

LYMPHOMA

RESEARCH • FOUNDATION

111 Broadway, NY, NY 10006; Tel: 212-349-2910; 800-235-6848
8800 Venice Blvd., Los Angeles, CA 90034; Tel: 310-204-7040; 800-500-9976

RESEARCH REPORT

September, 2006; Vol. 4, No. 2

REPORT FROM ASCO 2006

The American Society of Clinical Oncology met this year in Atlanta, Georgia, from June 2 to June 8, 2006. Many former and current Fellows and Awardees of the Lymphoma Research Foundation as well as members of the Scientific Advisory Board (SAB) presented the results of their research in the field of hematological malignancies, particularly lymphoma.

A number of these presentations and abstracts focused on mantle cell lymphoma (MCL). This is not surprising given the Mantle Cell Research Initiative of the Foundation, which has supported research in this area since 2003 with awards to gifted scientists working in productive laboratories in the United States and Europe.

LRF SCIENTIST LEADERS PRESENT AT ASCO

◆ Martin Dreyling PD, MD (University Hospital Grosshadern, Munich), an MCL Awardee working in the European MCL Research Network in Munich, Germany, spoke in the Education Session on the genetic basis of MCL, its relation to other lymphoproliferative cancers, and the importance of understanding the cell biology of this disorder to select appropriate therapeutic options.

Dr. Dreyling also presented the results of a study by the German Low Grade Lymphoma Study Group. This trial evaluated the effect of Rituximab maintenance, after induction of remission with Rituximab plus chemotherapy. Patients with advanced stage relapsed or refractory follicular lymphoma (FL) and mantle cell lymphoma (MCL) were eligible. After evaluating 176 cases the researchers concluded that this treatment was highly effective and improved progression-free survival of patients with relapsed FL and MCL.

◆ Results of two Phase II trials of the European MCL Network and the PLRG (Polish Lymphoma Research Group) also named Drs. Dreyling and Wolfgang Hiddemann, MD, Ludwig-Maximilians University, Munich, among the authors. These studies looked at the efficacy of radioimmunotherapy (RIT) with (⁹⁰Y) ibritumomab in relapsed or refractory mantle cell lymphoma. The study findings support applying RIT earlier in the treatment regimen of MCL following combined immunochemotherapy.

◆ Andrew Zelenetz, MD, PhD (Memorial Sloan-Kettering), a member of the LRF Scientific Advisory Board (SAB) also reported on the use of radioimmunotherapy (RIT) in mantle cell lymphoma. This study investigated the use of sequential RIT with tositumomab/iodine131 followed by CHOP chemotherapy as initial treatment for patients ineligible for, or unwilling to undergo, high dose therapy and stem cell transplantation. Twenty-four patients, all with advanced disease, were included in the study with 19 completing the planned therapy. The study showed that RIT with this agent is very active in

the treatment of MCL, but minimal residual disease is not effectively eliminated by subsequent CHOP chemotherapy. The investigators are planning to explore chemotherapy induction followed by RIT.

◆ David Inwards, MD (Mayo Clinic) described a phase II study, conducted by the North Central Cancer Treatment Group, of rituximab and cladribine in newly diagnosed MCL patients. A previous trial of cladribine as a single agent found it to be efficacious. This trial was designed to test whether the addition of rituximab to cladribine would improve outcomes as has been found with the addition of rituximab to other agents. The rituximab and cladribine were found to be well tolerated in a group including elderly patients. Fifty percent (50%) of the patients achieved a complete remission.

◆ Randy Gascoyne, MD (British Columbia Cancer Agency), an MCL Awardee, and Sandra Horning (Stanford University School of Medicine), an SAB member, were among the researchers presenting the results of a phase II study done by the Eastern Cooperative Oncology Group. This study evaluated rituximab plus CHOP (R-CHOP) followed by the radioimmunoconjugate, ⁹⁰Y-ibritumomab tiuxetan (⁹⁰Y-RIT) in patients with previously untreated mantle cell lymphoma. After evaluating response and toxicity in 56 patients, they concluded that ⁹⁰Y-RIT after 4 cycles of R-CHOP in untreated MCL is safe and improves the number and quality of responses. Further follow-up is needed to determine long-term efficacy.

