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Abstract

Background: Metastatic breast cancer (MBC) is breast cancer that has spread beyond the tissues of the breast. An estimated 150,000 women and men in the U.S. are living with metastatic breast cancer. 40,000 people in the U.S. die from metastatic breast cancer each year, accounting for 7% of all U.S. cancer deaths. Though treatments are improving, metastatic breast cancer is currently not curable. In order to make advances in our understanding of metastatic breast cancer, we need to be able to study tumor specimens from patients, ideally samples that are linked to updated clinical information. The challenge in studying tumors from patients with metastatic breast cancer has been that most tumors are not available for research, largely because the vast majority of patients are cared for in community settings where genomic studies are not conducted – which means that most patients have never been asked if they would like to contribute their tissue samples and medical information for research. To address this, we launched a nationwide study, *The Metastatic Breast Cancer Project*, which seeks to empower patients to accelerate research by sharing their samples and clinical information.

Methods: In collaboration with patients and advocacy groups, we developed a website to allow MBC patients to participate across the U.S. Enrolled patients are sent a saliva kit and asked to mail back a saliva sample, which is used to extract germline DNA. We contact participants' medical providers and obtain medical records and part of their tumor biopsy. Whole exome and transcriptome sequencing is performed on tumor and germline. Clinically annotated genomic data are used to identify mechanisms of response and resistance to therapies. The database is shared widely with researchers. Study updates and discoveries are shared with participants regularly.

Results: In the first 7 months, 2079 MBC patients enrolled. 1970 (95%) completed the 16-question survey about their cancer and treatments. Median age was 53 years (range 24-91). Median time between initial diagnosis (dx) of breast cancer and MBC was 2 yrs; 36% were dx'd with de novo MBC. More than 85% reported having a biopsy at or following their dx of MBC. Median time since MBC dx was 3 yrs; more than 100 reported having MBC >10 yrs. More than 600 reported being on a therapy for >2 yrs; more than 900 reported an "extraordinary response" to a therapy. For example, 117 reported long and/or extraordinary responses to capecitabine; 63 to platinum or PARP inhibitors, and 35 to everolimus. Initial medical records, saliva, and tumors have been received.

Conclusions: A direct-to-patient approach enabled rapid identification of large numbers of MBC patients willing to share tumors, saliva, and medical records. This includes many with rare phenotypes, a group that has been challenging to identify with traditional approaches. Genomic analysis of patients with extraordinary responses and with de novo MBC are underway. Patient reported data has also identified unanticipated research questions.

mbcproject.org

Your tumor and medical records could unlock discoveries.

Become part of the research movement. Have a direct impact on the future.

Here's how you can participate:

1. Tell us about yourself!
2. Give us permission to collect your samples and data.
3. Learn with us along the way.

Extraordinary Responders

Any therapy >2yrs?

- Yes: 1107
- No: 632
- Don't Know: 12
- No Response: 7

Any Extraordinary Response?

- Yes: 946
- No: 569
- Don't Know: 195
- No Response: 48

Years Since Diagnosis of Metastasis

Hundreds of patients with self-reported long-term and/or exceptional responses identified. >98% of respondents provided additional detail about the specific therapies involved. For example:

- **Capecitabine (Xeloda): 117**
- **Platinums (Carboplatin, Cisplatin) and PARP inhibitors: 63**
- **Everolimus: 36**

Participation in the the Metastatic Breast Cancer Project to Date

Over **2000 women and men with metastatic breast cancer** from all 50 states have joined the MBCproject in the 7 months since our launch in October 2015

Over **1100 have consented** to share medical records and allow next-generation sequencing on their tumor & saliva samples

~2000 participants have provided **detailed clinical and demographic data**, including information on treatments and responses

95% submitted the 16-question survey

98% response rate to each question (all are optional)

Median **6 minutes** to complete

Disease Characteristics:

- Dates of initial diagnosis
- Date of diagnosis with metastatic disease
- ER+, PR+, and HER2+ status

Treatment Response:

- Questions about extraordinary responses
- Free text about treatments
- Date of most recent biopsy

Demographics:

- Year of birth
- Race and ethnicity

Free text about anything additional

The Patient Voice

CultofPerfectMomhood @CultPerfectMoms - Oct 1
 The Boy says "Our family could be the key to unlocking a cure for cancer!" #mbcproject @corriePainter @NikhilWagle

Kelly Shanahan No, thank YOU for studying us! As someone who does not live near a research center and therefore cannot easily participate in trials, I finally feel like I can contribute!

