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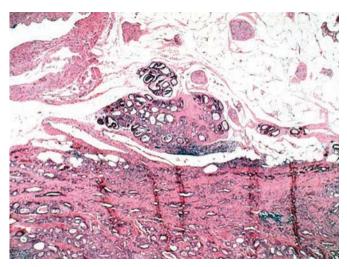
Novel Agents, Approaches Offer New Promise

olumbia and Weill Cornell researchers at NewYork-Presbyterian Hospital are taking a leading role in efforts to expand the therapeutic armamentarium available for the treatment of various cancers in both children and adults. Many of the resulting studies have received grant funding from the National Cancer Institute, with the Hospital as the lead study site.

Daniel Petrylak, MD, for instance, is the principal investigator of a Phase I safety study of docetaxel plus the antiangiogenesis drug lenalidomide for treatment-resistant prostate cancer. An internationally recognized leader in prostate cancer research, Dr. Petrylak treated the first prostate cancer patients with docetaxel and estramustine in 1996. Promising results seen in

the Phase I and II trials of this combination led to a large Phase III trial of docetaxel/estramustine in the Southwest Oncology Group, (SWOG 99-16) in the late 1990s. This trial was among the first to demonstrate a survival benefit for chemotherapy in patients with metastatic prostate cancer, and supported the FDA's approval of docetaxel for prostate cancer in 2004. Now, with the addition of lenalidomide, Dr. Petrylak hopes to further extend survival in patients with prostate cancer that have failed hormone therapy or surgical castration.

"Doxetaxel is the only chemotherapy that improves survival in this disease," he noted. "If the combination of doxetaxel and lenalidomide is effective, it will expand the spectrum of prostate cancer



An image of prostate cancer cells invading the tissue surrounding the gland. New therapies under study may improve outcomes in treatment.

therapy to include radiotherapy, surgery, hormonal therapy, and combination chemotherapy."

Docetaxel is FDA-approved for the treatment of certain types of breast, non–small-cell lung cancer, squamous cell carcinoma of the head and neck, and gastric and prostate cancer. Lenalidomide is FDA-approved for multiple myeloma and transfusion-dependent anemia due to myelodysplastic syndromes. Dr. Petrylak's Phase I trial is ongoing and is currently recruiting patients with treatment-resistant prostate cancer. Ultimately, this open-label study will enroll 50 patients. Patients will remain on the study drugs for as long as they respond to or tolerate the treatments. If treatment with the see Drug Therapies, page 7

Radiation Oncology Focuses on Customization

olumbia and Weill Cornell researchers at NewYork-Presbyterian Hospital constantly strive to find clues to one of the key unsolved mysteries in the field of oncology: that the same malignant disease can express itself differently among the patients who suffer from it. As part of this effort the Herbert Irving Comprehensive Cancer Center and Weill Cornell Cancer Center at NewYork-Presbyterian Hospital, like many cancer centers across the country,

have done away with the concept of one-size-fits-all care. Although cancer treatment is still modified for such variables as tumor location, grade, or histology, researchers are now focused on the individualization of treatment based on molecular features, paving the way for true customization of care.

"We are accumulating a great deal of information about how tumor metabolism and molecular see Radiation Oncology, page 6

Initiatives Seek to Educate, Support Breast Cancer Patients

olumbia and Weill surgeons at NewYork-Presbyterian Hospital are seeking to enhance the experience of care for breast cancer patients through initiatives focusing on doctor-patient communication, cosmesis, and empathy. At both NewYork-Presbyterian Hospital/Columbia University Medical Center and NewYork-Presbyterian Hospital/Weill Cornell Medical Center, the comprehensive Breast Centers offer each patient access to a team of specialists including surgeons, medical oncologists, pathologists, radiation oncologists, gynecologists, geneticists, psychiatrists, physical therapists, and nutritionists, in addition to physician assistants and specialized nurses. NewYork-Presbyterian/Weill Cornell has recently received funding for the Cosmetic Breast Cancer Surgery Center, which will open this fall with the goal of establishing protocols designed to produce optimal cosmetic results.

"We have an excellent surgery department, but the best outcome depends on a multidisciplinary team, and I think we excel in coordinating care and bringing multiple specialists together to direct patients to the best possible combination of modalities," noted Alexander J. Swistel, MD, Chief of the Breast Center at NewYork-Presbyterian/ Weill Cornell.

