

What's new in Research?

News from ASCO – Adjuvant PARP inhibitor makes a difference

The annual American Society of Clinical Oncology (ASCO) conference was held in June 2021, again virtually due to COVID-19 travel restrictions. The virtual platform attracted viewers from around the world, similar to the international conference that is usually held in Chicago. This conference showcases clinical data across oncology, ranging from practice-changing clinical trials to correlative studies, expanding our knowledge about biomarkers from clinical trial samples. Our faculty attended the meeting and provided some updates about the data presented.

This year among the likely practice-changing breast cancer trials presented was the long-awaited [OlympiA trial](#), a phase 3 trial studying the effect of **1 year of adjuvant Olaparib for patients with HER2-negative early-stage breast cancer who had documented BRCA1/2 mutations and had a high risk of relapse** after completing chemotherapy and surgery. Patients who had enrolled in the study were randomized to receive Olaparib or placebo, and their survival and recurrence outcomes were assessed. Olaparib is an oral PARP inhibitor that increases the amount of DNA damage in tumor cells, leading to their death if the tumor cells have lost BRCA1/2 function in a synthetic lethal manner. The results of the primary endpoint, iDFS (invasive disease-free survival), demonstrated that **patients assigned to receive Olaparib had a 42% lower risk of recurrence** than the placebo group when outcomes were assessed 3 years from starting the study (85.9% patients free of recurrence vs. 77.1% in the placebo group). Patients with TNBC in this study could not receive adjuvant capecitabine (Xeloda), which has recently become the standard of care, so we do not know if the Olaparib could be given concurrently with Xeloda or the magnitude of benefit of Olaparib versus Xeloda for this population. Patients with ER+ HER2- breast cancer were allowed to receive standard endocrine therapy along with Olaparib.

What relevance does this have for IBC patients? Previous data from our center has demonstrated that BRCA1/2 hereditary mutations occur at a similar rate to non-IBC patients, and stage 3 IBC patients with these mutations were allowed to participate in the study. Hence, once the FDA approves the use of Olaparib in this setting, which is expected in the coming months, we expect this will rapidly become the standard of care for IBC patients with BRCA1/2 mutations who have residual disease after chemo, surgery, and radiation.

Are all stage 4 IBCs alike? Maybe not!

With a very comprehensive workup, such as patients seen at MD Anderson, we have noticed that patients with IBC more often have contralateral nodal involvement at diagnosis. This means cancer which started in one breast has traveled to the lymph nodes on the opposite side. In up to 10% of IBC patients, this pattern of metastasis is identified either via complete bilateral ultrasound or PET-CT. Per the current AJCC staging criteria, patients in this category are considered stage 4 *de novo*, similar to patients with distant organ involvement (such as liver or lung). The purpose of categorizing a patient's stage is to estimate prognosis and guide the duration of systemic treatment offered. A recent analysis by graduating surgical oncology fellow [Dr. Lauren Postlewait](#), and her mentor, [Dr. Anthony Lucci](#), sought to **determine whether IBC patients with this diagnosis ("CAM") have similar outcomes to patients with distant organ metastasis**. This research was published in [Annals of Surgical Oncology](#) this Spring, the key finding being that among patients at MD Anderson with isolated CAM and no other organ metastases, **the outcome was not different from stage 3 IBC**. The authors note that aggressive treatment, including bilateral surgery and radiation, may be what's most important and raise the question of whether these results are validated with external larger databases, the staging criteria should be modified. For now, the **take-home message, however, is that identification of this pattern of spread is key to making the correct treatment decisions and demonstrates the importance of proper workup and diagnosis to optimal patient outcomes**.

ANNOUNCEMENTS

WELCOME

We are excited to extend a warm welcome to our newest IBC Connect team member from Texas – UT Health, Austin, Texas.

Location:

University of Texas at Austin UT Health Austin Clinical Practice

UT Health Austin's Breast Cancer specialty within the **Livestrong Cancer Institute** provides care for adult patients (18 years and older) of all genders with breast cancer diagnosis, including DCIS, early-stage, recurrent, and advanced or metastatic breast cancers.

Med Onc – Dr. Tara Kaufmann

 Facebook: www.facebook.com/UTHealthaustin

 Twitter: [@UTHealthaustin](https://twitter.com/UTHealthaustin)



UT Health Austin combines the latest research and methodologies with supportive care for the body, mind, and heart through an integrated and comprehensive approach designed to provide care, maintain balance and wellness through their breast cancer journey. Depending on patient needs, the treatment may include combinations of surgery, chemotherapy, immunotherapy, targeted therapy, hormone therapy, and radiation therapy.



