From icing to slicing the cake: the new hope of precision medicine for lung cancer

"Ετσι, δεν γνωρίζω" is the famous Socratic motto which stands for "I know, that I do not know". It was more than a humble outing, actually an open and virtuous learning method by a Greek philosopher of the fifth century. It should still be more than a feeling towards the progress made, particularly during the last decade, in the diagnosis and treatment of lung cancer. Over 30 years, we stepped forward to a genetic or genomic grounded medicine (namely, the precision-medicine) from previous tumour organ- and then morphology-based transitions. In the nineties, a diagnosis of lung cancer was enough to offer each patient a systemic treatment. From the twenties to twenty-tents, we offered different and more active treatments based on histological subtypes. There was an attitude to combine and escalate treatments based on their mechanisms of action in these two eras as the knowledge of tumour determinants was still poor. From the first decades of 2000, the progressive identification of gene alterations driving tumour progression alongside the discovery of effective targeted treatments has offered a new horizon for treating lung cancer based on a new translational approach (1). It entails further progress in lung cancer treatment are dependent on the genomic characterization for the hallmarks of the tumour at baseline and molecular dynamic monitoring for mechanisms of primary and secondary resistance to targeted therapies (2). After about a decade from the dawn of precision medicine, currently, about one every four patients with non-small cell lung cancer (NSCLC) can receive today a targeted agent addressing gene alterations in 8 different pathways of lung cancer progression (*EGFR*, *ALK*, *ROS1*, *BRAF*, *KRASG12C*, *MET*, *NTRK*, *RET*) (3-5). Targeted agents are more active and usually less toxic, and more convenient than chemotherapy. Moreover, some of those gene alterations might be drivers and actionable across different tumour subtypes (i.e., *BRAF*, *NTRK*, *RET*) and led to agnostic approval of anticancer agents based on new trial designs (like "basket" trials) (6). Besides genomic alterations, a high tumor cell expression of programmed cell death-ligand 1 (PD-L1) and/or tumour mutational burden (TMB) can be used to select patients with NSCLC for immunotherapy (7,8). At the same time, we have to face new complex diagnostic and therapeutic challenges. Despite these novel treatments and their transition to earlier disease stages, lung cancer remains incurable for most patients (9). We are still unable to detect or target tumour molecular drivers or deal with primary or acquired resistant mechanisms to targeted agents and immunotherapy (10,11). There is a need to harmonize diagnostic assays and make them widely available for molecular profiling and monitoring (12). These are the topics of this special series on precision medicine in thoracic oncology.

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References

1. Reck M, Heigener DF, Mok T, et al. Management of non-small-cell lung cancer: recent developments. Lancet 2013;382:709-19.
2. Haber DA, Gray NS, Baselga J. The evolving war on cancer. Cell 2011;145:19-24.
3. Addeo A, Banna GL, Friedlaender A. KRAS G12C Mutations in NSCLC: From Target to Resistance. Cancers (Basel) 2021;13:2541.
4. Friedlaender A, Drilon A, Banna GL, et al. The METeoric rise of MET in lung cancer. Cancer 2020;126:4826-37.
5. Frisone D, Friedlaender A, Malapelle U, et al. A BRAF new world. Crit Rev Oncol Hematol 2020;152:103008.
6. Thein KZ, Lemery SJ, Kummar S. Tissue-Agnostic Drug Development: A New Path to Drug Approval. Cancer Discov 2021;11:2139-44.
7. Banna GL, Cortellini A, Cortinovis DL, et al. The lung immuno-oncology prognostic score (LIPS-3): a prognostic classification of patients receiving first-line pembrolizumab for PD-L1 ≥ 50% advanced non-small-cell lung cancer. ESMO Open 2021;6:100078. Erratum in: ESMO Open 2021;6:100137.
8. Addeo A, Friedlaender A, Banna GL, et al. TMB or not TMB as a biomarker: That is the question. Crit Rev Oncol Hematol 2021;163:103374.
9. Addeo A, Banna GL, Friedlaender A. ADAURA: Mature Enough for Publication, Not for Prime Time. Oncologist 2021;26:266-8.
10. Friedlaender A, Banna G, Malapelle U, et al. Next Generation Sequencing and Genetic Alterations in Squamous Cell Lung Carcinoma: Where Are We Today? Front Oncol 2019;9:166.
11. Leonetti A, Sharma S, Minari R, et al. Resistance mechanisms to osimertinib in EGFR-mutated non-small cell lung cancer. Br J Cancer 2019;121:725-37.
12. Torres GF, Bonilla CE, Buitrago G, et al. How clinically useful is comprehensive genomic profiling for patients with non-small cell lung cancer? A systematic review. Crit Rev Oncol Hematol 2021;166:103459.

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