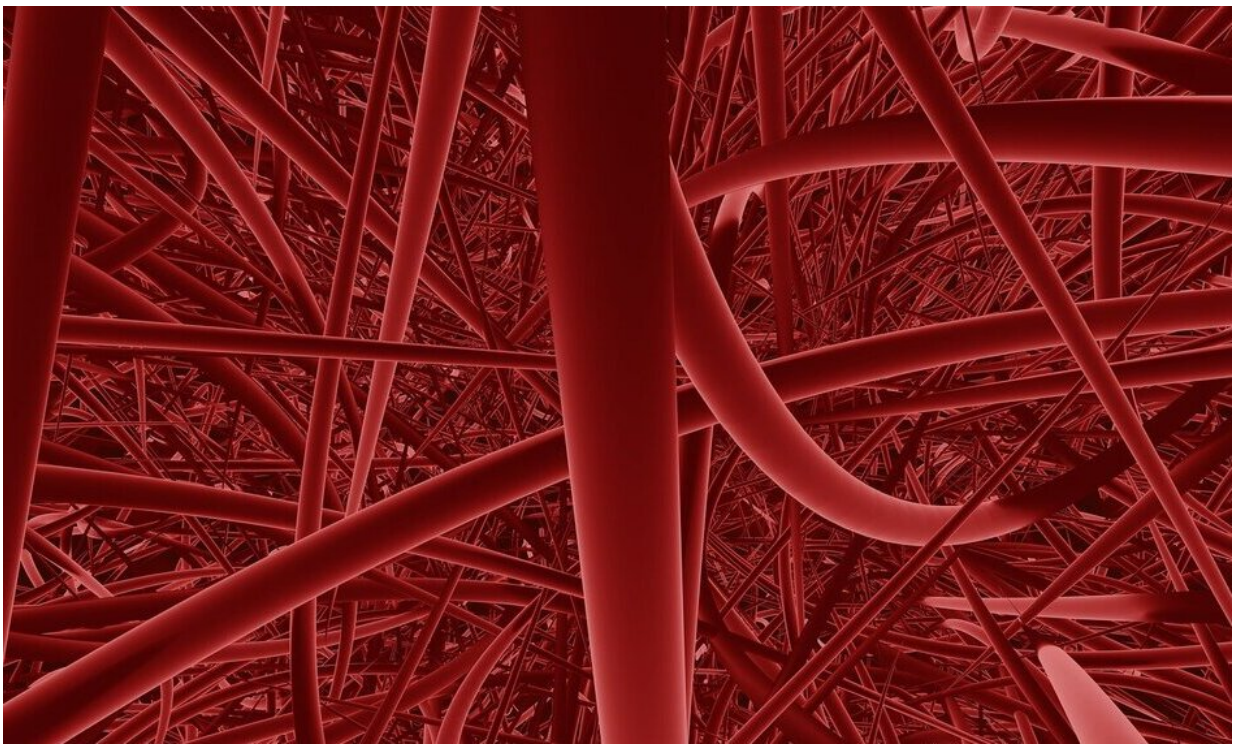
Medication keeps more patients with ANCA-associated vasculitis in remission than steroids

February 17 2021



Credit: Pixabay/CC0 Public Domain

A Phase 3 clinical trial showed a new medication that interferes with part of the immune system that causes inflammation was more effective than treatment with glucocorticoids ("steroids" such as prednisone) in

keeping patients with ANCA-associated vasculitis, a disease that causes the destructions of the body's small blood vessels, in remission for a year. The researchers behind the trial believe that a treatment approach that avoids the use of prednisone might significantly reduce many side effects patients experience. These results were published in the *New England Journal of Medicine* today.

"This is a whole new class of medication for the treatment of autoimmune disease that provides beneficial effects without the negatives we see when glucocorticoids like prednisone or other similar drugs are used," said the trial's co-primary academic investigator Peter A. Merkel, MD, MPH, the chief of Rheumatology in the Perelman School of Medicine at the University of Pennsylvania and director of the international Vasculitis Clinical Research Consortium. "Importantly, avacopan appears to work rapidly and thus may prevent the accumulation of disease-related damage in this form of vasculitis."

ANCA-associated vasculitis is a disease that occurs when the body's white blood cells attack and destroy the body's small blood vessels. This can affect many organs across the body, including kidneys, lungs, nerves, and other areas. Approximately one in 50,000 people are stricken with the disease, whose cause is undetermined. Untreated, it is deadly, but treatment markedly increases the disease's survivability.

Currently, treatment for ANCA-associated vasculitis typically involves use of high doses of a glucocorticoid like prednisone to tamp down the inflammation that breaks down blood vessels. But use of prednisone is associated with many serious side effects, such as increased risks of infection, diabetes, high blood pressure, weight gain, cataracts, and many other problems.

Seeking solutions that might cut out steroids entirely, Merkel, along with his co-primary academic investigator David Jayne, MD, a professor of

Nephrology at the University of Cambridge, worked with ChemoCentryx to develop avacopan for ANCA-associated vasculitis. The underlying premise is that C5a, a protein that acts as a "chemoattractant" for inflammatory cells, including neutrophils, provided an excellent opportunity to stop ANCA-associated vasculitis in its tracks.

"There is strong data from animal models that C5a is directly involved in the as-yet-unidentified cause of ANCA-associated vasculitis," Merkel explained. "Those models indicate that blocking C5a at the tissue level has the potential to rapidly stop at least part of the destructive inflammatory process in this disease."

To test this, the clinical trial (named ADVOCATE) enrolled 331 patients. They were randomized into two groups: the control group, which took prednisone as their standard of care; and the trial group, which received avacopan. Both groups also received cyclophosphamide (followed by azathioprine) or rituximab, other medications that are the standard for vasculitis. Every patient had their disease severity measured using a standard tool in trials of vasculitis, the Birmingham Vasculitis Activity Score (BVAS), which assisted in determining who had achieved remission.

First, the researchers measured whether patients reached remission from vasculitis 26 weeks (half a year) after the start of their respective treatments. Both groups achieved similar rates of remission, wi5th roughly 72 percent of avacopan-treated patients achieving remission and 70 percent of the prednisone-treated patients. This showed that avacopan performed just as well as prednisone.

However, by a year, the findings showed that patients avacopan were more likely to remain in remission. At that point, 66 percent of the original avacopan-treated patients were in remission, compared to 55

percent of the prednisone-treated patients.

Moreover, serious adverse events such as worsening vasculitis, serious infections, and also death occurred 33 percent more often in the prednisone group than the avacopan group.

Avacopan is currently under review by the U.S. Food and Drug Administration (FDA) for approval as a treatment for ANCA-associated vasculitis.

Provided by Perelman School of Medicine at the University of Pennsylvania