Improving Rates of Vaccination after Hematopoietic Stem Cell Transplant

By Bryan Tutt

Patients who have undergone a hematopoietic stem cell transplant (HSCT) for a hematological cancer usually lose the immunity they had acquired through vaccination. Although guidelines exist for vaccinating immunocompromised transplant recipients, many patients go unvaccinated or do not complete the series of vaccinations. An ongoing initiative at The University of Texas MD Anderson Cancer Center is using a multi-pronged approach to improve rates of vaccination after HSCT.

The underlying disease, radiation therapy and chemotherapy conditioning regimens, the transplant itself, and immunosuppressive drugs taken after the transplant all contribute to the loss of previously acquired immunity in patients who have undergone autologous or allogeneic HSCT. “It’s standard practice to re-vaccinate these patients with standard childhood vaccines, the so-called baby shots,” said Ella Ariza-Heredia, M.D., an assistant professor in the Department of Infectious Diseases, Infection Control, and Employee Health.

For various reasons, however, not all patients receive the recommended vaccines after HSCT. In some patients, vaccination is withheld or delayed intentionally, usually due to graft-versus-host disease treatment with certain drugs, such as corticosteroids or the anti-CD20 antibody rituximab. But a minority of patients who would benefit from post-HSCT vaccines do not receive them because of breakdowns in communication among clinicians or between clinicians and patients.

Dr. Ariza-Heredia is part of an effort to ensure that MD Anderson patients who have undergone HSCT receive the necessary vaccines. This joint endeavor by the Department of Stem Cell Transplantation and Cellular Therapy and the Department of Infectious Diseases, Infection Control, and...
Employee Health includes internal quality improvement initiatives, patient education programs, and improvements in communication between MD Anderson and referring physicians.

**Steps to ensure vaccination**

The first step in MD Anderson’s program to improve vaccination rates among HSCT patients was to adapt and streamline international and Infectious Diseases Society of America guidelines for post-HSCT vaccination into an internal standard operating procedures document (see table). This effort was led by clinical pharmacy services manager Alison Gulbis, Pharm.D., under the direction of Richard Champlin, M.D., a professor in and chair of the Department of Stem Cell Transplantation and Cellular Therapy. The streamlined vaccination schedule makes compliance easier for patients who receive their first round of vaccines at MD Anderson and then return to their primary care physicians for follow-up care.

Various tools are used to help patients and their community providers comply with vaccination schedules. For example, each patient is given an immunization tracking card that shows when the patient’s vaccinations are due. Face-to-face communication, however, remains the best tool. Nurses in MD Anderson’s Department of Stem Cell Transplantation and Cellular Therapy, in an effort spearheaded by Karen Stolar, A.P.N., have increased their efforts to educate patients and their families about the importance of completing the vaccine series.

“In some cases patients may not understand the importance of completing their vaccine series, and others simply forget because they are overwhelmed with new information,” Dr. Ariza-Heredia said. “I can see why vaccination can get lost in translation.” She added that a key component in the conversation between clinicians and patients and caregivers is to remind family members to remain current on their vaccinations so that they do not expose the immunocompromised patient to an infectious disease.

In addition, Dr. Ariza-Heredia said, “We realized that we needed to improve communication between the transplant teams and our patients’ primary care physicians. For the past 2 years, we’ve been doing this by hosting seminars for physicians, nurses, and physician assistants about posttransplant vaccination guidelines.”

Continuity of care, not just for vaccination but for all aspects of care, is essential for patients who have undergone HSCT. When a patient returns to his or her referring physician, MD Anderson physicians consult with the referring physician to discuss appropriate follow-up care, including the vaccination schedule. MD Anderson’s new electronic health record also helps by providing alerts when the patient’s next vaccination is due, and these notifications are sent to referring physicians through the EpicCare Link tool at myMDAnderson for Physicians.

