Evidence-Based Clinical Practices on Shared Decision Making in Metastatic Breast Cancer

Release date: May 1, 2017 · Expiration date: April 30, 2018 · Estimated time to complete activity: 1.5 hours

Target Audience

The target audiences for these activities are medical oncologists, pathologists, physician assistants, nurse practitioners, oncology nurses, nurse navigators/social workers, palliative/symptom management teams who care for patients with HER2-positive MBC and quality administrators responsible for their cancer center's adherence to value-based care delivery models. We will target centers participating in Centers for Medicare and Medicaid Services Oncology Care Model.

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Educational Objectives

At the conclusion of these educational initiatives, participants should be able to:

Carlos Arteaga, MD

- Develop evidence-based treatment approaches for patients diagnosed with HER2-positive breast cancer in the metastatic setting

Rachel Freedman, MD, MPH

- Consider fit/frailty status when contemplating evidenced-based treatment options for older patients with HER2+ MBC

Joanne Buzaglo, PhD

- Define clinician and patient perceived indicators of effective SDM for HER2-positive metastatic breast cancer
- Evaluate the clinician and patient perceived feasibility/satisfaction regarding using personalized treatment care plans to support shared decision making for HER2-positive metastatic breast cancer

Physician Continuing Medical Education

Accreditation Statement

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Module 1

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HER2-Positive Metastatic Breast Cancer

Carlos Arteaga, MD

I. Background

- The 5-year and 10-year survival rates for metastatic breast cancer (mBC) are 26% and 5% to 10%, respectively (Clements et al, 2012; American Cancer Society, 2016).
- For the 20% to 25% of patients with tumors that overexpress human epidermal growth factor receptor-2 (HER2), the disease course is more aggressive and associated with shorter survival times (Prat and Baselga, 2008).
- The advent of HER2-targeted therapies has dramatically improved patient outcomes in HER2-positive breast cancer (Santa-Maria et al, 2016); nevertheless, mBC eventually progresses.
- New molecular targets that can evade resistance mechanisms to HER2-directed therapies are being investigated in multiple ongoing trials.

II. Approved and Emerging Agents

A. Anti-HER2 Agents

- *Trastuzumab*, the first agent approved for the treatment of HER2+ BC, is a recombinant humanized monoclonal antibody that inhibits ligand-independent HER2 and HER3 signaling and also triggers antibody-dependent cellular cytotoxicity.
  - *Trastuzumab* was approved in 2006 as part of a treatment regimen containing doxorubicin, cyclophosphamide, and paclitaxel for the adjuvant treatment of women with node-positive, HER2-overexpressing BC.
  - The most important adverse event in the metastatic setting was cardiac dysfunction, which occurred in 27% of the group given an anthracycline, cyclophosphamide, and trastuzumab; 8% of the group given an anthracycline and cyclophosphamide alone; 13% of the group given paclitaxel and trastuzumab; and 1% of the group given paclitaxel alone (Slamon et al, 2001).
- *Pertuzumab*, a humanized monoclonal antibody that inhibits ligand-dependent signaling induced by HER2-HER3 dimers, was approved in 2012 in combination with trastuzumab and docetaxel for the treatment of patients with HER2+ mBC who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.
  - The most common (>30%) AEs in patients who received pertuzumab plus trastuzumab and docetaxel were diarrhea, alopecia, neutropenia, nausea, fatigue, rash, and peripheral neuropathy (Baselga et al, 2012).
- *ONT-380* is a small molecule inhibitor of HER2 that has been evaluated in a small phase 1b study in combination with capecitabine and/or trastuzumab following prior treatment with trastuzumuab and ado-trastuzumab emtansine (T-DM1) (Hamilton et al, 2015).
  - From 8 patients, 4 partial responses, 2 stable disease, and 2 progressive disease were reported.
  - Most toxicities were Grade 1 or 2, the most common being nausea, vomiting, diarrhea, palmar-plantar erythrodysesthesia, and fatigue.
  - A randomized, placebo-controlled, phase 2 trial is evaluating ONT-380 in combination with trastuzumab and capecitabine in heavily pretreated patients with HER2-positive mBC with or without brain metastases (NCT02614794).