◆ Patients with MCL, although they have a high response to chemotherapy, tend to relapse. In this study, Julie Vose, MD and James Armitage, MD both at the University of Nebraska and both SAB members, were among those investigating whether the use of dose-intensive induction therapy improves the results of **autologous stem cell transplant**¹ in these patients. They found that this treatment regimen did improve the long-term disease-free survival in this group of patients.

◆ Andre Goy, MD (The Cancer Center at Hackensack University Medical Center), a member of the MCL Consortium, described the findings of the PINNACLE study group's evaluation of the use of bortezomib (Velcade) in relapsed or refractory mantle cell lymphoma. This multi-center international study evaluated 155 patients and confirmed the activity of Velcade in relapsed/refractory MCL. The study results support its rapid development as a new treatment for this disorder. Velcade is a **proteasome inhibitor** that is also being studied as a first-line treatment in combination with standard chemotherapy.

◆ Johannes Drach, MD (University Hospital, Vienna), a 2004-07 Fellow, was among the authors of a paper describing the use of bortezomib, rituximab and dexamethazone (BORID) in heavily pretreated patients with mantle cell lymphoma. Bortezomib has been shown

to have activity in multiple myeloma and MCL. Preclinical studies suggest that it has synergistic activity with rituximab. This provides a rationale for exploring treatment combinations. In this study patients with relapsed/chemotherapy refractory MCL were treated with cycles of combination therapy every 3 weeks for a

total of 6 treatments. The data obtained suggest that the combination therapy has promising activity and manageable toxicity in patients with heavily pretreated MCL.

◆ The findings of a phase II multicenter study of bendamustine HCl plus rituximab in relapsed indolent B-cell lymphoma and mantle cell lymphoma were presented by Michael Williams, MD (University of Virginia, an MCL Awardee and Chairman of the MCL Consortium), Anil Tulpule, MD (Norris Cancer Center, Los Angeles, a 1994 Fellow) and Alberto Bessudo, MD (San Diego Cancer, a 1995 Fellow) among others. Bendamustine HCl is a novel alkylating agent whose mechanisms of action include cell death which occurs via both **apoptosis** and **mitotic catastrophe**. Sixty-seven patients (81% with indolent non-Hodgkins



Drs. Morton Coleman and Andre Goy.

¹ Bolded terms can be found in the *Glossary* on page 4.

lymphoma and 16% with mantle cell lymphoma) were treated with this regimen. The treatment was well tolerated and produced high response rates in this patient population. This suggests that bendamustine in combination with rituximab provides a potential benefit over rituximab alone.

◆ Nancy L. Bartlett, MD (Washington University, St. Louis, MO), a Career Development Awardee, addressed the management of advanced Hodgkin's lymphoma in the Education Session. She pointed out that, although the standard treatment for advanced Hodgkin's lymphoma, ABVD (Doxorubicin, Bleomycin, Vinblastine and Dacarbazine), is effective and cures about 70% of patients, in treatment one size does not fit all. Treatment should be based on stage and prognostic factors and new approaches are needed.

◆ Dr. Bartlett, along with Bruce Cheson, MD (Georgetown University Medical Center), an SAB member, and other colleagues reported on a phase II study of bortezomib in relapsed Hodgkin's lymphoma. The rationale for this study was that bortezomib, a proteasome inhibitor, leads to apoptosis (programmed cell death) of a Hodgkin's lymphoma cell line. However, it was found that, although it was well tolerated, bortezomib had no single agent efficacy in relapsed HL at the dose and treatment schedule used.

◆ Joseph M. Connors, MD, FRCPC (University of British Columbia), an SAB member, Dr. Gascoyne (British Columbia Cancer Agency), an MCL Awardee, and Kerry Savage, MD (British Columbia Cancer Agency), a 2001 Fellow, were among the authors of a paper discussing the impact of the initial treatment of advanced stage indolent lymphoma on the risk of transformation to aggressive disease. A large retrospective analysis of two consecutive phase II studies (conducted at the British Columbia Cancer Agency), which had identical inclusion criteria, provided evidence that the use of an anthracycline regimen as initial treatment for advanced indolent lymphoma is associated with a marked reduction in the risk of future transformation.



Drs. Andrew Zelenetz and Bruce Cheson converse with Dr. Randy Gascoyne in the background.

◆ SAB Members Morton Coleman, MD (Weill Medical College), and John Leonard, MD (Cornell Medical Center), also an MCL Awardee, were among the authors of a paper describing the results of a trial of a second-generation **humanized anti-CD20 antibody** [IMMU-106 (hA20)] in non-Hodgkin's lymphoma. Thirty-three patients (23 of whom had follicular lymphoma) completed all the infusions. Preliminary results were encouraging and the study is continuing to assess durability of response and to optimize the dose for future studies.

