

**METASTATIC BREAST CANCER ALLIANCE**  
METASTATIC BREAST CANCER  
CLINICAL TRIALS  
LANDSCAPE AND GAP ANALYSIS



Metastatic Breast Cancer Alliance, New York, NY; Breast Cancer Research Foundation, New York, NY

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# **The Metastatic Breast Cancer Alliance (MBCA)**

## **Metastatic Breast Cancer Clinical Trials Landscape and Gap Analysis**

### **PROJECT KNOWLEDGE AND RECRUITMENT GOALS**

- To build knowledge and awareness of clinical trials as options for care among patients, their families, and caregivers;
- To develop and promote best practices for metastatic breast cancer (MBC) patients to consider, understand, and decide about clinical trial opportunities; and
- To develop tools, systems, policies, and practices to support patients with MBC, caregivers, and providers in making decisions regarding clinical trial enrollment.

### **ACKNOWLEDGEMENTS**

The Metastatic Breast Cancer Alliance (MBCA) is grateful to the many MBCA member organizations and individuals who volunteered their time to be interviewed for this *Metastatic Breast Cancer Clinical Trials Landscape and Gap Analysis*, especially those living with MBC who shared their personal experiences and insights. The personal statements of MBC patients have been edited for brevity and focus on clinical trials.

We would also like to thank BreastCancerTrials.org, which so kindly shared access to their Metastatic Trial Search (MTS) tracking and analytic tools, with special thanks to Dr. Elly Cohen and Susan Colen for providing not only guidance and insight, but also data for the mapping analysis of metastatic clinical trials on the MTS system.

The project consultant was Deborah Vollmer Dahlke, DrPH, of DVD Associates, LLC, who is also an Adjunct Associate Professor and Senior Fellow at Texas A&M University's Center for Population Health and Aging. This project was overseen by Laurie Campbell, Executive Director of the MBCA; Christine Benjamin, Vice Chair of the MBCA; and the co-chairs of the MBCA Information Task Force, Janine Guglielmino and Andrea Hutton. Editing and special assistance were provided by Dana Mooney, MBCA Program Associate; and Kristine De La Torre, PhD, MBCA consultant and medical writer.

## FOREWORD

The Metastatic Breast Cancer Alliance was publicly launched on October 13, 2013, Metastatic Breast Cancer Awareness Day. It is a *union* of 32 nonprofit cancer organizations, 14 international pharmaceutical or biotech companies, and 30 individual patient advocates. *Together*, we develop and implement *awareness* initiatives that share how metastatic breast cancer (MBC) differs from early stage breast cancer, *research* initiatives that focus on advances that impact the outcomes of patients, and *information and support* initiatives that help newly diagnosed patients understand their disease and engage with their healthcare providers.

Women and men who receive a diagnosis of MBC, either as a first diagnosis (de novo disease) or as a recurrent diagnosis, desire to live as long as possible with the best quality of life. Newly diagnosed patients are often informed that a wide variety of treatment choices are available and if one treatment stops working, “there is another one we can try.” While that statement is comforting to hear, the reality is that the 5-year survival rate for MBC is 22 percent and the median survival is 3 years. Estimates are that by the end of 2020, 42,690 people in the U.S. will die from breast cancer. That annual number has hovered around 40,000 for over a decade.

Both metastasis and treatment resistance can contribute to death from MBC. The burden of cancer increases and, without another precise treatment, the death toll sadly rises. How can we assure patients that “another treatment” will be available for them when needed?

Only patient participation in clinical trials ensures that new treatments are identified and then made available in the clinic.

Working as a catalyst to change outcomes in MBC, the MBC Alliance undertook and completed a *Metastatic Clinical Trials Landscape and Gap Analysis*. The *Analysis* that follows describes challenges, gaps, and opportunities in clinical trial research. The leadership of the MBC Alliance developed a prioritized list of opportunities to effect change in access to and delivery of clinical trials. Guiding principles that facilitated the selection of priorities were urgency of need; known, active activities and partnerships among Alliance members; speed and likelihood of success; and the need for further or more diverse perspectives to move toward our goal.

**Priority 1: Address the Role of Disparities in Clinical Trial Access, Participation, and Completion**

**Priority 2: Play a Leadership Role in Encouraging Patient Participation in Trial Design**

**Priority 3: Work with Healthcare Professionals to Use MBC Connect and Metastatic Trial Search to Educate Patients About Clinical Trials**

**Priority 4: Facilitate the Use of MBC Connect and Metastatic Trial Search Among MBCA Members and Non-Members**

**Priority 5: Develop a Strategic, Coordinated Marketing Campaign to Increase Awareness of MBC Connect, Metastatic Trial Search, and Metastatic Trial Talk**

Unlike a single patient organization, the Alliance has the unique opportunity to collectively pursue initiatives that remove barriers to trial participation. Expanding trial eligibility criteria will, by itself, allow for “real-world” representation and accrual and significantly reduce ethnic, racial, and economic disparities in trials. With broad trial accrual, drugs that show efficacy, safety, and tolerable toxicity can be brought into the clinic and offered to patients who will have confidence that the new treatments were tested by patients who are similar to them.

It is an honor for me to lead the MBC Alliance and work with our committed members—nonprofit organizations, pharmaceutical and biotech industries, and individual patient advocates. We take seriously our responsibility to collectively pursue strategic initiatives identified in the *Metastatic Landscape Analysis* so that new and better treatments can be found, and better outcomes realized for all patients. *Together, we truly are greater than the disease!*

Shirley A. Mertz, MA, JD  
Chair  
Metastatic Breast Cancer Alliance

# TABLE OF CONTENTS

<b>1. Introduction and Rationale</b>	<b>7</b>
1.1 Current State of Enrollment in MBC Clinical Trials	10
1.2 Recent MBC Epidemiology and Statistics on Incidence, Prevalence, and Mortality	18
1.3 What's New: New Trial Types, Emerging Agents in Trials, and Diagnostics	23
1.4 Recent FDA Approvals: The State of the Science in MBC	27
1.5 The Importance of Clinical Trial Findings for People Living with MBC and Resources	30
<b>2. Clinical Trial Search and Matching Services for MBC</b>	<b>33</b>
2.1 Expanding Use of Clinical Trial Matching Services	34
2.2 Recent Changes that Affect Screening Criteria for Trial Matching	34
2.3 Consideration of Compensation in Addition to Reimbursement for Clinical Trial Participation	36
2.4 Overview of Clinical Trial Matching Services for MBC Patients and Their Families/Caregivers	37
<b>3. Key Findings and Results of Assessments of MBCA Member Websites and Social Media for MBC Clinical Trials</b>	<b>46</b>
3.1 Results of Assessments of MBCA Members' Websites and Social Media for Clinical Trial Education and Access	47
3.2 Opportunities and Best Practices to Expand Clinical Trial Education and Enrollment Through Social Media	49
<b>4. Results from Qualitative Interviews of MBCA Members and Key Thought Leaders about MBC Clinical Trial Barriers and Facilitators</b>	<b>50</b>
4.1 Qualitative Results of MBCA Interviews	51
4.2 Key Findings from Across the MBCA Interviews	51
4.3 MBCA Interview Responses from Academic, Business, and Minority Thought Leaders and Pharmaceutical Company Partners	54

# TABLE OF CONTENTS

<b>5. Discussion and Strategies for Best Practices and Innovations to Improve and Expand Access to MBC Clinical Trials</b>	<b>63</b>
5.1 Discussion of Results and Findings of Metastatic Breast Cancer Clinical Trials Landscape and Gap Analysis	64
5.2 Developing and Implementing Strategies to Improve MBC Clinical Trial Participation	64
5.3 Strategies to Address Policy, Institutional, and Structural Barriers to MBC Clinical Trial Participation	66
5.4 Strategies to Address Socio-Economic Barriers for MBC Patient Participation in Clinical Trials	68
5.5 Conclusions	69
<b>6. Appendices</b>	<b>70</b>
Appendix A: References	71
Appendix B: More information about terms used in this paper	75
Appendix C: Methods used in MBCA Clinical Trials Landscape and Gap Analysis	76
Appendix D: Advocate Interview Guide and Assessment Form	81
Appendix E: Thought Leader Interview Guide (Academia, Minority Advocacy, and Business Leaders)	87
Appendix F: MBC Patient Interview Guide	89
Appendix G: Hear Our Voice: Patient driven solutions to increase participation in clinical trials	91

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**INTRODUCTION  
AND RATIONALE**

# 1. INTRODUCTION AND RATIONALE

The vision of the Metastatic Breast Cancer Alliance (MBCA) is to transform and improve the lives of people living with metastatic breast cancer (MBC). This *Metastatic Breast Cancer Clinical Trials Landscape and Gap Analysis* reflects the key elements of the mission of the MBCA to “unify the efforts of MBC Alliance members to improve the lives of, and outcomes for, those living with metastatic breast cancer and their families through increasing awareness and education about the disease and advancing policy and strategic coordination of research funding – specifically focused on metastasis – that has the potential to extend life, enhance quality of life and ultimately... to cure.”

The MBCA is a true alliance, a group or union of nonprofit organizations, pharmaceutical companies, and individuals, formed with the shared goals of increasing knowledge, building understanding, and improving research progress in MBC. The MBCA is not static and continues to add new members; as of September 2020, members include 32 nonprofit cancer organizations, 30 individual patient advocate members, 5 founding international pharmaceutical companies, and 9 additional supporting or sustaining pharmaceutical or biotech companies.

The overarching goal of this project is to ensure that MBC patients, their caregivers, and providers know how, and are able, to access information about MBC trials as a treatment option. Among the questions the MBCA posed is “What is the current status of MBC trials?” The Alliance members recognized a greater interest in MBC trials in the past several years, as suggested by the focus on oral presentations and abstracts on MBC at the annual American Society of Clinical Oncology (ASCO) meetings as well as the San Antonio Breast Cancer Symposium (SABCS). The Alliance, however, sought a clearer understanding of the awareness about MBC trials from its advocate study to: 1) describe the current landscape of MBC trials; 2) identify any specific gaps in knowledge and education among its members; 3) assess the current changes in trials and therapies for MBC; and 4) identify changes in policy that might affect MBC trials and trial participation. The assessment included surveying its members and their patients’ access to information about metastatic clinical trials and the options, risks, and benefits of participating in a clinical trial.

A significant element of this landscape and gap research is focused on the Alliance’s partnership with BreastCancerTrials.org’s Metastatic Trial Search (**MTS**) and its new companion service, Metastatic Trial Talk (**MTT**). MTS launched in 2015 and was embedded on the websites of the MBCA and four founding Alliance members (Breastcancer.org, Living Beyond Breast Cancer, Young Survival Coalition, and Triple Step Toward the Cure) as a pilot. The objective of MTS was to expand access to MBC clinical trials and to provide people living with MBC an easy way to access and understand clinical trials in MBC. Because MTS involved Alliance members, Dr. Elly Cohen,



founder of BreastCancerTrials.org and MTS, began updating the Alliance's Research Task Force about the project. The Alliance formally joined the MTS project partnership in 2016 and expanded the Alliance's MTS membership to 13 sites that year.

In 2018, the Alliance was heavily involved in communications and dissemination of MTT to its members. The objective of MTT is to provide news and information about MBC clinical trials, including updates from oncology conferences, research news, resources and support, expert input, and personal stories. The Alliance continues to be an engaged and active partner in the design and ongoing development and deployment of MTS/MTT. In addition to describing Alliance member use of MTS/MTT, this report demonstrates the current digital environment of MBCA members and their use of MTS during 2018. We sought to learn about the plans that members have for education and programming for continued support of MTS and MTT.

Providing digital access to information and education is a key role for all Alliance members. The Alliance believes that this research project of reviewing and cataloging Alliance members' current and planned educational and outreach activities will better enable the Alliance to both target and expand efforts to inform members, patients, caregivers, and the larger cancer advocacy and professional healthcare community regarding participation in MBC clinical trials.

This report includes interviews with the leaders of Alliance member organizations, as well as Key Thought Leaders and people living with MBC. Their input provided the basis for better understanding the gaps, barriers, and opportunities for MBC patients who are seeking and considering enrollment in research studies for MBC. The interviews also will result in new opportunities for Alliance partners and expanded opportunities for education and outreach.

This research provides a snapshot of the landscape and gaps for clinical trial education and access among MBCA members, identifies barriers and gaps experienced by patients and providers, showcases MTS and other clinical trial matching services, and identifies best practices through case studies. In interviewing the patients, who are also advocates, we explored their experiences in learning about MBC trials, the barriers and facilitators to participating in trials, and what they believed was important to share about their experience living as a person with MBC. Their quotes about their experiences and insights are included throughout the document as side bars.

The Discussion, the last section of the report, provides suggestions and opportunities for the MBCA to increase outreach and expand programs and policy efforts to Alliance members. The hope is that these recommendations will help put into place best practices to enable caregivers, healthcare professionals, and people living with MBC to consider participation in clinical trials.

## 1.1 CURRENT STATE OF ENROLLMENT IN MBC CLINICAL TRIALS

### 1.1.A BARRIERS TO PATIENT ENROLLMENT IN MBC CLINICAL TRIALS

Understanding the barriers to patient enrollment in clinical trials is an ongoing area of research. The growth of social media advocacy from the MBCA and Alliance partners, along with their work in patient education, peer matching, navigation, and trial matching services, is increasing opportunities for those with MBC to learn about and consider cancer clinical trials as treatment options. Although patients and physicians indicate that clinical trial participation is a positive approach to cancer care<sup>1</sup> rates of enrollment have not greatly increased over time.<sup>1-6</sup> Research suggests that clinical trial systems that enroll patients more rapidly produce better results for treatment advances. Efficacious therapies proceed to approval faster with opportunities to be accelerated, and those studies that fail to demonstrate clinical effectiveness are halted earlier. Thus, increases in survival and quality of life, and reductions in mortality from MBC and other cancers, are enhanced by faster and more efficient accrual of study participants.<sup>2-6</sup> The issue at the heart of this analysis, in cancer clinical trials overall and in MBC trials specifically, is reducing barriers so that more MBC patients have opportunities to receive the newest advances in therapies.

Decisions about cancer treatment are complex and personal. Today, MBC cannot be cured, and time and quality of life are key factors in any decision. The additional prospect of considering clinical trials in the continuum of care adds levels of complexity, which often appear as barriers.

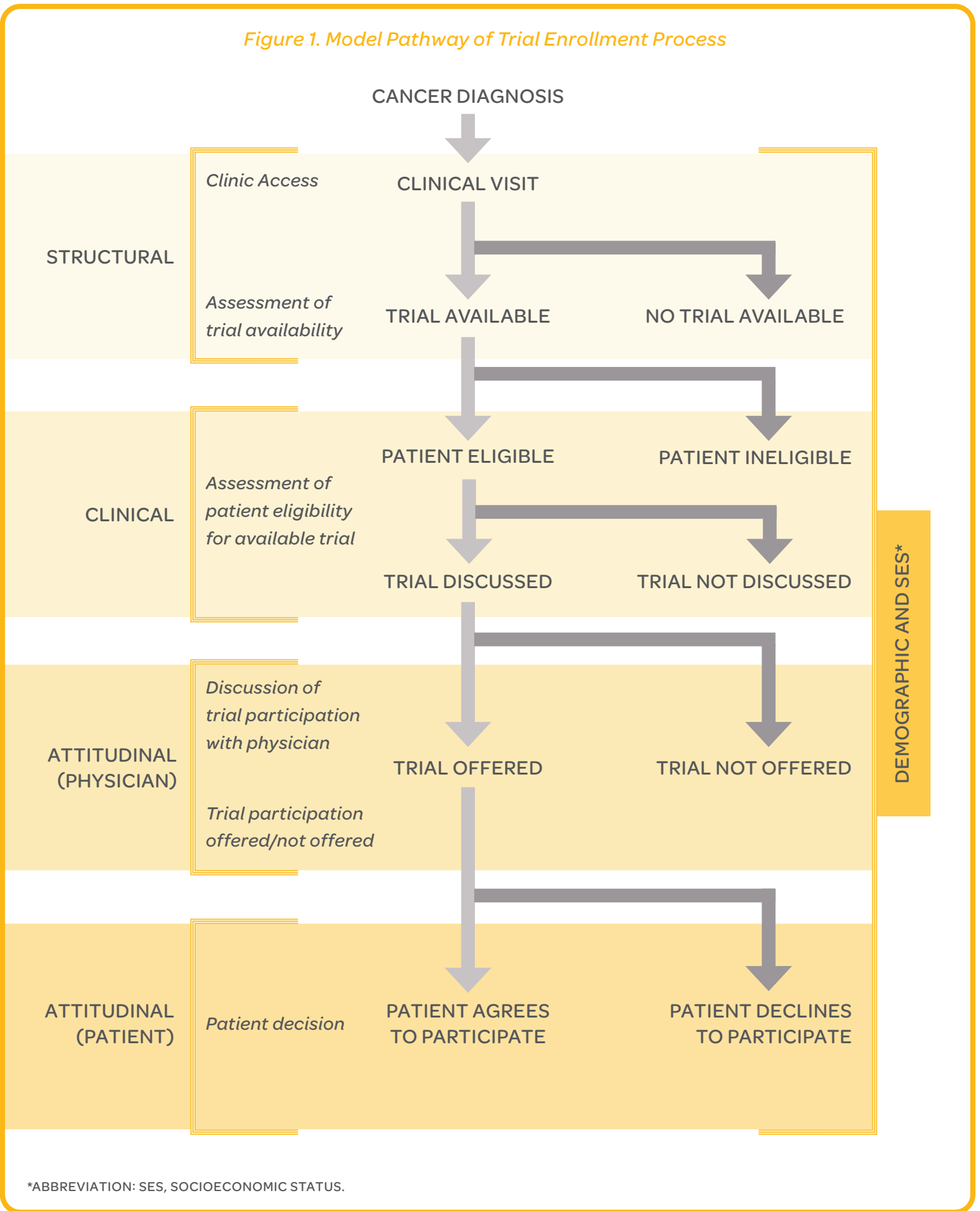
As a guide to understanding the decision-making process we discuss in this report, we included a simplified flow diagram (Figure 1) from an article by Unger et al. (2018) indicating the pathways an MBC patient travels to consider and eventually enroll in a trial.<sup>6</sup>

The Unger study assessed 13 studies spanning 15 years that involved over 8,800 patients. The researchers determined that 56% of patients did not

***If you ask any trialist, “What do you think barriers to participation are?” You don’t say “patient barriers.” They always think about barriers from a patient deficit perspective, where the patient situation makes it hard to participate: the patient can’t do this, the patient can’t do that. People will participate if they have the opportunity, if they have the resources, and if it’s made easier for them to participate. Another way of thinking about this is “What can we, as an institution, do to ease that burden of participating in this trial for that person and their family, and how can we design the trials so that there are fewer blood draws or that the number of times the patient needs to come in makes it easier?” We can’t just blame the patient when it is a system barrier of our own design.***

Lynne Nguyen,  
Director, Population and Community  
Core, Center for Community-Engaged  
Translational Research, MD Anderson  
Cancer Center

Figure 1. Model Pathway of Trial Enrollment Process



Source: Unger, J. M., Vaidya, R., Hershman, D. L., Minasian, L. M., & Fleury, M. E. (2019). Systematic Review and Meta-Analysis of the Magnitude of Structural, Clinical, and Physician and Patient Barriers to Cancer Clinical Trial Participation. *JNCI: Journal of the National Cancer Institute*, 111(3), 245-255

have a trial available at the institution where they were being treated, and nearly 22% were deemed ineligible for an available trial. Unger et al. concluded that combined structural and clinical factors are the main reasons why most cancer patients do not participate in trials.<sup>6</sup>

This model has been the basis for examining barriers to clinical trial participation in multiple studies,<sup>1,4-6</sup> and it categorizes the barriers to trial participation as structural (i.e., the lack of an available trial), clinical (i.e., patient not meeting inclusion/exclusion eligibility criteria), attitudinal (i.e., concerns of either the patient or physician), and demographic and socio-economic. For MBC patients, continual changes and shifts among these barriers may occur over time and as the disease progresses. Critically, the patient's decision making occurs at the end of the flow chart. Common thinking is that the barriers to clinical trial participation center around the patient, but this oversimplifies the issues and may detract attention from the root causes of the barriers.

