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DALLAS

CANCER UPDATE

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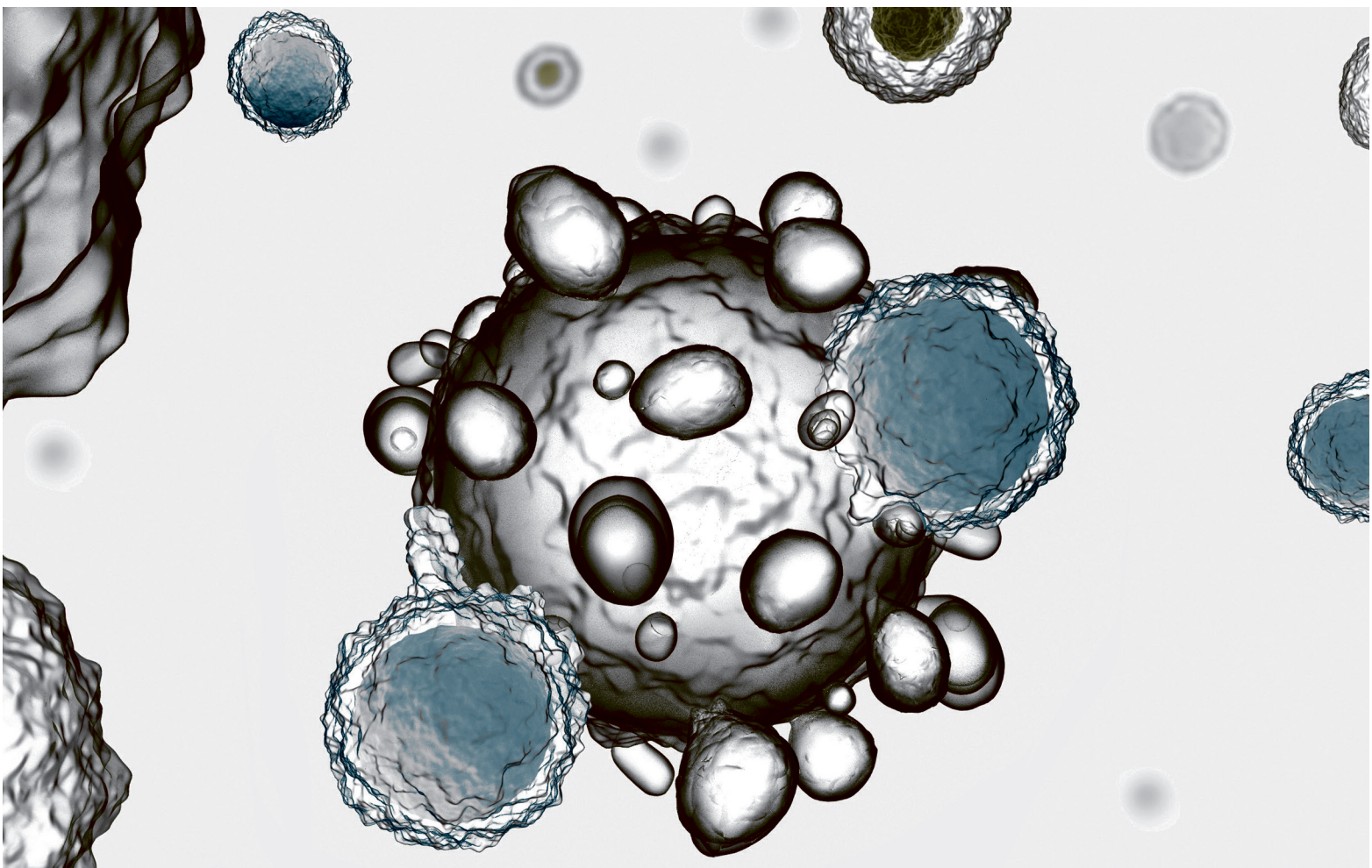

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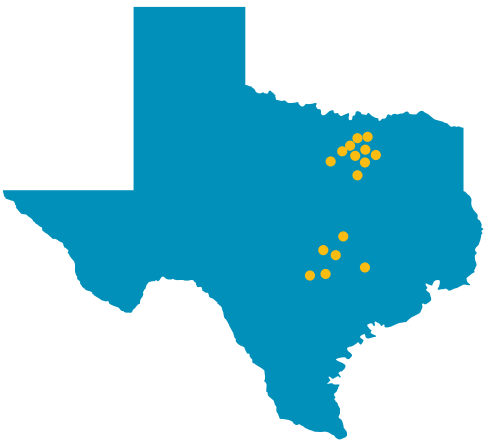
BAYLOR SCOTT & WHITE ONCOLOGY

Cancer research studies at Baylor Charles A. Sammons Cancer Center, located on the campus of Baylor University Medical Center, are conducted through Baylor Scott & White Research Institute, Texas Oncology and U.S. Oncology. Each reviews, approves and conducts clinical trials independently.

HOSPITAL-BASED CANCER PROGRAMS

Baylor Scott & White Health has the largest network of hospital-based cancer programs in Texas with 16 cancer centers.



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For more information, call **214.820.3535** or visit us at **BSWH.md/Oncology.**

FROM THE MEDICAL

DIRECTOR

Strong Building Blocks for an Even Stronger Future

The Royal College of Surgeons (RCSI) in Ireland has had a mission for more than 200 years to *educate, nurture and discover for the benefit of human health*. Johns Hopkins Medicine seeks to *improve the health of the community and the world by setting the standard of excellence in medical education, research and clinical care*. Like so many RCSI alumni and clinicians at Johns Hopkins, these values have left a lasting impression on me, and I am now delighted to align myself to the life changing work that is being carried out every day at Baylor Scott & White Health, *to promote the well-being of all individuals, families and communities*.

As a thoracic oncologist by training, I've served as a clinical investigator at the National Cancer Institute and spent nearly a decade of my career at John Hopkins establishing a portfolio of innovative lung and esophageal cancer trials. I also completed a master's degree in business administration approximately 20 years ago from University College Dublin with a focus on health economics and drug costs because of my interest in advancing the industry conversation around improving quality of care and enhancing value for patients.

My focus on discovering new therapies, as well as new operational practices, is part of what brought me to Baylor Scott & White. However, it was the size of the Baylor Scott & White network, expertise of its staff and clinicians as well as potential for future growth and medical advancement that were key in my personal decision to take on my new role. These were the building blocks that I identified as critical components needed to develop a world class oncology program.

Baylor Scott & White has a patient-centered approach that rings true across the System, and it's not something you see at many other programs in the US. Far too often, hospitals forget about the psychological toll cancer takes on patients and their families, but not here. Our offerings—like music therapy, art therapy, patient and nurse navigators, healthy eating classes, coping programs for children and caregivers of loved ones with cancer, and specialized rehabilitation clinics —are not the norm at other systems. Furthermore, the facilities here are second to none. The Baylor Charles A. Sammons Cancer Center and Baylor T. Boone Pickens Cancer Hospital are both on the campus of Baylor University Medical Center in Dallas. Together, they represent one of the largest cancer treatment centers in the nation. Across Texas, Baylor Scott & White has 16 cancer facilities, making up the largest hospital-based cancer network in the state, treating thousands of patients each year.

Additionally, our oncology program through the Baylor Scott & White Research Institute is investigating a number of exciting and highly novel immunotherapeutic strategies across multiple hematologic and solid tumors. Research successes seen in recent years using CAR-T and NK cells along with other cellular therapies are very promising. Our program is primed to be a standout immunotherapy center in the US—a destination for advanced immunotherapy oncology trials with an eye on the psychological, familial and spiritual support that patients and their loved ones need along their journey.

We're putting these building blocks together, and adding to them, to be an even stronger cancer program for the patients and families we serve today and those we'll serve in the future. I look forward to sharing more exciting news with you in coming issues as we expand our program.

Ronan Kelly, MD, MBA
Chief of Oncology, Baylor Scott & White Health - North Texas
Director, Baylor Charles A. Sammons Cancer Center - Dallas