B. EGFR Tyrosine Kinase Inhibitors (TKI)

- In 2007, lapatinib, a small-molecule inhibitor of HER1/EGFR and HER2 tyrosine kinases, was approved for use in combination with capecitabine for the treatment of patients with HER2+ advanced/metastatic breast cancer and who have received prior therapy including an anthracycline, a taxane and trastuzumab.
  - In 2010, *lapatinib* was also approved for use in combination with letrozole for the treatment of postmenopausal women with ER+ metastatic breast cancer that overexpresses HER2 and for whom hormonal therapy is indicated.
  - The most common adverse events associated with lapatinib are diarrhea, hand-foot syndrome, nausea, vomiting, fatigue, and rash distinct from hand-foot syndrome (Geyer et al, 2006).
- *Neratinib* is an irreversible tyrosine kinase inhibitor of HER1, HER2, and HER4 that has been investigated in a phase I/II trial in combination with capecitabine in patients with HER2+ mBC (Saura et al, 2014).
  - The most common drug-related AEs were diarrhea (88%) and palmar-plantar erythrodysesthesia syndrome (48%).
  - ORR was 64% in patients with no prior lapatinib exposure and 57% in patients previously treated with lapatinib; median PFS was 40.3 and 35.9 weeks, respectively.

C. mTOR Inhibitors

- mTOR inhibitors such as *everolimus* are hypothesized to reverse trastuzumab resistance via the hyperactivated PIK/AKT/mTOR pathway due to PTEN loss, by sensitizing PTEN-deficient tumors to trastuzumab (Hurvitz et al, 2015).
- The phase III BOLERO-1 trial assessed the efficacy and safety of adding everolimus to trastuzumab and paclitaxel as first-line treatment for 719 patients with HER2+ advanced BC (Hurvitz et al, 2015).
  - In the full population, median PFS was not statistically significant between the groups (14.95 months with everolimus versus 14.49 months with placebo).
  - The most common AEs were stomatitis (67% everolimus vs 32% placebo), diarrhea (57% vs 47%),

and alopecia (47% vs 53%).

  - In the HR-negative, HER2+ subgroup, a 7.2-month prolongation in PFS was reported with the addition of everolimus, warranting further investigation.

- In the BOLERO-3 trial, everolimus added to trastuzumab and vinorelbine significantly improved PFS for patients with trastuzumab-resistant previously treated mBC (André et al, 2014).

D. Phosphatidylinositol-3-kinase (PI3K) Inhibitors

- Constitutive activation of the PI3K pathway has been proposed as a mechanism of trastuzumab resistance in HER2+ mBC (Jain et al, 2015).
- The PI3K inhibitor *buparlisib* (BKM120) was investigated in a phase Ib trial of 17 patients with HER2+ advanced/metastatic breast cancer resistant to trastuzumab-based therapy (Saura et al, 2014).
  - Common (>25%) adverse events included rash (39%), hyperglycemia (33%), and diarrhea (28%).
  - At the recommended phase II dose, there were two (17%) partial responses, 7 (58%) patients had stable disease (≥6 weeks), and the disease control rate was 75%.
- *Alpelisib* (BYL719), the first oral PI3K inhibitor that selectively inhibits the PI3K alpha isoform, was evaluated in combination with T-DM1 in 8 patients with trastuzumab-refractory HER2+ mBC (Jain et al, 2015).
  - The most common treatment-related AEs were fatigue (86%), nausea (75%), aspartate aminotransferase increase (50%), and thrombocytopenia (50%); grade 3 AEs were rash (n = 3), hyperglycemia (n=1), hypertension (n=1), and thrombocytopenia (n=1).
  - ORR was 86% (1 confirmed CR, 2 confirmed PRs, and 3 unconfirmed PRs).

