Afatinib beyond progression in patients with non-small-cell lung cancer following chemotherapy, erlotinib/gefitinib and afatinib: phase III randomized LUX-Lung 5 trial


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Background: Afatinib has demonstrated clinical benefit in patients with non-small-cell lung cancer progressing after treatment with erlotinib/gefitinib. This phase III trial prospectively assessed whether continued irreversible ErbB-family blockade with afatinib plus paclitaxel has superior outcomes versus switching to chemotherapy alone in patients acquiring resistance to erlotinib/gefitinib and afatinib monotherapy.

Patients and methods: Patients with relapsed/refractory disease following ≥1 line of chemotherapy, and whose tumors had progressed following initial disease control (≥12 weeks) with erlotinib/gefitinib and thereafter afatinib (50 mg/day), were randomized 2:1 to receive afatinib plus paclitaxel (40 mg/day; 80 mg/m²/week) or investigator’s choice of single-agent chemotherapy. The primary end point was progression-free survival (PFS). Other end points included objective response rate (ORR), overall survival (OS), safety and patient-reported outcomes.

Results: Two hundred and two patients with progressive disease following clinical benefit from afatinib were randomized to afatinib plus paclitaxel (n = 134) or single-agent chemotherapy (n = 68). PFS (median 5.6 versus 2.8 months, hazard ratio 0.60, P = 0.003) and ORR (32.1% versus 13.2%, P = 0.005) significantly improved with afatinib plus paclitaxel. There was no difference in OS. Global health status/quality of life was maintained with afatinib plus paclitaxel throughout the entire treatment period. The median treatment duration was 133 and 51 days with afatinib plus paclitaxel and single-agent chemotherapy, respectively; 48.5% of patients receiving afatinib plus paclitaxel and 30.0% of patients receiving single-agent chemotherapy experienced drug-related grade 3/4 adverse events. Treatment-related adverse events were consistent with those previously reported with each agent.

Conclusion: Afatinib plus paclitaxel improved PFS and ORR compared with single-agent chemotherapy in patients who acquired resistance to erlotinib/gefitinib and progressed on afatinib after initial benefit. LUX-Lung 5 is the first prospective trial to demonstrate the benefit of continued ErbB targeting post-progression, versus switching to single-agent chemotherapy.

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Introduction

Patients with non-small-cell lung cancer (NSCLC) harboring activating epidermal growth factor receptor (EGFR) mutations are especially sensitive to first-line treatment with EGFR tyrosine kinase inhibitors (TKIs) [1]. However, almost all patients acquire resistance, leading to disease progression [2]. It has been hypothesized that, at the time of progression, NSCLC tumors comprise a heterogeneous mix of cells, some of which remain sensitive to EGFR inhibition [3]. Clinical observations are consistent with this hypothesis; withdrawal of an EGFR TKI at the onset of resistance can lead to rapid tumor growth [4, 5]. Therefore, there may be rationale for continued exposure to EGFR TKIs in combination with post-progression therapy. Indeed, recent retrospective [6] and single-arm [7] studies in patients with confirmed EGFR mutations suggested that continuation of EGFR TKIs beyond progression may improve outcomes in NSCLC patients.

Afatinib is a potent, irreversible ErbB family blocker that inhibits tyrosine kinase activity of EGFR, human epidermal growth factor factor 2 (HER2, ErbB2), ErbB4 and all relevant ErbB family dimers [8, 9]. Afatinib monotherapy has demonstrated progression-free survival (PFS) and overall survival (OS) benefits versus platinum-based doublet chemotherapy in previously untreated patients with NSCLC with activating EGFR mutations [10–12]. It has also demonstrated modest clinical activity in patients who had progressed following gefitinib and/or erlotinib [13, 14]. In order to prospectively evaluate the benefit of continued ErbB targeting beyond progression, this study was conducted in two parts. Part A enrolled patients who had failed ≥1 line of chemotherapy and progressed following ≥12 weeks’ clinical benefit on erlotinib/gefitinib. All patients received single-agent afatinib (50 mg daily) to identify patients who derive clinical benefit from ErbB blockade, from a uniformly treated (50 mg daily) to identify patients who derive clinical benefit from afatinib/gefitinib. All patients received single-agent afatinib after erlotinib/gefitinib. Phase B randomized patients with progression after ≥12 weeks’ clinical benefit from afatinib as third- or higher-line treatment. Afatinib was chosen as a combination partner based on preclinical evidence for synergism [15]. The safety and maximum tolerated dose (MTD) of the combination has been previously established [16]. As there is no established biomarker to predict clinical benefit from afatinib in a greater than or equal to third-line setting, ≥12 weeks of disease control from afatinib monotherapy were chosen as the primary selection criterion for enrollment in the randomized study.

