OncoLog
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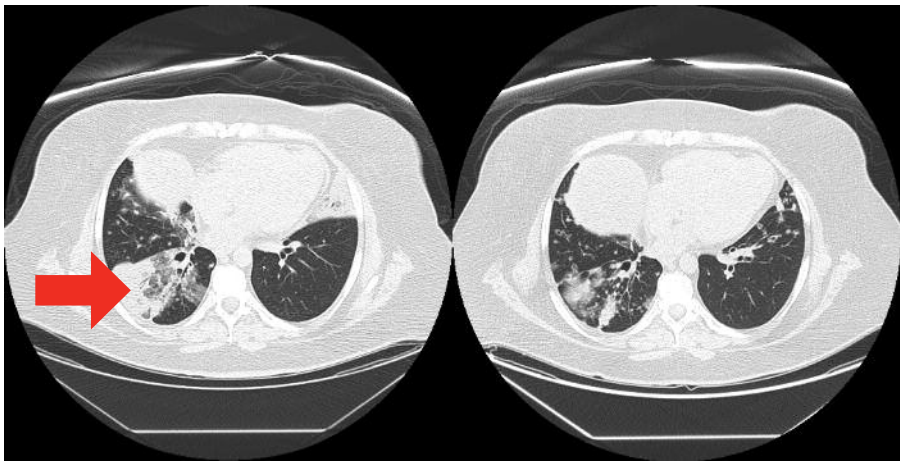
Biomarker-Driven Clinical Trials May Improve Personalized Treatment for Patients With Lung Cancer

By Stephanie Deming

Innovative clinical trials that assign patients to treatment arms based on tumor biomarkers could lead to increased treatment options for patients with lung cancer.



Computed tomography images show a lung tumor (arrow) before (left) and after treatment with sorafenib in the BATTLE-2 trial.

On June 16, SWOG (formerly the Southwest Oncology Group), in cooperation with the National Cancer Institute's (NCI) National Clinical Trials Network, activated a large biomarker-driven clinical trial of targeted therapies for squamous cell lung cancer, the Lung-MAP trial. The innovative design of this study is expected to result in highly efficient testing of personalized therapy. The lead national principal investigator of Lung-MAP and a member of the trial's oversight committee is Vali Papadimitrakopoulou, M.D., a professor in the Department of Thoracic/Head and Neck Medical Oncology at The University of Texas MD Anderson Cancer Center.

BATTLE studies helped lay foundation

According to Dr. Papadimitrakopoulou, Lung-MAP was inspired in part by two earlier biomarker-driven studies led by MD Anderson investigators, BATTLE and BATTLE-2.

In the BATTLE study, launched in 2005, investigators sought to determine whether certain biomarkers were useful for matching patients with non–small cell lung cancer with the targeted therapy most likely to be effective against their tumors. Patients had biopsies done just before treatment was started, and the biopsy specimens were analyzed for protein expression and genomic alterations. In the first stage of the trial, patients were randomly assigned to one of four targeted therapy regimens. However, in the second stage of the trial, information on biomarkers and disease control rates at 8 weeks in the first patients enrolled was used to adjust the randomization process for subsequent patients. Specifically, patients enrolled during the trial's second stage had a higher

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probability of assignment to the treatment regimen that had demonstrated the best disease control rate in earlier patients with the same biomarker profile.

The goal of this adaptive randomization process was to match patients with the therapies most likely to benefit them. "BATTLE was one of the first studies in the national arena that recognized the value of biomarker-driven treatment," Dr. Papadimitrakopoulou said. And the trial showed that biomarkers were indeed useful for guiding treatment selection.

