Metastatic Breast Cancer MBCalliance

*together we are stronger than the disease*

# METASTATIC BREAST CANCER ALLIANCE

# THOUGHT LEADER SURVEY REPORT

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

DECEMBER 2021

# TABLE OF CONTENTS

# TABLE OF CONTENTS

# TABLE OF CONTENTS

# 1.

# INTRODUCTION

As part of the MBCA's original Landscape Analysis published in 2014 entitled *Changing the Landscape for People Living with Metastatic Breast Cancer*, two members of the MBCA staff conducted a series of interviews with 59 key opinion leaders (KOLs) with knowledge of MBC research. Seven questions were asked with the goal of understanding the landscape of research in MBC. Interviewees included those working in academia, nonprofit breast cancer patient advocacy groups, government, industry, and the research community. Interviews with KOLs led to identification of four main gaps: (1) lack of a tissue bank that matches primary and metastatic tumors, (2) lack of standardization of metastatic preclinical models, (3) the need for redesigned clinical trials for MBC to measure new endpoints (beyond MBC tumor shrinkage and the Response Evaluation Criteria in Solid Tumors [RECIST] scale), (4) the need to coordinate trials across multiple investigators and institutions, and (5) the need for diversification of clinical R&D funds to invest in promising new targets, moving beyond "me too" drugs, such as PI3K inhibitors. Results were published in Chapter 2 of the original Landscape Analysis and formed much of the strategic planning for the MBCA for the subsequent ~5 years.

In 2020, the MBCA sought to update this section of Chapter 2 of the Landscape Analysis, report the current landscape of MBC research, and gather knowledge that will inform the 5-year MBCA strategic plan beginning in 2021. As a first step, in Fall 2020, the MBCA conducted 20 interviews with thought leaders (TLs; previously called KOLs) with knowledge of MBC research. A breadth of knowledge was sought, and thus interviewees comprised those working in academia, industry, government, nonprofit organizations, and the research community. The list of interviewees was developed by the Thought Leader Subcommittee with input from other members of the MBCA Research Task Force. Unlike in 2014, interviews in 2020 were also conducted with MBC patient advocates to provide the voice and perspective of people living with MBC. Interviews were conducted on Zoom by four representatives of MBCA member organizations, all with scientific backgrounds. Topics covered in the interviews included recent advances in MBC research, near-term impacts, new treatments, clinical trials, new technologies, roles for advocates in MBC research, and roles for the MBCA.

# 2.

# RESULTS FROM THE THOUGHT LEADER INTERVIEWS

A detailed TL Synthesis Report (**Appendix A**) of the learnings from the interviews was prepared and used to inform the next step in the process—development of a survey to a larger group of MBC TLs. A brief summary of the results from the TL interviews is shown below.

## 2.1 RECENT ADVANCES IN MBC RESEARCH OVER THE LAST ~5 YEARS AND OUTCOMES FOR PEOPLE LIVING WITH MBC.

TLs identified many drugs and drug classes (CDK4/6 inhibitors for hormone receptor-positive MBC, targeted therapy for HER2+ MBC, and immunotherapy for metastatic triple-negative breast cancer (TNBC)) as significant breakthroughs in the last 5 years, but most TLs reported that none of these drugs are game changers. Areas requiring more research include immunotherapy for other subtypes of MBC, antibody-drug conjugates, the role of the immune system, the role of the tumor microenvironment, genetics, and tumor heterogeneity. TLs reported that because MBC patients are living longer, closer attention must be paid to collateral damage (defined as the physical, functional, psychological, emotional, social, vocational, and financial concerns of women and men who have been diagnosed with cancer and/or the quality of life [QOL] of people living with MBC). TLs identified the need to understand not only a drug's efficacy, but also the impact of therapy on financial and psychosocial aspects, the impact on the person's QOL, and the toxicity associated with treatment.

## 2.2 NEAR-TERM IMPACTS FOR PEOPLE LIVING WITH MBC OVER THE NEXT ~5 YEARS.

TLs explained that research can be more effective with greater collaborations among patients and scientists. Greater understanding is needed of the metastatic process; tumor dormancy; the role of genetics, epigenetics, and genomics; and ways to exploit that knowledge. Increased attention is needed in the areas of brain metastases, immunotherapy, liquid biopsies, better preclinical models, expanded study of biopsies, biomarkers, treatment resistance, big data, and artificial intelligence. TLs also talked about the need to break down racial barriers to improve health equity.

## 2.3 CLINICAL TRIAL DESIGN AND PARTICIPATION.

TLs identified a number of concerns with clinical trials including strict eligibility criteria, trial locations that require travel, the need for patients to find trials and educate themselves about trials, and suboptimal trial design and endpoints. TLs stated that doctors should inform their patients about trials, trials should be designed with the patient in mind, and as much as possible should be learned from every patient in every trial. Data, both positive and negative, should be shared. Decentralization of trials is required, and telehealth may help achieve this goal. Trials should be representative of the populations that are going to be treated with the drugs being tested. Efforts are needed to improve representation of diverse and underserved patients in breast cancer clinical trials.

## 2.4 POSSIBLE ROLES FOR THE MBCA.

TLs suggested numerous roles that the MBCA can play in the near future. These include increasing conversations and communications about advances in MBC, especially in the Black community who tends to be less aware of the Alliance; facilitating collaborations and connections among various stakeholders; assisting with advocacy training efforts; initiating conversations with pharmaceutical companies to encourage data sharing, including positive and negative results, and collaboration to test drug combinations; and continuing to advocate nationally for investment in clinical trials.

# 3.

# DEVELOPMENT OF THE SURVEY QUESTIONS AND ANSWERS

In the next step, the MBCA worked with CBWhite, a consultancy that specializes in working with nonprofit organizations to develop strategies informed by marketing research. Survey questions were developed based on learnings from the TL interviews as reported in the TL Synthesis Report (**Appendix A**) and summarized above. Survey questions and answers were developed by the MBCA TL Subcommittee with input from CBWhite. The objectives of the survey were to 1. Understand the impact of recent **progress** (~5 years) in MBC research, 2. Assess the **potential** of new treatments to impact the lives of those living with MBC in the next ~5 years, 3. Assess areas of **research** and **technologies** with the most **potential** to advance our understanding of MBC and impact the lives of patients, 4. Understand the importance of various aspects of **clinical trial participation**, and 5. Inform **priorities** and roles for the MBCA in the next ~5 years (Table 1). The complete list of survey questions and answer options is shown in **Appendix B**.

The list of survey respondents included some TLs from the 2014 Landscape Analysis with additional respondents suggested by members of the MBCA Thought Leader Subcommittee and the MBCA Research Task Force Members. TLs were suggested based on their familiarity and expertise in MBC, including whether they held a leadership role in an academic institution or oncology association, whether they had published a relevant pivotal article, had been awarded a large breast cancer research grant, or were known for their contributions to research and/or clinical practice relative to MBC. Patient advocates/nonprofit staff were selected based on their role in leadership, in leadership training/review panel participation, or as an influencer. A digital survey was developed and distributed to 167 TLs (with overlap with the 20 TLs who participated in the interviews). A total of 119 confidential surveys were completed (71% completion rate).

*Table 1: 2021 SURVEY SAMPLE BREAKDOWN*

| QUESTIONS | SECTION | FOCUS |
|---|---|---|
| 1-11 | Introduction | Background/Demographics |
| 12-15 | 1 OF 4 | Research Progress/5-Year Look Back |
| 16-19 | 2 OF 4 | Research Potential/Next 5 Years |
| 20-24 | 3 OF 4 | Clinical Trials |
| 25-30 | 4 OF 4 | MBCA Priorities |

A comparison of the TL project in 2014 and 2021 is shown in Table 2.

*Table 2. THOUGHT LEADER COMPARISON 2014 VS. 2021*

| DESCRIPTION | 2014 | 2021 |
|---|---|---|
| Number of People that Participated | 59 | 20 Thought Leaders + 119 survey respondents (with some overlap) |
| Stakeholder Groups | Academia, nonprofit, breast cancer patient advocacy, government, industry, research community | Academia, industry, government, MBC patient advocates, nonprofits, professional societies, research community |
| Number of Questions Asked | 7 | 30 |
| Methodology | 59 in-person interviews conducted by two Alliance staff members | 20 Thought Leader interviews conducted via Zoom by four Alliance representatives; learnings informed the digital survey distributed to 167 Thought Leaders |
| Criteria for Nomination | KOL from leadership of MBCA members or scientist listed as PI in 6 grants taken from International Cancer Research Partnership's MBC Grants Dataset | Thought Leader of MBCA member organization (nonprofit and pharma), criteria rating for research community, and MBC patient advocates |

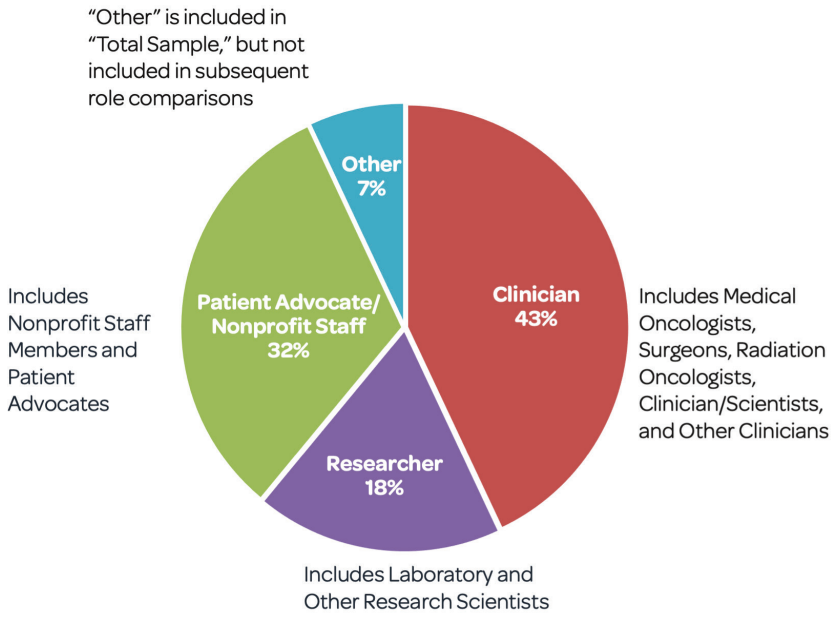
# 4.

# DEMOGRAPHIC DESCRIPTION OF SURVEY RESPONDENTS

Of the 172 digital surveys that were sent, five were returned as undeliverable, leaving 167 that were successfully delivered. Of these, 119 were completed and returned (71% response rate).

When looking at the self-identified role of the respondents, 43% were clinicians (mostly medical oncologists), 32% were nonprofit staff members or patient advocates, and 18% were researchers (mostly lab scientists) (Figure 1). According to their setting, more than half were affiliated with an academic institution, 18% were independent advocates, 12% were nonprofit staff members, and 9% were affiliated with a pharmaceutical company (Figure 2). "Role" and "setting" largely overlapped, and thus, in this report, data are described according to "role". The data are broken down according to three main roles: clinician (n = 51), researcher (n = 22), and patient advocate/ nonprofit staff (n = 38). Patient advocates and nonprofit staff were combined in the analysis because many of the nonprofit staff were also active patient advocates, responses were similar between these subgroups, and the sample size was small. After reviewing the similarity/differences in their responses, a decision was made to combine the categories. Many patient advocates/ nonprofit staff and researcher respondents spend a high proportion of their work in MBC (mode is 75% to 100%). Clinicians were more likely to spend a more "medium" proportion of their work in MBC (mode is 50% to 74%).

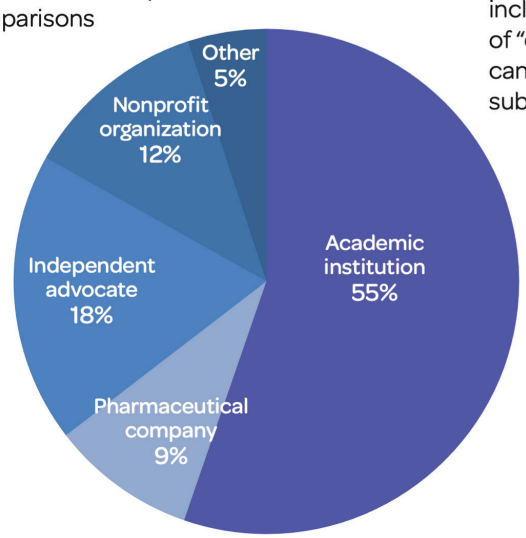
*Figure 1. Breakdown of survey respondents according to their role.*




| ROLE (full distribution) | n=119 |
|---|---|
| Clinician - medical oncologist | 30% |
| Clinician – surgeon | 3% |
| Clinician – radiation oncologist | 2% |
| Clinician – other | 2% |
| Clinician/Scientist | 6% |
| Research Scientist – laboratory scientist | 17% |
| Research Scientist – biostatistician | 0% |
| Research Scientist – computer scientist | 0% |
| Research Scientist – other | 2% |
| Nonprofit staff member | 5% |
| Patient advocate | 27% |
| Other professional role | 7% |

*Figure 2. Breakdown of survey respondents according to their setting.*

**Other** and **Does Not Apply** are included in the Total Sample, but not in subsequent setting comparisons



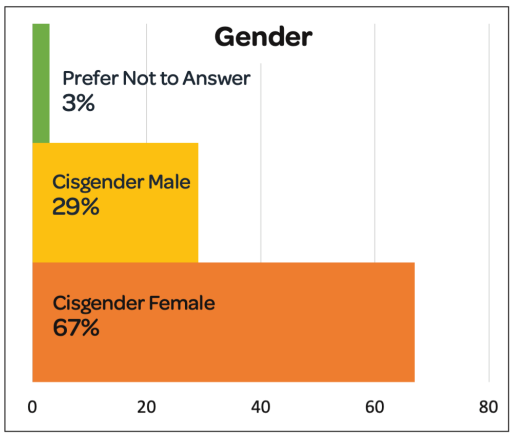

**Academic institution** includes a very small number of "community hospital/ cancer centers" in subsequent analysis

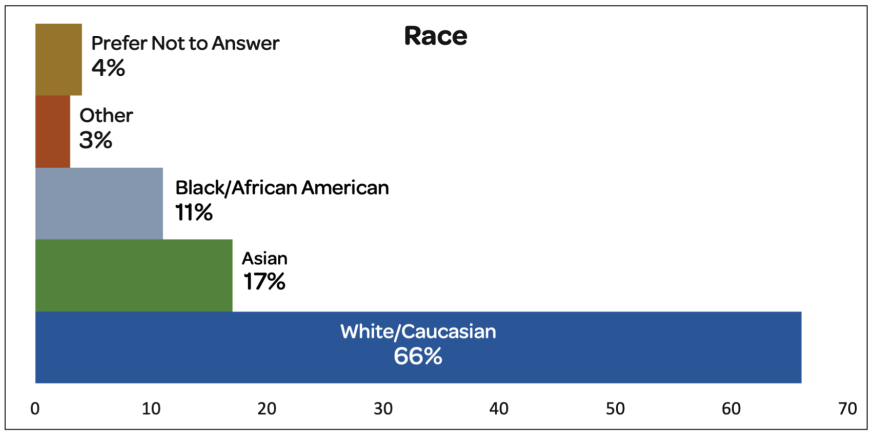
| SETTING | n=119 |
|---|---|
| Academically affiliated institution | 53% |
| Community hospital/cancer center | 3% |
| Pharmaceutical company | 9% |
| Nonprofit organization | 12% |
| Independent advocate | 18% |
| *Private practice* | *0%* |
| *Does not apply to me* | *1%* |
| *Other* | *4%* |

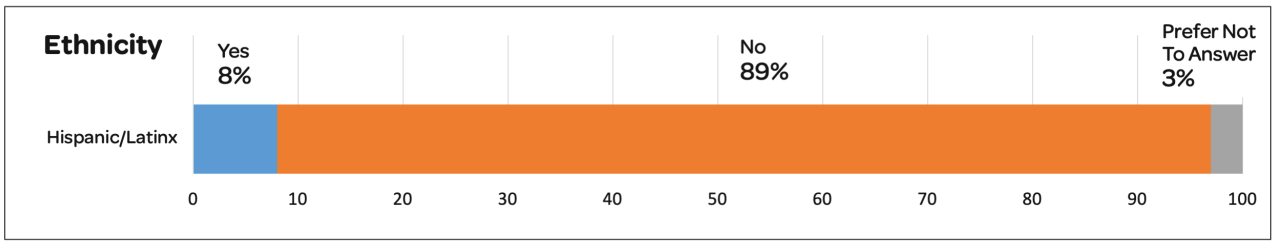
Two-thirds of survey respondents identified as female. Almost all patient advocates/nonprofit staff were female, clinicians were about 60% female, and researchers were about evenly distributed between males and females.

Two-thirds of survey respondents were white, 17% were Asian, and 11% were Black/African American. For ethnicity, 8% identified as Hispanic/Latinx (Figure 3). About three-quarters of patient advocates/nonprofit staff and researcher respondents identified as white/Caucasian. The next largest group was about one-fifth Asian among researchers and one-fifth Black/African American among patient advocates/nonprofit staff. Most clinicians identified as White/Caucasian (61%) or Asian (25%).

*Figure 3. Breakdown of survey respondents according to gender, race, and ethnicity.*



# 5.

# SURVEY RESULTS

Participants rated 90 items in four topics (Research Progress/5-Year Look Back, Research Potential/Next 5 Years, Clinical Trials, MBCA Priorities) that were presented in 14 question sets (**Appendix B**). Participants were asked to rate each of these 90 items on a scale from 1 to 5, as explained below for each topic. Participants could also select "don't know" or leave the statement blank. To report a single statistic for each item, we employed a commonly used approach that combines the responses for people who selected 4 or 5 on the five-point scale. Merging these two scale points gives a simple measure of strong enthusiasm for each item rated. Below we summarize combined responses of 4 or 5 for items considered in each of the four topics as reported by the three main roles: clinician, researcher, and patient advocate/nonprofit staff. We also consider the subset of people living with MBC (n = 22) among the patient advocates/nonprofit staff (n = 38). Their responses are stated separately when they appear quite different from the patient advocates/nonprofit staff as a whole. However, limitations with considering the subset of people living with MBC include: 1) a small number of respondents were in this group and; 2) given the small number of respondents who are living with MBC and the fact that they are all active advocates, interpretation of the differences that do exist is difficult. **Appendix C** shows the detailed responses from people living with MBC.

## 5.1 RESEARCH PROGRESS

The topic "Research Progress" was divided into three subtopics: new drugs, improving patients' QOL, and basic research. Survey participants responded to several items under each subtopic. Participants were asked about the amount of progress that has occurred over the last 5 years that has led to improved outcomes and/or QOL for people living with MBC and ranked each item on a scale from 1 to 5, with 1 being "insignificant progress", 4 being "major progress", and 5 being "significant progress". Below, we report the percentages of participants who selected 4 or 5 (combined).

### 5.1.1 NEW DRUGS

When asked about new drugs for MBC treatment, clinicians reported major or significant progress (i.e., a score of 4 or 5) in treatments for HER2-positive MBC (94%), hormone receptor-positive MBC (75%), and antibody conjugates (also called antibody-drug conjugates or ADCs; 76%). Compared to clinicians, researchers and patient advocates/nonprofit staff were less inclined to report major or significant progress for HER2-positive MBC (55% each) and hormone receptor-positive MBC (45% each), and even perceived less progress for antibody conjugates (researchers: 36%; patient advocates/nonprofit staff: 21%). All groups reported little progress for brain metastases in MBC (clinicians: 25%; researchers: 9%; patient advocates/nonprofit staff: 11%), vaccines for MBC (clinicians: 0%; researchers: 5%; patient advocates/nonprofit staff: 0%), and

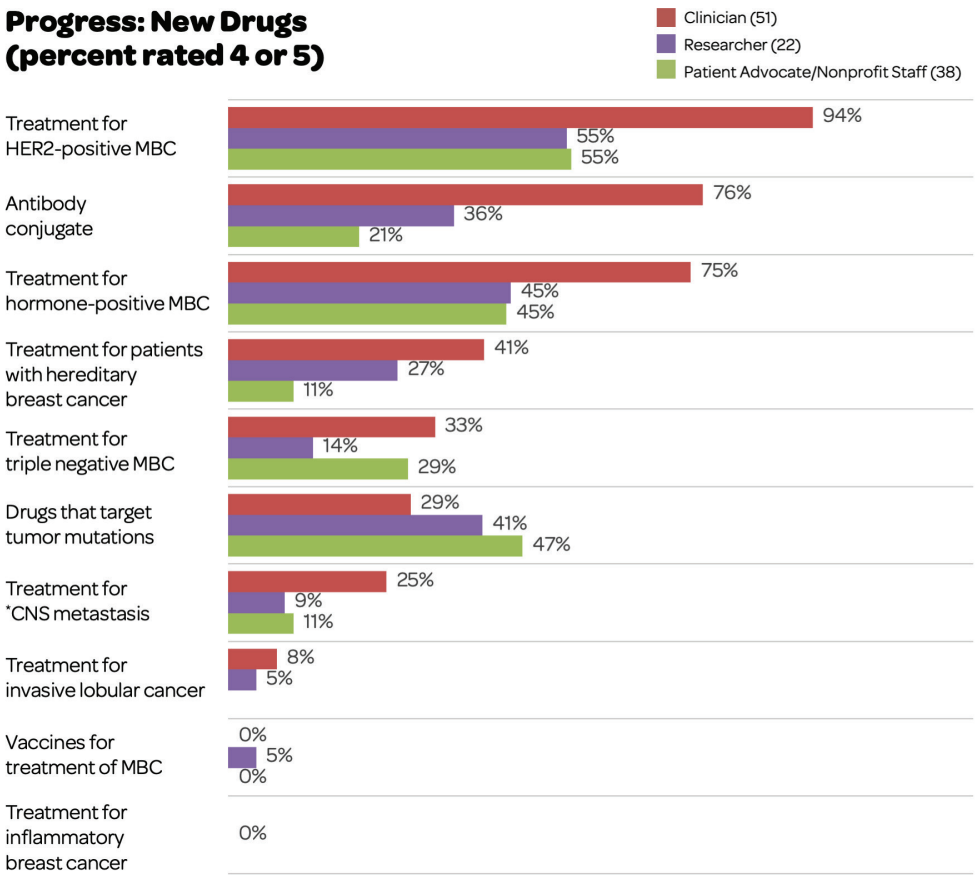
treatments for inflammatory and lobular MBC (lobular, clinicians: 8%; researchers: 5%; patient advocates/nonprofit staff: 0%. Inflammatory, 0% for all groups).

Overall, clinicians reported more progress and were more positive about that progress than researchers and patient advocates/nonprofit staff. Progress in HER2+ MBC has outpaced progress in other subtypes of breast cancer. Clinicians and researchers were less inclined than patient advocates/nonprofit staff to indicate that major improvements have been made in drugs that target specific mutations/biomarkers, although patients may be more hopeful and believe that more progress has been made.

Of note, 26% of patient advocates/nonprofit staff responded "don't know" when asked about antibody conjugates and brain metastases, 42% selected "don't know" when asked about lobular breast cancer, and 45% selected "don't know" when asked about inflammatory breast cancer.

> ***Possible action:*** These high percentages of "don't know" from patient advocates/nonprofit staff suggest an opportunity for increased education on these topics.

*Figure 4. Progress in new drugs (percent rated 4 or 5)*




| | **DK | N/A | DK | N/A | DK | N/A |
|---|---|---|---|---|---|---|
| Treatment for HER2-positive MBC | | | 5% | 9% | 13% | |
| Antibody conjugate | 6% | | 5% | 9% | 26% | 3% |
| Treatment for hormone-positive MBC | | | 5% | 9% | 5% | |
| Treatment for patients with hereditary breast cancer | | | 9% | 9% | 21% | 3% |
| Treatment for triple negative MBC | | 6% | 5% | 9% | 8% | 3% |
| Drugs that target tumor mutations | 2% | | 5% | 9% | 8% | |
| Treatment for *CNS metastasis | | 2% | 9% | 14% | 26% | 3% |
| Treatment for invasive lobular cancer | 4% | | 18% | 14% | 42% | 5% |
| Vaccines for treatment of MBC | 8% | 2% | 9% | 9% | 24% | |
| Treatment for inflammatory breast cancer | 4% | 2% | 18% | 9% | 45% | 5% |

*CNS, central nervous system.

**DK, don't know; N/A, no answer.

### 5.1.2 IMPROVING PATIENTS' QOL

When asked about progress in improving the QOL for people living with MBC, half of the researchers reported major or significant progress with liquid biopsies. Clinicians and patient advocates/nonprofit staff less frequently (clinicians: 20%; patient advocates/nonprofit staff: 21%) reported major or significant progress in this area. When considering the responses of the 22 participants living with MBC, 32% indicated major or significant progress in liquid biopsies. Researchers were more likely to rate liquid biopsies very highly compared with patient advocates/nonprofit staff and clinicians. This difference may represent advances in the research setting that have not progressed to the clinic.

Several areas were identified in which little progress has been made in the last 5 years. Fewer than half of respondents in all roles (clinicians: 45%; researchers: 27%; patient advocates/nonprofit staff: 34%; people living with MBC: 45%) reported progress in telehealth to improve access to care. Of note, this survey was conducted in the Spring of 2021 during the COVID-19 pandemic when the use of telehealth increased in general. In addition, little major or significant progress (0-18%) was noted by all groups in the areas of mitigating side effects of treatment, pain management, and mitigation of collateral damage (defined as the physical, functional, psychological, emotional, social, vocational, and financial concerns of women and men who have been diagnosed with cancer and/or the QOL of people living with MBC) due to MBC treatment and/or diagnosis; 9% of people living with MBC reported major or significant progress in each of these three areas. Overall, patient advocates/nonprofit staff reported little overall progress in improving the QOL of people living with MBC.