Methods

Patients had stage IIIB (wet) or IV NSCLC with measurable disease and had failed treatment with ≥1 line of chemotherapy (including platinum and pemetrexed) and erlotinib/gefitinib after ≥12 weeks of treatment, and must have attained ≥12 weeks’ clinical benefit on afatinib monotherapy [complete response (CR), partial response (PR) or stable disease (SD)] with subsequent progression according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Documentation of EGFR mutation status was not mandatory as this was not universal clinical practice at the time of study planning and conduct. Patients were ≥18 years old, had Eastern Cooperative Oncology Group (ECOG) performance status of 0–2 and life expectancy of ≥12 weeks. Exclusion criteria included absence of clinical benefit from afatinib monotherapy; abnormal hepatic, renal or hematologic function. Patients provided written informed consent before afatinib monotherapy and before randomization. This trial is registered at clinicaltrials.gov (NCT01085136).

Study design

Patients were randomized 2:1 to afatinib plus paclitaxel or investigator’s choice of single-agent chemotherapy. Randomization was stratified based on duration of benefit on prior gefitinib/afatinib (≥6 versus <6 months) and sex. Patients were treated until disease progression, unacceptable tolerability or withdrawal of consent. The primary end point was PFS. Secondary end points included OS, and objective response (OR). Other end points included health-related quality of life (QoL; defined as time-to-deterioration for cough, dyspnea and pain) (supplementary Methods S1, available at Annals of Oncology online) and safety.

The study protocol, designed in accordance with the Declaration of Helsinki, was approved by institutional review boards and the responsible regulatory authorities of each participating country. An independent Data and Safety Monitoring Committee (DMC) monitored study progress.

Treatments

Patients randomized to afatinib plus paclitaxel received 40 mg daily and 80 mg/m² weekly, respectively (the MTD) [16]. Patients who had two dose reductions on afatinib monotherapy during Part A (i.e. eventually received 30 mg daily) were permitted to start on 30 mg daily in Part B. Investigator’s choice of chemotherapy was administered according to the package insert. Up to two 10 mg dose reductions of afatinib were permitted if patients encountered any grade ≥3 drug-related adverse events (AEs; assessed according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 3.0), or grade 2 diarrhea lasting ≥2 days or nausea or vomiting for ≥7 consecutive days despite best supportive care. Paclitaxel dose reductions were conducted according to the Summary of Product Characteristics.

Assessments

Tumor assessments were carried out by computed tomography or magnetic resonance imaging of less than or equal to five target lesions at baseline and every 8 weeks thereafter. Response was evaluated by the investigator. AE assessments were carried out weekly. Patients were assessed for the likelihood of being EGFR mutation-positive based on a modification of published clinical enrichment criteria (higher clinical enrichment criteria: CR/PR or ≥48 weeks of benefit on erlotinib/gefitinib) [2].

