Individualized care for patients with advanced breast cancer

Canadian Breast Cancer Network
Réseau canadien du cancer du sein

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This is a summary of a roundtable held in collaboration with the Canadian Breast Cancer Network on Tuesday, December 4, 2018, at the Hilton Palacio Del Rio Hotel in San Antonio, as well as subsequent discussions on individualized care for patients with advanced breast cancer. The roundtable, moderated by Dr. Karen Gelmon, included Canadian leading experts in oncology, Drs. Christine Brezden-Masley, Sandeep Sehdev, Christine Simmons and Sunil Verma, and Jenn Gordon from the Canadian Breast Cancer Network.

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Introduction

By Cathy Ammendolea
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Cancer is about so much more than the disease. It's also about the individuals affected by it. Since 1994, the Canadian Breast Cancer Network (CBCN) has been dedicated to ensuring the best quality of life for all Canadians affected by breast cancer. The CBCN is a patient-directed organization, committed to voicing the views and concerns of breast cancer patients through education, advocacy activities and the promotion of information sharing.

Breast cancer is the most common malignancy among Canadian women, accounting for approximately 26% of new cancer cases in 2017.[1] Of those newly diagnosed, about 5% will have metastatic disease at diagnosis, but another 30% will relapse some time after their initial presentation.[2] Advanced breast cancer (ABC), including locally advanced and metastatic forms, has the poorest prognosis,[2] with a median overall survival of 3 years and a 5-year survival of only 25%.[3] This is a patient population in clear need of individualized support and improved treatments.

There are many key issues to consider in the treatment of patients with ABC. In particular, there is a need to:

- Recognize that ABC is a heterogenous disease
- Identify better predictive and prognostic biomarkers
- Further understand the evolution of the tumour
- Improve and individualize patient care

Heterogeneity of advanced breast cancer

Physicians who treat ABC must consider tumour heterogeneity and the clonal evolution of malignancies.

This means that treatments that have worked well in some instances of ABC may prove ineffective in others. Tumours evolve and develop resistance over time causing previously successful therapies to lose efficacy. Markers and biological features of tumours, such as hormone receptor and HER2 status, are currently used to help determine the prognosis and treatment selection.

When selecting optimal therapy, other characteristics, such as disease-free interval (the time from the initial presentation to the development of ABC) and the sites of metastases, may be considered. For example, when ABC develops shortly after the completion of adjuvant therapy or within the first 2 years of diagnosis, it is often a very aggressive form, which may be resistant to treatment.[4,5]

PROGNOSTIC factors in ABC may include:

- Patients with visceral metastases, especially those with a large burden of liver metastases or unresectable brain metastases, have poorer prognosis than those with bone-only metastases
- Patients who present with significant symptoms and a poor performance status have a poorer outcome
- Patients with multiple metastases may have poorer outcomes than those with single metastases, although this effect can vary based on sites and number of metastases

PREDICTIVE factors in ABC may include:

- Patients who present with rare, rapidly progressive metastases that need to be treated urgently may have a poor outcome if the cancer does not respond
- Patients who present with ABC at diagnosis and are otherwise reasonably well (good performance status) may respond better to first-line therapy than those who relapse on adjuvant therapy
- Cancers that do not respond to the first metastatic treatment may present with resistance and a more aggressive phenotype

Even beyond these factors, ABCs can vary greatly in their aggressiveness and response to treatment. Additional tumour markers and patient-related factors are needed to understand this variation and to develop effective, personalized treatment for patients with ABC.

The need for new biomarkers

The biomarkers used to predict prognostic outcomes for ABC require rethinking. Additional studies are needed to expand the markers in current use, and to define and validate new markers which may be useful to determine the best therapy for an individual patient. Current standard markers are ER and HER2. Some other commonly used markers, such as Ki-67 and even the progesterone receptor, may be less reliable because of inter-laboratory assay variability. The development of new and better standardized molecular tools and the optimization of breast cancer panels of markers would simplify treatment decisions for oncologists and patients.

The use of next generation sequencing (NGS) in ABC is being explored in the setting of clinical trials. While the use of NGS routinely in ABC needs further evaluation, it has, so far, led to the identification of important markers that are commonly mutated in ABC, which may prove to have predictive as well as prognostic significance. For example:

- PIK3CA mutations allow for selection of patients for treatment with newer PI3K inhibitors
- ESR1 mutations suggest more benefit from fulvestrant as an endocrine backbone therapy
- Homologous repair deficiency profiles and BRCA mutations may allow selective application of PARP inhibitors

Continued development of technology, to analyze peripheral blood samples to identify mutations in circulating tumour and circulating free DNA, will be of increasing importance in the future.

Confronting the dynamics of the tumour

ABC can vary not only among patients, but also in the same individual over time. When metastases develop, repeat biopsies can determine if the tumour genomics have evolved over time. The use of circulating tumour DNA, fine needle aspirates and biomarker panels (onco-panels) may simplify this task and allow for effective monitoring of the tumour, which may lead to a more rational selection of treatments and, hopefully, more effective therapies. A 'liquid biopsy' approach, for example, is essentially non-invasive, thus facilitating frequent monitoring of the patient's response to treatment and may provide the important data we need to improve response in ABC.

Onco-panels on core biopsy tissue supplemented with regular liquid biopsies may also provide insight in determining which tumours are resistant to specific therapies. This strategy will help clarify which patients are at heightened risk of developing resistance and will require more frequent monitoring.[6]

Improving care and empowering the patient

Each patient confronting a diagnosis of breast cancer has his or her own set of life goals. Physicians need to consider both clinical and patient-related factors when they choose a treatment approach, and in doing so prioritize the needs, values, preferences and concerns of the patient. By being involved as much as possible in their own cancer care, patients can ensure it is aligned with their own priorities and can make personal decisions.

For this reason, physicians, along with their multidisciplinary team of nurses, pharmacists, social workers, pain specialists, palliative care experts and patient groups, should support patients throughout their cancer care, from the time of diagnosis onward. Appropriate education can reassure the patient and help mitigate fear surrounding possible adverse effects and drug-drug interactions. When language barriers prevent easy communication in the clinic, physicians should bring in a medically educated translator to ensure patients understand and consent to treatment. Emotional and social support should be available for patients, especially for those with little family support.

A multidisciplinary team should be accessible for all patients with ABC, to provide psychosocial and emotional support of clinical efforts, both curative and palliative. Although it may not be possible to meet this ideal everywhere in Canada, even cancer centres with limited resources should offer ABC patients access to a good nursing team, to support them through their care.

Above all, patients deserve a chance to feel safe during their cancer care, and healthcare providers should look carefully for ways to offer each individual patient a greater sense of safety. Some patients feel safest, for example, when they are well-informed about the various treatment options available or when they are reassured that a multidisciplinary team is involved in their cancer care.

While urgent treatment may be required on clinical grounds, healthcare professionals must respect a patient's need for time to process the diagnosis. A patient should feel he or she is being treated as an individual, not defined by the disease.

Call to action

Healthcare professionals need to recognize that ABC is a heterogeneous disease that requires an individualized treatment approach. As new approaches emerge to assess, treat and monitor clinical response in ABC, the basic need remains for healthcare professionals to offer reassurance and emotional support appropriate to each patient individually.

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