Treatment of non-small cell lung cancer with gefitinib ('Iressa', ZD1839): the Greek experience with a compassionate-use program

E. Razis[a], D. Skarlos[b], E. Briasoulis[c], M. Dimopoulos[d], G. Fountzilas[e], S. Lambropoulos[a], S. Rigatos[f], P. Kopterides[b], H. Efstathiou[d], E. Tzamakou[c], C. Bakoyannis[a], D. Pectasides[g], T. Makatsoris[h], G. Varthalitis[i], S. Papadopoulos[a] and P. Kosmidis[a]

This is a retrospective analysis of 150 patients with advanced non-small cell lung cancer who had failed prior treatment or were unfit for chemotherapy and were treated with oral gefitinib ('Iressa', ZD1839; AstraZeneca) 250 mg/day. Thirty-two patients who received gefitinib for 3 weeks or less were not included in the analysis. For the remaining 118 evaluable patients, the mean age was 63.1 years; most patients had received prior chemotherapy (97.5%), Eastern Cooperative Oncology Group performance status scores 0–2 (97.4%) and stage IV disease (64.4%). The majority were symptomatic (84.6%). Disease control was observed in 30 patients (25.4%), of whom five had a partial response and 25 had stable disease; 18 (15.3%) were not evaluable. Median duration of treatment was 29.9 weeks in responding patients and 11.5 in patients with progressive disease ($p < 0.0001$). Median overall survival was 7.3 months (15.2 months for disease control) and median progression-free survival was 3.2 months. Gefitinib was well tolerated, with grade 3/4 skin rash and diarrhea seen in 2.5 and 4.2% of patients, respectively. Clinical benefit was evaluated using questionnaires before and following treatment with gefitinib. In 82 patients with completed questionnaires, evaluation revealed symptom improvement in 40.1% and improvement in general feeling in 31.4%. Epidermal growth factor receptor (EGFR) analysis found that efficacy did not correlate with tumor EGFR overexpression. Therefore, in this retrospective analysis, gefitinib treatment provided disease control in 25% of patients who derived significant palliative benefit.
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[a]HYGEIA Medical Center, Athens, Greece, [b]Henry Dunan Medical Center, Athens, Greece, [c]Ioannina University Hospital, Ioannina, Greece, [d]Alexandra University Hospital, Athens, Greece, [e]AHEPA Hospital, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece, [f]Agii Anargiri Hospital, Athens, Greece, [g]Attikon University Hospital, Athens, Greece, [h]Patras University Hospital, Patras, Greece and [i]Hania State Hospital, Hania, Greece.

Correspondence to E. Razis, Department of Medical Oncology, Hygeia Hospital, Er. Stavrou and Kifissias Avenue, 151 23 Maroussi, Athens, Greece.
Tel: +302106867165; fax: +302106867164;
e-mail: edrazis@hol.gr

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Introduction

Metastatic non-small cell lung cancer (NSCLC) is a common, fatal disease [1]. First-line chemotherapy with platinum-based combinations results in a 1-year survival rate of 30–40%, improves quality of life and is cost-effective [2–4]. However, patients who progress have few treatment options and second-line regimens yield response rates of 10%, with only modest improvements in survival [5,6]. Although further treatment beyond second-line therapy is occasionally employed, it is thought to be ineffective [7]. Furthermore, patients with NSCLC frequently have concurrent smoking-related and other illnesses, as well as poor performance status (PS). PS is the single most accurate predictor of response to chemotherapy and survival in the advanced NSCLC setting; patients with PS ≥ 2 are considered to derive little or no benefit from chemotherapy [8]. Therefore, treatment options for the management of unfit patients, or those who have relapsed after second-line treatment, are limited.