"From the beginning of my career, I have always tried to see the process through the patients' eyes," added Sheldon M. Feldman, MD, the new Chief of the Comprehensive

Breast Center at NewYork-Presbyterian/ Columbia. "We want to cure cancer, but we want to keep the care as patient-focused as possible. I am joining a program that is already extremely well regarded in its ability to lead breast cancer treatment toward better outcomes, but we can go beyond ensuring that patients consistently have access to the highest standards of care. I want to play a role in upgrading the experience of the care, so that patients consistently feel that they are our first priority."

"There are many techniques that we and others have developed, but no one has put this together before."

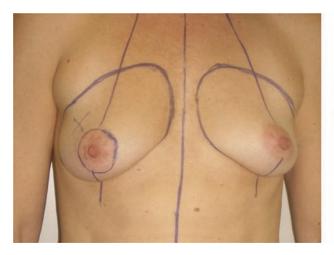
- Alexander J. Swistel, MD

As part of his new role, Dr. Feldman is planning to become involved in the logistics of care, working with staff to develop a system to ensure that phone calls are always returned promptly, that the e-mail system is responsive, and that physician-patient communication is optimized. Patients will be able to schedule appointments by e-mail. The goal is to provide timely, easily accessible, high-standard care. For physicians involved in the treatment of cancer, it is easy to overlook the ongoing concerns of the patient, particularly in the early period after the diagnosis.

"Patients have an enormous amount of information to digest, and the field just constantly grows more complex as we move toward individualization of care," said Dr. Feldman. "Generally, it is the breast surgeon who leads the team and is the person through whom the patient accesses the system, so we need to know the whole process, not just the surgical aspect."

Dr. Swistel also believes strongly in the role of the surgeon as a coordinator of care, with a focus on the contributions of nonsurgical departments to optimize breast cancer care. He noted that radiation oncologists at the Hospital have been leaders in targeted therapy after lumpectomy, and the genetics team has rapidly evolved into one of the best and busiest. Among the numerous recent innovations in the management of breast cancer that are evidence of the constant effort to find better ways to eradicate tumors and improve the patient's experience, Dr. Swistel said the Cosmetic Breast Cancer Surgery Center is "the biggest news." Long interested in defining and refining techniques for a cosmetically acceptable results after surgery, radiation, or both, Dr. Swistel called the new Center "a dream come true" for the increasing number of breast cancer survivors.

"There are many techniques that we and others have developed, but no one has put





Surgeons at NewYork-Presbyterian Hospital are perfecting nipple- and muscle-sparing procedures such as Deep Inferior Epigastric Perforator (DIEP) to improve the quality of life for breast cancer patients. At left, is the pre-op mark-up; at right, a patient's breasts post-op.

this together before," said Dr. Swistel. "Our goal is to apply strategies so that women look like they never had breast cancer." Initiatives in this area at NewYork-Presbyterian include a relatively new nipple-sparing oncoplastic surgery procedure for patients undergoing complete mastectomy that may also be useful in high-risk patients considering prophylactic mastectomy.

"With this technique, all of the breast tissue is removed except the skin and nipple," noted Dr. Feldman. "Other tissue or an implant is then inserted matching the volume lost and preserving the normal appearance of the breast. We now have a growing experience with this technique and can offer it to selected patients knowing that it is a safe option. For patients at high risk for breast cancer but reluctant to undergo mastectomy because of concern about the cosmetic result, this is an excellent approach to restoring the breast to its presurgical state."

According to Dr. Swistel, surgeons at the Hospital have also been active in performing oncoplastic reduction surgery, in which women with large breasts undergoing lumpectomy also have the size of their breasts reduced. For those with breasts large enough to cause back strain, the surgery can improve quality of life while possibly reducing the risk for breast cancer by decreasing the amount of breast tissue.

Some of the most exciting innovations in breast cancer surgery go beyond surgery in the conventional sense. As an example, Dr. Feldman cited a minimally invasive intraductal approach to the treatment of breast cancer called ductoscopy. In this procedure, miniaturized endoscopes are inserted through the nipple. Tumor cells within the milk ducts are ablated by energy or medication delivered through the scopes, so that many patients can ultimately avoid traditional surgery.