E. Antibody-drug conjugates

- *Ado-trastuzumab emtansine (T-DM1)*, an antibody-drug conjugate incorporating the HER2-targeted antitumor properties of trastuzumab with the cytotoxic activity of the microtubule-inhibitory agent DM1, was approved in 2013 for use as a single agent for the treatment of patients with HER2-positive mBC who previously received treatment with trastuzumab and a taxane, separately or in combination.
  - In the pivotal trial of 991 patients treated with T-DM1 or lapatinib plus capecitabine, the median PFS was 9.6 months and 6.4 months, respectively; the median OS (30.9 vs. 25.1 months) and ORR (43.6%, vs. 30.8%) were also improved with T-DM1 (Verma et al, 2012).
  - Rates of grade 3-4 AEs were higher with lapatinib plus capecitabine than with T-DM1 (57% vs. 41%); the incidences of thrombocytopenia and increased serum aminotransferase levels were higher with T-DM1, whereas the incidences of diarrhea, nausea, vomiting, and palmar-plantar erythrodysesthesia were higher with lapatinib plus capecitabine.
- *MM-302*, an antibody-drug conjugated HER2-targeted liposomal doxorubicin, was evaluated in a phase I trial of 69 heavily pre-treated patients administered MM-302 as monotherapy or in combination with trastuzumab or trastuzumab and cyclophosphamide (LoRusso et al, 2015).
  - Patients who received MM-302 plus trastuzumab had a median PFS of 7.6 months; those treated with the addition of cyclophosphamide had a median PFS of 10.6 months.
  - Adverse events occurring in more than 20% of patients included constipation, cough, decreased appetite, diarrhea, dyspnea, fatigue, nausea, neutropenia, stomatitis, and vomiting.
  - The ongoing randomized phase 2 HERMIONE trial is comparing MM-302 plus trastuzumab with chemotherapy of physician's choice plus trastuzumab, in anthracycline-naive HER2-positive, locally advanced/metastatic BC patients previously treated with pertuzumab and T-DM1.

II. NCCN Guidelines

Key NCCN guidelines for the treatment of HER2+ mBC are as follows (Gradishar et al, 2016):

- The identification of HER2 status in patients with mBC should be determined using fluorescence in situ hybridization and/or immunohistochemistry.
- Pertuzumab plus trastuzumab in combination with a taxane (docetaxel or paclitaxel) is the preferred option for first-line treatment of patients with HER2+ mBC; T-DM1 should be considered in patients not suitable for the preferred treatment, although published experience on the efficacy of T-DM1 after progression on trastuzumab/pertuzumab is limited.
- For patients with disease progression after treatment with trastuzumab-based therapy without pertuzumab, a line of therapy containing both trastuzumab plus pertuzumab with or without a cytotoxic agent (such as vinorelbine or taxane or an aromatase inhibitor for hormone receptor-positive tumors) may be considered; the regimen of capecitabine plus lapatinib is also an option.

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Module 2

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Managing the Older Patient with HER2-Positive Metastatic Breast Cancer

Rachel A Freedman, MD, MPH

I. Background

- Breast cancer is common in older women with nearly 100,000 cases of invasive breast cancer diagnosed annually in women aged 65 years or older (American Cancer Society, 2015)
- According to SEER-Medicare data, approximately 4.3% of all older women with breast cancer present with stage IV disease and about 5% present with stage III disease; older women with stage III disease have the highest risk for recurrence (Schonberg M, Marcantonio ER et al, 2011).
  - These numbers do not account for the fact that cancers will recur in many older patients and thus the number of older patients currently living with metastatic disease is significantly higher than 4%.
- The HER2-positive breast cancer subtype is not as common in older patients as it is in younger patients.
  - A report using cancer registry data suggested that approximately 11% of all breast cancer in those aged 65+ are HER2+ breast cancers,most of which is also hormone receptor-positive (Howlader N, Altekruse SF, et al, 2014).
  - The proportion of HER2+ cancers are similar for those aged 65 to 74 and those 75 or older (Howlader N, Altekruse SF, et al, 2014).
- Although the clear majority of older patients with breast cancer will die of other (non-breast cancer) causes, breast cancer remains the leading cause of death for older patients with stage III-IV, accounting for approximately 70% of deaths (Schonberg M, Marcantonio ER et al, 2011).
- However, we also know that outcomes for women with metastatic HER2+ disease are improving with the advent of new therapies, with the median survival now reaching 3.5 years from diagnosis (Olson EM, Najita JS, Sohl J, et al, 2013; Chia SK, Speers CH, D'Yachkova Y, et al, 2007; Vaz-Luis I, Lin NU, Keating NL et al, 2015).
- Our challenge as clinicians taking care of older patients with advanced breast cancer is how to optimally balance the side effects of therapy and potential functional decline with the benefits of therapy regarding symptom reduction and improved survival.
  - In the metastatic disease setting, the clear majority of women will need symptomatic relief over time, although the evidence base for treatment selection in this group of patients is very limited.
- Most clinical trials enroll few older patients, so little is known about their outcomes, treatment patterns, and toxicity profiles.
  - In a recent analysis of accrual of older patients to systemic treatment trials within the Alliance for Clinical Trials in Oncology (Freedman RA, Foster JC, Seisler DK, et al, 2017), only 24% of all patients on metastatic trials were age 65+ and only 13% were age 70+.
  - From 1985-2012, the proportion of patients enrolled on treatment trials decreased slightly for those with metastatic disease.
- The goals of therapy in this setting should be maximizing QOL, decreasing the burden of disease, tailoring treatment to the patient's wishes, and prolonging life and time to symptomatic disease as much as possible.

