

Aggressive Multimodality Salvage Therapy for Locally Recurrent Rectal Cancer Offers Hope to Patients

By Joe Munch

For patients with locally recurrent rectal cancer, multimodality salvage therapy presents the only chance for a cure. Such therapy is offered at just a handful of specialized referral institutions, including The University of Texas MD Anderson Cancer Center.

"We use a multidisciplinary approach to care for patients with locally recurrent rectal cancer and to help define their treatment. This disease is extremely complicated, and typically patients need surgery, chemotherapy, and radiation therapy plus other specialized treatments like reconstructive surgery," said Prajnan Das, M.D., M.P.H., an associate professor in the Department of Radiation Oncology.

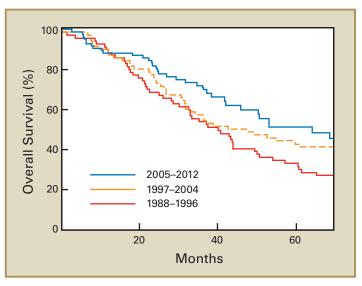
"This institution has a long tradition of offering aggressive multimodality salvage therapy with curative intent to selected patients with locally advanced rectal cancer," said Y. Nancy You, M.D., an associate professor in the Department of Surgical Oncology. "The stakes are high, and the whole salvage effort is much more difficult than treating the initial tumor."

Recurrent rectal cancer

Patients with locally recurrent rectal cancer are a heterogeneous group: the extent of their disease, their previous

therapies, and the biology of their tumors all vary widely. Similarly, the treatments they received for their initial rectal cancer may have failed for many different reasons.

"These patients might have had a complication after surgery that prevented them from healing well or from getting postoperative treatments like chemotherapy, or they might not have had optimal surgery or chemoradiation," Dr. You said. "Or maybe their tumors just had very aggressive biology and recurred."



Overall survival rates from the time of salvage surgery for locally recurrent rectal cancer have significantly increased (P = .044) as multimodality treatments have been implemented and improved over the years, according to a Cox regression analysis of patients treated at MD Anderson. Adapted from You YN, et al. Br J Surg. 2016. doi: 10.1002/bjs.10079.

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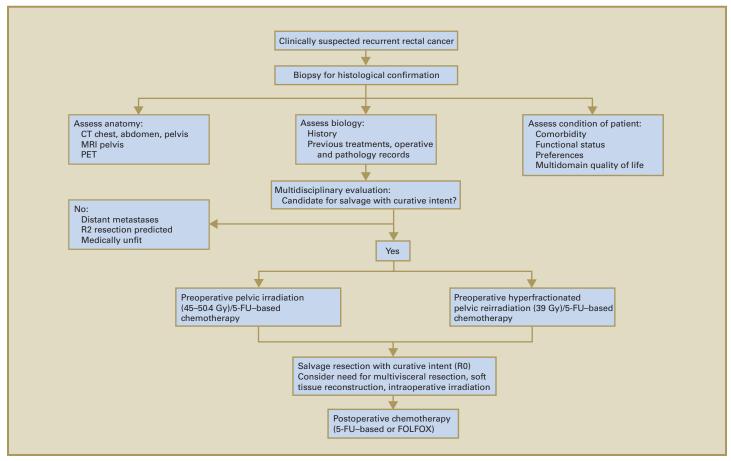




Making Cancer History®

Locally Recurrent Rectal Cancer

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The management algorithm for locally recurrent rectal cancer at MD Anderson. Abbreviations: 5-FU, 5-fluorouracil; CT, computed tomography; FOLFOX, 5-FU, oxaliplatin, and leucovorin; MRI, magnetic resonance imaging; PET, positron emission tomography. Adapted from You YN, et al. Br J Surg. 2016. doi: 10.1002/bjs.10079.

Given the group's heterogeneity. MD Anderson physicians carefully evaluate whether each patient with locally recurrent rectal cancer is a candidate for salvage therapy with curative intent. One key factor is whether the patient's disease can be surgically removed with R0 (microscopically negative) or R1 (microscopically positive) margins. Currently, patients with distant metastasis or disease that cannot be completely removed, i.e., predicted R2 (grossly positive) surgical margins, are not considered candidates for salvage therapy.

