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## **Immunomodulation**

Immunomodulation is modulation (regulatory adjustment) of the immune system. It has natural and human-induced forms, and thus the word can refer to the following:

Homeostasis in the immune system, whereby the system self-regulates to adjust immune responses to adaptive rather than maladaptive levels (using regulatory T cells, cell signaling molecules, and so forth) Immunomodulation is part of immunotherapy, in which immune responses are induced, amplified, attenuated, or prevented according to the rapeutic goals.

Cerebral venous thrombosis caused by vaccine-induced immune thrombotic thrombocytopenia (VITT-CVT) is a rare adverse effect of adenovirus-based SARS-COV2 vaccines. In March 2021, after autoimmune pathogenesis of VITT was discovered, treatment recommendations were developed. This comprised immunomodulation, nonheparin anticoagulants, and avoidance of platelet transfusion. The aim of the study was to evaluate adherence to these recommendations and their association with mortality.

Scutelnic et al. used data from an international prospective registry of patients with CVT after adenovirus-based SARS-CoV-2 vaccination. We analyzed possible, probable, or definite VITT-CVT cases included until 18 January 2022. Immunomodulation entailed the administration of intravenous immunoglobulins and/or plasmapheresis.

99 VITT-CVT patients from 71 hospitals in 17 countries were analyzed. Five of 38 (13%), 11/24 (46%), and 28/37 (76%) of patients diagnosed in March, April, and from May onwards, respectively, were treated in-line with VITT recommendations (p<0.001). Overall, treatment according to recommendations had no statistically significant influence on mortality (14/44 (32%) vs 29/55 (52%), adjusted OR 0.43 (95%CI 0.16-1.19)). However, patients who received immunomodulation had lower mortality (19/65 (29%) vs 24/34 (70%), adjusted OR 0.19 (95%CI 0.06-0.58)). Treatment with nonheparin anticoagulants instead of heparins was not associated with lower mortality (17/51 (33%) vs 13/35 (37%), adjusted OR 0.70 (95%CI 0.24-2.04)). Mortality was also not significantly influenced by platelet transfusion (17/27 (63%) vs 26/72 (36%), adjusted OR 2.19 (95%CI 0.74-6.54)).

In VITT-CVT patients, adherence to VITT treatment recommendations improved over time. Immunomodulation seems crucial for reducing mortality of VITT-CVT 1).

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