II. Current Treatment Patterns for Older Patients with Metastatic HER2+ Breast Cancer

- Data on the treatment patterns for older patients with breast cancer are limited.
- Studies repeatedly show that older women benefit just as much as younger patients with regard to breast cancer outcomes (Elkin EB, Hurria A, Mitra N, et al 2006; Giordano SH, Duan Z, Kuo YF, et al 2006; Muss HB, Woolf S, Berry D, et al, 2005), although toxicities and patient and provider preferences can significantly differ with age.
- In the registHER study, 1001 women with newly diagnosed metastatic HER2+ breast cancer in 2003-2006 were followed prospectively over time (Kaufman PA, Brufsky AM, Mayer M, et al, 2012).
  - Among the 209 women in this study who were 65+, 22% had de novo metastatic disease and 50% also had hormone receptor-positive tumors.
  - The oldest patients in this study were the least likely to receive trastuzumab-based therapy as first-line therapy (77% of women aged 75+, 81% of women aged 65-74, 85% of women aged <65), and they were more likely to receive trastuzumab monotherapy or trastuzumab with hormonal therapy.
  - Among women of all ages, those receiving trastuzumab-based therapy had improved outcomes (PFS and OS) compared with those not receiving this treatment.
- Further, studies using SEER-Medicare data have also demonstrated improved outcomes when patients receive first-line chemotherapy with trastuzumab (Griffiths RI, Lalla D, Herbert RJ, et al, 2011).
- Another study of over 4000 older women with de novo metastatic breast cancer during 1998-2009 demonstrated significant differences in outcomes by timing and duration of trastuzumab administration and disparities in outcomes were present, particularly for older black women (Vaz-Luis I, Lin NU, Keating NL et al, 2015).
- Although data on specific regimen use is not well reported in this setting, multiple studies in the adjuvant setting have shown lower rates of trastuzumab initiation and continuation, as well as substantial rates of administration of non-standard chemotherapy and non-standard trastuzumab-based regimens for older patients.

  - This may be appropriate in some patients but more often this represents under-treatment and under-utilization of available therapies (Freedman RA, Hughes ME, Ottesen RA, et al, 2013; Bouchardy C, Rapiti E, Fioretta G, et al, 2003; Hebert-Croteau N, Brisson J, Latreille J, et al, 1999; Freedman RA, Vaz-Luis I, Barry WT et al, 2014; Vaz-Luis I, Keating NL, Lin NU, et al, 2014; Vaz-Luis I, Lin NU, Keating NL, et al, 2016; Reeder-Hayes K, Hinton P, Meng K, et al, 2016).
- The concern is that the same is true in the metastatic disease setting, although this data is not yet mature.

