



Current status, challenges and perspectives: immunotherapy and tumour microenvironment in thoracic cancer

Immunotherapies have generated spectacular results in the clinic and changed the treatment scheme for cancer patients with thoracic cancers (1). Recent breakthroughs include checkpoint inhibitors and adoptive cellular therapies.

Immune checkpoint inhibitors, such as anti-PD-1 and anti-CTLA-4 antibodies present a major advance in the treatment of certain thoracic cancers. Since 2015, the US Food and Drug Administration (FDA) has approved a number of anti-PD-1/PD-L1 checkpoint blockade immunotherapies for lung cancers. For example, the anti-PD-1 antibodies Nivolumab and Pembrolizumab, and anti-PD-L1 Atezolizumab and Durvalumab were approved in treating patients with non-small cell lung cancer (NSCLC), and Atezolizumab and Durvalumab recently received FDA approval for treating metastatic small cell lung cancer (SCLC) patients. Anti-CTLA-4 antibody Ipilimumab was approved by FDA in 2011 for the treatment of melanoma and has since undergoing clinical trials for the treatment of different cancers. It was recently reported that Nivolumab plus Ipilimumab was effective and tolerable in treating advanced NSCLC (2). According to this exciting finding, the FDA has granted priority review to the Biologics License Application for this combination therapy for the first-line treatment of patients with metastatic or recurrent NSCLC.

Expansion of tumour-infiltrating T cells or chimeric antigen receptor (CAR) T cells demonstrated great promise in recent years. In early days, tumour infiltrating T cells were isolated and expanded from the tumours and reinfused back to patients for the treatment of melanoma. Although greater than 50% of the patients responded to the treatment (3), this therapy was proved difficult to use in other solid cancers. Subsequently, T cell receptor (TCR) or CAR transduced T cell therapy were developed and tested in the clinic. In particular, CAR T cell therapies have demonstrated their power in certain blood cancers and have received FDA approval for treating these hematologic malignancies. Although both TCR and CAR T cell therapies have only demonstrated moderate effect in solid cancers in the clinic, a number of recent preclinical studies (4-8) and clinical reports (9,10) have shown great promise.

The current challenge for cancer immunotherapies is that although some patients have benefited from the treatments, a number of the patients are resistant. Therefore, there is a strong interest in understanding resistant mechanisms and adopting new therapeutic approaches. One of the major focus in this field is to target the immunosuppressive tumour microenvironment (11,12).

This focused issue aims to provide an in-depth analysis of current literature and future directions for this important clinical topic. The articles collectively comment on the current status of the thoracic cancer treatments, including the treatments to their metastases, the challenges, and some controversial aspects that need to be further investigated in future.

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