

Lymphoma Vaccines

Expert review by:

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What are vaccines?

Most people are familiar with vaccines that prevent infections like tetanus, polio and measles. These so-called preventative vaccines use the body's immune system to resist or fight these infections. New kinds of experimental vaccines are now being studied as possible treatments for non-Hodgkin lymphoma (NHL). These lymphoma vaccines are not designed to prevent lymphoma, but rather, treat a lymphoma that already exists and therefore are called therapeutic vaccines. Therapeutic lymphoma vaccines are experimental and not yet approved by the U.S. Food and Drug Administration (FDA). Clinical trials of lymphoma vaccines are underway in lymphomas to determine whether they are a safe and effective treatment for lymphoma.

To understand lymphoma vaccines, it is important to know that lymphomas are cancers of the immune system. Our immune system is the body's natural protection against infections and other diseases. Our immune system is made up of specialized immune cells that include a certain type of white blood cell known as lymphocytes (B-cells and T-cells). Every lymphocyte has a unique feature, known as an idiotypic protein, which makes it different from every other lymphocyte in the body. When a lymphocyte becomes abnormal, or cancerous, it multiplies and carries with it the same idiotypic protein as that of the original cell. Therefore, each person's lymphoma is made up of cells with the same idiotypic protein. Thus, the idiotypic protein is a distinguishing feature of each person's lymphoma and a unique target for lymphoma vaccines.

What are lymphoma vaccines?

Lymphoma vaccines, also known as personalized immunotherapy, are custom-made for each patient. These vaccines are designed to work by stimulating the body's immune system to recognize and respond to lymphoma as if it were a foreign substance that does not belong in the body. If lymphoma vaccines stimulate or teach the immune system to fight and destroy lymphoma cells, it is hoped they will also provide long-lasting memory to react more quickly in the future, if the lymphoma recurs. The ability of the immune system to recognize and respond in this way is known as an immune response. Clinical trials suggest that development of an immune response against the lymphoma-specific idiotypic protein may be associated with tumor shrinkage, prolonged responses, and improvement in survival. Large Phase III randomized trials will definitively answer these questions.

Lymphoma vaccines target the unique idiotypic protein present on lymphoma cells and therefore, only cells with the unique idiotypic protein should be affected, while normal, healthy cells in the body are left unharmed. With normal cells spared, lymphoma vaccines may be associated with fewer side effects than other cancer treatments, like chemotherapy and radiation, which destroy both cancer cells and normal cells.

What are the different types of lymphoma vaccines?

Clinical trials are evaluating several different types of therapeutic lymphoma vaccines. Although lymphoma vaccines may differ, all therapeutic lymphoma vaccines are based on the same principle of using each person's immune system to fight their lymphoma.

Idiotypic vaccines start with a biopsy or tissue sample of each patient's lymphoma in order to identify the unique idiotype protein. These vaccines are developed based on genetic information obtained from the idiotype protein and contain a protein that is very similar to the protein found in each patient's lymphoma. This is the most common type of lymphoma vaccine.

Dendritic cell vaccines are made by mixing, or "pulsing," specialized immune cells called dendritic cells with a sample of a patient's tumor (either idiotype protein or killed lymphoma cells). Dendritic cells are derived from a patient's own blood using special laboratory procedures.

Tumor cell vaccines consist of pieces of a tumor (either whole, broken apart and/or combined with an immune stimulant) that are injected directly into a patient.

Heat shock protein vaccines consist of proteins purified from tumor cells that have been broken open to release these general immune stimulants.

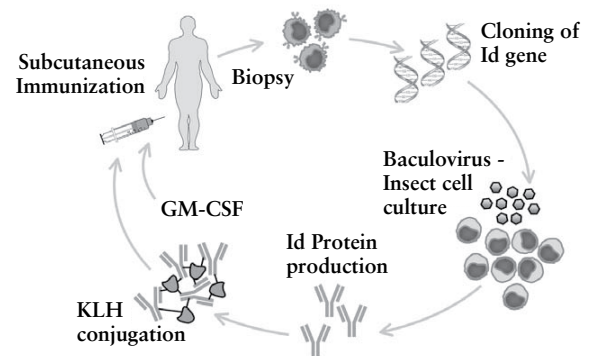
How are therapeutic lymphoma vaccines different from monoclonal antibodies (i.e. Rituxan)?

