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Practice Patterns Of Genetic Testing And Target Therapy Use In Metastatic Lung Cancer

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ABSTRACT

Introduction

All patients with metastatic non-small cell lung cancer (NSCLC) should undergo EGFR mutation testing and receive appropriate therapy, however, variation in testing and therapy use is a growing concern. The objective of this investigation was to identify physicians' practice patterns and predictors of physicians' genetic testing and targeted therapy use in metastatic lung cancer.

Methods

Approximately 360 physicians caring for CanCORS patients with lung or colorectal cancer completed a survey between 2012 to 2013 assessing attitudes and practices with respect to genetic testing and targeted therapies. The outcome variables were: (1) physicians' reports that they would likely recommend (a) EGFR testing and (b) ERCC1 testing for a hypothetical patient; (2) physicians' reports that they would choose Erlotinib as first-line regimen if a patient was found to have an EGFR mutation.

Results

Physicians who often obtained information from peer-reviewed medical literature reported that they would recommend EGFR testing more than those who rarely/never used this source ($p=0.068$). Physicians who were younger, had fewer years since graduation from medical school, graduated from a U.S./Canadian school, and were Asian or White chose Erlotinib more than physicians without these features ($p=0.008$, $p=0.011$, $p=0.068$, and $p=0.021$). Physicians who reported local/national guidelines as having a high impact on their test use, and those who reported obtaining information

often from local colleagues, national/international experts, or national guidelines, chose Erlotinib more than their counterparts (p=0.066, p=0.062, p=0.037, and p=0.041). Those with solo practice types were the least likely to recommend Erlotinib compared to other practice types (p=0.013). After adjustment, gender, age, race, practice type, impact of national guidelines, and obtaining information from national/international experts all remained significantly associated with choice of Erlotinib (OR[CI]=2.07 [1.12, 3.81] and OR[CI]=1.56 [0.96, 2.52], respectfully).

Conclusion

It can be inferred that the variation seen in testing and treatment in patients with NSCLC is largely due to the differences in physicians' knowledge, which are the result of diverse sources of information. The implications that follow the findings of the present paper include: the importance of considering the content and format of reports and guidelines directed towards clinicians; and the need for easily accessible interfaces that provide the knowledge and support for clinical decision-making.

INTRODUCTION

Background of NSCLC

Lung cancer accounts for 13% of all new cancer cases.[1] About two out of three people diagnosed with lung cancer are 65 or older, and fewer than 2% of all cases are found in people younger than 45. The average age at the time of diagnosis is about 70 years old.[2]

There are two types of lung cancer: Non-small cell lung cancer (NSCLC) which accounts for about 85-90% of lung cancers, and Small cell lung cancer (SCLC) which accounts for about 10-15% of lung cancers. Fifty-four percent of NSCLC patients are male and 46% are female.[1] Eighty-three percent of NSCLC patients are Caucasian, 10% are African American, 6% are Asian Pacific Islander, and 2.5% are Asian Pacific Islander female.[3]

The Role of EGFR in NSCLC

Epidermal growth factor receptor (EGFR) is a member of the ErbB family of cell surface tyrosine kinases[4] and is encoded on chromosome 7.[5] The receptor belongs to the HER/ErbB family of tyrosine kinases.[17] The function of the receptor is to regulate both cell proliferation and apoptosis via signal transduction pathways.[6] In a healthy cell, EGFR permits the cell to grow and divide. When there are too many receptors caused by a mutation, as is the case with cancer, the cancer cells continue to grow and divide.[7]

Approximately 60% of NSCLCs express EGFR and EGFR mutations occur in approximately 10-15% of tumors, which represents about 14,000 to 20,000 patients. Approximately 90% of these mutations are exon 19 deletions or exon 21 L858R point mutations.[8] These mutations increase the kinase activity of EGFR, leading to hyperactivation of downstream pro-survival signaling pathways.[9]

Given that more than 60% of NSCLCs express EGFR and 10-15% of these harbor mutations, EGFR has become an important therapeutic target for the treatment of these tumors.[10] Research studies have shown that EGFR mutations can predict whether certain types of drugs, called tyrosine kinase inhibitors (TKIs), can help treat lung cancer. In phase III randomized trials involving patients with advanced NSCLC and targeted therapy, EGFR mutation-positive (M+) status has been shown to be predictive of significant benefit from EGFR TKIs.[11,12,13] Findings from key clinical trials comparing EGFR TKI therapy with chemotherapy show a clinical benefit with EGFR TKI treatment – specifically in patients with EGFR M+ NSCLC.[12,13,14,15,16,17,18]

ERCC1 Expression in Lung Cancer

The excision repair cross-complementation group 1 (ERCC1) protein plays a role in repairing DNA damage.[19] Prior studies have shown that high tumor levels of ERCC1 predict a benefit of adjuvant chemotherapy in patients with NSCLC, however, the value

of testing has been questioned. Although the role of ERCC1 in DNA repair is important, ERCC1 expression, measured using commercially available antibodies, is not currently useful as a predictive biomarker of response to adjuvant chemotherapy in patients with NSCLC.[19]

Clinical Guidelines

EGFR mutation testing is recommended in patients with non-squamous NSCLC (i.e., adenocarcinoma, large cell carcinoma) or in NSCLC not otherwise specified (NOS).[20] Results of the test should guide treatment decisions to ensure patients receive treatment according to cancer type and mutation subtype.[21] Patients with NSCLC who test positive for an EGFR exon 19 deletion or exon 21 substitution mutation generally respond positively to treatment with an EGFR TKI (Erlotinib).

ERCC1 testing has not been recommended in national guidelines.[22]

Statement of problem

EGFR testing is a critical component when making treatment decisions in advanced NSCLC, as it helps match each patient with the most appropriate therapy as early as possible.[23] EGFR M+ patients are more likely to respond to EGFR TKIs, and so it is important to identify the biomarker status of all patients with advanced NSCLC.[11] On the other hand, ERCC1 testing has questionable utility in advanced NSCLC and has not been recommended in national guidelines. While genetic testing has been used to profile NSCLC with continued success, variation in genetic testing and targeted therapy use are a growing concern. A study done in 1996-1997 with 350 physicians from five difference clinical scenarios showed variability in treatment recommendations and perceived treatment efficacy both within and between specialties.[24] More recently, an international survey assessing EGFR mutation testing rates and treatment practices in lung cancer showed that almost a quarter of newly diagnosed NSCLC patients in the United States were not tested for EGFR mutation.[21] The main reasons for not testing patients, according to the surveyed oncologists, included: histology (tissue and cell type of tumor), insufficient tissue to perform the test, poor general health of the patient, and long turnaround time of the results.[21] According to the same survey, one in four patients in the United States treated by surveyed oncologists were started on first-line treatment before test results were received and 60% of oncologists do not determine their treatment decisions based on a patient's EGFR mutation subtype.[21] Furthermore, physicians' knowledge of and compliance with practice guidelines are generally low, which may result in too few recommendations for testing and subsequently improper treatment recommendations for therapy.[25] Another study on the beliefs of pulmonologists and thoracic surgeons in the therapeutic approach to NSCLC confirmed that some physician beliefs regarding treatment efficacy in NSCLC care did not reflect the results of randomized, controlled trials studying these therapies, underscoring how physician attitude toward the disease and available therapies may color treatment

recommendations.[26] This raises important questions about variable expertise of physicians, adherence to guidelines, and ultimately, the reliability of the physicians' guidance that crucially underpins the management and treatment of NSCLC.[27]

Objective(s) of Investigation

Because of the aggressive and incurable nature of metastatic NSCLC, selection of first-line therapy is a critical decision point in the treatment of advanced lung cancer. The objective of the investigation (thesis) is to identify practice patterns and predictors of genetic testing and targeted therapy use in metastatic lung cancer. The thesis will provide insight into reasons for variability in testing and therapy choice in order to identify areas of improvement to ultimately ensure that future patients will receive personalized treatment for their cancer type and mutation subtype.

