The Therapy of Osimertinib for EGFR Mutation—Non-small Cell Lung Cancer

Weiyi Lin 1,†, Zhuoyi Lin 2,† and Mengxue Zhang 3,*,†

1 School of bioscience, Northeast Agriculture University, Dongbei, China
2 School of chemistry and chemical engineering, Henan Normal University, Henan, China
3 School of chemistry, Chuangnam University, Deajeon, Korea

* Corresponding author: ZHANGMENGXE@cnu.ac.kr
†These authors contributed equally

Abstract. Lung cancer is still a disease cause of human beings mortality. Lung cancer is divided into numerous kinds, with non-small cell lung cancer (NSCLC) accounting for up to 85% of cases. KRAS, ALK, HER2, and PD-1 are currently identified targets for NSCLC therapy. And the therapy of lung cancer, molecular-targeted medicines have recently demonstrated encouraging outcomes and NSCLC was treated with a variety of molecular targeted drugs. In NSCLC, EGFR mutations are also quite prevalent. The human epidermal growth factor receptor (EGFR) belongs to the HER receptor family. When epidermal growth factor (EGF), transforming growth factor (TGF) and other ligands combine with EGFR, the downstream signaling pathway is activated, thereby regulating cell growth, proliferation, migration, anti-apoptosis. EGFR-TKI-targeted medicines are currently the most common treatment for NSCLC with an EGFR mutation. EGFR-TKI medicines of the first and second generations, such as erlotinib, gefitinib, and afatinib are used to treat EGFR NSCLC as first-line drugs. However, due to the emergence of medication resistance, a novel EGFR mutation-T790M has emerged. As a result, the EGFR-TKI medication has been upgraded to the third generation. The most representative of the three generations of medicines is osimertinib. It inhibits EGFR growth by targeting both EGFR and T790M mutant sites. Osimertinib also lessens some drug toxicity when compared to earlier first- and second-generation medicines. In this review paper, we will provide background information about EGFR NSCLC and the three generations of medications used to treat it.

Keywords: EGFR, lung cancer, non-small cell lung cancer, molecular targeted drugs, inhibitor, Osimertinib.

1. Introduction

According to the data on the official website of IARC, about 10 million people died of cancer in 2020. [1] Obviously, the medical burden caused by cancer is huge all over the world. We are not only facing the major problem that the development of drugs cannot keep up with the deterioration of the disease, but also facing the major problem that some cancers cannot be cured with drugs. DNA damage and epigenetic changes are the primary causes of cancer. Normal cell activities such as DNA repair, programmed cell death, and cell growth are all affected by these changes. The risk of cancer rises as more harm is done. [2] Because the genes of tumor cells are constantly changing, it is easy to produce drug resistance, so we cannot be satisfied with the existing treatment, we should continue to deepen the research on cancer. Over the three decades, lung cancer has rapidly developed into one of the highest mortalities and most common cancers in the world due to many factors such as smoking, air pollution and lamplight. [3] In 2020, roughly 1.8 million individuals will die from lung cancer, according to the study. [1] Therefore, we can see that it is an important topic to find more methods to treat lung cancer, which will help to improve the survival rate of lung cancer patients. Lung cancer may be parted into two categories based on histological characteristics: NSCLC and SCLC. It's worth noting that NSCLC take possession of approximately 85% of any and all cases of it. As a result, medical workers have never stopped exploring NSCLC.
People have always attached great importance to the treatment of NSCLC, because a reasonable and effective therapy may not only alleviate patients' agony, but also extend their lives. Radiation, chemotherapy, molecular targeted therapy, surgical surgery, and immunotherapy are now standard clinical treatment modalities for NSCLC.[4] Although there are so many treatment methods, there are still some disputes on how to choose treatment methods to develop the best curative effect because the principle of NSCLC is very complex.[5] In recent years, with the progress of research on signal pathway, human genomics and drugs that block the activity of pathway, people gradually find that targeted therapy has advantages over traditional treatment in safety.[6] When doctors create tailored treatment regimens for patients, they frequently employ molecular targeted therapy as a treatment option.[7] The ALK mutation, EGFR mutation and other mutations induced by the NSCLC driver gene are the most often. In 10% to 30% of patients, the EGFR mutation is present. We selected to research EGFR because it is not just widely used, but also because it is one of the most well-studied receptors.