“Community physicians need to be aware of the posttransplant vaccination recommendations because these providers are usually the ones who make sure the patients complete their vacci-
Bone Loss Prevention in Patients with Cancer

By Sarah Bronson

Patients undergoing cancer treatment are at an increased risk of fractures because many cancer therapies tend to weaken the bones. Researchers at The University of Texas MD Anderson Cancer Center are investigating treatments to prevent cancer-related bone loss and fractures as well as fracture-related sequelae such as immobility and blood clots.

Leading the effort to prevent bone loss and fractures are Huifang Lu, M.D., Ph.D., an associate professor in the Department of General Internal Medicine’s Section of Rheumatology and Clinical Immunology, and Mimi Hu, M.D., an associate professor in the Department of Endocrine Neoplasia and Hormonal Disorders. Drs. Hu and Lu rotate as the director of the Bone Health Clinic, a collaborative, interdisciplinary effort by MD Anderson clinicians who treat patients at risk for bone loss.

The Bone Health Clinic fills an unmet need, according to Dr. Lu. “Fracture risk in patients with cancer is an area that isn’t usually looked at,” Dr. Lu said. “Sometimes patients are referred to me for hip pain or back pain, and they actually have undiagnosed fractures. It’s really incapacitating.”

Bone loss in cancer patients

Many treatments for cancer decrease bone mineral density and increase the risk of fractures. Since bone maintenance is driven in part by hormones, hormonal therapies carry a significant risk of bone loss. Breast cancer patients and survivors, many of whom have received agents that reduce levels of estrogen, experience more severe bone loss after therapy than women in the general population do after natural menopause. Similarly, patients treated with testosterone blockers for prostate cancer often experience bone loss. Ablation of the ovaries or testicles to treat cancers affecting or affected by those organs also increases bone loss and the risk of fracture.

Other systemic therapies can also adversely affect bone. Cytotoxic chemotherapy drugs can cause bone loss most commonly by impairing gonadal function but also through direct toxic effects on bone cells. Drugs with these toxic effects include methotrexate, cyclophosphamide, ifosfamide, platinum compounds, and doxorubicin. Other

“For more information about communication between MD Anderson and referring physicians, visit www.mdanderson.org/for-physicians/refer-a-patient/mymdanderson-for-physicians.html, email physician relations@mdanderson.org, or call 713-792-2202 or 877-632-6789 and select option 1.

“Sometimes patients are referred to me for hip pain or back pain, and they actually have undiagnosed fractures.”

– Dr. Huifang Lu
Bone Loss Prevention

[Continued from page 3]

...cancer treatments that can increase bone loss and the risk of fracture are hematopoietic stem cell transplant, radiation therapy, and glucocorticoids.

Bone loss can also result from the cancer itself—especially cancers that affect the bone marrow, such as myeloma and leukemia—and from some conditions caused by the cancer. Decreased mobility, for example, can weaken the bones. Gastrointestinal malignancies may lead to malabsorption, and illness in general can cause patients to not get adequate nutrition; these conditions may deprive patients of vitamins and minerals needed for healthy bones, such as vitamin D and calcium. And these risk factors compound other risk factors for bone loss that patients with cancer may have, such as older age, postmenopausal status, and smoking history.

Bone loss and the resulting fractures in cancer patients are especially serious because fractures carry serious risks that could complicate cancer treatment. Hip fractures in any patient—with or without cancer—are associated with a mortality rate of 20% within 1 year, partly because of immobility and subsequent complications.

“The morbidity and mortality rates of fractures are very high,” Dr. Lu said. “And fractures seriously affect quality of life, so it is important that we prevent them in our patients. And fractures are largely preventable. We want to use the knowledge about and pharmaceutical developments for treating bone loss in the general population to benefit patients with cancer as well.”

Preventing bone loss in cancer patients

Several medications that are used to improve bone health in the general population, especially in postmenopausal women, can be used to prevent bone loss in patients undergoing cancer treatment. Bisphosphonates such as alendronate, risendronate, zoledronate, and ibandronate, which are used to treat or prevent osteoporosis, have been shown to improve or stabilize bone mineral density in patients receiving cancer treatments that can cause bone loss. This use of bisphosphonates has been well studied in clinical trials for patients with breast cancer and prostate cancer but remains to be established for patients with other cancers.

