ELSEVIER

Blood 142 (2023) 3752–3753

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

904.OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

Psychometric Evaluation of the PNH Symptom Questionnaire (PNH-SQ) Among Patients with Paroxysmal Nocturnal Hemoglobinuria from Three Phase 2 Clinical Trials with Pozelimab Monotherapy or in Combination with Cemdisiran

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Background: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired, life-threatening disease caused by chronic dysregulation of the complement system. PNH has a high symptom burden with significant impacts on the life of a patient. The PNH Symptom Questionnaire (PNH-SQ) is a PNH-specific patient-reported outcome (PRO) questionnaire designed to assess daily symptom severity in patients with PNH. The objective of this current study was to evaluate PNH-SQ psychometric properties among patients with PNH from three phase 2 clinical trials with pozelimab monotherapy or in combination with cemdisiran.

Methods: PRO data from three phase 2 PNH clinical trials, study 1852 (NCT03946748; pozelimab monotherapy; n=24), study 2092 (NCT04811716; combination therapy; n=24), and study 20105 (NCT04888507; combination therapy; n=6), were used for analysis. The PNH-SQ is a patient-reported daily diary that assesses 10 core symptoms of PNH using a five-point severity scale (none; very mild; mild; moderate; severe; very severe) for fatigue, shortness of breath, muscle weakness, headaches, abdominal pain, pain in back or legs, and chest discomfort, and a five-point difficulty scale (none, not at all, a little bit, somewhat, quite, very) for difficulty sleeping, difficulty thinking clearly, and difficulty swallowing. Prespecified psychometric analyses were performed after study database lock using blinded data. Analyses included quality of completion (ie ePRO prevented item-level missingness) and item responses over time. Reliability and validity of daily assessments with classical test theory (internal consistency and test-retest reliability, construct validity by observing correlations between pairs of PNH-SQ items and of the PNH-SQ daily score with other PRO scores from the EORTC QLQ-C30, FACIT-Fatigue and EQ-5D) and Rasch measurement theory (RMT) analyses were conducted. Test-retest reliability (within stable patients 4 weeks apart) and construct validity of various exploratory methods for aggregating daily scores over time were assessed.

Results: Completion rates of PNH-SQ items were higher in studies 20105 and 2092 (at Day 1: 54.2% in 1852 vs 83.3% in 20105 and 91.7% in 2092). Fatigue was consistently the most experienced symptom at baseline of the three studies, while difficulty swallowing was not experienced by any patient. A high proportion of 'none' responses were observed across all assessments. Cronbach's alpha calculated using all daily assessments was 0.75, indicating modest reliability. The correlation between each pair of items at Day 1 ranged between 0.11 and 0.93, with the lowest correlations being observed between pain items and sleep/cognitive items, and between abdominal pain and fatigue/dyspnea. At Day 1, PNH-SQ daily score trended higher according to the Patient Global Impression of Severity (PGIS)-symptoms categories and showed moderate correlations in expected direction with fatigue and pain, as assessed by FACIT-Fatigue and EORTC QLQ-C30, and lower correlations with dyspnea and overall health status (EQ-5D visual analog scale). RMT analyses of the daily PNH-SQ data highlighted that for response options "Very mild" for severity/"Not at all" for difficulty did not provide any useful information. RMT also uncovered a meaningful hierarchy of symptoms ranging from fatigue to difficulty swallowing. A fixed 7-day average led to the best test-retest reliability (intraclass correlation coefficient, 0.76).

Conclusions: Our analyses documented the PNH-SQ as an instrument to capture symptoms of PNH. The most frequent symptoms reported in our sample using the PNH-SQ, fatigue, dyspnea, and headaches, were aligned with observational study data. The sample of observations from the three trials was strongly skewed towards absence of symptoms, probably reflecting the low symptomatic severity of patients included in the study. Despite this restriction, early supportive data for the scoring of the PNH-SQ from a sample of patients with PNH were obtained, generating useful insights into the function of the response scales, opportunities for the creation of daily assessments of symptom severity, and for the creation of a measure

reflecting severity over a longer period, for which a fixed 7-day average appeared as a potential good scoring approach. Generating further evidence, especially in a sample of more symptomatic patients, is recommended to substantiate these results.

Disclosures Hartford: *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current holder of *stock options* in a privately-held company. **Eusebi:** *Modus Outcomes, a Division of THREAD:* Current Employment. **Kelly:** *Otsuka:* Honoraria; *Biologix:* Honoraria, Speakers Bureau; *Abbvie:* Membership on an entity's Board of Directors or advisory committees; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Astellas:* Honoraria, Speakers Bureau; *Pfizer:* Honoraria, Speakers Bureau; *Jazz:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Sobi:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Alexion:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. **Alin:** *Modus Outcomes, a Division of THREAD:* Current Employment. **Yang:** *Modus Outcomes, a Division of THREAD:* Current Employment. **Regnault:** *Geron:* Consultancy; *Modus Outcomes:* Current Employment. **Delevry:** *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current holder of *stock options* in a privately-held company. **Lum:** *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current holder of *stock options* in a privately-held company. **Rofail:** *Regeneron Pharmaceuticals, Inc.:* Current Employment, Current holder of *stock options* in a privately-held company.

https://doi.org/10.1182/blood-2023-181667