

## Clinical Trials: What's in it for me?

### **Q: What is a clinical trial?**

A: Clinical trials are **rigorous scientific studies** aimed at **finding better treatments** for diseases such as cancer. A wide variety of trial types exist, starting from small phase 1 trials which test the newest agents for safety and to identify potential signals of activity, all the way through to large multicenter phase 3 trials which randomize patients to a new treatment versus the standard of care. In addition to therapeutic trials, laboratory-based studies can **help companies/universities invent new diagnostic tools** or find ways to better tailor treatments based on blood biomarkers or tissue biomarkers.

### **Q: How do I know if I will get a placebo or inferior treatment?**

A: When your doctor presents a trial option to you, you will be **told whether a placebo is involved**. In cancer, we generally **don't have trials with only a placebo** – rather, a trial may compare the standard of care (for example, paclitaxel) with study drug X + paclitaxel. When trials are designed, before they can be opened to enrollment, several review steps, such as the IRB (institutional review board), reviews the protocol for scientific justification and safety monitoring. One of the aspects the IRB focuses on is whether the trial design represents scientific equipoise – *i.e.*, do we already know one of the treatments is inferior (either because of efficacy or toxicity). If the control arm is inferior, then the design is not appropriate, so the trial won't be approved.

For our IBC-related trials specifically, we are studying whether adding other agents (such as immunotherapy or targeted therapy) can increase the effectiveness of standard therapy, so **you can be assured of receiving at a minimum the standard treatment**.

### **Q: Why is a clinical trial important?**

A: Advances in treatment are made only because of patients who volunteer to participate in clinical trials. Clinical trials provide an opportunity to **access novel treatments years ahead of being commercially available that may improve your outcome while being carefully monitored for side effects**. The National Comprehensive Cancer Network (NCCN) guidelines even state that “NCCN believes the best management for any patient with cancer is in a clinical trial.”

### **Q: Will participating in a trial cost me more? Does the insurance cover the costs? Do I need to move to the trial hospital location to enroll?**

A: There should not be more direct medical costs, but there may additional indirect costs such as travel/parking if there are more visits than normal. **Some trials have reimbursement for travel expenses** either from the sponsor or institutional philanthropic funds, so ask your study team for information about any of these options. Insurance pays for the standard of care costs (such as lab work, standard chemotherapy, or surgery). The study sponsor usually provides the study drug at no cost to the participant. Your research nurse/study coordinator can give you the full details about the financial implications of the trial when you are first discussing whether to enroll. **Our trials do not require moving to Houston** – the treatments are given in the outpatient setting over a few hours, and many patients can safely travel home in the evening or the next morning.

### **Q: What's involved in participating in a trial? How do I find a trial?**

A: We recommend **asking your doctors to help find trials**. Once the doctor finds a potential trial, they will contact the trial team to screen you and determine whether a slot is currently available for enrollment. After you sign an informed consent document, the trial team will order any needed screening tests (like labs, scans, or necessary tissue screening tests) and set up your first appointment after your insurance clearance has been obtained. There are several online sites such as [clinicaltrials.gov](http://clinicaltrials.gov) or [breastcancertrials.org](http://breastcancertrials.org) to seek options; however, it is best to speak with your oncologist, who can help find the most appropriate options for you.

## Q: How do patients benefit from participating in clinical trials?

A: There are numerous benefits and risks to participating in a clinical trial, and each patient has their unique motivation on choosing to participate. Some patients are interested in the early access to **advanced, promising treatments** and close monitoring care from their physician and research professionals, while others participate for an opportunity to better understand their disease, play an active role in their care, and also **help the society** by **contributing to medical research, scientific research** and **discovery** of new therapies. If interested, you should discuss with your physician in detail; however, the decision to participate at any stage of the trial is always for the patient to make.

We realize that many advancements in IBC would not have been possible without our trial participants. Our team would like to take this opportunity to thank them for their generosity and participation in the clinical trials at our IBC program.

