# Safety and Efficacy of Radioimmunotherapy With Yttrium 90 Ibritumomab Tiuxetan (Zevalin)

Hossein Borghaei and Russell J. Schilder

**Patients with low-grade, follicular non-Hodgkin's lymphoma usually present with advanced disease, which is not considered curable with conventional therapies. New approaches are needed to improve the outcomes in patients with this disease. Yttrium 90 ibritumomab tiuxetan (Zevalin; Biogen Idec Inc, Cambridge, MA), is highly effective, with overall response rates of 73% to 83% and complete response rates of 15% to 51%, with a median duration of response in complete responders of 23 months. The response rates tend to be higher in patients who have been treated with fewer prior therapies, and $^{90}$Y ibritumomab tiuxetan may be suitable for use early in the course of therapy. Delayed myelosuppression is the most common adverse effect, and it is predictable, reversible, and manageable. Yttrium 90 ibritumomab tiuxetan has less nonhematologic toxicity than chemotherapy, with only minimal alopecia, mucositis, nausea, or vomiting, and a lower incidence of infections. The ibritumomab tiuxetan regimen is routinely and safely given in an outpatient setting and is completed in 7 to 9 days, and is thus more convenient for patients than chemotherapy.**


TREATMENT options for relapsed non-Hodgkin's lymphoma (NHL), and in particular for indolent B-cell NHL, have been expanded by the introduction of the monoclonal antibody to CD20 rituximab (Rituxan; Genentech, Inc, South San Francisco, CA, and Biogen Idec Inc, Cambridge, MA), which has gained near-universal acceptance, due in large part to its observed response rate as a single agent of up to 48%, with a median time to progression of 13 months.[1,2] Several strategies to increase the response rate and duration of response with rituximab have been evaluated, including the use of rituximab in combination with conventional chemotherapy, such as CHOP (cyclophosphamide/vincristine/doxorubicin/prednisone), and the use of high-dose rituximab.[2-4]

Radioimmunotherapy is particularly useful in B-cell lymphomas, which are highly radiosensitive. The radiolabeled monoclonal antibody yttrium 90 ibritumomab tiuxetan (Zevalin; Biogen Idec Inc, Cambridge, MA) has been shown to produce clinically significant responses in tumors of all sizes in patients with NHL, and it was the first radiolabeled monoclonal antibody approved for the treatment of lymphoma. In clinical trials, $^{90}$Y ibritumomab tiuxetan has achieved consistent overall response rates (ORRs) of 73% to 83%, with a complete response/complete response (unconfirmed) (CR/CRu) rate of 15% to 51% (Table 1).[5-13] The median duration of response in patients with a CR/CRu has been 23 months.[5] Yttrium 90 ibritumomab tiuxetan is well tolerated and has a good safety profile in the indicated population. The dose-limiting toxicity of $^{90}$Y ibritumomab tiuxetan is a delayed but transient myelosuppression.

## YTTRIUM 90 IBRITUMOMAB TIUXETAN

Yttrium 90 ibritumomab tiuxetan is indicated for the treatment of patients with relapsed or refractory low-grade, follicular, or transformed B-cell NHL, including patients with rituximab-refractory follicular NHL.[14] The murine IgG1 monoclonal antibody ibritumomab is the parent antibody of the chimeric monoclonal antibody rituximab. Ibritumomab has been shown to have antiproliferative effects and to induce apoptosis in vitro. It is covalently bound to the second-generation chelator tiuxetan, which forms a strong bond with the radionuclide (Fig 1). Tiuxetan provides a high-affinity chelation site for indium 111 (for imaging) or yttrium 90 (for therapy). Yttrium 90 is a pure beta emitter with a half-life of 64 hours, a maximum energy of 2.3 MeV, and a mean path length in soft tissue of approximately 5 mm. The high energy and long path length of $^{90}$Y help make $^{90}$Y ibritumomab tiuxetan effective both in relatively small tumors and in bulky or poorly vascularized tumors, as well as in tumors with heterogeneous CD20 expression. The ibritumomab tiuxetan regimen is routinely and safely given in an outpatient procedure because of the secure chelation of the $^{90}$Y radionuclide, and the fact that the beta radiation

*From the Department of Medical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

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*Address reprint requests to Russell J. Schilder, MD, Department of Medical Oncology, Fox Chase Cancer Center, 333 Cottman Ave, Philadelphia, PA 19111.*


