For years, researchers have studied various ways to boost the body's natural ability to fight cancer. While cytokines and monoclonal antibodies are routinely used in cancer treatment, research into other immunotherapies, like T cell therapies and therapeutic vaccines, is just beginning to pay off. In the past year, promising results have been reported for randomized clinical trials of therapeutic vaccines for several different types of cancer.

Some of these results have caught the attention of major media outlets. Successful phase III trials of a follicular lymphoma vaccine tested at The University of Texas MD Anderson Cancer Center led *Time* magazine to name the vaccine's developer, Larry Kwak, M.D., Ph.D. (a professor in and chair of the Department of Lymphoma and Myeloma), among this year's list of the world's 100 most influential people. Also making news was the successful trial of Dendreon Corp.'s sipuleucel-T (Provenge) vaccine, which received U.S. Food and Drug Administration (FDA) approval for use in patients with prostate cancer. Another ground-breaking phase III trial, which was conducted in patients with metastatic melanoma at MD Anderson and other centers, was among the first to demonstrate a positive effect of a vaccine against metastatic disease.

**Successful vaccines and their development**

“There have been some exciting breakthroughs in therapeutic vaccines,” said Patrick Hwu, M.D., chair of the Department of Melanoma Medical Oncology at MD Anderson and the senior investigator for the study of the
(Continued on page 2)
GP100 peptide vaccine in patients with metastatic melanoma. In this trial, patients who received the therapeutic vaccine plus interleukin 2, which is commonly used to stimulate the proliferation of T cells in patients with metastatic melanoma, had a 22.1% response rate, while those who received only interleukin 2 had a 9.7% response rate. Patients who received the vaccine plus interleukin 2 also had a longer median progression-free survival (2.9 months) than those receiving only interleukin 2 (1.6 months).

“The melanoma study showed us that combination therapy is more effective,” Dr. Hwu said. “The vaccine helps to make T cells, and interleukin 2 helps to drive those T cells. The T cells are the soldiers that kill the tumor cells.” He added that studies are under way or are being planned to combine other vaccines—including GlaxoSmithKline’s MAGE vaccine, which is now in phase III trials in patients with melanoma and other types of cancer—with cytokines like interleukin 2.

Dr. Kwak agreed that vaccines are only part of the overall treatment strategy. “In lymphoma, it is fairly easy to get patients into remission with standard chemotherapy,” he said. “The paradox is that they eventually relapse because chemotherapy doesn’t get rid of every last tumor cell. The role of the lymphoma vaccine is to come in during that minimal disease state and mop up the residual tumor cells.”

In a phase III trial of the lymphoma vaccine, 117 follicular lymphoma patients were given the idiotype protein vaccine or a placebo while in remission. The 76 vaccinated patients had a median time to relapse of 44.2 months, compared with 30.6 months for those who received the placebo. Dr. Kwak said researchers are in the process of submitting their data to the FDA for approval of the vaccine, and he added that several patients from an earlier trial of the vaccine are still in remission after 12 years of follow-up. “These patients have not needed anything else—not even rituximab, which is often given as maintenance therapy for lymphoma,” he said.

“We found that the vaccine keeps patients in remission longer, but our goal is to make that even better by developing a second generation of more potent vaccines,” said Sattva Neelapu, M.D., an assistant professor in the Department of Lymphoma and Myeloma and the principal investigator for the lymphoma vaccine’s phase III trial.

Dr. Neelapu said a therapeutic vaccine can induce two types of immune responses, an antibody response and a T cell response. “Right now we don’t know whether both are required or one is more dominant than the other for vaccine efficacy,” he said.

Dr. Neelapu’s laboratory is studying the mechanisms within the tumor cell microenvironment that impair immune response. “One of these mechanisms is mediated by regulatory T cells. If we can get rid of those regulatory T cells before or after vaccination, the vaccine is more likely to be effective,” he said. “The other mechanism we have found in lymphoma is that the antitumor T cells within the tumor upregulate an inhibitory molecule on the cell surface called programmed death-1. If we block this molecule—with an antibody, for example—then the T cells can recognize and kill the tumor much better.”

