Role of anaplastic lymphoma kinase inhibition in the treatment of non-small-cell lung cancer

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Lung cancer is the most common cause of cancer-related death in the United States for both men and women. An estimated 224,210 new cases of lung cancer were diagnosed in 2014, with an estimated 159,260 deaths. The disease is divided into two primary classifications: small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). NSCLC is more prevalent than SCLC, comprising 84% of all lung cancer diagnoses. Cigarette smoking is the primary risk factor for both NSCLC and SCLC, with 85–90% of all lung cancer diagnoses being attributed to smoking exposure. Five-year survival rates for patients with lung cancer are strongly dependent on the stage of disease at the time of diagnosis. Patients with early-stage disease have a five-year survival rate of 54%, while the prognosis for those with advanced-stage disease is much poorer, with reported five-year survival rates of 6–18%.

The treatment for early-stage lung cancer focuses on surgical resection with curative intent, with the possible use of chemoradiation depending on the extent of disease. In the advanced stages of lung cancer, the focus of treatment is palliation through the use of chemotherapy, radiation, or other targeted therapies. Standard cytotoxic chemotherapy for advanced lung cancer is platinum based; common two-agent regimens, or “platinum doublets,” include cisplatin or carboplatin in combination with docetaxel, gemcitabine, paclitaxel, or pemetrexed. In the last 10 years, there has been notable progress in the treatment of advanced-stage NSCLC with the development of mutation-targeted therapies. At diagnosis, patients with metastatic NSCLC who demonstrate a histology of adenocarcinoma or large-cell carcinoma, as well as those with unspecified histology, are tested for ALK mutation status. ALK-positive patients benefit from treatment with ALK inhibitors.

Purpose. Published data on the clinical efficacy, safety, dosage and administration, and costs of the anaplastic lymphoma kinase (ALK) inhibitors crizotinib and ceritinib in the treatment of non-small-cell lung cancer (NSCLC) are reviewed and compared.

Summary. The ALK protein functions as a transmembrane receptor tyrosine kinase; rearrangements of the ALK gene are associated with the development of NSCLC with adenocarcinoma histology. Crizotinib is an oral tyrosine kinase inhibitor approved in 2011 as a first-line therapy for patients with metastatic ALK mutation–driven NSCLC. Significantly improved response rates and progression-free survival (PFS) have been reported with the use of crizotinib therapy versus standard chemotherapy, but mutations conferring resistance to treatment develop in most cases. The second-generation ALK inhibitor ceritinib was approved in 2014 for the treatment of ALK-mutated NSCLC in patients who are intolerant or develop resistance to crizotinib. In a clinical trial of ceritinib involving 130 patients with ALK-positive NSCLC, the majority of whom had experienced disease progression during crizotinib use, patients receiving at least 400 mg of ceritinib daily had an overall response rate of 56% and median PFS of seven months. Adverse effects commonly reported with the use of either drug include visual disturbances, gastrointestinal disorders (e.g., diarrhea), and liver enzyme abnormalities.

Conclusion. The tyrosine kinase inhibitors crizotinib and ceritinib provide an effective treatment approach for patients with ALK-mutated NSCLC. Efficacy data for both crizotinib and ceritinib indicate improved response rates and PFS with the use of either drug as an alternative to standard chemotherapy.
for mutations in the genes coding for epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK). Based on the presence of EGFR and ALK mutations, a targeted therapy is selected as the first-line treatment. Approximately 15–25% of patients with adenocarcinoma test positive for one of these targetable mutations. EGFR mutations occur in 10–20% of patients with NSCLC adenocarcinoma. These patients are eligible for treatment with EGFR-directed therapies such as erlotinib and afatinib. The rate of ALK mutations in patients with NSCLC of adenocarcinoma histology is low, ranging from 2% to 8%. Higher rates of ALK mutation have been identified in patients who never smoked or have a light smoking history (<10 pack-years) and younger patients. Patients testing positive for an ALK mutation are eligible for treatment with targeted therapies that inhibit the expression of ALK. Current therapies available to target ALK-mutant tumors include the tyrosine kinase inhibitor (TKI) crizotinib and the newer TKI ceritinib. For patients without an actionable driver mutation, standard platinum-based chemotherapy is the first-line treatment of choice.

