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Disparities in Access to EGFR-Mutation Testing in Patients with Advanced NSCLC in Germany 2011

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Abstract

Background
The data from clinical trials show, that in patients with advanced non-small-cell lung-cancer and with activating EGFR-mutations first-line use of tyrosine kinase inhibitors (TKI) provides significant advantages in terms of response and progression free survival compared to standard doublet chemotherapy. [I,II,III,IV,V,VI] However, testing of all newly diagnosed patients with advanced NSCLC has been considered as a financial burden in daily clinical routine.
Objectives
The rate of EGFR-testing in daily practice was analyzed by institution type, histology, individual patient characteristics and by federal state. The EGFR-test processing was analyzed with respect to sampling, quality of samples, referral to the certified pathologists, reimbursement and coverage of costs.
Method
The online survey was performed in a representative sample of decision making physicians in 102 centres (21 university hospitals, 44 non-university hospitals, 32 office-based oncologists, 5 lung clinics) treating patients with advanced NSCLC in the 3rd quarter of 2011. The impact of relevant factors (test turn-around time, regional density of hospitals or specialist physicians, the type of test-initiating institution) on the likelihood of testing was assessed by using a two-sided Chi-square test.
Results
Only a minority of patients at the centres participating in this survey with NSCLC IIIb/IV (40%) had an access to EGFR-testing and to the respective treatment in case of a mutation in IIIrd quarter of 2011. Reasons may include the long waiting-time for test results (mean 9.2 d, range 5-14 d), the inadequate reimbursement of testing, esp. in lung clinics, and patient selection according to individual characteristics by the physician in order to reduce the test rates and the burden for clinical budgets. The regional data analysis indicates that patient access to EGFR-mutation testing is significantly related to the density of clinics and of specialized physicians in respective federal states.
Conclusions
Decentralized organization and funding of health care and diagnostics have led to significant regional disparities. Therefore, a detailed analysis of regional health care structures in oncology is necessary.

Background

The molecular testing is important in lung cancer because there are now a number of systemic therapies that are most effective in patients who have non-small-cell lung cancer (NSCLC) with specific molecular traits. The therapies and related molecular signatures include gefitinib (*Iressa*, AstraZeneca) or erlotinib (*Tarceva*, Roche) for patients with *EGFR* mutations and crizotinib (*Xalkori*, Pfizer) for patients with *ALK* mutations.

The EGFR mutation rate of German patients with advanced NSCLC is about 10%.[VII] In Germany the majority of patients with advanced NSCLC is considered to be treated outside of university hospitals or lung clinics in community hospitals or in oncological practices. [VIII] A major challenge now is to implement high-quality molecular diagnostics and personalized treatment strategies in routine clinical practice also outside of highly specialized academic centres.

Nevertheless, testing of all newly diagnosed patients with an advanced NSCLC has been considered as a burden for clinical budgets in daily clinical routine in Germany, since it has not been covered by DRGs. On the other side, it has been paid by the sick funds in the outpatient care.

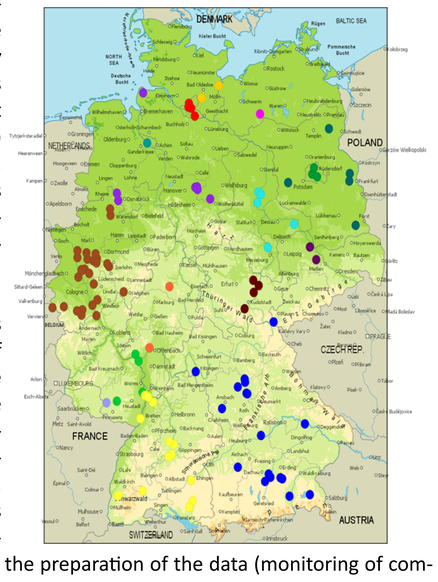
In a Dutch survey presented at ISPOR 2011 [IX], a mean of 70% pts with NSCLC IIIb/IV were tested. Extensive regional disparities were observed with 44% to 100%. In our survey the use of EGFR-testing in Germany and its limitations were assessed and analyzed with regard to the distribution of the treated prevalence in advanced NSCLC on the institution types.

Method

The survey was performed in a representative sample of centres with treatment decisions in advanced NSCLC in the IIIrd quarter of 2011. The basis for the sample was compiled from the O.I.s) address database with decision making physicians in hospitals and office-based practices. In order to construct the sample, 963 physicians (decision-makers) from the relevant specialties (665 oncologists, 161 pneumologists, 95 radiotherapists and 42 internists) at university hospitals at 682 centres (university hospitals, non-university hospitals, office-based practices and lung clinics) were informed of the project via mailing and invited to participate.

112 sites were recruited (a response rate of ca.12%); with a maximum of 1 physician per institution (decision makers in NSCLC IIIb/IV only), 102 sites distributed regionally according to population density participated: 21 university hospitals, 44 non-university hospitals, 5 lung clinics and 32 oncological practices). Regarding specialty, 80 oncologists, 14 pneumologists, 7 radiotherapists and 1 internist provided the data.