METHODS

Study Design & Participants

The CanCORS study was an observational study designed to evaluate cancer care and outcomes among patients with lung or colorectal cancer newly diagnosed from 2003 to 2005 and living in one of five geographic regions (northern California, Los Angeles, Alabama, Iowa, or North Carolina) or receiving care in one of five health maintenance organizations or one of 15 Veterans Affairs (VA) sites.[28,29] The characteristics of patients enrolled in CanCORS have been shown to be representative of patients identified by the Surveillance, Epidemiology, and End Results (SEER) Program for both lung and colorectal cancer.[30] Physicians caring for CanCORS patients were identified from a baseline patient survey, a follow-up survey 1 year after diagnosis, a follow-up survey in 2012, and medical records. The follow-up survey of CanCORS physicians was only performed from the summer of 2012 to the fall of 2013, and was the data used for this study's analysis.[29]

The study was conducted in two waves: the patient cohort was initially enrolled during the first wave (CanCORS I), and yielded 2,013 eligible participants with lung cancer and 4,223 with colorectal cancer who completed one of the baseline patient surveys. In the second wave (CanCORS II) additional data were collected on a subset of the patients and a physician survey was conducted with medical oncologists who were identified for the CanCORS I physician survey plus any new medical oncologists identified during the interviewers with members of the CanCORS II cohort. Approximately 900 physicians were asked to complete the survey by mail/web to assess attitudes and practices with respect to cancer survivor care and new, targeted cancer therapies. Of these 900, around 360 physicians completed the entire survey and were included in the final study sample.

Physician Survey

To understand how physicians' beliefs and characteristics influence the processes of care and outcomes of patients in the CanCORS study, physicians who made referrals for cancer care, treated cancer-related symptoms, or were involved in decisions about treatment were surveyed. The survey consisted of three primary domains: (1) physicians use and understanding of biomarkers and new biologic agents, (2) physician beliefs and practice re: cancer surveillance, and (3) physician practice characteristics and financial arrangements and demographics. The survey included two experiments in which vignettes (Appendix, questionnaire question 10 and 15) were modified in the three different versions of the survey. Respondents were randomly assigned one of these three versions. The experiment and subsequent vignette focused on in this study asks about EGFR testing for lung cancer and varies by race/ethnicity of the patient in the question (white vs. Asian vs. black). Enrollment began in July 2012 and ended October 2013.[31]

Physician Survey Content Used and Rationale for Use[31]

Domain	**Content**	**Rationale**
Physician demographic characteristics	Age, sex, race and ethnicity, year graduated from medical school, U.S./Canadian medical graduate	Potential predictors of care delivered to patients
Physician practice characteristics	Practice type, size, and ownership, and factors that influence income	Potential predictors of care delivered to patients
Volume of lung patients	Number of new lung cancer patients seen in a typical month	Potential predictor of cancer care delivery
Beliefs and utilization of biologic therapies recently approved by the FDA	Use of biologic therapies, understanding of recommendations and the supporting evidence, knowledge of potential benefits and toxicity for patients, and use of these drugs in certain clinical scenarios	Understand how physicians are using biologic therapies and if they are using them appropriately
Beliefs about the role of molecular biomarkers in the care of patients with lung cancer	Understanding and utilization of molecular profiling/genomic testing (EGFR mutations, clinical phenotypes, etc.) Personalization of treatment recommendations	Understand whether physicians are appropriately recommending molecular profiling of patients and using it to guide treatment

Outcome Variables

(1) Physicians' reports that they would likely recommend the following tests for the hypothetical patient (Appendix, questionnaire question 15):
   a. EGFR
   b. ERCC1

(2) Physicians' reports that they would choose Erlotinib as first-line regimen if a patient was found to have an EGFR mutation (Appendix, questionnaire question 16)

Statistical Analysis

Multiple imputation was used to adjust for missing item responses when analyzing the provider survey data. Frequency distributions were examined to develop groupings for responses to some survey items to facilitate their comparison and interpretation. For physician race/ethnicity, two race/ethnicity questions (Appendix, questionnaire question 36 and 37) were used to create four race categories: Non-Hispanic White, Asian, Other, and Unknown. Age was calculated by subtracting the physicians' reported birth year from the date the survey was taken. Specialty was grouped into 5 categories: oncology, hematology, oncology/hematology, specialized oncology/hematology (other, not lung), and lung hematology/oncology. For the first outcome variable on EGFR and ERCC1 testing (Appendix, questionnaire question 15), 'Very likely' and 'Somewhat likely' were combined and 'Very unlikely' and 'Somewhat unlikely' were combined. Aside from comparing the association between the hypothetical patients' race (Asian for survey A, black for survey B, and white for survey C) and EGFR or ERCC1 testing, the survey responses were combined across all three types. The second outcome variable was dichotomized with Erlotinib equal to 1 and all other treatment choices equal to 0.

Chi-square or Fisher's exact tests were used to determine physician demographic, practice characteristics, and beliefs associated with outcome variables (1) and (2), where appropriate. Means were compared used t-test and ANOVA, where appropriate. Variables that were significant at the 0.10 level in the bivariate analysis were included in a multivariable logistic regression model to determine the independent association of each variable with chosen outcomes. Because the study was more descriptive in nature, an alpha level of 0.10 was considered significant to allow for further analysis and discussion of potentially important variables.

All statistical analyses were performed using SAS University Edition (SAS Institute Inc., Cary, NC).

RESULTS

Demographic Characteristics

Description of the physician demographic characteristics can be found in Table 1. Among the 357 physicians who completed the survey, 75% were male and 25% were female. Median age was 54 years old, with the youngest physician being 36 and oldest being 82 years old. The majority of the sample identified as non-Hispanic White or Asian (66% and 23%, respectfully), while the remaining 9% of physicians identified as either non-Hispanic Black, Native Hawaiian, other race, or multiracial, and 2% said their race/ethnicity was unknown. More than half of physicians said that Oncology was their primary specialty and almost a third said that Hematology/Oncology was their primary specialty, while only 1% said that their primary specialty was Thoracic (Lung) Hematology/Oncology. The sample was evenly split between those that were involved with teaching medical students/residents and those that were not involved. A little more than three quarters of the sample graduated from a U.S./Canadian medical school, and the median years since graduation was 28 years.

Practice Characteristics

Description of the physician practice characteristics can be found in Table 2. The majority of physicians in the sample described their primary practice as a single specialty group and multi-specialty group (39% and 41%, respectfully), and one or more physicians, or a physician-owned corporation, was the most frequently reported owner of the practice (44%). The median reported percentage of the practice that included patients with lung cancer was 19%, with a range of 0-100%. Most physicians reported being paid by salary for their clinical work in 2011 (69%). Of those who were not paid by salary, exclusively fee-for-service and predominately fee-for-service best described personal income (46% and 37%, respectfully). When asked how, if at all, income is most likely to change as a result of prescribing/administering more chemotherapy and of ordering more genetic testing, most physicians said that income was not likely to change (70% and 88%, respectfully).