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**Table 1. Efficacy of $^{90}$Y Ibritumomab Tiuxetan in Clinical Trials**

| Investigators | Study Design | No. of Patients | Patients With OR | Patients With CR/CRu | Median Duration of CR/CRu |
|---|---|---|---|---|---|
| Witzig et al 1999[7] Witzig et al 2003[12] | Phase I-II several histologies | 51 | 73% | 51% | 23 mos |
| Wiseman et al 2002[10] Witzig et al 2003[12] | Phase II patients with mild thrombocytopenia | 30 | 83% | 47% | 23 mos |
| Witzig et al 2002[9] Witzig et al 2003[12] | Phase III randomized | 143 | 80% | 34% | 23 mos |
| Witzig et al 2002[13] | Phase II rituximab-refractory NHL | 57 | 74% | 15% | N/A |

Abbreviations: OR, overall response; CR, complete response; CRu, complete response (unconfirmed).

emitted by $^{90}$Y cannot escape the patient's body after $^{90}$Y ibritumomab tiuxetan has been administered.[15]

## EFFICACY OF $^{90}$Y IBRITUMOMAB TIUXETAN

Several clinical trials have established the efficacy of $^{90}$Y ibritumomab tiuxetan in patients with NHL (Table 1). Witzig et al[7] reported the results of a phase I-II multicenter trial in 51 patients with relapsed or refractory low-grade, intermediate-grade, or mantle cell CD20+ B-cell NHL. The study determined that a dose of rituximab 250 mg/m$^2$ is adequate for improving the biodistribution of the radiolabeled antibody and that the maximum tolerated single dose of $^{90}$Y ibritumomab tiuxetan that can be delivered in an outpatient setting without stem cell support is 0.4 mCi/kg in patients with a platelet count of 150 $\times$ 10$^9$/L or greater and 0.3 mCi/kg in those with a count of 100 $\times$ 10$^9$/L to 149 $\times$ 10$^9$/L. The ORR in this study was 73% (CR/CRu 51%).[5] In patients with low-grade NHL the ORR was 82% (CR 26%) and in those with intermediate-grade NHL it was 43% (CR 29%).[7] The adverse events were primarily hematologic, and correlated with the extent of marrow involvement with NHL and the platelet count before treatment.

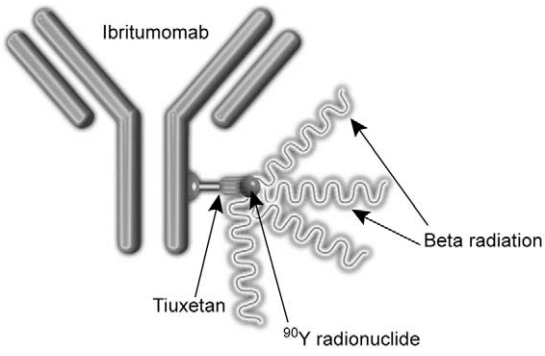


**Fig 1. The $^{90}$Y ibritumomab tiuxetan molecule.**

In the clinical studies of $^{90}$Y ibritumomab tiuxetan to date, patients with a lymphomatous marrow involvement of more than 25% were excluded. Significant thrombocytopenia is of particular concern, and a lower dose of $^{90}$Y ibritumomab tiuxetan (0.3 mCi/kg) has been found to be appropriate in patients with mild thrombocytopenia (100 $\times$ 10$^9$/L to 149 $\times$ 10$^9$/L).[10] In this open-label multicenter phase II study by Wiseman et al,[10] ORR was 83% in 30 patients, with a CR/CRu rate of 47%.[5]

Therapy with $^{90}$Y ibritumomab tiuxetan has been compared with rituximab therapy in a phase III trial in 143 patients with histologically proven relapsed or refractory follicular, low-grade, or transformed NHL.[9] Patients were randomized to one treatment with $^{90}$Y ibritumomab regimen 0.4 mCi/kg plus infusions of rituximab 250 mg/m$^2$ or to rituximab 375 mg/m$^2$/wk for 4 weeks. The primary endpoint in this study was ORR; responses were confirmed by a panel of independent blinded experts. The ORR in the $^{90}$Y ibritumomab tiuxetan group was 80% and in the rituximab group was 56% ($P$ = .002). This response rate in the rituximab control group was comparable to the 48% ORR in the pivotal trial of rituximab in 166 patients.[2] The CR/CRu rate was 34% in the $^{90}$Y ibritumomab tiuxetan group and 20% in the rituximab group ($P$ = .04).

