P840 A MATCHING-ADJUSTED INDIRECT COMPARISON OF THE EFFICACY OF PEGCETACOPLAN USING PRINCE TRIAL DATA VERSUS RAVULIZUMAB AND ECULIZUMAB IN COMPLEMENT-NAÏVE PATIENTS WITH PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

Topic: Bone marrow failure syndromes incl. PNH - Clinical

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Background: Pegcetacoplan (PEG) is a PEGylated peptide targeting proximal complement protein C3 that has been shown to control both intravascular and extravascular hemolysis and recently approved by the FDA and EMA for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). PRINCE (NCT04085601), was a phase-3, randomized, open-label trial assessing the efficacy and safety of PEG compared to control (CTL) treatment, excluding complement inhibitors among treatment naïve patients with PNH. PEG demonstrated superior efficacy to CTL by improving hemoglobin (Hb) levels and reductions in lactate dehydrogenase (LDH) levels in patients with PNH. To date, no head-to-head clinical trials exist comparing PEG to complement inhibitors in treatment naïve patients.

Aims: To assess the comparative effectiveness of PEG for complement-naïve patients with PNH against ravulizumab (RAV) and eculizumab (ECU) using matching-adjusted indirect comparison (MAIC) methodology to conduct cross-trial comparisons.

Methods: Individual patient data from PRINCE as well as aggregated published results of RAV and ECU in the ALXN1210-PNH-301 (“301”) study (Lee et al. 2019) were used. To adjust for cross-study differences, propensity score weighting was developed using logistic regression analyses and used to balance demographic and clinical characteristics between the PEG arm and RAV and ECU arms from 301. Outcomes were compared at 26 weeks using unanchored MAIC between PEG versus RAV and PEG versus ECU and included mean and percent change in LDH levels from baseline, LDH normalization (defined as LDH levels dropping <1xULN [246 U/L] in the absence of transfusions during the randomized controlled period), Hb stabilization (defined as the avoidance of a ≥2 g/dL decrease in hemoglobin level in the absence of transfusions during the randomized controlled period), and transfusion avoidance. Weighted Wald tests and 95% confidence intervals were computed for comparisons of categorical and continuous outcomes.

Results: A total of 34 patients were included in the PEG arm, 125 patients in the RAV arm, and 121 patients in the ECU arm. Prior to matching, significant differences existed between arms in the proportion of patients with White and American Indian or Alaska Native race, and mean LDH (all p<0.001). After matching the PEG to the RAV and ECU arms, separately, most patient characteristics were well balanced with a mean age of 43.8 years, 44.8 years, 46.2 years, respectively, 43.0-50.0% females, and a mean Hb of 9.4-9.6g/dL across arms; however, there were significant differences in Asian race and baseline LDH (all p<0.01). At week 26, patients in the PEG arm showed a significantly greater improvement in their LDH levels from baseline, with a mean of -523 U/L (-11.2%) compared to RAV and -578 U/L (-12.0%) compared to ECU (all p<0.001; Figure 1). Patients receiving PEG also showed significant improvements in LDH normalization (35.6% compared to RAV, p<0.001; 39.6% compared to ECU, p<0.001), Hb stabilization (28.2% compared to RAV, p<0.001; 31.7% compared to ECU, p<0.001), and transfusion avoidance (22.6% compared to RAV, p<0.001; 30.1% compared to ECU, p<0.001; Figure 1).
Summary/Conclusion: In the absence of head-to-head comparisons, this unanchored MAIC study shows that PEG is more efficacious versus RAV and ECU in complement inhibitors treatment naïve PNH patients in terms of significant improvements across all evaluated endpoints, Hb stabilization, LDH improvement, LDH normalization and transfusion avoidance.