When salvage therapy with curative intent is indicated, a team of surgical, medical, and radiation oncologists reviews each patient's case to create an individualized treatment plan that falls within the framework of a management algorithm for recurrent rectal cancer

(see figure above). In general, patients undergo preoperative chemotherapy or chemoradiation, then repeat pelvic surgery with or without intraoperative radiation and/or soft tissue reconstruction, and often postoperative adjuvant chemotherapy.

"Over time, we have learned that this multidisciplinary approach works really well," Dr. Das said. "And there have been incremental improvements in the techniques. Surgical techniques have evolved and have become more aggressive. We have become more aggressive in terms of radiation therapy, and systemic therapies have also evolved and improved."

Improvements in chemotherapy in particular have enhanced the success of salvage therapy. "A decade or two ago, we had only one drug, 5-fluorouracil, available for rectal cancer.

But in the past 10–15 years, we've had more effective cytotoxic chemotherapy agents like oxaliplatin and irinotecan and biologic agents like bevacizumab and cetuximab, so we have more options in terms of what drugs we can give," Dr. You said. "The response rates of colorectal cancer in general to those agents have improved. And more patients with locally recurrent rectal cancer are now receiving postoperative chemotherapy, which may help reduce their risk of further disease recurrence."

Achieving local control

"In the past, once rectal cancer recurred locally, performing re-operative pelvic surgery safely with negative tumor margins was very difficult because of significant inflammation, scarring, and tumor involvement of multiple structures in the tight space of the deep pelvis," Dr. You said. "But we've made some significant advances in the way we approach these patients."

In patients who will undergo surgery with curative intent for locally recurrent rectal cancer, preoperative three-dimensional conformal or intensity-modulated radiation therapy is given both to reduce the chances of a second local recurrence and to shrink the tumor to make it more amenable to resection. Patients who have not yet had radiation therapy receive conventionally fractionated radiation, typically to a dose of 50.4 Gy delivered in 28 daily fractions of 1.8 Gy each. But treating patients who have already had radiation therapy poses a bit more of a challenge.

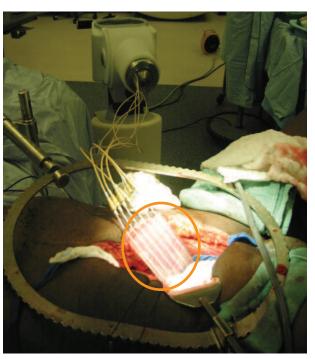
"The classic dogma in radiation therapy is that if you treat a part of the body once, you don't treat it again," Dr. Das said.

To overcome this challenge, radiation oncologists use hyperfractionated accelerated radiation therapy to deliver doses of 30–39 Gy in twice-daily fractions of 1.5 Gy each; the lower dose per fraction helps reduce the risk of side effects from the treatment.

"The key to re-irradiation is knowing when and in which patients this can be safely done. We have to pay attention to the surrounding normal tissues, and we have to pay attention to designing a radiation plan that is tolerable," Dr. Das said. "The treatment has to be individualized to the patient."

Intraoperative radiation—radiation delivered to the tumor bed in the open surgical field—also enhances the likelihood that salvage surgery will succeed. "Many of these patients with recurrences have tumors that are very close to the acceptable excision planes, which means that there is a potential that microscopic disease gets left behind," Dr. Das said. The aim of intraoperative radiation therapy is to eliminate this residual disease.

Intraoperative radiation is used selectively. Once the tumor has been



Intraoperative radiation is delivered via a flexible brachytherapy applicator (circled) during an abdominal perineal resection for locally recurrent rectal cancer. Image courtesy of Dr. Sam Beddar.

removed, if the surgical margin is found to be close, concentrated radiation in the form of high-dose-rate brachytherapy is used to destroy any tumor cells that may remain.

