Initiatives for the Benefit of MBC Patients

Anne Loeser, Updated Feb. 2021

Palliative Care:

Palliative Care (PC): Palliative Care should be made available immediately upon diagnosis to every MBC patient, and its services covered by insurance. - including recognition of and treatment for pain, neuropathy, fatigue, depression and anxiety The need for this is self-explanatory, especially since nearly 50% of patients report that their providers don't ask them about their symptoms & side effects, leaving it up to their patients to ask for help when they need it.

Provide Accurate, Up to Date Information that is Easy-to-Locate:

a. Expand Information: Information is perceived as a primary need by about 75% of MBC patients, and nearly 50% of MBC patients surveyed say they find the information they need difficult to locate and confusing. Furthermore, the information they are able to locate does not fully address their needs. Providing my Guide online will help, as will publishing it in hardcover and e-book format.
b. Messages to the Public: Ensure that messages convey accurate information:
   i. Do not imply that breast cancer is "preventable" and "curable."
   ii. Do not insinuate that mammograms are infallible.
   iii. Work with the public and Congress to enact a nationwide Breast Density Notification Law.
c. Allocate one week in October for public education about MBC, and one day specifically for male breast cancer.
d. Education Regarding Symptom Recognition: Ensure that medical staff and breast cancer patients of any stage are informed about the symptoms of MBC such as bone pain, shortness of breath, and chronic cough.
e. Education about Age: Educate medical personnel and the public to recognize that breast cancer and MBC can occur in young women, as well as in men. Too often, symptoms of breast cancer and MBC in young women and men are dismissed by the medical community.
f. Research Funding/Apportionment:
   i. Earmark 30% of all breast cancer research funding towards MBC, since one in three breast cancer patients will recur.
   ii. Apportion 1% of funds towards male breast cancer research.

Reduce Financial Toxicity: Reverse the current situation inhibiting Medicare from negotiating with pharmaceutical companies regarding drug prices.

Expand Drug Availability to Patients:

a. Expedite Drug Approvals: Encourage expansion of the FDA's expedited programs for drug approval (such as Fast Track Designation) so that new drugs may more quickly and cheaply reach those with terminal disease.
b. Patient Assistance Programs: Work with pharmaceutical companies to enable eligible Medicare and Medicaid patients to access drugs at a reduced rate via Patient Assistance Programs. Too often, eligibility is contingent upon the patient's non-participation in federal or state healthcare programs such as Medicaid or Medicare.

Research:

a. Eliminate Waste and Redundancy by working with the AllTrials Campaign and other methods to ensure that the results of all clinical trials - whether positive or negative - are published within 12 months of completion. As of 2014, 25% - 50% of clinical trial results were unpublished. https://www.ncbi.nlm.nih.gov/pubmed/24780575
b. Integrative Therapy Outcomes: Integrative therapies, whereby patients utilize conventional and complementary protocols, warrant consideration and assessment. An example is incorporating regular testing and adjusting for patients' Vitamin D levels because low levels of Vitamin D are associated with significantly worse prognosis. https://www.webmd.com/breast-cancer/news/20080516/vitamin-d-deficiency-worsens-breast-cancer#1
c. Identify and Track Recurrent MBC Patients in SEER: Since SEER currently only tracks de novo MBC patients, efforts must be undertaken to enable SEER to identify and track early stage breast cancer patients who subsequently present with MBC.
d. Explore the Efficacy of Existing Predictive Chemotherapeutic Models such as those in the Weisenthal Cancer Group and the Nagourney Cancer Institute in order to compare their outcomes with those of physicians' choice therapies.

CLINICAL TRIALS

This section is based upon a Metastatic Research Society Presentation by Kelly Shanahan, MD; Marina Kaplan, PhD; Patricia Wu, PhD; Leslie Falduto, RN, and additional thoughts from Anne Loeser.

