MedicalXpress

ANCA-associated vasculitis: The ADVOCATE study

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ANCA-associated vasculitis (AAV) is a systemic disease involving the formation of special autoantibodies (so-called anti-neutrophil cytoplasmic antibodies/ANCA) and vascular inflammation. There are several diseases associated with involvement of the kidneys, lungs, upper respiratory tract, heart, skin and the nervous system; potentially life-threatening courses of disease are also possible.

Immunosuppressive therapy is provided, which can lead to infections as a known side effect, among others. Modern immunosuppressants (e.g. rituximab, an anti-CD20 monoclonal antibody) do not block the entire immune system as corticoids, for example, do, but only parts of it, so other pathways of the immune system continue to work.

A role in AAV pathogenesis is also played by the complement system of the immune system, especially complement factor C5a. Neutrophil leukocytes have immunostimulating C5a receptors (C5aR). Avacopan (formerly CCX168) is an orally selective C5aR antagonist that inhibits C5a-induced activation of immune cells and thus AAV—as already demonstrated in two clinical Phase II trials.

The phase III ADVOCATE trial evaluated the safety and efficacy of avacopan—also with regard to lower doses of glucocorticoids being needed with avacopan. Patients were randomized 1:1 and received, over a total of 52 weeks, either the glucocorticoid prednisone (n=164) or avacopan (n=166) in combination with a) cyclophosphamide (oral or intravenous) followed by azathioprine or b) four infusions of rituximab

(RTX). Patients were stratified on the basis of treatment (RTX i.v., or orally administered cyclophosphamide), the specific type of ANCA and newly diagnosed or relapsing AAV disease. Response to treatment (remission, primary endpoint) was defined as BVAS=0 (disease activity according to the "Birmingham Vasculitis Activity Score") plus prednisone tapering (at least four weeks before week 26). Sustained remission was present if there was no relapse from week 26 to 52.

At Week 26, 72.3% subjects achieved remission in the avacopan compared to 70.1% in the prednisone group (p