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REPORT TO PHYSICIANS

DECEMBER 2008 VOL. 53, NO. 12

Oncology

Mantle Cell Lymphoma

Specialists are fighting this difficult-to-treat subtype with aggressive regimens.



By **Stephanie P. Deming**

Until about 20 years ago, most patients with the disease now known as mantle cell lymphoma (MCL) were classified as having either poor-prognosis lymphocytic lymphoma or poor-prognosis follicular lymphoma.

Then, in 1990, a breakthrough occurred: molecular, genetic, and immunohistochemical testing revealed that these patients, about 6%–10% of all patients with non-Hodgkin's lymphoma, actually had a distinct subtype of lymphoma affecting B cells in the lymph-node mantle zone. Investigators at The University of Texas M. D. Anderson Cancer Center were among the first to take advantage of this breakthrough and begin searching for the treatment strategies that would be most successful for patients with MCL.

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Dr. Jorge Romaguera and other M. D. Anderson investigators are testing new treatment strategies and new agents against mantle cell lymphoma. However, no standard therapy has emerged for this difficult-to-treat disease.

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Mantle Cell Lymphoma

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“When MCL was first identified, nobody really focused on it as a separate disease. It was just treated like other forms of lymphoma,” said Issa Khouri, M.D., a professor in the Department of Stem Cell Transplantation and Cellular Therapy at M. D. Anderson. “Then we started focusing on it back in the early ’90s. And by focusing on MCL, conducting clinical protocols, carefully studying what does and doesn’t work, and trying to understand the biology, we have made important progress.”

Despite this progress, MCL is one of the more difficult-to-treat subtypes of lymphoma—it tends to highly resist chemotherapy and to recur after treatment. In the early 1990s, the median survival time for newly diagnosed patients was only 3–4 years. Since then, this median survival time has increased, but only to about 5–6 years.

Investigators at M. D. Anderson and other institutions continue to test new treatment strategies and new agents and combinations to try to prolong patient survival. However, no single approach has yet proven to be clearly superior to the others, and today there is still no standard therapy for MCL.

Treating new MCL with intensive chemotherapy

A tiny fraction of patients with MCL have stage I or II disease at initial diagnosis—i.e., the disease is limited to lymph nodes on one side of the diaphragm. At M. D. Anderson, these patients are generally treated with either a combination of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) plus rituximab and radiation therapy or, if they are 65 years old or younger, an intensive regimen of alternating chemotherapy combinations (described below). In contrast, for the vast majority of patients who have stage III or IV disease at initial diagnosis, treatment generally consists of intensive cytotoxic immunochemotherapy, followed by high-dose chemotherapy and stem cell transplantation (SCT) in patients who do not achieve a complete remission after the first six cycles of therapy.

In the mid-1990s, physicians at M. D. Anderson were looking for an aggressive



Clinical nurse **Lisa J. Norman** and **Dr. Issa Khouri** review the records of a patient with mantle cell lymphoma. Dr. Khouri is studying the role of stem cell transplantation in the treatment of such patients.

treatment to improve the survival of patients with advanced MCL. They turned to a chemotherapy regimen that had been developed for children with acute lymphoblastic leukemia at St. Jude Children’s Research Hospital and then modified by Hagop Kantarjian, M.D., chairman of the Department of Leukemia at M. D. Anderson, for use in adult patients with leukemia and other hematologic malignancies.

“This experimental regimen consisted of two chemotherapy combinations given in an alternating fashion: hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (hyper-CVAD) and high-dose methotrexate,” said Jorge Romaguera, M.D., a professor in the Department of Lymphoma and Myeloma. “We really had nothing else for newly diagnosed, advanced mantle cell lymphoma that we thought would work, so we decided to try a clinical trial with the experimental regimen.” The regimen was followed by additional high-dose chemotherapy and either autologous SCT (using a patient’s own stem cells) or allogeneic SCT (using donor stem cells), depending on the patient’s age and whether a suitable stem cell donor was available.

Results were promising: the response rate was 93%, and at a median follow-up time of 49 months, the estimated 5-year overall and disease-free survival rates were 77% and 43%, respectively, better than rates in a historical control group treated with CHOP.