Statistical plan

PFS and OS were assessed using a stratified log-rank test. A stratified Cox proportional hazards model was used to derive the hazard ratios (HRs) and 95% confidence intervals (CIs). The Kaplan–Meier analysis was used to estimate the median survival and 95% CIs at landmark time points. Differences in objective response rate (ORR; CR plus PR) and disease control rate (DCR; ORR plus SD) were assessed by logistic regression.
For the primary analysis, 351 patients (279 PFS events) would be required to provide 90% power at a two-sided 5% significance level for the log-rank test, assuming an HR of 0.67 in favor of afatinib plus paclitaxel. Assuming an exponentially distributed median PFS of 8 weeks with afatinib monotherapy, 35% of patients would be alive and progression free at 12 weeks. Therefore, ~1100 patients needed to be treated with afatinib in Part A, assuming an ineligibility rate of 10%. Enrollment to Part B was lower than anticipated due to several unforeseen factors, including; patients’ desire for a break in treatment, patients’ refusal to proceed due to non-disease-related reasons and the requirement for screening to be within 14 days of progression under afatinib monotherapy. Consequently, the calculated number of 351 eligible patients (279 PFS events) was considered unachievable, and the protocol was amended following discussion with the DMC on 18 January 2013. The planned time points for the primary analysis of PFS and OS were amended to be undertaken once the final randomized patients had the chance to be followed for at least 6 months. Primary analysis was thus undertaken on 10 December 2013 after 163 PFS events had occurred.

results

patients

This trial was conducted in 115 enrolling centers in 23 countries. Between April 2010 and May 2011, 1154 patients were treated with afatinib monotherapy (supplementary Table S1, available at Annals of Oncology online). Of those, 223 patients with clinical benefit of at least 12 weeks were screened and 202 patients were randomized (134 to afatinib plus paclitaxel and 68 to chemotherapy; supplementary Figure S1, available at Annals of Oncology online). Reasons for not being randomized following afatinib monotherapy included <12 weeks of clinical benefit (n = 625) and exclusion at screening (n = 21). At the time of database lock, seven patients were still on treatment in Part A. Of the remaining 299 patients who were not randomized following progression on afatinib monotherapy, most declined participation due to general health deterioration, treatment-related, or other reasons (supplementary Table S1, available at Annals of Oncology online). The demographics and clinical characteristics of patients treated with afatinib monotherapy are shown in supplementary Table S2, available at Annals of Oncology online. There were no discernable differences in baseline characteristics between the 202 patients randomized to Part B and the 299 patients who were not randomized (supplementary Table S3, available at Annals of Oncology online).

Of the 202 patients randomized, 132 patients received afatinib plus paclitaxel and 60 received single-agent chemotherapy (Table 1). Few patients (13%) in the chemotherapy arm had received the same agent previously; six paclitaxel, one docetaxel and one pemetrexed.

primary efficacy end point

The median PFS was significantly longer with afatinib plus paclitaxel versus chemotherapy alone (5.6 versus 2.8 months, HR 0.60, 95% CI 0.43–0.85, P = 0.003, Figure 1A). PFS benefit was consistent across predefined subgroups (supplementary Figure S2, available at Annals of Oncology online) and was apparent versus individual chemotherapy regimens, although patient numbers in these analyses were small (supplementary Table S4, available at Annals of Oncology online). The median PFS attained in patients treated with paclitaxel monotherapy, the same agent previously; six paclitaxel, one docetaxel and one pemetrexed.

