Cancer Consult

Taussig Cancer Institute | August 2009

New Options for Image-Guided Radiation Therapy

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Dear Colleague:

I hope you enjoy this issue of Cancer Consult, which takes an in-depth look at Cleveland Clinic’s approach to cancer care. The Taussig Cancer Institute continues its mission of providing innovative, high-quality care through our commitment to meticulous clinical practice, augmented by a portfolio of clinical, translational and basic research, as well as undergraduate and graduate education.

As you will see in the pages that follow, we have had a busy year, with more than 600 publications (only a selection of which are listed in this magazine), more than 260,000 patient visits, and the acquisition of many new peer-reviewed grants, contracts and discoveries. We have participated in a number of quality assurance initiatives, and have developed several business tools to improve quality and consistency in our clinical products. We were gratified to be identified as the Top Cancer Center in Hospital Review’s recent article on the 11 top cancer centers in the United States.

We have been very active in research, achieving enrollment of more than 700 patients on clinical trials. We recently launched a clinical trials website to provide you and your patients with up-to-date information on available trials throughout our system, including our main campus and regional sites. Accrual from our regional oncologists continues to increase.

Our already robust translational research efforts were enhanced this year with the creation of a new Department of Translational Hematology and Oncology Research (THOR), with the world renowned clinician scientist Jaroslaw Maciejewski, MD, as its inaugural chairman. As you’ll see, our translational researchers continue to advance cancer diagnosis, prognosis and therapeutics.

In Radiation Oncology, we’ve added important new therapies including Ultimate Clarity™ for breast image-guided radiation therapy, hyperthermia, and Ambient MRI. We are participating in an exciting study of single fraction radiation therapy for breast cancer.

Studies initiated in our Bone Marrow Transplant Program have led to significant clinical advances that will give more patients an opportunity to mobilize stem cells for transplantation. We have further enhanced the program with the opening of a new, state-of-the-art bone marrow transplant cell processing laboratory, and expanded and renovated inpatient and outpatient areas.

We recently released a new edition of our Outcomes book, available online, which provides data on our clinical outcomes and volumes, as well as our patients’ experience throughout their continuum of care.

I hope you find this information to be interesting and useful in your own practice and look forward to continued collaboration with you.

Derek Raghavan, MD, PhD, FACP, FRACP
Chairman and Director, Taussig Cancer Institute
M. Frank & Margaret Domiter Rudy Distinguished Chair
Ultimate Clarity™ for Breast Image-Guided Radiation Therapy

Patients undergoing radiation treatment for early-stage breast cancer benefit from more accurate targeting of the treatment area with the Clarity™ Breast System. Clarity is an image-guided radiation therapy (IGRT) system that more accurately locates the treatment area for potentially fewer side effects and no additional risk to patients.

Available in Ohio only at Cleveland Clinic Taussig Cancer Institute, Clarity uses ultrasound images to help define the radiation treatment area. Ultrasound allows physicians to better visualize the area to be treated from the surrounding tissues than traditional computed tomography (CT) images alone. Because the target is more accurately visualized, a smaller volume of tissue needs to be treated with radiation, potentially resulting in fewer side effects. Since ultrasound does not use ionizing radiation, it is safe and poses no additional risks to patients.

Clarity is used for patients with breast cancer following lumpectomy for both whole breast irradiation with a “boost” and accelerated partial breast irradiation (APBI).
Ultrasound is very useful during treatment planning in helping to define the lumpectomy cavity to be treated, without any added risk to patients.

During simulation, Clarity provides clearer definition of the area to be treated than computed tomography (CT) scans alone.

“Ultrasound is very useful during treatment planning in helping to define the lumpectomy cavity to be treated, without any added risk to patients,” says Rahul Tendulkar, MD. “The Clarity system allows radiation oncologists to account for changes in the size, shape and position of the target, based on visualization of the actual anatomy.”

Image-guided systems like Clarity improve outcomes in terms of tumor control, minimize side effects, and improve the patient experience by decreasing treatment times and allowing for a shorter course of radiation treatment.

For more information on image-guided radiation therapy, call 216.444.5571, or email tendulr@ccf.org.
Single Fraction Intraoperative Radiation Studied for Breast Cancer

Partial breast irradiation for early stage breast cancer is commonplace in Europe and is gaining popularity in the United States. The benefit of this type of radiation is a reduction in the length of treatment time, from six to seven weeks of daily treatments to five, twice-a-day treatments.

Cleveland Clinic has performed intraoperative radiation utilizing the Intrabeam® System by Zeiss for colorectal tumors and brain tumors, and is now studying this option for the treatment of early stage breast cancer. This single intraoperative treatment has been shown to be effective as a replacement for the one-week boost received by women undergoing partial mastectomy with postoperative radiation. Jill Dietz, MD, Director of the Multidisciplinary Breast Cancer Program in the Ob/Gyn & Women’s Health Institute, and Rahul Tendulkar, MD, radiation oncologist in the Taussig Cancer Institute, will be the lead investigators in an ongoing international trial known as the TARGIT trial.

The Intrabeam device, the only of its kind in the state of Ohio, administers low voltage x-ray radiation that penetrates the breast tissue up to one centimeter from the intraoperative probe. In the operating room at the time of partial mastectomy, a team of surgeons, radiation oncologists, and physicists work together to place the sterile probe, ensure tissue conformity, and to establish the correct radiation dose for the patient. The intraoperative treatment lasts a total of less than 30 minutes. This device is currently used to replace the five-day boost treatment that is often added to external beam radiation treatments. The TARGIT trial is designed to evaluate whether a single intraopera-

By Jill Dietz, MD

For more information on Cleveland Clinic’s Breast Cancer Program, call Dr. Dietz at 216.445.3621, or email dietzj@ccf.org.
tive fraction can replace several weeks of external beam radiation treatment in low-risk breast cancer patients. This may be beneficial, especially in elderly women who tend to have smaller, lower risk tumors, and who may have difficulty traveling to a radiation facility five days a week for six to seven weeks. In addition, some women are choosing a complete mastectomy over a partial mastectomy due to the inconvenience of the daily commute for therapy. Intrabeam may provide an alternative since it can be provided the day of the patient’s breast surgery.

“Single fraction radiation therapy is not likely to replace other forms of radiation due to the continued presentation of women with various stages of breast cancer,” says Dr. Dietz. “However, the treatment may provide a welcome, more convenient option for women with low risk breast cancer. That’s why we are excited about joining the TARGIT trial.”

This new option adds to the expanding range of radiant options for women with breast cancer. At the Cleveland Clinic, these options include partial breast irradiation via a balloon catheter placement, as well as external beam radiation including 3-D conformal external beam radiation for high-risk patients.
Cleveland Clinic’s Bone Marrow Transplant Program, initiated in 1975, had performed 3,269 transplants by the end of 2008, making it the largest program in Ohio.

Cleveland Clinic physicians, scientists, nurses and the extended care team are renowned in the field of bone marrow transplantation. The goal of the team is to explore every potential laboratory and clinical breakthrough to improve survival.

Last year, the program benefited from the opening of Cleveland Clinic’s expanded campus when a new, state-of-the-art bone marrow transplant cell processing laboratory and blood bank opened in the 12-story Glickman Tower. The outpatient clinic has now been renovated, and in August the inpatient unit will be moving to new and expanded facilities, as well. The new unit, dedicated exclusively to transplant patients, will increase bed count from 17 to 25 in larger private rooms with the latest air handling system. The unit already scores above Centers for Medicare and Medicaid Services (CMS) benchmarks despite high patient acuity, but the new unit will add to the comfort of both patients and their family members.

Research

The Bone Marrow Transplant Program is driven by clinical and translational investigation. Cleveland Clinic was the second leading accruing institution in a recently completed multi-institutional study of a novel way to stimulate peripheral stem cells for transplantation. In December 2008, this molecule was FDA approved.

“This should be a significant clinical advance and give many patients the opportunity to mobilize stem cells for transplantation who might otherwise have been unable to do so,” says Program Director Brian Bolwell, MD.

The team currently is embarking on a novel protocol using lenalidomide and rituxan following autologous stem cell transplant in an attempt to improve patient outcomes. This protocol is part of the Leukemia and Lymphoma Society’s partnership with Cleveland Clinic.

2008 Stats

The Bone Marrow Transplant Program team performed 152 bone marrow/stem cell/umbilical cord blood transplants in 2008, including 32 autologous transplants for multiple myeloma, the most in the program’s history.

The most common disease indication for transplantation was non-Hodgkin lymphoma. This was followed by acute leukemias, multiple myeloma and Hodgkin lymphoma.

The program’s 100-day survival rate for autologous transplantation was 92 percent; and 80 percent for related allogeneic transplantation and all non-myeloablative allogeneic transplantation. These first 100 days are the most critically dangerous time for transplant patients.
New Liver Tumor Clinic Offers Comprehensive Approach

Hepatocellular carcinoma (HCC) is the most prevalent malignant hepatic tumor and has evolved into a significant worldwide health dilemma, resulting in more than 600,000 deaths annually.

This is partly due to the lack of effective therapies against hepatitis C, and inefficient preventive and screening policies in patients with hepatitis B and other etiologies of cirrhosis. In the United States, HCC induces more than 16,000 deaths yearly with a greater than two-fold increase between 1985 and 2002. The incidence of HCC is expected to continue to rise as a consequence of high hepatitis C infection rates between 1960 and 1990, and the average 20- to 30-year lag time between virus acquisition and the development of cirrhosis and carcinoma. Therefore, the treatment of HCC is a significant challenge.

