

Metastatic breast cancer

Metastatic disease is relatively common in cases of breast cancer.

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Approximately 40% of all patients with breast cancer will relapse, which represents a failure of adjuvant therapy to control micro-metastatic disease. Even though most patients will have a relapse within the first 5 years after treatment, they can relapse indefinitely; therefore breast cancer patients should be followed up for life.

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Metastatic disease is incurable, but because of improved therapy survival of patients has been prolonged. The overall median time of survival is 2 years from initial diagnosis of metastases, but in some circumstances patients may live much longer.

The following factors affect long-term survival of patients with metastatic disease:

- long disease-free interval
- positive oestrogen and progesterone receptors
- sustained response to previous hormone therapy
- single site of metastasis
- bone metastases only.

The aim of therapy is to improve and prolong quality of life by controlling symptoms and either stabilising or reducing disease burden with oncological therapy.

The following factors affect symptom control:

- age
- quality of life
- co-morbid disease
- clinical course of disease and previous therapy
- patient preference
- oestrogen, progesterone and HER2 neu (c erb2)-receptor status.

Once a metastasis has been diagnosed it is mandatory to re-stage the patient after determining its extent, site, new histological status, hormone status, and erb b2-receptor status, if possible.

Categories of relapse

- Locoregional disease
- Bone-only disease – most common, occurring in 30 - 40% of all first metastases

Table I. Management of relapse

Site of relapse	Problem	Management
Locoregional disease		Triple modality
Bone*	Pain	Analgesics, radiotherapy, bisphosphonates
	Fracture prevention	Stabilisation
	Hypercalcaemia	Bisphosphonates
Visceral disease – lung*	Solitary nodule	Excision
	Effusion	Drain pleurodesis
	Dyspnoea	Steroids, nebulisers Low-dose morphine (without O ₂ as result in home confinement)
Visceral disease – liver*	Nausea	Anti-emetics
	Weight loss, lethargy	Steroids
Brain		Excision, if possible Radiotherapy

* May be treated with hormone therapy and/or chemotherapy and/or trastuzumab as indicated.

All patients with metastatic disease are eventually considered for chemotherapy.

- Visceral disease
 - Lung – metastases recur in 15 - 25% of patients
 - Liver
- Brain metastases
- Multiple areas of metastatic disease.

For management of relapse see Table I and algorithm below.

Hormone therapy

Treatment of metastatic disease with hormone therapy will depend on the presence of hormone receptors, site of the metastasis, rapidity of disease progression, and quality of life. It will also depend on the menopausal status of the patient and previous hormone therapy, but any hormone that is administered in the adjuvant setting can be given in the metastatic setting.

