BaylorScott&White
BAYLOR UNIVERSITY MEDICAL CENTER
BAYLOR CHARLES A. SAMMONS CANCER CENTER
DALLAS

CANCER UPDATE

A **Baylor University Medical Center** Publication on Oncology Innovations

FALL 2020
VOLUME 9 | ISSUE 3

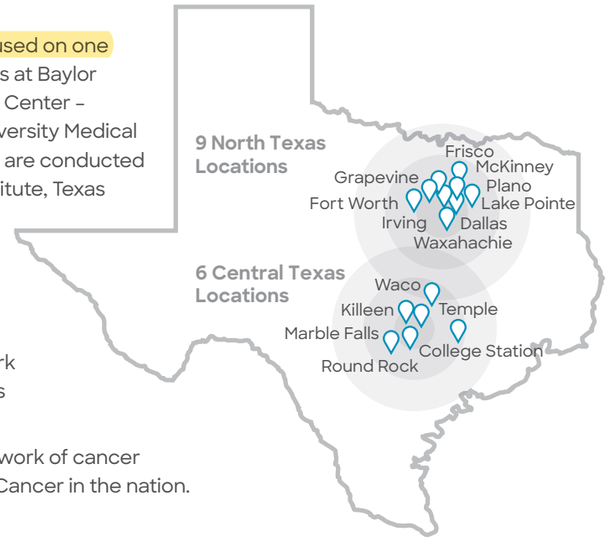
Feature Article | Page 6

TEXAS IMMUNO-ONCOLOGY BIOREPOSITORY

Also In This Issue

BAYLOR SCOTT & WHITE ONCOLOGY

Cancer hates pioneers. Because we're focused on one thing: Destroying it. Cancer research studies at Baylor Scott & White Charles A. Sammons Cancer Center – Dallas, located on the campus of Baylor University Medical Center, part of Baylor Scott & White Health, are conducted through Baylor Scott & White Research Institute, Texas Oncology and The US Oncology Network. Each reviews, approves and conducts clinical trials independently.



HOSPITAL-BASED CANCER PROGRAMS

Baylor Scott & White has the largest network of hospital-based cancer programs in Texas with 15 cancer centers.

Baylor Scott & White is the third largest network of cancer centers accredited by the Commission on Cancer in the nation.

CONTENTS

Our **COVID-19 Safe Care** measures are in place across our hospitals, surgery centers and clinics, in accordance with CDC guidance and recommendations by our clinical experts. Learn more at **BSWHealth.com/SafeCare**.

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

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FROM THE MEDICAL

DIRECTOR

It is my great pleasure to introduce the Autumn 2020 issue of the Baylor Scott & White Cancer Update. These newsletters will keep you up to date with the latest from Baylor Scott & White Charles A. Sammons Cancer Center – Dallas, a destination cancer research and treatment center located on the campus of Baylor University Medical Center (Baylor Dallas), part of Baylor Scott & White Health.

In this issue, we announce the opening of the Texas Immuno-Oncology Biorepository (TIOB) in September 2020. This ambitious project will collect longitudinal biological samples (blood, urine, stool, tissue and others) from a diverse population of Texans from early-stage to late-stage cancers in an attempt to study the evolving immunological changes that occur during a patient's entire duration with cancer. In addition, we will be studying samples from patients already being treated with a wide variety of immunotherapeutics from checkpoint inhibitors and cellular therapeutics (CAR-T, NK cells, T cell receptor) to oncolytic viruses and tumor-infiltrating lymphocyte therapy. As the largest not-for-profit health system in Texas, Baylor Scott & White intends to leverage its existing research infrastructure to build a research biospecimen resource at an unprecedented scale. The feature article describes how we will open the door to a new era of collaborative immuno-oncology research by realizing our goal of treating every patient and learning from every patient.

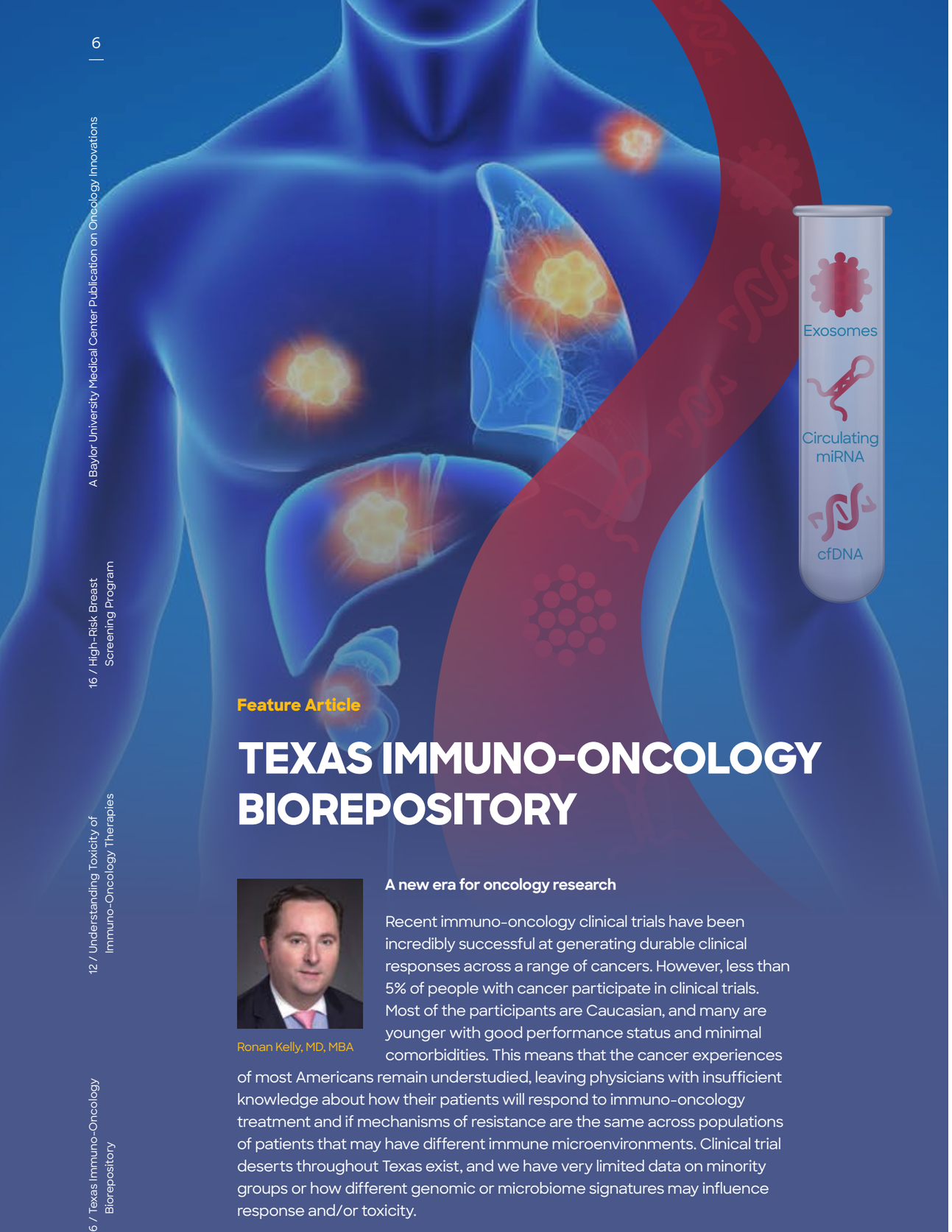
This issue will also tackle the concept of how we can utilize the TIOB to gain a more comprehensive understanding of which patients are more likely to have grade 3 – 5 immunological side effects from cellular immunotherapies and how we can develop strategies to mitigate adverse events.

