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REPORT TO PHYSICIANS

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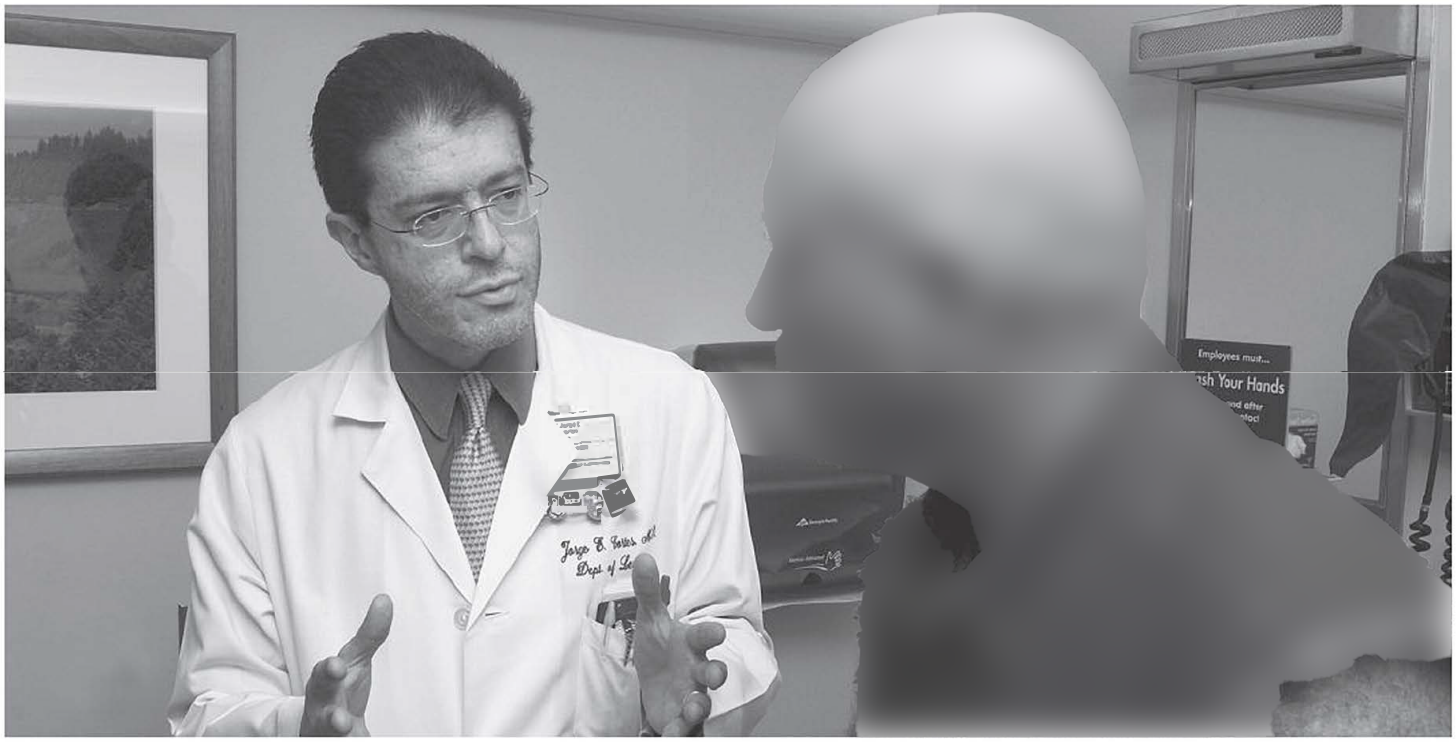
Chronic Myelogenous Leukemia: Refining Approaches to Treatment



Dr. Jorge E. Cortes, *conferring with patient* [redacted], *says results from recent trials of dasatinib and nilotinib suggest these agents may become the new standards of care for chronic myelogenous leukemia.*

By John LeBas

Just a decade ago, fewer than half of chronic myelogenous leukemia (CML) patients remained alive 7 years after their diagnosis. Then came the first-generation tyrosine kinase inhibitor imatinib (Gleevec), which reduced leukemia cells in most CML patients to almost undetectable levels. The drug's effects have proven remarkably durable, boosting the 7-year overall survival rate in CML to nearly 90%.