BAYLOR CHARLES A. SAMMONS CANCER CENTER

CURRENT CLINICAL TRIALS

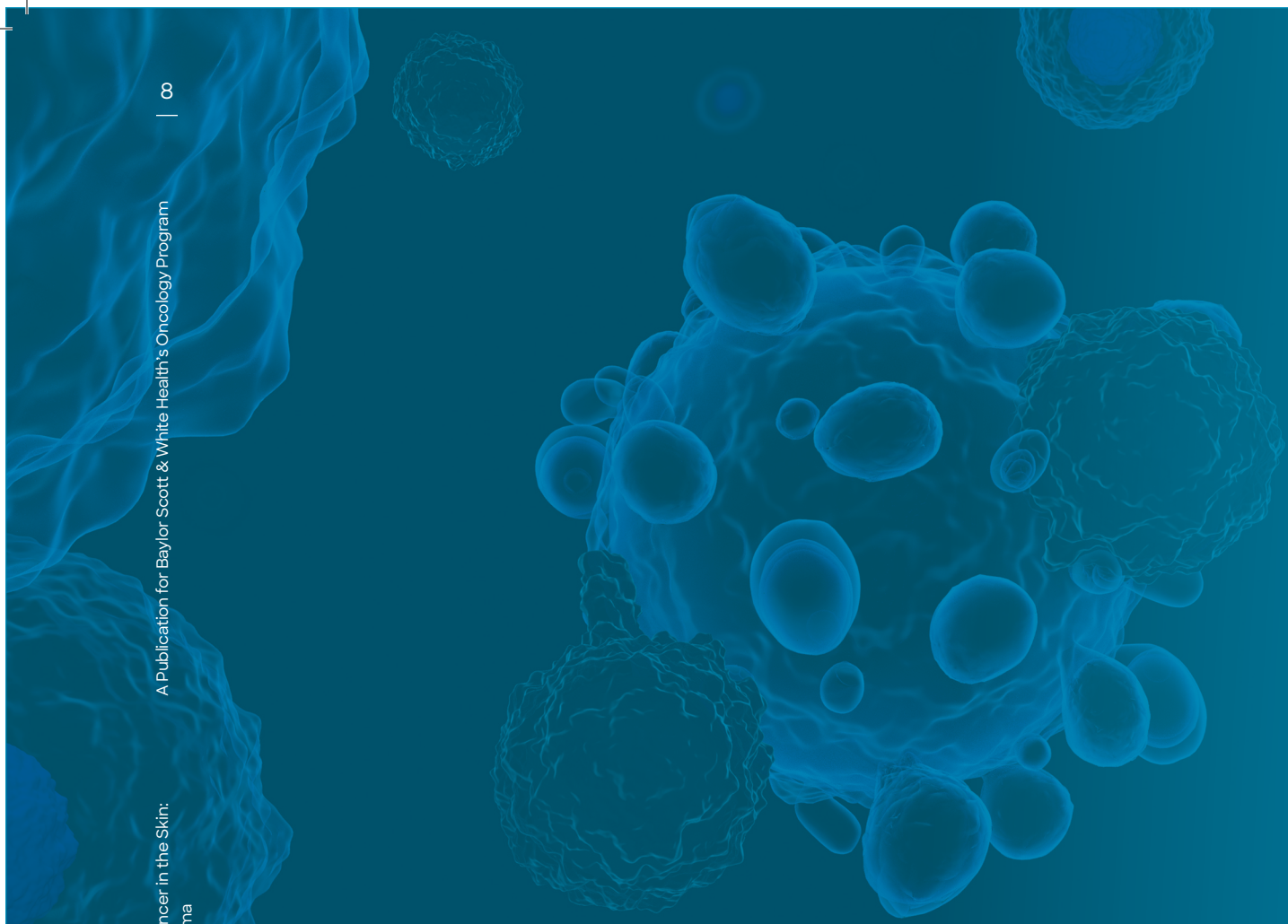
Site	Study ID	Location	Principal Investigator
Breast	017-478	Baylor Dallas	Joyce A. O'Shaughnessy, MD
	T01797	Texas Oncology - Dallas	Joyce A. O'Shaughnessy, MD
	18004	Texas Oncology - Dallas	Joyce A. O'Shaughnessy, MD
	18042	Texas Oncology - Dallas	Joanne Blum, MD, PhD, FACP
Lung	17199	Texas Oncology - Dallas	Kartik Konduri, MD
	17201	Texas Oncology - Dallas	Kartik Konduri, MD
	T01763	Texas Oncology - Dallas	Kartik Konduri, MD
GI	17186	Texas Oncology - Dallas	A. David McCollum, MD
	13195	Texas Oncology - Dallas	Carlos H.R. Becerra, MD
	18016 STAR	Texas Oncology - Dallas	A. David McCollum, MD
GU	15180	Texas Oncology - Dallas	Thomas E. Hutson, DO, PharmD
	T01761	Texas Oncology - Dallas	Thomas E. Hutson, DO, PharmD
Head & Neck	017-075	Baylor Dallas	Eric Nadler, MD, MPP

Study Title

A Phase 1, Multicenter, Open-label, Multiple Dose-escalation Study of ARX788, Intravenously Administered as a Single Agent in Subjects with Advanced Cancers with HER2 Expression
Phase 1a/2a Dose Escalation Trial to Determine Safety, Tolerance, MTD, and Preliminary Antineoplastic Activity of AVID100, in Patients With Advanced or Metastatic Solid Tumors of Epithelial Origin
Single Arm, Open Label Phase 1b/2 Study of SGN-LIV1A in Combination With Pembrolizumab for First-Line Treatment of Patients With Unresectable Locally-Advanced or Metastatic Triple-Negative Breast Cancer
A Phase 2, Non-randomized, Open Label, Single Arm, Multi-center Study Of Talazoparib For Neoadjuvant Treatment Of Germline Brca1/2 Mutation Patients With Early Triple-negative Breast Cancer
A Randomized Phase 2 Trial of AM0010 in Combination with Pembrolizumab vs. Pembrolizumab Alone as First-Line (1L) Therapy in Patients with Stage IV/Metastatic Wild Type (WT) Non-Small Cell Lung Cancer and Tumors with High Expression of PD-L1 (>50%).
A Randomized Phase 2 Trial of AM0010 in Combination With Nivolumab vs. Nivolumab Alone as Second-Line Therapy in Subjects With Stage IV / Metastatic Wild Type Non-Small Cell Lung Cancer and Low Tumor Expression of PD-L1
An Expanded Access Protocol For Lorlatinib For Treatment Of Patients With Advanced Non-small Cell Lung Cancer Harboring Specific Molecular Alterations
An Open-Label Exploratory Phase 2/3 Study of Nivolumab With Standard of Care Therapy vs Standard of Care Therapy for First-Line Treatment of Metastatic Colorectal Cancer
A Phase I/II Study of CX-4945 in Combination With Gemcitabine and Cisplatin in the Frontline Treatment of Patients With Cholangiocarcinoma
An International, Multicenter, Open-label, Randomized, Phase 3 Study of BLU-285 vs Regorafenib in Patients With Locally Advanced Unresectable or Metastatic Gastrointestinal Stromal Tumor (GIST)
A Multicenter, Open-Label Phase 1b/2 Trial of Lenvatinib (E7080) Plus Pembrolizumab in Subjects With Selected Solid Tumors
A Phase 1b Dose-Escalation Study of Cabozantinib (XL184) Administered Alone or in Combination With Atezolizumab to Subjects With Locally Advanced or Metastatic Solid Tumors (Urothelial carcinoma or Castrate-resistant Prostate Cancer)
A Multicentre, Randomized, Open-Label, Phase III Clinical Trial Of Gemcitabine And Carboplatin Followed By Epstein-Barr Virus-Specific Autologous Cytotoxic T Lymphocytes Versus Gemcitabine And Carboplatin As First Line Treatment For Advanced Nasopharyngeal Carcinoma Patients

Hematologic Malignancies	17212	Texas Oncology - Dallas	M. Yair Levy, MD
	018-019	Baylor Dallas	Edward Pearson, MD
	018-097	Baylor Dallas	Christopher Maisel, MD
	014-129	Baylor Dallas	M. Yair Levy, MD
	018-057	Baylor Dallas	Edward Pearson, MD
	018-127	Baylor Dallas	M. Yair Levy, MD
	018-128	Baylor Dallas	M. Yair Levy, MD
	018-170	Baylor Dallas	Houston Holmes, MD
	018-526	Baylor Dallas	Edward Pearson, MD
Skin	17060	Texas Oncology - Dallas	C. Lance Cowey, MD
	T01809	Texas Oncology - Dallas	C. Lance Cowey, MD
Pancreas	16187	Texas Oncology - Dallas	Carlos H.R. Becerra, MD
Solid Tumors	16106	Texas Oncology - Dallas	Carlos H.R. Becerra, MD
	18057	Texas Oncology - Dallas	Carlos H.R. Becerra, MD
	18020	Texas Oncology - Dallas	Carlos H.R. Becerra, MD
	18119	Texas Oncology - Dallas	Carlos H.R. Becerra, MD
	018-159	Baylor Dallas	A. Scott Paulson, MD

A Phase 1, Open-Label, Dose-Finding Study of INCB050465 in Combination With Investigator Choice of Rituximab, Bendamustine and Rituximab, or Ibrutinib in Participants With Previously Treated B-Cell Lymphoma (CITADEL-112)
A Multicenter, Double-Blind, Randomized, Placebo-Controlled, Phase III Study of Idasanutlin, an MDM2 Antagonist, with Cytarabine Versus Cytarabine Plus Placebo in Patients with Relapsed or Refractory Acute Myeloid Leukemia (AML)
A Phase 1/2 Study Evaluating the Safety and Pharmacokinetics of ABT-199 in Subjects with Relapsed or Refractory Multiple Myeloma
A Phase I Dose Escalation with Two Disease Specific Expansions, Multicenter, Open-label, Safety, Pharmacokinetic and Pharmacodynamic Study of APTO-253 in Patients With Relapsed or Refractory Acute Myelogenous Leukemia or High-Risk Myelodysplasia
A Phase 1b Study of TAK-659 in Combination With Venetoclax for Adult Patients With Previously Treated Non-Hodgkin Lymphoma
A Randomized Phase 3 Study to Evaluate the Efficacy and Safety of Enzastaurin Plus R-CHOP Versus R-CHOP in Treatment-Naive Subjects With High-Risk Diffuse Large B-Cell Lymphoma Who Possess the Novel Genomic Biomarker DGM1™
A Phase 1, Multi-center, Open-label Study of IMGN779 Administered Intravenously in Adult Patients with Relapsed / Refractory CD33-positive Acute Myeloid Leukemia
Long-term Follow-up Study of Subjects Treated With an Autologous T Cell Product Expressing an Antibody Coupled T Cell Receptor (ACTR)
A Phase 3, Randomized, Open-Label, Crossover Study of ASTX727 (Cedazuridine and Decitabine Fixed-Dose Combination) Versus IV Decitabine in Subjects With Myelodysplastic Syndromes (MDS) and Chronic Myelomonocytic Leukemia (CMML) [ASTX727-02]
A Phase 2, Open-Label, Single Arm Study to Evaluate the Safety and Efficacy of Pembrolizumab in Participants With Recurrent or Metastatic Cutaneous Squamous Cell Carcinoma (R/M cSCC)
A Phase I/2a Dose Escalation and Cohort Expansion Study of the Safety, Tolerability, and Efficacy of Anti-LAG-3 Monoclonal Antibody (BMS-986016) Administered Alone and in Combination With Anti-PD-1 Monoclonal Antibody (Nivolumab, BMS-936558) in Advanced Solid Tumors (Melanoma)
Randomized Study of AM0010 in Combination With FOLFOX Compared to FOLFOX Alone as Second-line Treatment in Patients With Metastatic Pancreatic Cancer That Has Progressed During or Following a First-Line Gemcitabine Containing Regimen
A Phase 1/1b, Open Label, Multiple Dose, Dose Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics and Antitumor Activity of the Anti-PD-1 Monoclonal Antibody BGB-A317 in Combination With the PARP Inhibitor BGB-290 in Subjects With Advanced Solid Tumors
A Phase 1/2 First-in-Human Study of BMS-986249 Alone and in Combination With Nivolumab in Advanced Solid Tumors
A Phase 1/2a Study of BMS-986253 in Combination With Nivolumab in Advanced Cancers
Phase I/II Pharmacokinetic Multi-Tumor Study of Subcutaneous Formulation of Nivolumab Monotherapy
A Multi-Center, Open-Label, Clinical Trial to Evaluate the Safety, Tolerability, Pharmacokinetics of Sulfatinib in Advanced Solid Tumors.