Drs. Hu and Lu sought to fill this gap through both retrospective and prospective analyses. Dr. Hu and colleagues performed a retrospective study that found that patients with medullary thyroid cancer with bone metastases who were treated with zoledronate or denosumab (a human monoclonal antibody used to treat bone loss and bone metastases) experienced fewer skeletal-related events, such as fractures or any need for radiation therapy to the bone, and fewer subsequent bone metastases at additional sites. These results were presented at the annual meeting of the Endocrine Society in April.

Dr. Lu and colleagues conducted a systematic review and meta-analysis (soon to be published) of patients with hematological cancers who were treated with bisphosphonates and found that the treatment prevented bone loss in the spine but not always in the hip bones.

Similarly, in a recently completed MD Anderson trial led by Dr. Lu, patients with hematological cancers who underwent hematopoietic stem cell transplant and received the bisphosphonate ibandronate for 1 year after the transplant had less bone loss in the spine than those who did not receive ibandronate. However, ibandronate was less effective in preventing bone loss in the hips. “This agent is not doing 100% of the job,” Dr. Lu said. “We will need to try new approaches, perhaps with new medications and different timing.”

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Bisphosphonates remain a promising treatment not only because of their ability to prevent bone loss in some cancer patients but also because of their favorable side effect profile. “Bisphosphonates are reasonably safe and easy to take,” Dr. Lu said. “In rare cases, however, these drugs can lead to serious effects such as jaw osteonecrosis or atypical femur fractures, which is why we don’t want to give these drugs to every patient but only to those at risk for fractures.”

Dr. Hu said, “Some of these side effects of bisphosphonates—such as abdominal discomfort, acid reflux, and musculoskeletal pain—are easy to manage, and some can be very serious but rare. We hope that talking to patients about these side effects using standard, uniform language will improve patient compliance and the effectiveness of their treatment.”

At MD Anderson, standard phrasing of recommendations is used to help patients adhere to their bone loss prevention regimens as well as precautionary practices to maintain bone health, such as resistance-based exercises and consuming adequate amounts of calcium and vitamin D.

Next steps

MD Anderson researchers and clinicians continue to seek ideal approaches for preventing bone loss not only through their efforts in the Bone Health Clinic but also by participating in a number of bone health initiatives. One such initiative is the Bone Health Program of Texas, a collaborative research program between academic institutions.

“I don’t believe that one approach fits all who happen to have low bone mass.”

– Dr. Mimi Hu
Experimental Drug
LOXO-101 Shrinks Tumors with NTRK Fusions

The drug LOXO-101 reduces the size of tumors with NTRK gene fusions, according to an ongoing multicenter phase I trial (No. 2014-1056) led by The University of Texas MD Anderson Cancer Center.

The trial’s goal was to find the highest tolerable dose of LOXO-101 that could be given to patients with advanced solid tumors. LOXO-101 is a selective pan-TRK inhibitor, and this is the first trial using it in humans.

Genomic testing revealed that six of the 41 patients enrolled in the trial had NTRK1 or NTRK3 gene fusions in tumors representing many types of cancer, including sarcoma, gastrointestinal stromal tumor, non–small cell lung cancer, papillary thyroid cancer, and mammary analog secretory carcinoma of the salivary gland.

Tumors in five of the six patients with NTRK fusions demonstrated partial responses to LOXO-101 according to Response Evaluation Criteria in Solid Tumors, and the sixth patient achieved a 21% tumor regression. All six patients continue to receive LOXO-101 and are into at least their seventh 28-day cycle of LOXO-101 without disease progression.

Thus far, LOXO-101 has been well tolerated at various once-daily and twice-daily doses. Common side effects have included fatigue, dizziness, and nausea. The highest tolerable dose for LOXO-101 has not been determined. Data from the phase I trial, which were presented at the American Association for Cancer Research’s annual meeting in April, suggest that LOXO-101 is well tolerated and capable of inducing durable disease control in patients who have tumors with NTRK fusions.

