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New lung cancer studies feature latest treatment advances

2019 Multidisciplinary Thoracic Cancers Symposium highlights include definitive therapy for oligometastatic disease, patient exposure to tailored guidelines and the use of prophylactic cranial irradiation

ARLINGTON, Va., March 12, 2019 — New research released today provides guidance for physicians who treat patients with lung cancer. Three authors will present their findings in an [online presscast](#) today and during the plenary session Thursday, March 14, at the [2019 Multidisciplinary Thoracic Cancers Symposium](#), held March 14-16 at the Hilton San Diego Bayfront. To schedule interviews with study authors and/or outside experts in lung cancer, contact ASTRO's media relations team at press@astro.org.

Following are summaries of each study selected for the presscast:

Local consolidative therapy linked to improved overall survival for oligometastatic NSCLC (Abstract 1)

This summary includes updated data not in the abstract.

A new analysis of nearly 200 patients treated with local consolidative therapy (LCT) for oligometastatic non-small cell lung cancer (NSCLC) finds that the intensive treatment approach is associated with improved overall survival. LCT, consisting of radiation therapy or surgery, extended median survival by six months for patients diagnosed with three or fewer metastases outside of the lungs.

"Though not all people with stage IV NSCLC are the same, there are treatment options for those with limited metastatic disease," said Erin Corsini, MD, presenting author of the study and a clinical research fellow at the University of Texas MD Anderson Cancer Center in Houston. "Specifically, in select populations of patients with oligometastatic NSCLC, local consolidative therapy to all sites of disease with surgery, radiation therapy or a combination of the two appears to show promise in prolonging overall survival. The patients who seem to gain the most benefit are those with more favorable disease characteristics, such as adenocarcinoma, early intrathoracic stage and absence of bone metastases."

For the study, researchers analyzed records of 194 patients treated for stage IV NSCLC at MD Anderson between 2000 and 2017. Eligible patients included those diagnosed with one to three synchronous metastatic tumors, with intrathoracic nodal disease counted as one site; most patients (70%) had two to three distant metastases. Nearly all patients (90%) received systemic therapy in addition to LCT.

Comprehensive LCT to all disease sites (i.e., the primary tumor and all distant metastases) was associated with improved overall survival. At a median follow-up of 52 months, the median overall survival was 29 months

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for patients who received LCT to all sites, compared to 23 months for patients who did not ($p=0.03$). The relationship held on multivariable analysis controlling for patient and disease characteristics ($p=0.03$).

LCT to the primary tumor was associated with improved control of local and regional recurrences. The rate of locoregional progression was 21 percent for patients who received LCT to the primary tumor, compared to 43 percent for patients who did not ($p<0.01$). LCT to the primary tumor also trended toward an association with improved overall survival ($p=0.08$), although this was not the case with LCT to distant metastases ($p=0.21$).

“Several recent clinical trials have shown that local consolidative therapy could provide a tangible survival benefit, and our results from evaluating a relatively large group of patients are not only consistent with, but arguably bolster, the previously reported findings,” said Dr. Corsini. “Taken together, these studies make a strong case for local consolidative therapy in patients with oligometastatic NSCLC.”

“As the evidence accumulates and we learn that there are options for patients with oligometastatic disease, it is important that providers, patients and families discuss these possibilities and how they align with their goals and priorities for treatment.”

Structured exposure to NSCLC patient guidelines fosters smoking cessation, biomarker testing (Abstract 3)

A new clinical trial finds that exposing patients to tailored versions of nationally-recognized treatment guidelines for non-small cell lung cancer (NSCLC) can help drive smoking cessation, testing for potential biomarkers and, for early-stage disease, more patient-centered use of chemotherapy following surgery. Findings demonstrate how evidence-based decision and communication aids can improve cancer care.

“The process of making treatment decisions can be extremely stressful for lung cancer patients, as treatment options are nuanced and may change significantly over the course of their staging workup,” said Susan Wu, MD, first author of the study and a radiation oncology resident at the University of California, San Francisco. “Educational tools can guide patients through the decision-making process and help them to synthesize the large amount of information available.”

Patients in the trial used an interactive web-based tool that presented treatment options tailored to their clinical characteristics, such as tumor stage and margin status following surgery. Options were based on National Comprehensive Cancer Network (NCCN) guidelines and included information about treatment sequencing as well as a timeline to help patients visualize the treatment trajectory. All 76 patients were introduced to the tool by a trained coordinator, who also used the tool to facilitate discussion during their consultation with an oncologist. A separate cohort of 159 patients seen at the same institution before the tool was available was used as a comparison group.

Structured exposure to guidelines was associated with several positive outcomes, including increased smoking cessation counseling/intervention among active smokers (80% vs. 4%, $p<0.001$) and increased molecular testing for EGFR and ALK mutations prior to systemic therapy among patients with metastatic disease (96% vs. 68%, $p=0.01$). Use of the tool was also correlated with decreased use of chemotherapy following surgery for stage IB-IIB NSCLC (0% vs. 50%, $p=0.02$), particularly among patients with negative margins following resection.