Encouraged by the success of the BATTLE study, investigators launched BATTLE-2 in 2011 to identify additional biomarkers for patients with non–small cell lung cancer. Because certain mutations are now well established as predictors of response to particular types of targeted therapy, patients who have these so-called sensitizing mutations and who have not previously received drugs that target these mutations are excluded from BATTLE-2 and offered those drugs. Patients who enroll in BATTLE-2 are randomly assigned to receive one of four different targeted therapies. The trial uses an adaptive randomization process similar to that used in the first BATTLE study, in which the assignment of patients to treatment arms later in the study depends on both the patients' tumor biomarkers and the outcomes observed in patients enrolled earlier. BATTLE-2 has reached its accrual goals for the first stage (200 participants), and the first-stage results are being analyzed.

Lung-MAP: efficient testing of targeted therapies

In Lung-MAP, the most recent biomarker-driven clinical trial for lung cancer patients, investigators have drawn on knowledge from the BATTLE trials and new data regarding the mutational background of squamous cell lung cancer to design a highly efficient approach to testing new targeted therapies for the disease. Squamous cell lung cancer remains a disease in which substantial developments in therapeutics have yet to be seen; the targeted therapies approved for treating non–small cell lung cancer are largely ineffective against the squamous cell variant.

"Many people in the cancer research community have been dreaming of this kind of (combined clinical trial) concept."

– Dr. Vali Papadimitrakopoulou

In Lung-MAP, each patient's tumor tissue is analyzed for more than 200 genomic alterations. The results of this analysis are then used to offer the patients participation in one of five phase II or III randomized trials, or substudies, within the Lung-MAP framework.

Four of the Lung-MAP substudies test new targeted therapies. For example, in one study, open to patients whose tumors harbor *PIK3CA* gene mutations, patients are randomly assigned to treatment with the PI3K inhibitor GDC-0032 or docetaxel. In a study open to patients whose tumors demonstrate *FGFR1*, *FGFR2*, or *FGFR3* gene amplification or mutations, patients are randomly assigned to treatment with the FGFR inhibitor AZD4547 or docetaxel. Patients without genetic alterations that match one of the tested targeted therapies are offered a randomized trial in which patients receive immunotherapy or docetaxel.

"There's really a lot of potential in the (Lung-MAP) study for the approval of drugs for patients with squamous cell lung cancer."

– Dr. Vali Papadimitrakopoulou

Another key feature of Lung-MAP is that if any of the phase II randomized trials shows that the experimental drug has substantial efficacy, then the trial proceeds to phase III, which can lead to drug approval by the U.S. Food and Drug Administration (FDA). If a phase II study shows that the experimental drug is not effective, the study will be replaced by a new study with a different drug or drug combination that addresses the same target. "There's really a lot of potential in the study for the approval of drugs for patients with squamous cell lung cancer," Dr. Papadimitrakopoulou said.

By gathering multiple randomized clinical trials together within one overarching trial infrastructure, the Lung-MAP investigators expect to attract large numbers of patients and increase enrollment in randomized trials of targeted therapy. The traditional approach to testing targeted therapies is to have different groups test different targeted therapies in different studies, each of which has its own genomic test for eligibility. With that approach, a patient who learns that his or her tumor is not a good match for a trial therapy must either look elsewhere or settle for standard treatment. In contrast, in Lung-MAP, patients have their eligibility tested for multiple studies simultaneously.

The Lung-MAP trial design is also expected to increase speed and efficiency through rapid clinical trial approval and avoiding duplication of resources. "MAP" in "Lung-MAP" stands for the "master protocol" specifying the overarching design of the trial. Within this master protocol, individual randomized trials can be stopped if the drugs they are testing do not show promise, and new randomized trials for targeted therapies that have demonstrated acceptable results in phase I trials can be developed and added quickly according

to prespecified guidelines. "It's a modular clinical trial," Dr. Papadimitrakopoulou said. The baseline testing for genetic alterations is performed by one company at a single site, and the statistical analyses for all the randomized trials will be performed by SWOG.