*If you have any additional questions about trials for IBC, please contact us via email at [ibcp@mdanderson.org](mailto:ibcp@mdanderson.org).*

*For more information please join our upcoming zoom Q&A on clinical trials:  
Thursday April 29<sup>th</sup> at 5pm CDT (6pm EDT, 3pm PDT)  
<https://mdacc.zoom.us/j/84342343927?pwd=cXdqaGFvTWdRSXBXbXhEOEN1dm56UT09>*

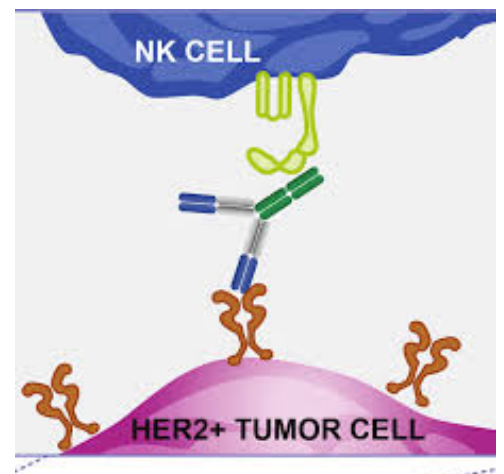
## MDACC COVID MASK MANDATE UNCHANGED

MD Anderson is committed to maintaining the safest environment for all our immunocompromised cancer patients, our employees, and our community. Our commitment to safety remains our greatest priority. As such, **MD Anderson will continue its previous masking practices**, even though the mask mandate for Texas has been lifted.

## Treatment-Related News for Patients

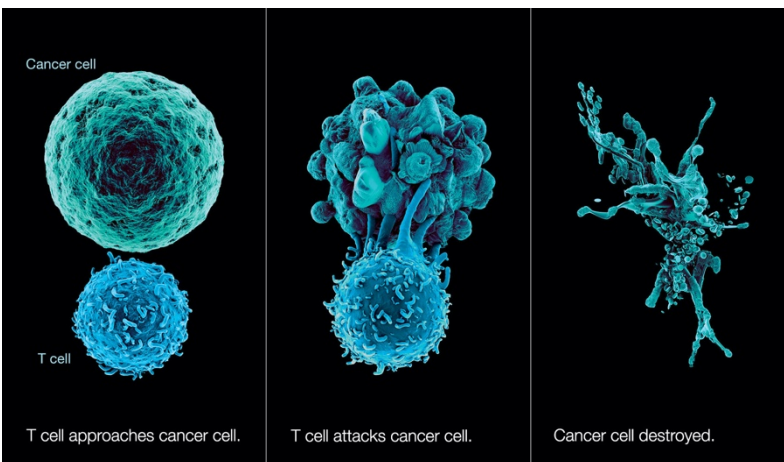
### *New HER2 approval*

We are pleased to share the news from late December that the **FDA has approved a new HER2-targeting drug, Margetuximab** (Margetux brand name) for patients with HER2-positive metastatic breast cancer, along with several choices of single-agent chemotherapy, for patients who have received at least 2 prior lines of HER2-based treatment. Margetuximab is a HER2 antibody similar to Herceptin; however, it is **engineered to more potently boost the immune response to cancer** by binding to receptors on immune cells to bring them into proximity with the tumor so that they can kill the cancer cells. In the phase 3 SOPHIA trial that led to this approval, it was noted that not all patients benefited equally. There are different forms of the CD16A receptor on the immune cells, and one specific form ("VV") predicted a greater benefit from Margetuximab. The FDA approved it for everyone since there is no clinical test to identify these receptor forms. However, it is likely in the future, a diagnostic test will be designed to give this treatment to the patients most likely to benefit.



## Update on Immunotherapy approval for early breast cancer

The breast medical oncology field had been anxiously awaiting news from the FDA about whether they would approve the use of Pembrolizumab (Keytruda) for patients with early-stage triple-negative breast cancer (TNBC). TNBC is the most aggressive subtype of breast cancer, and new treatments are urgently needed for these patients.



Pembrolizumab is a type of immune-checkpoint inhibitor that works to remove the brakes on the immune system to recognize cancer as foreign and kill it.