Another therapeutic vaccine developed at MD Anderson, the PR1 peptide vaccine, was given to patients with chronic and acute myelogenous leukemia in a phase II study. Jeffrey Molldrem, M.D., a professor in the Department of Stem Cell Transplantation, said that patients with minimal disease (less than 15% blasts in their bone marrow) responded best, but he added that 12 of the 53 patients not in remission at the time of vaccination had an objective clinical response, including eight who had a complete response and were still in remission up to 7 years after vaccination.

The PR1 vaccine is derived from two proteins (proteinase 3 and neutrophil elastase) that are overexpressed and aberrantly expressed in myelogenous leukemia cells—in the blasts and in the leukemia stem cells in particular. To help the immune system create a response to these proteins, the vaccine must first attach itself to leukemic cells to be recognized by the immune system. “The vaccine binds to a surface protein very frequently expressed in the Caucasian population, which makes up a large percentage of leukemia patients in the United States,” said Jorge Cortes, M.D., a professor in the Department of Leukemia and the principal investigator of an ongoing phase II trial of the PR1 vaccine combined with interferon in patients with chronic myelogenous leukemia. Enrollment in this study is on hold because the company that was manufacturing the vaccine decided to stop doing so. Dr. Cortes said there has been some response in the five patients currently participating in the trial—they received the full four-dose regimen and are being monitored—but there are too few patients to draw any significant conclusions. MD Anderson has begun manufacturing the vaccine, and Dr. Cortes hopes to resume enrolling patients soon.

The production of vaccines for research is being facilitated by a new partnership between MD Anderson and Texas A&M University System’s National Center for Therapeutic Manufacturing. “This new partnership will reduce costs of vaccine production and allow us to produce more vaccines, antibodies, and biologic agents such as recombinant cytokines for research,” said Dr. Molldrem. While vaccines derived from the PR1, GP100, or MAGE peptides can be mass-produced, the lymphoma vaccine is an idiotype protein custom-made for each patient from his or her own tumor cells. “My group is now looking at more streamlined methods of pro-
Ongoing vaccine studies in patients with various types of cancer (underlined) include:

A Double-Blind, Randomized, Placebo-Controlled Phase III Study to Assess the Efficacy of recMAGE-A3 + AS15 ASCI as Adjuvant Therapy in Patients with MAGE-A3 Positive Resected Stage III Melanoma (2008-0324). Principal investigator (PI): Merrick I. Ross, M.D. The primary objective of this study is to assess the efficacy of the recMAGE-A3 + AS15 antigen-specific cancer immunotherapeutic (ASCI) vaccine in patients who have undergone complete resection of stage III cutaneous melanoma and were found to have macroscopic lymph node involvement.

A Double-Blind, Randomized, Placebo-Controlled Phase III Study to Assess the Efficacy of recMAGE-A3 + AS15 Antigen-Specific Cancer Immunotherapeutic as Adjuvant Therapy in Patients with Resectable MAGE-A3-Positive Non Small Cell Lung Cancer (2007-0865). PI: David C. Rice, M.D. The primary objective of this study is to assess the efficacy of the recMAGE-A3 + AS15 ASCI vaccine versus placebo in patients with non–small cell lung cancer after complete surgical resection.

Activation of pDCs at the Tumor and Vaccine Site with a TLR Agonist (2008-0416). PI: Patrick Hwu, M.D. The primary objective of this phase II study is to compare the ability of the GP100 melanoma peptide vaccine in combination with a toll-like receptor (R848) to that of the vaccine alone to enhance the generation of circulating antigen-specific T cells in patients with metastatic melanoma.

