INTRODUCTION

Gefitinib (ZD1839, Iressa™, AstraZeneca) is an anilinoquinazoline that has been approved by the U.S. Food and Drug Administration (FDA) as a single-agent therapy for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) who have not responded successfully to chemotherapies with platinum (carboplatin, cisplatin) and docetaxel (Taxotere®, Aventis), two drugs that are the standard of care for this disease.1,2 Gefitinib is the first in a new class of anticancer drugs that inhibit epidermal growth factor receptor/tyrosine kinase (EGFR-TK) (Table 1).1,4 EGFR is expressed on both normal cells and solid tumor cells, including 40% to 80% of normal cells and solid malignant tumors, the mean half-life of gefitinib is estimated to be 60%.1

In a parallel-group, crossover study with healthy volunteers who received 50 mg of gefitinib, food intake decreased the Cmax by 34% and the area-under-the-curve (AUC) concentration by 14%.9 In another crossover study in healthy volunteers receiving 250 mg of gefitinib, both the Cmax and the AUC concentration were increased by 34% and 37%, respectively, with food ingestion.3 However, food does not have a clinically significant effect on bioavailability.3,9

The elimination half-life of gefitinib is 48 hours after intravenous (IV) administration.1 In a phase 1 trial of patients with solid malignant tumors, the mean half-life after a single 50-mg oral dose was 34 hours.10 After multiple-dose administration, the average mean half-life was 47.6 hours (range, 37–65 hours).10

Gefitinib is metabolized primarily by the cytochrome P-450 (CYP-450) hepatic enzyme 3A4.11 It is cleared predominantly by the liver and is excreted in the feces (86%), with less than 4% of the drug and its metabolites eliminated renally.1

PHARMACOKINETICS

Oral gefitinib exhibits a dose-proportional kinetic profile that is suitable for a once-daily regimen in cancer patients.9,10 The drug is absorbed slowly after oral administration and reaches peak plasma levels (maximal concentration [Cmax]) three to seven hours after administration in healthy volunteers.1,9 Steady-state plasma concentrations are reached within 10 days.1 The mean oral bioavailability of gefitinib is estimated to be 60%.1

In a parallel-group, crossover study with healthy volunteers who received 50 mg of gefitinib, food intake decreased the Cmax by 34% and the area-under-the-curve (AUC) concentration by 14%.9 In another crossover study in healthy volunteers receiving 250 mg of gefitinib, both the Cmax and the AUC concentration were increased by 34% and 37%, respectively, with food ingestion.3 However, food does not have a clinically significant effect on bioavailability.3,9

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CLINICAL TRIALS

The FDA approved gefitinib based on results from the Iressa Dose Evaluation in Advanced Lung Cancer (IDEAL-2), a phase II trial that included 216 patients, of whom 142 had not responded to both platinum-based and docetaxel chemotherapies. Approximately 10% of patients in this trial achieved a response rate defined as a decrease in tumor size by 50% after treatment with gefitinib.10,16,18 The results of published phase I/III clinical trials with gefitinib are summarized in Table 2.

Phase I Trials

Escalating oral doses of gefitinib were given to patients with NSCLC or other solid tumors for 14 days, followed by 14 days of observation10,11 or by 28 days of continuous observation.11 Patients were enrolled only if their solid malignant tumors were known to express or over-express EGFR.10,13,14

The Baselga Study13

Baselga et al. examined the safety, tolerability, and pharmacokinetic and pharmacodynamic effects of gefitinib in patients with solid tumors. Gefitinib was to be administered once a day as a single oral dose for at least 28 consecutive days at 150, 225, 300, 400, 600, 800, and 1,000 mg/day. If one patient experienced a dose-limiting toxicity (DLT) before completing a 28-day cycle at a specific dose, six or more patients had to finish one 28-day cycle at the same dose before other patients were allowed to begin the next dose level. The DLT was defined as:

- a drug-related toxicity of National Cancer Institute Common Toxicity Criteria (NCI–CTC), grade 3 or higher
Bioavailability: 60%

**Overview of Gefitinib**

Gefitinib monotherapy is approved for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after unsuccessful platinum-based and docetaxel chemotherapies.

**Mechanism of action**
Gefitinib inhibits the intracellular phosphorylation of numerous tyrosine kinases associated with transmembrane cell-surface receptors, including the tyrosine kinases associated with the epidermal growth factor receptor (EGFR-TK).

