

Zevalin

Expert review by:

Leo I. Gordon, MD, is the Abby and John Friend Professor of Cancer Research and Professor of Medicine at Northwestern University in Chicago, IL. He is Chief of the Division of Hematology/Oncology at the Northwestern University Feinberg School of Medicine and Associate Director for Clinical Sciences at the Robert H. Lurie Comprehensive Cancer Center at Northwestern University.

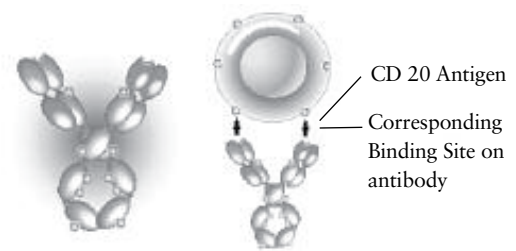
What is Zevalin?

Zevalin (Ibritumomab tiuxetan) was the first radioimmunotherapy treatment to be approved by the U.S. Food and Drug Administration (FDA) for the treatment of non-Hodgkin lymphoma (NHL). Zevalin has been approved for the treatment of patients with relapsed or refractory lowgrade, follicular, or transformed B-cell NHL, including patients with follicular NHL who are no longer responding to treatment with Rituxan (rituximab), a monoclonal antibody therapy.

“Treatment with the Zevalin regimen can be completed within a week on an outpatient basis.”

Zevalin is different in many ways from conventional chemotherapy or external beam radiation therapy. Zevalin combines the cell targeting ability of a monoclonal antibody with the additional cell killing ability of a radioactive particle, or radioisotope, called yttrium-90. Treatment with the Zevalin regimen can be completed within a week on an outpatient basis. It is generally well tolerated by patients, without the hair loss and nausea that often accompany chemotherapy treatments. The most common side effect is a temporary reduction in blood cell counts.

“It is generally well tolerated by patients, without the hair loss and nausea that often accompany chemotherapy treatments.”



Antibody targeting antigen on cell

What is a Monoclonal Antibody?

Antibodies are normal components of the body's immune system that can recognize and destroy foreign invaders such as bacteria and viruses. Scientists can now produce monoclonal antibodies designed to recognize very specific targets, or antigens, that are present on certain kinds of cancer cells. Rituxan was the first monoclonal antibody to receive FDA approval.

Therapy with a monoclonal antibody is an effective way of specifically targeting certain kinds of cancer cells, with a low degree of toxicity to normal cells. Monoclonal antibody therapy is administered by intravenous infusion, generally on an outpatient basis. Once in the bloodstream, monoclonal antibodies travel throughout the body and bind themselves to cells that have the specific target antigen, such as cancer cells. This activity alerts the body's own immune system to recognize and help destroy the bound cells. Although some normal cells that also have the specific target antigen may be affected, the body can replace these normal cells following treatment.

The monoclonal antibody used in the Zevalin regimen specifically recognizes and attaches to the CD20 antigen, which is found on the surface of lymphocytes, including the cancer cells in patients with B-cell NHL.

What is Radioimmunotherapy?

Radioimmunotherapy is a cancer therapy, involving the combination of a monoclonal antibody with a radioisotope, as a source of radiation. When a monoclonal antibody is combined with a radioisotope, it is said to be ‘radiolabeled.’ With radioimmunotherapy, the radiolabeled antibody targets and binds to a specific antigen present on cancer cells, delivering a dose of radiation directly to them. Not only does the radiation destroy the cell to which the antibody is bound, but it also destroys the surrounding cells, in what is called the “crossfire” effect.



Radiolabeled antibody killing off malignant cells

Products are currently on the market for Radioimmunotherapy?

There are two products currently approved by the FDA for radioimmunotherapy of patients with B-cell lymphomas: Zevalin and Bexxar. Both use radioactively-labeled mouse monoclonal antibodies targeting the CD20 antigen.

What are the differences between Zevalin and Bexxar?

Bexxar employs Iodine-131, a radiation-emitting form of iodine, attached to the monoclonal antibody tositumomab. Tositumomab seeks out and binds to CD20, found on the surface of B-cells. Once it is combined with Iodine-131, tositumomab is able to deliver its radiation to targeted cells. Iodine-131 emits beta and gamma radiation. Beta radiation is responsible for most of the tumorkilling effect. Gamma radiation allows gamma camera scans to evaluate the distribution and clearance of radiation from the patient’s body. Iodine-131 radiation is eliminated from the body mainly through the urine and by the natural decay of Iodine-131 (please see LRF’s Bexxar fact sheet for more information). The Zevalin regimen uses two different radioisotopes, indium-111 and yttrium-90. Indium-111 radiolabeled Zevalin is used for imaging studies. The amount of radiation associated with this imaging dose of

indium-111 Zevalin is very small, and patients do not need to observe any special safety precautions following this part of the regimen.

For treatment, Zevalin is combined with the yttrium-90 radioisotope, a pure beta emitter. The radiation from the therapeutic dose of yttrium-90 Zevalin is strong enough to damage and kill the targeted cancer cells and nearby cells, including some normal cells.

“In clinical trials involving patients with low-grade non-Hodgkin lymphoma, the reported response rates to Zevalin have been 70 percent to 80 percent.”

How is Zevalin given?

The Zevalin regimen is delivered over the course of about a week on an outpatient basis. Delivery of the regimen is coordinated by a team of healthcare professionals, including oncologists, nuclear medicine physicians or radiation oncologists, nurses, pharmacists and technicians. Because the Zevalin regimen involves the use of radioisotopes, it is necessary to involve persons specially trained in the safe handling of these substances at a licensed nuclear medicine or radiation oncology facility.