We also describe exciting new results emerging from our cancer program with the phase III global CheckMate577 esophageal/gastroesophageal junction cancer trial that utilized adjuvant nivolumab demonstrating a doubling in the primary end point of disease-free survival in patients with operable stage II/III disease. I had the pleasure of presenting the first results of this potentially practice-changing study during the Presidential/Plenary Symposium of the 2020 European Society for Medical Oncology (ESMO) conference. This study in esophagogastric cancers is the first trial after melanoma to demonstrate a benefit for the use of a PD-1 inhibitor in the adjuvant setting and signals the start of a whole new era in cancer care whereby we will be using checkpoint inhibitors in early-stage resectable disease for a wide range of tumor types both in the adjuvant and the neoadjuvant setting.

Finally, we introduce a highly novel and innovative program that we have launched for the early identification and treatment of breast cancer. Our High-Risk Breast Screening Program, which recently opened in North Texas, is realizing its mission of identifying women at increased risk of breast cancer and offering them enhanced counseling and screening options. The Breast Cancer Research and Treatment Center at Baylor Dallas has also expanded to offer new ways to promote efficiency and enhanced patient care for breast cancer surgery. The programs are both integrated with the TIOB, allowing patients the option to contribute to research during their cancer care journey.

We invite you to learn about these innovative programs here at Baylor Dallas.

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



Feature Article

TEXAS IMMUNO-ONCOLOGY BIOREPOSITORY

Ronan Kelly, MD, MBA

A new era for oncology research

Recent immuno-oncology clinical trials have been incredibly successful at generating durable clinical responses across a range of cancers. However, less than 5% of people with cancer participate in clinical trials. Most of the participants are Caucasian, and many are younger with good performance status and minimal comorbidities. This means that the cancer experiences of most Americans remain understudied, leaving physicians with insufficient knowledge about how their patients will respond to immuno-oncology treatment and if mechanisms of resistance are the same across populations of patients that may have different immune microenvironments. Clinical trial deserts throughout Texas exist, and we have very limited data on minority groups or how different genomic or microbiome signatures may influence response and/or toxicity.

Baylor University Medical Center, in collaboration with Baylor Scott & White Research Institute (BSWRI), has responded to this gap in knowledge by creating the Texas Immuno-Oncology Biorepository (TIOB). The TIOB, which opened in September 2020, will prospectively collect clinical data and biospecimens on an unprecedented scale across Baylor Scott & White's network, providing a unique opportunity to better understand how cancer treatment affects the health of everyone with cancer.

The goal of the TIOB is something entirely new: to both care for every patient and learn from every patient in a real-world environment throughout academic and community settings alike. This places the patients as partners in the larger journey toward understanding how cancer evolves and how the immune system can fight it. Over time, the TIOB will enroll patients across all cancer types to develop a more complete understanding of human cancer experiences.

According to Ronan Kelly, MD, MBA, director of oncology at Baylor Dallas and chief of oncology for Baylor Scott & White Health in North Texas, "As the largest network of hospital-based cancer programs in Texas and the third largest Commission on Cancer-accredited network of cancer hospitals in the US, we have access to an amazingly diverse population of people undergoing cancer treatment. These are people with a broad range of different ethnicities, different diets and different life experiences. It presents an excellent opportunity for us to usher in a new era of cancer research."

The TIOB will collect samples from patients undergoing treatment from stage 1 to stage IV disease in a longitudinal manner for a patient's entire journey with cancer. There also will be a particular emphasis on patients receiving immuno-oncology therapies, including checkpoint inhibitors and cellular therapies, in an attempt to understand mechanisms of resistance at a population level. Dr. Kelly explains why the TIOB will focus on therapies that boost the patient's own immune system. "Immuno-oncology is revolutionizing the way we treat cancer. We have come a long way in the last 10 years, but we really only have a surface-level understanding of the complexities of the tumor-adjacent immune microenvironment, which could reveal why some patients respond to therapy and some do not. It is time to dig deeper so we can realize the dream of long-term cancer control for everyone."

Building a unique biorepository

Sheila Dobin, PhD

Lucas Wong, MD

Developing the TIOB has required a strong commitment to coordination and quality assurance. Built on the networked clinical research infrastructure provided by BSWRI, the TIOB takes traditional tissue biorepositories to a new level.

Sheila Dobin, PhD, clinical cytogeneticist, medical geneticist and co-principal investigator for the TIOB in Central Texas, describes how the TIOB differs from a traditional biorepository, which typically only stores archival tissue. “The TIOB will collect samples prospectively on a regular schedule that coincides with the patient’s clinic visits. One of our big questions is why some people develop resistance to immuno-oncology therapies over time. By taking longitudinal samples, we can find that answer.” Participants will be asked to provide samples every three to 12 months, depending on their treatment schedule.

The TIOB will also collect more samples than a traditional biorepository, including blood, urine and stool, as well as any tumor tissue beyond what is needed for clinical care. By including these minimally invasive samples, researchers can investigate markers of cancer status that might reduce the need for biopsies and other invasive diagnostic approaches.

Lucas Wong, MD, a physician-researcher at Baylor Scott & White Medical Center – Temple, describes how the TIOB fits in with the existing clinical trial infrastructure at BSWRI. “We will also offer TIOB participation to people with early-stage disease and to those who are participating in our immuno-oncology clinical trials, including people who are no longer on active treatment. Although current clinical trials collect some research data, the focus is on the treatment and the trials end with limited follow-up asking ‘why?’ if the clinical response does not meet expectations. There are many missed opportunities for understanding how an individual’s response to treatment might be improved. Because this project is led in part by a network of academic medical centers, we now have the opportunity to look deeper and find new insights that could produce big results.”