**Dosage**
250 mg/day orally until disease progression occurs. In clinical studies, higher doses did not yield a better response and caused an increase in toxicity.

**Pharmacokinetics**
- Bioavailability: 60%
- Peak plasma levels: 3–7 hours
- Metabolism: hepatic (CYP-3A4)
- Excretion: fecal (86%)
- Elimination half-life: 48 hours

**Average wholesale price†**
$1,950 per bottle of 30 tablets

* Data from Iressa™ package insert. AstraZeneca Pharmaceuticals.1
† Data on file from the manufacturer.23

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Clinical and laboratory assessments were performed at the baseline evaluation and at two-week intervals. The investigators analyzed the pharmacokinetic parameters by taking venous blood (4 ml) before administering the dose on days one, eight, 15, 22, and 29; at 28-day intervals subsequently; at withdrawal from the trial; and two weeks after withdrawal from the trial. Skin biopsy specimens were collected for pharmacodynamic assessment before the first dose and after about 28 days of gefitinib therapy. Tumors were measured according to the revised World Health Organization criteria within two weeks before the start of therapy, at approximately 29 days, at 28 days thereafter, and at withdrawal.

Eighty-eight patients received dose-escalating (150 to 1,000 mg/day), continuous regimens of gefitinib. At 1,000 mg/day, five of the 12 patients experienced grade 3 diarrhea, and one had grade 3 somnolence. Grade 1 or 2 acne-like rash (64%) and diarrhea (47%) occurred frequently and were reversible once treatment ceased. Most patients had achieved steady-state concentrations by day seven. Inhibition of the EGFR signaling pathway was evident in the 28-day skin biopsy evaluation.

Of the 88 patients receiving gefitinib, 22 patients had NSCLC. In the NSCLC group, three patients had stable disease and received gefitinib for six months or more. Of the three patients, one was taking 150 mg/day and had had earlier radiotherapy and chemotherapy with carboplatin (Paraplatin®, Bristol-Myers Squibb) and fluorouracil and with docetaxel and gemcitabine (Gemzar®, Eli Lilly); one was taking 225 mg/day and had received radiotherapy and carboplatin; and the other was taking 300 mg/day and had previously undergone surgery and chemotherapy with gemcitabine and paclitaxel (e.g., Taxol®, Bristol-Myers Squibb).

The authors concluded that gefitinib was generally well tolerated.13 Most adverse drug events (ADEs) were controllable and reversible at doses up to 600 mg/day. Most DLTs occurred in patients receiving 800 to 1,000 mg/day. Stabilization of tumors was clinically meaningful, with multiple tumor types at various treatment doses.

**The Ranson Study**10

Ranson et al. conducted a phase I, escalating, multiple-dose trial to investigate the tolerability, pharmacokinetics, and antitumor activity of gefitinib in patients with solid malignant tumors. The study was designed to evaluate dose levels of 50, 100, 150, 225, 300, 400, 525, 700, and 925 mg/day. Additional patients could be recruited for the study if they had not completed the first 14-day daily dosing period for any reason other than the occurrence of DLT. DLT was defined as any NCI–CTC grade 3 or 4 drug-related toxicity, significant corneal epithelial change in two patients at a specific dose, or a PR interval of more than 217 milliseconds. Escalation of the dose was to continue up to 925 mg/day unless DLT was observed in two or more patients at a specific dose in the first 28 days.

Sixty-four patients received gefitinib treatment, with seven to 10 patients receiving each dosage. The dosage levels were 50, 100, 150, 225, 300, 500, 525, and 700 mg/day. As a result of a grade 3 or 4 drug-related DLT of diarrhea in three patients, the dose was not escalated above 700 mg/day.

Overall, patients had a variety of tumors, but the most common tumor was NSCLC (n = 16). All 16 patients had received at least one earlier chemotherapy regimen. There were 14 platinum-based regimens, 11 with gemcitabine, and five with vinorelbine tartrate (Navelbine®, GlaxoSmithKline) in addition to other chemotherapy agents.

