Gefitinib in patients with advanced non-small-cell lung cancer
Gefitynib u chorych na niedrobnokomórkowego raka płuc w zaawansowanym stadium

The authors report no financial disclosure.

Abstract

Introduction: Patients with advanced non-small cell lung cancer (NSCLC) have a very poor prognosis. Individualization of treatment and identification of therapeutic molecular targets may improve outcomes. Gefitinib was introduced recently among several other molecular-targeted drugs of activity in NSCLC. Gefitinib is indicated for patients diagnosed with advanced or disseminated NSCLC with an activating mutation in the EGFR (epidermal growth factor receptor) gene. The paper summarize experience with gefitinib in the Department of Lung and Thoracic Tumors of Maria Sklodowska-Curie Memorial Cancer Centre and Institute in Warsaw.

Material and methods: The group of 11 patients diagnosed with advanced NSCLC and activating mutations in the EGFR gene was analyzed. Patients were treated from April 2010 to April 2011. Tolerability, objective response rate (ORR) and progression free survival (PFS), which was calculated by the Kaplan-Meier method, were assessed.

Results: Median observation time from the start of gefitinib treatment was 14 months (range 4.8–19 months). The rate of one-year survival in this group of patients was 91% (10 patients) with 54% of patients (6 patients) surviving one year without progression of disease. The ORR rate of 82% and median PFS 11.4 months were reached. No treatment-related deaths were reported. Among the complications skin toxicity (82%) and diarrhea (45%) were most frequently observed, in most cases the Common Toxicity Criteria for Adverse Events (CTCAE) first grade.

Conclusions: The results confirm the literature data on the efficacy and safety profile of gefitinib in the treatment of patients with the diagnosis of advanced NSCLC and activating mutation in the EGFR gene.

Key words: gefitinib, non-small cell lung cancer, EGFR mutation
Se rate (ORR) is estimated at 20–35% and median overall survival (OS) is around 10 months [4]. Slightly better results were achieved in selected populations of patients with adenocarcinoma treated with cisplatin and pemetrexed (median OS around 12 months) [5].

Small molecule tyrosine kinase inhibitors (TKI) form a group of drugs that act through a different mechanism. They are administered orally, but their use in the general population of NSCLC patients does not give satisfactory results (ORR < 10%) [6, 7].

An improvement of outcome of advanced NSCLC treatment was achieved by the identification of molecular therapeutic targets and an individual therapeutic approach. Trials of TKI treatment in patients selected on the basis of epidermal growth factor receptor (EGFR) extracellular domain expression and amplification of the EGFR gene either failed or were inconclusive. It was, however, shown that activating mutation in the EGFR gene (that encodes EGFR protein) is an independent predictive factor of the response to the EGFR-TKI therapy [8].

The prevalence of EGFR gene mutation varies — in an Asiatic population it is present in 30–45% of patients [9,10] and in a Caucasian population in 10–16% [11, 12]. The prevalence of EGFR gene mutation is determined by some clinico-pathological factors: histopathological type of the cancer, sex, smoking status [11] (Table 1).

Gefitinib belongs to the group of EGFR-TKI drugs; it inhibits the intracellular domain of EGFR. The other representative of this group is erlotinib. The inhibition of the EGFR activated pathway may be also obtained with cetuximab — a monoclonal antibody directed against the extracellular domain of EGFR.

Gefitinib is indicated in an advanced and metastatic NSCLC in patients with present activating mutation of EGFR gene.

We want to share our experience of the use of gefitinib in patients with advanced NSCLC.

### Material and methods

#### Studied population

We report on the outcome of gefitinib therapy in 11 patients with advanced NSCLC, treated in the Department of Lung and Thoracic Tumours of Maria Sklodowska-Curie Memorial Cancer Centre and Institute in Warsaw (Table 2). The enrolment into the study took place between 1st April 2010 and 30th April 2011. At the time of entry to the study all patients had disseminated disease. Three patients had an earlier attempt at radical therapy due to initial stages of the disease II and III (the remaining patients had the disease diagnosed in the disseminated stage).
The activating mutation in the EGFR gene was confirmed in all patients with use of a direct sequencing method. In most of the cases (10 patients) the mutations affected exon 19 (detailed data are presented in Table 3).