Typically, this brachytherapy is delivered via a thin, flexible applicator. First, the applicator is secured to the surface of the tumor bed. Next, a pellet

"A subset of patients whose disease recurs after primary rectal cancer treatment can be cured by salvage therapy. And these patients deserve a multidisciplinary evaluation."

- Dr. Y. Nancy You

of a radioactive iridium isotope is passed through channels in the applicator and held at different points for a predetermined time; tissues immediately below the applicator receive a high dose of radiation, whereas those farther away receive little or no radiation. Once the radiation has been delivered, the applicator is removed, and the surgery is completed.

"Since all of this is done in the middle of surgery, we can move normal tissue away from the area where we're giving radiation, and we can put in lead shields to protect sensitive structures," Dr. Das said. "Specifically for recurrent rectal cancer, we've found that intraoperative radiation therapy is quite beneficial."

In addition to innovations in radiation therapy, improvements in surgical techniques themselves have advanced the treatment of locally recurrent rectal cancer.

Dr. You said that the most important surgical change over the past decade has been the emphasis on total mesorectal excision and, in some patients, even more extensive, multivisceral resection (i.e., the en bloc removal of adjacent involved organs or structures) or surgery in the extra-mesorectal tissue in the lateral pelvis to achieve a

"When we operate on a patient with rectal cancer or recurrent rectal cancer. we want to be sure to take out not only the rectum with the tumor in it but also the entire fatty tissue envelope around the rectum because the tumor may have metastasized to lymph nodes in that fatty envelope," Dr. You said. "By performing a total mesorectal excision, we're much more sure that all the tumor is removed, along with the potential lymph node spread. Following the same principles, when faced with recurrent rectal cancer that has spread beyond the rectum and the mesorectum, we aim to remove all structures involved by disease."

Additionally, Dr. You said, preopera-

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Surveillance for Success

fter finishing their treatments, most cancer patients undergo close surveillance for recurrent and secondary cancers. Patients who have completed treatment for rectal cancer are no exception, and catching recurrences early increases these patients' chances of being able to undergo salvage therapy with curative intent.

"Prompt diagnosis is extremely important," said Marta Davila, M.D., a professor in the Department of Gastroenterology, Hepatology, and Nutrition. "And once we have the diagnosis, we can begin aggressive treatment with curative intent."

At MD Anderson, Dr. Davila said, patients who have completed treatment for rectal cancer are followed up with scheduled colonoscopies and imaging studies. "Usually, these patients will have their first colonoscopy within 1 year of the initial resection and repeated evaluations over the next 5 years," she said. After 5 years, followup examinations are less frequent for asymptomatic patients.

"We have a very systematic follow-up, and we have a multidisciplinary approach. These two elements set us apart," Dr. Davila said.

tive planning in general has improved. "We are much more ready to involve other surgeons before the patient goes to surgery," she said, noting that in addition to colorectal surgeons, other surgeons—including urologists, gynecologists, vascular surgeons, orthopedic surgeons, and neurosurgeons—may be called to review a patient's case. "It's much better to assemble a multispecialty surgical team before surgery, get the surgeons' expert input, and have them on standby than to have to intraoperatively call in somebody who's unfamiliar with the case."

Improving patient selection

The key to successful salvage therapy for locally recurrent rectal cancer—especially salvage surgery—is appropriate patient selection. However, identifying the patients who are most likely to benefit from such therapy continues to vex even experienced oncologists. To help determine whom to select for salvage therapy, Drs. You and Das, along with other MD Anderson researchers, recently reviewed the institution's experience with treating patients with locally recurrent rectal cancer over the past 2 decades. Perhaps not surprisingly, they found that the ability to achieve an R0 resection and the avoidance of a second recurrence were independent predictors of the

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- Dr. Prajnan Das

long-term success of salvage therapy.