It is important to point out that lymphoma vaccines are still investigational, while the monoclonal antibody, Rituxan, is a FDA approved drug with known effectiveness against certain types of lymphoma. With that said, both therapeutic lymphoma vaccines and monoclonal antibodies represent a type of biologic therapy that works with the body's immune system to fight lymphoma. However, the important differences between these two types of immunotherapy lie in the immunologic approach. Monoclonal antibodies, generated in a laboratory, target a specific protein (CD20 protein in the case of Rituxan) found on the cell surface of normal and cancerous cells and are infused in a patient through a vein. Monoclonal antibodies use a "passive" immune approach whereby the immune system is stimulated to target cells tagged with the antibody and last only as long as the antibodies remain in the body. To the contrary, lymphoma vaccines target only the idiotype protein found on each patient's lymphoma cells and therefore, normal cells are left unharmed. Additionally, lymphoma vaccines use an "active" immune approach that involves a series of injections or "shots" and are designed to work by stimulating the immune system to recognize and respond to only those cells with the tumor-specific idiotype. The hope is that vaccines

will provide the immune system with a memory that will offer lifelong control against the lymphoma.

How are lymphoma vaccines made?

Scientists use different laboratory techniques to produce the various types of therapeutic lymphoma vaccines. In the case of idiotype vaccines, a biopsy, or lymphoma tissue sample is the first step in the process. Scientists then identify the unique genetic information or idiotype protein obtained from each patient's lymphoma cells and uses this as a template to produce a very similar protein that is used to produce an individualized, custom-made idiotype vaccine. Lymphoma vaccines are made up of two parts including: 1) the idiotype protein from each patient's lymphoma cells and 2) a protein called keyhole limpet hemocyanin (KLH). KLH is very "immunogenic," which means the immune system responds strongly to it.



During vaccine production, the idiotype protein is combined with KLH. In general, idiotype lymphoma vaccines require several months to manufacture, although scientists are continually testing methods to speed this process. Using modern molecular biology techniques, these vaccines are purified and produced in large quantities in the laboratory. Since idiotype vaccines are made specifically for each individual patient, once it is made, it can only be used for the patient from whom the biopsy, or tissue sample, was originally obtained.

Can anyone with lymphoma receive a vaccine and what is involved?

Presently, you must be enrolled in a clinical trial in order to receive a lymphoma vaccine. Since these vaccines are made individually for each patient, a biopsy or lymphoma tissue sample is needed. Each lymphoma vaccine trial has specific entry criteria, and you should discuss with your doctor

whether you might be eligible to participate in one of these clinical trials. Some trials require that you have never been treated for your lymphoma in the past. Others do not have this requirement. At present, the most advanced-stage testing of lymphoma vaccines is being done with idiotype vaccines. Randomized phase III clinical trials in lymphoma are designed to determine whether idiotype vaccines are effective in treating and/or preventing a lymphoma relapse (re-growth) after first reducing the lymphoma “tumor burden” with known effective treatments like Rituxan, chemotherapy, or a combination of Rituxan + chemotherapy. To date, researchers believe that patients have the best chance to respond to a vaccine when they have a low “tumor burden,” meaning no or only a small number of lymphoma cells are present in the body.

How are lymphoma vaccines given?

Lymphoma vaccine treatments involve two “shots” or injections, just beneath the skin, monthly for approximately 6 or more months. The first type of injection is the vaccine itself. The second type of injection is something designed to boost your immune system and is called Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF, Leukine). GM-CSF is administered as close to the vaccine injection site as possible. Your study doctor or healthcare provider must give all the vaccine injections at the health facility where the trial is being conducted. However, your doctor may permit you, a friend or family member to give subsequent shots of the GM-CSF for several days at home. These injections are typically given in the arm, the leg or the abdomen. Keep in mind, however, that each vaccine trial has distinct injection schedules and different rules, so check with your doctor about the specific requirements of the different trials.

Will the injections hurt or cause any side effects?

