

## Immunotherapy for Smoldering Myeloma

Clinical trials test PD-1, CD38 inhibitors to delay progression from premalignant disease to multiple myeloma

By Bryan Tutt

Until recently, patients with smoldering myeloma had no option but to watch and wait for the inevitable progression to malignancy. But now, two clinical trials of immunotherapy drugs offer patients with the precancerous condition a chance to delay disease progression and perhaps add years to their lives.

Smoldering myeloma has no symptoms and is diagnosed chiefly by levels of myeloma-produced proteins (e.g., monoclonal protein, free light chain proteins) in the serum and clonal plasma cells in the bone marrow. These levels help clinicians classify patients' disease as low, intermediate, or high risk.

Because smoldering myeloma is expected to progress to multiple myeloma, a patient's risk level indicates how soon this progression is likely to occur. Intermediate-risk smoldering myeloma, for example, indicates a 50%–74% chance of progression to multiple myeloma within 5 years. Patients' risk levels help determine the frequency of clinic visits to monitor their disease.

Although observation is the stan-



MD Anderson patient Robert Brown (right), a physician from Alabama, discusses his treatment with **Dr. Elisabet Manasanch**. Dr. Brown has been diagnosed with smoldering myeloma and receives the immunotherapy drug pembrolizumab in a clinical trial.

dard management strategy for smoldering myeloma, several clinical trials have evaluated the use of approved multiple myeloma chemotherapy regimens to delay the progression of smoldering

myeloma. One recent study, a multicenter phase II trial, evaluated a regimen of carfilzomib, lenalidomide, and dexamethasone in patients with high-risk smoldering myeloma. The results were

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# Immunotherapy for Smoldering Myeloma

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promising; however, the regimen was arduous for patients.

“Patients in that trial had two infusions a week for 8 months, plus stem cell collection for transplant-eligible patients,” said Elisabet Manasanch, M.D., an assistant professor in the Department of Lymphoma and Myeloma at The University of Texas MD Anderson Cancer Center and a co-investigator of that trial. “Patients who have smoldering myeloma usually are not feeling sick, so it’s difficult for them to accept a disruptive treatment.”

In search of less invasive treatments to delay the progression of smoldering myeloma, Dr. Manasanch and her colleagues turned to immunotherapy. She is the principal investigator of two ongoing clinical trials of different immunotherapy approaches.

## PD-1 inhibition

Pembrolizumab, which inhibits the immune checkpoint protein PD-1 (programmed cell death protein 1), is approved by the U.S. Food and Drug Administration (FDA) for the treatment of several advanced cancers and has been studied against multiple myeloma. Promising results from an early trial of pembrolizumab plus low-dose chemotherapy drugs in patients with relapsed/refractory multiple myeloma led to a similar phase III trial (No. 2015-1037), which is ongoing but no longer recruiting patients. To see if the drug can slow the progression of smoldering myeloma, Dr. Manasanch is leading a phase I trial (No. 2015-0371) of pembrolizumab.

The phase I trial began enrolling patients with intermediate- or high-risk smoldering myeloma in 2016 and has nearly completed enrollment. Patients receive one intravenous infusion of pembrolizumab per 3-week cycle for up to 24 cycles. The trial’s primary outcome measure is the response rate; response is defined as decreased levels of myeloma-produced proteins in the serum and urine and/or decreased levels of clonal plasma cells in the bone marrow.

Dr. Manasanch is encouraged by the

## Observational Study May Uncover Indicators of Smoldering Myeloma Progression

**Smoldering myeloma begins as** monoclonal gammopathy of undetermined significance (MGUS), which is characterized by low levels of myeloma-produced proteins in the serum. But the progression from MGUS to smoldering myeloma and then to multiple myeloma is not well understood.

“For some patients, it can take 20 years for their disease to progress; for others, it might be a couple of years or less,” Dr. Manasanch said.

Scales to stratify MGUS and smoldering myeloma have been developed by various groups, including the Mayo Clinic, Programa para el Tratamiento de Hemopatías Malignas, and SWOG; but these scales are not 100% accurate and are difficult to interpret. Furthermore, some of these scales rely on advanced flow cytometry and gene expression profiling, which are not commonly done outside large cancer centers.