At Cleveland Clinic, approximately 50 patients with HCC undergo liver transplantation and 20-30 patients receive hepatic resections (potentially curative therapies) each year. Approximately 100 new HCC patients were seen in the medical oncology clinic last year. Although the mainstay of therapy is surgical resection or liver transplant, the majority of patients are not eligible because of tumor extent or underlying liver dysfunction. These patients will then be candidates for non-curative approaches such as transarterial chemoembolization (TACE), transarterial radiotherapy or systemic therapy. Most recently, sorafenib became the first drug to be approved by FDA in treatment of advanced HCC.

Attempts to generate algorithmic approaches to the treatment of HCC are difficult due to the complex nature of HCC and the availability of multiple therapeutic approaches that tend to vary based upon the available expertise and institution.

A multidisciplinary approach that embraces physicians from different backgrounds such as oncology, interventional radiology, hepatology, pathology, radiation oncology and hepatobiliary/transplant surgery is pivotal in making treatment decisions for these patients. Cleveland Clinic has launched a comprehensive Liver Tumor Clinic to provide patients with a well-rounded approach to liver cancer and state-of-the-art treatment. The program offers extensive clinical service for patients with HCC, serves as a center of excellence in liver cancer research, and functions as a regional and national liver cancer educational resource.
The new clinic improves the patient experience by eliminating multiple appointments with different physicians at various locations. It provides referring physicians with a centralized point of contact, facilitating access and improving communication. It also creates an unprecedented, comprehensive tumor database that will enable team members to collect data and conduct research that may one day improve the care of patients.

The Liver Tumor Clinic provides therapeutic options including:

- Liver transplantation
  - Cadaveric
  - Living donation
- Liver resection
  - Open
  - Laparoscopic
  - Robotic
- Transarterial chemoembolization (TACE)
- Transarterial radiotherapy
- Radiofrequency ablation (RFA)
- Systemic chemotherapy
- Clinical trials of new approaches

Along with these standard treatment options, the Liver Tumor Clinic offers multiple clinical trials to determine the latest treatments for HCC, including a phase I trial using sorafenib + histone deacetylase inhibitors (HDAC inhibitors) in metastatic/unresectable HCC. Another planned trial will use local therapy such as TACE with doxorubicin bead in combination with sorafenib.

Vital Stats

- Cleveland Clinic is the fourth largest provider of liver transplants in the world.
- Average wait time for a liver transplant at Cleveland Clinic is six months — roughly half the time of other centers.
- Survival rates (one year) for liver transplants at Cleveland Clinic top 90 percent.
Clinical Trials Expand in Region

The evaluation of new therapies for cancer in the context of clinical trials is central to the mission of the Taussig Cancer Institute.

At present, around 10 percent of our patients are entered onto clinical trials — a number comparable with most other NCI-designated comprehensive cancer centers. There is an urgent need to increase this number, to ensure that our patients have access to state-of-the-art technology and promising new cancer therapies as quickly and easily as possible.

The barriers to clinical trial participation are well described. From the perspective of the investigator, the regulatory environment has become increasingly complex, contract and budget negotiations with sponsors are lengthy, and clinical research requires highly skilled and dedicated support staff and infrastructure. Explaining clinical trials to patients, obtaining informed consent and study-specific evaluations during the trial require major investments of time in busy schedules.

From a patient perspective, accessibility of new agents in clinical trials is often problematic. Many studies (especially phase I and II) are only conducted at major academic institutions, often at downtown locations. To enter these studies, patients may need to travel considerable distances to unfamiliar surroundings and an unfamiliar team of physicians and nurses. This adds additional burdens of cost and inconvenience to an already stressful and difficult situation.

Making these trials available at regional oncology centers where patients can be taken care of by their own team of physicians and nurses, close to their homes and families should overcome many of these barriers. Because of the integration between our main campus location and regional oncology centers, Taussig Cancer Institute is uniquely positioned to provide access to some early phase trials for our patients in the community.

To fully exploit this opportunity, Kim Kreller, Regional Research Manager for Taussig, has undertaken a major revision of personnel, infrastructure and policies in the regional centers to bring them in line with those at main campus. This integration of regional oncology with the main campus ensures uniform standards of care across the system. We are beginning to see examples of the results of this effort:

**2008 and 2009 Accrual at Regional Centers**

During 2008, a total of 161 patients were entered onto clinical trials at our regional oncology centers. Of these, 42 were entered on therapeutic trials and 119 on non-therapeutic (translational or correlative) studies. In the first three months of 2009, we reached a total accrual of 89 patients (18 therapeutic, 71 non-therapeutic/translational).

We have seen a consistent trend for increased accrual.

**LLS Center of Excellence for Clinical Trials in Hematologic Malignancies**

The partnership between Taussig and the Leukemia & Lymphoma Society (LLS) has been established as part of the LLS Therapy Acceleration Program, with the specific aim of making early phase trials in lymphoma and leukemia available at our regional centers. The second study funded by this partnership has now been opened at main campus, as well as Hillcrest and Fairview hospitals. This is a phase I/II study of AEG35156-204, a novel anti-sense molecule directed at the X-linked inhibitor of apoptosis (XIAP) in patients with relapsed and refractory low grade B-cell non-Hodgkin lymphomas.
We recently received approval from the LLS for the third study under our partnership agreement, using maintenance lenolidamide after autologous stem cell transplantation for patients with relapsed B-cell NHL, and anticipate opening this study at main campus and regional centers by Fall of 2009.

Thanks to the efforts of Ms. Kreller, research administrator Kristie Moffett, our investigators at regional centers and many others, we have seen a major improvement in our clinical research efforts in the region. We expect to continue to increase the number of trials available in the region. These trials need to be selected carefully. Phase I studies with requirements for intensive pharmacokinetic or pharmacodynamic studies will remain focused on main campus for now, and we will need to assess phase II studies on a trial by trial basis with respect to feasibility.
Locally advanced renal cell carcinoma (RCC) presents challenges to both the urologist and medical oncologist.

Locally advanced disease often is surgically difficult to resect entirely due to invasion of local organs, tumor size, bulky lymphadenopathy or involvement of critical structures like blood vessels. Further, such patients are at very high risk for recurrence and there is no proven effective adjuvant therapy.

Recent therapeutic advances in metastatic disease have included agents targeted against vascular endothelial growth factor (VEGF). These agents targeting circulating VEGF ligand (e.g. bevacizumab) or the tyrosine kinase portion of the VEGF receptor (e.g. sunitinib, sorafenib) have dramatically altered the therapeutic landscape of this disease and have become standards of care.

These agents initially were tested in patients with distant metastatic disease, most of whom had undergone previous primary tumor resection. One remarkable feature of all these agents is a high objective response rate of 10-40 percent, with approximately 70 percent of patients experiencing some degree of tumor burden reduction. Further, some reduction of primary tumor size has been observed in patients with primary tumor in place. As such, a natural extension of the use of these agents has been in several neoadjuvant settings:

1. prior to debulking nephrectomy,
2. prior to nephrectomy for locally advanced disease in an attempt to downstage the primary tumor,
3. prior to nephrectomy in localized disease, and
4. prior to consolidative metastasectomy in patients with a good response to drug and minimal residual disease. Existing data is limited to single institution case series and recent phase II clinical trials (Table 1).

A recently-published Cleveland Clinic retrospective experience administered sunitinib 50 mg four weeks on / two weeks off to 12 patients deemed unresectable because of invasion into adjacent organs, proximity to vital structures.

These initial experiences suggest the safety of these neoadjuvant approaches and efficacy in some patients.
### Prospective Clinical Trials

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<th>Approach</th>
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<th>Clinical results</th>
<th>Toxicity</th>
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<tr>
<td>Neoadjuvant sunitinib (CC)</td>
<td>‘Unresectable’ RCC (n=13 of 31 planned)</td>
<td>Primary tumor RECIST responses in 3 patients (25%)&lt;br&gt;Primary tumor shrinkage in 8 patients (67%)</td>
<td>No issues with wound healing, bleeding, or thromboembolic events were encountered</td>
<td>Viable tumor was present in all pathological specimens after nephrectomy.&lt;br&gt;Three patients underwent resection</td>
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<tr>
<td>Neoadjuvant sunitinib, sorafenib or bevacizumab (MDACC)</td>
<td>Prior to cytoreductive nephrectomy or resection of local recurrence (n=44)</td>
<td>Not reported</td>
<td>No surgical morbidity differences compared to matched group without neoadjuvant therapy</td>
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### Retrospective Series

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<tr>
<td>Neoadjuvant sunitinib (CC)</td>
<td>‘Unresectable’ RCC (n=12)</td>
<td>Primary tumor RECIST responses in 3 patients (25%)&lt;br&gt;Primary tumor shrinkage in 8 patients (67%)</td>
<td>No issues with wound healing, bleeding, or thromboembolic events were encountered</td>
<td>Viable tumor was present in all pathological specimens after nephrectomy.&lt;br&gt;Three patients underwent resection</td>
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#### Table 1: Selected neoadjuvant targeted therapy trials and experience in renal cell carcinoma