Treatment

Gefitinib was administrated orally in a standard single dose of 250 mg until progression of the disease or the occurrence of an unacceptable drug-related toxicity. The efficiency of the treatment was assessed with help of chest computed tomography (CT) and, in some cases, abdominal CT and imaging of the central nervous system (CNS). The above studies were performed every two months (every two cycles of the treatment). The response to the treatment was evaluated according to RECIST 1.1 criteria (Response Evaluation Criteria In Solid Tumours). The treatment toxicity was assessed according to the CTCAE scale (Common Toxicity Criteria for Adverse Events v.4.0). Karnofsky score and ECOG (Eastern Cooperative Oncology Group) score were used for evaluation of performance status. The standardised scale of quality of life in patients with NSCLC was not used.

Statistical Analysis

Statistica v.10.0 software was used. The progression-free survival (PFS) — i.e. time from gefitinib commencement to disease progression in imaging studies — was estimated with help of the Kaplan-Meier method. The endpoint for censored cases (patients continuing treatment) was the date of the last visit. The follow-up time was defined as the time from the diagnosis of metastatic NSCLC to the last patient’s visit or patient’s death.

Results

A group of 11 patients with NSCLC in stage IV and confirmed activating mutation in EGFR gene, treated with gefitinib, was analysed.

In 3 cases gefitinib was a second-line therapy, and in the remaining patients it was a first-line treatment. Median follow-up time from NSCLC diagnosis was 19 months (8–32 months), and from gefitinib commencement 14 months (4.8–19 months). One-year survival ratio was 91% (10 patients); 6 patients (54%) did not have progression of the disease during the first year. Median PFS in the whole group was 11.4 months (range 4.8–19 months) (Figure 1). In the subgroup of the first-line gefitinib treatment the median PFS was 12.6 months, and in 3 patients with second-line gefitinib treatment the PFS was 4.8 months and 9.4 months, respectively (the 3rd patient had been treated for 14 months without any radiological or clinical signs of progression).

Complete response (CR) or partial response (PR) was achieved in 9 patients (2 and 7, respectively). In 2 patients the disease stabilised (Table 4). The most prominent objective responses were observed after the first 2 treatment cycles (all CR were visible after 4 cycles; in these cases PR was seen after 2 cycles).

At the time of conducting these analyses, 4 patients were still on treatment (8.5–19 months), 2 died because of disease progression, and 1 was lost to follow-up after the progression was confirmed.

Among 7 patients with disease progression on gefitinib, 4 were given chemotherapy (cisplatin and pemetrexed, vinorelbine in monotherapy, docetaxel), and 2 were referred to palliative care due to worsening general condition in the course of the disease.

No standardised quality of life questionnaires for patients with cancer were used in this study. In 6 patients, however, improvement in performance status and subjective improvement in symptoms (cough, dyspnoea, pain) was achieved. The rest of the patients had very good performance status and only minimal symptoms from the respiratory system throughout the study duration.

We observed typical gefitinib related side effects (Table 5). The majority of patients suffered from skin problems (rashes and xeroderma) and diarrhoea of 1st degree according to CTCAE classification. In 2 patients a significant increase of liver transaminases and indices of cholestasis appeared (2nd and 3rd CTCAE degree), after 2 and 9 months of treatment, respectively. The therapy was stopped until the parameters normalised. When other potential causes of cholestasis were excluded, gefitinib was reintroduced. Liver abnormalities did not reoccur.

