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Trends among US oncologists in managing patients with nonsmall cell lung carcinoma: 2011-2013

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Abstract

Background: The management of patients with nonsmall cell lung carcinoma (NSCLC) is evolving rapidly. There have been Food and Drug Administration approvals for new therapies or expanded use of existing therapies in each of the last 6-year, with three approvals in the past year alone. This pattern is projected to continue with the advances of immunotherapies (e.g., programmed death-1 and programmed death-ligand 1 inhibitors), producing promising clinical trial results. With this continual stream of new options, it is important to understand oncologists’ grasp of the evidence supporting their use and their approach to incorporation into practice. Methods: To assess oncologists’ current approaches to managing patients with advanced local and metastatic lung cancer, we distributed a patient vignette survey to a cohort of practicing oncologists in 2011, 2012, and 2013 to assess trends in practice patterns of US oncologists in the management of patients with advanced local and metastatic lung cancer. Results: Shifts in practice patterns regarding testing and treatment for NSCLC were observed to be reflective of the shifts in the corresponding evidence. Oncologists have favorable perceptions of NSCLC immunotherapies, but lack familiarity with current immunotherapies and how they work.

Keywords: Lung cancer, practice patterns, case-based survey

INTRODUCTION

Despite the strides that have been made in diagnosis and treatment, lung cancer remains the leading cause of cancer death in the US. The number of new cases this year is estimated at 224,210. This is comparable to breast cancer (235,030) and prostate cancer (233,000). However, the mortality attributable to lung cancer is in stark contrast to these other indications: 159,260 deaths are estimated to occur in 2014 attributable to lung cancer, 4 times that of breast cancer and 5 times that of prostate cancer.1

Fortunately, the amount of development of new therapies for lung cancer over the years has been considerable, evidenced by the number of new lung cancer therapies approved by the Food and Drug Administration (FDA) over the past decade.2 Advances in understanding of the molecular aspects of the pathophysiology of lung cancer have spawned newer targeted therapies and biomarkers that inform treatment selection.3-6 These molecularly-targeted therapies have introduced new concepts and paradigms for treating lung cancer, requiring considerable efforts of oncologists to understand how to incorporate these new options into practice and stay up-to-date with the latest evidence.
To understand the approach that oncologists are taking to incorporate the latest evidence into practice and comprehend their educational needs, we conducted a 3-year study (2011-2013) of a cohort of US oncologists. The study used a clinical vignette-based survey that identified perceptions of and approach to management of patients with adenocarcinoma and squamous cell carcinoma. In addition, because of the significant advances that have occurred during this period in the development of immunotherapies for lung cancer, oncologists’ perceptions of this new field of therapies were assessed for 2013. These results provided trend analyses of how oncologists are incorporating evidence into their management decisions as well as identifying clinical areas that should be addressed in future continuing medical education.

**METHODS**

To quantify and assess the practice patterns of US-practicing oncologists in the testing and treatment of patients with lung cancer, a survey instrument with up to 28 questions was developed for dissemination to a random national sample of oncologists. This was initially done in March 2011 and then repeated in March 2012 and December 2013. The survey used three clinical vignettes of patients presenting with squamous cell carcinoma (SqCC) and adenocarcinoma in smoking and nonsmoking patients. A clinical vignette survey is a cost-effective tool that has been previously validated as a measure of clinical practice quality. Respondents made initial testing and treatment selections in first-line settings. In 2011, these selections were made in an open-ended format allowing respondents to write in their selections. In 2012 and 2013, cued responses were used in a multiple-choice format based on the 2011 open-ended responses, with multiple selections allowed. Responses were revised in each subsequent year to reflect the latest evidence-based options. This approach allowed direct comparison of the responses across the 3-year period. Respondents assessed their level of confidence in managing patients in each setting using a 10-point Likert scale format. Demographic information from each respondent was also obtained. For the 2013 study, questions regarding perceptions and awareness of immunotherapies for lung cancer were added to the survey. To obtain the initial study sample, the survey was distributed to a random national sample of oncologists. Participation in the study was limited to US-practicing medical oncologists or hematologic oncologists who see at least 11 patients with lung cancer per month. For the subsequent studies, the survey was distributed only to the 2011 respondents. Surveys were distributed by E-mail.