As we previously shared, Pembrolizumab is now approved for patients with metastatic TNBC who have PD-L1+ tumors, along with chemotherapy. A determination about the new approval for early-stage TNBC was promised by the end of March, and the results of this review have already been announced after the FDA advisory committee met in February to consider this application. The phase 3 study, KEYNOTE-522 was a large randomized

trial (>1100 patients enrolled) which was designed to determine whether patients with early-stage TNBC who received Pembrolizumab along with standard neoadjuvant chemotherapy and then after surgery (“adjuvant treatment” for 9 more cycles) had improved outcomes compared with the patients who only received standard chemotherapy on trial. The trial looked at both pathological complete response (pCR) at surgery as well as long-term outcomes known as event-free survival (what percentage of patients are alive without recurrence). The trial showed a statistically **significant increase in pCR rate for those patients on the Pembrolizumab arm** (64.8% versus 51.2%); however, the data on recurrence is still immature for final conclusions to be made whether the difference in pCR will translate to better long-term outcomes. Importantly immune checkpoint inhibitors such as Pembrolizumab have a risk for long-term side effects different from chemotherapy such as hypothyroidism, adrenal insufficiency, and pneumonitis (inflammation in the lung). These serious potential risks and immature long-term data led the **FDA committee to defer a final decision until more data on risks and benefits are available** from the ongoing studies. In conclusion, the results seen so far are quite interesting but not quite ready for prime time use in the clinic.

## IBC Webinar

Since January 2021, the **IBC program has restarted the webinar series for our IBC Connect colleagues** to discuss important medical topics that apply to the management of patients with IBC. We have been pleased with the interest and commitment of our sites to joining these zoom webinars and the discussion that the presentations have generated. This year's topics have included: Surgical Management of De Novo Stage 4 IBC given by Dr. Susie Sun, Immunotherapy updates in Breast Cancer, given by Dr. Sonia Ali from Scripps, and Pushing the Limits of Reconstruction in IBC given by Dr. Edward Chang.

## New Lab Study – Cancer Screening Diagnostic with Preferred Medicine Inc.

In the fall, we began a **new collaboration with Preferred Medicine Inc**, a company developing a new blood-based cancer detection test. The goal of the study, codenamed “DROPLET-BC,” is **to develop the AI algorithm to most accurately differentiate breast cancer from non-cancer**. The blood test being developed looks at small RNA molecules in the blood, which have different profiles in patients with cancer, and the objectives are to compare these profiles with standard screening methods such as mammograms. The first step is to optimize this method by obtaining blood from 600 patients newly diagnosed with breast cancer, including IBC, and 600 patients undergoing screening in the cancer prevention center without any history/diagnosis of breast cancer. To date, we have enrolled >400 patients and are actively consulting with the company about future implications that may improve the diagnosis of IBC.



## Faculty Spotlight Series: Dr. Bisrat Debeb



Dr. Debeb received his Doctor of Veterinary Medicine degree with high honors from Addis Ababa University in 1999 (during which he won the Gold Medal for excelling academically), Masters from Tuskegee University in 2005, and PhD from Texas A&M University in 2008. He immediately joined MDACC as a postdoctoral fellow under the mentorship of Dr. Wendy Woodward in the Department of Radiation Oncology. Since February 2017, he is a **tenure-track Assistant Professor in the Section of Translational Breast Cancer Research**, Department of Breast Medical Oncology.

His laboratory team members are the postdoctoral fellow Dr. Emilly S. Villodre and Dr. Xiaoding Hu and a research technician Anh Nguyen (expected start date May 2021).

**Dr. Debeb's laboratory's primary research focus is the identification of and targeting the molecular determinants of brain metastasis and understanding the molecular and cellular mechanisms underlying the unique pathobiology of inflammatory breast cancer (IBC)**, a rare but highly aggressive variant of breast cancer. Patients with brain metastases and/or IBC have poor survival outcomes despite multimodality treatment approaches, and no specific FDA-approved targeted therapies currently exist for these frequently fatal diseases. Our **research attempts to gain a richer understanding of the fundamental mechanisms of IBC aggressiveness and brain metastasis** that would enable the development of effective treatments to improve outcomes.

Currently, no effective treatments exist for patients with IBC and/or brain metastasis, and therefore, novel and effective therapies are urgently needed. Finding novel therapies requires a deeper understanding of the basic mechanisms underlying these diseases. The basic science research to identify and target unique drivers of IBC aggressiveness/ brain metastasis done in his laboratory will lay the groundwork for translation to clinical trials, leading to new and better treatments and survival outcomes for thousands of patients.