We proved the efficacy of gefitinib in patients with metastases to CNS. Two patients underwent palliative radiotherapy for the brain before gefitinib therapy was started. The regression of the disease during gefitinib treatment was also seen in CNS. In one patient clinical symptoms of increased intracranial pressure appeared after 9 months of treatment. Magnetic resonance imaging (MRI) revealed multiple small metastatic lesions in the brain. At the same time partial response in the chest was present and the patient tolerated gefitinib therapy very well. In this situation the patient was qualified for CNS palliative radiotherapy, and after irradiation was completed, gefitinib therapy was continued. Almost complete regression of metastasis.
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Race</th>
<th>Histological type</th>
<th>Type of mutation</th>
<th>Smoking status</th>
<th>Response to gefitinib</th>
<th>Adverse effects of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>71</td>
<td>Female</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>L858R mutation in exon 21</td>
<td>Never smoker</td>
<td>PR</td>
<td>Dry skin, rash</td>
</tr>
<tr>
<td>64</td>
<td>Male</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19; p.E746_S752</td>
<td>Previous smoker</td>
<td>CR</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>76</td>
<td>Female</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19</td>
<td>Never smoker</td>
<td>CR</td>
<td>Dry skin, diarrhoea, nausea</td>
</tr>
<tr>
<td>72</td>
<td>Female</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19</td>
<td>Never smoker</td>
<td>PR</td>
<td>Dry skin, diarrhoea, aminotransferase elevation (grade 2.)</td>
</tr>
<tr>
<td>50</td>
<td>Female</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19; p.K745-A750</td>
<td>Never smoker</td>
<td>PR</td>
<td>Dry skin, aminotransferase elevation (grade 3.)</td>
</tr>
<tr>
<td>75</td>
<td>Female</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19; p.E746-A750</td>
<td>Never smoker</td>
<td>PR</td>
<td>Dry skin, rash</td>
</tr>
<tr>
<td>40</td>
<td>Female</td>
<td>Caucasian</td>
<td>Squamous-cell carcinoma</td>
<td>Deletion of exon 19; p.E746-P753</td>
<td>Never smoker</td>
<td>SD</td>
<td>Rush</td>
</tr>
<tr>
<td>62</td>
<td>Female</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19; p.I747_P753</td>
<td>Never smoker</td>
<td>SD</td>
<td>Dry skin, rash</td>
</tr>
<tr>
<td>70</td>
<td>Female</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19; p.L747_T751</td>
<td>Never smoker</td>
<td>PR</td>
<td>Rush, diarrhoea</td>
</tr>
<tr>
<td>49</td>
<td>Female</td>
<td>Caucasian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19</td>
<td>Never smoker</td>
<td>PR</td>
<td>Dry skin, aminotransferase elevation</td>
</tr>
<tr>
<td>53</td>
<td>Male</td>
<td>Asian</td>
<td>Adenocarcinoma</td>
<td>Deletion of exon 19; p.E746_A750</td>
<td>Never smoker</td>
<td>PR</td>
<td>Rush, diarrhoea</td>
</tr>
</tbody>
</table>

*Toxicity was assessed according to the criteria CTCAE (Common Toxicity Criteria for Adverse Events v.4.0), in most cases it was first grade; CR - complete response; PR - partial response; SD - stable disease; ALT - alanine aminotransferase; AST - aspartate aminotransferase
The median age in the studied group at the start of therapy was 65 years (5 patients aged ≥ 70 years). The treatment tolerance in this subpopulation was good; no differences in toxicity profile were observed. No exacerbations of any comorbidities were reported. The comparison of treatment effectiveness between older and younger patients was not done due to the small numbers of patients in the studied group.

Discussion

We have presented a retrospective analysis of gefitinib treatment results in patients with disseminated NSCLC and an activating mutation of EGFR gene. 82% of objective responses were achieved. One-year survival was 91%, and median PFS was 11.4 months.

The presence of an activating EGFR mutation was an inclusion criterion. It is important to highlight the specific clinical profile of our patients: almost 80% were never-smoking women. Furthermore, in only one person was a squamous cell carcinoma diagnosed; in the remaining patients it was an adenocarcinoma. It stays in agreement with earlier observations in the Caucasian and Asian population on one hand, and on the other hand it indicates a patient profile in which it is reasonable to routinely perform molecular studies [7].