Feature Article

BAYLOR CHARLES A. SAMMONS CANCER CENTER
AND BAYLOR SCOTT & WHITE RESEARCH INSTITUTE

INNOVATIVE IMMUNO-ONCOLOGY CLINICAL TRIAL USING NATURAL KILLER CELLS

Immunotherapy has revolutionized the fight against cancer. Unlike traditional pharmaceuticals, immunotherapeutics harness the innate cell-killing power of the immune system to remove tumors. Researchers at Baylor Charles A. Sammons Cancer Center, located on the campus of Baylor University Medical Center (Baylor Dallas), part of Baylor Scott & White Health, and conducted through the Baylor Scott & White Research Institute and Fate Therapeutics, are testing a novel immunotherapy for difficult-to-treat solid tumors.

For many years, researchers suspected that it could be possible for the immune system to do the work in fighting cancer. However, cancers release factors that suppress the immune system. Once scientists began to discover how the tumor cells interact with the immune system, it became possible to design therapies that wake up the immune system and allow it to recognize and kill the cancer.

One class of immunotherapies uses modified immune cells as a "living drug" to harness the power of the immune system for killing cancer cells. The most well-studied of these cell-based immunotherapeutics is the chimeric antigen receptor (CAR) T cell. CAR-T cells are T lymphocytes that have been engineered to recognize proteins on the cancer cell surface. However, new breakthroughs have led researchers to consider anti-cancer treatments that use another type of immune cell: the natural killer (NK) cell.

According to Carlos Becerra, MD, medical director of the Swim Across America Innovative Clinical Trials Center at Baylor Sammons Cancer Center and study investigator, NK cells may have advantages over CAR-T cells for cancer therapy because of their innate cytotoxic capacity. "NK cells are the front lines of the army we have in the immune system to attack any invader. So they are ready to attack and kill foreign cells. T cells, on the other hand, have to be sensitized to know which cells are foreign." Although using NK cells might have therapeutic advantages, the safety and efficacy of these NK cell-based therapies in humans are not known.

FATE-NK100 study

This multicenter outpatient phase 1 study will test the safety of a new NK cell-based therapy, known as FATE-NK100, in patients with advanced metastatic solid tumors. The researchers hope to enroll 100 participants in the study. Baylor Dallas is one of only two sites in the study and the only site in the United States.

To generate FATE-NK100, NK cells are taken from the body of a related donor using a process called apheresis. Then, the cells are treated in a specialized facility for seven days using pharmacologic agents that inhibit glycogen synthase kinase 3 beta (GSK3B). Inhibition of GSK3B has been shown to induce maturation of NK cells and increase anti-tumor activity. This procedure induces a subtype of NK cells, known as adaptive NK cells, that behave more like the adaptive immune system and can be expanded ex vivo. The FATE-NK100 cell therapy is then delivered to the cancer patient, who is monitored for safety and efficacy.

This single-dose open-label dose-escalation trial includes three treatment regimens. One group will be treated with FATE-NK100 alone. In the second group, patients with human epidermal growth factor receptor 2-positive (HER2+) cancers, including breast and gastric cancer, will receive a HER2/neu receptor inhibitor in addition to FATE-NK100. In the third group, patients with epidermal growth factor receptor 1-positive (EGFR1+) cancers, including advanced colorectal cancer and head and neck squamous cell cancer, will receive an EGFR inhibitor in addition to FATE-NK100.

Natural killer cells in cancer therapy

Tumor-killing NK cells were first identified over 40 years ago as components of the innate immune system. These large granular lymphocytes use a set of positive and negative signals, including the expression of major histocompatibility complex (MHC) class 1 molecules, to distinguish the body's cells from those of invaders. Under normal conditions, NK cells act as a primary defense against a variety of pathogens. They also participate in tumor immunosurveillance, recognizing and destroying malignant cells. NK cells destroy tumor cells both directly, via the release of cytolytic granules, and indirectly, via cytokine release. Although anti-tumor NK cells are present in very low numbers, their potent capacity for identification and destruction of tumor cells make them an attractive target for anti-cancer therapy, especially when combined with strategies to expand and mature the NK cells ex vivo.

Clinical Trials at Baylor Charles A. Sammons Cancer Center

Novel clinical trials, such as the FATE-NK100 study, are made possible by the resources available at the Baylor Sammons Cancer Center at Baylor University Medical Center. The Swim Across America Innovative Clinical Trials Center at Baylor Sammons Cancer Center provides a single location for clinical trial participants to go for examinations, therapies and follow-up.

There are over 50 clinical trials currently active on campus. Baylor Sammons Cancer Center is also a member of the National Cancer Institute-sponsored Cancer Immunotherapy Trials Network and the Southwest Oncology Group.

> NK cells are the front lines of the army we have in the immune system to attack any invader. So they are ready to attack and kill foreign cells. T cells, on the other hand, have to be sensitized to know which cells are foreign.
>
> **Carlos Becerra, MD**
> Medical director of the Swim Across America Innovative Clinical Trials Center at Baylor Sammons Cancer Center and study investigator

In collaboration with Baylor Scott & White Research Institute, Baylor University Medical Center offers essential clinical trial infrastructure that is not available at most cancer centers. For the FATE-NK100 study, the NK cells are collected, processed, and delivered to participants on campus. The presence of an on-site FDA-regulated GMP resource for small-scale manufacturing of cell-based products facilitates the production and use of FATE-NK100 and other innovative cell-based therapeutics.

According to Dr. Becerra, "We are one of two sites that is preparing this approach with NK cells. Many others are using CAR-T cells, but this is a different approach. The NK cells don't need to be primed, so it may be a better approach."

To learn more about immuno-oncology clinical trials at Baylor University Medical Center, call **214.820.3535** or visit **BSWH.md/Oncology**.

WHAT ARE NEUROENDOCRINE TUMORS?

In the United States, approximately 15,000 to 25,000 people are diagnosed with a neuroendocrine cancer each year. Although neuroendocrine tumors (NETs) represent less than 2% of all diagnosed malignancies, their unique hormone-secreting properties and the propensity for metastasis make them important to find and treat.

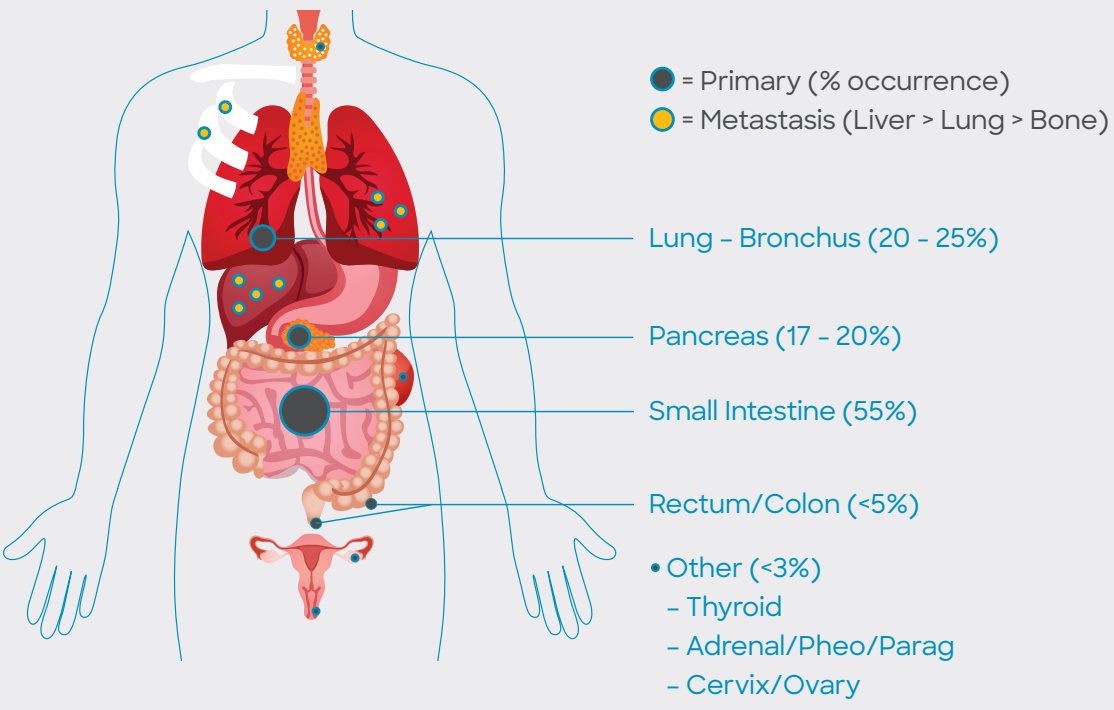
Types of neuroendocrine tumors

NETs are rare cancers that originate from hormone-producing cells located throughout the body. NETs can develop at a variety of sites and are extremely heterogeneous, both in the tumor biology and the clinical presentation (see Figure 1).

