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REPORT TO PHYSICIANS

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Oncology

Assessing Symptom Burden in Cancer

Researchers are aiming to help clinicians better manage the physical and emotional toll of disease and treatment.

By Joe Munch

Until recently, assessing the symptoms caused by cancer and its treatments—let alone managing them—often took a back seat to other aspects of clinical care.

Typically, symptoms were not treated until after they presented in patients, and when clinicians did address their patients' symptoms, they targeted the obvious—pain and fatigue—but tended to overlook other symptoms that interfered with their patients' lives. As cancer patients live longer, however, more clinicians are focusing not only on prolonging life, but also on improving quality of life. And that means addressing patients' symptoms *before* they become serious issues.

The Department of Symptom Research at The University of Texas M. D. Anderson Cancer Center is working toward that aim by assessing and exploring possible avenues of effectively treating patients' symptom burden—the physical and emotional toll of cancer and its treatments. The department is running clinical studies aimed at reducing or preventing symptoms in cancer patients, surveying patients to better define the characteristics and severity of those symptoms, and making an effort to understand their underlying causes.

Xin Shelley Wang, M.D., M.P.H., an associate professor of symptom research, is the principal investigator for many



Dr. Charles Cleeland and Dr. Xin Shelley Wang are taking symptom research beyond the realm of pain and fatigue.

of these studies. Much of her work focuses on the role of inflammatory cytokines in symptom burden. She and other researchers have discovered that certain symptoms seem to be correlated with each other—that they may in fact be caused by the same biologic mechanism. Investigating these mechanisms may lead to a more informed approach of treating symptom burden in cancer patients. “The goal is to target those mechanisms that cause

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Assessing Symptom Burden in Cancer

(Continued from page 1)

symptom burden so we can do a better job of managing and preventing symptoms,” Dr. Wang said.

The search for better data

The first step in locating and targeting the biologic mechanisms that cause symptom burden in cancer patients is identifying the symptoms and treatments that cause the most distress. However, many of the symptoms that contribute to a patient’s symptom burden—like fatigue, poor appetite, and drowsiness—cannot be measured easily or objectively. “You cannot just ask a patient, ‘Do you have hypertension?’ You need to measure it by taking that patient’s blood pressure,” Dr. Wang said. “But when you ask, for example, ‘Do you have pain, and how bad is it?’ no objective measure exists—you have to trust the patient.”

To better understand how symptoms interfere with patients’ lives, to better prepare patients for the symptoms of their cancer treatment, and ultimately, to use that information to help eliminate symptom burden, researchers in the Department of Symptom Research have been developing and are using symptom assessment tools—surveys designed to gauge the severity of symptoms patients experience while undergoing cancer treatments. Charles Cleeland, Ph.D., McCullough Professor of Cancer Research and chair of the Department of Symptom Research, has been at the forefront of the symptom research field for more than 20 years. In the late 1980s, while at the University of Wisconsin, he spearheaded the development of the Brief Pain Inventory, a tool that is used to assess pain and its effects on patients’ lives and that has become a major clinical trial and epidemiologic measure for pain in patients with cancer and other diseases. Later, after he arrived at M. D. Anderson, Dr. Cleeland and his colleagues developed the Brief Fatigue Inventory, a similar measure that is used to assess fatigue and its byproducts in patients. Yet, even as he and his colleagues were developing the Brief Fatigue Inventory, it became clear that pain and fatigue were not isolated problems and

“The goal is to target those mechanisms that cause symptom burden so we can do a better job of managing and preventing symptoms.”

– Dr. Xin Shelley Wang

that patients were, in fact, experiencing a constellation of symptoms.

“We thought that we still weren’t capturing the multitude of symptoms that patients have. We never will, but let’s go a little higher in the number we try to tackle,” Dr. Cleeland said. “So we did a lot of work with patients and tried to find out, at least for the patients here, what symptoms bothered them the most.”

Assessing the burden

To address this need, Dr. Cleeland and his colleagues in the Department of Symptom Research developed the M. D. Anderson Symptom Inventory, or MDASI, a brief, two-part, multiple symptom assessment tool modeled on the Brief Pain and Brief Fatigue inventories. On the survey, patients are first asked to rate on a 0 to 10 scale the severity of 13 “core” symptoms—pain, fatigue, nausea, vomiting, disturbed sleep, distress, shortness of breath, problems remembering things, lack of appetite, drowsiness, dry mouth, sadness, and numbness or tingling—experienced in the last 24 hours, with 0 representing “not present” and 10 representing “as bad as you can imagine.” Next, patients rate how those symptoms have interfered with six aspects of their lives—general activity, mood, work (including work around the house), relations with other people, walking, and enjoyment of life—with 0 representing “did not interfere” and 10 representing “interfered completely.”