> The TIOB will also collect more samples than a traditional biorepository, including blood, urine and stool, as well as any tumor tissue beyond what is needed for clinical care. By including these minimally invasive samples, researchers can investigate markers of cancer status that might reduce the need for biopsies and other invasive diagnostic approaches.
>
> **Sheila Dobin, MD**
> Clinical Cytogeneticist, Medical Geneticist, Co-Principal Investigator for the TIOB in Central Texas

As the director of the Cytogenetics laboratory at Baylor Scott & White Medical Center – Temple for over 35 years, Dr. Dobin developed a local biorepository that would serve as the precursor to the TIOB. According to Dr. Dobin, “We were lucky to have that experience with a tissue biorepository to get this project up and running more quickly. Small-scale testing of our processes is essential before integrating them into our system, and we already have a team in place that is dedicated to quality. This strong foundation has enabled us to succeed in managing the logistical complexities of the TIOB.”

The potential of the unprecedented scale of the TIOB requires a commitment to the highest levels of quality in sample collection, processing and storage. All samples are immediately de-identified with a unique identification number, so the participant’s protected health information is kept secure. All patient data, including clinical data, is stored in a centralized database. In addition, a trained BSWRI tissue coordinator is available to guide the patient through informed consent, collect specimens, and transport them to a secure, centralized facility for quality assessment and storage. The storage facilities are located both in Dallas and Temple, TX.

Dr. Wong describes how the centralized design of the TIOB can support collaboration, “A researcher might identify a great hypothesis and wonder how to test it. Because all our information is stored centrally, the data management team can quickly determine how the TIOB can accelerate that research. This gives us the opportunity to support many projects, each of which will enhance our understanding of how the immune system can be used to stop cancer.”

TIOB pathway

The patient gives written consent.

Baseline samples, including urine, blood and stool, are collected and possibly tissue biopsy (if indicated).

Next, the patient receives FDA-approved checkpoint inhibitors/CAR-T.

After 3 months, more samples are collected.

After 6 months, more samples are collected.

THEN:

Sample collection continues every 3 months. (Unless consent is withdrawn.)

If disease progresses, sample collection will continue with treatment as directed.

Enabling a new type of research

Daniel D. Von Hoff, MD, FACP

Mike Berhens, PhD

The large-scale data collection planned for the TIOB has opened the door to novel research endeavors that were previously not possible.
To stimulate this research, Baylor Dallas has established a collaborative relationship with the Translational Genomics Research Institute (TGen) to apply TGen's expertise in large-scale genomics and next-generation analytical capabilities to the TIOB resources with the goal of rapidly improving immuno-oncology cancer care.

Daniel Von Hoff, MD, an internationally recognized leader in oncology therapeutic development, describes some of the research that is made possible by the TIOB, "One area of great interest is the microbiome. As we learn more about the colonies of microbes that inhabit the human body, we have come to realize what an incredible impact they can have on health. We know the microbiome is extremely diverse among people and is affected in a complex way by cancer and its treatment. With the TIOB and advances in technology, such as next-generation sequencing, we can now start to ask how these interactions work on a large scale."

With the knowledge gained from the TIOB, the researchers envision the potential impact on cancer care, including using microbiome status as a prognostic indicator of treatment success and potentially modifying the microbiome for maximal therapeutic efficacy.

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>
> **Daniel D. Von Hoff, MD, FACP**

> Genomics analysis methods are constantly improving and, when combined with the latest advances in artificial intelligence and machine learning, provide a new opportunity to tame this vast quantity of information.
>
> **Michael Berens, PhD**

Dr. Berens' research includes the study of tumor interactions with patient host cells, which are studied using sophisticated microscopy techniques.

As part of the TIOB collaboration, BSRWI and TGen hope to also test the prognostic potential of cell-free nucleic acids (DNA and RNA) found in the blood. These circulating cell-free DNA and RNA fragments can serve as markers of cancer status. Another source of insight comes from extracellular vesicles (EVs), which are lipid bilayer-enclosed particles that are roughly 1,000 times smaller than the average human cell and are packed with nucleic acids, proteins and other cellular contents. Research on EVs dates to the 1940s, but they were only recently recognized as critical components of cell-cell communication in cancer metastasis and immune response. According to Dr. Von Hoff, "EVs act like an intranet for the body."

Michael Berens, PhD, an expert in translational therapeutics for cancer, describes the excitement around cell-free DNA and RNA, "Now that we have much more sensitivity to detect rare genetic markers in the blood, there is great potential to use this information. It is going to be transformative to medical care to use a blood or urine sample and start to learn from the circulating DNA and RNA about the cancer status of the patient. Is the tumor responding? Is the immune system benefiting from treatment? How is the tumor adapting to therapy? These are powerful opportunities to understand the disease state in real time without waiting for imaging or biopsy results."

Dr. Berens also describes how advances in computing power and bioinformatics can be leveraged to understand the massive amount of data generated by genomic analysis. "There are over 24,000 genes in the human genome and hundreds of thousands of DNA regions that are used to modify how those genes behave. This means we need to sort through hundreds of thousands of measurements to find the handful of DNA regions that are most instructive for an individual's health status. Genomics analysis methods are constantly improving and, when combined with the latest advances in artificial intelligence and machine learning, provide a new opportunity to tame this vast quantity of information."

The TIOB relationship represents a new chapter in the six-year-long collaborative relationship between TGen and Baylor Scott & White Research Institute.

UNDERSTANDING THE TOXICITY OF CELLULAR IMMUNO-ONCOLOGY THERAPIES

Houston Holmes, MD

The immuno-oncology boom of the past decade has ushered in new therapies with unprecedented potential to offer durable anti-tumor responses. Some are completely new, such as chimeric antigen receptor T cell (CAR-T) therapies, which take the patient's own T cells and engineer them to find and destroy cancer cells. The first CAR-T therapy was FDA-approved in 2017, and there are now three approved CAR-T therapies to treat blood cancers, including non-Hodgkin's lymphoma, mantle cell lymphoma and multiple myeloma. Despite the success of CAR-T cell clinical trials, some patients may be reluctant to try these new therapies due to the possibility for side effects. Houston Holmes, MD, hematologist and medical oncologist on the medical staff at Baylor University Medical Center, holds an interest in T cell therapy research and offers advice to physicians who might be apprehensive about referring patients for CAR-T therapy.

"We have come a long way with managing toxicities over the last few years. In the early studies, physicians were hesitant to give any kind of medicine that would suppress the immune system for fear that it would prevent the benefits of CAR-T cells. We now know that once the T cells have expanded, they don't lose their effectiveness. This means we can go ahead and treat side effects early in their course. It has made a big difference."