The most common NETs originate in the gastrointestinal system and lung, totaling about 12,000 cases per year. Low- and intermediate-grade tumors typically present with a well-differentiated cellular architecture with cancer cells that look normal and tend to grow slowly. High-grade tumors, known as neuroendocrine carcinomas, tend to be poorly differentiated. Poorly differentiated NETs are usually malignant and have a poor prognosis.

Diagnosis of these NETs relies on evaluation of multiple variables, including clinical symptoms, hormone levels, diagnostic imaging, and pathology results. The clinical judgment of an experienced multidisciplinary team is important at diagnosis because some tumors with a well-differentiated appearance can be highly aggressive.

Figure 1. Anatomical Distribution of Neuroendocrine Tumors



Second floor lobby for Baylor Charles A. Sammons Cancer Center at Baylor University Medical Center.

Symptoms and biomarkers

Neuroendocrine tumors are categorized as functional or nonfunctional. Functional tumors typically present with symptoms associated with increased hormone secretion, whereas nonfunctional tumors are often either asymptomatic or present with nonspecific symptoms related to the tumor location. Nonfunctional tumors are very difficult to detect. Even functional tumors present with diverse symptomatology, and over 50% of symptomatic patients have metastases at the time of diagnosis. Because of these factors, awareness of neuroendocrine tumors is often low among physicians.

Risk factors and genetic basis

Unlike many cancer types, most NETs have no clear environmental or lifestyle-associated risk factors. Heritable genetic risk factors are also largely absent. A small number of familial syndromes increase the risk of neuroendocrine tumor formation (see story on page 20). Although other heritable mutations may exist, the rarity of neuroendocrine cancer has made it difficult to identify familial variants. Thus, prevention and early detection strategies, which are important for other cancer types, such as breast and colon, cannot be applied to neuroendocrine tumors. Improvements in physician awareness and diagnostic imaging, however, have helped contribute to increasing the overall number of new neuroendocrine tumors identified.

More research is needed to understand NETs. According to Carlos Becerra, MD, oncologist on the medical staff at Baylor Charles A. Sammons Cancer Center at Dallas and medical director of the Swim Across America Innovative Clinical Trial Center at Baylor Dallas, there are several key areas of focus, "Trying to determine the underlying biology of the tumor is one area of importance. The second is trying to determine if there are any actionable molecular targets, including potential mutations that develop in the tumors and/or signaling pathways. Third, we are trying to bring new treatment modalities." He noted that researchers are already seeing an increase in the number of therapies available and more are on the horizon.

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BAYLOR UNIVERSITY MEDICAL CENTER

A MULTIDISCIPLINARY APPROACH TO NEUROENDOCRINE CANCER

These uncommon, rare tumors provide a unique set of challenges to the cancer care team as guidelines for treatment are still in development and treatment plans are highly customized. In particular, the course of diagnosis and treatment is often complicated and requires a range of expertise. The Neuroendocrine Research and Treatment Center at the Baylor Charles A. Sammons Cancer Center, located on the campus of Baylor University Medical Center (Baylor Dallas), addresses these challenges by bringing together a strong, multidisciplinary team (MDT) to discuss best practice standards and lead collaborative research with the aim to achieve excellence in patient care and support. This approach is enhanced by the use of innovative diagnostic and therapeutic tools. Because of the variability in the clinical presentation and underlying biology of each tumor, the management of NETs is an excellent domain for realizing the goals of personalized medicine.

The team at the Neuroendocrine Research and Treatment Center is well positioned to serve as a resource for multidisciplinary evaluation of NETs and to provide leadership in research and quality of care. According to Robert Goldstein, MD, chief of hepatobiliary surgery at Baylor Dallas, the overall goal is to create a “healing arts” program that combines the arts of surgery, medicine, and psychosocial support. “There has been an unbelievable transition due to the support that Baylor Dallas has given to cancer patients by recognizing that there is more than just the knife in medicine. For years and years, we thought that was all you needed. Now we realize there is much, much more to healing a patient.” The following sections review how the unique attributes of neuroendocrine tumors are approached by select specialties on the multidisciplinary team. In addition to these areas of expertise, the team also includes radiation oncologists, nuclear medicine specialists, endocrinologists, pathologists, nurses and patient navigators. This team meets twice a month to discuss ongoing treatment plans and offer expert opinions.

A MULTIDISCIPLINARY APPROACH TO NEUROENDOCRINE CANCER

MEDICAL ONCOLOGY

Medical oncologists often serve as the NET patient's primary contact for the medical system, coordinate and administer medication, and meet with the MDT to develop the treatment strategy. Their precise role depends on the state of the cancer at diagnosis. According to Scott Paulson, MD, co-medical director for the Neuroendocrine Research and Treatment Center at Baylor Dallas, "Fortunately, we have had a large number of new tools become available over just the past several years. Unfortunately, we are not quite sure of the optimal sequence, and further research is needed to answer those questions. In the meantime, therapies are sequenced based on the specifics of a particular patient's cancer."

For late-stage disease, traditional chemotherapies can be the best therapeutic option. Therapies such as everolimus (an mTOR inhibitor), sunitinib (a protein kinase inhibitor), capecitabine (a thymidylate synthetase inhibitor, via metabolism to 5-fluorouracil), and temozolomide (an alkylating agent) also show promise for specific indications. However, earlier stage disease is often indolent and does not respond well to chemotherapy. For these patients, targeted therapies are being heavily pursued. An exciting development for the treatment of gastroenteropancreatic NETs was the recent approval by the US Food and Drug Administration (FDA) of the targeted radiopharmaceutical ^{177}Lutetium (Lu)-DOTATATE (Lutathera), which falls into the class of peptide receptor radionuclide therapy (PRRT) (see story on page 24). These agents take advantage of the presence of the somatostatin receptor on the surface of many

NETs. In PRRT, a peptide that binds the somatostatin receptor is coupled to a radioactive payload, and this combined radiopharmaceutical then targets and destroys the cancer cells. PRRT is highly specific but challenging to administer. Baylor Dallas provides the specialized radiation oncology expertise and infrastructure needed for this advanced therapeutic strategy (see Figure 2).

Other therapies under development for NETs include immunotherapy and adoptive cell therapies. Such strategies, which help cells of the immune system recognize and kill the tumor, have been successful for other cancer types. According to Dr. Becerra, "When neuroendocrine tumors don't respond to standard therapy or clinical trials, then we have phase 1 trials, which is where new therapies are being studied." The Swim Across America Innovative Clinical Trials Center at Baylor Dallas enrolls new patients every year in phase 1 trials across various cancer types and contributes to nationwide clinical trial networks.

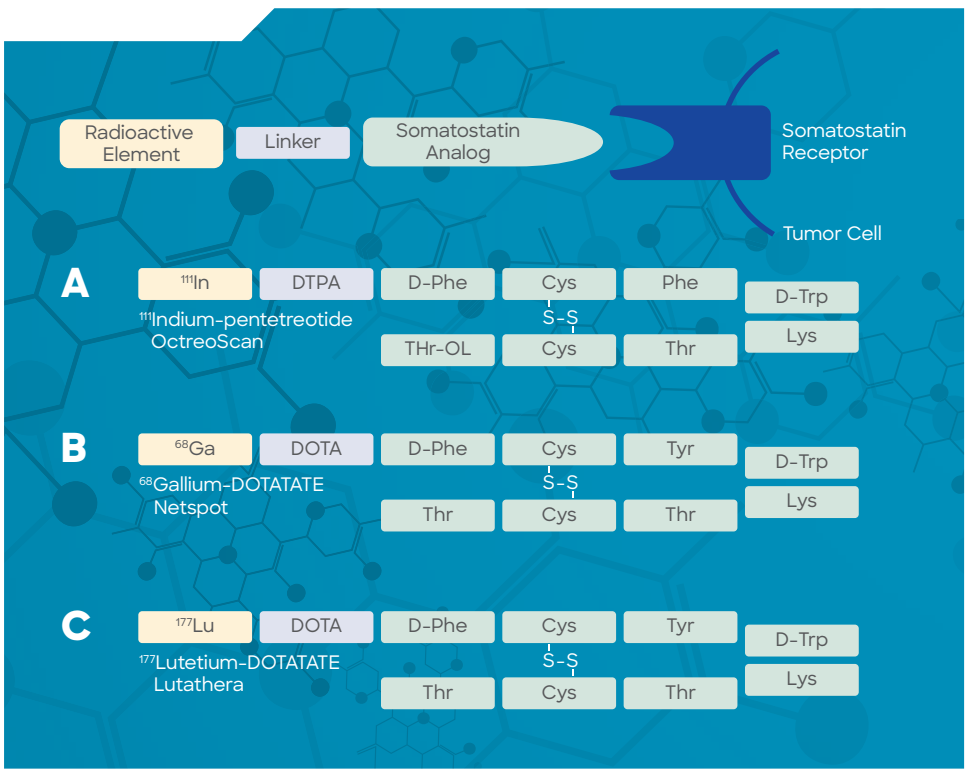


Figure 2. Schematic of radiopharmaceuticals for diagnosis and treatment of neuroendocrine tumors. For each radiopharmaceutical, a cyclic somatostatin peptide analog is linked to a radioactive element. Panels A and B show the imaging agents ^{111}Indium-pentetreotide (OctreoScan) and ^{68}Gallium-DOTATATE (Netspot). Panel C shows the therapeutic agent ^{177}Lutetium-DOTATATE (Lutathera).