“If you just ask patients, for example, ‘Do you have any pain?’ that’s an insuffi-

cient question because it doesn’t give you any boundaries,” Dr. Cleeland said. “But if you ask, ‘On a 0 to 10 scale, what is your pain?’ patients can give you some idea of the severity of it.”

Because each disease, stage, and treatment can cause different symptoms, the MDASI’s core items have been supplemented with symptoms that are specific to certain types of cancer and their treatment. For example, gastrointestinal cancer patients typically have problems with diarrhea, whereas advanced-stage lung cancer patients often use morphine and thus have problems with constipation. Neither of the symptoms is included among the core items on the MDASI, but they may seriously interfere with patients’ lives. These disease-specific “modules” enable the inclusion of disease-specific symptoms without making the surveys extremely long, as would be the case if all possible symptoms of all possible cancers were included.

Data collected with the MDASI in a large patient group can be used to help predict the severity of symptoms associated with a particular cancer or cancer treatment. That information in turn can be used to help health care provider and patient alike prepare for treatment. “For instance,” Dr. Cleeland said, “for certain head and neck cancers, chemotherapy is combined with radiation therapy, whereas the treatment used to be radiation therapy alone. We can use the MDASI to show that the difference in symptom burden associated with the combined therapies is significantly worse for the patient. You wouldn’t want to stop using the combined therapy, but with that knowledge you certainly could prepare better for making the patient more comfortable.”

While a handful of patients may manipulate their MDASI responses to draw attention to themselves, exaggerating the severity of their symptoms, Dr. Cleeland believes that the converse is probably a bigger problem. Patients who fear that their responses will bother the physician, instigate additional cancer treatments, or preclude them from participating in trials of experimental cancer therapies are more likely to

report their symptoms as less severe than they really are. However, Dr. Cleeland said, most of the responses are thought to be accurate self-assessments. “What we have seen in 20-plus years is that the majority of patients seem to use these assessment tools in the same way, and that for the majority of patients the numbers have a similar meaning, not only in the United States but across different cultures and countries,” he said.

Dr. Wang, who has been working with researchers from around the globe to validate foreign language versions of the MDASI, echoed Dr. Cleeland’s sentiments: “It doesn’t matter if your ‘5’ is equal to my ‘5’ or is equal to another person’s ‘5.’ Basically, when someone reports a ‘5,’ we observe impairment of the patient’s daily function. And when a patient goes from reporting a ‘0’ to reporting a ‘5,’ or goes to reporting an ‘8,’ for *that* patient, it’s a big change.”

And that big change needs to be addressed before a patient winds up in an emergency room.

Applications for intervention

According to Dr. Cleeland, one of the advantages of the MDASI is that it is “intuitively interpretable” by patients and physicians alike. Moreover, most patients can complete the survey in fewer than 5 minutes. Its uncomplicated, straightforward design makes the MDASI easily adaptable to a computer- and telephone-based interactive voice response (IVR) system that can be used to monitor patients at home. The IVR-MDASI is designed to keep clinicians in touch with patients’ needs throughout their disease courses: The system generates automated follow-up phone calls to outpatients; when prompted by the system, a patient reports the severity of his or her symptoms by pushing buttons on the telephone keypad. If the patient reports a sudden increase in symptom severity, the IVR-MDASI alerts the patient’s health care providers so that appropriate measures can be taken to help better manage the patient’s symptom burden.

“The end of the therapy doesn’t mean the end of the symptom burden,” Dr. Wang said. In some cases, she noted,

symptom burden actually increases after treatment ceases. “Even for patients who do not come back to the clinic on a weekly basis anymore because they have completed therapy, we still need to address how they’re dealing with their symptoms.”

Care providers rely on patients to report their symptoms. This does not present much of a problem if a patient is in the hospital and has almost constant contact with his or her care staff. However, Dr. Cleeland said, “We have shifted so much of our care to the outpatient setting. That, in turn, leaves it up to the patients to decide when they need to go in for unscheduled care, and it’s almost the rule that patients will wait way too long to do that. One of the things that intrigues us is whether, if we are monitoring these patients and finding that their symptoms are changing, we might be able to prevent some bad events from happening.”