Prospective, Randomized, Single-Blinded, Multi-Center Phase II Trial of the HER2/neu Peptide GP2 + GM-CSF Vaccine versus GM-CSF Alone in HLA-A2+ or the Modified HER2/neu Peptide AE37 + GM-CSF Vaccine versus GM-CSF Alone in HLA-A2– Node-Positive and High-Risk Node-Negative Breast Cancer Patients to Prevent Recurrence (2007-0125). PI: James Murray, M.D. The primary objective of this study is to determine whether either the GP2 or AE37 peptide vaccine combined with granulocyte-macrophage colony-stimulating factor (GM-CSF) can reduce the recurrence rate in patients with node-positive or high-risk node-negative breast cancer compared with GM-CSF alone.

Lymphodepletion Plus Adoptive Cell Transfer With or Without Dendritic Cell Immunization in Patients With Metastatic Melanoma (2004-0069). PI: Patrick Hwu, M.D. The primary objective of this phase II study is to determine whether T cell function will improve in patients receiving adoptively transferred, tumor antigen–specific T cells combined with high-dose interleukin 2 and a vaccine prepared from dendritic cells compared with patients treated with the T cells and high-dose interleukin 2 alone.

An Exploratory Study of Adjuvant Therapy of Pegylated Interferon-Alfa 2b Plus Melanoma Peptide Vaccine in Patients with Resected Stage II and III (N1a, N2a) Melanoma (2006-0816). PI: Wen-Jen Hwu, M.D. The primary objective of this phase I trial is to explore the safety and optimal dosing schedule of pegylated interferon-alfa 2b when combined with the GP100 melanoma peptide vaccine for eliciting a T-lymphocyte immune response to the vaccine.

Other immunotherapy research

In addition to vaccines, other approaches to stimulate patients’ immune systems are being investigated. Dr. Moldrem said his group has developed an antibody that recognizes both the PR1 peptide and the human lymphocyte antigen HLA-A2. “These are present on the surface of both leukemia cells and leukemia stem cells,” he said, “but very little of the combined molecule is present on the surface of normal hematopoietic cells.” In cell culture studies, the antibody killed leukemia cells but not bone marrow cells or cord blood cells from healthy donors. Animal studies have also been successful, and Dr. Moldrem expects trials of the antibody in patients to begin within the next year. “We’re also working on PR1-specific T cells for adoptive cell therapy in patients following stem cell transplant,” he said.

Clinical trials of T cell therapy for melanoma patients have already begun. “We’ve treated more than 25 patients who have metastatic melanoma by taking the tumor out and growing T cells from the tumor in the lab—up to 150 billion cells—which are then reinjected into the patient,” Dr. Hwu said. Response rates have ranged from 40% to 50%, with some responses lasting up to 2 years so far. “There are many ways to stimulate the immune system, and we have to combine them rationally,” he said. “In early stages of disease, we’re using vaccines plus interferon; in the later stages, we’re using vaccines plus interleukin 2 and T cell therapies. We’d like to combine these with antibodies that stimulate the immune system, like anti-CTLA-4, which takes the brakes off the immune system.”

Padmanee Sharma, M.D., Ph.D., an
Findings Could Alter Chronic Myelogenous Leukemia Treatment

Phase III trials show newer drugs yield better responses than imatinib

By John LeBas

Two second-line molecularly targeted therapies for chronic myelogenous leukemia (CML) have been shown to be even more effective than imatinib (Gleevec), the breakthrough therapy that made long-term survival possible for most CML patients.

In separate international phase III studies conducted at MD Anderson Cancer Center and other institutions, the drugs dasatinib (Sprycel) and nilotinib (Tasigna) yielded faster responses as first-line therapies for CML and were effective in more patients than imatinib.

Currently, dasatinib and nilotinib are approved as second-line CML therapies for patients who cannot tolerate or do not respond to imatinib.

The findings may lead to dasatinib and nilotinib becoming standard first-line treatments for CML, said Hagop Kantarjian, M.D., a professor in and chair of the Department of Leukemia at MD Anderson and corresponding author of the dasatinib trial report.

“CML patients who achieve a complete cytogenetic response, or the absence of the chromosomal abnormality that causes the disease, within 12 months of therapy are more likely to experience long-term survival,” explained Dr. Kantarjian, who also co-authored the nilotinib report. “Since dasatinib and nilotinib are more potent than imatinib, moving these newer drugs into first-line treatment is likely to improve long-term outcomes for CML patients.”

