

# Oncologists' Comprehension and Beliefs Surrounding Cancer Immunotherapy in Advanced NSCLC

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## INTRODUCTION

Lung cancer remains the leading cause of cancer-related death in the United States. With the recognition that lung cancer is an immune-modifiable disease and the approval of the first PD-1 inhibitor, immune checkpoint inhibitors represent a new treatment paradigm for patients with lung cancer, particularly those with previously-treated squamous cell lung cancer.

Since cancer immunotherapy is unique in its ability to target the immune system rather than the cancer itself, oncologists are likely to be unaccustomed to many of the nuances associated with its use. The objectives of this study were to evaluate oncologists' familiarity with cancer immunotherapy in the context of advanced non-small cell lung cancer (NSCLC) and to examine the impact of an educational curriculum on narrowing gaps in clinical practices.

## METHODS

An expert panel was convened to identify knowledge, competence, and practice gaps in the area of cancer immunotherapy. A series of 9 CME online activities (<http://www.medscape.org/sites/advances/immuno-oncology>) were developed, two of which were centered on advanced NSCLC and are the focus of this study.

- Content addressed pre-identified physician knowledge and clinical practice gaps
- Clinician-directed interactive and assessment questions were aligned with the learning objectives of the NSCLC activities
- Interactivity questions allowed learners to self-report their familiarity with immunotherapy concepts
- A case vignette and knowledge-based questions were constructed around evidence-based medicine and used to evaluate the effectiveness of the education

## ANALYSIS

- Responses to questions were collected from August 1, 2014 to February 1, 2015
- Confidentiality of survey respondents was maintained and responses were de-identified
- Answers to matching pre- and post-education outcomes questions were linked for comparative analysis of post-assessment responses relative to baseline self-assessment responses
- Learners served as their own controls
- Aggregate comparison served as a measure of the impact of the educational activity on improving the knowledge, skill, or performance of participating physicians
- Pearson's chi-squared test was used to determine the significance of pre- vs post-assessment responses; *P* values are shown as a measure of significance and *P* values less than .05 are statistically significant
- Effect sizes greater than 0.8 are large, between 0.8 and 0.4 are medium, and less than 0.4 are small

## RESULTS

Of the 1368 oncologists who participated in the 2 activities, an outcomes assessment was conducted on 103 participants who had pre- and post-assessment data. Approximately 58% of oncologists participating in this immunology curriculum indicated that they practice in a community setting, with the remaining 42% describing their practice setting as academic-based.

Analysis of each NSCLC activity demonstrated statistically significant improvements, with overall effect sizes of 1.165 (*P* < .05) and 0.883 (*P* < .05), respectively. Specific educational impact findings include:

- 17% improvement in comprehension of the immune system components necessary for T cell activation (*P* = 0.178)
- 16% improvement in comprehension of the role of an immune checkpoint in regulating the adaptive immune response (*P* = 0.116)
- 13% improvement in recognizing the link between T cell infiltration of a tumor and a decreased risk of recurrence (*P* = 0.066)

FIGURE 1 INDUCIBILITY OF PD-L1.

One of the limitations of using PD-L1 as a biomarker is:

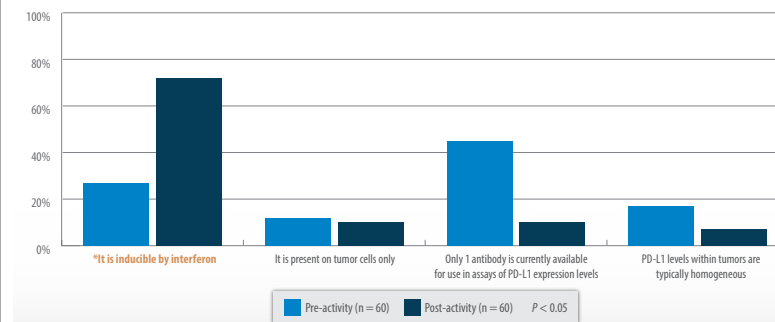


FIGURE 2 PSEUDOPROGRESSION VS DISEASE PROGRESSION WITH IMMUNE CHECKPOINT INHIBITORS

A 67-year-old man with stage IV squamous cell lung cancer is scheduled to receive single-agent ipilimumab in a clinical trial setting following disease progression on second-line chemotherapy with docetaxel. When monitoring this patient for evidence of tumor response using immune-related response criteria, which of the following observations would indicate that the patient was experiencing disease progression on ipilimumab?

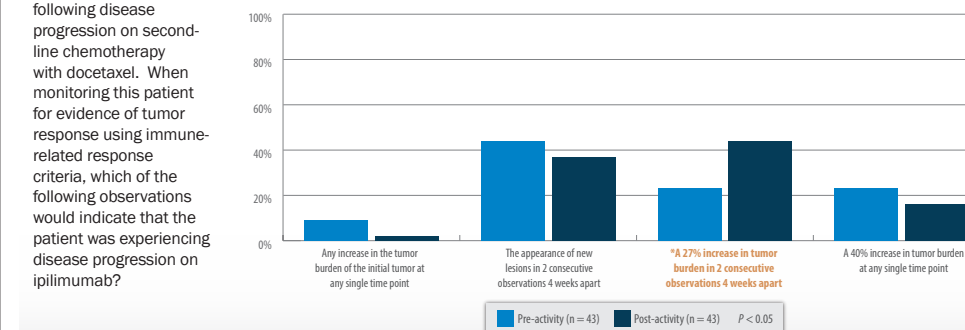


FIGURE 3 DURATION OF TREATMENT RESPONSE IN PATIENTS WITH ADVANCED NSCLC

A 63-year-old woman with heavily pretreated advanced NSCLC enrolled in a clinical trial evaluating single-agent nivolumab has experienced a response to treatment. Based on current evidence, which of the following choices would be a reasonable estimation of duration of response in this patient?

