Modeling the Patterns of Breast Cancer Early Metastases

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• In 2016, > 230,000 women in the US will be diagnosed with invasive breast cancer.

• Approximately 11% (26,000) of these will develop distant metastases after an initial diagnosis of no metastases.

  = our target patients

• These will account for nearly 2/3 of the total number (40,000) of breast cancer deaths annually.
• Current National Cancer Care Network (NCCN) guidelines for asymptomatic breast cancer survivors omit proactive imaging for the detection of early-stage metastatic disease, regardless of a patient’s metastatic risk.

• The presentation of an outward symptom (persistent cough, bone pain, headaches or dizziness, or abnormal laboratory findings), is typically associated with advanced metastatic disease -- multiple large masses afflicting multiple organs.

• Currently, metastatic breast cancer (MBC) carries a dismal 20% overall survival (OS) and 2% disease-free survival (DFS) at 5 years.
Limited efficacy of chemotherapy in recurrence

- The NCCN guidelines are based on 2 surveillance imaging studies performed in Italy from 1985-1993 where additional chemotherapy was the only treatment option (pre-dated image-guided surgery and SRT). Early detection and treatment did not prolong 5-year OS in the women who developed BC metastases.


Oligometastases (<=5 mets) treated using combined local + systemic therapy can achieve dramatically increased OS and DFS.

- **UF/Univ. of Rochester (2011):** 47% OS, 36% DFS at 8 years for Oligo-.
  

- **UM (2010-2014):** 80% vs 46% 5-year OS for oligo-/non-oligo.
  

- **48.5% 5-year OS for oligo-mets vs. 10.7% for non-oligo (1978-2005 data)**
  
IMAGING THE PATTERNS OF BREAST CANCER
EARLY METASTASES:
Clinical Trial Update

Cristiane Takita, MD, MBA
FACCA Retreat, Coral Gables, FL
03/04/16
BreastMetsPats

Primary Objectives

1. To determine how many high-risk breast cancer patients have oligometastatic presentation under proactive imaging.

2. To measure the incidence of metastases, their number and size at first instance, time to first instance, growth rates and target organs to define the optimal surveillance imaging protocol.

3. To relate the features of metastatic presentation with primary tumor factors (size, stage, ER/PR/HER2) and patient-specific factors (age, race, BRCA gene status).
1. To measure the local control rate, acute and late side effects for ablative local therapy in an intensive surveillance regimen compared with previous findings.

2. For secondary instance of distant metastases, measure their incidence, their number and size at, time to instance, growth rates and target organs.
Eligibility

Female patients with breast cancer who have presented within the last 48 months with a diagnosis that associates them with high risk (>30%) for developing metastatic disease but who at the time of enrollment are not known to have metastatic disease. Patients meeting this criterion are those that have any of the following presentations:

1. hormone receptor (or triple) negative breast cancer with 3 or more positive axillary lymph nodes;
2. a Stage III diagnosis (T1, N2 or T3, N1 or T4 or N3);
3. a primary tumor >2 cm and positive axillary lymph nodes (T2, N2);
4. multiple primary tumors with cumulative volume >= that of a single 2 cm tumor, and positive axillary lymph nodes
5. any number of lymph nodes with extranodal extension;
6. any internal mammary or supraclavicular nodes (N3);
7. any primary tumor that has grown into the chest wall or skin (T4);
8. or inflammatory breast cancer
1. All enrolled subjects will undergo a single body PET/CT scan that includes a diagnostic-quality CT scan with contrast acquired in the same imaging session; and a single brain MRI scan with contrast to be completed in separate imaging session but within 2 weeks of the PET/CT scan. Imaging will take place within 7 months after enrollment.

2. Medical records related to their cancer and care will be monitored for the duration of the patient’s life.
Clinical Trial Update

Timeline:

- 7/13/15: FACCA award starting date ($50,000)
- 9/3/2015: Protocol submission to UFHCC PRMC
- 9/29/2015 UF PRMC letter of approval
- 10/23/15: Submission to UM/SCCC PRC for expedited review
- 10/26/15: UM/SCCC PRC letter of approval
- 11/4/15: Protocol submission to UM/SCCC IRB
- 2/1/16: UM IRB letter of approval
- 1/29/2015: Protocol submission to UF IRB
- 2/1/16: 1st Site initiation visit for coordinators
- 2/22/16: Short version of Spanish ICF approved by IRB
- As of 2/29/16: 2 UM patients accrued, 1 patient screened
- 3/2/16: UF IRB review

Goal is to complete accrual by end of grant cycle
Active Surveillance in High Risk Breast Cancer

UF Health GNV & JAX

Imaging Research

Walter O’Dell
Paul Okunieff

Marc Lippman

UM/SCCC
Metastases Model Lab

FL High Risk Breast Cancer Survivor Population

Cristiane Takita
Youssef Zeidan

Outcomes Research

UM/SCCC

Walter O’Dell
Paul Okunieff

Marc Lippman

Cristiane Takita
Youssef Zeidan
Imaging and modeling the initial spread of metastases in breast cancer
PIs: Lippman/Takita (UM), Milano (URMC), O’Dell (UFHCC)

“Through this work we will forge a direct path through the NRG and RTOG for a national clinical trial to evaluate the benefit of combining proactive imaging with targeted therapy of breast cancer metastases.”
Aim 1. Prospectively measure patterns of first incidence of breast cancer metastasis.

Aim 2. Retrospectively measure patterns of metastasis presentation in breast cancer patients.

Aim 3. Model the dissemination of metastasis* to design optimal surveillance imaging protocol.

Original submission (4/2015): 3-yr, 2 institutions (UF+UM), $1M direct
Scored: 2.5 (good)
“This was a controversial review, and agreement on potential impact could not
be achieved. After a lengthy panel discussion, some panel members continued
to express high enthusiasm, but many agreed that the identified weaknesses
related to impact raised significant concerns that diminished enthusiasm.“

Planned resubmission (4/2016) 5-years, 3 institutions, $3.3M direct

A Phase IIIR/III Trial of Standard of Care Therapy With or Without
Stereotactic Body Radiotherapy (SBRT) and/or Surgical Ablation for
Newly Oligometastatic Breast Cancer
Pathway to a national trial of surveillance for metastases in breast cancer survivors.
PIs: Lippman (UM), Milano (URMC), O’Dell (UFHCC)
Planned submission: June 5, 2016

Aim 1. Prospectively measure patterns of breast cancer metastasis to design optimal surveillance imaging protocol.

Aim 2. Quantify the time-course of circulating tumor cells (CTCs) and additional blood markers to identify patients most likely to benefit from intensive surveillance and aggressive treatment.
Questions

Thanks again for your continued support