Preferences & Beliefs

Overall, the test predicting clinical benefit from specific treatments was reported to have the highest impact on the decision to request somatic genetic testing among the study sample (Table 3). Around 94% of physicians said that whether or not local or national guidelines have been issued on test use had a moderate or high impact on their decision to request genetic testing. On the other hand, FDA alerts about availability of testing or patient requests/inquires about the test was most commonly chosen as having a low impact on the decision to test among the sample.

Approximately three-quarters of the physicians in the study said that they often obtain information from national guidelines in order to learn about using a new somatic genetic test (Table 4). Peer-reviewed medical literature was the second most common source of information (66% said they often and 29% said they sometimes obtained information from literature). Most physicians said that they never or rarely obtain information from the test manufacturer or drug company website (32% and 44%, respectfully), test manufacturer or drug company representative (38% and 15%, respectfully), and FDA package insert (27% and 39%, respectfully). In addition, many physicians reported they rarely obtain information from local colleagues (28%) or foundation or government website (25%).

EGFR Testing

None of the physician demographic characteristics were associated with recommending EGFR testing (Table 5).

Who owns the practice was associated with recommending EGFR testing, with HMO, health plan, or insurance company ownership having the highest percentage of physicians recommending EGFR testing, followed by a university or medical school and one or more physicians or a physician-owned corporation (100%, 97%, and 97%, respectfully; p=0.080) (Table 6).

Physicians who said the test predicting toxicity from specific treatments had a low or high impact on their decision to request genetic testing recommended EGFR testing more than those who said toxicity from specific treatments had only a moderate impact (p=0.071) (Table 7). Low impact of a patient requesting/inquiring about a test on the decision to recommend genetic testing coincided with recommending EGFR testing more than moderate or high impact of patient requests/inquiries on decision-making (p=0.037). Physicians who reported that they rarely obtain information from peer-reviewed medical literature had the lowest percentage recommending EGFR testing compared to those who sometimes or often obtained information from this source (83% compared to 99% and 95%, respectfully; p=0.068) (Table 8).

ERCC1 Testing

Physicians who graduated from a medical school outside of the U.S./Canada said that they would request ERCC1 testing more than those who graduated from a U.S./Canadian medical school (p=0.103) (Table 9).

Solo practices and single specialty groups had the highest percentage of physicians recommending ERCC1 testing among the practice types (20% and 16%, respectfully; p=0.001) (Table 10). Who owns the practice also was associated with recommendation of ERCC1 testing, with university or medical school and one or more physicians or a physician-owned corporation having the highest percentage of physicians recommending

ERCC1 testing among all ownership types (13% and 16%, respectfully; p=0.073). Change in income as a result of ordering more genetic testing was also associated with recommendation of ERCC1 testing – physicians who said that ordering more genetic testing would likely increase their income recommended ERCC1 testing the most compared to those who said that ordering more genetic testing would likely decrease their income or not change their income (29% compared to 13% and 9%, respectfully; p=0.045). In addition, how the ERCC1 testing is usually requested or ordered in the practice was highly associated with whether the physician recommended ERCC1 testing -- physicians reporting that another surgeon or physician orders the test recommended ERCC1 testing the most compared to physicians who reported that they have never ordered/requested ERCC1 testing or physicians that said another oncologist orders ERCC1 testing (60% compared to 0% and 0%, respectfully; p<0.001).

Physicians who obtained information sometimes or often from local colleagues, national/international experts, national guidelines, and foundation or government websites recommended ERCC1testing more than those who never or rarely obtained information from these sources (p=0.062, p=0.037, p=0.041, and p=0.086, respectfully) (Table 12). Those who never or rarely reported obtaining information from test manufacturers or drug company websites recommended ERCC1 testing more than those who often obtained information from these sources (p=0.0260).

Recommendation of Erlotinib

Physician characteristics associated with Erlotinib are shown in Table 13. Physicians who chose Erlotinib as first-line regimen were younger and had less years since graduation from medical school compared to those who chose another treatment (p=0.008 and p=0.011, respectfully). Whether or not the physician graduated from a U.S./Canadian medical school was also associated with treatment choice, with 91% of those who did graduate from a U.S./Canadian medical school choosing Erlotinib compared to 83% of those who graduated from a medical school outside of the U.S. or Canada (p=0.068). Race/ethnicity was also associated with choice of Erlotinib, with 91% of Asian and Non-Hispanic white physicians choosing Erlotinib as the first-line regimen while only 70% of 'Other' races (non-Hispanic black, Native Hawaiian, other race, and multiracial) chose Erlotinib (p=0.021).

Practice characteristics associated with first-line regimen recommendation only included practice type – physicians who had a solo practice were the least likely to recommend Erlotinib (70%) while single and multi-specialty groups and other practice types were the most likely to recommend Erlotinib (89%, 90%, and 97%, respectively; p=0.013) (Table 14).

Physicians who said that whether or not local or national guidelines have been issued on test use had a high impact on their decision to request somatic genetic testing were more likely to choose Erlotinib compared to those who said national guidelines had a low

impact (92% and 78%, respectfully; p=0.066) (Table 15). Those who said they often obtain information from local colleagues, national/international experts, national guidelines, or foundation or government websites chose Erlotinib as first-line regimen more than those who never obtained information from these sources (p=0.062, p=0.037, p=0.041, and p=0.086, respectfully) (Table 16). On the other hand, those who say they often obtain information from test manufacturers or drug company websites chose Erlotinib the least compared to those who said they never or rarely use the source (p=0.026).

After adjusting for physician demographic characteristics, practice characteristics and preferences/beliefs, gender, age, race, practice type, impact of national guidelines on decision to request testing, and obtaining information from national/international experts on new somatic genetic testing all remained significantly associated with choice of Erlotinib as first-line regimen (Table 17). Male physicians have a higher odds of choosing Erlotinib as first-line regimen compared to females (OR=2.75; 95% CI=[1.07,7.05]; p=0.035). A one year increase in age decreases the odds of choosing Erlotinib by 7% (OR=0.93; 95% CI=[0.89, 0.98]; p=0.005). Physicians who identify as non-Hispanic black, Native Hawaiian, other race, or multiracial have a 73% decrease in odds of choosing Erlotinib as first-line regimen compared to white physicians (OR=0.27; 95% CI=[0.09, 0.77]; p=0.014). Those who graduated from a U.S./Canadian medical school have 2.36 times the odds of choosing Erlotinib compared to those who graduated from a medical school outside of the U.S./Canada (OR=2.36; 95% CI=[0.89, 6.26]; p=0.088). Physicians who believe that local or national guidelines issued on testing have a higher impact on the decision to request genetic testing have a higher odds of choosing Erlotinib compared to those who believe it has a lower impact (OR=2.07; 95% CI=[1.12, 3.871]; p=0.020). In addition, physicians who obtain information from national/international experts more often have a higher odds of choosing Erlotinib compared to those who obtain information from national/international experts less often or never (OR=1.56; 95% CI=[0.96,2.52]; p=0.073).

DISCUSSION

Most studies have been focused on patient characteristics, preferences, and knowledge of genetic testing and treatment decision-making. Although patient characteristics are important, the role of physician characteristics and preferences in decision-making has been overlooked. In the case of NSCLC, where substantial evidence and recommendation from guidelines exist on the use of EGFR testing and first-line treatment with Erlotinib, variation in use is concerning. The results of the study offer important insight into the provider perspective of decision-making in genetic testing and treatment recommendation.

