

Advanced breast cancer: What's new in treatment and care?

Despite growing precision in understanding the biology of breast cancer, progress in extending survival of people with metastatic disease remains frustratingly slow. Median survival is only about three years, having edged up only slightly in recent times, although there are signs that better care at ear-

lier stages is reducing the numbers of advanced cases. As indicated by the updates and additions to the guidelines arising from the 4th International Consensus Conference for Advanced Breast Cancer (ABC4), which are précised below, recent progress has been in the most common subtype – ER+ (oestrogen-receptor posi-

tive), luminal advanced breast cancer.

The ABC guidelines, drawn up under the auspices of the European School of Oncology and the European Society for Medical Oncology, cover both treatment and, increasingly, quality of life factors. This is in recognition of the need to apply evidence on the holistic wellbeing of people with

Précis of the key updates and additions from ABC4

• Quality and access

MDT care for advanced disease

At ABC4, the panel added several points about the organisation of care, including that all patients should have access to a specialist breast centre that includes a nurse experienced in advanced disease. In 2015, the European Parliament adopted a declaration that added metastatic breast cancer to its call for universal breast units, and the guidelines put more pressure on services to not isolate this patient group from integrated care.

Early palliative and supportive care

The offer of survivorship and palliative care services at an early stage in care was also added to the guidelines and recommendations, together with a quality assurance programme that covers the patient journey. The key is that care pathways and quality indicators in national breast unit certification systems currently omit the metastatic stage. This will also be addressed in the forthcoming quality assurance accreditation framework from the European Commission Initiative on Breast Cancer (EIBC), due for publication in 2020, and an update of the EUSOMA (European Society of Breast Specialists) 'Requirements of a breast centre', also underway, under the auspices of the ABC Global Alliance.

QoL tools for advanced disease

Also included is a call for tools that measure health-related quality of life of advanced breast cancer patients – this is another neglected area, where oncologists' reports have tended to take precedence over patient experiences: what doctors say often does not match what patients say about side-effects. The EORTC Quality of Life and Breast Cancer Groups are working on such a scale, and it is urgently needed given the expanding range of drug combinations that are now being trialled in successive lines of therapy, and the pressure

that severe side-effects can place on both the acute and community based health systems.

Biosimilars

On cost-effectiveness strong support is voiced for the use of new biosimilar drugs – a paper from the European School of Oncology this year will set out the latest issues on these, building on a paper from ESMO in 2016.

• Treatment statements

ER+ advanced breast cancer

Of the three main molecular subtypes – luminal (ER+/HER2-), HER2+, and triple negative – it is ER+ that has seen the most progress recently, and where the most impact could be seen as it is by far the most common type, at about 65% of advanced breast cancers. Two of the new statements on ER+ concern the new CDK4/6 inhibitors, two of which are approved in Europe with another on its way having gained US approval. ER+ cancer has been found to depend particularly on the CDK enzyme to grow, and the inhibitors are especially effective when combined with endocrine therapy.

However, there is no overall survival (OS) data yet for the combinations, but good evidence for progression free survival. The ABC panel has also added scores from the ESMO Magnitude of Clinical Benefit Scale to these statements to give a better guide about whether to offer them in practice. The addition of everolimus, a type of inhibitor (mTOR), to an aromatase agent also gets a statement, albeit without significant OS benefit.

The panel has made statements on the uncertainty of the sequence of endocrine-based therapy, and the lack of biomarkers other than the oestrogen receptor.

Pre-menopausal women

Expert opinion is given on the lack of trials in young women with ER+ advanced breast cancer, and there are strong words

advanced disease. In parallel, the wider ABC community has undertaken work on organisational and societal factors that affect metastatic patients, and this work has informed the consensus guidelines and indeed advocates are among the panel members (see *Advanced Breast Cancer Goes Global, Cancer World Winter 2017/18*).

The 4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC4) will be published in full in the Annals of Oncology.



in the commentary. The recommendation is that young women should receive ovarian suppression or ablation (removal of the ovaries) and be treated in the same way as postmenopausal women and allowed to enter the same clinical trials. “Resources should not be wasted running duplicate and separate trials for pre- and postmenopausal patients,” and the “ABC panel strongly advocates against unrealistic, unnecessary and sometimes expensive clinical trials requirements on contraception, with clear negative impact on quality of life, for pre-menopausal women who do not undergo suppression or ablation.” A definition of what adequate ovarian function suppression means in the context of ABC has also been added, and expert opinion that the impact of therapy on fertility should be discussed with all women of childbearing age.

HER2+ and triple negative

While anti-HER2+ therapy has been key to significant survival gains, there has been little to note in the past two years, although there are two new statements that follow latest trials on patients with ER+/HER+ ABC.

Triple negative ABC continues to have few advances, but PARP inhibitors are an option (see genetic testing).

Genetic testing and precision medicine

These are mostly new sections, and include statements on genetic testing for mutations in the BCRA1/2 genes, now that the PARP inhibitors have been approved, which are an option in triple negative and luminal breast cancer associated with BRCA mutations. This currently concerns only germline (hereditary) BRCA mutations, but could in future involve other hereditary gene mutations that confer risk. The commentary also calls for high-quality genetic counselling services. BRCA mutations can also arise somatically – i.e. not via genetic inheritance – but there is no clinical relevance yet. The panel added statements against the use of certain tools that are available

but not validated and so should not be used in routine clinical practice, such as next-generation multigene panels and circulating tumour DNA. Further, there is no clinical role yet for immunotherapy in advanced breast cancer.

Brain metastases

A statement on treatment of an uncommon condition, radionecrosis, has been added – it concerns an effect of using stereotactic radiotherapy that is now being seen more owing to longer survival of some patients with brain metastases from HER2+ breast cancer.

• Supportive and palliative care

Mucositis • Neuropathy • Hand & foot syndrome

The panel has added three statements on managing side-effects: on mucositis/stomatitis (mouth/lip inflammation), chemotherapy induced peripheral neuropathy, and hand and foot syndrome. As the commentary notes: “When adverse events are addressed systematically and at an early stage, they often become simple and inexpensive to treat, allowing for a higher probability of continuation of the planned therapy.”

• Integrative medicine

Exercise • Mindfulness • Hypnosis • Yoga • Acupuncture

Lastly, a new section has been added on what is termed ‘integrative medicine’ – this concerns therapies such as complementary medicines and physical exercise. It is recognised that many patients are using complementary therapies and the panel considers that some can reduce symptoms and improve quality of life. They find level I evidence in favour of physical exercise, ‘mindfulness-based’ stress reduction programmes, hypnosis, yoga and acupuncture. But there is evidence that some complementary medicines have no effect or can even make matters worse. Among these are antioxidants, herbs, high-dose vitamins and oxygen/ozone therapy.