OncoLog
MD ANDERSON'S REPORT TO PHYSICIANS ■ April 2014 Vol. 59, No. 4

New Fat Grafting Technique Improves Aesthetic Outcomes Following Head and Neck Reconstructive Surgery

By Zach Bohannan

A new fat grafting technique is enabling reconstructive surgeons to maximize aesthetic outcomes following major reconstruction for head and neck cancer treatment–related defects.

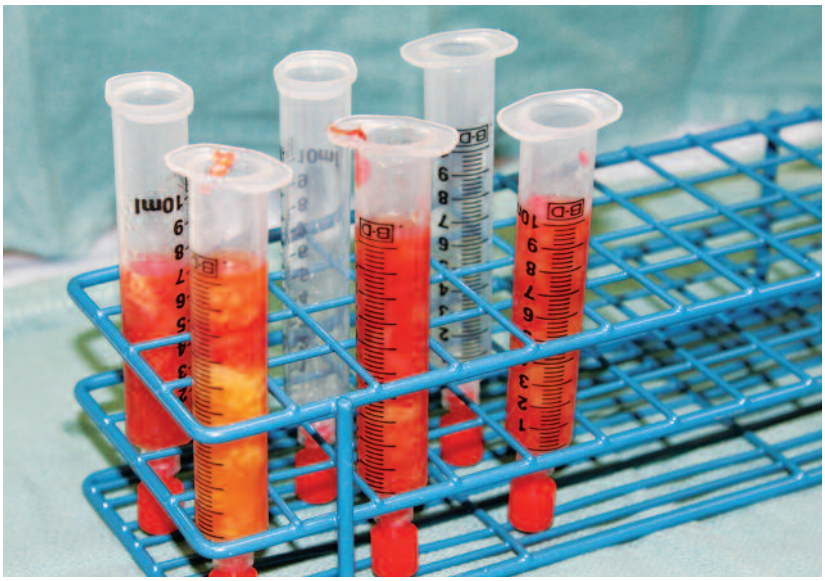
Because head and neck cancer resections can be extensive, can involve many structures, and may be followed by radiation or other secondary therapies, reconstructive surgery for head and neck cancer–related defects historically has limited aesthetic benefits and is mostly concerned with functional restoration.

Roman Skoracki, M.D., and Matthew Hanasono, M.D., both associate professors in the Department of Plastic Surgery at The University of Texas MD Anderson Cancer Center, are helping pioneer the use of fat cell isolation and injection to improve the quality and appearance of reconstructed tissue for head and neck cancer patients. "We can perform functional reconstructions very well here, but this new grafting technique allows us to refine the aesthetic qualities of the reconstructions," Dr. Skoracki said.

The procedure is currently used in some institutions to smooth the skin after breast reconstruction, but MD Anderson is among the first to use the technique in facial reconstruction following major cancer resections.

New hope for an old idea

Autologous fat transplants are traditionally small, to ensure an adequate blood supply for the fatty tissue, and often include nonfat tissue (such as skin), which may adversely affect aesthetic outcomes or limit the grafts' usefulness in many reconstructions. High-volume fat transplants often fail because much of their volume is either lost to resorption or



Fat harvested by liposuction (above) contains adipose tissue, liquid fat, blood, and sometimes other nonfat tissue. In a new approach to autologous fat transplantation, the pure fat cells are isolated by centrifuge for injection into the target area.

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

[Continued from **page 1**]

converted into scar tissue as a result of inadequate revascularization, which is needed to deliver oxygen and nutrients to each cell for survival. In fact, large autologous fat transplants sometimes form cysts that must be drained or surgically removed.

In the new approach to fat grafting, fat is first harvested by liposuction, using specialized cannulas, from a distant region of the body and subjected to centrifugation to quickly isolate the adipose tissue from liquid fat and blood. Then, many small amounts of the purified fat cells are injected into the target area. These multiple small transplants are arranged in a matrix over the target area, and this arrangement helps maintain the blood supply to each fat graft while still covering a relatively large area. These matrices of small grafts allow surgeons to precisely control the tissue thickness and aesthetics of the final result.