CML background

Little more than 10 years ago, the 7-year overall survival rate for newly diagnosed CML patients was less than 50%. Then came imatinib, a first-generation tyrosine kinase inhibitor that boosted the 7-year overall survival rate for CML patients to nearly 90%.

Imatinib works against the Philadelphia chromosome, a chromosomal ab-

Response Rates: Dasatinib vs. Imatinib

Response Rates: Nilotinib vs. Imatinib


normality present in about 95% of CML patients. The BCR-ABL gene resulting from the abnormality encodes a tyrosine kinase that promotes leukemia growth. Imatinib shuts down leukemia by inhibiting the activity of this tyrosine kinase.

Given daily as a pill, imatinib is generally well tolerated. But some patients cannot tolerate its side effects, which can include myelosuppression, fluid retention, muscle cramps, and diarrhea. And importantly, 30%-40% of CML patients do not experience a complete cytogenetic response to imatinib within 12 months, even though other measures of disease control may be favorable.

Dasatinib and nilotinib are second-generation tyrosine kinase inhibitors, similar to imatinib in how they inhibit the aberrant BCR-ABL protein. However, earlier studies showed nilotinib to be 50 times more potent than imatinib against the protein and dasatinib to be more than 300 times stronger. Those and other positive early results led to the development of the phase III trials, the results of which were reported this summer in the New England Journal of Medicine.

Study findings
In the dasatinib trial (Dasatinib versus Imatinib Study in Treatment-Naive CML Patients), the newer agent was studied head-to-head against imatinib in 519 patients with newly diagnosed CML. Dasatinib was shown to be superior in nearly all analyses.

Patients receiving dasatinib had a higher rate of confirmed complete cytogenetic response (77% vs. 66% for imatinib) after a minimum follow-up of 12 months. Furthermore, in patients receiving dasatinib, complete cytogenetic response was often achieved sooner: in 54% at 3 months and 73% at 6 months, compared with 31% and 59%, respectively, for patients receiving imatinib. Dasatinib also yielded a higher rate of major molecular response (defined as 0.1% or lower levels of the BCR-ABL oncoprotein as measured by a more sensitive test than cytogenetic analysis) in patients—46% vs. 28%—and did so faster than imatinib.

Estimated progression-free survival rates at 12 months were similar for dasatinib and imatinib. The safety of the two drugs was also similar, though dasatinib was associated with milder side effects.

The nilotinib study (Evaluating Nilotinib Efficacy and Safety in Clinical Trials—Newly Diagnosed Patients) included 836 patients with newly diagnosed CML. The patients were randomly assigned to receive nilotinib at one of two doses or imatinib at the standard dose.

Results were nearly identical for both groups receiving nilotinib: 80% and 78% of patients achieved a complete cytogenetic response by 12 months, while 44% and 43% achieved a major molecular response. In both nilotinib groups, less than 1% had experienced disease progression at 12 months. In contrast, among patients receiving imatinib, 65% achieved a complete cytogenetic response, 22% had a major molecular response, and 4% experienced disease progression by 12 months.

Additionally, patients who received nilotinib achieved a major molecular response (the primary endpoint of the study) earlier than those who received imatinib (median of 5.7 and 5.8 months compared with 8.3 months). Similar to dasatinib, nilotinib was considered as safe as imatinib but caused fewer side effects.

Next steps
Both reports point out that longer follow-up is needed to understand the long-term advantages and disadvantages of nilotinib and dasatinib compared with imatinib. However, given the effectiveness of the newer drugs, researchers are hopeful that the drugs will soon become the new standard of care.

Nilotinib-maker Novartis, which also makes imatinib, and dasatinib-maker Bristol-Myers Squibb are expected to seek U.S. Food and Drug Administration approval for the two drugs as first-line therapy for CML. And other tyrosine kinase inhibitors, including bosutinib, are currently being studied in CML clinical trials to see how they compare with imatinib.