To test the feasibility of the IVR-MDASI as an effective symptom assessment and tracking tool, researchers have recently incorporated it into clinical trials aimed at assessing the symptom burden in patients undergoing surgery for lung cancer, chemotherapy for non-small-cell lung cancer, and autologous blood or bone marrow transplantations.

Looking forward

In collaboration with other departments at M. D. Anderson, the Department of Symptom Research is

“If we are monitoring outpatients and finding that their symptoms are changing, we might be able to prevent some bad events from happening.”

– Dr. Charles Cleeland

doing research to determine the effectiveness of novel treatments designed to relieve patients’ symptom burden. Ongoing studies are exploring the possibility that various behavioral interventions, such as aural distraction or positive imagery, are effective at decreasing symptom burden during treatment; investigating the use of methylphenidate as an effective treatment of fatigue in breast cancer patients undergoing chemotherapy; and using functional magnetic resonance imaging to determine and measure the interaction between the activation sites in the brain that are associated with morphine, positive imagery, and pain in healthy volunteers.

For her part, Dr. Wang is working with the Department of Thoracic and Cardiovascular Surgery to study the prevalence, severity, and interference of multiple symptoms in advanced lung cancer after surgery or chemotherapy. She is also investigating the role of symptom-related cytokines in lung and gastrointestinal cancer patients undergoing chemotherapy and radiation therapy. Researchers draw blood samples and correlate cytokine levels with the symptoms patients experience from therapy.

The department’s research may one day lead to a clearer picture of symptom burden—and may help provide the means to target and eliminate it. In the meantime, the benefit of symptom research, Dr. Wang said, is that it sets the bar for practitioners: physicians now have a starting point when confronted with their patients’ symptoms.

“So many clinical trials have been done and so many symptom management guidelines have been published, and people are beginning to understand the importance of controlling symptom burden,” Dr. Wang said. “Today, you can actually do something to keep cancer patients from suffering from their symptoms. This you could not imagine 20 years ago.” ●

For more information, call the Department of Symptom Research at 713-745-3470 or visit www.mdanderson.org/departments/PRG.

Expanding Therapy Options for Advanced Cancer

M. D. Anderson's Department of Investigational Therapeutics is substantially increasing the number of experimental therapies being studied in people with metastasis or unresectable disease.

By Dianne C. Witter

Twenty-nine-year-old ██████ was not ready to die. But after her Ewing sarcoma metastasized to her lungs and neither surgery nor chemotherapy stopped its progression, further treatment options were limited, and her prognosis was not good.

That's when she looked to M. D. Anderson's Department of Investigational Cancer Therapeutics for alternatives, in the form of early clinical trials of new agents that showed promise in the laboratory. Since its inception in 2004 as the Phase I Program, the department has significantly increased the number of experimental agents available to patients who are essentially out of standard treatment options.

Phase I trials are a gamble; most patients don't experience a dramatic turnaround in their disease, but a few do. A few more may experience a partial remission or a reduction in tumor size. Traditionally, the primary purpose of phase I trials has been to gather dosing and toxicity data, but these trials also evaluate response to therapy.

"The old way of thinking was that phase I trials should look only at toxicity, that we weren't looking for response until phase II trials," said Razelle Kurzrock, M.D., chair of the Department of Investigational Cancer Therapeutics. "Our philosophy is completely different. One of the most important objectives of our trials is to look for response signals and identify which tumor type or types a drug is showing

some promise in, then expedite the transition to a phase II study of that drug in that type of cancer."

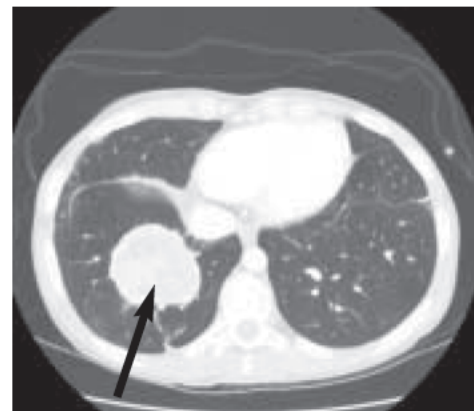
█████ wasn't in the lucky minority who benefited from the drug being studied in her first phase I trial; her disease continued to progress despite the new therapy. Nor did she respond to the drugs in her second or third phase I trials.

