The Oncologist®

Editorial

Immuno-Oncology in China

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China has a high incidence of malignant tumors, with nearly 4 million new cancer cases diagnosed each year. In particular, lung cancer has the highest incidence and mortality among all cancer types in China, followed by liver cancer and gastric cancer. In the face of this increasingly high cancer incidence, existing cancer treatment measures are insufficient for achieving ideal treatment outcomes. This particularly applies to China, as most patients present with advanced or metastatic cancer at diagnosis, limiting the selection of available treatment regimens and clinical benefits. Therefore, new drugs or treatments to increase the survival duration and improve the quality of life of patients with cancer are urgently needed.

Immuno-oncology as a breakthrough cancer treatment technique was heralded as one of the top 10 science and technology developments by *Science* journal in 2013. The rapid growth of this field in recent years has achieved outstanding results and attracted global attention. This new approach to treatment has not only revolutionized the care of patients with many types of tumors, including lung cancer, but also encouraged multiple pharmaceutical companies to embark on and deploy entirely new strategies for oncology research products.

Tumor immunotherapies currently in use internationally can be divided into two main categories. First, the targets of immunotherapy (checkpoints), such as programmed cell death protein 1 (PD-1) and its ligand (PD-L1) and cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4), antibodies of which are used to disrupt and inhibit the binding of receptors and ligands in the signaling pathway, relieve the inhibition of T cells, and establish the ability to kill tumor cells. Second, chimeric antigen receptor (CAR) T-cells produced through genetic modification of human T-cells via bioengineering, endow host cells with the ability to target and kill tumor cells.

In 2011, the CTLA-4 inhibitor, ipilimumab, was approved by the U.S. Food and Drug Administration (FDA) and became the first immune checkpoint inhibitor ever marketed. In 2014, nivolumab became the first PD-1 inhibitor marketed worldwide. Subsequently, many immune checkpoint inhibitors, such as PD-1/PD-L1 antibodies, were approved for treating various cancers. Five PD-1/PD-L1 antibodies have been approved for marketing by the FDA, including two PD-1 monoclonal antibodies, Keytruda (pembrolizumab) and Opdivo (nivolumab), as well as three PD-L1 monoclonal antibodies, Tecentriq (atezolizumab), Bavencio (avelumab), and Imfinzi (durvalumab). In 2017, two CAR-T drugs, Kymriah (tisagenlecleucel) and Yescarta (axicabtagene ciloleucel), were approved by the FDA for hematologic malignancies.

The approval of nivolumab in China in June 2018 for treating non-small cell lung cancer (NSCLC) in adult patients made available the first immune checkpoint inhibitor in China. One month later, pembrolizumab was approved for the treatment of melanoma.

Clinical applications require a considerable amount of exploration during preliminary research, potentially creating new opportunities for China. In recent years, as China's potential in biomedical sciences continues to be highlighted, we are participating in the global research and development of new drugs at an unprecedented rate. China is gradually occupying an indispensable role in global new drug development and clinical trials.

At present, 331 PD-1 monoclonal antibody studies against tumors are registered in the U.S. clinical trial database (ClinicalTrials.gov), of which 52 are being conducted in China; 270 PD-L1 monoclonal antibody studies, of which 20 are being conducted in China; 255 CTLA-4 monoclonal antibody studies, 6 of which are being conducted in China; and 277 CAR-T cell therapy studies, 173 of which are being conducted in China.

Through these studies, Chinese researchers, active on the world stage, have emerged as important contributors. In this special collection, Shukui Qin and Shun Lu et al. review the research progress of immune checkpoint inhibitors in liver and lung cancers and their clinical trials in China. They also describe a series of practical application questions, such as treatment gaps related to regional differences, variations between the best recommendations and actual clinical practices, and ethnic differences between Eastern and Western populations. Li Zhang et al. summarize 26 phase I immunotherapy trials in China focusing on pharmacodynamics and pharmacokinetics, which provide a cornerstone for the selection of clinical drug delivery models and the program planning for future large-scale phase II/III randomized controlled trials. Jinming Yu et al. elaborate on the current status as well as the initial results of combined radiotherapy and immunotherapy and suggest how combined modality clinical trials might be designed and executed. Ying Wang et al. summarize

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relevant data regarding the use of PD-1/PD-L1 immune checkpoint inhibitors in advanced NSCLC populations, and based on this, provide a forecast of future research directions in this domain. It is well known that the discovery and application of biomarkers, an important aspect of immunotherapy, have been interpreted under the concept of tumor targeted treatment. How to better identify, detect, and validate these biomarkers for patient selection remains a very important goal for clinical practice involving tumor immunotherapy.

The articles in this special collection describe the immunotherapy for some cancer types from different perspectives and have been published for the benefit of our readers. It should be noted that, although considerable progress has been made, there are still many unsolved questions in immuno-oncology, such as how to select the right patients for therapy and how to overcome primary/acquired drug resistance in immunotherapy. Are there any differences between various formulations in the same subdivision category? Are there other potential targets that can be identified to augment the effectiveness of current immunotherapies? These questions require continuous exploration.

We are currently witnessing an important moment in human cancer research. The development of tumor immunotherapy will benefit many Chinese patients, and Chinese scientists will continue their tireless exploration of tumor immunotherapy.

Disclosures

Bruce A. Chabner: PharmaMar, EMD Serono, Cyteir (C/A, H), Biomarin, Seattle Genetics, PharmaMar, Loxo, Blueprint, Bluebird, Immunomedics (OI), Eli Lilly & Co., Genentech (ET). Shun Lu indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board