Preface

I would like to welcome readers to this new book of AME Publishing Company. The purpose of this book is to provide you with the most recent and updated insights into the molecular background of lung cancer focusing on epidermal growth factor receptor (EGFR) mutations, targeted therapies with tyrosine kinase inhibitors (TKIs) and the molecular mechanisms underlying inherent or acquired resistance to these targeted therapies.

Lung cancer has been always considered a highly aggressive and difficult to treat disease and the majority of patients are diagnosed when the disease is in advanced stage. Chemotherapy has been for many decades the cornerstone of lung cancer treatment and few therapeutic options were available beyond cytotoxic chemotherapy for those patients with advanced disease. Fortunately, for the first time in many decades, we are witnessing dramatic changes in the way lung cancer is treated and conceptualized.

Two major ‘sightings’ have heralded the paradigm shift in the management of non-small cell lung cancer (NSCLC): the identification of alterations in genetic drivers with potential for target inhibition and the elucidation of the immunogenic properties of lung cancer. The incorporation in the clinical practice of comprehensive mutational analysis technologies has definitely accelerated the identification of several genetic drivers beyond EGFR, such as HER2, MET splice site mutation, BRAF mutations and gene rearrangements at ALK, ROS1, RET or NTRK and research efforts continue to identify other additional driver candidates (1,2). Today, the use of molecular targeted agents, designed to target driver mutations, and those that target immune checkpoints molecules have overcome a new standard for lung cancer treatment. Inconceivable a few years back and for the first time, both targeted therapies and immune checkpoints have displaced chemotherapy from first-line setting in a subset of molecular-selected lung cancer patients (3-6). Consequently, molecular testing is now crucial in the diagnostic algorithm of this disease.

Scientific community is now pooling all their expertise and knowledges towards a common goal: to convert lung cancer into a chronic disease. This is the real challenge of our time. To do so, we will need to overcome new obstacles in the way by identifying new prognostic and predictive markers of response, learning how to choose among different effective treatments (TKIs vs. chemotherapy vs. immunotherapy vs. combinations), developing novel and more potent inhibitors, understanding the mechanisms that lead resistance and learning how to enhance antitumor immune responses. It is through the tireless efforts of scientific community that we will be able to progress day by day providing new hope for lung cancer patients.

This new book highlights the most relevant cutting-edge advances in one of the ‘hot topics’ in the field, EGFR-mutant lung cancer. This book has been divided into several sections. The first section namely—EGFR mutation and lung cancer—offers a state of the art overview related to this molecular aberration, describing not only the most common types of EGFR mutations, indels and point mutations, but other less common genomic events such as duplications and rearrangements involving alternative sites of kinase domains. It also addresses current development of molecular assays for somatic mutation testing not only in tissue but by using novel and less invasive techniques that allow DNA mutation detection and monitoring in blood.

In the second section HER2-driven NSCLC is the focus of the topic discussing the genetic alterations that are felt to mediate its oncogenic functions in NSCLC, epidemiology and a detailed overview of new investigational anti-HER2 therapies that are currently explored in ongoing clinical trials applied to NSCLC.

In the next sections targeted therapies move back into attention addressing areas of huge interest for readers including an up-to-date review of available data from selected pivotal trials with first and second TKIs (focusing on afatinib), as well as an outline of new third generation irreversible and covalent inhibitors with potential to overcome the most frequent cause of acquired resistance related to T790M. This section makes attention to other hot topics in the field such as the controversial role of targeted therapies and immune checkpoint inhibitors with or without radiotherapy in the treatment of brain metastasis.

The last chapter outline the topic of acquired resistance in EGFR-mutated NSCLC patients and potential novel strategies to restore the sensitivity with new generation T790M inhibitors. Last but not least a mention to precision medicine, a clear example of implementation and success in lung cancer management.

I would not like to conclude without expressing our most sincere gratitude to all the authors who have contributed to this book. It is their knowledges and insights that have ensured the quality of the content. We extend our thanks to the editors-in chief, Dr./Prof. Yi-Long Wu and Dr./Prof. Rafael Rosell, who worked tirelessly to put this issue together.

We foresee that the content of this new book will be a valuable, helpful and an educational resource for all readers interested in lung cancer disease.
References


Noemi Reguart, MD, PhD
Consultant Thoracic Oncology, Medical Oncology Department, Hospital Clinic, IDIBAPS, Villarroel 170, 08036, Barcelona, Spain