Tara Kaufmann, MD, MSCE, Assistant Professor

Dr. Kaufmann is a board-certified medical oncologist in **UT Health Austin's Livestrong Cancer Institute** and assistant professor in the **Dell Medical School**, Department of Oncology. She is our newest member in IBC Connect and specializes in treating breast cancer patients.

Dr. Kaufmann's research focuses on improving supportive care services for patients with cancer. She conducts research to use **patient-reported outcomes (PROs)** to monitor patients for unmet care needs, such as physical symptoms, emotional needs, and support. Her goal is to improve symptom management during cancer treatment for patients and their families.

We are excited at the prospect of a new IBC Clinic at Austin in collaboration with IBC Connect in the near future.

IBC Registry Activation

We are pleased to share the news that **Scripps Health (San Diego, CA)** and **Covenant Health (Saginaw, MI)** have recently activated the IBC registry protocol at their sites to contribute to samples and clinical information being captured to facilitate more research into IBC. Further sites within the Cancer Network and IBC Connect may be added in the future.

Annual Zeta Tau Alpha (ZTA) Houston Alumnae Association Fellowship

We are pleased to announce the Annual Zeta Tau Alpha (ZTA) Houston Alumnae Association Fellowship in Inflammatory Breast Cancer (IBC) Research. **The ZTA Foundation has established an endowment through the MWIBCRPC to fund a fellowship in IBC research.** This year, the Program will award two grants, each receiving \$1,000, recognizing efforts with exceptional quality of IBC research and high impact (or potential impact) for our IBC patients. The awardee will be invited to present at our IBC research seminar at MD Anderson Cancer Center. However, due to COVID-19 and the current uncertainty of continued social distancing, the award winners may be expected to present virtually. For awardees outside of MD Anderson Houston and surrounding counties, Morgan Welch IBC will pay for travel.

If you are interested or know of someone who is interested and would like additional information regarding the annual ZTA Fellowship, please feel free to email us at ibcp@mdanderson.org.

IBC Team Profile - Susie Sun, MD, MS

Dr. Susie Sun is an Assistant Professor in the Department of Breast Surgical Oncology and a member of the Morgan Welch IBC Research Program and Clinic at MD Anderson. She is one of our **breast surgeons specializing in IBC** and supporting patient care at the IBC Multi-team clinic.

She received her undergraduate degree from Oberlin College with a major in Biochemistry and a medical degree from Boonshoft School of Medicine at Wright State University. She then completed her residency at Penn State Hershey Medical Center and her fellowship at MD Anderson.

Dr. Sun is the **recipient of numerous honors and awards** at national conferences such as the Annual Meeting Scientific Impact Award, George Peters Award: Best Presentation by a Fellow, Bristol-Myers Squibb Award in Population Science and Professionalism and Humanism in Surgery Award, just to name a few accomplishments in recent years.



Why is your research important, and what is your research (trials) focus?

“My areas of interest are clinical and outcomes research. There is currently a void in the study of the cost of oncologic treatments, especially in patients with breast cancer. **My goals are to better understand different aspects of the cost of care and their impact on long-term outcomes.** By associating the evaluation of cost in relation to both clinical and patient-reported outcomes, we can strive to provide the best value-based care to our patient population. “

Dr. Sun will be leading an upcoming clinical trial looking at the effect of **photoimmunotherapy for patients with IBC skin metastasis**, a protocol we are very excited to open in the coming months.

When she is not in the OR taking care of the IBC patients, she enjoys spending time with her husband and two children.

IBC Patient Focus



We appreciate our patients who share their stories online, either through MD Anderson media such as the CancerWise blog or otherwise. Ms. Dana Evans recently shared her experiences fighting metastatic HER2-positive inflammatory breast cancer since 2015. She notes how despite initial advice from her outside team to get her affairs in order due to having a poor prognosis, **she found hope and strength from her team led by Dr. Sadia Saleem at MD Anderson** and her family support, allowing her to participate in 5 clinical trials to date. She notes that upon hearing the recent FDA approval of Tucatinib, one of the first trials she participated in, she was ecstatic to have played a part in this process of discovering new treatments to extend her life and many other future patients. **Read more on her**

CancerWise article [here](#).