To better understand the rate of disease progression and to identify

molecular markers of such progression, Dr. Manasanch is enrolling patients with MGUS and smoldering myeloma in a 3-year observational study (No. PA15-0575). The patients’ disease is monitored by radiographic skeletal surveys at baseline and after 1, 2, and 3 years of follow-up; bone marrow aspiration and biopsies at baseline and after 3 years of follow-up; and standard blood and urine tests every 6 months. If signs of progression to multiple myeloma are seen, additional tests may be performed as clinically indicated.

“In the observational study and in our trials of pembrolizumab and isatuximab, we’re collecting data on the markers used to stratify MGUS and smoldering myeloma,” Dr. Manasanch said. “We hope this information will lead to a better scale for clinical use. We want to find markers that show when patients are going from a benign condition to something that can potentially be dangerous to their health.” ■

early results seen in the 12 patients who have begun treatment, and she plans to present these findings at the American Society of Hematology annual meeting in December 2017. “These results are a breakthrough,” she said.

## CD38 inhibition

CD38 is a glycoprotein that is found on the surface of many lymphocytes and overexpressed on myeloma cells. One drug that inhibits CD38, dara-

tumumab, is approved by the FDA for the treatment of relapsed/refractory multiple myeloma. A phase II clinical trial (No. 2015-0148) of another CD38 inhibitor, isatuximab, is currently enrolling patients who have high-risk smoldering myeloma.

Patients in the trial receive isatuximab intravenously every week for the first 28-day cycle, then every other week for five cycles, and finally every 4 weeks for up to 24 more cycles. The



primary outcome measure is the response rate. The safety and feasibility of the treatment will also be evaluated.

“Our goal is to achieve a 70% response rate after 6 months of treatment,” Dr. Manasanch said. She added that she hopes to have preliminary results ready to present in 2018.

**“We’re making major steps toward treating this disease.”**

– Dr. Elisabet Manasanch

### Expanding options

For patients with intermediate- or high-risk smoldering myeloma who wish to pursue treatment, immunotherapy drugs—with their lower toxicity profiles—are an attractive alternative to traditional chemotherapy regimens. Dr. Manasanch believes her research will help determine not only which immunotherapy drugs can best delay the progression of smoldering myeloma but also when patients need to be treated (See “Observational Study May Uncover Indicators of Smoldering Myeloma Progression,” p. 2).

“These are important studies, and we’re finding out important things already,” Dr. Manasanch said. “We’re making major steps toward treating this disease.” ■

### FOR MORE INFORMATION

Dr. Elisabet Manasanch.....713-745-5067  
eemanasanch@mdanderson.org

### FURTHER READING

Lee HC, Patel K, Kongtim P, et al. Multiple myeloma and other plasma cell dyscrasias. In: *The MD Anderson Manual of Medical Oncology*. 3rd ed. Kantarjian HM, Wolff RA, Eds. New York: McGraw-Hill Education; 2016:229–253.

# Malignant Pheochromocytoma and Sympathetic Paraganglioma Research

## Studies may expand treatment options for patients with rare neuroendocrine tumors

By Sarah Bronson

Malignant pheochromocytoma and sympathetic paraganglioma affect only about 100–200 people per year in the United States, but those who do develop these neuroendocrine cancers have only a 60% 5-year overall survival rate and limited options for effective treatment. Researchers at The University of Texas MD Anderson Cancer Center are conducting clinical trials of new treatments and studying the survival benefits of surgery to improve outcomes for patients with malignant pheochromocytoma and sympathetic paraganglioma.

Historically, response rates to standard treatment with chemotherapy or radiopharmaceuticals have been around 30% in patients with these cancers.