The twofold purpose of this article is to review the role of ALK mutations in NSCLC and to compare the clinical efficacy, safety, recommended dosage and administration, and costs of crizotinib and ceritinib therapy for the treatment of metastatic NSCLC.

**ALK rearrangements in NSCLC**

The ALK protein is a member of the insulin receptor family and functions as a transmembrane receptor tyrosine kinase. Soda and colleagues, in 2007, identified the fusion of the ALK gene with the gene coding for the protein echinoderm microtubule-associated protein-like 4 (EML4) in patients with NSCLC. The EML4 and ALK genes are both located on the short arm of chromosome 2. Fusion of these two genes occurs secondary to an inversion on chromosome 2 that causes the amino terminus of EML4 to join the intracellular catalytic domain of ALK. Fusions between EML4 and ALK can occur along different locations of chromosome 2, resulting in variations of the EML4-ALK fusion protein. Eleven different EML4-ALK variants have been described; however, differences in clinical outcomes, if any, associated with these variants have not been identified.

This fusion of EML4 with ALK results in constitutive activation of ALK, leading to dysregulation of downstream signaling pathways that control cell proliferation and apoptosis. The aberrant signaling of these pathways prevents apoptosis and causes excessive cell proliferation, contributing to the development of NSCLC (Figure 1).

Since the discovery of the EML4-ALK protein, fusions of ALK with genes other than EML4 have been identified in patients with NSCLC. These ALK fusion partners also have oncogenic potential and are sensitive to the currently approved ALK inhibitors, crizotinib and ceritinib.

Testing for ALK mutations in patients with NSCLC is recommended, along with testing for EGFR mutations, in all patients with adenocarcinoma or large-cell carcinoma and, possibly, in patients with poorly differentiated tumors. Fluorescence in situ hybridization (FISH) assay is the diagnostic method of choice for identifying aberrant ALK expression. FISH is also able to identify all possible ALK fusion variants, leading to greater sensitivity. Other possible testing methods include immunohistochemistry (IHC) and reverse transcriptase polymerase chain reaction. In many medical centers, IHC is performed initially as a prescreening evaluation and FISH is used for confirmatory testing.

Although ALK mutations are rare, patients with NSCLC with adenocarcinoma histology are routinely screened for such mutations at diagnosis. Patients testing positive for ALK mutations are considered eligible for ALK-directed therapies.

**ALK mutation-targeted therapies**

Since identification of the oncogenes ALK and EGFR, the development of targeted therapies has led to improved response rates and progression-free survival (PFS) in patients with metastatic NSCLC harboring ALK and EGFR mutations. Despite a pronounced response rate, ALK-targeted therapy does not improve overall survival, as resistance to therapy typically develops. There are currently two Food and Drug Administration (FDA)–approved agents to target ALK rearrangement in NSCLC, crizotinib and ceritinib.

Ceritinib is currently recommended for first- or second-line treatment in patients with metastatic disease who test positive for ALK mutations, while ceritinib is only approved for patients with resistance or intolerance to crizotinib therapy.

**Clinical pharmacology.** Crizotinib and ceritinib are both oral multikinase inhibitors that function to competitively inhibit ALK. Ceritinib is a second-generation ALK inhibitor with 20 times greater potency against ALK than that of crizotinib. Administration of crizotinib or ceritinib results in reduced phosphorylation of ALK, leading to reduced immature-cell proliferation and regression of tumors. Crizotinib also has inhibitory activity against the mesenchymal–epithelial transition (MET), hepatocyte growth factor receptor, and ROS proto-oncogene 1 (ROS1) tyrosine kinases, as well as the macrophage stimulating 1 receptor tyrosine kinase. Unlike crizotinib, ceritinib does not block the MET tyrosine kinase but does inhibit the insulin-like growth factor 1 receptor, insulin receptor, and ROS1 kinase, leading to variations in the adverse-effect profiles between the...
two drugs.\textsuperscript{18} The increased potency of ceritinib against ALK has resulted in favorable response rates in patients with NSCLC who are resistant to crizotinib treatment.

