

Radioimmunotherapy

Overview

Radioimmunotherapy (RIT) is a type of cancer therapy that combines a radioactive substance with a monoclonal antibody to kill cancer cells.

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 create monoclonal antibodies designed to recognize specific *antigens* (targets) that are present on the surface of certain cancer cells. Monoclonal antibody therapy can be administered by *intravenous* (IV; into a vein) or *subcutaneous* (under the skin) infusion, generally on an outpatient basis. Once in the bloodstream, monoclonal antibodies travel throughout the body and attach themselves to the target antigens on cancer cells. This helps the body's immune system identify and destroy the cancer cells. Sometimes normal cells that have the same target antigen on their surface may be affected as well, but the body can usually replace these cells following treatment.

What Is Radioimmunotherapy?

In RIT treatment, *radioisotopes* (radioactive particles) are attached to monoclonal antibodies and then infused into the body. Each time an antibody comes into contact with a cancer cell, the attached radioisotope delivers radiation directly to that cell. The major advantage of this approach is that it substantially reduces the exposure of healthy cells to radiation. Nuclear medicine physicians or radiation oncologists who specialize in the delivery of radiation, as well as other healthcare professionals such as oncologists or medical physicists, may be involved in the administration of RIT. Treatment is commonly administered by IV infusion, similar to monoclonal antibody therapy.

Ibritumomab Tiuxetan (Zevalin)

Ibritumomab tiuxetan (Zevalin) was the first RIT approved by the U.S. Food and Drug Administration (FDA). This RIT contains a radioisotope called yttrium-90 (Y^{90}) that kills cancer cells. Ibritumomab is a monoclonal antibody that targets the CD20 antigen expressed on the surface of malignant B cells. Tiuxetan is a *chelator* (connector) that links the Y^{90} molecule to the ibritumomab molecule. Ibritumomab tiuxetan has been approved for the treatment of patients with *relapsed* (disease returns after treatment) or *refractory* (disease

does not respond to treatment) low-grade or follicular B-cell non-Hodgkin lymphoma (NHL). It is also approved for use in previously untreated patients with follicular NHL who achieve partial or complete responses to first-line chemotherapy.

Patients being treated with ibritumomab tiuxetan (Zevalin) first receive two infusions of rituximab (Rituxan), another monoclonal antibody that also targets CD20 but does not carry any radioisotope, followed by a one-time infusion of ibritumomab tiuxetan. On day one, the patient receives premedication with acetaminophen (Tylenol) and diphenhydramine (Benadryl) followed by an IV infusion of rituximab that takes up to six hours. Seven to nine days later, the patient returns for a second infusion of rituximab followed by ibritumomab tiuxetan four hours later. Dosing is based on the patient's weight and platelet count.

Ibritumomab tiuxetan (Zevalin) is generally well tolerated, without the hair loss and nausea that often accompany chemotherapy. The most common side effect is a temporary decrease in blood cell counts, which start to occur two to three weeks after treatment. Blood cell counts typically return to near-normal levels within 10 weeks after receiving treatment. Platelet counts usually drop the most and can cause a patient to bruise more easily; in some cases, patients may bleed more easily. The most serious side effects are low blood counts that don't improve and having an allergic (anaphylactoid) reaction to the infusion. The side effects of rituximab (Rituxan) can include headache, nausea, *flushing* (involuntary, temporary reddening of the skin), indigestion, light-headedness, and mild fever and chills, especially after the first dose. This is not a complete list of side effects. Physicians will check for these and other effects during follow-up visits.

Radiation from ibritumomab tiuxetan does not escape outside the body, but a small amount may be present in body fluids such as blood and urine. Because of this, patients should wash their hands thoroughly after urination and use a condom during sexual intercourse. It is not necessary to avoid contact with friends or family during this time, and patients can typically return to work and their usual activities following treatment. Patients should speak with their physician regarding safety precautions.

Treatments Under Investigation

Y^{90} epratuzumab tetraxetan is an RIT agent currently under investigation for the treatment of certain types of NHL, including follicular NHL and diffuse large B-cell lymphoma. Epratuzumab is

a monoclonal antibody that targets CD22, a different antigen than the one targeted by ibrutinib, and tetraxetan is the *chelating* (binding) substance that links epratuzumab to the radioisotope Y⁹⁰. Y⁹⁰ epratuzumab tetraxetan is being investigated in combination with several agents, including rituximab (Rituxan) alone, R-CHOP (a combination of rituximab and chemotherapy), and another monoclonal antibody called velutuzumab.

Y⁹⁰ daclizumab, a CD25 antibody, is an RIT therapy that is currently being investigated for the treatment of Hodgkin lymphoma. One study of this RIT agent combines Y⁹⁰ daclizumab (Zinbryta) with a stem cell transplant and a chemotherapy regimen known as BEAM (carmustine, etoposide, cytarabine, melphalan).

Clinical Trials

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on the Lymphoma Research Foundation's (LRF's) website at www.lymphoma.org/publications, talk to their physician, or contact the LRF Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing helpline@lymphoma.org.

Follow-up

Patients with lymphoma should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required at various times during remission to evaluate the need for additional treatment.

Some treatments can cause long-term side effects or late side effects, which can vary based on the duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these side effects during follow-up care.

Patients and their caregivers are encouraged to keep copies of all medical records and test results as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any side effects resulting from treatment or potential disease recurrences. LRF's award-winning *Focus On Lymphoma* mobile app (www.FocusOnLymphoma.org) can help patients manage this documentation.

Patient and Caregiver Support Services

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. One-to-one peer support programs, such as LRF's *Lymphoma Support Network*, connects patients and caregivers with volunteers who have experience with lymphoma or chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), similar treatments, or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this information useful whether the patient is newly diagnosed, in treatment, or in *remission* (disappearance of signs and symptoms).

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and CLL/SLL including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts for people with lymphoma, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. To learn more about any of these resources, visit our website at www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

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Supported
through
grants from:



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