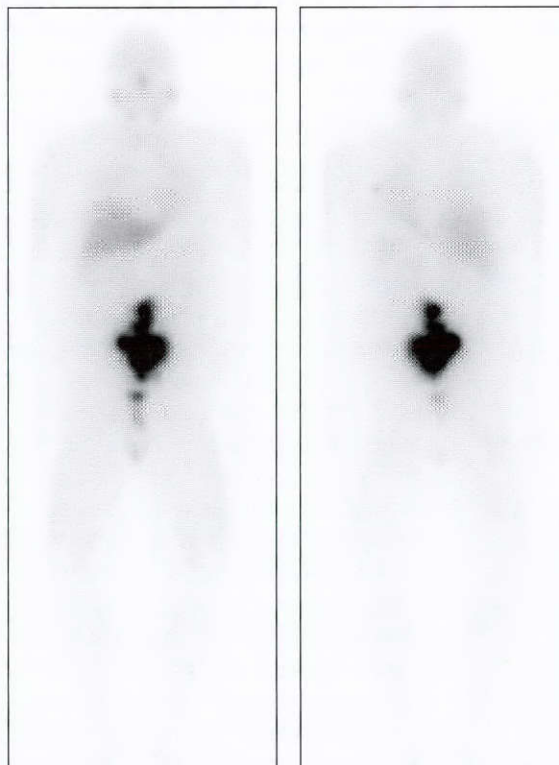
Surgery is another treatment for these patients; but it is not always feasible, and its impact on survival was unclear until recently.

Unfortunately, the small number of patients affected by these cancers has hindered progress. “We are the only institution that currently has multiple clinical trials devoted exclusively to patients with malignant pheochromocytoma and paraganglioma,” said Camilo Jimenez, M.D., an associate professor in the Department of Endocrine Neoplasia and Hormonal Disorders. Dr. Jimenez and his colleagues hope their efforts will improve the outlook for patients with these rare neuroendocrine tumors.

### Drug trials

#### UltraTrace iobenguane I 131

Introduced into clinical practice 30 years ago, the targeted radiopharmaceutical agent iobenguane I 131 enters cancer cells via the cell membrane norepinephrine transporter and has been used to both visualize and treat pheochromocytoma and paraganglioma. As an imaging aid, iobenguane I 131 shows where the cancer is and whether the cancer is taking up the agent. Patients whose tumors are



Anterior (left) and posterior (right) whole-body UltraTrace iobenguane I 131 images of a patient with metastatic paraganglioma show tumor involvement (black areas) in the abdomen and pelvis. Images courtesy of Dr. Aaron Jessop.



# Malignant Pheochromocytoma and Paraganglioma

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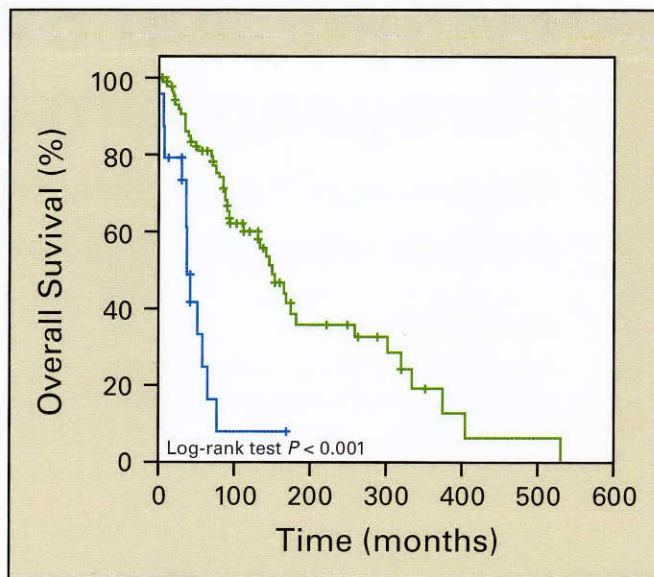
iobenguane avid on imaging may be given a higher, therapeutic dose to kill the cancer cells.

However, the original version of iobenguane I 131 is limited by the absence of radioactivity in most of its molecules. “Conventional iobenguane has an abundance of carrier molecules that are not radioactive but are bioactive, meaning they will cause side effects,” said Aaron Jessop, M.D., until recently an assistant professor in the Department of Nuclear Medicine at MD Anderson and now at another institution. “We want to make sure we’re treating the patient as aggressively as we can but without causing undue collateral damage.”

