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POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

The Change of Complement Deposition after Complement Inhibitor Treatment in Paroxysmal Nocturnal Hemoglobinuria Patients

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Background: Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired hematopoietic stem cell disease in which abnormal complement activation results in hemolysis and thromboembolic events (TEE). Complement inhibitors (CI) have been proved to be able to suppress intravascular hemolysis (IVH) and reduce the risk of TEE. Few studies were available on the changes of complement deposition after CI and their relationship with efficacy.
Methods: PNH patients treated with full dose eculizumab, crovalimab or iptacopan at Peking Union Medical Colleague Hospital from Oct 2021 to Jul 2023 were enrolled.Patients' clinical information and blood samples were collected after 0, 1, 3, 6, 9 and 12 months of treatment. The deposition of C5b-9, C3, C4b and factor B (FB) on peripheral red blood cells (RBC), white blood cells (WBC) and platelets (PLT) was detected by double-color staining flow cytometric assay. The efficacy of each CI was correlated with complement deposition levels on three blood lineages.
Results: 23 PNH patients were enrolled. Among them, 13 patients were treated with C5 inhibitors (4 with eculizumab and 9 with crovalimab), 10 were treated with iptacopan (FB inhibitor). For patients treated with eculizumab, C5b-9+/RBC and C5b-9+/WBC significantly decreased after 3, 6 and 12 months of treatment($P<0.05$); however, C3+/WBC and C3+/PLT significantly increased after 12 months ($P<0.05$). For covalimab-treated patients, C5b-9+/RBC significantly decreased after 6 and 12 months ($P<0.05$), while C3+/RBC, C3+/WBC, C4b+/RBC and C4b+/WBC increased ($P<0.05$) after 6 months. For those treated with iptacopan, after 1, 3, 6, 9 and 12 months, the deposition of C5b-9 on all three blood lineages significantly decreased ($P<0.05$), meanwhile, C3 and FB on all three lineages decreased ($P<0.05$); moreover, C4b+/WBC and C4b+/PLT decreased after 3, 6, 9 and 12 months ($P<0.05$). C5b-9+/RBC and C5b-9+/WBC were significantly associated with hemoglobin improvement after eculizumab treatment ($P=0.004$ and 0.018, respectively). C5b-9+/RBC was positively correlated with bilirubin ($P=0.023$) and C3+/RBC was positively correlated with absolute reticulocyte counts (Ret, $P=0.001$) after crovalimab treatment. After iptacopan treatment, C3+/RBC was positively correlated with Ret ($P=0.010$), C4b+/RBC was positively correlated with Ret ($P=0.032$) and lactose dehydrogenase (LDH, $P=0.003$), and FB+/RBC was positively correlated with LDH.
Conclusion: Complement inhibitors could effectively reduce C5b-9 deposition. Unlike C5 inhibitors, iptacopan also reduced the deposition of C3, C4b, and FB. C5b-9+/RBC may be correlated with the efficacy of inhibiting intravascular hemolysis. Upstream complement deposition is probably associated with breakthrough hemolysis or extravascular hemolysis.
Key words Paroxysmal nocturnal hemoglobinuria, complement inhibitor, complement deposition, flow cytometric assay, hemolysis

Disclosures No relevant conflicts of interest to declare.

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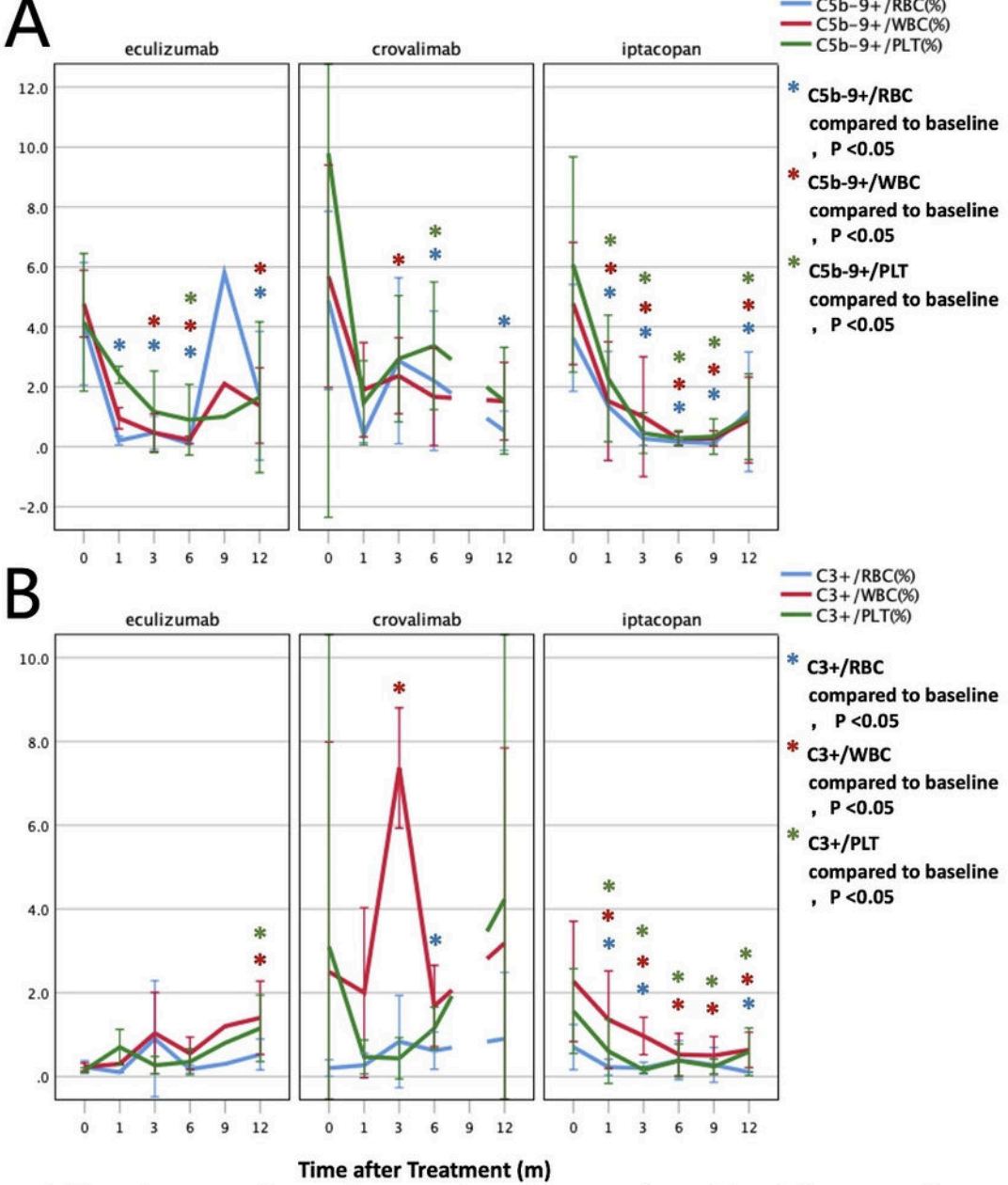

Figure 1. The changes of complement deposition on three blood lineages after eculizumab, crovalimab and iptacopan treatment compared with baseline

A. The changes of C5b-9+/RBC (%, mean ± standard deviation), C5b-9+/WBC and C5b-9+/PLT after each complement inhibitor treatment

B. The changes of C3+/RBC、C3+/WBC、C3+/PLT after each complement inhibitor treatment

Note: RBC，red bolld cell; WBC，white blood cell；PLT，platelet.

* This indicates a statistically significant difference from baseline at the time point.

Figure 1