VOLUME 27 · NUMBER 31 · NOVEMBER 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Phase II Study of Yttrium-90–Ibritumomab Tiuxetan in Patients With Relapsed or Refractory Mantle Cell Lymphoma

Michael Wang, Yasuhiro Oki, Barbara Pro, Jorge Enrique Romaguera, Maria Alma Rodriguez, Felipe Samaniego, Peter McLaughlin, Frederick Hagemeister, Sattva Neelapu, Amanda Copeland, Barry I. Samuels, Evelyne M. Loyer, Yuan Ji, and Anas Younes

From the Departments of Lymphoma, Myeloma, and Diagnostic Imaging and Division of Quantitative Science, The University of Texas M. D. Anderson Cancer Center, Houston, TX.

Submitted January 10, 2009; accepted May 21, 2009; published online ahead of print at www.jco.org on September 21, 2009.

Presented in part at the 48th Annual Meeting of the American Society of Hematology, December 9-12, 2006, Atlanta, GA.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Clinical Trials repository link available on JCO.org.

Corresponding author: Anas Younes, MD, Department of Lymphoma and Myeloma, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd, Unit 429, Houston, TX 77030; e-mail: ayounes@mdanderson.org.

0732-183X/09/2731-5213/$20.00

DOI: 10.1200/JCO.2009.21.8545

ABSTRACT

Purpose

This phase II trial evaluated the safety and efficacy of yttrium-90 (^{90}Y)–ibritumomab tiuxetan in patients with relapsed or refractory mantle cell lymphoma (MCL).

Patients and Methods

Patients with relapsed or refractory MCL were eligible for the study if they had adequate major organ function and performance status. Those with CNS disease, pleural effusion, circulating lymphoma cells ≥ 5,000/μL, or history of stem-cell transplant were ineligible. Patients with a platelet count ≥ 150,000/μL received a dose of 0.4 mCi/kg of ^{90}Y–ibritumomab tiuxetan, whereas those with a platelet count less than 150,000/μL received a dose of 0.3 mCi/kg.

Results

Thirty-four patients with a median age of 68 years (range, 52 to 79 years) received the therapeutic dose. The patients had received a median of three prior treatment regimens (range, one to six treatment regimens), including those that contained rituximab (n = 32) and bortezomib (n = 7). Of the 32 patients with measurable disease, 10 (31%) achieved complete or partial remission. After a median follow-up of 22 months (range, 2 to 72+ months), an intent-to-treat analysis revealed a median event-free survival (EFS) duration of 6 months and an overall survival duration of 21 months. The median EFS for those who achieved partial or complete remission was 28 months, while it was 3 months for those whose disease did not respond ($P < .0001$); it was 9 months for patients whose tumor measured less than 5 cm in the largest diameter before treatment and 3 months for those whose tumor measured ≥ 5 cm ($P = .015$).

Conclusion

The single-agent activity of ^{90}Y–ibritumomab tiuxetan and its favorable safety profile warrant its further development for the treatment of MCL.

J Clin Oncol 27:5213-5218. © 2009 by American Society of Clinical Oncology

INTRODUCTION

Mantle cell lymphoma (MCL) is a relatively rare type of B-cell non-Hodgkin's lymphoma (NHL) that accounts for approximately 5% of NHL cases in North America. The majority of patients with MCL present with advanced stage disease requiring systemic therapy; therefore, experience with external radiation therapy remains limited to the rare early-stage presentations and to palliation of relapsed disease.[1,2] While a variety of systemic combination chemotherapy regimens have been reported to produce high response rates, they remain noncurative: the durations of event-free survival (EFS) and overall survival (OS) remain short.[3-6]

Because the disease is disseminated in more than 90% of patients, we evaluated the potential therapeutic value of systemic radiation therapy delivered by the radioimmunotherapy (RIT) approach. While RIT has been shown to be effective for the treatment of relapsed indolent and transformed large B-cell lymphomas,[7-10] the clinical efficacy of this treatment modality in MCL is not well established. In this phase II clinical trial, we evaluated the safety and efficacy of a single standard dose of yttrium-90 (^{90}Y)–ibritumomab tiuxetan in patients with relapsed or refractory MCL.