Ultratrace iobenguane I 131 overcomes the inefficiency of the original agent through a production process that minimizes the number of molecules without radioactivity. “Compared with conventional iobenguane, this version is highly specific,” Dr. Jimenez said. “Therefore, the delivery of radioactivity to the tumor per dose is much higher.”

Dr. Jimenez is the principal investigator of a phase II trial of Ultratrace in patients with iobenguane-avid metastatic or recurrent pheochromocytoma or paraganglioma. So far, Ultratrace has been well tolerated by patients and has demonstrated significant activity, as measured by tumor shrinkage and reduced need for antihypertensive drugs.

These promising preliminary results



In a retrospective study, patients with metastatic pheochromocytoma or paraganglioma who underwent palliative resection of the primary tumor (green line,  $n = 28$ ) had longer median overall survival than those who did not (blue line,  $n = 24$ ). Adapted with permission from Roman-Gonzalez A, et al. *Ann Surg.* 2017. doi: 10.1097/SLA.0000000000002195.

led to the opening of an expanded access trial (No. 2009-0210) of Ultratrace in patients with malignant relapsed or refractory pheochromocytoma or paraganglioma. This trial is ongoing at MD Anderson and other institutions and will provide access to the radiopharmaceutical prior to its anticipated approval by the U.S. Food and Drug Administration (FDA).

## Cabozantinib

Another phase II trial at MD Anderson (No. 2014-0081) for patients with malignant pheochromocytoma and paraganglioma is testing cabozantinib, a tyrosine kinase inhibitor that has been approved by the FDA for the treatment of medullary thyroid cancer and kidney cancer. “This drug blocks the cMET receptor, which is important for the spread, growth, and survival of tumors and is upregulated when the tumors become resistant to other medications,” said Dr. Jimenez, the trial’s principal investigator. “So this is a drug that could be used to prevent resistance.”

The trial is enrolling patients with unresectable metastatic pheochromocytoma or paraganglioma. Because cabo-

zantinib also may benefit bone health, the trial includes an exploratory cohort of patients whose metastases are solely or predominantly in the bone—a group excluded from many trials.

So far, about 90% of patients treated in the trial have experienced a decrease in tumor size. Symptomatic improvement has been observed as well. Dr. Jimenez said, “It’s a drug that we believe can make a difference for many of these patients.”

## Pembrolizumab

A third approach being studied for this disease is immunotherapy. A phase II trial (No. 2015-0948) of the PD-1 (programmed cell death protein 1) inhibitor pembrolizumab is currently open to patients with any of several rare, advanced tumors, including malignant pheochromocytoma and paraganglioma.

“This study will add crucial information about the efficacy of pembrolizumab in patients with malignant pheochromocytoma and paraganglioma,” said Mouhammed Habra, M.D., an associate professor in the Department of Endocrine Neoplasia and Hormonal Disorders. “The results could establish the foundations for future immunotherapy-based trials in these diseases.”

## Expanding the use of surgery

Although novel drug treatments are not yet widely available, surgery may be used for treating malignant pheochromocytoma and paraganglioma in appropriately selected patients. As with other cancers, the use of surgery for these tumors depends on the extent of the disease. For patients whose disease is localized, Dr. Habra said, “Surgery is often our best hope for long-term survival.”

However, “If a patient has distant disease on initial evaluation or if the tumor is locally very invasive or aggres-

**“For the first time, we have options that seem to be less toxic than traditional chemotherapy.”**

– Dr. Camilo Jimenez



## Genetic Testing

### An important consideration in

the management of malignant or benign pheochromocytoma and sympathetic paraganglioma is their genetic basis. "Genetic counseling and consideration of genetic testing are indicated for all patients with pheochromocytoma or paraganglioma regardless of their family history, personal history, age, or disease characteristics because 30%–40% of these patients have an underlying hereditary predisposition," said Samuel Hyde, M.M.Sc., a genetic counselor in the Department of Clinical Cancer Genetics.