III. Treatment Considerations in the Older Patient with HER2+ Metastatic Disease

- Unlike the adjuvant setting where doublet agents are standard, the use of single-agent chemotherapy (along with HER2-directed therapy) can be very effective and will minimize toxicity over doublet chemotherapy without a detriment in outcome.
  - Unless a visceral crisis is occurring, single-agent chemotherapy is preferred.
- Fortunately, many biologic agents allow for the opportunity to administer HER2-directed therapy with limited toxicity and thus delay the need for traditional chemotherapy.
- The newest drug approvals in metastatic HER2+ disease are ado-trastuzumab emtansine (T-DM1) and pertuzumab, based on data from the EMILIA and CLEOPATRA studies respectively (Verma S, Miles D, Gianni L, et al, 2012; Baselga J, Cortes J, Kim SB, et al, 2012).
  - It is noteworthy that neither of these pivotal trials included a substantial proportion of older patients (median age of EMILIA was 53 years and median age of CLEOPATRA was 54 years).
- However, in a pooled analysis of T-DM1 trials (Dieras V, Harbeck N, Budd GT et al, 2014), the treatment was well tolerated in older age groups.
- Per NCCN guidelines, first-line treatment for HER2+ disease includes pertuzumab-taxane based regimens, followed by T-DM1 as second-line therapy.
- In older patients, clinicians should consider weekly taxane administration rather than every three-week administration because of potentially better tolerance (Tabernero J, Climent MA, Lluch A, et al, 2004; Baselga J, Tabernero JM, 2001; Eniu A, Palmieri FM, Perez EA, 2005).
- It is also of note that patients in the CLEOPATRA trial were permitted to stop taxane therapy after disease stabilization and continue antibody therapies until progression.
  - The ability to transition to an all-biologics regimen is a good option for the older patient who may experience cumulative toxicity with chemotherapy over time.
  - Pertuzumab and trastuzumab are also a stand-alone regimen if avoidance of chemotherapy is desired (Baselga J, Gelmon KA, Verma S et al, 2010).
- For patients who desire to avoid chemotherapy altogether, there are multiple studies showing the benefit of lower-intensity regimens.
  - Combinations such as lapatinib and trastuzumab can be very effective (Blackwell KL, Burstein HJ, Storniolo AM, et al, 2010; Lin NU, H Guo, Mayer IA et al, 2015).
  - Another trial underway directly addresses the efficacy and toxicity of this regimen in an older group of patients with metastatic, HER2+ disease, which will greatly inform clinical practice in this setting (NCT01273610).
- Trastuzumab monotherapy is also an option for some patients, particularly those who are frail and unable to tolerate standard combination therapy.
  - In first-line metastatic disease, trastuzumab monotherapy leads to a response rate of 34% and a median time to progression of 3.5 months (Vogel CL, Cobleigh MA, Tripathy D, et al, 2002).
  - Trastuzumab can also be combined with hormonal therapy in the setting of hormone receptor-positive disease.
- When combined with hormonal therapy, trastuzumab-treated patients have better outcomes than with hormonal therapy alone, with a median PFS of 4.8 months for the combination vs. 2.4 months with hormonal therapy (anastrozole) alone (Kaufman B, Mackey JR, Clemens MR, et al, 2009).
- Lapatinib with letrozole has also shown improved efficacy compared to letrozole alone in the metastatic setting (PFS 8.2 vs. 3.0 months), but the combination shows a higher frequency of diarrhea (Johnston S, Pippen J Jr, Pivot X, et al, 2009).
- These low-toxicity treatment combinations are appealing for older women with advanced comorbidity and/or minimal disease burden, and for those who have hormone receptor-positive disease.
  - The risk of cardiac dysfunction is likely higher in older patients than the rates reported in clinical trials (Bowles EJ, Wellman R, Feigelson HS, et al, 2012; Chen J, Long JB, Hurria A, et al, 2012; Vaz-Luis I, Keating NL, Lin NU, et al 2014).
- Figure 1 offers suggested approaches in treating older frail and non-frail patients
  - Widely available prognosis scales can be used to estimate frailty (e.g., http://eprognosis.ucsf.edu/).
  - Although these prognosis predictors are not validated for women with advanced breast cancer, they do allow clinicians to consider other medical conditions and mortality risk when making treatment decisions.

IV. New Anti-HER2 Agents

- There are many other agents in development for treatment of HER2+ breast cancer, including small molecule inhibitors (e.g., ONT-380, neratinib), mTOR inhibitors, PI3 kinase inhibitors, new antibody-drug conjugates (e.g., MM-302), CDK inhibitors, and immunotherapeutic agents.

- Given their targeted drug delivery, it is likely that these therapies will provide additional lower toxicity options for older patients, however this remains to be seen.
- Enrollment of patients in clinical trials whenever possible is key to increasing the evidence base for this group of patients.