Another potentially positive implication for the long-term treatment of CML is that dasatinib and nilotinib have side effects that are less pronounced than those of imatinib. Typically, maintenance therapy is recommended following initial remission because undetectable levels of CML may still be present. One of the problems with this approach is that patients can eventually tire of any side effects and choose to cease therapy, which may increase the chance of recurrence. With dasatinib and nilotinib, however, the incidence of side effects should be lower, enabling more patients to tolerate longer-term therapy.

“Now that we know dasatinib and nilotinib are more effective than imatinib against CML, we can focus on the long-term effects of these drugs in future studies,” Dr. Kantarjian said.

For more information, contact Dr. Kantarjian at 713-792-7026.

Clinical Trials in Chronic Myelogenous Leukemia

Ongoing studies of dasatinib and nilotinib include:

Therapy of Early Chronic Phase Chronic Myelogenous Leukemia (CML) with Oral Nilotinib (2005-0048).
Principal investigator: Hagop Kantarjian, M.D. The primary objective of this phase II clinical trial is to determine the percentage of patients who achieve a complete molecular response after 12 months of therapy with nilotinib.

Therapy of Early Chronic Phase Chronic Myelogenous Leukemia (CML) with Dasatinib (2005-0422).
Principal investigator: Jorge Cortes, M.D. The primary objective of this phase II clinical trial is to estimate the proportion of patients with previously untreated chronic phase CML attaining major molecular response within 12 months of dasatinib treatment.

For more information about these and other clinical trials in leukemia, visit the Department of Leukemia home page at www.mdanderson.org.
Vandetanib Shows Benefit When Combined with Docetaxel for Lung Cancer

An international phase III trial has shown that the oral targeted therapy vandetanib helps prolong progression-free survival for patients with advanced non–small cell lung cancer.

The findings, published in the July issue of Lancet Oncology, were the first to show the clinical benefit of a small molecule targeted agent added to standard chemotherapy for lung cancer.

“This study shows that an oral tyrosine kinase inhibitor can be combined with chemotherapy safely and effectively to provide a benefit,” said Roy Herbst, M.D., Ph.D., a professor in MD Anderson’s Department of Thoracic/Head and Neck Medical Oncology and the international study’s principal investigator. “Still, we need to build on this research and turn our focus toward better identifying the molecular markers involved, with the ultimate goal of personalizing our patients’ care.”

Vandetanib is unique in that it inhibits the tyrosine kinase activity of both the epidermal growth factor receptor (EGFR) and the vascular endothelial growth factor receptor (VEGFR). It is the first single agent in lung cancer to target both tyrosine kinase receptors, Dr. Herbst said. “Both receptors are active in lung cancer—EGFR on the tumor cells and VEGFR on the blood vessels. So with vandetanib, we’re really targeting the entire tumor environment at once,” he explained. “As a dual inhibitor, vandetanib also may provide cost savings to patients in that they can now potentially take one targeted therapy instead of two.”

The study enrolled 1,391 patients with non–small cell lung cancer from 198 centers between May 2006 and April 2008; all patients had received chemotherapy previously. Participants were randomized to receive either docetaxel and placebo or docetaxel and vandetanib. The median follow-up was 12.8 months, and the study’s primary endpoint was progression-free survival. Patients in the docetaxel and vandetanib arm had a median progression-free survival of 17.3 weeks. In contrast, the median progression-free survival in the control arm was 14 weeks. There was also a statistically significant prolongation of the time to worsening of symptoms in the docetaxel and vandetanib arm.

“Obviously, our ultimate goal is always to improve survival for our patients. However, the improved time to progression is also important, as is improvement in patient symptoms,” Dr. Herbst said. “If we could identify molecular parameters that predict response, we could someday take a group that’s receiving docetaxel and vandetanib and see them do even better. We’re not there yet, but hopefully this study will serve as the foundation for the merger of personalization and discovery with the now-proven safety and efficacy.”