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<tr>
<td>Prospective phase II study of sunitinib in unresectable RCC (CC)</td>
<td>‘Unresectable’ RCC (n=13 of 31 planned)</td>
<td>Three pts (23%) have undergone primary tumor resection; viable RCC present in all specimens&lt;br&gt;Median reduction in primary tumor was 11</td>
<td>No unexpected surgical morbidity&lt;br&gt;Surgical technique, feasibility, and complication rates not affected; no wound healing or bleeding issues</td>
<td>Unresectable defined as one or more of the following: tumor size, bulky lymphadenopathy, high level venous thrombosis or proximity to vital structures.</td>
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<tr>
<td>Neoadjuvant treatment with sorafenib for locally advanced RCC (UNC)</td>
<td>Locally advanced (≥T2) RCC received sorafenib 400 mg BID for 4–8 weeks until 24–48 hours prior to nephrectomy (n=25)</td>
<td>64% of primary tumors with some regression&lt;br&gt;Mean reduction in primary tumor size 11% (range, 0–40%)</td>
<td>Surgical technique, feasibility, and complication rates not affected; no wound healing or bleeding issues</td>
<td>Median 2 days off prior to surgery&lt;br&gt;Translational correlates including VHL analysis, gene / protein expression and metabolomic profiling ongoing</td>
</tr>
<tr>
<td>Neoadjuvant bevacizumab (+/- erlotinib) (MDACC)</td>
<td>Metastatic RCC pts prior to cytoreductive nephrectomy; treatment for 8 weeks (n=50)</td>
<td>51% of primary tumors with some regression</td>
<td>Two perioperative deaths occurred, and neither were attributable to study drug.&lt;br&gt;Wound dehiscence resulted in treatment discontinuation for three patients.</td>
<td>42 pts underwent nephrectomy</td>
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**Abbreviations**
- CC: Cleveland Clinic
- UNC: University of North Carolina
- MDACC: MD Anderson Cancer Center
- RCC: renal cell carcinoma
bulky regional lymph nodes or vascular invasion, with many patients possessing multiple such adverse features. Partial responses of the primary tumor were noted in three patients (25 percent). Primary tumor shrinkage was observed in eight patients (67 percent) with an average decrease of primary tumor size by 24 percent. Three patients demonstrated tumor size reduction enough to facilitate resection with mean primary tumor shrinkage of 16 percent. Viable tumor was present in all pathological specimens after nephrectomy. No issues with wound healing, bleeding, or thromboembolic events were encountered. A prospective trial of sunitinib in RCC patients with unresectable primary tumors (with or without distant metastases) is currently ongoing, with preliminary results showing a reduction in some primary tumors enough to permit subsequent surgical resection (Table 1, previous page).

Toxicity of such an approach is an important consideration. A recent report from MD Anderson Cancer Center evaluated perioperative complications in 44 patients treated with targeted molecular therapies (sunitinib, sorafenib or bevacizumab) before cytoreductive nephrectomy or resection of local renal cell carcinoma recurrence. There were no significant differences between study groups in the type or extent of surgical procedure or perioperative complications; approximately 30 percent in the group treated with neoadjuvant targeted therapy and a matched comparator group who underwent up front surgery. No clinical outcome data was reported.

Neoadjuvant therapy prior to a debulking nephrectomy may allow for determination of metastatic site drug sensitivity before subjecting a patient to nephrectomy. MD Anderson Cancer Center has reported a study of eight weeks of pre-nephrectomy bevacizumab (with or without erlotinib) in patients with metastatic RCC. Fifty-one percent of primary tumors demonstrated some degree of regression. A similar trial employing sunitinib in this setting is ongoing.

These initial experiences suggest the safety of these neoadjuvant approaches and efficacy in some patients. Continued investigation is needed to identify the optimal neoadjuvant setting and approach, timing of surgical intervention and to further define safety considerations such as time off of drug needed before and after surgery.

For a list of references, please email heinesm@ccf.org
Both physical and mental fatigue (often known as “chemobrain”) occur commonly during chemotherapy treatment. A portion of patients report persistent problems with cognitive function even after recovery from other effects of treatment.

Research into the prevention and treatment of “chemobrain” has been limited by the lack of objective measures of mental fatigue. It also can be difficult to distinguish effects of treatment from those of the cancer diagnosis itself and normal aging. Better understanding of the neurophysiology of cancer treatment related fatigue and cognitive dysfunction is essential for developing treatment and preventive strategies.

At Cleveland Clinic, we are piloting the use of electroencephalography (EEG) and Event Related Potentials (ERPs) to investigate chemotherapy associated fatigue and cognitive dysfunction. Patients receiving adjuvant chemotherapy for early stage breast cancer and a control group undergo a physical task and a mental task while brain activity is monitored. By following subjects over time, we will be able to compare results during treatment to baseline measurements and to see whether changes persist or resolve after treatment is complete. In addition, patient outcomes can be compared to the control group and to general population results. During each testing period, subjects undergo formal cognitive testing, as well as muscle strength testing. We also will evaluate subjects’ perception of fatigue and cognitive changes.

If we find we are able to objectively measure the phenomenon of “chemobrain,” we will have a platform upon which we can further study potential interventions for this important problem. Preliminary data from this pilot study will be used for future prospective studies, which may include interventions such as exercise, mental training or pharmacologic treatment.
Studies Show SNPs Useful in Predicting Toxicity

Drug toxicity is an inherent problem in treating cancer, but recent advances in pharmacogenomics have provided a unique opportunity to be able to identify patients who may be more susceptible to toxicity. Although there has been a renaissance in drugs available for the treatment of renal cancer, these don’t come without problems.

Ram Ganapathi, PhD, Director of the Clinical Pharmacology Program at the Taussig Cancer Institute, with his team in the Department of Translational Hematology and Oncology, are focused on identifying SNPs that predispose patients to toxicity, particularly hypertension following treatment with the angiogenesis inhibitor sunitinib.

“This drug has been extremely valuable because it has made remarkable inroads in managing patients with kidney cancer,” says Dr. Ganapathi. “But hypertension is a serious problem for patients treated with sunitinib.”

Last year, Dr. Ganapathi’s team studied SNPs that led to amino acid changes in key proteins that might predict for toxicity, and came up with a panel of 23 genes from an array that included 13,000 different genes. Then, using results from a study from Indiana University of a different angiogenesis inhibitor, they retrospectively screened 64 patients to evaluate the association among vascular endothelial growth factor (VEGF) SNPs and the development of hypertension in metastatic renal cell carcinoma patients receiving sunitinib.

“What we were able to determine is that one polymorphism clearly predicted for hypertension in this group,” says Dr. Ganapathi. The findings recently were shared in an oral presentation at the American Society of Clinical Oncology (ASCO) by Jenny Kim, MD, a clinical fellow in the Department of Hematology and Medical Oncology.
Next steps include trying to determine whether this polymorphism can predict toxicity with other drugs used in the treatment of kidney cancer; and whether the information can be used to determine dosing to reduce toxicity.

“Our goal is to uncover distinct signatures that could be used to develop personalized treatment to improve efficacy and, more importantly, to reduce toxicity,” says Dr. Ganapathi. “Addressing toxicity is so important to quality of life. We know this disease is a curse. We don’t need to make it worse. At Cleveland Clinic, we are at the leading edge of developing the strategies needed to personalize treatment.”

Dr. Ganapathi’s program is built on the strong belief that rational and effective treatment of cancer requires a comprehensive understanding of the biology of the tumor being treated, as well as the mechanisms of action and pathways that regulate resistance to anti-cancer drugs. The lab has been supported by the National Cancer Institute and the National Institutes of Health for more than 25 years.

“We have the resources of patients and excellent clinicians to do this kind of array work, which is not available everywhere,” he says. “We’re now in a position to use them intelligently.”

At Cleveland Clinic, we are at the leading edge of developing the strategies needed to personalize treatment.
A Cleveland Clinic collaborative project has created a new multidisciplinary model for colorectal cancer microsatellite instability testing to screen patients and their families for inherited cancers.

Many medical and genetic professionals agree that all colorectal cancer patients should be screened by microsatellite instability (MSI) or immunohistochemistry (IHC) testing to detect hereditary nonpolyposis colorectal cancer, otherwise known as Lynch syndrome, says Charis Eng, MD, PhD, Chair of the Cleveland Clinic Genomic Medicine Institute.

“While we know that 10 to 15 percent of sporadic (not inherited) colorectal cancers are MSI positive, virtually all colorectal cancers due to Lynch syndrome are MSI positive and IHC null,” Dr. Eng says. “Thus, MSI and IHC are an excellent first screening process for the possibility of Lynch syndrome.”

However, no studies have analyzed how this testing process should be practically implemented within an institution.

Analyzing the MSI/IHC screening process, led by Dr. Eng and Brandie Leach, MS, CGC, certified genetic counselor, became an important Cleveland Clinic initiative because CRC patients with Lynch syndrome have a 50 percent chance of developing a second colon cancer, as well as other types of cancer.

For more than a year, Dr. Eng and Ms. Leach analyzed the MSI/IHC process by collaborating with colorectal surgeons, gastroenterologists, genetic counselors, pathologists, nurses and other healthcare professionals from the Taussig Cancer Institute, the Digestive Disease Institute, and the Anatomic Pathology and Bioethics departments.

INCREASED RISK

CRC patients with Lynch syndrome have a 50 percent chance of developing a second colon cancer, as well as other types of cancer. For example:

- Women with Lynch syndrome have a 40 percent lifetime risk of developing uterine cancer, and a 12 percent lifetime risk of getting ovarian cancer.
- Lynch syndrome patients also are at risk for cancer of the stomach, small intestine, liver and biliary tract, brain and renal pelvis.
Specifically, the collaborative project retrospectively analyzed three models of the MSI/IHC testing process:

1. Sending test results to colorectal surgeons who were solely responsible for reporting results to patients and referring them for genetic counseling and genetic testing.

2. Colorectal surgeons and genetic counselors received MSI/IHC reports for triage of patients who were appropriate for genetic counseling and testing. The genetic counselor helped the colorectal surgeons identify these patients and make the referral for genetic counseling and testing.

3. MSI/IHC results were emailed to colorectal surgeons and genetic counselors. In collaboration with the surgeons, the counselors contacted the patients to discuss the abnormal results and facilitate a genetic counseling appointment.