Dr. Debeb was featured at The Scientist Magazine as one of the scientists to watch section. In the interview he shared his journey from a veterinarian student in Ethiopia to an assistant professor at MD Anderson. The interview is available at <https://www.the-scientist.com/scientist-to-watch/bisrat-debeb-models-how-cancer-spreads-to-the-brain-68575>.

## Recent Awards and Grants

**Bisrat Debeb, DVM, Ph.D.**, Assistant Professor, Department of Breast Medical Oncology-Research received the *Institutional Research Grant (IRG)* for \$75k through MD Anderson Cancer Center for his proposal entitled **“Deciphering the role of NDRG1 in inflammatory breast cancer tumor initiation and progression.”**

## Recent Publications and Abstracts

**Decorin-mediated suppression of tumorigenesis, invasion, and metastasis in inflammatory breast cancer.** Published by Communications Biology. **Authors:** Xiaoding Hu, Emily Schlee Villodre, et al. was accepted for publication.

**The Role of Mastectomy in de novo Stage IV Inflammatory Breast Cancer.** Published by Ann Surg Oncol (2021). **Authors:** Mediget Teshome, Carolyn Hall, Bora Lim, Vicente Valero, Wendy Woodward, Naoto Ueno, and Anthony Lucci, et al. <https://doi.org/10.1245/s10434-020-09392-8>

**Multi-omic molecular profiling reveals potentially targetable abnormalities shared across multiple histologies of brain metastasis.** Published by Acta Neuropathol. 2021 Feb;141(2):303-321 **Authors:** Fukumura K, Malgulwar PB, Fischer GM, Hu X, Mao X, Song X, Hernandez SD, Zhang XH, Zhang J, Parra ER, Yu D, Debeb BG, Davies MA, Huse JT.. doi: 10.1007/s00401-020-02256-1. Epub 2021 Jan 4. PMID: 33394124; PMCID: PMC7852029.

**Modeling Brain Metastasis Via Tail-Vein Injection of Inflammatory Breast Cancer Cells.** Published by J. Vis. Exp. (168) e62249. **Authors:** Hu, X., Villodre, E. S., Woodward, W. A., Debeb, B. G. doi:10.3791/62249 (2021).

## News/Events

The IBC program is growing! We are pleased to welcome the below new employees to our team.



### **Ms. Vivian Chiv, Senior Research Nurse**

Ms. Vivian Chiv has accepted the position as Senior Research Nurse for the IBC program to replace our recently retired RN, Charla Parker. Ms. Chiv has been with MD Anderson for many years, including previous experience as a research nurse in the Department of Breast Medical Oncology. Most recently, she comes to us from Clinical Research Finance, where she learned the business side of clinical research but missed the patient-care aspects of nursing. She will be in charge of various new clinical trials in the IBC program.



### **Dr. Mohd Mughees, Postdoctoral Fellow**

Dr. Mohd Mughees recently joined Dr. Bartholomeusz's Laboratory as a Postdoctoral Fellow in December 2020. He completed his Ph.D. degree in Biotechnology in 2019 and pursued a one-year postdoctoral Fellowship at Jamia Hamdard, New Delhi, India. His previous research was focused on the development of herbal-based nano-therapeutics for breast cancer. He was the recipient of the Senior Research Fellowship and Postdoctoral Fellowship from the Indian Council of Medical research. Besides, he also won the 'Merit Award' from ESMO and was awarded 4 travel awards from the Government of India and from ESMO to present his work at international conferences.

Currently, he is working on two projects, one focused on MEK Inhibitor Resistance in Breast Cancer (IBC and Non-IBC) and the other on the Role of EGR1 in metastasis of TNBC.



### **Ms. Giselle Ortiz, Research Assistant I**

Ms. Giselle Ortiz is our newest member of the IBC clinical laboratory team joining us in March 2021 from UT Health on a part-time basis to help with sample logistics given the current volume of collections. She is a graduate of Texas A&M with a degree in biomedical sciences in December 2019. Giselle will be involved in all of our laboratory and clinical trials with respect to blood and tissue collections.