Do you have a story you wish to share about your treatment at MD Anderson? Please contact us at ibcp@mdanderson.org, and we can refer you to our communications colleagues who manage the blog and social media channels.

MD Anderson's Institutional Update on Covid-19

Patient Visitors

As the impact of COVID-19 slows down, we are beginning to implement new changes within the institution - **MD Anderson is now accepting visitors on campus** to ensure patient comfort and safety. Patients in the Ambulatory (outpatient) and Acute Cancer Care Centers will be allowed one adult visitor or caregiver while on campus. Inpatients can provide the names of up to 5 visitors, but only 1 unique visitor will be permitted on any given day. Visiting hours will be **3-9 p.m. on weekdays** and **10 a.m.-9 p.m. on weekends**. Once a visitor leaves for the day, another visitor is not permitted until the next day.

Patient Testing

COVID-19 testing at MD Anderson for asymptomatic patients (domestic or international) will no longer be required prior to their first appointment. All other testing policies regarding patients will remain in place.

Personal Protective Equipment (PPE)

Patient-care areas will remain protected by a moat of heightened infection control protocols. **In moat-designated areas, MD Anderson-issued face masks must be worn by all.** In areas outside these mask-required zones, face masks will be recommended but not required.

In addition, **face shields are no longer required for routine patient care encounters.** MD Anderson-issued face shields must continue to be worn only by those performing high-risk and aerosol-generating procedures, administering COVID-19 tests, and working with COVID-19 patients. For those whose job role requires eye protection, such as safety glasses as standard PPE (e.g., research areas, certain EH&S staff), safety glasses will continue to be required.

Recent Awards and Grants

Emily Schlee Villodre, Ph.D., Postdoctoral Fellow in Dr. Bisrat Debeb's laboratory in Breast Medical Oncology-Research received **The Sheskey Family Fellowship for Breast Cancer Research award**. She also received the **2021 Education Week Trainee Award** at UT MD Anderson Cancer 2nd Place Oral Presentation in the category of Translational Research.

Dr. Naoto Ueno, Dr. Toshiaki Iwase, and Dr. Jangsoon Lee received the **Cancer Focus Fund for the Phoenix Molecular Design team**. The Cancer Focus Fund invests in promising therapies in late preclinical development through Phase I and Phase Ib/II clinical trials. The fund's objective is to provide support to accelerate the development of these therapeutics together with the clinical trials expertise and infrastructure of MD Anderson.

Dr. Naoto Ueno received Bridge Funding **Title: Developing a novel combination immunotherapy for triple-negative breast cancer.**

Dr. Xiaoping Wang received the DoD Rare Cancers Research Program Idea Development Award **Title: Enhancing Axl-Targeted Therapy in Inflammatory Breast Cancer.**

Recent Publications and Abstracts

Inhibition of resistant triple-negative breast cancer cells with low-dose 6-mercaptopurine and 5-azacitidine. Authors: Singh B., Sarli V. N., Lucci A. *Oncotarget*. 2021; 12: 626-637.
<https://www.oncotarget.com/article/27922/text/>

Prophylactic cranial irradiation reduces the incidence of brain metastasis in a mouse model of metastatic, HER2-positive breast cancer. Authors: Smith DL, Debeb BG, Diagaradjane P, Larson R, Kumar S, Ning J, Lacerda L, Li L, Woodward WA. *Genes Cancer*. 2021 Mar 13;12:28-38. doi: 10.18632/genesandcancer.212. eCollection 2021.

Gene expression profiles of inflammatory breast cancer reveal high heterogeneity across the epithelial-hybrid-mesenchymal spectrum. Authors: Chakraborty P, George JT, Woodward WA, Levine H, Jolly MK. *Transl Oncol*. 2021 Apr;14(4):101026. doi: 10.1016/j.tranon.2021.101026. Epub 2021 Jan 31.

Validation of Prognostic Stage and Anatomic Stage in the American Joint Committee on Cancer 8th Edition for Inflammatory Breast Cancer. Authors: Kida K, Hess KR, Lim B, Iwase T, Chainitikun S, Valero V, Lucci A, Le-Petross HC, Woodward WA, Krishnamurthy S, Hortobagyi GN, Tripathy D, Ueno NT. *Cancers (Basel)*. 2020 Oct 24;12(11):3105. doi: 10.3390/cancers12113105.

