**Research Article**

**EGFR Mutation Status and First-Line Treatment in Patients with Stage III/IV Non–Small Cell Lung Cancer in Germany: An Observational Study**

Wolfgang Schuette1, Peter Schirmacher2, Wilfried Ernst Erich Eberhardt3, Juergen R. Fischer4, J.-Matthias Graf von der Schulenburg5, Joerg Mezger6, Christian Schumann7, Monika Serke8, Silke Zaun9, Manfred Dietel10, and Michael Thomas11,12

**Abstract**

**Introduction:** EGFR mutations confer sensitivity to EGFR tyrosine kinase inhibitors (TKI) in advanced non–small cell lung cancer (NSCLC). We investigated the clinicopathologic characteristics associated with EGFR mutations and their impact on real-world treatment decisions and outcomes in Caucasian patients with advanced NSCLC.

**Methods:** REASON (NCT00997230) was a noninterventional multicenter study in patients (≥18 years) with stage IIIb/IV NSCLC, who were candidates for EGFR mutation testing and first-line systemic treatment, but not eligible for surgery or radiotherapy. Patients were followed up according to normal clinical practice and assessed for primary (correlation of mutation status with baseline characteristics) and secondary endpoints (first-line treatment decision).

**Results:** Baseline data were obtained for 4,200 patients; 4,196 fulfilled the inclusion criteria; EGFR mutations were detected in 431 patients; no EGFR mutations were detected in 3,590 patients; mutation status was not evaluable in 175 patients. In multivariate analysis, the odds of EGFR mutations were significantly higher ($P < 0.0001$) in females versus males (odds ratio: 1.85; 95% confidence interval, 1.48–2.32), never-smokers versus smokers (3.64; 2.91–4.56), and patients with adenocarcinoma versus other histologic subtypes (2.94; 2.17–4.08). The most commonly prescribed first-line systemic treatments were: EGFR-TKIs in EGFR mutation–positive NSCLC (56.6%) and combination chemotherapy in EGFR mutation–negative NSCLC (78.5%).

**Conclusions:** This represents the largest dataset for EGFR mutations in Caucasian patients and shows EGFR mutations to be most prevalent in females with adenocarcinoma who had never smoked.

**Impact:** These findings add to our understanding of the prognostic and predictive factors of NSCLC, supporting future improved treatment selection. *Cancer Epidemiol Biomarkers Prev;* 24(8): 1254–61. ©2015 AACR.

**Introduction**

Pivotal phase III trials have demonstrated longer progression-free survival with the EGFR tyrosine kinase inhibitors (TKI) erlotinib and gefitinib compared with chemotherapy in EGFR mutation–positive advanced non–small cell lung cancer (NSCLC; refs. 1–5). European guidelines therefore recommend EGFR mutation testing for all patients with advanced nonsquamous NSCLC, and first-line TKI treatment whenever activating mutations are detected (6). Mutations conferring sensitivity to TKIs occur in exons 18 to 21 of the EGFR tyrosine kinase domain. The predominant sensitizing mutations are exon 19 deletions (del 19) and the L858R amino acid substitution (exon 21; ref. 7).

EGFR mutations have been observed in 10% to 28% of all NSCLC tumors (8) and are associated with East Asian race, adenocarcinoma histology, female gender, and nonsmoking status (7–13). The prevalence of NSCLC EGFR mutations in East Asian populations (30%–50%) has been extensively studied (7). Analysis of epidemiologic studies has shown that compared with Caucasians with NSCLC, East Asian patients have a higher prevalence of EGFR mutation (~30% vs. 7%, predominantly among patients with adenocarcinoma and never-smokers), a lower prevalence of KRAS mutation (<10% vs. 18%, predominantly among patients with adenocarcinoma and smokers), and higher