First-line treatment

Gefitinib is a relatively new treatment option for advanced and disseminated NSCLC. Initial attempts to intensify therapy by implementation of gefitinib to standard chemotherapy failed (INTACT 1 and INTACT 2) [14, 15]. There was no advantage of gefitinib over placebo as a second and subsequent line of NSCLC treatment, either (Iressa Survival Evaluation in Lung Cancer [ISEL study]) [8]. However, molecular predictive factors were not used in any of the cited studies. Table 6 contains a summary of chosen gefitinib studies.

Together with the appearance of new data on intracellular signalling pathways and their role in the development of neoplasms, molecular targets for small molecule EGFR-TKI (including gefitinib) were identified. Initially, the attention was focused on the degree of EGFR extracellular domain expression evaluated with use of immunohistochemical methods, and on a number of the gene's copies in neoplastic cells with the use of fluorescent in-situ hybridization (FISH). Presently, mutations within the EGFR gene are considered to be the most significant.

The efficacy and safety profile of gefitinib in patients with NSCLC and an activating mutation in EGFR gene were investigated in several prospective randomised studies (table 7).

Retrospective analysis of the IPASS study confirms the predictive significance of an activating mutation in the EGFR gene in terms of ORR and PFS in patients treated with gefitinib. The importance of EGFR gene amplification weakens. Although the clinical benefit in patients with amplification was observed, it was seen only in patients with coexisting activating mutation in the EGFR gene (77% of patients with amplification) [7]. Patients without an activating mutation in the EGFR gene do not benefit from treatment with ge-
### Table 6. Phase III trials in NSCLC patients with unknown status of EGFR mutation

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>Treatment line</th>
<th>ORR (%)</th>
<th>PFS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giaccone, 2004 [14]</td>
<td>PG ± gefitinib</td>
<td>I</td>
<td>50.3 v. 51.2</td>
</tr>
<tr>
<td>Herbst, 2004 [15]</td>
<td>PG ± gefitinib</td>
<td>I</td>
<td>30 v. 30.4</td>
</tr>
<tr>
<td>Thatcher, 2005 [8]</td>
<td>Gefitinib v. placebo</td>
<td>II, III</td>
<td>8 v. 1.3</td>
</tr>
</tbody>
</table>

PG — cisplatyna + gemcytabina; ORR — overall response rate; PFS — progression-free survival

### Table 7. Phase III trials in NSCLC patients with EGFR positive mutation

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>Treatment line</th>
<th>ORR (%)</th>
<th>PFS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mok, 2009 [9]</td>
<td>Gefitinib v. PC</td>
<td>I</td>
<td>71.2 v. 47.3</td>
</tr>
<tr>
<td>(CI: 0.36–0.64; p &lt; 0.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitsudomi, 2010 [16]</td>
<td>Gefitinib v. DC</td>
<td>I</td>
<td>62.1 v. 32.2</td>
</tr>
<tr>
<td>(CI: 0.336–0.710; p &lt; 0.0001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maemondo, 2010 [17]</td>
<td>Gefitinib v. PC</td>
<td>I</td>
<td>73.7 v. 30.7</td>
</tr>
<tr>
<td>(CI: 0.22–0.40; p &lt; 0.001)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Han, 2012 [18]</td>
<td>Gefitinib v. CG</td>
<td>I</td>
<td>84.6 v. 37.5</td>
</tr>
<tr>
<td>(CI: 0.269–1.100; p = bd)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Results in the population of patients with activating mutation in the EGFR gene treated with gefitinib in comparison with chemotherapy treated patients; DC — docetaxel + cisplatina; PC — paclitaxel + carboplatin; CG — cisplatina + gemcitabin; ORR — overall response rate; PFS — progression-free survival; CI — confidence interval; bd — lack of data

The toxicity profile in our study was similar to that presented in the literature (skin problems, diarrhoea).

## Second-line treatment

The results of EGFR-TKI therapy as a second-line treatment in the general population of patients with NSCLC are similar to those obtained with chemotherapy (Table 9).

The data on EGFR-TKI as a second-line treatment in patients with an activating mutation in EGFR gene are available.

Almost half of a studied population (104 patients) were given erlotinib as a second- or a third-line therapy in the research carried out by a Spanish group [11]. PFS rates in any-line treatment groups were similar (median 14 months).

