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Blocking interferon results in clinical improvement for people with lupus

The type I interferon pathway contributes to the development of lupus.

INTRODUCTION

Systemic lupus erythematosus (also known as SLE or lupus) is an autoimmune disease. It typically affects women between the ages of 15 and 50, and symptoms flare up unpredictably. Lupus is caused by complicated interactions between the immune system and environmental factors leading to an imbalance in the way the immune system works. This imbalance causes inflammation which, if untreated, can lead to disability and shortened lifespan. Different factors may trigger lupus in different people, and symptoms may vary considerably. In some the illness is never life-threatening, but can cause chronic skin rashes or arthritis. Others develop potentially life-threatening disease in the kidneys, lungs or heart.

Sifalimumab belongs to a group of drugs known as biologics. Sifalimumab works by binding to a molecule called interferon alpha, which stops it from causing inflammation.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors hoped to find out whether blocking interferon alpha with sifalimumab would improve people's lupus. They also wanted to know whether sifalimumab would cause any side effects.

WHO WAS STUDIED?

The study looked at 431 people diagnosed with lupus that had not got better with other therapies such as steroids or disease-modifying antirheumatic drugs (also called DMARDs). The people included were all over the age of 18 and had all had lupus for at least 6 months, and were defined as having a moderate or severe form of the disease.

HOW WAS THE STUDY CONDUCTED?

This was a double-blind, randomised controlled trial, which means that patients were assigned by chance to one of four treatment groups to receive placebo (dummy drug) or one of three doses of sifalimumab for 52 weeks. Using chance in this way means that the groups will be similar and will allow the variable or treatment under investigation to be compared objectively. During the treatment neither the patients nor their doctors knew which group they were in.

WHAT WERE THE MAIN FINDINGS?

The main finding was that lupus got better in more people treated with sifalimumab than placebo. This was measured using the SLE Responder Index (also called SRI 4), which looks at several different symptoms and markers of lupus. Another important finding was that sifalimumab can give improvements in a variety of different ways. For example, as well as improving joint and skin symptoms, fatigue (tiredness) was also reduced in people taking sifalimumab. The results confirm that the type I interferon pathway contributes to the development of lupus. Blocking this pathway appears to result in significant clinical improvement for people with lupus.

The authors found that there were no unexpected side effects with sifalimumab. This suggests that the drug has an acceptable safety profile. There was an increase the number of people getting *Herpes zoster* infections (shingles) with sifalimumab compared with those receiving placebo: only 1 person taking placebo got a *Herpes zoster* infection, compared to 19 people taking sifalimumab. However, this side effect was expected because of the way the drug works. Importantly, all cases of *Herpes zoster* got better when treated.

ARE THESE FINDINGS NEW?

These findings confirm that blocking the type I interferon pathway is a promising approach for treating lupus. A previous study looking at rontalizumab (a molecule with similar way of working) did not achieve such good results.

ARE THERE ANY LIMITATIONS?

There are limitations in how the results from this study can be used. Importantly, the study took place over 1 year – therefore the longer term safety and efficacy of sifalimumab in people with lupus is not yet known.

The results might also not apply to all people with lupus. For ethical reasons, people who had active or severe and unstable types of lupus affecting their brain (neuropsychiatric lupus) or kidneys (renal lupus, or lupus nephritis) could not take part in this trial. This means that we cannot use the results of this study to say that sifalimumab will work in these types of lupus.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

AstraZeneca, the developers of sifalimumab, used these results to design studies for another new biologic called anifrolumab. Anifrolumab also works by blocking interferon. As assessment of the two drugs found that anifrolumab worked better, and so this drug is being developed further.

WHAT DOES THIS MEAN FOR ME?

If you have lupus, there are limited treatment options at the moment. The data from this study will help to continue to develop drugs that target interferon alpha, which may mean that there are better options for you in the future. If you are interested in taking part in clinical trials for new medicines, you should talk to your doctor.

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From: Khamashta, M. *et al*. Sifalimumab, an anti-interferon-α monoclonal antibody, in moderate to severe systemic lupus erythematosus: a randomised, double-blind, placebo-controlled study. *Ann Rheum Dis* 2016;75:1909–16.