---

1Department of Internal Medicine II, Hospital Martha-Maria, Halle-Dolau, Halle, Germany. 2Institute of Pathology, University Hospital Heidelberg, Heidelberg, Germany. 3Department of Medical Oncology, West German Tumor Centre, University Hospital Essen, University Duisburg-Essen, Essen, Germany. 4Medical Department II Oncology, Hospital Löwenstein LLC, Löwenstein, Germany. 5Center for Health Economics Research Hannover, Leibniz University Hannover, Hannover, Germany. 6Department of Internal Medicine II, Haematology, Oncology, Immunology, St. Vincentius-Kliniken, Karlsruhe, Germany. 7Department of Medical Oncology, University Hospital of Ulm, Ulm, Germany. 8Pulmonary and Thoracic Oncology, Lungenklinik Hemer, Hemer, Germany. 9Medical Affairs, AstraZeneca, Wedel, Germany. 10Institute of Pathology, Charité – Universitätsmedizin Berlin, Berlin, Germany. 11Department of Thoracic Oncology, Thoraxklinik at the University of Heidelberg, Heidelberg, Germany. 12Translational Lung Research Center Heidelberg (TLRC-H), Member of the German Center for Lung Research (DZL), Heidelberg, Germany.

**Note:** Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

W. Schuette and P. Schirmacher contributed equally to this article.

Current address for S. Zaun: Böckstr. 40, 10967 Berlin, Germany.

**Corresponding Author:** W. Schuette, Hospital Martha-Maria, Roentgenstr. 1, Halle-Dolau, 06120 Halle, Germany. Phone: 49-345-559-1440; Fax: 49-345-680-0376; E-mail: Wolfgang.Schuette@Martha-Maria.de

doi: 10.1158/1055-9965.EPI-14-1149

©2015 American Association for Cancer Research.
proportion of patients who are responsive to EGFR-TKIs (14). Real-world epidemiologic data on the prevalence of NSCLC EGFR mutations in Caucasian populations are limited. Recent studies in Caucasian populations have shown an EGFR mutation rate of 9% to 14%, associated with female gender and adenocarcinoma histology (15–17). However, these studies do not report outcomes such as treatment choices and healthcare resource use. In addition, data on the prevalence of uncommon EGFR mutations are still very limited.

Routine clinical practice management and outcomes data in Caucasian patients with EGFR mutation–positive NSCLC are limited to small, retrospective studies (18, 19). The Registry for the Epidemiological and Scientific evaluation of EGFR mutation status in patients with newly diagnosed locally advanced or metastatic NSCLC (REASON) was a noninterventional study (NIS) initiated to address this need for evidence of the epidemiology of EGFR mutation–positive NSCLC and pharmacoeconomic data on EGFR mutation–positive NSCLC. The study aims to gather data on the prevalence and associated clinicopathologic characteristics of EGFR mutations, and examines the treatment choices, outcomes, resource use, and quality of life in a large cohort of mostly Caucasian patients with EGFR mutation–positive NSCLC. These data will provide greater insight into current treatment of patients with advanced NSCLC in Germany. Herein, we report outcomes from the primary objective (prevalence and associated clinicopathologic characteristics of EGFR mutations) as well as first-line systemic treatment choices. Secondary objectives will be addressed in a separate manuscript.

Objectives

The primary objective of the study was to collect epidemiologic data on EGFR mutation status in a population of predominantly Caucasian ethnicity, and to correlate EGFR mutation status with clinicopathologic characteristics. Collection of data on first-line treatment decisions in all patients was a secondary endpoint.

Materials and Methods

In this NIS (registration ID: NCT00997230), patients were assessed under routine clinical practice. This differs from interventional studies where patients are selected according to strict inclusion and exclusion criteria to assess an investigational medicinal product. Decisions regarding diagnostic procedures and therapeutic management (type, dose, and duration of therapy) were at the discretion of the investigating physician. All patient data (including adverse events, serious adverse events, and adverse drug reactions) were recorded by the investigator using an electronic case report form (eCRF).