The efficacy of $^{90}$Y ibritumomab tiuxetan has also been evaluated in patients with rituximab-refractory follicular NHL.[13] Patients were considered to have refractory disease if they had not responded to rituximab 375 mg/m$^2$/wk or if they had durations of response of less than 6 months. Ninety-five percent of the patients had follicular histology and 90% had stage III or IV disease. This group of patients had been heavily treated, with a median of four prior chemotherapy regimens (range, 1 to 9), and many (>70%) had bulkier disease (≥5 cm) than the patients in the above-

**Table 2. Exclusion Criteria for $^{90}$Y Ibritumomab Tiuxetan**

- Presence of lymphoma in ≥25% of the bone marrow
- Prior myeloablative therapy with peripheral blood stem cell or bone marrow transplantation
- Platelet count $<100 \times 10^9$/L
- ANC $<1.5 \times 10^9$/L
- Hypocellular bone marrow (<15% cellularity)
- History of failed stem cell collection
- Prior external beam radiation to >25% active marrow

mentioned trial that directly compared $^{90}$Y ibritumomab tiuxetan therapy with rituximab therapy. The ORR was 74% (15% CR), which was not significantly affected by the presence or absence of bone marrow involvement or splenomegaly or by patient weight ≤80 kg or >80 kg ($^{90}$Y ibritumomab tiuxetan dose capped at 32 mCi). The response rate (74% *v* 80%) and median time to progression (6.8 months *v* 11.2 months) in this trial were slightly lower than those observed in the trial that compared $^{90}$Y ibritumomab tiuxetan with rituximab.[9] This may be attributable to the higher number of prior therapies in the patients in this trial than in the previous trial (median, 4 *v* 2). This result suggests that $^{90}$Y ibritumomab tiuxetan may be more effective when it is used earlier in the course of treatment.[16]

## SAFETY OF $^{90}$Y IBRITUMOMAB TIUXETAN

The ibritumomab tiuxetan regimen should be used only in appropriate patients, and the exclusion criteria should be strictly observed (Table 2). Patients with adequate bone marrow reserves and limited bone marrow involvement are optimal candidates. The most common adverse event with $^{90}$Y ibritumomab tiuxetan therapy is a transient but delayed myelosuppression. Unlike chemotherapy, treatment with $^{90}$Y ibritumomab tiuxetan is not associated with severe mucositis, hair loss, or persistent or prolonged nausea or vomiting.[12] Treatment with $^{90}$Y ibritumomab tiuxetan does not require that patients be isolated from others at any time, because those with whom patients have close contact are exposed to only minimal radiation, which is comparable to background levels.[15]

## HEMATOLOGIC EVENTS

The myelosuppression with $^{90}$Y ibritumomab tiuxetan may result in thrombocytopenia, neutropenia, and anemia. In the 349 patients in the registrational database who were treated with $^{90}$Y ibritumomab tiuxetan, the median nadirs were absolute neutrophil count, $0.8 \times 10^9$/L; platelets, $41 \times 10^9$/L; and hemoglobin level, 105 g/L (Table 3). In the randomized phase III trial that compared $^{90}$Y ibritumomab tiuxetan with rituximab alone, the nadirs for absolute neutrophil count (median, $0.9 \times 10^9$/L), platelets (median, $41 \times 10^9$/L), and hemoglobin level (median, 108 g/L) occurred at 42 to 49 days after the start of treatment, much later than the typical 10 to 14 days with chemotherapy. The myelosuppression with the ibritumomab tiuxetan regimen is, however, predictable, reversible, and manageable.

The median duration of severe hematologic toxicities (measured from the last day of grade 2 before the nadir to the first day of grade 2 after the nadir) was 27 days for the absolute neutrophil count, 23 days for the platelet count, and 15 days for the hemoglobin level.[9] The nadirs were somewhat lower in the patients with mild thrombocytopenia, who were treated with $^{90}$Y ibritumomab tiuxetan 0.3 mCi/kg, but this was not associated with a greater incidence of infections or bleeding than in the patients with higher platelet counts ($\geq 150 \times 10^9$/L), who were treated with $^{90}$Y ibritumomab tiuxetan 0.4 mCi/kg.[10]