The researchers also found that the 5-year overall survival rate of patients treated between 2005 and 2012 (50%) was significantly higher than that of patients treated between 1997 and 2004 (43%) or between 1988 and 1996 (32%). Several factors have contributed to the increased survival rate. In addition to advances in surgical techniques, radiation therapy approaches, and systemic therapies, the study period saw remarkable improvements in imaging studies: positron emission tomography/computed tomography is now used to ensure that patients do not have distant disease before they undergo surgery with curative intent, and high-resolution magnetic resonance imaging of the pelvis affords surgeons a clearer picture of the tumor's involvement with nearby structures and a better idea of whether the tumor can be resected with negative margins.

Challenges remain

Despite the myriad advances underlying the increase in the survival rates of patients with locally recurrent rectal cancer, challenges in treating the disease remain. When salvage therapy fails, it often fails because of distant metastasis. Having a method that more accurately identifies the patients in whom salvage therapy will fail—and that predicts those in whom it will fail distantly—would be good, Dr. You said, but being able to address distant disease itself would be better. A subset of patients who present with local recurrence may have some tumor cells in their blood that surgery cannot remove and radiation cannot kill; these cells may persist and become distant metastases. Dr. You and her colleagues are developing a protocol to identify circulating tumor cells and treat them before embarking on aggressive surgery in hopes of reducing the distant failure

"One of the questions we're raising is whether, rather than giving just pelvic radiation before surgery, we should actually be giving all patients systemic chemotherapy up front and try to reduce the volume of these microscopic circulating cells that can metastasize after surgery," Dr. You said.

Advances like these, she said, will help further improve outcomes in patients with recurrent rectal cancer. In the meantime, it is essential that such patients are considered for salvage ther-

"A subset of patients whose disease recurs after primary rectal cancer treatment can be cured by salvage therapy. And these patients deserve a multidisciplinary evaluation," Dr. You said. "We want to be able to help the patients who can be helped."

FOR MORE INFORMATION

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FURTHER READING

The Beyond TME Collaborative. Consensus statement on the multidisciplinary management of patients with recurrent and primary rectal cancer beyond total mesorectal excision planes. Br J Surg. 2013;100:1009-1014.

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Rapid Assessment, Clinical **Trials Could Improve Outcomes for Anaplastic Thyroid Cancer Patients**

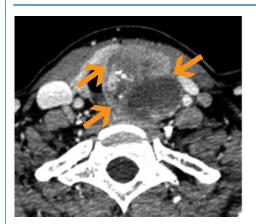
By Bryan Tutt

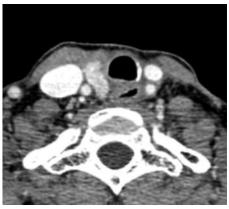
Anaplastic thyroid cancer is extremely aggressive—only 20% of patients survive 1 year after their diagnosis—so patients require immediate assessment and treatment. A program at The **University of Texas MD Anderson Cancer Cen**ter expedites the care of patients with this difficult-to-treat disease so that they can receive the best treatment possible, including access to clinical trials of promising new therapies.

Patients with anaplastic thyroid cancer typically present with advanced and symptomatic disease. In fact, all anaplastic thyroid cancers are considered stage IV disease, according to the AJCC Cancer Staging Manual, seventh edition. "Anaplastic thyroid cancer is difficult to manage because most patients typically are very ill and present with very large neck masses that compress the trachea," said Maria E. Cabanillas, M.D., an associate professor in the Department of Endocrine Neoplasia and Hormonal Disorders.

Although anaplastic thyroid cancer represents only 1% of thyroid cancers, its aggressive nature warrants awareness. "Any rapidly growing lower neck mass should raise suspicion for anaplastic thyroid cancer," said G. Brandon Gunn, M.D., an associate professor in the Department of Radiation Oncology. "I would encourage the referral of such patients to a tertiary care center for urgent evaluation."

"These tumors grow very fast, so the intervention also needs to be very fast," Dr. Cabanillas said. "The major chal-





Left: A pretreatment computed tomography scan shows a large anaplastic tumor (arrows) involving the left side of the thyroid gland. Right: A computed tomography scan of the same patient 18 months after surgery, chemotherapy, and radiation therapy shows no evidence of recurrence. Images courtesy of Dr. G. Brandon Gunn.