The epidermal growth factor receptor (EGFR) is thought to play a significant role in cancer cell proliferation, mediating its effects via a cascade of intracellular signaling events following the activation of the EGFR tyrosine kinase. Gefitinib ('Iressa', ZD1839; AstraZeneca) is a small molecule EGFR tyrosine kinase inhibitor (EGFR-TKI) that inhibits EGFR signaling, thereby blocking the proliferation and survival of cancer cells. Two large phase II trials ['Iressa' Dose Evaluation in Advanced Lung cancer (IDEAL) 1 and 2] studied oral gefitinib (250 and 500 mg/day) as second- and third-line treatment of metastatic NSCLC [9,10]; in those patients who received 250 mg/day gefitinib (the recommended dose in NSCLC), antitumor activity and disease control were observed in 12–18 and 42–54% of patients,

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respectively. Side-effects were relatively mild, consisting mainly of grade 1/2 acneiform rash and diarrhea. Notably, gefitinib 500 mg/day was associated with increased toxicity without additional clinical benefit. Further analysis revealed that certain subcategories of patients may derive more benefit from gefitinib therapy (e.g. patients with adenocarcinoma histology or poor PS, or female patients) [9]. Clinical trials have evaluated gefitinib in combination with platinum-based chemotherapy in the first-line setting for NSCLC on the premise that it may act synergistically. However, the combination of gefitinib with either paclitaxel/carboplatin or gemcitabine/cisplatin did not prove to be superior to either of these regimens alone [11,12]. Furthermore, comparable studies in NSCLC with another EGFR-TKI erlotinib have recently reported a similar absence of benefit when combining EGFR-TKIs with standard chemotherapy agents in the first-line setting. The reasons for this are unclear, but may be due either to poor synergy of TKIs with chemotherapy (in contrast to monoclonal antibodies) or to lack of selection of the subset of patients likely to respond to an EGFR-TKI. To date, gefitinib is the only EGFR-targeted agent to be approved by the US Food and Drug Administration for the management of patients with locally advanced or metastatic NSCLC after failure of both platinum- and docetaxel-based chemotherapies.

For those patients with no other treatment options, access to gefitinib has been possible through an Expanded Access Programme (EAP) at designated centers on a compassionate-use basis. The experience of using gefitinib in the EAP allows a better understanding of the advantages and risks of treatment, and may help in identifying patient subgroups likely to benefit from gefitinib therapy. As gefitinib targets the EGFR, it was thought likely that EGFR overexpression might correlate with gefitinib efficacy. While a prospective analysis of the IDEAL trials failed to show any correlation between gefitinib efficacy and EGFR overexpression [13], it remains possible that EGFR phosphorylation may be related to efficacy [14].

This study has retrospectively analyzed the experience of the EAP in Greece (in terms of tumor response, clinical benefit, survival, symptom improvement and tumor EGFR expression) in patients with advanced or metastatic NSCLC for whom no other treatment options existed.

Patients and methods

Patients

Patients with locally advanced or metastatic NSCLC who had failed prior treatment or who could not receive other treatment options were eligible to receive oral gefitinib 250 mg/day as part of the EAP. Relevant data were collected retrospectively from the records of all patients enrolled in the gefitinib EAP from 11 participating centers in Greece.

Efficacy

Patients treated with gefitinib as part of the EAP were assessed for response radiographically, using computed tomography scans according to standard practice or using what was thought clinically appropriate at each center. Tumor response to gefitinib therapy was assigned based on the managing physician's assessment.

Survival data, collected from all patients' records, were assessed from the start of gefitinib treatment to the date of death. Patients who died before disease progression was observed were categorized as having had progressive disease (PD). Patients who were still receiving treatment when the retrospective study closed were categorized as having completed therapy.

Analysis of clinical benefit

Improvements in disease-related symptoms were evaluated retrospectively; the managing physician completed a Clinical Benefit Questionnaire based on a review of patients' records before and after gefitinib therapy. The Clinical Benefit Questionnaire has been used previously to show improvements in clinical benefit using gemcitabine [15], and in NSCLC to show a correlation of symptom control with response and survival [16,17]. Clinical benefit was measured by analyzing the changes of nine symptoms (pain, cough, dyspnea, hemoptysis, nausea, vomiting, weakness, appetite and weight loss) following gefitinib treatment in comparison with baseline. General feeling was characterized as 'very good', 'good' and 'poor', and was compared before and after treatment.