He describes two characteristic toxicities of CAR-T cells: cytokine release syndrome (known as CRS) and immune cell-associated neurologic syndrome (known as ICANS). Cytokine release syndrome is caused by the expansion of the CAR-T cells, leading to a systemwide immune reaction that can manifest with symptoms such as fever, low blood pressure, fast heart rate, low oxygen levels and pulmonary infiltrates. Symptoms tend to begin two to three days after infusion. According to Dr. Holmes, "For most patients, CRS is mild and manageable. However, for some, it is serious and requires supportive care. We keep patients in the hospital for a week after the infusion to monitor and treat side effects as necessary."

ICANS, unlike CRS, manifests with cognitive impairment around four to six days after infusion. Dr. Holmes describes the proposed mechanism of ICANS. "We think ICANS is caused via a mechanism similar to CRS, but cytokines enter the central nervous system and cause the symptoms. However, these symptoms do not always appear together."

> We have come a long way with managing toxicities over the last few years. In the early studies, physicians were hesitant to give any kind of medicine that would suppress the immune system for fear that it would prevent the benefits of CAR-T cells. We now know that once the T cells have expanded, they don't lose their effectiveness. This means we can go ahead and treat side effects early in their course. It has made a big difference.
>
> **Houston Holmes, MD**

Dr. Holmes says that physicians often want to know if patients who are not candidates for autologous stem cell transplants can receive CAR-T cells. "The answer is often yes. There are many people who can tolerate CAR-T therapies but not autologous stem cell transplants. In fact, we have been pleased to note that in real-world treatment, many people can tolerate CAR-T therapies who were not considered candidates for the original clinical trials. We have learned so much."

Baylor Dallas is an authorized treatment center for all three FDA-approved CAR-T cell therapies and maintains an active portfolio of CAR-T cell clinical trials to drive the next generation of cellular therapeutics.

GROUNDBREAKING ADJUVANT IMMUNOTHERAPY ESOPHAGEAL/ GASTROESOPHAGEAL JUNCTION CANCER TRIAL

Practice changing results emerging from our program with the potential to change the standard of care for operable disease

Ronan Kelly, MD, MBA

The phase 3 randomized, multi-center CheckMate577 trial (NCT02743494) has announced that it met the primary endpoint of disease-free survival in patients with esophageal or gastroesophageal junction cancer at interim analysis, with a manageable safety profile. The trial compared adjuvant treatment with the anti-PD-1 immune checkpoint inhibitor nivolumab to placebo (current standard of care is close observation) in patients who had received neoadjuvant chemoradiation and surgical resection for stage II/III disease.

Esophageal cancer has a 20% five-year survival rate and is the 7th leading cause of cancer death.

According to Ronan Kelly, MD, director of Baylor Scott & White Charles A. Sammons Cancer Center - Dallas and international principal investigator on the CheckMate577 trial, “Only about 30% of patients will have a pathological complete response after standard of care neoadjuvant chemoradiation and surgery. Prior to this study, we had no data showing that additional chemotherapy might help the remaining 70% of people.”

CheckMate577 enrolled 794 patients across 27 countries, making it the largest adjuvant IO study to date for patients with operable esophageal or gastroesophageal junction cancer. It is also the first and only therapy to show improved disease-free survival for an adjuvant therapy in this patient population.

Nivolumab doubled the disease-free survival (22.4 months for nivolumab and 11.0 months for placebo, p=0.0003). The median treatment duration was 10 months for nivolumab compared to nine months for placebo. The safety profile was consistent with prior studies of nivolumab monotherapy. The rate of serious treatment-related adverse events of grade three and higher was 5% for nivolumab compared to 1% for placebo. Treatment-related discontinuation occurred in 9% of those taking nivolumab and 3% of those taking placebo.

Dr. Kelly described the potential for this therapeutic option to be rapidly incorporated into clinical practice. “These results give hope to a population of patients who had few to no treatment options available. The efficacy and safety observed in this trial is great news for these patients.”

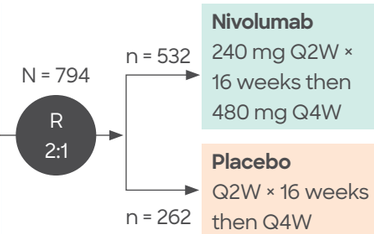
Nivolumab is also approved for adjuvant treatment of advanced, resected melanoma. The results of the CheckMate 577 study place esophageal/gastroesophageal junction cancer as only the second tumor type to show a benefit in the adjuvant setting for a PD1 inhibitor, likely heralding the start of a new era of IO use in early-stage disease.

These results were presented by Dr. Kelly in the Presidential/Plenary Symposium at the European Society for Medical Oncology 2020 virtual meeting in September.

CheckMate 577 is a global, phase 3, randomized, double-blind, placebo-controlled trial[a].

Key eligibility criteria
- Stage II/III EC/GEJC
- Adenocarcinoma or squamous cell carcinoma
- Neoadjuvant CRT + surgical resection (R0,[b] performed within 4 - 16 weeks prior to randomization)
- Residual pathologic disease – ≥ ypT1 or ≥ ypN1
- ECOG PS 0–1

Stratification factors
- Histology (squamous vs. adenocarcinoma)
- Pathologic lymph node status (≥ ypN1 vs. ypN0)
- Tumor cell PD-L1 expression (≥ 1% vs. < 1%[c])



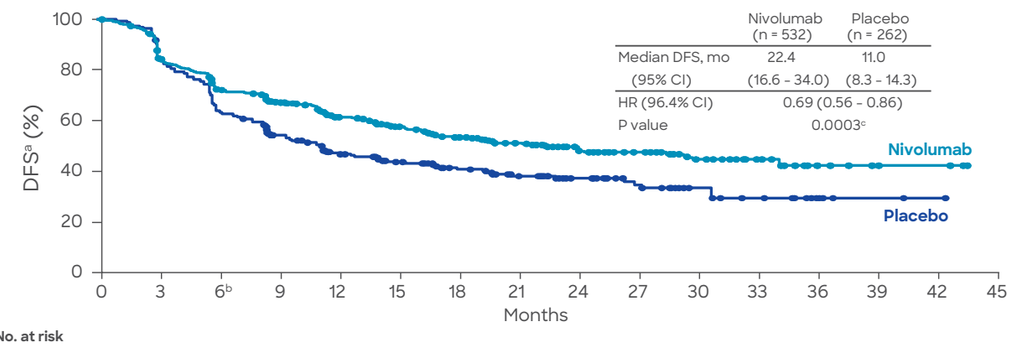
Primary endpoint:
- DFS[e]