Exposure to gefitinib increased after administration of doses greater than 50 mg/day. The Cmax and AUC concentration increased from 41 to 756 ng/ml and from 529 to 8,683 ng/hour per ml, respectively, after daily oral doses of 100 to 700 mg. When the plasma concentrations were elevated because of higher doses, skin and gastrointestinal ADEs occurred more often.
Table 2  Summary of Gefitinib Results in Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Endpoint</th>
<th>No.</th>
<th>Dose</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Phase I</td>
<td></td>
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<tr>
<td>Baselga et al.(^{13})</td>
<td>Safety Tolerability Pharmacokinetics Pharmacodynamics</td>
<td>88</td>
<td>150–1,000 mg/day dose escalation</td>
<td>Gefitinib was well tolerated, and side effects were reversible when the medication was discontinued. Disease progression was stabilized across a range of tumor types and doses. Inhibition of EGFR signaling was indicated by pharmacodynamic changes in skin.</td>
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<tr>
<td>Ranson et al.(^{10})</td>
<td>Tolerability Pharmacokinetics Antitumor activity</td>
<td>64</td>
<td>50–925 mg/day dose escalation</td>
<td>Gefitinib was well tolerated. Dose-limiting toxicity occurred at doses above that at which antitumor activity was seen. Once-daily dosing of gefitinib tablets was confirmed by pharmacokinetic analysis.</td>
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<tr>
<td>Uejima et al.(^{3,14})</td>
<td>Tolerability Pharmacokinetics Efficacy of intermittent daily oral dosing</td>
<td>31</td>
<td>50–700 mg/day intermittent dosing</td>
<td>Gefitinib was generally well tolerated at all doses with no dose-limiting toxicities occurring up to 525 mg/day. A confirmed partial response was demonstrated in 22% of patients.</td>
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<td>Phase II</td>
<td></td>
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<td>IDEAL-1(^{15,17})</td>
<td>Tumor response rate Safety Disease control rate Progression-free survival Overall survival</td>
<td>210</td>
<td>250 or 500 mg/day</td>
<td>There was no difference in response rate, disease control rate, progression-free survival, overall safety, or safety between groups. The 250-mg dose of gefitinib is as efficacious as the 500-mg dose with a more favorable side-effect profile. Gefitinib 250 mg showed clinically significant antitumor activity in patients who had previously received platinum-based therapy.</td>
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<tr>
<td>IDEAL-2(^{16,18})</td>
<td>Tumor response rate Disease-related symptom response Safety</td>
<td>216</td>
<td>250 or 500 mg/day</td>
<td>Tumor response rate, symptom response, and safety were similar among the two treatment groups. Clinically significant antitumor activity was demonstrated in both groups.</td>
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<tr>
<td>Phase III</td>
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<tr>
<td>INTACT-1(^{19})</td>
<td>Overall survival Progression-free survival Time to worsening of symptoms Symptom improvement Objective tumor response Disease control rate Quality of life Safety</td>
<td>1,093</td>
<td>CT* + placebo or CT + gefitinib 250 mg/day or CT + gefitinib 500 mg/day</td>
<td>Between the three groups, there were no statistically significant differences in overall survival, progression-free survival, or time to worsening of symptoms. Side effects were similar among all three treatment groups. CT plus gefitinib did not improve treatment outcomes.</td>
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<tr>
<td>INTACT-2(^{20})</td>
<td>Overall survival Progression-free survival Time to worsening of symptoms Symptom improvement Objective response rate Disease control rate Quality of life Safety Adverse-event profiling</td>
<td>1,839</td>
<td>CT† + placebo or CT + gefitinib 250 mg/day or CT + gefitinib 500 mg/day</td>
<td>There were no statistically significant differences in overall survival, progression-free survival, or time to worsening of symptoms between the three treatment groups. CT plus gefitinib failed to improve survival in this trial. Adverse events were similar in all treatment groups.</td>
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</table>

\(^{*}\) Chemotherapy = six cycles of gemcitabine (Gemzar\(®\)) 1,250 mg/m\(^2\) on days one and eight, plus cisplatin (Platinol\(®\)) 80 mg/m\(^2\) on day one.

\(^{†}\) Chemotherapy = carboplatin (Paraplatin\(®\)) (AUC = 6) + paclitaxel (Taxol\(®\)) (225 mg/m\(^2\)) every three weeks for six weeks.

AUC = area under the curve; CT = chemotherapy; EGFR = epidermal growth factor receptor.
Four patients with NSCLC had a partial response with doses of 300, 400, 525, and 700 mg/day. Three other NSCLC patients had stabilized disease with doses of 225, 400, and 525 mg/day. Six NSCLC patients continued to take the study drug regimen for three or more months. The authors concluded that gefitinib, when administered for 14 consecutive days every 28 days, was well tolerated. DLT occurred at a dose well beyond that at which antitumor activity was observed. The pharmacokinetic analysis demonstrated that oral gefitinib could be administered once daily.