Rituximab improves outcomes

In 1997, rituximab—a monoclonal antibody against CD20, which is over-expressed in MCL—was approved by the U.S. Food and Drug Administration for lymphoma treatment. Evidence of rituximab’s positive effect on outcomes of patients with MCL soon began to emerge.

In 1998, on the basis of preliminary observations in a small number of patients, Dr. Romaguera and colleagues at M. D. Anderson designed another clinical trial for MCL in which they added rituximab to an alternating hyper-CVAD and methotrexate-cytarabine regimen. If after six cycles of this regimen (rituximab-hyper-CVAD was considered one cycle and rituximab-methotrexate-cytarabine was another cycle) patients were in complete remission, as established by intensive testing, they skipped high-dose chemotherapy and SCT. The

complete response rate was 86%, and in 2005, at a median follow-up time of 40 months, the 3-year estimated overall and failure-free survival rates were 82% and 62%, respectively, for the entire cohort of patients age 41–80 years. The survival rates were even better for patients age 65 years or younger, who previously would have been offered consolidation with autologous SCT. As a result of the study, this rituximab-containing chemotherapy regimen is now widely used in patients with newly diagnosed MCL. A recent update of the

study showed that patients age 65 years or younger who received the regimen had a 52% failure-free survival rate at a median follow-up of 7 years, and only one failure in this age group occurred in the past 3 years.

In an effort to further improve failure-free survival, particularly for patients older than age 65 years, Dr. Romaguera and collaborator Andre Goy, M.D., from Hackensack University Medical Center, recently conducted a phase I clinical trial in which the proteasome inhibitor bortezomib was added to this regimen.

Bortezomib, a newer drug, has activity in relapsed MCL and was shown to have additive or synergistic effects when added to rituximab-hyper-CVAD and rituximab-methotrexate-cytarabine. The addition of bortezomib did not increase the risk of toxicity of the regimen. A phase II study is planned.

As expected with such an intense regimen as rituximab-hyper-CVAD alternating with rituximab-methotrexate-cytarabine, hematologic toxicity can be significant. About 4% of patients treated
(Continued on page 4)

Clinical Trials in Mantle Cell Lymphoma

A Study of Lenalidomide and Rituximab in the Treatment of Relapsed Mantle Cell Lymphoma and Diffuse Large B-Cell Non-Hodgkin's Lymphoma, Transformed Large Cell Lymphoma, and/or Grade 3 Follicular Lymphoma (RV-LYM-PI-0056) (2005-0461). Principal investigator (PI): Michael Wang, M.D. A goal of this clinical research study is to find the highest tolerable dose of lenalidomide that can be given with rituximab for relapsed mantle cell lymphoma.

A Phase II Study of 17-AAG in Patients with Relapsed/Refractory CD30+ Anaplastic Large Cell Lymphoma, Relapsed/Refractory Mantle Cell Lymphoma, and Relapsed/Refractory Classical Hodgkin's Lymphoma (2004-0792). PI: Anas Younes, M.D. This clinical research study will evaluate whether the investigational drug 17-AAG (a heat shock protein 90 inhibitor) can shrink or slow tumor growth.

A Phase II Study of Depsipeptide, a Histone Deacetylase Inhibitor, in Relapsed or Refractory Mantle Cell or Diffuse Large Cell Non-Hodgkin's Lymphoma (2005-0579). PI: Luis E. Fayad, M.D. This clinical trial will evaluate depsipeptide in the treatment of recurrent or refractory mantle cell or large B-cell non-Hodgkin's lymphomas. Specifically, researchers are studying activity in certain genes in blood cells.

An Open Label, Multi-Dose-Escalation, Safety and Pharmacokinetic Study of SAR3419 Administered as a Single Agent by Intravenous Infusion Every 3 Weeks in Patients with Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma (2006-1092). PI: Anas Younes, M.D. This clinical research study is designed to determine dosing, safety, and effectiveness of SAR3419, an anti-CD19 immunotoxin.

A Phase Ib Study to Evaluate the Safety and Tolerability of AMG 655 in Combination with Bortezomib or Vorinostat in Subjects with Relapsed or Refractory Lymphoma (2007-0906). PI: Anas Younes, M.D. This clinical research study is evaluating the safety of AMG 655 (a fully human monoclonal antibody) when it is given in combination with bortezomib or vorinostat to patients with lymphoma that has relapsed or has not responded to standard therapy.