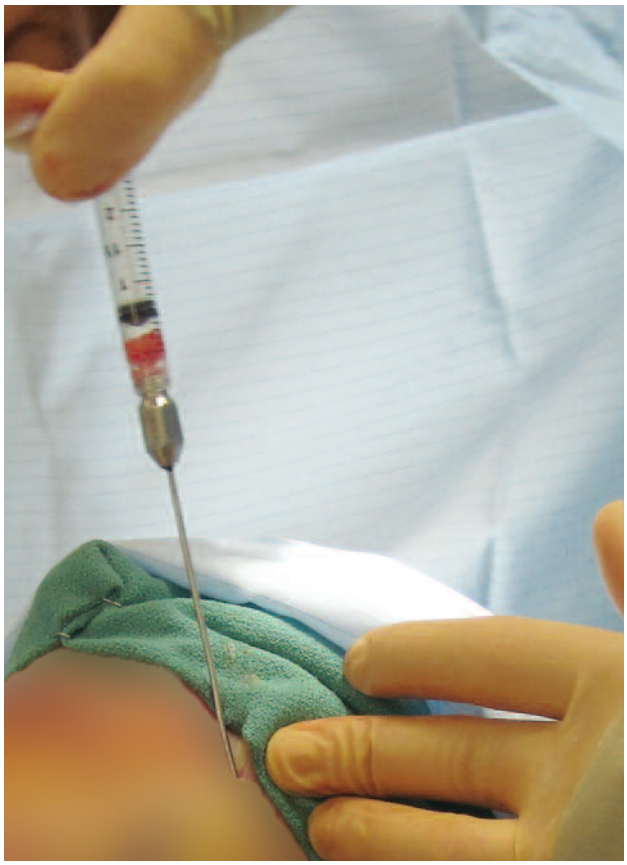
These fat cell grafting techniques may contribute to tissue improvement effects beyond aesthetics. Although these tissue improvement effects have not been fully characterized, Dr. Hanasono said, "The areas with the transplanted fat seem to be softer and more pliable than areas without the transplanted fat." Dr. Skoracki added, "Sometimes, for patients with poor tissue quality as a result of radiation or other damage, we can take a gradual approach in which the first fat graft procedure improves suppleness and flexibility and then subsequent procedures help fill out the reconstruction."

> **"It's mostly an outpatient procedure, so we can bring previous patients in and perform touch-ups relatively easily."**
>
> **– Dr. Matthew Hanasono**

Use in head and neck reconstructions

For head and neck cancer–related reconstructions, this fat grafting procedure is usually a touch-up procedure performed well after primary cancer treatment and reconstruction have been completed. Dr. Hanasono said, "This is really a post-treatment procedure that we use when the patient is stable and the wound area is relatively safe—6 months to several years after the cancer has been cured. We always consult the primary oncologist as well to ensure that oncologic outcomes are not compromised."

The speed and simplicity of these new fat grafts make them attractive to patients who are not satisfied with their existing reconstruction. Dr. Hanasono said, "It's mostly an outpatient procedure, so we can bring previous patients in and perform touch-ups relatively easily."



During an autologous fat transplant, a surgeon injects purified fat cells into the reconstructed area. Multiple small injections are made to ensure an adequate blood supply to each graft.

Most patients who have undergone head or neck reconstructive surgeries are eligible for this type of fat grafting procedure. Exceptions include patients with minimal subcutaneous fat—for example, those who are elite athletes or who have cachexia. Little fat is needed for a successful graft, but very low body fat percentages make it difficult to harvest a sufficient volume of fat for grafting.

For head or neck reconstructions, 100 mL of fat is typically harvested, but after purification, the total volume is generally half that. This is still more than enough material for a successful procedure, and Drs. Skoracki and Hanasono said they usually inject about 40 mL of fat at a time when performing head or neck reconstructions.

Potential complications

One persistent issue for fat grafts is the possibility of resorption, even in these small transplants. The amount of fat that remains resident after a transplant varies and is at least partially dependent on the state of the surrounding skin. Dr. Skoracki said, "There is some variability to the persistence of the fat, especially in patients who have a lot of scarring or skin damage from radiation therapy. In such patients, much of the fat gets resorbed, but the transplant still seems to improve the skin quality in the area."