In generalizing implications from this study, two fundamental assumptions become necessary: first, beliefs about therapy reveal knowledge about therapy; and second, beliefs about therapy influence actual practice.[26] Given these assumptions, the present

study supports the notion that sources of information and perceived impact of sources plays a substantial role in both the likelihood of genetic testing usage and recommendation of targeted therapy. In our study sample, physicians who obtained more information from 'credible' sources, such as national guidelines and peer-reviewed medical literature, were more likely to choose appropriate testing (EGFR testing) and properly recommend first-line treatment with Erlotinib given a patient with an EGFR mutation. On the other hand, physicians who obtained information from less 'credible' sources, such as drug company websites or test manufacturers, were less likely to recommend the proper treatment. Interestingly, physicians who reported obtaining information from more 'credible' sources, such as national guidelines and local colleagues, also reported higher use of ERCC1 testing, although national guidelines do not support its use. This may reflect the complexity and sheer magnitude of information on genetic testing and new therapies, and the difficulty for physicians in sorting through information and choosing evidence-based findings/recommendations to incorporate in practice. Overall, it can be inferred that the variation seen in testing and treatment in patients with NSCLC is largely due to the difference in knowledge of physicians, which is itself a result of the sources of information used and the perceived impact of those and other sources. These results are consistent with studies that have shown physicians' self-reported deficits in knowledge of genetic testing and guidelines.[32,33,34,35,36] Moreover, the implications that follow these findings include the importance of considering the content and format of reports/guidelines to clinicians and the need for easily accessible interfaces that provide the knowledge and support for clinical decisions.

In terms of demographic characteristics, younger physicians and those who have less years since graduation from medical school, two characteristics which are likely related, recommended Erlotinib as first-line regimen more than older physicians and those who have been out of medical school for longer. This may echo the changes in medical education and access to and/or familiarity with research databases and other sources of information. In terms of practice characteristics, the finding that physicians' with solo practices' use ERCC1 testing more and recommend Erlotinib less than other practice types can be said to further highlight the importance of knowledge – being in a solo practice limits the transfer of knowledge between physicians and others in the health system that is often present in a multi-specialty group or some larger network. This interpretation would further emphasize the importance of adequate knowledge, and of communication and discussion among members in the medical community.

Limitations

Although the results allow us to draw significant conclusions, there are some limitations to this study. An imputed data set was used for analysis, due to the missing responses for important variables, and so the validity of those responses may be questionable. Further analysis could have involved more than one type of imputed dataset and combined the results of each dataset to form conclusions from the final models. Moreover, the study results are based on self-reported indicators, and therefore actual use of testing and

treatment recommendation may not coincide with physician responses. Further research is needed with both physicians' self-reported indicators and actual practice patterns.

Sub-specialty of a physician may play a role in familiarity with proper testing and treatment recommendation, but the study was unable to perform meaningful comparisons due to the low number of physicians with a sub-specialty. However, it is more likely that patients with NSCLC will be under the care of general oncologists than specialized oncologists.

It is also possible that differences in guideline recommendations between professional organizations can play a role in some of the practice variability. In addition, physicians who completed this survey may be more interested/involved in research, and therefore have more knowledge of genetic testing and treatment choices than those who did not participate. This would, however, only further highlight the importance of the knowledge of physicians.

CONCLUSION

Summary of findings

Failing to be tested or to receive proper treatment may adversely affect patient outcomes by compromising access to treatment that is associated with an overall survival benefit and superior quality of life. Ideally, all patients who are fit for treatment of advanced disease should undergo EGFR mutation testing in a timely manner and subsequently receive appropriate therapy so as to not delay first-line treatment choices and, therefore, higher quality outcomes. Thus, the identification of practice patterns and predictors of genetic testing and targeted therapy use are important in helping us move toward the goal of properly testing and treating suitable patients. The results of this study have highlighted the importance of information sources and physicians' knowledge of novel testing and treatment recommendations. In particular, the variation in EGFR testing and subsequent recommendation of appropriate therapy in the management of NSCLC may be due to physicians' attitudes toward the impact of information sources and consequent knowledge attained from these sources. It is important that physicians follow national guidelines in order for patients to have the best possible outcomes; efforts should be directed to improving physicians' incorporation of guideline recommendations into their practice.

Implications & Recommendations

There will be an expanded need for physicians, particularly oncologists, knowledgeable in cancer genetics and novel treatments. Physicians must be aware of and understand the latest evidence-based guidelines for diagnosis and care, and must discuss test results and treatment recommendations with the patients. This will require new curricula, training, and facile knowledge transfer.[37]

To start, an easy checklist for oncologists dealing with advanced NSCLC patients may help ensure all patients receive testing and results prior to treatment recommendation. In terms of education, an annual conference or webinar could be used to update and/or tests physicians on the latest findings and recommendations in the specialty. This can be something established by national or professional associations, with the opportunity for physicians to count their completion of the conference/webinar toward a CME credit.

Education alone does not necessarily translate into adoption of appropriate practices. Additional research is needed to further characterize contextual factors influencing the incorporation of genetic testing and management into clinical practice, and the organizational changes needed within the healthcare system to provide cancer genetics services effectively.[38]

Table 1. Description of the physician sample characteristics.

Characteristic	N (%)*
Race/ethnicity	
Non-Hispanic White	237 (66.4)
Asian	82 (23.0)
Other†	32 (9.0)
Unknown	6 (1.7)
Age (years)	
Mean ± SD	54.00 ± 9.40
Median (Range)	54.00 (36, 82)
Years since graduation,	
Mean ± SD	27.73 ± 9.71
Median (Range)	28.00 (8, 55)
Sex	
Male	267 (74.8)
Female	90 (25.2)
Graduation from U.S./Canadian medical school	
Yes	272 (76.2)
No	85 (23.8)
Specialty	
Hematology	7 (2.0)
Oncology	224 (63.3)
Hematology and Oncology	108 (30.5)
Specialized Hem/Onc (Lung)	4 (1.1)
Specialized Hem/Onc (Other)	11 (3.1)
Involvement with teaching medical students/residents	
Yes	168 (47.1)
No	189 (52.9)

* Numbers may not sum to 357 due to missing data, and percentages may not sum to 100% due to rounding.

† Other includes non-Hispanic Black, Native Hawaiian, other race, and multiracial.

Table 2. Description of the physician sample practice characteristics.

Characteristic	N (%)*
Practice type	
Solo practice	27 (7.6)
Single specialty group	138 (38.7)
Multi-specialty group	147 (41.2)
Other	45 (12.6)
% PTs with lung cancer	
Mean ± SD	29.23 ± 27.44
Median (Range)	19.44 (0, 100)
Paid by salary for clinical work in 2011?	
Yes	245 (68.6)
No	112 (31.4)
Best describes personal clinical income	
Exclusively fee-for-service	52 (46.4)
Predominantly fee-for-service	41 (36.6)
Equal mix of fee-for-service & capitation	16 (14.3)
Predominantly capitation	2 (1.8)
Exclusively capitation	1 (0.9)
Who owns the practice	
University or medical school	58 (16.3)
Federal, state, or local government	16 (4.5)
1 or 1+ physicians/physician-owned corp	157 (44.0)
A hospital	66 (18.5)
HMO, health plan, or insurance company	43 (12.0)
Some other type of owner	17 (4.8)
Don't know	0 (0.0)
How, if at all, income is mostly likely to change as a result of prescribing/administering more chemotherapy	
Likely to decrease	32 (9.0)
Not likely to change	249 (69.8)
Likely to decrease	57 (16.0)
Don't know	19 (5.3)
How, if at all, income is mostly likely to change as a result of ordering more genetic testing	
Likely to decrease	8 (2.2)
Not likely to change	313 (87.7)
Likely to increase	21 (5.9)
Don't know	15 (4.2)

* Numbers may not sum to 357 due to missing data, and percentages may not sum to 100% due to rounding.

