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Phase II Clinical Trial of Gefitinib for the Treatment of Chemonaïve Patients with Advanced Non-small Cell Lung Cancer with Poor Performance Status

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ABSTRACT

BACKGROUND: Patients with advanced non-small cell lung cancer (NSCLC) have no curative treatment options; therefore, improving their quality of life (QOL) is an important goal. Gefitinib, an epidermal growth factor receptor (EGFR) inhibitor, is a safe oral agent that may be of benefit to a specific population of NSCLC.

PATIENTS AND METHODS: A Phase II clinical trial included chemonaïve patients with advanced NSCLC and poor performance status (PS). Response rate, progression-free survival, overall survival, QOL using the Functional Assessment of Cancer Therapy – Lung (FACT-L) questionnaire, and Trial Outcome Index (TOI) were evaluated.

RESULTS: Twelve out of 19 enrolled patients were evaluable. The median age for the evaluable patients was 68.8 years (59.7–74.6). Out of all the patients, 7 (58.3%) had adenocarcinoma and 5 (41.7%) had squamous cell carcinoma. The median duration of treatment was 62.5 days (26.5–115.0) in the evaluable patients. Grade 3/4 toxicities included fatigue, rash, diarrhea, and nausea. One patient had partial response, eight patients had stable disease (SD), and three patients progressed. The median overall survival for the evaluable population was 4.9 months (2.3–16). The median progression-free survival was 3.7 months (1.9–6.6). TOI was marginally associated with the overall survival, with a hazard ratio of 0.92 (95% confidence interval: 0.84, 1.0) ($P = 0.061$). FACT-L score and the TOI were highly correlated ($r = 0.96$, $P < 0.0001$). TOI scores were higher in African Americans compared to Caucasians and increased with age.

CONCLUSION: Our results suggest that gefitinib use in patients with NSCLC and poor PS may improve the QOL of older patients and African American patients.

KEYWORDS: advanced non-small cell lung cancer, poor performance status, gefitinib, quality of life

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Introduction

Lung cancer remains the leading cause of cancer-related death worldwide.[1] Non-small cell lung cancer (NSCLC) accounts for 80% of all lung cancers.[2] Nearly one-third of NSCLC patients present with advanced disease at the time of diagnosis,[3] at which time therapeutic options for patients who are unable to tolerate chemotherapy are limited. Improvements in quality of life (QOL) and symptom control are valuable endpoints in management of this group of patients. Patients with advanced NSCLC and poor performance status (PS) are often excluded from clinical trials and that decreases their chances of palliative cancer therapy and QOL improvement. Being underrepresented in clinical trials, patients with poor PS are managed in an empirical and inconsistent manner in clinical practice.[4]

The epidermal growth factor receptor (EGFR) has been found to be expressed or highly expressed in a variety of solid tumors, including NSCLC.[5] Gefitinib, an EGFR-inhibitor, is a safe oral agent with an acceptable toxicity profile that might be of benefit for this group of patients. Two pivotal Phase II studies, Iressa Dose Evaluation in Advanced Lung Cancer 1 and 2 (IDEAL 1 and 2), showed that gefitinib, in addition to the reported response rates of 18.4% and 11.8%, respectively, also provided symptom relief from the primary disease in nearly 40% of patients.[6,7] These two trials included patients who were previously exposed to chemotherapy, but excluded patients with poor PS.

In a worldwide compassionate use program, the Iressa expanded access program (EAP), patients with advanced NSCLC and no alternative therapeutic option received gefitinib.[8,9] Data from the EAP showed that in elderly, unfit or chemonaïve patients, the tolerability profile of gefitinib appeared to be similar to that seen in the IDEAL trials.[8]

The aim of our study was to evaluate the impact of this single-agent EGFR-inhibitor (gefitinib) on the QOL of chemonaïve patients with advanced NSCLC and poor PS.

Patients and Methods

This Phase II clinical trial was conducted from June 2004 up to and including December 2005. The primary objective was the assessment of QOL. The secondary objectives were the assessment of safety, response rate, progression-free survival, and overall survival.