### 1.1.B WHY DISPARITIES MATTER IN CLINICAL TRIALS

The Institute of Medicine has highlighted the need for increased participation in cancer clinical trials, a number that continues to be quite low for all cancer patients, and also addressed patient barriers to trials.<sup>1</sup> However, this is just an average, and the availability of trials is one of the barriers to enrollment that continues to contribute to disparities in care in general. The overall rate of participation in trials varies greatly based on the type of cancer center and the type of trials available. Across all cancers in the U.S., patient participation in National Cancer Institute (NCI) trials averages 3-5%, whereas participation at academic medical centers, including NCI-designated centers, averages 14.8%, and participation in community cancer centers, where nearly 85% of patients are treated, is about 6.3%.<sup>2</sup>

For MBC patients, availability of appropriate and early phase trials is likely another barrier to enrollment, especially because not all cancer centers offer Phase I and Phase II trials. Additional barriers to enrollment resulting in disparities in clinical trial participation include lack of patient and/or provider knowledge about clinical trials, general lack of health literacy, complexity of the eligibility requirements, expenses involved in participation, and difficulty with travel to trial sites. However, over 50% of eligible patients who are asked to enroll in cancer trials elect to participate.<sup>3</sup> Those who are asked and decide not to enter trials may cite concerns about use of placebos, concerns about randomization, fear of side effects, trust issues, and financial and logistical concerns.

Enrollment in a cancer clinical trial is a multi-stage process. Generally, participation and barriers to participation may be patient-related and family decisions. However, policy, provider, and institutional issues are also key to patient enrollment, and may play a much larger role in barriers to participation than is recognized. A 2018 study by the American Cancer Society Cancer Action Network (ACS CAN) entitled "**Barriers to Enrollment in Therapeutic Clinical Trials for Cancer: A Landscape Report**" analyzed studies across a variety of settings and found that:

- 56% of patients do not have a local trial available for their cancer
- 17% are ineligible for a trial due to exclusion criteria
- Many eligible patients are not asked by their provider to enroll
- Only 27% of cancer patients have the option to enroll in a local clinical trial

Research indicates that patients with higher socio-economic status enroll more frequently in cancer clinical trials than those with lower socio-economic status. Some patients have financial resources that enable them to bear the personal cost of enrollment in trials. In addition, more highly educated patients may better understand the potential benefits of the trial and the impact of research advances. Alternatively, elderly, uninsured, and minority patients, who may have more limited financial resources and access to information, are underrepresented in cancer clinical trials. Rural patients experience significant disparities in access to care.<sup>1-5</sup> A study by Unger et al.<sup>6</sup> indicated that rural MBC patients made up only about 20% of trial participants compared to those living in urban areas. These disparities have ethical implications in terms of which individuals have opportunities to participate in trials and also greatly decrease the generalizability of trial results by excluding some racial, ethnic, and demographic subgroups.

### **1.1.C MOLECULAR DIFFERENCES AND DISPARITIES**

For all breast cancer patients, and perhaps most importantly for MBC patients, disparities in care are partially explained by differential access to care through the quality of screening and healthcare resources, including accuracy at stage of diagnosis, and receipt of guideline-adherent treatment. Biological differences in breast cancer, especially between Black and white women, may be an underlying cause of disparities in outcomes, particularly in mortality rates, as Black women are more likely to be diagnosed with aggressive, hormone receptor (HR)-negative subtypes.<sup>7-11</sup>

Ongoing advances in molecular epidemiology provide evidence for racial differences in the aggressiveness and survival of breast cancer by receptor subtype. When classified according to the presence or absence of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2), patients diagnosed with the receptor-negative subtypes (ER-, PR-, and/or HER2-) experience the lowest survival rates compared with patients diagnosed with HR-positive (ER+, PR+) and/or HER2+ subtypes. Furthermore, the association between socio-economic status and breast cancer incidence and survival varies by HR subtype, with consistent associations in HR+ subtypes but not HR- subtypes.<sup>9,10</sup> Although the results of studies examining racial and socio-economic disparities in breast cancer mortality are somewhat inconsistent overall, the poor availability of healthcare resources clearly complicates MBC patient outcomes, especially for patients with the fast-growing and aggressive HR- subtypes, who are more likely to be Black women.<sup>7-14</sup>

### 1.1.D FINANCIAL TOXICITY AND DISPARITIES IN MBC PATIENTS

Financial distress as a result of disease or treatment options may be considered analogous to physical toxicity. “Financial toxicity” is emerging as a relevant variable in guiding cancer management decisions for both patients and physicians. Understanding how and among whom to best measure financial distress is critical to the design of future clinical studies for MBC patients, who are likely to have had multiple lines of treatment and participated in one or more studies. With the passage of the Affordable Care Act, the number of insured patients has increased, but overall cancer patients pay more out-of-pocket costs for trials due to increased cost sharing.<sup>15-20</sup>

In response to financial burdens imposed by care costs or participation in trials, patients may reduce spending on food and clothing, sell possessions or property, and decide not to adhere to aspects of their treatment plans. A 2018 survey of 1,513 MBC patients conducted by Wheeler et al. in collaboration with the Metastatic Breast Cancer Network (MBCN) found that one-third of patients were uninsured.<sup>17,21</sup> The uninsured in this study were more likely to identify as a racial or ethnic minority, have lower incomes, and stop working full-time. Compared to survey participants who were insured, the uninsured more frequently reported refusing or delaying treatment because of cost concerns. Compared to insured participants, the uninsured MBCN study participants more frequently reported not being able to meet monthly expenses, not being satisfied with their financial status, and not being “in control” of their financial situations.

The added costs of clinical trial enrollment can exacerbate the financial burden experienced by cancer patients, yet the existing scientific literature rarely addresses the financial aspects of clinical trial participation. Generally, in the research on developing clinical trials, cost discussions focus only on the costs to the trial sponsors and trial sites. Researchers, clinical sites, and contract research organizations (CROs) tasked with managing the studies rarely assess the financial burden to patients of their studies.

In January 2018, the FDA updated its [guidance](#) to institutional review boards (IRBs) and clinical

***Most people don't realize the personal and financial costs of living with metastatic breast cancer. It may be that we are living longer, but there are costs involved, and if you are under 65, the financial support is limited.***

***With regard to trials, I have never been offered one. In 2001, a year after breast reduction, I did not qualify as I did not have clean margins. I have always considered trials [a] “Hail Mary” option, as in, when all else fails...nothing will cure me, [and] every option I have tried has debilitated me to some extent. I am more open to trials these days, preferably more established ones over 1st stages. Especially ones that focus on improving a patient's quality of life.***

**Ann D.  
MBC patient since 2001\***

investigators to clearly allow reimbursements for lodging and travel to patients in clinical trials. Although paying patients for participation in clinical research may raise difficult questions that should be addressed by an IRB, reimbursements for travel expenses to and from trial sites do not raise concerns about undue influence, according to the agency's Office of Good Clinical Practice. The new FDA guidance explicitly defines the difference between compensation and reimbursement and is based on both advocacy inputs and published research.<sup>22-25</sup>

*In contrast to payment for participation, FDA does not consider reimbursement for travel expenses to and from the clinical trial site and associated costs such as airfare, parking, and lodging to raise issues regarding undue influence.*

*Other than reimbursement for reasonable travel and lodging expenses, IRBs should be sensitive to whether other aspects of proposed payment for participation could present an undue influence, thus interfering with the potential subject's ability to give voluntary informed consent. Payment for participation in research should be **just and fair**. The amount and schedule of all payments should be presented to the IRB at the time of initial review.<sup>26</sup> (The FDA Language letter guidance can be found [here](#).)*

When examining a protocol or clinical study design, IRBs separately consider reimbursement and payment. Based on the concepts of justice and equitable study participant selection, it is not appropriate for patients to pay out-of-pocket expenses to participate in research. Nevertheless, many cancer study protocols submitted to IRBs fail to include reimbursement for patients' out-of-pocket expenses, either in general or based on patient need. This may be an area for advocacy action and is highlighted in the [ASCO recommendations](#)<sup>27</sup> for reducing the financial burdens for patients considering clinical trials:

***“Recommendation 1:** Improve payer clinical trial coverage policies. Clinical trial cost payment policies should be revised so that they are made consistent, streamlined, and transparent to all stakeholders.”*

This includes recommending that the Centers for Medicare and Medicaid Services (CMS) revise the requirement that Medicare Advantage beneficiaries revert to fee-for-service while enrolled in a clinical trial and use its Innovation Center to explore how alternate payment models support increased participation in clinical trials.

***“Recommendation 2:** During the clinical trials development and enrollment process, provide patients with clear, transparent information about potential trial-related out-of-pocket costs, and include mechanisms to support patient financial/health literacy.”*

This policy statement recommends that trial sponsors conduct a trial-specific coverage analysis

that estimates all costs, including patient out-of-pocket and potentially covered costs, as coverage varies greatly among individuals. In addition, ASCO recommends that research sites consider offering financial counseling and suggests that trial designs avoid additional costs that are not necessary for the scientific objectives or for patient safety. Examples are low-value trial-specific visits to the clinic or CT/MRI or other scans, among other costs.

*“Recommendation 3: Remove impediments to ethically appropriate financial compensation for trial-related out-of-pocket costs. Provision of such financial support should not be considered ‘undue inducement.’”*

Despite the FDA guidance, pharmaceutical and biotech firms, CROs, and clinics often have misplaced concerns over financially supporting the out-of-pocket costs of clinical study participants. The FDA statement is intended to dispel the assumption that paying these costs would exert an influence over lower-income patients, pointing out that these reimbursements are tied solely to the clinical trial costs and do not add to the patient’s overall income. Rather, this type of reimbursement support may help patients and their families make independent decisions about their care that includes options previously unavailable to them.

*“Recommendation 4: Incentivize research that will better characterize patient costs incurred for participating in cancer clinical trials and support the longer-term development of tools to identify and mitigate the risk of trial-associated financial hardship.”*

Tools for assessing patient-reported outcomes are increasingly used in studies. They usually consider

***“You have to find the clinical trials for yourself—it is not easy. You have to be somewhat educated to even read the first sentence of the trial name to know if it applies to you. I live 4 hours from a cancer center, and the chance of finding a trial that matches to me is so very low—almost nil.***

***One of the barriers is for oncologists to recommend clinical trials to patients who they know can’t afford to get there and can’t afford to do it. Why give them the hope of something like a clinical trial that may help while knowing that there’s no way that they could make it happen?***

***Then there are the costs...that’s the big unknown. Patients are the only ones who aren’t getting paid any money. The doctors, the researchers, the techs who do your scans—everybody gets paid. The guy who valet parks your car or doesn’t valet park your car— you still pay for parking.***

***[Clinical trials] cost us time, money, and our bodies. People give their bodies, and we’re the only ones who don’t get any money or reimbursement for our time and our expenses. Even though the FDA says they can reimburse us, when you ask, they just say ‘No, we can’t do that.’ Something has to change so they can both pay us for our time and effort, and reimburse our expenses.”***

April Knowles - Metastatic Breast Cancer Patient Advocate and Rural Resident



symptom assessment and quality of life but may also include questions about patients' financial needs. The European Organization for the Research and Treatment of Cancer QOL Questionnaire C30 ([EORTC QLQ C30](#)) is a frequently used and validated instrument. It contains just one question about patient financial distress. Thus, although tools exist to monitor financial impacts and out-of-pocket costs associated with clinical trial participation, data on their use in general, and for MBC patients in particular, are limited.

Current published research studies lack information about the financial burden on clinical trial patients. Most charitable programs focus on pediatric patients enrolled in clinical trials. The National Institutes of Health offers a program through its foundation to provide financial support to adult patients for travel, meals, and lodging for trial participation, but only to those patients in treatment at NIH hospitals in Washington, DC. Many local and regional cancer centers have patient assistance programs, again often through nonprofit organizations, that may be available through social workers and navigators at the centers.

### *The Lazarex Foundation*

***The Lazarex Cancer Foundation, a national nonprofit organization, focuses on supporting patient access to clinical trials. In 2014, Lazarex partnered with Massachusetts General Hospital (MGH) to create a Cancer Care Equity Program, now known as IMPACT- Improving Access to Cancer Clinical Trials, to study the financial impact of clinical trial participation and to provide financial assistance for trial-related expenses. The 112 clinical trial participants in the program represented more than 10% of all cancer trial participants at MGH at that time: 71% were older than 50 years, 64% were women, 14% were racial or ethnic minorities, 5% did not speak English, 9% reported an annual income less than \$35,000 per year, and 64% lived out of state.***

***Most participants were enrolled in Phase I studies. On average, patients in the program spent more than \$600 per month for the additional costs of travel and lodging when enrolled in clinical trials at MGH. Those living in Massachusetts spent more than \$200 per month; those living in the New England region spent \$300 per month; and out-of-region patients spent more than \$900 per month.<sup>27</sup> In 2017, the results of Lazarex's 3-year study with MGH resulted in a 29% increase in overall participation and doubled minority participation.***

***Today, Lazarex has relationships with 47 of 50 NCI designated Comprehensive Cancer Centers, 6 of 12 NCI designated Cancer Centers, and 140 other cancer centers, for a total of 193 clinical trial sites. At the end of 2017, Lazarex had served over 3,000 cancer patients at those sites. Lazarex is spearheading a 3-year proof-of-concept plan to sustainably address financial gaps in cancer care through IMPACT. The IMPACT program facilitates a coordinated effort among academia, industry policy-makers, and cancer centers to create a replicable, boots-on-the-ground action plan. IMPACT is focused on bringing significant and sustainable change to the status quo of clinical trial recruitment, retention, minority participation, completion, and translational science.<sup>27</sup>***

## 1.2 RECENT MBC EPIDEMIOLOGY AND STATISTICS ON INCIDENCE, PREVALENCE, AND MORTALITY

### 1.2.A MBC EMERGING TRENDS AND RECENT EPIDEMIOLOGY

MBC, also known as advanced breast cancer, encompasses any breast cancer that has spread beyond the breast or nearby lymph nodes to a distant part of the body, such as the bones, liver, lungs, or brain. MBC includes metastases found at first diagnosis, called *de novo*, as well as recurrent cancers that are discovered months, years, or decades after a patient has been declared cancer-free after treatment following an earlier stage diagnosis. These cancers are considered stage IV, but only *de novo* diagnoses are captured in U.S. federal databases with this staging category.

Until 2017, neither the number of people living with MBC nor the incidence (the number diagnosed each year) was known. The mortality rate, or the number who die each year, was captured through death records, although not all death records capture cause of death. The landmark study [Estimation of the Number of Women Living With Metastatic Breast Cancer in the United States by Mariotto et al. \(2017\)](#)<sup>28</sup> was first published online by the American Association for Cancer Research. The MBCA was one of the study's sponsors, along with the Division of Cancer Control of the NIH, the NCI, and the Fred Hutchinson Cancer Center in Seattle, Washington.

Approximately 3.5 million people are living with a history of breast cancer in the U.S. In 2020, an estimated 279,100 new cases of invasive breast cancer will be diagnosed in women, and 2,620 cases will be diagnosed in men. Approximately 42,690 people (women and men) will die from breast cancer in 2020.<sup>29</sup> Based on the most recent data, the 5-, 10-, and 15-year survival rates for women diagnosed with breast cancer are 91%, 86%, and 80%, respectively. The incidence and stage of diagnosis for breast cancer are available from many sources including the American Cancer Society's annual [Facts and Figures](#)<sup>29</sup> and the [NCI's Surveillance, Epidemiology and End Results \(SEER\)](#) Program.<sup>30</sup> Although SEER and individual state registries could be used to estimate the numbers of women initially diagnosed with *de novo* MBC, the numbers of those diagnosed with early-stage breast cancer who experienced a distant or metastatic recurrence are not routinely collected. This information continues to not be collected by most SEER state contributors.<sup>31</sup>

## Metastatic Breast Cancer Prevalence

**Figure 2:**

Estimates and projections of MBC prevalence in the United States from 1990 to 2020 (yellow bars). Observes number breast cancer (BC) deaths (dashed line) as used as input in the back-calculation model and estimated number of new cases with new cases with *de novo* and recurrent MBC (solid line).

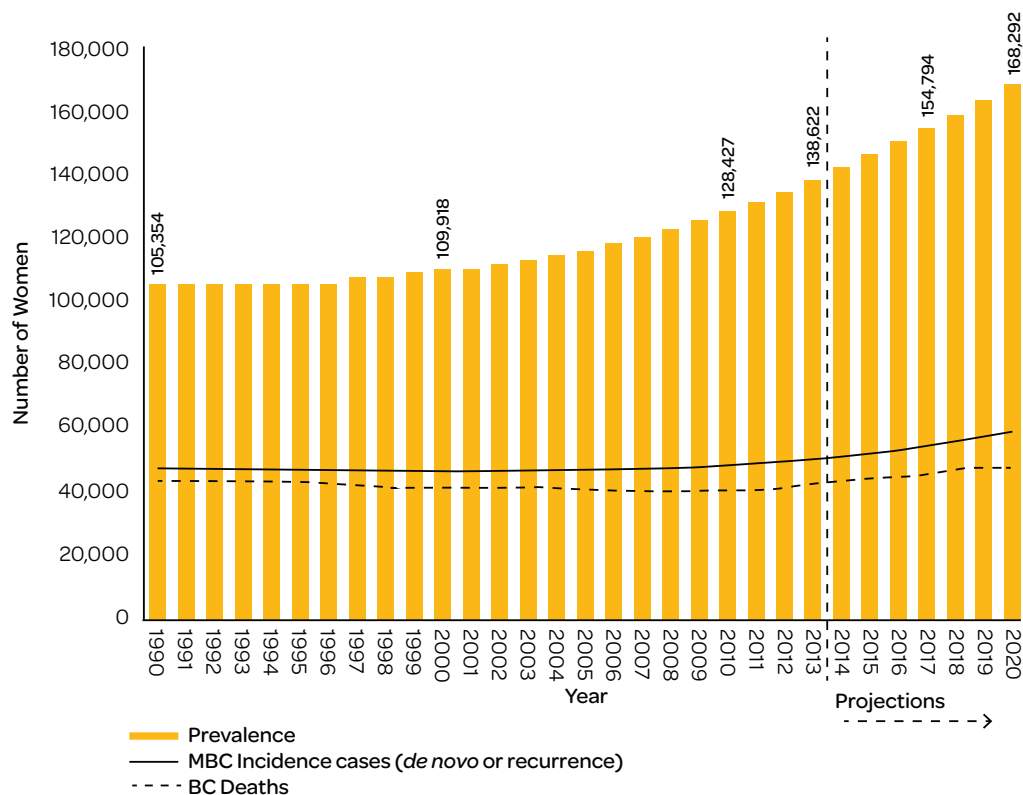
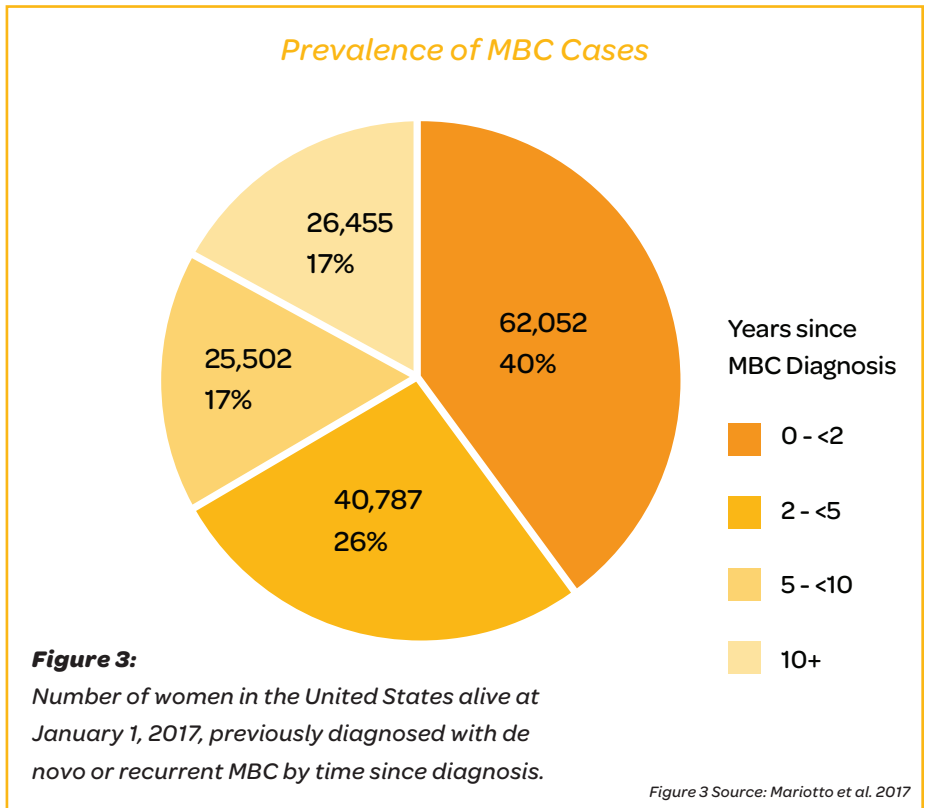


Figure 2 Source: Mariotto et al. 2017

To determine the full range of epidemiological data on MBC (incidence, prevalence, and mortality) as well as to develop a predictive model, Mariotto et al. utilized new calculation methods using data from SEER to estimate both the numbers of women diagnosed with *de novo* MBC, as well as those diagnosed with recurrent MBC.<sup>28,31,32</sup> In 2017, the estimated number of women living with MBC, both those diagnosed as *de novo* and recurrent, was 154,794, and the model estimated that by 2020, 168,292 women will be living with MBC (Figure 2).<sup>28</sup>

The results of this study show that large numbers of women in the U.S. are living with MBC. The number is increasing, most likely as a result of improved treatments but also because of the aging of the U.S. population (See Figure 3). Historically, a diagnosis of either *de novo* or recurrent MBC meant the patient would likely die within a few years. With optimal care and new treatments resulting from clinical trials, some people living with MBC can, and do, live for a number of years with a reasonable quality of life. Analysis of the SEER data in Mariotto et al. further revealed that 20% of breast cancer deaths in a given year originate from women diagnosed with *de novo* MBC, whereas 80% are deaths from women with recurrent MBC.<sup>28</sup> These results demonstrate the strong unmet need for new treatments and trials. Despite the overall poor prognosis of people living with MBC, a small, but still meaningful, percentage (11%) of those women diagnosed from 2000-2004 under age 64 survived 10 or more years.<sup>28</sup> However, researchers still have much to learn about MBC and the specific needs of those living with it.

