

## Preface for special issue “Advances in treatment and care in metastatic breast cancer”

More than 70% of patients with operable breast cancer who received the modern standard of care can be cured. On the other hand, patients with metastatic breast cancer (MBC) are still incurable and have poor prognosis with approximately 3 years of median survival time. However, the prognosis of MBC is gradually improving in step with advances in life science and technology and changes in the social environment.

New technologies such as next-generation sequencing (NGS), liquid biopsy, patient-derived xenograft model and systems biology provide us further understanding of breast cancer biology involving evolution of cancer, mechanism of metastasis, selection of subclones and emerging of resistant clones associated with treatment. Tumor microenvironments such as tumor-intestinal reactions, inflammatory reactions, tumor angiogenesis, immune responses are also investigated at the molecular levels.

Diagnostic systems for MBC are steadily progressing. In diagnostic imaging, modern computed tomography scan and magnetic resonance imaging can accurately detect and visualize clearly small lesions and tumor extent. In addition, molecular imaging such as HER2-positron-emission tomography (PET) and 17beta-estradiol-PET makes it possible to detect some of the characteristics and function of metastatic lesions. In pathological and molecular diagnosis, multiplex gene panel testing using NGS lead to detect driver and druggable mutations. Precision medicine based on such genetic analysis is already begun. Detection of mutated and methylated DNA in the blood using NGS and digital polymerase chain reaction is also expected as a prognostic/predictive and therapeutic monitoring marker.

Progress in treatment for MBC is also remarkable. Many molecular targeted agents are developed and some of them are applied clinically, resulting in improved patients' outcome. Especially, molecular targeted therapy based on the concept of oncogene addiction such as anti-HER2 therapy drastically improved the prognosis. Clinical application of cyclin dependent kinase 4/6 inhibitors and mTOR inhibitor has dramatically changed the treatment strategy in hormone receptor-positive/HER2-negative MBC. Poly (ADP-ribose) polymerase inhibitor has also a great impact on treatment of HER2-negative MBC.

The chemotherapy regimen is selected in consideration of various conditions such as tumor burden, general health condition, prior treatments and toxicities, and in particular patients' preferences depending on the purpose of treatment.

Immunotherapy such as immune-checkpoint inhibitors is also promising for certain population of breast cancer. Furthermore, bone modifying agents in case of bone metastases and supportive care for systemic therapy greatly contribute to maintain and improve the quality of life (QOL) in patients with MBC. Local treatment for the brain is also important to improve prognosis and QOL even in the presence of multiple brain metastasis, and it is time to develop a new treatment strategy based on biology.

Traditional treatment strategy for MBC would be changed along with emerging new treatments to improve the prognosis by the new modalities of treatment. One challenge is whether to improve prognosis by primary resection in patients with stage IV breast cancer in combination with modern systemic treatment. There might be a small subset of MBC patients who could be cured with current multidisciplinary approach, but we need to identify such a specific population of patients. The candidates are those of oligometastasis or complete response after 1<sup>st</sup> line systemic treatment.

Thus, in the near future, clinical application of precision medicine and courageous challenges in treatment modalities in the breast cancer field will achieve a drastic paradigm shift in the treatment strategy for MBC.

Advances in MBC treatment to date have given patients longer survival time than before. Therefore, MBC patients should be able to enjoy their daily life through improvement/maintenance of QOL and mental status. It is also important that patients, families and care providers communicate sufficiently each other during every stage of cancer trajectory and subsequent death. There are attempts of holistic approach such as introduction of palliative care and advanced care planning from the early-stage to MBC patients.

Treatment and care for MBC requires a multidisciplinary approach as described above. This special issue comprises comprehensive and informative review articles which cover virtually all aspects of recent advances in treatment and care in MBC. We believe that this special issue is very useful and informative to readers of the “*Chinese Clinical Oncology*”. Last but

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