A Phase I/II Study of Immunotherapy with Milatuzumab (hLL1) in Patients with Non-Hodgkin's Lymphoma and Chronic Lymphocytic Leukemia (2008-0075). PI: Felipe Samaniego, M.D. Goals of this clinical research study are to find the highest tolerable dose of milatuzumab and to determine whether milatuzumab can help to control disease.

A Phase I Study of SB1518 for the Treatment of Advanced Lymphoid

Malignancies (2008-0105). PI: Anas Younes, M.D. The goal of this clinical research study is to find the highest tolerable dose of SB1518 (an oral JAK2 inhibitor) that can be given to patients with lymphoid cancer.

An Open-Label, Phase I Study of MLN8237, a Novel Aurora A Kinase Inhibitor, in Patients with Advanced Hematological Malignancies (2008-0278). PI: Nathan Fowler, M.D. The goal of this clinical research study is to find the highest safe dose of MLN8237 that can be given to patients with a hematological cancer.

A Phase I Study of Multiple Intravenous Administrations of a Chimeric Antibody Against Interleukin-6 (CNTO 328) in Subjects with B-Cell Non-Hodgkin's Lymphoma, Multiple Myeloma, or Castleman's Disease (2004-0492). PI: Razelle Kurzrock, M.D. The goal of this clinical research study is to compare dose levels and schedules of CNTO 328, an anti-interleukin-6 antibody.

Allogeneic Stem Cell Transplantation with Rituximab-Containing Non-Ablative Conditioning Regimen for Advanced/Recurrent Mantle Cell Lymphoma (2004-0309). PI: Issa F. Khouri, M.D. This clinical research study will evaluate whether a transplant of blood stem cells after treatment with low-dose chemotherapy and rituximab will help control mantle cell lymphoma. ●

Mantle Cell Lymphoma

(Continued from page 3)

ed with this regimen experience fatal myelodysplasia while their MCL is in remission. And during therapy, intensive supportive care is necessary. Patients are always admitted to the hospital for the rituximab-methotrexate-cytarabine portion of therapy, and for the rituximab-hyper-CVAD regimen, physicians prefer to admit patients older than 65 years and those with certain comorbid conditions.

Autologous SCT: needed for new MCL?

One of the most important questions that remain to be resolved in the treatment of MCL is whether patients with newly diagnosed disease who have a complete remission or good response with intensive immunochemotherapy—for example, rituximab-hyper-CVAD alternating with rituximab-methotrexate-cytarabine—benefit from undergoing autologous SCT once this chemotherapy is finished.

According to Dr. Khouri, M. D. Anderson's results to date and results presented by the Nordic Lymphoma Group at the December 2007 American Society of Hematology meeting suggest that intensive rituximab-containing chemotherapy followed by autologous SCT may actually be able to cure MCL. The Nordic Lymphoma Group showed that in a large set of patients with newly diagnosed disease, a significant proportion of patients experienced long-term disease-free survival when treated with an intensive rituximab-containing chemotherapy regimen (similar to the one used at M. D. Anderson) followed by SCT. "We are

now having the courage to say that some patients may be cured with intensive immunochemotherapy with stem cell support," said Dr. Khouri. However, there has been no randomized trial to compare outcomes in patients in first remission who do and do not undergo autologous SCT after intensive immunochemotherapy.

For his part, Dr. Romaguera believes further study is warranted, since the Nordic study had a relatively short follow-up period (3.8 years) and because participants who developed molecular recurrence were treated with rituximab preemptively and were not counted as treatment failures.

Allogeneic SCT helps control recurrent MCL

For patients with recurrent MCL, the goal is to use chemotherapy to shrink disease—to the point of complete remission if possible—and then do allogeneic SCT. Autologous SCT is not used in patients with relapsed disease because studies at M. D. Anderson and elsewhere have shown that autologous SCT in this setting does not confer a benefit.