Many researchers responded "don't know" when asked about side effects (27%), collateral damage (27%), telehealth (32%), and pain management (50%), suggesting low levels of understanding of real-life experiences by people living with MBC and issues that are QOL related and of great importance to patients.

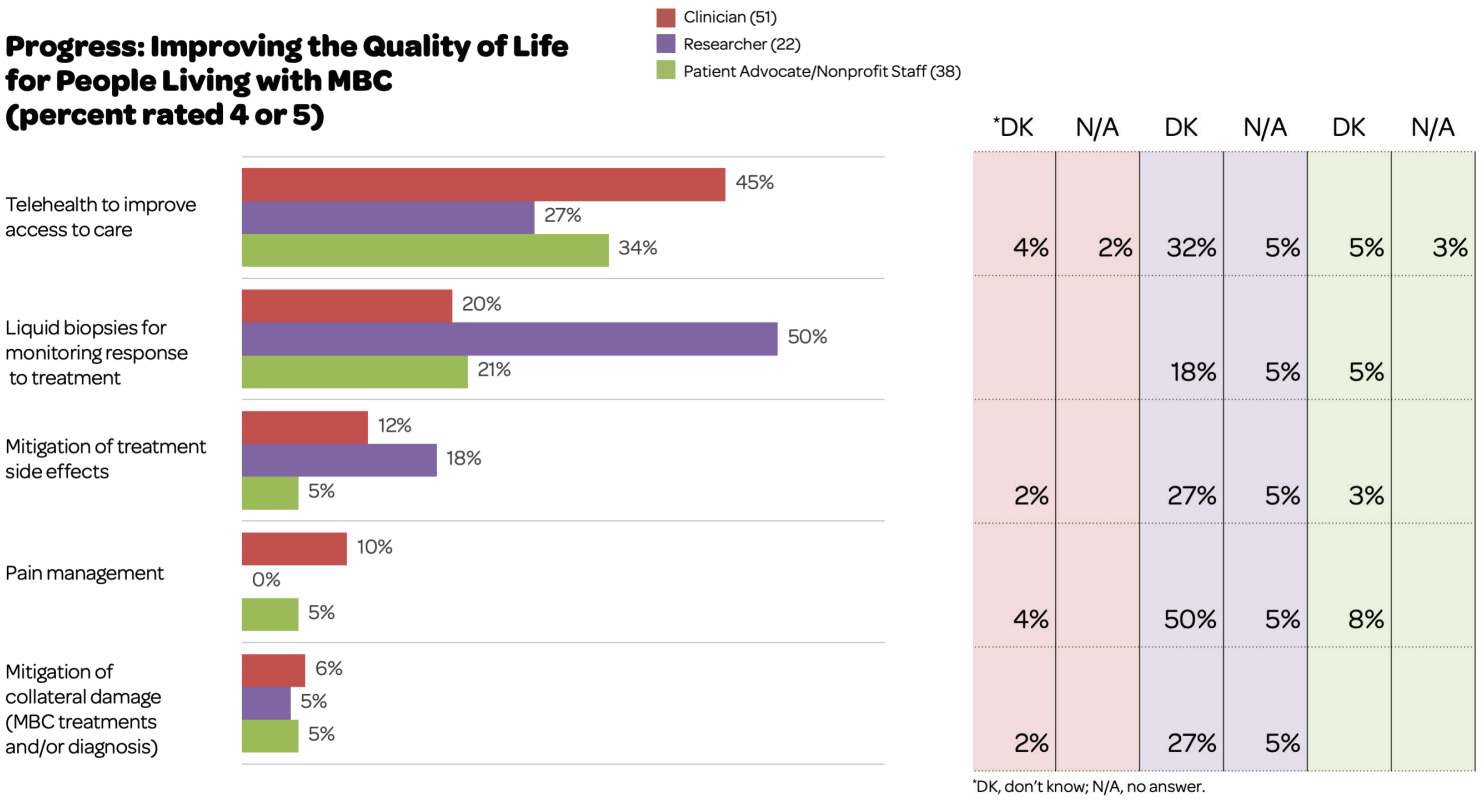
→ ***Possible action:*** Liquid biopsies: The MBCA can advocate for increased use of liquid biopsies in clinical trials.

> ***Possible action :*** Telehealth: The MBCA can monitor what happens with telehealth over time and advocate for increasing the use of telehealth for MBC patients, including those enrolled in clinical trials.

→ ***Possible action:*** Collateral damage: Peer support, although only one part of addressing collateral damage, may help mitigate these effects. The MBCA can perform an audit/inventory of efforts and gaps by its member organizations to mitigate collateral damage and determine if mitigation of side effects of treatment is part of collateral damage. The MBCA can also look into gaps and efforts by its member organizations to address financial toxicity.

> ***Possible action:*** Side effects, collateral damage, and pain management: Opportunities exist to educate scientists about the realities of living with MBC. MBCA member organizations may have ways to support this effort.

*Figure 5. Progress in improving patients' quality of life (percent rated 4 or 5)*




### 5.1.3 BASIC RESEARCH

Researchers frequently (55-68%) reported major or significant progress in multidisciplinary collaboration/translational science, understanding the immune system and the role of the tumor

microenvironment, tumor heterogeneity, and breast cancer genetics. In contrast, clinicians and patient advocates/nonprofit staff, including the subset of 22 people living with MBC, less frequently (13-37%) reported major or significant progress in these areas. Researchers also more frequently (41%) reported major or significant progress in preclinical model systems than clinicians and patient advocates/nonprofit staff (24% each). Researchers more frequently (36%) reported major or significant progress in sharing of data and resources than clinicians (22%) and patient advocates/nonprofit staff (16%; 9% of those living with MBC).

Several areas in which little progress has been made were identified. All groups reported little progress in access to serial biopsies for all populations (researchers: 5%; clinicians: 12%; patient advocates/nonprofit staff: 13%; people living with MBC: 9%). Researchers rated the amount of progress over the past 5 years higher than clinicians and patients, except for access to serial biopsies from all populations, where researchers do not see a lot of progress over the past 5 years. Collection of tissue for serial biopsies continues to present challenges, yet the need for them remains high.

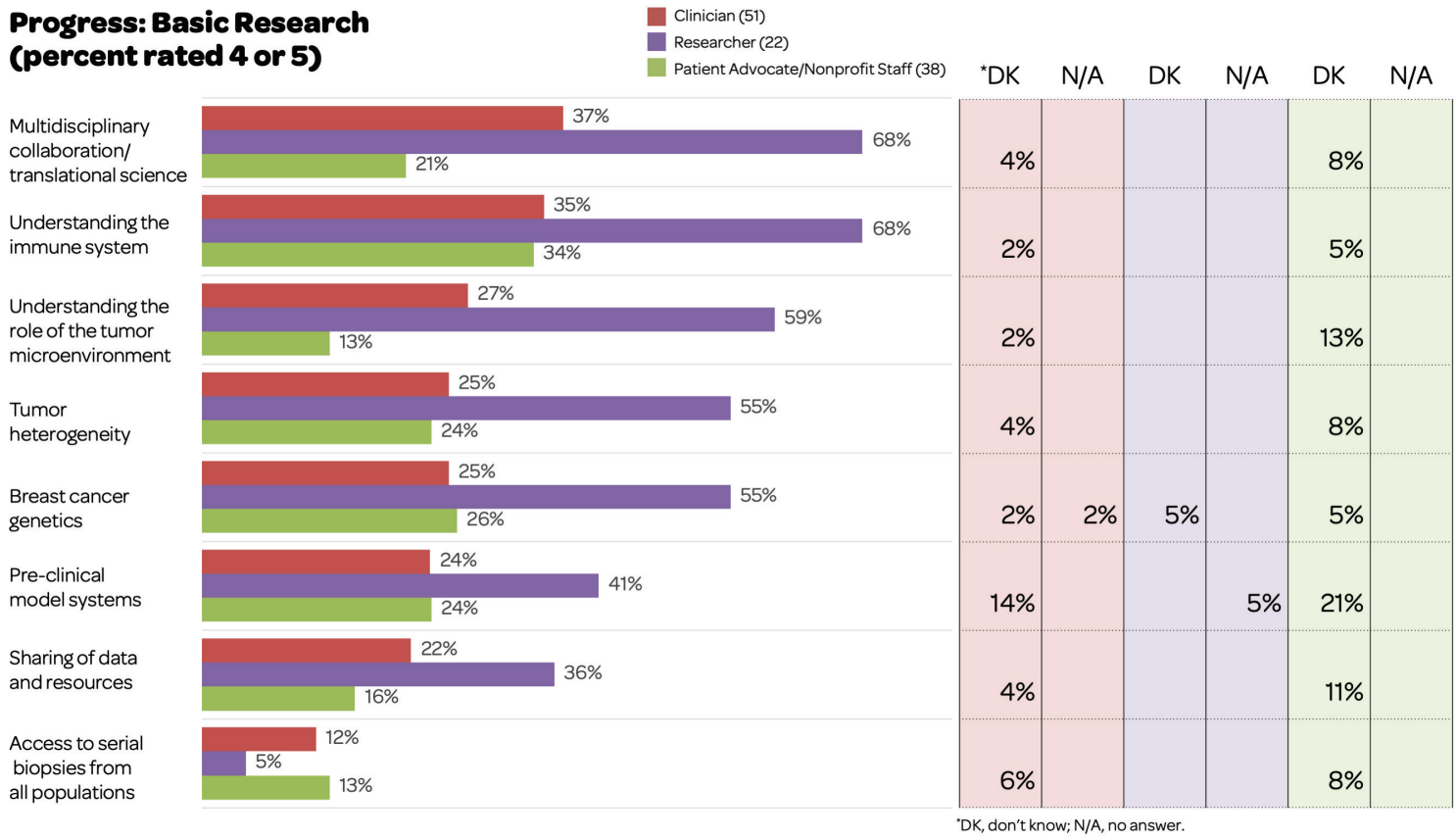
Encouragingly, very few respondents in all roles (≤21%; median, 5%) selected "don't know" for the basic research questions.

> ***Possible action:*** Opportunities exist for the MBCA to support and increase multidisciplinary collaboration, especially between researchers and clinicians, and to educate scientists about what constitutes a meaningful collaboration between patient advocates and researchers. The MBCA can continue to support the entire continuum of cancer work, so that it translates to people living with MBC.

> ***Possible action:*** Opportunities exist for advocate education in basic research in the areas of the tumor microenvironment (13% of patient advocates/nonprofit staff selected "don't know") and preclinical model systems (21% of patient advocates/nonprofit staff selected "don't know").

> ***Possible action:*** Advocate for access to serial biopsies from all populations by addressing the challenges that remain at all levels of the system.

*Figure 6. Progress in basic research (percent rated 4 or 5)*




### 5.1.4 FREE RESPONSES

Survey respondents were allowed to provide a free-text response to the question "Are there any other items that you would add to this list, when thinking about **progress** that has occurred over the **last five years** that has led to improved outcomes and/or QOL for people living with MBC (something that you might rate as a 4 or a 5)?" An increased focus was seen on research and general awareness of the needs of people living with MBC over the past 5 years. Increased capacity for clinical trial matching for MBC patients, greater inclusion of patient advocates, and more information on the web were identified as areas of progress. Additional comments included the need for patients to be educated about the FDA approval process and what accelerated approval actually means. The promise to date of precision medicine may be misleading to patients. A greater focus is needed in obtaining serial biopsies to understand metastatic disease and progression.

### 5.1.5 AREAS MOST FREQUENTLY REPORTED AS HAVING MAJOR OR SIGNIFICANT PROGRESS IN MBC RESEARCH

Overall, clinicians most frequently reported major or significant progress in treatments for HER2+ MBC (94%), hormone receptor-positive MBC (75%), and antibody conjugates (76%). Researchers most frequently reported major or significant progress in multidisciplinary collaboration/translational science (68%), understanding the immune system (68%), and understanding the role of the tumor microenvironment (59%). Patient advocates/nonprofit staff most frequently reported major or significant progress in treatments for HER2+ MBC (55%), drugs that target mutations (47%), and treatments for hormone receptor-positive MBC (45%).

## 5.2 RESEARCH POTENTIAL

The topic "Research Potential" was divided into three subtopics: basic research, biomarkers, and technologies. Participants responded to several items under each subtopic. Participants were asked about the potential for each item listed to lead to improved outcomes and/or QOL for people living with MBC over the next 5 years and ranked each topic on a scale from 1 to 5, with 1 being "insignificant potential", 4 being "major potential", and 5 being "significant potential". Below, we report the percentages of participants who selected 4 or 5 (combined).

### 5.2.1 BASIC RESEARCH

When asked about areas in basic research with the greatest potential to lead to improved outcomes and/or QOL for people with MBC, researchers ranked the tumor micro/immune/environment (91%), the immune system (86%), and the epigenome (73%) as the areas of greatest promise. The most highly ranked areas by clinicians were the immune system (73%), the tumor micro/immune/environment (65%), and genomics (63%). Patient advocates/nonprofit staff were more similar to clinicians than researchers, ranking the areas of greatest potential as the immune system (68%), the tumor micro/immune/environment (66%), and genomics (58%).

Overall, researchers saw greater potential than clinicians and patient advocates/nonprofit staff for basic research that will lead to improved outcomes and QOL for people with MBC. This is perhaps not surprising, as basic researchers are likely to be more familiar with recent advances in basic research than clinicians or patient advocates/nonprofit staff. A surprising finding was noted regarding genomics and genetics. A lot of money has been invested, but only 39-63% of participants in all groups noted major or significant progress in this area. This may be due in part to the relatively few targeted drugs that advance beyond early-stage clinical trials and limited clinical efficacy thus far of those that have. Perhaps this will change as we learn more about preventing resistance, the panel of mutated genes grows over the next 5 years, and drugs are discovered that target these mutations.

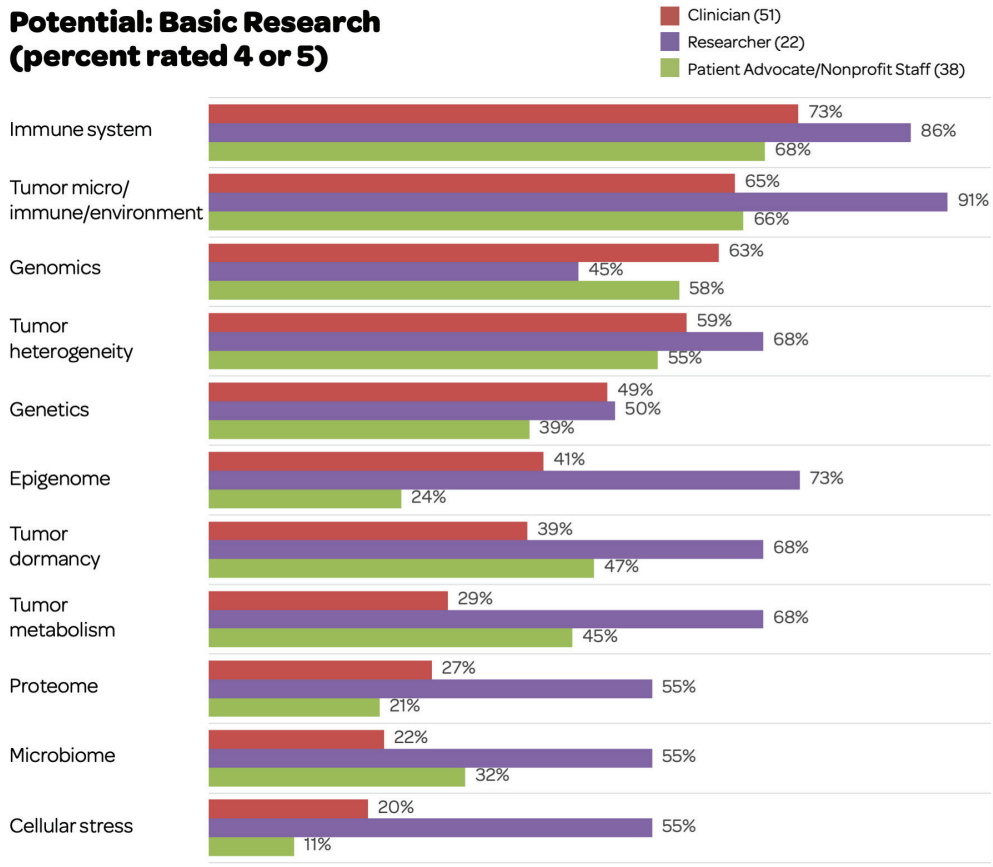
Notable differences between researchers and clinicians were seen in the areas of:

| | | |
|---|---|---|
| Genomics | Researchers: 45% | Clinicians: 63% |
| Tumor micro/immune/environment | Researchers: 91% | Clinicians: 65% |
| Epigenome | Researchers: 73% | Clinicians: 41% |
| Tumor metabolism | Researchers: 68% | Clinicians: 29% |

Patient advocates/nonprofit staff frequently selected "don't know" when asked about the proteome (42%), epigenome (32%), cellular stress (32%), and microbiome (24%).

→Possible action: Opportunities exist for advocate education in basic research in the areas of "omics" and cellular stress.

*Figure 7. Potential for basic research (percent rated 4 or 5)*




| | *DK | N/A | DK | N/A | DK | N/A |
|---|---|---|---|---|---|---|
| Immune system | 4% | | | | 3% | 5% |
| Tumor micro/ immune/environment | 4% | | | | 8% | 5% |
| Genomics | 2% | | | | 5% | 5% |
| Tumor heterogeneity | 4% | | | | 8% | 8% |
| Genetics | 2% | | | | 5% | 8% |
| Epigenome | 8% | | | | 32% | 11% |
| Tumor dormancy | 8% | | | | 8% | 11% |
| Tumor metabolism | 6% | | | | 18% | 8% |
| Proteome | 10% | 2% | | | 42% | 11% |
| Microbiome | 10% | | 5% | | 24% | 8% |
| Cellular stress | 10% | | 5% | | 32% | 8% |

*DK, don't know; N/A, no answer.

### 5.2.2 BIOMARKERS

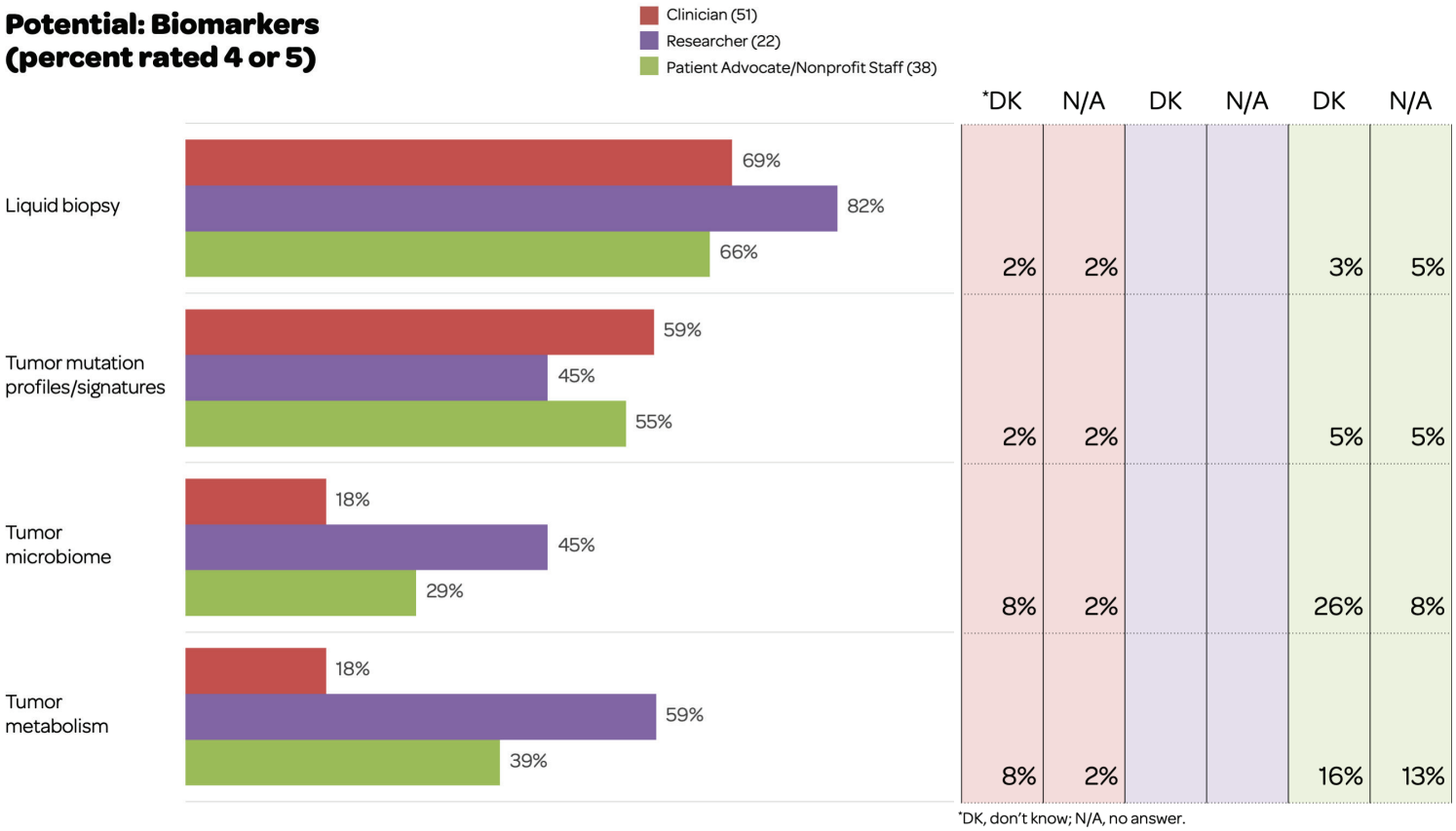
When asked about biomarkers with the greatest potential to lead to improved outcomes and/or QOL for people with MBC, researchers ranked liquid biopsies (82%) and tumor metabolism (59%) as the areas of greatest potential. Clinicians selected liquid biopsies (69%) and tumor mutation profiles/signatures (59%) as having the greatest promise. Similar to clinicians, patient advocates/nonprofit staff selected liquid biopsies (66%) and tumor mutation profiles/signatures (55%) as having the greatest potential. Thus, liquid biopsies, which could be used to follow disease progression, select treatment, and monitor mutations, were viewed as having major or significant progress by high numbers of researchers, clinicians, and patient advocates/nonprofit staff. Researchers (59%) saw more promise in tumor metabolism than clinicians (18%) and patient advocates/nonprofit staff (39%). The potential for tumor mutation profiling was viewed fairly similarly by researchers (45%), clinicians (59%), and patient advocates/nonprofit staff (55%).

For the tumor microbiome, 26% of patient advocates/nonprofit staff selected "don't know", and 16% selected "don't know" for tumor metabolism.

> ***Possible action:*** Opportunity exists for education related to the microbiome and tumor metabolism, which are active areas of research that have not reached the clinic.

> ***Possible action:*** Due to the enthusiasm among all groups for liquid biopsies, the MBCA could advocate for continued efforts to expand the use of liquid biopsies.

*Figure 8. Potential for biomarkers (percent rated 4 or 5)*




### 5.2.3 TECHNOLOGIES

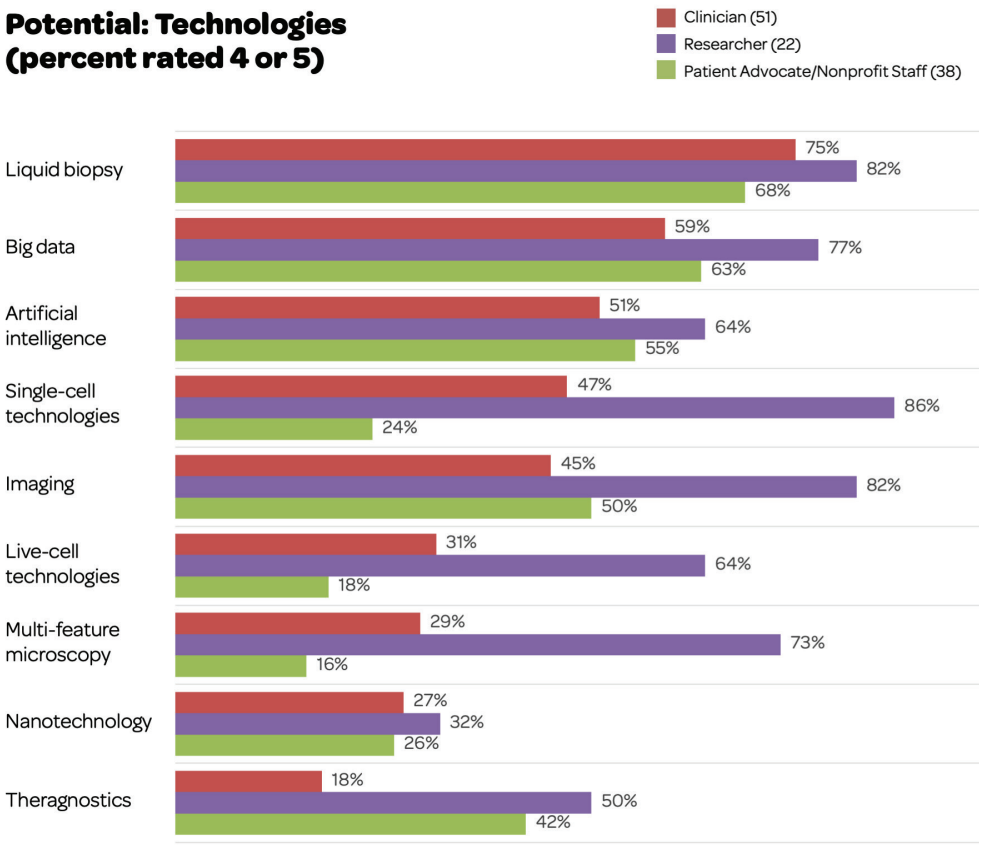
When asked about technologies with the greatest potential to lead to improved outcomes and/or QOL for people with MBC, researchers reported strong potential in single-cell technologies (86%), imaging and liquid biopsies (82% each), big data (77%), and multi-feature microscopy (73%). Clinicians reported strong potential for liquid biopsies (75%), followed by big data (59%) and artificial intelligence (51%). The three areas most frequently ranked as having major or significant potential by patient advocates/nonprofit staff were liquid biopsies (68%), big data (63%), and artificial intelligence (55%). Thus, all groups reported high potential in big data.

