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Evaluation of Patients with PNH Treated By Eculizumab: Real World Data from Turkey

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Introduction: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare disease which is characterized with complement mediated intravascular hemolysis, bone marrow failure and thrombosis. The prevelance of PNH is estimated 1 to 16 cases per million in USA. X-linked somatic mutation of phosphatidylinositol glycan#A (*PIGA*) gene in hematopoetic stem cells causes an impairment of glycosylphosphatidylinositol (GPI) anchored proteins. The absence of GPI#dependent molecules that are CD55 (decay accelerating factor; DAF) and CD59 (membrane inhibitor of reactive lysis; MIRL), normally protect the cell from complement#mediated hemolysis by preventing the formation of the membrane attack complex. The diagnosis is based on flow cytometry which can detect the deficiency of these two complement regulary proteins. We report a retrospective analysis of demographic and clinical characteristics of PNH patients from different centers.

Material and methods: We conducted a retrospective analysis of the patients' recorded data. Patients' demographics, medical and treatment history, comorbid conditions, PNH clone size, disease characteristics and outcomes, symptoms, PNH-specific treatments, PNH-related events, morbidity (including myeloproliferative disease, other malignancies, and infections), mortality. Clinical data captured include lactate dehydrogenase (LDH) levels, PNH clone size, hemoglobin levels, thrombotic events,

renal functional tests at the time of diagnosis, and other laboratory data. Specific information collected for eculizumab-treated patients includes dosage and dose adjustments and blood cell counts, reticulocyte count and LDH level after eculizumab treatment.

Results: 138 patients were included from 28 different centers. All patients were diagnosed by flow cytometry for GPI-linked antigens on red cells and neutrophils. The number of male (69/138) and female (69/138) patient was equal and the median age was 41 years. Median hemoglobin (hb) level was 8.75±2.13 gr/dL; Platelet (plt) level was 131× 10^9/L at the time of diagnosis. Overall, 49(35,5%) of the patients had been diagnosed with bone marrow failure, including aplastic anemia or hypoplastic anemia (n=31; 22,5%), myelodysplastic syndromes (n=18; 13%). A history of any prior thrombotic event was reported in 45 patients (32,6%). At the time of analysis, 12 (8,7%) patients had pulmonary hypertension. The median granulocyte and monocyte clone size was 63,6% (±32.26) and 66.76 ±28.75 respectively. Fatigue (58%) is the most commonly reported symptom and abdominal pain was seen in 8% of patients. After the eculizumab therapy, the median time for normalization of Hb and LDH level were 7 and 14,6 months, respectively. There was no correlation between thrombosis and clone size, hb, plt, LDH level at the time of diagnosis. LDH level was higher in fatigue patients compared with the patients who were not fatigue (p=0.021).

Discussion: PNH is a clonal but non malignant disease that is very rare and knowledge on large case series is really limited. The clinical findings and symptoms could be variable and unfortunately it takes very long time to diagnose because of unawareness of physicians. Eculizumab is a good option in treatment of PNH for improving symptoms of intravascular hemolysis but we still need better understanding of thrombosis mechanism of PNH to better management. In the future, novel inhibitors of the alternative pathway of complement will be used to improve survival and quality of life for PNH patients.

Disclosures

No relevant conflicts of interest to declare.

Author notes

*Asterisk with author names denotes non-ASH members.