To date, a majority of patients experience some type of reaction at the site of the vaccine/GM-CSF injections and may include skin redness, pain, itching and/or tissue swelling lasting 1-7 days. Roughly half of the people who have received experimental vaccine treatments also report symptoms similar to getting the flu, such as mild fevers, aches and pains in the muscles, bones, and joints, tiredness, nausea and headaches. These side effects generally only last a few days and can be treated fairly effectively with over-the-counter pain medicines, such as aspirin or acetaminophen. Remember, lymphoma vaccines are still investigational and

it is through clinical trials that we continue to learn all the potential side effects of this type of therapy.

Is vaccine therapy for me?

Speak to your doctor about whether you may be eligible to participate in a lymphoma vaccine trial. He or she will help you weigh the benefits and risks based upon your medical history, what type of lymphoma you have, as well as whether you have received prior treatment for your lymphoma. Your doctor may also factor in the results of blood tests and your overall disease prognosis as determined by the International Prognostic Index, a predictive tool researchers have developed to guide healthcare professionals in treating lymphoma.

Do vaccines work? Are they better than current NHL treatments?

At the present time, all lymphoma vaccines are still considered investigational treatments, so the definitive answer is not known. To know for sure, researchers must complete patient enrollment and carefully analyze the results of randomized, large-scale clinical trials. Several Phase III trials of idiotype vaccines are currently under way, and a number of smaller trials of other vaccine types are also in process. Early results of vaccine trials are promising. However, researchers do not yet know whether vaccine therapy will be effective in improving current treatments for lymphoma. At the least, the hope is that vaccine therapy, like other biologic therapy like monoclonal antibodies, will be less toxic than traditional therapies such as chemotherapy and radiation. Scientists are working hard to assess whether vaccine therapy can help patients with lymphoma. By participating in a vaccine trial, you can help researchers determine whether vaccines are effective in treating different types of lymphoma.

For the most up to date information about current lymphoma vaccine clinical trials, please contact the *Lymphoma Helpline and Clinical Trials Information Service* at 800-500-9976 or helpline@lymphoma.org.

The following websites will also have information about lymphoma vaccine studies.

www.favrille.com
www.biovest.com
www.genitope.com
www.clinicaltrials.gov

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The Lymphoma Research Foundation (LRF) offers a comprehensive series of patient education and support programs including:

- *Lymphoma Helpline & Clinical Trials Information Service*
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- Publications and newsletters
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Glossary of Terms

Dendritic cell vaccine: A vaccine that contains immune cells called dendritic cells that have been mixed, or "pulsed," with a sample of a patient's tumor

Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF, Leukine): A generalized immune stimulant that helps bring certain types of white blood cells to the vaccine site

Heat shock vaccine: A cancer vaccine that contains tumor cells that have been broken apart and mixed with an immune stimulant

Idiotype: A unique portion of an antibody present on the surface of cells

Idiotype vaccine: A lymphoma vaccine that is individualized and custom made for each patient to fight lymphoma. It contains a unique protein similar to that found on each patient's lymphoma cells, combined with KLH, an immune stimulant

Immunotherapy: Cancer treatment that uses each person's immune system to attack tumors

Keyhole limpet hemocyanin (KLH): A highly "immunogenic" protein that stimulates the immune system

Lymphoma vaccine: A form of cancer immunotherapy that uses a patient's immune system to fight his or her lymphoma Phase III trial: a large, randomized clinical study that compares the results of people receiving a new treatment with results of people receiving a standard treatment

Monoclonal antibody: A type of immunotherapy that uses an antibody, manufactured in the lab, and designed to target a specific antibody on the cell surface of normal and cancerous cells

Tumor cell vaccine: A cancer vaccine that consists of tumor cells (whole or broken apart) that have been mixed with an immune stimulant

Viral vaccine: A cancer vaccine that consists of a genetically engineered form of a virus such as adenovirus

About LRF

The mission of the Lymphoma Research Foundation (LRF) is to eradicate lymphoma and serve those touched by this disease. LRF is the nation's largest lymphoma-focused voluntary health organization devoted exclusively to funding lymphoma research and providing patients and healthcare professionals with critical information on the disease. Over 85 cents of every dollar spent goes to support research and education programming. People affected by lymphoma can receive free personalized information tailored to their diagnosis, help with finding a clinical trial, and easy-to-understand information on lymphoma, current treatments, and promising research. Please call 800-500-9976, email helpline@lymphoma.org, or visit the website www.lymphoma.org