Patient advocates/nonprofit staff were likely to mark "don't know" for many of the areas in which researchers see high potential, including live-cell technologies (45%), multi-feature microscopy (45%), single-cell technologies (39%), and nanotechnology (39%). Clinicians were most likely to mark "don't know" for live-cell technologies (22%), multi-feature microscopy (22%), and nanotechnology (18%).

> ***Possible action:*** Due to the high percent of "don't know" responses for several areas, the MBCA could perform an audit/inventory of its member organizations to understand what education efforts currently exist.

> ***Possible action:*** Due to the enthusiasm among all groups for big data, the MBCA could support member efforts in this area.

*Figure 9. Potential for technologies (percent rated 4 or 5)*




| | *DK | N/A | DK | N/A | DK | N/A |
|---|---|---|---|---|---|---|
| Liquid biopsy | 4% | | | | 3% | 5% |
| Big data | 2% | | | | 8% | 5% |
| Artificial intelligence | 6% | | | | 16% | 5% |
| Single-cell technologies | 12% | | | | 39% | 8% |
| Imaging | 2% | 2% | | | 5% | 5% |
| Live-cell technologies | 22% | | | | 45% | 8% |
| Multi-feature microscopy | 22% | | | 5% | 45% | 8% |
| Nanotechnology | 18% | | 5% | | 39% | 5% |
| Theragnostics | 14% | | | | 24% | 5% |

*DK, don't know; N/A, no answer.

### 5.2.4 FREE RESPONSES

Survey respondents were allowed to provide a free-text response to the question "Are there any other items that you would add to this list of items, when thinking about the **potential** for improved outcomes and/or QOL for people living with MBC over the **next five years** (something you might rate as a 4 or a 5)?" A wide variety of basic research areas, biomarkers, and technologies were

mentioned as having potential, and no single method with the greatest potential was identified. Many areas have great potential, and no agreement among respondents was found for a single pathway or route to successful treatment over the next 5 years.

### 5.2.5 AREAS MOST FREQUENTLY REPORTED AS HAVING MAJOR OR SIGNIFICANT POTENTIAL IN MBC RESEARCH

Overall, researchers most frequently reported major or significant potential in the areas of the tumor micro/immune/environment (91%), the immune system (86%), and single-cell technologies (86%). Clinicians most frequently reported major or significant potential in liquid biopsies (69-75%) and the immune system (73%). Patient advocates/nonprofit staff most frequently reported major or significant potential in the immune system (68%), liquid biopsies (66-68%), and the tumor micro/immune/environment (66%).

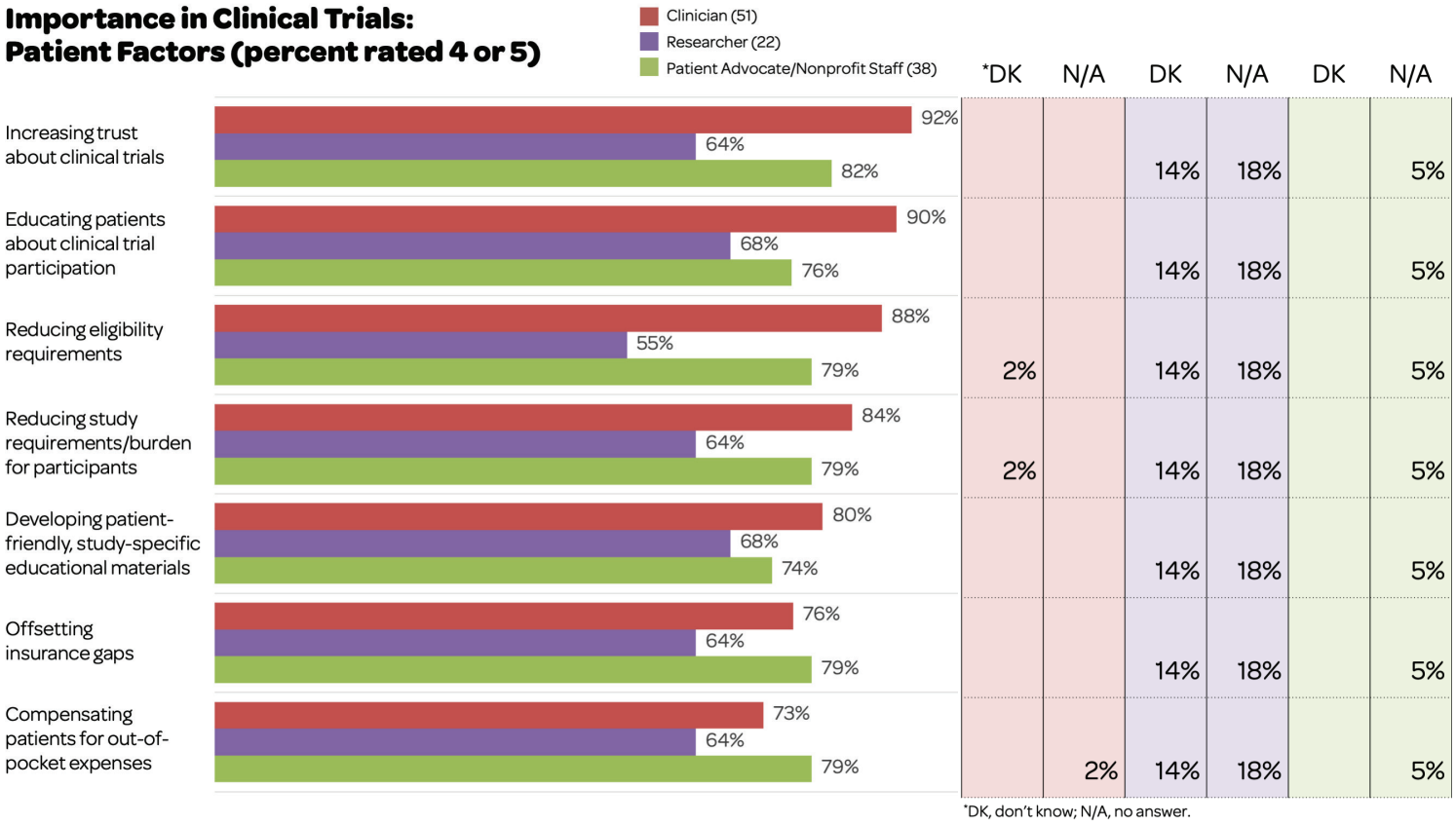
## 5.3 CLINICAL TRIALS

The topic "Clinical trials" was divided into four subtopics: patient factors, patient accrual planning, funding, and design factors. Participants responded to several items under each subtopic. Participants were asked about the importance of various factors in these subtopics related to clinical trial participation and design that may contribute to improved outcomes and/or QOL for people living with MBC and ranked each topic on a scale from 1 to 5, with 1 being "not important", 4 being "very important", and 5 being "extremely important". Below, we report the percentages of participants who selected 4 or 5 (combined).

### 5.3.1 PATIENT FACTORS

A similar pattern was seen in the responses about patient factors by researchers, clinicians, and patient advocates/nonprofit staff. Across all groups, the percentage of participants reporting that a patient factor was very or extremely important ranged from 55% to 92%. Although differences were small, clinicians and patients tended to agree, and researchers showed less enthusiasm for the various factors.

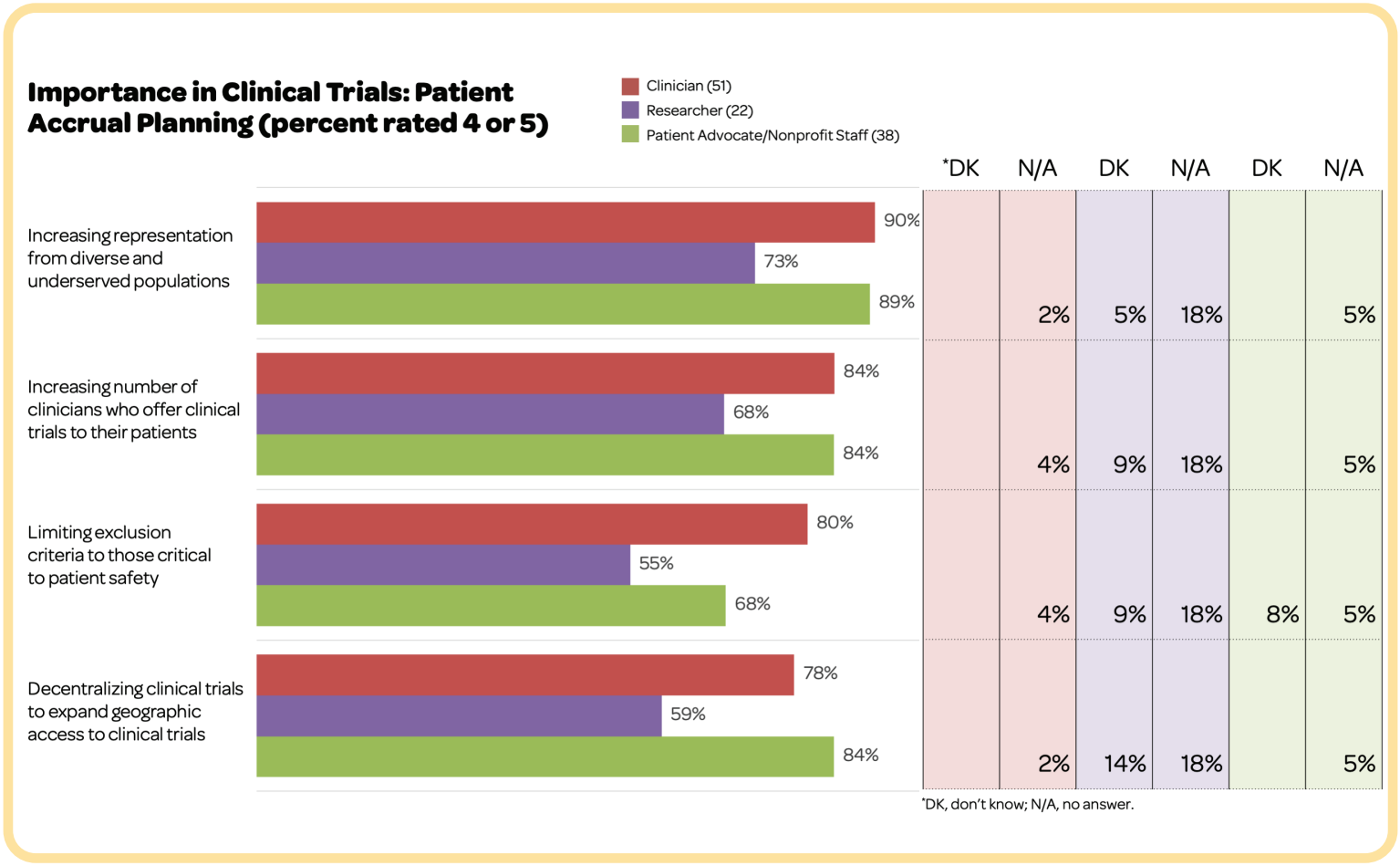
*Figure 10. Importance of patient factors in clinical trials (percent rated 4 or 5)*




### 5.3.2 PATIENT ACCRUAL PLANNING

A similar pattern was seen for the importance of factors related to patient accrual planning: clinicians and patients tended to agree, and researchers showed less enthusiasm. Across all groups, the percentage of participants reporting that a factor related to patient accrual planning was very or extremely important ranged from 55% to 90%. Factors frequently identified included representing diverse and underserved populations, increasing the number of physicians who offer clinical trials to their patients, limiting exclusion criteria to those critical for patient safety, and decentralizing clinical trials to expand geographic access to clinical trials. Increasing the number of community physicians who offer trials to their patients may require incentivization.

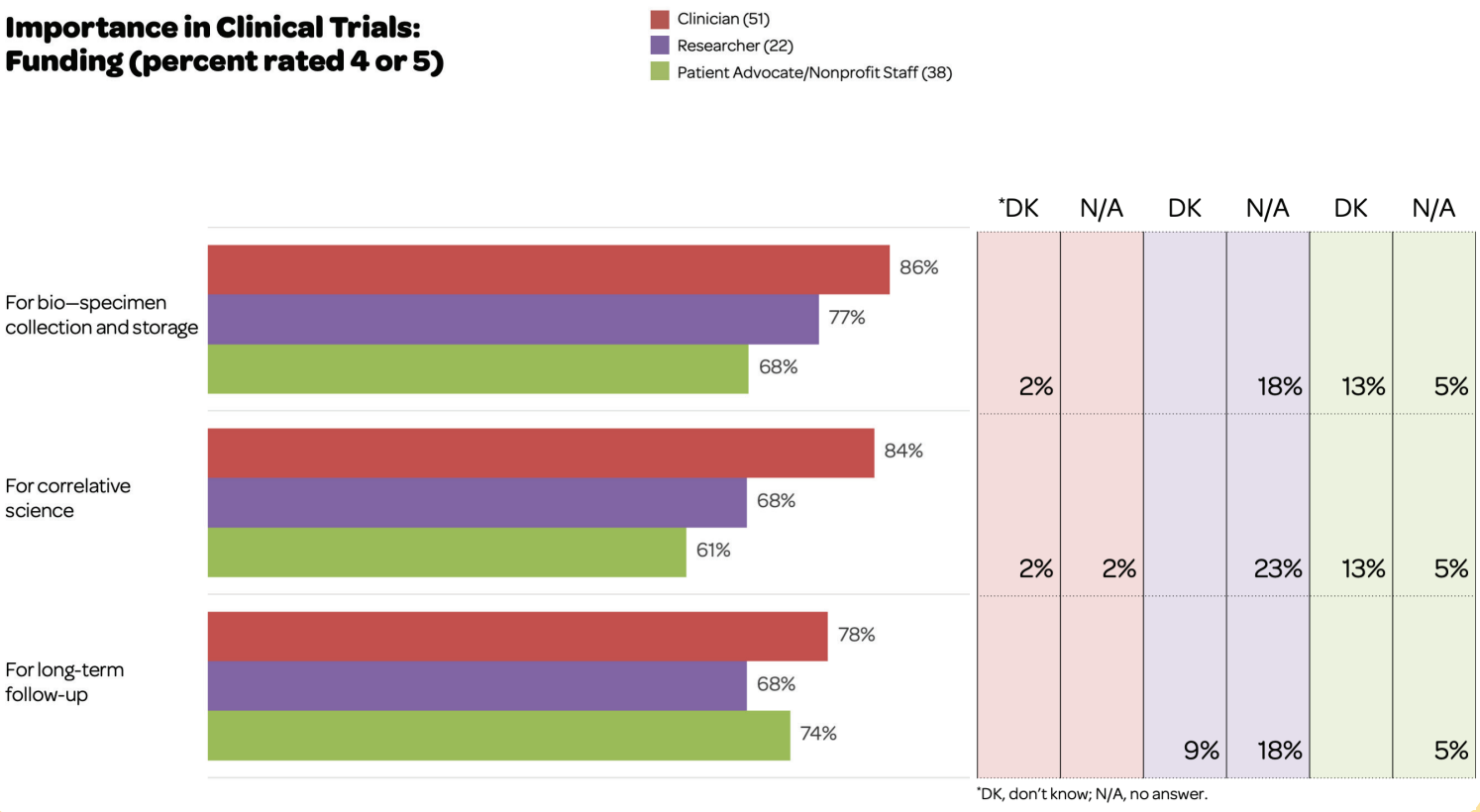
*Figure 11. Importance of patient accrual planning in clinical trials (percent rated 4 or 5)*




### 5.3.3 FUNDING

Fairly close agreement was seen among groups about factors related to funding. The range across groups was 61% to 86%. Patient advocates/nonprofit staff expressed more enthusiasm for the importance of funding for long-term follow-up (74%). Researchers typically do not receive specimens from clinical trials for correlative science, and they typically do not write clinical trial protocols. Thus, responses from researchers may be less informative, as their work does not typically involve clinical trials. Clinicians more frequently (86%) indicated the importance of funding for biospecimen collection than patient advocates/nonprofit staff (68%).

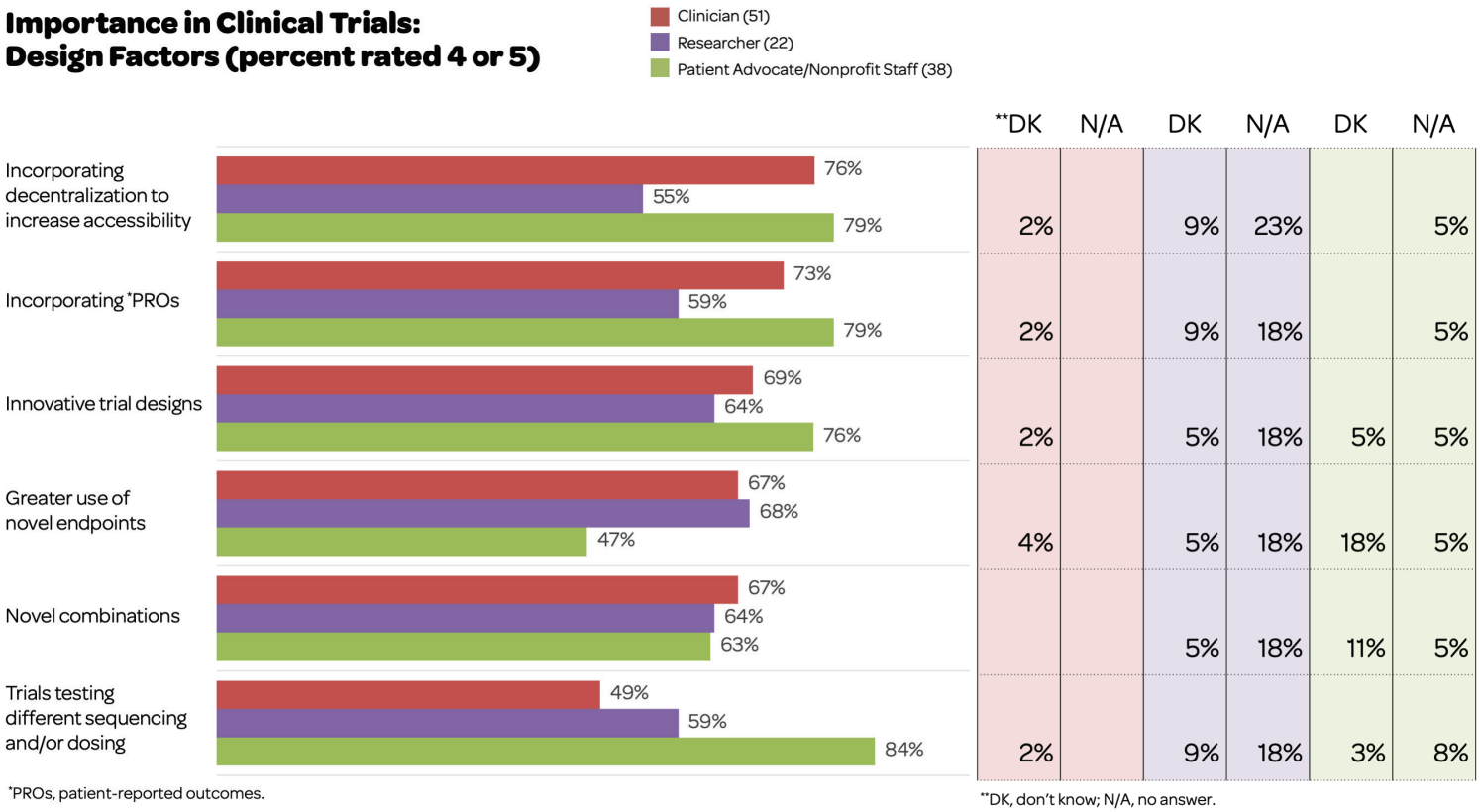
*Figure 12. Importance of funding in clinical trials (percent rated 4 or 5)*




### 5.3.4 DESIGN FACTORS

Clinicians and patients agreed on the importance of decentralizating trials to increase accessibility (clinicians: 76%; patient advocates/nonprofit staff: 79%), incorporating patient-reported outcomes into trials (clinicians: 73%; patient advocates/nonprofit staff: 79%), and innovative trial design (clinicians: 69%; patient advocates/nonprofit staff: 76%). An important point is that if physicians do not recommend trials to patients, patients may not ask about them. Thus, access to trials and awareness of trials are two different things. Patient advocates/nonprofit staff tended to be less enthusiastic about the importance of novel endpoints (47%). Clinicians were less enthusiastic (49%), and patient advocates/nonprofit staff were more enthusiastic (84%), about the importance of testing different sequencing/doses. Adding another arm to test an additional dose or treatment sequence is likely to increase cost, time to accrual, and the required number of participants, but may save patients some degree of toxicity (financial and physical) as a result. These two groups had different viewpoints on the importance of testing different sequencing/doses.

*Figure 13. Importance of design factors in clinical trials (percent rated 4 or 5)*




### 5.3.5 AREAS MOST FREQUENTLY REPORTED AS BEING VERY OR EXTREMELY IMPORTANT FOR CLINICAL TRIAL PARTICIPATION AND DESIGN THAT MAY CONTRIBUTE TO IMPROVED OUTCOMES AND/OR QOL FOR PEOPLE LIVING WITH MBC

Overall, researchers most frequently reported the following areas as being very or extremely important: funding for biospecimen collection or storage (77%); increasing representation from diverse and underserved populations (73%); and educating patients about clinical trials, developing patient-friendly education materials, increasing the number of clinicians who offer trials to their patients, funding for correlative studies and long-term follow-up, and greater use of novel endpoints (68% each). Clinicians most frequently reported the following areas as being very or extremely important: increasing trust about clinical trials (92%); educating patients about clinical trial participation and increasing representation from diverse and underserved populations (90% each); and reducing eligibility requirements (88%). Patient advocates/nonprofit staff most frequently reported the following areas as being very or extremely important: increasing representation from diverse and underserved populations (89%); and increasing the number of clinicians who offer trials to their patients, decentralizing trials to expand geographic access to trials, and testing different sequencing/dosing (84% each).

### 5.3.6 PEOPLE LIVING WITH MBC

Patient advocates/nonprofit staff (n = 38) were divided into those living with MBC (n = 22) and those not living with MBC (n = 16). Although the numbers of survey participants were small, and definitive conclusions were difficult, some trends were noted. People living with MBC were overall less enthusiastic about patient factors related to clinical trials than those without MBC. For example, 100% of those not living with MBC indicated that trust is very or extremely important, whereas 68% of those living with MBC responded this way. Similarly, 94% of patient advocates/nonprofit staff not living with MBC reported that educating patients about trials, offsetting insurance gaps, and reducing study requirements were very or extremely important, whereas 64-68% of people living with MBC responded this way. In the area of clinical trial design factors, 94% of those not living with MBC indicated that incorporating patient-reported outcomes and innovative trial designs were very or extremely important, whereas 64-68% of people living with MBC responded this way. Although the overall trend was positive regarding the importance of various factors in clinical trials, patients with MBC were less positive/optimistic that changes would result in improved outcomes. When comparing the responses from the overall 119 respondents with the responses from people living with MBC, the highest percentages of clinical trial factors reported by the overall group were increasing representation from diverse and underserved populations (87%); increasing trust about clinical trials (84%); increasing the number of clinicians who offer trials to their patients (82%); educating patients about clinical trial participation (82%); reducing eligibility requirements (79%); and increasing funding for biospecimen collection and storage (79%). Among the 22 patients living with MBC, the highest percentages for clinical trial factors reported were for increasing representation from diverse and underserved populations (82%); decentralizing clinical trials, increasing the number of clinicians who offer trials to their patients, and testing different sequencing/doses (77% each); and reducing eligibility requirements, compensating patients for out-of-pocket expenses, and incorporating decentralization to increase accessibility (73% each). Overall, people with MBC tended to view changes to trials as having a lower impact on outcomes than other groups. People living with MBC may place greater importance on factors that impact patients in the short term, but some of the items in the survey are expected to have longer-term impacts.

In the topic of clinical trials, researchers often answered "don't know" or didn't answer (up to 23% each). Clinical trials likely represent an area in which they have less knowledge and experience.

> ***Possible action:*** Opportunity exists for education of researchers about factors related to clinical trials.

> ***Possible action:*** Opportunity exists for education for patient advocates about novel endpoints.

> ***Possible action:*** The MBCA can take inventory to see what its member organizations are doing in these areas related to clinical trials and work to improve communication.