Whole-genome sequencing of phenotypically distinct inflammatory breast cancers reveals similar genomic alterations to non-inflammatory breast cancers. Authors: Li X, Kumar S, Harmanci A, Li S, Kitchen RR, Zhang Y, Wali VB, Reddy SM, Woodward WA, Reuben JM, Rozowsky J, Hatzis C, Ueno NT, Krishnamurthy S, Pusztai L, Gerstein M. *Genome Med*. 2021 Apr 26;13(1):70. doi: 10.1186/s13073-021-00879-x.

ASO Visual Abstract: Contralateral Axillary Metastasis in Patients with Inflammatory Breast Cancer. Authors: Postlewait LM, Teshome M, Adesoye T, DeSnyder SM, Lim B, Kuerer HM, Bedrosian I, Sun SX, Woodward WA, Le-Petross HT, Valero V, Ueno NT, Lucci A. *Ann Surg Oncol*. 2021 May 29. doi: 10.1245/s10434-021-10200-0. Online ahead of print.

Contralateral Axillary Metastasis in Patients with Inflammatory Breast Cancer. Authors: Postlewait LM, Teshome M, Adesoye T, DeSnyder SM, Lim B, Kuerer HM, Bedrosian I, Sun SX, Woodward WA, Le-Petross HT, Valero V, Ueno NT, Lucci A. *Ann Surg Oncol.* 2021 Jun 14. doi: 10.1245/s10434-021-10148-1. Online ahead of print.

Identification of JNK active triple-negative breast cancer cluster associated with immunosuppressive tumor microenvironment. Authors: Takashi Semba, Xiaoping Wang, Xuemei Xie, Evan N. Cohen, James M. Reuben, Kevin N. Dalby, James P. Long, Lan Thi Hanh Phi, Debu Tripathy, and Naoto T. Ueno, has been accepted for publication by JNCI.

PI3K and MAPK Pathways as Targets for Combination with the Pan-HER Irreversible Inhibitor Neratinib in HER2-Positive Breast Cancer and TNBC by Kinome RNAi Screening. Authors: Jangsoon Lee, Huey Liu, Troy Pearson, Toshiaki Iwase, Jon Fuson, Alshad S. Lalani, Lisa D. Eli, Irmina Diala, Debu Tripathy, Bora Lim, and Naoto T. Ueno has been accepted for publication by MDPI Biomedicines.

Antibody-drug conjugates with dual payloads for combating breast tumor heterogeneity and drug resistance. Authors: Chisato M Yamazaki, Aiko Yamaguchi, Yasuaki Anami, Wei Xiong, Yoshihiro Otani, Jangsoon Lee, Naoto T Ueno, Ningyan Zhang, Zhiqiang An, Kyoji Tsuchikama. *Nature Communication.* 2021 Jun 10;12(1):3528. doi: 10.1038/s41467-021-23793-7.

Chemical generation of small molecule-based bispecific antibody-drug conjugates for broadening the target scope. Authors: Aiko Yamaguchi, Yasuaki Anami, Summer Y Y Ha, Travis J Roeder, Wei Xiong, Jangsoon Lee, Naoto T Ueno, Ningyan Zhang, Zhiqiang An, Kyoji Tsuchikama. *Bioorganic & Medicinal Chemistry.* Volume 32, 15 February 2021, 116013

Changes in Overall Survival over Time for Patients with de novo Metastatic Breast Cancer. Authors: Toshiaki Iwase, Tushaar Vishal Shrimanker, Ruben Rodriguez-Bautista, Onur Sahin, Anjali James, Jimin Wu, Yu Shen, Naoto T Ueno. *Cancers (Basel).* 2021 May 28;13(11):2650. doi: 10.3390/cancers13112650.

The Prognostic Impact of Body Composition for Locally Advanced Breast Cancer Patients Who Received Neoadjuvant Chemotherapy. Authors: Toshiaki Iwase, Aaroh Parikh, Seyedeh S. Dibaj, Yu Shen, Tushaar Vishal Shrimanker, Sudpreeda Chainitikun, Kumiko Kida, Maryanne E. Sapon, Onur Sahin, Anjali James, Andrea Yizel Delgado Medrano, Ann H. Klopp, and Naoto T. Ueno. *Cancers (Basel).* 2021 Feb; 13(4): 608.

