



## Targeted therapy and non-small cell lung cancer: a new era!

Non-small cell lung cancer (NSCLC) represents the principal cause of death for cancer worldwide, with an incidence of 1,350,000 new diagnosis each year and mortality of 1,180,000 deaths each year (1). In the last 10 years, predictive molecular pathology and precision medicine led to a revolution in NSCLC clinical management, encouraging the incorporation of tumor genotyping into therapeutic decision making and the development of new therapeutic options, such as first and second generations of tyrosine kinase inhibitors (TKIs) molecules for oncogene addicted NSCLC patients (e.g., *EGFR*, *ALK*, *ROS1*) (2-4). More recently, the advent of third generation TKIs also allowing the treatment of first or second generations resistance NSCLC patients, but unfortunately, also for these patients, several mechanisms of acquired resistance are now described (5).

In addition to oncogene addicted treatment strategies, the recent understanding of cancer immune evasion biological mechanisms lead to the implementation in clinical practice of new class of immunomodulatory agents able to reactivate host immune-response, leading to remarkably changed of first and second line therapeutic algorithms (6). In particular, for *EGFR*, *ALK*, and *ROS1* wild-type patients, expressing  $\geq 50\%$  of PD-L1 on neoplastic cells, Pembrolizumab represents the best choice in first-line setting. Moreover, different therapeutic combination regimens (anti-PD-1/anti PD-L1 plus chemotherapy and anti-PD-1 plus anti-CTLA4) could become newer options also for non-oncogene addicted NSCLC patients expressing  $\leq 50\%$  of PD-L1 (6,7).

In this very exciting scenario, to find the right way for the right patients, the correct biomarkers assessment for optimal patient selection through the implementation of more sensitive and specific methodologies in association with integration among different biological sources of material (e.g., tissue, blood, exosomes) became the key weapon to minimize the adverse events and to improve the clinical outcome of NSCLC patients (8,9). Considering all together the papers published in the special issue “Targeted therapy and non-small cell lung cancer: a new era?” represent a critical point of view on well established therapeutic options and new perspectives in the very complex field of NSCLC patients management with also an interesting focus on communicational issues in the precision medicine era (10), to support the oncologist to select the best therapeutic approach for advanced NSCLC patients.

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