The study also suggests that cancer registries are critical for collecting information and data on the experiences of MBC patients across the life course to enable patients, researchers, and epidemiologists to better understand the impact of MBC.



## 1.2.B A MORE RECENT STUDY ON MBC EPIDEMIOLOGY

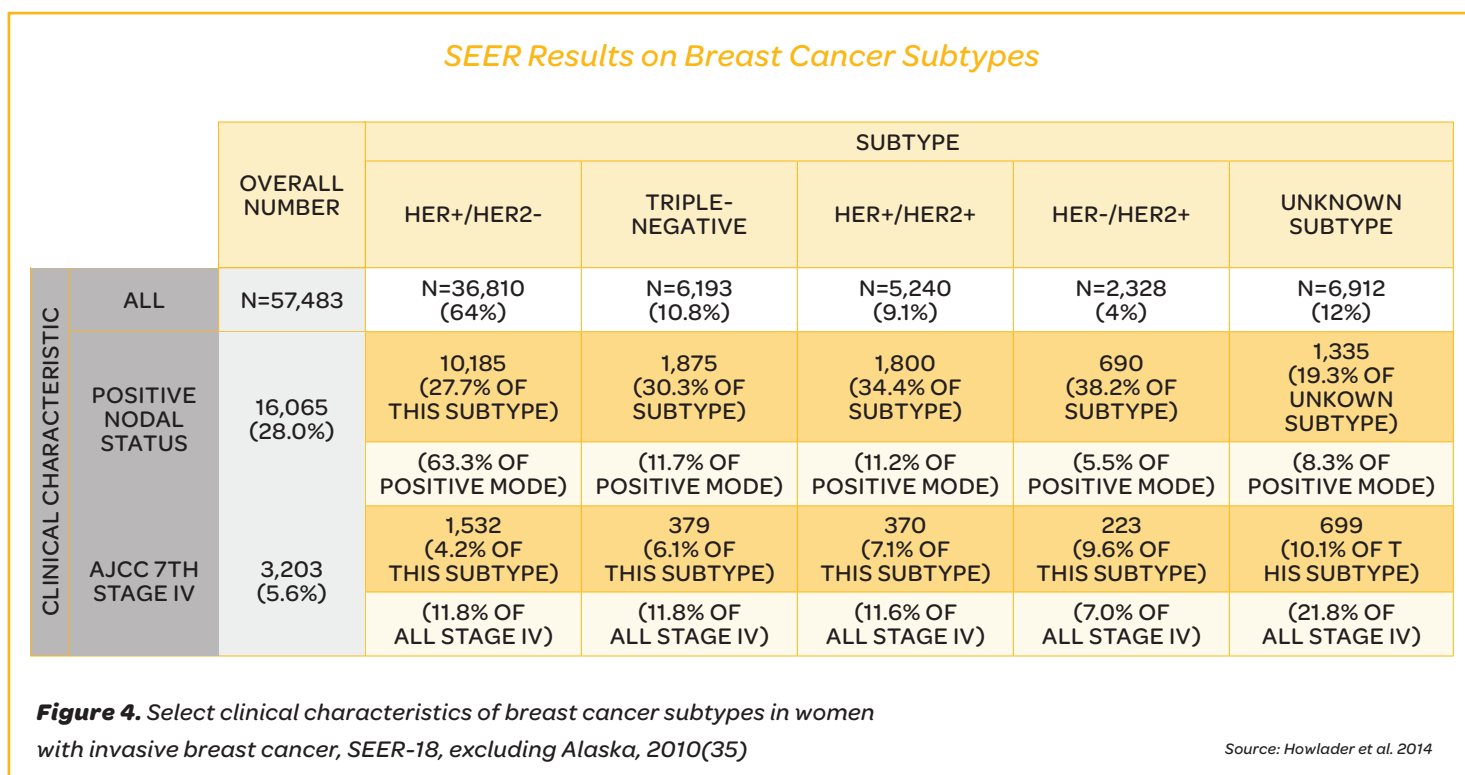
**Examination of a paradox: recurrent metastatic breast cancer incidence decline without improved distant disease survival: 1990–2011** by Malmgren et al. (2019),<sup>32</sup> which appeared in *Breast Cancer Research and Treatment* in September 2019, studied 8,292 women with stage I-III invasive breast cancer, 964 of whom (11.6%) were later diagnosed with recurrent MBC. The authors found a significant decline in recurrent MBC over time but no increase in survival. Survival after a recurrent MBC diagnosis decreased over time, from 23% in the years between 1990 and 1998, to 21% between 1999 and 2004, and to 13% between 2005 and 2011.<sup>32</sup>

## 1.2.C WHY DO THESE STATISTICS MATTER TO MBC PATIENTS AND ADVOCATES?

To effectively support MBC policies, patients and patient advocates need evidence-based data to inform their public communications about MBC prevalence and mortality. These epidemiology studies support effective advocacy informed by data, rather than tradition or speculation. For early stage drug developers, understanding current MBC statistics is vital to estimate important parameters and to answer the questions that matter most to patients and their families. For example, do drugs in development extend life or potentially offer cures? What is their impact on the cost of care? What is their impact on patient quality of life?

Today, few research studies in MBC address these questions, and studies of population data collections, such as statewide registries that feed into SEER, are lacking in collection of important data about recurrent MBC patients, both male and female. Most state registries collect only newly

diagnosed incident data, initial treatment, and mortality. In 2018, SEER entered into a number of pilot studies to begin collecting more information than cancer subtype and grade to include data on genetics, biomarkers, and recurrences, as well as information on oral therapies.<sup>31</sup> Figure 4 shows SEER results with additional information on breast cancer subtypes from a study by Howlader et al. (2014). The findings, which draw from data on HER2 status that SEER began collecting in 2010, suggests the potential for richer data sets to inform key research questions<sup>33</sup>



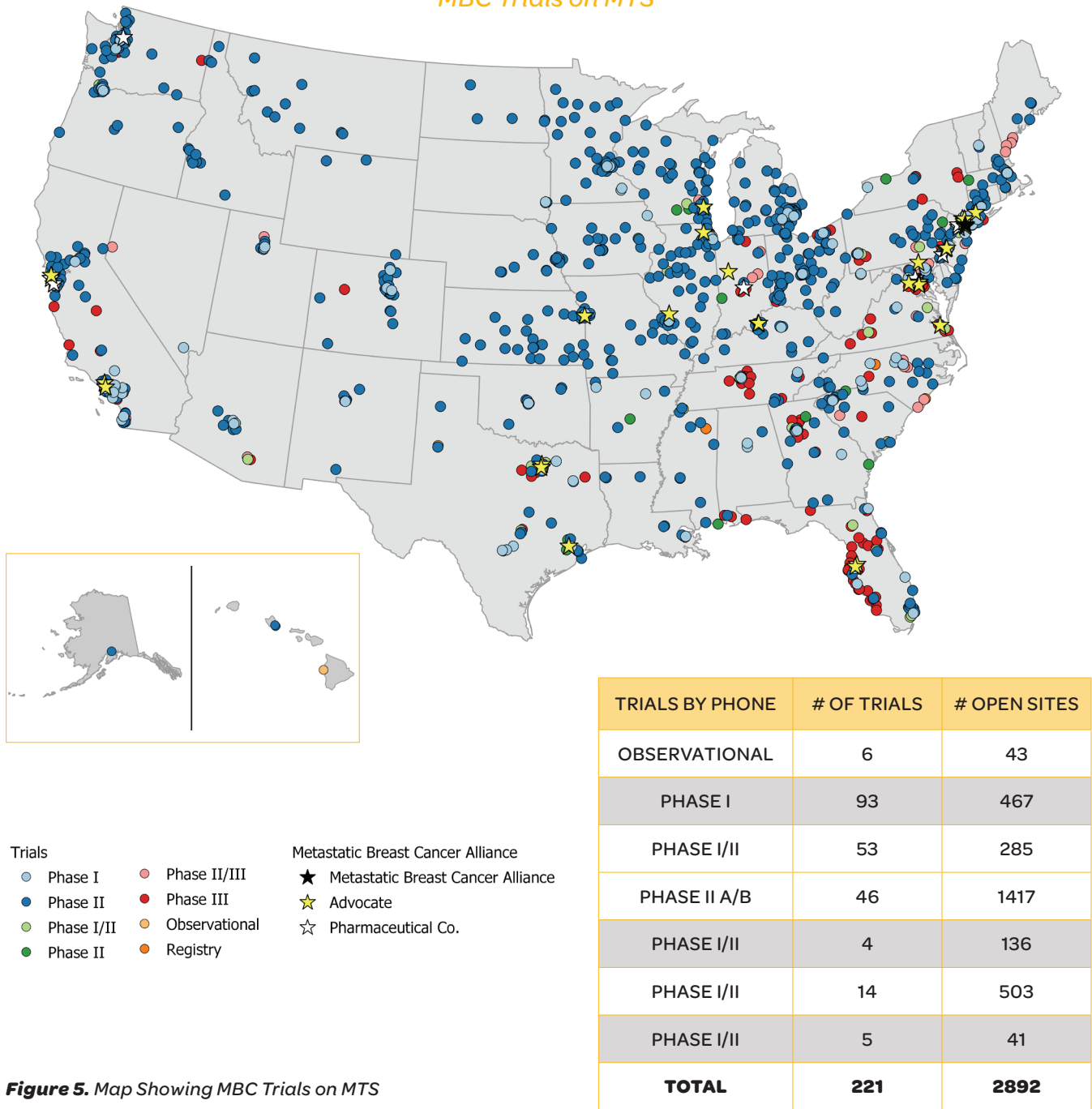
## 1.2.D AVAILABILITY OF CLINICAL TRIALS FOR MBC

In 2018, the **Pharmaceutical Research and Manufacturers of America** (PhRMA) reported that over 1,100 medicines and vaccines (or other immunotherapies) were in clinical testing for the treatment of cancer, including at least 108 specific to breast cancer.<sup>34</sup>

The number of clinical trials changes regularly as new drugs are advanced; existing standard of care (SOC) drugs are tested in combination with new, not yet approved, agents; and unsuccessful drugs are removed from the development pipeline. A February 2018 search of Clinicaltrials.gov identified 1,638 registered trials recruiting for drug interventions for breast cancer. Of these, only 236 are indicated for metastatic or recurrent breast cancer.

Groups that report on metastatic clinical trials assess these trials differently. For example, up to 1,459 open, but not yet accruing, trials that include MBC could be included in combination trials, and various Phase I or Phase I/II trials that are solid tumor trials or basket trials according to

### MBC Trials on MTS



**Figure 5.** Map Showing MBC Trials on MTS as of November 2018

Source: Data pulled from BreastCancerTrials.org in February 2018; map designed by author.

research (unpublished) by [The Storm Riders Network](#) could be included. As shown in Figure 5, a search of [BreastCancerTrials.org](#) for “Metastatic Breast Cancer Trials” in February 2018 revealed a total of 221 trials open to MBC patients. Importantly, 91% of the interventional or treatment trials (n = 210) are Phase I, I/II, or II, indicating an early phase of research for most MBC therapies. The map shows many areas of the U.S. where few MBC trials are available, especially in the northern and southwestern states where patients living in rural and small communities would need to travel great distances to participate in trials.

Because trials open and close on a daily basis and many combination trials may not be well labeled by the sponsor, determining exactly how many interventions and trials are available to MBC patients at any one time is challenging. For patients and their families, the value of clinical trial matching services is that they allow narrowing of the search function to trials that have the characteristics important to them. The number of interventions and trials in MBC is expanding, but the expected impact on cure, quality of life, and mortality remains unknown. Innovations like immunotherapies and combination therapies continue to emerge, but the most critical need remains finding people with MBC to participate in trials to accelerate the rate of drug development and make progress in research to end MBC.

***“If I could change anything that is fundamental to research, it would be the hope that more patients participate in clinical trials and that more funding comes along to further new research.”***

**James P. Allison, PhD Nobel Prize Laureate - 2018 Nobel Prize in Physiology or Medicine**

## **1.3 WHAT'S NEW: NEW TRIAL TYPES, EMERGING NEW AGENTS IN TRIALS, AND DIAGNOSTICS**

A variety of developments in the structure and administration of clinical trials, as well as in the medical treatment of people with MBC, influence the direction of the MBCA's advocacy supporting patient access to clinical trials. In this section, we review several core recent developments of importance to patients and advocates.

### **1.3.A PRECISION MEDICINE AND NEW TRIAL DESIGNS AND DIAGNOSTIC METHODS**

As treatments for breast cancer become more complex, the challenges of enrollment in clinical trials become more complex and personalized as well. Today, a variety of approaches are under development, such as treatment with immunotherapy, methods to measure treatment criteria and effects with biomarker tests and liquid biopsy, and novel clinical trial designs such as basket and umbrella trials. The complexities and the rapid pace of precision medicine demand that member organizations of the Alliance work collaboratively to drive progress forward.

### 1.3.B PRECISION MEDICINE

Until recently, most cancer therapies were considered empiric; in many cases, that approach to therapy remains in effect today. Empiric therapy or empirical therapy is medical treatment or therapy based on experience and, more specifically, therapy begun based on a clinical “educated guess” in the absence of complete or perfect information. Physicians give patients the FDA-approved standard of care (SOC) treatment that seems to work best for most patients with that type of cancer. If that treatment fails to work, or if the side effects are too extreme, other alternatives are tried. Metastatic patients commonly experience a progression and go through multiple rounds of empiric therapies.

Today, evidence-based decision-making, in which scientific methodology and the associated results rather than tradition or “guessing” drive treatment selection, is becoming the gold standard. Precision medicine begins with testing and analysis of the individual patient and his or her tumor or system to provide evidence to suggest which treatment may be optimal for that patient. Testing may occur through a biopsy of the tumor or testing for other drug-specific biomarkers.

The MBCA provides patient and advocate information on precision medicine through [The Right Track Organizational Framework](#) that teaches newly diagnosed patients with MBC, and those with progression, how to access the right healthcare team, the right tests, and the right treatments to achieve the best possible outcomes, while sharing their data to inform research. The Research Advocacy Network offers a free self-study course in [Precision Medicine](#) that may be of interest to both patients and advocates.

***Biomarkers in Precision Clinical Trials:*** A number of emerging types of precision medicine may be considered for MBC patients, many of which are targeted therapies, which hone in on a particular gene or protein, set of genes or proteins, or pathway specific to a patient type.

In precision medicine clinical trials, biomarkers are often used in multiple ways:

**(1) Risk assessment:** To help a person determine how likely he or she is to develop breast cancer. For example, *BRCA1* and *BRCA2* tests can be used for assessing breast and ovarian cancer risk; **(2) Prognostic:** To forecast the aggressiveness of the metastatic disease process or how a patient can expect to fare in the absence of therapy, or both; **(3) Predictive:** To help identify which patients will respond to which drugs. For example, epidermal growth factor receptor (EGFR) mutations may be used as a predictive biomarker when evaluating MBC patients with brain metastases to select patients for anti-EGFR drug therapy; and **(4) Monitoring:** To determine how a patient is doing over time, either on or off therapy. For example, some researchers are evaluating the identification of circulating miRNA specific to MBC as an opportunity for early disease identification and for monitoring disease burden. Other new biomarkers may be used as exploratory tools during the course of the trial to determine to what extent the new agent is effective.



**Genomics in Precision Medicine and Clinical Trials:** Researchers in clinical trials are more frequently exploring genomics through the study of tumor samples, from either fresh or frozen biopsies or stored tumor samples. In the past, researchers focused on single genes because they lacked the technology and methods to study how multiple genes interact. The new and more affordable technology for sequencing DNA supports genomic research. The term *oncogenomics* refers to the study of genes within cancer. The term genetics refers more broadly to the science dealing with heredity and variation of single genes, whereas the term genomics typically refers to multiple interacting genes, often those found in tumor samples. The Research Advocacy Network offers an excellent tutorial on [Genomics in Cancer](#) for advocates and patients.

### 1.3.C INNOVATIONS IN CLINICAL TRIAL DESIGNS

Clinical trials are performed as a series of phases. Learn more about clinical trials and clinical trial phases [here](#).

**Crossover in Trials:** The use of crossover as a design feature of randomized trials is becoming more common. Reports indicate that up to 22% of all randomized controlled trials utilize this feature.<sup>35</sup> In cancer medicine, crossover typically refers to unidirectional crossover at the time of progression, meaning patients assigned to a placebo group are offered access to the investigational agent, but not vice versa (bidirectional). Crossover in cancer trials is typically specified by the protocol, because all cancer trials have to include SOC drugs and may, when randomized, include a new drug + SOC as well as placebo + SOC. The decision on crossover in the design occurs before any action is taken by the monitoring committee. A trial may allow patients to cross over to the active drug after un-blinding, and this use of crossover is a prerequisite to ethical trial design.<sup>35</sup>

**Basket Trials:** A more recent change in oncology clinical trials is the development of what is known as a basket study. These trials include patients with a certain somatic mutation (a mutation acquired by the tumor cells) in common, regardless of the site of origin of cancer in the body. For example, patients in a basket study may all have the same *TRK* somatic mutation but have primary cancer at a variety of sites, such as lung, breast, prostate, etc. Basket studies are sometimes referred to as bucket studies and have also been described as tissue agnostic or pan-tumor studies. Basket trials can be relatively simple in design to include specific treatment arms or “baskets” for cancers of different origins or locations. The design can also become more complex with the baskets including more than one somatic mutation across multiple cancer locations, or designed to evaluate multiple drugs across a selected number of somatic mutations and cancer locations.

***Umbrella Trials:*** An umbrella trial may investigate one or a combination of different targeted cancer agents in the same trial within independent groups or cohorts of patients. The patient groups and disease types are often defined by biomarkers or specific molecular signals or alterations that could predict sensitivity to the cancer agent or combination of agents under investigation in the study. In breast cancer, four subtypes (luminal A, luminal B, HER2, and basal-like) are confirmed and can be used to group patients in umbrella trials. Umbrella trials allow researchers to develop study designs that target individual subtypes within one type of cancer simultaneously. For example, a study might look at all four subtypes, but each group or arm in the umbrella study might be given a different therapy or combination of therapies.<sup>31,35,36</sup>

***Adaptive Study Trial Design:*** An adaptive design allows modifications to the trial or statistical procedures of the trial, or both, after its initiation without undermining its validity and integrity. The purpose is to make clinical trials more flexible, efficient, and fast. For breast cancer researchers and advocates, the most well-known example of an adaptive trial design is the I-SPY trial.<sup>37</sup> A major advantage for I-SPY 2 is the sophisticated informatics system that addresses the need to integrate and interpret enormous amounts of complex and disparate data (genomics, proteomics, pathology, and imaging) from many investigators. This allows researchers real-time access to study data and enables the adaptive elements of the trial, which include introducing new agents. The I-SPY 2 trial, performed in the neoadjuvant setting, focuses on women with high-risk, locally advanced breast cancer identified at a stage when a cure is considered possible. The adaptive design approach is an important and innovative model to rapidly assess novel Phase II drugs and identify effective drugs and drug combinations that can help determine which breast cancer subtypes will be most responsive. Unique to adaptive trial design is rapid learning as the trial proceeds, and the use of information from each patient may potentially inform subsequent treatment assignments. What makes the I-SPY trials truly transformative in breast cancer research is the use of adaptive trial design, including existing and developing biomarker candidates and test drugs and the potential to learn what works within months rather than years.<sup>38</sup>

### 1.3.D TYPES OF TARGETED THERAPIES IN MBC TRIALS

In addition to chemotherapy for MBC, newer, more effective treatments can attack specific breast cancer cells without harming normal cells. Targeted therapy drugs selectively impact molecules in cancer cells that help drive the cancer and are thus designed to dampen an improper or over-active molecule or cellular process in the cancer cell. Currently, these targeted methods are commonly used in combination with traditional chemotherapy, and new targeted therapies are among those being tested in trials. In general, targeted drugs have less severe side effects than standard chemotherapy drugs.