**Table 3. Hematologic Toxicity With $^{90}$Y Ibritumomab Tiuxetan**

| $^{90}$Y Ibritumomab Tiuxetan Dose | Median Nadir | Patients With Toxicity Grade 3 | Patients With Toxicity Grade 4 | Duration | |
|---|---|---|---|---|---|
| | | | | All Patients | Patients With Grade 3 or 4 |
| Neutropenia | | | | | |
| 0.3 mCi/kg | $0.6 \times 10^9$/L | 40% | 35% | 23 days | 29 days |
| 0.4 mCi/kg | $0.8 \times 10^9$/L | 28% | 30% | 14 days | 22 days |
| Thrombocytopenia | | | | | |
| 0.3 mCi/kg | $24 \times 10^9$/L | 66% | 14% | 29 days | 34.5 days |
| 0.4 mCi/kg | $41 \times 10^9$/L | 52% | 10% | 15 days | 24 days |
| Anemia | | | | | |
| 0.3 mCi/kg | 100 g/L | 12% | 8% | 0 days | 14 days |
| 0.4 mCi/kg | 105 g/L | 14% | 3% | 0 days | 14 days |

**Table 4. Incidence of Nonhematologic Adverse Events Occurring in ≥5% of Patients in Clinical Trials With $^{90}$Y Ibritumomab Tiuxetan During the Treatment Period*[14] (N = 349)**

| | All Grades no. (%) | Grade 3/4 no. (%) |
|---|---|---|
| Any Adverse Event | 318 (91.1) | 70 (20.1) |
| Infection | 100 (28.7) | 16 (4.6) |
| Chills | 82 (23.5) | 1 (0.3) |
| Fever | 58 (16.6) | 2 (0.6) |
| Abdominal pain | 54 (15.5) | 9 (2.6) |
| Pain | 44 (12.6) | 3 (0.9) |
| Hypotension | 22 (6.3) | 3 (0.9) |
| Nausea | 107 (30.7) | 2 (0.6) |
| Vomiting | 41 (11.7) | 0 (0.0) |
| Diarrhea | 31 (8.9) | 1 (0.3) |
| Anorexia | 27 (7.7) | 0 (0.0) |
| Peripheral edema | 28 (8.0) | 2 (0.6) |
| Arthralgia | 26 (7.4) | 2 (0.6) |
| Myalgia | 23 (6.6) | 1 (0.3) |
| Dizziness | 35 (10.0) | 1 (0.3) |
| Dyspnea | 47 (13.5) | 7 (2.0) |
| Pruritus | 32 (9.2) | 1 (0.3) |
| Rash | 29 (8.3) | 1 (0.3) |

*Treatment period is the time interval from first infusion to 12 weeks after $^{90}$Y ibritumomab tiuxetan treatment. All adverse events are included regardless of cause.

## NONHEMATOLOGIC EVENTS

The most common nonhematologic toxicities observed in the clinical trials of $^{90}$Y ibritumomab tiuxetan are shown in Table 4. These tend to reflect the nonhematologic toxicities of rituximab, and may be attributable to the preinfusions of rituximab, which account for most of the total amount of antibodies given.

## INFECTIOUS EVENTS

The incidence of infectious complications in the first 3 months after the start of therapy is 29% (Table 5).[14] This is substantially lower than the typical incidence of infectious complications with CHOP chemotherapy of 65%.[17] These infections included febrile neutropenia, sepsis, pneumonia, cellulitis, diarrhea, osteomyelitis, and urinary tract and upper respiratory tract infections. In an integrated safety database of 349 patients the overall incidence of hospitalization because of serious infection was 7%.[14] The incidence of hospitalization because of febrile neutropenia was 2%.[12]

