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Oncology

REVISION: BREAST METASTASIC CANCER AND RECURRENT, PART 2

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ABSTRACT

SUMMARY: The purpose of this review is to guide physicians in particular on the generalities to be taken into account regarding the treatment of metastatic breast cancer for which pubmed and google scholar updated literature were searched.

INTRODUCCION

Metastatic breast cancer at the moment remains an incurable disease with a median overall survival of approximately 3 years, and a 5-year overall survival of approximately 25%, and although it seems a slow growth we have had encouraging results in studies that have Demonstrated increase in overall survival (OS) especially targeting the epidermal growth factor receptor 2 (HER-2). (1–4)

GENERAL INFORMATION REGARDING TREATMENT

The choice of treatment should take into account:

1. Hormone receptor status and HER2
2. Previous therapies and their toxicities
3. Tumor load (defined as number and site of metastasis)
4. Biological age
5. Performance status or ECOG
6. Comorbidities (including organ dysfunctions)
7. Menopausal status (for endocrine therapy)
8. Need for rapid control of the disease / symptoms
9. Socioeconomic and psychological factors
10. Therapies available in the patient's country and patient preferences.

The patient's age should not be the only reason to stop therapy (elderly patient) or to over-treat (young patients), age alone should not determine the intensity of treatment. (5)

In the absence of medical contraindications, anthracycline or taxane-based regimens would be considered as first-line chemotherapy for HER2-negative metastatic breast cancer, as well as those patients who have not received these regimens as neoadjuvant or adjuvant treatment, however, there are other options. available and effective, such as capecitabine and vinorelbine, particularly if avoiding alopecia is a priority for the patient. (5)

The objective of systemic treatment in a patient with metastatic or recurrent breast cancer should focus on prolo nging survival accompanied by a good quality of life and explaining that its purpose is not curative. (6)

ENDOCRINE THERAPY

Patients with metastatic or recurrent breast cancer with estrogen or progesterone receptor expression are appropriate candidates for initial endocrine therapy, even in the presence of visceral disease, unless there is a visceral crisis or endocrine resistance. (6)

For premenopausal women, for whom endocrine therapy was decided, OFS / OFA combined with additional endocrin therapy is the preferred option. (5)

In pre-menopausal women without prior exposure to an antiestrogen, the initial treatment is with a selective estrogen receptor modulator or complete ovarian ablation / suppr ession plus endocrine therapy as for menopausal women. (7)

For pre-menopausal women who have primary endocrine resistance, second-line treatment will focus on complete ovarian ablation / suppression plus endocrine therapy as for menopausal women. (6)

Endocrine therapy for post menopausal patients includes non-steroidal aromatase inhibitors (letrozole / anastrozole), steroidal aromatase inhibitors (exemestane), selective estrogen receptor modulators (tamoxifen), estrogen receptor antagonists (fulvestrant) and recently several new combin ations with new agents such as exemestane with everolimus, palbociclib with letrozole / fulvestrant. (6)

According to some studies in postmenopausal women, aromatase inhibitors appear to have superior results compared to tamoxifen, although the differences are modest. (8–12)

A Cochrane review also suggests a survival benefit in favor of aromatase inhibitors over other endocrine therapies altho ugh the advantages are small. (13–15)

A randomized phase III study compared the combination of tamoxifen plus exemestane as the first line of treatment in postmenopausal patients with metastatic breast cancer, showing no significant differences in either progression-free survival or overall survival. (12)

Fulvestrant appears to be at least as effective as anastrozole in patients who progressed to their disease by using tamoxifen before. (6)

In contrast, in a phase II study, the use of Fulvestrant to the progression to the use of aromatase inhibitor, a partial response of 14.3% is reported and 20.8% of patients presented stability for at least 6 months. (6)

Given the intrigue of combined therapy, the FACT study the Anastrozole / Fulvestrant combination was not superior to Anastrozole alone, while in another S0226 study the Anastrozole / Fulvestrant combination was superior. (6)

Palbociclib, a selective inhibitor of CDK kinase activity 4/6, has played an important role in treating patients with metastatic breast cancer in combination with endocrine therapy. (6)

The phase III study (PALOMA-3) compared the combination of palbociclib / Fulvestrant and Fulvestrant in pre or post-menopausal patients with positive hormonal receptors, HER-2 negative, progression-free survival (PFS) was 9.2 months for the combination versus 3.8 months for Fulvestrant. (6)

Resistance to endocrine therapy in women with positive hormonal receptors is common, a mechanism of resistance to endocrine therapy is the activation of mTOR. (6)

The Phase III study (BOLERO-2) randomized postmenopausal women with hormonal receptors and who progressed to aromatase inhibitors to receive exemestane with or without everolimus (mTOR inhibitor), with a PFS of 11 versus 4.1 months in favor of the combination . (7)

In men the preferred therapy is LHRH agonist. (5)

HER-2 THERAPY FOR METASTASIC / RECURRENT BREAST CANCER.