Secondary endpoints:
- OS[f]
- OS rate at 1, 2, and 3 years

- Total treatment duration of up to 1 year[d]
- Median follow-up of 24.4 months (range, 6.2 - 44.9)[g]
- Geographical regions: Europe (38%), US and Canada (32%), Asia (13%), rest of the world (16%)

[a]ClinicalTrials.gov number, NCT02743494
[b]Patients must have been surgically rendered free of disease with negative margins on resected specimens defined as no vital tumor present within 1 mm of the proximal, distal or circumferential resection margins.
[c]< 1% includes indeterminate/nonevaluable tumor cell PD-L1 expression
[d]Until disease recurrence, unacceptable toxicity or withdrawal of consent
[e]Assessed by investigator, the study required at least 440 DFS events to achieve 91% power to detect an average HR of 0.72 at a 2-sided α of 0.05, accounting for a pre-specified interim analysis.
[f]The study will continue as planned to allow for future analysis of OS.
[g]Time from randomization date to clinical data cutoff (May 12, 2020)

Nivolumab provided superior DFS with a 31% reduction in the risk of recurrence or death and a doubling in median DFS versus placebo



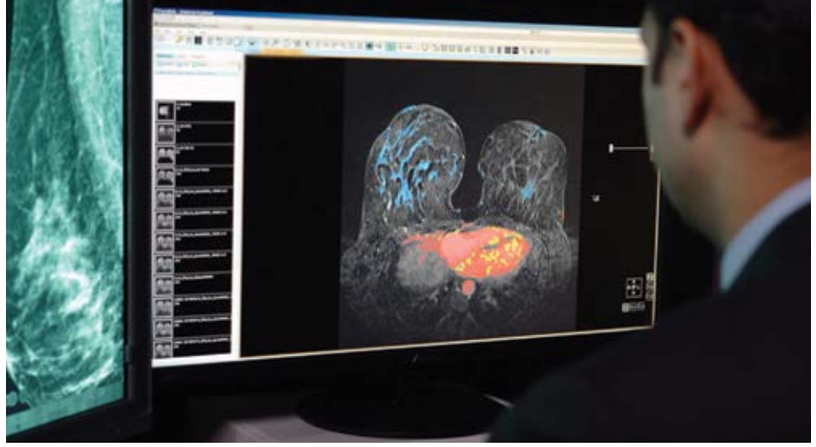
No. at risk

Nivolumab	532	430	364	306	249	212	181	147	92	68	41	22	8	4	3	0
Placebo	262	214	163	126	96	80	65	53	38	28	17	12	5	2	1	0

[a]Per investigator assessment
[b]6-month DFS rates were 72% (95% CI, 68 - 76) in the nivolumab arm and 63% (95% CI, 57 - 69) in the placebo arm.
[c]The boundary for statistical significance at the pre-specified interim analysis required the P value to be less than 0.036.

Summary

- Nivolumab is the first adjuvant therapy to provide a statistically significant and clinically meaningful improvement in DFS versus placebo in resected EC/GEJC following neoadjuvant CRT.
  - 31% reduction in the risk of recurrence or death and a doubling in median DFS
  - DFS benefit across multiple pre-specified subgroups
- Nivolumab was well tolerated with an acceptable safety profile.
  - Incidence of serious TRAEs and TRAEs leading to discontinuation were ≤ 9% with nivolumab and 3% with placebo
- These results represent the first advance in years for this group of patients, potentially establishing adjuvant nivolumab as a new standard of care.



HIGH-RISK BREAST SCREENING PROGRAM

Sean Raj, MD

Yearly mammograms are the standard of care for women at average risk of developing breast cancer. However, for women at higher risk of breast cancer, this screening method may not be enough to catch these cancers early. To improve early breast cancer detection, the Darlene G. Cass Women's Imaging Center at Baylor Dallas has launched the High-Risk Breast Screening Program. Its goal is to identify women at an increased risk for breast cancer and offer them personalized counseling and screening services.

Sean Raj, MD, breast radiologist on the medical staff at Baylor Dallas, is the medical director of the High-Risk Breast Screening Program. He describes his journey toward founding this program: "Breast cancer has always stood out to me as one of the most profound medical problems. One in eight women—an incomprehensibly massive number of women—will be affected by this disease. It really led me to wonder how we could diagnose breast cancer smarter and earlier."

Dr. Raj began to think about typical screening programs and how the one-size-fits-all model provides inadequate care to those at highest risk.

The threshold for high-risk status is a 20% lifetime breast cancer risk. Approximately 15% of women fall into this category, and most don't even know it. Risk factors can be hereditary, such as mutations in the *BRCA1* or *BRCA2* breast cancer susceptibility genes. Personal factors, such as cancer history, obstetric history, lifestyle choices and age, also contribute to risk.

According to Dr. Raj, "We were fortunate to have the crucial support of the Baylor Scott & White Health Foundation - Dallas and the annual Celebrating Women funding campaign to develop this innovative program. Because women at high risk often have more aggressive cancer, it is essential that we identify these cancers as soon as possible."

The High-Risk Breast Screening Program opened in March 2020 and offers personalized and patient-centered risk assessment and initial counseling services at no cost.

Patients are first identified as potentially at high risk based on their screening mammogram. The program's dedicated nurse navigator then personally engages the patient, and a Cancer Risk Assessment survey is completed together, which provides a risk classification score using models of lifetime risk. Dr. Raj says that the initial enthusiasm for the project has been amazing. "Over 40% of these patients classified as high risk based on the preliminary screening mammogram have engaged in our program, learned about their risk and have created a plan that will lead to a healthier future. This level of interest has exceeded all expectations, and we are thrilled to be impacting the lives of women in North Texas."

The team takes an individualized and comprehensive approach to every woman confirmed as high risk, including discussing strategies for risk-reduction, proposing adjunctive screening for potentially aggressive breast cancers, and recommending follow-up care with geneticists and other specialists (breast surgery and oncology), as needed. For many women, this means considering supplementary screening with automated breast ultrasound, contrast-enhanced mammography or abbreviated MRI.

Dr. Raj says, "Many studies in the last decade have shown a dramatic benefit of adjunctive screening for high-risk women in addition to screening mammography. By shortening the interval between screenings, it is possible to detect these aggressive cancers early. This means smaller surgeries with less scarring, potentially less toxic chemotherapy and less morbidity, as well as fewer breast cancer related deaths."

The program is intended to supplement the relationship with the patient's referring physician, and all communications with the patient are documented for the referring physician, including the patient's calculated risk score, strategies and suggestions.

The High-Risk Breast Screening Program is also integrated with the TIOB (see page 6). According to Dr. Raj, "We now have an opportunity to learn from women predisposed to developing aggressive cancers and can harness this information to create smarter, more effective therapeutics through partnerships with the TIOB and the pharmaceutical industry."