Tolerability

Adverse events (AEs) were coded using MedDRA, and graded and recorded using WHO guidelines at the same time points as response. Causality was assigned by the managing physician.

Tumor EGFR analysis

Formalin-fixed and paraffin-embedded tissue sections from previous biopsy samples were analyzed immunohistochemically for tumor EGFR expression using an EGFR monoclonal antibody (EGFR.113 clone; Novocastra, Newcastle, UK) in 1/10 dilution with the Ventana NexES automated stain system. Antigen retrieval was performed in a 350-W microwave oven for 15 min in a citrate buffer (pH 7.0).

Statistical analysis

Summary statistics were provided for all variables. Categorical variables were summarized by frequency distribution tables, while measures of central tendency

(mean, SD, SE, median, interquartile range) were provided for all continuous variables. The association of patient response to treatment with categorical parameters of interest was investigated using a χ^2-test with continuity correction (or using Fisher's exact test, as appropriate). In addition, a logistical regression model was used to confirm univariate analysis results. For this purpose, responses were grouped as follows: partial response (PR) and stable disease (SD) versus PD.

Log-rank statistics were employed to evaluate overall survival (OS) distributions and progression-free survival (PFS) distributions. The associated distribution curves were illustrated according to the Kaplan–Meier method. Multivariate analyses for OS and PFS were performed using the Cox proportional hazard model. All tests were two-sided and the level of statistical significance was set at 5%.

Results

Patient characteristics

One hundred and fifty patients entered the EAP between September 2001 and August 2003. Of these, 32 patients were not evaluable for efficacy because they had received therapy for ≤ 3 weeks and the effect of gefitinib could not be assessed. As patients were first seen 1 month after starting gefitinib, safety data were not collected on these 32 patients. Therefore, 118 patients were evaluable for both efficacy and safety.

Patient demography for the 118 evaluable patients is shown in Table 1. Twenty-four patients had undergone surgery as initial therapy and 29 had received radiotherapy; of these, only nine had received both surgery and radiotherapy. Few patients had received adjuvant or neoadjuvant chemotherapy (seven and four patients, respectively). Three patients were chemonaive and, of the 115 patients who had received prior chemotherapy, 78 had been treated with platinum-based chemotherapy. The majority of patients (60.9%) had completed their previous chemotherapy regimens, with objective responses experienced by 30 patients (two complete responses and 28 PRs). Most patients (81.3%) were smokers and 35.6% suffered concurrent illness (mostly cardiovascular disease). At the time of treatment in the EAP, the majority of patients (84.6%) were symptomatic (Table 2), but, despite their symptoms, most patients did not feel poorly, as reflected by the majority of PS scores being 0–1 (90.6%).

Treatment

Mean duration of treatment was 18.3 weeks (range 3–85.7). Gefitinib was given as second-line treatment in 33.1% of patients, third-line treatment in 38.1% of patients, and fourth-line treatment and beyond in 28.8% of patients.

Table 1 Patient characteristics

Patients (*n*)	118
Median age [years (range)]	63.1 (37–88)
Gender [*n* (%)]	
male	92 (78.0)
female	26 (22.0)
ECOG PS [*n* (%)]	
0	64 (54.2)
1	43 (36.4)
2	8 (6.8)
3	2 (1.7)
3	2 (1.7)
Disease stage on presentation [*n* (%)]	
I	3 (2.5)
II	5 (4.2)
IIIA	15 (12.7)
IIIB	19 (16.1)
IV	76 (64.4)
Histology[a] [*n* (%)]	
adenocarcinoma	75 (65.8)
squamous cell carcinoma	24 (21.1)
large cell carcinoma	6 (5.3)
mixed	3 (2.6)
undifferentiated	5 (4.4)
not classified	1 (0.9)
Histological grade[b] [*n* (%)]	
well differentiated	3 (3.7)
moderately differentiated	32 (39.0)
poorly differentiated	44 (53.7)
undifferentiated	3 (3.7)
Tumor EGFR status[c] [*n* (%)]	
0	19 (55.9)
I	11 (32.4)
II	2 (5.9)
III	2 (5.9)
Chemotherapy regimens[d]	
1	38 (33.1)
2	44 (38.1)
3	26 (22.9)
≥ 4	7 (5.9)

[a]$n=114$; [b]$n=82$; [c]$n=34$; [d]$n=115$.

