New hope for patients with SLE with one-a-day oral medicine

Summary from Hermann V, et al. First use of cenerimod, a selective $S1P_1$ receptor modulator, for the treatment of systemic lupus erythematosus: a double-blind, randomised, placebo-controlled, proof-of-concept study
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INTRODUCTION

Systemic lupus erythematosus (SLE), often just called lupus, is an autoimmune disease. It causes immune cells in the body to become hyperactive and produce antibodies that attack the body's own cells. It is not known exactly what triggers SLE, and symptoms can vary from patient to patient. It typically affects women between the ages of 15 and 45, but can start in younger children. People with SLE are often very tired, have joint pain, skin rashes and their skin may be sensitive to sunlight. SLE can also lead to internal organ damage, and severe forms that affect the kidneys or brain are called Lupus nephritis or Neuropsychiatric lupus.

Sphingosine-1-phosphate 1 (shortened to $S1P_1$) receptors are found on the surface of certain cells. They play a role in different biological processes, including moving a type of immune cell called a lymphocyte from lymph nodes into the bloodstream. In patients with SLE, once lymphocytes are in the blood they travel to places in the body and cause inflammation. Cenerimod is a new medicine under development that works by blocking these $S1P_1$ receptors, to prevent lymphocytes from leaving the lymph nodes and reaching other places in the body. This action helps to reduce levels of inflammation.

WHAT DID THE AUTHORS HOPE TO LEARN?

The authors wanted to see whether cenerimod could reduce the number of circulating lymphocytes in the bloodstream of people with SLE.

WHO WAS STUDIED?

The study looked at 67 people with mild or moderate SLE. Everyone was over the age of 18, and had been diagnosed for at least 6 months – with at least 4 of the 11 criteria used to diagnose SLE. Everybody taking part also had evidence of specific antibodies in their blood.

People were not able to take part if they had certain types of SLE that affected their kidneys, central nervous system, lungs or heart, or if they had very severe SLE with a high level of disease activity.

HOW WAS THE STUDY CONDUCTED?

This was a randomised, double-blind trial, which means that people were sorted by chance to one of five treatment groups, and neither the patients nor their doctors knew which treatment group they were in. Randomly dividing patients into treatment groups means that on average the groups are similar and allows the treatment under investigation (different doses of cenerimod) to be compared objectively. Four of the groups received one capsule per day of cenerimod, at a dose of either 0.5, 1, 2 or 4 mg. The fifth group received one capsule per day of placebo (dummy drug). During the study, everyone carried on taking their

normal SLE medicine as well. The study lasted for 12 weeks, and then people had check-ups 6, 11, and 16 weeks after their last dose of medicine.

Throughout the study, blood samples and tests were done to monitor changes in people's disease activity. These included measuring levels of lymphocytes and antibodies in the blood, scoring disease activity with a tool called the SLEDAI-2K, and recording any side effects or tolerability issues.

WHAT WERE THE MAIN FINDINGS?

The study found that cenerimod lowered the number of circulating lymphocytes and has the potential to reduce disease activity. There was a larger decrease in disease activity for the people taking the higher doses of cenerimod. At the highest dose (4 mg), cenerimod significantly decreased levels of anti-dsDNA antibodies in the blood. These findings suggest that cenerimod causes biological changes in the body that reduce the effects of SLE on patients.

ARE THESE FINDINGS NEW?

Yes, this kind of medicine has not been investigated in SLE before.

WHAT ARE THE LIMITATIONS OF THE STUDY?

The study included only people with mild-to-moderate SLE, so we do not know how well the drug will work in patients with more severe disease. In addition, the study was only 12 weeks long, so it is not possible yet to say whether cenerimod will keep working over longer periods of time.

ARE MORE STUDIES PLANNED?

Yes, a larger study including 500 people with moderate-to-severe SLE is underway. It is a randomised study with a longer duration than this current study, and will evaluate the effectiveness and safety of cenerimod, in addition to standard treatment (ClinicalTrials.gov: NCT03742037). The new study will also look at whether taking cenerimod for SLE can change people's overall quality of life and improve important symptoms like fatigue.

WHAT DOES THIS MEAN FOR ME?

If you have SLE, there are currently limited treatment options. But these results offer some hope that in the future there will be 'one-a-day' tablets to treat the underlying disease and its symptoms. If you are interested in taking part in a trial for a new medicine, please speak to your doctor.

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