Even as the phase I trial of LOXO-101 continues to enroll patients, a phase II trial (No. 2015-0728), which includes only patients whose tumors test positive for NTRK gene fusions, is under way. Patients in the phase II trial receive 100 mg of LOXO-101 twice daily.

“We are currently enrolling patients with all solid tumor types with NTRK fusions for a phase II trial,” said David Hong, M.D., an associate professor in the Department of Investigational Cancer Therapeutics. “NTRK fusions have been found in nearly every tumor type. The phase II trial is important for generating additional data about LOXO-101 in patients with NTRK fusion cancer, but we also anticipate it will further broaden the range of tumor types that we’ve tested thus far.”

FOR MORE INFORMATION
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Dr. Huifang Lu ...................... 713-563-8866

Local Consolidative Therapy for Oligometastatic Non–Small Cell Lung Cancer Triples Progression-Free Survival

Aggressive treatment with surgery, radiation therapy, or both following induction chemotherapy for patients with non–small cell lung cancer with three or fewer metastatic lesions (oligometastatic disease) yielded longer progression-free survival times than did standard therapy in a recent phase II clinical trial.

All patients in the trial received induction chemotherapy and then were randomly selected to receive standard treatment or aggressive local consolidative therapy. Standard treatment was determined by the treating physician and consisted of observation only or systemic maintenance therapy without surgery or radiation therapy. Local consolidative therapy was determined by a multidisciplinary team of medical, sur-

“\textit{We are currently enrolling patients with all solid tumor types with NTRK fusions for a phase II trial.}”

– Dr. David Hong

www.mdanderson.org/oncolog
gical, and radiation oncologists and consisted of surgery only, radiation therapy only, or both.

For patients who received local consolidative therapy, surgery could be performed on the primary tumor and/or one or more metastases. Radiation therapy could be delivered by three-dimensional conformal radiation therapy, intensity-modulated radiation therapy, stereotactic radiosurgery, or proton therapy.

“With this study, we wanted to be pragmatic and allow the breadth of treatments that are now available to patients in general practice,” said Daniel Gomez, M.D., an associate professor in the Department of Radiation Oncology at The University of Texas MD Anderson Cancer Center. Dr. Gomez was the principal investigator of the multi-institutional trial.

Although local consolidative therapy for non–small cell lung cancer has shown promise in previous studies, patients in those studies were carefully selected for favorable risk factors. “Our research is the first randomized prospective study of oligometastases in lung cancer to look at treating patients aggressively and comparing the results to standard therapy, which typically is maintenance therapy or observation,” Dr. Gomez said.

The prospective phase II trial, which was designed for 94 patients, ceased enrollment at 49 patients because of the benefit seen in the patients who received local consolidative therapy. At a median follow-up of 18.7 months, the median progression-free survival times were 11.9 months for patients who received local consolidative therapy and 3.9 months for patients who received standard treatment. The majority of patients who received standard treatment crossed over to receive local consolidative therapy after disease progression.

“These findings provide evidence and enthusiasm to offer aggressive local treatment and, with validation, could pave the way to treat tens of thousands of lung cancer patients with curative intent,” said Dr. Gomez, who presented the trial’s results at the American Society of Clinical Oncology’s annual meeting in June. Further results from the phase II trial will assess the patients’ overall survival and quality of life, and follow-up trials are being planned.

Immunotherapy Drug Nivolumab Reduces Tumor Burden in Patients with Metastatic Bladder Cancer

The immune checkpoint inhibitor nivolumab reduced tumor burden in 24.4% of patients with metastatic bladder cancer, according to the early results of an ongoing multi-institutional clinical trial of the drug in patients with various solid tumor types.

