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Letter

Complement inhibition in severe COVID-19 – Blocking C5a seems to be key

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With great interest we read the report by Annane and colleagues describing the effect of blocking complement factor C5 with the antibody eculizumab in patients with severe COVID-19 [1]. Results of this non-controlled study show an important proof of principle of complement inhibition therapy in patients with severe COVID-19. Increasing evidence point towards a critical role of the proinflammatory anaphylatoxin C5a in the pathogenesis of severe COVID-19 [2–4]. A previous study showed that controlling the anaphylatoxin C5a in disease requires a specifically targeted inhibition [5].

The authors mention that frequency and dosage of eculizumab had to be increased during the study to achieve complete and sustained complement inhibition [1]. Concentrations of C5a during the study of patients treated with or without high or higher dose eculizumab may provide important information about the potential of complement inhibition in COVID-19. Alternatively, selective approaches blocking C5a could be preferred. We recently published results of a phase 2 trial, showing that selective C5a inhibition with vilobelimab is safe in patients with severe COVID-19, with secondary outcome results in favour of vilobelimab [4]. Because blockade of an upstream component in the complement pathways will inevitably affect the formation of the membrane attack complex, such upstream intervention might put patients with COVID-19 at risk of secondary bacterial infections. The authors could provide more insight in this issue by presenting C5a concentrations of patients treated with eculizumab, with a breakdown for initial and high dose of eculizumab.

Declaration of Competing Interest

Dr. Vlaar reports personal fees from InflaRx, outside the submitted work. All other authors declare no competing interests.

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