(Continued on page 2)

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"We've clearly changed the natural history of this disease with imatinib, but it doesn't work for everybody," said Jorge E. Cortes, M.D., a professor in the Department of Leukemia at The University of Texas M. D. Anderson Cancer Center. "We still need to improve therapy, in both newly diagnosed and resistant disease."

So today, clinicians are focused on refining the treatment of CML, which is diagnosed in about 4,500 Americans each year. Effective treatment approaches have been found to help many of the patients for whom imatinib does not work, thanks to a better understanding of treatment resistance. As happened with imatinib a decade ago, some of the more recent efforts are meeting with remarkable success, according to Dr. Cortes and other specialists at M. D. Anderson.

"The development of second- and third-generation drugs has been based, in part, on our understanding of CML's genetic variability and mechanisms of resistance."

– Dr. Hagop Kantarjian

Mechanisms of success

The success of imatinib lies in a common molecular aberration in CML. About 95% of CML patients have the Philadelphia chromosome, an abnormality characterized by a translocation between chromosomes 9 and 22. The resulting *Bcr-Abl* gene encodes a tyrosine kinase that promotes leukemia growth. Imatinib, approved by the U.S. Food and Drug Administration in 2001, acts by inhibiting the activity of this tyrosine kinase, halting the cancer's proliferation.

Generally, imatinib is easy to administer (it is given as a pill) and is well tolerated. Its more common side effects include myelosuppression (characterized by anemia, thrombocytopenia, and neutropenia), fluid retention, muscle cramps, and diarrhea. Rarely, congestive heart failure has been identified in patients receiving imatinib. Initial myelosuppression usually goes away and does not recur following a temporary cessation of imatinib, but recurrent myelosuppression can occur in some patients and may be treatable with hematopoietic growth factors without further cessation of tyrosine kinase inhibitor therapy. Cardiac effects usually can be managed with dose alteration.

However, some patients cannot tolerate the side effects of imatinib despite optimal management of the side effects. Additionally, 20%–25% of CML patients do not respond well to the drug or relapse after experiencing an initial response, even if the imatinib dose is increased. It is these patients who are perhaps the most in need of new treatment options, for they do not benefit from an otherwise highly effective therapy.

Fortunately, two agents have been found particularly effective as second-line therapies: dasatinib (Sprycel) and nilotinib (Tasigna). In fact, two recent studies showed that dasatinib and nilotinib, which are currently approved in the United States for treatment of CML after imatinib, elicited even better responses than imatinib in previously untreated patients. Also, toxicity so far has been low. "We think such findings may lead to these drugs becoming the standard of care in the near future," Dr. Cortes said.

Dasatinib and nilotinib, both second-generation tyrosine kinase inhibitors, are similar to imatinib in that they inhibit the activity of the cancer-promoting Bcr-Abl protein. Nilotinib is considered to be 50 times more powerful than imatinib in its inhibition of Bcr-Abl. And dasatinib is some 300 times stronger against Bcr-Abl, plus it inhibits other tyrosine kinases as well. Investigators believe the effectiveness of dasatinib and nilotinib against imatinib-resistant CML is due to their ability to inhibit Bcr-Abl protein variants that may occur when imatinib stops working. Dasatinib also works against Src family kinases, which may have a role in CML.

A third investigational tyrosine kinase inhibitor, bosutinib, also appears to be active against CML. Early data from an ongoing international phase II trial also suggest that bosutinib has safety and side effect profiles comparable to those of dasatinib and nilotinib, Dr. Cortes said. "Bosutinib could give us yet another option to treat patients for whom existing front-line therapy is not ideal," he added.

Applying past experience

Another treatment quandary is represented by the very small percentage of patients whose CML does not respond or becomes refractory to two or more of the kinase-inhibiting agents. Such patients may be eligible for early-phase testing of drugs that target more specific pathways of CML progression.