Patients were recruited at University of Cincinnati Oncology Clinics. The approval of University of Cincinnati Institutional Review Board was obtained (Protocol #1839US/0288), and all patients signed consent forms. Patients' confidentiality was maintained throughout the study. The research complied with the principles of the Declaration of Helsinki.

Inclusion criteria. Patients with pathologically diagnosed NSCLC in either American Joint Committee on Cancer (AJCC) stage IIIB with malignant pleural effusion or stage IV and with Eastern Cooperative Oncology Group (ECOG) PS 3 were included. All patients had to have measurable disease according to the Response Evaluation Criteria in Solid Tumors (RECIST 1.0) and adequate laboratory values, including absolute neutrophil count >1500/mm^3; platelet count >100,000/mm^3, and total bilirubin <1.5× institutional upper normal level; aspartate aminotransferase (AST) and alanine aminotransferase (ALT) <3× institutional upper normal level; and serum creatinine <1.5× institutional upper normal level.

Exclusion criteria. Patients with known severe hypersensitivity to gefitinib or with second primary malignancy that was clinically detectable at the time of consideration for study enrollment were excluded. Patients who were using phenytoin, carbamazepine, barbiturates, rifampin, or St. John's wort were excluded from the study because of their potential to modify hepatic enzyme activity and interfere with anticancer drug action. Patients who were treated with a non-approved or investigational drug within 30 days before day 1 of the trial treatment, who had incomplete healing from previous oncologic or other major surgery, who were pregnant or breastfeeding, or who were unable to swallow were also excluded from the study. Patients with severe or uncontrolled systemic disease or with any evidence of clinically active interstitial lung disease were excluded as well.

Patient population. The initial aim of the study was to enroll 40 patients; however, because of the negative results of the ISEL (Iressa Survival Evaluation in Lung Cancer) study, which did not show an advantage with gefitinib as a second-line therapy,[10] it was difficult to justify enrolling more patients in this study. Thus, the enrollment was stopped at 19 patients.

The patient received gefitinib 250 mg per day orally until disease progression or unacceptable toxicity was encountered. Patients were considered evaluable if they received at least one dose of gefitinib and had adequate follow-up imaging for re-evaluation. Patients who did not fulfill one or both of these criteria were considered non-evaluable. Twelve patients were evaluable for response, which included exploratory analysis of QOL and efficacy analyses of progression-free survival. Safety analyses were conducted for patients who received at least one dose of gefitinib (n = 18). Demographic summaries and overall survival were obtained for all study participants (n = 19).

Evaluation criteria. RECIST criteria were used for the evaluation of the objective tumor response. All baseline measurements were performed as close as possible to the treatment start date, with a maximum of 4 weeks prior to the start of therapy.

A sum of the longest diameter (LD) for all target lesions (maximum 10 target lesions and maximum 5 lesions per organ) was calculated and reported as the baseline sum LD.

Complete response (CR) was defined as the disappearance of all target and non-target lesions, and partial response (PR) was defined as at least 30% decrease in the sum of the LD of the target lesions using the baseline LD as a reference. Progressive disease (PD) was defined as either at least 20% increase in the sum of the LD of the target lesions using the smallest sum LD recorded as the reference, or the appearance of one or more new lesions. Stable disease (SD) was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.

Quality of life. The Functional Assessment of Cancer Therapy – Lung (FACT-L) questionnaire (version 3) was used to assess QOL and was administered at baseline (before the start of study treatment) and weekly thereafter until the end of the study. The Functional Assessment of Cancer Therapy – General (FACT-G) core instrument has 27 questions designed to measure social, emotional, physical, and functional well-being of the patients and to be sensitive to change.[11] The lung cancer-specific portion of the FACT-L questionnaire has nine additional questions, seven of which were used in

the QOL assessments. Each question was scored on a scale of 0–4, so the total score could range from 0 to 136. In addition, the Trial Outcome Index (TOI) was calculated using the physical, functional, and lung cancer-specific subscales. These subscales were selected because they are most likely to change in a chemotherapy trial.[11,12]

Safety. Duration of treatment (days), number of cycles taken (1, 2–3, or ≥4), and the toxicities observed following treatment were assessed. Toxicities were graded according to the National Cancer Institute (NCI) Common Toxicity Criteria version 2.[13]

Statistical analysis. The primary endpoint was the QOL of the patients assessed using the FACT-L questionnaire. The secondary endpoints were safety, response rate, progression-free survival, and overall survival. No formal sample size calculation was conducted. The sample size was typical for small Phase II studies and was based on clinical judgment and previous gefitinib experience. The null hypothesis was that the single-agent EGFR-inhibitor (gefitinib) did not significantly improve the QOL of chemonaïve patients with advanced NSCLC and poor PS. The alternative hypothesis was that gefitinib significantly improved the QOL of these patients.