“We can empower patients to make decisions that align with their priorities and goals for treatment with evidence-based tools. For example, data from patients with breast cancer suggests that those who may derive limited benefit from adjuvant therapy are more likely to forego it. We similarly found that patients with completely resected early-stage NSCLC had a tendency not to pursue additional chemotherapy,” said Dr. Wu.

Exposure to the guideline tool did not impact some outcomes, including the frequency of pathologic mediastinal staging performed prior to surgery ($p=0.70$) or nonsurgical treatment ($p=0.55$) in patients with

stage III disease, nor did it influence the use of upfront chemoradiation therapy in stage III patients who were ineligible for surgery (p=0.55).

“Our goal was to help patients feel more comfortable making treatment decisions and become more active participants in the decision-making process,” said Dr. Wu. “While implementing a decision support tool does require substantial resources, such as the time and effort to develop the tool and introduce it to patients, these tools can help empower our patients, and in some cases meaningfully impact their care.”

Declining number of physicians use prophylactic cranial irradiation (PCI) for extensive-stage SCLC (Abstract 5)

This summary includes updated data not in the abstract.

A new survey of radiation oncologists points to a sharp decline in the use of prophylactic cranial irradiation (PCI) for patients with extensive-stage small cell lung cancer (ES-SCLC), indicating a rapid change in standard practice for the disease following publication of a major clinical trial in 2017.

“Small cell lung cancer has a tendency to spread past the lungs to the brain, and brain metastases substantially diminish a patient’s quality of life. PCI is preventative radiation therapy given after first-line treatment to eliminate cancerous cells before they become symptomatic metastases,” said Olsi Gjyshi, MD, PhD, first author of the study and a radiation oncology resident at the University of Texas MD Anderson Cancer Center.

“Radiation oncologists largely adopted PCI for ES-SCLC following the 2007 publication of a randomized EORTC trial that linked its use to extended overall survival ([Slotman et al., NEJM](#)). However, with the recent publication of a Japanese trial showing no survival benefit from PCI compared to MRI surveillance ([Takahashi et al., Lancet Oncology](#)), it is important to come to a consensus on how best to treat these patients. Our survey indicates that most providers no longer routinely use PCI for patients with extensive-stage disease that responds to chemotherapy.”

To determine the extent of practice changes, researchers surveyed attending radiation oncologists at academic cancer centers across the United States (24% survey response rate). Anonymous email surveys were collected in September 2018, more than a year after the Takahashi et al trial was published, and the same year National Comprehensive Cancer Network (NCCN) guidelines were updated to reflect its findings.

All 49 radiation oncologists who specialize in treating thoracic cancers were aware of the Takahashi et al trial, and two-thirds (67%) had altered their practice in response to its findings. Specifically, fewer than half of those who offered PCI for ES-SCLC prior to 2017 continued to do so after it was published (78% vs. 38%, p<0.001).

Researchers confirmed the trend of shifting away from PCI in a subsequent nationwide survey of radiation oncologists (N=431). The trend was consistent across private practices and academic centers. One-fourth of these physicians reported a decline in PCI referrals by medical oncology for patients with extensive-stage SCLC, and 12 percent also reported fewer referrals for limited-stage SCLC.

“With extensive-stage disease, PCI may best be reserved for patients who are likely to benefit from it, such as those with excellent performance status, younger age (<70 years) and excellent cognitive functions at baseline,” said Dr. Gjyshi. “Caution should be used in extrapolating the Takahashi et al. data to patients with limited-stage disease, and further trials may be necessary to address this question.”

“Declining PCI use could impact enrollment in future clinical trials, however, so careful consideration should be given to future studies and trials that plan to investigate the role of PCI in this patient population.”

Attribution to the 2019 Multidisciplinary Thoracic Cancers Symposium requested in all coverage.

Study and Presentation Details

- All three abstracts will be presented in the same presscast and scientific session
- Presscast: Tuesday, March 12, 11:00 a.m. – 12:00 p.m. Eastern, <http://bit.ly/thoracic19>
- Plenary Session: Thursday, March 14, 10:45 a.m. – 12:15 p.m. Pacific, Indigo Ballroom Salons ABEF (Level 2), Hilton San Diego Bayfront

Resources on Lung Cancer and Radiation Therapy

- Digital brochure: [Radiation Therapy for Lung Cancer](#); ([Spanish version](#))
- Video: [Radiation Therapy for Lung Cancer](#); ([Spanish version](#)), [An Introduction to Radiation Therapy](#); ([Spanish version](#))
- ASTRO's [clinical guidelines](#)
- Additional [patient brochures, videos and information](#) on radiation therapy from RTAnswers.org

ABOUT THE SYMPOSIUM

The 2019 Multidisciplinary Thoracic Cancers Symposium is a two-and-a-half-day meeting that convenes radiation and medical oncologists, thoracic surgeons and all members of the treatment team for a practical and comprehensive examination of current thoracic cancer care. Scientific, interactive and case-based educational sessions will cover the latest research on multidisciplinary therapies, clinical applications and new treatment strategies, supportive care and toxicity mitigation. The meeting is cosponsored by the [American Society for Radiation Oncology](#) (ASTRO), [the American Society of Clinical Oncology](#) (ASCO) and [The Society of Thoracic Surgeons](#) (STS).