Breast cancer targeted therapy uses drugs that block the growth of breast cancer cells in specific ways. Targeted therapy may block the action of an abnormal protein (such as HER2) that stimulates the growth of breast cancer cells.

Several types of existing and emerging targeted therapies in breast cancer treatment and MBC treatments include:

- Hormonal therapies: selective estrogen receptor modulators (SERMS), selective estrogen receptor degraders (SERDS), aromatase inhibitors
- Monoclonal antibodies: these drugs target and bind to specific antigens, such as HER2
- Small molecule target inhibitors: tyrosine kinase inhibitors (TKIs) and poly ADP-ribose polymerase (PARP) inhibitors
- Immunotherapies: checkpoint inhibitors of PD-L1, vaccines, and T-cell therapies

For the most updated information about FDA-approved and emerging targeted therapies in MBC, visit the websites of MBCA members.

## 1.4 RECENT FDA APPROVALS: THE STATE OF THE SCIENCE IN MBC

People living with MBC who choose to participate in clinical trials are among the first to receive a treatment before it is available to the public (See New Trial Designs in Section 1.3.C). Clinical trials or research studies approved by the FDA are the only way to make scientific advances toward approval. Here we focus on some recently approved therapies for MBC and promising treatment options still in trials. For additional information, including updates from the 2018-2020 ASCO Annual Meetings and San Antonio Breast Cancer Symposiums, visit the websites of MBCA members.

### 1.4.A NEWLY APPROVED THERAPIES IN MBC

In the course of developing this study, from 2018 through 2020, the FDA approved several medications for people with MBC.

- In January 2018, the FDA approved a new indication for olaparib (Lynparza) in women with deleterious or suspected deleterious germline *BRCA*-positive, HER2-negative MBC. Olaparib was the first PARP inhibitor approved for this patient population. A second PARP inhibitor, talazoparib (Talzenna), was FDA approved in October 2018 for a similar group of patients.<sup>39</sup>

- In 2018, the FDA approved new and expanded indications for the CDK inhibitors abemaciclib (Verzenio)<sup>40-42</sup> and ribociclib (Kisqali).
- In late 2018, the first biosimilar to trastuzumab (Herceptin) was approved, called Herzuma (trastuzumab-pkrb, Celltrion Inc.). In subsequent months, several other biosimilars were approved, and many have been introduced to the market.
- In March 2019, the FDA granted accelerated approval to atezolizumab (Tecentriq) in patients with unresectable locally advanced or metastatic triple negative breast cancer (TNBC) whose tumors express PD-L1, along with a companion diagnostic test to identify those potentially eligible for the treatment.
- In May 2019, the FDA approved alpelisib (Piqray), the first phosphatidylinositol-3 kinase (PI3K) inhibitor available for HR-positive MBC with a *PIK3CA* mutation.
- In December 2019, the FDA approved fam-trastuzumab deruxtecan-nxki (Enhertu), a topoisomerase inhibitor conjugate, for patients with unresectable or metastatic HER2-positive breast cancer who received two or more prior anti-HER2 regimens for metastatic disease.
- In February 2020, the FDA approved neratinib (Nerlynx) in combination with capecitabine for adults with advanced or metastatic HER2-positive breast cancer who received two or more prior anti-HER2 based regimens for metastatic disease.
- In April 2020, the FDA granted accelerated approval to sacituzumab govitecan-hziy (Trodelvy) for adults with metastatic TNBC who received at least two prior therapies for metastatic disease.
- Also in April 2020, the FDA approved tucatinib (Tukysa) in combination with trastuzumab and capecitabine, for adults with advanced unresectable or metastatic HER2-positive breast cancer, including those with brain metastases, who received one or more prior anti-HER2-based regimens in the metastatic setting.

As this manuscript goes to press, other medications and methods to treat MBC are under study. To learn more about these approaches, as well as the clinical trials that support FDA approvals, visit the websites of the Alliance members.

#### **1.4.B INNOVATIONS IN CANCER TESTING: LIQUID BIOPSIES AND BIOANALYTIC ASSAYS**

Early detection of cancers with a simple blood test or plasma from blood, often called liquid biopsy, is another facet of diagnostics that has been gaining traction. Some recent studies have shown that a blood test that assesses multiple potential markers, including both genes and

proteins, may be sensitive enough to potentially diagnose cancer. One such test, CancerSEEK<sup>43</sup>, detects eight common types of cancer by assessing eight protein biomarkers and tumor-specific mutations in circulating DNA found in blood samples. Although not yet ready for the clinic, this diagnostic establishes a conceptual foundation for a single, multi-analyte blood test for early detection of many types of cancers. To establish the clinical utility of CancerSEEK, prospective studies of all incident cancer types in a large population are needed.

The federally funded study of CancerSEEK analyzed the blood of approximately 1,000 patients previously diagnosed with cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung, or breast and compared those results to blood sample analyses from 850 healthy people. CancerSEEK detected evidence of cancer with a sensitivity (the positive results were accurate) of 69% to 98% and a specificity (the negative results were accurate) of greater than 99% (this study was funded in part by NCI and the National Institute of General Medical Sciences). The study authors suggest that **CancerSEEK** may be able to be developed as a universal blood test for the early diagnosis of cancer.<sup>43</sup>

A recent study by Ye et al. (2019) performed one of the largest genomic characterizations of metastatic TNBC mutations using liquid biopsy to conduct low coverage genome-wide sequencing of circulating free DNA (cfDNA).<sup>44</sup> cfDNA is degraded DNA fragments released into the blood and includes various forms of DNA freely circulating in the bloodstream, such as circulating tumor DNA and cell-free fetal DNA. Elevated levels of cfDNA are observed in cancer, especially in advanced disease. This study demonstrated the value of using a liquid biopsy to better characterize metastatic TNBC and could potentially lead to an improved understanding of the evaluation of the tumor fraction in patients without a physical biopsy. It may suggest opportunities for prognostic analyses of metastatic TNBC patients.

The validity and standardization of liquid biopsy tests for solid tumors are still underway, leading many physicians to be reluctant to order the studies. In addition, follow-up genome sequencing may be required. Some liquid biopsies are being used as exploratory tests in early stage clinical trials. In these situations, the cost is covered by the trial.

Most insurance companies appear reluctant to cover the costs. This is emerging as an important clinical and financial issue for MBC patients and patients with other malignancies who are interested in novel cancer drugs and may need to know if their tumors are a potential match to therapies being offered in precision medicine clinical studies. In 2018, CMS finalized a National Coverage Determination that covers diagnostic laboratory tests using next-generation sequencing for patients with advanced cancer (i.e., recurrent, metastatic, relapsed, refractory, or stages III or IV cancer).<sup>45</sup> CMS believes that when these tests are used as a companion diagnostic to identify patients with certain genetic mutations that may benefit from FDA-approved treatments, these tests can assist patients and their oncologists in making more informed treatment decisions. Additionally, when a known cancer mutation cannot be matched to a treatment, then results from

the diagnostic lab test using next-generation sequencing can help determine a patient's candidacy for cancer clinical trials.<sup>46</sup>

To date, the FDA has approved one test that covers multiple cancers, **FoundationOne CDx**; as this report went to press, a pan-tumor liquid biopsy test, FoundationOne Liquid CDx, had just been FDA approved and become available. FoundationOne typically does not disclose how much the companies will pay to cover its tests, but the amount will be something less than the price non-insured patients would have to pay for it or \$5,800 per test for FoundationOne and \$7,200 for its test for blood cancers called FoundationOne Heme.<sup>46</sup>

## 1.5 THE IMPORTANCE OF CLINICAL TRIAL FINDINGS FOR PEOPLE LIVING WITH MBC AND RESOURCES

Learning about what is new in cancer clinical trials and aspects of trials such as biomarkers, liquid biopsies, and new trial designs is daunting, not just for patients and their families, but also for community oncologists, nurses, and navigators whose time is spent not in research, but in treating patients. The members of the MBCA educate both patients and providers by providing resources online via social media and in conferences to help increase understanding and awareness of new therapies and innovations in clinical trial operations.

### *MBC Patient Advocate on Myths and Barriers to Trials and Advocacy*

***“[There are] mental and cultural barriers that might stop a woman in our community from moving forward... but [also] other uncertainties. Will I be treated properly and equally? Will I be respected? If it’s not working or the side effects are too harmful, can I leave?... What are my choices and what happens to me? Unfortunately, some people still believe African-Americans in our community are used only as test subjects. It may mean they’re not receiving the proper medication. It’s as if they’re getting only the placebo as their disease’s condition is advancing. I work with African-American women and individuals of other ethnic groups that have been diagnosed with metastatic breast cancer. These women come from various socio-economic backgrounds... they may not have much understanding about health literacy in clinical trials. And so, the first thing I say is, if they’re African-American, we cannot change history, but we can look beyond it. It’s number one. The history is there, but we’ve got to advance. The other thing I express is ... You don’t know how women in our community are going to be affected because you took this step forward. You’re contributing to the improvement of science, medicine, and the healthcare community.”***

Felicia Johnson, Patient Advocate, Metastatic Breast Cancer

Understanding the current barriers and enablers to participating in a clinical trial is even more important for people living with MBC, their families, providers, and caregivers. Although multiple barriers exist, advantages to trial participation are also present. The myths associated with clinical trials need to be understood from an individual and cultural perspective and addressed in clear, simple language that patients and their families can easily understand. This is especially the case for many minority and under-resourced patients. (See Side Bar-Patient Advocate Addresses Myths and Barriers in the African American Community)

In the past, participation in Phase I studies was considered a “last ditch effort” for patients who had few or no options for additional therapy. Today, that is no longer true, and many Phase I/II studies offer patients access to innovative treatment. Additionally, clinical trial participants may receive enhanced care and attention. However, participation in any trial is an important decision, and MBC patients and their families should carefully consider all their options.

### **1.5.A QUESTIONS TO ASK YOUR DOCTOR AND THE RESEARCH STAFF ABOUT A TRIAL YOU MAY BE CONSIDERING**

- What is the main purpose of this study? Is it a Phase I study or some variation of Phase I/II or a Phase II/III?
- If it is an early stage trial with a continuation study (i.e., Phase I/II), will patients whose cancers progress on the study drug be allowed to cross over?
- If the treatment works for me, can I keep using it after the study? At what cost?
- Does the study involve a placebo or a SOC treatment that is already on the market? What is the SOC therapy and does the physician have a choice?
- How will I receive the treatments—will they be oral, intravenous, or intradermal?
- Will I be randomized? When will I learn my treatment assignment?
- How will participation in this study affect my quality of life?
- How long is the study going to last, and while I am a participant, what will I need to do? How many visits will I make to the clinic and over what period?
- Do I have to pay for any part of the study, such as scans or biopsies? Will my insurance cover these costs?
- Is there any reimbursement for travel costs, lodging, childcare, or eldercare?
- What will researchers learn about the study treatment and will they publish the study results? When will I be given access to the study results?
- Will I be able to see my own doctor?

- Have prior studies observed any major/minor side effects? If so, what are they?
- Can anyone find out whether I'm participating in the clinical trial?
- Will I receive any follow-up care after the study has ended?
- What will happen to my medical care if I stop participating in the study?
- Does the physician/investigator have any financial/special interest in the clinical study?
- What are the credentials and research experience of the physician and study staff?

The Alliance recently developed a downloadable [Clinical Trials Checklist for Patients](#) who are considering participation in a clinical trial. The checklist contains 10 statements related to trial participation that patients should understand and feel confident they can answer to make the best decision for themselves about taking part in a clinical trial. Many MBCA members also have tools and resources to help patients evaluate whether to participate in a clinical trial.

### **1.5.B HELPFUL RESOURCES FOR MBC PATIENTS WHO EXPERIENCE BARRIERS OR WANT MORE INFORMATION ABOUT ACCESSING TREATMENT THROUGH CANCER CLINICAL TRIALS**

In addition to the included list of questions, multiple resources in various types of media (print, online, pdf, and video) can help address barriers and better educate MBC patients and their families about cancer clinical trials as a treatment option. A few are listed below. We also encourage patients, providers, and caregivers to explore the [extensive library of MBC and clinical trial resources](#) of Alliance advocacy groups and pharmaceutical partners.

- [ASCO's Cost of Cancer Care Booklet](#)
- [Association of Community Cancer Centers' Library on Metastatic Breast Cancer](#)
- [Coalition of Cancer Cooperative Groups: Clinical Trials 101](#)
- [Lazarex Cancer Foundation](#)
- [Myths and Facts about Breast Cancer Clinical Trials](#)
- [Seven Things People with Metastatic Breast Cancer Want You to Know About Joining a Trial](#)
- [Young Survival Coalition's Metastatic Trial Navigator](#)



**2.**

**CLINICAL TRIAL  
SEARCH AND  
MATCHING SERVICES  
FOR MBC**

## 2. CLINICAL TRIAL SEARCH AND MATCHING SERVICES FOR MBC

### 2.1 EXPANDING USE OF CLINICAL TRIAL MATCHING SERVICES

Clinical trial matching services for people living with MBC can help patients and their families learn about the availability and location of trials, even if no decision on trial participation is imminent. Some clinical trial matching services provide additional information such as support services available at a trial site, trial education materials, and professional trial navigation services. Navigators can help patients better understand their options and formulate questions to ask their physicians or the physicians and staff at the trial site.

In this listing of clinical trial matching services, all the services provide a list of trials. Some are specific to MBC, and others are general cancer trial lists. The availability of the types of services varies greatly from general lists to tailored lists developed through screening tools based on eligibility and location to fully navigated matching and enrollment services based on patient eligibility, geographic location, and patient considerations or preferences.

### 2.2 RECENT CHANGES THAT AFFECT SCREENING CRITERIA FOR TRIAL MATCHING

As of February 2019, [www.clinicaltrials.gov](http://www.clinicaltrials.gov) indicated that approximately 339 open and accruing (or recruiting) interventional or therapy studies for MBC were available. In addition to the therapeutic trials, 11 supportive care trials and one registry trial were also listed. Trials that have closed or are anticipated to open are also listed on this site. Although hundreds of MBC clinical trials are underway in the U.S., any specific MBC patient would only qualify for a small portion of the open and accruing trials, because researchers design each trial's eligibility criteria, called inclusion and exclusion criteria, that determine who may be eligible to participate. Eligibility for a clinical trial may be determined by factors such as prior treatment history, presence of other diseases, overall health and functionality, whether the patient's cancer has molecular markers that affect the cancer's response to treatment, age, sex, medical history, and the particular type of cancer and its stage. Some trials request tumor tissue from fresh, frozen, or preserved samples. By defining the characteristics of the study population in this way, researchers can better understand the efficacy and toxicity of the study treatment and minimize the impact of confounding factors on

interpretation of the study results. However, with more stringent eligibility criteria, fewer patients qualify to participate, making the results less applicable to treating the more diverse patient populations seen in routine clinical practice. Such criteria can also influence the rate of accrual, potentially slowing the speed of medical research.

ASCO and Friends of Cancer Research (FOCR) launched a collaborative effort in early 2016 based on research to modernize eligibility criteria to promote greater patient participation in cancer clinical trials. The two organizations worked closely with the FDA. In October 2017, ASCO and FOCR published a [joint research statement](#) that provides a comprehensive examination of eligibility criteria for cancer clinical trials with recommendations to address eligibility criteria in five areas. On August 8, 2018, ASCO and FOCR submitted recommended language to the FDA for five guidance documents on ways to broaden eligibility criteria for cancer clinical trials. The five areas addressed are: minimum age requirements for trial enrollment, HIV/AIDS status, brain metastases, organ dysfunction, and prior and concurrent malignancies.<sup>47</sup> The areas most relevant to MBC are:

- **Brain metastases:** *The incidence of brain metastases is increasing in specific cancers, particularly affecting patients with melanoma and cancers of the lung and breast. Excluding patients from clinical trials may mean under-representing one-half to one-third of patients with certain types of cancer.*
- **HIV/AIDS, hepatitis B, and hepatitis C:** *Expanding cancer clinical trial eligibility to be more inclusive of patients with managed HIV, hepatitis B virus, or hepatitis C virus infections is justified in most cases and may accelerate the development of effective cancer therapies for patients with these chronic viral infections.*
- **Organ dysfunction:** *Patients with organ dysfunction are often excluded from clinical trials, regardless of specific drug metabolism or clearance mechanisms. However, as the general population is aging, an increasing number of patients with renal disease, hepatic dysfunction, and cardiac disease will also develop cancer. If a drug does not directly affect particular organs or when organ dysfunction does not directly impact drug metabolism or clearance, patients with lower organ function could participate in a trial. In addition, as data on toxicity become available during drug development, protocols should be revised to include patients with compromised organ function where safe parameters have been determined.*
- **Prior and concurrent malignancies:** *An increasing number of patients has prior or concurrent malignancies or comorbidities. By excluding individuals with previous or concurrent cancers or comorbidities, older patients may be prevented from participating.*

On November 29, 2018, the FDA accepted and put these suggestions into a guidance document with the expectation that new protocols submitted to NCI's Cancer Therapy Evaluation Program on or after November 1, 2018, will use these eligibility requirements.

## 2.3 CONSIDERATION OF COMPENSATION IN ADDITION TO REIMBURSEMENT FOR CLINICAL TRIAL PARTICIPATION

In January 2018, the FDA's Office of Good Clinical Practice issued an informative and important guidance paper: [\*\*Payment and Reimbursement to Research Subjects - Information Sheet\*\*](#).<sup>26</sup> This document provides guidance and helps IRBs, clinical trial centers, and investigators designing trials to clarify concerns and considerations for providing reimbursement and compensation to clinical trial participants.

In the past, IRBs, pharmaceutical companies, and clinical trial sites expressed concerns about undue influence that might occur in providing reimbursement for trial participation expenses (e.g., travel, childcare, eldercare, lodging, food, etc.). This type of patient support is seldom included in the financial negotiations between drug development companies and the CROs that may manage the trials and the clinical trial sites. However, this document clearly states that pharmaceutical companies and CROs may provide these funds as part of the negotiations with trial sites and that such consideration should be provided to the IRBs as part of the trial protocol approval process. These statements are only guidelines, and the FDA clearly states that "This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public." The document continues this theme:

*"Paying research subjects in exchange for their participation is a common and, in general, acceptable practice. Payment to research subjects for participation in studies is not considered a benefit that would be part of the weighing of benefits or risks; it is a recruitment incentive. FDA recognizes that payment for participation may raise difficult questions that should be addressed by the IRB. For example, how much money should research subjects receive, and for what should subjects receive payment, such as their time, inconvenience, discomfort, or some other consideration."*

## 2.4 OVERVIEW OF CLINICAL TRIAL MATCHING SERVICES FOR MBC PATIENTS AND THEIR FAMILIES/CAREGIVERS

Clinical trial matching services are one way of addressing crucial barriers to clinical trial participation. The research indicates that structural barriers preclude patient participation for about half of cancer patients. Among patients for whom a trial is available, approximately 25% (half of those who might participate) are not eligible for the trial due to trial exclusion factors. In many cases, patients who might be eligible are not offered trials by their physicians.<sup>6</sup> Trial matching services put the opportunity to find trials in the hands of the patients and their caregivers and provide patients with information that enables them to return to their physicians and discuss possible trials.

Social media and access to the internet are increasing opportunities for both MBC patients and their physicians to more rapidly learn about trial opportunities, thus supporting opportunities for faster access to trials.<sup>48</sup>

Clinical trial matching services may also help increase diversity and address under-representation of minorities in clinical trials, especially when services are better targeted through social media. Diversity of participants in breast cancer trials is vital due to the multiple identified types of breast cancer. Research suggests that some racial and ethnic groups have higher risk factors than white groups. A recent study analyzing the inclusion of women and minorities in cancer clinical trials indicated that 82.9% were white, 6.2% were African American, 3.3% were Asian, 2.2% were Latinas, and 0.1% were Native Americans.<sup>49</sup>

The actions of the MBCA and those featured in the following examples of trial matching services suggest the potential for compelling relationships between advocacy-stimulated clinical trial education and access to and improvements in MBC patient participation.