Crizotinib and ceritinib are both metabolized by and inhibit cytochrome P-450 (CYP) isozyme 3A4/5, leading to potential drug–drug interactions. Strong CYP3A4/5 inhibitors or inducers may alter plasma crizotinib and ceritinib concentrations and should be avoided. Ceritinib’s manufacturer specifically recommends a dose reduction of around 33% (rounded to the nearest 150-mg dosage strength) if strong CYP3A4/5 inhibitors are used concomitantly.\textsuperscript{14} Grapefruit and grapefruit juice should also be avoided with concomitant crizotinib or ceritinib use due to grapefruit’s ability to inhibit CYP3A4/5.\textsuperscript{14,15} Drugs metabolized by CYP3A4/5 substrates should be avoided or the doses reduced if there is a narrow therapeutic window. Ceritinib also has inhibitory activity against the CYP2C9 isozyme. Concurrent use of medications with a narrow therapeutic index, such as warfarin, may require a dose reduction and should be monitored appropriately.

**Clinical efficacy.** *Crizotinib.* Crizotinib was initially evaluated for safety and tolerability in an open-label Phase I trial involving 37 patients with advanced malignancy.\textsuperscript{19} Evaluation of dose-escalation cohorts established 250 mg twice daily as the maximum tolerable dose. During this initial investigation, 2 patients with NSCLC associated with ALK rearrangements exhibited a substantial response relative to other trial participants, leading to an expanded cohort investigation in patients with ALK mutation–driven NSCLC.\textsuperscript{19,20} The patients (\(n = 149\)) were typically lifetime nonsmokers or former smokers (99%) with adenocarcinoma histology (97%); the median age was 52 years. Crizotinib had demonstrated efficacy in this population, with an objective response rate (either a partial or a complete response) of 60.8%. The median time to response was 7.9 weeks, and the median duration of response was 49.1 weeks.\textsuperscript{20} This trial provided the basis for FDA approval of crizotinib in patients previously treated with ceritinib.

Since the promising results of crizotinib treatment were demonstrated in the Phase I investigation, Phase II and III trials have been conducted.\textsuperscript{21–23} Preliminary results of an ongoing Phase II trial of crizotinib therapy for advanced ALK-mutated NSCLC indicated an objective response rate of 59.8% in 259 patients previously treated with one or more chemotherapy agents.\textsuperscript{21} The median time to treatment re-
response was 6.1 weeks, and median PFS was 8.1 months (95% confidence interval [CI], 6.8–9.7 months). As in the Phase I trial, most of these patients had adenocarcinoma histology (94%) and were lifetime nonsmokers or former smokers (95%).

In Phase III trials, crizotinib has been studied as both first- and second-line therapy. A recently published randomized, open-label Phase III trial compared the effects of crizotinib and standard second-line chemotherapy. Three-hundred forty-three patients with ALK-positive, previously treated patients with NSCLC were randomly assigned to receive crizotinib 250 mg by mouth twice daily or standard i.v. chemotherapy with either pemetrexed 500 mg per square meter of body surface area (500 mg/m²) or docetaxel 75 mg/m² every three weeks. Crizotinib was superior to single-agent second-line standard chemotherapy, with overall response rates of 65% and 20%, respectively (p < 0.001). PFS was also significantly improved in the crizotinib group (median, 7.7 months versus 3.0 months with docetaxel or pemetrexed [p < 0.001]). In addition to improved response, crizotinib was associated with subjective improvements (relative to standard second-line chemotherapy) in quality of life (as reported by patients on the European Organization for Research and Treatment of Cancer quality-of-life questionnaire for lung cancer) (p < 0.001) and lung cancer symptoms (cough, dyspnea, fatigue, alopecia, insomnia, and pain; p < 0.001 for all comparisons). No significant between-group differences in overall survival were noted; however, 64% of the chemotherapy group crossed over to crizotinib therapy, likely confounding the results.