Some clinicians hypothesize that fat grafting improves tissue texture because fat contains stem cells. Researchers have previously shown that fat does contain inactive stem cells, but the data remain inconclusive about whether fat grafting can somehow activate the stem cells. Although active

stem cells may help to reverse some of the scarring caused by radiation and surgery, there is the hypothetical concern that the stem cells could also contribute to second cancers. However, only one laboratory study has suggested this possibility, and it was performed in mice. None of the clinical studies performed to date have found evidence of fat-derived second cancers. Nevertheless, the American Society of Plastic Surgeons recommends that surgeons exercise caution when transplanting autologous fat into patients with a high risk of second cancer. "We have very little evidence that this technique carries a risk of second cancer, but we do try to be cautious when working with patients who have higher second cancer risks," Dr. Skoracki said.

Future refinements

Some researchers at MD Anderson and other institutions are working to refine the new fat grafting technique to improve its effectiveness for use in a variety of reconstructive procedures such as breast reconstruction after lumpectomies. The use of autologous fat transplants in such procedures has been limited because they require larger volumes of fat than does head or neck reconstruction. The need for larger fat volumes may make it difficult to obtain adequate fat for transplantation and increase the chance of resorption or scarring.

Some equipment manufacturers are trying to reduce the time and increase the yield of the centrifugation process, which may facilitate fat transplants to more substantial parts of the body or for larger reconstructions.

Even as surgeons strive to improve the technique, Dr. Hanasono said the procedure has made a profound difference for his patients. He said, "For us, this has been a game changer because we can go from good reconstruction to much better." ■

FOR MORE INFORMATION

Dr. Matthew Hanasono.....713-794-1247
Dr. Roman Skoracki.....713-794-1247

IN BRIEF

Invasive Bladder Cancer Subtypes Resemble Breast Cancer Subtypes

Researchers have found that the gene expression pattern of muscle-invasive bladder cancer is remarkably similar to that of breast cancer. This resemblance has important implications for treating the most lethal form of bladder cancer.

Scientists at The University of Texas MD Anderson Cancer Center, working with researchers at The University of Texas Graduate School of Biomedical Sciences and other institutions, reported that the gene expression profiles of muscle-invasive bladder cancer fall into three molecular categories that closely resemble three of the four major subtypes of breast cancer.

The researchers analyzed the genetic profiles of 73 flash-frozen muscle-invasive bladder cancer tissue samples from MD Anderson and then validated the initial findings in a set of 57 formalin-fixed, paraffin-embedded muscle-invasive bladder tumor samples, also from MD Anderson. The researchers also performed subtype analyses on muscle-invasive bladder tumor samples collected in clinical trials performed at MD Anderson, Fox Chase Cancer Center, and Thomas Jefferson University Hospital in Philadelphia.

David McConkey, Ph.D., a professor in the Department of Urology, and his colleagues identified a basal subtype of muscle-invasive bladder cancer that is similar to basal (triple-negative) breast cancer; a luminal subtype that is similar to luminal A and B breast cancer subtypes; and a "p53-like" luminal subtype that is also similar to luminal A breast cancer but is characterized by activated wild-type *TP53* gene expression.

The basal subtype of muscle-invasive bladder cancer expressed genes that are biomarkers for basal breast cancer (*CD44*, *KRT5*, *KRT6*, and *CDH3*) and indicate the presence of cancer stem cells and other treatment-resistant features. Like its breast cancer counterpart, the basal bladder cancer subtype was found to be biologically aggressive if left untreated but was sensitive to cisplatin-based chemotherapy. Cisplatin-based chemotherapy followed by cystectomy is the standard of care for muscle-invasive bladder cancer.

The luminal subtype of muscle-invasive bladder cancer expressed gene biomarkers shared by the luminal A and B subtypes of breast cancer (*CD24*, *FOXA1*, *GATA3*, and *ERBB2*). Luminal bladder cancers were estrogen receptor–positive and had activating mutations in *FGFR3*, which encodes a growth factor receptor. Drugs that target these receptors may be effective in patients with this bladder cancer subtype.

