Neoadjuvant Immunotherapy for Melanoma

Trial investigates immune checkpoint blockade in patients with resectable stage III or oligometastatic stage IV disease

By Bryan Tutt

The immune checkpoint inhibitors nivolumab and ipilimumab have transformed the treatment of melanoma, but thus far their use has been limited mostly to therapy for unresectable metastatic disease. An ongoing clinical trial may show that the two drugs can also be used as neoadjuvant treatment for patients with resectable stage III or oligometastatic melanoma.

Patients with resectable stage III or oligometastatic (i.e., resectable stage IV disease in three or fewer sites excluding the bone and central nervous system) melanoma have a 70% chance of disease recurrence after standard treatment with surgery followed by systemic therapy, according to Rodabe Amaria, M.D., an assistant professor in the Department of Melanoma Medical Oncology at The University of Texas MD Anderson Cancer Center. She thinks neoadjuvant therapy could improve outcomes for such patients.

“Neoadjuvant therapy doesn’t have a track record in melanoma,” Dr. Amaria said. “And many patients don’t see a medical oncologist until after the surgery is done. I think that’s a missed opportunity for this population of patients who have such high-risk disease.”

Neoadjuvant immunotherapy trial

Dr. Amaria is the principal investigator of a phase II clinical trial (No. 2015-0041) of neoadjuvant therapy with nivolumab alone or combined with ipilimumab. Nivolumab, which inhibits PD-1 (programmed cell death protein 1), and ipilimumab, which inhibits CTLA-4 (cytotoxic T lymphocyte antigen 4), are each approved by the U.S. Food and Drug Administration as monotherapy for metastatic melanoma; and the combination of nivolumab and ipilimumab was approved in 2016 for patients who have unresectable metastatic melanoma.

But the current trial is one of the first studies to use these agents as neoadjuvant therapy for resectable melanoma.

Patients in the trial’s monotherapy arm receive up to four doses of nivolumab (3 mg/kg intravenously every 2 weeks) before surgery; patients in the...
combination therapy arm receive up to three doses of nivolumab (1 mg/kg intravenously every 3 weeks) and ipilimumab (3 mg/kg intravenously every 3 weeks) before surgery. After surgery, patients in both arms receive nivolumab (3 mg/kg intravenously) every 2 weeks for 6 months.

Outcome measures and concerns

The trial’s primary outcome measure is pathological response, which is determined by the number of viable tumor cells on hematoxylin and eosin staining of a surgical sample. “Our hypothesis is that the more tumor necrosis or the less viable melanoma you have at the time of surgery, the better the patients’ long-term outcomes,” Dr. Amaria said. She added that the hypothesis was derived from the success of neoadjuvant therapy for breast cancer, in which complete pathological responses correlate with better survival outcomes.

The secondary outcome measures are the 12-month recurrence-free and overall survival rates as well as the objective response rate to neoadjuvant therapy. Responses are assessed using imaging and the Response Evaluation Criteria in Solid Tumors.

The safety of nivolumab and ipilimumab is also being evaluated, and patients are monitored closely for adverse events. “Any of these immunotherapy drugs can cause side effects related to overactivation of the immune system,” Dr. Amaria said. The side effects—which typically resolve with treatment—may include rash, pneumonitis, diarrhea, and thyroid or pituitary gland dysfunction.

Another concern is tumor progression. “These drugs don’t work as quickly as targeted therapies,” Dr. Amaria said. “So there’s a possibility that some patients’ tumors will grow during treatment. But we’re seeing good responses in both treatment arms.” Although not enough patients have been treated to enable a preliminary analysis, Dr. Amaria said that about half the patients have had a good response to neoadjuvant immunotherapy—including multiple patients who had no viable tumor cells in their surgical specimens—while half the patients have gone to surgery with a considerable volume of viable tumor cells.

Biomarker studies

The trial’s randomization process is set up to assign equal numbers of patients whose tumors express PD-L1 (the PD-1 ligand) to the two treatment arms. Patients whose tumor biopsy slides are seen on page 1 shows a scalp nodule (left, arrow) before therapy. After 9 weeks of neoadjuvant therapy with ipilimumab and nivolumab, the patient experienced a complete radiological response, as evidenced by resolution of the nodule (right, arrow). Images courtesy of Dr. Rodabe Amaria.

