

case report

Erlotinib in previously treated non-small-cell lung cancer

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Background. Erlotinib is a novel biological anti-tumour agent in the treatment of advanced non small cell lung cancer. It represents the molecularly-targeted therapy which has been studied extensively.

Case report. We present a case of a patient who suffered from advanced non-small-cell lung cancer. After the progress of disease following a prior chemotherapy he was treated with erlotinib with remarkable effect which was shown at chest x ray and symptoms were quite reduced.

Conclusions. In selected patients with advanced non-small-cell lung cancer Erlotinib improves survival and symptom control as it results in presented case.

Key words: carcinoma, non-small-cell lung; antineoplastic agents

Introduction

In Europe lung cancer ranks first among all cancers and cancer related deaths in men and fourth in women. Similarly in Slovenia lung cancer ranks first in men with 787 new cases in year 2002 and fifth in women with 258 cases.¹ Between 80 - 85% of cases are non small cell lung cancers. A majority of patients is presented in advanced or locally advanced stages, and therefore these patients are not candidates for potentially curative resection. In patients with advanced disease our current treatment of choice is platinum based

chemotherapy with the newer agents, mostly with gemcitabine in the initial setting.^{2,3} For patients who progress after achieving response to the primary treatment therapeutic option is the treatment with taxanes (e.g.docetaxel),⁴ pemetrexed⁵ or a novel antitumour agent in a clinical trial.⁶⁻⁸

Over the past few years, a number of new agents have become available for the treatment of metastatic non-small-cell lung cancer, including the inhibitors of receptors of tyrosine kinase.^{9,10} Such a novel biological antitumor agent is erlotinib (Tarceva).^{11,12} Erlotinib is a small molecule inhibitor of HER1/EGFR tyrosine kinase; chemically it belongs to the quinazoline class and is orally available.¹³ It binds to an intracellular part of epidermal growth factor receptor and decreases tumour proliferation, invasion, metastases formation angiogenesis and tumour cell adhesion, while it increases apoptosis and probably also the sensitivity to

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Figure 1. Lung tumour after chemotherapy; visible nonhomogenous lung infiltrates

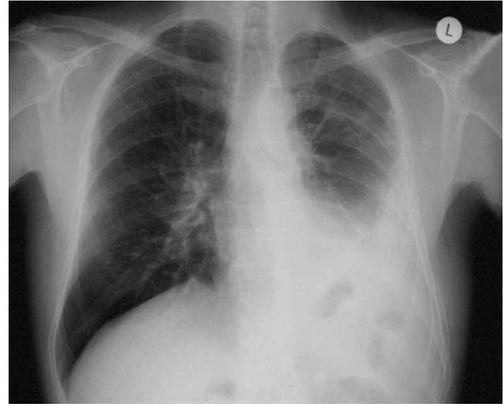


Figure 2. Lung tumour two months after therapy with erlotinib; lung infiltrates in regression

chemotherapy. Among patients with non-small-cell lung cancer who receive erlotinib, the presence of an EGFR mutation may increase responsiveness to the agent, but it is not indicative of a survival benefit.^{14,15}

In 2005 we enrolled in the study treatment with erlotinib through Tarceva EAP (extended access protocol). In this report we would like to present a case of our first patient treated with erlotinib.

Case report

Fifty-eight-year old male patient was presented for the first time in year 2003. He suffered from fatigue and dyspnoea on exercise. These symptoms lasted for two years.

The patient was a former smoker who smoked for 30 years up to 20 cigarettes a day; seven years ago he stopped smoking.

On chest X ray there was a left sided pleural effusion and indurated right hilus.

Bronchoscopy revealed stenosis of the middle lobe bronchus and bronchus for the 6th left lobe, where mucosa was also granulated and bled at touch.

Histologically invasive adenocarcinoma was confirmed in specimen taken at bronchoscopy. Cytology of pleural effusion was twice negative at malignant cells.

At the clinical examination we found a lymph node at the right supraclavicular region.

The initial stage at diagnosis was T4N3Mx; re-evaluation of native chest X rays showed metastatic lesions in both lungs, therefore the stage was T4N3M1.

The patient was in good condition, Karnofsky performance status at the time of diagnosis was assessed at 80%.

The patient received chemotherapy with cisplatin and gemcitabine in the prolonged infuse for 6 cycles, the maximal response was stagnation. The leading symptom was dyspnoea.

Ten months after the completion of treatment chest X ray showed a progressing in lung, while the performance status deteriorated gradually.

In February 2005 the patient started the treatment with erlotinib. At the beginning of the treatment chest x ray showed the left sided pleural effusion, with patchy infiltrates centrally in both lungs, while in the periphery there were multiple small nodular lesions (Figure 1).

After a month of the treatment with erlotinib the patient's general condition improved and his breathing improved too. Of the adverse effects he presented with GII rash.

The improvement was seen also in chest X ray, with diminishing and rarefication of nodes shown in the periphery and also with the improvement of centrally located infiltrate.

After two months of the treatment there was a further regression of all lesions seen on X ray (Figure 2).

The patient resumed with his work as a public employee.

Until January 2006 the patient was in a partial remission. He was employed; his only complaint was rash, which persisted.

Upon progression the patient had more infiltrates on X ray, his performance status was still excellent (Karnofsky 90).

The patient continued treatment with chemotherapy with paclitaxel and carboplatinum.

Discussion

In advanced non small cell lung cancer the aim of the treatment is to improve the survival and the quality of life (ref. meta-analysis).³

The survival in advanced non small cell lung cancer is still not as good as in some other types of advanced cancer (e. g. breast).^{16,17} The treatment with platinum based doublets had achieved some degree of the disease control but the survival remains in range of 9 months to 1 year.^{16,18} This has been improved slightly by the introduction of the second line chemotherapy with docetaxel or pemetrexed, which have a moderate efficacy and is reasonably well tolerated.^{4,5,8}

However, the mode of action of erlotinib differs from that of less specific agents - both, in terms of anti-tumour activity and side effects.¹⁹ The use of erlotinib is not connected with any significant degree of nausea and vomiting, the main side effect remains rash, which is usually well manageable and does not interfere with everyday functioning.²¹

Care should be taken of diarrhoea, which can be potentially life threatening so it is vital to ensure the patient's compliance with regimen and understanding of specific side effects.²² Oral medication is usually preferred over i. v. infusion. But one must bear in mind that specific targeting of erlotinib means also that a significant proportion of patients receiving the drug will not benefit from it and that those would therefore benefit from early discontinuation and change of the treatment strategy.

We can, therefore, presume that in selected patients, erlotinib not only improves the survival, but also improves the quality of life.^{8,15} According to the study by Sheppard *et al.*, this beneficial effect is not restricted only to female Asian non-smokers with lung adenocarcinoma but also to other patients as our patient witness.⁶

However, a careful monitoring of patient is needed and a discontinuation of the treatment at first signs of progressive disease and the reconsideration of other treatment options is warranted.

Our patient was not chemonaive, but received only the first line chemotherapy, so there is still a chance that he will respond to the second line chemotherapy. Furthermore, as his performance status improved, he is now probably a better candidate for the further treatment.

Conclusions

The patient we are presenting has clearly benefited from the treatment with erlotinib. However, even though he has progressed after a year of the treatment he is still in a better clinical condition as before the treatment, likewise, despite his progression, radiologically his tumour burden is still smaller than before the treatment.

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