"The field is moving so quickly toward new technologies that eradicate malignancy that I can envision a time when people look back at surgery as quite primitive," he said. "With many of the techniques, the promise is not just a better result but a much easier experience for the patient."

Contributing faculty for this article: Sheldon M. Feldman, MD; Alexander J. Swistel, MD

NewYork-Presbyterian Oncology

is a publication of the Cancer Centers of NewYork-Presbyterian Hospital. The Cancer Centers are at the forefront of cancer prevention and screening, diagnosis, treatment, basic science, and clinical research. The Cancer Centers serve more than 6,500 new cancer patients each year, who receive state-of-the-art multidisciplinary care. The Cancer Centers include the NCI-designated Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian Hospital/Columbia University Medical Center and the Weill Cornell Cancer Center at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, which are respectively comprised of faculty from Columbia University College of Physicians and Surgeons and Weill Cornell Medical College.

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NewYork-Presbyterian Hospital's Cancer Prevention Newsletter

and Web site offer information for professionals on the latest developments in the field of cancer prevention and screening. Visit nypcancerprevention.org.

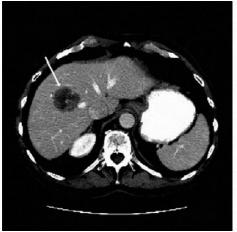
Team Seeks to Apply Radioembolization to Liver Cancer

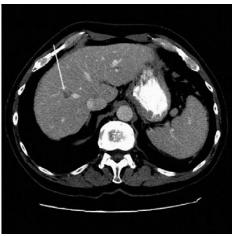
or patients who have primary hepatic malignancies or metastases that cannot be managed with resection, chemotherapy, or external beam radiation, the treatment options have been limited until recently. Researchers at the Herbert Irving Comprehensive Cancer Center and Weill Cornell Cancer Center at NewYork-Presbyterian Hospital, however, are spearheading the development of a new treatment: radioembolization. With this technique, radioactive microspheres are deposited within the liver precisely at the site of the malignancy. Localizing the radiation to the tumor makes possible a highly targeted kill of malignant cells, preserving healthy liver tissue that would likely be lost with another, more traditional approach.

"Only a small number of centers have developed an active program with this approach; for some patients, it is really the only intervention with the potential to control disease," noted David L. Sherr, MD. When distributed optimally, "radioembolization is so conformal that most of the normal adjacent liver cells are unaffected."

"For the patients who will be considered for this procedure, there is really no other option at this point," agreed David C. Sperling, MD. Noting that survival periods have more than doubled in some of the clinical trials in which patients were treated with radioembolization, Dr. Sperling added that the quality of the survival is also good. Because the dose is localized, the treatment offers the advantages of both efficacy and safety. "This is another weapon in the armamentarium," he said. "But it can be a very important new option for selected patients."

The FDA has approved 2 similar systems for the treatment of liver metastases secondary to colorectal cancer. They differ in the composition of the microspheres to which the radioactive isotope yttrium 90 (90Y) is bound, which may be important, but both deliver the microspheres via a catheter threaded to the hepatic artery, which supplies blood to both malignant and normal liver tissue. In general, the advantage of the microspheres is that they emit a high dose of radiation over a very short distance. Studies suggest that the dose of radiation is wholly contained within the patient's body, and only a small fraction reaches the skin surface. With the system currently in use at NewYork-Presbyterian Hospital, all





CT scans of patients with liver tumors who underwent radioembolization with microspheres. The procedure offers the benefit of targeted kills of cancer cells and increased safety.

but 2.5% of the delivered radioactivity dissipates 14 days after administration of the microspheres, which are not flushed out of the liver but remain there after they have become inactive.

"Radioembolization can be very effective in the right patient... It is an excellent complement to current therapies."

-Jason Funderburk, MD

"The goal is not usually cure but increased survival. However, the results can be dramatic. There are frequent cases of a complete response, even with large tumors," said Jason Funderburk, MD. "These kinds of results are very encouraging in a group of patients for whom we really have had nothing else to offer."