Although Lung-MAP could in theory continue indefinitely, at present the study is projected to last approximately 5 years. Up to 300 sites around the United States are expected to participate, and the investigators are in active discussions to try to expand the trial to Canada. There is also interest in expanding the study to other countries. At present, it is expected that 500–1,000 patients will enroll each year, but those numbers could change as the number of randomized trials within the Lung-MAP framework changes.

Another outcome of Lung-MAP will be the creation of a central tissue bank, overseen by SWOG. "This is going to be an unprecedented repository of squamous cell lung cancer tissues," Dr. Papadimitrakopoulou said.

New wave of clinical trials

In designing Lung-MAP, investigators were responding to a mandate from the Institute of Medicine and the NCI to conduct more efficient studies. "The organizations are concerned about waste of resources: patient and personnel time from screening patients who don't end up being eligible for a particular trial, and taxpayer money in the case of NCI-funded research," Dr. Papadimitrakopoulou said.

Trials similar to Lung-MAP are being planned for other types of cancer and are expected to become increasingly common. "Many people in the cancer research community have been dreaming of this kind of concept," Dr. Papadimitrakopoulou said. "If we can prove that this trial design works, it will lead a lot of other groups to conduct similar trials." ■

FOR MORE INFORMATION

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New Antibody-Chemotherapy Combinations Show Promise Against Acute Lymphoblastic Leukemia

By Bryan Tutt

Two investigational agents—inotuzumab and ofatumumab—show promise when combined with cytotoxic chemotherapy drugs for the treatment of acute lymphoblastic leukemia (ALL) in adults.

The early results of two ongoing clinical trials, which are available only at The University of Texas MD Anderson Cancer Center, were reported in June at the 2014 American Society of Clinical Oncology Annual Meeting by Elias Jabbour, M.D., an associate professor in the Department of Leukemia, and colleagues.

Dr. Jabbour said the studies are important because they provide a new avenue of treatment for adult ALL patients, who tend to have more aggressive disease, lower tolerance for chemotherapy, and worse outcomes than do children with the disease. "Although great success has been seen in the treatment of pediatric ALL, unfortunately outcomes for adults have lagged behind," Dr. Jabbour said. The cure rates for children and adults with ALL are around 90% and 40%, respectively.

Monoclonal antibodies that target surface antigens such as CD20 and CD22 on ALL cells have become a mainstay in the treatment of ALL. The standard of care for patients in whom CD20 is expressed on at least 20% of ALL cells is the anti-CD20 monoclonal antibody rituximab combined with cytotoxic chemotherapy. However, rituximab is not effective in patients whose tumor cells have lower levels of CD20 expression or in the tiny percentage of patients whose disease does not express CD20 at all.

Second-generation monoclonal antibodies such as inotuzumab and ofatumumab could extend the use of antibody-chemotherapy combinations to a broader group of ALL patients.

Inotuzumab

When the CD22 inhibitor inotuzumab ozogamicin was found to be active as a single agent against ALL in early studies, researchers saw the opportunity to reduce the doses of cytotoxic chemotherapy drugs. "In the beginning, we thought about treating elderly patients with the drug because many elderly patients cannot tolerate chemotherapy very well," Dr. Jabbour said. "In one study, treatment-naïve patients 60 years or older with ALL were given chemotherapy at half the standard dose plus inotuzumab. Responses were excellent."

Those results led to the current study—led by Hagop Kantarjian, M.D., a professor in and chair of the Department of Leukemia—in which treatment-naïve ALL patients 60 years or older or patients of any age with relapsed or refractory ALL are given inotuzumab and low-intensity cytotoxic chemotherapy. Patients in the study receive 8 cycles of a chemotherapy regimen that comprises reduced doses of cyclophosphamide, dexamethasone, methotrexate, and cytarabine; during the first 4 cycles, patients are also given rituximab and inotuzumab. Patients then receive maintenance therapy with mercaptopurine, methotrexate, vincristine, and prednisone (POMP) for 4 years.