Retrospective analysis of the INTEREST study showed significant improvement in PFS and ORR in patients with the activating mutation. In patients having the mutation and treated with gefitinib, an ORR of 41% (vs. 21% in patients treated with docetaxel) and median PFS of 7 months were observed. There were no differences in overall survival. There was no difference found in efficacy between gefitinib and docetaxel in patients without the mutation in EGFR gene, either [23].

The results of the retrospective analysis of erlotinib efficacy as a second-line treatment in advan-
A median PFS of 5.9 months was achieved in patients with an activating mutation in the EGFR gene (vs. 1.5 months in patients without the mutation) [24]. The results of the second-line treatment (EGFR-TKI vs. chemotherapy) in patients with confirmed activating mutation in the EGFR gene were summarised in a meta-analysis (13 randomised studies, including 3 studies on the second-line treatment and 10 on the first-line and a supportive treatment) [25]. In patients treated with EGFR-TKI, an ORR of 47.4% was achieved (vs. 28.5% in patients treated with chemotherapy).

In our group there were 3 cases of gefitinib used as second-line treatment. PFS were 5 and 9.4 months, and the third patient still continues the treatment (14 months) without signs of disease progression.

### Treatment in patients with metastatic disease in the brain

Metastases of NSCLC to CNS are common, especially in adenocarcinoma. It is estimated that metastases to the brain appear in 25–30% of patients. Involvement of the CNS is associated with worse prognosis [26]. The efficacy of chemotherapy and other routinely used methods of treatment (palliative radiotherapy, neuro- or radiosurgery in some cases) remains poor. The estimated survival time in such patients is 4–6 months.

Small molecule EGFR-TKIs act in a specific way. It has been postulated that they are very active towards lesions in CNS. In a population of patients with pulmonary adenocarcinoma and CNS metastases, who underwent palliative radiotherapy and/or chemotherapy previously, objective responses to the treatment and improvement in general condition were observed in 10–30% of cases [27, 28]. In patients with an activating mutation in the EGFR gene 70% of objective responses to gefitinib treatment was noted [29]. The above-mentioned data concerned patients with confirmed mutation in the EGFR gene and asymptomatic metastases in CNS, who did not have radiotherapy before. Median PFS was 6 months, and median overall survival was 19.8 months. It was also noted that the prognosis depended on the type of mutation. Better results were achieved in patients with mutation within exon 19 [29]. The protective role of EGFR-TKI drugs on the metastases to CNS has also been suggested [30].

In our group, metastases in CNS at the time of cancer diagnosis were present in two cases, and in another one clinical signs of increased intracranial pressure appeared during the treatment (however, she did not have any imaging studies of CNS per-
formed before, so it cannot be excluded that the metastases were present before the therapy was applied. All patients underwent palliative radiotherapy of the brain, and subsequently regression of the lesions in CNS during gefitinib therapy was observed. One of these patients still continues the treatment, and two of them died due to disease progression (only in one of these two cases progression of CNS metastases occurred, after 7 months from radiotherapy and gefitinib commencement).

**Hepatotoxicity**

It is estimated that in about 50% of patients on gefitinib, elevated activity of liver transaminases occurs (in 26% CTCAE degree 3 or 4). Gefitinib is metabolised in the liver by CYP3A4–5, CYP1A1, and CYP2D6 isoenzymes of P450. Polymorphism of genes encoding CYP2D6 is probably connected to gefitinib’s hepatotoxicity [31]. The lower activity of cytochrome results in higher serum levels of gefitinib, which leads to higher cytotoxicity. Medications inhibiting the cytochrome (i.e. ketoconazole, voriconazole, or clarithromycin) are contraindicated during gefitinib therapy. Among substances that induce the cytochrome activity are: phenytoin, carbamazepine, rifampicin, barbiturates, and St John’s wort. These medications decrease gefitinib serum levels and its efficacy [32]. The risk of liver injury is higher in patients with a chronic liver disease or in those abusing alcohol. An increase of the transaminases and bilirubin levels may be the only sign of hepatotoxicity, but acute liver failure has also been described. In the case of liver injury of the 3rd or higher degree, according to CTCAE, it is recommended to temporarily withhold the treatment until normalisation of the parameters. Gefitinib reintroduction in the initial or at a reduced dose may be considered. There are some reports about replacing gefitinib with erlotinib (as they have different metabolic pathways), which allowed for safe continuation of the treatment [33, 34].