Because of their analysis, the third model was adopted by Cleveland Clinic. The biggest lesson learned from this analysis, concludes Dr. Eng: “Implementation of MSI/IHC testing within an institution requires integration of a multidisciplinary team including pathology, colorectal surgery, bioethics and genetics to ensure the seamless process of results delivery and that our patients get the most comprehensive health care they need.”
Moving Targeted Therapies into the Treatment of Early Stage Non-Small Cell Lung Cancer

Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related death in the United States, with only 15 percent of patients surviving five years from diagnosis. Despite these grim statistics, patients with earlier stages of disease can have a significantly better prognosis, with cure rates as high as 70 percent in stage I patients treated with surgery.

For patients with either large tumors or with local lymph node involvement, adjuvant chemotherapy given after surgery has shown a modest improvement in survival. Nonetheless, when even patients with the smallest and most curable lung cancers have almost a one in three chance of relapsing and eventually dying of their disease, there is a large unmet need for better treatments.

For the past decade, much of the focus of clinical research in NSCLC has been in the development of so-called “targeted agents:” drugs designed to specifically target one or more important proteins or cellular pathways in cancer cells. In particular, two targeted agents have made an important impact in the treatment of patients with advanced or metastatic NSCLC, and here at Taussig Cancer Institute we are helping to investigate the role of these agents in the early stage setting.

The first of these agents is bevacizumab (Avastin®), which is a monoclonal antibody against vascular endothelial growth factor (VEGF), a protein critically important in the formation and maintenance of cancer blood vessels. Bevacizumab, in combination with chemotherapy, was approved by the Food and Drug Administration (FDA) in 2006 for the treatment of advanced or metastatic NSCLC after a large phase III trial showed improved survival with the combination compared to chemotherapy alone.

In an attempt to see if the survival benefit seen in advanced NSCLC patients translates into the early stage setting, we are currently enrolling stage IB-IIIA NSCLC patients as part of a nationwide randomized phase III trial of standard adjuvant chemotherapy with or without bevacizumab after surgery. Patients will receive four cycles of platinum-doublet chemotherapy with or without bevacizumab, and those randomized to the bevacizumab arm will then continue bevacizumab alone for up to one year. The primary outcome of this trial will be improved overall survival.

The second major targeted drug to make an impact in the treatment of NSCLC is erlotinib (Tarceva®), which is an oral small molecule inhibitor of the epidermal growth factor receptor (EGFR). EGFR is critically important to the growth and survival of lung cancer cells, and erlotinib has also been FDA approved for the treatment of patients with advanced or metastatic NSCLC who have failed first- or second-line chemotherapy.

Erlotinib is particularly effective when used in patients with activating mutations in the EGFR gene, which are present in about 10 percent of NSCLC patients in the United States. These mutations occur more frequently in female patients, those with adenocarcinoma histology, and those who have never smoked. If a mutation is present, 70 percent or more of patients will respond to erlotinib, and average survival tends to be about twice as long as in patients without EGFR mutations.
Given the effectiveness of erlotinib in advanced NSCLC patients with EGFR mutations, it makes sense to investigate this drug in the adjuvant setting. We are currently enrolling stage I-IIIA patients, all of whom must have EGFR mutations present in their tumors, in a phase II trial of erlotinib given daily for two years after surgery. Patients can still receive standard adjuvant chemotherapy after surgery prior to starting erlotinib, and are eligible for enrollment if they are within six months of their surgery. The goal will be to show an improvement in the number of patients who are alive and free of recurrence two years after surgery.

Improvements in cancer treatment tend to come in small increments, and can be frustratingly few and far between. By moving proven effective treatments from the advanced disease setting where cure is not possible, into the earlier stage setting where cure is possible, there is the potential to make a much bigger impact on patients’ lives.

The primary outcome of this trial will be improved overall survival.
Internationally Renowned Researcher Heads Translational Hematology and Oncology Research

Jaroslaw Maciejewski, MD, PhD, an international authority on bone marrow failure syndromes, was named chairman of the newly created Department of Translational Hematology and Oncology Research (THOR) in February.

Dr. Maciejewski’s appointment represents another opportunity for the Taussig Cancer Institute to evolve its research agenda and to provide an even higher level of care and translational research for patients across the United States and beyond. The department will focus on the study of molecular and biochemical mechanisms leading to cancer with the goal of directly improving diagnosis and treatment for cancers and leukemia as well as other related disorders. The research topics include molecular pathogenesis, cancer stem cells, tumor immune surveillance and development of new targeted cancer therapeutics.

Dr. Maciejewski, a staff physician at Taussig for eight years, is widely respected as an expert on myelodysplastic syndrome, pre-leukemic states and molecular prognostication. He holds more than $10 million in peer-reviewed grants, has published manuscripts in many highly cited journals, is on the editorial board of Blood, and has mentored many translational researchers.

“Dr. Maciejewski has been instrumental in our research efforts regarding hematologic diseases, resulting in several major discoveries since he joined our team,” says Derek Raghavan, MD, PhD, Chairman of the Taussig Cancer Institute. “His leadership in the Department of Translational Hematology and Oncology Research will help us achieve even greater innovation in this field.”

Dr. Maciejewski, who specializes in bone marrow transplantation and has been named one of America’s Best Doctors, is also Associate Professor of Medicine at the Cleveland Clinic Lerner College of Medicine at Case Western Reserve University. He attended the Medical School Charite, Humboldt University, in Berlin.

“Patients will benefit greatly from the heightened focus on hematologic and oncologic research, which we intend to use to improve individual outcomes,” says Dr. Maciejewski. “Our new department is a response to the challenge to improve cure rates through biomedical innovation and research excellence.”

To discuss Taussig Cancer Institute translational research projects, call Dr. Maciejewski at 216.445.5962, or email maciejewski@ccf.org
Brain metastases occur in up to 25 percent of all patients with cancer, particularly in those with lung, breast and kidney cancers and melanoma. The incidence of brain metastasis continues to rise, in part due to improved systemic therapy and longer survival times. In patients who receive either surgery or stereotactic radiosurgery as local therapy for 1-3 brain metastases, adjuvant WBRT improves relapse rate but not time of neurologic independence or survival when compared to no further treatment.

The efficacy of chemotherapeutic agents for malignancies in the brain has been limited and their use restricted to those cancer types that are relatively chemo-sensitive. This is partly because the CNS has traditionally been regarded as a sanctuary site, with the blood-brain barrier (BBB) acting as an impediment for chemotherapies to reach brain tumors. But agents like sunitinib that target angiogenesis do not need to cross the BBB as they target vasculature on the abluminal side of the BBB.

While the role of this class of drugs has not been established in the setting of brain metastases, their pharmacologic target and their relatively low toxicity profile in comparison to cytotoxic chemotherapy drugs makes their use in this group of heterogeneous diseases attractive.

During the trial, patients with stable systemic disease on a treatment regimen (e.g., breast cancer patient on trastuzumab) will continue the regimen provided it has a safety record when combined with sunitinib. The protocol contains an extensive list of such regimens, which is updated on a regular basis. Given the concern for neurocognitive toxicity, neurocognitive function also will be measured in this study.
Institute Physician-Researcher Discovers Two Genes Linked To Breast, Thyroid and Kidney Cancers

Early detection is critical to ensure the best odds to survive cancer, and for patients with Cowden Syndrome (CS) and a CS-like disease, the odds are improving.

Lerner Research Institute staff have discovered two new genes (SDHB and SDHD) that may improve detection of breast, thyroid and kidney cancers. Research led by Charis Eng, MD, PhD, Chair, Genomic Medicine Institute (GMI), points toward the advent of personalized healthcare, whereby patients will be screened for cancer risk based on their individual genetic profile.

“Our discovery is an example of how to apply genetics to clinical practice and of the future of personalized medicine,” says Dr. Eng. “Physicians and genetic counselors now have another diagnostic tool available for the screening, detection and prevention of breast and thyroid cancers.”

Normally, a gene called PTEN acts to suppress cancers. In 1997, Dr. Eng discovered that certain mutations in PTEN determined susceptibility to CS, a syndrome characterized by tumor-like growths and a high risk of developing breast and thyroid cancers. However, some individuals with normal PTEN still get the disease.

Now, 11 years later, SDHB and SDHD have been identified as markers of CS susceptibility for such individuals. Dr. Eng’s current study indicates that mutations in these two genes confer a higher risk of breast, thyroid and kidney cancers as compared to PTEN mutations alone.

“Clinicians should consider SDH testing for patients who have a strong personal history and/or family history of breast, thyroid and/or kidney cancers, especially when their PTEN is normal,” says Dr. Eng. “Patients with SDH mutations should be more rigorously screened for these cancers.”

Rigorous screening may reveal a cancer at an earlier stage, which leads to earlier intervention and improved outcomes, Dr. Eng says.

The study examined DNA extracted from blood samples from 375 patients with CS and a CS-like disorder and a family history of PTEN mutation negative. Dr. Eng’s team then looked at the sequence of three related genes, SDHB, SDHC and SDHD. When mutated, these three genes are responsible for a rare tumor completely unrelated to CS called paraganglioma. Dr. Eng chose to study those genes after noticing that in one to four percent of individuals with SDHB mutations, kidney and thyroid cancers developed.

This research appeared the American Journal of Human Genetics (www.ajhg.org/). Dr. Eng is the director of the Genomic Medicine Institute and holds the Sondra J. and Stephen R. Hardis Chair of Cancer Genomic Medicine.
Jackson Laboratories has developed a new strain of immunocompromised mouse called the NSG mouse (NOD-SCID-IL2rGamma). For growing human tumor explants, this is a vast improvement over athymic nude mice, or NOD-SCID mice, or even NOG mice since NOD-SCID mice possess an intact IL2 gamma receptor and NOG mice retain a truncated IL2 receptor gamma chain that still signals. The success rate for engraftment of human tissue into athymic nude or NOD-SCID mice is typically 10-15 percent.