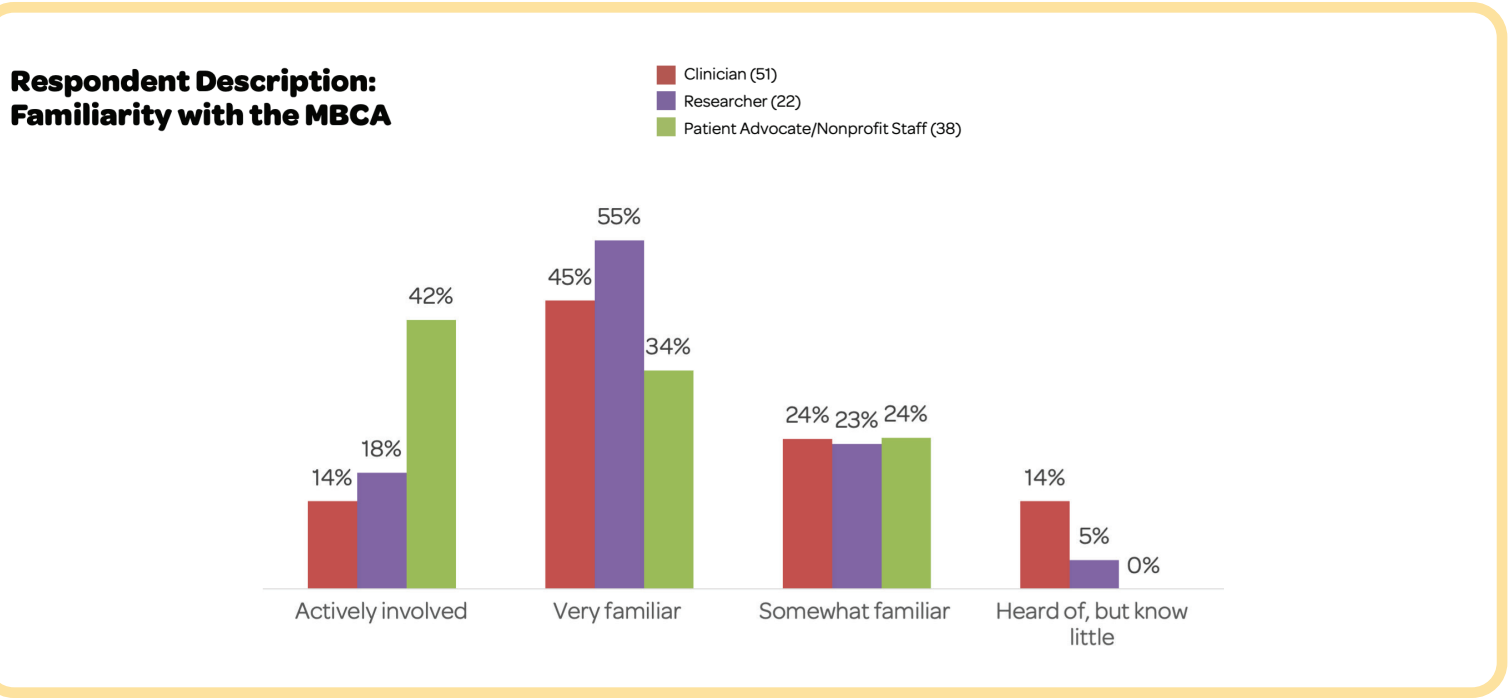
> ***Possible action:*** Drive more connection between the MBCA and member organizations to reach common goals. Ongoing efforts about clinical trials should be prioritized.

## 5.4 MBCA PRIORITIES

The topic "MBCA Priorities" was divided into four subtopics: awareness and education, collaboration, funding, and other. Participants responded to several items under each subtopic. Participants were asked about the degree of priority the MBCA should place on each topic and ranked each topic on a scale from 1 to 5, with 1 being "very low priority", 4 being "high priority", and 5 being "very high priority". Below, we report the percentages of participants who selected 4 or 5 (combined).

Respondents were asked about their familiarity with the MBCA. About three-quarters of researchers and patient advocates/nonprofit staff were actively involved or very familiar with the MBCA, with advocates more likely to be "actively involved" (42%). Almost 60% of clinicians were actively involved or very familiar with the MBCA. Overall, nearly all respondents were somewhat familiar, very familiar, or actively involved with the MBCA. The respondents' familiarity with the MBCA was considered to be sufficient for weighing in on priorities for the MBCA.

*Figure 14. Familiarity with the MBCA*



### 5.4.1 AWARENESS AND EDUCATION

For clinicians, a group that is likely interested in increasing accrual to clinical trials, the highest areas of priority for the MBCA in awareness and education were patient awareness about clinical trials (92%), public understanding of science and its breakthroughs (86%), and healthcare provider awareness about clinical trials (84%). For researchers, the highest areas of priority were patient awareness about clinical trials (91%), conversations about MBC in all breast cancer communities (91%), healthcare provider awareness about clinical trials (86%), and patient education about the importance of biospecimen donation (86%). For patient advocates/nonprofit staff, the highest areas of priority were patient awareness about clinical trials (76%), healthcare provider awareness about clinical trials (71%), conversations about MBC in all breast cancer communities (68%), and patient awareness about genetic testing and tumor profiling (68%). Only 42% of patient advocates/nonprofit staff selected public understanding of science and its breakthroughs as a high priority, perhaps because they do not see an immediate impact of public understanding of science on patient outcomes.

Clinicians (53%) and patient advocates/nonprofit staff (61%) less frequently reported patient education about the value of patient registries as an area of high priority for the MBCA compared to researchers (82%), raising the question of how familiar oncologists, surgeons, and radiologists who answered the question are with registries. MBC Connect, a patient registry sponsored by the MBCA, has not been marketed to clinicians and researchers yet. Scientists saw a greater impact for such registries. The reason that patient advocates/nonprofit staff less frequently reported this as an area of priority is not clear.

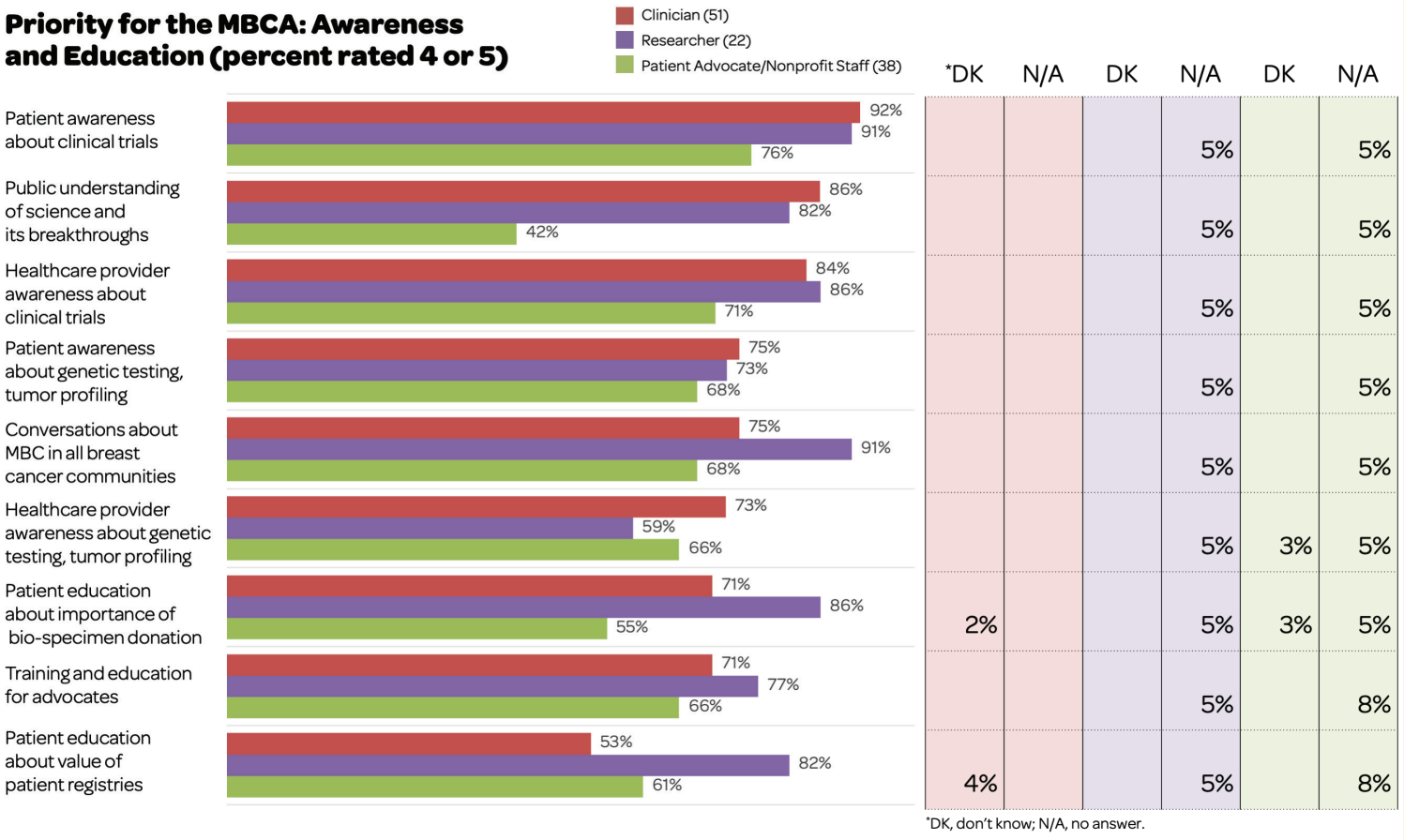
> ***Possible action:*** The MBCA may want to consider how to promote the value of MBC Connect with the patient advocacy and clinical communities.

> ***Possible action:*** Opportunities exist for education of clinicians and patients about the value to researchers of registries in general and MBC Connect in particular.

> ***Possible action:*** The MBCA can further patient education/awareness about genetic testing, tumor profiling, and biospecimen donations.

> ***Possible action:*** The MBCA could work to ensure that conversations about MBC occur in all breast cancer communities. Current efforts by MBCA member organizations may be identified through an audit/inventory, as described above.

*Figure 15. Priorities for the MBCA: awareness and education*



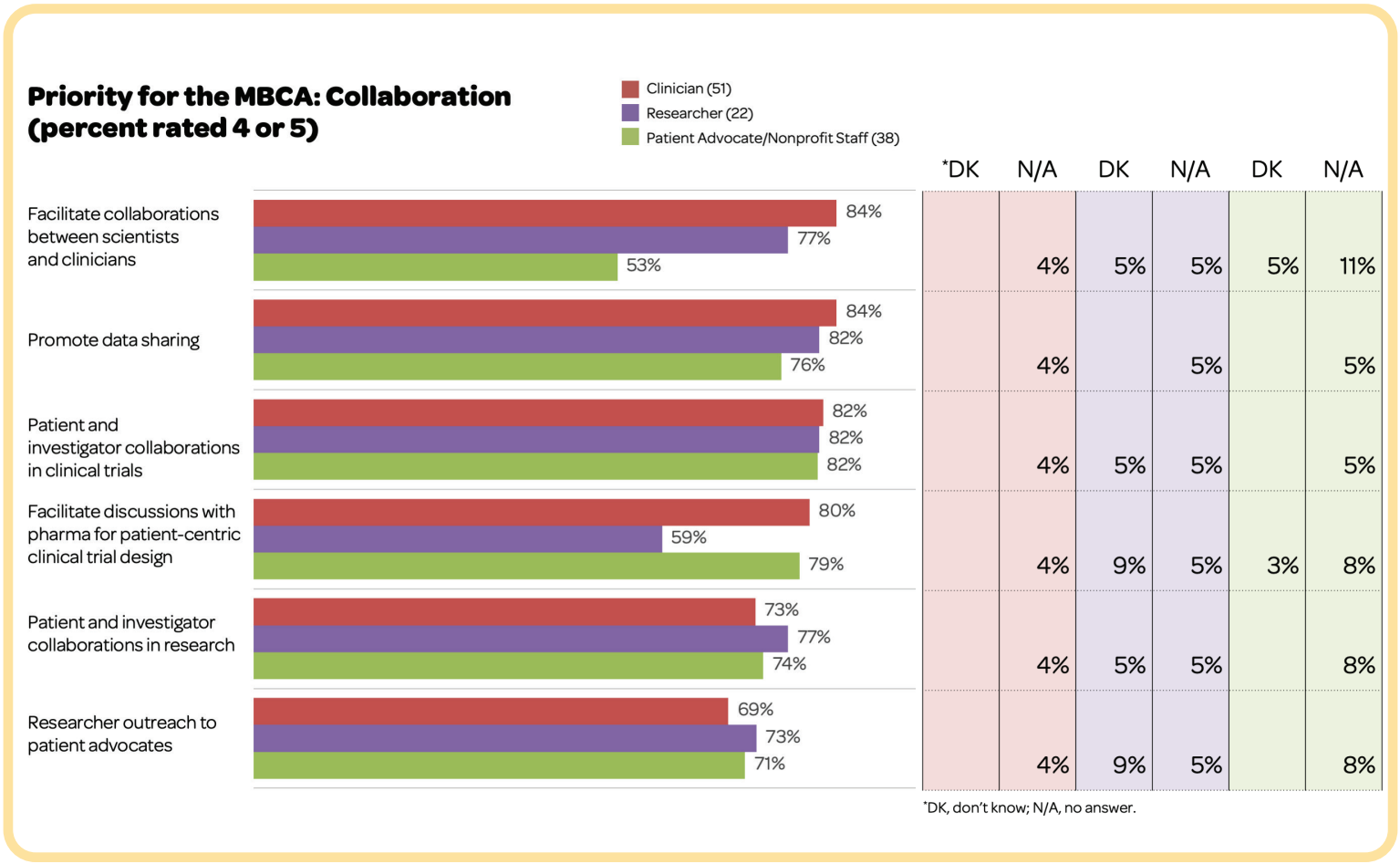

### 5.4.2 COLLABORATION

For clinicians, the highest areas of priority for the MBCA in collaboration were facilitating collaborations between scientists and clinicians (84%), promoting data sharing (84%), and patient and investigator collaboration in clinical trials (82%). For researchers, the highest areas of priority were promoting data sharing (82%), patient and investigator collaboration in clinical trials (82%), facilitating collaborations between scientists and clinicians (77%), and patient and investigator collaboration in research (77%). For patient advocates/nonprofit staff, the highest areas of priority were patient and investigator collaboration in clinical trials (82%), facilitating discussions with pharma for patient-centric clinical trial design (79%), and promoting data sharing (76%). Although data sharing may not have short-term impacts, respondents considered this to be a high priority for the MBCA. Patient advocates/nonprofit staff showed less enthusiasm (53%) than researchers

(77%) and clinicians (84%) for facilitating collaborations between scientists and clinicians, perhaps because patients are not included in these collaborations. Areas that deepen patient engagement in all phases of research were a priority for all groups. This includes data sharing. Promoting collaborative research should be a part of the MBCA mission because all three groups believed that together they should be partners in research. Collaboration may also close education gaps noted (e.g., section 5.1.1, 5.1.3, etc.). Identification of areas in which individuals, nonprofits, and industry align may facilitate collaboration. The MBCA can promote collaboration, especially in areas that engage patients. Only 59% of researchers reported that facilitating discussion with pharma for patient-centric clinical trial design was an area of high priority for the MBCA, whereas 79% of patient advocates/nonprofit staff and 80% of clinicians rated this as an area of high priority. The low percentage among researchers may reflect a lack of understanding among researchers that restrictive clinical trial requirements can be removed through such discussions.

> ***Possible action:*** The MBCA should work to advocate for open data sharing within clinical trials and registries.

*Figure 16. Priorities for the MBCA: collaboration*



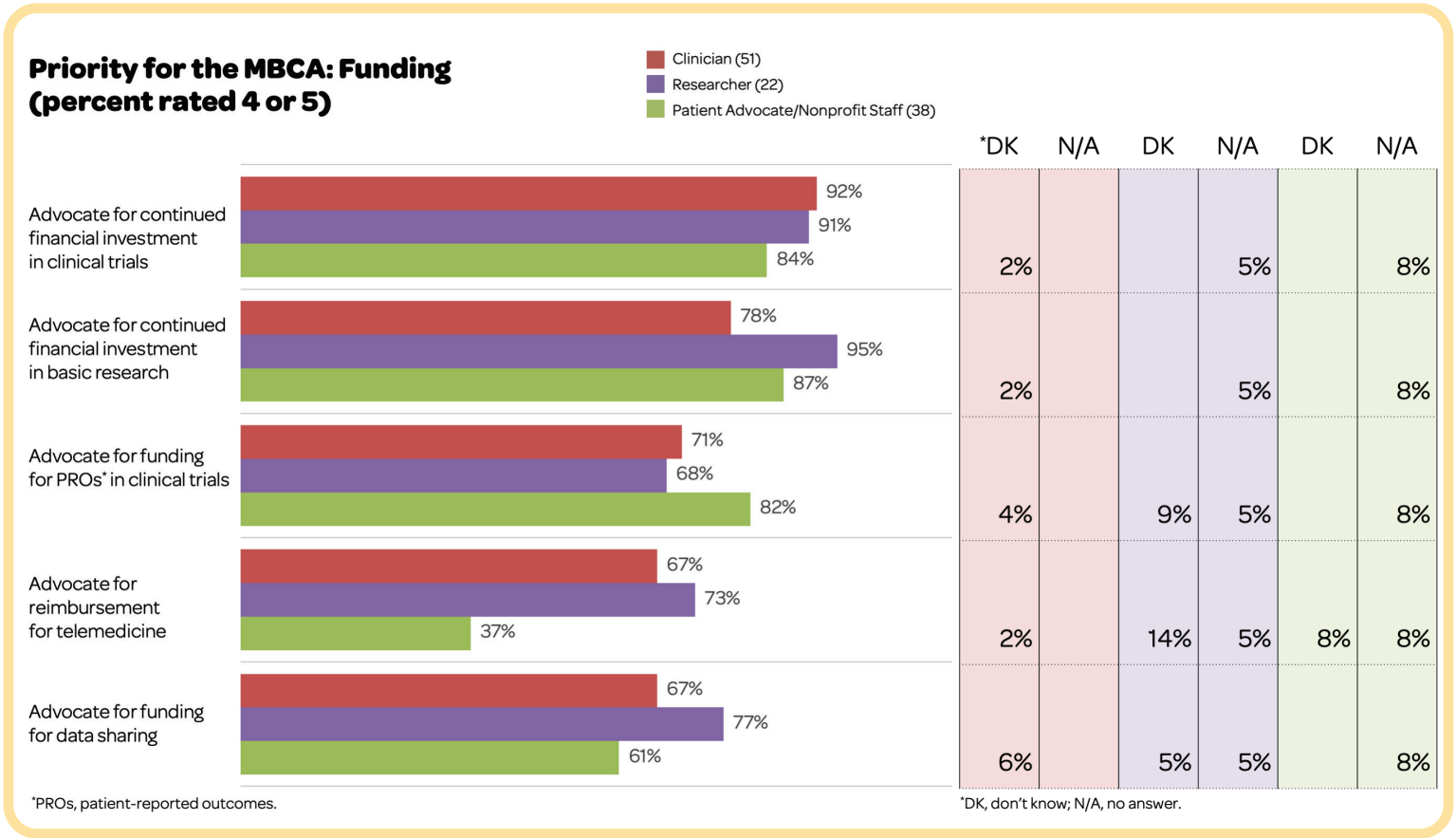
### 5.4.3 FUNDING

For clinicians, the highest areas of priority for the MBCA in funding were to advocate for continued investment in clinical trials (92%), continued investment in basic research (78%), and funding for patient-reported outcomes in clinical trials (71%). For researchers, the highest areas of priority were to advocate for continued investment in basic research (95%), continued investment in clinical trials (91%), and funding for data sharing (77%). For patient advocates/nonprofit staff, the highest areas of priority were to advocate for continued investment in basic research (87%), continued investment in clinical trials (84%), and funding for patient-reported outcomes in clinical trials (82%). Thus, investments in clinical trials and basic research were considered areas of high priority for the MBCA by all groups. Advocates placed high priority on patient-reported outcomes in clinical trials. The MBCA can advocate for data sharing but not advocate for funding for data sharing, as funding may not be a major barrier to data sharing.

Telemed was not frequently selected as an area of high priority by patient advocates/nonprofit staff (37%). The reason telemed was not frequently given high priority by patient advocates/nonprofit staff is unclear and is an area that could be further explored.

> ***Possible action:*** The MBCA can advocate for data sharing.

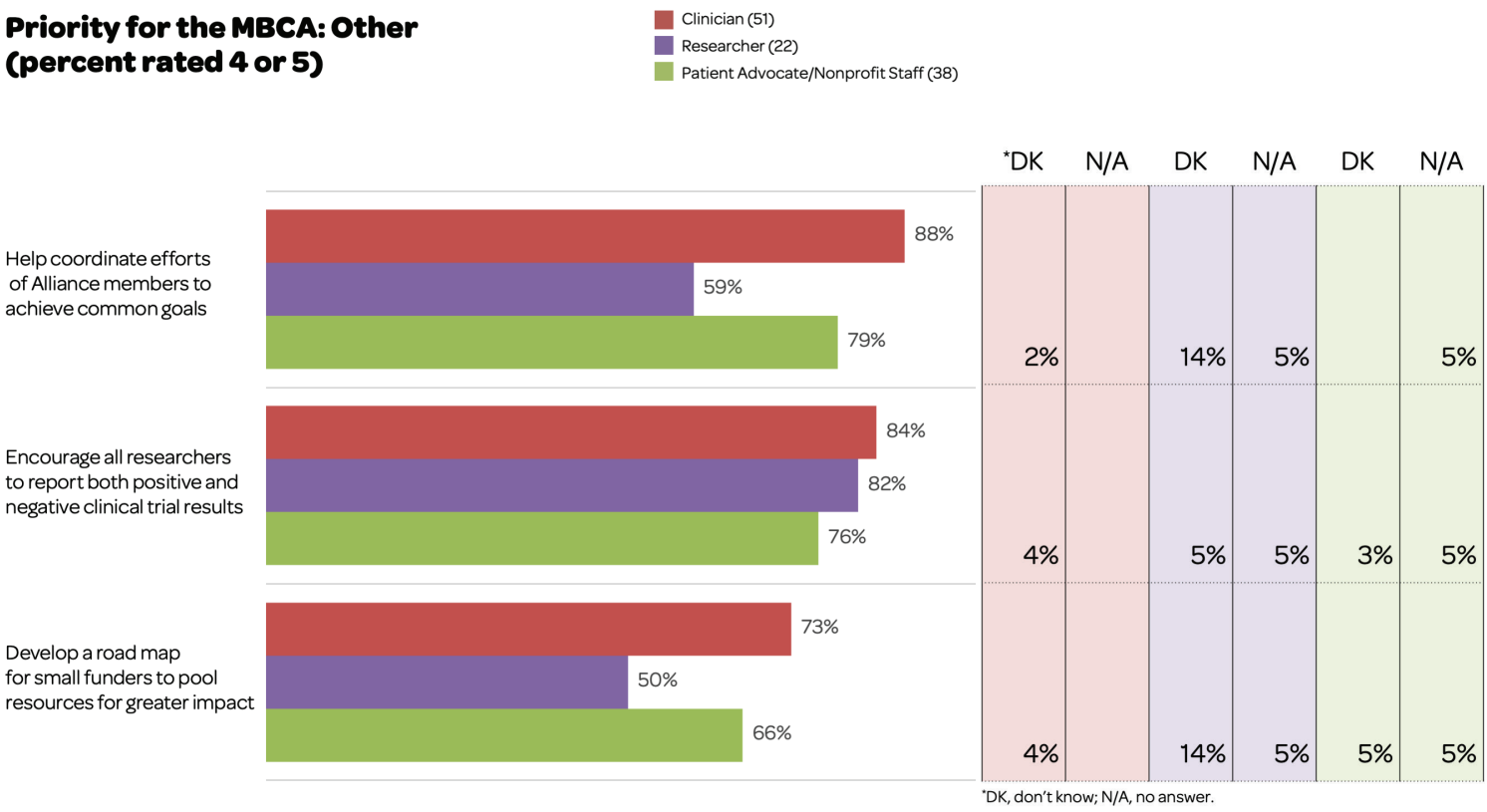
*Figure 17. Priorities for the MBCA: funding*



### 5.4.4 OTHER

Clinicians (88%) and patient advocates/nonprofit staff (79%) reported that helping coordinate efforts of Alliance members to achieve common goals is a high priority for the Alliance. Only 59% of researchers selected this as an area of high priority. In addition, 14% of researchers selected "don't know", suggesting that this may not be an area in which they have much knowledge.

*Figure 18. Priorities for the MBCA: other*




The percent of participants responding "don't know" in the topic of priorities for the MBCA was very low. Overall, participants understood the topic and associated questions and weighed in.

### 5.4.5 AREAS MOST FREQUENTLY REPORTED AS BEING OF HIGH OR VERY HIGH PRIORITY FOR THE MBCA

Overall, researchers most frequently reported the following areas as being of high or very high priority for the MBCA: patient awareness about clinical trials (92%); advocating for continued

investment in clinical trials (92%); and helping coordinate efforts of Alliance members to achieve common goals (88%). Clinicians most frequently reported the following areas as being of high or very high priority: advocating for continued investment in basic research (95%); advocating for continued investment in clinical trials (91%); patient awareness about clinical trials (91%); and conversations about MBC in all breast cancer communities (91%). Patient advocates/nonprofit staff most frequently reported the following areas as being a high or very high priority: advocating for continued investment in basic research (87%); advocating for continued investment in clinical trials (84%); advocating for funding for patient-reported outcomes in clinical trials (82%); and patient and investigator collaborations in clinical trials (82%).

The three groups were highly invested in patient and investigator collaboration in clinical trials, advocating for funding for clinical trials, and inclusion of patient-reported outcomes in clinical trials. Significant unified agreement was seen among the three groups that data should be shared and for clinical trial researchers to report both positive and negative clinical trial results. Greater patient and healthcare provider awareness about clinical trials and their importance is needed. This may be particularly true for healthcare providers in community settings, where access to clinical trials is more limited.

> ***Possible action:*** The MBCA should promote patient and investigator collaboration in clinical trials, advocate for patient-centric clinical trial designs, and promote the inclusion of patient-reported outcomes in clinical trials.