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Early results from a clinical trial indicate that neoadjuvant therapy with BRAF inhibitors improves recurrence-free survival in melanoma patients who have resectable stage III or oligometastatic melanoma with BRAF V600E or V600K mutations compared with a group of patients who were offered standard therapy.

In the trial (No. 2014-0409), which is ongoing but no longer enrolling patients, patients were randomly assigned to a control arm to receive the standard of care or an experimental arm to receive neoadjuvant and adjuvant therapy with the oral BRAF inhibitors dabrafenib and trametinib. Patients in the control arm underwent surgery within 4 weeks of enrollment followed by standard adjuvant therapy selected by the treating physician. Patients in the experimental arm received dabrafenib (150 mg twice daily) and trametinib (2 mg once daily) for 8 weeks followed by surgery, and they will continue to receive the study drugs for up to 44 weeks after surgery.

An interim analysis showed an overall response rate of 77% on imaging and a pathological complete response rate of 58% at week 8 for the patients in the experimental arm. The estimated 6-month recurrence-free survival rates were 100% for the experimental arm but only 28% for the control arm, so enrollment was closed.

Drs. Amaria and Wargo and their colleagues presented these results at the 2016 Society for Melanoma Research International Congress in November.
arms. Previous studies have identified PD-L1 expression as a potential biomarker for response to nivolumab and ipilimumab, so the researchers want to see whether PD-L1 expression affects outcomes in either arm.

Dr. Amaria—along with Jennifer Wargo, M.D., an associate professor in the Department of Surgical Oncology, and other collaborators in the trial—also hopes to discover new biomarkers for response to immune checkpoint inhibitors. “Our trial is heavy on the collection of blood and tumor tissue so that we can assess what happens in the tumor and blood over the course of therapy,” Dr. Amaria said.

For each patient, tumor biopsy samples are taken before treatment and at least once during treatment. These samples and those from the surgical specimen undergo immune and molecular assays. “The serial samples will generate data that may help us understand why some patients have excellent responses and other patients do not respond as favorably,” Dr. Amaria said.

Building a neoadjuvant therapy program
The immunotherapy trial is the second MD Anderson trial to investigate neoadjuvant therapy for stage III or oligometastatic melanoma. The first trial, led by Dr. Wargo, is ongoing but is no longer enrolling patients, and the preliminary results are promising (see “Neoadjuvant Therapy with BRAF Inhibitors for Patients with Melanoma,” p. 2).

“We’re working to build a neoadjuvant therapy program for melanoma patients,” Dr. Amaria said. “With the advances in treatment we’ve seen in recent years, neoadjuvant therapy has become a viable option.”

FOR MORE INFORMATION
Dr. Rodabe Amaria ..............713-792-2921
Dr. Jennifer Wargo ..............713-745-1553

Radiation May Enhance Immunotherapy for Solid Tumors
Clinical trials combine immune checkpoint inhibitors with radiation therapy against lung cancers, other solid tumors

By Joe Munch

Immunotherapy drugs are revolutionizing the treatment of many cancer types, but not all patients treated with these new drugs respond. To enhance the efficacy of immunotherapy, researchers at The University of Texas MD Anderson Cancer Center are exploiting a rare phenomenon of radiation therapy in clinical trials for patients with lung cancer and other solid malignancies.

“Radiation has been used for a hundred years to do one thing: achieve local control,” said James Welsh, M.D., an associate professor in the Department of Radiation Oncology. “We are now combining it with immunotherapy for systemic control, and that’s pretty exciting.”

Seeking synergy

Alone, drugs that inhibit immune checkpoints—CTLA-4 (cytotoxic T lymphocyte antigen 4), PD-1 (programmed cell death protein 1), or PD-L1 (the PD-1 ligand)—can elicit impressive responses in some cancer patients, even in those with metastatic disease. However, immunotherapy eliminates distant disease in perhaps only 20% of patients with metastatic cancer; Dr. Welsh hopes to use radiation to push that rate to 30% or even 40%.

At first glance, the logic of combining radiation therapy with immunotherapy to fight cancer seems obvious. Radiation, which kills cancer cells by damaging their DNA, is given locally; immunotherapy is given to ramp up the immune system to attack the disease systemically. But this is only a partial explanation of how the combination might assault the disease. Rather than one treatment providing just local disease control and the other providing just systemic control, the therapies may work synergistically. One area of synergy is that radiation can stimulate immunogenic cell death and sensitize cancer cells to immunotherapy by promoting the expression of major histocompatibility complex (MHC) class I molecules and other apoptosis-mediating proteins.