**The Uejima Study**

Uejima et al. examined the tolerability, pharmacokinetics, and efficacy of intermittent daily oral dosing of gefitinib in Japanese patients with solid tumors (n = 31, 23 with NSCLC). Initially, patients were given a single oral dose of gefitinib and were then observed for 10 to 14 days. Thereafter, escalating oral doses of gefitinib (50–900 mg/day) were to be given for 14 days, followed by 14 days of observation.

The most frequent ADEs were skin reactions, gastrointestinal symptoms, and elevated transaminase levels. Grade 3 elevations in aspartate and alanine transaminases (SGOT and SGPT) were observed in two patients, one who received 225 mg and one who received 525 mg. After multiple dosing for 14 days, gefitinib exhibited dose-related increases in mean Cmax and AUC concentration (73.8–384 ng/ml and 1,236–5,875 ng/hour per ml, respectively); the half-life was 45 hours.

Five patients with NSCLC (22%) showed a confirmed partial response at the following doses: 225 (one patient), 400 (one patient), 525 (two patients), and 700 mg (one patient); these responses persisted for four months, six or more months, one month, three or more months, and two or more months, respectively.

**Phase II**

IDEAL-1 and IDEAL-2 were two randomized, double-blind phase II trials that investigated tumor response and safety of oral gefitinib in patients with locally advanced or metastatic NSCLC. In IDEAL-1, patients had not responded to one or two chemotherapy regimens, of which one had to be platinum-based therapy. IDEAL-2 patients had not responded to two or more chemotherapy regimens containing platinum and docetaxel, given simultaneously or separately. Patients in both studies were given 250 or 500 mg/day of gefitinib continuously until their disease progressed or the doses reached unacceptable levels of toxicity.

The Functional Assessment of Cancer Therapy–Lung (FACT-L) and its disease-specific, seven-item Lung Cancer Subscale were also used in the IDEAL-1 and IDEAL-2 studies to assess disease-related symptoms and quality of life. Over a four-week time frame, increases in the FACT-L by six or more points and in the Lung Cancer Subscale by two or more points, respectively, were defined as an improvement in disease-related symptoms and quality of life.

**IDEAL-1**

In the IDEAL-1 study (n = 210), patients were unresponsive to one (56%) or two (44%) previous chemotherapy regimens. In the 250- and 500-mg/day groups, tumor response rates were 18.4% versus 19%, and progression-free survival was 2.7 versus 2.8 months, respectively. In general, tumor response rates were also similar when gefitinib was used as a second-line or third-line treatment (17.9% vs. 19.8%). More patients taking 500 mg/day experienced drug-related grade 3 or 4 ADEs (30.2%) and withdrawals (9.4%); patients taking 250 mg/day experienced grade 3 ADEs (8.7%) and fewer withdrawals (1.9%).

The authors evaluated symptom improvement and compliance in 140 IDEAL-1 patients. Overall, quality of life improved within 29 days in 24% of patients receiving gefitinib 250 mg/day and in 22% of patients receiving 500 mg/day. The authors concluded that gefitinib provided clinically significant antitumor activity, symptom relief, and improved quality of life in patients with advanced NSCLC who had previously undergone a platinum-based regimen.

**IDEAL-2**

Outcomes in IDEAL-2 were similar to those of IDEAL-1. IDEAL-2 included 216 patients who had not responded to two previous chemotherapy regimens (41%), three regimens (33%), or four or more regimens (25%). In the groups receiving 250 and 500 mg/day, tumor response rates were 11.8% (95% confidence interval [CI], 6.2–19.7) and 8.8% (95% CI, 4.3–15.5). Median survival was 6.1 (95% CI, 4.8–7.7) and 6.0 (95% CI, 4.3–7.2) months, respectively. Grade 3 or 4 drug-related ADEs occurred in 6.9% of the patients taking gefitinib 250 mg/day and in 17.5% of the patients taking 500 mg/day.

The symptom response rate was a primary endpoint of IDEAL-2; therefore, patients with disease-related symptoms, as assessed by a score of 24 or higher on the Lung Cancer Subscale, were included in the study. Symptom response was seen in 43% of patients taking 250 mg/day and in 34% of patients taking 500 mg/day. Improved quality of life occurred in 34% of patients taking 250 mg/day and in 23% of patients taking 500 mg/day. Longer survival was observed in patients with symptom response (8.1 months) than in patients who did not show symptom response (3.7 months).