† If not paid by salary

Table 3. Description of physician preferences: impact of variables on requesting somatic genetic testing.

Characteristic	N (%)*
Whether or not local or national guidelines have been issued on test use	
Low impact	20 (5.6)
Moderate impact	108 (30.3)
High impact	229 (64.2)
FDA alerts about availability of test	
Low impact	97 (27.2)
Moderate impact	165 (46.2)
High impact	95 (26.6)
Test sensitivity and specificity	
Low impact	14 (3.9)
Moderate impact	125 (35.0)
High impact	218 (61.1)
Prevalence of genetic alteration	
Low impact	50 (14.0)
Moderate impact	181 (50.7)
High impact	126 (35.3)
Test predicts clinical benefit from specific treatments	
Low impact	1 (0.3)
Moderate impact	37 (10.4)
High impact	319 (89.4)
Test predicts toxicity from specific treatments	
Low impact	24 (6.7)
Moderate impact	151 (42.3)
High impact	182 (51.0)
Test predicts prognostic information	
Low impact	21 (5.9)
Moderate impact	150 (42.0)
High impact	186 (52.1)
Patient requests/inquires about test	
Low impact	97 (27.2)
Moderate impact	206 (57.7)
High impact	54 (15.1)

* Numbers may not sum to 357 due to missing data, and percentages may not sum to 100% due to rounding.

Table 4. Description of physician sources of information: how often they obtain information from the following sources in order to learn about using a new somatic genetic test.

Characteristic	N (%)*
Local colleagues	
Never	27 (7.6)
Rarely	101 (28.3)
Sometimes	163 (45.7)
Often	66 (18.5)
National/international experts	
Never	9 (2.5)
Rarely	43 (12.0)
Sometimes	141 (39.5)
Often	164 (45.9)
Test manufacturer or drug company representative	
Never	53 (14.9)
Rarely	134 (37.5)
Sometimes	139 (38.9)
Often	31 (8.7)
National guidelines	
Never	4 (1.1)
Rarely	12 (3.4)
Sometimes	75 (21.0)
Often	266 (74.5)
Scientific meetings and conferences	
Never	1 (0.3)
Rarely	22 (6.2)
Sometimes	121 (33.9)
Often	213 (59.7)
Peer-reviewed medical literature	
Never	4 (1.1)
Rarely	13 (3.6)
Sometimes	104 (29.1)
Often	236 (66.1)
Foundation or government website	
Never	19 (5.3)
Rarely	90 (25.2)
Sometimes	142 (39.8)
Often	106 (29.7)
Evidence-based, synthesized websites	
Never	25 (7.0)
Rarely	55 (15.4)
Sometimes	111 (31.1)

Often	166 (46.5)
Test manufacturer or drug company websites	
Never	114 (31.9)
Rarely	158 (44.3)
Sometimes	77 (21.6)
Often	8 (2.2)
FDA package insert	
Never	97 (27.2)
Rarely	139 (38.9)
Sometimes	101 (28.3)
Often	20 (5.6)

* Numbers may not sum to 357 due to missing data, and percentages may not sum to 100% due to rounding.

Table 5. Unadjusted associations between physician characteristics and respondents who reported they were 'Very Likely' or 'Somewhat Likely' to order EGFR.

Characteristic	N*	% Very/Somewhat Likely (EGFR)	p†
Race/ethnicity			0.760
Non-Hispanic White	209	95.2	
Asian	70	97.1	
Other†	30	93.3	
Unknown	6	100.0	
Age (years), mean ± SD			0.397
Very/Somewhat Likely	54.27 ± 9.29		
Very/Somewhat Unlikely	56.43 ± 9.65		
Years since graduation, mean ± SD			0.490
Very/Somewhat Likely	28.12 ± 9.55		
Very/Somewhat Unlikely	29.93 ± 9.84		
Sex			1.000
Male	236	95.3	
Female	79	96.2	
Graduation from U.S./Canadian medical school			0.347
Yes	237	96.2	
No	78	93.6	
Specialty			0.815
Hematology	5	100.0	
Oncology	194	94.9	
Hematology and Oncology	106	97.1	
Specialized Hem/Onc (Lung)	4	100	
Specialized Hem/Onc (Other)	3	100	
Involvement with teaching medical students/residents			0.564
Yes	136	96.3	
No	179	95.0	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 6. Unadjusted associations between practice characteristics and respondents who reported they were 'Very Likely' or 'Somewhat Likely' to order EGFR.

Characteristic	N*	% Very/Somewhat Likely (EGFR)	p†
Practice type			0.340
Solo practice	27	92.6	
Single specialty group	130	96.9	
Multi-specialty group	122	95.9	
Other	36	91.7	
% PTs with lung cancer, mean ± SD			0.316
Very/Somewhat Likely	29.73 ± 27.44		
Very/Somewhat Unlikely	22.19 ± 27.35		
Paid by salary for clinical work in 2011?			0.154
Yes	210	94.3	
No	105	98.1	
Best describes personal clinical income†			1.000
Exclusively fee-for-service	50	98.0	
Predominantly fee-for-service	37	97.3	
Equal mix of fee-for-service & capitation	15	100.0	
Predominantly capitation	2	100.0	
Exclusively capitation	1	100.0	
Who owns the practice			0.080
University or medical school	36	97.2	
Federal, state, or local government	14	92.9	
1 or 1+ physicians/physician-owned corp.	152	96.7	
A hospital	59	91.5	
HMO, health plan, or insurance company	41	100.0	
Some other type of owner	13	84.6	
Don't know	0	0.0	
How, if at all, income is mostly likely to change as a result of prescribing/administering more chemotherapy			0.877
Likely to decrease	30	96.7	
Not likely to change	211	95.7	
Likely to decrease	57	94.7	
Don't know	17	94.1	
How, if at all, income is mostly likely to change as a result of ordering more genetic testing			0.188
Likely to decrease	8	100.0	
Not likely to change	279	96.1	
Likely to increase	16	87.5	
Don't know	12	91.7	

How the test is usually requested or ordered in your practice			0.656
Self	285	95.1	
Another oncologist	0	0.0	
Pathologist	28	100.0	
Surgeon or other physician	1	100.0	
This test has not been ordered/requested	1	100.0	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 7. Unadjusted associations between impact of sources on requesting genetic testing and respondents who reported they were 'Very Likely' or 'Somewhat Likely' to order EGFR.

