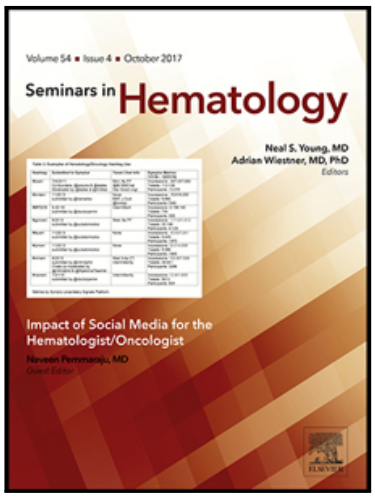

C3-mediated extravascular hemolysis in PNH on eculizumab: mechanism and clinical implications

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C3-mediated extravascular hemolysis in PNH on eculizumab: mechanism and clinical implications.

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Abstract

The introduction of eculizumab, a human monoclonal antibody against the C5 component of complement, has changed radically the management of paroxysmal nocturnal hemoglobinuria (PNH). The blockade of the terminal complement pathway by eculizumab eculizumab abrogates intravascular hemolysis, reduces the transfusion requirement and the risk of thrombosis in most of hemolytic PNH patients. However, in almost all PNH patients on eculizumab arises a fraction of PNH red cells that bind fragments of C3 and become a potential target of phagocytosis by macrophages. Eventually, this phagocytosis results in a variable degree of extravascular hemolysis that may reduce clinical benefits of eculizumab and, in fact, about one fourth of patients remain transfusion-dependent.

The treatment of the few PNH patients in which this *de novo* extravascular hemolysis become clinically relevant is still unsatisfactory. Nevertheless, the investigations of the mechanisms responsible of the extravascular hemolysis on eculizumab have resulted in the development of novel strategies for complement blockade that could overcome this condition.