

Abstract

Introduction

In recent years, new oncological treatments with targeted effects on cellular level have been introduced into the clinical practice. Some of these agents can cause specific changes affecting skin, skin appendages and mucosa. Currently, the most significant cutaneous side effects in the clinical practice are observed during treatment with inhibitors of the epidermal growth factor receptor (EGFR). Papulopustular exanthema is the most frequent adverse effect of EGFR inhibitors. Skin changes have a crucial impact on the quality of life can cause an interruption or even termination of the oncological treatment, thus worsening the patient prognosis.

Objectives

The objective of this study was to evaluate the incidence, severity and time of onset of papulopustular exanthema in patients with non-small cell lung cancer (NSCLC) treated with erlotinib. The study also aimed to assess the correlation between papulopustular exanthema and patient prognosis and the incidence of EGFR gene mutations. Another objective was to create informational materials for patients with EGFR inhibitors skin toxicity, its prevention, treatment and recommended regime measures.

Methods

This was a prospective, open-label, uncontrolled study in which patients with non-small cell lung cancer stage III B and IV treated with erlotinib in any line of anticancer treatment have been followed since 2006. Patients were followed-up in monthly intervals to monitor NSCLC and to assess the presence and severity of papulopustular exanthema and paronychia induced by anti-EGFR treatment. Presence of activating mutations in EGFR gene was examined in a subgroup of patients. After one month of erlotinib treatment patients were assigned to the groups according to the presence and severity of exanthema and the presence of activating EGFR mutations. The correlation of the presence and severity of papulopustular exanthema with overall survival (OS) and progression-free survival (PFS) and the correlation between incidence of papulopustular exanthema and presence of activating EGFR mutations were assessed.

Results

In total, 580 patients were enrolled in the study. Activating mutations in EGFR gene were examined in 337 patients. Papulopustular exanthema was diagnosed in 300 (51.7%) out of 580 patients. Grade 1 exanthema was described in 118 (20.3%) patients, grade 2 in 141 (24.3%) patients, grade 3 in 34 (5.9%) patients and grade 4 in 7 (1.2%) patients. Paronychia were described in 27 (4.7%) patients. Exanthema occurred within one month in 272 (91.3%) patients, after one month in 26 (8.7%) patients. The mean time to develop papulopustular exanthema during erlotinib treatment was 26 days (median 22 days). Activating mutations of EGFR gene were confirmed in 38 (6.5%) patients, wild-type EGFR was found in 299 (51.6%) patients. Analysis of the subgroup of 308 patients (treated with erlotinib at least one month and examined for activating EGFR mutations) found significantly higher incidence of exanthema in patients with EGFR mutations (25 out of 35 patients, 71.4%) when compared to patients without mutations (140 out of 273 patients, 51.3%) ($p=0.030$). After one month of erlotinib treatment, 523 (90.2%) patients out of 580 patients were eligible for overall survival analysis and 396 (68.3%) patients were eligible for progression-free survival analysis. The median overall survival in the group of patients with exanthema (267 out of 523 patients) was 12.3 months; in the group of patients without exanthema (256 out of 523 patients), it was 6.6 months. The difference between the groups was statistically significant ($p < 0,001$). The median progression-free survival in the group of patients with exanthema (208 out of 396 patients) was 2.7 months; in the group of patients without exanthema (188 out of 396 patients), it was 1.1 months. The difference between the groups was statistically significant ($p < 0,001$). Both median overall survival and median progression-free survival were prolonged with increasing exanthema grade.

Conclusions

The incidence and severity of papulopustular exanthema correlated with overall survival and progression-free survival in patients with NSCLC treated with erlotinib. Papulopustular exanthema developed in the majority of the patients within one month after initiation of the treatment. Higher incidence of exanthema was found in the subgroup of patients with activating EGFR mutations.