As mentioned before, we had 3 cases of hepatotoxicity in our group. In these cases the treatment was temporarily suspended and re-established in the same dose after levels of transaminases decreased.

**Treatment of the elderly**

It is estimated that around 50% of patients with diagnosis of NSCLC are older than 65 years [35]. It is understandable that efficacy and safety of the treatment, including molecularly targeted methods, should be investigated in that specific population. It has been observed that in the general population of patients in advanced age gefitinib efficiency is not superior to vinorelbine efficiency, but the tolerance of the treatment is significantly better [36]. If an activating mutation in the EGFR gene was present, an ORR of 60–65% was observed. Also, an improvement in general condition in 80% of patients, whose pre-treatment performance status was 3–4 according to the WHO scale, was seen [37]. Median PFS was from 6.5 [37] to 13 months [35, 36]. There were no treatment-related deaths, and the most common complications were elevation of liver transaminases and anaemia [37–39]. In the opinion of the authors of the papers cited above, gefitinib is an effective and well-tolerated therapeutic option in patients in advanced age, even with more impaired performance status.

The median age at the time of gefitinib commencement in our group was 65 years, and 5 patients were older than 70 years. As mentioned, treatment tolerance was good, and median PFS in the subgroup of patients with advanced age was 14 months.

**Quality of life**

Reliable assessment of quality of life is an important part of prospective, randomised studies. The impact of the treatment on the quality of life often affects the final appreciation of a therapeutic method. Among the tools used for quality of life assessment are *Functional Assessment of Cancer Therapy-Lung* (FACT-L) and *Lung Cancer Subscale* (LCS). FACT-L consists of 5 modules assessing a patient’s emotions, social aspects, clinical symptoms, and general wellbeing. LCS focuses on complaints from the respiratory system. These tools have been applied for the evaluation of quality of life in patients treated with gefitinib, for example in the INTEREST and IPASS studies. The superiority of gefitinib over docetaxel and double-medication chemotherapy based on paclitaxel and carboplatin was shown [22, 40]. In patients with an activating mutation in the EGFR gene, treated with gefitinib, the time to clinical progression was significantly longer (15.6 months vs. 3 months in patients treated chemotherapy). Significantly more patients declared an improvement in health-related quality of life (HRQL) [39]. The median time to an improvement based on the questionnaires score (increase in FACT-L scale ≥ 6 points and in LCS scale ≥ 2 points, lasting for at least 21 days) was 8 days. This parameter was only measured in patients treated with gefitinib [40].

We did not use the FACT-L questionnaire in our study. We based our assessment on the Karno-
fsky and WHO performance status scales. We also collected data on symptoms related to the respiratory system (dyspnoea, cough, and haemoptysis). The reduction in the intensity of these symptoms in all patients could be seen in the first weeks of the treatment.

Conclusions

A group of 11 patients with disseminated NSCLC was presented. It was homogenous in terms of the presence of an activating mutation in the EGFR gene, but also in terms of clinical profile (sex, negative smoking history, diagnosis of adenocarcinoma). The presence of an activating mutation in the EGFR gene was the factor determining the choice of therapy. On the basis of the available published data and registered indications for gefitinib, patients were qualified for treatment with this medication. In total, 82% of ORR was achieved, 1-year survival rate was 91%, and median PFS was 11.4 months. The obtained results are in agreement with data published thus far and support the thesis about the efficiency of EGFR-TKI medications in the Caucasian population.

Gefitinib applied as the first-line treatment in patients with an activating mutation in the EGFR gene significantly improves 1-year survival and rate of responses; the tolerance of treatment is good. The benefit of improved overall survival was not shown.

Conflict of interest

The authors declare no conflict of interest.

References