Whereas autologous SCT is done as supportive therapy to allow patients to survive high-dose chemotherapy, allogeneic SCT actually has a direct effect against the lymphoma, known as a graft-versus-lymphoma effect. "In the 1990s," said Dr. Khouri, "we used to give patients getting a donor transplant high-dose chemotherapy, as we do with the autologous transplant. But one third of the patients died within 30 days. Then, we realized that it was the high-dose chemotherapy that was causing these deaths. And also we realized that it is actually the donor cells inducing the cure, not the high-dose chemotherapy."

Dr. Khouri, Dr. Romaguera, and colleagues began offering patients with recurrent MCL nonmyeloablative chemotherapy (chemotherapy that does not completely destroy the bone marrow) followed by allogeneic SCT. The chemotherapy facilitates engraftment of the donor stem cells, which, once they are taken into the patient's

(Continued on page 8)

Sparing the Ni

New surgical techniques pre

By Virginia M. Mohlere

In recent years, skin-sparing mastectomy has gained acceptance for the treatment of early-stage breast cancer and for prophylactic treatment in women at high risk of developing the disease. However, even though skin-sparing mastectomy allows breast surgeons to find a better balance between good oncologic results and good cosmetic results, nipple reconstruction remains a challenge. Nipples surgically created from skin grafts can flatten, tattooed areolae can lose color, and reconstructed nipples have no erectile capability and, worse, little or no sensation.

But recent studies by M. D. Anderson researchers and others have found that the incidence of nipple involvement in early-stage breast cancer ranges widely and that when primary tumors are at least 2 cm away from the nipple, the rate of nipple involvement is only about 6% (Laronga et al., *Ann Surg Oncol* 1999;6:609–13). Thus, preservation of a nipple-areolar complex (NAC) may be considered in select patients with breast cancer or those who are considering mastectomy for prevention. Unfortunately, researchers do not know the risk of local recurrence if the patient undergoes NAC-sparing mastectomy for oncologic purposes. Nevertheless, in the past few years, breast cancer surgeons have begun to consider saving the NAC using a variety of surgical techniques during skin-sparing mastectomy.

Saving the NAC is tricky. The goal is to preserve the appearance of the nipple, along with the hope there may be sensation and erectile function. However,

We are now having the courage to say that some patients may be cured with intensive immunochemotherapy with stem cell support."

– Dr. Issa Khouri

Nipples During Mastectomy

preserve appearance and function in some patients

Surgeons successfully spared the nipple-areolar complex in this patient, who had surgery to remove breast cancer 6 months earlier.

the NAC is supplied by a complex group of blood vessels and nerves. Even in a skin-sparing mastectomy, it is difficult to save enough vessels and nerves to allow the NAC to live.

Because the surgery is so complex, NAC-sparing mastectomies performed in an oncologically safe fashion have been performed for only a few years. This means that there are very few comprehensive data about the best approaches, most appropriate patients, and outcomes. To determine outcome, Gildy Babiera, M.D., an associate professor in M. D. Anderson's Department of Surgical Oncology, and her colleagues have embarked on a prospective study of NAC-sparing mastectomy. They will use intraoperative frozen-section and final histopathologic examination and follow-up to monitor rates of NAC involvement and breast cancer recurrence, as well as collect data on NAC survival.

Procedure and patients

To start the NAC-sparing mastectomy, the location of the incision is determined. Factors that influence the site of

incision include previous scars, the location of the tumor, and access to blood vessels important for reconstruction and cosmesis.

After the incision is made, skin flaps are created and the breast tissue is oriented and marked before being removed. The specimen is sent for pathologic review, and the tissue underneath the NAC is microscopically examined during the surgery. If it is deemed cancer-free, the NAC and surrounding skin are left intact. Patients undergo immediate breast reconstruction. Follow-up includes visits at 1, 3, and 6 months and 1, 2, and 5 years and consists of a physical examination and, if needed, imaging or biopsy procedures.

Patient selection is critical to achieving the best results both oncologically and in terms of each patient's satisfaction with her reconstructed breast. "We don't claim to work miracles here," Dr. Babiera said as she described the importance of making sure that patients are well informed and have realistic expectations: given the level of difficulty of the surgery, not every NAC will remain

viable, and cancer recurrence is a possibility. "First we treat the cancer," Dr. Babiera said, "and if in 1 or 2 years you have a living nipple, that's a freebie."