Descriptive statistics were presented for continuous parameters as median and interquartile range (IQR), and for categorical parameters as number (*n*) and proportion (%).

Response rate, progression-free survival, and QOL were calculated for the evaluable patients. Progression-free survival (months) was defined as the time from start of study treatment to the date of disease progression. Overall survival (months) was calculated in all patients as the duration between the date of consent till the date of death. Duration of treatment was calculated in days as the duration between start date of study treatment and end date of study treatment.

A Cox regression model was used to determine the joint effect of age, race, gender, duration of treatment, and baseline QOL scores on the overall survival of the patients.

A linear mixed-effects model was utilized to examine the impact of potential covariates (age, race, gender, response, and duration of treatment) on the outcome of QOL scores over time (FACT-L, FACT-G, and TOI).

All statistical analyses were conducted using the Statistical Analysis Software (SAS) version 9.1 (SAS® Institute, Cary, NC).

Results

Patient characteristics. Nineteen eligible patients were enrolled in our study; however, only 12 out of the 19 patients were clinically evaluable for response rate, progression-free survival, and QOL assessments. Patients were excluded from the evaluable population because they did not have follow-up imaging for re-evaluation mainly because of loss to follow-up (n = 6) or did not start treatment after enrollment into the study (n = 1). The patient characteristics are presented in Table 1. The median age for the evaluable patients was 68.8 years (59.7–74.6), and for the non-evaluable patients was 71.8 years (70.2–79.2). Among the evaluable patients, eight (66.7%) were male, while four (33.3%) were female. Among the non-evaluable patients, the corresponding numbers are six (85.7%) and one (14.3%), respectively. Regarding race, the evaluable patients were composed of eight (66.7%) Caucasians and four (33.3%) African Americans, while in the non-evaluable patients, the numbers were six (85.7%) and one (14.3%), respectively. Out of the evaluable patients, seven (58.3%) had adenocarcinoma and five (41.7%) had squamous cell carcinoma (not shown).

Impact on QOL. The total FACT-L score and the TOI were highly correlated (correlation coefficient (r) = 0.96, P = 0.0001) (not shown). Table 2 shows the QOL indices at baseline, week 5, and week 8. There were no significant differences in the FACT-G, FACT-L, or subscale scores between baseline, week 5, and week 8. Notably, in contrast to the FACT-G and FACT-L scores, an increasing trend in the TOI was observed, ranging from 33.8 at baseline to 42.0 at weeks 5–45.0 at week 8, although this trend was not significant (Fig. 1).

Duration of treatment was significantly associated with survival with a hazard ratio of 0.97 (95% confidence interval: 0.94, 1.0) (P = 0.049). Of the QOL scores examined, only baseline TOI was marginally associated with the overall survival, with a hazard ratio of 0.92 (95% confidence interval: 0.84, 1.0) (P = 0.061) (not shown).

A mixed effects linear model was utilized to examine the impact of potential covariates (age, race, gender, response, and duration of treatment) on the QOL scores (FACT-L, FACT-G, and TOI) over time. Race and age were significantly associated with TOI. TOI scores were higher in African Americans compared to Caucasians and increased with age ($P < 0.05$) (Table 3).

Response rate, progression-free survival, and overall survival data. One patient had a partial remission (8.3%), eight patients had SD (66.7%), and three patients progressed (25.0%) (Table 1). The median progression-free survival in the evaluable patients was 3.7 months (1.9–6.6) (Table 1). The median overall survival for the evaluable population was 4.9 months (2.3–16), and for the non-evaluable population was 1.5 months (1.2–3.7).