Chemotherapy is often relatively ineffective in controlling liver tumors, particularly when they are large. Newer ablation techniques offer several advantages over surgical resection, including less morbidity, but neither ablation nor resection is an option for patients with large or diffuse liver tumors. A dose of externally administered radiation sufficient to eradicate a large tumor would at the same time also be likely to damage enough normal liver tissue to cause liver failure.

Appropriate mapping of the tumor and control of the blood flow are necessary for

delivery of the microspheres to provide an optimal kill of malignant cells with minimal adverse effects on healthy tissue; it is particularly important to avoid outflow that would carry the radioactive beads to other organs. A multidisciplinary team of radiation oncologists and interventional radiologists collaborate on each procedure to ensure these goals are achieved.

The potential benefits of radioembolization may not yet be fully realized. In patients with primary tumors of the liver, this technique may be able to shrink the mass sufficiently for them to meet the criteria for liver transplantation, a potentially curative procedure; this strategy is currently under investigation. Dr. Funderburk also reported that it is not yet clear how to use radioembolization in patients with complicating features, such as previous exposure to bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor.

"Bevacizumab affects the body's vasculature and is not a good match with radioembolization, so this can be an issue for someone exposed to this or other biologics that affect the blood supply," Dr. Funderburk noted. "We expect to accumulate one of the largest data sets anywhere on the use of radioembolization. This procedure is an excellent complement to current therapies. It can be very effective in the right patient, and it is gratifying to see a good response in a patient for whom there was really nothing else to offer."

Contributing faculty for this article: Jason Funderburk, MD; David L. Sherr, MD; David C. Sperling, MD

Technology Expands Offerings in Rectal Cancer Surgery

Due to several important initiatives, Columbia and Weill Cornell surgeons at NewYork-Presbyterian Hospital have been leading efforts to redefine minimally invasive rectal cancer resections with procedures such as transanal endoscopic microsurgery (TEMS) and minimally invasive techniques such as laparoscopy and endolumenal procedures.

"The whole concept of endolumenal surgery is moving rapidly because of new designs of scopes and tools that are expanding what we can achieve from a minimally invasive approach," said Jeffrey W. Milsom, MD. "We have been participating in formal arrangements with industry to help design the tools going forward. We are not just adapting the new technologies; we are contributing to the advances."

One of the major attributes of minimally invasive surgery is a quick recovery, but the Columbia and Weill Cornell investigators at NewYork-Presbyterian are proceeding only when it is clear that the quality of surgery will not be compromised. As the word "minimally" implies, the degree of invasiveness can range widely, depending on the procedure. Surgeons at NewYork-Presbyterian Hospital/Weill Cornell Medical Center are leading a multicenter study in which the hypothesis is that hand-assisted laparoscopy will be superior to straight laparoscopy in the treatment of rectal cancer, even though it requires an extra incision. Previous studies have already demonstrated significant reduction in operating time (Table).

"The laparoscopic approach to rectal cancer has been controversial because of initial reports that minimally invasive procedures led to an increase in positive margins, higher recurrence rates, and a higher rate of

complications, such as anastomotic leaks," noted Sang Lee, MD, principal investigator of a multicenter, randomized study involving both Columbia and Weill Cornell surgeons that compares instrument-only laparoscopy to hand-assisted laparoscopy. He added that a European study has already indicated that laparoscopy can be as effective for rectal cancer resection as an open procedure. Dr. Lee suggested that it might be possible to build on the advantages of laparoscopy simply by adding an extra incision to the procedure that will reduce operating time.

"We are moving directly to a comparison of two laparoscopic techniques," he said. "The primary outcome is operating time, but we will be looking at a variety of end points, including positive radial margin, number of harvested lymph nodes, sexual and urinary functions, recovery time, complications, and relapse. We think that the hand-assisted approach will accelerate the process. Not long ago, there was substantial resistance from laparoscopic purists about hand-assisted procedures, but I think many of us are now changing our perspective. There really seems to be no downside to the extra incision."