Crizotinib was evaluated as a first-line treatment option in a randomized, open-label Phase III trial. Three-hundred forty-three patients with advanced ALK-mutated NSCLC who had received no prior treatment were assigned to receive crizotinib 250 mg by mouth twice daily or i.v. chemotherapy. The chemotherapy used in this study consisted of pemetrexed 500 mg/m² with either cisplatin 75 mg/m² or carboplatin (adjusted to attain a target area under the concentration–time curve of 5–6 mg/mL/min) administered every three weeks for six cycles. Median PFS was significantly longer in the crizotinib group than in the chemotherapy group (10.9 months versus 7.0 months, p < 0.001). The objective response rate was also superior in the crizotinib group relative to the chemotherapy group (74% versus 45%, p < 0.001). There was no significant difference in overall survival between the two groups; however, 70% of patients in the chemotherapy group crossed over to crizotinib therapy.

Ceritinib. Ceritinib was approved for the treatment of ALK-mutated NSCLC in patients who are resistant to or unable to tolerate crizotinib. Its approval was based on results from one Phase I dose-escalation study of 130 patients with ALK-positive metastatic NSCLC. A total of 114 of these patients received at least 400 mg of ceritinib per day and were found to have an overall response rate of 58% (95% CI, 48–67%). PFS in this group was 7.0 months (95% CI, 5.6–9.5 months). The majority of patients in the study population had previously received treatment with crizotinib (68%). The overall response rate in the crizotinib-treated group was 56% (95% CI, 45–67%), as compared with a response rate of 62% (95% CI, 44–78%) among patients who had not received previous crizotinib treatment. Of the patients treated with at least 400 mg of ceritinib daily, 64% (95% CI, 50–74%) had a duration of response of 6 months or longer. Unlike crizotinib, ceritinib was also demonstrated to have activity against metastatic central nervous system (CNS) lesions. Overall survival for this study was not reached at the data collection cutoff.

Safety

Although crizotinib and ceritinib have similar toxicity profiles, there are notable distinctions between the two. The most common reported toxicities (all grades) of crizotinib in clinical trials included visual disorders, such as visual impairment, photopsia, blurred vision, floaters, diplopia, and photophobia (62% of patients who had one or more of these events); edema (38%); and gastrointestinal (GI) events, including nausea (57%), diarrhea (49%), vomiting (45%), and constipation (38%). Visual events generally occurred within two weeks of initiation of therapy and were reversible with crizotinib discontinuation. No permanent effects on vision were noted in clinical trials. Approximately 4% of adverse effects were classified as grade 3 or 4. Rare but serious adverse events reported with crizotinib included pneumonitis, neutropenia, elevated liver transaminases, and Q-Tc interval prolongation.

Like crizotinib, ceritinib was commonly associated with GI events during clinical trials; however, the reported rates of these adverse effects are higher with ceritinib. In the Phase I dose-escalation study of ceritinib, reported GI adverse effects (all grades) included nausea (82%), diarrhea (75%), and vomiting (65%). Supportive care strategies for managing the GI toxicity associated with crizotinib and ceritinib, including the administration of anti-emetics and fluid replacement therapy, should be used as needed.

Unlike crizotinib, ceritinib does not commonly cause visual disturbances. In clinical trials, the overall reported rate of visual dysfunction (grade 1 or 2) with ceritinib was 9%, as compared with the 60% rate reported with crizotinib. In patients with baseline visual dysfunction, such as cataracts, and patients whose activities of daily living require visual acuity, ceritinib may be a more preferable option. Other common
adverse effects (any grade) reported in association with ceritinib use include fatigue (47%), hyperglycemia (49%), and increased levels of liver transaminases (35%).

During clinical development, ceritinib use was associated with higher rates of serious (grade 3 or 4) adverse events than were reported in trials of crizotinib, including elevations in alanine transaminase (ALT) (27% of study participants) or aspartate transaminase (AST) (13%), hyperglycemia (13%), diarrhea (6%), and increased lipase levels (10%). Overall, a total of 59% of study participants required a dose reduction due to toxicity, and 10% of patients required permanent discontinuation of ceritinib. The majority of adverse effects were reversible with treatment discontinuation.