PATIENTS AND METHODS

Patients

Patients were required to have histologically confirmed relapsed or refractory MCL with less than 25%

bone marrow involvement with lymphoma, age ≥ 18 years, Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2, and adequate bone marrow (absolute neutrophil count ≥ 1,500/μL, platelets ≥ 100,000/μL), liver, and kidney function. Patients were excluded if they had undergone prior stem-cell transplantation or RIT, or if they had a history of CNS lymphoma, human immunodeficiency virus infection, pleural effusion, human antimouse antibody reactivity, or circulating lymphoma cell count ≥ 5,000/μL. All patients were required to sign a written informed consent approved by the institutional review board in accordance with the Declaration of Helsinki.

Study Design and Treatment

This phase II, open-label, single-arm, single-center study was designed to assess the safety and efficacy of ibritumomab tiuxetan RIT in patients with advanced relapsed or refractory MCL and was approved by the institutional review board. The components of the ibritumomab tiuxetan treatment regimen are described in detail elsewhere.[11,12]

Patients initially received one course of rituximab (250 mg/m^2) and immediately thereafter an intravenous injection of an imaging dose of indium-111 (^{111}In)–ibritumomab tiuxetan (5 mCi [185 MBq]; 1.6 mg). One week later, patients with favorable imaging results received a second infusion of rituximab (250 mg/m^2) and a therapeutic intravenous injection of ^{90}Y–ibritumomab tiuxetan at a dose based on body weight and platelet count. Patients with a pretreatment platelet count ≥ 150,000/μL received a dose of 0.4 mCi ^{90}Y/kg (maximum dose 32 mCi), whereas those with a platelet count of 100,000 to 150,000/μL received 0.3 mCi ^{90}Y/kg.

Assessment

Duration of EFS was calculated from the date of registration onto the study to the date of documented relapse, disease progression, or death from any cause. Duration of OS was calculated from the date of registration onto the study to the date of death from any cause. Tumor assessments were performed on all target lesions identified by computed tomographic scans (neck, thorax, abdomen, and pelvis) at baseline, every 3 months for 1 year, every 4 months during year 2, every 6 months during years 3 to 5, and yearly thereafter. Changes in the sum of the products of the largest perpendicular diameters of measurable lesions were used to establish partial remission (PR) and complete remission (CR) as defined by the International Workshop Response Criteria, which do not incorporate positron emission tomography findings.[13] Adverse events were graded according to the National Cancer Institute Common Toxicity Criteria version 3.

Statistical Analysis

The primary end point of the study was the overall response (CR + PR) rate, and the secondary end points were EFS, OS, and toxicities. The study used a MiniMax two-stage design, in which 18 patients were recruited in the first stage. If five or more responses were observed in the first stage, an additional 15 patients were recruited in the second stage. The two-stage design was based on $\alpha = .05$, power = 0.8, undesirable response rate = 20%, and desirable response rate = 40%. Statistical analyses for patients' characteristics, response rates, and adverse events were descriptive. Analysis of EFS and OS was performed on an intent-to-treat basis and was calculated by the Kaplan-Meier method.[14] Comparison between curves was performed by using a two-sided log-rank test (significance level of $\alpha = .05$).

RESULTS

Patient Characteristics

Thirty-five eligible patients were enrolled between April 2002 and June 2006. Thirty-four of these patients received the therapeutic ^{90}Y–ibritumomab tiuxetan dose and were evaluable for treatment toxicity. One patient withdrew consent after receiving the imaging dose. Patients entering the study had been treated previously with a median of three therapeutic regimens (range, one to six treatment regimens). Twenty-two patients had been previously treated with fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (hyperCVAD) alternating with methotrexate+cytarabine,[15] seven with bortezomib,[16] and 32 with rituximab. Sixty-three percent of the patients had low-risk features according to the MCL International Prognostic Index (MIPI).[17] Patient characteristics are summarized in Table 1.