Characteristic	N*	% Very/Somewhat Likely (EGFR)	p†
Whether or not local or national guidelines have been issued on test use			0.802
Low impact	17	94.1	
Moderate impact	92	95.7	
High impact	206	95.6	
FDA alerts about availability of test			0.646
Low impact	85	94.1	
Moderate impact	144	96.5	
High impact	86	95.4	
Test sensitivity and specificity			0.669
Low impact	13	92.3	
Moderate impact	111	95.5	
High impact	191	95.8	
Prevalence of genetic alteration			0.264
Low impact	44	100.0	
Moderate impact	157	94.3	
High impact	114	95.6	
Test predicts clinical benefit from specific treatments			1.000
Low impact	1	100.0	
Moderate impact	29	96.6	
High impact	285	95.4	
Test predicts toxicity from specific treatments			0.071
Low impact	22	100.0	
Moderate impact	134	92.5	
High impact	159	97.5	
Test predicts prognostic information			0.470
Low impact	20	100.0	
Moderate impact	132	96.2	
High impact	163	94.5	
Patient requests/inquires about test			0.037
Low impact	90	97.8	
Moderate impact	179	94.4	
High impact	46	95.7	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 8. Unadjusted associations between how often physicians obtain information from the following sources in order to learn about using a new somatic genetic test and respondents who reported they were 'Very Likely' or 'Somewhat Likely' to order EGFR.

Characteristic	N*	% Very/Somewhat Likely (EGFR)	p†
Local colleagues			0.972
Never	25	96.0	
Rarely	90	94.4	
Sometimes	148	96.0	
Often	52	96.2	
National/international experts			0.381
Never	9	100.0	
Rarely	35	94.3	
Sometimes	126	97.6	
Often	145	93.8	
Test manufacturer or drug company representative			0.132
Never	44	97.7	
Rarely	117	95.7	
Sometimes	124	96.8	
Often	30	86.7	
National guidelines			0.846
Never	4	100.0	
Rarely	7	100.0	
Sometimes	69	97.1	
Often	235	94.9	
Scientific meetings and conferences			0.614
Never	1	100.0	
Rarely	20	100.0	
Sometimes	112	96.4	
Often	182	94.5	
Peer-reviewed medical literature			0.068
Never	4	100.0	
Rarely	12	83.3	
Sometimes	92	98.9	
Often	207	94.7	
Foundation or government website			0.340
Never	17	100.0	
Rarely	79	96.2	
Sometimes	127	92.9	
Often	92	97.8	
Evidence-based, synthesized websites			0.268
Never	23	91.3	
Rarely	49	91.8	

Sometimes	97	96.9	
Often	146	96.6	
Test manufacturer or drug company websites			0.192
Never	104	98.1	
Rarely	137	94.2	
Sometimes	67	95.5	
Often	7	85.7	
FDA package insert			0.575
Never	88	97.7	
Rarely	119	95.0	
Sometimes	92	94.6	
Often	16	93.8	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 9. Unadjusted associations between physician characteristics and respondents who reported they were 'Very Likely' or 'Somewhat Likely' to order ERCC1.

Characteristic	N*	% Very/Somewhat Likely (ERCC1)	p†
Race/ethnicity			0.578
Non-Hispanic White	169	10.1	
Asian	58	10.3	
Other†	22	18.2	
Unknown	6	0.0	
Age (years), mean ± SD			0.788
Very/Somewhat Likely	53.56 ± 9.52		
Very/Somewhat Unlikely	54.06 ± 9.12		
Years since graduation, mean ± SD			0.853
Very/Somewhat Likely	27.59 ± 9.83		
Very/Somewhat Unlikely	27.95 ± 9.33		
Sex			0.836
Male	193	10.4	
Female	62	11.3	
Graduation from U.S./Canadian medical school			0.103
Yes	193	8.8	
No	62	16.1	
Specialty			0.678
Hematology	5	20.0	
Oncology	162	10.5	
Hematology and Oncology	81	8.8	
Specialized Hem/Onc (Lung)	3	0.0	
Specialized Hem/Onc (Other)	1	0.0	
Involvement with teaching medical students/residents			0.850
Yes	109	11.0	
No	146	10.3	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 10. Unadjusted associations between practice characteristics and respondents who reported they were 'Very Likely' or 'Somewhat Likely' to order ERCC1.

Characteristic	N*	% Very/Somewhat Likely (ERCC1)	p†
Practice type			0.001
Solo practice	20	20.0	
Single specialty group	108	15.7	
Multi-specialty group	98	2.0	
Other	29	13.8	
% PTs with lung cancer, mean ± SD			0.632
Yes	171	9.9	
No	84	11.9	
Paid by salary for clinical work in 2011?			0.877
Very/Somewhat Likely	29.72 ± 27.88	89.2	
Very/Somewhat Unlikely	25.24 ± 23.57	88.6	
Best describes personal clinical income†			0.928
Exclusively fee-for-service	41	12.2	
Predominantly fee-for-service	28	10.7	
Equal mix of fee-for-service & capitation	13	15.4	
Predominantly capitation	1	0.0	
Exclusively capitation	1	0.0	
Who owns the practice			0.073
University or medical school	32	12.5	
Federal, state, or local government	10	0.0	
1 or 1+ physicians/physician-owned corp.	120	15.8	
A hospital	50	8.0	
HMO, health plan, or insurance company	32	0.0	
Some other type of owner	11	0.0	
Don't know	0	0.0	
How, if at all, income is mostly likely to change as a result of prescribing/administering more chemotherapy			0.504
Likely to decrease	8	8.0	
Not likely to change	166	10.8	
Likely to decrease	50	8.0	
Don't know	14	21.4	
How, if at all, income is mostly likely to change as a result of ordering more genetic testing			0.045
Likely to decrease	8	12.5	
Not likely to change	225	8.9	
Likely to increase	14	28.6	
Don't know	8	25.0	

How the test is usually requested or ordered in your practice			<0.001
Self	79	27.9	
Another oncologist	6	0.0	
Pathologist	7	28.6	
Surgeon or other physician	5	60.0	
This test has not been ordered/requested	158	0.0	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 11. Unadjusted associations between impact of variables on requesting somatic genetic testing and respondents who reported they were 'Very Likely' or 'Somewhat Likely' to order ERCC1.

Characteristic	N*	% Very/Somewhat Likely (ERCC1)	p†
Whether or not local or national guidelines have been issued on test use			0.479
Low impact	13	15.4	
Moderate impact	74	13.5	
High impact	168	8.9	
FDA alerts about availability of test			0.560
Low impact	64	7.8	
Moderate impact	118	12.7	
High impact	73	9.6	
Test sensitivity and specificity			0.738
Low impact	12	8.3	
Moderate impact	87	12.6	
High impact	156	9.6	
Prevalence of genetic alteration			0.553
Low impact	38	13.2	
Moderate impact	129	8.5	
High impact	88	12.5	
Test predicts clinical benefit from specific treatments			0.750
Low impact	1	0.0	
Moderate impact	23	13.0	
High impact	231	10.4	
Test predicts toxicity from specific treatments			0.302
Low impact	19	21.1	
Moderate impact	106	9.4	
High impact	130	10.0	
Test predicts prognostic information			0.246
Low impact	16	0.0	
Moderate impact	116	9.5	
High impact	123	13.0	
Patient requests/inquires about test			0.525
Low impact	70	7.1	
Moderate impact	147	11.6	
High impact	38	13.2	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 12. Unadjusted associations between how often physicians obtain information from the following sources in order to learn about using a new somatic genetic test and respondents who reported they were 'Very Likely' or 'Somewhat Likely' to order ERCC1.