Dr. Babiera's group hopes to enroll 30 women in the NAC-sparing mastectomy study; so far, they have enrolled 15 patients with 22 breasts requiring surgery.

Women who may be candidates for the trial are those undergoing prophylactic mastectomy with immediate reconstruction and those with stage 0, I, or II cancer who are candidates for skin-sparing mastectomy with immediate reconstruction. In addition, primary tumors must be located 2.5 cm or more from the NAC.

Women who are not eligible include:

- smokers
- those with cancer of the NAC, subareolar tumors, or tumors less than 2.5 cm from the NAC
- those with inflammatory breast cancer or cancer involving the breast skin
- those with collagen vascular disease or Paget's disease of the nipple
- those desiring reduction mammoplasty as part of reconstruction
- those with a history of previous surgery involving a periareolar incision
- those with a body mass index greater than 40 kg/m²
- those with a prior history of breast irradiation

The hope for this study is that enough data will be collected to present a clearer picture of attempts to try to save the NAC and their success rates. So far, Dr. Babiera and other key contributors from the Departments of Surgical Oncology and Plastic Surgery, including research nurse Laura Pantoja, R.N., and former surgical oncology fellow Regina Fearmonti, M.D., have seen favorable results in patients who have had the surgery. There have been no cancer recurrences, and all NACs that have been preserved remain relatively healthy. ●

For more information, call Dr. Babiera at 713-745-1563.

Tumor-Suppressing Cell Surface Receptor May Provide New Options in Colorectal Cancer

The cannabinoid cell surface receptor 1 (CB1), already known for its role in relieving the side effects of radiotherapy and chemotherapy, plays a tumor-suppressing role in colorectal cancer, according to a recent study by researchers at M. D. Anderson and Vanderbilt-Ingram Cancer Center.

CB1 receives cannabinoids, a group of compounds that serve a variety of cell-signaling roles. (Among these is tetrahydrocannabinol, the active ingredient in marijuana.) Cannabinoids have been shown to induce apoptosis in cancer cells in vitro.

“We found that CB1 expression is lost in most human colorectal cancers, and when that happens, the cancer-promoting protein survivin is free to inhibit cell death,” said senior author Raymond DuBois, M.D., Ph.D., a professor in the Departments of Gastrointestinal Oncology and Cancer Biology and M. D. Anderson’s provost and executive vice president. By reactivating CB1, Dr. DuBois and his colleagues found that they could inhibit the expression of survivin, which is overexpressed in most tumors, and increase apoptosis in colorectal cancer cells.

In the study, CB1 was largely inactive in 18 of 19 human colorectal tumor specimens but was active in adjacent normal mucosa. CB1 was also inactive in 9 of 10 colorectal cancer cell lines. The researchers discovered that, in human colorectal cancers, the gene that encodes the CB1 protein, *Cnr1*, was not damaged but rather silenced by methylation. Treating the cell lines with decitabine, a demethylating agent that is used to treat some types of leukemia, restored normal gene expression in seven of eight cell lines and restored full CB1 expression in three lines.

Using a mouse model known to spontaneously develop precancerous polyps in the intestine, the group also found that mice in which the *Cnr1* gene had been deleted developed 2.5-

–3.8 times more polyps in the small intestine and colon than control mice did. Deleting the gene also increased by 10 times the number of large growths in the intestine—the type most likely to become cancerous.

Dr. DuBois and his colleagues also found that mice with the *Cnr1* gene that were treated with a cannabinoid agonist—a synthetic molecule that binds specifically to CB1 and enhances its function—developed fewer polyps in the small intestine and colon than control mice did. The researchers found as well that CB1 is required for the agonist to have a tumor-inhibiting effect.

Given this finding, “Just increasing the levels of cannabinoids to treat colorectal cancer won’t work if CB1 is not present,” Dr. DuBois said. Instead, giving patients a demethylating agent such as decitabine to reactivate CB1 in the tumor and then administering a cannabinoid might be an effective way to treat colorectal cancer. Less toxic demethylating agents that could also work are being developed.