Efficacy

Thirty-two patients had bidimensionally measurable disease before starting study therapy. Of these, 21 patients (67%) had tumor reductions ranging between 14% and 85% after therapy (Fig 1). Ten (31%) of the 32 patients with measurable disease achieved a major response (five CR and five PR), while 11 patients had stable disease. In 10 of the patients with at least one tumor measuring ≥ 5 cm in

Table 1. Patient Characteristics

Characteristic	No.	%
Registered	35	100
Received therapeutic dose	34	97
With measurable disease before treatment	32	89
Sex		
Male	28	80
Female	7	20
Age, years		
Median	66	
Range	49-77	
Prior treatment regimens		
Median	3	
Range	1-6	
HyperCVAD therapy	24	68
Rituximab	32	91
Bortezomib	7	20
Elevated LDH	9	26
Stage at relapse		
I	6	17
II	8	23
III	12	34
IV	9	26
Largest tumor diameter, cm		
≥ 5	10	28
< 5	25	72
Response to last therapy		
CR	18	51
< CR	17	49
MIPI score		
0-3	22	63
4-5	11	31
> 5	2	6
IPI score		
0-1	13	37
2-3	21	60
4-5	1	3

Abbreviations: hyperCVAD, fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone; LDH, lactate dehydrogenase; CR, complete remission; MIPI, mantle cell lymphoma international prognostic index; IPI, international prognostic index.

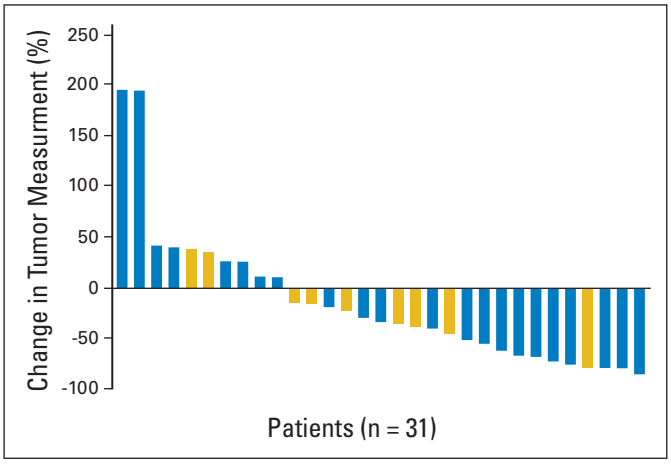

Fig 1. Waterfall chart demonstrating change in tumor measurements for 31 patients with measurable tumor at baseline who received the therapeutic dose of yttrium-90–ibritumomab tiuxetan. Patients with tumor measuring less than 5 cm in largest diameter (blue bars) had a higher response rate than those with tumor measuring ≥ 5 cm in largest diameter (gold bars).

diameter, a response to therapy was seen in one (10%). In contrast, nine (41%) of the 22 patients with a tumor size of less than 5 cm achieved a major response (Fig 1). Furthermore, patients who had received one or two prior regimens (n = 16) had a higher response rate than those who had received at least three prior regimens (44% *v* 19%, respectively). Similarly, there was a trend for a higher response rate among patients who did not receive hyperCVAD than among those who did (50% *v* 23%, respectively). Among the four patients who received a dose of 0.3 mCi ^{90}Y/kg, one achieved a CR and the others had progressive disease.