Characteristic	N*	% Very/Somewhat Likely (ERCC1)	p†
Local colleagues			0.062
Never	26	73.1	
Rarely	90	91.1	
Sometimes	149	89.9	
Often	52	90.4	
National/international experts			0.037
Never	9	55.6	
Rarely	36	88.9	
Sometimes	127	89.0	
Often	145	91.0	
Test manufacturer or drug company representative			0.237
Never	44	93.2	
Rarely	118	91.5	
Sometimes	125	87.2	
Often	30	80.0	
National guidelines			0.041
Never	4	50.0	
Rarely	8	100.0	
Sometimes	69	84.1	
Often	236	90.7	
Scientific meetings and conferences			0.346
Never	1	100.0	
Rarely	20	95.0	
Sometimes	114	85.1	
Often	182	90.7	
Peer-reviewed medical literature			0.116
Never	4	50.0	
Rarely	12	91.7	
Sometimes	94	87.2	
Often	207	90.3	
Foundation or government website			0.086
Never	17	70.6	
Rarely	80	88.8	
Sometimes	127	91.3	
Often	93	89.3	
Evidence-based, synthesized websites			0.425
Never	23	87.0	
Rarely	49	83.7	

Sometimes	99	87.9	
Often	146	91.8	
Test manufacturer or drug company websites			0.026
Never	104	87.5	
Rarely	138	94.2	
Sometimes	68	82.4	
Often	7	71.4	
FDA package insert			0.351
Never	88	88.6	
Rarely	121	92.6	
Sometimes	92	84.8	
Often	16	87.5	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 13. Unadjusted associations between physician characteristics and choice of Erlotinib as first-line regimen.

Characteristic	N*	% choosing Erlotinib	p†
Race/ethnicity			0.021
Non-Hispanic white	210	90.5	
Asian	70	91.4	
Other†	31	71.0	
Unknown	6	100.0	
Age (years), mean ± SD			0.008
Erlotinib	53.88 ± 9.16		
Other	58.26 ± 9.46		
Years since graduation, mean ± SD			0.011
Erlotinib	27.70 ± 9.36		
Other	32.06 ± 10.12		
Sex			0.597
Male	238	89.5	
Female	79	87.3	
Graduation from U.S./Canadian medical school			0.068
Yes	239	90.8	
No	78	83.3	
Specialty			0.634
Hematology	5	80.0	
Oncology	195	90.3	
Hematology and Oncology	107	86.9	
Specialized Hem/Onc (Lung)	4	100	
Specialized Hem/Onc (Other)	3	100	
Involvement with teaching medical students/residents			0.258
Yes	137	91.2	
No	180	87.2	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 14. Unadjusted associations between practice characteristics and choice of Erlotinib as first-line regimen.

Characteristic	N*	% choosing Erlotinib	p†
Practice type			0.013
Solo practice	27	70.4	
Single specialty group	130	89.2	
Multi-specialty group	123	90.2	
Other	37	97.3	
% PTs with lung cancer, mean ± SD			0.363
Erlotinib	29.72 ± 27.88		
Other	25.24 ± 23.57		
Paid by salary for clinical work in 2011?			0.877
Yes	212	89.2	
No	105	88.6	
Best describes personal clinical income†			0.646
Exclusively fee-for-service	50	92.0	
Predominantly fee-for-service	37	83.8	
Equal mix of fee-for-service & capitation	15	86.7	
Predominantly capitation	2	100.0	
Exclusively capitation	1	100.0	
Who owns the practice			0.597
University or medical school	38	92.1	
Federal, state, or local government	14	100.0	
1 or 1+ physicians/physician-owned corp.	130	85.5	
A hospital	53	89.8	
HMO, health plan, or insurance company	38	92.7	
Some other type of owner	12	92.3	
Don't know	0	0.0	
How, if at all, income is mostly likely to change as a result of prescribing/administering more chemotherapy			0.289
Likely to decrease	30	80.0	
Not likely to change	213	88.7	
Likely to decrease	57	93.0	
Don't know	17	94.1	
How, if at all, income is mostly likely to change as a result of ordering more genetic testing			0.452
Likely to decrease	8	87.5	
Not likely to change	280	88.6	
Likely to increase	16	100.0	
Don't know	13	84.6	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 15. Unadjusted associations between impact of variables on requesting somatic genetic testing and choice of Erlotinib as first-line regimen.

Characteristic	N*	% choosing Erlotinib	p†
Whether or not local or national guidelines have been issued on test use			0.066
Low impact	18	77.8	
Moderate impact	93	85.0	
High impact	206	91.8	
FDA alerts about availability of test			0.367
Low impact	86	90.7	
Moderate impact	145	90.3	
High impact	86	84.9	
Test sensitivity and specificity			0.822
Low impact	13	84.6	
Moderate impact	111	88.3	
High impact	193	89.6	
Prevalence of genetic alteration			0.185
Low impact	44	95.5	
Moderate impact	159	86.2	
High impact	114	90.4	
Test predicts clinical benefit from specific treatments			0.245
Low impact	1	100.0	
Moderate impact	30	80.0	
High impact	286	89.9	
Test predicts toxicity from specific treatments			0.297
Low impact	22	90.9	
Moderate impact	135	91.9	
High impact	160	86.3	
Test predicts prognostic information			0.818
Low impact	20	85.0	
Moderate impact	133	88.7	
High impact	164	89.6	
Patient requests/inquires about test			0.673
Low impact	90	86.7	
Moderate impact	181	89.5	
High impact	46	91.3	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 16. Unadjusted associations between how often physicians obtain information from the following sources in order to learn about using a new somatic genetic test and choice of Erlotinib as first-line regimen.

Characteristic	N*	% choosing Erlotinib	p†
Local colleagues			0.062
Never	26	73.1	
Rarely	90	91.1	
Sometimes	149	89.9	
Often	52	90.4	
National/international experts			0.037
Never	9	55.6	
Rarely	36	88.9	
Sometimes	127	89.0	
Often	145	91.0	
Test manufacturer or drug company representative			0.237
Never	44	93.2	
Rarely	118	91.5	
Sometimes	125	87.2	
Often	30	80.0	
National guidelines			0.041
Never	4	50.0	
Rarely	8	100.0	
Sometimes	69	84.1	
Often	236	90.7	
Scientific meetings and conferences			0.346
Never	1	100.0	
Rarely	20	95.0	
Sometimes	114	85.1	
Often	182	90.7	
Peer-reviewed medical literature			0.116
Never	4	50.0	
Rarely	12	91.7	
Sometimes	94	87.2	
Often	207	90.3	
Foundation or government website			0.086
Never	17	70.6	
Rarely	80	88.8	
Sometimes	127	91.3	
Often	93	89.3	
Evidence-based, synthesized websites			0.425

Never	23	87.0	
Rarely	49	83.7	
Sometimes	99	87.9	
Often	146	91.8	
Test manufacturer or drug company websites			0.026
Never	104	87.5	
Rarely	138	94.2	
Sometimes	68	82.4	
Often	7	71.4	
FDA package insert			0.351
Never	88	88.6	
Rarely	121	92.6	
Sometimes	92	84.8	
Often	16	87.5	

* Numbers may not sum to total due to missing data.

† P-value for χ^2 test or Fisher's Exact test, where appropriate.

Table 17. Final logistic regression model predicting choice of Erlotinib as first-line regimen.