Antibody-Chemotherapy Combinations for ALL

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"Going forward with the antibodies we have available to us, the future is bright for ALL patients."

– Dr. Elias Jabbour

At the trial's interim analysis, the overall response rates for patients with newly diagnosed ALL and relapsed/refractory ALL were 95% and 75%, respectively. "We have not seen significant adverse effects, and the 1-year survival rate was about 80%," Dr. Jabbour said.

Ofatumumab

The anti-CD20 molecule ofatumumab, which binds to CD20 at a site different from that of rituximab, is already approved for the treatment of chronic lymphoblastic leukemia. Dr. Jabbour is the principal investigator of a phase II clinical trial of cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with methotrexate and cytarabine (hyper-CVAD) plus ofatumumab as a frontline treatment for patients with ALL.

In the study, patients with CD20-positive ALL who are newly diagnosed or have undergone 1 cycle of chemotherapy receive the first 4 cycles of the hyper-CVAD regimen with ofatumumab followed by 4 cycles of hyper-CVAD without ofatumumab. Patients then receive maintenance therapy with POMP for 30 months. The maintenance therapy is interrupted with intensification therapy comprising methotrexate plus pegaspargase in months 6 and 18 and hyper-CVAD plus ofatumumab in months 7 and 19.

Of the first 25 patients enrolled in the study, 24 were in complete remission as of June. Dr. Jabbour said there were no safety concerns associated with the treatment. "Obviously the follow-up is short at 14 months," he said. "But if these results are maintained a year from today, that will be a major breakthrough in the treatment of patients with ALL."

Future is bright

In addition to inotuzumab and ofatumumab, other monoclonal antibodies, such as obinutuzumab, blinatumomab, SGN-CD19A, and epratuzumab, are being investigated for the treatment of ALL in clinical trials at MD Anderson and other institutions. Dr. Jabbour is optimistic that combinations of such agents and cytotoxic chemotherapy drugs will improve cure rates for pediatric and adult ALL patients alike. He said, "Going forward with the antibodies we have available to us, the future is bright for ALL patients." ■

FOR MORE INFORMATION

Dr. Elias Jabbour.....713-792-4764

To see the abstracts about these studies presented at the 2014 American Society of Clinical Oncology Annual Meeting, visit http://meetinglibrary.asco.org/abstracts and search for Abstract No. 7019 (inotuzumab) or 7065 (ofatumumab).

To learn more about the ongoing clinical trials of chemotherapy plus monoclonal antibodies for the treatment of ALL, visit www.clinicaltrials.org and select study No. 2010-0991 (inotuzumab) or 2010-0708 (ofatumumab).

Deep Inspiration B Cardiotoxicity in P

By Joe Munch

Patients with left-sided breast cancers have an increased risk of heart damage from adjuvant radiation therapy given after lumpectomy or mastectomy.

To minimize cardiotoxicity from incidental cardiac irradiation in these patients, radiation oncologists at The University of Texas MD Anderson Cancer Center are using a technique called "deep inspiration breath hold" during radiation delivery.

"Radiation to the heart is not a good thing, and any effort to keep the dose to the heart as low as reasonably achievable should be in our patients' best interests," said Benjamin Smith, M.D., an associate professor in the Department of Radiation Oncology. "Deep inspiration breath hold is an elegant innovation to help keep that dose as low as possible."

Radiation risks

The majority of breast cancer patients who undergo lumpectomy for early-stage disease, as well as many breast cancer patients who undergo mastectomy for more extensive disease, receive adjuvant radiation therapy. In patients with left-sided breast cancers, radiation delivered to the target volumes—the tumor bed and/or regional lymph nodes—can also intersect the heart. The potential complications arising from this incidental cardiac irradiation depend on which part of the heart is irradiated. Possible complications include ischemic heart disease, heart failure, valvular disease, or even death from heart disease.