The median observation period was 22 months for the entire group (range, 2 to 72+ months) and 34+ months for patients who are alive at the time of this report (range 30+ to 72+ months). On the basis of intent-to-treat analysis, the median OS duration was 21 months and the median EFS duration was 6 months (Fig 2). As shown in Figure 3, the median EFS duration was longer for patients who achieved PR or CR than for those who did not (28 *v* 3 months; $P <$ .0001), for those with a tumor measuring less than 5 cm than for those with larger tumors (9 *v* 3 months; $P = .015$), and for those who had relapsed disease from prior CR than for those who did not achieve a CR after their last regimen (11 *v* 3 months; $P = .0005$). Conversely, the number of prior treatment regimens, prior exposure to the hyperCVAD regimen, age, MIPI score, and IPI score had no influence on EFS duration (Fig 3, and data not shown).

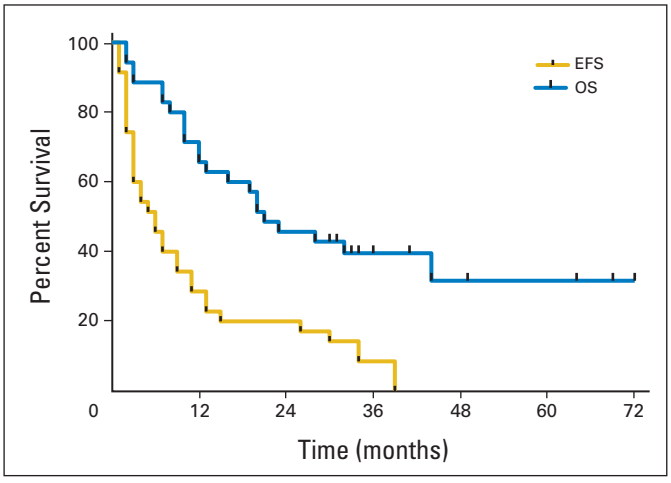

Fig 2. Event-free survival (EFS) and overall survival (OS) durations based on intent-to-treat analysis of all 35 registered patients.

Safety

Toxicity was similar to what has been reported with the same dose and schedule of ^{90}Y–ibritumomab tiuxetan in other types of lymphoma and was primarily hematologic, transient, and reversible.[8,18] The most common nonhematologic toxic effects were grade 1 and included fatigue (50%), nausea (40%), chills (37%), and diarrhea (15%). Grade 3/4 thrombocytopenia was observed in 24% of the patients, with a median time to nadir platelet count of 41 days. Grade 3/4 neutropenia was observed in 32%, with a median time to nadir neutrophil count of 48 days. One patient developed neutropenic fever, and three developed grade 1/2 nonneutropenic fever. Two patients developed myelodysplastic syndrome (MDS) 20 and 48 months after receiving therapy and remained alive 33 and 72 months, respectively, after study entry.

DISCUSSION

In the past few years, little progress has been made in the management of MCL, and the search for new active agents is ongoing.[17] Here, we report the results of what, to the best of our knowledge, is the first completed clinical trial using single-agent RIT in patients with relapsed MCL. In this study, we demonstrate that ^{90}Y–ibritumomab tiuxetan yielded a 32% response rate in 35 heavily pretreated patients with MCL, of whom 91% had previously received rituximab, 68% the hyperCVAD regimen, and 20% bortezomib. This single-agent activity compares favorably with that of other single agents when used in patients who had previously received rituximab, with remarkable similarity to bortezomib- and temsirolimus-induced remission rates and progression-free survival duration (Table 2). Furthermore, ^{90}Y–ibritumomab tiuxetan therapy offers the advantage that the treatment can be completed within 1 to 2 weeks, while bortezomib and temsirolimus require protracted treatment duration. In addition, ^{90}Y–ibritumomab tiuxetan has fewer adverse effects than these agents. The single-agent activity of ^{90}Y–ibritumomab tiuxetan in this study is similar to that in a smaller European study that was recently presented.[22]