As early recognition of the program's success, the High-Risk Breast Screening Program was named as a finalist for the 2020 *D CEO's* Excellence in Healthcare awards. Looking toward the future, Dr. Raj says the goal is to expand the High-Risk Breast Screening Program throughout Baylor Scott & White and beyond. "We truly believe that if we can identify breast cancer earlier through smarter personalized screening, we can change the way breast cancer is diagnosed and defeated."

To improve early breast cancer detection, the Darlene G. Cass Women's Imaging Center at Baylor Dallas has launched the High-Risk Breast Screening Program. Its goal is to identify women at increased risk for breast cancer and offer them personalized counseling and screening services.

16 / High-Risk Breast Screening Program

12 / Understanding Toxicity of Immuno-Oncology Therapies

6 / Texas Immuno-Oncology Biorepository

EXPANDED BREAST CANCER SURGERY SERVICES

Lucy Wallace, MD

The Breast Cancer Research and Treatment Center at Baylor Dallas has expanded its surgical offerings to promote efficiency and enhance the patient experience. Lucy Wallace, MD, co-medical director of the Breast Cancer Research and Treatment Center and breast surgeon on the medical staff at Baylor Dallas, has infused the program with a passion for innovation.

One improvement in breast cancer surgical care is the introduction of a wireless localization system for lumpectomies and excisional biopsies in patients with non-palpable breast lesions. Previously, using a wire localization system, patients had to report to multiple departments throughout our center on the morning of surgery, a multi-step process that was stressful for patients and led to delays in the operating room.

According to Dr. Wallace, “Now, the patient can have the localization device placed on a flexible schedule, even weeks before surgery. This flexibility is better for both the patient and physicians. This technology also allows easy identification of positive lymph nodes prior to neoadjuvant chemotherapy, so we can be sure to retrieve the previously positive node at the time of surgery to accurately determine whether the axillary disease is gone.”

A right skin-sparing mastectomy with sentinel lymph node biopsy with a left prophylactic skin-sparing mastectomy.

Another improvement is the addition of a lighted retractor system to the operating room to enhance visibility in the surgical cavity. This process improvement has increased the ease of performing nipple-sparing mastectomies and other procedures that are performed through small surgical incisions. Dr. Wallace says, “The addition of more specialized lighted equipment facilitates a more cosmetic approach to surgery, and that is something I am very passionate about.”

In addition to these innovations in perioperative care, the Breast Cancer Research and Treatment Center is closely aligned with new initiatives including the High-Risk Breast Screening Program (see page 16) and the TIOB (see page 6). Dr. Wallace describes the collaborative relationship. “Baylor Dallas is committed to improving services for people at high risk for developing breast cancer. For every patient who comes into Baylor Dallas, we calculate his or her lifetime risk for developing breast cancer using the Tyrer-Cuzick model and refer them to the High-Risk Breast Screening Program if they meet the threshold. We also discuss the TIOB with each new breast cancer patient and refer them to the research coordinator for participation.”

Looking toward the future, the Breast Cancer Research and Treatment Center will apply for 2022 accreditation with the National Accreditation Program for Breast Centers (NAPBC), a quality program of the American College of Surgeons. This process will increase multidisciplinary communication, guide quality initiatives on campus and strengthen community outreach. According to Dr. Wallace, “We look forward to the opportunity to formalize our commitment to excellence through NAPBC accreditation, which will benefit our program, our patients and the community.”

June 1, 2020, through September 30, 2020

RECENT PUBLICATIONS

FROM BAYLOR SCOTT & WHITE SAMMONS CANCER CENTER

Abraham P, Wang L, Jiang Z, Gricar J, Tan H, Kelly RJ. Healthcare utilization and total costs of care among patients with advanced metastatic gastric and esophageal cancer [published online ahead of print, 2020 Sep 30]. *Future Oncol.* 2020;10.2217/fon-2020-0516. doi:10.2217/fon-2020-0516

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BAYLOR SCOTT & WHITE SAMMONS CANCER CENTER

CURRENT CLINICAL TRIALS

Study ID	DX	NCT#	Principal Investigator	Study Title
014-129	AML, MDS	NCT02267863	Levy, M Yair	(APTOSE) A Phase Ia/b Dose Escalation and Expansion, Multicenter, Open-label, Safety, Pharmacokinetic and Pharmacodynamic Study of APTO-253 in Patients With Relapsed or Refractory Acute Myelogenous Leukemia or High-Risk Myelodysplasia
015-312	MCL	NCT02601313	Holmes, Houston	A Phase 2 Multicenter Study Evaluating the Efficacy of KTE-X19 in Subjects With Relapsed/Refractory Mantle Cell Lymphoma (r/r MCL)
016-068	MM	NCT02884102	Levy, M Yair	Clinical-grade Molecular Profiling of Patients With Multiple Myeloma and Related Plasma Cell Malignancies (MMRF-002)
016-077	Other	n/a	Levy, M Yair	(ROC) (AMPS) A Two-Stage Blinded Study to Assess Accelerometry-Tracked Pre-Treatment Physical Activity as Surrogate Indicator of Clinical Performance Status
016-126	AML	NCT0266506	Koshy, Nebu	A Multicenter, Pivotal Phase 3 Study of Iomab-B Prior to Allogeneic Hematopoietic Cell Transplantation Versus Conventional Care in Older Subjects With Active, Relapsed or Refractory Acute Myeloid Leukemia
016-260-5	MM	n/a	Levy, M Yair	(TGen Sample Study) Characterizing Mechanisms of Resistance to Novel Agents in Multiple Myeloma
016-264	ALL, CML	NCT02629692	Whiteley, Andrew	A Two-Part Phase 1/2 Study to Determine Safety, Tolerability, Pharmacokinetics, and Activity of K0706, a Novel Tyrosine Kinase Inhibitor (TKI), in Healthy Subjects and in Subjects With Chronic Myeloid Leukemia (CML) or Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia (Ph+ ALL)
018-127	DLBCL, Lymphoma	NCT03263026	Levy, M Yair	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™
018-503	AML	NCT03435848	Burch, Micah	A Phase 2b Open Label, Single Arm, Multi-Center Study to Assess the Efficacy and Safety of BST-236 as a Single Agent for the Treatment of Adult Patients With Newly Diagnosed Acute Myeloid Leukemia (AML), Not Eligible for Standard Induction Therapy
018-566	MM	NCT03544281	Levy, M Yair	(DREAMM-6) A Phase I/II, Open-label, Dose Escalation and Expansion Study to Evaluate Safety, Tolerability, and Clinical Activity of the Antibody-Drug Conjugate GSK2857916 Administered in Combination With Lenalidomide Plus Dexamethasone (Treatment A), or Bortezomib Plus Dexamethasone (Treatment B) in Participants With Relapsed or Refractory Multiple Myeloma
018-617	DLBCL, NHL	NCT03575351	Holmes, Houston	A Global Randomized Multicenter Phase 3 Trial to Compare the Efficacy and Safety of JCAR017 to Standard of Care in Adult Subjects With High-Risk, Transplant-Eligible Relapsed or Refractory Aggressive B-Cell Non-Hodgkin Lymphomas (TRANSFORM)
018-634	ALL, AML, MDS, Other	NCT03555955	Burch, Micah	A Phase 1 Trial to Evaluate the Potential Impact of Renal Impairment on the Pharmacokinetics and Safety of CPX-351 (Daunorubicin and Cytarabine) Liposome for Injection Treatment in Adult Patients With Hematologic Malignancies
018-635	DLBCL, Lymphoma, NHL	NCT03677154	Holmes, Houston	A Phase I/II Trial of Mosunetuzumab (BTCT4465A) as Consolidation Therapy in Patients With Diffuse Large B-Cell Lymphoma Following First-Line Immunochemotherapy and as Therapy in Patients With Previously Untreated Diffuse Large B-Cell Lymphoma Who Are Unable to Tolerate Full-Dose Chemotherapy