Because NSG are so immunosuppressed, they will accept normal human bone marrow and human tumor explants (xenografts) that have previously been impossible to grow in athymic or NOD-SCID mice. NSG mice do not possess the undesirable property of NOD-SCID mice which uniformly develop lymphoma at 6-9 months of age.

Daniel Lindner, MD, PhD, of the Animal Tumor Core (ATC), is working with Brian Rini, MD, Solid Tumor Oncology, to implant biopsies of renal carcinoma; and with Jaroslaw Maciejewski, MD, PhD, Translational Hematology and Oncology Research, and Yogen Saunthararajah, MD, Hematologic Oncology and Blood Disorders, to implant bone marrow specimens derived from acute myelogenous leukemia and myelodysplastic syndrome patients. The team hopes these new murine models will allow development of new therapeutic modalities.

The ATC, part of Cleveland Clinic’s Research Core Services, was established in 2002 to help principal investigators perform tumor experiments, angiogenesis studies and pharmacokinetic studies in mice. The ATC conducts syngeneic murine tumor experiments, and human xenograft tumor experiments. Research Core Services are critical to advancing treatment of disease, providing investigators with access to technology and instrumentation that is too costly, complex, or otherwise inaccessible to individual laboratories.
Miniature 3-D Scaffold is a Better Way to Test Cancer Drugs

It has been difficult, if not impossible, to predict the effectiveness of new cancer drugs accurately because they often work disappointingly less well in patients’ tumors than in laboratory cell cultures.

Responding to this need, Vinod Labhasetwar, PhD, Biomedical Engineering and Director of the Cancer NanoMedicine Program, recently reported results from a novel 3-D tumor scaffold intended to yield findings that more closely mimic those found in patients’ tumors.

Dr. Labhasetwar’s research team surface-engineered large and porous biodegradable polymeric microparticles as a 3-D scaffold on which to grow human breast cancer cells into a tumor-like structure in culture. They then evaluated those 3-D cells against cells grown on a “2-D” single layer in culture plates, which is a commonly used technique to study cancer cells. Researchers compared the effects of the drugs doxorubicin, paclitaxel and tamoxifen on cancer cells from both 2-D monolayers and 3-D scaffolds. They found that the 3-D tumor model showed lower drug accumulation, less slowing of tumor growth by the drug, and higher drug resistance than cells grown in monolayer. In short, the 3-D tumor model more closely mimicked the effects the drugs have in human patients.

Surprisingly, gene changes were also found in cancer cells grown on 3-D scaffolds, a finding possibly explained by differences in how cells signal each other when they’re grown in 3-D versus 2-D monolayer.

“The results underscore the significant roles played by cell structure, variations in the cells’ genes, and how cells are organized in determining how efficiently drugs are transported and how effectively they are able to combat cancer cells,” Dr. Labhasetwar says. “A well-characterized 3-D tumor model can be particularly useful for rapid screening of a large number of therapeutics for their ability to affect cancer cells during the drug discovery phase.”
For his achievement, the American Association for Cancer Research (AACR) recognized Dr. Stark's work as a seminal discovery in cancer research. The AACR is the oldest and largest scientific organization in the world focused on every aspect of high-quality, innovative cancer research, and it selected Dr. Stark’s discovery to represent the year 1979 during its recent centennial.

More than 30 years ago, the accepted way to measure the amount of molecules called mRNA was labor intensive and time consuming. mRNA is critical to correctly producing the basic building blocks of all cells called protein. Simply, a cell’s DNA (located in a cell’s nucleus) contains that cell’s genetic blueprint. The DNA expresses, or produces, mRNA to carry the blueprint to another structure within the cell called the ribosome, which then creates the proteins necessary for the cell’s function and survival. This process happens in all cells, and any misstep along the way disrupts proper cell behavior.

“We wanted to determine the amount of a specific mRNA in some drug-resistant cells that we had developed,” says Dr. Stark, Molecular Genetics. “The available methodology involved separating the mRNAs by size in a tube gel, freezing the gel, cutting it into about 100 sections with a device resembling an egg slicer, transferring each slice to a separate tube, and interrogating each with a radioactive probe for the RNA of interest.

“We did this experiment once and vowed never again — what a pain!”

At the time, British molecular biologist Sir Edwin Southern, FRS, had developed a technique for separating DNA fragments in a slab gel and transferring them to cellulose, where they could be identified and quantified with a radioactive probe. Dr. Stark saw no reason why this would not also work for mRNA. But the problem was that mRNA did not adhere to the cellulose being used.

“So we brought chemistry into the picture. We made a derivative of the cellulose that would link to the mRNA, immobilizing it in a form suitable for further analysis,” he says. “It worked like a charm, and our ‘diazotized paper’ was very popular for a few years.”

Eventually, others discovered supports for mRNA that did not require chemical coupling, and these have been used ever since. In a related development, Dr. Stark also helped to develop the popular Western technique, in which proteins separated in gels were transferred to the chemically reactive diazotized paper, and identified and quantified with antibodies. Again, the need for the chemistry soon disappeared as better supports were developed by others.

“The ability to identify the sizes and amounts of individual mRNAs in a simple and reliable way has been extremely valuable, and the Northern method is still in very wide use,” Dr. Stark says. “Virtually every molecular biology lab does this method, and the Western blot as well, on a routine basis. Also, both techniques have been widely used in clinical tests, for example, until very recently for the diagnosis of AIDS.”

But why “Northern” and “Western” blots? Sir Southern’s technique is universally known as, well, the “Southern blot.” With a wink and a nod to the inspiration, Dr. Stark thought the directional names were quite fitting.
Selected Leadership Roles
Professional Groups and Societies 2008-2009

American Academy of Hospice and Palliative Medicine
T. Declan Walsh, MD
Founding Member

American Association for the Advancement of Science
Ernest Borden, MD
Charis Eng, MD, PhD
Derek Raghavan, MD, PhD
Robert Silverman, MD
Roy Silverstein, MD
John Sweetenham, MD
Fellows

American Board of Radiology
John Suh, MD
Section Head, CNS/Pediatric Section for Oral Board Exam in Radiation Oncology & Oral Board Examiner

American Cancer Society
Derek Raghavan, MD, PhD
Ohio Division Board of Directors
Cuyahoga County Unit Board of Directors
Hope Lodge Board of Directors

American College of Physicians
Brian Bolwell, MD
Ernest Borden, MD
G. Thomas Budd, MD
Dale Cowan, MD
Robert Dreicer, MD
John Hines, MD
Leonard Horwitz, MD
Matt Kalaycio, MD
Ruth Lagman, MD
Susan LeGrand, MD
Derek Raghavan, MD, PhD
Timothy Spiro, MD
T. Declan Walsh, MD
Kenneth Weiss, MD
Fellows

American College of Radiology
John Suh, MD
Member, ACR Appropriateness Criteria®
Expert Panels on Radiation Oncology
Gregory Videtic, MD
Vice-Chairman, ACR Appropriateness Criteria®, Radiation Oncology-Brain Panel Listing; Member, Guidelines & Standards Committee; Member, Radiation Oncology Committee

American Society of Chest Physicians
Mellar Davis, MD
Fellow

American Society of Clinical Oncology
Robert Dreicer, MD
Chairman, Steering Committee 2008 GU Cancer Symposium; Member, Ethics Committee
Derek Raghavan, MD, PhD
Member, Cost Containment Task Force; Past Chair, Diversity Task Force
Brian Rini, MD
Scientific Program Track Team Leader, GU Oncology
John Sweetenham, MD
Member, Cancer.net Editorial Board

American Society of Hematology
Brian Bolwell, MD
Member, Communications Committee
Yogen Saunthararajah, MD
Member, Red Cell Scientific Committee
Mikkael Sekeres, MD
Member, Committee on Educational Affairs; Chair, Education Session: Myelodysplastic Syndromes

American Society of Human Genetics
Charis Eng, MD, PhD
Board of Directors, Expert Speakers Bureau

American Society of Therapeutic Radiology and Oncology
John Suh, MD
Reviewer
Ping Xia, MD
Member, Evaluation Subcommittee of Emerging Technology Committee; Co-Chair, Practical Aspects of IMRT Practicum

Aplastic Anemia and MDS International Foundation
Mikkael Sekeres, MD
Co-Chair, Medical Advisory Board

Center for International Bone Marrow Transplant Research
Brian Bolwell, MD
Co-Chairman, Late Effects Committee
Eastern Cooperative Oncology Group
Robert Dreicer, MD
Chair, Bladder Cancer Subcommittee
John Sweetenham, MD
Member, Lymphoma Care Committee

European Association for Palliative Care
T. Declan Walsh, MD
Founding Member

Foundation for the Accreditation of Cellular Therapy
Ronald Sobecks, MD
U.S. Inspector

International Stereotactic Radiosurgery Society
John Sun, MD
Director of Membership Committee

Leukemia Research (United Kingdom)
John Sweetenham, MD
Chairman, Clinical Trials Advisory Panel

National Cancer Institute
David Adelstein, MD
Co-Chairman, Previously-Untreated Locally Advanced Disease Task Force, Head and Neck Cancer Steering Committee
Brain Bolwell, MD
Member, Subcommittee H
Derek Raghavan, MD, PhD
Member, Clinical Oncology Grant Review Committee (Study Section)
Mikkael Sekeres, MD
Member, PDQ® (Physician Data Query) Editorial Board

National Comprehensive Cancer Network Guidelines
Charis Eng, MD, PhD
Special Consultant

National Heart, Lung and Blood Institute
Yogen Saunthararajah, MD
Member, Sickle Cell Disease Advisory Board

