.98)	0.50 (0.00, 2.50)	19	3.05 (2.20)	3.00 (1.00, 4.00)	0.046
FACIT Fatigue							
Total Score ↑	12	42.08 (8.37)	44.50 (40.00, 48.00)	19	23.11 (7.39)	21.00 (18.00, 31.00)	<.001
Neuro-QOL Item Bank v2.0 – Cognitive Function – SF							
Total Score ↑	12	52.12 (11.93)	51.80 (42.15, 64.20)	19	40.44 (7.25)	38.40 (34.80, 46.50)	0.008
PROMIS Item Bank v1.0 – Dyspnea Functional Limitations – SF 10a							
Total Score	12	44.12 (10.59)	42.55 (34.80, 45.60)	19	52.19 (7.38)	52.80 (48.50, 56.70)	0.010

↑ Indicates that higher scores are better; for all other domains, higher scores are worse.

Possible score ranges: PROMIS 29+2 Profile physical functioning: 22.5-57.0, anxiety: 40.3-81.6, depression, 41.0-79.4, fatigue: 33.7-75.8, sleep disturbance: 32.0-73.3, ability to participate in social roles and activities: 27.5-64.2, pain interference: 41.6-75.6, cognitive functioning: 29.5-61.2, pain intensity: 0-10, FACIT Fatigue: 0-52, Neuro-QOL Item Bank v2.0 – Cognitive Function – SF: 17.3-64.2, PROMIS Item Bank v1.0 – Dyspnea Functional Limitations – SF 10a: 29.7-76.7

P-values for PROMIS 29+2 fatigue, sleep disturbance, and cognitive functioning domains, NeuroQOL cognitive function short form, and PROMIS dyspnea functional limitations short form are based on t-tests; all others based on Mann-Whitney test for non-normally distributed variables.

Abbreviations: IQR, interquartile range; PNH, paroxysmal nocturnal hemoglobinuria; SD, standard deviation; SF, short form

Figure 1

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