Adapted with permission from Okavari SM. Peptide-based radiopharmaceuticals and cytotoxic conjugates: Potential tools against cancer. *Cancer Treatment Reviews.* 2008; 34(1):13-26 and Fani M, Maecke HR, Okarvi SM. Radiolabeled Peptides: Valuable Tools for the Detection and Treatment of Cancer. *Theranostics* 2012; 2(5):481-501.

A MULTIDISCIPLINARY APPROACH TO NEUROENDOCRINE CANCER

SURGICAL ONCOLOGY

Surgery plays a critical role in the treatment of NETs, and the surgical oncologist works with the MDT to evaluate the risk-to-benefit ratio of intervention. In particular, risks associated with the tumor's hormone secretion must be managed along with any surgical consideration. If the cancer is diagnosed early, surgery is often very important and can substantially improve the prognosis. In the middle stages, where the disease has spread but there may or may not be symptoms, careful evaluation is required to determine whether surgery is right for the patient. In the late stages, surgery once again plays an important role to debulk metastases. Although the primary tumor may be very small, the metastases can often be three to five times larger than the original tumor, and the disease is often only recognized once the metastatic lesions are large enough to cause symptoms. For instance, 40% of intestinal and 60 to 70% of pancreatic NETs present with liver metastases at diagnosis. In these cases, the goal of surgery is to improve quality of life for the patient.

Carcinoid syndrome, which occurs in approximately 5% of NETs, can play an important role in the decision to perform surgery to improve quality of life for late-stage NET patients. In this syndrome, the tumor produces serotonin, which can overwhelm the metabolic capacity of the liver, especially in the presence of liver metastases. The serotonin overload causes a variety of dangerous symptoms including gastrointestinal distress, skin flushing,

and cardiomyopathy. Debulking surgery is a common strategy to reduce the serotonin levels and stabilize symptoms. A new therapy, telotristat ethyl, which blocks the rate-limiting step in serotonin production, was FDA approved in 2017 for carcinoid syndrome. Thus, the MDT must work together to consider the latest medical and surgical strategies in each patient's treatment sequence.

The surgeon is typically a key contributor to the MDT throughout a long cancer management process. Sometimes the tumor is indolent and is monitored for years before treatment; also, recurrence is common. Dr. Goldstein noted that it is important to seek specialized expertise because the treatment strategy for NETs is so different from the treatment for other tumors in the same organ. "Unless you are really dedicated to neuroendocrine tumors, you probably can follow the plans that are given by a multidisciplinary team, but it is hard to come up with a good plan independently."

A MULTIDISCIPLINARY APPROACH TO NEUROENDOCRINE CANCER

RADIOLOGY AND NUCLEAR MEDICINE

Diagnostic imaging of NETs can be challenging, as very small lesions can have a major impact on the clinical course and treatment selection. Computed tomography (CT) and magnetic resonance imaging comprise the first line of anatomical imaging, but molecular imaging with nuclear medicine, which uses radioactively labeled compounds for diagnosis and treatment, plays an essential role in neuroendocrine cancer. Nuclear medicine agents target tumor-specific proteins, such as somatostatin receptors, or NET cells.

The somatostatin receptor-binding peptide ^{111}Indium(In)-pentetreotide (OctreoScan) was FDA approved in 1994 and is widely used for routine nuclear imaging of NETs (see Figure 3 on page 16). However, optimal results require long imaging sessions over two days and a single-photon emission computed tomography (SPECT) camera that incorporates simultaneous CT imaging (SPECT/CT) to generate co-registered anatomic and molecular image "slices" throughout the body. Another nuclear imaging modality, positron emission tomography (PET; typically combined with simultaneous CT as PET/CT), uses different types of radioactive agents, with higher resolution for small tumors and shorter imaging times.

> A positive imaging result with 68Ga-DOTATATE has been shown to help predict the patient's response to Lutathera, making targeted diagnostic imaging a crucial component of personalized medicine.
>
> **Landis Griffeth, MD, PhD**
> Radiologist specializing in nuclear medicine and chairman of the Committee on Radiation Safety and Radiopharmaceuticals at Baylor Dallas

According to Landis Griffeth, MD, PhD, radiologist specializing in nuclear medicine and chairman of the Committee on Radiation Safety and Radiopharmaceuticals at Baylor Dallas, "Multiple somatostatin analogs for neuroendocrine tumors have been evaluated in PET/CT research trials with ^{68}Gallium(Ga)-DOTATATE (NetSpot) earning FDA approval in 2016. The DOTATATE molecule also can be labeled with ^{177}Lu to form the PRRT agent, ^{177}Lu-DOTATATE (Lutathera). A positive imaging result with ^{68}Ga-DOTATATE has been shown to help predict the patient's response to Lutathera, making targeted diagnostic imaging a crucial component of personalized medicine."

Optimal nuclear imaging of NETs requires advanced technology and expertise. ^{111}In-OctreoScan and ^{68}Ga-DOTATATE imaging are best performed on state-of-the-art SPECT/CT and PET/CT cameras, respectively, with specialized image reconstruction techniques and high-quality CT correlative imaging. Then, a dedicated team of experienced nuclear imaging subspecialists is needed to interpret the studies, incorporating the latest research findings into practice. Nuclear medicine specialists at Baylor Dallas collaborate closely with surgeons to precisely localize tumors for surgery (see story on page 14) and with oncologists to select the best treatment strategy, such as PRRT (see story on page 24).