# 6.

# THE LANDSCAPE OF MBC RESEARCH IN 2014 AND 2021

In 2014, the MBCA conducted interviews with 59 key opinion leaders (KOLs; now referred to as Thought Leaders). KOLs were asked seven questions, but overall they cautioned against focusing on only these questions. Some of the main topics identified are shown in Table 3 (see Table 5 in Chapter 2 of the original LA). Many of the topics covered in 2014 were also discussed in 2020-2021 in the TL Synthesis Report (**Appendix A**) and the TL survey and are also summarized in Table 3.

*Table 3.*

| TOPIC | 2014 | 2020-2021 | ADDITIONAL OBSERVATIONS |
|---|---|---|---|
| Targeted therapies | Targeted therapies hold great promise. CDK4/6 inhibitors, PARP inhibitors, and HSP90 inhibitors are the most advanced in the drug development pipeline. | CDK4/6 inhibitors and PARP inhibitors are important drugs now available for treating some people with MBC | HSP90 drugs were not mentioned by TLs in 2020-2021. |
| Brain metastases | Controlling brain metastases is an unmet need. | Survey participants reported little progress in treating brain metastases (Figure 4). | There have been some recent efforts to include patients with both active and stable brain metastases in clinical trials (https://files.constantcontact.com/b642a850501/d5b075bf-15e5-42e9-b21b-9e755cfbd710.pdf). Tucatinib has recently been approved for use in patients with HER2+ MBC and brain metastases and is being tested to prevent breast cancer brain metastases (FDA approves tucatinib for patients with HER2-positive metastatic breast cancer \| FDA). |
| ER+ MBC | KOLs identified the need to understand late relapse of ER+ MBC and how to treat it. | 45-75% of survey participants identified major or significant progress in treatments for HR+ MBC (Figure 4). | This topic remains urgent because most patients on CDK4/6 inhibitors will eventually recur. A new class of drugs, oral selective estrogen receptor degraders, are being developed. |

| TOPIC | 2014 | 2020-2021 | ADDITIONAL OBSERVATIONS |
|---|---|---|---|
| HER2+ MBC | KOLs identified the need for long-term, safe treatments for controlling HER2+ MBC. | 55-94% of survey participants identified major or significant progress in treatments for HER2+ MBC (Figure 4). | Recent clinical trials (ATEMPT and COMPASS) focused on de-escalating therapy for patients HER2+ early-stage breast cancer with good prognosis have resulted in new approaches to treatment. This concept is under investigation in MBC. |
| TNBC | KOLs identified the need for more effective treatments of TNBC. | Only 14-33% of survey participants identified major or significant progress in treatments for TNBC (Figure 4). | Since 2014, an increasing number of agents has been approved including immunotherapy, with limited benefit for most patients. |
| Inflammatory breast cancer (IBC) | KOLs identified the need for more effective treatments for IBC. | 0% of survey participants indicated significant progress in new drugs for IBC. 45% of patient advocates/nonprofit staff and 18% of researchers selected "don't know" for this question (Figure 4). | The survey results indicate a lack of knowledge about IBC by patient advocates/nonprofit staff and researchers who were survey participants. |
| Lobular breast cancer (LBC) | | 42% of patient advocates/ staff and 18% of researchers selected "don't know" for this question (Figure 4). | The survey results indicate a lack of knowledge about LBC by patients who were survey participants. The LBC Alliance is working hard to change this. |
| Understanding the process of metastasis | KOLs identified the need for greater understanding of the biology in the steps of metastasis to improve targeted therapy. | TLs mentioned multiple areas of active research on this topic as well as new technologies, e.g., single-cell analysis. | |
| Vulnerable populations | KOLs identified the need to study MBC tissue from different populations such as young women and underserved ethnic minorities. | Survey participants reported little progress in access to serial biopsies from all populations (Figure 6). | Addressing cancer health disparities and inferior outcomes for Black and Brown people living with MBC remains an urgent priority. |

| TOPIC | 2014 | 2020-2021 | ADDITIONAL OBSERVATIONS |
|---|---|---|---|
| Tumor biopsies | KOLs identified the need for matched primary and metastatic tumors and blood samples collected at various time points. | One example of a successful effort is the AURORA Study (TL interviews). | More efforts are needed, and collaboration is an area of opportunity. |
| Preclinical models | KOLs identified the need for validated, standardized preclinical MBC model systems including reproducible in vivo models. | 24-41% of survey participants reported major or significant progress in preclinical models (Figure 6). | More progress is needed in the development of predictive preclinical models. |
| Cancer cells and interactions with the tumor microenvironment | KOLs identified the need to understand cancer stem cells, cell invasion, MBC-related cell signaling and proliferation, tumor dormancy, the immune system, and the microenvironment. | For the immune system, 34-68% of survey participants reported major or significant progress. For the microenvironment, 13-59% of survey participants reported major or significant progress (Figure 6). | This area of research has not yet translated to significant benefit to MBC patients. |
| Microbiome | KOLs identified the need to understand the role of the microbiome in health, immune function, and response to therapy. | 22-55% of survey participants reported major or significant potential for the microbiome in basic research (Figure 7). 18-45% reported major or significant potential for the microbiome as a biomarker (Figure 8). | Research related to the microbiome has not yet had an impact on patients living with MBC. |
| Liquid biopsies | KOLs identified the need for a better understanding of circulating tumor cells and circulating tumor DNA and what they mean clinically. | 66-82% of survey participants reported major or significant potential for liquid biopsies (Figures 8 and 9). | TL responses suggest progress over the last 5 years in advancing the utility of liquid biopsy for research and clinical application. |
| Patient accrual to clinical trials | KOLs indicated that recruiting patients to clinical trials is challenging. | Survey participants identified many topics as being very or extremely important in patient recruitment to clinical trials (Figures 10 and 11). | There is increasing awareness of the urgent need to include diverse populations and limit eligibility criteria. |

| TOPIC | 2014 | 2020-2021 | ADDITIONAL OBSERVATIONS |
|---|---|---|---|
| Patient-reported outcomes | KOLs indicated that QOL measures are needed in all clinical trials. | 59-79% of survey participants identified patient-reported outcomes as being very or extremely important to include in clinical trials (Figure 13). | Progress has been made, including the FDA's support of patient-reported outcomes (FDA In Brief: FDA Provides Guidance on Measuring Patient-Reported Outcomes in Cancer Clinical Trials \| FDA), but more progress is needed. |
| Clinical trial endpoints | KOLs identified a need for clinical trial endpoints beyond tumor shrinkage and the RECIST scale, such as time to new metastases. | 47-68% of survey participants identified novel endpoints as being very or extremely important to include in clinical trials (Figure 13). | More patient-centric endpoints are needed. |

# 7.

# ACTION ITEMS FOR THE MBCA

Based on areas of enthusiasm, areas of concern, and areas in which a lack of knowledge was identified, possible action items for the MBCA were identified in the following categories:

## 7.1 EDUCATION IS NEEDED:

**For patients/advocates about:**

- Rare subtypes of MBC including lobular and inflammatory
- Emerging drugs, including drugs for brain metastases
- Emerging areas of basic and translational research in MBC, including the tumor microenvironment, preclinical model systems, tumor profiling, the microbiome, and tumor metabolism
- Novel endpoints in clinical trials
- The value of registries including MBC Connect, and biospecimen donations
- Recent progress in treating people with HER2+ MBC with brain metastases

**For scientists about:**

- The realities of living with MBC
- What constitutes a meaningful collaboration between patient advocates and researchers
- Factors related to clinical trials

**For clinicians about:**

- The value of registries including MBC Connect to researchers
- The value patient advocates place on dosing and sequencing studies

The MBCA can partner with its member organizations to elucidate what online education is available, inventory ways to educate patients and other stakeholders, develop a guide for patients, and assemble study groups of interested patients. Doing so will improve the ability of advocates to serve as grant reviewers. The MBCA could also strive for collaborative education in which collective knowledge is shared among clinicians, researchers, and patient advocates. In addition, providing opportunities for greater communication between clinicians and researchers in areas in which they disagree and that are of specific interest to the MBCA could be beneficial.

## 7.2 THE MBCA SHOULD PERFORM AN AUDIT/INVENTORY OF EFFORTS AND GAPS BY ITS MEMBER ORGANIZATIONS:

→

- To mitigate collateral damage and financial toxicity
- To understand what education efforts currently exist, especially about those topics listed in section 7.1
- In areas related to clinical trials, such as including patient-reported outcomes in trial reporting, increasing representation from diverse and underserved populations, and reducing eligibility requirements to include only those necessary for safety
- To ensure that conversations about MBC occur in all breast cancer communities

## 7.3 THE MBCA SHOULD ADVOCATE:

- For the use of liquid biopsies in clinical trials
- For telehealth options for MBC patients
- To increase access to serial biopsy tissue/blood from all populations and to help clinical trial participants understand their importance
- For data sharing
- For patient-centric clinical trial designs
- For the inclusion of patient-reported outcomes in clinical trials

## 7.4 THE MBCA SHOULD:

- Support multidisciplinary collaboration, especially between researchers and clinicians
- Support its member efforts in big data
- Support connections between the MBCA and member organizations to reach common goals
- Promote the value of MBC Connect
- Promote patient and investigator collaboration in clinical trials
- Create a database of trained patient advocates

# ACKNOWLEDGMENTS

Report prepared by Kristine De La Torre, PhD, with input and guidance from Elizabeth Frank, Jane Perlmutter, Margaret Flowers, PhD, the Thought Leader subcommittee, and other MBCA members and representatives of MBCA member organizations. The MBCA is grateful to the individuals who participated in the interviews and survey.

# 8.

# APPENDICES

# APPENDIX A:
# SYNTHESIS REPORT OF THE THOUGHT LEADER INTERVIEWS

METASTATIC BREAST CANCER ALLIANCE:
THOUGHT LEADER SURVEY RESULTS

DECEMBER 2021

## Topic 1: Significant breakthroughs or advances in MBC research

**Breakthroughs and impacts on patients with MBC**

Patient/nonprofit TLs

According to several patient/nonprofit thought leaders (TLs), a lot more attention has been focused on MBC over the last 5 years than before due to patient advocacy. Patient advocacy, which is a source of pride for patients, has a different impact on MBC research than advocacy by scientists and large organizations. Many new drugs are available, including drugs for heavily pretreated patients, and this gives patients hope and confidence that a treatment is available that will work. Although the impact of these drugs, both positive and negative, is unclear because they are so new, patients stated that they are living longer. The increase in the number of options for MBC patients is important. However, most patient/nonprofit TLs did not view these new drugs as game changers, although one patient indicated that MBC may be close to becoming a chronic disease. One patient stated that she thought there would be more breakthroughs, and she was initially baffled by the disconnect between science and patients. She now feels empowered by being involved in science and being heard by researchers, and feels like metastatic disease is now part of early stage conversations.

Many patient/nonprofit TLs cited many *drugs and classes of drugs* that are now available to treat MBC, including:

- CDK4/6 inhibitors (abemaciclib, ribociclib, palbociclib) for hormone receptor-positive MBC
- Antibody-drug conjugates
- HER2-targeted drugs for HER2+ MBC (DS-8201 [trastuzumab deruxtecan]; Kadcyla [trastuzumab-DM1, T-DM1, an antibody-drug conjugate that may have activity in the brain])
- Trodelvy (sacituzumab govitecan) for metastatic triple-negative breast cancer (TNBC)
- Immunotherapy for metastatic TNBC
- Drugs that target somatic mutations
- Drugs that control bone metastases

Patient/nonprofit TLs stated that because of research over the last 5 years, *we now have a better understanding* of the following topics:

- Drug targets
- The immune system
- Tumor heterogeneity
- The tumor microenvironment
- The genetics of breast cancer, how genes and mutations that are identified through genomic testing impact the growth of cancer and are part of the course of the disease, and how they can change because of treatment.

One nonprofit TL stated that basic research continues to be important to keep potential new drugs and drug targets in the drug development pipeline. Important tools now available for research include registries such as MBC Connect and MBC Project, and tissue banks that provide access to tissue.

Research TLs

Research TLs also stated that although many drugs are now available to treat specific subtypes of MBC, none are game changers. For the most part, they provide minor survival advantages, with changes in progression-free survival typically under a year.

Research and industry TLs also cited the following *drugs and classes of drugs* as providing survival advantages:

- Checkpoint immunotherapy is approved for TNBC (Tecentriq [atezolizumab]). However, although immunotherapy provides successful treatment for patients with melanoma and non-small cell lung cancer, these successes with immunotherapy are not happening to the same extent in MBC.
- CDK4/6 inhibitors. An industry TL described CDK4/6 inhibitors as "groundbreaking".
- Sacituzumab govitecan. One research TL stated that sacituzumab govitecan may be a game changer for MBC.
- Tucatinib (Tukysa, a small molecule inhibitor of HER2, with possible efficacy on brain metastases)
- fam-trastuzumab deruxtecan-nxki
- DS-8201
- The PIK3CA inhibitor, alpelisib (Piqray)
- Antibody-drug conjugates
- PARP inhibitors for *BRCA1* and *BRCA2* mutated MBC

Research TLs identified the following important *areas of research* that have emerged in the last 5 years. Increased understanding of many of these areas may provide new drug targets and novel strategies for treatment.

- The role of the immune system including its role in metastatic spread and keeping metastases and primary tumors in check. Researchers now understand that breast cancers develop new and unique ways to escape immune system detection. Researchers have an improved understanding about regulatory T cells and other immunosuppressive cells such as macrophages that make the tumor microenvironment resistant to immune checkpoint therapies. New sets of drugs are targeting and activating the immune system.
- The tumor microenvironment and increased understanding of the crosstalk between the tumor and specific microenvironments such as bone. The niche may support metastatic development in different organs.
- Understanding the underlying mechanisms of metastatic disease. Metastasis is a natural by-product of the cell adapting to stress, both in primary and metastatic tumors. No "metastasis gene" may be present. Rather, genes that promote cell fitness may be important and only needed when the cell is under stress. Agents that target those fitness factors combined with factors that cause stress (chemotherapy, radiation, or immunotherapy) may be important new treatment strategies. Researchers may need to think outside the box and conceptually change how they approach the question of metastasis and the question of drug development based on those new concepts. Eventually, new thinking will translate into new clinical trial designs and new endpoints.

- Evolutionary selection of subsets of cells with specific mutations that could allow metastasis, and understanding that a majority of the cells in a primary breast cancer are not capable of metastasis. The notion of polyclonal seeds, in which multiple tumor cells leave the primary cancer in the breast and move to a metastatic site. Many tumor cells probably need to work together to form a metastasis, rather than a single tumor cell leaving the primary site. This feature is fairly common in TNBC. This understanding may have clinical implications for designing strategies that would inhibit the spread of the disease.
- Mutations and changes in gene expression that occur within the cancer cells and the concept of genes that are recurrently mutated in subsets of breast cancers. Not every mutation is present in every cell, leading to genomic heterogeneity.
- Inherent differences between people and increased understanding of the true meaning of personalized oncology.
- Multiomics when the tumor is taken out of the patient
- Increased understanding that liquid biopsy will be revolutionary in helping stratify patients. Cell-free DNA detected in blood-based assays may be useful to indicate the presence of tumor cells or to measure disease burden or response to treatment.

**Collateral Damage**

Collateral damage is defined as the physical, functional, psychological, emotional, social, vocational, and financial concerns of women and men who have been diagnosed with cancer and/or the quality of life of people living with MBC.

Patient/nonprofit TLs

Several patient/nonprofit TLs reported that MBC patients are living longer due to the new treatments that are available. Patients want to not only live longer but live better. One patient told her doctor "I know I'm a metastatic patient, but don't treat me like I'm dying. Treat me as I'm living. You do all you can and I'll do all I can to keep me alive." Patients and doctors should strive for open communication and to establish a partnership.

Many *challenges* remain in terms of collateral damage. One patient reported that new breakthroughs are actually addressing survival more and are not necessarily addressing quality of life. In contrast, another patient stated that companies are investing in quality of life and supportive services. The financial cost of these drugs continues to be a burden. One patient suggested that patient advocates be compensated for their contributions, similar to the compensation of doctors and researchers. One patient indicated that the public structure of our healthcare system needs to catch up with the science, because metastatic patients may encounter waiting periods before they can receive coverage for their care. Oral treatments should be considered not just a prescription, but a treatment, and exorbitant copays should be eliminated. Another patient expressed concern that patients will not be able to keep or get a job, which equates to psychological, emotional, social, and vocational tolls. A new drug takes an emotional toll because the patient is hoping that this drug is going to be the miracle drug that works. Nausea and fatigue take an emotional and financial toll. Although a drug may keep a patient's cancer under control, the drug may also exacerbate pain. Another patient recommended reexamination of the concept of the maximum tolerated dose. Instead, doses should be individualized so that people can live a higher quality of life while being on the treatment.

Patient/nonprofit TLs reported some *success and progress* in terms of reducing collateral damage. A new drug can be a confidence builder if the drug is working. Having a confidence builder in the back of a patient's mind is a good thing for MBC patients. Another patient stated that because of better alternatives to chemotherapy, she does not have to go to the hospital all the time, does not have as many side effects, and the treatments are less invasive and less intrusive, which all lead to an improved quality of life.

Research TLs

In terms of *challenges* regarding collateral damage, research TLs acknowledged that the goal is always to extend life while also improving the quality of life. Although a cure may be difficult, there is hope that the disease can be controlled for an extended period of time. As survival times increase, quality of life also needs to increase. One research TL commented that clinical trials have not comprehensively looked at the patient experience. Many of the complications from metastatic disease such as fractures or nerve compression from bone metastases are severe. Oncologists should tailor treatments based on each patient's comorbidities and after careful discussion with the patient about all the potential toxicities. All of the drugs currently in use have some side effects. The side effect profile has to consider financial toxicity as well. Research TLs acknowledged that for a patient, continuing to live with a disease that cannot currently be cured is an emotional hardship.

Research TLs described *success and progress* in addressing collateral damage. As treatments are moving more towards targeted therapies and selecting patients who might have the highest chance of benefit, patients are spared a lot of the side effects and toxicities of a treatment if the treatment is not going to have any chance of working. Although targeted therapies have a lot of side effects, knowledge in the ability to address side effects is increasing. An industry TL called CDK4/6 inhibitors "groundbreaking" due to their synergism with estrogen suppression. This industry TL stated that although this combination is not curative, it has dramatically changed quality of life, because it delays disease progression, has fewer side effects, requires fewer lab tests, and can be taken by mouth rather than requiring IV administration. More treatment choices are available than ever before, and if a patient has side effects that are rate-limiting or that impact their quality of life, whether it is emotional, social, or other, an oncologist can try a different drug. Research TLs expect that blood-based measures will be cheaper, faster, and easier and allow closer monitoring of disease and guide specific therapy decisions to improve everything, including quality of life while extending survival times. Immunotherapy has shown some benefits on quality of life and needs to be improved. One TL stated that physicians are incorporating palliative care into their practice to address the emotional, financial, and psychological issues that are associated with having metastatic cancer. Patient advocacy has led to realignment of the variables that are taken into account when selecting a treatment in a manner that considers how the patient feels the therapy impacts her life or his life. Physicians are now looking at socio-emotional symptomatology including the long-term consequences. Physicians are also looking much more at the whole person and the impact of MBC and treatments on long-term relationships, mobility, financial stressors, sex, and intimacy. The spectrum of toxicities has shifted, and physicians' understanding of how to deliver symptomatic relief for traditional chemotherapies has increased tremendously, making chemotherapy a lot more tolerable.

## Topic 2: Opportunities, gaps/barriers, and possible solutions in MBC treatment

Patient/nonprofit TLs

In general, patients discussed research and treatment opportunities that could make MBC chronic if not cured. With MBC, research is needed that is will provide more options, more time, and ultimately, cures. With patients living longer, greater understanding is needed of the long-term impacts of drugs on the nervous system, respiratory issues, the heart, etc. Accountability should be part of NCI standards and NCCN guidelines. Ensuring precision medicine and addressing inequities should become standard of care. A comprehensive model is needed for the care of MBC patients that factors in all issues (financial, insurance, nutrition, exercise, etc.), not just medical factors. Patients who are newly diagnosed with MBC need to understand their disease, but the burden should not be on the patient to be assertive and to seek out support resources. A possible solution is enhanced publication and distribution of the Right Track approach that was developed at the Harvard Broad Institute that the MBC Alliance has on its website. This informs patients about finding the right doctor, obtaining a second opinion at a comprehensive cancer center, undergoing the right test, and receiving the right treatment based on the molecular makeup of that patient's disease. One patient pointed out that overcoming barriers can be difficult because not enough conversations are focused on MBC. Much focus is still on early stage breast cancer, and trying to obtain funding for late stage breast cancer is difficult because people may not want to think about people dying. One way to move forward is to adopt the model of HIV/AIDS work in which funding and efforts were allocated to understand what is killing people. Two patient TLs and two research TLs mentioned the success of the HIV/AIDS advocacy movement as a model for MBC advocacy due to a focus on what people are dying from and the unwillingness to accept siloed behavior when people's lives are at stake.

Patient/nonprofit TLs also talked about opportunities to *break down racial disparities*. One patient stated that addressing health disparities is a "low-hanging fruit". A white patient stated that the onus should be on white allies to gain the trust of the Black and Brown communities. In addition, doctors need to work to bridge that gap and ensure trust. Decentralization of trials will increase access to trials for people living in rural communities and in communities of color. Researchers should engage metastatic patients of color in clinical trials and research to help understand why some patients live a few years with metastatic disease and some live for decades. For patients who are outliers, their lifestyle choices (real-world evidence, which is information collected outside a clinical trial) should be investigated to understand the factors that impact them living a longer life. A burden on the Black patient remains, because the health care system was not built to serve this community. The system that was built created barriers, and the barriers have created disparities. The way the system was built needs to be dismantled, and then barriers and disparities will be dismantled. A nonprofit TL described an inclusion pledge and other commitments to ending disparities and barriers. This effort is moving towards investing in Black principle investigators and Black people in STEM and focusing on research that could impact Black women with breast cancer.

Patient/nonprofit TLs discussed ways that *research can be more efficient and effective*. More patients should be engaged in the research system, which will help make cancer more human for scientists. More synergy and collaboration among scientists is needed, and silos need to be broken down so that engineers, biologists, social scientists, etc. can work together. A feedback loop of information between patients and scientists is important; one patient TL commented that scientists typically welcome this.

Challenges exist within academic institutions about publishing and tenure. Changes are needed in how research is incentivized. As a possible solution, collaborative teams should be funded to reduce the importance of publications. Funding of collaborative teams will also facilitate different types of scientists working together, as mentioned above. Academia needs to work with industry more to figure out how to properly set up these kind of teams. Negative results should be published. More funding for breast cancer research is needed, including funding of young researchers in particular.

Many aspects of MBC need to be understood before they can be overcome. Opportunities in *research* discussed by patient/nonprofit TLs included the need to understand:

- How cancer spreads including all the factors from the tumor and the host (i.e., the tumor microenvironment), what causes cancer to come back, and what is happening at the time of a recurrence
- The immune system
- Tumor dormancy and how to maintain it
- Early detection of metastatic disease
- The heterogeneity of MBC
- The biology of MBC
- How to target specific proteins or mutations
- Genomic information that could help tailor treatments
- The epigenome

Another research challenge is the lack of primary and metastatic breast cancer samples, but this is improving due to AURORA.

New opportunities and challenges regarding *treatments for MBC* that were discussed by patient/nonprofit TLs included:

- Diagnosis, imaging, monitoring, and interventions for MBC patients with brain metastases and leptomeningeal disease. These patients are often overlooked and underserved. Doctors do not have standardized guidelines to follow. Only one drug has been approved for brain metastases (tucatinib), and it is only for HER2-positive patients.
- Treatments are needed for patients with not only stable brain metastases but also progressing or untreated brain metastases. Antibody-drug conjugates are being tested in such patients.
- Drugs are needed that cross the blood-brain barrier to treat brain metastases. CDK inhibitors are small molecule inhibitors, and may have this capability.
- PARP inhibitors can cross the blood-brain barrier.
- More effective use of immunotherapy. Immunotherapy is effective in melanoma and lung cancer, but progress in MBC is way behind these other cancers. Achieving success with immunotherapy in MBC may take more than 5 years. Only a small percentage of MBC patients with PD-L1-positive tumors receive a benefit from immunotherapy. Most breast cancers are considered “cold” tumors, meaning that they are not readily recognized by the immune system.
- Treatments for patients with metastatic TNBC

Opportunities for *better monitoring of disease and response to treatment* included:

- Liquid biopsy. Upon progression, a biopsy or liquid biopsy may provide information so that a patient is not given drugs that are not going to work, because their cancer no longer has particular factors. Liquid biopsies may help detect development of resistance.

- Oncologists should encourage or require their newly diagnosed MBC patients to have genetic testing upon diagnosis, and those who have been living with MBC to have genetic testing upon progression. This should be in the NCCN guidelines.

Research TLs

One research TL commented that the process of studying MBC is fractured and not very effective. Many patients do not enroll in a clinical trial and are never studied. The genomes of many patients are not captured, and no data pooling occurs. One research TL discussed the difficulties with sharing genetic data. Six to 12 months are often required to get data sharing agreements in place between two institutions, and data set restrictions limit the use of the data. This problem is slowing down research. This TL suggested that the government and NIH rewrite some of the existing rules and work toward standardized consent because going back for re-consent is difficult. This TL stated that protecting a person's genetic information is of the utmost importance, but that we may have gotten too conservative. Several research TLs commented that MBC and metastasis work are still underfunded. Funding should not dictate whether we test for say, cell-free tumor DNA or just circulating tumor cells; these choices should be based on science. Another TL suggested changing the wording from "MBC is incurable" to "MBC is currently incurable" to provide hope. Until the last decade or so, MBC patients were not wanted in support groups because they would be a downer to the rest of the group. Within the last decade, several groups that the MBC Alliance has worked with have worked to change this, which has been incredibly helpful.