Personalized Medicine Coalition
Charis Eng, MD, PhD
Chair, Clinical Sciences Committee

Radiation Therapy Oncology Group
Gregory Videtic, MD
Member, Lung Cancer Committee

Radiological Physics Center
Ping Xai, MD
Ad Hoc Committee Member, Annual Site Visit
Royal Australian College of Physicians
Derek Raghavan, MD, PhD
Fellow
Royal College of Physicians (Edinburgh)
T. Declan Walsh, MD
Fellow
Royal College of Physicians (London)
John Sweetenham, MD
T. Declan Walsh, MD
Fellows
Sino-American Network for Therapeutic Radiology and Oncology
Ping Xai, MD
Founding Board Member

Southwestern Oncology Group
G. Thomas Bud, MD
Board of Governors
Mikkael Sekeres, MD
Member, Leukemia Committee
Gregory Videtic, MD
Member, Lung Cancer Committee

The American Association of Physicists in Medicine
F. Chris Deibel, MD
Treasurer, Penn-Ohio Chapter
Allan Wilkinson, MD
Co-Chair, Partners in Physics Program;
Curator, International Organization for Medical Physics/AAPM Library Program

U.S. Food and Drug Administration
Mikkael Sekeres, MD
Member, Oncologic Drug Advisory Committee
Critical to Taussig Cancer Institute’s success is the complete partnership established with Cleveland Clinic’s nationally recognized teams of cancer care specialists. The following leaders from other Cleveland Clinic institutes collaborate with Taussig staff to provide the most advanced oncologic care to our patients:

**Cole Eye Institute**
Arun Singh, MD

**Dermatology & Plastic Surgery Institute**
Allison Vidimos, MD
Philip Balin, MD, MBA
Wilma Bergfeld, MD
Christopher Gasbarre, DO
David Hamrock, MD
Douglas Kress, MD
Edward Maytin, MD, PhD
Jonelle McDonnell, MD
Jon Meins, MD
Melissa Piliang, MD
Christine Poblete-Lopez, MD
Apra Sood, MD
James Taylor, MD
Kenneth Tomecki, MD
Rebecca Tung, MD

**Endocrinology & Metabolism Institute**
Allan Siperstein, MD

**Glickman Urological & Kidney Institute**
Steven Campbell, MD, PhD
Monish Aron, MD
Ryan Berglund, MD
Khaled Fareed, MD
Amr Fergany, MD
Michael Gong, MD
J. Stephen Jones, MD
Jihad Kaouk, MD
Eric Klein, MD
Venkatesh Krishnamurthi, MD
David Levy, MD
Robert Stein, MD
Andrew Stephenson, MD
James Ulchaker, MD

**Digestive Disease Institute**
Federico Aucejo, MD
Carol Burke, MD
Sricharan Chalikonda, MD
James Church, MD
Gary Falk, MD
Victor W. Fazio, MD
John Fung, MD, PhD
Michael Johnson, MD
Ian Lavery, MD, BS
K.V. Narayanan Menon, MD
James Merlino, MD
Charles Miller, MD
Feza H. Remzi, MD
Matthew R. Walsh, MD

**Head & Neck Institute**
Daniel Alam, MD
Michael Benninger, MD
Brian Burkey, MD
Michael Fritz, MD
P. Daniel Knott, MD
Joseph Scharpf, MD
Peter Weber, MD
Benjamin Wood, MD

**Miller Family Heart & Vascular Institute**
Thomas Rice, MD
David Mason, MD
Sudish Murthy, MD

**Ob/Gyn & Women’s Health Institute**
Joseph Crowe, MD
Jill Dietz, MD
Richard Drake, MD
Pedro Escobar, MD
Alicia Fanning, MD
Katherine Lee, MD
Lawrence Levy, MD
Chad Michener, MD
Holly Pederson, MD
Peter Rose, MD

**Orthopaedic & Rheumatologic Institute**
Michael Joyce, MD
Steven Lietman, MD

**Pulmonary Institute**
Rendell Aston, MD
Thomas Gildea, MD
Michael Machuzak, MD
Peter Mazzone, MD
Madhu Sasidhar, MD

**Pediatric Institute & Children’s Hospital**
L. Kate Gowans, MD
Eric Kodish, MD
Michael Levien, MD
Gregory Plautz, MD
Tanya Tekautz, MD
Margaret Thompson, MD, PhD
Thirteen Named to America’s Best

Thirteen physicians were recognized by Castle Connolly Medical Ltd. as “America’s Top Doctors for Cancer.” Physicians listed are nominated by peers and thoroughly reviewed by the Castle Connolly’s physician led research team. Learn more about Castle Connolly Medical Ltd by visiting castleconnolly.com/doctors/index.cfm?source=ccf.

Cleveland Magazine’s Best Doctors list recognized 29 oncologists in the March 2009 issue. “Best Doctors” is a biennial peer review representing 40,000 doctors in more than 40 medical specialties. Learn more about Best Doctors in America® by visiting bestdoctors.com/bd/experts.php

Aplastic Anemia
Jaroslav Maciejewski, MD, PhD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors

Bladder Cancer
Vinit Makkar, MD
Cleveland Magazine Best Doctors
Derek Raghavan, MD, PhD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
Brian Rini, MD
Cleveland Magazine Best Doctors
Jay Ciezki, MD
Cleveland Magazine Best Doctors
Jerold Saxton, MD
Cleveland Magazine Best Doctors

Bone Marrow Transplant
Brian Bolwell, MD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
Brad Pohlmam, MD
Cleveland Magazine Best Doctors
John Sweetenham, MD
Cleveland Magazine Best Doctors

Brain Tumor, Adult & Peds
David Peereboom, MD
Cleveland Magazine Best Doctors
John Suh, MD
Castle Connolly Top Doctors

Breast Cancer
Thomas G. Budd, MD
Castle Connolly Top Doctors
Robert Dreicer, MD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
Charis Eng, MD, PhD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
Rogor Macklis, MD
Castle Connolly Top Doctors
Gary Schnur, MD
Cleveland Magazine Best Doctors

Cancer Genetics
Charis Eng, MD, PhD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors

Esophageal Cancer
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Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
Gregory Videtic, MD
Cleveland Magazine Best Doctors

Gastrointestinal Tumors
Robert Pelley, MD
Cleveland Magazine Best Doctors

Genitourinary Cancer
Derek Raghavan, MD, PhD
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Cleveland Magazine Best Doctors

Gynecological Cancers
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Cleveland Magazine Best Doctors

Head & Neck Cancer
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Castle Connolly Top Doctors
Vinit Makkar, MD
Cleveland Magazine Best Doctors
Jerold Saxton, MD
Cleveland Magazine Best Doctors

Hematologic Malignancies
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Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
Alan Lichtin, MD
Cleveland Magazine Best Doctors
Jaroslav Maciejewski, MD, PhD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
John Sweetenham, MD
Cleveland Magazine Best Doctors

Immunotherapy
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Castle Connolly Top Doctors
Cleveland Magazine Best Doctors

Kidney Cancer
Ronald Bukowski, MD†
Castle Connolly Top Doctors
Brian Rini, MD
Cleveland Magazine Best Doctors

Leukemia
Edward Copelan, MD
Cleveland Magazine Best Doctors
Matt Kalaycio, MD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
Mikkael Sekeres, MS, MD
Cleveland Magazine Best Doctors

Lung Cancer
David Adelstein, MD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors

Malignant Cysts
Edward Copelan, MD
Cleveland Magazine Best Doctors

Musculoskeletal Malignancies
Edward Copelan, MD
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Nephroblastoma
Edward Copelan, MD
Cleveland Magazine Best Doctors

Ovarian Cancer
Charis Eng, MD, PhD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors

Prostate Cancer
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Castle Connolly Top Doctors
Cleveland Magazine Best Doctors

Radioimmunotherapy of Cancer
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Castle Connolly Top Doctors

Research Hematologic Oncology and Blood Disorders
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Cleveland Magazine Best Doctors

Sarcoma Vaccine Therapy
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Castle Connolly Top Doctors
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Stem Cell Transplant
Jaroslav Maciejewski, MD, PhD
Castle Connolly Top Doctors
Edward Copelan, MD
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Stereotactic Radiosurgery
John Suh, MD
Castle Connolly Top Doctors
Gregory Videtic, MD
Cleveland Magazine Best Doctors

Testicular Cancer
Derek Raghavan, MD, PhD
Castle Connolly Top Doctors
Cleveland Magazine Best Doctors
Exploring Less Toxic Cancer Treatments

• Yogen Saunthararajah, MD, led a study that suggests cancer could be treated in a novel way that is much less toxic to healthy cells. Dr. Saunthararajah and his team found that the mechanisms that cause cancer cells to divide and grow uncontrollably often are different from the mechanisms that drive the growth of health stem cells. They altered an existing chemotherapy drug to selectively stop the growth of cancer cells and encourage the growth of healthy cells. The approach soon may be tested in clinical trials.

• New technologies employed by physicians and specialist in the Department of Radiation Oncology include the Clarity™ Breast System, an image-guided radiation therapy system for breast cancer that more accurately locates the treatment area for potentially fewer side effects. For patients with surface and recurrent tumors, hyperthermia therapy is used in conjunction with standard radiation therapy to make cells more sensitive to radiation so the dose delivered can be increased while minimizing damage to surrounding tissue.

Meeting Diverse Patient Needs

• As the population ages, so too does the number of older and elderly adults who face a cancer diagnosis in their lifetime. To meet the unique needs of older adults with cancer, the Taussig Cancer Institute Geriatric Oncology Program carefully assesses each individual to maximize the cancer treatment benefits and conducts clinical trials to evaluate effective cancer treatments for older adults.