Chemotherapy

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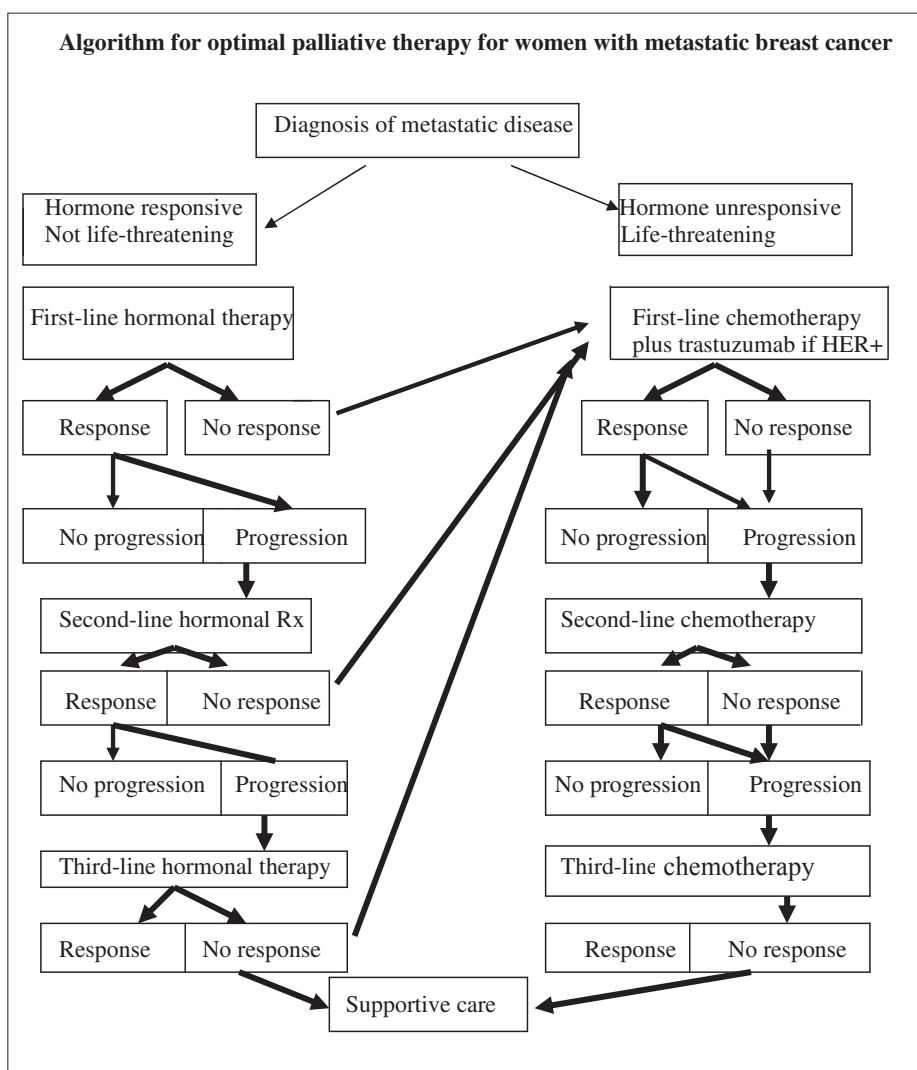
As a rule single agents are given sequentially and are used to control symptoms, except in fit young patients with a first diagnosis of metastatic disease and whose disease is progressing rapidly. In these patients combination chemotherapy can control disease progression and thus improve symptoms quickly. The agents used will depend on which drug and dosage were administered as adjuvant treatment. Newer oral chemotherapy agents such as vinorelbine tartrate and capecitabine are well tolerated and effective and used only in metastatic disease.

Newer therapies

Trastuzumab (Herceptin) is a humanised monoclonal antibody which blocks the extracellular domain of the HER2 neu receptor and is administered as adjuvant therapy. In combination with chemotherapy drugs synergistic and additive effects have been shown to improve the response rate, time to progression and survival time. If trastuzumab has not been used as adjuvant treatment, and the tumour has been shown to be HER2 neu (c erb b2) positive and FISH positive, the drug can be considered at this stage. It should be noted that trastuzumab is very expensive and its cost may not be covered by all medical aid plans.

Two other drugs for the treatment of metastatic breast cancer will soon be registered:

- **Lapatinib** – a small-molecule tyrosine kinase inhibitor which seems to be active in patients who relapse after trastuzumab therapy.
- **Bevacizumab** – a monoclonal antibody with anti-angiogenic properties. It is effective in oestrogen receptor-negative and HER2 neu receptor-negative patients.



When metastatic disease has been confirmed, it is essential to discuss prognosis and expectations with the patient and her family. If treatment should fail, it should therefore not be too traumatic to start palliative care.

Treatment of metastatic breast cancer is given on an individual basis as many factors come into play. However, maintaining quality of life is the prime goal of treatment and support should be given to patients and their families, as they are subjected to profound psychological

stress. A team approach is necessary, which includes the attending oncologist, the general practitioner, and the psychologist, as well as hospice care.

Further reading

- Bonadonna G, Hortobagi G, Valagussa P, eds. *Breast Cancer Guide to Therapy*. 3rd ed. 2006.
- Guidelines – Metastatic Breast Cancer – Recommendations Proposal From European School of Oncology (ESO) MBC Task Force. *The Breast* 2007; 16(1).
- Silva O, Zurrida S, eds. *Breast Cancer – A Practical Guide*. 3rd ed. 2006.

In a nutshell

- Metastatic breast cancer treatment is not curative and has only a modest impact on survival, but can prolong time to disease progression.
- Quality of life and tumour palliation are the main therapeutic goals.
- Hormone therapy and single-agent chemotherapy protocols are used to control tumour progression.
- Quality of life is improved by control of symptoms such as pain, dyspnoea, nausea and vomiting, and depression. It can be done in combination with active treatment or continued after tumour treatment has been discontinued.
- The patient and her family should receive psychological support, as well as help from trained counsellors.