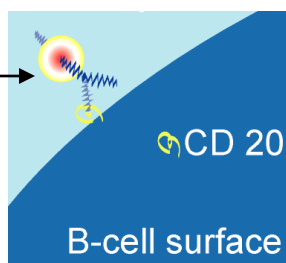


What is RIT: Radioimmunotherapy?

When your body detects something that does not belong, such as bacteria, one way it eliminates it is to produce antibodies that bind to the protein shapes that are specific to the pathogen.

RIT agents are man-made antibodies with different radiation components attached, designed to bind to a protein shape called CD20, which sticks out of mature B lymphocytes (immune cells), both malignant and nonmalignant (cancerous and normal).



... Importantly, the cd20 shape (or antigen / receptor) is **not** found on precursor b-cells – immature b-cells which can later mature to replenish the supply of normal mature b-cells.

There are two approved RIT therapies for b-cell lymphomas: Bexxar and Zevalin.

RIT is considered a targeted therapy, because the antibodies that deliver the radiation are specific to one type of cell. RIT is more potent than unlabeled antibody therapy, such as Rituxan, but it also has unique potential risks.

Clinical data shows that RIT is very potent and can induce complete responses that are very durable (measured in years), even in heavily pretreated patients.

RIT is given in therapeutic steps:

(1) The initial antibody dose ("cold" or "naked" antibody) clears the body of normal b-cells so that subsequent doses will be more focused on tumor cells.

(2) The second "warm" dose likely has anti-tumor effects, but also helps calculate the optimal and safe final dose. For Bexxar the dose is calculated based on individual clearance rates as determined by imaging of the gamma radioactive element.

(3) The final "hot" dose has the most potent anti-tumor effects, and is focused on tumor cells.

Ways that radio-immunotherapy are thought to lyse (destroy) tumor cells

When radio-labeled antibody binds to tumor cells it can cause tumor killing by:

(1) Inducing self-killing (apoptosis), which is programmed cell death triggered by the binding of the antibody to the cell receptor.

(2) Complement-dependent cytotoxicity (CDC) - where antibody leads to fixing of complement by the immune system.

(3) Antibody-dependent cellular cytotoxicity (ADCC) - where effector cells (immune cells) kill antibody-engaged tumor cells.

(4) Ionizing radiation from the radioisotope damages the tumor cells, leading to cell death.

(5) Possible vaccine-like effect - leading to adaptive immunity against cells that may survive initial treatment. This mechanism is not proven but suggested by the time to optimal response – as long as two years.

WHEN TO CONSIDER RADIOIMMUNOTHERAPY

For Lymphoma Patients and Caregivers

Providing evidence-based resources on lymphoma and its treatments – and informed perspectives on clinical research and clinical trial design – independent of health industry funding



Lymphomation.org

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Guiding Principle:

The routine discussion and full consideration of all reasonable treatment options for lymphomas, including clinical trials – informed consent.

Objectives:

The under-utilization of RIT has been cited by experts in the field, the media, and in medical journals.

Our objective is to encourage patients and treating physicians to include RIT as an option when treatments of b-cell lymphomas are being considered.

When might RIT be appropriate, indicated or deserving of your consideration?

FDA approved indications for RIT: "for the treatment of relapsed or refractory low grade, follicular, or transformed B-cell non-Hodgkin's lymphoma (NHL)."

Important: Treatment decisions are complex and require input from well-trained, experienced lymphoma specialists. All therapies have risks and outcomes will vary. Please discuss the risks and benefits of all reasonable therapies when consulting your physician. Items below marked with * indicate investigational uses. See *Locating RIT-based Clinical Trials*.

- As first primary treatment, perhaps as an alternative to chemotherapy, particularly if chemotherapy is not indicated for you. *
- As consolidation therapy? *
Consolidation therapy is a treatment given shortly after another treatment with the goal

of improving on the response. (Also called sequential therapy.)

- As second primary treatment, particularly following a short or insufficient response to prior treatment?
Primary treatment is one that is given with intent to achieve a significant and long lasting response, as opposed to palliative therapy where the goal might be to relieve symptoms.
- When you have relapsed from prior treatment and the goal of your next therapy is to achieve a durable complete remission.
- As a possible alternative to stem cell transplantation (SCT), particularly if SCT is indicated, but not suitable for you because of age or other factors. *

- As part of the conditioning therapy of stem cell transplantation? *
- As a possible alternative to maintenance Rituxan

Maintenance is the regularly scheduled administration of Rituxan with the goal of maintaining the response to prior induction treatment.

- When transformation is suspected and you are not a candidate for SCT, or combination chemotherapy, such as CHOP-Rituxan?

Transformation is a change in the indolent lymphoma cells that leads to more aggressive clinical behavior and/or resistance to standard treatment.

Locating RIT-based Clinical Trials

- Go to www.lymphomation.org
- Select **Clinical Trials**
- Select by **Treatment Type**
- Select **Radioimmunotherapy**
- Select desired query type:

All lymphoma studies utilizing radioimmunotherapy (RIT)

RIT for previously untreated lymphoma

RIT as part of Stem Cell transplantation

RIT-based sequential therapy

DLBCL and Radioimmunotherapy

High dose, or maximum tolerated doses of treatment with RIT

Non-clinical factors that may contribute to the underutilization of RIT

- Lack of awareness of the potential of RIT to result in higher remission rates and longer remissions.
- When insurance carriers do not cover treatment out of network/area, and the patient's treating physician does not offer nuclear medicine.
- Not all physicians can offer nuclear medicine in their local practice.
- The risks* of RIT may be overestimated or not fully understood.

** RIT, like all cancer treatments, has potential risks and benefits. Please discuss with your doctors the clinical factors – such as your age, areas of involvement, previous therapies – that may increase or reduce risk.*