The p53-like subtype of muscle-invasive bladder cancer was distinguished by its activated wild-type *TP53* gene expression signature. The tumors in this category were resistant to cisplatin-based combination chemotherapy. Dr. McConkey said that a recent clinical trial of presurgical chemotherapy for breast cancer found that breast tumors with normal *TP53* gene expression signatures also responded poorly to chemotherapy. One explanation for this chemotherapy resistance is that besides promoting cell death, the p53 protein also can simply arrest cell growth and division. Dr. McConkey said, "These dormant cells evade chemotherapy, which preferentially kills dividing cells."

The report of the study was published in the February edition of *Cancer Cell*. The researchers are developing streamlined methods for identifying these muscle-invasive bladder cancer subtypes so that the information can be used to guide treatment decisions. ■

New Kinase Inhibitors Hold Promise for Chronic Lymphocytic Leukemia, Other B-Cell Malignancies

By Joe Munch

New targeted therapies against chronic lymphocytic leukemia (CLL) are eliciting overall response rates similar to those achieved using standard chemoimmunotherapy but with fewer toxic effects.

As these targeted drugs—inhibitors of the B-cell receptor (BCR) pathway—are increasingly combined with other agents and long-term follow-up data accrue, a more permanent role for these agents in the treatment of CLL and other B-cell malignancies is beginning to emerge.

BCR pathway inhibitors

The main advantage of BCR pathway inhibitors over standard treatments for CLL is that the targeted drugs do not induce the classic, sometimes life-threatening side effects of cytotoxic chemotherapy.

"One of the biggest issues in treating CLL is that up until now, most of the therapies we had caused myelosuppression," said Susan O'Brien, M.D., a professor in the Department of Leukemia at The University of Texas MD Anderson Cancer Center. "In a CLL patient who has an elevated white blood cell count, we want the white count to come down, but we don't want the nonspecific effects of lowering the platelets or hemoglobin, which could cause the patient to need a transfusion."

Because BCR pathway inhibitors do not cause myelosuppression, they also carry a lower risk of infection than do cytotoxic chemotherapy drugs. These qualities make the targeted agents ideally suited for CLL patients whose advanced age or comorbidities preclude traditional chemotherapy. Numerous clinical trials are now investigating BCR pathway inhibitors alone or in combination with other agents in these and other populations.

BCR pathway inhibitors target CLL cells more specifically than do cytotoxic agents. The inhibitors work by disabling enzymes in the BCR signaling pathway, which are aberrantly activated in CLL, to render the pathway nonfunctional. For example, ibrutinib inhibits Bruton tyrosine kinase, and idelalisib inhibits phosphoinositide 3-kinase δ; both enzymes are critical to BCR signaling. As a result of this interrupted signaling, CLL cells lose not only their ability to proliferate and survive but also their ability to home in on, invade, and remain in the lymph nodes, which would otherwise serve as havens for further CLL growth. Deprived of these abilities, the bulk of CLL cells in the lymph nodes are dislodged into the peripheral blood.

The rapid redistribution of the cells causes transient lymphocytosis; in early trials of BCR pathway inhibitors, this was mistakenly viewed as a reason to stop treatment. "The patient's lympho-

CLINICAL TRIALS: Chronic Lymphocytic Leukemia

Randomized study of ibrutinib versus ibrutinib plus rituximab in patients with relapsed chronic lymphocytic leukemia (2013-0703). Principal investigator (PI): Jan Burger, M.D. The primary objective of this phase II trial is to compare the 2-year progression-free survival rate of patients treated with single-agent ibrutinib (PCI-32765) to that of patients treated with ibrutinib plus rituximab. Secondary objectives are to determine the regimens' safety and tolerability, overall response rates, estimated progression-free survival, changes in immune parameters (lymphocyte subpopulations, immunoglobulin levels), and biomarker responses.