## **Best Practice Example:**

### **Collaboration Among Pharmaceutical Companies and Advocacy Groups in Recruiting MBC Patients into Clinical Trials**

**Increasingly, pharmaceutical companies recognize the power of patient advocacy groups to educate patients about clinical trials and as partners to enhance and speed trial accruals. For these companies, a significant consideration is the competition to get a new drug approved and the medication into the market. Patients, too, want to see new drugs enter the market and become available to all patients, not just trial participants, quickly and safely.**

**A successful example of industry-advocacy collaboration was the partnership between Pfizer and patient advocacy groups to recruit for the EMBRACA trial. Medivation, a biotechnology company that Pfizer acquired, had begun partnering with several members of the MBCA that serve patients with BRCA mutations, the primary audience for the EMBRACA trial of a PARP inhibitor. Pfizer continued these activities after the acquisition, from July to August 2016.**

**Medivation announced the launch of a patient-friendly site to 27 breast cancer and pan-tumor advocacy organizations. As a result, a variety of MBCA member organizations promoted the trial to their constituents.**

**One notable example is recruitment assistance provided by FORCE. The organization posted the trial in its newsletter and on its Featured Research page on its website. Monthly, it promoted EMBRACA on Facebook, and it invested in a week of Facebook ads pointing to a blog post and webinar. FORCE also promoted the trial to healthcare professionals.**

**As a result of rapid patient accrual to the EMBRACA studies, on October 16, 2018, the FDA approved talazoparib (Talzenna™, Pfizer Inc.), the PARP inhibitor, for patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2-negative locally advanced or metastatic breast cancer.**

**The FDA also approved a companion diagnostic alongside the PARP inhibitor, the BRACAnalysis CDx™ test (Myriad Genetic Laboratories, Inc.), to identify patients eligible for the treatment. Pfizer has continued to work with advocacy organizations through a dedicated clinical trial patient recruitment team.**

Beth Burnett, Strategic Alliance Director,  
Pfizer Oncology

## **MBC Connect**

*In October 2018, the MBCA launched MBC Connect™, an application that collects, via the use of a mobile app or a website, general patient characteristics and demographics, disease characteristics, genetics and tumor mutations, treatment history, quality of life data, and clinical trial experience from patients living with MBC. MBC Connect is an interactive, web- and mobile-friendly patient experience registry that empowers patients in the U.S. to collaborate with researchers to advance MBC research. All patient information is kept private and encrypted. MBC Connect is available in English and Spanish.*

*A new feature of MBC Connect, known as MBC Connect 2.0, was released December 2019. MBC Connect 2.0 provides automatic clinical trial matching. Although not a web-based search engine like the other trial matching websites mentioned in this section, this feature of MBC Connect will use survey answers and treatment information entered by patients to automatically match patients to MBC clinical trials that may be of interest, thus avoiding the current, complex trial search process. Clinical trial matching requires that MBC Connect participants respond to Demographics and Disease History surveys. Completion of a Treatment History and Genetics Survey will provide more targeted clinical trial matches.*

*MBC Connect 2.0 greatly simplifies the current trial search process that prevents many patients from discovering potentially life-saving available treatments. Previously, researching potential clinical trials required significant time and an overwhelming*

*amount of ongoing research. As a result, both physicians and their patients are often unaware of clinical trial options. This is one of the contributing factors for the extremely low participation rate for clinical trials, despite many patients expressing a willingness and desire to participate.*

*MBC Connect 2.0 was designed with MBCA partner BreastCancerTrials.org via its technology partner, Quantum Leap Health Care Collaborative. Information about clinical trials is sourced from ClinicalTrials.gov. The trial information is curated and presented in lay-friendly language via BreastCancerTrials.org. Matching to new clinical trials occurs nightly, ensuring an up-to-date list of MBC clinical trials for each user. MBC Connect participants who have entered pertinent information into the application will see a list of MBC clinical trials in the application when they log on. Trials are listed in geographic order, with the closest trials listed first. Clicking on a trial in the list shows a description that includes the purpose, who the trial is for, a Google map of the trial's location, a description of what is involved, links to learn more, and other information. Users can:*

- *filter their trial list according to parameters such as different types of treatment trials (e.g., targeted therapy, chemotherapy), non-treatment trials (e.g., support/education, managing side effects), and phase (I, II, or III);*
- *save trials of particular interest in a separate list;*
- *dismiss trials that are not interesting; and*
- *share trials (via text or email) with family members, friends, and their health care team.*

## CLINICAL TRIAL SERVICE:

### National Library of Medicine's Clinicaltrials.gov

(<https://clinicaltrials.gov/>)

**ACCESS:** Mobile Web-based Interface, Toll Free Phone Support, and Live Chat

**TELEPHONE:** 1-800-4-CANCER (1-800-422-6237)

**HOURS OF OPERATION:** Monday-Friday 9 A.M. to 9 P.M. ET

**LIVE HELP ONLINE CHAT:** [LiveHelp](#) Monday-Friday 9 A.M. to 9 P.M. ET

**E-MAIL:** [E-mail Us](#)

**DESCRIPTION:** Clinicaltrials.gov is a public access resource of the U.S. National Library of Medicine that lists clinical trials in the U.S. and around the world. It features clinical studies on a broad range of trials for a variety of indications, including cancer. Patients and providers find trials by using the systems predictive search tools that support finding trials based on disease indication, trial phase, and basic attributes of the trials, such as inclusion/exclusion criteria. Clinicaltrials.gov was designed as a trial registry for medical and research professionals. Patients and caregivers may find the medical jargon confusing and difficult to understand.

**PATIENT DATA REQUIRED TO IDENTIFY MATCHES:** Minimal. Users can run a basic search on a diagnosis or a type of therapy and can include location.

**FEATURES OF CLINICAL TRIALS DATABASE:** The service shows where specific types of trials are located on a mapping tool. Users can download and print their selected list of trials to share with their physicians and medical professionals.

**MATCHING PROCESS:** The service utilizes predictive text entered into text boxes to help guide patients to the appropriate search term. After running an initial search, patients can narrow the search by a limited number of parameters by utilizing a series of check boxes and data fields on the results page. However, as a basic service that aims to provide patients and their proxies with an overview of open trials, it does not have many features to identify the most appropriate trials.

**USER EXPERIENCE:** The search results do not contain patient education materials or help patients understand the clinical trial descriptions.



## CLINICAL TRIAL SERVICE:

### Facing Our Risk of Cancer Empowered (FORCE)

(<https://www.facingourrisk.org/research-clinical-trials>)

**ACCESS:** Web-based Interface, Peer Support Navigators, and a Help Line in English and Spanish.

**TELEPHONE:** 1-866-288-RISK (7475).

**E-MAIL:** [E-mail Contact Form](#)

**DESCRIPTION:** FORCE focuses on adult hereditary cancers, including hereditary ovarian, pancreatic, and prostate cancers; melanomas; and early and metastatic breast cancers. The FORCE Research Study search tool allows users to select the type of hereditary cancer study of interest: Treatment trials; Prevention; Detection and Risk trials; Quality of Life and Well-being studies; and Surveys, Registries, and Interview studies. Users can filter searches by location, type or stage of cancer, and other details. FORCE supports ABOUT, the first research registry created and governed by and for people affected by hereditary breast or ovarian cancer. The ABOUT Network is a patient-powered research registry that is part of the National Patient-Centered Clinical Research Network (known as PCORnet), which works to ensure the patient voice and experience is considered at all phases of the research cycle. FORCE's Peer Navigation Program has the ability to match patients interested in clinical trials with others who have participated.

**PATIENT DATA REQUIRED TO IDENTIFY MATCHES:** Minimal. Users can run a basic search on a diagnosis and type of mutation, or stage of breast or other hereditary cancers.

**FEATURES OF CLINICAL TRIALS DATABASE:** Identifies highlighted trials for MBC with easy-to-understand information on the trial, locations, and contact information. Provides users easy access to additional trials related to hereditary cancers on the Clinicaltrials.gov database.

## CLINICAL TRIAL SERVICE:

### Breast Cancer Trials (BCT)

(<https://www.breastcancertrials.org/BCTIncludes/index.html>)

**ACCESS:** Web-based service. Users can call or email for assistance or information

**TELEPHONE:** 415-476-5777 (available 9 A.M.-5 P.M. PT Monday-Friday)

**E-MAIL:** [Help-desk@bctrials.org](mailto:Help-desk@bctrials.org)

**DESCRIPTION:** Breast cancer patients or their caregivers have choices to view all trials, view trials specific to a cancer type or treatment type without creating a profile, or complete an extensive clinical profile to assist with an intelligent algorithm matching platform. The service partners with trial sponsors to ensure that trial information in the BreastCancerTrials.org database is updated on a regular basis to facilitate more accurate matching and to avoid matching patients to closed or otherwise unavailable studies.

**AMOUNT OF PATIENT DATA REQUIRED TO IDENTIFY MATCHES:** The BCT profile creation offers users the opportunity to provide many clinical data points, including lab and imaging results and treatment history. This helps narrow the choices returned to the user. The exact amount of patient data required to conduct a search varies based on where the patient is in her/his treatment course (e.g., newly diagnosed but not yet started treatment, or currently on hormone treatment after surgery) and responses to questions (certain responses trigger additional questions).

**FEATURES OF CLINICAL TRIALS DATABASE:** BCT has a proprietary breast cancer-specific database that is based on data from Clinicaltrials.gov that has been augmented with updated data from researchers. BCT has the capability to create specific trial type filters such as that created for Metastatic Trial Search, as well as disease-specific filters beyond breast cancer.

**MATCHING PROCESS:** The service leverages checkboxes and branching logic to ensure that patients enter accurate and pertinent search parameters, thus increasing the likelihood the search will yield relevant trials. Users can mouse over the terms in the boxes to learn more or access the definition. Based on the checkboxes that the patient selects, the service identifies additional relevant data fields to narrow the search (e.g., if the patient indicates they received chemotherapy, the service includes additional data fields and checkboxes for the type of chemotherapy the patient received).

**USER EXPERIENCE:** BCT staff converts the medical terminology in clinical trial descriptions into lay-friendly language. The user interface is easy to navigate, allowing patients to quickly see pertinent details, such as the distance from multiple matched trial sites (using Google Mapping) and anticipated treatment frequency. Users can save specific matched trials to their profile page, use a secure email system to send their profile to a specific trial site and coordinator, and sign up for a Trial Alert system that notifies them of new trials that match their profile.

## CLINICAL TRIAL SERVICE:

### Metastatic Trial Search (MTS) and Metastatic Trial Talk (MTT)

**ACCESS:** Mobile Web-based service optimized for mobile iOS and Android platforms

**TELEPHONE:** 415-476-5777 (available 9 A.M.-5 P.M. PT Monday-Friday)

**E-MAIL:** [MetastaticTrialSearch@gmail.com](mailto:MetastaticTrialSearch@gmail.com)

**DESCRIPTION:** Metastatic Trial Search (MTS) is a clinical trial search application designed specifically for and with MBC patients. MTS launched in 2015 as a part of BreastCancerTrials.org (BCT), an organization within the Quantum Leap Health Collaborative. MTS is housed at the University of California in San Francisco and continues to be powered through the BreastCancerTrials.org systems and platforms. MTS was designed in collaboration with several breast cancer advocacy groups with coordination supported by the MBCA. In March 2018, MTS relaunched and added a monthly social blog, Metastatic Trial Talk (MTT), which runs in parallel on the embedded MTS websites and provides carefully curated and monthly updated news and features about MBC research, including listings of trials recently added to BCT and MTS. Today, MTS is embedded on 17 MBCA breast cancer websites and is heavily featured in their social media activities. Users can subscribe to MTT to receive monthly updates.

**AMOUNT OF PATIENT DATA REQUIRED TO IDENTIFY MATCHES:** MTS is built specifically for MBC patients based on a thoughtfully designed and user-tested filtering system using an advanced and intelligent search algorithm. Initial data points include breast cancer type based on hormone receptors, potential sites, areas with metastases (e.g., brain, bone, liver, lung, none, or other), sex, menopausal status for females, birth year, and zip code. Users can further filter and narrow trial choices by key word search (e.g., PARP inhibitors), trial type, phase, and radius distances with trial locations shown on a Google Map. MTS staff curate the MTS trials, re-writing for health literacy and identifying key trial design elements important to users such as trial purpose, eligibility criteria, and time/clinic visit requirements.

MTS users can send trial information via email, post on Twitter or Facebook, print copies to share with their families and physicians, save specific matched trials to their profile page, use a secure email system to send their profile to a specific trial site and coordinator, and sign up for a Trial Alert system that notifies them of new trials that match their profile.

**FEATURES OF CLINICAL TRIALS DATABASE:** MTS is based on a second and more flexible database design than the original BCT with the capabilities to provide indication-specific trials for other cancers and chronic diseases with custom filters. It captures data from Clinicaltrials.gov that may be augmented with updated data from researchers. Clinical terminology in the database is translated into patient-friendly language. MTT/MTS are easily embedded at no cost to advocacy groups as buttons or widgets on their sites.

**MATCHING PROCESS:** The service leverages the initial MTS filters with additional checkboxes and branching logic to ensure patients enter accurate and pertinent search parameters, thus increasing the likelihood the search will yield relevant trials.

**USER EXPERIENCE:** MTS ensures data entry is easy for patients through the use of checkboxes, patient-friendly language, and presentation of search results in an easy-to-navigate format. Additional current education is provided via MTT.

## CLINICAL TRIAL SERVICE:

### Storm Riders Network

(<https://thestormriders.org/science-research/clinical-trials/>)

**DESCRIPTION:** The Stormriders Clinical Trial Matching Service is broader than other MBC trial matching and listing services. The website includes MBC trials in the U.S. and internationally. Trials are updated every 2 weeks from the NIH registry and are filtered onto the list to include trials for:

- MBC patients
- Targeted therapy: biological or hormonal
- Drugs that have been FDA approved for other cancers

**AMOUNT OF PATIENT DATA REQUIRED TO IDENTIFY MATCHES:** The trial filters are relatively rudimentary and include breast cancer type, a selection of categories based on the types of drugs being tested in the study (e.g., immunotherapy; serine-threonine kinase inhibitor; tyrosine kinase inhibitor; endocrine (hormone) therapy; and miscellaneous inhibitor). The user can select only one site of metastasis (e.g., brain) and can select the trial phases of interest.

**FEATURES OF CLINICAL TRIALS DATABASE:** The database of trials may be larger than that of MTS and possibly EmergingMed because it includes many Phase I and Phase I/II trials for multiple solid tumors that are likely filtered out in the current structure of those services.

**USER EXPERIENCE:** The service is ambitious and continues to evolve.

## CLINICAL TRIAL SERVICE:

### EmergingMed Clinical Trial Navigation Service

(<https://app.emergingmed.com/cca/home>)

**HOURS OF SERVICES FOR NAVIGATION:** 8:00 A.M. to 5:00 P.M. ET

**TELEPHONE:** Toll Free Number 1-877-601-8601

**ACCESS:** Mobile Web-enabled with concierge-like trained clinical trial navigators delivering highly personalized services. Patients can fill in their personal information to create a profile and view trial matches based on cancer indication and trial criteria filters. Patients can also request a call or email contact from the navigators, who will assist in educating them about trials and aid them in their searches. EmergingMed will also, if requested, update patients when new trials and sites open that match the patient's profile.

**DESCRIPTION:** EmergingMed provides specialized services to cancer advocacy groups, including MBCA member SHARE, and to pharmaceutical and biotech companies using a subscription fee-for-service mode as a turn-key hosting. Services to patients and physicians are free.

**FEATURES OF EMERGINGMED'S DATABASE:** EmergingMed's database is drawn primarily from [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and supplemented with trials reported directly by trial sponsors and sites.

**MATCHING PROCESS:** EmergingMed uses predictive matching based on the criteria patients enter into its online forms, including the ability to specify or limit the trials to a geographic area. The Clinical Trial Navigators enter data gathered from the patients via phone or email to support their creation of a matching profile.

# 3.

## **KEY FINDINGS AND RESULTS OF ASSESSMENTS OF MBCA MEMBER WEBSITES AND SOCIAL MEDIA FOR MBC CLINICAL TRIALS**

### 3. KEY FINDINGS AND RESULTS OF ASSESSMENTS OF MBCA MEMBER WEBSITES AND SOCIAL MEDIA FOR MBC CLINICAL TRIALS

#### 3.1 RESULTS OF ASSESSMENTS OF MBCA MEMBER WEBSITES AND SOCIAL MEDIA FOR CLINICAL TRIAL EDUCATION AND ACCESS

The 2017-2018 assessments of MBCA members, which were conducted using the quantitative assessments shown in Figure 6, indicate that one-third of Alliance members (11/33, as of April 2019) include MTS/MTT on their websites and in their social media efforts (e.g., Facebook, Twitter, blogs, and Instagram). Of MTS users, two also use EmergingMed or their own matching systems.

In July 2018, BreastCancerTrials.org made a significant change to MTS by adding MTT as an enhanced education function. Based on the 2017 statistical analysis of the prevalence of persons living with MBC by Mariotto et al.,<sup>28</sup> the current reach of the combined MTS and EmergingMed's search engines in 2018 equals ~8% of the prevalent population. The percentage change from 2017 to 2018 is notable in several areas: 1) A very slight change in the number of page views occurred in 2018, but the number of sessions of individual and unique users increased by over 170%. (Search robots that can artificially inflate page views and sessions were excluded from the analyses.) This finding suggests that although more individuals are using MTS, they are using it more precisely and thus accessing fewer pages; 2) In 2018, the number of individuals who requested that the system "show trials" increased by nearly 17%. Those who asked to learn more and included their contact information to receive information on new trials and sites as they are added to MTS increased by nearly 6.5%. Overall, average screen time among site users decreased by ~22.6%. That finding may indicate that users are identifying the information and trials they want more easily. An additional finding is that new users to all MBCA member sites increased by over 108%, and return visitors increased by nearly 350%.

**Table 1: Tally of MBCA Member Assessment of Clinical Trial Education and Access to MBC Clinical Trials**

	MBCA PAGE VIEWS	MBCA SESSIONS	MBCA SHOW TRIALS	LEARN MORE/ CONTACT INFO	AVERAGE SCREEN TIME (MINUTES)	MBCA NEW USERS*	MBCA RETURN VISITORS
2017	21,898	5,190	29,906	4,602	4.30	3,475	1,144
2018	22,170	14,058	3,390	4,900	3.33	7,233	5,147
<b>% CHANGE</b>	<b>1.24%</b>	<b>170.87%</b>	<b>16.66%</b>	<b>6.48%</b>	<b>-22.56%</b>	<b>108.14%</b>	<b>349.91%</b>

Table 2 provides a comparison of the assessment scores of the MBCA advocacy groups to MBCA pharmaceutical company members.

**Table 2. Comparison of MBCA Advocacy Group to Pharmaceutical Firm Assessments of Clinical Trial Education and Access to MBC Clinical Trials**

	AWARENESS OF TRIALS (E.G. EXPLAINS PHASES)	KNOWLEDGE SHARING	INTEREST IN METASTATIC BREAST CANCER	ACTION POTENTIAL FOR CLINICAL TRIAL ACCESS OR ENROLLMENT	<b>TOTAL</b>
MBCA ADVOCATE MEMBERS	15.8	16.6	17.1	16.3	<b>65.7</b>
MBCA PHARMA MEMBERS	15.3	13.3	15.8	16.2	<b>60.5</b>

Table 3 provides a scored analysis of MBCA member use of social media to educate and inform their members and people living with MBC on information and programming about MBC and clinical trials.

**Table 3. MBCA Members Use of Social Media Outreach**

	FACEBOOK FOLLOWERS	TWITTER FOLLOWERS	INSTAGRAM POSTS	INSTAGRAM FOLLOWERS	YOUTUBE SUBSCRIBERS	PINTEREST	LINKEDIN
MBCA ADVOCATE MEMBERS	2,394,916	273,645	212	100,888	16,963	2,564	34,626
MBCA PHARMA MEMBERS	118,358	53,649	121	31,080	99,359	1,489	3,954,863



## 3.2 OPPORTUNITIES AND BEST PRACTICES TO EXPAND CLINICAL TRIAL EDUCATION AND ENROLLMENT THROUGH SOCIAL MEDIA

The opportunity for ongoing growth and success of MTS/MTT rests on the collaborative efforts of Alliance members to push out information on MTS/MTT in various ways across multiple social media channels. However, it is important to recognize that each advocate member has its own messages and programming and that MTS/MTT and metastatic clinical trials are only one of many messages important to any individual advocacy group member. Because only one-third of members place MTT/MTS on their websites, the Alliance should make it a priority to increase the number of members utilizing the service. Providing financial incentives or offering free technical assistance to the smaller, less well funded advocacy groups may increase participation and use of MTS/MTT. MTS/MTT may also become part of a menu of options that the Alliance offers.

Some Alliance members, such as Breastcancer.org, SHARE, and FORCE, are savvy about threading information on MTS and MTT into existing programming. Some include it in messaging for moderators on Facebook or during Twitter chats, or mention it on Instagram, on Pinterest tiles, and in YouTube videos. In examining Table 3 above, clearly, there is strength in numbers among the advocacy members on Facebook and Twitter, but those channels have noise as well. This suggests the need for a concerted, planned, and strategic effort to provide ongoing stimulants to the advocacy members to communicate regularly about MTS/MTT. Examples could include a schedule or calendar of Twitter feeds and image or poster tiles that could be used, shared, and re-shared on a variety of social media channels.