**RESULTS**

**Sample demographics**

A sample of 152 oncologists was obtained for the 2011 study. These oncologists were primarily in private practice (74% group, 14% solo). They had been in practice an average of 24-year and managed an average of 64 patients with lung cancer each month. Of the original sample of 152 respondents, 100 participated in the 2012 study, and 87 participated in the 2013 study.

**Management of a life-long smoker with squamous cell carcinoma**

Study participants were presented a patient case vignette of a 58-year-old man who had smoked 1–2 packs of cigarettes per day for 40-year. His symptoms included cough and occasional hemoptysis. A positron emission tomography scan was positive in the upper lobe of the left lung, hilum, mediastinum, and adrenal gland. The lung mass was biopsied as SqCC.

In selection of molecular testing for this patient, most oncologists (53–60%) would not include any options provided (epidermal growth factor receptor [EGFR], K-ras, anaplastic lymphoma kinase [ALK], excision repair cross-complementation 1 [ERCC1], programmed death-ligand 1 [PD-L1]), an appropriate action given the lack of information these test results would provide in the setting of a life-long smoker with SqCC. However, many oncologists did order molecular tests for the patient, with a third of respondents ordering EGFR (34% in 2011, 33% in 2012, 28% in 2013) and approximately a fifth ordering ALK (22% in 2011 and 2012, and 15% in 2013). In 2011, 17% of respondents included ERCC1, but this percentage dropped to 6% in 2012 and 2013. In 2013, 10% also included PD-L1 testing (a new option provided in the 2013 study). In considering first-line therapy for the patient, oncologists remained relatively divided between 2 evidence-based regimens: Carboplatin/paclitaxel and carboplatin/gemcitabine [Figure 1]. Of note, in both 2012 and 2013, 6% of respondents selected carboplatin/pemetrexed, although pemetrexed is not indicated for SqCC.

![Figure 1: First-line therapy for a 58-year-old man, life-long smoker, with squamous cell lung carcinoma with cough and occasional hemoptysis](http://www.cconcology.com/content/2014/1/1/6)
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http://www.cconcology.com/content/2014/1/1/6

Carboplatin/protein-bound paclitaxel, an agent approved for nonsmall cell lung carcinoma (NSCLC) in October 2012, was added as an option for 2013, and 35% of the 2013 respondents considered it for treatment as well.

Management of a light smoker with lung adenocarcinoma

In the initial management of a 52-year-old woman who smoked half a pack per day for 30-year, with moderately differentiated adenocarcinoma and osseous metastases, almost all oncologists included EGFR testing (97%) and ALK testing (94%) in 2013. These percentages are marginally higher than in 2012 but much higher than in 2011 (80% EGFR, 42% ALK). K-ras testing has been very consistent, with a third including it each year. In 2013, 10% included PD-L1, and 9% included ROS1.

Notable shifts in approaches to first-line chemotherapy for this patient have occurred over the past 3-year [Figure 2]. In 2011, respondents were almost evenly divided on their approach, with 35% selecting a doublet, carboplatin/pemetrexed, and 32% selecting a triplet, carboplatin/paclitaxel/bevacizumab. A significant shift occurred in 2012, with 62% of respondents selecting a different triplet, carboplatin/pemetrexed/bevacizumab. This triplet was also the most frequently selected regimen in 2013 by 52% of respondents.

In each year, almost all respondents offered maintenance therapy to the patient rather than expectant care (94% in 2011, 99% in 2012 and 2013) and were most likely to recommend pemetrexed (72% in 2011, 90% in 2012, and 81% in 2013). Other maintenance selections were composed primarily of either bevacizumab (14% in 2011, 8% in 2012, and 9% in 2013) or erlotinib (7% in 2011, 6% in 2012, and 5% in 2013).

