

STUDY TITLE:

IBC and ME - International Inflammatory Breast Cancer Registry

PRINCIPAL INVESTIGATOR:

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CO-INVESTIGATORS:

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Check any **applicable** boxes in the table below – you will be asked for further detail on these topics later in the protocol form:

<p>Indicate Vulnerable Population(s) to be Enrolled</p>	<p><input type="checkbox"/> Children (you must complete Appendix A in addition to this protocol document if you plan to enroll children)</p> <p><input type="checkbox"/> Cognitively Impaired Adults</p> <p><input type="checkbox"/> Pregnant Women (IF the research activities will affect the pregnancy or the fetus)</p> <p><input type="checkbox"/> Prisoners (or other detained/paroled individuals)</p>
<p>International Research (check this box if you will collect data from individuals located outside the United States)</p>	<p><input type="checkbox"/></p>
<p>Research involving external collaborators (some research activities will be carried out by individuals not employed by Northwestern or NU affiliates)</p>	<p><input type="checkbox"/></p>
<p>Research has U.S. Federal government funding via direct award or a sub-award (e.g., NIH, NSF, other federal agencies or departments)</p>	<p><input type="checkbox"/></p>

1.0 Purpose and rationale of the study:

The purpose of this registry is to learn about the characteristics of Inflammatory Breast Cancer and to be used as a launching pad for future research studies with interested participants.

Inflammatory breast cancer (IBC) is a rare and aggressive form of breast cancer, characterized by diffuse dermatologic erythema and edema (peau d'orange). It accounts for 0.5 to 2 percent of invasive breast cancers diagnosed in the United States, but may be higher elsewhere. In the United States, its incidence appears to be increasing, particularly among white women [1-3]. The incidence of IBC is higher in black Americans compared with whites, and black women are diagnosed at a younger age [1,2]. Data on risk factors are limited and inconclusive [1] which necessitates further understanding of the etiology,

risk factors, and treatment responses of this disease. The typical presentation of IBC is different than non-inflammatory Breast Cancer and may include breast pain, a rapidly growing, self-diagnosed breast lump [4], tenderness, firmness, enlargement, or itching of the breast.

On presentation, almost all women with IBC have lymph node involvement, and approximately one-third have distant metastases [5-7]. IBC tends to have a higher preponderance of visceral metastases compared with other forms of breast cancer due to earlier and more aggressive hematogenous spread. Given the atypical and rapid onset of symptoms, many IBC patients are initially treated with antibiotics for presumed mastitis without clinical improvement, prompting further evaluation. IBC is designated as T4d in the American Joint Committee on Cancer (AJCC) Tumor, Node, Metastasis (TNM) staging system [8] with the following diagnostic criteria [9]: (1) Rapid onset of breast erythema, edema and/or peau d'orange, and/or warm breast, with or without an underlying palpable mass; (2) Duration of history no more than six months; (3) Erythema occupying at least one-third of the breast; and (4) Pathologic confirmation of invasive carcinoma.

In general, women with IBC without distant metastatic disease are approached similarly to those with non-inflammatory LABC. The main exception is that breast conservation therapy (BCT) and sentinel lymph node biopsy (SLNB) are inappropriate for women with IBC, even in the presence of a strong response to neoadjuvant therapy [10]. Management of the disease includes neoadjuvant chemotherapy and locoregional treatments such as surgery (mastectomy with axillary dissection) and radiation therapy. Using biomarkers, further specifications of treatment can be recommended both in neoadjuvant and adjuvant settings. For example, HER2-positive tumors may respond to targeted agents such as Trastuzumab and Pertuzumab; Hormone receptive-positive disease may benefit from endocrine therapy.

Despite improvements in treatment, the survival rate for patients with IBC remains significantly worse compared with women with non-inflammatory, locally advanced breast cancer (LABC). In a report from the SEER database, for breast cancer cases diagnosed between 2004 and 2007, the two-year breast cancer-specific survival rate of patients with IBC versus non-inflammatory LABC was 84 versus 91 percent (hazard ratio [HR] for death 1.43, 95% CI 1.10-1.86) [11]. Given the relative rarity of this disease and the need for more information about the efficacy of drugs against IBC, inflammatory breast cancer patients should be made aware of clinical trials for which they are eligible.