| Table 1. Patient demographics and clinical characteristics |
|------------------|------------------|------------------|
| Characteristic   | Afatinib plus paclitaxel (n = 134) | Chemotherapy (n = 68) |
|                  | Female, n (%)     | Median age (years) | Baseline ECOG status, n (%) | Race, n (%) | Smoking status, n (%) | Clinical stage at screening, n (%) | Tumor histology, n (%) | Higher clinical enrichment criteria, n (%) | Prior EGFR TKI therapy, n (%) | Lines of prior chemotherapy, n (%) | Previous pemetrexed, n (%) | Previous taxane, n (%) |
|                  | 65 (48.5)         | 60.0             | 47 (35.1)                   | 52 (38.8)   | Never smoked           | 1 (0.7)                          | 113 (84.3)               | Positive                              | 96 (71.6)               | 0                           | Yes                           | 6 (4.5)                  |
|                  | 34 (50.0)         | 60.5             | 14 (20.6)                   | 30 (44.1)   | <15 pack-years, stopped | 3 (4.4)                          | 61 (89.7)                | Negative                              | Gefitinib               | 1                           | Yes                           | 3 (4.4)                  |
|                  |                  |                  | 46 (67.6)                   | 24 (35.3)   | >1 year before diagnosis | 2 (1.5)                          | 8 (12.8)                 | Higher clinical enrichment criteria, n (%) | Erlotinib               | >1 year before diagnosis | Yes                           | 3 (4.4)                  |
|                  |                  |                  | 8 (11.8)                    | 2 (2.9)     | Current/other ex-smoker | 3 (4.4)                          | 6 (8.8)                  | Prior EGFR TKI therapy, n (%) | Gefitinib               | ≥1 year before diagnosis | No                            | 2 (0.3)                  |
|                  |                  |                  |                              |            |                          | 2 (1.5)                          | 1 (1.5)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 5 (0.7)                  |
|                  |                  |                  |                              |            |                          | 3 (4.4)                          | 1 (0.7)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |
|                  |                  |                  |                              |            |                          | 2 (2.9)                          | 3 (4.4)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |
|                  |                  |                  |                              |            |                          | 12 (17.6)                         | 2 (0.3)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |
|                  |                  |                  |                              |            |                          | 28 (41.2)                         | 2 (0.3)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |
|                  |                  |                  |                              |            |                          | 26 (38.2)                         | 3 (0.5)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |
|                  |                  |                  |                              |            |                          | 39 (57.4)                         | 3 (0.5)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |
|                  |                  |                  |                              |            |                          | 29 (42.6)                         | 3 (0.5)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |
|                  |                  |                  |                              |            |                          | 38 (55.9)                         | 3 (0.5)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |
|                  |                  |                  |                              |            |                          | 30 (44.1)                         | 3 (0.5)                  | Prior EGFR TKI therapy, n (%) | Both                   | ≥1 year before diagnosis | No                            | 3 (0.5)                  |

CR, complete response; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; PR, partial response; TKI, tyrosine kinase inhibitor.

*aPaclitaxel (35.0%), docetaxel (15.0%), pemetrexed (26.7%), vinorelbine (8.3%), gencitabine (6.7%), carboplatin (1.7%), non-protocol defined chemotherapy (6.7%).

bChina, Taiwan or Korea.

cDue to local regulations that did not allow the collection of such information.

dDefined as CR or PR to prior EGFR TKI or ≥48 weeks’ treatment with prior EGFR TKI.
Clinical benefit rate (74.5 versus 45.6%, OR 3.41, 95% CI 1.85–6.26, P < 0.0001) and ORR (32.1 versus 13.2%, OR 3.41, 95% CI 1.41–6.79, P = 0.005) were superior with afatinib plus paclitaxel versus chemotherapy (Table 2). The median maximum percentage decrease from baseline sum of target lesion diameters was 15.1% and 1.2%, respectively (supplementary Figure S3, available at Annals of Oncology online). Tumor response and PFS for patients treated with afatinib monotherapy are shown in supplementary Table S5 and Figure S4, available at Annals of Oncology online.

There was no difference in the median OS between treatment arms (12.2 versus 12.2 months, HR 1.00, 95% CI 0.70–1.43, P = 0.994, Figure 1B). Approximately 60% of patients received greater than or equal to one post-progression therapy. More patients in the chemotherapy arm received two additional lines of therapy than in the afatinib plus paclitaxel arm (36% versus 15%, supplementary Figure S5 and Table S6, available at Annals of Oncology online). Time to deterioration of global health status/quality of life and predefined symptoms was not adversely affected by treatment with afatinib plus paclitaxel versus single-agent chemotherapy (supplementary Table S7, available at Annals of Oncology online).