HPV-Positive Tumor Status Indicates Better Prognosis in Patients with Oropharyngeal Cancer

Oropharyngeal cancer patients whose tumors test positive for the human papillomavirus (HPV) have higher rates of 3-year overall and progression-free survival than patients with HPV-negative disease, researchers from MD Anderson Cancer Center reported recently in the New England Journal of Medicine.

The study—the largest and most definitive of its kind to date, conducted with the support of the Radiation Therapy Oncology Group (RTOG) and in collaboration with RTOG investigators—showed that tumor HPV status is a strong and independent prognostic factor for survival in oropharyngeal cancer patients. Follow-up data from the study were presented at the 44th annual meeting of the American Society of Clinical Oncology.

“This is the strongest prognostic factor we have ever identified for head and neck cancer,” said K. Kian Ang, M.D., Ph.D., professor in MD Anderson’s Department of Radiation Oncology and lead author of the paper. “Its value is stronger than other prognostic factors we have used, such as the size of the tumor or the presence of tumor in lymph nodes. Knowing that the tumor is associated with HPV tells the patient that the prognosis is excellent with currently available treatments.”

The phase III clinical trial examined overall survival and progression-free survival in 323 patients with stage III or IV oropharyngeal cancer treated with a combination of radiation therapy and chemotherapy. Of those patients, 206 had HPV-positive tumors and 117 had HPV-negative tumors. The 3-year overall survival rate for patients with HPV-positive tumors was 82.4%, compared with 57.1% for patients with HPV-negative cancer. The 3-year progression-free survival rates for the two groups were 73.7% and 43.4%, respectively.

When researchers adjusted for other significant determinants of survival, including patient age, race, tumor and nodal stage, and tobacco use, patients with HPV-positive cancer had a 58% reduction in risk of death compared with patients with HPV-negative tumors. The study noted that tobacco use substantially increased the risk of death. The results will allow physicians to stratify patients enrolled in clinical trials into risk groups based on HPV status, tobacco use, and cancer stage. This information can then be used to better determine which patients are candidates for more intensive investigational therapies.

While it remains unclear why patients with HPV-positive tumors have better outcomes than those with HPV-negative tumors, researchers speculate it may be a result of biologic and immunologic properties that render HPV-positive cancers inherently less malignant or better able to respond to treatment. How the HPV vaccine, made available to the public in 2006, will affect the incidence of HPV-related head and neck cancers is unknown but a topic of research interest.

Visit www.mdanderson.org/newsroom for more information.
Long touted as a way to ease muscle strain and foster relaxation, massage is now being used to relieve some of the side effects of cancer and cancer treatment. As a complementary therapy, massage assists circulation, restores energy, and enhances emotional well-being.

Massage has been shown to reduce the fatigue, pain, anxiety, and nausea that cancer patients often experience, according to Ki Y. Shin, M.D., a rehabilitation physician and an associate professor in MD Anderson Cancer Center’s Department of Palliative Care and Rehabilitation Medicine. Although not a treatment for cancer, massage seems to ease symptoms of the disease and to help patients cope with the side effects of treatment. It can improve their satisfaction with hospital stays and can improve quality of life, Dr. Shin said.

Types of massage

Massage has been around for centuries. Originating in traditional Chinese medicine, it was also once used to treat illness in Japan and India and in ancient Egypt, Greece, and Rome. Massage can be done while the recipient is seated in a chair, lying on a table, or lying in a hospital bed.

Massage is a touch therapy in which a client’s muscle groups are stroked, kneaded, or stretched. Among the various forms of massage is Swedish massage, which is very popular in the United States and which uses kneading actions to enhance circulation or long, gentle strokes to communicate calmness to the skin. Deep tissue massage focuses on the deeper underlying areas of muscle.

Another type of massage is manual lymphatic drainage, which uses light pressure in gentle rhythmic motions to increase the flow of lymph fluid out of swollen tissues. The U.S. National Cancer Institute says that this form of massage is an effective therapy for lymphedema, the retention of proteins and water in the tissues that can result from cancer treatment. Because of potential side effects and injury, manual lymphatic drainage massage techniques should be performed only by a health practitioner with lymphedema-specific training and certification.