Research TLs discussed several *research challenges*. The *need for better models* was highlighted by several research TLs. One TL commented that many current models for metastasis are informative if done correctly. Nevertheless, good ER-positive breast cancer models are needed, as are models of dormancy and metastatic recurrence. Several TLs acknowledged that current models are not perfect, and that researchers should recognize the limitations of models. For example, patient-derived xenografts are limited as models because they lack immune components. One research TL stated the need to increase the number of patient-derived xenograft samples from African American communities, and then these models should be available to everybody. Potential solutions to better models include teaming up with an expert in another cancer (e.g., melanoma) to ask why checkpoint therapy is not working better in breast cancer, and facilitating the ability of clinicians and translational researchers to work together. Mice with a humanized immune system will help with modeling of disease. One barrier to model development is that not a lot of incentive (publications, funding) is present to develop models and that NIH and other big funding agencies no longer fund model development. One research TL described culturing live cells from a patient and testing their drug sensitivity as a way toward addressing the limitations of model systems. This TL acknowledged that this has not yet improved survival in patients but is the next frontier. Patients with MBC load in their body do not have the luxury of lots of failures, and need decisions at the time metastasis first happens. One TL recommended that scientists share models to increase the likelihood of getting a particular research finding into patients.

Another *research challenge* discussed by research TLs is the *problem of drug resistance*. Cancer is a constantly changing group of cells. Drug resistance is a result of genetic and genomic instability. One TL indicated the need to look at the changes in the tumor microenvironment in patients who are responding to immunotherapy or other therapies compared to those who are not responding. Researchers need to look holistically at the situation, the tumor, the patient, and their microbiome to move the field forward. One possible opportunity is to assess recurrently mutated genes and understand the therapeutic vulnerabilities that are engendered by those mutations to develop

mutation-specific therapies. Unfortunately, many of these mutations are not common.

Instead of treating patients with the same drug regimen until it stops working, one TL envisioned clinicians being smarter and using better tools to monitor disease in real time. He suggested that instead of treating a patient with several drugs at the same time, a different strategy is to design sequential drug regimens that will prevent or delay resistance from occurring in the majority of patients. Treating a patient sequentially with drugs such as CDK4/6 inhibitors may be a better approach. Testing this approach could be challenging because a drug company may not want to invest because their drug is perhaps only one of several different drugs in a sequential approach.

Another TL described the need to find ways to reduce the emergence of drug resistance or to be able to deal with resistance in a longer-term manner. Liquid biopsies may help researchers understand breast cancer evolution in near real time. Another TL stated that metastatic TNBC patients develop resistance quickly and that research is needed to understand this better and what genetic changes could be targeted.

Research TLs also discussed *expanding the use of biopsies*. Serial biopsies and more biospecimens from patients when they have progressed are needed. Every tumor in every patient is different, and every tumor in a different place in a patient is different. The ability to target the tumor cells using a targeting strategy will be the most helpful. Although sampling tumors is invasive, one TL stated that clinicians under-sample. Many patients, but not all, understand that researchers need to know more and are willing to have another biopsy.

Metastatic biopsies are more difficult to obtain because of where in the body they are located, although one TL stated that metastatic biopsies have become standard of care. Primary tumor samples are harder to get now because they may have been obtained years or decades ago and were thrown out, are degraded, or are small due to neoadjuvant treatment. Although a lot of centers are banking tissue, an organized database and archived primary and metastatic samples that can be shared are needed. Biopsy samples may only be sent to the pathology department and not go to scientists. One TL talked about a program at his institution in which multiple biopsy samples are obtained at one time so that both the pathology department and scientists can study them. Such an approach can be expanded to community settings where persons of color or vulnerable patients are being treated, thus allowing better assessment of specimens to improve care for minorities and collection of specimens for research from a more diverse population. This model can be replicated in other places.

One TL stated that every metastatic patient should have next generation sequencing done to identify targets that may or may not be standard of care. Expanded analysis of biopsies could increase understanding of the molecular etiology of the disease, which is the foundation for treatments and a cure. The diagnosis of cancer in each individual patient needs to be investigated for better, more precise, and less toxic therapies. An opportunity to do such an analysis is to use a series of omics technologies to take an unbiased look at the tumor's DNA, RNA, protein, phosphoprotein, and potentially other omic levels to assemble individual computational maps that drive the disease. If a patient has a breast cancer relapse, genomic and ultimately proteogenomic, analyses of the tumor are needed. Then, a national consortia, such as the NCI-ComboMATCH program, will be needed to study disease subsets. This TL then described an example of such an approach that resulted in drug repurposing when the biology was understood. A subset of estrogen receptor-positive breast cancers lose the neurofibromatosis protein. Drugs called MEK inhibitors are approved to control malignancies associated with neurofibromatosis. The ComboMATCH protocol provides one such drug called binimetinib to patients with loss of this protein in their metastatic cancers. Another opportunity is that regional centers of excellence for MBC can provide advice about the best treatment or trial for a

particular patient.

*Liquid biopsies* could be used for *better monitoring* and could have an immediate benefit. Patients approve of the idea of liquid biopsies because they are less invasive, and physicians approve because they have the potential to identify who is in the process of recurring, even though traditional methods would not detect such a recurrence. Results from a liquid biopsy could be actionable very quickly. Current studies are working to identify a marker that can predict the likelihood of developing breast cancer in the first place, and MBC in the second place, before tumors ever occur. Additional improvements will be made by identification of genetic markers and common mutations for which a personalized treatment is available. One TL stated that in 5 to 10 years, liquid biopsy will probably be the predominant way that disease burden is measured and response to therapy is monitored.

A *treatment challenge* discussed by many research TLs is how to improve the efficacy of *immunotherapy* for more MBC patients. Research TLs stated the need to understand why immunotherapy works in a small subset of breast cancer patients and why a large majority of patients show no good response. The efficacy of immunotherapy among MBC patients needs to improve to make a substantial change in survival. This is seen in patients with melanoma and lung cancer, and needs to be translated into MBC. For a small subset of MBC patients, immunotherapy may provide a durable response or even a cure. Biomarkers beyond PD-L1 are needed to identify who will respond to immunotherapy. Research is needed to compare the tumors from patients who are responding to immunotherapy to those who are not. Research should continue to build on the promise of immunotherapy in the next 5 years.

Other *research and treatment challenges and opportunities* identified by research TLs include:

- Understanding the tumor microenvironment
- Understanding how metastasis occurs, what the key drivers are, and how to target them
- Integrating physical sciences, chemistry, biophysics, and other fields
- New antibody-drug conjugates
- Vaccines
- The need to educate the community about biosimilars (drugs that are just as effective and cheaper) to help address financial toxicity
- Improvements in treatment for brain metastases or prevention of brain metastases
- The opportunity to treat patients with HER2-positive MBC with a curative intent. A series of very good drugs is available, and HER2 is a fairly stable target. Challenges include measuring success and recruiting for these trials because there are fewer HER2+ MBC patients. This TL cautioned against concluding that HER2-positive MBC is not a problem because most people are cured in the early stage.
- Expanded use of inhibitors of other CDKs such as CDK2 in combination with other methods of estrogen suppression such as selective estrogen receptor modulators. New all-oral combinations may improve quality of life, provide more options, reduce side effects, and mitigate the development of resistance.
- Research in better prediction, monitoring, and management of cancer-related toxicities. Better research to prevent or manage multiple toxicities is crucial, as many patients are living longer with their cancer. An important challenge is that pharmaceutical companies do not have incentives to run these types of trials, and increased funding from government/NCI is therefore needed.
- Recurrent alterations in estrogen receptor-positive breast cancer that can potentially be targeted, such as mutations in FGFR, ESR1, and PIK3CA
- Acquired HER2 mutations

- Understanding and exploiting the abscopal effect in which radiation of one area of the body results in shrinkage of tumors in other places

*Telehealth* is another opportunity to improve MBC treatment. Tumor boards can be entirely online and function to obtain second opinions. Community physicians can call in and obtain a consult so the patient does not have to travel to an academic medical center. Dissemination of knowledge of new therapies to the community can sometimes take a decade. Virtual molecular tumor boards can help disseminate knowledge more quickly and can be used for assessment of genetic sequencing reports to help physicians and providers interpret them. Because of the virtual nature of these tumor boards, community hospitals, academic centers, and international sites are involved. This should be available to every single patient. Social media and direct-to-patient engagement can be used to ensure that MBC patients know that options are available that they might not have discussed with their oncologist. One barrier to the use of telehealth and virtual tumor boards is that insurance agreements are needed so that that the doctor's time and the time of the persons who are providing the molecular second opinion can be billed. The COVID-19 pandemic has forced long overdue changes such as Centers for Medicare and Medicaid Services (CMS) reimbursement for telehealth. An industry TL emphasized the importance of not going backwards from this advancement.

An industry TL discussed the challenges with new drug development and how to incorporate research findings into clinical practice. The rules for changing the standard of care in this country are complicated. Big trials and evaluation of the activity of every component of the therapy are required. Another challenge is the complex and lengthy regulatory process. A partnership among the regulatory authorities, patient advocate associations, and the scientific community is needed to evaluate how the trials can be expedited so that treatments can move into clinical practice more quickly and more cost-effectively.

## Topic 3: New effective therapies, combination therapies, and possible solutions

Patient/nonprofit TLs

Patient/nonprofit TLs stated several *challenges* to new treatments. One patient stated the need for expansion of treatment for hormone receptor-positive MBC and metastatic TNBC to mirror the success that has been achieved with HER2-positive MBC. Although treatments provide decent success in controlling bone metastases, better understanding of other sites of metastases is needed, and better control of brain metastases in particular is needed. Better models of metastases are needed to aid in these efforts. Better understanding is needed of the proper timing of combination treatments and how much time should elapse between treatments to control a patient's cancer. Immunotherapy in MBC needs to improve beyond metastatic TNBC. For all efforts, racial disparities must be addressed, and data must be used that reflect the characteristics of the community that a new therapy is designed to treat.

Potential *solutions* that may facilitate increased understanding and implementation of new treatments for MBC include the following. Better biomarkers are needed to identify who will respond to what drug. One nonprofit TL stated that biopsies should be studied to address basic biology questions, increase understanding of how drugs are working and who is and is not benefiting, and to increase understanding of tumor heterogeneity. Patients stated that genomic testing and genetic testing should be part of standard of care, with every recurrence or progression, and should be included in NCCN guidelines. Genomic profiles should inform treatment decisions. Data obtained from these studies should be shared

rather than siloed. The entities that hold the data in silos should be pressured to share their data and embrace collaboration. A COVID-19-like urgency approach to cancer research is needed. Pharmaceutical companies need to cooperate to develop combination therapies.

Research TLs

Several research TLs discussed *preclinical challenges* to new therapies. Researchers do not have enough models of MBC, especially models of luminal, hormone receptor-positive, and male MBC, and the ones that are available are not great. The NIH and other large funding agencies do not fund model development anymore. Patient-derived xenograft models are powerful but very limited because they do not consider the immune system. To assess whether an effect is an artifact of a particular model, drugs should be tested in multiple models of MBC, not just a few. One of the important challenges to developing new effective therapeutic combinations is the increased rate of toxicities related to combination therapies. Using better preclinical models to predict these toxicities before initiating phase I trials could be a potential solution. One research TL stated that guidelines are in place for what constitutes success in clinical trials and that those same rules should be applied to the pre-clinical setting. This TL said that if a drug is given to a mouse model, and the drug slows tumor growth, that is considered a success. However, in a patient, if a drug only slows tumor growth, the effect is called progressive disease and is not a success. If a higher bar was set in preclinical studies, we might have fewer clinical trials, but they would be more likely to succeed. Another challenge in preclinical studies is obtaining drugs from companies to test.

One basic science TL talked about the challenges of moving from basic science discoveries to early stage clinical trials. The space between these steps is the so-called "zone of death" where a lot of exciting research gets lost. Many resources are needed to progress from screening a compound, to lead development, to development of a compound with suitable pharmacological profiles, safety, and clinical efficacy, to a state that excites venture capitalists or big pharma so that they are willing to invest and acquire the target. At institutions that focus on basic research, efforts are needed to bridge the gap between basic research and venture capitalists and other investors. One of the major roadblocks for basic scientists is that they are typically not experts in medicinal chemistry, drug design, structure-activity relationships, and other basic pharmacological aspects. Resources are often not available for this. Other considerations include legal aspects, intellectual property, and protection.

An industry TL stated that moving from preclinical testing to clinical trials is a long process with many regulatory steps, some that may not be needed. Discussion is needed among stakeholders about how to expedite this process. Good preclinical evaluation, as discussed above, may help.

One research TL reported that the biggest challenge to new treatments is that more research is needed. This TL stated that HER2+ MBC has been cured in some patients, but that more research is needed to understand the exceptional responses in those HER2+ patients and the genetic underpinnings that prevent others from achieving that same type of response. Research is needed to understand the biology of the patient, and how he or she metabolizes drugs. This information will suggest potential targets and therapeutic vulnerabilities that will lead to development of appropriate drugs that will ultimately lead to better outcomes. Antibody-drug conjugates hold great promise, and treatments that cross the blood-brain barrier for brain metastases are needed.

One TL stated that a lot of basic and translational research needs to be done before key clinical trials of combinations can be initiated. Enough single drugs are available, but more combinations are needed. A much better understanding of companion drugs, of the concept of synergy, and how to augment the power of certain drugs is needed. Molecular therapies based on the tumor makeup need to be added to immunotherapy to augment the power of boosting the immune system.

Several research TLs and one patient TL stated that a major *barrier to new drug combinations* is that drugs may be manufactured by two different pharmaceutical companies that may be unwilling to work together to test that combination. However, one industry TL stated that such collaborations between companies "happen frequently" due to mutual agreements that are established to protect intellectual property; these collaborations may not be in the public view. Challenges related to companies working together, as stated by an industry TL, include legal issues, conflict of interest, proprietary concerns, and contract considerations. A potential solution to this problem, suggested by two research TLs, is for the federal government to step in and fund such a study. A government TL stated that some agreements with companies are in place at the NCI through The Cancer Therapy Evaluation Program (CTEP).

An additional *barrier is cost*. Compared to industry, drug development is less expensive in academia, because of the standards and regulatory approval involved. The process of drug development should be tailored according to unmet needs, the tumors, and how significant a preclinical discovery is. The FDA's expedited process has helped shorten the period between completion of a study and approval of the drug, allowing earlier access to the drug by patients. The expedited process also works globally and can be sought in multiple countries at the same time.

## Topic 4: Challenges and solutions to more effective clinical trials

Patient/nonprofit TLs

Patients/nonprofit TLs discussed *challenges and problems* with clinical trials. *Problems* included:

- Too much bureaucracy
- Too much status quo
- Waiting periods
- Insurance gaps
- Trials may be too far away from a patient's home.
- Exclusions due to comorbidities
- Strict eligibility criteria often result in exclusion of patients with brain metastases, or lobular breast cancer or inflammatory breast cancer who do not have measurable tumors.
- Patients feel like finding trials is their responsibility, because trials are not suggested to them by their doctors.
- Patients are already overwhelmed, and finding a trial is too much of a burden.
- Patients may not understand trials and may have reservations about having a conversation with their doctor.
- Not as much information is obtained from trials as possible.
- Determining a maximum tolerated dose in the beginning of the trial process is not an ideal strategy. Instead, determining the minimal effective dose is preferred. This would allow more appropriate management of side effects by eliminating some of them in the beginning.

Patient/nonprofit TLs stated that *trials should be*:

- Overhauled
- Streamlined
- Decentralized
- Available in rural communities
- More accessible in the community, which may help with transportation and childcare issues
- Transparent
- Suggested to patients by their care team. Doctors should be initiating conversations about clinical trials, but often they do not.
- Smarter and innovative in their design
- Incorporated into standard of care
- More inclusive to get patients into trials and to provide more solutions quicker and sooner
- Representative of the populations that are going to receive the drugs. For example, if a drug is going to be used to treat people who have had multiple lines of therapies, then people with multiple lines of therapy should be in the trial. This comment also pertains to inclusion of diverse populations. See below for more details.

Patient/nonprofit TLs also stated that data and samples should be shared and better reported, including negative data. Trialists should collect outcomes reported by patients, who may report an outcome differently than a doctor. Trialists should not lose sight of the patient and should focus on how to make treatments less burdensome. Patient/nonprofit TLs indicated that physicians need to be more open to talking about clinical trials without assuming that their patients are going to say no or because of fear that they will lose their patients to clinical trials. Another suggestion was that compassionate use could be an automatic feature of a clinical trial. Patients should be educated so that they understand that they can drop out of a trial at any time, that not every patient will experience every side effect, and that many side effects can be managed so that a patient can stay on a trial.

Patient/nonprofit TLs discussed *solutions to improving clinical trials*. One patient/nonprofit TL described a successful effort by her group to bring a new site for an existing clinical trial to her local area so that patients would not have to travel. They paid for a clinical trial manager and a staff person to open this new site. She reported that this was “not that hard”. She reported that they now they have doctors talking to patients about trials and educating them. Other solutions include requesting input from patients and trained advocates to improve trial design and protocols, and to provide insight on the number of biopsies, visits, and blood draws. In addition to doctors telling patients that trials exist, advocacy groups can promote a trial or tell people about a trial. Advocates can serve as clinical trial navigators to help patients through the consent process using a peer-to-peer discussion.

Patient/nonprofit TLs discussed *barriers to including more diverse populations* in clinical trials. Trials should be representative of the populations that are going to receive the drugs being tested, but the Black population is generally not as involved in clinical trials as their white counterparts. Trust is often a problem, Black people have felt marginalized in the healthcare system, and people of color may not understand why trials are important. Especially in the Black community, patients think they are guinea pigs. Historically, racism has been present in the healthcare system. A system was built that works for the white population, but not for Black patients. Some doctors assume that minorities and people of color would not want to join a trial so they do not even approach them. Conversations between patients and physicians should take place so that patients understand that trials are a treatment option.

Some *proposed solutions to improving diversity* were also discussed. One patient stated the need to talk about racism and bias before we can solve it. Improving diversity in trials takes work in the communities and intention. Both Black and white patient/nonprofit TLs referred to their counterparts as "allies" and expressed a desire to work together to facilitate change. Allies need to work together so that people of color are viewed as people and not just recruitment subjects. Black patient-led organizations and other leadership by Black patients and Black advocates are expected to be effective. Some solutions to the trust problem include helping people understand the trauma and mistrust that the Black population has faced historically, which has created a "them and us" barrier. The pain should be honored, but then stakeholders should look forward to the promise of innovation. These efforts need to be respectful and ethical. One Black patient TL suggested a way to increase accrual of Black patients: "Ask us. Explain it to us. Help us understand it." This patient TL also talked about recruitment strategies for the Black community, which could include recruitment at churches, public service announcements that show somebody that is culturally like them, and meeting people where they are such as barbershops, beauty salons, community hospitals, and Veterans administration care facilities. She stated that many avenues exist for reaching Black people to educate them about clinical trials. Regarding results from clinical trials, real-world evidence could be used to better understand toxicities in diverse populations.

Research TLs

Research TLs discussed the *need to learn as much from clinical trials as possible*, including how the tumor changes in response to treatment, and not to just look at the question clinical trials are designed to answer. Researchers need to collect tissue samples for research in every single case to understand the biology. Several research TLs stated the need to complete a loop in which what is learned in the lab is applied to the clinic but also what is learned in the clinic is taken back to the lab. Consent for broad research will help researchers increase what they can learn from clinical trial specimens.

A *challenge to learning as much from a trial* as possible is related to analysis of biospecimens. Most grants from the government and nonprofits do not pay to acquire the biopsies but usually pay for the studies that researchers want to do on those biopsies. Government and nonprofit grants typically only pay for the correlative studies. The money that helps to pay for research biopsies comes from pharmaceutical companies in the context of an investigator-initiated trial in that budget. However, another research TL stated that when industry funds a trial, they provide funding to do the trial and collect serum. They almost never fund assessment of pre- and post-treatment biopsies of metastatic disease. Samples beyond serum are also valuable, such as cerebrospinal fluid to understand specifically what is happening in the brain. Other barriers include the way that the systems are set up in terms of incentives, promotions, intellectual property, and commercialization. An industry TL stated that an academic trial can be much cheaper than a comparable industry trial.

*Trial end points and trial designs should be adjusted* based on new advances in research and understanding about metastatic disease, because typical end points may not provide an accurate readout. As an example, one TL talked about long-term vs. short-term outcomes. Measures of tumor burden and tumor size may not make a big difference in the short term. But in the long term, shrinking the tumor improves survival. Following treatment with some immunotherapies, the tumor initially becomes bigger, and if tumor size is used as an end point initially, the trial would be a failure. A different end point such as long-term survival should be used. Control of metastatic disease should be considered a success. Another example is trials that target dormancy; those trials would require a very long trial time, a large number of patients, and would be expensive. Thus, new markers are needed to serve as end points. Another research TL discussed the need to change RECIST criteria regarding the definition of a drug that is working by keeping tumor cells dormant. A revision of RECIST is needed to state that stable disease that lasts multiple years is acceptable for quality of life. These different end points and

the correlative studies should be built into the trial's design so that researchers learn as much as possible from every patient in every trial. An industry TL stated that the COVID-19 pandemic has led to unprecedented transparency in terms of end points and timing of vaccine development due to public demands. This should happen in breast cancer too.

Research TLs discussed *new trial designs* including adaptive trials such as ISPY-2, basket trials, and umbrella trials that may also be informative. A research TL indicated the need to rethink clinical trial design because a one-size-fits-all design may often not be optimally informative. In standard trial design, standard of care is given to all patients, and then half the patients receive a placebo and half receive the new drug. Historical parameters of progression-free survival and overall survival are then measured. This design needs to be rethought, and the possibility of adding drugs sequentially should be considered. Clinical trials need to be designed based on the science of the molecules they purport to test. Researchers need to invent new ways to test drugs and to follow patients in innovative ways. One barrier to new trial designs is that standard trial design advances careers, whereas innovative trial design may not. National clinical trials with large consortiums will help with examination of rare mutations.

An industry TL stated that trials should be designed through the patient's lens rather than through the investigator's lens. Efforts should be centered on what the patient needs and can do. Trial investigators should put the patient first and take the trial to where the patients are. Some trial data can be collected from the patient through a smartphone. Lab work and imaging can be performed in community settings. Collection of data can be expedited by a central hub doctor who works with community doctors. Quality of life considerations should be incorporated into trials. Studies should be designed that patients will want to participate in with end points that matter, including assessment of quality of life. Trial investigators undermine their ability to conduct a trial when these issues are not considered. Trial investigators should work in collaboration and in partnership to accomplish these goals.

An industry TL reported that collaboration and discussion are needed between academia and industry in development of better and smarter clinical trials, and many times that does not happen because goals are different. The goal in industry is obtaining approval of a drug and starting to sell the drug. The goal of a scientist is advancing his/her career. This TL suggested having a conversation with the FDA to develop innovative ways to evaluate new drugs or new combinations that would include a team consisting of companies and regulatory authorities to expedite the process and determine what is essential and what is not needed that can be eliminated. An example of a successful collaboration that happened among industry, patients, regulatory authorities, and the scientific community is the new approach in patients with MBC with brain metastases. This was an unmet need. The four entities have worked together and written guidelines to include brain metastasis patients in clinical trials. They now view brain metastasis in a different way. This is an important point that regulators, industry, and scientists need to think about when they are developing a clinical trial.

One research TL discussed the important distinction between clinical investigations and clinical trials. With a clinical investigation, the patient is the focus of interest. In a clinical trial, the drug is the focus of interest. A clinical investigation may involve serial blood samples, assessment of quality of life, and how a patient is responding to standard drugs. A clinical investigation involves getting the patient's tumor into the lab where it can be studied, perhaps as a patient-derived xenograft or a cell line. Clinical investigations are greatly underfunded. Clinical investigations are important for learning, for example, predictors for why some patients do not respond or cease responding to a standard of care drug, which opens up a new field of pharmacology. Clinical investigations can also be used to better understand

immunotherapy, the tumor microenvironment, and the immune response to the tumor. As much patient-oriented research as possible is needed. Each patient is an n of 1. Acquiring biospecimens and making models from them is being done by patient-derived xenograft consortiums such as the PDXNet consortiums at the NCI.

Research TLs discussed *patient accrual challenges and solutions*.

- Trials should be smarter, faster, safer, and easier.
- Patients are willing and eager to participate in trials, but access to trials is a challenge because patients may not know how to get involved and if any preconditions would prevent them from enrolling in a trial. Many patients are confused and frustrated with the lack of access and information. Informed consent language is a burden because it can be confusing. Many doctors are not very informed about what patients understand. Better outreach to frontline doctors who see the patients and who could recommend them to trials is needed. One research TL stated that it is very difficult for physicians in practice to find trials for their patients. Trial accrual is in part due to how a doctor presents and explains a trial to a patient. This can take a long time, about 1.5 hours for a new patient. One research TL who is a clinical researcher stated that she presents a trial to a patient as an option and does not pressure the patient. In her practice, she tries to have a trial for every single patient, so that everybody has options.
- Another research TL stated that the site of disease in a patient's body should not be an exclusion criterion. In particular, including patients with brain metastases was called out by several research TLs.
- Trials should be decentralized, because most people are treated in the community where only a few trials are open.
- One research TL stated that testing of new drugs with unknown toxicity should be fairly centralized, but trials of more advanced drugs could be more flexible in terms of where a patient receives care or treatment. Some study drugs can be administered by a patient's local doctor.
- Virtual visits and shipping of drugs can allow visits to be spaced out from every 3 weeks to every 6 or 9 weeks. The COVID-19 pandemic has shown how medical care can be flexible. Implementing these changes could increase trial enrollment.
- The accrual lag of a year or more is a very important barrier in terms of quickly moving treatments forward. An industry TL stated that working together as an oncology community may help expedite trial enrollment. In addition, this industry TL mentioned the rapid accrual to COVID-19 vaccine trials because people understand what is at stake and want to participate. Advocacy efforts to help MBC patients understand what is at stake may increase enrollment in MBC trials.
- Another challenge is the need to dispel the notion that doctors "own" their patients. Doctors may fear losing patients as a source of revenue if they enroll in a trial.
- To encourage people to enroll in trials, a patient should be informed that when he or she is in a randomized clinical trial, the patient is at least getting the standard of care (what clinicians think is the best care) and possibly what clinicians think is the next best option. Patients should view trials as a first resort rather than a last resort, and that trials do not put patients at a disadvantage.