The study was published in the journal *Cancer Research*. ●

Blocking Overexpressed Protein TG2 May Change Disease’s Course

Tissue type transglutaminase (TG2), already implicated by M. D. Anderson researchers in drug-resistant metastatic melanoma, pancreatic cancer, and breast cancer, is now also linked with increased chemoresistance and metastasis in ovarian cancer. Moreover, M. D. Anderson researchers have found that blocking the TG2 protein in ovarian cancer might lead to new treatment options.

“Drug resistance and metastasis are major impediments to the successful treatment of ovarian cancer, and until now we had little information about the role TG2 played in ovarian cancer,” said Anil K. Sood, M.D., a professor in the Departments of Gynecologic Oncology and Cancer Biology.

Dr. Sood and Kapil Mehta, Ph.D., a professor in the Department of Experimental Therapeutics, found that over-

expression of TG2 is associated with decreased overall survival in metastatic ovarian cancer and that blocking the protein in mouse models decreased tumor volume, especially when the mice also received docetaxel. The findings were reported in the journal *Cancer Research*.

“Liposomal siRNA targeted to TG2 is exciting because it takes out TG2 completely.”

– Dr. Kapil Mehta

Dr. Sood and Dr. Mehta, who first studied the protein in tissue samples and cell lines, found that inhibiting TG2 with targeted siRNA delivered via liposomes reversed tumor progression, including cancer cell proliferation and blood vessel development. As another of the study’s authors, Gabriel Lopez-Berestein, M.D., a professor in Experimental Therapeutics, explained, “While it remains to be seen if these results will translate to humans, targeting TG2 could eventually be an attractive option against advanced ovarian cancer.”

Dr. Mehta also noted that TG2 seems to promote a variety of molecular pathways in cancer development, not only those related to tumor progression but also those involved in the tumor’s defenses against chemotherapy. That makes the promise of a drug that inhibits TG2 much more powerful, as it would fight cancer on several fronts.

“This aberrant protein [TG2] is doing so many different things, you would have to develop a small-molecule drug to block each function,” Dr. Mehta said. “Liposomal siRNA targeted to TG2 is exciting because it takes out TG2 completely, blocking everything that it does.”

The next step for M. D. Anderson researchers is to design phase I clinical trials of the TG2-targeted siRNA for ovarian cancer. Similar research is being done in pancreatic cancer. ●



Taking Medicine? Be Aware of Food-Drug Interactions

You probably know that certain medications shouldn't be taken together because of how they interact. But did you know that the food you eat can also interact with your prescription drugs?

While some food-drug interactions may be mild, others can cause serious health effects or prevent you from receiving a drug's full benefit.

Fortunately, you can avoid food-drug interactions by simply watching what you eat and when you eat it. Elderly patients should be especially careful with their diets because they usually take more than one medication at the same time. However, all patients should know the risks for their prescription drugs.

Below are some commonly prescribed medications listed with foods to avoid while taking them. Keep in mind that this is not a complete list of potentially harmful food-drug combinations. Before taking any medicine for the first time, be sure to ask your physician, pharmacist, nurse, or clinical dietitian about possible side effects, how the medication should be taken, and if what you eat will interact with the drug. ●