In patients with left-sided breast cancers who receive adjuvant radiation

Breath Hold Protects Against Radiation-Induced Patients With Left-Sided Breast Cancers

therapy, the heart usually receives a glancing blow of radiation, with the superficial portions of the heart—the pericardium and the coronary arteries—receiving the highest radiation dose. The pericardium is generally fairly tolerant of radiation, and radiation-induced pericarditis is uncommon among patients with left-sided breast cancers. Much more susceptible to the adverse effects of radiation are the coronary arteries.

"Radiation to the arteries increases the risk of atherosclerotic disease, and this can be a very late effect of radiation," Dr. Smith said. "It's been reasonably well established that there's a radiation dose–response relationship; the higher the dose to those blood vessels, the more likely the patient will have a late effect. So trying to minimize the dose to those blood vessels is very meaningful for minimizing a patient's long-term risk of heart damage."

To illustrate this point, Dr. Smith described a breast cancer patient who in 1980 was one of the first treated with lumpectomy and radiation; 34 years later, she had a heart attack that was at least partially attributable to her radiation therapy. "So radiation causes this injury that can be silent for decades, but after some time, the patient reaches a critical tipping point and begins having clinical manifestations of the injury," Dr. Smith said.

Patients with preexisting cardiac risk factors or coronary heart disease may be more likely to develop radiation-related heart problems later in life. In addition, many systemic agents used to treat breast cancer are potentially cardiotoxic—including traditional chemotherapy drugs such as doxorubicin, targeted agents such as trastuzumab, and hormonal therapies such as tamoxifen—and they may act in synergy with radiation to damage heart tissue.

Minimizing the radiation dose

Several techniques can be used to minimize the radiation dose to the heart. One strategy is to use a cardiac block—essentially placing a slab of lead in front of the heart to shield it from radiation. Now achieved with a multileaf collimator integrated with the radiation delivery system, a cardiac block can be used effectively in most patients with upper-quadrant breast tumors but may compromise the dose to the target volume in patients with lower-quadrant breast tumors.

Another common approach is to use intensity-modulated radiation therapy to shape the radiation beam to the target volume while avoiding the heart; however, such treatment may also result in a higher radiation dose to other organs at risk in the thorax.

A third option is to use respiratory gating—synchronizing the delivery of radiation with the patient's breathing to limit the amount of tissue beyond the target volume that receives radiation. One type of respiratory gating is deep inspiration breath hold, in which the patient takes a deep breath to inflate the lingula of the left lung. The inflated lingula temporarily displaces the heart inferiorly and posteriorly, thereby increasing the distance between the heart and the chest wall and moving the organ out of the radiation beam's path. Dr. Smith says he employs the technique in almost all of his patients with left-sided breast cancers.

"With other techniques, you sometimes have to decide whether to protect the heart or adequately treat the tumor bed to minimize the risk of recurrence," Dr. Smith said. "But with deep inspiration, you can usually have the best of both worlds. It allows us not only to lower the dose of radiation to the heart—and the dose can be lowered pretty dramatically—but also to deliver enough radiation to treat the tumor bed effectively."

Example of radiation treatment plans for whole-breast irradiation in a woman with ductal carcinoma in situ using the standard free breathing (left) or deep inspiration breath hold (right) technique. The mean radiation doses to the heart are 1.8 Gy with free breathing and 0.8 Gy with deep inspiration breath hold. Colored lines depict the minimum radiation dose: red, 50 Gy; purple; 45 Gy; green, 25 Gy; orange, 5 Gy; yellow, 2 Gy; aquamarine, 1 Gy. Reprinted from Smith 2014, with permission from The ASCO Post.