Table 2 Sites of metastatic disease and patients' general feeling at the start of the EAP

Sites of metastatic disease [*n* (%)]	
lung	118 (100)
bone	72 (61.0)
liver	59 (50.0)
lymph nodes	29 (24.6)
adrenal glands	22 (18.6)
pleura	17 (14.4)
brain	16 (13.6)
other	8 (6.8)
Symptomatic patients [*n* (%)]	99 (84.6)
1 symptom	22 (18.8)
2 symptoms	20 (17.1)
3 symptoms	20 (17.1)
>3 symptoms	37 (31.7)
Most common symptoms [n^a (%)]	
pain	54.7
dyspnea	52.1
cough	40.2
weakness	40.2
appetite loss	27.2
weight loss	20.5
General feeling [n^a (%)]	
very good	51 (43.6)
good	25 (21.4)
poor	41 (35.0)

[a]$n=117$.

Efficacy

Response

One-hundred patients (84.7%) were evaluable for response, while 18 patients (15.3%) were non-evaluable due to death ($n = 9$), refusal to continue ($n = 3$), toxicity ($n = 2$) or being lost to follow-up ($n = 4$) (Table 3). Disease control (PR plus SD) was confirmed radiographically in 30 patients (25.4%), of whom five had a PR and 25 had SD. Median duration of treatment was significantly longer in patients with disease control ([29.9 weeks; 95% confidence interval (CI) 4.1–85.7] compared with those whose disease progressed (11.5 weeks; 95% CI 3.0–66.4; $p < 0.0001$) (Fig. 1).

Survival

At the end of the EAP, 53 patients were still receiving treatment, 61 had died (60 due to disease progression and one due to an unknown cause) and four were lost to follow-up. Median disease-specific OS from the start of gefitinib therapy was 7.3 months for all evaluable patients; however, for patients with PR and SD this increased to 13.3 and 15.2 months, respectively, with the median OS for patients experiencing disease control being 15.2 months (Fig. 2). Median PFS was 3.2 months.

Improvements in disease-related symptoms

Clinical Benefit Questionnaires were completed for 82 patients. Thirty-three patients (40.2%) experienced some symptom improvement and symptoms deteriorated in the remainder. Cough improved in 42.4% of patients (Fig. 3). Pain, dyspnea and hemoptysis improved in approximately one-third of patients, while weakness and loss of appetite or weight improved in approximately one-quarter of patients (Fig. 3). Overall, 31.4% of patients experienced an improvement in their general feeling having received therapy with gefitinib.

Table 3 Best response of patients treated with gefitinib

	Patients [*n* (%)]	95% CI
PR	5 (4.2)	0.6, 47.8
SD	25 (21.2)	13.8, 28.6
PD	70 (59.3)	50.5, 68.1
Not evaluable	18 (15.3)	8.8, 21.8

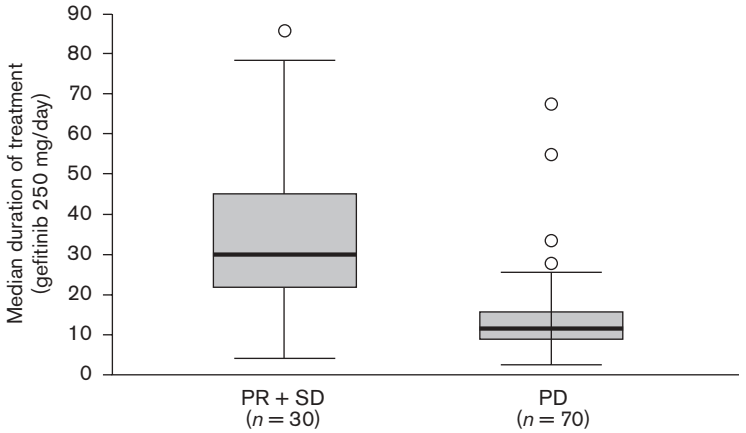
Analysis of factors that may predict efficacy