If a patient with pheochromocytoma or paraganglioma tests positive for a hereditary condition associated with his or her disease, the patient's long-term surveillance becomes more intensive because the patient could be at risk for other tumors. "Patients with these hereditary conditions need to come back and see us more often," Mr. Hyde said. "They need to be screened for tumors in other parts of their body and have other blood tests." The presence of such a hereditary condition also means that family members should

be tested for the same mutations.

The number of patients with pheochromocytoma, paraganglioma, and other neuroendocrine tumors seen at MD Anderson has enabled Mr. Hyde to build expertise in genetic testing for these patients while keeping up with advances in the field. "There are often subtleties to family histories or personal histories that can make us more suspicious of one condition over another," he said.

Hereditary conditions associated with pheochromocytoma and paraganglioma include mutations in *SDHB*, *SDHC*, *SDHD*, and *SDHAF2*, each of which predisposes patients to a distinct disease phenotype. These and other mutations associated with pheochromocytoma and paraganglioma are becoming better understood, and the tools for detecting them are becoming capable of evaluating more genes at once.

Patients seeking genetic counseling or testing at MD Anderson can fill out a self-referral form at <https://my.mdanderson.org/RequestAppointment> or call the Clinical Cancer Genetics Program at 855-711-9908. ■

sive, surgical resection may not be a viable option," said Paul Graham, M.D., an assistant professor in the Department of Surgical Oncology's Section of Surgical Endocrinology. In these cases where the disease burden precludes surgery, medical treatment may be given first in hopes of stabilizing or shrinking the disease for future surgical consideration. In patients with metastatic disease, resection of the primary tumor may be used to palliate symptoms of catecholamine overproduction.

To determine the effect of surgery on survival in patients with metastatic pheochromocytoma and paraganglioma, Drs. Habra and Jimenez and their colleagues compared overall survival in patients who underwent primary tumor

resection and those who did not. In the retrospective analysis, resection of the primary tumor was associated with longer overall survival (see graph, p. 4) and, in patients with hormonally active tumors, improvement of symptoms of catecholamine excess. These findings indicate that surgery may be beneficial in an expanded subset of patients. However, prospective studies will be needed to determine the full benefit of primary tumor resection for patients with metastatic disease.

### Expanding options

As a result of the ongoing research and mounting expertise on malignant pheochromocytoma and paraganglioma at MD Anderson and partner institu-

tions, new paths of care for patients with these little-seen diseases are opening up. "For the first time, we have options that seem to be less toxic than traditional chemotherapy," Dr. Jimenez said. "Having these options, I suspect, will help extend the survival of these patients while preserving an acceptable quality of life."

The current trials also will help determine which patients should receive which of these new treatments. "If you can see certain predictors of who is going to respond to a treatment, then you can include or exclude certain patients from studies of that drug or that class of drugs," Dr. Habra said. "And we'll take the patients who do not respond and look for more effective treatment options for them." ■

### FOR MORE INFORMATION

Dr. Paul Graham .....936-446-5246  
[phgraham@mdanderson.org](mailto:phgraham@mdanderson.org)  
Dr. Mouhammed Habra .....713-792-2841  
[mahabra@mdanderson.org](mailto:mahabra@mdanderson.org)  
Dr. Camilo Jimenez .....713-792-2841  
[cjimenez@mdanderson.org](mailto:cjimenez@mdanderson.org)

### FURTHER READING

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To learn more about the ongoing clinical trials for patients with pheochromocytoma or paraganglioma, visit [www.clinicaltrials.org](http://www.clinicaltrials.org) and select study No. 2009-0210, 2014-0081, or 2015-0948.