Enrollment of 4,000 patients was planned at 149 sites all over Germany. The sample size was defined to provide high level of precision in EGFR mutation rates (95% confidence interval (CI) ≤5% above or below point estimates), based on existing epidemiologic evidence in Caucasian populations. Study sites included 127 hospitals and 22 oncologists in private practice. Sites were selected based on expertise in advanced NSCLC treatment and conducting clinical trials.

Eligible patients were aged ≥18 years with histologically confirmed locally advanced or metastatic NSCLC (stage IIIb/IV), not eligible for curative surgery or radiotherapy but considered typical candidates for first-line systemic treatment. The staging system in effect at the time of the original protocol was the 6th edition of the TNM classification (20), during the course of the study, it was replaced by the 7th edition (21). Overall, 421 patients (10.0%) were classified based on the 6th edition and 3,563 patients (84.8%) according to the 7th edition; data are missing for the other patients (5.1%). Patients were required to have EGFR mutation status, and suitable tumor tissue was available. All patients provided signed, written informed consent to participate in the study. Patients with mixed histology of small-cell and NSCLC were not included. Patients’ follow-up was done according to standard clinical practice.

All patients fulfilling the inclusion criteria were assessed for EGFR mutation status, as per the primary objective of REASON. We also report analysis of baseline characteristics and first-line treatment decision for all patients, as per the secondary objective of collecting first-line treatment decisions in patients with EGFR mutation–positive status, EGFR mutation–negative status, or where mutation status is not evaluable. Other secondary objectives of collecting clinical outcome data (progression-free survival, overall survival, and objective response rate), pharmacoeconomic data, and second-line and further treatment decisions were restricted to patients with EGFR mutation–positive NSCLC who were not participating in other clinical trials (Fig. 1). Safety and tolerability data were only analyzed in patients receiving gefitinib.

Mutation analysis was performed in a decentralized manner by institutes of pathology that had been certified by the Quality assurance Initiative Pathology (QuIP), an independent certification institution of the German Society of Pathology (DGP; ref. 22). Testing for EGFR mutations of exons 19 and 21 was mandatory, whereas testing of exons 18 and 20 was optional. No specific testing method was stipulated in the study protocol; the method used was recorded in the eCRF. At the time of patient enrollment into REASON, there was no consensus over a preferred EGFR mutation testing methodology, and a number of different methodologies were available, such as direct sequencing and Amplification Refractory Mutation System (ARMS).

Evaluation of data was performed with descriptive methods of statistics by means of frequency tables and cross tabulations. Ninety-five percent confidence limits of proportions were calculated to determine precision of results. Correlation of EGFR mutation status with the three key variables (gender, smoking habit, tumor histology, each dichotomized) was analyzed using a multivariate logistic regression model. Secondary endpoints related to clinical outcome, safety and tolerability, and pharmacoeconomic data (resource use) were also evaluated using descriptive statistics. Binary, categorical, and ordinal parameters were summarized by means of absolute and percentage numbers (including “missing data” as valid category). Numerical data were summarized by means of standard statistics (i.e., number of available data, mean, SD, minimum, median, maximum, lower, and upper quartile). Wherever useful, the summary statistics were presented for all patients and by EGFR mutation status (positive, negative, and mutation not evaluable).

Statistical tests were performed two-sided at a 5% level of significance. However, the P values of all statistical tests are to be interpreted only in a descriptive-exploratory way. Two-sided CIs are displayed for important variables. Appropriate methods were used to derive CIs, depending on data nature and distribution. All safety and tolerability data are presented in a purely descriptive manner.
Results

Between November 2009 and March 2011, 4,243 patients were enrolled at 149 sites throughout Germany. By the cutoff date of October 31, 2012, baseline documentation was available for 4,200 patients, and 4,196 patients were compliant with the inclusion and exclusion criteria.

EGFR mutations were detected in 432 patients (10.3%). No EGFR mutations were detected in 3,593 patients (85.5%). EGFR mutation status could not be determined in 175 patients (4.2%; Table 1).