## IBC Program Presentations

### **HiPlex Technologies for Immune Profiling**

*Sandesh Subramanya, Ph.D., MBA  
Scientific Project Director  
Department of Translational Molecular Pathology*

### **Contribution of cellular plasticity and immune cells to cancer metastasis**

*Sendurai A. Mani, Ph.D. Professor  
Department of Translational Molecular Pathology*

### **Identification of novel molecules that enhance neratinib efficacy in triple-negative breast cancer by high-throughput RNA interference**

*Jangsoon Lee, Ph.D., Assistant Professor  
Department of Breast Medical Oncology*

### **Mechanisms of action and resistance to CDK4/6 inhibitors in breast cancer**

*Khandan Keyomarsi, Ph.D. Professor  
Department of Experimental Radiation Oncology*

### **HER2-targeting macrophage CARs Therapy**

*Naoto T. Ueno, M.D., Ph.D., Professor  
Department of Breast Medical Oncology*

### **Mechanism of MEK inhibitor resistance in triple-negative breast cancer**

*Moises J. Tacam, BS., Research Assistant II  
Department of Breast Medical Oncology-Research*

## Current Clinical IBC Trials Open for New Patient Enrollment

### **Neoadjuvant (newly diagnosed):**

2016-0177 – A randomized phase II study of neoadjuvant Carboplatin/Paclitaxel (CT) versus Panitumumab/Carboplatin/Paclitaxel (PaCT) Followed by anthracycline-containing regimen for newly diagnosed primary triple-negative inflammatory breast cancer

- 2016-0537 - A phase 1b study of neratinib, pertuzumab, and trastuzumab with taxol (3HT) in metastatic and locally advanced breast cancer, and phase II study of 3HT followed by AC in HER2 + primary IBC, and neratinib with taxol (NT) followed by AC in HR+ /HER2- primary IBC
- 2018-0002 - Phase II study of combination ruxolitinib (INCB018424) with preoperative chemotherapy for triple-negative inflammatory breast cancer

### **Adjuvant (after surgery and radiation):**

- 2016-0096 - A phase II study of anti-PD1 (Pembrolizumab) in combination with hormonal therapy in patients with hormone-receptor (HR)-positive localized inflammatory breast cancer (IBC) who did not achieve a pathological complete response (pCR) to neoadjuvant chemotherapy
- 2018-0550 - Atorvastatin in triple-negative breast cancer (TNBC) patients who did not achieve a pathologic complete response (pCR) after receiving neoadjuvant chemotherapy, a multicenter pilot study

### **Radiation:**

- SWOG1706 - A phase II randomized trial of olaparib administered concurrently with RT vs. RT alone for inflammatory breast cancer

### **Metastatic IBC:**

- 2014-0533 - A phase II study of anti-PD1 (MK-3475) therapy in patients with metastatic inflammatory breast cancer (IBC) or non-IBC triple-negative breast cancer (TNBC) who have achieved clinical response or stable disease to prior chemotherapy.
- 2016-1096 - A Phase I Study of OTS167PO, a MELK inhibitor, to Evaluate Safety, Tolerability, and Pharmacokinetics in Patients with Advanced Breast Cancer and Dose-Expansion Study in Patients with Triple Negative Breast Cancer.
- 2016-0890 - A phase II study of triple combination of Atezolizumab, Cobimetinib, and Eribulin (ACE) in patients with chemotherapy-resistant metastatic inflammatory breast cancer
- 2018-0493 - An open-label, multicenter, phase 1b/2 Study of Rebastinib (DCC-2036) in combination with paclitaxel to assess safety, tolerability, and pharmacokinetics in patients with advanced or metastatic solid tumors

We are currently actively developing several new clinical trials for patients with newly diagnosed IBC and patients with metastatic disease and will share more details once activated.

### **Current Clinical IBC Lab Studies:**

We currently have 7 open clinical IBC laboratory studies that collect blood and tissue for analysis of host and tumor biology and clinical correlations.

 Facebook: [www.facebook.com/InflammatoryBreastCancer](https://www.facebook.com/InflammatoryBreastCancer)  Twitter: [www.twitter.com/InflammatoryBCa](https://www.twitter.com/InflammatoryBCa)

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