

Treatments being studied for lupus

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Resource Content

What treatments are being studied for lupus?

Many drugs, both old and new, are now being studied in people with lupus. The drugs described below are not a complete list of all the drugs currently in development for lupus, and they may not all end up as approved medications. However, the variety of scientific approaches reflects the growing interest in lupus at all levels of the biomedical and pharmaceutical industry.

Much has been learned about trial designs for lupus studies. There is continued interest in lupus by many biomedical and pharmaceutical companies worldwide, offering realistic hope that we will see additional treatments for lupus in the not-too-distant future.

Clinical Trials

Before any drug can be approved for use as a medical treatment, a strict process has to be followed. Clinical testing is done in several phases, and this can take as much as 15 years. Generally, as part of the clinical trial designs, some of the volunteers receive placebo (an inactive substance). These trials are also "double blind" meaning that neither the investigating team or the volunteer know whether they are receiving the real treatment or the placebo--at least not until the study is over. This is done to make sure the results are scientific.

There will be no new drugs for lupus without clinical trial volunteers! While participation in research studies is not for everyone, people with lupus, as well as people without lupus, can make a profound contribution by participating in clinical trials.

There is no guarantee that a drug being studied will provide any benefit, and of course there are always risks with all drugs, whether investigational treatments in trials or standard of care treatments, commonly prescribed in general medical care. In early phase clinical trials, less is known about the side effects to be expected. The

longer a drug has been used, and the larger number of people that have tried it, the more is known about its potential risks and benefits.

Treatments Under Investigation

We have listed these investigational drugs in alphabetical order. Some have already been approved by the FDA for treating other conditions, and are now being studied in lupus. Other treatments listed here are not yet approved for any diseases, and are not on the market or available to any individuals except those in clinical trials.

Abatacept (Orencia®) targets the T cells, a type of white blood cell that plays an important role in regulating the immune response. Levels of these T cells are higher than normal in lupus and other autoimmune disorders. Orencia has been approved by the FDA to treat rheumatoid arthritis (RA). This type of treatment is known as a biologic because it is made to mimic the actions of real proteins that exist in biology. Orencia is made to be a combination of parts of an antibody and of a special protein called CTLA4. It interferes with signals that are sent between T cells and B cells, which, in lupus, may control the hyperactivity of both cells. Anti-TNF-alpha drugs are biologics that have been approved for rheumatoid arthritis for a long time. They interfere with the action of tumor-necrosis factor-alpha (TNF- α). TNF- α plays key roles in inflammation, anti-tumor responses, and infections. Enbrel®, Humira®, Cimzia®, Simponi® and Remicade® are all anti-TNF- α therapies approved for RA. Although anti-TNF-alpha agents have been found to cause drug-induced lupus in some people (reversible when the medicine is stopped), some scientists think they may be helpful in treating some features of lupus. There are some reports about this in the medical literature, but more research is needed.

Anti-interferon-alpha antibody targets interferon-alpha (INF- α), a chemical the body makes to fight viruses. Too much INF- α can lead to immune problems, and levels of INF- α are higher than normal in lupus and other autoimmune disorders. Stopping the overproduction of INF- α may reduce disease activity in lupus. This is in the biologics class of drugs.

Blisibimod is also a biologic. Like belimumab (Benlysta®), it has been designed to block signals that come from a protein called BAFF (or BlyS) that stimulates B cells. Blisibimod is currently in late stage development.

Leflunomide (Arava®), approved for the treatment of RA, might help with the arthritis caused by lupus. It has been tried in many lupus patients and works by stopping the overproduction of immune cells, which leads to swelling, inflammation, stiffness, and joint pain. This is in the immunosuppressives (immune modulators)

class of drugs. Small studies of leflunomide have been published but more research is needed.

Lupuzor™ was developed to change the behavior of a specific type of T cell involved in lupus disease activity. This is in the biologics class of drugs. It is still in mid-stage development for lupus but a later stage trial is being planned.

Medi 546 (Anifrolumab) is a new biologic treatment, not yet approved for any disease, that blocks the protein that transmits signals into immune cells from interferon-alpha (INF- α). INF- α is an important soldier in the immune defense against viruses. Too much INF- α can lead to immune problems, and levels of INF- α are higher than normal in lupus and some other autoimmune disorders. Stopping the signals from INF- α that crank up inflammatory responses by immune cells might reduce disease activity in lupus. The next step is to figure out the best dose to dampen lupus disease activity without too much increased risk of viral infections. Results of mid-stage testing of anifrolumab are very promising, but it won't be certain that this drug is on its way for general use in patients until the late phase testing is completed.

Prograf® works by interfering with T cell function. This is in the organ transplant anti-rejection class of drugs.

Rapamycin (Sirolimus, Rapamune®), is used in combination with other medications to prevent rejection of kidney transplants. This treatment has unique effects on T Cells and inhibits a certain form of a control point in the cell called MTOR (Mammalian Target of Rapamycin) that is known to be imbalanced in lupus. There have been few studies so far, but there is growing interest in this approach to treating lupus.

Rituximab (Rituxan®) is a biologic approved for the treatment of lymphoma and rheumatoid arthritis that targets a specific protein called CD20 on the surface of B cells. Rituxan attaches to CD20 to attack and kill B cells. Clinical trials in lupus did not demonstrate better efficacy than placebo, but there were some concerns about the trial design, including very aggressive treatments given to the placebo group as background therapy. Many published reports have suggested that rituximab might be helpful for certain types of severe lupus, and it has been widely used in clinics in the United States and Europe. A current trial is looking to see if rituximab and mycophenolate mofetil (Cellcept) can be given together without steroids for lupus nephritis. Newer agents that have the same mechanism of action as rituximab may also be tested for lupus in the future. Stem cell transplantation is studied in people with severe, life-threatening autoimmune conditions who have not responded to any other treatments. Stem cells are the most basic type of cell, and are able to become different types of cells; they also have the ability to self-renew to produce more stem cells. The procedure works by eliminating the immune system that has become imbalanced and replacing it with a new, healthy system. Stem cell transplants use bone marrow cells from self (autologous), or stem cells from donors (allogenic). Both self and donor stem cell transplantation have been under

investigation for many years in Europe and in the U.S. The use of mesenchymal stromal cells (MSCs) in stem cell transplantation has also been studied in China and Europe. MSCs are unique adult stem cells with immunosuppressive properties and also may play a key role in preventing autoimmunity. When successful, disease symptoms become more easily controlled, and the need for medications reduced. However, some people may experience a recurrence of their symptoms over time, and there are serious risks from the procedure.

TACI-Ig (Atacicept) is a biologic designed to block signals from BAFF (or BlyS) similarly to blisibimod and belimumab. However, it also blocks signals from another molecule called APRIL which sometimes works in partnership with BAFF to control B Cell inflammation. This treatment has not been approved for any diseases at this time, but it is in late stage development for lupus.

Tacrolimus (Prograf®) works by interfering with T cell functions. This is approved for patients with organ transplants, to avoid rejection. It has been used quite a bit in lupus clinics, especially for lupus nephritis. Several studies from China suggest that it may be a useful treatment for lupus. Ustekinumab (Stelara®) is a biologic that targets a protein that becomes unregulated due to a particular imbalance in how T Cells develop in lupus. It is currently undergoing a middle stage clinical trial for lupus patients.

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