Anaplastic Thyroid Cancer

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lenge in anaplastic thyroid cancer is getting the patients seen quickly by a specialist for anaplastic thyroid cancer before they become very sick, preventing them from receiving any therapy."

Rapid access

To make sure patients with anaplastic thyroid cancer receive timely attention, Dr. Cabanillas and her colleagues—notably Stephen Lai, M.D., Ph.D., an associate professor in the Department of Head and Neck Surgery—initiated a program called Facilitating Anaplastic Thyroid Cancer Specialized Treatment (FAST). Initiated in 2014, the FAST program coordinates with administrative and clinical staff to ensure that patients with anaplastic thyroid cancer are identified and given rapid access to care.

"In developing the program, we worked with the administrative staff to make sure they understood the urgency of getting these patients in to be seen,' Dr. Cabanillas said. "We also made sure the administrative staff knew all the synonyms for anaplastic thyroid cancer squamous cell carcinoma of the thyroid, sarcoma of the thyroid, giant cell thyroid cancer, and others—so that patients referred to us with these diagnoses were identified as having anaplastic thyroid cancer."

Once identified, patients with anaplastic thyroid cancer are given top priority. The FAST program initiated an arrangement for physicians with expertise in treating anaplastic thyroid cancer to keep open slots in their clinic schedule that are specifically reserved for new patients with the disease. "These patients need to see a lot of physicians an endocrinologist, a head and neck medical oncologist, a head and neck radiation oncologist, a head and neck surgeon, and a palliative care specialist," Dr. Cabanillas said.

Specialists such as Charles Lu, M.D., a professor in the Department of Thoracic/Head and Neck Medical Oncology, understood the importance of the program at its outset and were eager to participate. "We're focusing on rapid assessment to get these patients in to see a doctor within a couple of days because many of these patients have

a lot of symptoms," Dr. Lu said.

So far, the program has been successful. The average referral-to-disposition time (the time from when the patient contacts MD Anderson to the time the first appointment is scheduled) for patients with anaplastic thyroid cancer is now half a day, and in fact the first available appointment is often too soon for patients who have to travel long distances. Dr. Cabanillas said, "We get patients in to see all of these anaplastic thyroid cancer specialists within a week of their first appointment, so patients have a treatment plan that can be initiated the second week they're here."

Challenges to diagnosis and treatment

In addition to patients' advanced disease stage, other factors complicate the management of anaplastic thyroid

"The pathologic diagnosis of anaplastic thyroid cancer is difficult to make," Dr. Cabanillas said, adding that tumors may contain spindle cells, giant cells, and/or squamous cells. "So we think it's very important for any patient with a tumor suspected to be anaplastic thyroid cancer to have the diagnosis confirmed by an expert thyroid cancer pathologist because the diagnosis makes a difference in the patient's treatment."

For differentiated thyroid cancer, the most common type of thyroid cancer, the mainstay of treatment is surgery. "But patients with anaplastic thyroid cancer commonly present with advanced tumors that are not amenable to surgery," Dr. Gunn said.

Another challenge in the treatment of anaplastic thyroid cancer is that the chemotherapy drugs used—taxanes and/or platinum drugs—are not very effective. "With standard chemotherapy agents, the tumor shrinkage rates for anaplastic thyroid cancer are low, and the duration of response tends to be short," Dr. Lu said.

Radiation, therefore, plays a central role in the treatment of anaplastic thyroid cancer, either to achieve local tumor control or for palliation. According to Dr. Gunn, intensity-modulated radiation therapy (IMRT) is the standard

modality used in such treatment. IMRT is often used in conjunction with radiosensitizing chemotherapy agents.

Standard therapy

Stage IVA anaplastic thyroid cancers (T4a, any N, M0), which are considered resectable, are typically treated with surgery followed by IMRT with radiosensitizing chemotherapy agents such as paclitaxel. Unfortunately, the disease tends to recur within 7 months.