V. Treatment Selection

- Increasing attention is being paid to toxicity and functional decline in older patients; models have been developed to prospectively predict who will develop severe toxicity (Hurria A, Togawa K, Mohile SG, et al, 2011; Extermann M, Boler I, Reich RR, et al, 2012).
- Further validation is underway in specific disease subtypes, but these models will help clinicians with decision-making on who is most at risk for treatment-related toxicities.
- Consider renal function (beyond creatinine alone), liver dysfunction, and functional reserve when choosing a treatment and dose.
  - Also, consider incorporating tools such as the geriatric assessment, which aids in the assessment of a patient's functional status and risk but does not add a significant burden to your practice (Hurria A, Cirrincione CT, Muss HB, et al, 2011).

VI. Summary

- HER2+ metastatic disease is heterogeneous and so are patients.
- We need to make thoughtful treatment decisions with our patients that focus on patient priorities and wishes.
- Careful monitoring and early intervention of toxicities are critical.
- Optimize other medical problems.
- Enroll in clinical trials whenever possible.

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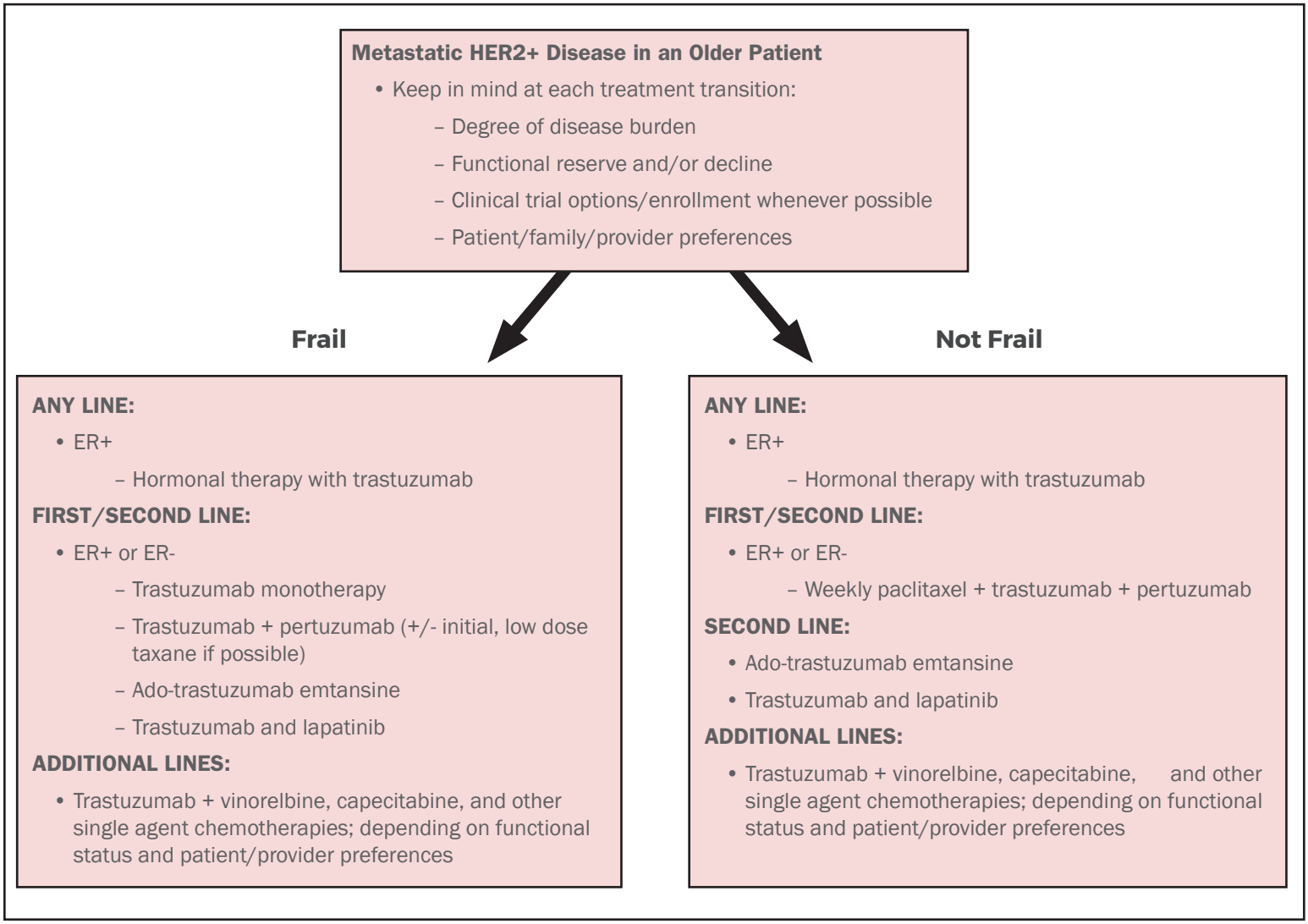
Figure 1