"Whenever I was told that a treatment wasn't working, I just asked, 'What are we going to do next?'" said ██████. "Never give up. You never know if the next drug will be the one to work." Her physician, Robert Benjamin, M.D., worked closely with Dr. Kurzrock, trying to determine which trials would have the best chance of working for her, based on what was known about the biology of her disease.

In December 2006, ██████ started her fourth trial, that of a monoclonal antibody that targets the insulin-like growth factor-1 receptor. This time, she hit the jackpot. Her tumors shrank remarkably, and she has had a sustained response since that time. She is still receiving therapy and says she is feeling great, has better stamina, and is working full time.

While success stories like this are the exception rather than the rule in phase I studies, they have helped fuel the fast growth of Investigational Cancer Therapeutics. From an initial two active trials, the research has expanded to 71 trials—and the program recently became a formal department.

The goal of the department is to quickly expand the pipeline of newly developed drugs. These drugs are for the most part developed by the pharmaceutical industry. Some are sponsored by the National Cancer Institute, and a small—but increasing—number of new drugs are developed at M. D. Anderson. The department also has



Computed tomography images show ██████ tumor before (above) and after therapy with an experimental monoclonal antibody. It was the fourth phase I trial in which ██████ participated.

several phase I trials looking at new combinations of drugs that are already approved, on the premise that hitting several targets at once may more effectively shrink the tumors.

"We now know a lot more about which molecular changes drive the growth of tumors," said Dr. Kurzrock. "We try to pick drugs that are likely to have the greatest impact on the signaling pathways that are abnormal in cancer, and then we try to match specific drugs with specific tumor types." The goal is to make new drugs available to

“In our phase I trials, we try to match specific drugs with specific tumor types.”

– Dr. Razelle Kurzrock

patients for whom standard therapy has been ineffective and to more efficiently move drugs that elicit response in early trials into phase II trials.

People with a variety of cancers are included in any given study, allowing researchers to quickly evaluate the potential effectiveness of a drug or combination therapy across tumor types. This approach can identify efficacies that weren't apparent in mouse models and that otherwise may never have been identified. For example, explained Dr. Kurzrock, since the program started, nine drugs that showed unexpected benefits in cancers other than the ones they were developed for have been transitioned into phase II studies for those cancers.

For example, the insulin-like growth factor-1 receptor inhibitor ██████████ responded to was not originally developed for Ewing sarcoma, but seeing some dramatic responses in these patients made the investigators rethink how this drug should be developed. It is

now entering phase II studies by a global collaboration of sarcoma investigators. The study will look at Ewing sarcoma patients as well as patients with other specific sarcomas that are thought to have the same biological pathways. Similarly, several new drugs elicited response in thyroid cancer, which is rarely studied in preclinical models, and this has led to further trials in this disease.

The most likely candidates for the Department of Investigational Cancer Therapeutics program are patients who have no standard treatment options available, who are in good health other

than their cancer, who want experimental treatment, and who can stay in Houston for treatment for 1 to 2 months, Dr. Kurzrock said.

The program also has specialized trials for patients who often have difficulty finding clinical trials appropriate for them, such as people with brain metastasis, those with liver or kidney failure, people older than 60 years, and children.

“We're entering a whole new era of drug development,” Dr. Kurzrock said. “We want to make sure our early clinical trials are efficiently linking the many patients looking for experimental therapy with the new drugs becoming available.” ●

For more information or to refer a patient for a phase I study in the Department of Investigational Cancer Therapeutics, contact Christie Carver-Fryer, R.N., B.S.N., at 713-563-9819 or visit www.mdanderson.org/departments/phase1.

Phase I Clinical Trials

- **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).** Principal investigator (PI): Razelle Kurzrock, M.D. This antibody targets B lymphoproliferative disorders such as multiple myeloma, lymphoma, and Castleman's disease.
- **Phase I Study of Tipifarnib and Sorafenib in Patients with Biopsiable Advanced Cancers (2005-0363).** PI: David Hong, M.D. This combination study uses a farnesyltransferase inhibitor and an RAF kinase inhibitor to target *Ras*-mutated genes, which are found in a variety of solid and hematologic malignancies.
- **Multiple Ascending Dose (MAD) Phase I Study of the IGF-1R Antagonist R1507 Administered as an Intravenous Infusion on QW and Q3W Schedules in Patients with Advanced Solid Tumors,**

Non-Hodgkin's Lymphomas, or Hodgkin's Lymphoma (2005-0806). PI: Razelle Kurzrock, M.D. R1507 is a fully humanized monoclonal antibody to the insulin-like growth factor-1 receptor that is being used in patients with various solid tumors, non-Hodgkin's lymphoma, and Hodgkin's lymphoma.