Stage IVB cancers (T4b, any N, M0), which are confined to the neck but cannot be removed surgically, are treated using IMRT with radiosensitizing chemotherapy agents for local tumor control or for palliation. "We do the best we can to control the tumor in the neck—because it is so symptomatic, affecting breathing and swallowing—with chemotherapy," Dr. Lu said. "But we will be the first to acknowledge that it's not highly successful." Occasionally, however, the combination of chemotherapy and radiation can shrink the tumor enough that surgery can be considered.

Stage IVC anaplastic thyroid cancer (any T, any N, M1) has no effective standard treatment. In such cases, chemotherapy or targeted therapy is usually the first treatment, to slow the growth of the metastases; and IMRT, with or without chemotherapy, may be used on the primary tumor for palliation. "The problem is that if we don't address the tumor in the neck with radiation, the patient may asphyxiate," Dr. Cabanillas said.

Patients with stage IVB and IVC anaplastic thyroid cancer have dismal outcomes: radiation fails within 5 months in most patients. "Traditional therapies have reached their limit for effectiveness against anaplastic thyroid cancer," Dr. Gunn said.

Changing the standard of care

Recognizing the need for new treatments, MD Anderson physicians encourage their patients with anaplastic thyroid cancer to participate in clinical trials when possible. One such study, a multicenter clinical trial (RTOG0912), is currently enrolling patients with anaplastic thyroid cancer. "The study is investigat-

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Skin Cancer Prevention

Avoiding ultraviolet rays from the sun and indoor tanning devices will help keep your skin healthy



About 1 in 5 people will someday develop skin cancer, the most common cancer in the United States. The most



common skin cancers in older adults are basal cell and squamous cell carcinoma. Melanoma, the most fatal type of skin cancer, also occurs in older adults and is one of the most common cancers in adolescents and young adults—and the number of new melanoma cases increases each year.

Tips for avoiding sun-damaged skin

Most skin cancers are caused by ultraviolet (UV) rays from the sun. These rays can damage your skin even on a cloudy day. The following tips for avoiding and blocking UV rays can help keep skin healthy, young looking, and cancer free.

- Limit sun exposure during the middle of the day, between 10 a.m. and 4 p.m. This is the time when the sun is directly overhead and sunburn-causing UV rays are most damaging.
- Wear clothes that cover as much skin as possible. Wide-brimmed hats; socks and shoes that cover the entire foot; shirts with sleeves to the elbow or longer; and long shorts, skirts, or pants are good choices to help block sunlight. Tightly woven fabrics give the best protection. Some companies even sell sun-protective laundry additives or clothing specifically designed to block UV rays.
- Stay in the shade.
- Wear sunscreen on all skin not covered by clothing, even on cloudy days or when in the shade, because UV rays can cut through clouds and reflect off bright-colored surfaces,

- concrete, water, or snow. Many moisturizers, foundations, and lip balms contain sunscreen. All exposed areas—including the scalp, ears, and toes—should be protected.
- Wear sunglasses, especially wraparound designs that protect the eyes and surrounding skin. Select sunglasses that block 99%–100% of the sun's UV rays; this information will be on the label. Melanoma can develop in the eyes and on the eyelids.
- Consider your location. UV rays are most intense at high altitudes and near the equator.
- Be prepared for less obvious exposures to the sun's rays, such as while driving in a car or sitting near a window. During these activities, covering your skin will limit exposure.
- Never tan, indoors or outdoors. Indoor UV tanning is a known risk factor for melanoma.
- Examine moles and spots on the skin. Large, asymmetrical, or multicolored moles or spots should be checked by a doctor, as should any mole or spot that changes size, shape, color, or texture.
- Have regular skin exams by a dermatologist. Also, regular dilated eye exams by an optometrist or ophthalmologist can help check for damage inside the eyes.
- Learn your family history of skin cancer. A doctor can help identify any hereditary risk factors.
- Begin prevention early. Infants should be covered up and out of the sun. Children 6 months or older should have sunscreen applied before going outside. Teaching children good sun protection habits like wearing sunscreen and staying in the shade will help them live healthfully.