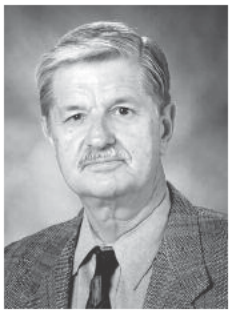
One of those agents, AP24534, inhibits CML-promoting proteins encoded in patients with the T315I genetic mutation—an anomaly associated with resistance to imatinib, dasatinib, nilotinib, and bosutinib. A second agent, homoharringtonine, so far appears to reduce CML levels in patients who have the T315I mutation or have failed kinase-inhibitor therapy. Other agents, including DCC-2036, PHA-739358, and XL-228, may have similar effects and are also being investigated in the clinic.

The investigation of tyrosine kinase inhibitors in this disease has resulted in the understanding that multiple previously unknown genetic mutations are at work in CML. "This is one disease in which we know virtually all patients share one molecular abnormality, the Philadelphia chromosome," Dr. Cortes said. "But since the introduction of ima-

tinib, the varied responses to therapies targeting the Philadelphia chromosome have allowed us to realize how heterogeneous CML actually is. We are learning that the expression of certain genes is very different in different patients."

The interplay of this varied gene expression with the main chromosomal defect appears to create difficult-to-decipher effects on response—and resistance—to therapy. For example, genetic variations between seemingly similar CML patients might cause them to metabolize a drug very differently. Or, some patients might have a form of CML with greater genetic instability, making it more likely to become therapy-resistant or increasing the chance of a blast crisis.

"Research in this area is very active," said Hagop Kantarjian, M.D., professor and chair of the Department of Leukemia. "The development of second- and third-generation drugs has been based, in part, on our understanding of CML's genetic variability and mechanisms of resistance." In one example, dasatinib, which was shown in preclinical studies to inhibit Src, was tested against CML after some patients who relapsed while receiving imatinib were found to have high levels of Src proteins. In another example, Dr. Kantarjian designed the clinical trials that led to the approval of nilotinib as a second-line CML therapy based on the known action of tyrosine kinase inhibition against mutant kinase expression in CML.



Dr. Ralph Arlinghaus

Ralph Arlinghaus, Ph.D., chair of the Department of Molecular Pathology, said mutations of the *Bcr-Abl* gene—and mutations of other genes in CML patients who undergo disease progression—likely hold the key to future therapeutic ap-

(Continued on page 8*)*

Clinical Trials in Chronic Myelogenous Leukemia (CML)

Therapy of Early Chronic Phase CML with Dasatinib (BMS-354825) (2005-0422). Principal investigator (PI): Jorge E. Cortes, M.D. The goal of this phase II clinical research study is to learn whether dasatinib can help control previously untreated CML in the chronic phase.

Therapy of Early Chronic Phase CML with Oral Nilotinib (2005-0048). PI: Hagop Kantarjian, M.D. This phase II clinical trial aims to determine the percentage of CML patients who achieve a molecular complete response after 12 months of therapy with nilotinib.

A Phase II Open-Label Study of the Subcutaneous Administration of Homoharringtonine (Omacetaxine Mepesuccinate; OMA) in the Treatment of Patients with CML Who Have Failed or Are Intolerant to Tyrosine Kinase Inhibitor Therapy (2006-0926). PI: Dr. Cortes. The goal of this clinical research study is to find out whether homoharringtonine can help control CML in patients who relapsed on or could not tolerate treatment with imatinib and dasatinib.

A Phase I, Open-Label, Dose Escalation Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of INNO-406 in Adult Patients with Imatinib-Resistant or Intolerant Philadelphia Chromosome-Positive (Ph+) Leukemias (2006-0278). PI: Dr. Kantarjian. INNO-406 is a multikinase inhibitor whose safety and efficacy in various cancers are being studied.

A Phase Ib Study Evaluating the Safety and Exploring the Molecular and Cytogenetic Response of Combination Therapy with Dasatinib and Ipilimumab in Patients with Chronic or Accelerated Phase Myeloid Leukemia (2008-0157). PI: Dr. Cortes. The goal of this clinical research is to learn the safety of ipilimumab, a monoclonal antibody designed to stimulate the immune system, in combination with dasatinib in CML patients who lost a previously achieved major molecular response or a complete cytogenetic response while on dasatinib.