2.0 Enrollment Criteria (who can be in your study and who would not be eligible to participate in your study):

- Adults (>18 years old)
- Self report as having received a diagnosis of Inflammatory Breast Cancer

- Able to sign the online consent form, provide contact information, answer health background questionnaire
- Be in the United States of America

3.0 Sample Size:

This is a registry, so we are aiming to include as many participants as possible. In the US alone, we estimate 2000 women (which would be our upper limit) to be diagnosed annually with IBC, and we recognize that only a fraction of them would have the opportunity to participate in the registry.

4.0 Recruitment and Screening Methods:

Recruitment will be through an online survey intended for participants who self-identify as having been diagnosed with Inflammatory Breast Cancer. The link to the survey will be disseminated via listservs and social media via known IBC patient advocacy and professional research organizations such as: the Inflammatory Breast Cancer International Consortium. There will be controls / stops within the online survey instrument that will not allow the enrollment to proceed unless the potential subject indicates that they are currently in the United States.

5.0 Research Locations:

All activities of this registry (e.g. patient consent registration, questionnaires, and follow up contact) will be done via internet communications: email and a secure web server. The server hosting the data will be hosted by the Feinberg School of Medicine at NU (REDCap). The REDCap project is set up so that the consent and surveys will only proceed once the participants indicate that they are in the United States at the time of participation in the research.

6.0 Multi-site Research (research that involves external collaborating institutions and individuals):

N/A

7.0 International Research (where data collection will occur outside the United States and U.S. territories, including online activities)

Not at this time. We will submit an amendment before we do.

8.0 Procedures Involved:

Please check the boxes for all applicable data collection procedures you plan to use:

- One-on-one interviews
- Focus Groups
- Questionnaires/surveys
- Analysis of secondary data (medical record data, educational records, government or private sector datasets, etc.)
- Ethnographic observation
- Physiological measurements (e.g., EEG, EKG, MRI)
- Biospecimen collection (saliva samples, blood draws, hair samples, etc.)
- Mobile applications/data collection devices (e.g., Fitbits, actigraphs, etc.)
- Behavioral decisionmaking tasks (e.g., puzzles, interactive games, etc.)
- Physical activities such as walking and other forms of exercise
- Other procedures (briefly list types of procedures here if not covered by the check-boxes above): _____

Initial Recruitment: Participants will be directed to an online survey. Participants will provide their consent electronically through the first page of the survey (online consent language attached to protocol). As part of the consent, they will provide their email for subsequent follow up. They will proceed to answer a brief ~10 minute survey asking for basic demographics, family history, health history, and information about their IBC diagnosis and treatment. They will finally be asked to indicate whether they consent to being contacted for participation into future research projects should they be a good match.

Annual Follow-up Survey: Participants will receive annual follow up surveys asking for updates related to their IBC diagnosis and treatment if any exist. They will be also given an opportunity to review and update their previous information.

Matching with Clinical Trials: Investigators interested in recruiting patients from the registry into IBC-related research protocols will not have access to the data directly. Information about the content of the registry will provided to investigators in one of two manners:

- 1) Aggregate information (record counts) to help them assess the feasibility of research. This will not require IRB approval.
- 2) If they provide an IRB-approved protocol with explicit recruitment criteria, the study team (we) will contact participants in the registry who match those criteria on the investigators' behalf. We will not release the emails of the participants directly to the

investigators, instead we will act as honest brokers. We will offer a description of the study to the participants and will provide them with the contact information of the investigator. If they chose to participate, they can then contact the investigator directly.

9.0 Research with Vulnerable Populations (if children are the ONLY vulnerable population you plan to enroll, do NOT complete this section -- instead fill out Appendix A)

N/A

10.0 Incomplete Disclosure or Deception:

N/A

11.0 Consent Process:

Consent will be provided electronically through a REDCap secure online form. It was derived from the consent template downloaded from the NU IRB website was used. A draft of the online version can be viewed on the link below. A PDF version of this form is attached.

12.0 Waiver of Participant Signature on Consent Form:

N/A

13.0 Waivers and Alterations of Consent Information:

N/A

14.0 Financial Compensation:

N/A

15.0 Audio/Video Recording/Photography

N/A

16.0 Potential Benefits of this Research:

The main benefit of participation is contribution along with a growing online community of patients to the patient-powered understanding of Inflammatory Breast Cancer; another main benefit is the enhanced opportunity to enroll into clinical trials.