Tips for choosing sunscreen

When choosing sunscreen, you can start with the sun protection factor

(SPF). Most experts recommend using sunscreen with an SPF of 30. SPF 30 sunscreens filter out or block 97% of UV rays. Next, you should make sure the sunscreen is broad spectrum, protecting against both types of UV rays: UVA and UVB.

It's also good to look at the ingredients. Most sunscreens are oil based, but people with sensitive skin may prefer alcohol-based sunscreens. Some people are allergic to certain ingredients, so if you have a reaction to one sunscreen, try one with different active ingredients. You can test the new sunscreen by rubbing a small amount on the inside of your wrist and waiting 24 hours to see if your skin reacts to it.

Aside from choosing the right sunscreen, it is important to generously apply it on all skin not covered by clothing. Most people do not apply the amount of sunscreen needed to reach the SPF level of protection written on the label. The average adult should use 1 ounce of sunscreen—enough to fill a shot glass—each time sunscreen is applied. For best results, sunscreen should be applied to dry skin 30 minutes before going outside.

Sunscreen should be reapplied frequently, every 1–2 hours and after swimming or sweating. No sunscreen is truly waterproof, and sunscreens labeled "water-resistant" now tell how much time a user can expect to get the declared SPF level of protection while swimming or sweating.

The most effective sunscreen is the one you and your family will use, so find what works best for you and start using it daily, along with other skin-healthy steps, to prevent skin damage.

–K. Werner

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Anaplastic Thyroid Cancer

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ing whether adding targeted therapy to standard chemoradiation can improve patient outcomes," said Dr. Gunn, the principal investigator for the trial's MD Anderson

Patients in the study receive a standard regimen for anaplastic thyroid cancer-IMRT and paclitaxel—and are randomly assigned to receive a placebo or the experimental drug pazopanib. Pazopanib is an antiangiogenic tyrosine kinase inhibitor approved for the treatment of advanced renal cell carcinoma and soft tissue sar-

Although interim results are not yet available, the multicenter trial has already been successful in proving that it is possible to recruit enough patients with this rare disease for a trial. "This is encouraging to patients and investigators," Dr. Gunn said.

In addition, patients with anaplastic thyroid cancer may be eligible for clinical trials of targeted agents that are open to patients with any solid tumor that has a specific genetic mutation. "Because the prognosis is so poor, we immediately request molecular profiling for any patient with anaplastic thyroid cancer rather than wait to see how the patient does with standard treatment," Dr. Lu said. "Less than half of patients with anaplastic thyroid cancer have targetable mutations, but those who do may benefit from targeted agents in a clinical trial."

For example, BRAF mutations are seen in 25% of anaplastic thyroid tumors, so Drs. Lu and Cabanillas and their colleagues refer patients with such mutations to a clinical

trial or off-label treatment with dabrafenib, which inhibits the BRAF kinase, plus trametinib, which inhibits the MEK kinase along the same signaling pathway. "We've had some promising results so far," Dr. Cabanillas said.

In addition to the ongoing studies, more clinical trials are being planned for patients with stage IVB and IVC anaplastic thyroid cancer. For example, patients without a targetable mutation will be offered lenvatinib, a multiple kinase inhibitor, in a clinical trial scheduled to open in the next few months. Also opening soon is a trial to test neoadjuvant systemic therapies that boost the immune system or target a specific genetic mutation. Depending on the response to neoadjuvant therapy, the patients' thyroid tumors will be treated with surgery followed by IMRT or with IMRT only.

"Five years ago, we had nothing to offer other than the standard of care for patients with anaplastic thyroid cancer. We now have some very promising studies," Dr. Cabanillas said. "We are trying to improve the standard of care for anaplastic thyroid cancer."

FOR MORE INFORMATION

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For more information about ongoing clinical trials, visit www.clinicaltrials.org. To learn more about the FAST program, visit http://bit.ly/1RO2jxL.

OncoLog

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