ORIGINAL RESEARCH PAPER

Oncology

REVISION: BREAST METASTASIC CANCER AND RECURRENT

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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 management of metastatic breast cancer for which pubmed and google scholar updated literature were searched and basic concepts were established to help understand this topic.

INTRODUCTION

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)

Studies by Malmagren and Holzel have been able to demonstrate a better survival in those de novo care patients, on the other hand, it becomes a lower survival and difficult management in patients in recurrence. (5.6)

The management of metastatic and recurrent cancer is complex and involves a multidisciplinary team that must be comprised among other specialties by: clinical oncologist, surgeon oncologist, radio-oncologist, image experts, pathology, social work, nursing and pisco-oncologists. (7)

1.- BASIC DEFINITIONS

1.1.- METASTASIS.-

Dissemination to distant organs of a cancer, generally occurring by blood or lymphatic route. (8)

1.2.- RECURRENCE.-

Reappearance of the cancer after an apparent disappearance of the same after surgical or medical treatment, being able to be local or remote. (8)

1.3.-VISCERAL CRISIS.-

Severe organic dysfunction evaluated by signs and symptoms, laboratory studies and rapid disease progression. The visceral crisis is not only the presence of visceral metastases, but it implies an important visceral compromise that leads to a clinical indication for a faster and more effective therapy. (7)

1.4.- PRIMARY ENDOCRINE RESISTANCE.-

Relapse during the first 2 years of adjuvant endocrine therapy, or progression within the first 6 months of first-line endocrine therapy. (7)

1.5.- SECONDARY ENDOCRINE RESISTANCE.-

Relapse after the first 2 years while in adjuvant endocrine therapy, or progression after 6 months after starting endocrine therapy, or a relapse within 12 months of completing adjuvant endocrine therapy. (7)

1.6.- OLIGOMETASTATIC DISEASE.-

Disease with a limited number and size of metastatic lesions (up to 5 and not necessarily in the same organ), potentially susceptible to local treatment, with the aim of achieving a state of complete remission. (7)

1.7.- MENOPAUSE.-

Permanent cessation of menstruation, due to the deep and permanent decrease of estrogen synthesis by the ovaries, to determine menopause, it must include the following

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parameters. (9)

- Bilateral Prior Oforectomy
- Age greater than or equal to 60 years
- Age less than 60 years with a history of amenorrhea of 12 months or more in the absence of chemotherapy, tamoxifen or ovarian suppression with the presence of follicle stimulating hormone (FSH) and estradiol within postmenopausal ranges.
- Age under 60 years of age taking tamoxifen with the presence of follicle stimulating hormone (FSH) and estradiol within postmenopausal ranges.

1.8.- OVARIAN FUNCTION SUPPRESSION (OFS) .-

Is the induction of menopause by bilateral ovariectomy or continuous use of agonists of luteinizing hormone releasing hormone (LHRH) analogs (7)

1.9.- OVARIAN FUNCTION ABLATION (OFA) .-

It is the induction of menopause by pelvic radiotherapy (the latter is not always effective being the least preferred option) (7)

2.- STADIFICATION

The staging evaluation of metastatic or recurrent breast cancer includes medical history and physical examination; Complete blood count, liver function tests, bone gammagraphy, bone x-ray of any limb that presents pain or abnormality to bone gammagraphy, chest-abdomen tomography and whether or not pelvis, PET / SCAN will be considered only in cases of suspicion of difficult diagnosis. (9) Brain imaging should not be performed routinely in asymptomatic patients, including those with a triple negative profile report or positive for HER-2. (7)

3.- PATHOLOGY

A biopsy of a metastatic lesion, if easily accessible, should be performed to confirm the diagnosis, particularly when a metastasis is first diagnosed. (7)

The presence of metastatic disease or recurrence should be biopsied as a fundamental pillar of treatment to determine the histology of the tumor as well as biomarkers to determine the selection of the appropriate treatment. (9)

Biological markers (especially hormonal receptors (HR) and HER2) should be reassessed at least once in the metastatic environment if feasible. (7)

If the results of tumor biology in metastatic lesion differ from the primary tumor, the recommendation is to consider the use of targeted therapy (HT or anti-HER2 therapy) when the recipients are positive in at least one biopsy, regardless of the time. (7)

It is necessary to determine the status of hormonal receptors (estrogen and progesterone) as well as HER 2 every time that the diagnostic tissue has been obtained, it must be taken into account that hormonal receptors can be falsely positive or falsely negative as well as mismatch between the tumor and metastasis. (10.11)

The reason why there may be disagreement of the status of receptors between the tumor and metastasis may be due to changes in the biology of the disease, a differential effect between the primary treatment and the clonal subset, tumor heterogenicity, imperfection in accuracy and tissue reading reproducibility. (eleven)

Retesting is recommended to assess recipient status in patients with unknown prior diagnosis, previous negative or non-expressed receptors, while for patients who clinically study with positive hormonal receptors or previously had positive hormonal receptors, follow-up with endocrine therapy is reasonable regardless of the new hormone receptor report. (9)

4.- GENERAL INFORMATION REGARDING TREAT MENT

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 discontinue a therapy (elderly patient) or to over-treat (young patients), age alone should not determine the intensity of treatment. (7) 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. (7)

The objective of systemic treatment in a patient with metastatic or recurrent breast cancer should focus on prolonging survival accompanied by a good quality of life and explaining that its purpose is not curative. (9)

4.1.- SUPPORT THERAPY IN OSEAS METASTASIS

The treatment target is to act against osteoclast activity, with the main objective of avoiding bone fractures, reducing bone pain, spinal cord compression and hypercalcemia. (12,13)

For these problems one of the treatments to follow is radiot herapy, as well as zoledronic acid or pamidronate bisphosphonates have been used for this purpose, and a wide variety of clinical trials have shown the benefits of avoiding skeletal-related events, finally Denosumab is a monoclonal antibody directed against the RANK ligand an osteoclast function meter. (12)

Bisphosphonates and Denosumab are associated with a higher risk of causing jaw necrosis, so a prior dental check-up must be performed before starting these treatments, since once they have been established, any dental procedure should be avoided. (12,14)

Prior to the onset of bisphosphonates or Denosumab, an initial evaluation of calcium, phosphorus, magnesium levels as well as follow-up is important as cases of hypocalcemia, hypopho sphatemia and hypomagnesemia have been reported. (9)

4.1.1.- BIFOSPHONATES

An intravenous bisphosphonate (pamidronate, zoledronic acid) in combination with a supplement with oral calcium citrate and vitamin D should be used in women with bone metastases, especially if the bone has lost weight or has lysis, bisphosphonates can be administered with chemotherapy or With endocrine therapy, it should be taken into account that zoledronic acid may be superior to pamidronate in lytic metastases. (14–21)

The use of bisphosphonates in patients with bone metastases is a palliative management, it will reduce the risk of bone lesions but does not affect or modify the overall survival, although research has shown that zoledronic acid or

pamidronate can be administered every 3 to 5 weeks, more data Recent reports have indicated that there is no difference between administering every 4 or every 12 weeks with event rates related to bone accidents of 22% vs. 23.2%. (15)

4.1.2.- DENOSUMAB

Patients with metastatic bone cancer may be candidates for bisphosphonates as well as being able to be considered for treatment with Denosumab, clinical trials have shown a decrease in related bone events but also there was no difference in overall survival, we must consider that in broad strokes The risk of this treatment is unknown as well as treatment time. (12)

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