A Phase II Study of INCB018424 in Patients with Advanced Hematologic Malignancies (2007-0925). PI: Farhad Ravandi-Kashani, M.D. The purpose of this study is to observe the antitumor effects of INCB018424, a Jak kinase inhibitor, in patients with relapsed/refractory acute non-lymphocytic leukemia, acute lymphocytic leukemia, myelodysplasia, and blast phase or tyrosine kinase–refractory CML.

A Multicenter Phase I Clinical and Pharmacokinetic Study of DCC-2036 in Subjects with Philadelphia Chromosome-Positive Leukemias (2008-0732). PI: Dr. Cortes. This study aims to determine the safety of DCC-2036, an experimental kinase inhibitor, and also to determine the agent's effect against Bcr-Abl kinase, which is known to be active in CML.

A Phase I Study of PHA-739358 in Adult Patients with CML and Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia Resistant or Intolerant to Imatinib and/or Other 2nd Generation c-ABL Therapy (2007-0939). PI: Dr. Cortes. PHA-739358, an inhibitor of multiple kinases, is undergoing early testing in various blood cancers.

A Phase I Dose-Escalation Study of the Safety, Pharmacokinetics, and Pharmacodynamics of XL228 Administered Intravenously to Subjects with CML or Philadelphia Chromosome-Positive Acute Lymphocytic Leukemia (Ph+ ALL) (XL228-001) (2007-0502). PI: Dr. Cortes. This clinical study aims to determine dosing for XL228, an inhibitor of multiple kinases known to be active in CML. ●

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

Advancing the Treatment of Lymphedema

A new surgical procedure provides treatment for painful lymph build-up, while new imaging techniques aim to shed light on its causes.

By Maude Veech

Not many areas of medicine still draw heavily from 19th century knowledge, but the understanding of the lymphatic system has been hampered in just such a way. Thus, it has been impossible to prevent or cure lymphedema, a painful dysfunction of the lymphatic system that can result from cancer treatments.

Today, M. D. Anderson researchers are breaking barriers in lymphatic medicine. Not only is the institution developing new ways to image the almost invisible lymphatic system, it is also among the first to offer surgery to treat lymphedema. With further research, specialists hope to better understand metastasis via the lymphatic system and to prevent lymphedema altogether.

"You'd think that in 2009 we'd have a good understanding of the lymphatic system, but we don't," said David W. Chang, M.D., a professor in the Department of Plastic Surgery and clinical medical director of the Plastic Surgery Center. "Not fully understanding the lymphatic system and its anatomy—as we do with the vascular system, for instance—is one reason it is so hard to prevent and treat lymphedema. It also prevents us from explaining why some patients develop lymphedema and others do not."

Lymphedema basics

Lymphedema, characterized first by swelling and later by inflammatory fibrosis in tissues near damaged or missing lymph nodes, is caused by a failure of the lymphatic system to drain properly. Primary lymphedema develops spontaneously, while secondary lymphedema is caused by treatment, injury, or infection. About 200 million people worldwide suffer from secondary lymphedema caused by parasites, mostly in underdeveloped regions.

In developed nations, lymphedema is usually a byproduct of cancer treatment—in fact, it is one of the worst side effects of removing one or more lymph nodes, which is often done to determine how far a cancer has spread. Radiation treatment to cancerous lymph nodes can also cause lymphedema. Breast cancer patients are among those most likely to develop lymphedema, with about 20%–30% experiencing it to some extent, usually in the upper arms. However, lymphatic system problems can also develop in the legs or elsewhere following treatment for cancers in the pelvis or other locations.

Historically, the only treatments readily available for lymphedema were compression, massage, and other palliative measures. "Some physicians have tried using liposuction or taking the radical approach of removing skin and muscle to offer relief to patients," Dr. Chang added. However, the effectiveness of such approaches remains controversial.

New treatment option

M. D. Anderson is one of the first centers to offer a new procedure known as lymphaticovenular bypass to reroute the fluid that has built up. The procedure is performed using general anesthesia and is minimally invasive, requiring two to five small incisions. Using microsurgical tools, the surgeon redirects lymphatic fluid into tiny veins, allowing it to drain out of the affected area. Patients generally can return home within 24 hours.