HER-2 is a cell surface protein that is found in approximately 20% of breast cancer cases and is involved in cell growth and migration. (6)

Tumor tissue status in relation to HER2 can be analyzed by various laboratory analyzes: immunohistochemistry (IHC), fluorescence in situ hybridization (FISH) or chromogenic in situ hybridization (CISH). (6)

A cancer is positive for HER-2 when the result of the IHC analysis is 3+ (crosses) or the result of an FISH or CISH test is positive according to the pathology report. (6)

Anti-HER2 therapy should be offered as a first line of treat ment to all patients with metastatic breast cancer that is positive for HER-2. (6)

Both guides such as NCCN and ESMO recommend pertuzumab plus trastuzumab in combination with a taxane as a preferred first-line treatment in patients with HER-2 breast cancer, ESMO also recommends that the choice of anti-HER2 agent will depend on the specific availability of the country , the specific anti-HER2 therapy previously administered and the relapse-free interval. (5)

In patients who achieve complete remission, the optimal duration of anti-HER2 maintenance therapy is unknown and should be balanced with treatment toxicity, logistic load and cost. (5)

For patients who previously received anti-HER-2 therapy with trastuzumab, it is recommended to continue blocking HER-2. (6)
T-DM1 is an antibody-chemotherapeutic conjugate, composed of the anti-HER2 trastuzumab antibody and the cytotoxic antimicrotubule agent, DM1 (emtansin), bound by a stable bond. (6)

The selective release of emtansin in the HER2 positive cell causes systemic toxicity to be limited, making it a very well tolerated drug by most patients. (6)

THERAPY FOR NEGATIVE TRIPLE BREAST CANCER

Chemotherapy remains the only non-investigative systemic treatment option available for metastatic or recurrent triple negative breast cancer with non-mutated BRCA, without specific recommendations regarding the types of agents, with the possible exception of platinum compounds. (5)

Regardless of the BRCA status in cases of recurrence, patients previously treated with anthracyclines with or without taxanes in the (neo) adjuvant setting, carboplatin demon strated comparable efficacy and a more favorable toxicity profile, compared to docetaxel. (5)

Those patients with triple negative breast cancer who have androgen receptors to the research should emphasize that there is no standardized method to analyze androgen receptor, so the data is very limited and suggests a low level of efficacy for antagonistic agents of Androgenic receptor such as bicalutamide and Enzalutamide, so at this time, these agents should not be used in normal clinical practice. (6)

PARP inhibitors (olaparib or talazaparib) may become a reasonable treatment option for patients with triple negative metastatic breast cancer associated with BRCA, previously treated with an anthracycline with or without taxane, since its use is associated with a benefit of Progression-free survival, improvement in quality of life and a favorable toxicity profile. (5)

BRAIN METASTASIS

Patients with a single metastasis or a small amount of potentially resectable brain metastases should be treated with surgery or radiosurgery, being radiosurgery is also an option for some unresectable brain metastases. (5)

Total brain radiotherapy is a good option but this should be discussed in detail with the patient, balancing the longer duration of intracranial disease control and the risk of neurocognitive effects. (5)

Because patients with HER-2 positive brain metastases can live for several years, consideration of long-term toxicity is

important and less toxic local therapy options (for example, stereotactic RT) should be preferred. (5)

HEPATIC METASTASES

There are no random data that support the effect of local therapy on survival, local therapy should only be proposed in highly selected cases, with limited hepatic involvement, without extrahepatic lesions, after adequate systemic therapy has demonstrated disease control. (5)

MALIGN PLEURAL SPILLS

Malignant pleural effusions require systemic treatment with or without local treatment, thoracentesis should be performed for diagnosis, recommending drainage in patients with symptomatic and clinically significant pleural effusion. (5)

REALITY AS TO COSTS

Aware of the cost of treatment, balanced decisions must be made in all cases; Patient well-being, life span and prefer ences should always guide decisions. (5)

For decision-making of high-cost medicines it is necessary to follow the recommendations on the use of objective scales, such as ESMO-MCBS or ASCO Value Framework, to assess the real magnitude of the benefits provided by a new treatment and help prioritize funding, particularly in countries with limited resources like ours. (5)

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