At NewYork-Presbyterian, increasing numbers of procedures are being evaluated in which "minimally invasive" means circumventing the need for any external incisions. One of the best examples is the TEMS procedure, which allows removal of rectal polyps not accessible with standard instruments through the anus. In TEMS, a circular piece of the rectal wall with the polyp in its center is excised through a special anoscope, which provides access to polyps that are otherwise out of reach. The wound is then closed with special sutures. Unlike laparoscopy, the majority of patients after TEMS

can return home after only an overnight hospitalization. Characteristic of endolumenal procedures being pursued at the Hospital, TEMS is redefining minimally invasive surgery.

"TEMS is technically challenging, but we have been deeply involved in minimally invasive surgery for several years and have a deep pool of surgeons with good skills in these types of techniques," said Richard L. Whelan, MD, who credited Daniel Feingold, MD, with refining the TEMS approach at NewYork-Presbyterian Hospital/Columbia University Medical Center. "Selecting the right candidate is important. However, for those who are suitable, TEMS has the potential to substantially reduce the dangers of and the trauma associated with a standard rectal cancer resection."

TEMS is seen as another step on the road to a reorientation in gastrointestinal surgery at NewYork-Presbyterian. According to Dr. Milsom, the Hospital recently recruited Fred Cornhill, DPhil, previously Director of the Institute of Biomedical Engineering at the University of Oxford, to participate in their effort to rethink approaches to minimally invasive surgery that include not only better instrumentation, but better intraoperative imaging.

"What we are seeing is a drastic redesign of the operating room that will allow imaging to play a far more important role in guiding the procedure," Dr. Milson said, adding that the Helmsley Operating Room at NewYork-Presbyterian/Weill Cornell has been designed so that intraoperative 3-dimensional imaging can be used to achieve a precision that is as good as or better than that achieved in open surgeries. In general, the advances at the Hospital are expected to facilitate a growing number of resections for rectal tumors to be performed without any external excisions. Whenever a minimally invasive procedure can be substituted for an open technique with similar results, it yields major benefits for the patient.

"We are dedicated to this concept and are helping to bring it forward," Dr. Whelan said. "For the right patient, minimally invasive surgery allows us to greatly improve the experience of surgery for the patient without compromising the result."

Table. Hand-Assisted Laparoscopic vs. Straight Laparoscopic Colorectal Surgery

	Hand-Assisted	Straight
No. of Patients	47 (33 sigmoid/left colectomy, 14 total colectomy)	48 (33 sigmoid/left colectomy, 15 total colectomy).
Mean operative time sigmoid/ left colectomy, min ^a	175±58	208±55
Mean operative time total colectomy, min ^b	127±31	184±72

^a P=0.021 ^b P=0.015

Source: Dis Colon Rectum. 2008;51(6):818-826.

Contributing faculty for this article: Sang Lee, MD; Jeffrey W. Milsom, MD; Richard L. Whelan, MD

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differences should influence treatment decisions," said K.S. Clifford Chao, MD. "The whole field is moving to this individualization of care based on a broader and more detailed characterization of tumor features."

In a step designed to further coordinate research efforts in this area at both NewYork-Presbyterian/Columbia and NewYork-Presbyterian/Weill Cornell, Dr. Chao has been appointed to the newly created position of Director, Combined Program in Radiation Oncology. This is the first oncology program at the Hospital to be combined under a single leader. The goal is to integrate the research and treatment expertise at both centers to ensure patients are receiving the best care possible.

"Regardless of the first point of contact, patients will get radiation therapy individualized to suit their specific needs," said Dr. Chao. "The goal is to integrate our strengths across facilities. Radiation oncology has become increasingly complex, and it is reasonable to expect that the specialization that generates advances in one area has the potential to complement other equally important approaches. We are very aware of these relative strengths and weaknesses. By better integrating our capabilities, we can consistently play to our strengths."

The individualization of treatment is not a new concept to Dr. Chao; it has been the main focus of his research for years. At the University of Texas M.D. Anderson Cancer Center, Houston, Dr. Chao pioneered functional image-guided intensity-modulated radiation therapy (IMRT), which combines positron emission tomography (PET) and

computed tomography (CT) images to customize radiation treatment. This concept of individualized care based on the molecular signature of a tumor is pivotal to the future of IMRT.

"The goal is to integrate our strengths across facilities. Radiation oncology has become increasingly complex.... By better integrating our capabilities, we can play to our strengths."