Enhance Patient Recruitment:

a. Simplify Consent Forms. They are too long and technical.
b. Unbundle Clinical Trials from Major Institutions and brick and mortar locations; make them more portable and convenient (this should also include related tests).
c. Endeavor to Increase Enrollment of MBC Patients of Color and the Underserved Community by liaising with hospitals, local churches, and community leaders.
d. Patient Reimbursement: Patients should be adequately compensated for participation, including travel and related expenses. Furthermore, any additional drugs required to manage the side effects of their experimental treatment should be recompensed.
e. Eliminate the Standard Washout Period: The 28-day washout period is unacceptable because patients have died during that period. Instead, personalize each prospect's admission requirements based upon their specific prior treatment (and half-life), their health status, and other criteria..
f. Decrease Scan Frequency: Undergoing scans every 6 weeks is overkill that is detrimental to the patient's physical and mental health (unless the patient's condition obviously worsens). Explore opportunities for scanning every 3 or more months depending upon the patient's symptoms and the aggressiveness of their disease. Furthermore, liquid biopsies should be leveraged relative to potential substitution for scans in this context.
g. Access to Test Results: Required tests for admission into clinical trials should be done by CLIA-certified laboratories and patients should have access to their results so that they can be leveraged for other clinical trials as well as treatment decisions.
h. Crossover: In a randomized clinical trial, if/when it becomes clear that a certain drug or combination of drugs in one arm is more efficacious than those in another arm, patient crossover to the more effective arm should be a viable option.
i. Report on Outcomes from Earlier Related Trial Phases: If a patient is considering a Phase II or III clinical trial, then readily being able to access efficacy and toxicity information available from the earlier phase would be enormously helpful. This information should also incorporate Patient Reported Outcomes (PROs) relative to patients' experiences with the experimental therapy.
j. Encourage the Development of More Trials for MBC Patients with Leptomeningeal Metastases (LM). This is the most difficult-to treat metastatic area, and there is a growing population of LM patients. Yet few options are available to LM patients and their median survival is 9 months.
k. Accommodate Patients whose Disease Cannot be Measured by RECIST: In order to use RECIST to measure disease, there must be at least one tumor that can be measured on X-rays, CT scans, or MRI scans. Since lobular MBC does not present as a solid tumor, and the tumors of patients with bone metastasis (or bone marrow metastasis) cannot always be measured via RECIST, patients with these conditions are routinely excluded from clinical trials. An alternative measurement mechanism (such as CTCs/liquid biopsies) needs to be established for these individuals so that they may enter clinical trials.
l. Prior Lines of Therapy: Typically, patients who have had more that 2 or 3 lines of therapy are excluded from enrolling in clinical trials. This is due to the fact a patient's response to therapy generally decreases with each successive line of therapy, and therefore treatment-naïve patients or those with minimal prior therapies are more desirable with respect to clinical trials. Yet as patients are living longer and are undergoing increasingly more therapies, it is essential to assess whether an experimental drug has efficacy with regard to this heavily pre-treated population.
m. Re-evaluate the General Exclusion of Patients with CNS Metastases from clinical trials. As MBC patients' lifespans increase, more patients are presenting with CNS metastasis. Excluding these patients thus skews results away from the real world and denies this population of the opportunity to leverage potentially beneficial therapies. Additionally, an experimental drug may actually be helpful for patients with CNS metastasis, yet there would be no way of knowing this if these patients are routinely excluded from clinical trials.
n. Co-Morbidities/Past Illnesses: Often, patients with co-morbidities or who have had other types of diseases in the past are excluded from clinical trials. Unless these health issues and/or the medications taken for them may impact the patient's response to therapy, these patients should be considered for inclusion
o. MBC Disease Burden: In some instances, the size and number of a patient's tumors can preclude them from entering a clinical trial.

Enhance Clinical Trial Measurements:

a. Revisit dosages: Challenge the use of the Maximum Tolerated Dose as opposed to the Minimum Effective Dose, and personalize drug dosages in the clinic. All too often after a new drug is released into the market, its patient toxicity levels cause doctors to lower the dose and/or reduce the frequency of administration. Excellent article: http://ascopubs.org/doi/full/10.1200/jco.2012.43.4233

b. Drug Rating: Each patient in a clinical trial who receives the experimental drug should be able to rate it based upon a 5-star rating (similar to restaurant and hotel ratings). Ratings should be based upon the patient's perception of the drug's toxicity, the patient's QOL and side effects, and other relevant factors. These ratings should be published (via a star rating along with explanatory verbiage) in tandem with the more traditional endpoints of PFS, OS, etc. Ideally, a weighted scoring system that integrates all factors - such as Overall Survival (OS), Progression Free Survival (PFS), degree of toxicity, and patients' ratings - would be exceptionally helpful for patients when determining whether they wish to enroll in a Phase II or III clinical trial, since they could view the ratings from a prior trial. For example, if the average rating for a drug in a Phase I trial was 4 of 5 stars, patients may find it more attractive in terms of Phase II recruitment.