The overall survival for the evaluable population stratified by the median duration of treatment is shown in Figure 2. The overall survival in evaluable patients with a duration of treatment of 62.5 days or less (n = 6) was 2.3 months (95% confidence interval = 1.3–4.5), while the overall survival in those with a duration of treatment greater than 62.5 days (n = 6) was 15.2 months (95% confidence interval = 5.3–26.5) (P = 0.02 using the log-rank test).

Safety data. The median duration of treatment was 62.5 days (26.5–115.0) in the evaluable patients, and 34.0 days (10–36) in the non-evaluable patients. Out of

Table 1. Patient characteristics.

CHARACTERISTIC	EVALUABLE (N = 12)				NON-EVALUABLE (N = 7)			
	MEDIAN	(IQR)	N	(%)	MEDIAN	(IQR)	N	(%)
Age (years)	68.8	(59.7, 74.6)			71.8	(70.2, 79.2)		
Duration of treatment (days)*	62.5	(26.5, 115.0)			34.0	(10.0, 36.0)		
Overall Survival (months)	4.9	(2.3, 16.0)			1.5	(1.2, 3.7)		
Progression-free survival (months)	3.7	(1.9, 6.6)						
Gender								
Male			8	(66.7)			6	(85.7)
Female			4	(33.3)			1	(14.3)
Race								
Caucasian			8	(66.7)			6	(85.7)
African American			4	(33.3)			1	(14.3)
Response								
Stable disease			8	(66.7)				
Progressive disease			3	(25.0)				
Partial response			1	(8.3)				
Stage								
IIIB			1	(8.3)			2	(28.6)
IV			11	(91.7)			5	(71.4)
Cycles*								
1			4	(33.3)			3	(50.0)
2–3			2	(16.7)			0	
≥4			5	(41.7)			0	
Missing			1	(8.3)			3	(50.5)

Notes: *Duration of treatment and cycles were assessed in the safety population (12 evaluable patients, and 6 non-evaluable patients). Percentages for cycles were calculated based on the safety population ($n = 18$).
Abbreviation: IQR, interquartile range (lower quartile, upper quartile).

the evaluable patients, four (33.3%) had one cycle of study treatment, two (16.7%) had two to three cycles, and five (41.7%) had four or more cycles. Only three (50.0%) of the non-evaluable patients had one cycle, and none had more than one cycle.

There were no detrimental side effects and no treatment-related death. The treatment was well tolerated. Toxicities were graded according to the NCI Common Toxicity Criteria version 2.[13] Grade 3/4 toxicities included fatigue, rash, diarrhea, and nausea (Table 4).

Table 2. QOL ($n = 12$).

CHARACTERISTIC	BASELINE			WEEK 5			WEEK 8		
	N	MEDIAN	(IQR)	N	MEDIAN	(IQR)	N	MEDIAN	(IQR)
Physical	8	19.0	(15.42, 24.83)	7	21.0	(8.0, 23.3)	3	20.0	(20.0, 25.0)
Social /Family	9	22.0	(21.0, 26.0)	6	20.4	(18.7, 25.0)	3	18.0	(16.0, 24.0)
Emotional	9	20.0	(18.0, 23.0)	6	20.0	(16.0, 24.0)	2	17.5	(17.0, 18.0)
Functional	9	13.0	(7.0, 19.0)	7	16.0	(15.4, 19.0)	3	17.0	(14.0, 20.0)
Lung cancer subscale	11	16.0	(14.0, 22.2)	9	17.0	(16.0, 20.0)	3	15.0	(14.0, 18.7)
FACT-G total	9	75.0	(61.8, 90.0)	8	58.2	(36.7, 84.5)	3	72.0	(55.0, 82.0)
FACT-L total	11	75.8	(57.0, 106.0)	9	60.7	(46.4, 103.7)	4	70.5	(42.0, 86.3)
TOI	11	33.8	(25.0, 60.0)	9	42.0	(30.4, 61.0)	4	45.0	(27.0, 54.8)

Abbreviation: IQR, interquartile range (lower quartile, upper quartile).