17.0 Potential Risks to Participants:

The primary risk of participation is loss of privacy concerning participants' self-reported disease information due to unauthorized access to the data.

18.0 Provisions to Protect Participant Privacy and Data Confidentiality:

The privacy of the participants will be paramount. The contact information they provide will *only* be used for the follow up surveys and for letting them know that they may be a match for a given trial (see above). The survey will be administered via Northwestern University instance of the Research Electronic Data Capture (REDCap) system. REDCap is a secure online data capture system that is optimized for human subject research and survey data management. It is routinely backed-up and monitored by FSM IT Department. All communication in and out of the REDCap system will be encrypted via SSL protocols. REDCap also provides a complete audit trail of every record operation (including record views). Access to the REDCap forms data will only be given to Authorized Personnel List on this protocol. For analysis, e.g. to determine patients who are eligible for given clinical trials or to report aggregate statistics about the registry, data will be stripped of all identifiers. Participant locations will be maintained at the state level. Dates of diagnosis and treatment events will be analyzed at the year level (no months or days). Where more granularity is needed for temporal analysis (e.g. duration between diagnosis or treatment) a relative interval will be calculated (e.g. the interval will be reported using length in days without the start and end dates) to further mitigate risk of re-identification. A copy of the data will be routinely stored on the FSMResFile drive which is encrypted at rest and protected by FSM IT.

19.0 Data Monitoring Plan to Ensure the Safety of Participants:

N/A

20.0 Long-term Data and Specimen Storage and Sharing:

Long Term Storage and Archival of the Research Information will be via the FSM-sanctioned and secure platforms of REDCap and FSMResFiles. We do not plan to include identifiers in any data disclosure.

21.0 Qualifications of Research Team to Conduct the Research:

Dr. Cristofanilli is a medical breast oncologist and world-renowned expert on IBC. He is the president of the Inflammatory Breast Cancer International Consortium (IBCIC); he is the co-founder of the IBC Foundation and is its medical advisor.

Ms. Donahue was diagnosed with Stage 3B Inflammatory Breast Cancer in April 2007 at the age of 26. She was misdiagnosed before receiving the diagnosis of IBC. She firmly believes in the value of Patient Advocacy and Education in the fight against IBC. She is Program Coordinator of the Lurie Cancer Center OncoSET Program at NM; a member of the board of the IBC Foundation; and Executive Coordinator of the IBCIC organization.

Dr. Wehbe is the Chief Research Informatics Officer of the Feinberg School of Medicine at Northwestern University. He is an associate professor of Preventive Medicine, division of Health and Biomedical Informatics, and of Pathology. He is the director of informatics operations for the Lurie Cancer Center OncoSET Precision Oncology Program and for the OncoSET Registry and Biobank.

Consent to Participate in Research

Page 1 of 4

Title of Research Study: IBC and ME International Registry

Principal Investigator: *Massimo Cristofanilli, MD, FACP*

Supported By: This research is supported by Northwestern University Feinberg School of Medicine.

Conflict of Interest Disclosure:

Key Information about this registry:

The following is a short summary of this registry to help you decide whether to be a part of it.

The purpose of this registry is to learn about the global characteristics of Inflammatory Breast Cancer and to be used as a launching pad for future research studies with interested participants.

You will be asked to provide information through an online survey about yourself, how to contact you, your health, your family history, and to specify which kinds of potential research studies you would be interested in participating. You will receive every 6 months, a brief email surveys for follow up.

We expect that you will be in this registry for 15 years or until this registry is closed whichever is first.

The primary risk of participation is loss of privacy due to unauthorized access to the data.

The main benefit of participation is contribution to the understanding of Inflammatory Breast Cancer and the opportunity to be recruited into clinical trials.

Why am I being asked to take part in this registry?

You are being asked to take part in this registry because you have received a diagnosis of inflammatory breast cancer.

How many people will be in this registry?

We expect about 2000 or more people will be in this registry.

What should I know about participating in a registry?

- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You do not have to answer any question you do not want to answer.

What happens if I say, “Yes, I want to be in this registry”?

