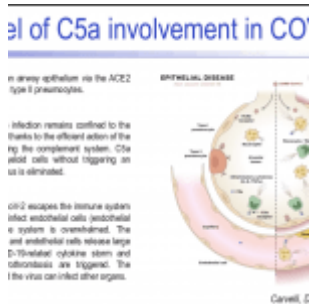


IUIS Webinar: Involvement of C5a-C5aR1 axis in COVID-19 pathology



In a recent IUIS Webinar, Eric Vivier presented data on longitudinal analysis of immune responses in the blood and bronchoalveolar lavage fluid (BALF) of patients at various stages of COVID-19 severity: paucisymptomatic, pneumonia and acute respiratory distress syndrome (ARDS). Highlights of his webinar include:

- Description of how SARS-CoV-2 (as well as SARS-CoV, MERS-CoV) N proteins bind to MASP-2, which leads to activation of complement component 5a (C5a) and aggravated lung damage. C5a has also been shown to drive pathogenesis of several viral-induced pneumonia and ARDS, and he specifically showed that levels of C5a increased with COVID-19 disease severity.
- C5a can bind to C5a receptor 1 (C5aR1) which is expressed on neutrophils and myeloid cells. He presented data that demonstrated upregulation of C5aR1+ cells in BALF from COVID-19 patients.
- Anti-C5aR1 therapeutic monoclonal antibodies, Avdoralimab, prevented C5a-mediated human myeloid cell recruitment and activation and inhibited acute lung injury (ALI) in human C5aR1 knockin mice. These results support C5a-C5aR1 axis blockade as a means of limiting myeloid cell infiltration in damaged organs and preventing the excessive lung inflammation and

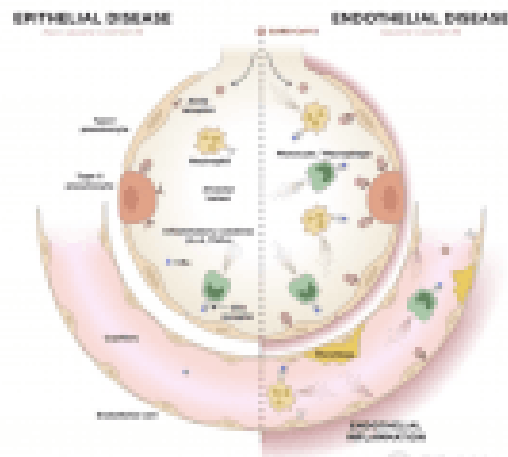
endothelialitis associated with ARDS in COVID-19 patients. (Proposed mechanism is described in the figure below)

A model of C5a involvement in COVID-19

SARS-CoV-2 infects the human airway epithelium via the ACE2 receptors located primarily on type II pneumocytes.

In non-severe COVID-19, the infection remains confined to the epithelium (epithelial disease), thanks to the efficient action of the innate immune system involving the complement system. C5a allows the recruitment of myeloid cells without triggering an inflammatory storm, and the virus is eliminated.

In severe COVID-19, SARS-CoV-2 escapes the immune system and crosses the epithelium to infect endothelial cells (endothelial disease). The innate immune system is overwhelmed. The myeloid cells recruited by C5a and endothelial cells release large amounts of IL-6. The COVID-19-related cytokine storm and endothelialitis-associated microthrombosis are triggered. The patient's condition worsens and the virus can infect other organs.

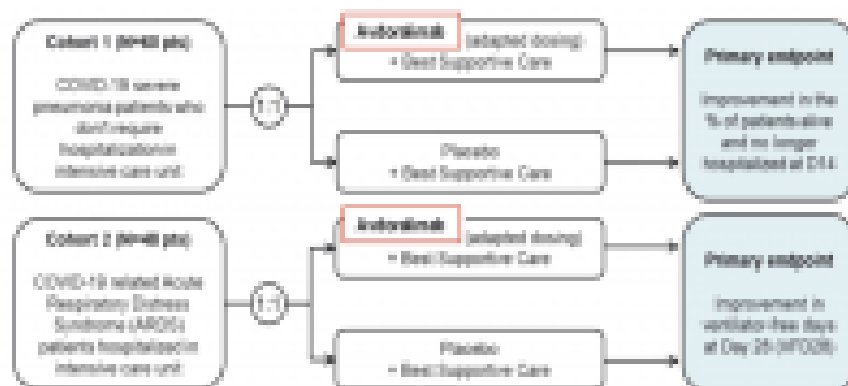


- [Finally, he ended his talk describing the design of a randomised clinical trials that will test Avdoralimab as a potential COVID-19 treatment](#)

Clinical trial – Force

Avdoralimab as a potential treatment for COVID-19 pneumonia

1. Objective: to reduce disease morbidity and/or mortality in a clinically relevant manner in Patients with COVID-19 pneumonia or COVID-19 ARDS



Summary by Cheleka AM Mpande