Baseline demographic characteristics and EGFR mutation status are shown in Table 1. The predominant characteristics of the total study population were male gender, former or current history of smoking, adenocarcinoma, stage IV disease, and Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1. The mean (SD) age in the overall population was 66 (10.4).

Multivariate analyses (logistic regression, binary variables) indicated that the probability of having an EGFR mutation was significantly higher \( (P < 0.0001 \text{ for all}) \) in female versus male patients (odds ratio: 1.85; 95% CI 1.48–2.32), patients who never smoked versus those with a history of smoking (3.64; 2.91–4.56), and patients with adenocarcinoma versus other histologies (2.94; 2.17–4.08).

EGFR mutations were observed in 6.4% of men compared with 16.7% of women, 6.8% of patients who had ever smoked compared with 26.2% in never-smokers, and 3.8% of patients with nonadenocarcinoma histology compared with 13.1% with adenocarcinoma.

In patients with stage IV NSCLC and who had a description of metastases entered in the eCRF \( (n = 3,558) \), the mean number of organs with metastases per patient was 1.65 (SD 0.93). Table 2 shows the location of metastases in patients with stage IV disease. Bone \( (P < 0.001, \text{ Fisher exact test}) \), pleura \( (P < 0.001) \), and brain \( (P = 0.01) \) metastases were significantly more common in patients with EGFR mutations than in those without EGFR mutations. Conversely, adrenal gland metastases were significantly
more common in patients without EGFR mutations than in those with EGFR mutations \((P < 0.01)\).

The individual mutations detected on each exon are shown in Table 3, with additional analyses by tumor tissue source reported in Supplementary Table S1. Mutations were detected in four exons, including those where testing was not mandatory (18 and 20). Twelve patients had two documented mutations (double mutations). Direct sequencing was the most common method for EGFR testing (recorded in 80.9% of all patients; Supplementary Table S2). Similarly, for those patients testing positive for exon 18 and 20 mutations, direct sequencing was the most common method reported (85.7% of patients). The methodology used for testing was missing or not available in the eCRF for 14.3% of all patients. The majority of samples for EGFR mutation analyses were taken from primary tumor tissue (81.8%; Supplementary Table S3). The rate of EGFR mutations was higher in patients whose tissue samples were taken from distant metastases (16.5%) compared with primary tumors \((9.3\% ; \ P = 0.00002; \text{Fisher exact test})\). The EGFR mutation rate in lymph node metastases was 11.5%. Post hoc analysis suggests a difference in testing methodology between primary tumor and metastatic tissue sources (Supplementary Table S2).

Figure 2 shows the treatment decisions in patients who received systemic first-line treatment, according to EGFR mutation typing. Combination chemotherapy (predominantly platinum-based doublets) was the most common first-line treatment overall and in the EGFR mutation–negative population. Just over half of the patients with EGFR mutation–positive NSCLC received EGFR-TKI monotherapy as first-line treatment; combination chemotherapy was the next most
frequent treatment in patients with EGFR mutation–positive disease.

Of patients receiving first-line treatment, 88.0% had ECOG performance status of 0 to 2 (Table 4). Among patients who received combination chemotherapy or chemotherapy plus anti-

body treatment (predominantly bevacizumab), there was a trend toward lower performance status score compared with patients who received single-agent chemotherapy. Patients receiving EGFR-TKI monotherapy had a comparable performance status distribution to the overall population.

Discussion

The REASON study represents the largest dataset for EGFR mutations and related outcomes for advanced NSCLC in Caucasian patients.

Lung cancer is a major cause of mortality in Germany, resulting in more than 44,000 deaths in 2012 (23). EGFR mutation testing is available to most German patients with advanced NSCLC. Direct sequencing (Sanger or pyro) was the standard testing method, and was in used in at least 80% of tests in this study. Other techniques were admissible as long as the Institute of Pathology had passed the strict certification procedure of the DGP (QuIP, ref. 22).

