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New drug tabalumab offers limited efficacy in lupus

Tabalumab will not be developed any further for lupus, but may offer insights into future trial design for other treatment options.

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 rashes or arthritis. Others develop potentially life threatening disease in the kidneys, lungs or heart.

Tabalumab belongs to a group of drugs known as biologics. Tabalumab works by blocking a protein that regulates the immune system called BlyS. This prevents the stimulation of a type of white blood cell called a B lymphocyte that can be overactive in people with lupus, working like specialized factories that make antibodies. In people with lupus antibodies are formed that react with the body's own tissues (autoantibodies), causing inflammation and disease.

Another treatment that blocks BlyS, belimumab, has already been approved for people with lupus. Belimumab blocks any of the BlyS protein that is loose in the bloodstream. Tabalumab blocks both the loose BlyS and a form that is carried on the surface of other white blood cells.

WHAT DID THE AUTHORS HOPE TO FIND?

The authors were testing whether tabalumab is safe and effective to use for people with lupus.

WHO WAS STUDIED?

This summary combines two published papers from two similar studies of tabalumab – called ILLUMINATE-1 and ILLUMINATE-2. In total, they looked at 2288 people with lupus. All people included were over the age of 18.

HOW WAS THE STUDY CONDUCTED?

These were both randomised, double-blind, placebo-controlled clinical trials, which means that patients were assigned by chance to one of three treatment groups to receive either tabalumab every 2 weeks, tabalumab every 4 weeks, or a placebo (dummy drug). Using chance in this way means that the groups will be similar and the treatment can be compared in a scientific way. During the treatment neither the patients nor their doctors knew which group they were in. This is done to minimise the chance of bias in the results.

People in the studies continued taking their usual treatment for lupus, such as steroids, immunosuppressants or antimalarial drugs. The studies both lasted for 52 weeks.

WHAT WERE THE MAIN FINDINGS OF THE STUDY?

In ILLUMINATE-1 tabalumab did show some activity against auto-antibodies, which means that the drug did have some impact. However, the study did not demonstrate that people on tabalumab every 4 weeks fared better than those receiving placebo.

In ILLUMINATE-2, people treated with tabalumab 120 mg every 2 weeks did better than those receiving placebo, with more people responding to treatment (38% compared to 28%).

There was an important difference between these two studies which could explain the different results. In both studies other medicines such as steroids and immunosuppressive drugs were given together with the tabalumab or placebo. In the first study, people who changed the background treatments they were taking in any way (either increasing them or decreasing them) were counted as non-responders. In the second study if you increased your medications you were counted as a non-responder, but if you decreased them and continued to do well, you were counted as a responder.

Tabalumab had similar safety to placebo in both studies, and most side effects were not serious. Serious adverse events and deaths were similar in the tabalumab and placebo groups, and similar numbers of people stopped taking the study treatments due to side effects.

ARE THESE FINDINGS NEW?

Yes, these are the first large-scale clinical results for tabalumab in people with lupus.

WHAT ARE THE LIMITATIONS OF THE STUDIES?

Most patients in both studies were people with the most common active features of lupus, mainly affecting their joints and skin.

Because people did not stop taking their usual lupus medicines in the study, it is not known whether different medicines could have been affecting the results of tabalumab. Different medicines can interact in different ways: they can promote each other, they can inhibit each other, or they can be doing the same thing as each other. With all these background medications that have unknown effects on what tabalumab does, the interpretation of studies can be uncertain.

WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

At the present time Eli Lilly, the manufacturer of tabalumab has announced that it will not develop tabalumab any further at this time, but will be focusing on other treatments for lupus.

WHAT DOES THIS MEAN FOR ME?

If you have lupus, there are treatment options available at the moment, but there is a need for more progress. Even though tabalumab is unlikely to become available, the data from this study will help to work out better ways to test new drugs for lupus and other complicated autoimmune diseases. It is hoped that this work will provide better options for you in the future.

If you are interested in taking part in clinical trials for new medicines, you should first talk to your doctor about whether this is a reasonable option for you. If you would like to learn more about available trials or about what is being done to design these trials better, you can contact the Lupus Foundation of America www.lupus.org.

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Joint summary from:

- ▶ Merrill, JT. *et al.* Efficacy and safety of subcutaneous tabalumab, a monoclonal antibody to B-cell activating factor, in patients with systemic lupus erythematosus: results from ILLUMINATE-2, a 52-week, phase III, multicentre, randomised, double-blind, placebo-controlled study. *Ann Rheum Dis* 2016;75:332–40. doi:10.1136/annrheumdis-2015-207654
- ▶ Isenberg, DA. *et al.* Efficacy and safety of subcutaneous tabalumab in patients with systemic lupus erythematosus: results from ILLUMINATE-1, a 52-week, phase III, multicentre, randomised, double-blind, placebo-controlled study. *Ann Rheum Dis* 2016;75:323–31. doi:10.1136/annrheumdis-2015-207653

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