A randomized, multicenter, open-label, phase III study of the Bruton tyrosine kinase inhibitor PCI-32765 versus chlorambucil in patients 65 years or older with treatment-naïve chronic lymphocytic leukemia or small lymphocytic lymphoma (2012-1007). PI: Dr. Burger. The primary goal of this trial is to compare the effectiveness of ibrutinib to that of chlorambucil in older patients with chronic lymphocytic leukemia or small lymphocytic lymphoma. The safety of these drugs will also be compared.

A phase I study to investigate the safety and clinical activity of idelalisib in combination with chemotherapeutic agents, immunomodulatory agents, and anti-CD20 monoclonal antibody in subjects with relapsed or refractory indolent B-cell non-Hodgkin lymphoma, mantle cell lymphoma, or chronic lymphocytic leukemia (2010-0811). PI: Nathan Fowler, M.D. The primary goal of this trial is to learn about the safety of idelalisib (CAL-101, GS-1101) when combined with rituximab, ofatumumab, bendamustine, fludarabine, chlorambucil, everolimus, bortezomib, and/or lenalidomide in patients with non-Hodgkin lymphoma, mantle cell lymphoma, or chronic lymphocytic leukemia. Researchers will also study the efficacy of these drug combinations.

cyte count will go up initially. But this should not be interpreted as a sign of progressive disease, and the patient should not be taken off the drug for that reason," Dr. O'Brien said.

Clinical trials

Of the BCR pathway inhibitors, idelalisib and ibrutinib have generated the most excitement, as both drugs have advanced to phase III studies against multiple B-cell malignancies.

Trials of idelalisib against relapsed CLL or treatment-refractory indolent non-Hodgkin lymphoma have had encouraging results, and applications for the drug's use in patients with these conditions are pending approval by the U.S. Food and Drug Administration (FDA).

Ibrutinib, approved by the FDA in November 2013 for the treatment of mantle cell lymphoma in patients who have received at least one prior therapy, made headlines again in February when it was approved for the treatment of CLL in patients who have received at least one prior therapy. And a recent phase Ib/II study demonstrating ibrutinib's safety and efficacy in treatment-naïve patients older than 65 years who had CLL or small lymphocytic lymphoma is likely a harbinger of the approval of the drug for use in additional populations of patients with B-cell malignancies.

"These new agents are going to raise a lot of interesting questions about potential combinations that in the long run may get us away from the use of cytotoxic chemotherapy entirely."

– Dr. Susan O'Brien

Patient selection

"At this point, we can clearly recommend ibrutinib for elderly patients who are not candidates for chemoimmunotherapy or for patients who have high-risk disease," said Jan Burger, M.D., an associate professor in the Department of Leukemia, "especially if they have the 17p deletion."

The 17p chromosomal deletion is a negative prognostic factor that almost invariably portends suboptimal responses to chemoimmunotherapy. In contrast, ibrutinib has elicited relatively good responses in patients who have the 17p deletion and is likely to have a role as

and Other B-Cell Malignancies

A phase III, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of GS-1101 (CAL-101) in combination with bendamustine and rituximab for previously treated chronic lymphocytic leukemia (2012-0411). PI: Susan O'Brien, M.D. The primary goal of this trial is to find out if adding idelalisib to rituximab and bendamustine is more effective than rituximab and bendamustine plus a placebo in controlling chronic lymphocytic leukemia. The safety of these two treatment combinations will also be studied.

A phase II, open-label study evaluating the efficacy, safety, tolerability, and pharmacodynamics of GS-9973 in combination with idelalisib in subjects with relapsed or refractory hematologic malignancies (2013-0319). PI: Dr. O'Brien. The primary goal of this trial is to learn if the combination of GS-9973 with idelalisib can help control chronic lymphocytic leukemia. The safety of these drugs will also be studied.

A phase I, multicenter, open-label, and dose-escalation study of ACP-196 in subjects with chronic lymphocytic leukemia (2013-0907). PI: Dr. O'Brien. The primary goal of this trial is to find the highest tolerable dose of the Bruton tyrosine kinase inhibitor ACP-196 that can be given to patients with chronic lymphocytic leukemia. Researchers will also study the safety of ACP-196 and whether it can help control the disease. This is the first study using ACP-196 in humans.