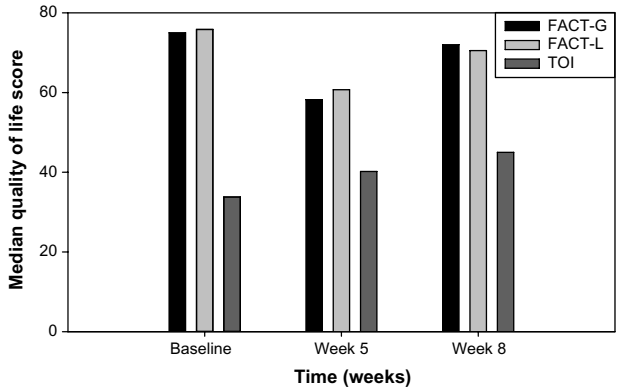

Figure 1. Quality of life scores in all the evaluable patients ($n = 12$).

Discussion

PS is a significant prognostic factor for predicting survival. In earlier studies on patients with NSCLC who were treated with four different chemotherapy regimens, patients with PS of 0 had a median survival of 9.4 months compared to 3.3 months in patients with a PS of 2. Patients with a PS of 2 or worse are more likely to experience toxicity of chemotherapy.[14] Consequently, patients with poor PS have been traditionally excluded from clinical trials. Our study, however, focused on this group of patients with PS of 3. The median overall survival for the evaluable patients was 4.9 months, and for the non-evaluable patients was 1.5 months.

In a similar, but a retrospective study done in Taiwan, out of 52 patients with poor PS, 82.7% had ECOG PS of 3 and the rest had ECOG PS of 4. They were all diagnosed with advanced NSCLC and received single-agent gefitinib 250 mg once daily, where the best response rate was 25% in 13/52 chemonaïve patients, followed by 13.3% in 2/15 patients who previously failed one line of chemotherapy, and 18.8% in 3/16 patients who previously failed two or more lines of chemotherapy.[15] The median overall survival for the cohort was 2.5 months, but the response group had a median survival of 9.1 months, the SD group had 3.1 months, and the PD group had 0.8 months ($P < 0.001$). In another study for the evaluation of gefitinib in Chinese patients with NSCLC and poor ECOG PS of 3 and 4, 42 patients were evaluated. The objective tumor response was 40.4%, and the SD rate was 26.2%. Also the median overall survival and the progression-free survival in that study were 10.1 and 5.7 months, respectively, which again were higher than in our study.[16] Furthermore, rash and diarrhea were among the main side effects, similar to our study. In general, other studies follow the trend of a higher objective tumor response and lower SD rate compared to our study.[17] These data suggest that gefitinib might be well tolerated with similar efficacy and safety among patients with poor PS with no other therapeutic option, and that it has a reasonable safety profile making it worthy for further study in this specific patient population.

Unlike our study, the QOL analysis was not available in these two studies. Gefitinib thus seems to be a good treatment choice for patients with poor PS especially as a frontline therapy given that it is non-chemotherapy, has a low toxicity profile, and is an oral formulation.[12] It has been used as a frontline therapy for advanced NSCLC with severe comorbidity, poor PS, or refusal of chemotherapy.[18,19]

In the IDEAL-1 trial, 17% of the patients had a PS of 0, 70% a PS of 1, and 13% a PS of 2, and none had a PS of 3 or 4.[6] In that trial, gefitinib showed response rates of 18.4% and 19% among the 250 and 500 mg daily doses with symptom improvement rates of 40.3% and 37%, respectively, in previously treated patients. The median progression-free survival was 2.7 and 2.8 months, and the median overall survival times were 7.6 and 8 months, respectively, in the good PS previously treated population. In IDEAL-2 trial, a similar outcome was observed with gefitinib 250 mg daily dose with fewer side effects.[7] In both trials, gefitinib showed better symptom control. In contrast, our sample consisted of PS 3 patients who were administered 250 mg per day of gefitinib. Although the median overall survival was lower than that reported in these studies, we observed that it significantly differed by duration of treatment. The overall survival in evaluable patients with a below-median duration of treatment was 2.3 months. However, it drastically increased to 15.2 months among those with a duration of treatment longer than the median.

Our results provide an alternative approach to improve QOL for patients with advanced NSCLC who have no other therapeutic option. We observed that the QOL index, TOI score, which has been shown to be more reflective of clinical change, consistently increased over time and was marginally associated with overall survival. Our data also showed that in a selective patient population, patients with older age and African American race, an EGFR-inhibitor could be a good option for improving the QOL. In another similar

Table 3. The effect of various covariates on the outcome of QOL using the mixed model approach ($n = 12$).