You will be asked to fill out an online survey which includes questions about your contact information (email), your IBC diagnosis and treatment history, your other health history, your family’s history. You

Consent to Participate in Research

will also indicate whether you would be interested in participating in future research studies. You will receive every 6 months via email a brief survey for follow up. After securing the proper approvals for research, investigators for studies related to IBC will contact us asking for potential matches. If you are a match for those criteria, and if you have indicated your willingness to participate, you will be contacted separately for those studies. You always have the right to decline and opt out from further contact.

Will being in this registry help me in any way?

We cannot promise any benefits to you or others from your taking part in this registry. However, possible benefits include being matched to a clinical trial or study that is relevant to you.

Is there any way being in this registry could be bad for me?

A possible risk for any research is that confidentiality could be compromised – that is, that people outside the registry might get hold of confidential registry information. We will do everything we can to minimize this risk, as described in more detail later in this form.

What happens if I do not want to be in this research, or I change my mind later?

You can decide not to participate in this research or you can start and then decide to leave the research at any time and it will not be held against you. To do so, simply exit the survey. Any data already collected will not be saved. You can leave the research at any time and it will not be held against you.

If you decide to withdraw from this registry, the researchers will ask you if information already collected from you can be used. If not, any data already collected from you will be destroyed.

How will the researchers protect my information?

Efforts will be made to limit the use and disclosure of your personal information, including the study personnel who need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution.

This survey is being hosted by the Research Electronic Data Capture (REDCap) system. REDCap is a secure, web-based application designed exclusively to support data capture for research studies. REDCap provides: encryption between the data entry in your browser and the server; and audit trails for tracking data manipulation and export procedures. The application and data are housed on servers provided by the Northwestern University Feinberg School of Medicine (FSM). These servers are located within the FSM secure data center. All information will be kept on a password-protected device and only accessible by the research team.

The results obtained from this registry may be published, but your name will never be used.

Who will have access to the information collected in this registry?

Efforts will be made to limit the use and disclosure of your personal information, including research records, to people who have a need to review this information. We cannot promise complete secrecy.

Consent to Participate in Research

There are reasons why information about you may be used or seen by other people beyond the research team during or after data collections. Examples include:

- University officials, government officials, study funders, auditors, and the Institutional Review Board may need access to the registry information to make sure the research is done in a safe and appropriate manner.
- The research team may give information to appropriate authorities for reasons of health and safety – for example, if you indicate that you plan to harm yourself or others, or for public health reasons.

We will not ask you about child abuse, but if you tell us about child abuse or neglect, we may be required or permitted by law or policy to report to authorities.

How might the information collected in this registry be shared in the future?

We will keep the information we collect about you for the registry's recordkeeping and for potential use in future research projects. Your name and other information that can directly identify you will be stored securely and separately from the rest of the research information we collect from you.

The researchers plan to contact you again as part of this registry to update your record.

De-identified data from this registry may be shared with the research community, with journals in which registry statistics are published, and with databases and data repositories used for research. We will remove or code any personal information that could directly identify you before the registry data are shared. Despite these measures, we cannot guarantee anonymity of your personal data.

We would like to contact you on behalf of other researchers for future research studies. We will ask for your consent to do so at the end of this form. You can be in this current registry without agreeing to future research use of your identifiable information.

Aggregate data from this registry could be shared in articles and presentations, but will not include any information that identifies you unless you give permission for use of information that identifies you in articles and presentations.

Will I be paid or given anything for taking part in this registry?

There is no payment or reimbursement for participating in this registry.

Who can I talk to?

If you have questions, concerns, or complaints, you can contact the Principal Investigator please email contact@ibcic.org.

This research has been reviewed and approved by an Institutional Review Board ("IRB") – an IRB is a committee that protects the rights of people who participate in research studies. You may contact the IRB by phone at (312) 503-9338 or by email at irb@northwestern.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.

Consent to Participate in Research

- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Please indicate your agreement with the following:

The researcher may keep my contact information in order to contact me in the future to see whether I am interested in participating in other research studies.

If you want a copy of this consent for your records, you can print it from the screen.

If you wish to participate, please click the “I Agree” button and you will be taken to the survey.

If you do not wish to participate in this registry, please select “I Disagree” or select X in the corner of your browser.