# Hypofractionated Partial-Breast Irradiation

## Clinical trial tests 10-day external-beam radiation therapy regimen after lumpectomy for patients with early-stage breast cancer

By Bryan Tutt

Partial-breast irradiation is an effective strategy to prevent breast cancer recurrence after breast-conserving surgery. However, brachytherapy, the most-studied method of delivery, is invasive and not widely available; and accelerated partial-breast external-beam radiation therapy has had unacceptable levels of toxicity in some studies. In search of a less invasive and less toxic but still rapid adjuvant radiation therapy technique, researchers at The University of Texas MD Anderson Cancer Center are conducting a clinical trial of hypofractionated partial-breast external-beam irradiation for early-stage breast cancer patients.

Hypofractionated dosing, in which external-beam radiation is delivered at higher doses in fewer fractions than in standard fractionated dosing, has been proven safe and effective for whole-breast irradiation following lumpectomy and is more convenient and less expensive for patients (see “Shorter Course of Whole-Breast Irradiation for Breast Cancer,” *OncoLog*, January 2015). In fact, hypofractionated whole-breast irradiation is now standard practice at MD Anderson for patients who have

undergone lumpectomy for early-stage breast cancer.

“Our trial of hypofractionated partial-breast irradiation is the next natural step: taking some of the advantages of partial-breast irradiation and some of the advantages of hypofractionated whole-breast irradiation and making those two concepts meet in the middle,” said Benjamin Smith, M.D., an associate professor in the Department of Radiation Oncology.

“We want to find the most convenient and least toxic way to deliver partial-breast irradiation,” added Elizabeth Bloom, M.D., a professor in the Department of Radiation Oncology.

### Benefits and limitations of standard partial-breast irradiation

Compared with whole-breast irradiation, partial-breast irradiation has a smaller radiation field, which translates into fewer radiation-related toxic effects. For example, whole-breast irradiation sometimes causes cosmetic alterations or scar tissue in the breast or underlying muscles. Such damage could potentially be avoided with partial-breast irradiation because a smaller

volume of tissue is treated.

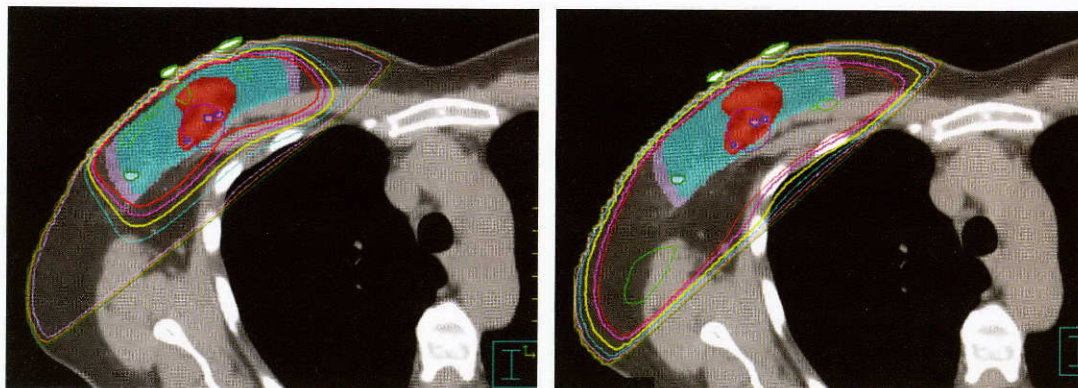
Partial-breast irradiation using brachytherapy is safe and effective, but it has some drawbacks. First, the catheters used to deliver the radioactive beads can be uncomfortable for patients and must remain in place for the duration of treatment. Second, the catheters carry a risk of infection. Finally, because placement of the catheters requires specialized training, the treatment is not widely available. “Brachytherapy works very well,” Dr. Bloom said, “but a limited number of people in the country know how to do it well.”

In contrast to brachytherapy, external-beam radiation therapy is widely available but is not commonly used for partial-breast irradiation owing to its reputation for having undesirable side effects. “Several studies have shown that partial-breast external-beam irradiation has higher risks of breast tissue scarring and poor cosmetic outcomes than expected with brachytherapy,” Dr. Smith said. However, he added that those studies treated patients twice a day for 5 days because such an accelerated dosing schedule had worked for brachytherapy.