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Module 3

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Shared Decision Making in the Context of Metastatic Breast Cancer: Physician and Patient Barriers

Joanne Buzaglo, PhD

Shared decision making (SDM) is the keystone of patient-centered care. It improves patients' understanding of treatment options, results in more conservative care choice, and leads to lower healthcare costs (Fowler FJ, Levin CA, Sepucha KR, 2011); yet its elements are still not well understood and there are numerous misconceptions as to what SDM is.

In short, SDM is best defined as when "the physician and the patient make health-related decisions collaboratively, based on both the best available evidence and the patient's values, beliefs, and preferences." (Bernabeo E, Holmboe ES, 2013) The word "collaboratively" is important; one misconception is that shared decision making is simply when physicians share a treatment decision with their patients and their patients simply follow their new treatment regimen. Others are wary of SDM because they believe it means that patients make all decisions and physicians follow their desires without question, which could potentially result in harm to the patient.

More recent thinking about SDM has been critical of its narrow focus on individual patient autonomy (Brom L, De Snoo-Trimp JC, Onwuteaka-Philipsen BD et al, 2015; Clayman ML, Gulbrandsen P, Morris MA, 2017). Shortcomings include its focus on the individual without full regard for the patient's relationships, including family members, and the cultural context of the individual patient. Second, emphasis is placed on a single medical encounter, rather than a focus on an ongoing process that begins prior to the first treatment decision encounter and continues well after the treatment decision consultation. Patients frequently search for information, and discuss their concerns and considerations with their partners and peers prior to meeting with the doctor. Ideally, patients have an opportunity to reflect on what they learn during the consultation that ultimately can inform treatment planning. Third, the patient is not just a person in the clinic. The patient is a person in the world with social roles and functions that translate into personal goals that are often not understood or met by the oncology team. Clayman et al. (2017) advocates for a model of "person-centered decision making" that takes into account factors related to patient values and goals, relationships and cultural context as well as a longer view of decision making that maps onto the continuum of care. This is particularly relevant for a person living with metastatic breast cancer for whom there can be many decisional twists and turns along the treatment trajectory, including end-of-life decisions.

In actual practice, SDM depends on physicians and patients taking different roles in the clinical interaction and treatment decision. In SDM, the physician's role is to present all treatment options in an unbiased way, provide patients with the best available evidence for the recommended treatment plan, help the patient weigh risks vs. benefits, discuss uncertainties and treatment alternatives, and check on the patient's understanding. Patients also have several important roles and responsibilities if they are to be thoughtful participants in shared decision making. Patients must want to participate in shared decision making; and must define and clarify their values, preferences, and goals relating to treatment. Finally, patients and physicians must listen carefully to each other, ask questions, and request additional information when necessary. (Frosch DL, 2013)

Although SDM may seem an intuitive practice, there are several barriers to its practice, both on the physicians' and patients' side of the desk. Physicians, for example, may believe that SDM allows the patient to dictate to the physician regardless of the physician's best judgment. (Center for Advancing Health, 2014; Lin GA, Halley M, Rendle KA, et al, 2013) Physicians may also perceive SDM to take too much time and effort in an already too-short time-frame (Lin GA, et al, 2013). They may also object to sharing all information about treatment options, particularly cost (Hibbard JH, Greene J, Sofaer S, et al. 2012). Finally, a given physician's institution or hospital may not provide infrastructure that supports patient engagement or shared decision making (Center for Advancing Health, 2014). Patient barriers to SDM include low health literacy (Coulter A, Ellins J, 2007), and disinclination to engage in shared decision making (Elwyn G, Frosch D, Thomson R, et al, 2012) due to either cultural or psychosocial factors.

People living with metastatic breast cancer face a range of challenges that can cause significant distress, including frequent medical procedures, pain, fatigue, cognitive impairment, sexual dysfunction, and work and family related issues (e.g., MBC Alliance, 2014; Mosher CE, et al, 2016; Buzaglo JS, et al, 2014a; Cancer Support Community, 2014).