### safety

The median exposure to afatinib plus paclitaxel was longer than for chemotherapy alone (133 versus 51 days). Eighty-two percent of patients started on the 40 mg afatinib dose. A total of 27.3% and 4.5% of patients required one or two afatinib dose reductions, respectively; 23.5% and 35.6% of patients required one or two paclitaxel dose reductions, respectively.

The most common treatment-related AEs in the combination arm were diarrhea (53.8%), alopecia (32.6%), asthenia (27.3%), decreased appetite (22.0%) and rash (20.5%, Table 3). The incidence of treatment-related peripheral neuropathy was 9.1% versus 8.3% with chemotherapy. Serious treatment-related AEs were reported in 11.4% and 3.3% of patients in the combination and chemotherapy arms, respectively. Dose-reduction rates due to AEs were 36.2% in the combination arm and 11.7% with chemotherapy. Discontinuation rates due to drug-related AEs were 18.9% in the combination arm and 6.7% with chemotherapy. One patient experienced a fatal AE of pneumonia that was considered treatment-related (attributed to paclitaxel).

### secondary efficacy end points

Clinical benefit rate (74.5 versus 45.6%, OR 3.41, 95% CI 1.85–6.26, P < 0.0001) and ORR (32.1 versus 13.2%, OR 3.41, 95% CI 1.41–6.79, P = 0.005) were superior with afatinib plus paclitaxel versus chemotherapy (Table 2). The median maximum percentage decrease from baseline sum of target lesion diameters was 15.1% and 1.2%, respectively (supplementary Figure S3, available at Annals of Oncology online). Tumor response and PFS for patients treated with afatinib monotherapy are shown in supplementary Table S5 and Figure S4, available at Annals of Oncology online.

There was no difference in the median OS between treatment arms (12.2 versus 12.2 months, HR 1.00, 95% CI 0.70–1.43, P = 0.994, Figure 1B). Approximately 60% of patients received greater than or equal to one post-progression therapy. More patients in the chemotherapy arm received two additional lines of therapy than in the afatinib plus paclitaxel arm (36% versus 15%, supplementary Figure S5 and Table S6, available at Annals of Oncology online). Time to deterioration of global health status/quality of life and predefined symptoms was not adversely affected by treatment with afatinib plus paclitaxel versus single-agent chemotherapy (supplementary Table S7, available at Annals of Oncology online).
In conclusion, this study demonstrates that, in a clinically enriched population with a high correlation to blinded independent central review and does not bias trial outcomes [17, 18]. Another limitation was our failure to enroll the planned number of 351 patients in the randomized study. Since the randomized patients were recruited from the afatinib-treated pool in Part A which was fully recruited before the high attrition was recognized, a decision was made in discussion with the independent DMC to analyze the randomized part of the trial without going back to increase recruitment in Part A. Based on this experience, future trials of fourth-line therapies will have to expect such high attrition rates. Also, EGFR mutation testing was not mandated in this study, reflecting community practice at the time of patient recruitment (2010–2011). Instead, we clinically enriched patients for continued ErbB dependency before randomization.

Given the likelihood of several lines of post-progression therapy after study discontinuation, PFS was chosen as the primary end point. Randomized patients had received (and responded to) greater than or equal to two prior TKIs and most subsequently received greater than or equal to one line of post-study treatment. Moreover, there was an imbalance in the number of post-progression therapies between treatment arms. Hence, it was not surprising that no difference in OS was observed. The absence of OS benefit necessitated that the clinical meaningfulness of PFS was validated by patient-reported outcomes and safety. Notably, global health status/QoL was not significantly different with afatinib plus paclitaxel, despite a doubling of median treatment time versus chemotherapy. The AE profile of afatinib (±paclitaxel) was consistent with previous studies [10, 11, 13, 14]. The frequency and severity of AEs was higher in the afatinib plus paclitaxel arm versus chemotherapy (possibly reflecting prolonged treatment exposure) and discontinuation was higher in the afatinib plus paclitaxel arm. However, differences in AEs between arms did not seem to impact on global health status/QoL.