The rare but serious adverse effects (any grade) associated with ceritinib are similar to those associated with crizotinib and include interstitial pneumonitis (4% of patients) and Q-Tc interval prolongation of >60 msec (3% of patients). Patients receiving either crizotinib or ceritinib should be monitored for shortness of breath and coughing during therapy. Crizotinib or ceritinib use should be discontinued if interstitial pneumonitis is suspected. Patients with congenital long Q-T syndrome should not be treated with crizotinib or ceritinib. Electrolyte and electrocardiography monitoring are suggested for patients with baseline cardiac dysfunction and those who are taking other medications known to prolong the Q-Tc interval.

Overall, the safety profile of ceritinib is similar to that of crizotinib; however, the severity of adverse effects appears to be more pronounced with ceritinib treatment (Table 1). It is important to note the higher rate of grade 3 or 4 diarrhea reported with ceritinib versus crizotinib use (6% versus 0%), as well as the high rates of hyperglycemia (13% versus 0%), liver enzyme abnormalities (27% versus 17%), and grade 3 or 4 nausea (4% versus 1%), in clinical trials. The overall rate of visual disturbances (any grade), however, was much lower with ceritinib use than with crizotinib use in clinical trials (9% versus 60%); ceritinib also offered advantages in terms of reported rates of grade 3 or 4 neutropenia (0% versus 12%) and edema of any grade (0% versus 31%).

Limitations
Unfortunately, the dramatic response to crizotinib often seen in patients with ALK-mutated NSCLC is not permanent. Resistance to crizotinib typically develops within one to two years of treatment initiation. Resistance mechanisms emerge through mutations in the ALK kinase domain, EML4-ALK amplification, or dominant expression of other oncogenic drivers. Mutations

Table 1. Adverse Effects of Crizotinib and Ceritinib Reported in Clinical Trial Participants

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Crizotinib (n = 172)</th>
<th>Ceritinib (n = 255)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grade 3 or 4 (%)</td>
</tr>
<tr>
<td>Severe adverse events</td>
<td>2.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q-Tc interval prolongation</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Visual disorders</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>42</td>
<td>2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
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<td>1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>47</td>
<td>1</td>
</tr>
<tr>
<td>Other disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Edema</td>
<td>31</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td>Laboratory test abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT elevations</td>
<td>76</td>
<td>17</td>
</tr>
<tr>
<td>AST elevations</td>
<td>61</td>
<td>9</td>
</tr>
<tr>
<td>Hyperglycemia</td>
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<td>0</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>Lipase elevations</td>
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<td>0</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>51</td>
<td>9</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>49</td>
<td>12</td>
</tr>
</tbody>
</table>

*ALT = alanine transaminase, AST = aspartate transaminase.*
in the ALK kinase domain have been detected in 29% of crizotinib-resistant patients, while amplification of EML4-ALK expression has been identified in 9%.36,32,33 The most common mutations in the ALK kinase domain conferring resistance to crizotinib are L1196M and G1269A.16

Ceritinib was developed to overcome the treatment resistance observed with crizotinib use. In cell line models, ceritinib was demonstrated to have activity against crizotinib-resistance mutations in the ALK kinase domain, including the L1196M, G1269A, I1171T, S1206Y, and C1156Y mutations.25,28

Despite initial activity against crizotinib-resistant NSCLC, patients treated with ceritinib inevitably relapse, sometimes due to the emergence of new resistance mutations. Little is known about the mechanisms that confer resistance to ceritinib; in one small study, 5 of 11 patients with progressive NSCLC despite ceritinib therapy had acquired mutations in the ALK kinase domain at position G1202 or F1174.28

Along with the development of resistance, poor CNS activity is another limitation of ceritinib therapy. Case reports have described the ineffectiveness of ceritinib in controlling brain metastases in patients with NSCLC.29,31 Furthermore, in the Phase I and II trials of ceritinib, the brain was the most common site of relapse in patients with disease progression.

