There were an estimated 19.3 million new cancer cases worldwide in 2020, among which 2.26 million were new breast cancer cases. For the first time, breast cancer now tops the list of the most commonly diagnosed cancers, surpassing lung cancer. The disease burden of breast cancer is also high in China. Up to 420,000 new breast cancer cases were diagnosed in China in 2020, accounting for almost 1 in 5 newly diagnosed breast cancer cases globally.

Since 2017, the Chinese Society of Clinical Oncology-Breast Cancer (CSCO-BC) Task Force has developed guidelines that are more relevant and applicable to clinical settings, with an attempt to address the real-world needs of Chinese patients and promote the standardized treatment of breast cancer. The first edition of the CSCO BC guidelines was published in 2017, which gave consideration to the regional diversity of development, accessibility of diagnosis/treatment means, and social value of tumor treatments, and were dedicated to providing the optimal treatment protocols to oncologists in China and other countries and regions. Since then, 4 update editions have been published, and more than 300,000 copies have been distributed. In April 2021, the new edition of the guidelines was released as scheduled. With ensured accuracy and timeliness, this new edition will continue to guide the standardized treatment of breast cancer in China.

Unlike the treatment for patients with early stage breast cancer, the treatment of advanced breast cancer requires a whole course management. Only appropriate treatment protocols and personalized patient management can increase the long-term survival rates.

Trastuzumab is the standard of care for human epidermal growth factor receptor 2 (HER2)–positive breast cancer patients, and trastuzumab-based regimens are preferred in patients who are trastuzumab-naive or are eligible for trastuzumab reuse. In terms of trastuzumab selection, the HOPES study showed that inetetamab in combination with vincristine significantly prolonged progression-free survival (PFS). In addition, clinical studies have shown that some marketed trastuzumab biosimilars have the same clinical efficacies as trastuzumab; according to the principle of indication extrapolation, these biosimilars may be approved for all indications of the originator drug. Therefore, either trastuzumab and its biosimilars or initumumab can be used as anti-HER2 monoclonal antibodies for treating breast cancer.

Now, the question is this: what treatment should a patient choose after trastuzumab treatment? The National Comprehensive Cancer Network (NCCN) recommends ado-trastuzumab emtansine (T-DM1) as a preferred treatment and lapatinib as the second-line therapy. However, since T-DM1 has not been approved for the treatment of advanced breast cancer, the CSCO-BC guidelines have different recommendations on the targeted therapy options after trastuzumab treatment. Two phase III clinical trials initiated by Chinese investigators, the PHENIX study and the PHOEBE study, showed that pyrotinib combined with capecitabine could improve the prognosis of breast cancer patients after previous trastuzumab treatment, and this regimen became another China-initiated standard of care for breast cancer after trastuzumab treatment.

Chemotherapy has been the mainstay of treatment for triple-negative breast cancer (TNBC). In recent years, however, the advances in immunotherapy have made available more treatment options to this breast cancer type. The IMpassion 130 study and the KEYNOTE-355 study demonstrated the value of programmed cell death protein 1/programmed death-ligand 1 (PD-1/PD-L1) inhibitors in TNBC patients. Considering that different studies had different drug combinations, target populations, and predictors, and that immune checkpoint inhibitors are not currently approved to treat breast cancer in China, the CSCO BC panel encourages patients to actively participate in clinical studies. However, caution should be exercised in current clinical settings. In addition, for patients with HER-2–negative advanced breast cancer with *BRCA*1/2 germline mutations, olaparib can significantly prolong PFS compared with chemotherapy. Therefore, the panel generally agrees that patients with *BRCA*1/2 germline mutations can receive treatment with olaparib or actively participate in relevant clinical trials. However, limited by the drug accessibility, this regimen is a class III recommendation in the CSCO BC guidelines.

Endocrine therapy is a key therapeutic option for hormone receptor (HR) positive breast cancer patients. The PALOMA studies confirmed the value of palbociclib combined with endocrine therapy in treating HR positive MBC. The combination of palbociclib with aromatase inhibitor (AI) has also been approved in China as the first-line treatment of hormone receptor–positive advanced breast cancer (HR+ MBC); however, the combination of palbociclib with fulvestrant has not yet been approved in China. The results of the MONARCH plus study, a double-blind cohort study initiated by Chinese investigators, showed that abemaciclib in combination with either nonsteroidal AI (NSAI) or fulvestrant significantly improved the PFS of BC patients. Accordingly, China has approved the use of abemaciclib in combination with AI as the first-line endocrine

therapy in postmenopausal BC patients and also approved the combination of abemaciclib with fulvestrant for patients with disease progression after previous endocrine therapy. The new edition of CSCO BC guidelines reasonably distinguishes the use of different CDK4/6 inhibitors in patients who have received different previous endocrine treatments and suggests that CDK 4/6 inhibitors and their combinations should be carefully selected according to the inclusion criteria and baseline conditions in a clinical trial. In addition, the ACE study, which was also conducted by Chinese scientists, investigated the role of chidamide (the first successful epigenetic modulator in the field of solid tumors) in treating breast cancer. Rooted in scientific evidence, this study increased clinical drug accessibility and helped to bring the treatment of HR-positive advanced breast cancer into an era of endocrine therapy plus targeted therapy.

The past decade has witnessed the transformation of Chinese oncologists in the field of breast cancer from followers of international guidelines to developers of Chinese-version guidelines and to advocates of the "Chinese Practice and International Contribution". Their contributions to breast cancer treatment have been increasingly recognized. It is believed that more effective, less toxic therapies, as well as more tailored treatment protocols, will be available in China for patients with advanced breast cancer, and these options will assuredly bring new benefits for breast cancer patients both in China and abroad.

Zefei Jiang
The Fifth Medical Center of the PLA General Hospital,
Beijing, China