In a recently reported prospective analysis, Dr. Chang found that 19 of 20 breast cancer patients with lymphedema who underwent lymphaticovenular bypass had significant improvements in their symptoms. Researchers compared measurements of patients' affected arms and healthy arms to quantify the benefits of the surgery. After bypass, there was a mean reduction in the volume difference between the healthy and affected arms of 29% at 1 month, 33% at 3 months, 39% at 6 months, and 25% at 1 year.

Dr. Chang has performed more than 30 such surgeries, and his group now has data documenting sustained symptom alleviation over 3 years. Though the surgery appears to be most effective before fibrosis develops, almost any breast cancer patient with stage I, II, or III

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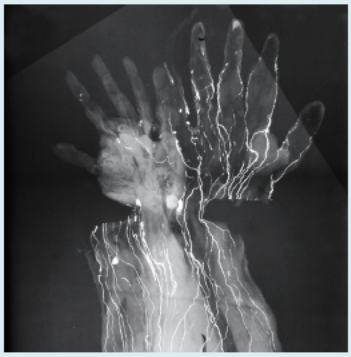

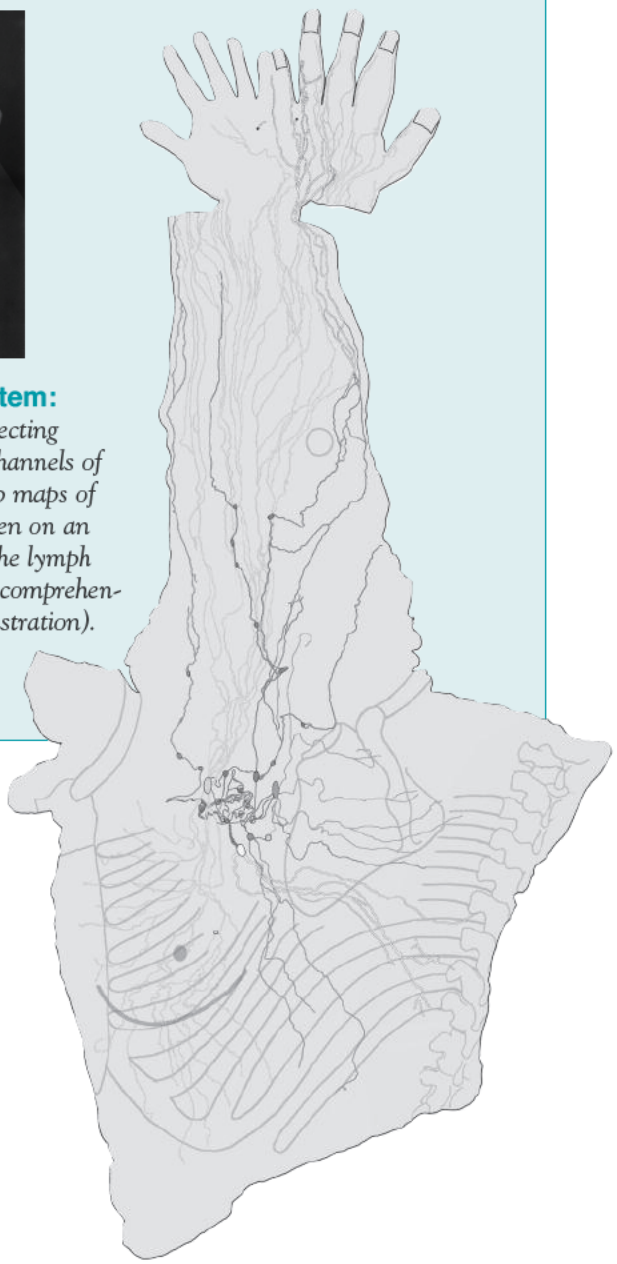

Mapping the lymphatic system:
Dr. Hiroo Suami's *method of injecting radiocontrast dye into the lymph channels of cadavers is enabling him to develop maps of the lymphatic system. The dye (seen on an x-ray image above) travels along the lymph channels, allowing the paths to be comprehensively charted (as shown in the illustration).*

lymphedema of the upper extremities is a candidate, and the procedure can also be performed for lymphedema in the legs. Dr. Chang is now planning a larger prospective trial of lymphaticovenular bypass for upper and lower extremity lymphedema in conjunction with collaborators from the Department of Surgical Oncology.