◆ Another paper, on follicular lymphoma, was presented by Dr. Leonard. This study looked at the immune response of patients treated with a personalized vaccine directed against specific proteins on the surface of the patient's tumor. Patients had been pretreated with chemotherapy and rituximab. It was found that an immune response could be measured in these patients, but it appeared to be less robust than in patients who had not been treated with rituximab.

◆ Jonathan Friedberg, MD (University of Rochester), 2002-05 Career Development Awardee, and SAB Members, Drs. Zelenetz (Memorial Sloan-Kettering), and Vose (University of Nebraska) were among the investigators for a National LymphoCare Study of the initial therapeutic strategies used for follicular lymphoma (FL). In this study data were collected from 1493 patients with FL enrolled at 237 sites in the US. Initial treatment

strategies were:

- Chemotherapy + Rituximab 51%
- Observation 19%
- Rituximab 13%
- Radiation 5%
- Chemotherapy 4%

Thus many different treatment strategies are used as initial regimens for FL. Few patients are treated in clinical trials. Differences between regions and types of treatment centers suggest that physician preference drives initial therapy. Further studies like this one are needed to understand how initial therapy affects short and long-term outcomes.

◆ Issa Khouri, MD and Richard Champlin, MD (both at M.D. Anderson Cancer Center), MCL Awardees, were among the authors of a study looking at **allogeneic hematopoietic stem cell transplantation** for cutaneous T-cell lymphoma (CTCL). Results of this study suggest that this therapy is effective in these patients, who usually have a poor prognosis, and it should be further evaluated.

◆ Drs. Cheson and Horning with Dr. Richard Fisher (University of Rochester), all SAB members, along with Dr. Gascoyne, and other members of the International Harmonization Project, presented recommendations for revised response criteria for malignant lymphomas. They pointed out that “standard response criteria are needed to interpret and compare clinical trials and for approval of new therapeutic agents by regulatory agencies.” Although the International Working Group criteria of 1999 were widely adopted, these are now out of date because of recent technological advances.

Therefore revised criteria have been proposed. Their adoption by study groups and regulatory agencies should facilitate the development of more effective therapies for lymphoma.

From this selection of the work presented at ASCO 2006 it is clear that there are promising new therapeutic approaches for lymphoma and that scientists supported by the Lymphoma Research Foundation are making important contributions.

Glossary

Allogeneic bone marrow transplantation:

A procedure in which patients receive bone marrow or stem cells donated by another person.

Apoptosis: Programmed cell death.

Autologous bone marrow transplantation: A

type of bone marrow or stem cell transplantation in which a patient receives their own cells.

Hematopoietic cells: Blood forming cells found in bone marrow.

Mitotic catastrophe: An alternative form of cell death induced by anti-cancer agents (note apoptosis above).

Proteasome inhibitor: Proteasomes are enzymes found in cells, and play a role in regulating cell function and growth. Proteasome inhibitors, such as Velcade, block the activity of proteasomes leading to the death of cancer cells.

Anti-CD20 antibody: An antibody directed against CD20, a protein found on the surface of normal and malignant B cells. In patients with B-cell NHL, such antibodies, for instance, Rituximab (Rituxan), are used to reduce circulating B cells in patients by binding to CD20.

Editor:

Kathleen Brown, MPA, CAE, Director of Research Grant Administration and Professional Programs

Writer:

JoAnne K. DeVries, PhD

Consultant:

Marc Hurlbert, PhD, *Scientific Director, Science Information Solutions, Inc.*

Layout:

Deborah Dwoskin, MPA, Manager, Research Grants and Professional Programs

Photographs:

Leslie E. Kossoff, *LK Photos*

Printing:

Intergraphics Litho Corp.

**www.lymphoma.org —www.mantlecelllymphoma.org—www.lymphoma.org
E-mail: researchgrants@lymphoma.org**

Los Angeles Office

8800 Venice Boulevard
Suite 207
Los Angeles, CA 90034
310.204.7040 • 800.500.9976
310.204.7043 fax

New York Office

111 Broadway
19th Floor
New York, NY 10006
212.349.2910 • 800.235.6848
212.349.2886 fax