Body composition and breast cancer risk and treatment: mechanisms and impact. Authors: Toshiaki Iwase, Xiaoping Wang, Tushaar Vishal Shrimanker, Mikhail G Kolonin, Naoto T Ueno. *Breast Cancer Res Treat.* 2021 Apr; 186(2):273-283.

Nonphosphorylatable PEA15 mutant inhibits epithelial-mesenchymal transition in triple-negative breast cancer partly through the regulation of IL-8 expression. Authors: Jihyun Park*, Moises J. Tacam*, Gaurav Chauhan, Evan N. Cohen, MariaGagliardi, Lakesla R. Iles, Naoto T. Ueno, Venkata L. Battula, Yoo-Kyoung Sohn, Xiaoping Wang, Hak-Sung Kim, Savitri Krishnamurthy, Natalie W. Fowlkes, Morgan M. Green, Geoffrey A. Bartholomeusz, Debu Tripathy, James M. Reuben, Chandra Bartholomeusz. * Equal First authors has been accepted for publication in *Breast Cancer Research and Treatment.*



News/Events

Save the date: MD Anderson Virtual Boot Walk: Nov 6th, 2021



MD Anderson will host the **6th Annual Boot Walk to End Cancer®** event on **Saturday, Nov 6, 2021** with a goal of generating funds to advance research. Team IBC Wranglers is excited to participate in the virtual Boot Walk once again this year and we look forward to your support for our team. The IBC program has participated every year as the "IBC Wranglers" team and raised over \$300,000 in the past 5 years, used to support basic/translational and clinical research, including support for patients participating in our clinical trials. The boot walk will continue to be a virtual event this year so you can walk **WHEREVER WE ARE, ON ANY DAY AND AT ANY TIME.**

IBC Events Update

The program participates in multiple October Breast Cancer Awareness events including the annual IBC High Tea. However, this year due to the continuing COVID-19 restrictions limiting in-person events, we will be unable to conduct any events onsite. **However, we look forward to in-person events and meetings in the future.**

IBC-IC Conference postponed to December 2022

MD Anderson is honored to host the **7th International IBC- IC Conference**, held bi-annually to foster collaboration and networking among local and international IBC researchers, clinicians, patients, advocates and the IBC community to enable scientific discussions and innovation IBC research.

However, COVID restrictions continue to be in place for most healthcare institutions, with limitations on in-person meetings, business travel etc. Therefore, the IBC Conference planning committee decided to **postpone the conference scheduled in December 2021 until next year**, keeping in mind MD Anderson's core value of Safety and providing a safe environment for our employees, patients, advocates, and all conference participants. We look forward to a successful conference in December 2022.

IBC Program Presentations

Identifying mechanisms of immune resistance through analysis of the T cell repertoire in NSCLC

*Alexandre Reuben, Ph.D., Assistant Professor
Department of Thoracic/Head and Neck Medical Oncology*

Chemobrain, accelerated aging and peripheral neuropathy as a result of chemotherapy: mechanisms and treatment with cell therapy

*Cobi J. Heijnen, Ph.D., Professor
Chair, Department of Symptom Research*

Mesenchymal Stromal Cells as a Therapeutic Target in Carcinoma Treatment

Mikhail Kolonin, Ph.D., Professor

Harry E. Bovay, Jr. Distinguished University Chair in Metabolic Disease Research, Director, Center for Metabolic and Degenerative Diseases, The Brown Foundation Institute of Molecular Medicine, McGovern Medical School, University of Texas Health Science Center

IBC Program Update

*Naoto T. Ueno, MD, Ph.D., Professor
Breast Medical Oncology*

*Wendy Woodward, MD, Ph.D., Professor
Radiation Oncology*

*Anthony Lucci, MD, Ph.D., Professor
Surgical Oncology*

The spatial localization of CD163+ tumor-associated macrophages predicts prognosis and response to therapy in inflammatory breast cancer

*Christophe Van Berckelaer, MD, PhD Student
2020 ZTA-IBC FELLOWSHIP AWARD WINNER
Translational Cancer Research Unit
University of Antwerp*

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

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 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 5 open clinical IBC laboratory studies that collect blood and tissue for analysis of host and tumor biology and clinical correlates.

Newsletter Committee

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Swetha Bopparaju Emily Schlee Villodre
Jie Willey Hope Murphy Naoto Ueno

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