EGFR mutations were detected in 10.3% of patients. Although this EGFR mutation rate is similar to that reported in other studies of Caucasian populations (6, 15–17), other reports quote 5% to 23% (19, 24–28). This variability may arise from the design of the studies, which all included fewer patients than the REASON study. Most of these studies were not designed to evaluate the prevalence of EGFR mutations in the broader NSCLC population, and strict eligibility criteria may limit the external validity of the reported rates. The studies were heterogeneous in terms of the histology, gender, and smoking status of the patients enrolled, so clinical selection bias cannot be excluded. Other factors may also affect the recorded prevalence of EGFR mutations, such as KRAS mutation–negative preselection, differences in mutation testing method, number of sequenced exons, and tumor source tested (primary vs. metastasis). In addition, mutations were not comprehensively analyzed in these studies, so mutation rates may have been underestimated to different extents.

In this cohort, the odds of having an EGFR mutation were nearly 2-fold higher in women than in men, more than 3.5-fold higher in never-smokers than in smokers, and nearly 3-fold higher in patients with adenocarcinoma than in those with other histologic entities. This observation confirms the previously reported higher rates of EGFR mutation in these groups. The presence of mutations in patients with other characteristics, however (men, smokers, nonadenocarcinoma histology), reinforces the

Table 2. Number and locations of metastases in patients with stage IV disease

<table>
<thead>
<tr>
<th>Location</th>
<th>Frequency of detected mutations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer, contralateral</td>
<td>31.2 (1.4)</td>
</tr>
<tr>
<td>Brain</td>
<td>5.2 (0.2)</td>
</tr>
<tr>
<td>Liver</td>
<td>1.0 (0.2)</td>
</tr>
<tr>
<td>Adrenal gland</td>
<td>1.0 (0.2)</td>
</tr>
<tr>
<td>Pleura</td>
<td>2.0 (0.2)</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>2.0 (0.2)</td>
</tr>
<tr>
<td>Other</td>
<td>2.0 (0.2)</td>
</tr>
<tr>
<td>Total</td>
<td>37.4 (1.4)</td>
</tr>
</tbody>
</table>

Abbreviations: EGFR Mut., EGFR mutation positive; EGFR Mut., no EGFR mutation detected; EGFR Mut.x, EGFR mutation status not evaluable.

© 2015 American Association for Cancer Research. cbep.aacrjournals.org Downloaded from cbep.aacrjournals.org on November 15, 2017.
importance of testing all patients with advanced NSCLC for EGFR mutations (9).

Recent reports from phase III studies have not contributed to a definitive prevalence of EGFR mutation–positive NSCLC in Caucasian patients. Rosell and colleagues screened for EGFR mutations in 2,105 Spanish patients and reported a 16.6% mutation rate. However, a selection bias applied favoring inclusion of patients with adenocarcinoma, females, and never-smokers (29). The Sequential Tarceva in Unresectable NSCLC (SATURN) study reported mutation status only for the subgroup of patients whose disease did not progress after initial platinum-based chemotherapy and only screened for L858R and del 19 mutations (30, 31). The European Tarceva study versus Chemotherapy (EURTAC) study was the first prospective phase III trial of erlotinib versus chemotherapy in non-Asian patients with EGFR mutation–positive NSCLC (32). In a recent retrospective analysis of specimens from the EURTAC study, 225 of 1,044 screened patients tested positive for EGFR exon 19 deletion or L858R mutations based on laboratory-developed tests (LDT), suggesting an EGFR mutation rate of 22% (33). This EGFR mutation rate is higher than that reported in REASON and other studies in Caucasian patients (15–17); however, the reasons for this discrepancy are not known and the authors do not discuss the EGFR mutation rate obtained from LDTs.

Our study has some limitations, which should be considered for the correct evaluation of its relevant results. Principally, the study was not designed to determine the overall prevalence of EGFR mutations in the German NSCLC population. Thus, some pathology services assessed EGFR mutations on exons 18 to 21, but some tested only the mandatory exons 19 and 21. Mutations in exons 18 and 20 were observed in some patients (16.9%), so the overall EGFR mutation rate is an underestimate of the true prevalence.