To reach a more professional audience such as researchers, pharmaceutical and biotech leaders, and clinicians, LinkedIn offers valuable opportunities (See Table 3). The examples from Katherine O'Brien's use of LinkedIn, including her most recent foray on February 10, 2019, "[Choosing an Oncologist-A 10 Year Retrospective](#)", suggest that LinkedIn may be an important venue to explore, especially to reach professional audiences.

When considering social media use, strategizing and understanding how age groups, communities, and populations select social media and how they use it are important. For example, Latinos and African Americans communicate by text more frequently than whites, and younger users will use text, WhatsApp, Snap Chat, Instagram, or Twitter almost exclusively rather than using the phone to actually call someone or to read an email. Latinos also frequently use WhatsApp.<sup>50</sup> A recent [study](#) by the Pew Research Center can help the Alliance strategize for increased social media use, especially among Latinos and African Americans.

# 4.

## **RESULTS FROM QUALITATIVE INTERVIEWS OF MBCA MEMBERS AND KEY THOUGHT LEADERS ABOUT MBC CLINICAL TRIAL BARRIERS AND FACILITATORS**

## 4. RESULTS FROM QUALITATIVE INTERVIEWS OF MBCA MEMBERS AND KEY THOUGHT LEADERS ABOUT MBC CLINICAL TRIAL BARRIERS AND FACILITATORS

### 4.1 QUALITATIVE RESULTS OF MBCA INTERVIEWS

As part of this effort to better understand the landscape and gaps and identify best practices, we interviewed over 30 leaders from the MBCA advocacy groups; leaders from academia, industry, and nonprofit organizations; and individuals living with MBC.

The goal of the interviews with MBCA members was to better understand their current activities and plans for the future, including efforts to increase awareness of MTS/MTT and other educational and patient assistance efforts, as well as to learn how the MBCA might better serve them as Alliance members. This is a representative sample and examples of best practices from the many interviews in which MBCA advocate leaders so graciously gave their time and insights.

For the thought leaders from the pharmaceutical industry, academia, and other nonprofit groups, we wanted to gain insight into what they saw as urgent priorities, gaps, and opportunities for policy and process for improving access to MBC clinical trials.

In interviewing patients, many but not all of whom are active as advocates, we wanted to learn more about their experiences in learning about MBC trials, the barriers and facilitators to participating in trials, and what they believed was important to share about their experiences living as a person with MBC. In addition, Marina Kaplan\*, an MBC patient advocate, presented a poster at SABCs 2019 in which she explored MBC patient attitudes towards clinical trial participation and possible solutions to increase participation from the MBC patient's perspective (Appendix G).

### 4.2 KEY FINDINGS FROM ACROSS THE MBCA INTERVIEWS

Each interview guide was tailored to the specific type of individual or organization (e.g., MBCA member, Academic or Minority Thought Leader, Pharmaceutical Thought Leader), but some key themes emerged.

*\* This contributor is deceased. We are grateful to her and to her family for the gift of her time and expertise for this endeavor.*

### ***Education and Knowledge Sharing:***

- Among the advocate leaders of larger organizations, the use of digital education and knowledge sharing is extensive. Most have annual plans and strategies in place for the next 12-18 months to extend MBC and clinical trial education efforts among their members. Nearly all the advocate leaders stated that peer matching, live programming, and navigation are needed to provide personalized human interaction for people living with MBC, especially those considering clinical trials.
- Interactive digital communication was deemed vital for individualized outreach. Examples included private Facebook groups, interactive Twitter chats, and the presence of MBCA members at booths during large regional and national meetings.
- Interviews with smaller nonprofit breast cancer groups (not current MBCA members) suggested opportunities exist for increased use of the MTS/MTT widget. Under-resourced nonprofits lacked the skill or financial resources to include the widget on their pages. Current small MBCA members would also likely welcome such assistance.
- Interviews with smaller nonprofits suggest that opportunities exist for the MBCA to provide non-branded MTS clinical trials education, in English and Spanish, for posting on these groups' websites.

### ***Healthcare Professional Engagement:***

One objective of the interview guide was to learn more about how advocacy group members engage with healthcare professionals. Nearly all those interviewed have oncology healthcare professionals on their advisory boards or scientific advisory boards. Groups that publish blogs or articles, including feedback on trials or on drug types or reports from national conventions, nearly always have one or more oncologists review the materials prior to publication. Several groups utilize healthcare professionals, usually medical oncologists but also radiation oncologists, oncology nurses, and dieticians, in live or recorded webinars to provide education.

Few advocacy leaders reported having educational programming specifically for healthcare professionals. Susan G. Komen is the exception. An example of one Komen program is the **2019 Breast Cancer Conference: Advancing the Practice of Patient-Centered Care**. This Continuing Medical Education course is nationally accredited for physicians, physician assistants, nurses, and nurse practitioners. Other professionals including fellows, pharmacists, care managers such as community health workers, and dieticians are awarded a certificate of completion that may count toward their required hours of professional education.

This may be an opportunity for the MBCA to strategize with members about how best to educate healthcare professionals in the use of MTT/MTS. Among the groups mentioned for

consideration were minority physicians and minority-focused medical schools. An additional group for consideration, especially among minority communities, is Promotores de Salud or Community Health Workers (P/CHW). A number of states have certification programs for P/CHW, and most require annual continuing education credits. Texas, for example, requires certification and P/CHW Continuing Education Units focused on breast cancer clinical trials navigation training and outreach.

### ***Areas Where the MBCA Could Better Serve Its Members:***

Among the questions we asked MBCA members was what the Alliance could do better, do more of, or do differently. Unanimously, the MBCA members were pleased with their engagement in the Alliance. Most stated that the Alliance was true to its purpose and that their organizations had benefited from participating. Several noted the importance of having an alliance focused on MBC.

Similar to recommendations already discussed, member leaders requested additional support, services, or engagement from the Alliance to:

- Conduct an engagement audit of MTS/MTT among users and non-users and engage with those members who do not have MTS/MTT on their sites to find out how it might be added.
- Review changes in FDA policy and guidance and create a policy and action agenda on how to engage with researchers, pharmaceutical firms, biotech, and cancer center IRBs to promote the use of the new guidelines on trial inclusion/exclusion and guidelines on reimbursement for trial participation expenses.
- Engage with groups like [Metavivor](#), [Lazarex](#), [Friends of Cancer Research](#), and ASCO to collaborate on policy activities and capture best practices.
- Create continuing education programming to better educate community oncologists, oncology nurses, navigators, social workers, pharmacists, and others including P/CHW in minority communities on MTS/MTT and MBC trials as a treatment option.
- Better understand the cost/benefits of having clinical trial navigators available for live, on-line phone calls or chats to assist patients and caregivers in using MTS/MTT and educating people about MBC clinical trials and emerging treatments.
- Consider engagement with the American College of Surgeons accredited cancer clinics, minority medical education centers, and others for use of MTS/MTT and education on MBC.
- Engage with pharmaceutical MBCA members to develop a strategy to use MBC patient advocates more deeply in the design, planning, recruitment, and retention of MBC patients in trials, especially minority MBC patients.
- Determine an improved way of sharing member information on MBC and MBC trials and resources such as registries and apps.

### ***Engagement and Opportunities with MBCA Pharmaceutical Members:***

The pharmaceutical leaders interviewed shared examples of and opportunities for patient and physician education.

- They expressed openness to the MBCA working with their companies to better educate MBC advocates and patients to review MBC clinical study designs, informed consent, education, and recruitment materials, with the understanding that patients and advocates may need training in clinical trial language and processes.
- They expressed a lack of awareness of the recent FDA guidance on reimbursement of expenses. One interviewee suggested this was an area for cancer centers to provide funding. The company representatives expressed concerns about undue influence, which relates to FDA concerns prior to the most recent guidance.

## **4.3 MBCA INTERVIEW RESPONSES FROM ACADEMIC, BUSINESS, AND MINORITY THOUGHT LEADERS AND PHARMACEUTICAL COMPANY PARTNERS**

The following is a collection of responses by key thought leaders from academia, business, pharmaceutical, and minority advocates in best practice suggestions regarding MBC clinical trials, minority participation, and patient navigation:

## Key Thought Leaders from Academia, Business, and Minority Advocates Responses

Best practice suggestions regarding MBC clinical trials, minority participation, and patient navigation

*Abby Kahler, Advanced Nurse Practitioner (APN) and Metastatic Patient Navigator, MD Anderson Cancer Center*

*“One of the barriers has to do with insurance. A lot of patients’ insurance and co-pays are an issue. Because I’m a Nurse Practitioner I can bill for my services. That means I cannot see the patient on the same day as the medical oncologist. So, I have to see the patient on the day of a scan [or] on a day on an ancillary referral: supportive care, nutrition, radiation, surgery, something like that. It’s a barrier trying to work with patients to coordinate appointments.”*

*“Having the right kind of insurance coverage is part of the process of getting into MD Anderson and is one of the largest barriers. But then, [many of my patients] don’t live in Houston, but they may live in San Antonio or Austin or New Orleans. So, there’s still a commute involved. They still need a hotel room, even though they’re within driving distance. And so, they would face the same barriers that someone who comes via a plane flight may face.”*

*“Many of my metastatic patients want to get started on treatment yesterday. A potential barrier is a lot of the pre-trial screening, and if there’s any more scans involved or, if there’s a biopsy. Some of my patients are like, ‘Yeah, biopsy, no problem.’ Others really have to consider if that’s something that they want to pay for or if their insurance will pay for it.”*  
*“One of the things that I’m currently working on is to create a peer-to-peer network. So,*

*through our volunteer services, we’re trying to come up with a way in which a newly diagnosed patient can be matched with a survivor so that journeys can be shared. My patient advocates feel that they are the missing link to be able to portray the necessity of my role in “lessons learned” types [of] conversation.”*

*“MD Anderson [is] a big place, and a new patient will have a lot of questions. Doing a little bit of extra support through the process can help us retain some patients who might not feel comfortable or cared for. They have to make certain decisions in certain time periods and a lot of things can get lost in translation. Most of our physicians are very open to the idea of working with a local oncologist. So, you may not have to travel here but for re-staging scans once every three months. And then, if it’s a clinical trial, working with the study coordinator as well as our social worker as to what assistance is available, whether it’s through the clinical trial, their insurance, MD Anderson, or the community. Often the patient’s not going to know about all of those different avenues that they can check for assistance. Being a patient navigator and trained as an APN allows me to make sure that we’ve exhausted all options, and being the person that oversees all of those different players has been helpful.”*

## Key Thought Leaders from Academia, Business, and Minority Advocates Responses

Best practice suggestions regarding MBC clinical trials, minority participation, and patient navigation

*Dr. Armin Weinberg, Retired, Clinical Professor at Baylor College of Medicine, Founder of the Intercultural Cancer Council and Principal Investigator of the “Eliminating Disparities in Clinical Trials (EDICT)” Project.*

*“When you look at innovation in metastatic breast cancer or in other areas, it reminds me a lot of some of the challenges that we saw in the early days when cardiovascular risk factors were becoming identified back to the late 60’s, early 70’s. One of the things that we learned from part of our research in the cardiovascular area was that the public’s understanding could drive more interest in these advances, which in turn could drive changes in position and provider behavior. One of the most frustrating things about clinical trials is how there is this lack of real knowledge about their availability and how often they are not offered as a part of the frequent options.”*

*“Public education and opportunity is something I feel still needs to be really pushed forward. In particular, with some of the disparity populations, I know that there has been progress in these areas. I think partnering between some of the more traditional organizations that are involved in clinical trials and those entities that are advocacy based, or even professional groups that are primed to deal with this have not been very effective. They are not well supported.”*

*“For example, let’s take the minority-serving institutions in this country. Both Hispanic and African-American, the black, and historically*

*black universities and others. There has been a deficit in their clinical programming that occurred, [but] we’re making progress. [However], we haven’t quite accelerated to where those institutions are providing some of the early impetus and infrastructure to really engage their communities. There’s a tendency for the majority of institutions to take advantage of, in a positive way, their service to minorities in hospital-based activities, for example county hospital systems. That’s often how they will fill their quotas or their goals or improvements of these studies. Those people who are in those minority-serving institutions really often have to play doubly hard, because the majority of the high-level clinical trials and the early trials are not serving those communities. There’s a need shift with this kind of flow of funds, activities, and opportunities to those institutions. And it’s been slower than I would have liked.”*

*“What you have to acknowledge when you are talking about clinical trial participation in metastatic breast cancer is the patient’s time. Think about the time it takes to inform people in [our] healthcare system about a change or an opportunity. The public engagement side and other providers in the healthcare system can really start to play a role [in providing this information].”*



## Key Thought Leaders from Academia, Business, and Minority Advocates Responses

Best practice suggestions regarding MBC clinical trials, minority participation, and patient navigation

Courtney Hudson, Founder/CEO of EmergingMed

*“The most beneficial situation for both patients and trials today is to get more therapies tested and approved or discarded faster. This is the scenario where patients consider clinical trial options at each step along the way in their journey, at each treatment decision point. It helps greatly if your doctor is informing you of trials and planning along with you, but you can also do it on your own once you become educated and learn about the trials.”*

*“If you don’t plan out your consideration of trials for which you potentially are eligible, it is likely you will miss windows of opportunity. Precision medicine means that trials are getting more specific, so you need to understand your own profile. Especially for metastatic patients—with every drug you take,*

*with every week that passes your eligibility changes at each treatment window.”*

*“If you identify trials that are somewhere new—you have to schedule a new patient visit, to send over your records, and have a conversation with your own doctors and family members. You have to be pretty darn motivated, and it’s all going to take some time, and the odds of you having the weeks to do that if you’re just starting from scratch—let’s say the day you find out that your localized breast cancer has metastasized, you’ve got a very limited amount of time [to] work with, and whether your doctor is helping you or not, it can be tough to pull that off. That is why I think every patient should learn about and consider trials as a treatment option as early as possible and just keep informed.”*

## Key Thought Leaders from Academia, Business, and Minority Advocates Responses

Best practice suggestions regarding MBC clinical trials, minority participation, and patient navigation

Venus Ginés, Founder/Executive Director, Dia de la Mujer Latina

*“It’s difficult getting Latinas interested in any clinical research but especially into a Phase 1 trial ... due to all the myths and rumors about medical abuse and especially the sterilization abuse of Latinas in the past. As a breast cancer survivor, I want to share about the opportunity that exists to receive the newest therapies if they chose to participate in a clinical trial.”*

*“They have to be computer-literate to log in and read about the trial and do the data entry in English, even the fairly simple questions, on MTS. At Dia de la Mujer Latina’s office at the multi-service center, we developed a plan to have one day where our Spanish-speaking Community Health Workers/Promotores are available to assist [patients] in setting up an email, logging in, and creating an account. We have been successful with the NIH’s All of Us initiative. The more we provide this assistance, the more interested they will be in all the clinical research that’s available.”*

*“But there’s still mistrust. Some Latina women are concerned that when they apply for citizenship or their Green Card, they may face the Public Charge clause, which will disqualify*

*them and mark them as being a burden on the system. Furthermore, there is a lot of general fear and mistrust of the medical community overall. And unfortunately, some of the Latino doctors that I have spoken with about clinical trials have reservations about offering [trials] to their patients, especially Latinas. When I have spoken to women with breast cancer, I ask them if their doctors discussed clinical trials and especially those with metastatic breast cancer say ‘no.’ That is a problem for us patient advocates.”*

*“Although we have trained over 3,000 Promotoras/es, our small grassroots organization wants to do a better job in addressing the low participation rate of Latinas in clinical trials, especially in breast cancer. What would be helpful for us would be example texts in Spanish that we could send out on Facebook, Twitter, text messages, or WhatsApp—those are the social media vehicles most used in our communities. Also, if we had access to non-branded information on clinical trials in Spanish, we could add it to our website. I’d like to have the MTS/MTT button on my website, but we might need either financial or technical assistance.”*

## Interviews with Pharmaceutical Thought Leaders

Responses to questions regarding current/planned MBC clinical trial education, healthcare professional education, and roles in patient advocacy in pharmaceutical trials

*Pfizer Pharmaceuticals – Pfizer Oncology*

*Michael J. Zincone, Director/Team Leader Advocacy and Professional Relations and*

*Beth Burnett, Strategic Alliance Director*

### **On Clinical Trial Participation**

*“If we start at the highest level and then go to the patient level, we are participating with the Pharmaceutical Research and Manufacturers of America (PhRMA) as a partner in trying to expand clinical trial participation, not just in oncology, but across all therapeutic areas. All of the large pharmaceutical organizations recognize the challenges and have been attempting to both increase awareness of clinical trials as well as provide for policy and coverage opportunities that would increase the likelihood for participation and the coverage of participation through third-party payers.”*

*“[At] Pfizer Oncology, we have specifically worked to increase awareness within all patient populations by using websites for a spectrum of clinical trials. Some of them are within metastatic breast cancer, and others have been within other therapeutic areas in oncology. This has helped to provide things like frequently asked questions about the opportunities to enroll, where the clinical trial sites are, and provides a much more user-friendly interface to help patients understand an individual study and potential opportunities.”*

*“We recognize that clinical trial participation—both at the patient and*

*healthcare professional levels—is not a one-sided problem. It has multiple facets, and some solutions tend to be more local in nature. There are impediments to clinical trial participation from a range of things, for example lack of transportation and geographical remoteness. Pfizer has a Clinical Trial Innovation Group that is working on things like allowing remote participation so that participants don’t necessarily have to travel to attend a principal investigator’s site in order to be enrolled in a study. The group also developed Pfizerlink – a clinical trial community for patients who complete Pfizer clinical trials. Participants in this program get a Lay Summary of the overall clinical trial purpose and results at the end of the trial not less than 1 year after completion. We are also working to use this platform to return their personal data (e.g., labs, biomarker tests, etc.) for use as the patient deems appropriate.”*

*“The other aspect is designing trials in a way that fosters patient participation [and] reduces patient burden and exclusion criteria so that the average person with a disease would be able to enroll. Throughout the industry we’ve had enrollment criteria that have been rigid, such that the normal person with a disease might not be able to enroll. Thus, we’ve artificially reduced the number of patients who can participate.”*

## Interviews with Pharmaceutical Thought Leaders

Responses to questions regarding current/planned MBC clinical trial education, healthcare professional education, and roles in patient advocacy in pharmaceutical trials

*Pfizer Pharmaceuticals – Pfizer Oncology*

*Michael J. Zincone, Director/Team Leader Advocacy and Professional Relations and*

*Beth Burnett, Strategic Alliance Director*

### **On Physician Education**

*“We’ve worked with a grant program to Avon to help BreastCancerTrials.org get the Metastatic Trials Search (MTS) engine up to speed. On our own Pfizer pages, for both patients and healthcare professionals, we’ve tried to make it easier and simpler to find and understand trials and list the site. We’ve even included a Google mapping tool to make it easier to find the sites where the trials are open.”*

*“Within our global medical grants program, we have also funded patient level education including an enduring piece on WebMD regarding treatment for metastatic breast cancer. Through a grants program with the National Comprehensive Cancer Network (NCCN), we meet with the grant recipients to learn from their experiences in trying to improve access [to] care, [which] includes clinical trial awareness and availability. Those cycles of grants have been very instructional and helped us learn what some best practices are in trying to maintain accessibility to the best standard of care. One of the programs that we found to be very successful was funded through Dana Farber, named project EMBRACE. The principle behind it was that a community oncologist could refer to Dana Farber for another opinion or to get a review of a treatment program or assessment of whether or not clinical trials were the right choice for a patient, but not lose them to their local care. The program is designed to foster communication between the referring*

*physician and Dana Farber and return the patient back to the referring practitioner, but allow the patient to benefit from the expertise at a tertiary care center, and that also includes access to clinical trials and awareness. We provided an additional \$2 million in funding at the end of 2018, which will be used in the upcoming 12 to 18 months to expand this to multiple academic medical centers.”*

*“The patient and the physicians [both] benefit.”*

*“Pfizer has worked with FORCE in current efforts to support hereditary breast, ovarian, and related cancers, which includes many metastatic breast cancer patients. Also included were efforts to advance our EMBRACA study for metastatic patients. The trial was accelerated by engagement with multiple advocacy groups engaged in metastatic breast cancer patient support.”*

*“We are increasing our efforts to include patient and advocate input into our study design and recruitment.”*

*“We have advocates providing input on patient-reported outcomes programming in trials. Changes made include a simplified informed consent document form; a patient gratitude program thanking patients at the start, mid-way, and end of a trial for their participation; and now involving patients and/or advocates at the protocol concept stage (before the draft is written) to provide input. This is the same time we would engage key researchers.”*