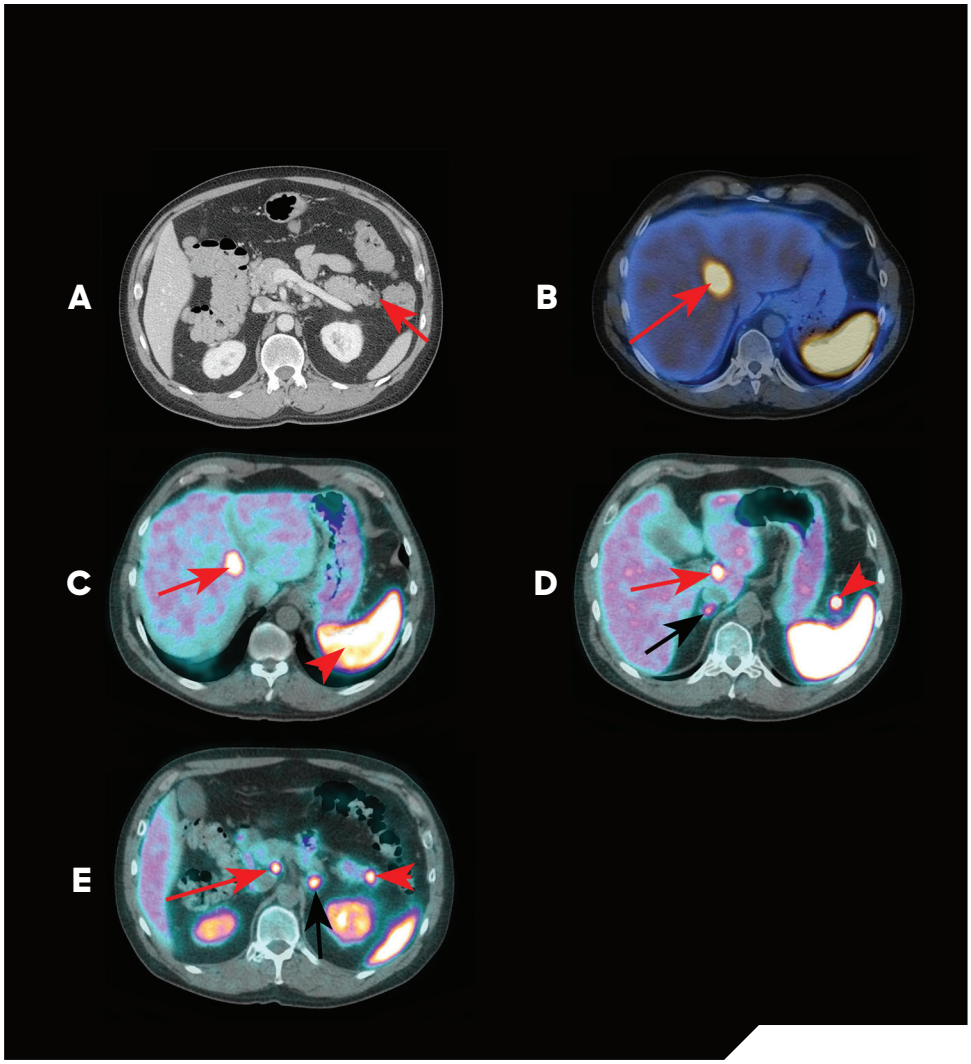


Figure 3. A patient had gastric ulcer disease related to an elevated gastrin level, believed to be due to a gastrinoma. A CT scan (Panel A) and MRI scan (not shown) showed a cystic lesion in the tail of the pancreas (arrow), with benign characteristics and no evidence of a gastrinoma or of metastases. A ^{111}In-pentetreotide scan (OctreoScan SPECT/CT; Panel B) demonstrated a single somatostatin-receptor-positive lesion in the right lobe of the liver (arrow), consistent with metastasis, but no primary tumor. Conversely, a ^{68}Ga-DOTATATE PET/CT scan (Panel C) showed the same right hepatic lobe metastasis, but showed several additional lesions, including a second hepatic metastasis in the caudate lobe (Panel D, red arrow). Additional, very small, somatostatin-receptor-positive metastases were demonstrated in subcentimeter lymph nodes in the splenic hilum (Panel D, arrowhead) and the periceliac region (Panel E, red arrow). Finally, ^{68}Ga-DOTATATE imaging also revealed focal tracer uptake consistent with the primary gastrinoma in the tail of the pancreas (Panel E, arrowhead), involving the medial aspect of the cystic lesion that had appeared benign on CT and MRI. Note also that Ga-DOTATATE demonstrates intense and variable uptake in a number of normal structures (e.g., kidneys, spleen [Panel C, arrowhead], and adrenal glands [Panels D and E, black arrow]) and benign lesions, which necessitates skilled and meticulous interpretation of such studies.

MULTIDISCIPLINARY APPROACH TO NEUROENDOCRINE CANCER

PSYCHOSOCIAL SUPPORT

At the Baylor Sammons Cancer Center at Dallas, psychosocial support is based on an integrative approach known as behavioral health oncology. Shannon Poppito, PhD, clinical psychologist on the allied health professional staff in behavioral health oncology services at Baylor Dallas, describes her multifactorial approach to caring for cancer patients in the following way: "We combine cancer-related supportive care, healthy lifestyle management, pain management, and sleep management, along with the psycho-oncology approach of helping patients cope with cancer-related anxiety, depression, and demoralization. Then, there are also the deeper existential-spiritual issues of facing mortality and helping people find meaning and purpose in life, even in the face of cancer."

> The goal of this approach is to educate and empower patients to engage in healthy bio-psycho-spiritual self-care, which is especially important due to the unique nature of neuroendocrine tumors.
>
> **Shannon Poppito, PhD**
> Clinical psychologist and founder of the Behavioral Health Oncology Service

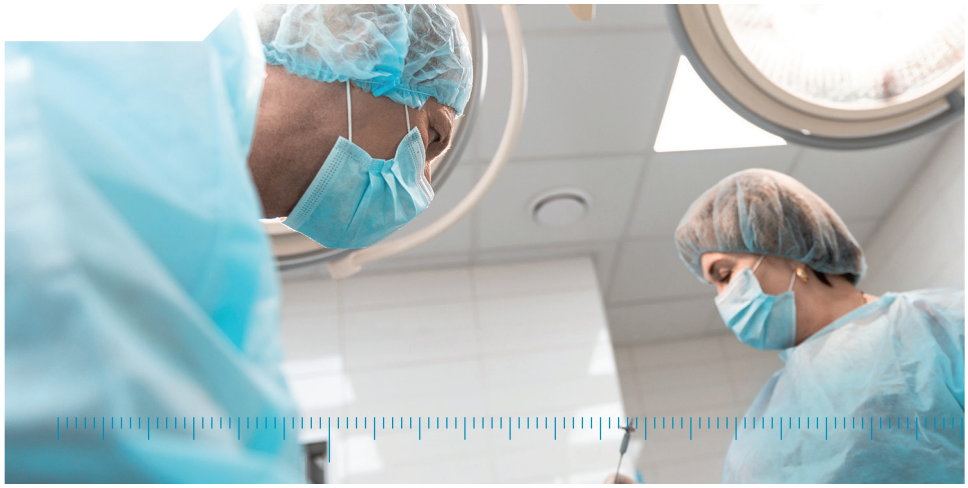
The goal of this approach is to educate and empower patients to engage in healthy bio-psycho-spiritual self-care, which is especially important due to the unique nature of NETs.

First, because these cancers are so rare, it is easy for NET patients to feel isolated and alone in their illness. The magnitude of the effects can vary depending on the tumor type and if the tumor is actively secreting hormones. Typically, not only do patients need education about their neuroendocrine tumor, but their families, healthcare providers, and insurance companies need targeted education as well.

Second, hormone dysregulation is caused by the endocrine nature of the tumors. This hormone dysregulation may cause heightened levels of anxiety, anger, and agitation, which can be more extreme than with other cancers. The hormone-associated mood dysregulation can further affect self-worth and guilt for feeling like a burden to loved ones, causing strain on relationships. One key aspect of education is helping family members and caretakers understand and anticipate this mood dysregulation and avoid taking the difficult emotions personally.

A third challenge is pain management. If the NET is diagnosed during the late stages, the patients can have considerable pain associated with metastasis, especially in the liver. This is worsened by metabolic dysregulation, which is often associated with the endocrine component of the cancer. Therefore, the behavioral health oncologist can serve as a link to engage patients in stress, coping, and pain reduction strategies and initiate referrals to palliative care for medical pain management.

Behavioral health oncology services at Baylor Dallas contribute to the MDT approach through physician referrals and by serving as a referral resource to connect patients to palliative, psychiatric, and symptom management teams to meet their multifactorial needs. At the heart of the psychosocial support network at Baylor Sammons Cancer Center at Dallas is the Cvetko Patient Resource Center. This center hosts a range of activities and patient resources in a comfortable environment, including 12 support groups. Among these is the Carcinoid Cancer Texas Survivors group, which meets monthly to support neuroendocrine cancer patients.



BAYLOR CHARLES A. SAMMONS CANCER CENTER

HERITABLE NEUROENDOCRINE TUMORS

Some neuroendocrine tumors (NET) derive from heritable genetic mutations, which cause multisymptomatic neuroendocrine syndromes. Although most of the mutations are inherited, they can also appear *de novo* in patients with no family history. Examples of autosomal dominant heritable neuroendocrine syndromes are listed in Table 1.

Specialized expertise is required to diagnose and monitor patients with these rare heritable disorders. Furthermore, patients with these syndromes are presented at the multidisciplinary conferences at Baylor Charles A. Sammons Cancer Center at Baylor University Medical Center (Baylor Dallas) to develop an individually designed treatment plan.

Pheochromocytoma and paraganglioma

Pheochromocytoma and paragangliomas are often classified together because both of these rare genetically linked tumors secrete catecholamines. Approximately 500 to 1,000 patients are diagnosed with these tumors per year. Although both tumor types derive from chromaffin cells of the neural crest, pheochromocytomas originate in the medulla of the adrenal gland while paragangliomas originate from the ganglia of the autonomic nervous system anywhere from the head to the abdomen. These tumors present with symptoms such as heart palpitations, high blood pressure, headaches, anxiety, diabetes, and weight loss. Although many are benign, about 10% of pheochromocytomas and 25% of paragangliomas are malignant. Given the severity of the endocrine symptoms, these tumors can still be life-threatening. Diagnosis starts

Table 1. Heritable neuroendocrine syndromes that increase the risk of neuroendocrine cancer

Disease	Frequency[1]	Mutated gene (protein function)	Neuroendocrine tumor types
Von Hippel-Lindau syndrome	1 in 36,000	*VHL* (tumor suppressor)	Pheochromocytoma
Neurofibromatosis type 1	1 in 3,000 – 4,000	*NF1* (tumor suppressor)	Pheochromocytoma
Multiple endocrine neoplasia type 1	1 in 30,000	*MEN1* (tumor suppressor)	Parathyroid tumors, neuroendocrine tumors of the pancreas, and pituitary tumors
Multiple endocrine neoplasia types 2A and 2B and familial medullary thyroid cancer	1 in 30,000	*RET* (proto-oncogene)	Medullary thyroid cancer, pheochromocytoma
Familial paraganglioma-pheochromocytoma	1 in 1,000,000	*SDH* (mitochondrial metabolic protein)	Paraganglioma, pheochromocytoma

[1]Data from National Library of Medicine Genetics Home Reference (https://ghr.nlm.nih.gov/).

with a biochemical workup. Patients who have laboratory results consistent with a pheochromocytoma or paraganglioma undergo imaging to determine the location of the tumor. Prior to any surgical intervention, the patient is given alpha-blockade and possible subsequent beta-blockade to avoid a hypertensive crisis during surgery.

Surgery on the adrenal gland is usually laparoscopic. This operation can be performed from the anterior approach or the posterior retroperitoneoscopic approach. Posterior retroperitoneoscopic adrenalectomy is a technique offered at Baylor Dallas. This technique allows direct access to the adrenal gland from the back, thereby avoiding mobilization of abdominal organs encountered during the laparoscopic anterior approach. The recovery time is short, and patients can often go home the next day. Recurrence only occurs in 10% of patients, but predicting malignancy is challenging and monitoring is necessary.

Bilateral tumors, which occur in approximately 10% of pheochromocytomas and are often due to hereditary syndromes, pose an additional surgical challenge. Complete bilateral adrenalectomy would require the patient to take steroid medications to compensate for the loss of the steroid-producing outer rim of the adrenal gland, known as the cortex. However, long-term steroid use can cause debilitating side effects. Therefore, surgeons on the medical staff at Baylor Dallas offer cortical-sparing adrenalectomy, whereby the tumor-containing adrenal medulla is resected in a manner that retains the adrenal cortex. This method reduces the risks associated with long-term steroid use, including osteoporosis, ulcers, and changes in fat distribution.

