CURRENT AND FUTURE HORIZONS IN THE MANAGEMENT OF PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

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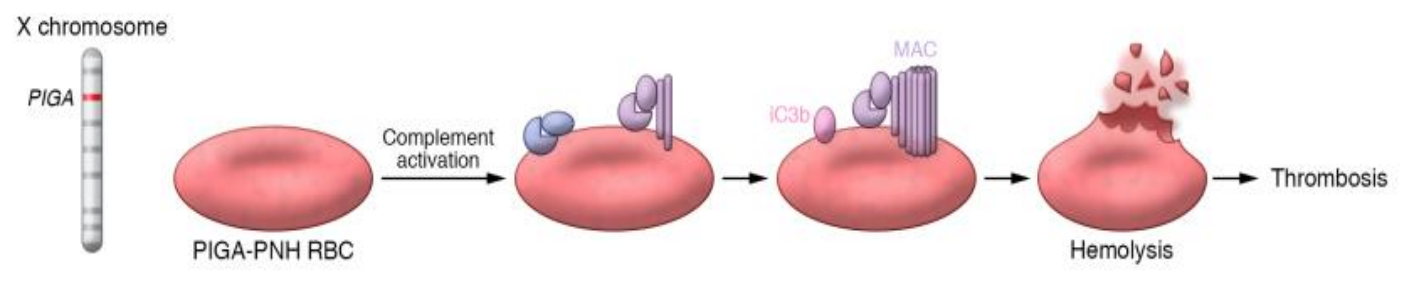
Introduction: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal hematopoietic stem cell disorder characterized by hemolysis, bone marrow dysfunction, and thrombosis, primarily due to a somatic mutation in the PIGA gene. Here, we explore the current therapeutic strategies and emerging treatments for PNH.

Material and Methods: A literature review was conducted using PubMed and Scopus databases to identify relevant studies published from 2016 to 2024. Keywords such as Paroxysmal Nocturnal Hemoglobinuria, PNH treatment, Eculizumab, Ravulizumab, Complement inhibitors, Gene therapy PNH, Emerging therapies PNH, Factor D inhibitors, and Factor B inhibitors were utilized.

Results: The introduction of eculizumab, a complement C5 inhibitor, has revolutionized PNH treatment by significantly improving patient outcomes and altering the disease's natural history. However, emerging unmet clinical needs have driven the development of novel complement inhibitors targeting different components of the complement cascade. Ravulizumab, another C5 inhibitor with more favorable pharmacokinetics, has been approved and offers the advantage of less frequent dosing. Additionally, pegcetacoplan, a C3 inhibitor, has been introduced to address C3-mediated extravascular hemolysis, providing a broader complement pathway inhibition. Novel anti-C5 agents, including long-lasting monoclonal antibodies, small molecules for subcutaneous administration, and small interfering RNA, are in clinical development, aiming to enhance patient compliance and achieve more profound C5 inhibition. Upstream complement inhibitors, such as compstatin and its derivatives, and inhibitors of complement factors D and B are also being explored to prevent intravascular and extravascular hemolysis, potentially leading to improved hematological responses.



Robert A. Brodsky, Paroxysmal nocturnal hemoglobinuria without GPI-anchor deficiency, J Clin Invest. 2019;129(12):5074-5076.

Conclusion: In conclusion, the landscape of PNH treatment is rapidly evolving, with a shift towards targeted therapies that address the underlying complement dysregulation characteristic of the disease.