Visualizing the lymphatic system

Dr. Chang has also worked closely with Hiroo Suami, Ph.D., clinical research program coordinator in the Department of Plastic Surgery, who has been studying the anatomy of the lymphatic system since 2001. A specialist in gross anatomy, Dr. Suami is employing a novel method for imaging the lymphatic system and aims to develop a modern map of the system.

The maps of the lymphatic system currently taught in medical schools originated in France over 100 years ago. "They made a diagram—not photos, but a diagram. We don't know how accurate that is," Dr. Suami said. Modern imaging can help create a better anatomical model and illustrate how lymphedema occurs, he added.

But Dr. Suami's research goes beyond exploring the mechanisms of lymphedema. "We want to understand how the lymphatic system works so we can understand its role in spreading cancer," he said, noting that the lymph nodes are among the most common sites of early cancer metastasis. To do this, Dr. Suami has developed animal models that allow him to inject orange lead oxide directly into the lymphatic vessels of living rats and mice. He has also had a great deal of success with human cadavers, using a microscope to guide the injection and then studying differences between cadavers with and without lymphedema.

To visualize the lymphatic system, Dr. Suami injects the orange lead oxide directly into the lymphatic vessels. A contrast medium, lead oxide can be recorded by radiography, computed tomography, or three-dimensional computed tomography. "We also plan to use an infrared camera system in the near future to study the lymphatic vessels in living animals," Dr. Suami said.

Currently, only limited visualization of the lymphatics can be obtained in clinical practice. For example, during sentinel lymph node biopsy, physicians inject dye and radioactive tracers to identify the lymph nodes closest to a tumor, those that are most likely to contain metastasis. "However, the sentinel lymph node biopsy technique can only identify the nodes and surrounding vessels near the injection area," Dr. Suami said. "By injecting lead oxide into the lymphatic vessels, I can delineate comprehensive pathways."

Another difference is that sentinel node biopsy is only used in primary operative cases because previous operations disturb lymph flow, Dr. Suami said. "But my technique can be applied in postoperative cases to see changes in the lymphatics," he explained.

Future implications

If reliable methods of mapping the lymphatic system can be developed, cancer surgeons could spare more of the healthy lymphatic system during lymph node removal. "Perhaps we can keep the lymphatic vessels visible using colored dye during operations for cancer," Dr. Chang said. "That would help us preserve the essential lymphatics and remove cancerous lymph nodes without damaging others."

And while lymphaticovenular bypass surgery can potentially relieve the misery of lymphedema, Drs. Chang and Suami hope that someday their research will make the surgery obsolete.

"Right now, we can help reduce lymphedema, but there is no cure. Once we learn why lymphedema develops in some cases and not others, we may be able to prevent it," Dr. Chang said. ●

For more information, call Dr. Chang or Dr. Suami at 713-794-1247.

Dramatic Increases in Metastatic Colorectal Cancer Survival Documented

Patients with metastatic colorectal cancer are surviving much longer than they did two decades ago, thanks to novel chemotherapy and biological agents and surgical advances in liver resection, an M. D. Anderson study has found.

The median overall survival duration for patients diagnosed with advanced colorectal cancer is now nearly 30 months, compared with 8 months for patients diagnosed before 1990. Also, the 5-year overall survival rate of patients diagnosed after 2004 is projected to be more than 30%, according to the study, which was published in the *Journal of Clinical Oncology*.

> "As chemotherapy improves, we can remove more tumors, and as surgery for metastatic disease is more commonly performed, then patients can receive more chemotherapy."
>
> **– Dr. Scott Kopetz**

Recently, the U.S. Food and Drug Administration approved numerous chemotherapeutic agents that are effective against metastatic colorectal carcinoma, said Scott Kopetz, M.D., corresponding author on the study and an assistant professor in the Department of Gastrointestinal Medical Oncology. Also, over the past decade, the concept that specific metastatic liver lesions can be surgically removed has become more widely accepted as practice. Thus, more emphasis is now placed on identifying candidates for resection of liver metastasis.