The first treatment option for NSCLC is EGFR-TKI, which is a targeted medication. [5] Erlotinib and Gefinib, both first-generation medicines, have showed promising clinical results. [8, 9] After around 10 months of medication, however, most patients acquire drug resistance. [10] As a result of studying the DNA sequence of drug-resistant patients, a new mutation site T790M was discovered in the DNA sequence. [10, 11] Hence, the researchers modified the EGFR-TKI medication. Afatinib, second-generation medicines, demonstrated effective suppression of the EGFR signaling pathway but inadequate targeting of the T790M mutant site. [12, 13] However, Osimertinib, the third generation of EGFR-TKI, not only inhibits the T790M mutation site but also has a considerable effect in blocking the EGFR signaling pathway. [11, 12] It has a good clinical effect in the treatment of EGFR NSCLC at the moment. [10] We'll go over some EGFR signaling pathways, EGFR NSCLC, and the treatment of Osimertinib in this article.

2. The reason for treating NSCLC with EGFR as one of the objectives

As human genome research and precision oncology have evolved, the prognosis of NSCLC had already changed considerably. Patients experience a lot of treatment-related side responses when they rely on chemotherapy to treat cancers since chemotherapy destroys both tumor cells and normal cells when it works. We must confess that Chemotherapy is no longer a major therapeutic option for NSCLC patients, since sequencing the human genome has opened up a new notion of tailored therapy.[14] We no longer rely solely on traditional treatment schemes for treatment, but innovatively combine many treatment methods and use combination therapy to hinder the deterioration of tumor cells. Human beings have increasingly established the presence of gene mutation types directly associated to NSCLC, thanks to the rapid growth of cancer genome screening. EGFR mutations, ALK mutations and so on are the most prevalent forms of gene mutations. We can achieve continuous progress in cancer emerging therapeutics by concentrating on the pathogenic genes associated with NSCLC. [15]

2.1. EGFR and mutation sites of EGFR leading to cancer

The EGFR / HER1 is a tyrosine kinase receptor discovered on human chromosome 7.[15] An exterior binding affinity region, a cytoplasmic region, and an internalized protein tyrosine area make up the structure of the EGFR protein. As show in Fig. 1. It binds to ligands and activates the tyrosine kinase region in cells, which then pass the signal to the downstream path such as the STATs system, the PI3K/ AKT pathway and so on, influencing cell proliferation, differentiation, angiogenesis, and apoptosis inhibition. Malignant tumors, particularly NSCLC, use these signaling pathways to grow, metastasize, and invade. In NSCLC patients, exons 18-21 are the most common locations of EGFR mutations. The most frequent site changes are exon 19 deletion as well as exon 21, which take possession of 80–90 percent of any and all site changes. Exon 19 mutant NSCLC sufferers responded to EGFR TKIs at a substantially higher rate than exon 21 mutant NSCLC patients. [16]
2.2. Relationship between EGFR and NSCLC

According to the study process of lung cancer, the EGFR genetic condition is among the most important findings in lung cancer clinical research in the twenty-first century. As show in Table 1, because EGFR has a role in the suppression of tumor cell death, we can deduce that abnormal EGFR expression influences tumor cell number, tumor blood vascular transfer, and tumor cell mortality.

Table 1. In diverse groups of NSCLC sufferers, the average prevalence of EGFR mutations was found.\[17\]

<table>
<thead>
<tr>
<th>Group classification</th>
<th>Average prevalence</th>
<th>Tests of heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>All NSCLC patients</td>
<td>32.3%</td>
<td>(&lt;0.001)</td>
</tr>
<tr>
<td>NSCLC patients in Asia</td>
<td>38.4%</td>
<td>(&lt;0.001)</td>
</tr>
<tr>
<td>NSCLC patients in America</td>
<td>24.4%</td>
<td>(&lt;0.001)</td>
</tr>
<tr>
<td>NSCLC patients in Europe</td>
<td>14.1%</td>
<td>(&lt;0.001)</td>
</tr>
</tbody>
</table>

From these research data, we can conclude that the abnormality of EGFR signal transduction accounts for a large proportion in the cause of NSCLC. Because EGFR mutation belongs to tumor specific mutation, this mutation mainly exists in tumor cells, and this phenomenon hardly exists in normal cells.