- Metastatic breast cancer patients most frequently indicate that physical (e.g., fatigue) and/or emotional (e.g., anxiety) symptoms are distressing because they disrupt their lives and interfere with their ability to remain active and fulfill their goals and social functions (Mosher CE, et al, 2016). Yet, while most MBC patients suffer multiple symptoms of disease and side effects of treatment that disrupt their lives—most common are fatigue, pain, and sleep problems, 50% of patients say they are not routinely asked about their symptoms and express concern about "bothering" their doctors (MBC Alliance, 2014).
- Further, women with metastatic breast cancer are at greater risk for emotional distress characterized by anxiety, depression and fear of recurrence (e.g., Vehling S, et al, 2011; Yang HD, Thornton LM, Shapiro CL, et al., 2008).
- Finally, MBC places a significant financial burden on patients, which can result in significant distress and significantly impact their quality of life and health outcomes (Buzaglo JS, et al, 2016b).

Metastatic breast cancer diagnosis and treatment can involve complex considerations from both the patient and physician perspective, especially given the life-threatening nature of the diagnosis, the looming uncertainty for the patient, and the complexity of treatment options.

- Individualized information about MBC is critical for informed participation in treatment decision making. Yet many MBC patients do not receive adequate information from their physicians and health care teams to enable them to understand the disease and its treatments, identify their questions and concerns, and take part in shared decision making (MBC Alliance, 2014; Mayer, M, Grober SE, 2013).
- MBC patients' understanding of the nature of the disease and goals of treatment is often poor; many believe they will be cured (MBC Alliance, 2014).
- Treatment information needs to be clearly presented in a manner that supports:
  - Patient understanding and literacy
  - Patient-driven dialogue with questions and concerns
  - Patient's values and goals
  - Time for the patient to think about treatment options, and revisit later with the oncologist and health care team (e.g., nurse)

A key component of shared decision making is to identify the patient's values and goals. Yet, eliciting these goals can be difficult from both the physician and patient perspective.

- Patients are not always able to identify their goals in treatment and may not have enough information to understand their options (Boeckxstaens P, Willems S, Lanssens M, et al, 2016).
- Doctors are not trained to elicit patient preferences and values (Zeuner R, Frosch DL, Kuzemacha MD et al, 2014).
- Doctors may feel more comfortable providing treatment-related information rather than eliciting patient values when deliberating over a treatment decision with a patient. In a qualitative study of oncologists, all of the clinicians expressed the importance of providing information, especially to address patient worry even though most patients do not recall the majority of the information presented (Golden SE, Thomas CR, Moghanaki D, et al, 2016). When patients expressed distress, physicians expressed empathy and were more likely to offer more information but were less likely to elicit patient preferences and values.

The challenges challenge to promote shared decision making are real, especially in the context of end-of-life decisions.

- Oncologists may frequently couch the option of not opting for a second- or third-line treatment as 'doing nothing', (Brom L, et al., 2015, p 80).
- Yet, 'no treatment' or 'doing nothing' does not fully convey the full range of options that are defined by palliative care, including psychosocial support and pain management (Brom et al., 2015).
- Metastatic breast cancer patients indicate on average that quality of life plays a more critical role in their treatment decision making compared to length of life (Buzaglo JS, Miller MF, Longacre ML, et al, 2016). Given that quality of life is often a priority factor among MBC patients, shared decision making, especially in the last phase of advanced disease, can be enhanced by eliciting patient preferences and exploring palliative care options that are designed to improve quality of life (Brom et al, 2015).
- Another important bias among oncologists is that continuing treatment or offering second- and third-line treatment can provide "hope" to the patient and family. Taking away the sense of hope is frequently associated with concern that it would harm the patient's wellbeing. Thus, oncologists refrain from offering palliative care options when they may actually may be more in line with the patient's goals than active treatment (Brom et al., 2015).

While providing treatment-related information is necessary and essential to the patient, it is not sufficient to support shared decision making. Oncologists should be encouraged to elicit patient values, goals, and preferences, especially as the disease progresses; and to encourage discussions about all treatments, their risks and benefits, and options for palliative care over the course of care.

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