A multi-center phase I/Ib study evaluating the efficacy and safety of ublituximab, a third-generation anti-CD20 monoclonal antibody, in combination with TGR-1202, a novel PI3k delta inhibitor, in patients with B-cell malignancies (2013-0566). PI: Dr. O'Brien. The primary goal of this trial is to learn the highest tolerable dose of the combination of ublituximab and TGR-1202 that can be given to patients with B-cell lymphoma, chronic lymphocytic leukemia, or other B-cell lymphoproliferative disorders. The safety of this drug combination will also be studied.

A multicenter phase II study of the Bruton tyrosine kinase inhibitor PCI-32765 for treatment of relapsed hairy cell leukemia (2013-0299). PI: Farhad Ravandi-Kashani, M.D. The primary goal of this trial is to learn if ibrutinib can help control hairy cell leukemia and variant hairy cell leukemia. The safety of this drug will also be studied.

A phase II study of ibrutinib plus rituximab in patients with relapsed/refractory mantle cell lymphoma (2013-0090). PI: Michael Wang, M.D. The primary goal of this trial is to learn if a combination of ibrutinib and rituximab can help control relapsed or refractory mantle cell lymphoma. The safety of this drug combination will also be studied. ■

FOR MORE INFORMATION

Visit www.clinicaltrials.org.

frontline therapy for the 5%–10% of CLL patients who have this deletion at diagnosis.

"In patients with relapsed, refractory disease who have the 17p deletion, the median progression-free survival duration with ibrutinib is about 2 years," Dr. O'Brien said. "That is better than any published median progression-free survival duration—which is typically 1 year—for patients with the 17p deletion receiving frontline chemotherapy," Dr. O'Brien said. "Right now, I would not hesitate to treat a patient with the 17p deletion up front with ibrutinib because I know such patients don't do well with cytotoxic chemotherapy."

According to Dr. Burger, ibrutinib and idelalisib both represent excellent options for the treatment of CLL. Whether patients receive one or the other may ultimately depend on the patients' ability to tolerate the side effects of the drugs or whether other agents are being given concurrently. For example, ibrutinib, which can increase the risk of bleeding, may not be ideal for patients taking certain anticoagulants, such as warfarin.

"Only time will tell whether one drug is a little better than the other in patient subgroups," Dr. Burger said. "We have followed up patients treated with these drugs for only 3–3.5 years. That's a relatively short time for follow-up."

The main advantage of BCR pathway inhibitors over standard treatments for CLL is that the targeted drugs do not induce the classic, sometimes life-threatening side effects of cytotoxic chemotherapy.

"These patients who didn't have other options wouldn't be here with us without this [ibrutinib-rituximab] treatment."

– Dr. Jan Burger

Long-term data may hold answers

Without sufficient long-term follow-up data, some vexing questions about the use and action of BCR pathway inhibitors remain. Chief among these is the issue of why patients treated in a frontline therapy setting, where one might expect to see a more robust treatment response, overwhelmingly have partial rather than complete responses. However, responses to BCR pathway inhibitors are very slow to occur; given that these patients have been followed for only a short time, additional complete responses may yet be observed.

"I think some patients who have partial responses to these drugs as frontline therapy will eventually transition to a complete response. How many will actually become complete responders is very hard to know because we don't have long-term follow-up data yet," Dr. O'Brien said.

The lack of long-term follow-up data also clouds researchers' understanding of the side effects of BCR pathway inhibitors.

"Once larger populations get treated, then there could be safety issues that did not come up in the earlier clinical trials," Dr. Burger said. "Kinase inhibitors can have cardiovascular side effects. That relationship may still emerge in the case of BCR pathway inhibitors, and that's something we need to be cautious about."

Additional long-term data may also provide insight into CLL cells' development of resistance to BCR pathway inhibitors. This resistance is not yet common but remains a prime concern.

"These agents target one pathway, which is clearly an important pathway, but malignant cells rarely have only one abnormal pathway," Dr. O'Brien said. "Targeting one pathway may not be enough."