“External-beam radiation given in twice-daily fractions doesn’t provide enough time between treatments for the normal breast tissue to repair itself,” Dr. Smith said. And standard fractionation (i.e., given over 6 weeks) for partial-breast external-beam irradiation would have the same disadvantages of inconvenience and expense that it has for whole-breast irradiation.

Drs. Smith and Bloom and their co-investigators hypothesized that once-daily

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External-beam radiation treatment plans show that partial-breast irradiation (left) delivers significantly lower radiation doses to healthy breast, rib, and lung tissues than does whole-breast irradiation (right). Images courtesy of Dr. Elizabeth Bloom.





# Support for Cancer Patients

## Patients, caregivers find many types of support from various organizations

**Even when they are surrounded by friends and family, cancer patients can feel isolated because no one around them understands what they are going through.**

Likewise, caregivers sometimes need help coping with the changes brought about by a loved one's cancer. Fortunately, support services such as support groups, educational programs, social events, or one-on-one mentoring from a fellow cancer survivor are available.

Many patients benefit from support services, especially one-on-one mentoring. "Evidenced-based research shows that trained cancer peer mentors can reduce patients' anxiety and can hasten patients' recovery," said Debbie Schultz, a director in the Department of Volunteer Services and Merchandising at The University of Texas MD Anderson Cancer Center. Ms. Schultz is responsible for leading myCancerConnection, a collection of psychosocial support programs for cancer patients.

### Choosing a support organization

Although many organizations and Web sites offer various support services, patients and caregivers should be careful to choose trusted, credible organizations. "If you go to a support Web site you're not familiar with and talk to someone online, you don't know whether they've been trained and whether your information will be kept confidential," Ms. Schultz said.

When support services are sponsored by large nonprofit organizations such as the American Cancer Society or hospitals such as MD Anderson, patients and caregivers have some assurance that the volunteers have been vetted and trained. Many smaller organizations also provide excellent services, but patients and caregivers should do a little research before contacting these organizations. The Better Business Bureau ([www.bbb.org](http://www.bbb.org)), GuideStar

([www.guidestar.org](http://www.guidestar.org)), Charity Navigator ([www.charitynavigator.org](http://www.charitynavigator.org)), and other watchdog groups can provide information about nonprofit support organizations.

### Available resources

Below are a few nonprofit support organizations and the services they provide.

**The American Cancer Society** ([www.cancer.org](http://www.cancer.org)) maintains a nationwide database that can be searched by location and cancer type to find in-person support groups. In addition to supplying information on treatment and financial aid, the organization provides a live chat tool on its Web site and a toll-free help line.

**CancerCare** ([www.cancercare.org](http://www.cancercare.org)) offers educational resources, counseling by social workers, and support groups. Some of these support groups meet in person in New York City, Long Island, New Jersey, and Connecticut; others meet online or by teleconference. Some support groups are specific to a certain cancer type, some are for young adults, and some are for caregivers or bereaved family members.

**Cancer Support Community** ([www.cancersupportcommunity.org](http://www.cancersupportcommunity.org)) offers information on cancer-related topics and online support groups led by licensed counselors. In-person education and support programs are available at more than 150 locations in the United States, Canada, Israel, and Japan.

**Caregiver Action Network** ([www.caregiveraction.org](http://www.caregiveraction.org)), formerly known as the National Family Caregivers Association, provides online discussion forums and educational resources for caregivers of patients with chronic illnesses or disabilities. The organization's Caregiver Community Action Network is a group of more than 100 volunteers, all current or former caregivers, who provide one-on-one

support or counseling to caregivers.

**Cancer180** ([www.cancer180.org](http://www.cancer180.org)) hosts support groups, social events, conferences, and educational offerings for young adults with cancer. The MD Anderson-sponsored program is open to all cancer patients in their 20s and 30s.

**myCancerConnection** ([www.mdanderson.org/mycancerconnection](http://www.mdanderson.org/mycancerconnection)) offers a variety of support and education programs for patients treated at MD Anderson and elsewhere. An annual Survivorship Conference is held in September and is open to all cancer survivors. Also available to all cancer patients is one-on-one peer mentoring. myCancerConnection has a cadre of more than 2,300 trained volunteers who are current or former cancer patients. When someone requests a peer mentor, myCancerConnection staff search their database for a mentor who has had a similar diagnosis.