Due to the high mutation frequency of EGFR in NSCLC and NSCLC depends on EGFR mutation to maintain the characteristics of malignant tumors, we have reason to prove that EGFR is the best characterized gene in NSCLC. \[18\] EGFR has been extensively acknowledged as a molecular target to treat NSCLC patients at various stages as one of the most thoroughly explored targets in lung cancer treatment. This conclusion is also supported by the patient's favorable clinical outcomes with targeted medications. We should search for genetic abnormalities once individuals have been diagnosed with NSCLC. We may acquire distinct prognostic features based on different EGFR mutation types, and we can integrate the genetic evaluation of EGFR mutation status into the treatment plan for each NSCLC patient. \[16\] Furthermore, using EGFR as the primary target for lung cancer therapy, we must investigate gene mutation locations that may increase patient overall survival rates. \[19\]
3. Targeted therapy for EGFR NSCLC

3.1. Current NSCLC treatment

NSCLC is a diverse type of cancer with numerous treatment options. Surgical procedures, radiation, chemotherapy, and molecular targeted therapy are all options. Systemic therapy is critical for patients with metastatic NSCLC.[9] Therefore, chemotherapy and molecular targeted therapy are the treatments of choice.[20] Some cancer cells, on the other hand, contain unique biomarkers, such as EGFR, HER2, and PD-1. Hence, molecular targeted treatments, such as EGFR, can be chosen.[9] In clinical practice, chemotherapeutic medications have a good effect on cancer cell development and diffusion throughout the body, but their mechanism is cytotoxicity, which has a lot of negative side effects on the human body. [6] The mechanism of molecular targeted drugs, on the other hand, is to address specific targets, which increases the accuracy of anticancer drug therapy by not only limiting cancer cell proliferation but also minimizing drug toxicity and side effects. [13, 14] Thus in the treatment of NSCLC, molecular targeted treatments have shown great clinical results. [18] Exon 19 deletions (EGFRdel19) and exon 21 L858R mutations (EGFRL858R) are common activating EGFR mutations in tumors that respond well to EGFR-TKI therapy. [14, 15] And EGFR-TKI therapy drugs have updated to third-generation. As shown in fig.2.this demonstrates that such medications are always fixing the flaws.

![Figure 2. The therapy for NSCLC.](image-url)

3.2. Approved drugs for EGFR NSCLC

Surgery has been superseded as the first-line treatment for cancer by chemotherapy and molecular targeted therapy.[9] Molecular targeted medications have made considerable advances in cancer therapy in recent years. When compared to cell toxicity medications, the selectivity of molecular therapies has helped patients feel less pain. [20]. As shown in table 2, as one of the most popular anti-cancer treatments, the FDA has approved a number of molecular targeted drugs that have shown clinical efficacy in the treatment of a variety of cancers, including breast, lung, and stomach cancer, among others. [20, 21]
Table 2. Clinical application molecular targeted drugs for EGFR NSCLC.

<table>
<thead>
<tr>
<th>Name</th>
<th>Targeted point</th>
<th>Patient’s stage</th>
<th>Phase</th>
<th>Line of treatment</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetuximab</td>
<td>EGFR</td>
<td>Advanced NSCLC, EGFR positive</td>
<td>III</td>
<td>First</td>
<td>FDA</td>
</tr>
<tr>
<td>Nimotuzumab</td>
<td>EGFR</td>
<td>NSCLC</td>
<td>II</td>
<td>First</td>
<td>FDA</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>EGFR-TKI</td>
<td>Advanced NSCLS, EGFR positive</td>
<td>III</td>
<td>First</td>
<td>FDA</td>
</tr>
<tr>
<td>Osimertinib</td>
<td>EGFR-TKI</td>
<td>Advanced NSCLC, EGFR positive</td>
<td>III</td>
<td>First</td>
<td>FDA</td>
</tr>
<tr>
<td>Afatinnib</td>
<td>EGFR-TKI</td>
<td>NSCLC</td>
<td>III</td>
<td>First</td>
<td>FDA</td>
</tr>
</tbody>
</table>