## Interviews with Pharmaceutical Thought Leaders

Responses to questions regarding current/planned MBC clinical trial education, healthcare professional education, and roles in patient advocacy in pharmaceutical trials

*Eli Lilly Oncology*

*Patrick Bubach, Global Medical Affairs Education Advisor, Breast Cancer and Sarcoma for Eli Lilly Oncology*

*“Lilly started working on education in metastatic breast cancer in 2016 in parallel to our research work and results from the MONARCH trial. We built a whole educational campaign, partnering with Medscape, that started with breast cancer as a disease, and [then] different types of breast cancer, and then metastatic cancer. Whenever there is a trial update at national or international medical meetings, we share updates looking at the whole class of drugs that are available, and what’s new in therapies.”*

*“Lilly is educating all types of physicians working in oncology, and in the U.S., we do that through Medscape or WebMD. It’s really hard to identify a community oncologist versus an oncology expert.”*

*“Strategically and historically, usually we start with a physician that is actually making a decision, who needs to be educated at a different level. One of our strategic objectives is to provide education treatment decisions. The other objectives center on the management of the disease and the therapy. That’s usually more centered around pharmacists and nurses, depending on the country.”*

## Interviews with Pharmaceutical Thought Leaders

Responses to questions regarding current/planned MBC clinical trial education, healthcare professional education, and roles in patient advocacy in pharmaceutical trials

*Devon McGoldrick, Oncology Advocacy & Professional Relations at Eli Lilly and Company*

*“In 2018, Lilly, in partnership with leaders of the MBC community, commissioned a national survey of people living with MBC, their loved ones, and healthcare professionals to better understand the unique challenges people living with MBC face every day. Findings include:*

*Health care professionals may not be aware of how eager their patients are to have information about treatment options, including trials:*

- *82% (n = 297) of people living with MBC are interested in learning about all of the treatment options available to them, while 80% of the oncologists (n = 201) were not aware that patients wanted this information.*
- *Health care professionals (both oncologists and oncology nursing*

*professionals) want to know more about current treatments and want patients to know their options (including clinical trials):*

- *73% of oncologists say it is important to know about all treatment options (n = 201)*

- *91% of oncology nurses say it is important to know about all treatment options (n = 150)*

- *Regarding interest in education about treatment options:*

- *74% of oncologists want to learn more about treatment options (n = 201)*

- *77% of oncology nurses want to learn more about treatment options (n = 150)”*

# 5.

## **DISCUSSION AND STRATEGIES FOR BEST PRACTICES AND INNOVATIONS TO IMPROVE AND EXPAND ACCESS TO MBC CLINICAL TRIALS**

## 5. DISCUSSION AND STRATEGIES FOR BEST PRACTICES AND INNOVATIONS TO IMPROVE AND EXPAND ACCESS TO MBC CLINICAL TRIALS

### 5.1 DISCUSSION OF RESULTS AND FINDINGS OF METASTATIC BREAST CANCER CLINICAL TRIALS LANDSCAPE AND GAP ANALYSIS

As part of this analysis, we identified areas of support and progress among MBCA members, especially in providing access to MTS and MTT and some exceptional examples of peer support, social media outreach, and engagement. One striking feature is the strong degree of support for and awareness of the value and benefits of collaboration among Alliance members. We also identified areas that remain neglected, especially among the smaller and minority/ethnic-focused advocacy group members as well as among patients in general.

### 5.2 DEVELOPING AND IMPLEMENTING STRATEGIES TO IMPROVE MBC CLINICAL TRIAL PARTICIPATION

Throughout this report, we illustrated the nature of barriers to clinical trial enrollment and retention. Efforts to improve awareness of and access to metastatic clinical trials are clearly needed. Advocate leaders, MBC patients, and key academic and pharmaceutical business thought leaders noted the barriers and the facilitators to patients enrolling in clinical trials. They made it very clear that many of the barriers are not patient barriers but rather clinical communications, policy, structural, and financial barriers that disrupt the potential for MBC patients to consider, enroll in, and remain in clinical trials.

This section of the report summarizes suggestions from evidence-informed research and from the qualitative and quantitative analyses conducted as part of this Landscape and Gap Analysis. Clearly, the issues related to clinical trial recruitment remain multifactorial. However, the work of the Alliance and its members has moved the effort forward, and the evidence in this report suggests that the initiatives are growing and strengthening. One of the major efforts is MTS/MTT, which continues to grow in its outreach to provide access and information via the MBCA partners. However, ongoing efforts for patient registries, peer matching, MBC patient navigation, and a multitude of educational and training efforts must continue, as people continue to be diagnosed every day with MBC and may or may not have ever considered clinical trials as a treatment option.



## ***Local and MBCA Advocacy Group Strategies***

**Social Media:** Increasingly, social media platforms provide opportunities to communicate directly with patients, trialists, researchers, and the public about metastatic clinical trials. Some suggested considerations for social media use include:

### ***Initial Strategies***

- The MBCA and its members should agree and establish the rationale and ethics for the application of social media directed at target populations. Should materials be reviewed by patients and medical advisors? What key messages should be delivered, and to whom?
- The MBCA and its members may want to establish ground rules to continue to address the privacy and confidentiality concerns of the social media applications they elect to use.
- All social media communications should be vetted for harms and benefits, even if the content does not require IRB approval.
- Providing and agreeing upon summary statements about important MBC community issues regarding the intent to use and share social media should consider its intended uses and potential abuses.
- Statements issued by the MBCA should make clear both the intended use as well as ways in which the statement should not be used.
- If user-generated content is allowed or encouraged, which is usually essential for robust online communities, are agreed-upon guidelines available for monitoring and protecting the advocacy group—or if a trial is involved, the trial’s integrity?

### ***Advanced Social Media Strategies***

The power of the Alliance stems from the willingness of its members to work collaboratively on key efforts. This type of collaboration can be greatly enhanced by planned and concerted efforts to use social media and to seek different and increasingly innovative ways to communicate key messages, especially to minority and under-resourced advocates and their constituents. Because technology and communication consistently evolve, social media outreach should be an ongoing, persistent communication and dissemination strategy. It could be framed as an MBC “Learning Collaborative” where members test and share new and best practices in social media.

- Enhancing access to information on metastatic clinical trial information for small, less well-resourced advocacy groups could extend reach into minority and hard-to-recruit populations. Excellent metastatic clinical trial resources exist in multiple languages that could be accessed and distributed by the Alliance. These resources could be bundled

together with the widget for MTS/MTT with information on MBC Connect.

- The Alliance may want to explore ways for the MTS/MTT widget to be more broadly communicated and utilized. The Alliance should consider how such a campaign could be integrated into campaigns for MBC Connect.

## 5.3 STRATEGIES TO ADDRESS POLICY, INSTITUTIONAL, AND STRUCTURAL BARRIERS TO MBC CLINICAL TRIAL PARTICIPATION

### 5.3.A EXPANDED ELIGIBILITY ACCESS

The recent [joint research statement](#) from the FDA, suggested by ASCO and Friends of Cancer Research to modernize and expand eligibility criteria for clinical trials, is an essential and fundamental shift in the clinical trial enterprise.<sup>47</sup> It requires not only a culture shift in the mindset and practices of the researchers and clinicians who design and conduct trials, but also among the CROs that work with researchers to contract for trials at clinical sites and among the IRBs that review and approve the trial protocols. The Alliance can further explore this issue to determine any impact for MBC patients who previously would have been excluded from many current trials. The development of standard inclusion, rather than exclusion, criteria for these patients provides a significant opportunity for increased trial invitations and partitions, but only if this new policy guidance is carefully and thoughtfully shared.

Current efforts across several ongoing and future clinical trials will likely demonstrate the feasibility of expanding clinical trial eligibility. Future FDA guidance will likely assist industry sponsors and clinical researchers in designing trials that represent these expanded populations. The Alliance may consider collaboration with ASCO and Friends of Cancer Research to work with the clinical trial community, especially the MBC research community, to encourage incorporation of these recommendations in new and forthcoming trials and to establish methodologies to support recruitment and evaluation among people living with MBC.

### 5.3.B GENERAL PHYSICIAN AND CLINICAL BARRIERS TO PATIENT EDUCATION AND ENGAGEMENT IN CLINICAL TRIALS

As the individual usually linking patients to clinical trials, the oncologist plays an integral role in encouraging and supporting patient recruitment. Surveys of oncologists in community cancer centers indicate that most agree clinical trials may provide a high quality of care (87%), and patients may benefit from enrollment (83%).<sup>48</sup> Nevertheless, multiple studies suggest that nearly half of potentially eligible patients are not offered or are actively discouraged from participating in clinical trials because of physician decision, non-communication, or preference. Historically,

at least four significant barriers to oncologist recruitment are present: 1) Lack of awareness: Even when the patient brings information to the physician, s/he may lack confidence or sufficient knowledge about the study agents to feel comfortable recommending the trial; 2) Communication issues: These are related to time to research and explain the trial to the patient, and communicate with the trial PIs or coordinators to learn more about the patient's eligibility; 3) Financial disincentives: Concern about losing the patient or using clinic resources to support the patient's enrollment. Community oncology offices often lack the resources required to support a patient's consent and enrollment into a trial at their site; and 4) Eligibility: Concerns or assumptions that the patient is likely ineligible for the trial. Although rarely explored in the scientific publications, physician beliefs about cost considerations, insurance coverage, or the financial capacity of the patient to participate in the trial may factor in some oncologists' decisions not to encourage trial participation.

To participate in a trial, an individual must first have access to the trial, which can be influenced by many factors, including insurance coverage, transportation, time off work, travel distance, and access to childcare or eldercare. Once those issues have been addressed, significant additional barriers remain that are based on the cancer histology, stage, and the individual's state of health, including co-morbidities. Other clinical barriers may include the patient's medical history with other therapies and the time off or on existing SOC drugs.

Strategies the Alliance might consider to address the issue of lack of physician referral include:

- Continue to support patient advocates in educating *de novo* and recurrent MBC patients on the ease of use and access to MTS/MTT
- Support adult nurse practitioners and nurse navigators in collaboration with clinical trial matching services to educate potential participants and develop decision guides for trial participation
- Collaborate with the Oncology Nursing Society or the Academy of Oncology Nurse Navigators to create continuing education, webinars, and programming to educate professionals about resources like MTS/MTT and to in turn educate their metastatic patients
- Collaborate with Lazarex and MBCA members in communicating opportunities for patient reimbursement support at participating comprehensive cancer centers

## 5.4 STRATEGIES TO ADDRESS SOCIO-ECONOMIC BARRIERS FOR MBC PATIENT PARTICIPATION IN CLINICAL TRIALS

Similar to the recent FDA guidance on inclusion factors for trial participation, the two recent FDA practice guidelines regarding reimbursement and compensation for trial participation could potentially create major cultural and policy shifts among trial sponsors and CROs. Historically, cancer centers and even some CROs created foundations to provide financial support to under-resourced cancer patients to facilitate participation in clinical trials. Financial pressure on patients continues to grow with increased co-pays and ever higher costs for SOC drugs, as well as pre-screening scans, biopsies, and other tests that may not be covered by the trial or the clinic. Although these costs are expected to be covered by the patient's health insurance, they may influence a patient's ability to consider participation in clinical trials.

A national survey investigated the extent and severity of negative financial effects of cancer among more than 1,000 women with MBC. The study, led by University of North Carolina Lineberger Comprehensive Cancer Center researchers, found that nearly one-third of women had no insurance, and many felt significant or catastrophic financial effects from cancer. **The preliminary results were presented at the American Society of Clinical Oncology's Quality Care Symposium**, in Phoenix, Arizona, in September 2018. Uninsured individuals more often refused or delayed treatment because of cost (98% vs. 41% of insured,  $P < 0.001$ ). They were also more likely than insured patients to report not paying non-medical bills (40% vs. 16%,  $P < 0.001$ ), quitting their job after diagnosis (65% vs. 46%,  $P < 0.001$ ), or being contacted by a collections agency (77% vs. 36%,  $P < 0.001$ ). Insured participants reported higher cost-related emotional distress, including being "quite a bit" or "very" stressed about not being sure of cancer costs (53% vs. 32%,  $P < 0.001$ ) and about financial stress on their family members due to their cancer (52% vs. 27%,  $P < 0.001$ ).<sup>17</sup>

Our interviews with patients and patient advocates supported the notion that many people living with MBC are in financial distress due to the costs of their treatment. The added potential financial burden from participating in a clinical trial could be a daunting disincentive.

The Alliance may have multiple options to address this issue from a policy and communications perspective:

- No survey of cancer clinic and hospital foundation policies and procedures has been conducted. Researching the resources available at major academic and other research cancer centers offering metastatic clinical trials may be worthwhile.
- The Alliance should investigate how patient advocacy groups can interact with groups outside the breast cancer space. Consider seeking opportunities to collaborate or form coalitions to encourage **PhRMA** and BIO as well as pharmaceutical clinical trial sponsors,

CROs, and major NCI centers and institutional sponsors to discuss options and possible responses to the FDA guidance documents on reimbursement and compensation, now that providing these funds does not necessarily create undue influence. Communication strategies should clarify MBC patient perspectives, whose lives and quality time may be lessened without being able to consider trial participation.

- The Alliance may engage with the Lazarex Foundation to explore new and additional tools and strategies to support patient reimbursement for trial expenses, especially among older, under-resourced, and minority patients, whose participation is greatly needed to ensure generalizability of trial results.

## 5.5 CONCLUSIONS

Metastatic patients, patient advocates, physicians, and researchers regard clinical trial participation as an important and critical approach to improving metastatic cancer care and the movement toward cures. Despite this shared value, the complexity of new trials in precision medicine and the potential barriers that exist at multiple levels in the system—not just patient barriers—make successful enrollment in a clinical trial an uphill battle. Published research studies and qualitative studies such as ours support the importance of a more thorough understanding of the barriers and facilitators for metastatic patients considering trials as a treatment option, at any stage of their care.

Today, more than ever, as we stand on the edge of innovation in MBC care, increasing and easing accrual into clinical studies is vital. Faster accrual means that drugs get to patients faster. And drugs that fail will fail faster. Supporting diversity among trial participants to ensure generalizability of results is important. For all these reasons, the Metastatic Breast Cancer Alliance should harness the power of its members to develop and grow strategies that will dismantle systemic barriers to clinical trial participation.

**6.**

**APPENDICES**

## APPENDIX A: REFERENCES

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## APPENDIX B: MORE INFORMATION ABOUT TERMS USED IN THIS PAPER

Doctors often use medical terms to talk about cancer and clinical trials. For more information about some of the terms you may see when reading this document or when you are thinking about being in a clinical trial, please visit [cancer.gov](https://www.cancer.gov).

## APPENDIX C: METHODS USED IN MBCA CLINICAL TRIALS LANDSCAPE AND GAP ANALYSIS

### Objectives of Landscape and Gap Analysis Data Collection

This section has the following objectives:

- To better understand and capture for our *Metastatic Clinical Trials Landscape and Gap Analysis* the work the MBCA member advocacy groups and pharmaceutical companies are doing to educate their constituents (e.g., patients, members, caregivers, providers, and community) about opportunities for care through MBC clinical trials;
- To understand organizations' future plans for programming around MBC clinical trials, including the use of MTS, with a particular focus on the period between September 2018 and December 2019, and;
- To better understand how the MBCA can aid or assist member organizations in providing such education.

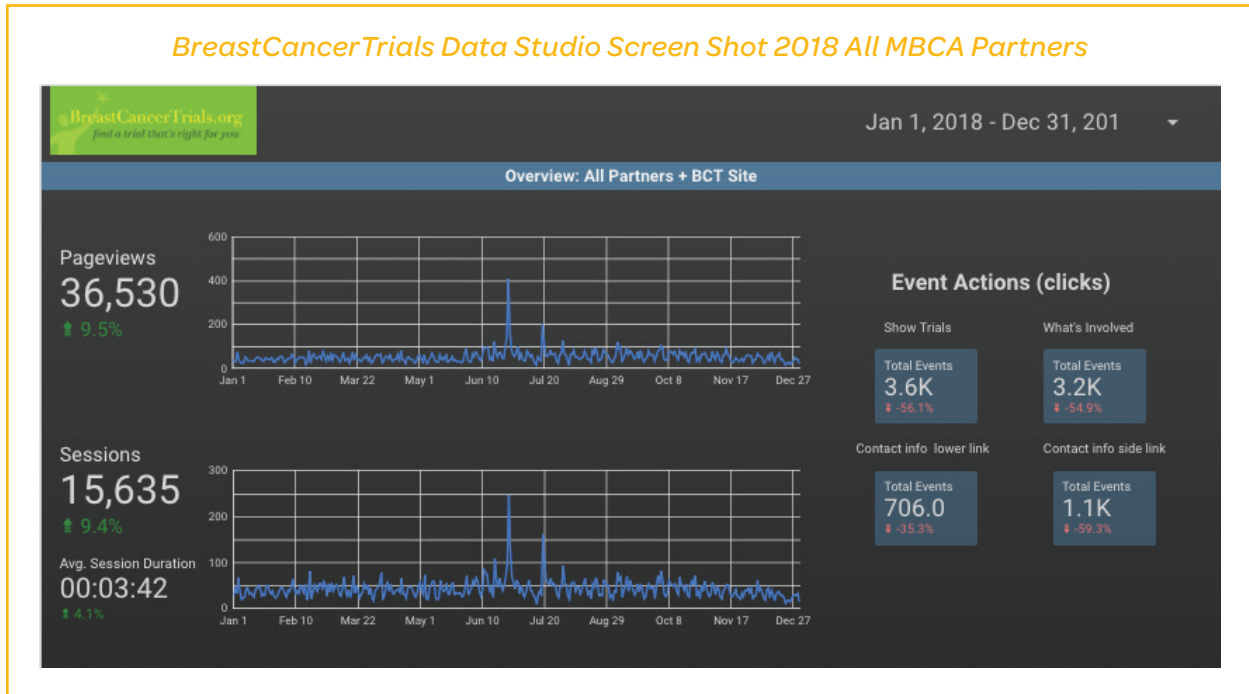
### METHODOLOGY

Our mixed methods approach included quantitative aspects (classification and rating of MBCA members' websites and social media for awareness, education, and access for users to find and enroll in MBC clinical trials) and qualitative aspects (Table 1). Interviews reviewed the assessments among several MBCA advocate group leaders, and we conducted interviews with key thought leaders in clinical trials that included pharmaceutical company representatives and a diverse group of MBC patients.

*Table 1: Role and Purpose of Mixed Methods Qualitative and Quantitative Research*

	QUALITATIVE RESEARCH	QUANTITATIVE RESEARCH
OBJECTIVE/PURPOSE	To gain an understanding of underlying reasons and motivations. To provide insights into the setting of a problem, generate ideas, and/or clarify or confirm hypotheses for or from initial quantitative research.	To quantify data and generalize results from a sample to the population of interest. To measure the incidence of various views and opinions in a chosen sample. Sometimes followed by qualitative research, which is used to explore some findings.
SAMPLE (WHO IS INVOLVED)	Usually a number of cases representing the population of interest (e.g., thought leaders from pharma, academia, minority groups, and MBC patients).	Respondents selected to fulfil a given quota (e.g., MBCA advocate leaders and their websites/social media, academia, minority groups, and MBC patients).
DATA COLLECTION	Unstructured or semi-structured techniques (e.g., individual depth interviews or group discussions).	Structured techniques such as ranked assessments and questionnaires, sometimes followed by on-line or telephone interviews.
DATA ANALYSIS	Non-statistical.	Statistical data are usually in the form of simple statistics and tabulations (tables). Findings are conclusive and usually descriptive in nature.
OUTCOME	Exploratory and/or investigative. Findings are not conclusive and cannot be used to make generalizations about the population of interest. Develop an initial understanding and sound base for further decision making.	Used to recommend or inform a course of action or policy direction.

The first element of our quantitative methodology involved using the results from the MTS tracking tool, which was provided to the project by BreastCancerTrials.org.



This was followed by the second quantitative element, which included a list of MBCA members’ websites and online clinical trial search engines to assess the websites of 33 MBCA members (as of 2018). Special attention was paid to those 11 MBCA members whose websites included MTS/MTT in 2018 to provide an analysis of their websites in 2017 compared (to date of the assessment) to those in 2018.

### Screen Shot of MTT and MTS as They Appear on MBCA Member Websites

Find metastatic breast cancer trials that are right for you

Two individuals rated each of the websites and then discussed any differences or additions to arrive at a collaboratively agreed-upon assessment. As part of this effort, the team also assessed each MBCA member’s social media efforts, with special attention paid to those advocacy groups whose social media included information and education on MBC clinical trials.

The protocol and criteria on which each of the 33 MBCA websites (as of 2018) were assessed include the following using a scale of 1 to 5 with 5 being “high” for a total potential score of 100 (See Appendix D for Example Assessment Tool).