• To address the disparities in cancer treatment and outcomes along race, ethnicity and socio-economic lines, Taussig Cancer Institute has developed a Patient Navigation Program. The program is offered at Huron Hospital and involves an outreach effort to provide education and cancer screenings in the community, and
to remove barriers to care or treatment for those with suspicious findings.

Cancer Findings from the Genomic Medicine Institute

- Charis Eng, MD, PhD, has discovered what may become a new way to assess the risk of some people developing inherited cancers. She has identified 16 specific locations in the human genome where imbalances of alleles made an individual more prone to prostate and breast cancer, and head and neck tumors.

Genetic mutations alone may not increase a patient’s risk for developing certain cancers. Dr. Eng and her team identified two enablers (microRNA) that appear to turn off tumor fighting genes, making it more likely that the cells will grow uncontrollably and cause cancer.

Improving Treatment Options

- Research to investigate and develop new and better treatment options for patients with cancer is ongoing at Taussig Cancer Institute. In 2008, more than 700 patients enrolled in research trials at Taussig Cancer and 80 percent of those patients participated in investigator-initiated trials. Participation in some clinical trials is available to patients at Taussig Cancer Institute regional sites located throughout the Cleveland area.

- Manjula Gupta, PhD, has developed the first blood test to distinguish thyroid cancer from non-cancerous nodules, reducing the need for surgery.

Clinical Trials and Translational Research

- The Department of Translational Hematology and Oncology Research conducts internationally recognized research to bring advances in cancer treatment and detection. As more is known about the human genome and its significance for cancer biology, abnormalities in malignant cells can serve as markers for the development of new drugs and diagnostics.
The Cleveland Clinic Taussig Cancer Institute is dedicated to providing exceptional cancer care and support to individuals with cancer. More than 250 cancer specialists, nurses and technicians work together to plan and implement treatment plans designed to meet the individual needs of each patient. The best in high-quality treatment, access to the latest technology and research, and the all encompassing “Patients First” philosophy make Taussig Cancer Institute a leading cancer center.

Taussig Cancer Institute encompasses both a comprehensive clinical cancer treatment facility and cancer research laboratories that conduct more than 350 clinical trials a year and produce internationally recognized, innovative translational research results. In 2008, more than 28,000 patients with cancer received treatment at the Cleveland-based Taussig Cancer Institute and at 10 locations throughout Northeast Ohio. Taussig Cancer Institute was rated number one in Ohio by U.S. News & World Report and number one in the United States by Hospital Review.

The institute is comprised of the following departments:

- Solid Tumor Oncology (Chair: Robert Dreicer, MD, FACP)
- Hematologic Oncology and Blood Disorders (Chair: Brian Bolwell, MD, FACP)
- Radiation Oncology (Chair: John Suh, MD)
- Regional Oncology (Chair: Tim Spiro, MD, FACP) and
- Translational Hematology and Oncology Research (Chair: Jaroslaw Maciejewski, MD, PhD).

In addition to these departments, the institute includes:

- Center for Clinical Research (Director: John Sweetenham, MD, FRCP) and
- Section of Palliative Medicine (Chair: Terence Gutgsell, MD).

High Quality Treatment Programs

In developing treatment plans for patients, Taussig Cancer Institute specialists collaborate in multidisciplinary teams across many specialties utilizing the best standard of care, as well as new and emerging technologies and treatments. Treatment clinics and programs for solid tumor and hematologic malignancies include:

Brain and Spinal Cord Tumors – The Brain Tumor and Neuro-oncology Center utilizes Gamma Knife technology for nonsurgical treatment for patients with a wide range of brain tumors including brain metastases, which afflict nearly one-quarter of cancer patients.

Breast Cancer – Taussig's cancer specialists and the Cleveland Clinic Breast Center collaborate to use innovative therapies for breast cancer, including treatment that may reduce the risk of onset or progression of the disease. The center also offers patients the latest treatments for breast cancer, including minimally invasive techniques and reconstructive surgery performed alone or together with therapeutic cancer surgery and precision-targeting radiation.

Colorectal Cancer – Cleveland Clinic’s colorectal surgeons pioneered the “no touch” technique that prevents the accidental spread of cancer cells during colorectal surgery. What's more, our surgeons are among a few in the Midwest performing transanal endoscopic microsurgery, an incision-free method of removing polyps and selected cancers in the colon and rectum.

Gastrointestinal Cancer – Patients with cancers of the esophagus, gall bladder, liver, pancreas and stomach are treated by multidisciplinary teams of medical oncologists, surgeons, and radiologists who work closely with specialists from our renowned Digestive Disease Institute. Our cancer specialists were among the first in the nation to offer radiofrequency thermal ablation for patients with liver metastases.
The Cleveland Clinic Taussig Cancer Institute is dedicated to providing exceptional cancer care and support to individuals with cancer. More than 250 cancer specialists, nurses and technicians work together to plan and implement treatment plans designed to meet the individual needs of each patient. The best in high-quality treatment, access to the latest technology and research, and the all encompassing “Patients First” philosophy make Taussig Cancer Institute a leading cancer center.

Taussig Cancer Institute encompasses both a comprehensive clinical cancer treatment facility and cancer research laboratories that conduct more than 350 clinical trials a year and produce internationally recognized, innovative translational research results. In 2008, more than 28,000 patients with cancer received treatment at the Cleveland-based Taussig Cancer Institute and at 10 locations throughout Northeast Ohio. Taussig Cancer Institute was rated number one in Ohio by U.S. News & World Report and number one in the United States by Hospital Review.

The institute is comprised of the following departments:

- Solid Tumor Oncology (Chair: Robert Dreicer, MD, FACP)
- Hematologic Oncology and Blood Disorders (Chair: Brian Bolwell, MD, FACP)
- Radiation Oncology (Chair: John Suh, MD)
- Regional Oncology (Chair: Tim Spiro, MD, FACP) and
- Translational Hematology and Oncology Research (Chair: Jaroslaw Maciejewski, MD, PhD).

In addition to these departments, the institute includes:

- Center for Clinical Research (Director: John Sweetenham, MD, FRCP) and
- Section of Palliative Medicine (Chair: Terence Gutgsell, MD).

**High Quality Treatment Programs**

In developing treatment plans for patients, Taussig Cancer Institute specialists collaborate in multidisciplinary teams across many specialties utilizing the best standard of care, as well as new and emerging technologies and treatments. Treatment clinics and programs for solid tumor and hematologic malignancies include:

**Brain and Spinal Cord Tumors** – The Brain Tumor and Neuro-oncology Center utilizes Gamma Knife technology for nonsurgical treatment for patients with a wide range of brain tumors including brain metastases, which afflict nearly one-quarter of cancer patients.

**Breast Cancer** – Taussig’s cancer specialists and the Cleveland Clinic Breast Center collaborate to use innovative therapies for breast cancer, including treatment that may reduce the risk of onset or progression of the disease. The center also offers patients the latest treatments for breast cancer, including minimally invasive techniques and reconstructive surgery performed alone or together with therapeutic cancer surgery and precision-targeting radiation.

**Colorectal Cancer** – Cleveland Clinic’s colorectal surgeons pioneered the “no touch” technique that prevents the accidental spread of cancer cells during colorectal surgery. What’s more, our surgeons are among a few in the Midwest performing transanal endoscopic microsurgery, an incision-free method of removing polyps and selected cancers in the colon and rectum.

**Gastrointestinal Cancer** – Patients with cancers of the esophagus, gall bladder, liver, pancreas and
Selected Publications
2008-2009

**JOURNALS**


Bae SI, Cheriyath V, Jacobs BS, Reu FJ, Borden EC. Reversal of methylation silencing of Apo2L/TRAIL receptor 1 (DR4) expression overcomes resistance of SK-MEL-3 and SK-MEL-28 melanoma cells to interferons (IFNs) or Apo2L/TRAIL. *Oncogene.* 2008 Jan 17;27(4):490-498.


Campbell SC. Editorial comment [Radical nephrectomy for pT1a renal masses may be associated with decreased overall survival compared with partial nephrectomy]. J Urol. 2008 Feb;179(2):472.


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Davis MP, Angst M. In reply [Opioid-induced hyperalgesia may be more frequent than previously thought]. J Clin Oncol. 2008 Mar 20;26(9):1565.


Gibson SE, Schade AE, Szpurka H, Bak B, Maciejewski JP, Hsi ED. Phospho-STAT5 expression pattern with the MPL W515L mutation is similar to that seen in chronic myeloproliferative disorders with JAK2 V617F. *Hum Pathol*. 2008 Jul;39(7):1111-1114.


Raghavan D, Klein EA. Prostate cancer: moving forward by reinventing the wheel...but this time it is round. *J Clin Oncol.* 2008 Oct 1;26(28):4535-4536.


Rini BI. Editorial comment [Risk score and metastasectomy independently impact prognosis of patients with recurrent renal cell carcinoma]. *J Urol.* 2008 Sep;180(3):878.


**BOOKS**


**BOOK CHAPTERS**


Cancer patients and their family members may attend weekly High Tea in the Taussig Cancer Institute Bistro to drink tea, eat pastries, listen to music and relax.
Supporting and caring for patients is the number one priority at Taussig Cancer Institute. In addition to clinical and research expertise, Taussig provides a large variety of programs and services to assist patients and their caregivers with the challenges of their cancer experience.

**Support Groups** – providing patients, families, and friends an opportunity to have their concerns, fears, and hopes reaffirmed by others who are experiencing similar life challenges. Support groups are led by our cancer institute’s oncology social workers, oncology nurses and psychologists who are specialists in providing reliable and helpful information in an atmosphere of encouragement.