-K.S. Clifford Chao, MD

"The CT scans with or without MRI provide the anatomical information, while PET provides information about both molecular features and metabolic activity," said Dr. Chao, who has published multiple articles and written a well-regarded textbook on this topic. "You can obtain details about the molecular make-up of a tumor through biopsy, but PET is noninvasive, which is a significant advantage when trying to minimize the morbidity of cancer care."

According to Dr. Chao, the customization of radiation treatment leads to improved outcomes for obvious reasons: More targeted therapy can result in more damage to the tumor while reducing toxicity to healthy tissue. Learning in advance which tumors are vulnerable and which are resistant to radiation may result in a completely new therapeutic approach, he said, channeling patients to their best opportunity for a treatment response. In a published study, Dr. Chao and colleagues found that a computer-assisted contouring system reduced the variation in target volume delineation among physicians with different experiences in head and neck IMRT and saved contouring time (Int J Rad Onc Biol *Phys*, 2007;68(5):1512–1521).

"At NewYork-Presbyterian, where there are dozens of research protocols underway at any one point in time, there is a very active effort to make specialists in one area fully aware about what specialists in another area can offer their patients," he explained. "With a single infrastructure for radiation oncology, we have an enormous opportunity to deliver the highest quality of cancer treatment in a consistent fashion."

Dr. Chao will continue his research on IMRT and molecular imaging at NewYork-Presbyterian, where it will integrate with similar efforts in other oncology departments to understand the distinctive features of individual malignancies that make them more or less vulnerable to any single strategy. Although the ultimate goal is curing malignancies, Dr. Chao said that individualized care also has a great deal to offer for reducing the long-term toxicity of cancer treatments, which in turn will affect the patient's quality of life.

"Limiting toxicity can be a major advance, even if response rates remain the same," he noted. "There is much greater concern of preserving quality of life in patients with cancer, which can greatly relieve the psychological burden."

> Contributing faculty for this article: K.S. Clifford Chao, MD

Table. Time Analysis for Use of IMRT in Patient with Base of Tongue Cancer

Frequent HN IMRT physicians				Sporadic HN IMRT physicians					
Physician no.	CFS time (min)	CAT time (min)	Ratio	Time saving (min)	Physician no.	CFS time (min)	CAT time (min)	Ratio	Time saving (min)
8	24	29	1.21	-5	2	43	24	0.56	19
6	38	31	0.82	7	1	65	16	0.25	49
7	45	29	0.64	16	3	50	37	0.74	13
5	69	20	0.29	49	4	60	35	0.58	25
Average	44	27	0.74	17	Average	55	28	0.53	27

CAT, computer-assisted target volume delineation; CFS, contouring from scratch; HN, head and neck; IMRT, intensity-modulated radiation therapy Source: Int J Rad Onc Biol Phys. 2007;68(5):1512-1521.

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combination of doxetaxel and lenalidomide proves safe, Dr. Petrylak plans to begin a Phase II trial to assess efficacy.

Dawn Hershman, MD, MS, and Katherine Crew, MD, MS, meanwhile, have been awarded a National Cancer Institute grant to study the safety and tolerability of polyphenon E, an ingredient in green tea that may help prevent new breast cancer from developing in women with a history of hormone receptor—negative breast cancer.

"One of my main interests is cancer survivorship in breast cancer, and one of the components of survivorship is reducing the risk of secondary malignancy," said Dr. Hershman, an oncologist and epidemiologist. "Women who have breast cancer are at the highest risk of developing cancer in the other breast. For women with hormone receptor-positive cancer, we can treat them with tamoxifen and aromatase inhibitors to reduce this risk-but for women who had hormone receptor-negative breast cancer, we don't have any medications for preventing new cancers. There is a considerable amount of epidemiologic data and some preclinical laboratory evidence that polyphenon E, a compound in green tea, can reduce the risk of recurrent cancer, possibly because of its very high antioxidant level."

"The problem with just drinking green tea is that it is usually caffeinated, and you have to drink a lot of it to possibly have these preventive effects, so we decided to test the active compound, polyphenon E, in a Phase I tolerability and toxicity study," added Dr. Crew. "In addition, we hope to find the best dose that we can use in a prevention study in the future if the Phase I study is successful."