Who should not receive massage

Patients with certain medical conditions could be harmed by receiving a massage. Those who should not get massage therapy, Dr. Shin said, include patients with blood clots, fractures, or active disease in the area to be massaged. Patients taking blood-thinning or anticoagulant medications or those who have a low platelet count, bone metastasis, and certain blood disorders should not receive deep tissue massage. A variety of other medical conditions, such as skin fragility after radiation treatment or chemotherapy, infections, bone metastasis, excess fluid around the lungs, or lymphedema, may require adjustments in massage therapy.

The massage therapist

It is important for a person with cancer to pick a massage therapist who has training in the special needs of cancer patients, Dr. Shin said. Such a therapist will screen each person to see whether a massage is appropriate and, if necessary, will modify the massage to accommodate the client’s medical condition. This might mean, for instance, reducing the pressure of the massage therapist’s touch in order not to irritate a client’s swollen tissues or avoiding certain areas near a tumor or a surgical incision. It is vital for a massage therapist to consult with a patient’s oncologist before treatment, and it is also important for physicians to know when a patient is undergoing this complementary therapy.

Additional resources

To find a qualified massage therapist with experience working with cancer patients, contact the American Massage Therapy Association by calling 1-877-905-2700, or visit the association’s Web site at www.amtamassage.org. Visit www.mdanderson.org/cimer for information on studies of massage in cancer patients.
Therapeutic Vaccines against Cancer

(Continued from page 3)

assistant professor in the Department of Genitourinary Medical Oncology, has been working with anti-CTLA-4, an antibody that blocks an intrinsic regulatory mechanism on T cells. Blocking the inhibitory signal allows the T cells to work for longer periods and to be more effective against tumors. A phase III clinical trial of anti-CTLA-4 in patients with metastatic prostate cancer is currently enrolling patients at MD Anderson and other institutions. “It’s an exciting agent, and it has shown dramatic, durable responses in a previous trial with melanoma patients,” Dr. Sharma said. She explained that because the antibody targets a molecule on T cells, it is not a tumor-specific agent and may therefore boost immune responses against various types of cancer.

In a previous trial of the NY-ESO-1 DNA vaccine in patients with metastatic prostate adenocarcinoma, Dr. Sharma’s group found that the vaccine induced an immune response, but that the response was suppressed by regulatory T cells and other mechanisms that regulate immune responses. Because the NY-ESO-1 DNA vaccine activates T cells and anti-CTLA-4 blocks an intrinsic inhibitory mechanism in T cells, Dr. Sharma and her group are in the process of planning a trial combining the two drugs. “We need to be able to turn on antitumor immune responses and simultaneously block inhibitory pathways that act to turn them off,” she said.

Individualized treatment

Now that their lymphoma vaccine has had a positive trial, Dr. Neelapu said he and other researchers at MD Anderson are doing follow-up studies to learn why certain patients responded to the vaccine and others did not. “We are looking at genetic markers and immunological markers from these patients,” he said.

“None of these studies were home runs,” said Dr. Hwu. “In our melanoma study, the response rate doubled from 10% to 20%, but that still leaves 80% who did not respond.” His lab continues to study biomarkers in patients from the previous trial of the GP100 vaccine and in patients participating in ongoing studies. “We’re trying to customize treatment with the MAGE vaccine by looking at the expression of certain genes in the tumor to develop profiles that will determine who responds to the vaccine and who doesn’t,” said Dr. Hwu. In fact, he added, MD Anderson has an immune-monitoring core laboratory to analyze cell-mediated immune responses in samples from participants in clinical trials of new immunotherapies or drugs.

“I think response rates from vaccines are going to get incrementally better as we learn how to target these therapies,” Dr. Hwu said. “I’m excited about the future.”

For information about ongoing clinical trials, visit www.mdanderson.org.