“We developed a model of resistance to PD-1 inhibition in my lab. Tumor cells lose the expression of MHC class I molecules, which present antigens to cytotoxic T cells,” Dr. Welsh said. “Radiation can make tumor cells express...”

“Tumor cells lose the expression of MHC class I molecules, which present antigens to cytotoxic T cells. Radiation can make tumor cells express those molecules and respond to immunotherapy.”

– Dr. James Welsh
those molecules and respond to immunotherapy. We’ve shown that in mice and a few humans so far.”

In addition to sensitizing irradiated tumor cells to immunotherapy, radiation can cause the cells to release tumor antigens that prime T cells to attack other tumor cells in the body, including those at distant, non-irradiated sites.

“Effectively, radiation can turn the tumor into a vaccine,” Dr. Welsh said.

This phenomenon of radiation shrinking the tumor locally while inducing an immune response systemically is known as the abscopal effect. The addition of immunotherapy, the thinking goes, helps maintain the effect by preventing T cell activation from becoming downregulated by CTLA-4 or PD-1/PD-L1.

The key to exploiting the abscopal effect to kill tumor cells systemically with radiation, Dr. Welsh said, is fractionation. Conventionally fractionated radiation therapy, in which the radiation dose is given in many small fractions over 6 or 7 weeks, doesn’t work well with immunotherapy because the long-term, almost constant delivery of radiation exhausts the T cells that, given the chance, would go on to attack non-irradiated tumors. Hypofractionated radiation therapy, in which the radiation dose is given in a few large doses over just a week or two, gives those T cells that chance and may prove to have advantages when combined with immunotherapy.

“We need to hit the tumor and then get out of the way,” Dr. Welsh said. “We need to disrupt the tumor with radiation to try to turn it into a vaccine, and then we need to stop treating it and let the T cells come in and do their work.

“What we’ve previously done for patients with multiple sites of metastatic disease is to hit one site with radiation to try to turn it into a vaccine and then see if the other sites respond,” Dr. Welsh continued. “But now, we’re hitting four or five disease sites with radiation to make the tumor a better vaccine, so to speak, and combining radiation with immunotherapy.”

Immunotherapy is also being added to radiation to help improve local control in patients with stage I disease. “If you can’t get the radiation dose high enough to eradicate the tumor, adding immunotherapy can help with local control,” Dr. Welsh said. “So we’re using the combination for almost all stages of cancer, because almost every patient could benefit from either better local or better distant control.”

**Clinical trials**

Dr. Welsh is heading up several clinical trials to investigate the potential use of the immunotherapy–radiation therapy combination across the cancer spectrum, with a focus on metastatic disease. Enthusiasm for the studies has been strong. The first such trial—a large one looking at the CTLA-4 inhibitor ipilimumab plus radiation in patients with any cancer type who have metastatic or primary lesions in the lungs or liver—has accrued almost all of its nearly 100 planned participants.

In that trial (No. 2013-0882), Dr. Welsh said, “We’ve definitely had some interesting cases where it seems that radiation has really added a benefit.”

One case was particularly striking. One of the early patients enrolled in the trial had anaplastic thyroid cancer, a highly aggressive disease associated with a median survival time of only about 2 months. “The patient had about five metastases in the lung; I treated one with radiation, and all the others just went away for a year,” Dr. Welsh said. “That’s remarkable; it’s something we’ve never seen in anaplastic thyroid cancer. Now there are several trials looking into the combination of immunotherapy and radiation therapy for anaplastic thyroid cancer.”

Although initial results of Dr. Welsh’s study have been promising, some questions remain.

“We can’t yet prove that the radiation caused or helped cause the responses we’ve seen. The patients were receiving both the immunotherapy drug and the radiation, and their disease might have responded to the drug alone,” Dr. Welsh said. “In some of our newer studies, we’re randomly selecting patients to receive either immunother-
A treatment plan for palliative stereotactic radiation therapy to the liver shows the dose to target areas (red) and decreasing doses to the surrounding area. This patient received 36 Gy in 5 fractions, after which non-irradiated tumors in the lungs shrank. Image used with permission from Cancer J. 2016;22:130–137.