## SECONDARY MALIGNANCIES

In a recent update reported by Czuczman et al,[18] myelodysplastic syndrome or acute myelogenous leukemia had developed in 10 (1.3%) of 770 patients treated with $^{90}$Y ibritumomab tiuxetan over the past 9 years. The onset of a secondary cancer occurred at 4 to 34 months after treatment with $^{90}$Y ibritumomab tiuxetan and 1.5 to 14 years after the diagnosis of NHL. The overall risk of the development of myelodysplastic syndrome/acute myelogenous leukemia reported in the literature on patients with NHL treated with chemotherapy ranges from 0.6% to 8% at 10 years. Thus far, the incidence of secondary malignancies after treatment with $^{90}$Y ibritumomab tiuxetan is well within the range expected in patients who have previously been treated with multiple potentially leukemogenic therapies (eg, regimens containing alkylating agents).[19] Of the 10 patients in whom secondary malignancies developed after treatment with $^{90}$Y ibritumomab tiuxetan, one patient developed acute myelogenous leukemia 4 months after treatment with $^{90}$Y ibritumomab tiuxetan. It is unlikely that the development of acute myelogenous leukemia in as little as 4 months after treatment with $^{90}$Y ibritumomab tiuxetan is related to this regimen, but cytogenetic analyses before treatment with $^{90}$Y ibritumomab tiuxetan were not available. All of the patients in whom secondary malignancies developed had a significant history of treatment with alkylating agents. Longer follow-up is necessary to more precisely assess the potential risk of secondary malignancy. There was one patient who developed a grade 1 meningioma.

## FEASIBILITY OF THERAPIES SUBSEQUENT TO $^{90}$Y IBRITUMOMAB TIUXETAN

It was shown in a recent review of clinical trials of $^{90}$Y ibritumomab tiuxetan that therapies given subsequent to $^{90}$Y ibritumomab tiuxetan were safe and effective.[20] A total of 152 patients with NHL from five clinical trials received treatment subsequent to $^{90}$Y ibritumomab tiuxetan therapy. These treatments included single alkylating agents, CHOP, and other intensive chemotherapy regimens. Some patients were treated with bioimmunotherapy or high-dose chemotherapy followed by peripheral blood stem cell

**Table 5. Infectious Events in Clinical Trials With $^{90}$Y Ibritumomab Tiuxetan**

| | 0 to 3 Months After Treatment | 3 to 48 Months After Treatment |
|---|---|---|
| Total | 29% | 6% |
| Grade 1 or 2 | 84% | 3% |
| Grade 3 or 4 | 16% | 2% |

support. Responses were seen with all of the types of subsequent therapy, with ORRs comparable to those in patients with NHL who had not been previously treated with $^{90}$Y ibritumomab tiuxetan. Ansell et al[21] also showed that the rate and severity of adverse events with subsequent treatment in 58 patients who had been treated with $^{90}$Y ibritumomab tiuxetan at a single institution were no different from those in similar patients who had not been treated with $^{90}$Y ibritumomab tiuxetan. Eight patients in this study were treated with autologous stem cell transplantation, in seven of whom peripheral blood stem cells were collected after growth factor mobilization. Bone marrow collection was required in one patient, because of low peripheral blood stem cell counts despite the use of growth factor. Another patient had an allogeneic transplant. All patients recovered adequate blood cell counts after transplantation, at rates similar to those in historical controls who had not been treated with $^{90}$Y ibritumomab tiuxetan.

Yttrium 90 ibritumomab tiuxetan is highly effective, with ORRs of 73% to 83% and CR/CRu of 15% to 51% in clinical trials, with a median duration of response in complete responders of 23 months. Yttrium 90 ibritumomab tiuxetan may be particularly suitable for use early in the course of therapy, because the ORRs tend to be higher in patients who have been treated with fewer prior therapies. Delayed myelosuppression is the most common adverse event, and it is predictable, reversible, and manageable.

Treatment with $^{90}$Y ibritumomab tiuxetan is better tolerated than chemotherapy, with minimal nonhematologic toxicities such as mucositis, alopecia, or severe or prolonged nausea or emesis. The incidence of infections is also lower, and the $^{90}$Y ibritumomab tiuxetan regimen is more convenient for patients. The ibritumomab tiuxetan regimen is routinely and safely given in an outpatient setting and is completed in 7 to 9 days.

## REFERENCES


1. Cheson BD: Rituximab: Clinical development and future directions. Expert Opin Biol Ther 2:97-110, 2002

2. McLaughlin P, Grillo-Lopez AJ, Link BK, et al: Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: Half of patients respond to a four-dose treatment program. J Clin Oncol 16:2825-2833, 1998

3. Keating M, O'Brien S: High-dose rituximab therapy in chronic lymphocytic leukemia. Semin Oncol 27:86-90, 2000 (suppl 12)

4. Dillman RO: Radiolabeled anti-CD-20 monoclonal antibodies for the treatment of B-cell lymphoma. J Clin Oncol 20:3545-3557, 2002

