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508.BONE MARROW FAILURE: ACQUIRED

Real-World Treatment Outcomes of Paroxysmal Nocturnal Hemoglobinuria (PNH) Patients Treated with Pegcetacoplan and Complement Protein 5 Inhibitors (C5i)

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Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, potentially fatal disease characterized by complement-mediated hemolysis which clinically manifests with symptoms including fatigue, weakness and, in severe cases, thrombosis. Previous disease-modifying treatments solely comprised of complement protein 5 inhibitors (C5i) which effectively reduce intravascular hemolysis (IVH) in most patients with PNH. However, due to residual IVH and emerging extravascular hemolysis (EVH), complement protein 3 inhibitor (C3i), pegcetacoplan (PEG) has been recently approved to target the complement cascade further upstream, tackling both IVH and EVH. The aim of this study was to report real-world outcomes of PEG-treated and C5i-treated patients.

Data were drawn from the Adelphi PNH Disease Specific Programme (DSP)™, a real-world, cross-sectional survey of physicians and their patients with PNH in France, Italy, Germany, Spain and the United States of America from January - November 2022. Patients were eligible for inclusion if they had received PEG for ≥1 month. Physicians recorded patient demographics, hemoglobin (Hb) levels, treatment administration and hospitalizations. The same patients were invited to self-report on symptomatology, fatigue via the Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) questionnaire, and impact on work and productivity via the Work Productivity and Activity Impairment (WPAI) questionnaire. Descriptive statistics were reported for patients receiving PEG from the DSP and from previously published data describing patients receiving C5i treatment (Panse, J et al. Eur J Haematol. 2022 Oct;109(4):351-363 [1]; Sicre de Fontbrune F et al. Hematology. 2022 Dec;27(1):1140-1151 [2]).

Fourteen physicians reported data for 61 patients receiving PEG. Mean (standard deviation; SD) age was 37.1 (11.3) years and 59.0% of patients were male. Mean (SD) time since diagnosis was 3.7 (3.3) years and mean (SD) time receiving PEG was 5.9 (4.0) months. All patients received 1080 mg dose of PEG, with 98.3% of patients receiving this dose twice weekly. For PEG-treated patients mean (SD) Hb from the most recent result was 11.5 (1.6) g/dL and 34.4% of patients had Hb >12 g/dL. Published literature based on a real-world survey reported C5i-treated patients had a mean (SD) Hb of 10.2 (2.0) g/dL and 14.3% had Hb >12 g/dL [1]. C5i-treated patients had mean (SD), 0.4 (1.0) emergency room (ER) visits during the 12-months prior to data collection [2]. In the DSP sample, no patients required ER visits during the time they were receiving PEG. Thirty PEG-treated patients provided self-reported data with less reporting to experience shortness of breath (23.3% vs 46.5%), difficulty swallowing (10.0% vs 19.7%) and abdominal pain (16.7% vs 19.7%) at the time of survey than C5i-treated patients [1]. At the time of survey 83.3% of PEG-treated patients reported fatigue (63.4% C5i patients in the literature [1]). PEG-treated patients reported a mean (SD) FACIT-F score of 37.4 (8.6). C5i-treated patients reported 35.0 (13.7) [1]. 73.5% of PEG-treated patients were employed, 2.5% reported absenteeism and 22.4% reported overall activity impairment. For previous literature regarding C5i patients this was 57.7%, 10.2% and 37.5%, respectively [1].

We assessed previously published literature of C5i-treated patients and demonstrated favorable outcomes for PEG-treated patients across the endpoints assessed in this analysis. Patients receiving PEG reported higher Hb and FACIT-Fatigue scores than C5i-treated patients. More PEG-treated patients remained in paid employment and reported less impact on their daily

activities than C5i-treated patients. Further research is required to explore the real-world effectiveness of PEG compared to other therapeutic options and understand how newer therapies can improve outcomes for patients with PNH.

Disclosures Majerus: *Alexion:* Speakers Bureau; *Apellis:* Membership on an entity's Board of Directors or advisory committees; *Genetech:* Membership on an entity's Board of Directors or advisory committees; *Spark therapeutics:* Membership on an entity's Board of Directors or advisory committees. **Wilson:** *Swedish Orphan Biovitrum AB:* Current Employment. **Fishman:** *Apellis Pharmaceuticals:* Current Employment, Current equity holder in publicly-traded company. **Mellor:** *Swedish Orphan Biovitrum Ltd:* Consultancy. **Earl:** *Swedish Orphan Biovitrum Ltd:* Consultancy. **Roeth:** *Novartis:* Consultancy, Honoraria; *Biocryst:* Consultancy, Honoraria; *Roche:* Consultancy, Honoraria, Research Funding; *Bioverativ:* Consultancy, Honoraria; *Sanofi:* Consultancy, Honoraria; *Alexion, AstraZeneca Rare Disease:* Consultancy, Honoraria; *Apellis Apellis Pharmaceuticals:* Consultancy, Honoraria.

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