Compared with crizotinib, ceritinib is thought to have increased CNS penetration. Patients with crizotinib-resistant disease with CNS involvement experienced reductions in CNS lesions with ceritinib treatment in clinical trials.34 It is currently unknown if ceritinib should be used as first-line therapy before crizotinib in patients with CNS metastatic disease at presentation.

Dosage and administration

The recommended dosage of crizotinib is 250 mg orally twice daily, to be administered with or without food.15 Treatment with crizotinib should be continued until disease progression or the development of intolerance to therapy. For patients experiencing intolerable adverse effects with initial dosing (e.g., grade 3 or 4 bradycardia, liver function abnormalities, hematologic toxicities), it is recommended to reduce the dosage to 200 mg twice daily; a further dosage reduction to 250 mg once daily may be necessary in some cases. No formal studies have been conducted to investigate the effects of severe renal or hepatic impairment on ceritinib dosing, but the manufacturer recommends dosage reduction to 250 mg once daily in patients with a creatinine clearance of <30 mL/min and not requiring dialysis.

The recommended dosage of ceritinib in patients with ALK-positive metastatic NSCLC is 750 mg orally once daily, to be taken until disease progression or intolerable toxicity. The manufacturer recommends a dose reduction of 150 mg (to 600 mg daily) for Q-Tc prolongation of >500 msec, severe intolerable nausea, vomiting or diarrhea, persistent hyperglycemia (defined as a blood glucose value of >250 mg/dL), bradycardia requiring intervention, or severe hepatic impairment (defined as an elevation of ALT or AST to a level greater than five times the upper limit of normal along with an elevation of the total bilirubin concentration of less than or equal to two times the upper limit of normal).14

Both crizotinib and ceritinib have advantages and disadvantages with regard to dosing and administration. Ceritinib’s once-daily administration schedule is more convenient than the twice-daily schedule required with crizotinib use. However, the need to administer ceritinib on an empty stomach may be inconvenient for some patients; they might prefer crizotinib, which can be administered without regard to meals. The pill burden is more substantial with the use of ceritinib versus crizotinib (patients must take five ceritinib capsules to obtain the daily dose). These differences in dosing and administration considerations may become more relevant if ceritinib is approved for first-line use.

Cost considerations

The monthly cost of crizotinib is approximately $14,382, with additional costs required for prescreening genetic testing.32,33 The cost for a full year of therapy is upward of $173,000. The manufacturer of ceritinib (Pfizer) offers copayment assistance programs for eligible patients to reduce the out-of-pocket expense. An analysis of the cost-effectiveness of crizotinib versus standard platinum doublet chemotherapy estimated a relative gain of 0.379 quality-adjusted life years (QALYs) at an additional cost of $95,043 (in Canadian dollars) with crizotinib therapy; the incremental cost-effectiveness ratio was $250,632 per QALY gained, leading the investigators to conclude that crizotinib is likely not a cost-effective therapy.

The cost of ceritinib, like that of crizotinib, is substantial; at the full dosage of 750 mg once daily, the monthly cost is approximately $16,197. Relative to crizotinib therapy, the use of ceritinib could potentially cost almost $2,000 more per month.32,35 The manufacturer of ceritinib (Novartis) also offers copayment assistance.

Assessment of patient-specific costs and access to therapy should be conducted prior to initiation of ceritinib or crizotinib therapy.

Future directions

Ongoing studies are investigating the effects of new tyrosine kinase inhibitors in the treatment of ALK-positive NSCLC.28 Several novel ALK inhibitors with increased potency and targeted selectivity are currently in development. The emergence of drug
Therapy Update

Non-small-cell lung cancer

Resistance will continue to provide challenges for future development.

Conclusion

The tyrosine kinase inhibitors crizotinib and ceritinib provide an effective treatment approach for patients with ALK-mutated NSCLC. Efficacy data for both crizotinib and ceritinib indicate improved response rates and PFS with the use of either drug as an alternative to standard chemotherapy.

References