The authors concluded that in patients who had had an earlier platinum or docetaxel chemotherapy regimen, both doses of gefitinib demonstrated clinically significant antitumor activity and had an acceptable tolerability profile. As in IDEAL-1, symptom improvement was correlated with tumor response.

**Phase III**

The Iressa NSCLC Trials Assessing Combination Treatment (INTACT-19 and INTACT-20) were two randomized, double-blind, placebo-controlled studies of chemotherapy plus gefitinib in patients with NSCLC. Study participants were chemotherapy-naïve patients with stage III or IV disease, age 18 years or older, and a performance status of 0 to 2. The patients were randomly selected to receive chemotherapy plus placebo, chemotherapy plus 250 mg/day of gefitinib, or chemotherapy plus 500 mg/day of gefitinib. Treatment with gefitinib or placebo was continued until disease progressed.

In both studies, the primary endpoint was overall survival. Secondary endpoints included progression-free survival and time to worsening of disease-related symptoms. Symptom improvement, objective tumor response rate, disease
control rate, quality of life, and ADEs were also evaluated.

**INTACT-1**

The chemotherapy regimen consisted of six cycles of gemcitabine 1,250 mg/m² on days one and eight, plus cisplatin (Platino®), Bristol-Myers Squibb) 80 mg/m² on day one. Across all three arms (placebo, 250 mg, and 500 mg), there were no statistically significant differences in overall survival. The median for overall survival was 11.1 (CI, 10.1–11.9) for the placebo group, 9.9 (CI, 8.7–10.8) for the 250-mg group, and 9.9 (CI, 8.8–11.4) for the 500-mg group. In addition, progression-free survival and time to worsening of symptoms were not statistically significant.

The toxicity profile was similar across all three groups, except for additive dose-dependent diarrhea and skin rash.

The authors concluded that combination therapy with gefitinib plus two other chemotherapy agents did not improve outcomes (overall survival, time to progression, or tumor response rates) in patients with advanced NSCLC.

**INTACT-2**

The chemotherapy regimen consisted of carboplatin (AUC = 6) plus paclitaxel (225 mg/m²) every three weeks for at least six cycles. In the placebo arms (250 and 500 mg), there were no statistically significant differences in overall survival. The median for overall survival was 9.9 (CI, 8.9–11.1) for the placebo group, 9.8 (CI, 8.4–10.6) for the 250-mg group, and 8.7 (CI, 8.0–10.3) for the 500-mg group. Moreover, progression-free survival and time to worsening of symptoms were not statistically significant.

As in INTACT-1, combination therapy with gefitinib did not improve survival in patients with stage III or IV NSCLC, and the dose-dependent ADEs of diarrhea and skin rash occurred at a higher rate in the patients receiving gefitinib.

**DRUG INTERACTIONS**

In two open, randomized, crossover trials in healthy male volunteers, the mean AUC concentration and Cmax were decreased by 83% and 65%, respectively, when patients (n = 18) were given 500 mg of gefitinib alone on day 10 of a 16-day dosing regimen of 600 mg/day of rifampicin (e.g., Rimactone®, Geneva), a potent CYP-3A4 inducer. In the second trial, two cohorts (n = 24 each) received 500 mg or 250 mg of gefitinib on the fourth day of a 12-day dosing regimen of iraconazole (Sporanox®, Janssen, Ortho Biotech) 200 mg/day, a potent CYP-3A4 inhibitor. In this group, the AUC concentration increased by 58% in the patients taking 250 mg and by 80% in those taking 500 mg; the Cmax increased by 32% in the 250-mg group and by 51% in the 500-mg group. Inducers of CYP-3A4 increase the metabolism of gefitinib and decrease its plasma concentrations, whereas inhibitors of CYP-3A4 decrease gefitinib metabolism and increase gefitinib plasma concentrations.1

When gefitinib 500 mg/day was given in combination with metoprolol (Lopresor®, Novartis) to patients with solid tumors for 28 days, there was a 30% increase in levels of metoprolol, which is a substrate of CYP-2D6. Gefitinib inhibited CYP-2C19 by 24% and CYP-2D6 by 43% at study concentrations of 5,000 ng/ml.1 Renitidin (Zantac®, Glaxo-SmithKline) with sodium bicarbonate, used to maintain the gastric pH above 5.0, reduced the mean gefitinib AUC concentration by 44%. Elevations in the International Normalized Ratio (INR) and bleeding events have been reported in patients taking warfarin sodium (Coumadin®, DuPont) while they were also taking gefitinib.1