Combination therapies

Given their success as single-agent therapies, their good tolerability, and the fact that they are oral agents, BCR pathway inhibitors such as ibrutinib and idelalisib are being given with other agents against CLL in the hopes of eliciting even better treatment responses.

The findings of ongoing phase II trials of combinations of the targeted therapies and cytotoxic chemotherapy are promising, although combining these therapies sacrifices the BCR pathway inhibitors' advantage of not causing myelosuppression.

A more promising approach may be to combine the inhibitors with monoclonal antibodies to treat CLL. For example, Dr. Burger recently completed a pilot study of ibrutinib plus rituximab—the monoclonal antibody that has had a major impact on survival in CLL—in which 38 of 40 patients (95%) had a complete or partial response. The only patients who did not respond exited the

[Continued on **page 8**]

Animal-Assisted Therapy

Interacting with pets helps recovery

HOUSE•CALL PATIENT INFORMATION SHEET

Pets can help people feel better. But pets trained in animal-assisted therapy can actually help during recovery for patients who have cancer or other serious illnesses.

The goal of animal-assisted therapy is to help therapists improve patients' physical, social, emotional, and cognitive function.

What is animal-assisted therapy?

Many programs provide animal-assisted therapy to help patients recover functions that have been affected by a serious illness or its treatment. For example, at The University of Texas MD Anderson Cancer Center, doctors can prescribe animal-assisted therapy through the Welcoming Animals Giving Support (WAGS) program.

Each Saturday, six to eight volunteer handlers bring their dogs to MD Anderson to participate in WAGS, which celebrates its 10th anniversary this year. The dogs and handlers have gone through an extensive training program sponsored by Caring Critters, a nonprofit animal-assisted therapy group.

Current dog volunteers include golden retrievers, German shepherds, fox terriers, poodles, and dachshunds. Each dog serves a special function in helping patients achieve their physical therapy goals. For example, patients who need to work on standing for long periods of time might groom or pet a small dog on a table. Small dogs also can curl up in patients' laps to help them work on their sensory or fine motor skills through petting. Other patients who are working on balance might walk with a large dog on a leash. Large dogs also can help patients develop coordination by playing fetch and other games.

Benefits

In addition to helping patients achieve specific therapeutic goals, the dogs help patients emotionally and

socially. Marifel Malacara, P.T., D.P.T., a physical therapy supervisor in the Department of Rehabilitation Services, said, "There was one little boy who did not want to get out of bed or participate in physical therapy. He would cry every time we tried to get him up. When he saw the dog, though, he got very excited and energetic. The transformation in his attitude was amazing."

The dogs can make the hospital environment seem more like home and help remind patients about life outside of the hospital. The dogs also encourage and motivate patients to get better so that the patients can return home and see their own pets.

Research has shown that dogs can have positive physiological effects on humans. One study showed that levels of beta-endorphin, oxytocin, and dopamine—chemicals that promote a sense of well-being and help reduce stress and anxiety—increase in both humans and dogs after a positive interaction. These interactions also lower people's levels of cortisol, which is sometimes called the "stress hormone" because it is released as a response to anxiety or stress.

Other studies have been published on patients' pain levels after interacting with pets. One study found that patients who sat quietly for 20 minutes reported four times more pain than did patients who interacted with an animal for the same amount of time. Because animals can help reduce pain, many centers that offer animal-assisted therapy use animals to distract and comfort children who are undergoing medical procedures.

The National Institutes of Health established a research fund in 2008 to further explore the science behind human-animal interaction.

Contraindications

Animal-assisted therapy is not for all patients, however. Patients with allergies, low white blood cell counts, infection control issues, or psychiatric disorders are not candidates for animal-assisted therapy.

The dogs themselves do not contribute to infection risk. WAGS, like most animal-assisted therapy programs, requires dogs to be screened by a veterinarian before they can participate in the program. Also, several studies have shown that animals do not increase infection rates in hospitals. A study of 2,381 dog visits to 1,690 patients at Huntington Memorial Hospital in California found no increase in zoonotic (spread from animals to humans) infections over a 5-year period.