The proportion of squamous cell carcinoma was lower (19.2%) than expected for an unselected sample of patients with NSCLC (34). Therefore, the possibility cannot be excluded that individual centers may have applied selection bias for enrollment or for EGFR mutation testing of patients with specific clinical characteristics. Moreover, the introduction during the trial period (2009) of new standard rates for all German statutory health insurance companies may have been a factor in favor of study participation.

A higher EGFR mutation rate was observed in tissue samples taken from metastatic tissue (16.5%) compared with primary tumor tissue (9.3%). This phenomenon has been reported previously (35) and raises the possibility that EGFR mutation is

Table 4. ECOG performance status by first-line therapy, % of patients

<table>
<thead>
<tr>
<th>ECOG performance status</th>
<th>Total n = 1,320</th>
<th>Combination chemotherapy n = 2,297</th>
<th>Monotherapy Chemotherapy plus antibodyn = 360</th>
<th>Chemotherapy plus antibodyn = 299</th>
<th>EGFR-TKI monotherapy n = 241</th>
<th>Other (not assignable)n = 117</th>
<th>Other combinationsn = 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>31.6</td>
<td>31.8</td>
<td>17.8</td>
<td>40.5</td>
<td>29.5</td>
<td>51.3</td>
<td>16.7</td>
</tr>
<tr>
<td>1</td>
<td>47.4</td>
<td>48.0</td>
<td>48.1</td>
<td>46.8</td>
<td>46.5</td>
<td>35.0</td>
<td>66.7</td>
</tr>
<tr>
<td>2</td>
<td>9.0</td>
<td>8.6</td>
<td>15.6</td>
<td>5.0</td>
<td>10.4</td>
<td>3.4</td>
<td>16.7</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>1.7</td>
<td>4.4</td>
<td>0.3</td>
<td>3.3</td>
<td>2.6</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>0.2</td>
<td>0.2</td>
<td>0.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Not available</td>
<td>0.9</td>
<td>9.7</td>
<td>13.9</td>
<td>7.4</td>
<td>10.4</td>
<td>7.7</td>
<td>0</td>
</tr>
</tbody>
</table>

*Predominantly bevacizumab.
*Experimental therapies, free-text entries.
*TKI plus chemotherapy (n = 5), antibody alone (n = 3).
positively correlated with tumor progression. We also observed different patterns of metastatic locations between patients with EGFR mutation–positive and mutation–negative NSCLC. This may suggest a difference in the natural history of the EGFR mutation–positive versus wild-type disease. This observation merits prospective validation.

Of the patients with EGFR mutation–positive disease, 43.4% did not receive first-line treatment with an EGFR-TKI, which contrasts with current guideline recommendations for treatment (6, 36–38). We believe that some patients with acute symptoms may have been initiated on first-line chemotherapy while waiting for EGFR mutation test results, and may subsequently have been switched to an EGFR-TKI once a positive mutation test was confirmed. The TKI use would therefore be recorded as second-line in the eCRF. In a recent retrospective study of 1,164 patients with NSCLC who received chemotherapy at a single Korean hospital (39), EGFR-TKI therapy was received by 88.0% of patients with EGFR mutation–positive NSCLC. Of the 441 patients referred for EGFR testing, 51 (11.6%) were started on EGFR-TKI therapy, before the results of their EGFR test were available. EGFR-TKIs were used most frequently in second-line therapy, but first-line use was not reimbursed in Korea at the time of the study.