Research TLs discussed *including diverse populations in clinical trials*. Research TLs agreed that underserved communities and diverse populations of patients should be enrolled in not only clinical

research trials, but also clinical research studies of various types. When research includes patients across diverse economic, racial, ethnic, etc. lines, those advances can then go back out to all communities. Having a diverse presence in the trial population is critical, because clinicians want the treatment to work for everyone not just the most frequently enrolled group. One research TL stated that race-associated toxicities may exist, and these need to be identified before the drug is approved. A tumor has changes in its genetic makeup, the tumor interacts with the host, and every host is different. Thus, including diverse patients in terms of the genetic makeup of different populations and different ethnicities is very important.

*Barriers to enrollment of diverse patients* may include financial barriers, insurance barriers, trust barriers, cultural barriers, socioeconomic challenges, and geographical barriers. Researchers also need to understand the effects of stress and of lifelong deprivation of opportunities that have real biological signatures. When diverse populations from all experiences of the human condition in society are not included in trials, a lot remains unclear. Another barrier is that the number of patients seen each day in a clinic that works with underserved populations is high. The amount of staffing in such clinics is not conducive to clinical research, because clinical research takes more time.

One research TL stated the need to chip away little by little at various barriers to make a difference. *Solutions to the diversity problem in trials* suggested by research TLs included the need for the federal government and the NIH to have federally designated underserved clinics. This designation can be expanded to provide special funding to clinical trials in research to accrue in those settings. Resources are needed to do clinical research in clinics that work with underserved populations. Infrastructure can be efficiently set up in almost any clinic to enroll patients in clinical research; this needs to become a priority. The federal government is very likely to end up having to pay for the drugs once they are approved, because they are currently the major insurer of underrepresented populations. Thus, saving money by providing better care will help save money in the long run. Providing the best care up front is preferred over addressing neglected problems, which is the current state of underserved populations.

## Topic 5: Promising technologies and new areas of research

Patient/nonprofit TLs

Better *imaging and monitoring* are needed. Better methods are needed to identify lobular breast cancer. Imaging modalities should be combined and added to molecular biomarkers to monitor disease less invasively. TLs also called out liquid biopsies as a new and emerging technology that is expected to improve point of care, provide faster results, reduce the anxiety of patients regarding scans, and reduce the cost of disease monitoring by reducing the number of scans needed.

One patient indicated that new technology could be used to better understand targeted mutations, targeted proteins, immunotherapies, what makes a cancer thrive, and how to target or disrupt that process in the tumor microenvironment. A treatment that is currently used to treat patients with very few metastases is stereotactic body radiation therapy.

A nonprofit TL commented that applied use of *data science* and artificial intelligence may help improve how health care is delivered in different places. Electronic health records (EHRs) need to be improved. Currently, EHRs do not have a field for genetic test results. EHRs also contain non-structured data, and thus, the power of data mining cannot be used to make sure that patients get the treatment they need. Patient TLs also indicated that technology could be used to increase the capacity of advocate training

and that clinical trials should have an app to show where a patient can get a test other than the trial site and what other trials are available.

Research TLs

Research TLs also discussed the potential of ***liquid biopsies***. For patients living with MBC, the key is to identify effective second line, third line, fourth line, etc. therapies that continue to control their disease effectively and reduce morbidity. The goal is to be able to precisely predict the outcome of a certain drug. Dynamic biopsy and real-time analysis of the dynamic landscape of the tumor that is still in the patient is critical for predicting the response. This will require advances in technologies such as the capture and analysis of individual tumor cells in a liquid biopsy to identify tumor DNA, and use of this information as a predictive marker to identify additional lines of therapy that are likely to be effective. Liquid biopsy analysis requires standardization, so that the results are reliable and reproducible. Many therapies are available, but the critical question is whether a certain treatment will be effective or not. Combining liquid biopsy with low-cost effective single-cell analysis to look at the composition of the tumor is an important goal because the tumor may have grown and changed, and the mutation landscape evolves in response to therapies. Tumor or liquid biopsies will be important to understand the heterogeneity within each subtype. Another hope is that liquid biopsies and cell-free DNA will be able to guide physicians clinically in determining who is really cured after standard of care therapies and who is not. Liquid biopsies may provide evidence of micro-metastatic disease in a patient's body and quantification to assess tumor burden in a patient. The hope is that cell-free DNA or circulating tumor DNA in a liquid biopsy can be used as a surrogate real-time biomarker to facilitate changing a treatment sooner than is currently done with scans, in weeks rather than months. Although a scan may look good, circulating tumor DNA may show that cancer cells are still present.

Research TLs highlighted several new and emerging types of ***imaging***. Targeted imaging and molecular imaging involve a specific probe that identifies a specific protein or disease process (e.g., proliferation or angiogenesis). This technology could be used to more deeply understand the actual state of different lesions. In MBC, a lesion is very different depending on whether it is present in the brain, liver, lung, etc. A particular drug may work in one place and not another. This type of technology could be used to detect a very early response. Live-cell technologies and single-cell technologies could be used to understand the role of single cells in great detail and to define immune cell subsets that are infiltrating lesions. Another related area is theranostics (therapy + diagnostics). Theranostics markers not only allow identification and location of a tumor, but also identify biomarkers that could be effective therapeutic targets. Developments in nanotechnology and biomarker development for theranostics markers combined with efforts in single-cell and circulating liquid biopsy analysis may provide more powerful assessment of the disease state. Spatial imaging allows scientists to look at 50-100 markers while also understanding the spatial microscopic organization. Multi-feature microscopy, sampling of individual cells or small groups of cells, sequencing their genomes, and gene expression profiling of thousands of genes are possible while maintaining spatial information. Spatial imaging will be informative to determine how cells communicate with each other and the role of the microenvironment.

In terms of ***treatments***, research TLs stated that new technology can be applied to antibody-drug conjugates and immunotherapy drugs. Various new technologies and platforms can be used to measure effectiveness and prevent the emergence of drug resistance in an adaptive trial design. New

technologies can be used to visualize what cells are present, what factor(s) and receptor(s) a cell is making, and what treatments can be used to interfere with those processes.

Research TLs identified emerging opportunities and challenges regarding the use of *big data, artificial intelligence, and deep learning*. Although volumes of data are being generated, understanding what is important and what is not remains a challenge. An unbiased eye is needed to identify patterns. Research TLs indicated the need to be able to get the most out of data. One research TL pictured a scenario in which the data for every person who had a liquid biopsy were in a database with every treatment regimen that person had ever received before and after the liquid biopsy, along with how that person responded to the various treatments. Such a research database would be enormously valuable to understand what happens with various drug resistance mechanisms and to predict response. No national database of this type exists. This information could be very valuable to oncologists from a standard of care standpoint and also from a trial matching standpoint. The data that exist are not in a standard format, and are not integrated in a way that allows learning from the data. Data from thousands of patients could be mined in very interesting ways. Scientists need to accumulate knowledge from "n of 1" studies and put the information in a shared database. Then an oncologist can compare that information to his/her own patient to inform treatment decisions. One research TL stated that establishing communication and data transmission security should be priorities.

Physicians need more than just the genomics and genetics of a patient. That information needs to be linked to the patient's clinical records. Obtaining access to patient records and obtaining the patient's permission is paramount to making genomics data useful. As a solution, AACR Project Genie and the Biopharma Consortium is partnering with pharmaceutical companies to liberate patients' data and medical records, combined with the genomic analysis.

Another emerging use of technology is *telehealth and telemedicine* to set up a second opinion precision oncology clinic.

## Topic 6: Including advocates and advocate organizations in MBC research

**Current patient advocate involvement**

Patient/nonprofit TLs

Patient/nonprofit TLs talked about how involving patient advocates helps drive better research by informing researchers what people with MBC are concerned about. Patients can help researchers understand what they should focus on, blind spots that they are not seeing, clinical trial design, the patient experience, and real-world implications for patients. For clinical trials, patient advocates can help researchers understand the importance of how often a patient will have to travel, how many appointments and tests they will have to undergo, what side effects may occur, and whether patients can incorporate a trial into their normal life. One patient TL helped establish a program called GRASP (Guiding Researchers and Advocates to Scientific Partnerships) to bring advocates and researchers together for a sustainable relationship to help researchers understand how research is going to help patients. Patient advocates also help researchers learn how to talk to the public and how to work with oncologists, radiologists, surgeons, researchers, pathologists, and universities about clinical trial design or the results from an NCI review. One patient TL stated that she appreciates that researchers listen to

her point of view and incorporate suggestions into their grant applications. Another patient/nonprofit TL stated that small organizations can pool their money to make an impact.

A nonprofit TL stated that there is now more intention to include and work with patients in research because some nonprofits have made it a requirement. In addition, the FDA has released guidance about how pharmaceutical companies and drug sponsors should be working with patients.

Advocates are also active in the Black community. They work to inform the MBC community and the Black community as well. Their work supports recruitment to ensure a reflective, diverse population of patients, and to dispel inequity in epidemiology and social determinants of health.

Patient/nonprofit TLs stated their *current involvement in the research process*:

- Testifying to the FDA
- Being active at the patient's particular cancer center
- Informing content and co-creating programs
- Working on papers to incorporate scientific input and research to inform the MBC community
- Grant reviews for the DoD and METAvivor
- Working with Specialized Programs of Research Excellence (SPORE) established by NCI
- Helping write grants and providing support letters

Patients talked about *training opportunities for advocates*:

- The National Breast Cancer Coalition has established the Project LEAD workshop, Clinical Trials Project LEAD, and Quality Care Project LEAD.
- Living Beyond Breast Cancer has a Young Advocate Training program.
- Tigerlily Foundation's Chrysalis Initiative provides training for industry for the comprehensive care model, ideal patient navigation, patient education, and incorporating technology to increase capacity.

Research TLs

All research TLs who were asked reported that they currently work with patient advocates, and overall, their assessment of working with patient advocates was enthusiastic and positive. They described these interactions as "critical", "very, very valuable all around", "it's great to have their input. They give us focus and a lot of practical input, particularly on some of the clinical trial designs", "brings to a conscious level what we might otherwise dismiss", "help[ed] me hone my message, provide accurate lay messaging", "changes everything", and "advocates are a major component of all the decisions [that our group makes]". Patient advocates can identify the most important needs of the patient as opposed to what researchers and clinicians think are the important things. In the era of the COVID-19 pandemic, most meetings with patient advocates are virtual, which may make working with advocates easier.

Research TLs described the following *current interactions with and roles for patient advocates*:

- Advocates visit the basic research lab, serve on graduate student dissertation committees, and talk to and inspire lab members and especially young students to understand why the work they are doing is important. Advocates provide feedback about what really matters to them such as what research questions really excite them or directions that the lab should focus on.

- Advocates speak in graduate and college-level classes where they describe their experience as they are undergoing treatment for cancer. These interactions are highly ranked by students.
- Advocates work with nonprofits to create financial support for patient advocates to travel to meetings and to create webinars in which patient advocates can ask basic scientists questions. A basic science TL reported that these interactions are mutually beneficial so that they know what walls divide them. He reports that the patients and researchers have a lot of common ground and common goals and that they want to work hand-in-hand. Advocates bring in other advocates.
- Advocates provide input in clinical trial design and through the Translational Breast Cancer Research Consortium (TBCRC). One research TL stated that researchers need to understand the concerns of the community. They provide focus and a lot of practical input, particularly on some of the clinical trial designs. Advocates provide input to ensure that trials are designed in such a way that patients will join them. Sometimes a patient will say "I wouldn't go on that trial." This allows the researcher to fix the problem. Advocates help bring the researchers back to what is most important for advancing clinical care.
- As an example of successful advocate input, an industry TL stated that at the TBCRC, someone proposed to have biopsies in every single patient with metastatic disease as a way to learn how drugs work or don't work. Because this was a smart, good idea, this changed immediately. Now at the TBCRC, every single trial obtains biopsies of metastatic disease.
- An industry TL stated that the relationship between patient advocates and industry is currently more about drugs that have been already approved and management of side effects.
- Advocates have helped expedite drug approval in multiple countries.
- Advocates helped develop a 100-person advocate community called PIVOT (Patients and Investigator Voices Organizing Together) that is their community sounding board and trains patients in how to be advocates for every kind of cancer.
- Advocates are active at Dana Farber in the EMBRACE Metastatic Breast Cancer Program. They help with organizing data, outreach and education, development of newsletters, webcasts, and educational forums related to MBC. They performed a survey study to understand coping mechanisms. Advocates review all of this content for language and tone.
- Advocates provide comments on grants including SPORE grants. One research TL stated that her group does not submit any grants that the advocacy organization has not read.
- Advocates serve on advisory boards.
- Advocates are involved in capturing the patient experience.

**Opportunities for more patient involvement**

Patient/nonprofit TLs

Patient/nonprofit TLs reported the *following opportunities for more advocacy involvement*:

- Increased involvement in DoD research studies
- Review posters
- Review papers
- Co-create solutions versus just being given a solution

- Involvement in the entire research process from the beginning of study design, through R&D, commercialization, and marketing
- Communication of findings in plain language with story telling. This will help patient involvement in other areas.
- Creation of a research advocacy program. Many researchers are very eager to work with patients, but are not sure how to go about it.
- Continue to ensure that patient advocates are partners of researchers, not adversaries.

Patient/nonprofit TLs also stated that they want to see more published papers in journals. They stressed the importance of getting patients at the table with scientists, researchers, clinicians, pharmaceutical companies, and other entities; collaborating on research; and helping design all aspects of a research program from beginning to end. Advocates should be involved early and often to ensure that research continues to be patient-centric. This concept is innovative, and there is room for more of that to happen.

Research TLs

Research TLs suggested the following *opportunities for more advocacy involvement*:

- Involvement in cooperative groups
- Working with the FDA and other agencies to improve trials specifically for metastatic disease and trials for metastasis preventing agents
- Encourage the distribution of drugs from pharmaceutical companies for preclinical studies to speed the process of testing novel combinations.
- Help facilitate two companies working together to test a drug combination in clinical trials when the two drugs are from two different companies; advocates currently work very little in industry.
- Participate in cutting-edge research including the design of trials and in helping mold research to the real needs of patients.
- Make their voices heard by policymakers in government, academia, industry, and all stakeholders to facilitate learning from one another about ways to advance patient care and improve patient outcomes.
- Working in underserved areas to raise the level of patient care

**Patient advocacy training**

Patient/nonprofit TLs discussed current *needs for patient advocacy training*. A training needs analysis needs to be done to assess what training is available and by which organization(s) and what training is lacking. Resources for advocacy training are lacking. Most patient advocates are self-taught. Curricula, either newly developed or already available, should be used, and a skill building course to help a patient frame his/her story in a way that is interesting needs to be created. Training modules for each stage of the research spectrum are needed. The training should be divided into segments such as being an advocate for basic research, for translational research, for clinical trials, in the governmental space, etc. This will allow advocates to "specialize" and help avoid advocate burnout.

## Topic 7: Possible roles for the MBCA

Patient/nonprofit TLs suggested the following *roles for the MBCA* to facilitate MBC research that will impact MBC patients:

- Continue to increase conversations about MBC.
- Be more vocal, especially in the Black community; many Blacks do not know about the MBCA.
- Report novel breakthroughs that are coming up the pipeline.
- Do MBC interviews with people about what they think is most important.
- Help patients and researchers make connections, initiate a conversation, or get a seat at the table.
- Facilitate collaborations between researchers and patients.
- Facilitate advocates working with young researchers.
- Develop a university course for researchers in how to work with an advocate or with the public.
- Assist with advocacy training: develop a strategy that is effective in the community and embrace the passion of a particular patient.
- Facilitate new advocates talking to more experienced advocates.
- Share the work the MBCA is doing via a newsletter or via virtual events to promote the work being done. Describe what the MBCA and their member organizations are doing to keep MBC patients up to date about MBC, from financial to research. Let them know that the organizations that are part of the MBCA are “out there fighting for you."
- Create a roadmap or framework for small funders to help prioritize, be strategic, pool resources, and have the greatest impact.
- Have nonthreatening conversations with pharmaceutical companies about data sharing including sharing of negative results. The MBCA could help put pressure on those who hold data in siloes to share their data. One industry TL reported that her company is committed to sharing its study results, whether positive or negative.
- Gather representatives from pharmaceutical companies who do the research and who set the priorities within their company to facilitate combination therapeutics; this is possible and needs to be a priority.
- Create a medical advisory board, which would facilitate pharmaceutical company involvement in combination therapy.
- Increase awareness of clinical trials by all patients.
- Promote MBC Connect more.

Research TLs suggested the following *roles for the MBCA*:

- The MBCA can extend its leverage by publishing a position paper in a high-impact journal such as the *New England Journal of Medicine* or *Journal of Clinical Oncology*. The MBCA can get people's attention and say, "We demand these changes”. The position paper could say "You should not run a trial without looking at collateral damage." The paper could also call for companies to work together.
- Promote collaborations between basic scientists and clinicians. Bridge the gap between universities and industry by engaging the MBCA’s industry partners.
- Create a portal or platform so that people who are doing basic science and are interested in further development of a compound have access to medicinal chemistry expertise to help them think or provide advice.
- Provide advice about legal aspects, intellectual property, and protection.

- Provide a database platform so that patients can search and access, in a user-friendly way, trials in which they could participate based on their geographical location, personal background information, disease status, etc. Improve minority accrual to trials.
- Continue to advocate on a national level for investment in clinical trials.
- Promote or facilitate the use of telemedicine to provide access to metastatic second opinions, particularly in underserved communities.
- Be active in very low service areas with underserved populations.
- Provide patient education.
- Emphasize the importance of studying people in “clinical investigations” not just studying drugs as is done in “clinical trials”.
- Encourage patients to submit their samples, both primary and metastatic, to appropriate studies along with annotation of the patient's clinical journey so that each patient can be studied.
- Facilitate development of a platform to accumulate data on MBC patients.
- Facilitate patients informing patients of new treatment options and trials.
- Help engage community providers. NCCN centers can serve as hubs to reach community providers.
- Help with the drug matching problem. Ensure that a patient's tumor is profiled, and then ensure that the patient is aware of what the drug matching process looks like, and get them access to specialists and drugs that could be repurposed.
- The MBCA consists of different organizations with different outreach styles, different target audiences, and different face-forwarding groups. The MBCA could optimize the common strengths of all the organizations by promoting joint efforts to facilitate achieving common goals and activities such as lobbying with the federal government and with funding agencies.

# APPENDIX B:
# THOUGHT LEADER SURVEY QUESTIONS

## Metastatic Breast Cancer - Thought Leader Survey

### Welcome!

**Thank you for participating in the Metastatic Breast Cancer Alliance survey. You have been identified as a Thought Leader on the topic of metastatic breast cancer (MBC).**

**We recommend taking the survey on a tablet or computer (larger screen than a phone).**

**We are requesting responses by March 24th. Your confidential responses will go directly to our outside researcher. The Alliance will know who completed the survey but will not know who said what.**

**We hope you will share your expertise on the following pages. Your thoughts will help the Alliance shape its priorities. We commit to sharing the information we gather and are eager for your input that will make it as robust as possible.**

## Metastatic Breast Cancer - Thought Leader Survey

***This section asks a few questions about you and your work background related to metastatic breast cancer (MBC):***

* 1. Please choose the category and title that most accurately describes your **primary** role related to metastatic breast cancer:

- ◯ Clinician: Medical Oncologist
- ◯ Clinician: Surgeon
- ◯ Clinician: Radiation Oncologist
- ◯ Clinician: Other (PLEASE DESCRIBE IN COMMENT BOX BELOW)
- ◯ Research Scientist: Laboratory Scientist
- ◯ Research Scientist: Biostatistician
- ◯ Research Scientist: Computer Scientist
- ◯ Research Scientist: Other (PLEASE DESCRIBE IN COMMENT BOX BELOW)
- ◯ Nonprofit Staff Member
- ◯ Patient Advocate
- ◯ Other professional role (PLEASE DESCRIBE IN COMMENT BOX BELOW)

If you chose one of the "OTHER" options above, please briefly describe your primary role related to MBC:

## Metastatic Breast Cancer - Thought Leader Survey

* 2. Are you living with metastatic breast cancer?

- ◯ No
- ◯ Yes (Please fill in box below)

If Yes, how many years have you been living with MBC:

## Metastatic Breast Cancer - Thought Leader Survey

* 3. Are you living with metastatic breast cancer?

- ◯ No
- ◯ Yes (Please fill in box below)

If Yes, how many years have you been living with MBC?

4. As a Patient Advocate, what organization(s) are you primarily affiliated with? (Please list below)

## Metastatic Breast Cancer - Thought Leader Survey

* 5. Which of the following most accurately describes the setting in which you do your MBC work?

- ◯ Academically affiliated institution
- ◯ Community hospital/cancer center
- ◯ Pharmaceutical company
- ◯ Nonprofit organization
- ◯ Private practice
- ◯ Does not apply to me
- ◯ Other (please briefly describe)

* 6. What proportion of your current work is directly related to MBC?

- ◯ 75% - 100%
- ◯ 50% - 74%
- ◯ 25% - 49%
- ◯ Less than 25%

* 7. How many years have you been involved in MBC-focused work? (Please enter the **numeral only** below.)

* 8. Please indicate your gender identity: (Please select one)

- ◯ Cisgender Female (assigned female at birth and identify as female)
- ◯ Cisgender Male (assigned male at birth and identify as male)
- ◯ Transgender Female (assigned male at birth and identify as female)
- ◯ Transgender Male (assigned female at birth and identify as male)
- ◯ Genderqueer or Non-Binary (neither exclusively male nor female)
- ◯ Another gender category
- ◯ I prefer not to answer

* 9. Are you of Hispanic or Latino(a) origin or descent? (Please select one)

- Yes
- No
- I prefer not to answer

* 10. What is your race?

- American Indian/Alaska Native
- Asian
- Black/African American
- Native Hawaiian or Other Pacific Islander
- White/Caucasian
- I prefer not to answer
- Other (please specify)

* 11. How familiar are you with the Metastatic Breast Cancer Alliance? (Please select one)

- I am actively involved with the MBC Alliance
- While not actively involved, I am very familiar with the MBC Alliance
- I am somewhat familiar with the MBC Alliance
- I've heard of the MBC Alliance, but know little about it
- I have never heard of the MBC Alliance

## Metastatic Breast Cancer - Thought Leader Survey

Section 1 of 4

***The following set of questions asks about your thoughts on the amount of progress that has occurred over the last five years, leading to improved outcomes and/or quality of life for people living with MBC.***

***For each item, please select a number from 1 to 5, where 1 represents insignificant progress for patients over the past five years and 5 represents significant progress.***
***As you see the topics on a page, if you feel you cannot weigh in, feel free to scroll down and click "Next" to proceed.***

***Remember:*** ***Please rate progress over the last five years leading to improved outcomes and/or quality of life for people with MBC.***

12. New Drugs for MBC specific to:

| | Insignificant progress 1 | Minor 2 | Moderate 3 | Major 4 | Significant progress 5 | Don't know |
|---|---|---|---|---|---|---|
| Treatment for Hormone-positive MBC | ○ | ○ | ○ | ○ | ○ | ○ |
| Treatment for HER2-positive MBC | ○ | ○ | ○ | ○ | ○ | ○ |
| Treatment for Triple Negative MBC | ○ | ○ | ○ | ○ | ○ | ○ |
| Treatment for patients with hereditary breast cancer | ○ | ○ | ○ | ○ | ○ | ○ |
| Treatment for Inflammatory Breast Cancer | ○ | ○ | ○ | ○ | ○ | ○ |
| Treatment for Invasive Lobular Cancer | ○ | ○ | ○ | ○ | ○ | ○ |
| Treatments for CNS metastasis | ○ | ○ | ○ | ○ | ○ | ○ |
| Antibody conjugates for the treatment of MBC | ○ | ○ | ○ | ○ | ○ | ○ |
| Vaccines for the treatment of MBC | ○ | ○ | ○ | ○ | ○ | ○ |
| Drugs that target tumor mutations (e.g. PIK3CA) | ○ | ○ | ○ | ○ | ○ | ○ |

13. Improving Patient's Quality of Life

| | Insignificant progress 1 | Minor 2 | Moderate 3 | Major 4 | Significant progress 5 | Don't know |
|---|---|---|---|---|---|---|
| Mitigation of side effects related to treatments | ○ | ○ | ○ | ○ | ○ | ○ |
| Mitigation of collateral damage (functional, emotional, financial) related to treatment for and/or diagnosis of MBC | ○ | ○ | ○ | ○ | ○ | ○ |
| Telehealth to improve access to care | ○ | ○ | ○ | ○ | ○ | ○ |
| Liquid biopsies for monitoring response to treatment | ○ | ○ | ○ | ○ | ○ | ○ |
| Pain management | ○ | ○ | ○ | ○ | ○ | ○ |

14. Basic Research

| | Insignificant progress 1 | Minor 2 | Moderate 3 | Major 4 | Significant progress 5 | Don't know |
|---|---|---|---|---|---|---|
| Pre-clinical model systems (cell lines, 3-D modeling, animal models, etc.) | ○ | ○ | ○ | ○ | ○ | ○ |
| Access to serial biopsy tissue/blood derived from all populations including diverse and underserved populations | ○ | ○ | ○ | ○ | ○ | ○ |
| Understanding the immune system | ○ | ○ | ○ | ○ | ○ | ○ |
| Understanding the role of the tumor microenvironment | ○ | ○ | ○ | ○ | ○ | ○ |
| Breast cancer genetics | ○ | ○ | ○ | ○ | ○ | ○ |
| Tumor heterogeneity | ○ | ○ | ○ | ○ | ○ | ○ |
| Multidisciplinary collaboration/translational science | ○ | ○ | ○ | ○ | ○ | ○ |
| Sharing of Data and resources (e.g., bio-specimens) | ○ | ○ | ○ | ○ | ○ | ○ |

15. Are there any other items that you would add to this list, when thinking about **progress** that has occurred over the **last five years** that has led to improved outcomes and/or quality of life for people living with MBC (something that you might rate as a 4 or a 5)?

