

Metastatic breast cancer (MBC) is the most advanced stage of breast cancer and is usually regarded as an incurable disease. Breast cancer has different molecular subtypes, which require tailored treatment options. Once recurrence and metastasis occur and the disease enters a more advanced stage, the biological characteristics of the malignancy become even more complex and diverse, which makes the clinical treatment particularly challenging. Multiple dimensions must be considered when developing a treatment strategy. In addition to the molecular subtypes, other considerations may include drug resistance, visceral metastasis/visceral crisis, and length of disease-free survival. In an era of molecular typing and precision therapy, the availability of a variety of molecularly targeted drugs has dramatically improved the prognosis of patients with advanced breast cancer, which has led to significant changes in treatment concepts and patient outcomes.

“Survival with tumor” has been one of the most important treatment concepts for MBC. The vast majority of MBC cases are incurable. Thus, the toxicities or side effects of medications must be considered in addition to their efficacy, which is often referred to as “effective and less toxic” options. Most MBCs are hormone receptor (HR)-positive, for which endocrine therapy is an “effective and less toxic” option and is also suitable for long-term maintenance. Therefore, endocrine therapy is the preferred treatment for HR-positive MBC in most guidelines. Anti-human epidermal growth factor receptor 2 (HER2)-targeted drugs have been available for HER2-positive advanced breast cancer patients. For these patients, the chemotherapy dose intensity may be properly lowered after the dose intensity of targeted drugs is ensured. In addition, suspending the chemotherapy while continuing the maintenance therapy with targeted drugs may be feasible after the tumor is effectively controlled. This type of maintenance therapy also represents one of the new ideas in antitumor treatment in which not only is the continuity of the care ensured but the toxicity alleviation and patient recovery accounted for. “Still water runs deep,” is an apt description of the concept of survival with tumor.

More encouragingly, with the introduction of precise treatments of specific advanced breast cancer subtypes, the marketing of novel antitumor drugs, and the updating of treatment concepts, MBC patients are more likely to move from a “survival with tumor” status to one that is “partially curable”. Cure of MBC presents a challenging goal—one that may seem unattainable; however, with the stunning progress made in treatments for other tumors in recent years, achieving a cure for MBC may not just be a dream. In fact, the survival rate of breast cancer patients is extremely high: globally, breast cancer is the most common cancer in women (2.26 million in 2020) but ranks only the sixth in deaths (about 680,000 deaths). Even after surgery and various adjuvant treatments, about 30–40% of early breast cancer patients will ultimately experience recurrence and metastasis; in addition, about 5–10% of treatment-naïve breast cancer patients are already in the advanced stage. Thus, MBC patients constitute a huge population. However, the annual mortality rate is less than one-third of the annual incidence rate, which is mainly attributed to the use of new antitumor drugs, especially anti-HER2-targeted drugs and endocrine medications. Therefore, there is new hope toward a cure for some MBC patients. The response rates of first-line treatments for MBC patients are more than 50% and have reached 60–70% in some reports. Although the rate of complete remission (CR) is still low, some patients with a partial remission (PR) can achieve a tumor-free status following both systemic and local therapies. This long-term tumor-free status is similar to the initial CR status in terms of survival and outcome and therefore can also be defined as CR. A successful first-line treatment also paves the way for excellent outcomes after second- and higher-line therapies and increases the chances of reaching CR. Some large studies have indicated that the combinations of cyclin-dependent kinases 4 and 6 (CDK 4/6) inhibitors with endocrine therapies as first- and second-line treatments in hormone receptor (HR)-positive advanced breast cancer have achieved an overall survival of 4 to 5 years, with many CR patients being able to maintain CR status for a long period of time. In the CLEOPATRA trial, HER2-targeted therapy with dual blockade achieved an 8-year overall survival (OS) rate of 37% (which then slowly entered a plateau), and it was expected that the 10-year OS rate could still reach 30%. The long-term survival of CR patients has also been demonstrated in quite a few case reports and small-sample case analyses.

It is evident that the therapeutic efficacy for MBC is constantly improving as treatment concepts, therapeutic tools, and drugs are updated. Many patients can survive with tumor for a long period of time, and there remains a good chance for cure in some patients who have achieved clinical CR. It is time for clinicians to seize the opportunity and overcome this challenge.

The treatment concept and expected outcome of advanced breast cancer have undergone drastic changes. Based on the

authors' clinical practice of more than 30 years and a large number of clinical research results, we attempt to define the concept of a cure for advanced breast cancer. It is hoped that we can work together to care for patients with advanced breast cancer from the survival with tumors to cure. Just as the mission of the ABC Global Alliance, it is our goal to improve and extend the lives of women and men living with ABC in all countries worldwide and to fight for a cure.

Acknowledgements

Funding: This work was supported by grants from Major Science and Technology Projects of Zhejiang Province (2012C13019-1), Key research and development projects in Zhejiang Province/International cooperation technology research and development and demonstration promotion projects (2019C04001,2020C04012), National Key research and development program/International cooperation in science and technology innovation/key special projects of Hong Kong, Macao and Taiwan cooperation in science and technology innovation (2019YFE0196500).



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