Planning and delivering radiation

When the deep inspiration breath hold technique is used, radiation treatment is planned meticulously to ensure a minimal radiation dose to the heart while allowing a sufficient dose to the target volume. During treatment simulation, the patient lies on her back, and a reflector box is taped to her abdomen. An infrared camera mounted at the foot of the treatment couch tracks the up-down movement of the box as the patient breathes. The patient wears video goggles showing a yellow bar moving up (representing her inhalation) and down (exhalation) below a blue "target" rectangle. When the patient inhales deeply, the yellow bar rises into the blue rectangle and turns green. The patient then holds her breath for about 15 seconds while computed tomography images are taken to map the patient's anatomy for treatment planning.

Deep Inspiration Breath Hold

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During the actual radiation treatment, the patient is again outfitted with the reflector box and goggles and asked to inhale until the yellow bar rises into the blue target rectangle and turns green, at which point the radiation beam is activated. For the beam to be activated, the yellow bar must be in the blue rectangle. Because radiation is given only when the patient has inhaled sufficiently, the patient effectively controls the delivery of the radiation, and movements due to coughing or sneezing do not interfere with therapy delivery.

"For the vast majority of patients, we can get good radiation plans," Dr. Smith said. "And the data we have indicate that these patients' risk of long-term cardiac side effects from radiation should be very low."

Benefit in specific scenarios

Deep inspiration breath hold is particularly beneficial in a number of clinical scenarios.

"There is significant variation in patients' anatomy," Dr. Smith said. "Some patients have a heart that's right up against the rib cage, so without deep inspiration breath hold it can be extremely difficult to avoid the heart and still cover the tumor area that needs to be treated."

Other patients likely to benefit greatly from the breath hold technique are those with tumors in the lower half of the breast. Without this technique, such tumors are difficult to treat effectively while still avoiding irradiation of the heart. Although patients with these tumors may be treated in the prone position, with the affected breast falling down and away from the body, it can still be difficult in some patients to miss the heart.

"When the patient is prone, both the breast and the heart fall forward, and so the heart may be even closer to the tumor bed," Dr. Smith said. "The prone plan has certain advantages, but in some patients, you can't reliably deliver a good dose to the tumor bed and be confident that you would also miss the heart at each treatment session."

Patients who need treatment to the internal mammary nodes, which are close to the heart, also benefit from the breath hold approach.

"For patients who underwent lumpectomy for breast tumors close to the heart, we can routinely get mean heart doses that are less than 1 Gy. And for patients who require treatment of the internal mammary lymph nodes after mastectomy, we can get mean heart doses between 2 Gy and 4 Gy," Dr. Smith said. "Without breath hold, those mean heart doses are a lot higher."

There are few contraindications to using deep inspiration breath hold to move the heart out of harm's way, Dr. Smith said.

"A few patients can't hold their breath because they have lung issues or they're anxious, but most patients seem to be able to do it well and reproducibly," Dr. Smith said. "People who are 80 years old have undergone this procedure, so age doesn't seem to be a contraindication."

Deep inspiration breath hold often is not necessary for patients who also have chronic obstructive pulmonary disease. One of the hallmarks of chronic obstructive pulmonary disease is hyperinflation of the lingula, which often displaces the heart just as deep inspiration breath hold would do.

Although deep inspiration breath hold is used primarily in patients with left-sided breast cancers, it can also be used in select patients with tumors in the right breast to help minimize the radiation dose to the lung.

Drawbacks

Deep inspiration breath hold is not without its drawbacks. Treatment simulation with deep inspiration breath hold takes about 15 minutes longer than simulation for treatment without the technique, and treatment itself can take 5–10 minutes longer depending on the complexity of the treatment plan. The extra time needed for deep inspiration breath hold could be burdensome for a radiation oncology clinic already operating at full capacity.

"Deep inspiration breath hold also introduces another layer of uncertainty in the setup of patients," Dr. Smith said. "Particularly with complicated plans with a lot of different fields, there's some theoretical concern that you might not deliver the radiation to the same place each day."

Overcoming barriers

Dr. Smith estimates that at MD Anderson, deep inspiration breath hold is used to reduce cardiac irradiation in 300–400 patients with left-sided breast cancers each year. However, widespread adoption of the technique outside major cancer centers has been hindered by the additional time and equipment (and thus cost) it requires.

