Liquid biopsy in lung cancer immunotherapy : Between hope and hype in routine practice

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The increasing treatment strategies using immunotherapy in thoracic oncology certainly require urgent needs for the discovery, validation and subsequent adoption of robust, sensitive and specific predictive and prognostic biomarkers for clinical daily practice use. These biomarkers have to be develop both in tissue and liquid biopsies. Until now, anti-PD-L1 immunohistochemistry (IHC) on tissue sections has been the only validated companion diagnostic test for first-line immunotherapy for advanced and metastatic cancer non-small-cell lung cancer (NSCLC). However, detection of this biomarker presents many limitations that have stimulated the development of other biomarkers and other approaches. Within this context, the use of a liquid biopsy (LB) could provide an important complementary or alternative added strong value to PD-L1 IHC. LBs have been used in the field of immuno-oncology (I-O) to predict response, relapse or adverse advents for patients undergoing immune-checkpoint inhibitor (ICI) therapy (anti-PD-1/PD-L1 and CTLA-4) in many clinical trials. However nowadays none of these circulating biomarkers have been approved for routine clinical practice, and therefore there is a gap between many promising results obtained in clinical research field and their application in daily practice. Circulating tumor cells , cell-free DNA, proteins and cytokines detected in plasma as well as circulating T-lymphocytes can be potential sources for developing new I-O biomarkers. The quantification of cfDNA as a predictive biomarker, as well as its sequencing for the determination of tumor mutational burden, are certainly new opportunities for using liquid biopsy in the onco-immunology field. Additionally, the quantification of PD-L1 from CTCs, bound on exosomes or free in plasma, as well as the determination of cytokines, are also being actively investigated with promising results. Lastly, analysis of T-lymphocytes, especially by analyzing the T-cell receptor, has recently emerged as a valuable biomarker that might become relevant for the prediction of response to ICIs. While LBs have not yet been implemented in routine I-O clinical practice rapidly advancing technologies indicate that this approach has the potential to soon personalize the clinical management of lung cancer patients receiving ICIs. In this presentation we will present the main recent results concerning the use of liquid biopsy in the field of immunotherapy in thoracic oncology.