- **Multi-Arm, Complete Phase I Trial of Valproic Acid-Based 2-Agent Oral Regimens for Patients with Advanced Solid Tumors (2007-0170).** PI: Siqing Fu, M.D., Ph.D. Clinical synergism between valproic acid and either sorafenib, sunitinib, dasatinib, erlotinib, lapatinib, or lenalidomide is being monitored in this study. By using multiple treatment regimens in tandem, the hope is to see clinical activity in a variety of solid tumors.
- **Phase I Dose-Escalation Study of the Safety and Pharmacokinetics of XL184 Administered Orally to Subjects with Advanced Malignancies (2005-0396).** PI: Razelle

Kurzrock, M.D. This study uses an RET/VEGF inhibitor to target metastatic or unresectable solid tumors.

- **Phase I Trial of Bevacizumab and Bortezomib in Patients with Advanced Malignancy (2006-0764).** PI: Razelle Kurzrock, M.D. This study uses a combination of an antiangiogenic agent and proteasome inhibitor for the treatment of metastatic or unresectable advanced malignancies.
- **Open-Label Phase I Study to Evaluate the Effects of Patupilone on the Pharmacokinetics of Midazolam and Omeprazole in Patients with Advanced Malignancies (2006-0563).** PI: Razelle Kurzrock, M.D. Patupilone is a natural, microtubule-targeting cytotoxic agent that induces mitotic cell cycle arrest and eventual apoptosis in human cancer cells. Advanced solid tumors are being targeted. ●

For more information on these and other clinical trials at M. D. Anderson, visit www.clinicaltrials.org.

Vaccine Shows Response in Some Leukemia Patients

A peptide vaccine helped certain patients with leukemia live longer without relapse, M. D. Anderson researchers reported at the annual meeting of the American Society of Hematology in December 2007. The PR1 vaccine, which attempts to elicit an immune response to kill cancer cells in myelodysplastic syndrome, acute myelogenous leukemia, and chronic myelogenous leukemia, was tested in a phase I/II clinical trial from 2000 to 2006.

Patients in whom the vaccine triggered an immune response had an 8.7-month relapse-free survival, compared to 2.4 months for nonresponders. Also, clinical responses—including complete remission—were observed in 36% of the patients with immune responses, compared to 10% of nonresponders. Among the 13 patients who were in remission when they started the trial, four remained in remission for a median of 30.5 months. “We were quite pleased to see the clinical responses and improved relapse-free survival, since we did not expect it in the beginning,” said Muzaffar Qazilbash, M.D., an associate professor in the Department of Stem Cell Transplantation and Cellular Therapy. The vaccine was developed by Jeffrey Molldrem, M.D., a professor in the department.

Disease-specific phase II trials of the vaccine for chronic myelogenous leukemia and myelodysplastic syndrome are planned or under way. To be eligible, patients must be positive for HLA-A2, a histocompatibility molecule.

For more information, contact Dr. Qazilbash at 713-792-8750 or mqazilba@mdanderson.org. ●

Drug’s Redesign Lessens Danger to the Heart

Imatinib (Gleevec)—a drug that has dramatically improved the long-term survival rate for patients with chronic myelogenous leukemia (CML)—has

been redesigned to kill gastric cancer cells with a lower risk of cardiotoxicity. Researchers at M. D. Anderson produced and tested the altered form of imatinib, which was redesigned at Rice University. The development of the new drug, called WBZ-4, is being described as a novel “bottom-up” approach, in which small changes in an agent’s chemical structure are designed to elicit specific, intended effects on biological processes.

