Emerging role of EGFR and lung cancer treatments

Abstract

Tyrosine kinase inhibitors (TKIs) against targetable mutations such as epidermal growth factor receptor (EGFR) are highly efficient in treating advanced stage lung cancers. The usage of EGFR inhibitors (EGFR) is associated with an improved response rate and improved progression-free survival (PFS) compared to chemotherapy. Frequently expressed EGFR mutants include 19del, T790M, L858R and recently discovered secondary mutation C797S. There is also some possibility to improve outcome by focusing on better EGFR and/or combining EGFR with other therapies like chemotherapy, vascular endothelial growth factor (VEGF) inhibitors and immunotherapy. This review provides an overview of the current status and potential future for EGFR therapies and LUNG CANCER treatments.

Keywords: EGFR mutation, treatments, chemotherapy, lung cancer

Introduction

Cancer incidence rates are growing rapidly globally and according to the estimation from the World Health Organization (WHO), there will be 21.7 million people diagnosed with cancer. At present, cancer is the second leading cause of death around the globe. Most of the increase is expected to be concentrated in developing countries due to heavy smoking, poor diet, physical inactivity and environmental pollutions. In 2012, it was observed that the lung cancer was among the 10 most commonly founded cancers that are frequently diagnosed worldwide (Lung cancer statistics). The third-most commonly diagnosed cancer in both men and women is lung cancer (Cancer statistics, 2017).

Since epidermal growth factor receptor discovered in 1986, the EGFR Gene has emerged as an essential factor for the development and growth of human malignancies, including lung cancer. The EGFR is found to be associated with the direct cell proliferation, growth, differentiation, and apoptosis. As biomarkers, EGFR is a high-ranking member as it regulates a variety of cellular processes, including cell growth, production, and progression. In fact, in multiple tumorigenic processes such as proliferation of cancer cells, angiogenesis, and metastasization, EGFR signal transduction network play a key role. Every time, EGFR aberrant activation is prognostic in NSCLC, which provided a solid foundation for the development of EGFR-targeting strategies for NSCLC. The EGFR TKI, gefitinib, erlotinib, and afatinib, they show improved progression-free survival (PFS) compared with standard chemotherapy. Unfortunately, patients develop resistance, including acquired EGFR mutations such as T790M and C797S. To combat this resistance, second- and third-generation EGFR TKIs have been developed; however, therapeutic resistance still persists. It has been observed that about NSCLC, mutations in EGFR are common. Frequent genetic polymorphisms and inactivation of tumor suppressor genes damage to chromosomes 3p, 5q, 13q, and 17p are predominantly regular in small cell lung carcinoma. 1-7

Lung cancer in India

According to estimates published in The Lancet today around 5,55,000 people died of cancer in 2010, 8 Reliable information on new cancer cases is provided by the population-based cancer registries in India and forms the basis for the national incidence estimates available in the IARC’s GLOBOCAN database. In a recent study, tobacco-related cancers represented around 42% of male and 18% of female cancer deaths. 9 In India, approximately 63,000 new lung cancer cases are reported every year. 10 In Bengaluru and Chennai, lung cancer is the second, and the third leading cancer site, respectively. In women, lung cancer is one of the 10 leading sites in 4 of the 6 cancer registries, i.e., in Bhopal, Chennai, Delhi, and Mumbai. 11 The national cancer registry program under the Indian council of medical research, after studying the lung cancer incidence rate over 24 years (1982-2005), has found that lung cancer is the subsequent leading cause of cancer in women and has increased by a yearly percentage change of 2.7 in Bengaluru, 4.6 in Chennai, and 2 in Delhi. 12

EGFR mutations and lung cancer

The molecular targeted anticancer drugs have paved a way for new treatments in the molecular pathogenesis of the lung cancer. The most established target of lung cancer EGFR. It is a member of the ErbB kinase family. It is structurally related receptor tyrosine kinases. ErbB proteins play a vital role in the regulation of cellular proliferation,
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and their dysregulation has been identified in a variety of cancers.\textsuperscript{17,18} For example, somatic mutations of EGFR have been reported in approximately 50% of Asian patients and 10-15% of Caucasian patients with lung adenocarcinoma,\textsuperscript{19,20} with the most common mutations in these populations being exon 19 deletions (Del19), and an L858R point mutation (L858R). The most prevalent secondary or acquired mutations in the EGFR gene are T790M and C797S, the presence of which correlates with resistance to first, second and third line of tyrosine kinase inhibitors. This Mini review describes the clinically significant EGFR gene mutations, and the efficacy of small molecule EGFR TKIs as targeted therapies for these gene mutations. Therapeutic strategies to overcome resistance, including selected emerging and novel therapies are discussed.\textsuperscript{21}

Conclusion

Advanced NSCLC testing for mutations in EGFR paved the way in the treatment-decision making pathway. In Indian, NSCLC patients, EGFR TKIs either added to or given after standard chemotherapy may also improve results, but additional evidence is necessary.\textsuperscript{22,23} as a maintenance therapy after first-line, erlotinib has also shown a role in non-progressive patients alone after platinum-based chemotherapy or in combination with bevacizumab after a bevacizumab and cisplatin regimen.\textsuperscript{24,25} In addition, wide research on individual patient’s tumor biology may be necessary for appropriate targeted therapy. This individual patient approach would finally result in improved PFS and overall survival for the diverse category of lung cancer patients. EGFR-TKIs comprised a major part of the treatment strategy, especially for patients with poor PFS lung cancer in the real world. Further to this, the real challenge is therapeutic agents into the management of patients with earlier stage disease diagnosis with the hope of truly improving rates of cure for the devastating illness that is lung cancer.

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Conflict of interest

The author declares no conflict of interest.

References

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