EGFR expression was assessed in tumor biopsies from 34 patients, with four found to overexpress the receptor. Immunohistochemical evaluation of EGFR expression found that response to gefitinib, PFS and OS were not correlated with EGFR overexpression (Table 4).

In terms of predictors of response, earlier stages of disease at presentation tended to correlate with disease control, but no other patient demography criterion correlated with response. Among pretreatment symptoms, only the presence of pain was associated with response to gefitinib. However, there was a very strong association between response and improvement in symptoms and general feeling (Fig. 4).

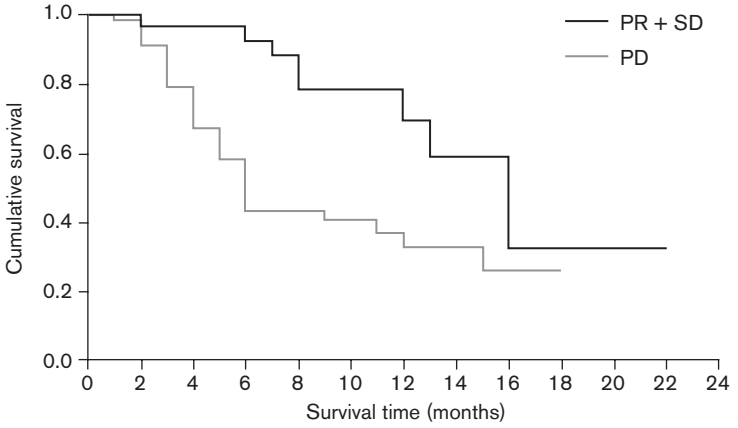
Interestingly, symptom improvement correlated with longer OS ($p = 0.0001$). There was no correlation between OS and gender, smoking history, disease stage, PS, previous surgery or the number of prior chemotherapy regimens. However, baseline disease-related symptoms such as pain, hemoptysis, weakness, and loss of appetite and weight were all significantly ($p < 0.03$ for all) associated with worsened OS, while cough, dyspnea and the presence of a pleural effusion were not. The presence of bone ($p \leq 0.0001$) and lymph node metastases

Fig. 1



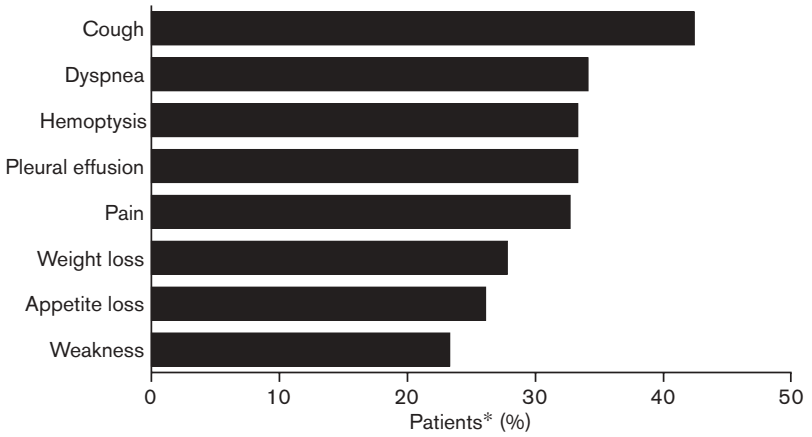
Median duration of treatment in patients with disease control (PR + SD) or disease progression. $p < 0.0001$; patients with disease control received treatment for longer than patients with PD.