4. Novel drug therapy--Osimertinib

Surgical resection, radiation, chemotherapy, immunotherapy, and targeted therapy are now used to treat EGFR NSCLC [20, 21]. However, for many patients with advanced NSCLC, surgical excision is not an option. Chemotherapy and targeted therapy have thus become the primary therapeutic options for advanced EGFR-mutated NSCLC, with postoperative recurrence also a possibility. Hence, improving the survival rate of advanced and recurrent NSCLC patients with EGFR mutations is critical. As a result, researchers created EGFR-TKI for the treatment of EGFR-mutated NSCLC patients, which had a good therapeutic impact and became the EGFR-mutated NSCLC patients first-line therapy option.[22] The epidermal growth factor receptor (EGFR) has been found to have mutations, EGFR-TKI can enter cells and operate directly on the intracellular region of EGFR to prevent phosphorylation of Tyrosine kinase and its substrate, effectively stopping aberrant Tyrosine kinase signaling.[22] Molecular-targeted medications give more precise treatment than classical cytotoxicity.[6, 10] Hence, EGFR-TKI is playing a bigger role in the development of EGFR NSCLC anticancer medicines. The first- and second-generation EGFR TKIs, such as erlotinib, gefitinib, and icotinib, have repeatedly demonstrated improved therapy efficacy and reduced toxicity as compared to some first-line anti-cancer drugs, such as cisplatin drugs, and are now the judgment criteria of care for EGFR-mutated advanced NSCLC patients. [5, 8] Due to the emergence of drug resistance, EGFR mutations, bypass signaling pathways, and histologic have changed resulted. [11] Third-generation EGFR-TKIs, Osimertinib approved were developed in response to changed tumor resistance patterns after treatment and hazardous side effects that have a negative influence on patient quality of life. [11] Third-generation inhibitors, on the other hand, target the T790M mutation specifically, which increases Tyrosine kinase downstream signaling of EGFR to promote cancer cells growth and liberation, and leads to treatment is difficult. [21, 22] Hence, throughout therapy, Osimertinib has been demonstrated to spare basic EGFR and T790M, minimizing non-specific binding and lowering toxicity.[10]

4.1. Mechanism of Osimertinib

Osimertinib is an oral use mono-anilino-pyrimidine compound which is a kinase inhibitor class of drugs and was designed to penetrate the blood brain barrier (BBB).[22] It promotes lung cancer cell growth by blocking aberrant proteins from passing information on to EGFR farther downstream. This may help decrease tumors by halting or slowing the spread of cancer cells. Cancer cells establish a signaling pathway when they have mutations in the EGFR gene, and it is critical to block this signaling pathway with medications to stop cancer cells from growing. [11, 22] Osimertinib is an EGFR-TKI that binds to specific EGFR mutations and preoccupies the majority of NSCLC tumors after first-line EGFR-TKI treatment. [22, 23] As a third-generation tyrosine kinase inhibitor, Osimertinib targets the T790M mutation of the portal vein guard protein, which increases ATP binding activity to EGFR. This mutation inhibits the medication from binding to this location, providing resistance. Because some cancer cells that have spread to the brain can benefit from this
feature. Osimertinib, an irreversible third-generation EGFR-TKI, is an authorized therapeutic choice (The recommended daily dose is 80mg.) for patients with EGFRm advanced NSCLC and T790M(side-mutation point) NSCLC who have progressed on EGFR-TKIs.[22,23] Despite the fact that Osimertinib is a substrate for the efflux transporters for permeability glycoprotein and cancer resistance protein, in vitro evidence has demonstrated that, unlike other EGFR-TKIs, its permeability is sufficient to overcome this efflux. [22] Osimertinib is an oral medicine that is processed in the body by digestive organs like the liver--first pass metabolism. Two primary metabolites, AZ5104 and AZ7550, are generated after metabolism. Because the goal of the third generation of medications is to increase the therapeutic efficacy of EGFR NSCLC by addressing the T790M mutation induced by treatment resistance. The basic EGFR signal route is well inhibited by AZ7550, while the new mutation site T790M is well inhibited by AZ5104.[22] Hence, the novel medication can inhibit both EGFR-TKI-sensitizing mutations as well as the T790M resistant mutation. As shown in fig.3, Osimertinib demonstrated low off-target kinase activity when tested against a variety of different kinases. [22, 23]

![Figure 3. The Mechanism of Osimertinib.](image)

A complete and long-lasting response to daily oral long-term dosages of oximitinib was observed in these EGFR-mutated xenograft tumors, with no evidence of tumor development after 200 days of treatment, and the animals were well tolerated, losing just 5% of their initial body weight. [22, 23] Finally, osimertinib caused a considerable reduction in tumor size in transgenic mice with EGFR L858R or L858R+T790M mutations, confirming its anticancer efficacy. The pharmacodynamics of oximitinib inhibition of its target and downstream pathways were validated using these models.[23]