Because genetic mutations often cause pheochromocytoma and paraganglioma, genetic testing is a key component of the diagnostic procedure. Germline mutations in the *SDH* genes occur in 15% of cases, and mutations in *VHL*, *RET*, and *NF1* are associated with up to 10% of cases. Information about the specific mutation can predict the location of the tumor and the severity. For instance, mutation of *SDHB* causes familial paraganglioma type 4, which is associated with increased malignancy, and mutations of *SDHC* (familial paraganglioma type 3) and *SDHA* (familial paraganglioma type 5) are associated with reduced tumor formation. Understanding why various subunits of a

single protein would cause divergent symptomatology is an active area of research.

Recent advances in the management of pheochromocytoma include progress in classifying these extremely rare tumors. Christine Landry, MD, FACS, surgical oncologist on the medical staff at Baylor Dallas, specializes in surgical endocrinology and contributed to the *Cancer Manual* (8th edition) from the American Joint Committee on Cancer Staging. She commented on the importance of this work: "Prior to this time, there has not been a staging system for neuroendocrine tumors of the adrenal gland, the reason being that they are incredibly rare. On this panel, we are trying to figure out: can we have a staging system, and do we have enough information?" This panel is working to gather variables that will be used to create a staging system for malignant pheochromocytoma and paraganglioma, which will help cancer care teams treat these rare tumors.

Medullary thyroid cancer

Medullary thyroid cancer is a rare hereditary form of thyroid cancer that derives from the parafollicular C cells, which are in the upper thyroid. These cells make calcitonin, a peptide hormone that regulates calcium and phosphate levels in the blood. Medullary thyroid cancer represents only 5 to 10% of all thyroid cancers and can be aggressive. Approximately 70% of these cancers will spread to the lymph nodes. Five-year survival rates are above 80% for stage I to II disease but remain low (28%) for stage IV disease. As such, early detection and treatment are critical. Treatment involves removing the thyroid and associated lymph nodes, and potentially removing the lymph nodes in the lateral portion of the neck. Although radioactive iodine or thyroid hormone suppression are used for other thyroid cancer types, they are not effective against medullary thyroid cancer.

Familial medullary thyroid cancer accounts for about 25% of these tumors. According to Dr. Landry, "Knowing which mutation an individual has can predict the aggressiveness of the medullary thyroid cancer. In fact, patients with some mutations should have the thyroid removed within the first year of life because the medullary thyroid cancer is extremely aggressive." In addition, the mutation type might predict the presence of disease in other organs. For instance, if the medullary thyroid cancer is associated with multiple endocrine neoplasia type 2A, these patients are at risk of developing parathyroid disease, which could be addressed during the thyroid surgery.

As with the other NETs, the development of new therapies has been slow due to the rarity of the disease and the lack of similarity to other cancers. The protein kinase inhibitors vandetanib and cabozantinib were FDA approved within the last 10 years for the treatment of advanced medullary thyroid cancer, and trials of everolimus are ongoing. Promising future areas of development include RET-specific inhibitors, combination therapies, and immunotherapy.

NEUROENDOCRINE CANCER IN THE SKIN: MERKEL CELL CARCINOMA

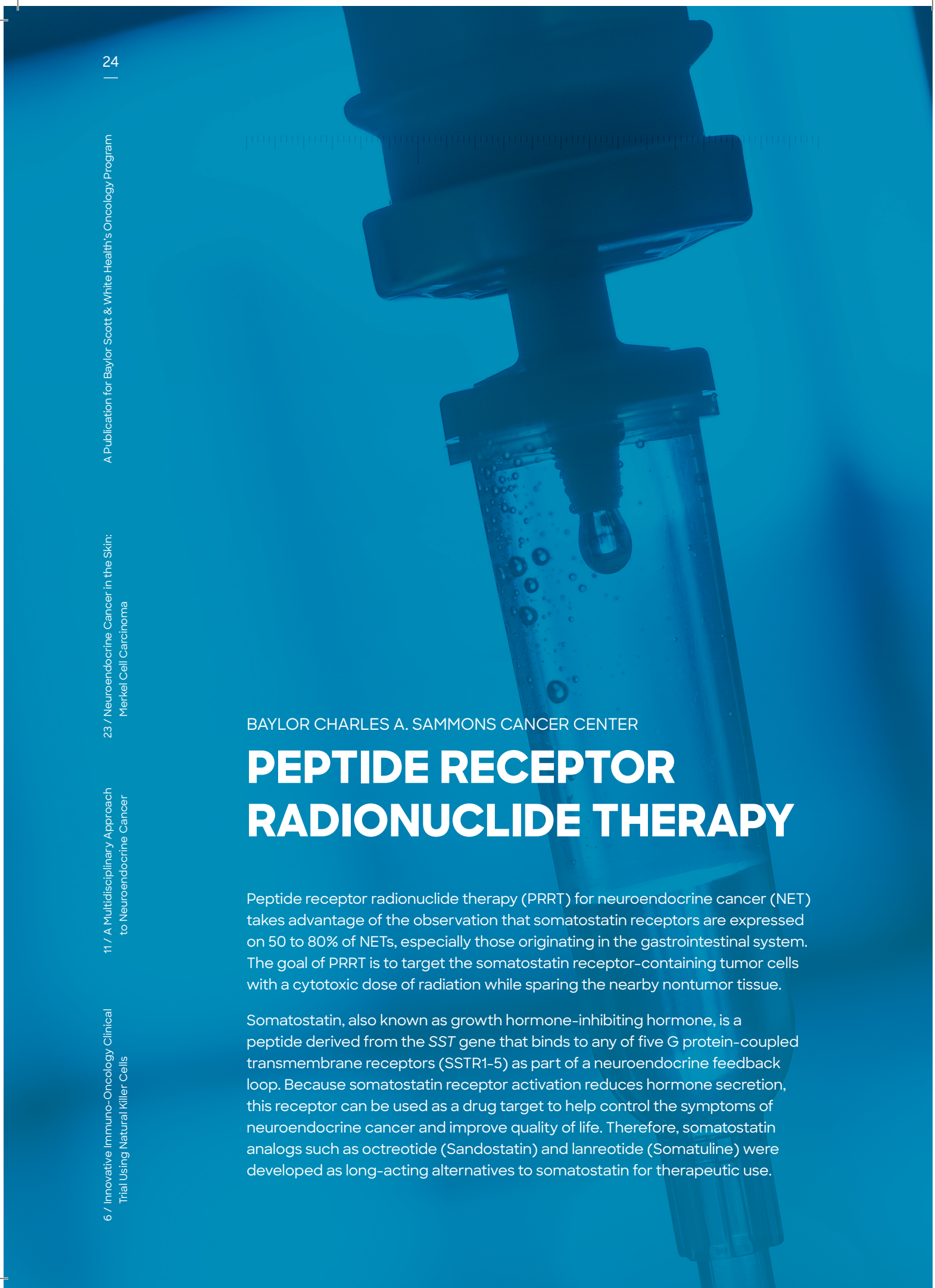
Merkel cell carcinoma is a rare neuroendocrine tumor (NET) of the skin. Approximately 2,500 cases are diagnosed in the US per year and the rates are rising, likely due to the aging of the US population. This tumor, which is often painless and looks like a small nodule in the skin, is commonly misdiagnosed. Therefore, at presentation, 23 to 25% have lymph node involvement and 6 to 16% have distant metastases, with five-year mortality ranging from 41 to 71% depending on the stage at presentation. Typical treatment includes wide local excision and sentinel lymph node biopsy, followed by radiation. If there is evidence of spread, additional surgical and medical intervention is recommended. Christine Landry, MD, FACS, surgical oncologist on the medical staff at Baylor Dallas, noted that despite the rarity of these disorders, Baylor Dallas typically sees half a dozen patients per year. She commented, "We treat aggressively because the cancer is so aggressive, and it can come back." More than half of the tumors recur within the first two to three years, and over 30% of patients will eventually develop metastatic disease.

Key challenges for the treatment of Merkel cell carcinoma include a lack of data on the molecular mechanisms of tumorigenesis, lack of outcomes data on therapeutic strategies and lack of treatment options. For instance, for stage IV disease, the top therapeutic recommendation is a clinical trial. Although the genetic basis for most Merkel cell carcinoma is unknown, there are several known risk factors. These include a suppressed immune system, extensive ultraviolet phototherapy, sun exposure, increasing age, Caucasian race, and male gender.

One important breakthrough was the discovery, in 2008, of a disease biomarker: the Merkel cell polyomavirus. This virus is found in approximately 80% of Merkel cell cancers and is associated with a less aggressive course. This discovery not only provides mechanistic insight into

the development of Merkel cell cancer, but it also provides a biomarker for monitoring treatment progression. For patients who have the virus, Merkel cell polyomavirus antibodies can be measured at various intervals to detect recurrence and guide treatment. However, resources for virus testing are limited. Therefore, the team at the Neuroendocrine Research and Treatment Center has created a workflow wherein the blood is drawn locally and shipped to the University of Washington for virus testing as a standard component of the diagnostic workup.