Study ID	DX	NCT#	Principal Investigator	Study Title
018-651	Other, MDS	NCT03682536	Whiteley, Andrew	A Phase 3, Open-Label, Randomized Study to Compare the Efficacy and Safety of Luspatercept (ACE-536) Versus Epoetin Alpha for the Treatment of Anemia Due to IPSS-R Very Low, Low or Intermediate Risk Myelodysplastic Syndromes (MDS) in ESA Naïve Subjects Who Require Red Blood Cell Transfusions
018-679	DLBCL	NCT03570892	Holmes, Houston	Tisagenlecleucel Versus Standard of Care in Adult Patients With Relapsed or Refractory Aggressive B-Cell Non-Hodgkin Lymphoma: A Randomized, Open Label, Phase III Trial (BELINDA)
018-741	MM	NCT03269136	Levy, M Yair	A Phase I, Open-Label Study to Evaluate the Safety, Pharmacokinetic, Pharmacodynamic and Clinical Activity of PF-06863135, a B-Cell Maturation Antigen (BCMA) - CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Advanced Multiple Myeloma
019-029	AML	NCT03504410	Levy, M Yair	A Phase III, Multicenter, Open-Label Randomized Trial to Evaluate Efficacy and Safety of CPI-613® (Devimistat) in Combination With High Dose Cytarabine and Mitoxantrone (CHAM) Compared to High Dose Cytarabine and Mitoxantrone (HAM) in Older Patients (≥ 50 Years) With Relapsed/Refractory Acute Myeloid Leukemia (AML)
019-030	Other	NCT03394365	Pineiro, Luis	Multicenter, Open-Label, Phase 3 Study of Tabelecleucel for Solid Organ Transplant Subjects With Epstein-Barr Virus-Associated Post-Transplant Lymphoproliferative Disease After Failure of Rituximab or Rituximab and Chemotherapy (ALLELE)
019-046	CLL, Leukemia	NCT03624036	Holmes, Houston	(ZUMA-8) A Phase 1/2 Multicenter Study Evaluating the Safety and Efficacy of KTE-X19 in Adult Subjects With Relapsed/Refractory Chronic Lymphocytic Leukemia
019-088	MZL + FL B-cell Non-Hodgkin Lymphoma		Levy, M Yair	An Open-Label, Phase 1b/2 Study of Acalabrutinib Alone or in Combination Therapy in Subjects With B-Cell Non-Hodgkin Lymphoma
019-101	AML, Other	NCT03386513	Holmes, Houston	A Phase 1/2, Multi-Center, Open-Label Study of IMGN632 Administered Intravenously in Adult Patients With Relapsed/Refractory CD123-Positive Acute Myeloid Leukemia and Other CD123-Positive Hematologic Malignancies
019-137	MM	NCT03651128	Holmes, Houston	A Phase 3, Multicenter, Randomized, Open-Label Study to Compare the Efficacy and Safety of bb2121 Versus Daratumumab (DARA) in Combination with Pomalidomide (POM) and Low-dose Dexamethasone (dex) (DPd) in Subjects With Relapsed and Refractory Multiple Myeloma (RRMM)
019-140	GvHD	NCT03657160	Pineiro, Luis	A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Vedolizumab in the Prophylaxis of Intestinal Acute Graft-Versus-Host Disease in Subjects Undergoing Allogeneic Hematopoietic Stem Cell Transplantation
019-157	CLL, Leukemia	NCT03331198	Levy, M Yair	(TRANSCEND) An Open-Label, Phase 1/2 Study of JCAR017 in Subjects With Relapsed or Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma (017004)
019-177	MPN	NCT02718300	Holmes, Houston	A Phase 2 Study of the Safety, Tolerability, and Efficacy of INCB05465 in Combination With Ruxolitinib in Subjects With Myelofibrosis
019-207	NHL	NCT01796171	Maisel, Christopher	A Phase I/II Study of Lutetium (177Lu)-Lilotomab Satetraxetan (Betalutin®) Antibody-radionuclide-conjugate for Treatment of Relapsed Non-Hodgkin Lymphoma
019-227	AML	NCT03217838	Levy, M Yair	A Phase I/II, Open-Label, Multicentre 2-Part Study to Assess the Safety, Tolerability, Pharmacokinetics, and Efficacy of AZD2811 Nanoparticle as Monotherapy or in Combination in Treatment-Naïve or Relapsed/Refractory Acute Myeloid Leukemia/Myelodysplastic Syndrome Patients Not Eligible for Intensive Induction Therapy