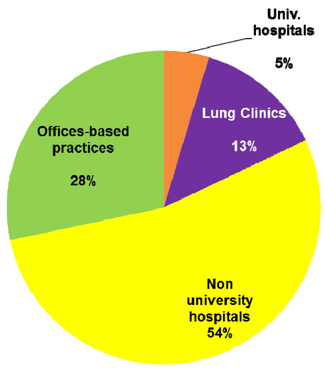
The total of NSCLC pts, stage IIIb/IV, reported in this sample amounts to 3834 pts. This sample covers 14% of the treated prevalence of NSCLC pts, stage IIIB/IV, in the IIIrd quarter of 2011 in Germany (estimated as 27700 pts). Physicians took part in an online survey (KeyPoint Version 5.5, optionally paper and pen) based on a structured questionnaire. The descriptive statistical analysis was done in KeyPoint™ Version 5.5, Microsoft Excel™ 2010 and Visokio Omniscope™.



The impact of relevant predictive factors (days to availability of test, density of hospitals or specialist physicians, the type of test-initiating institution) on the likelihood of testing was assessed separately for each potentially relevant factor by using a two-sided Chi-square test. For all comparisons a p-value of less than 0.05 was considered to be statistically significant. Both the field work and the preparation of the data (monitoring of completeness and accuracy, queries) for the statistical analysis and presentation were carried out entirely by O.I.s).

Results

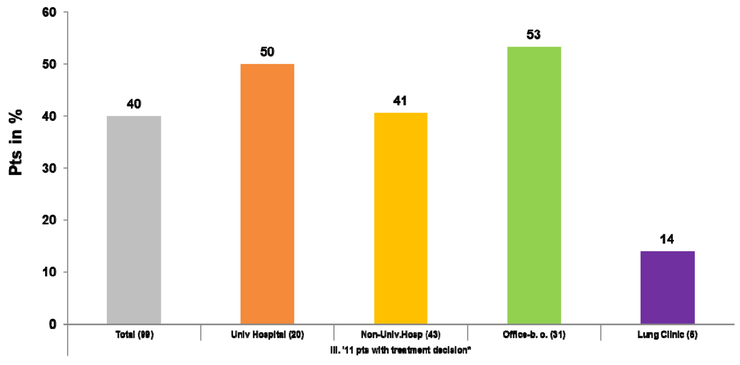
According to the analysis of reported data the treated prevalence was distributed among the institutions as follows: 5% university hospitals (UH), 54% non-university hospitals (NUH), 28% office based oncologists (OBO), 13% lung clinics. The majority of pts. in advanced NSCLC is treated outside of academic or specialized centres in NUH or in OBO.



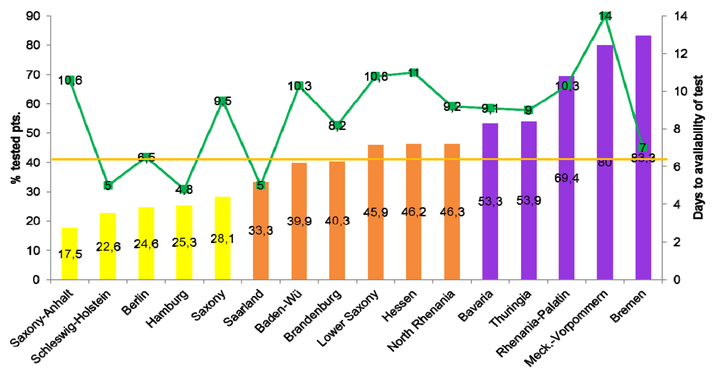
Apparently, there are no general limits for the processing of EGFR-testing in NUH or in OBO. The EGFR-mutation test has been applied in the vast majority (97%) of responding centres (100% lung clinics, 95% UH, 98% NUH, and 97% OBO). Moreover, the centres reported a sufficient quality in 85% of samples (median value). In comparison, EML4-ALK fusion gene status test was performed in 31% centres (80% lung clinics, 57% UH, 32% NUH, 6% OBO) only.

Only a minority of pts. (40%) was tested. The results of this German survey confirmed the data from Netherlands [VIII] . The test ratio seems to be higher than in Germany (mean 40% in IIIrd quarter of 2011), but the regional disparities reported in Germany correspond with the Dutch data (from 17.5% to 83.3%).

The differences in test rate between the institutions are significant (p < 0.0001): lung clinics 14% pts (Range: 9.0% - 27.8%), NUH 41% pts (Range: 0.0% - 100.0%), UH 50% pts (Range: 0.0% - 100.0%), OBO 53% pts (Range: 0.0% - 90.9%).