The researchers wanted to determine whether those changes in therapy resulted in longer survival in a large group of patients. The retrospective study included 2,470 patients with newly diagnosed metastatic colorectal cancer who were treated at M. D. Anderson or Mayo Clinic between 1990 and 2006.

No significant change in overall survival was found in patients diagnosed between 1990 and 1997. But by 2006, the median overall survival duration had increased to 29.2 months. Five-year overall survival also increased over time: from 9.1% (diagnosed 1990–1997), to 13% (diagnosed 1998–2000), to 19.2% (diagnosed 2001–2003). Five-year survival for patients diagnosed in 2004–2006 has not yet been determined but is projected to be more than 30%. The findings were confirmed through analysis of survival data in the U.S. National Cancer Institute's Surveillance, Epidemiology and End Results cancer registry.

"We found not only a significant improvement in the overall survival of metastatic colorectal cancer patients, but we also demonstrated that the degree and rapidity of the improvement are of a magnitude that is rarely seen in metastatic cancers," Dr. Kopetz said.

The researchers noted two periods in which survival increased the most: in the late 1990s, when surgeons started performing higher numbers of hepatic resections, and beginning around 2004, following the approval of the agents cetuximab, bevacizumab, and oxaliplatin.

"However, surgery and chemotherapy are not independent and certainly complement each other," Dr. Kopetz said. "As chemotherapy improves, we can remove more tumors, and as surgery for metastatic disease is more commonly performed, then patients can receive more chemotherapy."

Despite the study's reported gains, metastatic colorectal cancer remains incurable for most patients, and continued research is needed to further extend survival, Dr. Kopetz said.

The study was funded by grants from the National Cancer Institute. ●

Acupuncture Relieves Dry Mouth Following Radiation Therapy, Study Shows

Researchers at M. D. Anderson have found that acupuncture made patients less likely to experience xerostomia—severe dry mouth—following repeated radiation therapy for head and neck cancers.

In the study, 19 patients suffering from xerostomia due to radiation therapy underwent twice-weekly acupuncture sessions for 4 weeks. The patients were then tested for saliva flow and completed questionnaires designed to gauge the effects of the acupuncture sessions on their quality of life. "Patients in the study had improvements in their physical well-being and in subjective symptoms," said Mark S. Chambers, D.M.D., a professor in the Department of Head and Neck Surgery and a study author. "Although the patient population was small, the positive results are encouraging and warrant a larger trial to assess patients over a longer period of time."

In fact, a phase III, placebo-controlled trial is planned and is currently under review, said M. Kay Garcia, Dr.P.H., first author on the pilot study. In other studies, M. D. Anderson researchers are examining whether acupuncture can prevent—not just treat—xerostomia in head and neck cancer patients who receive radiation.

People who have cancers of the head and neck typically receive large cumulative radiation doses, which can leave the salivary glands incapable of producing adequate saliva. Saliva substitutes, lozenges, and chewing gum bring only temporary relief, and a commonly prescribed medication (pilocarpine) may have short-lived benefits and bothersome side effects. Acupuncture may bring relief by increasing blood flow to the affected area through the stimulation of precise points, though further study is needed.

Results of the M. D. Anderson study were reported online in the journal *Head & Neck*. ●

HOUSE•CALL

Hospice: Comforting Care When the End Is Near

When seriously ill patients run out of treatment options, many choose to enter a final phase of care designed to make them as comfortable as possible—hospice care.

In hospice care, treatments aimed at fighting the disease are stopped. Instead, hospice patients receive palliative treatments—those aimed at relieving symptoms— along with social, emotional, and spiritual support.

Depending on the program and the patient's needs, hospice services can include 24-hour nursing care, supplies and medications, help with daily tasks, and counseling.

The basics

Most hospice programs provide care in the patient's home, but hospice care is also available in some facilities, such as assisted-living residences, nursing homes, hospitals, and private hospices. When hospice care is given at home, family members usually serve as the main caregivers, with support from doctors, nurses, home health aides, social workers, therapists, and trained volunteers. At-home hospice patients still may be admitted for short in-patient hospital stays so that troublesome symptoms can be managed. In facility-based hospice programs, health professionals provide the care, but family members can usually be by the patient's side all the time.