Management of a never-smoker with metastatic lung adenocarcinoma

The patient, a 45-year-old man who had never smoked, presented with dyspnea and left hip pain. A chest X-ray revealed large right pleural effusion. A 5 cm mass in the right lower lung was detected and was determined to be adenocarcinoma. Staging demonstrated metastatic disease in the left hip.

Similar to the testing pattern observed for the other adenocarcinoma presentation, at least 94% of respondents in 2012 and 2013 included EGFR and ALK testing for this nonsmoking patient. In 2011, although 88% included EGFR, only 58% included ALK. Also, as was observed in the previous presentation, a third of respondents included K-ras, and 2013 respondents also included PD-L1 (10%) and ROS-1 (9%).

In 2013, respondents were more likely to wait for testing results before initiating systemic therapy (64%, compared to 52% in 2012 and 49% in 2011).

In making treatment selections, respondents remain divided among doublet and triplet regimens, but significant shifts have occurred since 2011 [Figure 3]. In 2011, the most frequently considered regimen was carboplatin/pemetrexed (39%), with 21% considering monotherapy erlotinib, and 20% considering the carboplatin/paclitaxel/bevacizumab triplet. In 2012, the most frequently selected regimen shifted significantly to carboplatin/pemetrexed/bevacizumab (56%; 54% in 2013). A notable portion of 2013 respondents selected monotherapy erlotinib (18%) or crizotinib (13%), although no testing results were provided in the case vignette.

Perceptions and knowledge of immunotherapies for nonsmall cell lung carcinoma

To assess oncologists’ level of familiarity with some of the scientific concepts associated with immuno-oncology, 2013 respondents rated their familiarity (on a 1–10 scale, with 1 = not at all and 10 = extremely) with these concepts.
specific aspects: The role of the immune system in cancer pathophysiology and in cancer immunosurveillance, and the safety and efficacy data of available immunotherapies. In none of the four aspects queried did >31% consider themselves “very” familiar (8–10 on the 10-point scale) with the majorities (63–74%) considering themselves “somewhat” familiar (4–7 on the 10-point scale) with each of these aspects. To assess if any demographic characteristics were statistically significant with regard to familiarity with these immuno-oncology topics, an ANOVA analysis was performed. The analysis demonstrated that respondents’ year of graduation from medical school (a surrogate for respondent age) was the only demographic trait where significant differences were found: Those that were more familiar were significantly younger ($P = 0.017$) than those that were less familiar with the topics.

Respondents also rated the importance of immunotherapies in improving the outcomes of patients with advanced lung cancer. Almost equal percentages considered it either “very” important (8–10 on a 10-point scale) or “somewhat” important (4–7 on a 10-point scale), 45% and 44%, respectively; 11% considered immunotherapy “not important.”

In assessing at what stage of lung cancer they believe immunotherapy would be most useful, the majority of respondents expected immunotherapies to be most useful in later stages of disease, stage III (23%) or stage IV (51%). The remaining oncologists were equally divided between stage I (13%) and stage II disease (13%).

**DISCUSSION**

The cohort of oncologists was a well-experienced sample of community-based physicians who manage patients with NSCLC on a daily basis. They provide a representative sample of front-line lung cancer treaters. Patient scenarios presented in the study included both squamous cell and adenocarcinoma settings to assess approaches to management. Although, encouragingly, most oncologists made evidence-based management decisions, notable shifts in practice were observed as shifts in evidence have occurred, along with some potential gaps in care.

In the setting of SqCC, molecular tests such as EGFR and ALK are of limited value due to the low frequency that the relevant mutations occur in this type of NSCLC. However, in each year, almost a third of oncologists tested the patient for an EGFR mutation, and approximately 20% tested for ALK. Although these mutations can occur in SqCCs, current NCCN recommendations consider these tests reasonable only in the setting of never-smokers, small biopsy specimens, or mixed histology. None of these contingencies were present in this particular case vignette. Given the high cost-to-benefit ratio of molecular tests in the setting of SqCC, the issues that are driving these testing decisions among oncologists need to be addressed.