The response rate and progression-free survival duration achieved with ^{90}Y–ibritumomab tiuxetan in this study is promising and is typical of other single agents used in similar patient populations (Table 2). It is possible, however, that these results may be improved when RIT is used in rituximab-naïve and/or previously untreated patients with low tumor burden. To test this hypothesis, Zelenetz et al[23] examined the single-agent activity of tositumomab in patients with newly diagnosed MCL (rituximab- and chemotherapy-naïve) and reported an overall response rate of 86%, confirming the radiosensitive nature of this disease. In our study, patients with tumors measuring less than 5 cm in their largest diameter had a higher response rate and longer EFS than those who had a larger tumor. Thus, it seems logical to use cytoreductive chemotherapy to decrease the

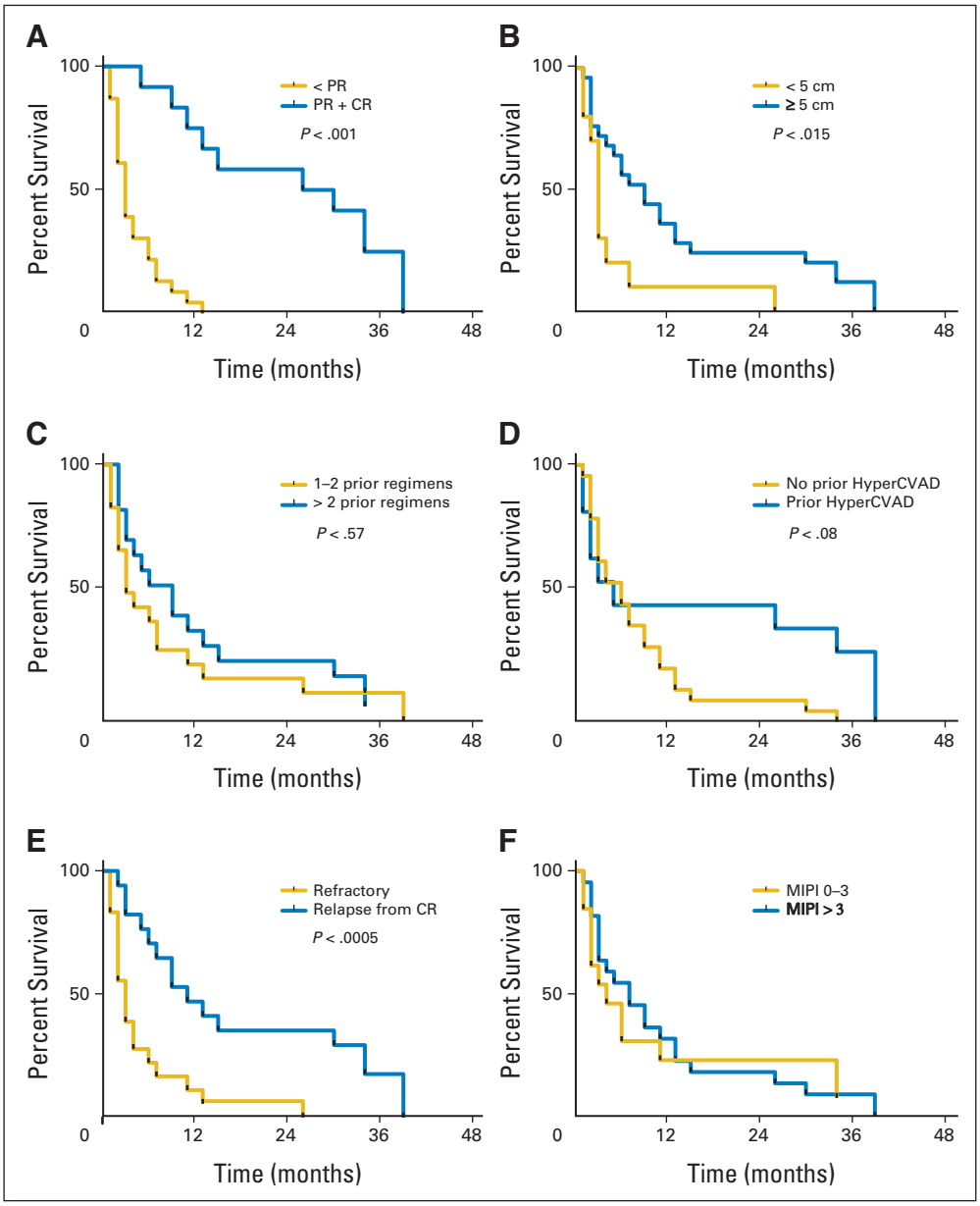

Fig 3. Event-free survival (EFS) duration according to clinical parameters. (A) EFS for patients with partial remission (PR) and complete remission (CR) patient groups combined. (B) EFS for patients with tumor size measured at its largest diameter. (C) EFS for patients who received one or two prior treatment regimens or more than two prior treatment regimens. (D) EFS for patients who received prior treatment with or had no prior treatment with fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (hyperCVAD). (E) EFS for patients who had refractory mantle cell lymphoma (MCL) or had relapsed from CR. (F) EFS for patients according to their MCL international prognostic index (MIPI).

tumor burden before administering RIT. To test this strategy, Smith et al[24] treated patients with newly diagnosed MCL with R-CHOP (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy followed by ^{90}Y–ibritumomab tiuxetan consolidation, with promising early results.