Study ID	DX	NCT#	Principal Investigator	Study Title
019-256	CLL, Lymphoma, NHL	NCT03786926	Burch, Micah	A Phase 1, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of HMPL-689 in Patients with Relapsed or Refractory Lymphoma
019-377	AML, MDS	NCT03248479	Whiteley, Andrew	A Phase 1b Trial of Hu5F9-G4 Monotherapy or Hu5F9-G4 in Combination with Azacitidine in Patients With Hematological Malignancies
019-451	AML	NCT03969420	Burch, Micah	A Phase 2, Open-Label, Randomized, Two-Stage Clinical Study of Alvocidib in Patients With Relapsed/ Refractory Acute Myeloid Leukemia Following Treatment with Venetoclax Combination Therapy
019-491	AML	NCT03616470	Burch, Micah	A Phase III Randomized, Double-Blind Trial to Evaluate the Efficacy of Uproleselan (GMI-1271) Administered with Chemotherapy Versus Chemotherapy Alone in Patients With Relapsed/Refractory Acute Myeloid Leukemia (GMI-1271-301)
020-025	Peripheral T Cell Lymphoma	NCT03372057	Reynolds, Jana	(PRIMO) A Multi-Center Phase 2 Open-label, Parallel Cohort Study of Efficacy and Safety of Duvelisib in Patients With RR Peripheral T Cell Lymphoma (PTCL)
011-113	Other	n/a	Preskitt, John	Creation and Maintenance of a Longitudinal Surgical Oncology Clinical Research Database (SOCRD)
013-249	Pancreatic Cancer	n/a	Preskitt, John	(Pancreas MDT) A Retrospective and Prospective Longitudinal Pancreas Data Collection Study for Multidisciplinary Tumor Conferences (MDTC)
014-197	Melanoma	n/a	Preskitt, John	(Melanoma MDT) A Retrospective and Prospective Longitudinal Melanoma Data Collection Study for Multidisciplinary Tumor Conferences (MDTC)
014-248	Lung Cancer	n/a	Preskitt, John	(Lung MDT) A Retrospective and Prospective Longitudinal Lung Data Collection Study for Multidisciplinary Tumor Conferences (MDTC)
015-196	Pancreatic Cancer	n/a	Celinski, Scott	(ROC) (w/TGen) Circulating Tumor DNA, Non-Coding RNA, and DNA Methylation Biomarkers for Early Detection of Recurrence and Prognostication of Pancreatic Cancer: A Pilot Study.
016-130	Anaplastic Astrocytoma	NCT02796261	Fink, Karen	A Phase 3, Randomized, Open-Label Study to Evaluate the Efficacy and Safety of Eflornithine With Lomustine Compared to Lomustine Alone in Patients With Anaplastic Astrocytoma That Progress/Recur After Irradiation and Adjuvant Temozolomide Chemotherapy
016-137	Pancreatic Cancer, Gastric and Prostate	NCT02744287	Becerra, Carlos	A Phase 1/2 Feasibility, Safety, and Activity Study of PSCA-Specific Chimeric Antigen Receptor Engineered T Cells (BPX-601) in Subjects With Previously Treated Advanced Solid Tumors
016-266	Pancreatic Cancer	n/a	Celinski, Scott	Retrospective Assessment of Candidate Molecular Prognosticators in Pancreas Cancer Patients With Localized Disease
017-200	Pancreatic Cancer	n/a	Celinski, Scott	(TGen) Integrated Genomic Biomarkers for the Early Detection of Pancreatic Cancer
017-330	Lung, Pancreatic, Solid Tumors, Urothelial Cancer	NCT03139370	Becerra, Carlos	A Phase 1 Study Evaluating the Safety and Efficacy of MAGE-A3/A6 T Cell Receptor Engineered T Cells (KITE-718) in HLA-DPB1*04:01 Positive Subjects With Advanced Cancers

Study ID	DX	NCT#	Principal Investigator	Study Title
017-478	Breast Cancer	NCT03255070	O'Shaughnessy, Joyce	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
018-159	Solid Tumors	NCT02549937	Paulson, Scott A	A Multi-Center, Open-Label, Clinical Trial to Evaluate the Safety, Tolerability, Pharmacokinetics of Surufatinib (HMPL-012), Previously Named Sulfatinib in Advanced Solid Tumors
018-745	Breast		O'Shaughnessy, Joyce	Pilot Clinical Trial of Treatment with Oral LY302023414 to Inhibit Homologous Recombination (HR) Followed by Prexasertib in Patients with Chemotherapy-Pretreated Metastatic Triple Negative Breast Cancer
019-021	Esophageal, Gastroesophageal	NCT03044613	Kelly, Ronan	Phase IB Trial of Induction Nivolumab or Nivolumab/Relatlimab Prior to Concurrent Chemoradiation in Patients With Operable Stage II/III Esophageal/ Gastroesophageal Junction Cancer
019-038	Gastric / Cholangiocarcinoma	NCT03656536	Paulson, Scott A	A Phase 3, Open-Label, Randomized, Active-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib (INCB054828) vs Gemcitabine Plus Cisplatin Chemotherapy in First-Line Treatment of Participants with Unresectable or Metastatic Cholangiocarcinoma With FGFR2 Rearrangement
019-074	GBM	NCT03018288	Fink, Karen	A Randomized, Double Blind Phase II Trial of Radiation Therapy Plus Temozolomide and Pembrolizumab With and Without HSPPC-96 in Newly Diagnosed Glioblastoma (GBM)
019-075	Neuroendocrine	NCT04042714	Paulson, Scott A	An Open-Label, Phase II Investigation of TAS-102 in Patients With High Grade, Extrapulmonary Neuroendocrine Carcinoma
019-350	Solid Tumors		Kelly, Ronan	The Texas Immuno-Oncology Biorepository: Collection of Patients' Biospecimens for Analysis of Immunological and Molecular Biomarkers that Predict Benefit/Resistance to Cancer Immunotherapies
019-410	Head & Neck	NCT03937141	Nadler, Eric	A Phase 2 Efficacy and Safety Study of ADU-S100 and Pembrolizumab in Adults With Head and Neck Cancer
020-008	Breast Cancer		O'Shaughnessy, Joyce	Pilot Clinical Trial of Treatment With Bortezomib to Inhibit Homologous Recombination (HR) Followed by Pembrolizumab and Cisplatin in Patients with Chemotherapy-Pretreated Metastatic Triple-Negative Breast Cancer
020-031	Melanoma	NCT04068181	Cowey, Lance	Phase 2 Study of Talimogene Laherparepvec in Combination With Pembrolizumab in Subjects With Unresectable/Metastatic Stage IIB-IVM1d Melanoma Who Have Progressed on Prior Anti PD-1 Based Therapy
020-063	Glioma	NCT04164901	Fink, Karen	A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of AG-881 in Subjects With Residual/Recurrent Grade 2 Glioma With an IDH1 or IDH2 Mutation (AG881-C-004)
020-095	Pancreatic Cancer	NCT04121442	Becerra, Carlos	A Phase I/IIa, Open-Label Dose Escalation Trial With Isunakinra Alone and in Combination With a PD-1/ PD-L1 Inhibitor in Patients With Metastatic or Unresectable, Locally Advanced Malignant Solid Tumors
020-203	Solid Tumors	NCT04208958	Kelly, Ronan	Phase 1 Study of VE800 and Nivolumab in Patients with Selected Types of Advanced or Metastatic Cancer

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