Nivolumab blocks programmed cell death protein 1 (PD-1) by binding to the PD-1 ligands (PD-L1 and PD-L2). In May, atezolizumab, which inhibits PD-L1 but not PD-L2, became the first drug to be approved by the U.S. Food and Drug Administration for the treatment of metastatic bladder cancer. Because PD-L1 expression on tumor cells is considered a prognostic marker for response to PD-L1 inhibitors, a secondary endpoint of the nivolumab clinical trial was to see whether expression of the ligand on pretreatment tumor biopsy specimens correlated with response to nivolumab treatment. The primary endpoint of the trial was the objective response rate.

In the phase I portion of the trial, which has completed enrollment, patients with metastatic cancer receive nivolumab (3 mg/kg intravenously every 2 weeks) until their disease progresses or treatment is discontinued because of adverse events. The early results for the trial’s cohort of patients with metastatic bladder cancer, all of whom had previously received at least one line of platinum-based chemotherapy, were reported at the annual meeting of the American Society of Clinical Oncology in June.

The overall response rate was 24.4% for the 78 patients with metastatic bladder cancer treated in the phase I portion of the study: five patients had complete responses, and 14 had partial responses. An additional 22 patients had stable disease, and 30 patients experienced disease progression. Grade 3 or 4 side effects occurred in 16 patients, and two patients died of treatment-related effects.

“The response rate is better than we’ve seen for other potential second-line treatments, and nivolumab is really well tolerated, which is important because bladder cancer patients are a fragile group after front-line treatment with platinum chemotherapy,” said Padmanee Sharma, M.D., Ph.D., a professor in the Department of Genitourinary Medical Oncology and The University of Texas MD Anderson Cancer Center’s principal investigator for the trial.

Dr. Sharma added that there was no significant difference in response to nivolumab between patients whose tumors expressed PD-L1 and those whose tumors did not. “We can get good results without choosing to treat patients based on PD-L1 status,” Dr. Sharma said.

In the phase II portion of the trial, patients will receive nivolumab plus ipilimumab, which inhibits the immune checkpoint known as cytotoxic T lymphocyte–associated protein 4.

“The response rate is better than we’ve seen for other potential second-line treatments.”

– Dr. Padmanee Sharma

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– Dr. Padmanee Sharma
Common Terms Used in Cancer Surgery

Cancer surgery is done in many ways for many reasons

Surgery is one of the most common treatments for cancer, but the thought of having surgery can be as frightening as the cancer itself. Understanding as much as possible about the surgery can ease these fears. If you or a loved one is going to have surgery, the terms below will be useful to know.

Types of cancer surgery

Curative surgery removes the entire cancer and is an attempt to cure the disease. Curative surgery is most helpful for cancers that are in only one part of the body. Chemotherapy, radiation therapy, or both may be given before or after curative surgery.

Palliative surgery eases pain or symptoms by removing all or part of a cancer. Palliative surgery does not cure cancer, but it helps improve patients’ quality of life.

Preventive or prophylactic surgery keeps cancer from happening. For example, a woman might have her breasts removed to prevent breast cancer if the disease runs in her family.

Reconstructive surgery is performed after cancer treatment to restore appearance and function.

Staging surgery helps doctors see where a cancer is located and how advanced it is.

Supportive surgery prepares a patient for other types of cancer treatment. For example, a patient might have a port (see below) put under the skin before receiving chemotherapy.

Open and minimally invasive approaches

Minimally invasive surgery, also called keyhole or laparoscopic surgery, uses cuts less than an inch long.

Open surgery means the surgeon makes a cut large enough to see into the body.

Robotic surgery uses one or more robotic arms controlled by a surgeon. These robotic arms can hold tiny instruments or laparoscopes (see below). This type of minimally invasive surgery helps keep surgeons’ hands from becoming too tired.

Surgical techniques

Ablation destroys cancers by making them very hot or cold. Surgeons use thin probes to heat or freeze the cancers.

Biopsy is the removal and study of small amounts of tissue from the body. The tissue can be taken after the cancer has been removed by surgery, in a separate surgery to remove only the tissue sample, or by a needle without surgery. Biopsies help doctors make an exact diagnosis.