The safety of RIT that includes ^{90}Y–ibritumomab tiuxetan is now well documented. In our study, the observed toxicity was similar to what has been described when ^{90}Y–ibritumomab tiuxetan was used to treat other types of B-cell lymphoma. Both ^{90}Y–ibritumomab tiuxetan and tositumomab have been reported to induce secondary MDS and acute myelogenous leukemia. In a study of 746 patients with NHL treated with ^{90}Y–ibritumomab tiuxetan in registration and compassionate-use trials, Czuczman et al[25] reported that 19 patients (2.5%) developed MDS or acute myelogenous leukemia a median of 1.9 years (range, 0.4 to 6.3 years) after receiving RIT. In our study, two patients (5.7%) developed MDS 20 and 48 months, respectively, after completing therapy with ^{90}Y–ibritumomab tiuxetan, both of whom had previously received intensive therapy with the hyperCVAD regimen and who were older than age 65 years at the time of study entry. These patients remained alive 33 and 72 months from study registration. Finally, it is important to note that, although the median EFS duration in this study was 6 months, many patients were able to tolerate subsequent therapy, contributing to the median OS duration of 21 months.[26]

In summary, ^{90}Y–ibritumomab tiuxetan has promising activity as a single agent in relapsed MCL, especially in patients with a small-volume disease and those who have previously achieved CR with their last therapy. Further investigation of regimens that include ^{90}Y–ibritumomab tiuxetan after induction therapy in newly diagnosed patients with MCL is warranted.

Table 2. Activity of Selected Single Agents in Relapsed or Refractory MCL

Single Agent	No. of Patients With Prior Rituximab Therapy	%	Response Rate (%)	CR (%)	Median EFS/ PFS (months)	Study
Rituximab	12	0	33	NR	NR	Coiffier et al[19]
Rituximab	35	0	37	14	NR	Foran et al[20]
^{90}Y–Ibritumomab tiuxetan	35	91	32	16	6	Wang et al*
Temsirolimus	34	89	38	3	6.5	Witzig et al[21]
Bortezomib	144	96	33	8	6.2	Fisher et al[16]