Expand Trial Outputs:

Report Trial Outcomes Separately by Patient Groupings:

a. *Atypical Responders:* Clinical trial results should be expanded to report results relative to Exceptional Responders and Rapid Progressors. Outcomes for patients who are Exceptional Survivors based upon the date of their MBC diagnosis should also be reported on separately.
b. *Lobular MBC:* Since Lobular MBC often follows a different metastases and treatment trajectory than ductal MBC, studies should segregate these patients in terms of therapeutic outcomes.
c. *Male MBC:* Reporting specifically about outcomes of male MBC patients will help treatments for this population to become more effective.
d. *People of Color/Ethnicities:* Reporting specifically about outcomes of patients of color and ethnicities will help treatments for this population to become more successful.
e. *Patients with CNS Metastases:* Assuming their inclusion in clinical trials, the efficacy of the experimental drug on patients with CNS metastases should be specifically evaluated and reported. This could benefit not only the patients, but also the pharmaceutical company if the drug is successful in treating this population.
f. *Patients Receiving a Dose Reduction:* The outcomes of patients in clinical trials whose dose was reduced due to Adverse Events should be compared to the outcomes of patients remaining on the standard (Maximum Tolerated/MTD) dose. This reporting stratification will provide valuable information regarding the relative efficacy of lower doses (PFS, OS) in addition to toxicity-related quality of life information.

Leverage Opportunities for Innovative, "Out of the-Box" Studies

a. Study Re-use of a Previously Taken Effective Drug: It is currently unknown when a successful prior drug can be successfully re-administered, and when. This is a valuable area of research that has been under-studied.
b. Obtain "Real-World" Data Regarding the Efficacy of Lower Allowed Doses in the Clinical Setting: The outcomes of patients receiving FDA-approved treatment whose dose needed to be reduced due to treatment-related side effects should be compared with outcomes of patients who continue to receive the standard (MTD) dose of the same drug. Over time, these data will provide valuable insights regarding the relative efficacy of lower allowed dosages when compared to the standard dose in addition to quality of life implications. Comprehensive real-world data is needed for oral, injected, and intravenously-administered FDA approved drugs.
c. Re-evaluate the Use of Older Drugs: Estrogen has been FDA-approved for MBC, as have Megace and Halotestin. These drugs deserve re-evaluation for a potential "fit" in the current therapeutic arena, possibly as later-line treatment. Estrogen is especially interesting inasmuch as it has been known to re-sensitize hormone therapy-resistant MBC to standard hormonal therapies. Estrogen also has a proven clinical efficacy, and once it fails, the act of withdrawal can be of favorable impact in and of itself.
d. Determine Optimal Drug Sequence: The ideal sequence of administering currently available therapies for hormone receptor positive (and HER2+) MBC is unknown and deserves attention.

e. Assess Synergies between Existing Therapies and Other Factors such as CIM, lifestyle, etc. that may improve patient outcomes. To this end, provide for the collection of a common set of data elements, including health-related quality of life measures, across clinical practice and clinical trials.

f. Explore Ways to Transform TNBC into a More Treatable Subtype such as hormone receptor positive or HER2 positive MBC. (Preliminary successful work has been done in mice by co-administering cruciferous vegetables and green tea to in order transform TNBC into ER+ MBC). http://www.newsmax.com/Health/Health-News/dietary-combo-broccoli-green-tea/2017/10/18/id/820552/

g. Investigate Methods of Transforming Aggressive MBC into Indolent MBC.

h. Study the Impact of a Treatment Hiatus when a patient has been NED or NEAD for specific period of time. It is possible that a hiatus will enable a patient who relapses to become more responsive to a prior therapy, and it may help the patient regain energy and strength.