"There's also a learning curve to figuring out the process of setting up patients on a daily basis and making sure the setup is accurate," Dr. Smith said. "At MD Anderson, we have really great therapists and physicists who work through a systematic process to do that, but it takes time to build up that kind of expertise."

Another potential barrier to widespread use of the technology is that, until recently, deep inspiration breath hold lacked a Current Procedural Terminology code that would enable physicians to be reimbursed for performing the procedure. However, such a code has been introduced, and this should allow radiation oncologists to recoup some of the additional costs associated with the procedure and thus make the procedure more widely available.

Ultimately, Dr. Smith said, it is important to provide patients with the best treatment options available. This may mean referring some patients to institutions that can provide radiation therapy with deep inspiration breath hold.

"If I had a family member with left-sided breast cancer, I would definitely want her to have access to this technology," Dr. Smith said. ■

Dr. Benjamin Smith contributed to this article.

FOR MORE INFORMATION

Dr. Benjamin Smith 713-563-8495

FURTHER READING

Smith BD. Reducing incidental cardiac irradiation during breast radiotherapy. *The ASCO Post.* May 15, 2013.

Books Can Help Patients Deal With Cancer

Fiction and nonfiction can provide encouragement and education

Books about cancer, whether novels or more practical books about how to cope with treatments or side effects, can be beneficial for both patients and caregivers. In fact, bibliotherapy—treatment in the form of self-help books, novels, or poetry—has been prescribed for other disorders such as anxiety and depression.

Self-help books

Several practical books can help cancer patients cope with the side effects of cancer or its treatment. Many of these books focus on nutrition.

The Cancer-Fighting Kitchen: Nourishing, Big-Flavor Recipes for Cancer Treatment and Recovery (Ten Speed Press, 2009), by Rebecca Katz with Mat Edelson, is not merely a cookbook. Ms. Katz points out in the introduction that as many as 80% of cancer patients are malnourished, and she cites the growing body of scientific evidence that supports nutrition as a key aspect of cancer treatment and prevention. Each recipe describes the nutritional value of its ingredients, and the book includes a "Culinary Pharmacy" table that provides information about the anticancer properties of commonly used ingredients in the recipes.

Louise Villejo, the executive director of the Patient Education Office at The University of Texas MD Anderson Cancer Center, said that one of the most highly requested books in the Learning Center at MD Anderson is *Anticancer: A New Way of Life* (Penguin, 2009) by David Servan-Schreiber, M.D., Ph.D. *Anticancer* discusses nutritional changes that can help in cancer recovery and also recommends other lifestyle changes, such as stress reduction, that can help fortify the body's defenses against cancer. Dr. Servan-Schreiber, who had brain cancer, describes the book as "the story of how I used my skills as a physician and scientist to find out everything in the medical literature that would help me change the odds."

Memoirs

Reading memoirs written by cancer survivors can help inspire and encourage patients currently struggling with the disease. These books can also help patients and their loved ones articulate their feelings or discuss difficult topics. *The Cancer Survivors Club* (CKG Publishing, 2012), edited by Chris Geiger, is a collection of essays written by survivors of common and rare cancers.

Lance Armstrong's memoir written with Sally Jenkins, *It's Not About the Bike: My Journey Back to Life* (Penguin Putnam, 2001), describes in detail the cyclist's struggle with testicular cancer, treatments, and survivorship. He writes, "I've read that I flew up the hills and mountains of France. But you don't fly up a hill. You struggle slowly and painfully up a hill, and maybe, if you work very hard, you get to the top ahead of everybody else. Cancer is like that, too."