Fig. 2



Median PFS in patients with disease control (PR + SD) or PD.

Fig. 3



Improvements in disease-related symptoms following treatment with gefitinib. *$n = 0.82$.

Table 4 EGFR expression in tumor biopsies taken at baseline ($n = 34$)

Response to gefitinib	EGFR status		Total
	0 + I [*n* (%)]	II + III [*n* (%)]	
PR + SD	10 (41.7)	1 (25.0)	11 (39.3)
PD	14 (58.3)	3 (75.0)	17 (60.7)
Total	24	4	28[a]

EGFR is not significantly associated with response, $p = 1.0$.
[a]Six patients with reported EGFR expression were not evaluable for response.

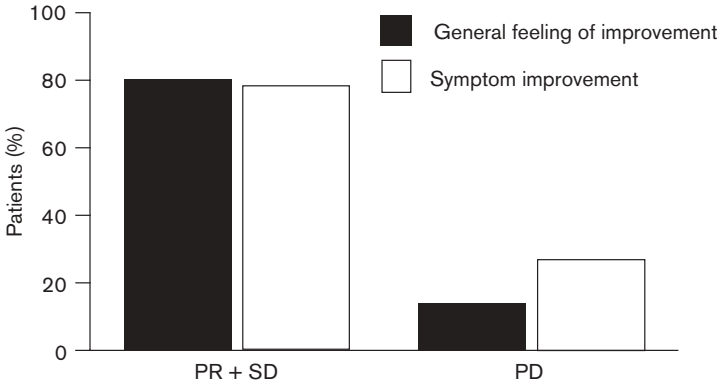
($p = 0.0005$) were also associated with poor OS, unlike the presence of liver, brain, adrenal and pleural metastases.

Pain and weakness appeared to correlate with worse PFS, as did brain metastases. In the Cox proportional regression multivariate model, disease stage ($p = 0.027$), pain ($p = 0.018$) and cough ($p = 0.045$) all correlated with worsened PFS, while the presence of brain metastases remained a significant predictor of poor PFS ($p = 0.002$).

Tolerability

AEs by Common Toxicity Criteria grades that were experienced by the 118 evaluable patients are shown in Table 5, with the majority being mild to moderate grade 1/2 events. Grade 1/2 skin rash was seen in 50 patients (42.4%) and 42 patients (35.6%) had diarrhea. Weight loss was observed in 10 patients (8.5%), and, of the remaining AEs, only dysphagia and nausea and vomiting occurred in > 5% of patients (5.9% for both; grade 1/2). Grade 3 AEs experienced by 10 patients were diarrhea ($n = 4$), skin rash and weight loss ($n = 2$ each), and fatigue and

Fig. 4



Association between response, general feeling and symptom improvement in patients treated with gefitinib.

infection ($n = 1$ each). Two grade 4 AEs were seen: skin rash and diarrhea.

Six patients experienced AEs that were considered serious by the investigator, three of which were considered to be related or possibly related to gefitinib; one patient had severe grade 4 diarrhea (as described above), one had possible interstitial lung disease (ILD, plus hypotension and dehydration considered unrelated to gefitinib) and another patient had a decrease in cardiac ejection fraction (possibly also attributed to their medical history of heart disease). The three patients with serious AEs that were not considered to be related to gefitinib included one patient with a chest infection, one patient with dyspnea and hypotension (due to PD), and one patient with disseminated intravascular coagulation (due to PD) and myocardial infarction. The latter three patients died, two due to disease progression and one due to the myocardial infarction.

Discussion

This retrospective analysis of the Greek EAP experience has found that gefitinib provides clinical benefit (response rate, OS, PFS, symptom improvement) and is well tolerated by patients with NSCLC. Recent concerns that some patients may develop ILD following treatment with gefitinib have since subsided, with one patient developing possible ILD that was gefitinib related in this analysis; when safety data from $> 92\,000$ patients were analyzed, the worldwide frequency of ILD was $< 1.0\%$ [18].