Imatinib inhibits proteins including C-Kit kinase, which is involved in the development of gastrointestinal stromal tumor (GIST), and Bcr-Abl kinase, which is involved in CML. The cumulative incidence of complete cytogenetic response in CML with imatinib therapy was 91%, according to a recent M. D. Anderson study led by Hagop Kantarjian, M.D., a professor in and chair of the Department of Leukemia. However, imatinib does carry a low risk of heart failure (one M. D. Anderson study showed that 1.7% of 1,276 patients taking imatinib had symptoms that may have been caused by heart failure). Researchers believe this risk may be related to the inhibition of Bcr-Abl activity.

WBZ-4, unlike imatinib, targets C-Kit but not Bcr-Abl. As a result, the potential for cardiotoxicity is even lower, researchers found in laboratory, animal, and computer testing. WBZ-4 appears to be as effective against GIST as imatinib—but, of course, it has no effect on CML since it does not inhibit the function of the leukemia-associated protein. The new drug was created by adding just four atoms to imatinib at a precise location in its molecular structure, which allowed a reaction with C-kit but not Bcr-Abl.

“This is excellent proof that we can enhance the selectivity of a drug by making a small but significant change in its structure,” said Gabriel Lopez-Berestein, M.D., a professor of experimental therapeutics at M. D. Anderson, who helped oversee testing of WBZ-4 by computer, in cell culture experiments, and in mouse models of GIST and CML. “We know exactly how WBZ-4 works. It’s a completely novel approach

that could be applied to the redesign of other drugs in a way that allows for greater control of their effects.”

Results were published in the *Journal of Clinical Investigation*. Human trials have not been set. ●

Aerosol Therapy May Offer Hope to Infection-Prone Patients

Researchers at M. D. Anderson have developed an aerosol therapy that stimulates an immune system response within the lungs, killing airborne pathogens on contact. Though the therapy has so far been tested only in mice, investigators are hopeful it will lead to new protection for cancer patients and others at risk of infection because of compromised immune systems.

Dubbed the aerosolized lung innate immune stimulant (ALIIS), the therapy is a purified extract of a common bacterium that causes ear and sinus infections in children. When inhaled, ALIIS apparently prompts the innate immune system to flood the thin layer of fluid lining the lungs with polypeptides that destroy invading microbes. What’s more, the ALIIS-stimulated innate immune system appears to wipe out invaders before the adaptive immune system is fully activated and before neutrophils are summoned. That could be important for immunocompromised cancer patients, whose neutrophils are often killed off by chemotherapy, said Burton Dickey, M.D., a professor in and chair of the Department of Pulmonary Medicine at M. D. Anderson and senior author of the ALIIS research.

All mice treated with ALIIS 4 to 24 hours before exposure to the most common pneumonia bacterium survived. When administered 2 hours before exposure, ALIIS was found to prompt an effective response against the bacterium in 83% of exposed mice. Likewise, ALIIS was effective against several other types of bacterial pneumonia, influenza virus, and the mold *Aspergillus*.

The findings were presented at the annual meeting of the American Society for Cell Biology in December 2007. ●



Helping Kids Make Smart Food Choices

The age-old problem of getting kids to eat their veggies might be tougher than ever. Today's parents have to compete with fast food, vending machine snacks, sodas, and other options that are quick and easy—and often far from healthy. But you can help your children develop better eating habits.

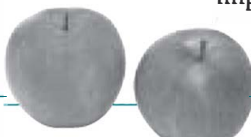
Learning about groceries

You might be surprised to learn that children will usually pick nutritious foods when given the choice. But it's up to parents to give them those choices, and spicing up your trips to the grocery store is a great place to start. "Getting kids involved in the grocery shopping teaches them how to pick out produce and other ingredients," said Kristen Bardon, R.D., L.D., senior clinical dietitian in the Department of Clinical Nutrition at The University of Texas M. D. Anderson Cancer Center. "It also helps them learn how to prepare healthy meals."

Have your kids help put together the shopping list, and be sure to suggest lots of fresh fruits and vegetables. That way you can talk about healthy choices before ever getting to the store. Children will be more interested in food that's good for them when they have a chance to make some of the decisions. And you'll learn more about what they like and don't like.

