Immunotherapy in other thoracic malignancies and uncommon populations

The advent of immune checkpoint inhibitors (ICIs) has rapidly transformed the treatment paradigm for multiple cancer types, including thoracic malignancies. In advanced non-small cell lung cancer (NSCLC), ICIs have shifted treatment paradigm and improved overall survival (OS). In patients with advanced NSCLC and a programmed death ligand 1 (PD-L1) expression ≥50%, monotherapy with ICI has undoubtedly broken the former glass ceiling of almost no patients alive at 5 years (1), and set up a new bar regarding long-term survival reaching almost one third of patients alive at 5 years. For PD-L1 <50% NSCLC chemotherapy with immune-strategy or combination of ICI have also become a new standard of care worldwide based on improved survival compared with chemotherapy alone. However, it still remains some relevant clinical questions to be answered, as not all patients included in clinical trials reflect daily practice population. Therefore, the role of immune-strategy in elderly population, in patients with poor performance status, autoimmune disorders or brain metastases, as well as in oncogenic addicted tumors are challenging questions. Indeed, new patterns of progressive disease on ICI have been reported and the biological explanation behind these patterns merit further evaluation. Similarly, ICI have also modified the therapeutic strategy in first-line setting in patients with extensive disease small cell lung cancer (SCLC) shifting treatment paradigm in this orphan and recalcitrant disease without any survival improvement in the last 15 years (2,3). Despite this significant improvement, the magnitude of benefit of immune strategy in SCLC remains modest in comparison with the benefit reported in advanced NSCLC. Finally, ICI have stablished a step forward in the therapeutic strategy in the malignant pleural mesothelioma (MPM). The ICIs strategy have reported to improve the OS compared with chemotherapy in first-line setting (4), and significantly improved the OS compared with placebo in patients with MPM previously treated with platinum-based chemotherapy (5). Again, this phenomenon is of huge relevance as MPM was also considered orphan disease without any significant improvement in the therapeutic strategy in the first-line setting during the last 15 years, and no standard treatment in second line. This is even more clinically relevant as asbestos exposure is still a burden worldwide and legislative action is needed to obtain a full ban. Indeed, the peak of incidence of MPM is expected in the coming years in some European countries. and some countries continue to use asbestos, leading that worldwide rates of mesothelioma are still increasing (6). Therefore, therapeutic improvement for this disease may help to improve the outcome of these patients, as MPM is usually diagnosed at advanced stages due to the absence of early symptoms, which reduces the options for radical-curative approaches. Finally, thymic epithelial tumors (TETs) are the last thoracic malignancy where ICI have reported some light of efficacy. However, as up to one third of patients with thymoma may have an autoimmune disorder, and based on the risk of autoimmune disorder flare and sever immune-related adverse events under ICI, these drugs are not considered standard of care. Therefore, the role of immune-strategy in TETs is only being explored in thymic carcinoma and B3-thymoma, the TETs with the lowest incidence of autoimmune disorders.

In this special series of *Translational Lung Cancer Research* about "Immunotherapy in other thoracic malignancies and uncommon populations", a group of renowned international specialists involved in the management of thoracic malignancies present a comprehensive and timely review of state-of-the-art of ICI in thoracic malignancies, discussing the lights and shadows of ICIs, either in under-represented patients with NSCLC in clinical trials, as well as the efficacy of ICIs in thoracic malignancies other than NSCLC. We hope that the readers of *Translational Lung Cancer Research* will find this special series useful for their everyday practice and as an inspiration for research efforts.

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