Data obtained in this study are consistent with published data from the phase II IDEAL 1 and 2 studies (Table 6) [5,6,9,10,19–22]. In these studies, administration of gefitinib as second- and third-line therapy was well tolerated and provided disease control in 42–54% of patients with advanced or metastatic NSCLC. In fact,

Table 5 AEs [*n* (%)] in the Greek EAP occurring in more than one patient[a]

AE	Grade 1	Grade 2	Grade 3	Grade 4
Rash	34 (28.8)	16 (13.6)	2 (1.7)	1 (0.8)
Diarrhea	28 (23.7)	14 (11.9)	4 (3.4)	1 (0.8)
Weight loss	8 (6.8)	2 (1.7)	2 (1.7)	0
Dysphagia	5 (4.2)	2 (1.7)	0	0
Nausea and vomiting	4 (3.4)	3 (2.5)	0	0
Fatigue	3 (2.5)	1 (0.8)	1 (0.8)	0
Hoarseness	3 (2.5)	0	0	0
Infection	2 (1.7)	2 (1.7)	1 (0.8)	0
Anemia	1 (0.8)	2 (1.7)	0 (0.0)	0

[a]A patient could have >1 AE.

the OS and PFS data between our retrospective analysis and the IDEAL trials are similar (Table 5), although our disease control rate is lower, probably due to the more advanced patients in this programme and the irregular monitoring of response. In both IDEAL trials, 205 patients with NSCLC received 250 mg/day gefitinib. Disease control was experienced by 54.3% (18.4% had PR, 35.9% had SD) and 42.2% (11.8% had PR, 30.4% had SD) of patients in IDEAL 1 and 2, respectively. Duration of response in IDEAL 1 was 13 months (range 2.0, 19.8 +) while in IDEAL 2 it was 7.0 months (range 3.4, 9.0 +). OS was 7.6 and 6.5 months and PFS was 2.7 and 1.9 months in IDEAL 1 and 2, respectively. As in our study, symptom data were available in 75–80% of patients in the IDEAL trials, with gefitinib improving disease-related symptoms in 40.3 and 43.1% of patients in IDEAL 1 and 2, respectively. Serious drug-related AEs were uncommon, occurring in three patients (grade 2 diarrhea, grade 3 bundle branch block and grade 3 dehydration) in IDEAL 1 and in four patients (two with asthenia, one with thrombocytopenia and epistaxis, and one with peripheral edema) in IDEAL 2.

Table 6 shows data for 73 patients from the Italian EAP [19]. These patients showed a higher response rate

Table 6 Comparison between gefitinib and docetaxel in the advanced NSCLC setting

	Gefitinib (250 mg/day)			Docetaxel (75 mg/m^2) versus		
	Greek EAP (n=118)	IDEAL 1 [9] (n=103)	IDEAL 2 [10] (n=102)	Italian EAP [19] (n=73)	BSC [5] (n=55)	Vinorelbine or ifosfamide [6] (n=120)
Response (%)[a]						
PR	4.2	18.4	11.8 [20]	9.6	5.5	6.7
SD	21.2	35.9	30.4	43.8	47.3	36.0
Duration of response [months (range)]	–	13 (2.0, 19.8+)	7.0 (3.4, 9.0+)	4 (2, 7)	6.5 (6.2, 6.7)	9.1
Median OS (months)	7.3	7.6	6.5 [9]	4	7.5	5.7
Median PFS (months)	3.2	2.7	1.9	–	–	–
Improved quality of life (%)	31.4	23.9	34.3	ND	significantly less deterioration using docetaxel [21]	improved [22]
Improved symptoms (%)	20	40.3	43.1	ND	significantly less pain using docetaxel [21]	improved [22]
Serious AEs	1 diarrhea, 1 possible ILD, 1 dehydration, 1 dyspnea, 2 hypotension, 1 disseminated intravascular coagulation and myocardial infarction, and 1 chest infection	1 diarrhea, 1 bundle branch block and 1 dehydration	2 asthenia, 1 thrombocytopenia and epistaxis, and 1 peripheral edema	1 grade 3 diarrhea	1 death (pneumonia); 67% of patients with grade 3/4 neutropenia	54% of patients with grade 4 neutropenia

BSC, best supportive care; ND, not determined.
[a]Data are based on the intent-to-treat population for our study, IDEAL 2, the Italian EAP and the docetaxel versus BSC trial. Data for IDEAL 1 and docetaxel versus vinorelbine or ifosfamide are from the per protocol populations.