In previous studies, modest activity has been demonstrated with afatinib monotherapy in some patients with acquired resistance to first-generation EGFR TKIs [13, 14, 19]. Recently, emerging third-generation EGFR inhibitors, such as AZD-9291, rociletinib and HM-61713, have shown much greater response rates (>50%) in patients with EGFR T790M-positive NSCLC [20–22]. Consequently, the role of afatinib monotherapy in this setting may, ultimately, be limited. However, third-generation EGFR inhibitors are less active in patients with EGFR T790M-independent resistance mechanisms. This leaves up to 50% of patients with acquired resistance to first-generation EGFR TKIs underserved, thus constituting a major unmet medical need. Therefore, novel afatinib-based combination regimens, including afatinib plus paclitaxel, warrant consideration in these patients, as well as in patients who are unsuitable for tumor rebiopsy. Indeed, recent data have demonstrated that afatinib plus cetuximab may be particularly effective post-erlotinib/gefitinib in both EGFR T790M-positive and -negative tumors [23].

In conclusion, this study demonstrates that, in a clinically selected patient population, continuous ErbB blockade with afatinib in patients with NSCLC who had failed platinum-based chemotherapy, gefitinib/erlotinib and afatinib monotherapy...

### Table 3. Drug-related AEs reported in >10% of patients (ordered by rate of occurrence in afatinib + paclitaxel arm)

<table>
<thead>
<tr>
<th>Clinical characteristic</th>
<th>Afatinib + paclitaxel (n = 132)</th>
<th>Chemotherapy (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All grades, n (%)</td>
<td>Grade ≥3, n (%)</td>
</tr>
<tr>
<td><strong>Patients with any drug-related AE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>71 (53.8) 16 (12.1)</td>
<td>4 (6.7)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>43 (32.6) 1 (0.8)</td>
<td>9 (15.0)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>36 (27.3) 11 (8.3)</td>
<td>17 (28.3)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>29 (22.0) 2 (1.5)</td>
<td>10 (16.7)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>27 (20.5) 6 (4.5)</td>
<td>9 (15.0)</td>
</tr>
<tr>
<td>Rash</td>
<td>27 (20.5) 2 (1.5)</td>
<td>6 (10.0)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>24 (18.2) 15 (11.3)</td>
<td>8 (13.3)</td>
</tr>
<tr>
<td>Nausea</td>
<td>23 (17.4) 2 (1.5)</td>
<td>10 (16.7)</td>
</tr>
<tr>
<td>Paronychia</td>
<td>23 (17.4) 3 (2.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>21 (15.9) 3 (2.3)</td>
<td>4 (6.7)</td>
</tr>
<tr>
<td>Anemia</td>
<td>20 (15.2) 5 (3.8)</td>
<td>3 (5.0)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>20 (15.2) 6 (4.5)</td>
<td>7 (11.7)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>16 (12.1) 0 (0)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>13 (9.8) 2 (1.5)</td>
<td>2 (3.3)</td>
</tr>
<tr>
<td>Mucosal inflammation</td>
<td>12 (9.1) 1 (0.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>10 (7.6) 0 (0)</td>
<td>3 (5.0)</td>
</tr>
<tr>
<td>Dry skin</td>
<td>6 (4.5) 0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

AEs, adverse events.
improves PFS and ORR, but not OS, when combined with paclitaxel. This is the first prospective evidence to support the concept for maintaining target inhibition beyond formal disease progression in oncogene-addicted lung cancer.

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disclosure

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references

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Dacomitinib versus erlotinib in patients with EGFR-mutated advanced nonsmall-cell lung cancer (NSCLC): pooled subset analyses from two randomized trials


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Background: The irreversible epidermal growth factor receptor (EGFR) inhibitors have demonstrated efficacy in NSCLC patients with activating EGFR mutations, but it is unknown if they are superior to the reversible inhibitors. Dacomitinib is an oral, small-molecule irreversible inhibitor of all enzymatically active HER family tyrosine kinases.

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appendix

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