Dr. Malacara believes that the benefits far outweigh the risks of animal-assisted therapy. "Animal-assisted therapy is a collaborative, positive program—especially for cancer patients. They benefit physically, mentally, and emotionally," she said. "The change in the patients after interacting with the dogs is remarkable. Our patients really look forward to their Saturday sessions." ■

– J. Delsigne

FOR MORE INFORMATION

- *Visit Caring Critters at www.caringcritters.org*
- *To find an animal-assisted therapy program in your area, visit www.petpartners.org*
- *Call* askMDAnderson *at 877-632-6789*

The University of Texas
MD Anderson Cancer Center
OncoLog-1725/142100-10-100104-11
PO Box 301407
Houston, TX 77230-1407

New Kinase Inhibitors Hold Promise

[Continued from **page 6**]

study early owing to side effects or treatment complications.

"I have one patient for whom eight or nine lines of therapy had failed; he really didn't have any options left. I enrolled him in the ibrutinib-rituximab trial, and 2 years into this treatment, he's doing fine and traveling throughout Europe," Dr. Burger said. "These patients who didn't have other options wouldn't be here with us without this treatment. And there's quite a large number of these patients."

As in the case of patients treated with single-agent ibrutinib, most patients receiving the ibrutinib-rituximab combination had partial responses; only about 10% of patients had complete remissions. However, Dr. Burger said that the patients' CLL did respond faster than is typically seen in patients who receive ibrutinib alone, and this may translate into longer progression-free survival. The combination is now being compared with rituximab alone in a trial enrolling 208 CLL patients at MD Anderson.

Dr. Burger is optimistic about the future of BCR pathway inhibitors and other targeted drugs for CLL treatment. "Patients have been waiting for drugs like these. The feedback that I get from the patients I enroll in the studies of these drugs is extremely positive," Dr. Burger said. "Moving forward, we're going to use them more often and more broadly. I'm hopeful that these more targeted approaches will offer more benefit than side effects for a large majority of patients."

"I think what people like to envision for CLL is non-cytotoxic therapy," Dr. O'Brien said. "These new agents are going to raise a lot of interesting questions about potential combinations that in the long run may get us away from the use of cytotoxic chemotherapy entirely." ■

> **"I'm hopeful that these more targeted approaches will offer more benefit than side effects for a large majority of patients."**
>
> **– Dr. Jan Burger**

FOR MORE INFORMATION

Dr. Jan Burger.....713-563-1487
Dr. Susan O'Brien.....713-792-7543

FURTHER READING

Burger JA. Inhibiting B-cell receptor signaling pathways in chronic lymphocytic leukemia. *Curr Hematol Malig Rep.* 2012; 7:26–33.

OncoLog®

The University of Texas MD Anderson Cancer Center

President
Ronald A. DePinho, M.D.

Provost and Executive Vice President
Ethan Dmitrovsky, M.D.

Senior Vice President for Academic Affairs
Oliver Bogler, Ph.D.

Director, Department of Scientific Publications
Kathryn Carnes

Managing Editor
Bryan Tutt

Assistant Managing Editors
Zach Bohannan Sarah Bronson Joe Munch

Contributing Editors
Melissa G. Burkett Stephanie Deming
Jill Delsigne Mark Picus
Ann M. Sutton

Design
Janice Campbell, The Very Idea®

For questions or comments about *OncoLog*, please email scientificpublications@mdanderson.org or call 713-792-3305. Current and previous issues are available online in English and Spanish at www.mdanderson.org/oncolog.

Made possible in part by a gift from the late Mrs. Harry C. Wiess.

NATIONAL® CANCER INSTITUTE
A Comprehensive Cancer Center Designated by the National Cancer Institute

To Refer a Patient

Physicians: To refer a patient or learn more about MD Anderson, contact the Office of Physician Relations at 713-792-2202, 800-252-0502, or www.physicianrelations.org.

Patients: To refer yourself to MD Anderson or learn more about our services, call 877-632-6789 or visit www.mdanderson.org.