"I would like to participate in your trial because knowledge is power and I am thrilled you are studying metastatic breast cancer for a cure! I want to live and watch my children grow up, but if I can't then I want to leave a legacy and a cure."

Tracy Oliphant @TKO365 5/24/16
 .@corriePainter & @NikhilWagle Giving us HOPE for the future and if not for some us, for our families. @MBC_Project

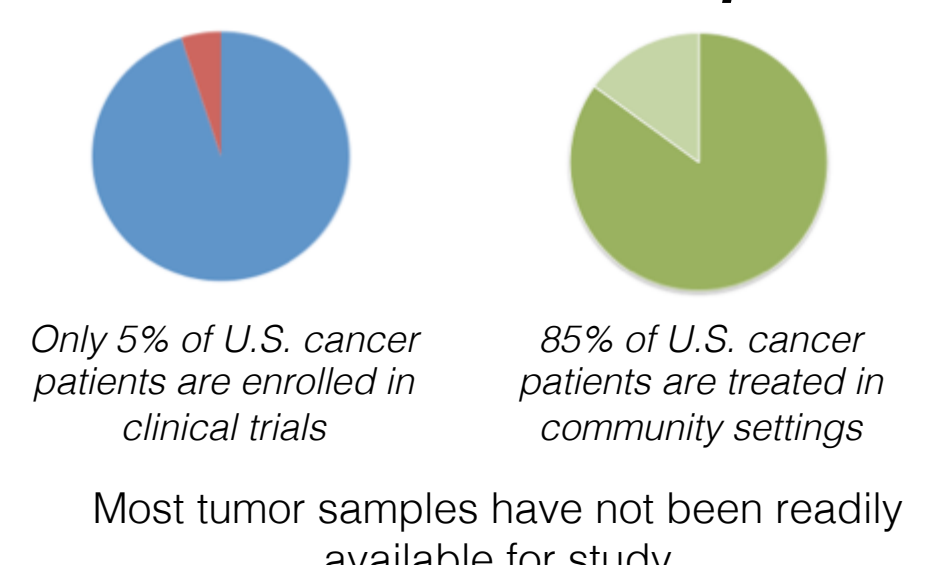
Amazing how happy that little box makes you feel! I felt like a 2 year old. Let me help! I feel a sense of pride and belonging because of this."

Twitter: @mbc_project
Email: info@mbcproject.org

Facebook: The Metastatic Breast Cancer Project
Phone: 617-800-1622

Patients have been involved from day 1 in conceiving, designing, implementing, testing, and refining this project. Feedback from patients is an essential element of the MBCproject

Challenges of Studying Patient Tumor Samples



Partnering Directly with Patients

GOAL: To empower patients and their families to accelerate research through sharing samples and clinical information

Advocacy Partners



Approach

Online Consent	Medical History	Tissue and Saliva	Genomic Analysis	Data Interpretation	Reporting / Data Sharing
Electronic consent form asks for permission to obtain tumor tissue and medical records.	Medical records are obtained by the study team and centrally reviewed and abstracted	Tumor blocks are requested from local pathology depts by the study team. Patients are sent a saliva kit for germline DNA.	Patient specimens are characterized by whole exome sequencing and transcriptome sequencing	Genomic data is interpreted in the context of clinical data at the individual level and in aggregate across similar patients	Deidentified genomic / clinical data shared widely with research community. Overall findings regularly communicated directly to patients

Identified groups of rare patients who have been challenging to study with traditional approaches:

- Patients with extraordinary responses to therapies
- Patients who present with advanced disease (de novo MBC)
- Patients diagnosed with MBC at a young age
- Patient groups that have been previously underrepresented

Current Age of Respondents

Average age of the respondents is 53 yrs (range 24-91 yrs)

Years Between Initial Diagnosis and Metastatic Disease

613 (36%) diagnosed with de novo MBC

Age at Diagnosis

591 (35%) diagnosed before age 40

Summary and Conclusions

- A direct-to-patient approach using social media & patient/advocate partnerships enabled rapid identification of large numbers of MBC patients willing to share tumors, saliva, & medical records.
- This includes many with rare phenotypes, a group that has been challenging to identify with traditional approaches
- Genomic analysis of tumors and saliva from patients with extraordinary responses, patients with de novo MBC, and young patients is underway.
- A pilot of cell free DNA sequencing from blood biopsies to study resistance, tumor evolution, and heterogeneity is planned
- All de-identified clinically-annotated genomic data will be shared widely with the research community as it is generated
- This study may serve as model for patient-driven research in other cancer types

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