(9.6%) and disease control rate (43.8%) than patients in our study, probably due to closer monitoring of response and a higher percentage of patients being treated with second-line gefitinib. Interestingly, both the EAP studies and IDEAL trials found that gefitinib improved general feeling and disease-related symptoms in most patients whose disease either responded to or stabilized with gefitinib. Furthermore, in the IDEAL trials, symptom improvement correlated with improved OS and PFS [9,10,23]. For these patients the benefit is great, as it is achieved with minimal toxicity and by oral administration. Our retrospective analyses are also compared with data from two studies that led to the FDA approval of docetaxel as second-line chemotherapy for NSCLC (Table 6) [5,6]. Similar to the observations of the IDEAL trials (where 500 mg/day gefitinib did not have additional clinical benefit but was associated with increased toxicity compared with 250 mg/day), the docetaxel trials found that response, OS and quality-of-life benefits were similar whether using 75 or 100 mg/m^2 docetaxel, although the higher dose caused unacceptable toxicity (grade 4 hematological AEs in 54% of patients and the deaths of six patients) [5,6,22]. Compared with placebo, docetaxel increased OS, but at present no such comparison is available for gefitinib.

Data from our study have not identified specific predictive markers for response or other characteristics that would identify patients who are more likely to benefit from gefitinib. Response to gefitinib did not correlate with adenocarcinoma histology, female gender or smoking history, in contrast to other publications [9,24]. Unlike the Italian EAP study, we did not find that overexpression (assessed in 25 patients in the Italian EAP study) correlated with response to gefitinib [19]. Indeed, analysis of the IDEAL data has shown that EGFR overexpression (recently shown to be a marker for poor survival [25]) does not seem to identify patients who are more likely to respond to gefitinib [13]. One EGFR marker that appears to be related to gefitinib response is EGFR phosphorylation [14]. Data from an EAP analysis of 84 evaluable patients treated with gefitinib support this; higher response rates were seen in patients with high versus low baseline phosphorylated mitogen-activated protein kinase (26.3 versus 6.4%) or Akt staining (21.0 versus 0.0%) [26]. Unfortunately, we were unable to perform an analysis of EGFR phosphorylation in our patients because at the time this technology was not available in Greece.

Apart from EGFR phosphorylation, characterization of other markers may identify subgroups of patients likely to benefit from gefitinib. For another EGFR-TKI erlotinib, acneiform rash has been suggested to be associated with efficacy, although this has yet to be proven [27]; a phase II trial is underway to investigate the possible association. However, for gefitinib, data to date suggest that rash is not a good predictor of response [28].

The best predictor of response and survival following treatment with gefitinib seems to be symptom improvement. There is clearly great need for translational

research in order to clearly identify patients who will benefit most from gefitinib therapy and the experience of using gefitinib in the EAP setting may allow a better understanding of this.

In spite of the fact that this analysis is retrospective, with all the limitations this entails, it provides significant information about the efficacy and tolerability of gefitinib that is similar to other prospective studies.

Conclusion

Data from this study support the results obtained from two large phase II trials of gefitinib (IDEAL 1 and 2). In our study, 250 mg/day gefitinib was well tolerated in patients with NSCLC and provided disease control in 25% of patients. Many patients also derived a significant palliative benefit. There was no clear correlation between markers and efficacy, and until patients who are likely to benefit from gefitinib treatment are identified, all patients with NSCLC who have received first- and second-line chemotherapy or who are unable to receive chemotherapy are candidates for treatment with gefitinib.

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