5. Witzig TE, Emmanouilides C, Molina A, et al: Yttrium-90 ibritumomab tiuxetan radioimmunotherapy (RIT) induces durable complete responses (CR/CRu) in patients with relapsed or refractory B-cell non-Hodgkin's lymphoma (NHL). Proc Am Soc Clin Oncol 22:597, 2003 (abstr 2400)

6. Knox SJ, Goris ML, Trisler K, et al: Yttrium-90-labeled anti-CD20 monoclonal antibody therapy of recurrent B-cell lymphoma. Clin Cancer Res 2:457-470, 1996

7. Witzig TE, White CA, Wiseman GA, et al: Phase I/II trial of IDEC-Y2B8 radioimmunotherapy for treatment of relapsed or refractory CD20$^+$ B-cell non-Hodgkin's lymphoma. J Clin Oncol 17:3793-3803, 1999

8. White CA, Halpern SE, Parker BA, et al: Radioimmunotherapy of relapsed B-cell lymphoma with yttrium 90 anti-idiotype monoclonal antibodies. Blood 87:3640-3649, 1996

9. Witzig TE, Gordon LI, Cabanillas F, et al: Randomized controlled trial of yttrium-90-labeled ibritumomab tiuxetan radioimmunotherapy versus rituximab immunotherapy for patients with relapsed or refractory low-grade, follicular, or transformed B-cell non-Hodgkin's lymphoma. J Clin Oncol 20:2453-2463, 2002

10. Wiseman GA, Gordon LI, Multani PS, et al: Ibritumomab tiuxetan radioimmunotherapy for patients with relapsed or refractory non-Hodgkin lymphoma and mild thrombocytopenia: A phase II multicenter trial. Blood 99:4336-4342, 2002

11. Parker BA, Vassos AB, Halpern SE, et al: Radioimmunotherapy of human B-cell lymphoma with $^{90}$Y-conjugated antiidiotype monoclonal antibody. Cancer Res 50:1022s-1028s, 1990 (suppl 3)

12. Witzig TE, White CA, Gordon LI, et al: Safety of yttrium-90 ibritumomab tiuxetan radioimmunotherapy for relapsed low-grade, follicular, or transformed non-Hodgkin's lymphoma. J Clin Oncol 21:1263-1270, 2003

13. Witzig TE, Flinn IW, Gordon LI, et al: Treatment with ibritumomab tiuxetan radioimmunotherapy in patients with rituximab-refractory follicular non-Hodgkin's lymphoma. J Clin Oncol 20:3262-3269, 2002

14. Zevalin (ibritumomab tiuxetan) prescribing information: San Diego, CA, IDEC Pharmaceuticals, 2002

15. Wagner HN Jr, Wiseman GA, Marcus CS, et al: Administration guidelines for radioimmunotherapy of non-Hodgkin's lymphoma with $^{90}$Y-labeled anti-CD20 monoclonal antibody. J Nucl Med 43:267-272, 2002

16. Emmanouilides CE, Witzig TE, Molina A, et al: Improved safety and efficacy of yttrium-90 ibritumomab tiuxetan radioimmunotherapy when administered as 2nd or 3rd line therapy for relapsed low-grade, follicular, and transformed B-cell non-Hodgkin's lymphoma (NHL). Proc Am Soc Clin Oncol 22:595, 2003 (abstr 2392)

17. Coiffier B, Lepage E, Briere J, et al: CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. N Engl J Med 346:235-242, 2002

18. Czuczman M, Witzig TE, Gaston I, et al: Zevalin radioimmunotherapy is not associated with an increased incidence of

secondary myelodysplastic syndrome (MDS) or acute myelogenous leukemia (AML). Blood 100:357a, 2002 (abstr 1386)

19. Leone G, Mele L, Pulsoni A, et al: The incidence of secondary leukemias. Haematologica 84:937-945, 1999

20. Schilder RJ, Witzig T, Gordon L, et al: $^{90}$Y ibritumomab tiuxetan (Zevalin) radioimmunotherapy does not preclude effective delivery of subsequent therapy for lymphoma. Proc Am Soc Clin Oncol 21:267a, 2002 (abstr 1064)

21. Ansell SM, Ristow KM, Habermann TM, et al: Subsequent chemotherapy regimens are well tolerated after radioimmunotherapy with yttrium-90 ibritumomab tiuxetan for non-Hodgkin's lymphoma. J Clin Oncol 20:3885-3890, 2002