**ADVERSE DRUG REACTIONS**

Gefitinib has been well tolerated in phase I, II,10,13,14, II,15–18 and III10,19 clinical trials in patients with NSCLC. The most commonly reported ADEs were dose-dependent and reversible skin rash, gastrointestinal symptoms (diarrhea, nausea, vomiting, constipation, abdominal pain), anemia, and elevated hepatic transaminases.10,13,14,15–20 Other common reactions in the study by Ranson et al.10 were conjunctivitis, dyspnea, increased cough, asthenia, somnolence, and headache.

There were reports of eye pain and corneal erosion or ulcer, sometimes in association with aberrant eyelash growth.20 In a study by Herbst et al.,4 one patient withdrew from the study because of corneal epithelial damage, caused by an ingrown eyelash; however, the damage was reversed following gefitinib withdrawal and supportive care measures.23

Postmarketing studies in Japan have reported the occurrence of interstitial lung disease (ILD).

**Skin Reactions**

In all three phases of the clinical trials, skin reactions occurred in the majority of patients.10,13,14,15–20 Reactions generally occurred between days 10 and 14 of treatment and resolved during the off-treatment period, with a decrease in frequency observed over each treatment period.10 Most reactions were grade 1 or 2 acne-like rash on an erythematous base.10,13,14 Rashes were transient in most cases, and there were no reports of scarring or other permanent skin changes.10,13,14 Grade 3 or 4 reactions were observed primarily at doses greater than 400 mg/day.10,13,14

**Diarrhea**

Diarrhea also occurred in all three phases, most commonly during the first treatment period.10,13,14,15–20 It was described as a watery or loose stool that was negative for blood or mucus.13 Usually, grade 1 or 2 diarrhea was observed, but doses as low as 300 mg/day were associated with grade 3. Diarrhea usually resolved with cessation of therapy and supportive care measures.10,13,14

**Pulmonary Toxicity**

(Interstitial Lung Disease)

In Japan, acute ILD occurred in about 1% to 2% of patients receiving gefitinib.21 Overall, ILD has occurred in approximately 1% of patients receiving gefitinib, and fatalities have occurred in about one-third of patients with ILD.1 Generally in those who received previous radiation therapy (31%), earlier chemotherapy (57%), and no prior therapy (12%).1 Symptoms of ILD include acute-onset dyspnea and an occasional cough or low-grade fever that may worsen and require hospitalization.1 Increased mortality was observed in patients with lung comorbidities whose condition deteriorated with gefitinib therapy.1,21

**DOSEAGE AND ADMINISTRATION**

Gefitinib is administered as an oral 250-mg tablet to be taken with or without food.1 In clinical trials, higher doses resulted in greater toxicity and did not provide a superior response.10,13,14,15–18 Dosage adjustments are not required on continued on page 655
the basis of the patient’s age, weight, sex, ethnicity, or renal function. In patients with hepatic impairment caused by liver metastases, bioavailability levels were similar to those observed in patients with normal liver function, signifying that there is no need for dose modification.22

Gefitinib therapy should be withheld if an acute onset or worsening of pulmonary symptoms occurs, and it should be discontinued if ILD is confirmed.1 In patients receiving a potent CYP-3A4 inducer, such as rifampicin or phenytoin (Dianin®, Pfizer), clinicians should consider increasing the dose of gefitinib to 500 mg daily and should monitor patients for drug reactions, clinical response, and ADEs.1 Therapy should be withheld if eye pain or other related eye symptoms occur, and the aberrant eyelash, if present, should be removed.1

CONCLUSION

Gefitinib is the first in a new class of agents.3 It is indicated as monotherapy for the treatment of patients with locally advanced or metastatic NSCLC after failure of both platinum-based and docetaxel chemotherapies.1 Unlike the side-effect profile associated with most other cytotoxic agents, gefitinib has an acceptable tolerability profile, and most drug-related ADEs are mild and reversible.1,13,14,15–20.

In clinical studies, improved quality of life seemed to correlate with those patients who had partial responses to therapy or stable disease.15–16 Gefitinib is a safe and effective second-line treatment option available for patients with advanced NSCLC.

REFERENCES


Disclosure

Dr. Ruffin and Dr. Harris have no commercial or industry relationships to disclose in relation to this article.