For example, the phase II portion of an ongoing trial of the PD-1 inhibitor pembrolizumab plus conventional wide-field or stereotactic radiation therapy for patients with non–small cell lung cancer (No. 2014-1020) includes two treatment arms in which patients receive concurrent pembrolizumab and radiation (conventional in one treatment arm and stereotactic in the other) and two in which patients receive only pembrolizumab for 5 weeks; conventional or stereotactic radiation therapy, depending on the treatment arm, is added for patients whose disease progresses. The 3-month progression-free survival rates of the patients treated with pembrolizumab alone will be compared with those of patients in the concurrent radiation arms.

Other ongoing or upcoming trials of immunotherapy combined with radiation therapy at MD Anderson include a trial in which patients with small cell lung cancer will receive immunotherapy plus standard-of-care chemoradiation (No. 2014-1003); a trial in which patients receiving any immunotherapy drug whose disease is progressing will receive salvage radiation therapy while continuing maintenance doses of their immunotherapy drug if appropriate (No. 2015-0936); and a trial in which patients with brain metastases will receive immunotherapy plus stereotactic radiation to the brain. Studies of immunotherapy combined with radiation therapy in patients with prostate, breast, head and neck, and other cancers also are being planned or are underway.

Moving forward

Increasing interest in cancer immunotherapy has led to a flood of new immunotherapeutic agents. Identifying which agents work well with radiation therapy—and which don’t—and determining how to best sequence combinations of the agents with radiation therapy to elicit an optimal tumor-destroying immune response will be research focuses moving forward.

“We want to make the synergy between immunotherapy and radiation therapy reproducible, so it doesn’t just happen once in a while; and we want to make sure we can do this in a safe manner,” Dr. Welsh said. “We think future studies will help us refine our technique and find the optimal sequencing, doses, and combination of agents.”

FOR MORE INFORMATION
Dr. James Welsh........................................
JWelsh@mdanderson.org

FURTHER READING

CLINICAL TRIALS: Immunotherapy and Radiation Therapy

Phase I trial of MK-3475 and concurrent chemo/radiation for the elimination of small cell lung cancer (2014-1003). Principal investigator (PI): Dr. James Welsh. The goal of this study is to find the highest tolerable dose of the combination of pembrolizumab and radiation therapy (either conventional or stereotactic). The goal of the study’s phase II portion is to learn if this combination therapy can help to control metastatic non–small cell lung cancer.

Phase I/II trial of ipilimumab (immunotherapy) and hypofractionated stereotactic radiation therapy in patients with advanced solid malignancies (2013-0882). PI: Dr. Welsh. The goal of this study is to determine the safety and effectiveness of ipilimumab and stereotactic body radiation therapy given simultaneously as well as sequentially.

Phase II trial of salvage radiation therapy to induce systemic disease regression after progression on systemic immunotherapy (2015-0936). PI: Dr. Welsh. The goal of this study is to learn if radiation therapy can help to control solid tumors in patients whose disease has gotten worse after receiving immunotherapy.

FOR MORE INFORMATION
IN BRIEF

Nivolumab Plus Azacitidine Shows Promise in Relapsed Acute Myelogenous Leukemia

The addition of the immunotherapy drug nivolumab to standard salvage therapy with azacitidine may benefit some patients with acute myelogenous leukemia (AML) for whom prior therapy failed. The nivolumab–azacitidine combination yielded an encouraging response rate and median overall survival duration in a preliminary analysis of an ongoing clinical trial (No. 2014-0861) at The University of Texas MD Anderson Cancer Center.

The MD Anderson group previously found that treatment resistance and poor overall survival outcomes in AML patients treated with the epigenetic agents azacitidine or decitabine may be linked to the upregulation of immune checkpoint proteins such as PD-1 (programmed cell death protein 1). Nivolumab, which inhibits PD-1, may help overcome such resistance and improve response rates and survival durations.

“The combination of azacitidine and nivolumab showed a response rate of 34%, which compares favorably to a historical response rate of 12%–15% in patients with relapsed AML treated with azacitidine alone,” said Naval Daver, M.D., an assistant professor in the Department of Leukemia. He added that the complete remission rate in the trial was 22%, and all but one of these remissions has lasted at least 7 months.

Fifty-three patients in the single-arm phase II trial of azacitidine and nivolumab were eligible for survival analysis, which showed a median overall survival of 6.0 months. A historical cohort of patients with AML who received salvage therapy with azacitidine alone had a median overall survival of 4.1 months. For patients in the trial who had received only one prior course of therapy, the median overall survival was 9.3 months, which compared favorably with historical durations of 4.5 months in similar patients.