Variable	OR (95% CI)	p
Male	2.75 (1.07, 7.05)	0.035
Age	0.93 (0.89, 0.98)	0.005
Race		0.031
Non-Hispanic White	1.00	--
Asian	1.52 (0.47, 4.88)	0.483
Other*	0.27 (0.09, 0.77)	0.014
Unknown†	--	0.987
Graduation from U.S./Canadian medical school	2.36 (0.89, 6.26)	0.088
Practice type		0.149
Solo practice	1.00	--
Single specialty group	1.71 (0.52, 5.67)	0.378
Multi-specialty group	1.88 (0.53, 6.66)	0.327
Other	15.87 (1.51, 167.19)	0.021
Impact on requesting somatic genetic testing		
Whether or not local or national guidelines have been issued on test	2.07 (1.12, 3.81)	0.020
How often physicians obtain information from sources in order to learn about using a new somatic genetic test		
National/international experts	1.56 (0.96, 2.52)	0.073

* Other includes non-Hispanic Black, Native Hawaiian, other race, and multiracial.

† Quasi-complete separation of data points --- the maximum likelihood estimate does not exist.

APPENDIX

Appendix 1. Questions used from survey:

1. How much impact does each of the following have on your decision to request **somatic genetic testing**?

(MARK **ONE BOX** IN EACH ROW)	Little or no impact	Moderate impact	High impact
a. Whether local or national guidelines have been issued on test use	1☐	2☐	3☐
b. Food and Drug Administration (FDA) alerts about availability of testing	1☐	2☐	3☐
c. Test sensitivity and specificity (ability of test to detect a genetic change if it is present or exclude if not present)	1☐	2☐	3☐
d. Prevalence of genetic alteration	1☐	2☐	3☐
e. Test predicts clinical benefit from specific treatments	1☐	2☐	3☐
f. Test predicts toxicity from specific treatments	1☐	2☐	3☐
g. Test provides prognostic information	1☐	2☐	3☐
h. Patient requests/inquiries about tests	1☐	2☐	3☐

3. How often do you obtain information from the following sources in order to learn about using a new **somatic genetic test** in your clinical practice?

(MARK **ONE BOX** IN EACH ROW)	Never	Rarely	Sometimes	Often
a. Local colleagues	1☐	2☐	3☐	4☐
b. National/international experts	1☐	2☐	3☐	4☐
c. Test manufacturer or drug company representative	1☐	2☐	3☐	4☐
d. National guidelines (e.g., NCCN or ASCO)	1☐	2☐	3☐	4☐
e. Scientific meetings and conferences	1☐	2☐	3☐	4☐
f. Peer-reviewed medical literature	1☐	2☐	3☐	4☐
g. Foundation or government websites (e.g. ASCO or NIH)	1☐	2☐	3☐	4☐
h. Evidence-based, synthesized websites (e.g. UpToDate)	1☐	2☐	3☐	4☐
i. Test manufacturer or drug company websites	1☐	2☐	3☐	4☐
j. FDA package insert	1☐	2☐	3☐	4☐

14. Genetic testing can be obtained by a variety of providers. For each test listed, select the one answer that best reflects how each test is usually requested or ordered in your practice.

(MARK **ONE BOX** IN EACH ROW)	I request/ order this test	Another oncologist requests/ orders this test	A pathologist routinely requests/ orders this test	A surgeon or other physician requests/ orders this test	This test has not been requested/ ordered
a. *EGFR*	1☐	2☐	3☐	4☐	5☐
b. *KRAS*	1☐	2☐	3☐	4☐	5☐
c. *EML4-ALK*	1☐	2☐	3☐	4☐	5☐
d. ERCC1	1☐	2☐	3☐	4☐	5☐

Next, we will ask you about a hypothetical patient.

15. Mrs. K is a 62 year-old Asian female who has never smoked and was recently diagnosed with stage IV adenocarcinoma of the lung. She has bilateral lung nodules and an adrenal metastasis. She has a good performance status, minimal symptoms, and is interested in starting therapy. She has no hemoptysis or history of cardiovascular disease or blood clots. At this point in time, how likely are you to recommend the following tests on her core biopsy?

(MARK **ONE BOX** IN EACH ROW)	**Very unlikely**	**Somewhat unlikely**	**Somewhat likely**	**Very likely**	**I have limited experience with this test**
a. *EGFR*	1☐	2☐	3☐	4☐	5☐
b. *KRAS*	1☐	2☐	3☐	4☐	5☐
c. *EML4-ALK*	1☐	2☐	3☐	4☐	5☐
d. ERCC1	1☐	2☐	3☐	4☐	5☐

16. Assume Mrs. K underwent *EGFR* testing, and was found to have an *EGFR* mutation (deletion in exon 19). Which of the following first-line regimens are you most likely to recommend? (MARK **ONE** BOX)

1☐ Erlotinib
2☐ Platinum doublet
3☐ Platinum doublet+ bevacizumab
4☐ Platinum doublet + cetuximab
5☐ Other regimen (specify _____)
6☐ No chemotherapy
7☐ Would review further with pathologist or other colleagues before making chemotherapy decisions

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29. In what year were you born? 19_____
YEAR

30. In what year did you graduate from medical school? _____
YEAR

31. Did you graduate from either a U.S. or Canadian medical school?

1☐ Yes
2☐ No

32. What is your primary specialty (i.e., the one specialty in which you spend most of your time)?

_____
SPECIALTY

---

35. What is your gender?

1☐ Male
2☐ Female

36. Are you of Hispanic origin or ancestry?

1☐ Yes
2☐ No

37. Which do you feel best describes your race or ethnicity? (MARK ALL THAT APPLY)

1☐ White
2☐ Black or African-American
3☐ Asian
4☐ Native Hawaiian or other Pacific Islander
5☐ American Indian
6☐ Alaskan Native
8☐ Other, please specify: _____

38. Are you **currently** involved with teaching medical students and/or residents?

1☐ Yes ➔ GO TO QUESTION 38b
2☐ No ➔ GO TO QUESTION 39

38b. In a **typical month**, on how many days do you teach for at least some of the day?

1☐ 0 to 1 day per month
2☐ 2 to 5 days per month
3☐ 6-15 days per month
4☐ More than 15 days per month

39. Is your primary practice a:

1☐ Solo practice→GO TO QUESTION 40
2☐ Single specialty group→GO TO QUESTION 40
3☐ Multi-specialty group→GO TO QUESTION 39b
8☐ Other, please specify: _____→GO TO QUESTION 40

41. Who owns this practice? Is it:

1☐ A medical school or university
2☐ Federal, state or local government
3☐ One or more physicians, or a physician-owned corporation
4☐ A hospital
5☐ An HMO, health plan or insurance company
8☐ Some other type of owner (please specify: _____)
9☐ Don't know

44. Still thinking about the practice where you see most of your cancer patients if you have more than one practice site, please consider how you were paid for your clinical work in 2011 (excluding bonuses).

44a. Were you paid by salary?

1☐ Yes → GO TO QUESTION 44b
2☐ No → GO TO QUESTION 45

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45. If you were not paid by salary in 2011, which best describes *your* personal clinical income (excluding bonuses)? *(Under capitation, a fixed amount is paid per patient per month regardless of services provided.)*

1☐ Exclusively fee-for-service
2☐ Predominantly fee-for-service
3☐ Equal mixture of fee-for-service and capitation
4☐ Predominantly capitation

---

47. For many providers, income is influenced by prescribing and/or ordering practices. How, if at all, is your income most likely to change as a result of …

(MARK **ONE BOX** IN EACH ROW)	**Likely to decrease**	**Not likely to change**	**Likely to increase**	**Don't know**
a. Prescribing/administering more chemotherapy	1☐	2☐	3☐	9☐
b. Ordering more genetic testing	1☐	2☐	3☐	9☐
c. Providing survivorship care for asymptomatic patients after completion of active cancer treatment	1☐	2☐	3☐	9☐

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