**Reflections Wellness Program** – offering a variety of complementary and aesthetic services to Cleveland Clinic Taussig Cancer Institute patients. All treatments are designed to reduce anxiety and promote healing while patients are undergoing cancer treatments and leave them feeling their best.

**Late Effects Clinic** – following up with cancer survivors years after successful treatment to stave off or detect minor or serious side effects as early as possible.

**Fertility Preservation for Cancer Patients** – offers options prior to treatment for cancer patients who hope to eventually become parents.

**Scott Hamilton CARES Initiative** – the Scott Hamilton Cancer Alliance for Research, Education and Survivorship (CARES) initiative, created by the champion figure skater after successful treatment at Cleveland Clinic Taussig Cancer Institute, promotes cancer awareness, education and research.

**Chemocare.com** – developed jointly by Taussig Cancer Institute and the Scott CARES initiative, this website takes the mystery out of chemotherapy.

**The 4th Angel Mentoring Program** – a key component of the Scott CARES initiative, this patient-mentoring program matches newly diagnosed patients with trained volunteers who are cancer survivors.

**Cancer Answer Line** – For questions or concerns about cancer, or to schedule a second opinion, Monday through Friday, 8 a.m. to 4:30 p.m., call 216.444.7923 or toll-free 866.223.8100.

**Medical Concierge** – A complimentary service for patients and families who travel from out-of-state. Call 800.223.2273, ext. 55580, or email medicalconcierge@ccf.org

**Global Patient Services** – Complimentary assistance for national and international patients and families. Call 001.216.444.8184 or visit clevelandclinic.org/gps.

**Helen Meyers McLoraine Patient Resource Center**

Staffed by two clinical nurse specialists and an administrative coordinator, the Patient Resource Center is located in the northeast corner of Taussig Cancer Institute and is open from 8 a.m. to 4:30 p.m., Monday through Friday.

**Resources include:**
- Free pamphlets and informational brochures
- Computer terminals for searches
- A room for nurse/patient discussions, subcutaneous self-injection teaching and educational video viewing
- Listings and registrations for support groups and other patient-related events
- Listings of resources, such as wigs, transportation and lodging
An interview with Olympic ice-skating champion and cancer survivor Scott Hamilton

This year, the Scott Hamilton CARES Initiative celebrates its 10th anniversary. In this Q & A, Mr. Hamilton reflects on the first 10 years of his collaboration with Taussig Cancer Institute.

**Q:** How do you feel about the accomplishments of the Scott Hamilton CARES initiative so far?

**A:** Coming out of the gates, I wanted to be an active fundraiser to provide funding for research, and I’m still doing that. But ultimately, I realized that there were other important needs to be met. There really wasn’t a good resource for finding information about cancer care, and there’s a real strength and power in information. So we launched chemocare.com, which gives patients information that is user friendly, that’s not written in medical journals. It’s very technical and deep information, but it’s presented in a way that gives you a true understanding of the chemotherapy experience — what the drugs are and some of the side effects and issues involved. It’s a global entity since it’s on the World-Wide Web. A lot of oncology nurses are using it to give patients the information they need to understand what they are about to go through. So chemocare.com was a huge undertaking and a great success for us.

The 4th Angel Mentoring Program was very important as well. Going through the cancer experience, I realized that I was asking a lot of people for information, but I was asking people who never had cancer and had just watched others go through it. So I realized that if I could get the information from another cancer patient, another survivor, someone who had the same type of cancer as me and had been through it, they could understand the questions that I was asking and better answer what’s in store for me. I just thought that would be a good thing to have. The 4th Angel Mentoring Program has grown rapidly and they are doing a great job matching patients with survivors of similar cancer and treatment.

**Q:** How do you feel you have been most able to change the lives of cancer patients?

**A:** It’s just information. When you are going through a cancer experience, you want to be able to understand what it takes to properly combat the situation. And information is just so important. Obviously the research is being done. It’s what ultimately is going to save your life. But to know where you stand is so much healthier.

And learning how to cope with the new issues in your life is extremely important. It not only adds a better understanding, but also gives you great comfort and a quality of life that you may not have been able to achieve without that information. With the right information and the right perspective, you’re better able to combat the disease and live more happily day to day.

**Q:** What made Cleveland the right place to launch Scott Hamilton CARES?

**A:** I was very familiar with the hospital, being treated here. I’m an Ohio guy, which gives me kind of a local perspective. And I just really loved the way I was treated at the Taussig Cancer Institute. I became a huge fan of the hospital by being a resident of the place, and it just filled me with confidence. It was a fantastic experience, but I realized the help that was needed in just filling in the gaps in the overall cancer experience for each patient.

**Q:** A lot of people look up to you. Who do you most admire?

**A:** I admire anyone and everyone who is enduring this moment in their lives when they are dealing with cancer. It’s very frightening. But when I see and meet these patients who are going through chemotherapy or radiation, surgeries, or whatever, and they are dealing with their cancers effectively and with great courage and determination, I’m inspired. Away from all of that, in my everyday life I’m inspired, because I see all of these people being champions in life.
Q: What do you most want to say to other people who might today be facing a cancer diagnosis?

A: Help is on the way. We’re doing everything we can to fund young, brilliant minds to find the next answers, to treat and cure cancer. I lost my mother to cancer. I’ve survived cancer. I’ve had so many dear, dear friends be exposed to this disease, whether personally or members of their families, and it’s ultimately curable. We just need to keep funding research and driving the message home that this is something we can accomplish. We just need to get busy.
Cancer Consult provides information from Cleveland Clinic Taussig Cancer Institute specialists about innovative research and diagnostic and management techniques.

**Please direct correspondence to**
Brian Rini, MD, Medical Editor
rinib2@ccf.org
Taussig Cancer Institute/R35
Cleveland Clinic
9500 Euclid Avenue
Cleveland, OH 44195

Cleveland Clinic Taussig Cancer Institute annually serves more than 26,000 cancer patients. More than 250 cancer specialists are committed to researching and applying the latest, most effective techniques for diagnosis and treatment to achieve long-term survival and improved quality of life for all cancer patients. Taussig Cancer Institute is part of Cleveland Clinic, an independent, not-for-profit, multispecialty academic medical center.

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Brian Rini, MD
Solid Tumor Oncology

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Services for Physicians

Physician Directory: View all Cleveland Clinic staff online at clevelandclinic.org/staff.

Physician Liaison: Referring physicians have a dedicated personal liaison at Cleveland Clinic with our Physician Liaison to help with any interaction involving Cleveland Clinic. Contact Physician Liaison Kate Kenny at clevelandclinic.org/ContactKate.

Critical Care Transport Worldwide: Cleveland Clinic’s critical care transport team serves patients of all ages and complex patients across the globe. This team, which comprises mobile ICU vehicles, helicopters and fixed-wing aircraft. The transport teams are staffed by physicians, nurse practitioners, critical care nurses, technicians and ancillary staff, and are customized to meet the needs of the patient. Critical care transport is available for children and adults.

To arrange a transfer for STEMI (ST elevated myocardial infarction), acute stroke, ICH (intracerebral hemorrhage), SAH (subarachnoid hemorrhage) or aortic syndromes, call 877.279.CODE (2633).

For all other critical care transfers, call 216.444.8302 or 800.553.5056.

Track Your Patient’s Care Online: Whether you are referring from near or far, DrConnect offers secure access to your patient’s treatment progress at Cleveland Clinic. To establish a DrConnect account, visit clevelandclinic.org/drconnect or email drconnect@ccf.org.

Remote Consults: Request a remote medical second opinion from Cleveland Clinic. MyConsult is particularly valuable for patients who wish to avoid the time and expense of travel. Visit clevelandclinic.org/myconsult, email clevelandclinic@ccf.org or call 800.223.2273, ext 43223.

Outcomes Data Available: The latest Outcomes book from Cleveland Clinic Taussig Cancer Institute is available. Our ongoing book contains clinical outcomes data and information on volumes, in addition to system and publications. To view our latest book, go to clevelandclinic.org/quality.

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CME and Custom Learning Opportunities

Neuro-Oncology 2009: Current Concepts
September 11-12, 2009
The Ritz Carlton Hotel
Cleveland, Ohio
Target Audience: neurosurgeons, radiation oncologists, medical oncologists, neurologists and allied health professionals who work with patients with tumors

Multidisciplinary Breast Cancer Summit
September 11-12, 2009
InterContinental Hotel and Bank of America
Cleveland, OH
Target Audience: physicians and allied health professionals in medicine, surgery, plastic surgery, medical oncology, radiation oncology, radiology and genetics

Society for Hematopathology 2009 Workshop
The Spectrum of Immunoproliferative Disorders and the Border Between B-Cell Lymphoma and Plasma Cell Neoplasms
September 24-26, 2009
InterContinental Hotel and Bank of America Conference Center
Cleveland, Ohio
Target Audience: pathologists, practicing and in training.

7th Annual Innovation Summit
Improving the Prognosis: Cancer Cures Through Innovation
October 5-7, 2009
InterContinental Hotel and Bank of America Conference Center
Cleveland, Ohio
Target Audience: senior healthcare industry executives, venture capitalists, researchers, and other service providers.

9th Annual Multidisciplinary Genitourinary Oncology Course
November 18, 2009
InterContinental Hotel and Bank of America Conference Center
Cleveland, OH
Target Audience: medical oncologists, urologists, radiation oncologists, pathologists and nurses.

ASTRO Review
December 9, 2009
Embassy Suites Hotel
Independence, OH
Target Audience: radiation oncologists, medical oncologists, hematologists, physicists and nurses.

For more information, including a list of international programs and online CME topics, please call the Cleveland Clinic Continuing Education Department at 800.238.6750 or visit clevelandclinicmeded.com/cancered.

To arrange an in-house, custom presentation by one of our staff, email masonm@ccf.org.