Another recent breakthrough was the 2017 FDA approval of avelumab, a monoclonal antibody that inhibits the programmed cell death protein 1 (PD-1) pathway, to treat metastatic Merkel cell carcinoma in patients 12 years and older. This therapy falls into a larger class of anticancer immunotherapies that help the body's immune system kill tumor cells. In a trial of 88 patients, 33 experienced complete or partial shrinkage of the tumors. The duration of response was over 12 months for 45% of patients who responded to treatment. Additional trials of immunotherapies and combination therapies are underway.



BAYLOR CHARLES A. SAMMONS CANCER CENTER

PEPTIDE RECEPTOR RADIONUCLIDE THERAPY

Peptide receptor radionuclide therapy (PRRT) for neuroendocrine cancer (NET) takes advantage of the observation that somatostatin receptors are expressed on 50 to 80% of NETs, especially those originating in the gastrointestinal system. The goal of PRRT is to target the somatostatin receptor-containing tumor cells with a cytotoxic dose of radiation while sparing the nearby nontumor tissue.

Somatostatin, also known as growth hormone-inhibiting hormone, is a peptide derived from the *SST* gene that binds to any of five G protein-coupled transmembrane receptors (SSTR1-5) as part of a neuroendocrine feedback loop. Because somatostatin receptor activation reduces hormone secretion, this receptor can be used as a drug target to help control the symptoms of neuroendocrine cancer and improve quality of life. Therefore, somatostatin analogs such as octreotide (Sandostatin) and lanreotide (Somatuline) were developed as long-acting alternatives to somatostatin for therapeutic use.

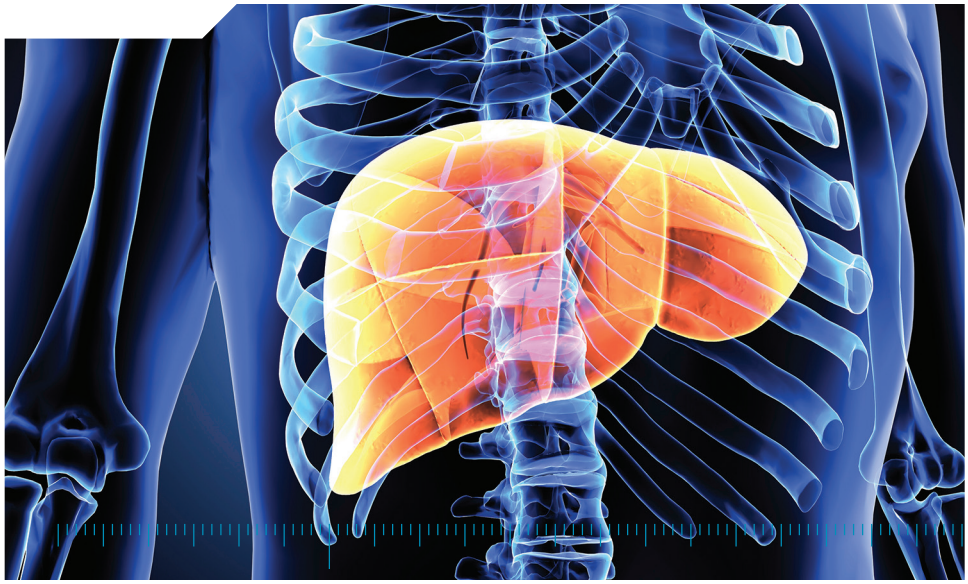
In PRRT, the long-acting somatostatin analog is coupled to a bifunctional chelator, which binds a radioactive element. One such somatostatin analog is DOTATATE, which combines tyrosine^3-octreotate with the bifunctional chelator DOTA. This peptide is combined with ^{177}Lutetium (Lu), and the radiopharmaceutical can bind somatostatin receptors, undergo endocytosis to enter the cell, and deliver beta particles to damage nearby molecules, thus killing the cancer cell.

In January 2018, the FDA approved intravenous ^{177}Lu-DOTATATE for adults with advanced neuroendocrine cancer in the pancreas or gastrointestinal tract. This approval was based partially on the NETTER-1 phase 3 clinical trial, which included research administered through Baylor Scott & White Research Institute at Baylor Charles A. Sammons Cancer Center at Dallas. The NETTER-1 trial compared ^{177}Lu-DOTATATE to long-acting octreotide in 229 somatostatin receptor-positive patients with advanced neuroendocrine tumors of the midgut. The following results were published in the *New England Journal of Medicine* (Strosberg et al, 2017):

- 79% reduction in the risk of disease progression or death during the 20-month evaluation period.
- 18% response rate, which is the percentage of patients with tumor shrinkage (compared to 3% for the control group). This is the first time a response rate of over 5% was observed for a systemic therapy in this patient population.

^{177}Lu-DOTATATE is delivered as four injections given every other month. The timing of ^{177}Lu-DOTATATE therapy requires careful consideration by an experienced multidisciplinary team, including radiation oncologists. Although the initial results for ^{177}Lu-DOTATATE were very promising, there is also a risk of serious side effects, including lymphopenia, and the risks and benefits must be carefully considered. In addition, the infrastructure for handling and delivering radiopharmaceuticals must be in place, including specialized training for the cancer care team. This necessary expertise and infrastructure are in place at Baylor Charles A. Sammons Cancer Center at Dallas, making it one of two sites in Texas approved to deliver ^{177}Lu-DOTATATE therapy.

The Bridge of Hope connects Baylor Charles A. Sammons Cancer Center at Dallas and Baylor T. Boone Pickens Cancer Hospital, making the combined facilities one of the largest cancer institutions in the U.S.



LIVING DONOR LIVER TRANSPLANT FOR NEUROENDOCRINE CANCER

Patients with neuroendocrine cancer (NET) of the pancreas and gastrointestinal tract now have new options for treatment. Although the primary neuroendocrine tumor (NET) may not cause symptoms, NETs often metastasize to the liver and can diminish quality of life by disrupting liver function. Therefore, liver transplant can reduce the disease burden in selected patients with advanced NET. Due to liver transplantation requirements, living donor liver transplant is the best transplantation option for advanced NET.

Physicians on the medical staff at Baylor University Medical Center (Baylor Dallas) have established an internationally recognized living donor liver transplant program through the Baylor Scott & White Annette C. and Harold C. Simmons Transplant Institute. The liver transplant program is working with the Neuroendocrine Cancer Research and Treatment Center at Baylor Charles A. Sammons Cancer Center at Dallas to develop living donor liver transplant as a therapeutic option for NET patients.

Living Donor Liver Transplant

Living donor liver transplant is a complicated procedure that involves the partial resection of the donor's liver. The liver recipient undergoes a full liver resection and the partial donor liver is transplanted into the recipient. Over the next two months, the livers of both the donor and recipient will grow to full size. This procedure is very challenging and requires a transplant team with a wide range of expertise.

Only a few hospitals in the country have built the infrastructure to handle living donor liver transplant. According to Robert Goldstein, MD, FACS, chief of hepatobiliary surgery at Baylor Dallas and co-director of the Neuroendocrine Research and Treatment Center, "The technical requirements for living donor transplant are much greater than for a cadaveric transplant. You must take the liver out safely from the donor and put it back into the recipient, and both sides of the operation are challenging. A unique skill set is required, and it is much more labor intensive with little room for error."

Neuroendocrine Patient Criteria for Liver Transplant

For an adult NET patient to be eligible for living donor liver transplant, the disease must not be curable with pharmacological therapy and be unresectable. Furthermore, all detectable disease must be localized to the liver and not to other organs, such as the lymph nodes, bones, or chest. In addition, if the disease is symptomatic, liver transplant will be strongly considered.

Dr. Goldstein notes, "Many neuroendocrine cancers occur in the intestine, causing the intestinal blood supply to go through the superior mesenteric vein and the portal vein which is filtered in the liver. Therefore, a lot of the metastases go to the liver and, after resection of the primary tumor, the only remaining tumor cells might be in the liver. In selected patients, replacement of the liver is a very viable option to consider."

Living Donor Transplant Resources at Baylor Dallas

The liver transplant program at Baylor Dallas is one of the most robust and well-regarded centers in the country. The surgeons at Baylor Dallas and Baylor Scott & White All Saints Medical Center – Fort Worth have transplanted over 4,000 livers. The transplant team includes nine transplant surgeons on the medical staff and an experienced team of transplant support staff. This skilled infrastructure allows Baylor Dallas to be the only site in North Texas to offer living donor liver transplant.

Collaboration between the Baylor Scott & White transplant team and the Neuroendocrine Cancer Research and Treatment Center at Baylor Sammons Cancer Center allows Baylor Dallas to offer advanced and specialized treatment options, including transplantation strategies, for uncommon and challenging NET cancers.

Liver transplant may be a late-stage intervention for NET, but Dr. Goldstein recommends that physicians engage the transplant team at Baylor Dallas early in the patient's treatment journey. Early monitoring is important even for indolent disease. According to Dr. Goldstein, "It is never too early to get an opinion from an advanced research and treatment center. You may end up learning about treatment options that might not be available elsewhere."

New Directions for Research on Neuroendocrine Cancer

Researchers at Baylor Dallas are also seeking new strategies for treating NET. In particular, researchers are interested in investigating whether new adjuvant therapies might be combined with living donor liver transplant. One adjuvant therapy of interest is Peptide Receptor Radionuclide Therapy (PRRT), which uses octreotate, a somatostatin analog, to deliver a radioactive payload specifically to neuroendocrine tumor cells (see article on page 26). Furthermore, this living donor transplant strategy might be useful for colon cancer and other cancers that metastasize primarily to the liver. Their overall goal is to reduce the liver disease burden of cancer and thereby improve the patient's quality of life over the long term.

August 2018 to January 2019

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