Abbreviations: MCL, mantle cell lymphoma; CR, complete remission; EFS, event-free survival; PFS, progression-free survival; NR; not reported; ^{90}Y–Ibritumomab tiuxetan, yttrium-90 ibritumomab tiuxetan.
*This study.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following author(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Employment or Leadership Position: None **Consultant or Advisory Role:** Peter McLaughlin, Eli Lilly (C), Biogen Idec (C), Genentech (C), Millennium Pharmaceuticals (C); Anas Younes, Amgen (C), Gloucester Pharmaceuticals (C), Seattle Genetics (C), Millenium Pharmaceuticals (C) **Stock Ownership:** None **Honoraria:** Michael Wang, Celgene, Millennium Pharmaceuticals; Peter McLaughlin, Millennium Pharmaceuticals, Genentech, Eli Lilly, Bayer Pharmaceuticals; Frederick Hagemeister, Biogen Idec, Millenium Pharmaceuticals, Genentech, Cephalon, Amgen; Anas Younes, Biogen Idec, Genentech, Seattle Genetics, MethylGene, Pharmion, sanofi-aventis, Xencor, Amgen **Research Funding:** Michael Wang, Celgene, Millennium Pharmaceuticals, Proteolix, Novartis; Barbara Pro, Gloucester Pharmaceuticals, Allos Therapeutics, Merck, Ortho Biotech; Jorge Enrique Romaguera, Celgene, Wyeth, Millennium Pharmaceuticals; Maria Alma Rodriguez, Ortho Biotech, Amgen, Biogen Idec; Peter McLaughlin, Bayer Pharmaceuticals, Millennium Pharmaceuticals, Genentech, OSI Pharmaceuticals; Frederick Hagemeister, Novartis; Anas Younes, Genentech, sanofi-aventis, Tanox, Xencor, S*Bio, Seattle Genetics, Novartis, Nereus Pharmaceuticals **Expert Testimony:** None **Other Remuneration:** None

AUTHOR CONTRIBUTIONS

Conception and design: Anas Younes
Administrative support: Anas Younes
Provision of study materials or patients: Michael Wang, Yasuhiro Oki, Barbara Pro, Maria Alma Rodriguez, Felipe Samaniego, Peter McLaughlin, Sattva Neelapu, Anas Younes
Collection and assembly of data: Michael Wang, Yasuhiro Oki, Amanda Copeland, Barry I. Samuels, Evelyne M. Loyer, Anas Younes
Data analysis and interpretation: Michael Wang, Yasuhiro Oki, Yuan Ji, Anas Younes
Manuscript writing: Michael Wang, Yasuhiro Oki, Anas Younes
Final approval of manuscript: Michael Wang, Yasuhiro Oki, Jorge Enrique Romaguera, Sattva Neelapu, Barry I. Samuels, Anas Younes

REFERENCES

1. Rosenbluth BD, Yahalom J: Highly effective local control and palliation of mantle cell lymphoma with involved-field radiation therapy (IFRT). Int J Radiat Oncol Biol Phys 65:1185-1191, 2006

2. Leitch HA, Gascoyne RD, Chhanabhai M, et al: Limited-stage mantle-cell lymphoma. Ann Oncol 14:1555-1561, 2003

3. Jares P, Colomer D, Campo E: Genetic and molecular pathogenesis of mantle cell lymphoma: Perspectives for new targeted therapeutics. Nat Rev Cancer 7:750-762, 2007

4. Hiddemann W, Dreyling M: Mantle cell lymphoma: Therapeutic strategies are different from CLL. Curr Treat Options Oncol 4:219-226, 2003

5. Witzig TE: Current treatment approaches for mantle-cell lymphoma. J Clin Oncol 23:6409-6414, 2005

6. O'Connor OA: Mantle cell lymphoma: Identifying novel molecular targets in growth and survival pathways. Hematology Am Soc Hematol Educ Program 2007:270-276, 2007

7. Witzig TE: Efficacy and safety of 90Y ibritumomab tiuxetan (Zevalin) radioimmunotherapy for non-Hodgkin's lymphoma. Semin Oncol 30:11-16, 2003

8. Morschhauser F, Illidge T, Huglo D, et al: Efficacy and safety of yttrium-90 ibritumomab tiuxetan in patients with relapsed or refractory diffuse large B-cell lymphoma not appropriate for autologous stem-cell transplantation. Blood 110: 54-58, 2007