If You Take These Drugs:	You Should Know:
<ul style="list-style-type: none"> • Monoamine oxidase inhibitors (or MAOIs), such as phenelzine (Nardil), tranylcypromine (Parnate), isocarboxazid (Marplan), or selegiline (Eldepryl)—used to treat depression and Parkinson's disease • Isoniazid (INH or Nydrazid)—used to treat or prevent tuberculosis infection • Procarbazine (Matulane)—a chemotherapy drug used to treat Hodgkin's lymphoma and brain tumors 	<p>The interaction of these drugs with some foods can cause a dangerous, sudden increase in blood pressure. Patients taking these drugs should not drink alcohol and should not eat soy sauce, canned soups, packaged gravies or sauces, most cheeses, and certain meat products. In addition, avoid eating canned figs, raisins, avocados, bananas, raspberries, red plums, sauerkraut, soybeans, tofu, fava and broad beans, snow peas, and kimchi.</p>
<ul style="list-style-type: none"> • Linezolid (Zyvox)—used to treat bacterial infections 	<p>This medication also can cause a sudden increase in blood pressure when combined with caffeine-containing foods. Patients taking this drug should not drink alcohol and should limit their consumption of coffee, cola, tea, and chocolate.</p>
<ul style="list-style-type: none"> • Warfarin (Coumadin)—an anticoagulant used to prevent or decrease blood clots 	<p>Suddenly changing the amount of vitamin K in your diet may reduce the drug's effectiveness. Vitamin K is found in green leafy vegetables, soybean oils, meats, dairy products, egg yolks, and liver. Do not drink alcohol, consume more than one serving a day of caffeine-containing foods or beverages, go on a weight-reduction diet, or consume ginseng, garlic, ginkgo, or vitamin E.</p>
<ul style="list-style-type: none"> • Imatinib (Gleevec)—used to treat certain cancers • Statins, such as atorvastatin (Lipitor), lovastatin (Mevacor), pravastatin (Pravachol), and simvastatin (Zocor)—used to lower cholesterol • Buspirone (BuSpar)—used to treat anxiety • Carbamazepine (Tegretol)—used to treat epilepsy and bipolar disorder • Nifedipine (Procardia, Adalat) and verapamil (Calan, Isoptin, Verelan)—used to treat high blood pressure 	<p>Grapefruit and grapefruit juice can affect the concentration of these drugs in the blood. Patients taking imatinib should avoid eating grapefruit or drinking grapefruit juice and should take the medication with food and a full glass of water. Patients taking the other drugs listed should not make a sudden change in their consumption of grapefruit or grapefruit juice.</p>
<ul style="list-style-type: none"> • Potassium-sparing diuretics, such as amiloride (Midamor), spironolactone (Aldactone), and triamterene (Dyrenium); and ACE inhibitors, such as benazepril (Lotensin), captopril (Capoten, Capozide), enalapril (Vasotec), fosinopril (Monopril), lisinopril (Prinivil, Zestril), moexipril (Univasc), perindopril (Aceon), quinapril (Accupril), ramipril (Altace), and trandolapril (Mavik)—used for controlling high blood pressure and treating heart disorders 	<p>Patients taking a potassium-sparing diuretic or ACE inhibitor should not use salt substitutes and should limit their consumption of foods high in potassium.</p>

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Mantle Cell Lymphoma (Continued from page 4)

bone marrow, attack the lymphoma. “The donor stem cells recognize the lymphoma cells through a certain mechanism that we don’t understand fully,” Dr. Khouri said. “The biological activity of the donor stem cells is probably the most potent activity against the disease—and an activity that we’re not able to reproduce with any form of chemotherapy.” Nonmyeloablative conditioning regimens are now widely used in patients receiving allogeneic SCT, and this change in therapy represents one of the major advances to date in the treatment of MCL.

If allogeneic SCT is so powerful, why is it not used in all patients undergoing transplant? Dr. Khouri points out that allogeneic SCT is associated with a significant risk of graft-versus-host disease or death—about 10%–15% of patients die even with the nonmyeloablative conditioning regimens. Thus, allogeneic transplantation is generally reserved for patients with relapsed disease or newly

**In the future,
molecular testing may
allow individualized
treatment for mantle cell
lymphoma based on
each patient’s
disease features.**

diagnosed disease with high-risk features such as blastic histology.

Another factor that influences treatment planning is that patients who have no suitable related donor and who are from a racial or ethnic group underrepresented in donor registries may never be able to undergo allogeneic transplantation. Such patients may be more likely to be offered autologous SCT at the time of initial diagnosis.

What does the future hold?

Efforts are ongoing to elucidate the molecular features of MCL, which will provide clues about which agents and treatment strategies may be most effective against this disease. Also, in the future, molecular testing may be done for each patient so that treatment can be individualized on the basis of each patient’s disease features. Among the many new agents being tested are inhibitors of mammalian target of rapamycin inhibitors, Bcl-2 inhibitors, vaccines, siRNAs, and histone deacetylase inhibitors.

There is also great interest in identifying prognostic factors for MCL. Mutations in the *p53* gene and blastoid cytology have been confirmed to predict poor prognosis. Other predictors of poor prognosis include high Ki-67 expression, high beta-2-microglobulin level, and the presence of minimal residual disease on molecular testing after high-dose chemotherapy and autologous SCT. ●

For more information, contact Dr. Romaguera at 713-792-2860 or Dr. Khouri at 713-745-3219.

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