### 4.2. Clinical therapy

Clinical trials are essential for determining whether Osimertinib is effective and safety in treating patients with NSCLC EGFR-mutated with EGFR T790M mutation. A clinical trial of Osimertinib, AURA, began after FDA approval. Two experimental results were primarily employed in clinical trials to establish if the medicine had a therapeutic effect: progression-free survival and overall survival. A total of 682 were treated by Osimertinib in Phase I-III. The higher dose of Osimertinib (intravenous 20-240mg single dose or once a week) did not result in greater toxicity, and its
pharmacokinetics was dose-dependent, according to phase I trials. A total of 87 patients were treated for 11 months in the phase II trial (80mg/ day). Due to anti-cancer treatment Because anticancer medication therapy involves the use of more than one drug, Osimetinib will be used in combination with chemotherapy drugs in the III trial to see if the therapeutic impact can be improved and the drug toxicity is within acceptable limits. A total of 253 patients were tested with Osimertinib combination with chemotherapy in Phase III. Phase I-III therapy has had a clinical effect. The result as figure 4.[23]

<table>
<thead>
<tr>
<th>Phase</th>
<th>No.of patients</th>
<th>Progression-free survival (months)</th>
<th>Response rate (%)</th>
<th>Overall survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I/II</td>
<td>253:</td>
<td>- 31 (dose-escalation cohorts) - 222 (dose-expansion cohorts)</td>
<td>- T790M + : 9.6 (95% CI 8.3–NR) - T790M - : 2.8 (95% CI 2.1–4.3)</td>
<td>- T790M + : 61 (95% CI 52–70) - T790M - : 21 (95% CI 12–34)</td>
</tr>
<tr>
<td>II</td>
<td>210</td>
<td>9.9 (95% CI 8.5–12.3)</td>
<td>70 (95% CI 64–77)</td>
<td>--</td>
</tr>
<tr>
<td>II</td>
<td>411 (T790M +)</td>
<td>12.3 (95% CI 9.5–13.8)</td>
<td>62 (95% CI 54–68)</td>
<td>--</td>
</tr>
<tr>
<td>III</td>
<td>416:</td>
<td>- experimental arm (279) - chemotherapy arm (140)</td>
<td>10.1 (95% CI 8.3–12.3) 4.4 (95% CI 4.2–5.6)</td>
<td>71 (95% CI 65–76) 31 (95% CI 24–40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HR 0.30; (95% CI 0.23–0.41)</td>
<td>Odds ratio 5.39;</td>
<td>95% CI 3.47–8.48; p&lt;0.001</td>
</tr>
</tbody>
</table>

Note: HR- hazard ratio; NR- not reached

Figure 4. Osimertinib clinical trials data.[23]

Based on these data, multiple molecular pathways of osimertinib resistance have been discovered, indicating tumor heterogeneity and adaptability. From the clinical trial results data graph, osimertinib has a good therapeutic impact, according to the data and results from the clinical trial, efficiently overcoming the resistant mutant gene and improving patient treatment. Hence, accomplishment the purpose of design a third-generation medicine that can be presented to the FDA for approval and can help more lung cancer patients survival rate. Oxitinib's indication was expanded to first-optional therapy for patients with EGFR-mutated NSCLC in April 2018. It introduces a new therapy option for patients.

5. Drug toxicity and adverse reactions

5.1. Toxicity

So far, the toxicity of EGFR-Tkis has been found to be mainly interstitial lung disease, pneumonitis, cardiomyopathy, keratitis and embryo-fetal toxicity.

5.2. Adverse reactions

With the increase in clinical use of osimertinib, its adverse reactions (ADR)have gradually emerged. Compared with chemotherapy, EGFR-TKI drugs have particular adverse reactions, such as
rash, diarrhea, thyroiditis, oral mucositis, liver injury, interstitial lung disease. Among them, the most common ADR were diarrhea, rash, and loss of appetite, ADR involved organs or systems, mainly respiratory system and digestive system, in addition to cardiovascular system, blood system, skin and eyes.

As shown in table 3, the incidence of oral mucositis caused by Osimertinib is about 15%–29%. The incidence of grade 3 and above is less than 1% [24, 25]. The incidence of diarrhoea in phase III clinical trials about Osimertinib is about 41%, and the incidence of grade 3 and above is about 1% [24], meanwhile, the incidence of diarrhoea about the second-generation EGFR TKIs afatinib is about 88.3%–95.2% [26, 27], the incidence rate is much lower. The incidence of acne-like rash caused by Osimertinib is about 34%, the incidence of grade 3 and above is less than 1% [24], meanwhile, the incidence of acne-like rash caused by afatinib is about 80.8%–89.1% [26, 27] (table4).