Once at the store, take the children on a scavenger hunt for healthy foods, Ms. Bardon suggests. This will make shopping exciting and helps them look beyond the junk food aisles. Try these tips for a successful scavenger hunt:

- Show your kids a picture of a fruit or vegetable and ask them to find it.
- Have them describe



Healthy Diet Recommendations

You can find a world of information about food recommendations for children on the Internet. Here are a couple of sources to help you get started.

www.americanheart.org

The American Heart Association offers an eating pattern for families at its Web site. Highlights include:

- ✓ Eat foods that are low in saturated fat, trans fat, cholesterol, sodium, and added sugars.
- ✓ Serve whole-grain and/or high-fiber breads and cereals. Look for "whole grain" as the first ingredient on the food label.
- ✓ Serve a variety of fruits and vegetables each day, but limit the amount of juice kids drink. Each meal should contain at least one fruit or vegetable.
- ✓ Don't overfeed your kids. Typical calorie needs are about 900 per day for a 1-year-old child, 1,800 per day for a 14- to 18-year-old girl, and 2,200 per day for a 14- to 18-year-old boy (or more for active teens).

www.fruitsandveggiesmatter.gov

For recipes and eating tips, visit the Web site "Fruits and Veggies—More Matters." The site includes a calculator that you can use to figure out specific food serving information for your child. The "More Matters" program is sponsored by the U.S. government and private partners.



the shape, color, and size of fruits and vegetables they see.

- Have them count fruits and vegetables.
- Encourage them to find fruits and vegetables that they haven't eaten before.

Benefits of a healthy diet

By being a good role model for healthy eating, you also can set children on a lifelong path of making the right food choices.

"It's important for kids to start eating healthy early in life," Ms. Bardon said. "Healthy eating can help prevent many problems as they get older, including obesity, diabetes, heart disease, and some cancers."

Not only can eating well help prevent problems down the road, it's important for growing kids to take in the nutrients provided by fruits, vegetables, and other healthy



foods. But these nutrients are even more important for children who have cancer or another major illness.

"These children need a healthy, well-balanced diet sufficient in protein and calories," Ms. Bardon said. "Protein helps the body heal, and calories produce energy and help kids keep up their weight." ●



For more information, talk to your physician, or:

- call askMDAnderson at 1-877-632-6789
- visit the Department of Clinical Nutrition's Web site at www.mdanderson.org/departments/nutrition
- visit www.mdanderson.org

OncoLog, February 2008
J. LeBas

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DiaLog Making Headway in Hematology

By **Guillermo Garcia-Manero, M.D.**

The annual meeting of the American Society of Hematology (ASH), which was held in December 2007, showcased the complex and fascinating research taking place in the field of hematology, from the laboratory to the clinic.

For instance, a lot of promising work on myelodysplastic syndrome (MDS) is taking place at our institution and around the world. A prospective, randomized phase III study presented at ASH demonstrated that 5-azacitidine, a hypomethylating agent, significantly improved survival in patients with higher-risk MDS. In this study, the probability of survival at 2 years was approximately double in patients treated with 5-azacitidine versus other interventions, including cytarabine-based chemotherapy. Overall survival increased by nearly 10 months. These results establish 5-azacitidine as the current standard frontline therapy in higher-risk MDS.

Two important studies were presented that identified new molecular alterations in 5q- syndrome (a subset of MDS characterized by deletion of part of the long arm of human chromosome 5). Both papers discussed the use of short hairpin RNA (shRNA) technology and identified two genes (*RPS14* and *HSPA9B*) as potential key molecular mediators of this syndrome. The relationship between these two genes and 5q- syndrome in MDS now needs to be clarified.

Multiple discoveries were reported in

leukemia and lymphoma, including new therapeutic agents and molecular markers. Researchers from M. D. Anderson reported on two drugs showing promise as frontline therapy in chronic myelogenous leukemia (CML), dasatinib and nilotinib, which are currently used as second-line agents in imatinib-resistant CML. Also from M. D. Anderson, exciting initial data were presented on the use of two JAK2 inhibitors in myeloproliferative disorders, as well as the results of a study of combination epigenetic therapy in acute myelogenous leukemia and high-risk MDS.

In multiple myeloma, several studies established the role of the proteasome inhibitor bortezomib and the immunomodulatory drug lenalidomide. Finally, data were presented indicating the safety of cord blood transplantation and establishing the role of mini-transplantation in multiple myeloma. (More information on ASH-presented research is on page 6. — Ed.)

It's an exciting time for the field of malignant hematology, given the new drugs coming into clinical use and our growing understanding of these diseases. Important findings are being quickly translated into clinical practice—and that translates into better outcomes. ●



Dr. Garcia-Manero is an associate professor in M. D. Anderson's Department of Leukemia.

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