On day one of the regimen, the patient first receives an intravenous infusion of Rituxan, which takes a few hours. Following the Rituxan infusion, the patient will go to a nuclear medicine or radiation oncology facility to receive an imaging dose of indium-111 Zevalin. This intravenous infusion will take approximately 10 minutes. A nurse or technician will stay with the patient during treatment.

On day one or day two, whole body images will be taken with a gamma camera. Then, on day two or day three, additional images will be taken. The physician may recommend that additional images be taken on day four or five, between 90 to 120 hours after the infusion of indium-111 Zevalin. The physician uses these images to view the path of indium-111 Zevalin in the body.

Approximately one week after the initial treatment day, the patient will return for a second infusion of Rituxan followed by yttrium-90 Zevalin, the therapeutic portion of the Zevalin regimen. After receiving Rituxan, the patient will again go to the nuclear medicine or radiation oncology facility, this time to receive yttrium-90 Zevalin. Yttrium-90

Zevalin is administered by an intravenous infusion that is completed in about 10 minutes. Imaging studies are not necessary after this infusion.

What precautions are necessary after receiving yttrium-90 Zevalin?

Radiation from yttrium-90 Zevalin does not escape outside the body, but a small amount of radiation may be present (for about a week following treatment) in body fluids, such as blood and urine. Minimal radiation safety precautions are required. Patients should wash their hands thoroughly after urination and use a condom during sexual intercourse. In general, it is not necessary to avoid contact with friends or family during this time and isolation is not required. Patients can usually return to work and their usual activities following treatment. Patients should speak with their physician regarding recommended safety precautions and any questions or concerns that they may have.

What side effects are associated with Zevalin?

Because the Zevalin regimen involves the administration of Rituxan, side effects of Rituxan and Zevalin are discussed. The most common side effects associated with Rituxan are mild, flu-like symptoms. Physicians will often provide medications such as Tylenol and Benadryl to manage these temporary side effects.

The administration of yttrium-90 Zevalin usually results in no infusion-related toxicities. However, because of the radioactivity of this treatment, blood cell counts will be lowered. The period of lowered blood cell counts generally occurs 4 to 6 weeks following therapy, with recovery of counts 2 to 3 weeks later. It is important to note that Zevalin is not associated with hair loss or with the nausea and vomiting typically seen with chemotherapy.

Who is a candidate for Zevalin?

Zevalin has been approved for the treatment of patients with relapsed or refractory B-cell lymphomas of the following subtypes: low-grade and/or follicular, or transformed B-cell NHL, including patients who are no longer responding to Rituxan treatment. Zevalin is not currently recommended for patients with greater than 25 percent bone marrow involvement, impaired bone marrow reserve or for patients with platelet counts less than 100,000.

How effective is Zevalin?

In clinical trials involving patients with low-grade NHL, the reported response rates to Zevalin have been 70 percent to 80 percent. Zevalin produced responses in patients who were no longer responding to treatment with chemotherapy, were no longer responding to treatment with Rituxan, and those who had bulky disease.

“Importantly, there are patients who are still in remission over 5 years after treatment with a single dose of Zevalin.”

In a randomized Phase III clinical trial for patients with relapsed and refractory indolent lymphoma, comparing Rituxan and Zevalin treatments, 50 percent of patients responded to Rituxan and 80 percent of patients responded to Zevalin. The patients who were treated with Zevalin had a complete response rate of 30 percent, compared to 20 percent of Rituxan patients. Patients had a median age of 60, with an average of two prior therapies. The median duration of response was 13.9 months with Zevalin compared to 11.8 months with Rituxan. The subgroup of patients with follicular lymphoma had a median duration of response of 16.7 months. Importantly, there are patients who are still in remission over 5 years after treatment with a single dose of Zevalin.

Does Zevalin therapy “burn ridges” for future treatments with other products?

It is not believed that Zevalin will limit future treatment options. Data reported that NHL treatments such as chemotherapy, Rituxan, radiation therapy and stem cell transplant are all feasible following Zevalin therapy.

Contact Us

For more information about *Getting the Facts* or information about the



Please contact:

Los Angeles

Patient Education, Services and Support
8800 Venice Boulevard, Suite 207
Los Angeles, CA 90034
(310) 204-7040
(310) 204-7043 fax

New York

Research Grants, Professional Education,
Public Policy, Finance and Development
115 Broadway, 13th Floor
New York, NY 10006
(212) 349-2910
(212) 349-2886 fax

Helpline: (800) 500-9976

Website: www.lymphoma.org

Email: LRF@lymphoma.org
Helpline@lymphoma.org

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

- *Lymphoma Helpline & Clinical Trials Information Service*
- *Lymphoma Support Network*
- Patient Aid Grant Program
- Publications and newsletters
- Informational teleconferences and webcasts
- In-person conferences
- National Chapter Network

©2008 Lymphoma Research Foundation

Getting the Facts is published by the Lymphoma Research Foundation for the purpose of informing and educating readers. Because each person's body and response to treatment is different, no individual should self-diagnose or embark upon any course of medical treatment without first consulting with his or her physician. LRF is not responsible for the medical care or treatment of any individual.

Last Updated March 2008

Information Resources

To learn more about lymphoma, treatments and ongoing clinical trials, contact LRF's *Lymphoma Helpline* at 800-500-9976, helpline@lymphoma.org or visit www.lymphoma.org.

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

For more information about Zevalin, please consult Zevalin Prescribing Information, call 1- 866-298-8433, visit www.zevalin.com or speak with your physician.