"Being able to talk to someone who's been there, had the same diagnosis, and taken the same treatments is helpful to patients," Ms. Schultz said.

Recently, myCancerConnection worked with other peer mentoring organizations, including **Cancer Hope Network** ([www.cancerhopenetwork.org](http://www.cancerhopenetwork.org)) and **Imerman Angels** ([www.imermanangels.org](http://www.imermanangels.org)), to pool their resources into a nationwide peer mentoring group. If one organization cannot find a peer mentor to match a particular patient, it can find one through one of the other organizations. "Together," Ms. Schultz said, "we can help anybody, anywhere." ■

### FOR MORE INFORMATION

- Ask your physician
- Call askMDAnderson at 877-632-6789
- To request a myCancerConnection peer mentor, call 713-792-2553 or 800-345-6324



## Hypofractionated Partial-Breast Irradiation

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hypofractionated dosing could avoid the side effects seen in the previous studies of partial-breast external-beam irradiation. In March, they began enrolling patients in a clinical trial of hypofractionated partial-breast external-beam irradiation at MD Anderson clinics in the Texas Medical Center, The Woodlands, Sugar Land, the Bay Area, and Katy—all of which are in the Houston area.

### Clinical trial

The phase II trial, called OPAL (No. 2016-1035), is currently enrolling women 50 years and older who have ductal carcinoma in situ or early-stage (T1 or T2, N0, M0) invasive breast cancer. Invasive tumors must be smaller than 3 cm and estrogen receptor-positive.

After undergoing breast-conserving surgery and, if desired, immediate oncoplastic reconstruction, patients receive hypofractionated partial-breast external-beam radiation therapy. A total dose of 35 Gy is delivered in once-daily fractions on 10 consecutive treatment days (excluding weekends and holidays). Patients whose tumors had resection margins narrower than 2 mm receive an additional 9-Gy boost in three fractions. The regimen was evaluated by radiobiologist Howard Thames, Jr., Ph.D., a professor in the Department of Biostatistics, to ensure that the dose was equivalent to the standard regimen used for whole-breast irradiation.

The trial's primary outcome measure is the rate of grade 2 or higher toxic effects from the start of radiation therapy through

the 6-month follow-up visit. "Our goal is for this rate to be lower than the lowest rate from our most recent study of hypofractionated whole-breast irradiation," Dr. Smith said, "because the patients in our current trial, like almost any patient who's had a lumpectomy, would also be candidates for that treatment."

The secondary outcome measure is patient-reported cosmetic results. Patients complete questionnaires about how their breast looks and feels at baseline, at the 6-month follow-up visit, and at five yearly follow-up visits afterward. These results will be compared with data from the recent study of hypofractionated whole-breast irradiation.

If the outcomes of the OPAL trial are satisfactory, Drs. Smith and Bloom and their co-investigators may propose a randomized trial to directly compare outcomes from hypofractionated partial-breast irradiation and hypofractionated whole-breast irradiation. Dr. Bloom said, "Why treat more healthy tissue if you don't have to?" ■

### FOR MORE INFORMATION

Dr. Elizabeth Bloom ..... 281-646-2244  
[ebloom@mdanderson.org](mailto:ebloom@mdanderson.org)  
Dr. Benjamin Smith ..... 713-563-2380  
[bsmith3@mdanderson.org](mailto:bsmith3@mdanderson.org)

For more information about the OPAL trial, visit [www.clinicaltrials.org](http://www.clinicaltrials.org) and select study No. 2016-1035.

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### To Refer a Patient

**Physicians:** To refer a patient or learn more about MD Anderson, contact the Office of Physician Relations at 713-792-2202, 800-252-0502, or [www.physicianrelations.org](http://www.physicianrelations.org).

**Patients:** To refer yourself to MD Anderson or learn more about our services, call 877-632-6789 or visit [www.mdanderson.org](http://www.mdanderson.org).