#### **PROTOCOL FOR SEARCHING FOR MBC TRIALS INFORMATION:**

- 1) Access website and other digital properties (Facebook, Twitter, blogs from spreadsheet provided by MBCA)
- 2) If no specific MBC or clinical trial information is found on the home page, use the website search function
- 3) Use “clinical trials,” “metastatic breast cancer,” and “metastatic breast cancer clinical trials” as initial search words/phrases
- 4) Capture any links, blog sites, and digital materials regarding education, information, or meetings regarding MBC clinical trials and place in MBCA Dropbox
- 5) Each of the two reviewers reviews individual assessments and reaches an agreement on any differences in material captured or the final scoring
- 6) Selected MBCA members will be asked to review their organization’s assessment as an “ongoing assessment,” and any necessary changes in scores or materials will be updated based on the interviews

#### **EXAMPLES OF SCALE FOR EACH CATEGORY OF THE ASSESSMENT**

**Awareness of Clinical Trials:** **1)** No information on trials; **2)** Includes reference to trials as part of a treatment decision; **3)** Describes trials briefly with suggestions for 2nd opinion at a location where trials may be more available (e.g., NCI Center; American College of Surgeons Commission on Cancer Clinics ACoS-CoC); **4)** Describes trials by phase and what each phase may mean for a patient; may link to [EmergingMed](#), [www.Clinicaltrials.gov](#), or the pharmaceutical or biotech company’s own trial matching system; **5)** Links to [www.BreastCancerTrials.org](#) and/or [MTS](#).

**Knowledge Sharing Related to MBC:** **1)** Little or no mention or information; **2)** Discusses MBC as a type as well as other types/stages; **3)** Includes information on understanding pathology of breast cancer; **4)** Provides very specific information without extreme searching; clear mentions of MBC; **5)** Addresses MBC in depth and offers valued resources including trial referral.

**Interest in MBC:** **1)** Little or no information on MBC; **2)** Includes references to MBC as a type but devotes little attention in digital or print materials; **3)** Includes information on MBC in materials but no specific educational events or materials; **4)** Provides very specific information on MBC and

includes groups, digital materials, or print materials; **5)** Provides very specific information on MBC in multiple forms of materials and may include multiple languages.

**Action Potential for MBC Clinical Trial Access or Enrollment:** **1)** Little or no potential due to lack of information or focus; **2)** Low action potential due to level of information; **3)** Encourages patients to consider trials as a treatment option and discusses pros/cons; **4)** Has referral links to EmergingMed, MTS, or the pharmaceutical company or biotech’s own trial matching system; **5)** Conducts outreach for clinical trial training/education events, seminars, or blogs. (See Appendix D for Breastcancer.org’s example of the MBCA Member Assessment Tool)



## APPENDIX D: ADVOCATE INTERVIEW GUIDE AND ASSESSMENT FORM

### **Interview Guide**

#### **MBC Clinical Trial Landscape and Gap Analysis Project**

*Introduction from Deborah Vollmer Dahlke, DrPH*

*Thank you for taking the time to speak with us. This interview should take about 40 minutes but will not extend beyond the hour you have so kindly allocated. We will use Zoom, an online communications tool that will allow us to see each other, share screens, and record the conversation (with your permission).*

*The purpose of this interview and the overarching goals of MBCA's Clinical Trial Landscape and Gap Analysis are three-fold:*

- 1) To better understand and capture for our Landscape and Gap Analysis the work your organization is doing to educate your constituents (e.g., patients, members, caregivers, providers, and community) about opportunities for care through MBC clinical trials;*
- 2) To understand your organization's plans for the next 12-18 months for education/training activities/materials/events regarding MBC clinical trials; and*
- 3) To better understand how the MBCA can aid or assist you in providing such education.*

*I would like your permission to record this interview. It will help in capturing your thoughts and ideas. We will de-identify all comments and statements in the interview in our overall landscape assessment; however, we may request your permission to use and attribute a specific quote and/or to build a small case study regarding your organization's efforts.*

*We promise to share our findings with you in our final report and may also request your participation in an online focus group to review our draft report.*

#### **May I begin recording now?**

**Question 1:** *Education & Knowledge Sharing: Can you provide an overview of the types of educational activities your organization is currently conducting or materials you are making available to educate your constituents about metastatic breast cancer clinical trials? Do you have any metrics related to metastatic breast cancer patients who visit your website or attend/participate in webinars, twitter feeds, or live meetings? Can you please share this data?*

**Question 2:** *Plans for Metastatic Trial Education: What are your organization's plans for the next 12-18 months for educating constituents about metastatic breast cancer clinical trials as a therapeutic option? Do you have plans for promoting the latest version of Metastatic Trial Search and recently launched Metastatic Trial Talk? For example, will you be creating new online materials (PDFs, sections of your website)? Are you planning webinars, blogs, or live meetings?*

**Question 3:** *Healthcare Professional & Pharma Partnerships: Do you have active relationships and partnerships with local or national physicians such as oncologists, gynecologists, radiologists, nurses or hospitals and clinics or pharma companies? In what ways do they support your efforts in metastatic breast cancer clinical trials education?*

**Question 4:** *Review of Draft Assessment Form: We would like to take a few minutes to review your organization's draft assessment. Are there missing elements or areas you would like to discuss, or suggest we amend? (Note: I can share this on screen while we are talking)*

**Question 5:** *Ideas & Suggestions for Metastatic Trial Education: Do you have ideas or suggestions for ways the Alliance can better assist you in educating your constituents regarding Metastatic Breast Cancer trials as a therapeutic option?*

## **Closing**

*As a breast cancer advocate and researcher, I greatly appreciate all that you do for your constituents including both patients and caregivers. MBCA will share the results of the MBC Clinical Trial Landscape and Gap Analysis with you later this year. We may invite you to review the draft report results as part of an online focus group. We are also planning a survey later this fall and may ask your help in identifying participants.*

*Thank you for your participation in this interview and for your ongoing support of MBCA initiatives.*

BCO ASSESSMENT FORM – A FRAMEWORK FOR EVALUATING PRINT AND DIGITAL COLLATERAL FOR MBC CLINICAL TRIAL EDUCATION

SCALE OF 1-5

(1 = little or no information; 2 = low level/general; 3 = moderate level; 4 = high level; 5 = superior)

*Additional Notes from BCT/MTS Search for 2018*

The screenshot shows a table with the following data:

	Full Referrer	Traffic Type	Campaign	Pageviews
1.	google	organic	(not set)	1,786
2.	breastcancer.o...	referral	(not set)	581
3.	m.facebook.co...	referral	(not set)	415
4.	yahoo	organic	(not set)	125
5.	(direct)	direct	(not set)	83
6.	bing	organic	(not set)	42

1 - 6 / 6 < >

2018 Notes – Updates and changes since MTS relaunch of MTS/MTT

NAME /TYPE OF ORGANIZATION	AWARENESS OF TRIALS (E.G., EXPLAINS PHASES)	KNOWLEDGE SHARING	INTEREST IN MBC	ACTION POTENTIAL FOR CLINICAL TRIAL ACCESS OR ENROLLMENT	MTS PAGE VIEWS + TRIAL APPLICATIONS
WWW.BREASTCANCER.ORG	5	5	5	5	Total visitors December 31, 2017 = 2886. Of those, 2078 asked to see trials.
TYPE OF MATERIAL: (E.G., PRINT, DIGITAL, VIDEO, BLOG, OTHER) DOWNLOADABLE	5	5	5	5	From Jan. 1-June 26, 2018, the average # of MTS visitors was 10.5. From June 26 to Aug. 20, the average was 19.1.
CONTENT DESCRIPTION	<p>Very thorough and easy to navigate. Blogs and Podcasts easiest to access via the webpage itself</p> <p><b><u>Stage IV and Metastatic Breast Cancer ONLY</u></b> 21,843 Topics, 513,861 Posts</p> <p><b><u>Clinical Trials, Research News, Podcasts, Study Results</u></b> 5,700 Topics, 24,898 Posts</p>				<p><b>2017 MTS</b> notes Average session was 3:37 minutes. 72.9% of users were new users, and 27.1% were returning users to the site.</p>
CONTENT RANKING	5	5	5	5	
POTENTIAL REACH	5	5	5	5	
POTENTIAL MBC PATIENT TARGET AUDIENCE EFFECT	5	5	5	5	
<b>TOTAL SCORE</b>	<b>25</b>	<b>25</b>	<b>25</b>	<b>25</b>	<b>Score = 100</b>

## BCO ASSESSMENT FORM – A FRAMEWORK FOR EVALUATING PRINT AND DIGITAL COLLATERAL FOR MBC CLINICAL TRIAL EDUCATION

### SCALE OF 1-5

(1 = little or no information; 2 = low level/general; 3 = moderate level; 4 = high level; 5 = superior)

### NOTES:

31% are new users.

415 users come from Facebook.

In 2018 thus far, 955 have asked to see trials, and the average time spent on MTS was 4:03 minutes.

From June 26 to August 18, 2018, Breastcancer.org had 1410 visitors or ~30% of all of this year's users.

### PROTOCOL FOR SEARCHING FOR MBC TRIALS INFORMATION:

- 1) Access website and other digital properties (Facebook, Twitter, blogs from MBCA-provided spreadsheet).
- 2) If no specific MBC or clinical trial info is found on the home page, use the website search function.
- 3) Use "clinical trials", "metastatic breast cancer", or "metastatic breast cancer clinical trials" as initial search words/phrases.
- 4) Capture any links, blog sites, and digital materials regarding education, information, or meetings regarding MBC clinical trials and place in MBCA Dropbox.

### EXAMPLES OF SCALE FOR EACH CATEGORY ON THE ASSESSMENT:

**Awareness of Clinical Trials:** 1) No information on trials; 2) Includes reference to trials as part of a treatment decision; 3) Describes trials briefly with suggestions for second opinion at a location where trials may be more available (e.g., NCI center; ASCO Clinics); 4) Describes trials by phase and what each phase may mean for a patient. May link to [EmergingMed](#) or [www.Clinicaltrials.gov](#); 5) Links to breastcancertrials.org's [MTS](#).

**Knowledge Sharing Related to Metastatic Breast Cancer:** 1) Little or no mention or information; 2) Discusses MBC as a type as well as other types/stages; 3) Includes information on understanding the pathology of breast cancer; 4) Provides very specific information without extreme searching; clear mentions of MBC; 5) Addresses MBC in depth and offers valued resources including trial referral.

**Interest in Metastatic Breast Cancer:** **1)** Little or no information on MBC; **2)** Includes references to MBC as a type but devotes little attention in digital or print materials; **3)** Includes information on MBC in materials but no specific educational events or materials; **4)** Provides very specific information on MBC and includes groups, digital materials, or print materials; **5)** Provides very specific information on MBC in multiple forms of materials and may include multiple languages.

**Action Potential for MBC Clinical Trial Access or Enrollment:** **1)** Little or no potential due to lack of information or focus; **2)** Low action potential due to level of information; **3)** Encourages patients to consider trials as a treatment option and discusses pros/cons; **4)** Has referral links to EmergingMed or MTS; **5)** Conducts outreach for clinical trial training/education events, seminars, and blogs.

**Action Potential for MBC Clinical Trial Access or Enrollment:** **1)** Little or no potential due to lack of information or focus; **2)** Low action potential due to level of information; **3)** Encourages patients to consider trials as a treatment option and discusses pros/cons; **4)** Has referral links to [EmergingMed](#) or [MTS](#); **5)** Conducts outreach for clinical trial training/education events, seminars, and blogs.

## APPENDIX E: THOUGHT LEADER INTERVIEW GUIDE (ACADEMIA, MINORITY ADVOCACY, AND BUSINESS LEADERS)

OCTOBER-NOVEMBER 2018

*Thank you for taking the time to speak with us. This interview should take about 40 minutes but will not extend beyond the hour you have so kindly allocated. We will use Zoom, an online communications tool that will allow us to see each other, share screens and record the conversation (with your permission).*

*The purpose of this interview with you as a Key Opinion Leader (KOL) for MBCA's Clinical Trial Landscape and Gap Analysis are as follows:*

- 1) To better understand what you believe are key clinical opportunities and barriers for men and women with metastatic breast cancer to participate in clinical trials, especially early stage trials;*
- 2) To capture your thoughts on what MBCA and its member organizations can do to help educate their constituents regarding these clinical opportunities and barriers, including the use of BreastCancerTrials.org's tools—Metastatic Trial Search and Metastatic Trial Talk ([https://www.Breastcancer.org/treatment/clinical\\_trials/metastatic-trials-tool](https://www.Breastcancer.org/treatment/clinical_trials/metastatic-trials-tool))*
- 3) To gain your thoughts on economic, demographic and socio-economic barriers to trial participation and what MBCA can do to help address those barriers; and*
- 4) To better understand how MBCA and its advocate member organizations can aid or assist you and other professionals in providing education and training for both patients and healthcare professionals regarding metastatic breast cancer clinical trials.*

*I would like your permission to record this interview. It will help in capturing your thoughts and ideas. We will de-identify all comments and statements in the interview in our overall landscape assessment; however, we may request your permission to use and attribute a specific quote and/or to build a small case study regarding your organization's efforts.*

*We promise to share our findings with you in our final report.*

**May I begin recording now?**

**Question 1:** *What are examples of opportunities for participation in early stage clinical trials for patients with metastatic breast cancer? Many of these may be Phase 1A/B solid tumor trials that include metastatic breast cancer patients as potential participants. It may be the case that both patients and their community oncologist may lack awareness of these trials. How should patients best address potential participation in such trials, especially if their oncologist lacks knowledge about the trials?*

**Question 2:** *In your experience, what are the most common clinical barriers to patients' participation in metastatic breast cancer trials? How might some of these be addressed? For example, ASCO and Friends of Cancer Research have submitted joint research statement to the FDA for expanding cancer clinical trial participation.<sup>47</sup> The organizations recommend addressing minimum age requirements, HIV/AIDS status, brain metastases, organ dysfunction, and prior and concurrent malignancies.*

**Question 3:** *Diversity of patients, including men and women of color, minority participation as well as older and younger adults in clinical trials, is a persistent issue. What, if any, steps have your organization taken to support these patients' consideration of metastatic breast cancer trials? What suggestions can you offer to increase diversity, specifically in metastatic breast cancer clinical trials?*

**Question 4:** *From what sources do most of your patient referrals for metastatic breast cancer clinical trials come? Did you have an opportunity to explore: [https://www.Breastcancer.org/treatment/clinical\\_trials/metastatic-trials-tool](https://www.Breastcancer.org/treatment/clinical_trials/metastatic-trials-tool)*

**Question 5:** *What are educational or informational actions that MBCA could take to better educate both patients and professionals regarding metastatic breast cancer clinical trials?*

## **Closing**

*As a breast cancer advocate and researcher, I greatly appreciate all that you do for your constituents including both patients and caregivers. MBCA will share the results of the MBC Clinical Trial Landscape and Gap Analysis with you later this year. We may invite you to review the draft report results as part of an online focus group. We are also planning a survey later this fall and may ask your help in identifying participants.*

*Thank you for your participation in this interview and for your ongoing support of MBCA initiatives.*



## APPENDIX F: MBC PATIENT INTERVIEW GUIDE

*Thank you for taking the time to speak with us. This interview should take about 40 minutes but will not extend beyond the hour you have so kindly allocated. We will use Zoom, an online communications tool that will allow us to see each other, share screens and record the conversation (with your permission).*

*The purpose of this interview with you, as a person living with metastatic breast cancer, is to help us ensure that the patient's perspective is included in the MBCA's Clinical Trial Landscape and Gap Analysis*

*We hope our interview helps the MBCA to:*

- 1) Better understand what you believe are key clinical opportunities and barriers for men and women living with metastatic breast cancer to participate in clinical trials;*
- 2) Capture your experience in being educated about, recruited into, and/or participating in metastatic breast cancer clinical trials;*
- 3) Gather your thoughts and ideas about what the MBCA and its member organizations can do to help educate individuals living with MBC, their families, and their caregivers regarding clinical trial opportunities, including the use of BreastCancerTrials.org's tools— **Metastatic Trial Search** and **Metastatic Trial Talk**; and*
- 4) Hear your thoughts on the kinds of informational, economic, demographic, and socio-economic barriers to your and other patients' participation in clinical trials (both treatment and supportive care trials), and what MBCA can do to help address those barriers.*

*I would like your permission to record this interview. It will help in capturing your thoughts and ideas. We will de-identify all comments and statements in the interview in our overall landscape assessment; however, we may request your permission to use and attribute a specific quote and/or to build a small case study regarding your organization's efforts. If that is the case, we will contact you for your permission.*

*We promise to share our findings with you in our final report that will be published on the Alliance website.*

**May I begin recording now?**

**Question 1:** *There are a range of types of opportunities for participation in clinical trials for patients living with metastatic breast cancer including treatment trials, supportive care, and palliation trials. Additionally, there are many Phase 1A/B solid tumor trials that include metastatic breast cancer patients as potential participants. It may be the case that both patients and their community oncologist may lack awareness of these trials. What has been your experience in learning about metastatic breast cancer clinical trials?*

**Question 2:** *Historically, how have you learned about metastatic breast cancer clinical trials? For example, did your oncologist or oncology nurse suggest a trial? Did you use an advocacy group online resource to learn more about trials? What, if any, search tools have you used to find relevant clinical trials?*

**Question 3:** *Do you try to stay educated about new trials and therapies? If so, what are your major sources of information? What works best for you?*

**Question 4:** *In your experience, what are the most common barriers you might have in making a decision to participate in a metastatic breast cancer clinical trial? What kinds of things might encourage you to participate in a trial (either supportive or treatment)? What might discourage you or cause you concern?*

**Question 5:** *What are educational or informational actions that MBCA could take to better educate both patients and professionals regarding metastatic breast cancer clinical trials?*

**Question 6:** *Is there anything else you would like to share?*

## **Closing**

*As a breast cancer advocate and researcher, I greatly appreciate your sharing your experiences as a patient—the one who stands at the center of this research. The Alliance will share the results of the MBC Clinical Trial Landscape and Gap Analysis with you later this year. We may invite you to review the draft report results as part of an online focus group. We are also planning a survey later this summer and may ask your help in responding and helping identify participants.*

*Thank you for your participation in this interview and for your ongoing support of MBCA initiatives.*

## APPENDIX G: HEAR OUR VOICE: PATIENT DRIVEN SOLUTIONS TO INCREASE PARTICIPATION IN CLINICAL TRIALS

In a [poster](#) presented at the San Antonio Breast Cancer Symposium in 2019, patient advocate Marina Kaplan\* studied the barriers to clinical trial participation and possible solutions from the MBC patient's perspective. She conducted a survey of 496 MBC patients.

She discovered that MBC patients' attitudes are really not barriers. Patients in the MBC setting are very willing to participate in clinical trials. Respondents generally reported positive attitudes toward trial participation. The opportunity to receive innovative treatments, help others with MBC, and contribute to research were rated as extremely important. Potential disadvantages included fear of side effects, the possibility that the trial drugs may not be effective, and financial toxicity.

System-level barriers were identified such as exclusion criteria that are too broad and eligibility criteria that are too strict. Sometimes centers offering trials do not take people's insurance, eliminating a substantial segment of the population. MBC patients were also concerned about the washout period being too long. In addition, getting to trials can be difficult because few trials that they would qualify for may be available close to where they live.

Fifty-two of the respondents were interviewed. Patients felt that trials should reflect the "real world", and that opening up eligibility criteria would increase diversity and the number of potential participants. Possible solutions to break down trial participation barriers were identified:

- Rigid eligibility and exclusion criteria should be addressed. Oncologists and scientists should develop protocols where the exclusion and inclusion criteria are absolutely critically necessary, not just for the science of the study, but also for patient safety.
- Patient advocates who are informed and educated on the science of trials and the methodologies should be consistently included in research design, protocol development, and policy decisions.
- Oncologists often do not bring up clinical trial opportunities at the first or second restaging visit. They often wait until the patient has progressed a lot, which then in turn excludes them from trials because they have been heavily pretreated. Thus, one solution is that the oncology field as a whole should be talking to patients about trial participation at every restaging visit.
- Access to necessary information to weigh benefits vs. risks should be provided.
- The washout period should be based on the half-life of the last drug.
- To reduce isolation, patients should be enabled to connect with one another if they wish.

*\* This contributor is deceased. We are grateful to her and to her family for the gift of her time and expertise for this endeavor.*

- Geographic, logistical, and financial barriers should be addressed by using more “portable” multi-institution trials and by providing transportation and adequate reimbursement for patients’ expenses.
- Labs and scans should be limited to the minimum necessary.
- Current community-based patient-led initiatives should be identified and built on to reduce disparities.

Ms. Kaplan identified an important next step, which is to collaborate with the minority community and to replicate this study as far as it makes sense in that community to obtain actionable data for minority populations.