Fiction

Novels, like memoirs, can help patients and their loved ones process emotions and can provide a scaffold for discussing difficult issues. John Green's *The Fault in Our Stars* (Penguin, 2012) has become a *New York Times* bestseller and a film. The story is narrated by Hazel, a 16-year-old girl with thyroid cancer that has metastasized to her lungs. Suffering from depression, she goes to a cancer support group meeting, where she meets Augustus, a boy who has lost a leg to osteosarcoma. This novel is a young adult love story, but it also explores fundamental philosophical questions.

My Sister's Keeper (Washington Square Press, 2004), a novel by Jodi Picoult that has been turned into a film, raises difficult questions about what it means for a family to live with cancer. In the story, Anna was genetically engineered to be a perfect bone marrow match for her older sister Kate, who has leukemia. Throughout Anna's life, she has provided Kate with blood transfusions, bone marrow, and stem cells; but when Kate needs a kidney transplant, Anna decides to sue her parents for the right to choose what happens to her body.

Historical books

Understanding the history of cancer can help demystify the disease, and learning about advances in cancer treatment can give hope to patients. Siddhartha Mukherjee, M.D., an oncologist, won a Pulitzer Prize for his book *The Emperor of All Maladies: A Biography of Cancer* (Scribner, 2010). This book chronicles the advances in research from Herodotus's 440 BC account of Atossa, a Persian queen who had a slave cut a tumor from her breast, to the nineteenth-century surgeons who performed radical and disfiguring mastectomies, to the age of systemic chemotherapy beginning in the 1960s, to the current era of molecularly targeted therapies.

Helping patients cope

Although none of these books would be considered typical light summer reading, they may help patients cope with cancer by providing practical advice and encouragement. ■

– J. Delsigne

FOR MORE INFORMATION

- *Call MD Anderson's Learning Center at 713-745-8063*
- *Visit the Learning Center at www.mdanderson.org/patient-and-cancer-information/guide-to-md-anderson/places-to-visit/the-learning-center.html*

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IN BRIEF

Large-Scale Molecular Data Analysis Yields Multiple Benefits

Diverse molecular data from a large group of patients with multiple types of tumors can be combined with clinical variables to help predict patients' overall survival durations, a recent study found. The study also showed that a large-scale analysis of multiple tumor types can detect important genetic alterations that would likely be missed in an analysis of a single tumor type.

In the multi-institutional study, researchers analyzed several types of molecular data (somatic copy-number alteration; DNA methylation; and mRNA, microRNA, and protein expression) from 953 samples of four cancer types (clear cell renal cell carcinoma, glioblastoma multiforme, ovarian serous adenocarcinoma, and squamous cell carcinoma of the lung). Also studied were clinical variables such as patient age and tumor stage from the same set of patients. The molecular and clinical data came from The Cancer Genome Atlas.

Statistical models developed by Han Liang, Ph.D., an assistant professor in the Department of Bioinformatics and Computational Biology at The University of Texas MD Anderson Cancer Center, and his colleagues showed that the combination of molecular data and clinical factors predicted overall survival more accurately than did clinical factors alone in three of the four cancer types studied (renal, ovarian, and lung cancer).

"In contrast to previous studies driven by a single cancer or data type, we could evaluate patient survival prediction from different molecular data and describe the potential prognostic and/or therapeutic relevance across multiple cancers," Dr. Liang said.

An additional analysis of 12 cancer types identified 10,281 somatic alterations in clinically relevant genes. Dr. Liang said that in an analysis of a single tumor type, many of these alterations would not have been revealed at a frequency that would justify further investigation.

"By analyzing data from multiple cancer types, we were able to systematically evaluate prognostic models and more thoroughly identify gene alterations that led to tumor formation," Dr. Liang said. "This would have not been obtained by looking at tumor data from just one cancer type."

Dr. Liang added that future studies of independent patient cohorts will be needed to determine how large-scale molecular profiling data might be used with clinical variables to stratify cancer patients into various risk groups to help guide surveillance and treatment strategies.

The study's report was published in June in the online version of *Nature Biotechnology*. ■

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