The 6-month study will enroll 40 patients (active drug, 30; placebo, 10) with a prior history of estrogen receptor—negative breast cancer previously treated with surgery, chemotherapy, or radiation. More than half of the participants have already been enrolled. In addition to NewYork-Presbyterian Hospital/Columbia University Medical Center, the lead institution in the study, patients will enroll at M.D. Anderson Cancer Center, Houston; Baylor College of Medicine, Houston; and Memorial Sloan-Kettering Cancer Center, New York City.

Also in the area of breast cancer research, Linda Vahdat, MD, and her team at NewYork-Presbyterian Hospital/Weill Cornell Medical Center are currently involved in 9 trials studying the safety and efficacy of several therapeutic options for metastatic and recurrent disease. Study drugs include eribulin, ixabepilone, ZK-Epothilone, CR011, CLN-20, SAHA (suberoylanilide hydroaxamic acid), and tipifarnib combinations with paclitaxel or fulvestrant. The team is also looking at the role of the amino acid glutamine in the reduction of neuropathic pain associated with breast cancer and its treatment. In addition, in conjunction with pediatric oncologists David C. Lyden, MD, and Rosandra Kaplan, MD, Dr. Vahdat and her team have 3 studies under way to understand the role of bone marrowderived hematopoietic stem cells in the trafficking of metastases in women with various stages of breast cancer.

determine the maximum allowable dose of bevacizumab, a vascular endothelial growth factor (VEGF)-neutralizing antibody in pediatric patients, based on safety and toxicity. The team's work paved the way for the soon-to-be-initiated Phase II trials of the drug, which will study bevacizumab in combination with chemotherapy in dosing schedules similar to adults.

Dr. Glade-Bender's work was part of a larger effort within the Herbert Irving Division of Child & Adolescent Oncology Center at Morgan Stanley Children's Hospital to expand the role of its physicians in the oft-underfunded area of pediatric cancer research, according to Michael Weiner, MD. The Center is among 20 Phase I developmental therapeutic sites managed by the

"Doxetaxel is the only chemotherapy that improves survival prostate cancer. If the combination of doxetaxel and lenalidomide is effective, it will expand the spectrum of prostate cancer therapy to include radiotherapy, surgery, hormonal therapy, and combination chemotherapy."

-Daniel Petrylak, MD

"From a clinical point of view, to prevent metastases in women with breast cancer and a high risk of relapse, we are studying the ability of a copper-depletion compound called tetrathiomolybdate to keep the 'angiogenic switch' in the 'off' position, keeping the patients metastasis-free," noted Dr. Vahdat. "We are very excited to be able to offer an additional option that has the hope of being beneficial to our patients with breast cancer at high risk of relapse."

Since chemotherapy's side effects, especially peripheral neuropathy, can be debilitating, Dr. Vahdat's group is also collaborating with scientists at Rockefeller University, New York City, to understand the effects of chemotherapy on the peripheral nerves. It is expected that the results of that study will help clinicians understand and treat the problem.

Julia Glade-Bender, MD, a pediatric oncologist at Morgan Stanley Children's Hospital of NewYork-Presbyterian/Columbia, was the principal investigator of a recent successful Phase I trial of bevacizumab, an antiangiogenic agent. The goal of the study (*J Clin Oncol* 2008;26[3]:399-405) was to

Children's Oncology Group, a national consortium sponsored by the National Cancer Institute and dedicated to clinical trials for children, adolescents, and young adults with cancer. In addition, it has joined other leading pediatric cancer centers in 2 smaller consortia focused on clinical trials for patients with refractory neoplastic diseases: NANT (New Approaches to Neuroblastoma Therapy) and TACL (Therapeutic Advances in Childhood Leukemia).

"One of the gratifying aspects of treating childhood cancers is that they are very responsive to treatment," said Dr. Weiner, "but children's cancers are different diseases from adult cancers, and merit different therapeutic approaches. Our program includes 15 pediatric oncologists, nurse practitioners, research nurses, data managers, and others on the clinical team that allow us to conduct 15 to 20 Phase I trials at any one time."

Contributing faculty for this article: Julia Glade-Bender, MD; Katherine Crew, MD, MS; Dawn Hershman, MD, MS; Daniel Petrylak, MD; Linda Vahdat, MD; Michael Weiner, MD

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