“Longer follow-up is required to confirm the durability of the responses and the overall survival benefit,” Dr. Daver said. “It will be especially important to follow the tail of the survival curve and see if responders attain long-term survival, as this has been the major benefit of checkpoint inhibitor–based strategies in solid tumors.”

One patient in the trial died of pneumonitis/epiglottitis. Other adverse events included nephritis, skin rash, and colitis, all of which were managed with systemic steroids.

Dr. Daver and his colleagues presented their preliminary findings in December at the 58th Annual Meeting of the American Society for Hematology.

Acute Myelogenous Leukemia, Myelodysplastic Syndrome Study Questions Standard Exclusion Criteria for Conventional Trials

Patients with acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) who are excluded from conventional clinical trials because of comorbid conditions may benefit from participation in trials of low-intensity interventions, a new study’s findings indicate.

“Most clinical studies for AML and MDS exclude patients with comorbidities, active or recent malignancies of other types, organ dysfunction, or poor performance status,” said Guillermo Garcia-Manero, M.D., a professor in the Department of Leukemia at The University of Texas MD Anderson Cancer Center. “But how these criteria protect the drug or intervention being studied rather than the patient.”

Dr. Garcia-Manero and his colleagues sought to determine whether patients who would be excluded from conventional studies for the reasons listed above could be treated in a clinical trial. The two-phase study included stopping rules for survival, response, and toxicity.

In the initial single-arm phase of the study, 30 patients (16 with MDS and 14 with AML) received low doses of azacitidine plus vorinostat. The overall and complete response rates were 40% and 27%, respectively; the 60-day overall survival rate was 83%; and the median overall survival and event-free survival durations were 7.8 and 5.1 months, respectively. The main adverse events were grade 1 or 2 gastrointestinal toxic effects.

In the subsequent randomized phase of the study, 79 patients (47 with MDS and 32 with AML) received low doses of either azacitidine alone (27 patients) or azacitidine plus vorinostat (52 patients). The monotherapy and combination therapy groups’ 60-day survival rates (67% and 85%, respectively), overall response rates (48% and 46%, respectively), overall survival durations (6.1 and 7.6 months, respectively), and event-free survival durations (3.0 and 5.5 months, respectively) did not differ significantly. Again, the main adverse events were grade 1 or 2 gastrointestinal toxic effects, which occurred more frequently in the combination therapy group (81%) than in the single-therapy group (56%).

A univariate analysis revealed that a performance score of 3 or more, a creatinine or bilirubin concentration of 2 mg/dL or more, and the presence of another malignancy did not adversely affect 60-day survival, overall survival, or event-free survival. In addition, an Adult Comorbidity Evaluation-27 index score of 2 or 3 did not reduce survival duration.

Dr. Garcia-Manero and his colleagues concluded that the standard exclusion criteria used in clinical trials for AML and MDS patients should be re-evaluated. According to the team, relaxing the criteria could make experimental agents available to the patients whose poor prognoses make them the most likely to benefit.

The results of the study were presented in December at the 58th Annual Meeting of the American Society for Hematology.
Social Media Groups for Cancer Patients

Twitter chats, online groups for patients, caregivers

People affected by cancer—including patients, survivors, advocates, and health care providers—can use social media to raise awareness and create support networks. Twitter and other social media play a big role in fostering online communities for people to find support, share information or experiences, and cope with the challenges that come with cancer diagnosis, treatment, and survivorship.

Tweet chats

A tweet chat, or organized conversation on Twitter, allows Twitter users to meet online at a preplanned time to discuss a topic. Participants include a specific hashtag—a pound sign (#) followed by a word or phrase (without spaces) indicating the chat’s topic or organizing group—in their tweets to contribute to the discussion.

Tweet chats include moderators who keep the conversation going by asking questions and encouraging replies. Conversations aimed at patients and other individuals concerned about or affected by cancer cover topics such as diagnosis, emotional support, treatments, resources, and survivorship.