A variety of hospice services are available, depending on the program and the patient's needs. Services may include:

- Care provided by a hospice doctor or the patient's primary care physician
- For at-home hospice patients, regular home visits by hospice nurses and 24-hour on-call nursing support
- Help with bathing, cooking, cleaning, or other daily needs
- Counseling for the patient and family members
- Social services
- Respite care (provided for at-home hospice patients so that their caregivers can get a break)
- Medications and medical equipment, such as a hospital bed, oxygen, and a wheelchair
- Bereavement support for the family following the death
- Visits from a chaplain or other spiritual counselors, if requested
- Arrangements for specialized services such as physical, occupational, and speech therapy and nutritional counseling

Many people receiving hospice care have cancer, but others have heart disease, dementia, obstructive pulmonary disease, or any number of life-ending conditions.

For hospice care to be covered by insurance, a doctor usually must certify that the patient is expected to live no more than 6 months. That is the guideline used by Medicare, which pays for most hospice care costs. Many private insurers have adopted the same policy.

Choosing a program

How do you decide which hospice program is the best choice? To start, find out whether the program is accredited by a nationally recognized group, such as the Joint Commission, and if it is certified by Medicare. Ask the agency that provides the program for a brochure or other written information about available services, eligibility rules, costs, and payment procedures.

Doctors, nurses, and social workers are also good sources of information about specific programs, as are area agencies on aging and elderly services organizations. The Eldercare Locator (1-800-667-1116 or www.eldercare.gov) can connect you with the right agency. Other helpful resources are the National Hospice Foundation (www.hospiceinfo.org); the Hospice Foundation of America (www.hospicefoundation.org); and Hospice Net (www.hospicenet.org).

Often, hospice care is not started until the patient is very near death, but entering a program earlier might be beneficial, according to hospice experts. The longer a patient receives hospice care, the better the chances are that the patient will have a peaceful and high-quality experience. For that reason, it's important to explore options for end-of-life care sooner rather than later. ●

For more information, talk to your physician, or:

- *visit www.mdanderson.org*
- *call* askMDAnderson *at 1-877-632-6789*

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Chronic Myelogenous Leukemia

(Continued from page 3*)*

proaches against advanced stages of CML. "Numerous compounds under investigation have been shown to kill imatinib-resistant cells, except in patients with one prevalent type of mutation (T315I). At least in cell culture, drugs that inhibit the Jak2 tyrosine kinase can overcome all forms of imatinib resistance—including those resulting from the T315I mutation—by interrupting the *Bcr-Abl/Jak2* pathway," said Dr. Arlinghaus, among the first to describe this pathway in CML. "Further investigation might enable the development of these compounds as clinically useful agents."

"The varied responses to therapies targeting the Philadelphia chromosome have allowed us to realize how heterogeneous CML actually is."

– Dr. Jorge E. Cortes

Downsides of long-term therapy

Although the current strategies for managing CML have been highly successful, they are not without flaws. "Whether we can achieve a long-term remission is still the main question in CML, because it is difficult to say whether a successfully treated patient is actually free of disease," Dr. Cortes said. "The most sensitive test for CML, polymerase chain reaction, is very powerful—but when the results are negative, that just means the disease is undetectable. Even patients with undetectable CML can eventually relapse."

For that reason, long-term maintenance therapy is usually recommended. But this approach inherently creates another treatment problem for which there is no good solution. Some patients, such as those who suffer side effects or those who cannot afford the medication long-term, simply cannot continue therapy indefinitely. Other patients sometimes tire of daily therapy, especially when they appear to be perfectly healthy, and choose to stop. Patients who do not continuously take therapy are at a greater risk of relapse.

But researchers think they may eventually be able to help such higher-risk patients. As more tolerable agents become available, the incidence of side effects should decrease. Also, immune-stimulating vaccines and other treatment options now under investigation in patients with minimal residual disease could spur the body to keep CML at bay over the long term, negating the need for maintenance therapy.

And perhaps then, the remaining problems in CML treatment could be solved for good. ●

For more information, call Dr. Cortes at 713-794-5783.

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