Metastatic Breast Cancer - Thought Leader Survey

Section 2 of 4

***The following set of questions asks your thoughts on the potential for each item listed to lead to improved outcomes and/or quality of life for people living with MBC over the next five years.***

***For each item, please use a scale from 1 to 5 as indicated below, where 1 indicates insignificant potential and 5 indicates significant potential.***
***As you see the topics on a page, if you feel you cannot weigh in, feel free to scroll down and click "Next" to proceed.***

***Remember: Please rate the potential over the next five years for the item to lead to improved outcomes and/or quality of life for people with MBC.***

16. Basic Research

| | Insignificant potential 1 | Minor 2 | Moderate 3 | Major 4 | Significant potential 5 | Don't know |
|---|---|---|---|---|---|---|
| The immune system | ○ | ○ | ○ | ○ | ○ | ○ |
| Tumor micro/immune/environment | ○ | ○ | ○ | ○ | ○ | ○ |
| Tumor heterogeneity | ○ | ○ | ○ | ○ | ○ | ○ |
| Tumor dormancy | ○ | ○ | ○ | ○ | ○ | ○ |
| Tumor metabolism | ○ | ○ | ○ | ○ | ○ | ○ |
| Cellular Stress | ○ | ○ | ○ | ○ | ○ | ○ |
| Epigenome | ○ | ○ | ○ | ○ | ○ | ○ |
| Proteome | ○ | ○ | ○ | ○ | ○ | ○ |
| Microbiome | ○ | ○ | ○ | ○ | ○ | ○ |
| Genomics | ○ | ○ | ○ | ○ | ○ | ○ |
| Genetics | ○ | ○ | ○ | ○ | ○ | ○ |

17. Biomarkers

| | Insignificant potential 1 | Minor 2 | Moderate 3 | Major 4 | Significant potential 5 | Don't know |
|---|---|---|---|---|---|---|
| Tumor mutation (gene expression) profiles/signatures | ○ | ○ | ○ | ○ | ○ | ○ |
| Liquid biopsy | ○ | ○ | ○ | ○ | ○ | ○ |
| Tumor metabolism | ○ | ○ | ○ | ○ | ○ | ○ |
| Tumor microbiome | ○ | ○ | ○ | ○ | ○ | ○ |

18. Technologies

| | Insignificant potential 1 | Minor 2 | Moderate 3 | Major 4 | Significant potential 5 | Don't Know |
|---|---|---|---|---|---|---|
| Liquid biopsy | ○ | ○ | ○ | ○ | ○ | ○ |
| Imaging | ○ | ○ | ○ | ○ | ○ | ○ |
| Multi-feature microscopy | ○ | ○ | ○ | ○ | ○ | ○ |
| Single cell technologies | ○ | ○ | ○ | ○ | ○ | ○ |
| Live-cell technologies | ○ | ○ | ○ | ○ | ○ | ○ |
| Nanotechnology | ○ | ○ | ○ | ○ | ○ | ○ |
| Theragnostics (molecules that deliver therapeutics coupled to radioisotopes used in tumor imaging) | ○ | ○ | ○ | ○ | ○ | ○ |
| Artificial intelligence | ○ | ○ | ○ | ○ | ○ | ○ |
| Big Data (integration and anaylsis of large complex data sets from multiple sources) | ○ | ○ | ○ | ○ | ○ | ○ |

19. Are there any other items that you would add to this list of items, when thinking about the **potential** for improved outcomes and/or quality of life for people living with MBC over the **next five years** (something you might rate as a 4 or a 5)?

Metastatic Breast Cancer - Thought Leader Survey

Section 3 of 4

***This section is specific to clinical trials and how certain factors related to clinical trial participation and design may contribute to improved outcomes and/or quality of life for people living with MBC.***

***Please use the following scale where 1 indicates the item is not important and 5 indicates it is extremely important.***
***As you see the topics on a page, if you feel you cannot weigh in, feel free to scroll down and click "Next" to proceed.***

***Remember: Please rate the importance of how each factor related to clinical trials may contribute to improved outcomes and/or quality of life for people living with MBC. Even if many items seem like 5's, please try to use the whole scale.***

20. Patient Factors

| | Not important 1 | Slightly 2 | Somewhat 3 | Very 4 | Extremely important 5 | Don't know |
|---|---|---|---|---|---|---|
| Reducing eligibility requirement (e.g., inclusion of CNS disease) | ○ | ○ | ○ | ○ | ○ | ○ |
| Reducing study requirements/ burden for clinical trial participants (e.g. number of in-person visits) | ○ | ○ | ○ | ○ | ○ | ○ |
| Offsetting insurance gaps (e.g., co-pays, deductibles) | ○ | ○ | ○ | ○ | ○ | ○ |
| Compensating patients for out of pocket expenses (e.g., travel, child-care) | ○ | ○ | ○ | ○ | ○ | ○ |
| Educating patients about clinical trial participation | ○ | ○ | ○ | ○ | ○ | ○ |
| Increasing trust about clinical trials | ○ | ○ | ○ | ○ | ○ | ○ |
| Developing patient-friendly, study-specific educational materials (e.g., Informed Consent Forms, patient brochures, study website) | ○ | ○ | ○ | ○ | ○ | ○ |

21. Patient Accrual Planning

| | Not important 1 | Slightly 2 | Somewhat 3 | Very 4 | Extremely important 5 | Don't know |
|---|---|---|---|---|---|---|
| Decentralizing clinical trials to expand geographic access to trials | ○ | ○ | ○ | ○ | ○ | ○ |
| Increasing representation from diverse and underserved populations | ○ | ○ | ○ | ○ | ○ | ○ |
| Increasing the number of clinicians who offer clinical trials to their patients | ○ | ○ | ○ | ○ | ○ | ○ |
| Limiting exclusion criteria to those that are critical to patient safety | ○ | ○ | ○ | ○ | ○ | ○ |

22. Funding

| | Not important 1 | Slightly 2 | Somewhat 3 | Very 4 | Extremely important 5 | Don't know |
|---|---|---|---|---|---|---|
| Increased funding for long term follow-up | ○ | ○ | ○ | ○ | ○ | ○ |
| Increased funding for Bio-specimen collection and storage | ○ | ○ | ○ | ○ | ○ | ○ |
| Increased funding for correlative science | ○ | ○ | ○ | ○ | ○ | ○ |

23. Clinical Trial Design Factors

| | Not important 1 | Slightly 2 | Somewhat 3 | Very 4 | Extremely important 5 | Don't know |
|---|---|---|---|---|---|---|
| Greater use of novel endpoints | ○ | ○ | ○ | ○ | ○ | ○ |
| Novel combinations | ○ | ○ | ○ | ○ | ○ | ○ |
| Incorporating patient reported outcomes | ○ | ○ | ○ | ○ | ○ | ○ |
| Innovative trial designs such as basket trials, umbrella trials, adaptive trials | ○ | ○ | ○ | ○ | ○ | ○ |
| Trials testing different sequencing and/or dosing of drugs | ○ | ○ | ○ | ○ | ○ | ○ |
| Incorporating decentralization to increase accessibility | ○ | ○ | ○ | ○ | ○ | ○ |

24. Are there any other items that you would add to this list, when thinking about **clinical trials** and the item leading to improved outcomes and/or quality of life for people living with MBC (something you might rate as a 4 or a 5)?

Section 4 of 4

***As a patient-focused advocacy organization, the MBC Alliance may be uniquely positioned to impact issues affecting people living with MBC.***

***Please indicate the degree of priority you believe the MBC Alliance should place on each item, where 1 indicates very low to 5 indicates very high priority.***

***As you see the topics on a page, if you feel you cannot weigh in, feel free to scroll down and click "Next" to proceed.***

***Remember*: Please rate the priority you feel the MBC Alliance should place on the item. Even if many items seem like 5's, please try to use the whole scale.**

25. Awareness and Education

| | Very low priority 1 | Low 2 | Medium 3 | High 4 | Very high priority 5 | Don't know |
|---|---|---|---|---|---|---|
| Public understanding of science and its breakthroughs | ○ | ○ | ○ | ○ | ○ | ○ |
| Conversations about MBC in all breast cancer communities | ○ | ○ | ○ | ○ | ○ | ○ |
| Patient education about the importance of bio-specimen (e.g. tissue/blood) donation | ○ | ○ | ○ | ○ | ○ | ○ |
| Patient education about the value of patient registries | ○ | ○ | ○ | ○ | ○ | ○ |
| Training and education for advocates | ○ | ○ | ○ | ○ | ○ | ○ |
| Patient awareness about clinical trials | ○ | ○ | ○ | ○ | ○ | ○ |
| Healthcare provider awareness about clinical trials | ○ | ○ | ○ | ○ | ○ | ○ |
| Patient awareness about genetic testing and/or tumor profiling | ○ | ○ | ○ | ○ | ○ | ○ |
| Healthcare provider awareness about genetic testing and/or tumor profiling | ○ | ○ | ○ | ○ | ○ | ○ |

26. Collaboration

| | Very low priority 1 | Low 2 | Medium 3 | High 4 | Very high priority 5 | Don't know |
|---|---|---|---|---|---|---|
| Patient and investigator collaborations in research | ○ | ○ | ○ | ○ | ○ | ○ |
| Patient and investigator collaborations in clinical trials | ○ | ○ | ○ | ○ | ○ | ○ |
| Researcher outreach to patient advocates | ○ | ○ | ○ | ○ | ○ | ○ |
| Facilitate discussions with pharma for patient-centric clinical trial design | ○ | ○ | ○ | ○ | ○ | ○ |
| Facilitate collaborations between scientists and clinicians (Team science) | ○ | ○ | ○ | ○ | ○ | ○ |
| Promote data sharing | ○ | ○ | ○ | ○ | ○ | ○ |

27. Funding

| | Very low priority 1 | Low 2 | Medium 3 | High 4 | Very high priority 5 | Don't know |
|---|---|---|---|---|---|---|
| Advocate for continued financial investment in basic research | ○ | ○ | ○ | ○ | ○ | ○ |
| Advocate for continued financial investment in clinical trials | ○ | ○ | ○ | ○ | ○ | ○ |
| Advocate for the funding for patient reported outcomes in clinical trials | ○ | ○ | ○ | ○ | ○ | ○ |
| Advocate for funding for data sharing | ○ | ○ | ○ | ○ | ○ | ○ |
| Advocate for reimbursement for telemedicine | ○ | ○ | ○ | ○ | ○ | ○ |

28. Other

| | Very low priority 1 | Low 2 | Medium 3 | High 4 | Very high priority 5 | Don't know |
|---|---|---|---|---|---|---|
| Help to coordinate the efforts of the MBC Alliance members to achieve common goals | ○ | ○ | ○ | ○ | ○ | ○ |
| Develop a road map for small funders to pool their resources for greater impact | ○ | ○ | ○ | ○ | ○ | ○ |
| Encourage all researchers (including pharma) to report both positive and negative results from clinical studies | ○ | ○ | ○ | ○ | ○ | ○ |

29. Are there any other items that you would add to this list, when thinking about the degree of **priority** you believe the MBC Alliance should place on an item (something you might rate as a 4 or a 5)?

30. Is there anything else you would like us to know?

## Metastatic Breast Cancer - Thought Leader Survey

Thank you for taking the time to complete the survey.

# APPENDIX C:

## BREAKDOWN OF RESPONSES FROM PEOPLE LIVING WITH MBC (N = 22), PATIENT ADVOCATES/NONPROFIT STAFF NOT LIVING WITH MBC (N = 16), AND THE ENTIRE SAMPLE OF SURVEY RESPONDENTS (N = 119)

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0012_000_2

Summary of Frequencies: TOP 2 BOX q0012_0001 to q0012_0010

## PROGRESS

| Total | 119 | 22 | 16 |
|---|---|---|---|
| Treatment for Hormone-positive MBC | 72 | 11 | 6 |
| | 61% | 50% | 38% |
| Treatment for HER2-positive MBC | 88 | 10 | 11 |
| | 74% | 45% | 69% |
| Treatment for Triple Negative MBC | 38 | 8 | 3 |
| | 32% | 36% | 19% |
| Treatment for patients with hereditary breast cancer | 35 | 2 | 2 |
| | 29% | 9% | 13% |
| Treatment for Invasive Lobular Cancer | 5 | - | - |
| | 4% | | |
| Treatments for CNS metastasis | 20 | 2 | 2 |
| | 17% | 9% | 13% |
| Antibody conjugates for the treatment of MBC | 60 | 3 | 5 |
| | 50% | 14% | 31% |
| Vaccines for the treatment of MBC | 1 | - | - |
| | 1% | | |
| Drugs that target tumor mutations (e.g. PIK3CA) | 46 | 11 | 7 |
| | 39% | 50% | 44% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0013_000_2

Summary of Frequencies: TOP 2 BOX q0013_0001 to q0013_0005

PROGRESS

| Total | 119 | 22 | 16 |
|---|---|---|---|
| Mitigation of side effects related to treatments | 14 | 2 | - |
| | 12% | 9% | |
| Mitigation of collateral damage (functional, emotional, financial) related to treatment for and/or diagnosis of MBC | 6 | 2 | - |
| | 5% | 9% | |
| Telehealth to improve access to care | 46 | 10 | 3 |
| | 39% | 45% | 19% |
| Liquid biopsies for monitoring response to treatment | 31 | 7 | 1 |
| | 26% | 32% | 6% |
| Pain management | 7 | 2 | - |
| | 6% | 9% | |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0014_000_2

Summary of Frequencies: TOP 2 BOX q0014_0001 to q0014_0008

## PROGRESS

| Total | 119 | 22 | 16 |
|---|---|---|---|
| Pre-clinical model systems (cell lines, 3-D modeling, animal models, etc.) | 31 | 4 | 5 |
| | 26% | 18% | 31% |
| Access to serial biopsy tissue/blood derived from all populations including diverse and underserved populations | 13 | 2 | 3 |
| | 11% | 9% | 19% |
| Understanding the immune system | 49 | 7 | 6 |
| | 41% | 32% | 38% |
| Understanding the role of the tumor microenvironment | 36 | 3 | 2 |
| | 30% | 14% | 13% |
| Breast cancer genetics | 40 | 5 | 5 |
| | 34% | 23% | 31% |
| Tumor heterogeneity | 38 | 5 | 4 |
| | 32% | 23% | 25% |
| Multidisciplinary collaboration/translational science | 44 | 3 | 5 |
| | 37% | 14% | 31% |
| Sharing of Data and resources (e.g., bio-specimens) | 28 | 2 | 4 |
| | 24% | 9% | 25% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0016_000_2
Summary of Frequencies: TOP 2 BOX q0016_0001 to q0016_0011

## POTENTIAL

| | | | |
|---|---|---|---|
| Total | 119 | 22 | 16 |
| The immune system | 89 | 16 | 10 |
| | 75% | 73% | 63% |
| Tumor micro/immune/environment | 84 | 15 | 10 |
| | 71% | 68% | 63% |
| Tumor heterogeneity | 71 | 11 | 10 |
| | 60% | 50% | 63% |
| Tumor dormancy | 56 | 9 | 9 |
| | 47% | 41% | 56% |
| Tumor metabolism | 50 | 9 | 8 |
| | 42% | 41% | 50% |
| Cellular Stress | 29 | 1 | 3 |
| | 24% | 5% | 19% |
| Epigenome | 49 | 3 | 6 |
| | 41% | 14% | 38% |
| Proteome | 36 | 2 | 6 |
| | 30% | 9% | 38% |
| Microbiome | 40 | 6 | 6 |
| | 34% | 27% | 38% |
| Genomics | 68 | 11 | 11 |
| | 57% | 50% | 69% |
| Genetics | 58 | 9 | 6 |
| | 49% | 41% | 38% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0017_000_2

Summary of Frequencies: TOP 2 BOX q0017_0001 to q0017_0004

POTENTIAL

| | | | |
|---|---|---|---|
| Total | 119 | 22 | 16 |
| Tumor mutation (gene expression) profiles/signatures | 68 | 11 | 10 |
| | 57% | 50% | 63% |
| Liquid biopsy | 83 | 13 | 12 |
| | 70% | 59% | 75% |
| Tumor metabolism | 41 | 8 | 7 |
| | 34% | 36% | 44% |
| Tumor microbiome | 34 | 6 | 5 |
| | 29% | 27% | 31% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0018_000_2
Summary of Frequencies: TOP 2 BOX q0018_0001 to q0018_0009

## POTENTIAL

| | | | |
|---|---|---|---|
| Total | 119 | 22 | 16 |
| Liquid biopsy | 88 | 13 | 13 |
| | 74% | 59% | 81% |
| Imaging | 65 | 11 | 8 |
| | 55% | 50% | 50% |
| Multi-feature microscopy | 40 | 2 | 4 |
| | 34% | 9% | 25% |
| Single cell technologies | 56 | 5 | 4 |
| | 47% | 23% | 25% |
| Live-cell technologies | 41 | 3 | 4 |
| | 34% | 14% | 25% |
| Nanotechnology | 34 | 5 | 5 |
| | 29% | 23% | 31% |
| Theragnostics (molecules that deliver therapeutics coupled to radioisotopes used in tumor imaging) | 39 | 7 | 9 |
| | 33% | 32% | 56% |
| Artificial intelligence | 67 | 10 | 11 |
| | 56% | 45% | 69% |
| Big Data (integration and anaylsis of large complex data sets from multiple sources) | 76 | 13 | 11 |
| | 64% | 59% | 69% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0020_000_2

Summary of Frequencies: TOP 2 BOX q0020_0001 to q0020_0007

## CLINICAL TRIALS

| TOTAL ANSWERING | 119 | 22 | 16 |
|---|---|---|---|
| Reducing eligibility requirement (e.g., inclusion of CNS disease) | 94 | 16 | 14 |
| | 79% | 73% | 88% |
| Reducing study requirements/ burden for clinical trial participants (e.g. number of in-person visits) | 93 | 15 | 15 |
| | 78% | 68% | 94% |
| Offsetting insurance gaps (e.g., co-pays, deductibles) | 89 | 15 | 15 |
| | 75% | 68% | 94% |
| Compensating patients for out of pocket expenses (e.g., travel, child-care) | 89 | 16 | 14 |
| | 75% | 73% | 88% |
| Educating patients about clinical trial participation | 98 | 14 | 15 |
| | 82% | 64% | 94% |
| Increasing trust about clinical trials | 100 | 15 | 16 |
| | 84% | 68% | 100% |
| Developing patient-friendly, study-specific educational materials (e.g., Informed Consent Forms, patient brochures, study website) | 91 | 15 | 13 |
| | 76% | 68% | 81% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0021_000_2

Summary of Frequencies: TOP 2 BOX q0021_0001 to q0021_0004

## CLINICAL TRIALS

| Total | 119 | 22 | 16 |
|---|---|---|---|
| Decentralizing clinical trials to expand geographic access to trials | 93 | 17 | 15 |
| | 78% | 77% | 94% |
| Increasing representation from diverse and underserved populations | 104 | 18 | 16 |
| | 87% | 82% | 100% |
| Increasing the number of clinicians who offer clinical trials to their patients | 97 | 17 | 15 |
| | 82% | 77% | 94% |
| Limiting exclusion criteria to those that are critical to patient safety | 87 | 14 | 12 |
| | 73% | 64% | 75% |

Table q0022_000_2

Summary of Frequencies: TOP 2 BOX q0022_0001 to q0022_0003

| Total | 119 | 22 | 16 |
|---|---|---|---|
| Increased funding for long term follow-up | 91 | 15 | 13 |
| | 76% | 68% | 81% |
| Increased funding for Bio-specimen collection and storage | 94 | 14 | 12 |
| | 79% | 64% | 75% |
| Increased funding for correlative science | 88 | 11 | 12 |
| | 74% | 50% | 75% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0023_000_2

Summary of Frequencies: TOP 2 BOX q0023_0001 to q0023_0006

## CLINICAL TRIALS

| | | | |
|---|---|---|---|
| Total | 119 | 22 | 16 |
| Greater use of novel endpoints | 73 | 9 | 9 |
| | 61% | 41% | 56% |
| Novel combinations | 79 | 13 | 11 |
| | 66% | 59% | 69% |
| Incorporating patient reported outcomes | 87 | 15 | 15 |
| | 73% | 68% | 94% |
| Innovative trial designs such as basket trials, umbrella trials, adaptive trials | 85 | 14 | 15 |
| | 71% | 64% | 94% |
| Trials testing different sequencing and/or dosing of drugs | 77 | 17 | 15 |
| | 65% | 77% | 94% |
| Incorporating decentralization to increase accessibility | 88 | 16 | 14 |
| | 74% | 73% | 88% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0025_000_2

Summary of Frequencies: TOP 2 BOX q0025_0001 to q0025_0009

MBCA PRIORITIES

| | | | |
|---|---|---|---|
| Total | 119 | 22 | 16 |
| Public understanding of science and its breakthroughs | 85 | 8 | 8 |
| | 71% | 36% | 50% |
| Conversations about MBC in all breast cancer communities | 92 | 15 | 11 |
| | 77% | 68% | 69% |
| Patient education about the importance of bio-specimen (e.g. tissue/blood) donation | 81 | 12 | 9 |
| | 68% | 55% | 56% |
| Patient education about the value of patient registries | 75 | 12 | 11 |
| | 63% | 55% | 69% |
| Training and education for advocates | 86 | 16 | 9 |
| | 72% | 73% | 56% |
| Patient awareness about clinical trials | 104 | 16 | 13 |
| | 87% | 73% | 81% |
| Healthcare provider awareness about clinical trials | 97 | 17 | 10 |
| | 82% | 77% | 63% |
| Patient awareness about genetic testing and/or tumor profiling | 87 | 15 | 11 |
| | 73% | 68% | 69% |
| Healthcare provider awareness about genetic testing and/or tumor profiling | 83 | 15 | 10 |
| | 70% | 68% | 63% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0026_000_2

Summary of Frequencies: TOP 2 BOX q0026_0001 to q0026_0006

MBCA PRIORITIES

| | | | |
|---|---|---|---|
| Total | 119 | 22 | 16 |
| Patient and investigator collaborations in research | 90 | 17 | 11 |
| | 76% | 77% | 69% |
| Patient and investigator collaborations in clinical trials | 99 | 18 | 13 |
| | 83% | 82% | 81% |
| Researcher outreach to patient advocates | 85 | 17 | 10 |
| | 71% | 77% | 63% |
| Facilitate discussions with pharma for patient-centric clinical trial design | 92 | 17 | 13 |
| | 77% | 77% | 81% |
| Facilitate collaborations between scientists and clinicians (Team science) | 87 | 11 | 9 |
| | 73% | 50% | 56% |
| Promote data sharing | 98 | 16 | 13 |
| | 82% | 73% | 81% |

| IN THESE TABLES, PERCENTAGES OF RESPONDENTS SELECTING "4" OR "5" (I.E. TOP 2 BOX) ARE COMPUTED WITHIN COLUMNS. IT IS THE PERCENT OF THE **SAME** COLUMN'S 'TOTAL ANSWERING' ROW. | TOTAL ANSWERING (includes all 119) | Patient Advocates Living with MBC | Patient Advocates and Staff without MBC |
|---|---|---|---|

Table q0027_000_2

Summary of Frequencies: TOP 2 BOX q0027_0001 to q0027_0005

MBCA PRIORITIES

| Total | 119 | 22 | 16 |
|---|---|---|---|
| Advocate for continued financial investment in basic research | 101 | 20 | 13 |
| | 85% | 91% | 81% |
| Advocate for continued financial investment in clinical trials | 107 | 20 | 12 |
| | 90% | 91% | 75% |
| Advocate for the funding for patient reported outcomes in clinical trials | 90 | 18 | 13 |
| | 76% | 82% | 81% |
| Advocate for funding for data sharing | 82 | 14 | 9 |
| Advocate for reimbursement for telemedicine | 72 | 7 | 7 |
| | 61% | 32% | 44% |

Table q0028_000_2

Summary of Frequencies: TOP 2 BOX q0028_0001 to q0028_0003

| Total | 119 | 22 | 16 |
|---|---|---|---|
| Help to coordinate the efforts of the MBC Alliance members to achieve common goals | 96 | 18 | 12 |
| | 81% | 82% | 75% |
| Develop a road map for small funders to pool their resources for greater impact | 81 | 13 | 12 |
| | 68% | 59% | 75% |
| Encourage all researchers (including pharma) to report both positive and negative results from clinical studies | 97 | 16 | 13 |
| | 82% | 73% | 81% |