Most Twitter accounts hosting a tweet chat will post rules on their account or accompanying Web site. Here are some tips on participating in a tweet chat:

- create a Twitter account at www.twitter.com;
- include the identified hashtag in a post so it becomes part of the chat;
- preface a question or answer, respectively, with Q1, Q2 or A1, A2, and so forth;
- retweet (forward a tweet using the retweet button or copy and paste the tweet and username into a draft of a new tweet) a question or answer that interests you if it gets lost in the quick pace of the conversation; and
- keep posts 140 characters or fewer as Twitter has a character limit.

Social media accounts

Below are Twitter accounts (which begin with an @ symbol) and hashtags that patients and those affected by various types of cancer may find useful. The hashtags shown are used during the groups’ tweet chats or at any time for posts related to their topic. The hashtags also can be used to find posts related to the topic on Facebook and Instagram.

**Brain tumors**

Brain Tumor Social Media (@BTSMchat, #BTSM) is a patient-run Twitter community offering patients support and the latest information on brain tumor research. The #BTSM tweet chat occurs at 8 pm central time (CT) on the first Sunday of each month.

#BrainTumorThursday is a separate hashtag that often appears alongside #BTSM. Though #BrainTumorThursday doesn’t have its own organized tweet chat, every Thursday people use the hashtag to post new information, questions, and experiences related to brain tumors.

**Breast cancer**

Breast Cancer Social Media (@BCSMchat, #BCSM) offers support, information, and the latest research pertaining to the disease. Two survivors of breast cancer founded the #BCSM community with the idea that social media could be used to “unite, educate, and empower those affected by breast cancer.” The #BCSM tweet chat occurs at 8 pm CT every Monday.

**Lung cancer**

Lung Cancer Social Media (@LCSMchat, #LCSM) doesn’t use endorsements or advertisements and therefore claims to provide a neutral voice for patients. The group’s Web site, www.lcsmchat.com, includes transcripts of past tweet chats and a schedule with the topic for the upcoming tweet chat. The #LCSM tweet chat occurs at 7 pm CT every other Thursday.

**Cancer in young adults**

Stupid Cancer (@StupidCancer, #StupidCancer) was founded by a survivor of brain cancer to build a community, improve the quality of life, and provide meaningful survivorship for young adults who are cancer patients or survivors. The group’s Web site, www.stupidcancer.org, defines young adult patients as those 15–39 years old. Stupid Cancer also has a mobile app called Instapeer, which enables patients to instantly and anonymously connect with each other one-on-one.

**Other cancer-related topics**

The easiest way to find an organized tweet chat, informal conversation, or post about cancer or a cancer-related topic is to search the subject prefaced by a hashtag and without spaces (e.g., #prostatecancer for prostate cancer) on Twitter or other social media platforms. A useful Web site is www.symplur.com, which provides a platform for healthcare communities and allows users to search for specific healthcare hashtags. If you can’t locate a group that addresses your interests, perhaps you can create the group yourself.

—Z. Ahmed

**FOR MORE INFORMATION**

- Talk to your physician
- Visit www.mdanderson.org
- Call MD Anderson at 877-632-6789
- Follow OncoLog on Twitter: @OncoLogNews and @OncoLogEspanol

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Physicians who refer patients to specialty hospitals are often stymied by red tape or concerned that their patients will face long waits for appointments. To help avoid such difficulties, The University of Texas MD Anderson Cancer Center has streamlined its referral process and made it easy for physicians to refer patients online or by phone. As a result, most local patients are seen within 48 hours of contacting MD Anderson.

MD Anderson’s online system for health care professionals, myMDAnderson for Physicians, expedites referrals and enables physicians to contact the MD Anderson care team throughout the treatment process. Through myMDAnderson for Physicians, physicians can not only refer patients but also access their patients’ electronic medical records and appointment schedules, review test results, and receive notifications about their patients’ statuses. If the information a physician wants isn’t available on myMDAnderson for Physicians, he or she can submit a question through the portal’s secure messaging system.

Physicians who prefer person-to-person communication can refer patients by calling the Physician Access Center between 8 am and 5 pm, central time. The Physician Access Center can also provide information about:
- clinical trials,
- referral status,
- MD Anderson programs for referring physicians,
- use of myMDAnderson for Physicians, and
- other concerns or issues that affect the referring physician experience.

More information about the patient referral process, including hospital-to-hospital or international referrals, is available at www.mdanderson.org/for-physicians/refer-a-patient.html. Physicians can log in to myMDAnderson for Physicians at mylink.mdanderson.org or call the Physician Access Center at 713-792-2202 or 800-252-0502, option 1.