<table>
<thead>
<tr>
<th>EGFR-TKI</th>
<th>Area</th>
<th>Incidence of diarrhoea(%)</th>
<th>Incidence of rash/acne-like rash(%)</th>
<th>Incidence of stomatitis/mucositis(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afatinib</td>
<td>The global</td>
<td>95.2[26]</td>
<td>89.1**[26]</td>
<td>72.1[26]</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>The European</td>
<td>57[28]</td>
<td>67**[28]</td>
<td>No relevant data are mentioned</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>East Asia</td>
<td>46.6[29]</td>
<td>66.2**[29]</td>
<td>17[29]</td>
</tr>
</tbody>
</table>

In 2019, FORTE M J et al reported a case of diffuse alveolar hemorrhage after four months of taking Osimertinib, and then improved after mechanical ventilation and hormone therapy [30]. In addition, there are also reports of Osimertinib combined with other drugs leading to cardiac toxicity and death due to ineffective treatment [31].

6. Drug resistance

Unfortunately, although Osimertinib is effective for patients, tumors will inevitably come to be acquiring resistance to EGFR TKI and reduce its long-term efficacy, including Osimertinib. Drug resistance has become a bottleneck restricting its further improvement. At present, the mechanisms of EGFR-TKI acquired drug tolerance mainly include T790M mutation, C797S mutation, and MET amplification.

7. Development in the future

Third generation EGFR-TKI drugs are highly selective and effective against EGFR-TKI acquired T790M resistance, which is not possible with first-generation and second-generation drugs.

But Osimertinib, a third-generation EGFR-TKI drug, will eventually become resistant. Some studies have pointed out that Osimertinib resistance is related to mutation of C797S gene, but other studies believe that the mechanism of drug tolerance of the third-generation drug is more complex, possibly involving 9 genes. All this means that drug tolerance to the third-generation EGFR-TKI drug is harder to overcome.

Pharmaceutical companies at home and abroad have also been researching new drugs with better treatment effects, lower drug resistance and stronger safety. In 2020, Cancer Research reported the IACS-13909 inhibitor, which is a specific and effective Scr homologous 2-domain phosphatase allostERIC inhibitor, in NSCLC treated with Osimertinib with EGFR-independent and independent drug resistance mechanisms, Osimertinib alone or in combination can induce tumor regression in vivo and inhibit tumor multiplication in vitro.[32] In the same year, Nature reported a new generation of targeted drug EAL045 that may overcome Osimertinib resistance, which can be used in the sick with
first-generation drug resistance and T790M mutation, or in patients with oxitinib resistance and C797S mutation.[33]

EGFR-TKI provides a therapeutic option for the sick with EGFR-mutation-positive NSCLC, but with the emergence of first generation, second generation, and third-generation drug resistance, the therapeutic option is more demanding. Studies on combination therapy and four generations of drugs have provided ideas for overcoming resistance, but the feasibility is still questionable, and EGFR-TKI treatment still has a long way to go.

8. Conclusions

EGFR mutations account for about 10% - 30% of NSCLC patients. As epidermal growth factor receptor is expressed or overexpressed on the outside of many tumor cells in NSCLC, for the study of molecular targeted drugs of EGFR, the therapeutic effect of drugs is closely related to the sensitivity and drug resistance of EGFR TKIs. EGFR TKIs is momentous for the therapy of targeting oncogene addiction and tumor specific adaptive drug resistance. This has turned the treatment of NSCLC from routine chemotherapy to targeted treatment for sick with specific EGFR mutation, which has become a reality.

With the accumulation of toxicity and the emergence of drug resistance caused by the long-term use of previous EGFR TKIs, in order to prolong the progression free survival of the sick in the first-line treatment of lung cancer, the third-generation drugs have been successfully listed through the unremitting efforts of drug researchers. Osimertinib not only has relatively mild side effects, but also has better clinical efficacy and tolerance. Osimertinib showed good CNS penetration in both first-line and second-line patients.

There is no doubt that Osimertinib is the preferred drug for the therapy of NSCLC in the advanced stage of EGFR mutation. However, as a drug, Osimertinib will inevitably face two challenges: how to reduce side effects and how to solve the problem of drug resistance. Therefore, clinical treatment still needs to choose drugs according to factors such as efficacy, toxicity and economic conditions of patients.

References