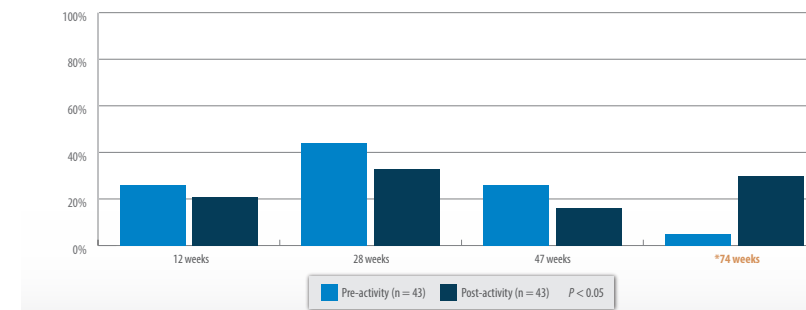


FIGURE 4 RECOGNITION OF UNIQUE SIDE EFFECT PROFILE ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS IN NSCLC

A patient diagnosed with advanced nonsquamous NSCLC not characterized by an activating *EGFR* mutation or *ALK* translocation who is currently receiving first-line chemotherapy asks for information about future enrollment in a clinical trial investigating the safety and efficacy of immune checkpoint inhibitors. Although he has been tolerating chemotherapy well he is particularly concerned about the potential adverse effects of immunotherapy. Which of the following adverse effects is least likely to be experienced by a patient receiving this type of treatment?

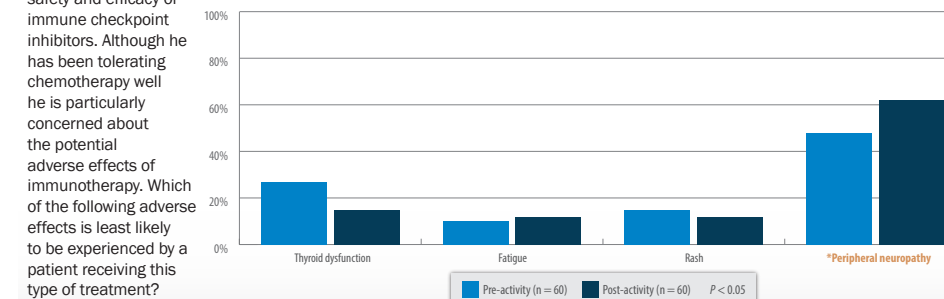
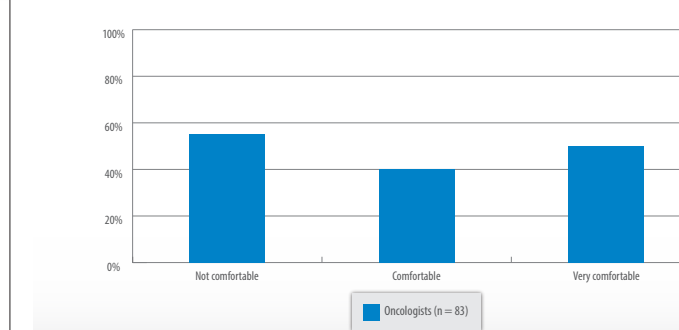


FIGURE 5 ONCOLOGIST COMFORT WITH IMMUNE CHECKPOINT INHIBITOR-RELATED SIDE EFFECTS.

How comfortable are you with monitoring adverse effects with immune checkpoint inhibitors?



## CONCLUSIONS & IMPLICATIONS

This study demonstrates that oncologists who participated in the NSCLC activities included in this year-long curriculum demonstrated improvement in their comprehension of basic immunology and the role of the immune system in targeting cancer, as well as the clinical efficacy and safety of immune checkpoint inhibitors in advanced NSCLC. However, several gaps in knowledge regarding the use of immune checkpoint inhibitors in patients with advanced NSCLC remained post-education including:

- 55% of oncologists remain uncomfortable with monitoring immune checkpoint inhibitor-related side effects, while 38% still failed to correctly identify peripheral neuropathy as a side effect that is not associated with cancer immunotherapies. As immune checkpoint inhibitors are now a part of the treatment paradigm for lung cancer, it is critical that oncologists have an improved comfort level with this concept so they can identify treatment-related side effects in a timely manner in order to improve patient outcomes and quality of life
- More than 55% of oncologists could not distinguish between pseudoprogression and disease progression, which may result in patients either being taken off therapy prematurely or kept on therapy when discontinuation and consideration of alternative therapies should take place
- 27% of oncologists remain uncertain about the potential pitfalls of PD-L1 as a biomarker; because the role of PD-L1 expression as a biomarker has yet to be fully determined and/or may be linked to individual therapies, oncologists must comprehend the limitations of PD-L1 and its implications to practice.

Additional education is needed to continue to improve oncologists' competence in the use of cancer immunotherapies in the management of NSCLC.

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