Preface

Immunotherapy & thoracic cancers

Thoracic malignancies present a significant global health burden with the incidence and mortality of both lung cancer and malignant pleural mesothelioma (MPM) increasing by year. Lung cancer, including non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), is the leading cause of cancer-related deaths, worldwide. The incidence and mortality rates of MPM, still considered a "rare disease", have not yet peaked but they are increasing yearly. Thymic tumors are the most common tumors in the anterior mediastinum, being part of the thoracic. Survival rates for all these cancers are poor, as the majority of patients are diagnosed with late stage disease.

NSCLC, including adenocarcinoma, squamous cell and large cell carcinoma, represents about 85% of all new lung cancer diagnoses. Patients who are not suitable for surgery and who do not have a specific treatable mutation are currently given platinum-based doublet chemotherapy in the vast majority of the cases. Overall, the 5-year survival of any stage NSCLC patients is <10%. Therefore, there is an urgent need to identify novel therapeutic approaches in all these diseases.

Naturally, the immune system is able to detect and destroy the abnormal cells preventing the development of cancers. On the other hand, cancer cells are sometimes able to avoid detection and destruction by the immune system. In fact, cancer cells may reduce the expression of tumor antigens on their surface, making it harder for the immune system to detect them. They may express proteins on their surface that induce immune cell inactivation and they may induce cells in the microenvironment to release substances suppressing immune responses and promoting tumor cell proliferation and survival.

Immunotherapy is an emerging therapeutic modality that either increase the strength of the human immune system against cancer cells or counteract signals produced by cancer cells that suppress immune responses. This approach is a new frontier for the management of cancers with practice-changing trials already reported for unresectable or metastatic malignant melanoma, advanced NSCLC, and advanced renal-cell carcinoma. Monoclonal antibodies targeting three main targets, cytotoxic T-lymphocyte antigen 4 (CTLA-4), programmed cell death-1 (PD-1) and programmed death-ligand 1 (PD-L1) are already available in the clinical practice.

It is our pleasure to extend to you a very warm welcome to this special issue of the *Journal of Thoracic Disease*, in which experts from around the world discuss the role of, and associated challenges with, the use of immunotherapeutics for the treatment of thoracic malignancies. This special issue contains a compendium of updated, interesting and perceptive peer-reviewed articles, encompassing a variety of immunotherapy and thoracic malignancies topics. The knowledge about the methods, platforms and antibodies employed for the detection of PD-L1 expression and their implications in the current practice is addressed as well as the characteristics of immune system activity and the basis for its modulation in thoracic malignancies, considering the rationale for immunotherapy and the duration of treatment in completely resected thoracic cancers patients. The role of immunotherapy within the multi-modality approach for the management of locally-advanced NSCLC and the to date available clinical results in the treatment of metastatic NSCLC are also discussed. Ultimately, topic chapters touch on the role of immunotherapy in MPM, SCLC, and thymic cancers with the discussion of the available guidelines to assist clinicians in their practice. The early diagnosis and the correct management of immune-related adverse events are also explored. Finally, looking to the future, an updated review looks at the growing body of evidence concerning the potential further targets for immunotherapy and its potential role in the future algorithm of thoracic malignancies strategic approaches.

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