Performance status was considered as a possible confounding factor in the first-line treatment decisions for patients in this study, because of the known tolerability concerns with systemic anticancer therapy. We observed a majority of patients with good performance status in each treatment group. This is consistent with ESMO guidelines for advanced NSCLC (6), which recommend systemic therapy be offered to all patients with performance status of 0 to 2. The guidelines suggest patients with poor performance status (3 or 4) and EGFR mutation–positive disease could be offered TKI therapy, but in our study, only 3.3% of those patients receiving TKI monotherapy had a poor performance status (all with performance status of 3). The highest proportion of patients with performance status of 3 or 4 (4.7%) was observed in the group who received monochemotherapy, suggesting that monochemotherapy is often chosen when there are concerns about patients’ ability to tolerate platinum-based regimens, EGFR-TKIs, or antibody therapy. In the Korean retrospective study (39), patients with poor performance status were also statistically significantly more likely to receive EGFR-TKI therapy, as were women and patients with EGFR mutation–positive disease. The autonomy of physicians and pathologists in determining how to manage their patients’ disease and establish EGFR mutation status was central to the design of the REASON study. Therefore, the results provide insights into routine clinical practice regarding diagnosis and management of EGFR mutation–positive NSCLC in a large, primarily Caucasian population.

Disclosure of Potential Conflicts of Interest
W. Schuette is a consultant/advisory board member for Amgen, AstraZeneca, and Roche. W.E.E. Eberhardt reports receiving commercial research grant from Eli Lilly; has received speakers bureau honoraria from Astellas, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Eli Lilly, Merck, Novartis, Pfizer, and Roche; and is a consultant/advisory board member for AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Daiichi Sankyo, Eli Lilly, Medimmune, Merck, Novartis, Pfizer, Roche, and Teva. M. Serke has received speakers bureau honoraria from AstraZeneca, Boehringer, Lilly, MSD, Pfizer, Pierre Fabre, and Roche; and is a consultant/advisory board member for AstraZeneca, Boehringer, Roche, Lilly, MSD, and Pfizer. M. Thomas has received speakers bureau honoraria from AstraZeneca. No potential conflicts of interest were disclosed by the other authors.

Authors’ Contributions
Conception and design: W. Schuette, W.E.E. Eberhardt, M. Serke, S. Zaun, M. Dietel
Development of methodology: W.E.E. Eberhardt, M. Dietel
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): W. Schuette, W.E.E. Eberhardt, J. Mezger, C. Schumann, M. Serke, M. Dietel, M. Thomas
Writing, review, and/or revision of the manuscript: W. Schuette, P. Schirmacher, W.E.E. Eberhardt, J. Mezger, C. Schumann, S. Zaun, M. Dietel, M. Thomas
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): P. Schirmacher, J.R. Fischer
Study supervision: W.E.E. Eberhardt, S. Zaun

Acknowledgments
The authors thank Dr. Isabelle Leach, from iMed Comms, who provided medical writing support funded by AstraZeneca.

Grant Support
This study was sponsored by AstraZeneca.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received October 13, 2014; revised May 7, 2015; accepted May 26, 2015; published OnlineFirst June 12, 2015.

References


1260 Cancer Epidemiol Biomarkers Prev; 24(8) August 2015 Cancer Epidemiology, Biomarkers & Prevention

Downloaded from cebp.aacrjournals.org on November 15, 2017. © 2015 American Association for Cancer Research.


Cancer Epidemiology, Biomarkers & Prevention

EGFR Mutation Status and First-Line Treatment in Patients with Stage III/IV Non–Small Cell Lung Cancer in Germany: An Observational Study

Wolfgang Schuette, Peter Schirmacher, Wilfried Ernst Erich Eberhardt, et al.

Cancer Epidemiol Biomarkers Prev 2015;24:1254-1261. Published OnlineFirst June 12, 2015.

Updated version
Access the most recent version of this article at:
doi:10.1158/1055-9965.EPI-14-1149

Supplementary Material
Access the most recent supplemental material at:
http://cebp.aacrjournals.org/content/suppl/2015/06/16/1055-9965.EPI-14-1149.DC1

Cited articles
This article cites 35 articles, 8 of which you can access for free at:
http://cebp.aacrjournals.org/content/24/8/1254.full#ref-list-1

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, use this link
http://cebp.aacrjournals.org/content/24/8/1254.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.