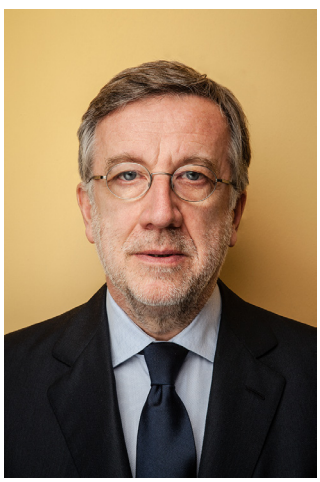
In the era of molecular and personalized therapeutics, the discovery of sensitizing in epidermal growth factor receptor (EGFR) in 15%–20% of lung adenocarcinomas and the associated response to EGFR-targeting tyrosine kinase (TK) inhibitors have provided a successful avenue of attack in high-stage adenocarcinomas. In a period of time of approximately 15 years we had the tremendous clinical opportunity to test and implement in our clinical practice three different generation of EGFR-TKI, learning progressively about respective level of activity and toxicity profiles as well as understand every year better the biological basis of acquired resistance to EGFR-TKI. There is no question that in the appropriate subgroup of patients as defined by molecular screening these agents have shown a clear-cut superiority over cytotoxic chemotherapy and significantly prolonged survival.

While most of the clinical development has been focused on common sensitizing mutations more recently investigators started focusing on uncommon mutations and the contribution of HER2 associated genomic changes in lung cancer to better understand if a consensus may be obtained around those rare clinical conditions. In the specific case the rarity of the molecular alterations leads to the uncertainty of clinical evidence and in this setting dedicated trials have to be implemented.

The straightforward clinical improvements have been paralleled by significant achievements on the diagnostic side. While up to few years ago to monitor molecular changes in the context of the EGFR-mutated tumor the only viable option was the repeated tissue biopsy with all associated hurdles such as size and site of progression or relapse, tumor necrosis, side effects related to the diagnostic procedure among others. Nowadays we are entering in a new diagnostic era where several genomic tests are feasible in different biological fluids, from blood to urine, pleural effusion and cerebral-spinal fluid. While some blood-based tests are already approved for clinical use the vast majority of these tests are still restricted to the context of clinical trials but they will definitively represent a step forward to better understand tumor heterogeneity and will contribute to a real-time monitoring of the disease. In a long-term perspective those tests will be potentially useful in early detection strategies, in monitoring tumor dynamics, evaluation of early treatment response and monitoring of minimal residual disease.

This book represents an outstanding piece of work with the contribution of several key opinion leaders in the field that summarizes the state of the art about the current and future knowledge for the appropriate application of targeted therapies in the context of non-small cell lung cancer.



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