9. Horning SJ, Younes A, Jain V, et al: Efficacy and safety of tositumomab and iodine-131 tositumomab (Bexxar) in B-cell lymphoma, progressive after rituximab. J Clin Oncol 23:712-719, 2005

10. 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

11. Borghaei H, Schilder RJ: Safety and efficacy of radioimmunotherapy with yttrium 90 ibritumomab tiuxetan (Zevalin). Semin Nucl Med 34:4-9, 2004

12. Gordon LI: Practical considerations and radiation safety in radioimmunotherapy with yttrium 90 ibritumomab tiuxetan (Zevalin). Semin Oncol 30:23-28, 2003

13. Cheson BD, Horning SJ, Coiffier B, et al: Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI sponsored International Working Group. J Clin Oncol 17:1244, 1999

14. Kaplan EL, Meier P: Non-parametric estimation from incomplete observations. J Am Stat Assoc 53:457-481, 1958

15. Romaguera JE, Fayad L, Rodriguez MA, et al: High rate of durable remissions after treatment of newly diagnosed aggressive mantle-cell lymphoma with rituximab plus hyper-CVAD alternating with rituximab plus high-dose methotrexate and cytarabine. J Clin Oncol 23:7013-7023, 2005

16. Fisher RI, Bernstein SH, Kahl BS, et al: Multicenter phase II study of bortezomib in patients with relapsed or refractory mantle cell lymphoma. J Clin Oncol 24:4867-4874, 2006

17. Hoster E, Dreyling M, Klapper W, et al: A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma. Blood 111:558-565, 2008

18. 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

19. Coiffier B, Haioun C, Ketterer N, et al: Rituximab (anti-CD20 monoclonal antibody) for the treatment of patients with relapsing or refractory aggressive lymphoma: A multicenter phase II study. Blood 92:1927-1932, 1998

20. Foran JM, Rohatiner AZ, Cunningham D, et al: European phase II study of rituximab (chimeric anti-CD20 monoclonal antibody) for patients with newly diagnosed mantle-cell lymphoma and previously treated mantle-cell lymphoma, immunocytoma, and small B-cell lymphocytic lymphoma. J Clin Oncol 18:317-324, 2000

21. Witzig TE, Geyer SM, Ghobrial I, et al: Phase II trial of single-agent temsirolimus (CCI-779) for relapsed mantle cell lymphoma. J Clin Oncol 23: 5347-5356, 2005

22. Weigert O, von Schilling C, Rummel MJ, et al: Efficacy and safety of a single-course of yttrium-90 (90Y) ibritumomab tiuxetan (Zevalin(R)) in patients with relapsed or refractory mantle cell lymphoma (MCL) after/not appropriate for autologous stem cell transplantation (ASCT) - A phase II trial of the European MCL Network. ASH Annual Meeting Abstracts 106:4786, 2005

23. Zelenetz AD, Noy A, Pandit-Taskar N, et al: Sequential radioimmunotherapy with tositumomab/iodine I131 tositumomab followed by CHOP for mantle cell lymphoma demonstrates RIT can induce molecular remissions. J Clin Oncol 24:436s, 2006 (suppl; abstr 7560)

24. Smith MR, Zhang L, Gordon LI, et al: Phase II Study of R-CHOP Followed by 90Y-Ibritumomab Tiuxetan in Untreated Mantle Cell Lymphoma: Eastern Cooperative Oncology Group Study E1499. Blood (ASH Annual Meeting Abstracts) 110:389, 2007

25. Czuczman MS, Emmanouilides C, Darif M, et al: Treatment-related myelodysplastic syndrome and acute myelogenous leukemia in patients treated with ibritumomab tiuxetan radioimmunotherapy. J Clin Oncol 25:4285-4292, 2007

26. 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