The time to obtaining the test results is 9.2 days (d) in average, the time does not differ significantly (p=0.901) regarding type of institution: 7.9 d (Range: 3 d – 15 d) in UH, 8.7 d in NUH (Range: 3 d – 21 d), 9.6 d in lung clinics (Range: 3 d – 14 d) and 11 d in OBO (Range: 4 d – 30 d). The reported mean time to availability of test results varies considerably among the federal states: 5 days to 14 days, the ratio of EGFR-mutation by tested pts. from 7% to 60%. Nevertheless, the ratio of tested pts. is not explainable by the time to availability of test results (as a measure for the feasibility of test). (p=0.186)



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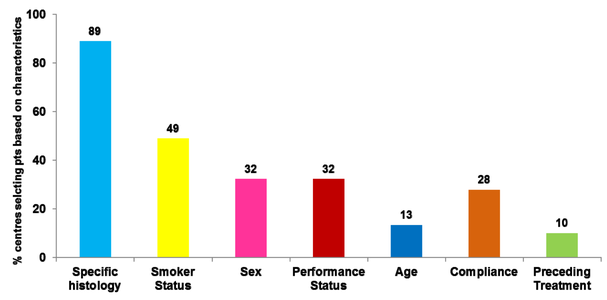
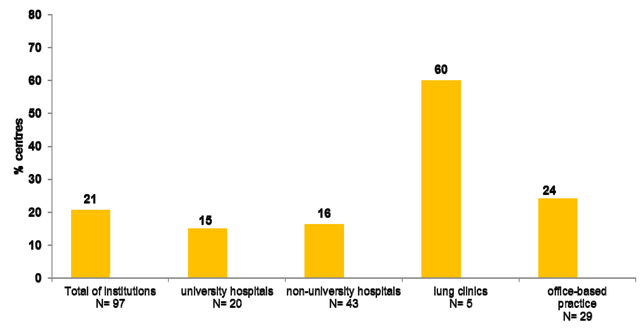
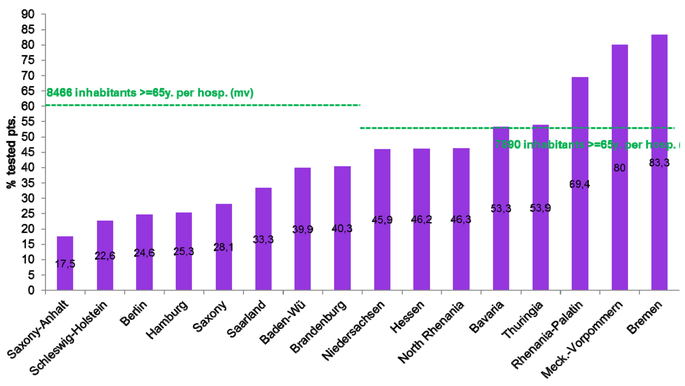
In general (reported by 91% centres) the test was performed only in pts. with specific clinical criteria (100% lung clinics, 95% UH, 95% NUH, 81% OBO). The clinical criteria used most frequently are the known predictors for clinical response: histology (89% centres), smoker status (49% centres), gender (32%). Furthermore, the patients eligible for the EGFR-test were selected by individual characteristics as performance status (32% centres), compliance (28% centres), age (13%) and preceding treatment (10%).



Due to the distribution of patients at different institutions the reimbursement patterns vary considerably: the hospitals calculate the test costs within DRGs, the vast majority of office-based practices invoice the compulsory health insurance (CHI) directly. The costs of the EGFR-test have been transferred to the pathologists or to the out-patient sector. Nevertheless, the costs of EGFR-testing present a restriction for EGFR-testing in 21% of centres and esp. in lung clinics (60%).



As in Germany the age structure of the population differs significantly by federal states, we performed a regional analysis for population older than 65 years, as the majority of cancer patients is older than 65 years. [X] In federal states with a test ratio of <=40% (mean value) the population >=65 y. per hospital is significantly higher (mean value 8446, p<0.001) than in states with a test ratio >40% (7890 inh.>=65 y./hospital). The regional analysis indicates a predicting value of health care situation on the access of patients to the EGFR-mutation testing. The federal stated with a lower density of hospitals present a test ratio below the mean level of 40%.



Conclusions

Only a minority of patients with NSCLC IIIb/IV (40%) had an access to the EGFR testing in IIIrd quarter of 2011 and to the respective treatment in case of mutation. Reasons may be the long waiting-time for test results (mean 9.2 days) or the inadequate reimbursement of testing, esp. in lung clinics. The physicians select the patients not only by predictors for clinical response but in addition by individual patient characteristics, perhaps/likely, in order to avoid the costs of testing. The regional data analysis indicates that the patient access to the EGFR-mutation test is significantly related to the health care structure in the respective federal state. Decentralized organization and funding of health care and diagnostics have led to significant regional disparities. However, the large regional disparities plead for a detailed analysis of regional health care structures in oncology.

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[IX] Diagnostics and treatment of pts with NSCLC in daily practice: HM Blommestein, HJM Groen[2], EF Smit[3], E.Thinnissen[3], CA Uyl-de Groot[1]
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[X] Robert Koch-Institut (Hrsg.) (2010) Verbreitung von Krebserkrankungen in Deutschland.Entwicklung der Prävalenzen zwischen 1990 und 2010. Beiträge zur Gesundheitsberichterstattung des Bundes. RKI, Berlin

O.I.s)