COVARIATE	BETA COEFFICIENT	STANDARD ERROR	*P*-VALUE
Age (years)	0.88	0.27	<0.05
Duration of treatment	0.08	0.07	0.30
Gender			
Female	–3.32	9.10	0.74
Male	Reference		
Race			
African American	32.78	11.51	<0.05
Caucasian	Reference		
Response			
Progressive disease	–17.51	10.20	0.16
Partial response	11.01	8.15	0.25
Stable disease	Reference		

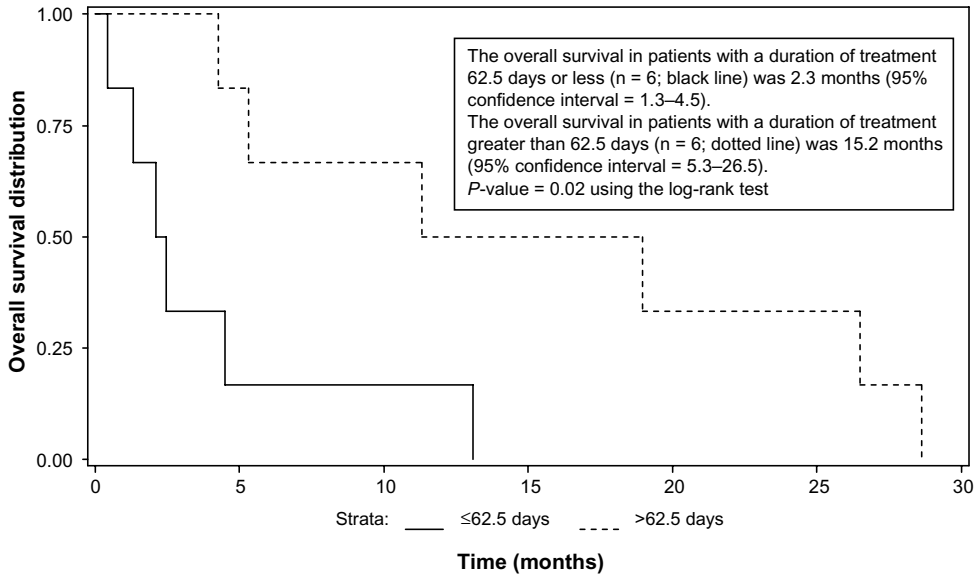

Figure 2. Overall survival distribution of all the evaluable patients ($n = 12$) stratified by duration of treatment (months).

study evaluating the QOL of patients with advanced NSCLC who were not responding to treatment or progressed, a trend toward improvement for fatigue, dyspnea, insomnia, and constipation was observed after 1 month of therapy.[20] The study did not identify any subgroup-specific benefits like we observed in our study. QOL was also assessed in 216 symptomatic patients with NSCLC who were previously treated with at least two chemotherapy regimens, showing similar beneficial effects.[21] Gefitinib has also shown beneficial effects including improvements in QOL and severity of adverse effects compared to other anticancer agents in patients with advanced NSCLC.[22]

The efficacy of gefitinib was reported not only in poor PS patients, but it was shown as well among one of the several case reports noted that it had no cross-resistance with the conventional chemotherapy. Moreover, disappearance of brain metastases with gefitinib therapy 6 months away from radiation therapy was also noted in the same report.[23]

Table 4. Treatment-related toxicity (NCI Common Toxicity Criteria Evaluation version 2) ($n = 18$).

TOXICITY	I N (%)	II N (%)	III N (%)	IV N (%)
Fatigue	3 (16.7)	1 (5.6)	2 (11.1)	1 (5.6)
Rash	2 (11.1)	3 (16.7)	1 (5.6)	
Diarrhea	2 (11.1)		1 (5.6)	
Nausea	1 (5.6)		1 (5.6)	
Thrush		1 (5.6)		
Fever	2 (11.1)			
Renal toxicity	1 (5.6)			
Anemia		2 (11.1)		
Pain	1 (5.6)	2 (11.1)		

The number of patients in our study was too small for definitive conclusions, and thus the results should be interpreted with caution. Despite this limitation, our results demonstrate that the overall survival was significantly increased with increasing duration of treatment. Furthermore, we provide preliminary data on the impact of gefitinib on the QOL of this underserved patient population. It was not clear to us why the QOL analysis showed that African Americans had better improvement in the QOL status. This result was notable despite the smaller number of African Americans compared with Caucasians, and warrants further clinical and genetic investigations.