Resection or excision means removal through surgery. If you see a word that ends in -ectomy, that tells you that all or part of an organ or structure is going to be removed. For example, a lumpectomy is the excision of a lump, and a nephrectomy is the excision of all or part of a kidney.

Surgical devices

Catheters are flexible tubes used to put liquids into or take liquids out of the body.

Drains are tube-like devices that take fluid out of a wound or part of the body.

Endoscopes, laparoscopes, and thorascopes are thin, tube-like instruments with lights and lenses that doctors can use to see inside the body. Sometimes, these instruments have tools attached that doctors use to operate.

Ports or port-a-caths are small devices that are implanted under the skin and that lead into a blood vessel. Drugs can be given and blood can be drawn through these devices so that patients do not need multiple needle sticks.

Shunts are passageways that allow fluid to move from one part of the body to another. For example, a surgeon may use a shunt to redirect blood.

Words describing cancers or other tissues

Bilateral cancers affect both the right and left sides of the body. For example, bilateral breast cancer is found in the right and left breasts and might be treated with a bilateral mastectomy (removal of both breasts).

Inoperable cancers cannot be treated with surgery. Other treatments such as radiation and chemotherapy may be used instead.

Obstructions block passages in the body. For example, colon cancers sometimes cause bowel obstructions (the colon is part of the large bowel or large intestine) and have to be removed.

Operable cancers can be treated with surgery.

Resectable cancers that can be removed completely by surgery.

Unilateral cancers affect only one side of the body. For example, unilateral breast cancer affects only one breast.

If you hear your medical team use words that aren’t familiar to you, be sure to ask for an explanation. Your team will be happy to help. You can also find a glossary of cancer terms at http://bit.ly/28KKMv4.

– L. Russell

For more information

- Ask your physician
- Call askMDAnderson at 877-632-6789
- Visit www.mdanderson.org
Cancer Treatment Algorithms

Cancer treatment is constantly evolving as new drugs and new surgery and radiation therapy techniques are introduced. To help physicians follow current best practices when caring for their cancer patients, The University of Texas MD Anderson Cancer Center offers treatment algorithms for most types of cancer.

The cancer treatment algorithms reflect detailed, multidisciplinary approaches to patients’ diagnostic work-up, treatment according to disease stage, and ongoing surveillance. Treatment algorithms are available for the following disease types:

- **Brain cancer**: leptomeningeal, 1–3 metastatic lesions, more than 3 metastatic lesions, and diffuse glioma
- **Breast cancer**: invasive, noninvasive, Paget disease, phyllodes tumor, and breast cancer during pregnancy
- **Gastrointestinal cancer**: colon, esophageal, gastric, hepatocellular, pancreatic, and rectal
- **Genitourinary cancer**: bladder, prostate, renal, and testicular
- **Gynecologic cancer**: cervical, endometrial, and ovarian
- **Head and neck cancer**: larynx and oral cavity
- **Leukemia**: acute lymphoblastic leukemia and lymphoblastic lymphoma, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, and myelodysplastic syndrome
- **Lung cancer**: non–small cell and small cell
- **Lymphoma**: AIDS-related B cell, Burkitt and double-hit, diffuse large B cell, follicular (grades 1 and 2), gastric mucosa–associated lymphoid tissue, Hodgkin, mantle cell, non–gastric mucosa–associated lymphoid tissue, peripheral T cell, and primary mediastinal large B cell
- **Melanoma**: cutaneous
- **Myeloma**: multiple myeloma, solitary and extramedullary, plasmacytoma, and Waldenström macroglobulinemia
- **Pediatric cancer**: osteosarcoma
- **Sarcoma**: primary bone cancer and soft tissue (clinical stage III)
- **Unknown primary cancer**

The cancer treatment algorithms were developed by multidisciplinary teams of clinicians and researchers at MD Anderson. The algorithms are frequently updated, and some algorithms may be unavailable while revisions are being made. The algorithms are not a replacement for physicians’ clinical judgement but are intended to help physicians make evidence-based recommendations to their patients.