In both 2012 and 2013, in selecting first-line therapy for the patient with SqCC, oncologists were almost evenly divided between 2 evidence-based doublets, carboplatin/gemcitabine or carboplatin/paclitaxel. With the FDA’s approval of protein-bound paclitaxel for NSCLC in October 2012, 35% of oncologists in 2013 also considered this agent in combination with carboplatin. Of note were the small but significant percentages (13% in 2012, 8% in 2013) that considered a triplet with bevacizumab, given that bevacizumab is indicated only for nonsquamous histology and contraindicated in patients with hemoptysis. In addition, a smaller subset in 2012 and 2013 (6%) considered pemetrexed for the patient, although it is not recommended for use in SqCC.

Molecular test selection for both presentations of adenocarcinoma, a 52-year-old female light smoker and a 45-year-old male never-smoker, was relatively uniform, with at least 94% of oncologists appropriately selecting both EGFR mutation and ALK rearrangement for these patients as supported by current evidence. These findings represent a notable shift from testing patterns observed in 2011, when at least 80% of oncologists included EGFR mutation testing in both patient cases, but only 40% included ALK testing for the light-smoker patient and 58% included it for the never-smoker patient. For the never-smoker patient, it is interesting that oncologists appear to be becoming more reliant on molecular testing results to guide treatment selection. A greater percentage in 2013 withheld treatment until test results were obtained than in the preceding years.

Treatment selections for both cases of adenocarcinoma were also similar in that in both 2012 and 2013, the most frequently selected regimen was carboplatin/pemetrexed/bevacizumab by a majority of respondents (light-smoker: 62% in 2012, 52% in 2013; never-smoker: 56% in 2012, 54% in 2013). This regimen demonstrated improved progression-free survival and a better toxicity profile (less neuropathy) compared to the taxane-based triplet regimen. By comparison, in 2011 there was lower consensus, with the most frequently selected regimens for the light-smoker patient being carboplatin/pemetrexed (35%) and carboplatin/paclitaxel/bevacizumab (32%). For the never-smoker, it was carboplatin/pemetrexed (34%), erlotinib monotherapy (21%), and carboplatin/paclitaxel/bevacizumab (20%).

For the light-smoker patient, 99% of oncologists in 2012 and 2013 recommended maintenance therapy and were most
likely to select pemetrexed maintenance, regardless of their choice in first-line therapy.

Immunotherapies for NSCLC, such as anti-programmed death-1/PD-L1 and other checkpoint inhibitors, have demonstrated considerable efficacy in recent NSCLC clinical trials and appear ready to make a significant impact in the treatment. Although oncologists are currently not very familiar with the role of the immune system in either cancer pathophysiology or treatment, the majority have a favorable outlook on immunotherapy’s potential to improve patient outcomes. However, even though immunotherapies may represent a new paradigm in cancer treatment, oncologists appear to be considering them in a more conventional sense akin to chemotherapies that initially, are commonly indicated for later-stage disease. Most oncologists expect immunotherapies to have the greatest impact in later-stage disease rather than in early stages.

The results of this study have demonstrated the changes that have occurred since 2011 in oncologists’ testing and treatment approaches for patients with NSCLC as the evidence that guides those decisions has shifted. Encouragingly, based on the contemporaneous information, most oncologists have made evidence-based treatment choices over the past 3-year. Although the consensus in treatment has increased in this period, it remains relatively low and will likely continue to be so until sufficient comparison data are available to provide more guidance in treatment selection. Moreover, with the coming immunotherapies for lung cancer on the horizon, evidence will likely shift at an even more rapid pace, placing an even greater burden on the oncologist to stay current with the latest evidence and on the oncologist educator to provide effective education.

REFERENCES

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