However, in a study from Italy, gefitinib seemed to benefit selective groups of patients. Response rate was significantly higher in women, non-smokers, and patients with EGFR mutations; specifically, EGFR and HER2-polysomy were significantly associated with response to gefitinib therapy.[24] In the IDEAL-1 study, 102 Japanese patients experienced more benefits, suggesting that there might be ethnic differences in gefitinib efficacy.[6] This was also addressed in the Chinese study mentioned earlier.[16]

Our study did not analyze the EGFR status of the studied patients, which was not available for analysis as this would have given us more insight on the benefit of the drug. In the Italian study mentioned above, a total of 137 patients with advanced NSCLC received gefitinib either as a first-line treatment or after failure of chemotherapy. The positivity for EGFR mutations was significantly associated with response to gefitinib therapy. The results of the univariate analysis showed that patients with EGFR mutation had median survival of 14.9 months compared to patients without mutations who had median survival of 5 months ($P < 0.05$).[24]

In contrast to our study, Leidner et al suggested less benefit of the EGFR-inhibitors in the African American

population in terms of achieving major remissions.[25] Leidner et al studied the frequency of EGFR pathway aberrancies among African American patients with NSCLC. African Americans were significantly less likely to harbor activating mutations of EGFR than White patients (2% v 17%; $P = 0.022$). Only one EGFR mutation was identified, a novel S768 N substitution. EGFR Fluorescence In Situ Hybridization (FISH) assay was more frequently positive for African Americans than for White patients (51% v 32%; $P = 0.018$). In that study, no data to address the QOL assessment in this group of patients were available, which constitutes the main focus of our study.

A meta-analysis was conducted on four randomized studies that compared gefitinib with chemotherapy in the first-line treatment of patients with advanced NSCLC: IPASS, North-East Japan, West Japan, and first-SIGNAL studies. Selection of patients was based on either the known presence of EGFR mutations or on clinicopatholgical criteria associated with high likelihood of these mutations (non-smokers with adenocarcinomas). In this population of patients, upfront gefitinib or chemotherapy was found to be associated with similar OS. However, gefitinib was associated with less fatigue, myelosuppression, and nausea compared to systemic chemotherapy. On the other hand, gefitinib consistently caused more skin rash, diarrhea, and pneumonitis. Patients who received gefitinib were found to have improved QOL compared to those who received chemotherapy. This meta-analysis supported considering EGFR-inhibitors use as an appropriate first-line choice in such group of patients.[26]

Over the last few years, our data were further confirmed by multiple larger studies on gefitinib for advanced NSCLC with positive EGFR mutation.[27–31] Although the outcome was poor in this population, these studies showed a longer disease-free survival and a better side-effect profile for patients treated with gefitinib compared to other chemotherapies. Another study on gefitinib for elderly patients aged 75 or older with advanced NSCLC also showed a good tolerability and mild toxicity with strong anti-tumor activity.[32]

Conclusion

The single-agent EGFR-inhibitor (gefitinib) is an active and well-tolerated therapy for NSCLC patients with poor PS with a trend of the TOI observed for improvement in QOL.

Inspite of the small number of the studied patients, our results suggest that increasing age and African American race had higher TOI scores and thus improved QOL status.

Gefitinib could thus be an option for therapy in patients with advanced NSCLC for whom standard chemotherapy is not recommended because of poor performance status.

Author Contributions

Conceived and designed the experiments: ARJ. Analyzed the data: SM. Wrote the first draft of the manuscript: NAK. Contributed to the writing of the manuscript: AZ, SP. Agree with manuscript results and conclusions: NAK, SM, AZ, SP, ARJ. Jointly developed the structure and arguments for the paper: NAK, ARJ. Made critical revisions and approved final version: ARJ. All authors reviewed and approved of the final manuscript.

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