ABOUT ASTRO

The American Society for Radiation Oncology (ASTRO) is the world's largest radiation oncology society, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals who specialize in treating patients with radiation therapies. The Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes three medical journals, [International Journal of Radiation Oncology • Biology • Physics](#), [Practical Radiation Oncology](#) and [Advances in Radiation Oncology](#); developed and maintains an extensive patient website, [RT Answers](#); and created the nonprofit foundation [Radiation Oncology Institute](#). To learn more about ASTRO, visit our [website](#), sign up to [receive our news](#) and follow us on our [blog](#), [Facebook](#), [Twitter](#) and [LinkedIn](#).

ABOUT ASCO

Founded in 1964, the American Society of Clinical Oncology (ASCO) is committed to making a world of difference in cancer care. As the world's leading organization of its kind, ASCO represents more than 40,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation. Learn more at www.ASCO.org, explore patient education resources at www.Cancer.Net, and follow us on Facebook, Twitter, LinkedIn, and YouTube.

ABOUT STS

Founded in 1964, The Society of Thoracic Surgeons is a not-for-profit organization representing approximately 7,200 cardiothoracic surgeons, researchers, and allied health care professionals worldwide who are dedicated to ensuring the best possible outcomes for surgeries of the heart, lung, and esophagus, as well as other surgical procedures within the chest. The Society's mission is to enhance the ability of cardiothoracic surgeons to provide the highest quality patient care through education, research, and advocacy.

Abstract 1: Improved Overall Survival with Local Consolidative Therapy in Oligometastatic Non-Small Cell Lung Cancer: Results from a Cohort of 194 Patients with Synchronous Disease

K. G. Mitchell¹, A. Farooqi², E. B. Ludmir², E. M. Corsini¹, A. A. Vaporciyan¹, S. G. Swisher¹, J. Heymach³, J. Zhang³, D. R. Gomez², and M. Antonoff¹; ¹*Department of Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX*, ²*Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*, ³*Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX*

Purpose/Objective(s): Treatment strategies consisting of aggressive local therapy represent an evolving paradigm for select patients with advanced non-small cell lung cancer (NSCLC) who present with a limited burden of metastatic disease. We hypothesized that local consolidative therapy (LCT) to the primary lesion and metastatic foci would be associated with improved overall survival (OS) among patients with synchronous oligometastatic NSCLC.

Materials/Methods: Patients presenting to a single institution (2000-2017) with stage IV NSCLC and ≤ 3 synchronous metastatic lesions were identified. Intrathoracic nodal disease was counted as one site. Univariable and multivariable Cox regressions were performed to identify factors associated with overall survival. A ninety-day landmark analysis was performed to limit survivorship bias.

Results: Of 194 patients (median age 62 years; male 111 [57%]), 146 (75%) had adenocarcinoma. 136 (70%) had 2-3 sites of non-regional metastasis, with 86 (44%) brain, 51 (26%) bone, and 36 (19%) adrenal as the most common sites of distant disease. Systemic therapy was administered in 175 (90%). LCT to the primary lesion was used in 145 (75%), to all distant metastases in 147 (76%), and to all disease sites in 121 (62%). Rates of locoregional progression were lower in patients who received LCT to the primary tumor (30/145, 21%) than those who did not (21/49, 43%) ($p < 0.01$). After a median follow-up of 52.3 (IQR 29.9-98.0) months, median OS for the cohort was 26.5 (CI 23.0-30.0) months. Though the site of metastatic disease was not associated with prognosis on univariable analysis, progression on first-line systemic therapy was associated with an increased hazard of death (HR 1.87, CI 1.15-3.02, $p = 0.01$). Comprehensive LCT to all sites of disease was associated with improved OS (HR 0.67, CI 0.47-0.96, $p = 0.03$); a similar trend toward improved survival was observed with receipt of LCT to the primary lesion (HR 0.71, CI 0.49-1.05, $p = 0.08$). In contrast, LCT to distant metastases was not associated with a survival benefit (HR 0.77, CI 0.52-1.16, $p = 0.21$). On multivariable analysis, receipt of comprehensive LCT to all sites of disease (HR 0.68, CI 0.47-0.97, $p = 0.032$) and adenocarcinoma histology (HR 0.71, CI 0.56-0.90, $p = 0.004$) remained independently associated with improved OS.

Conclusion: Aggressive consolidative therapy to the primary lesion and all metastatic sites was associated with improved overall survival in this large, retrospective series of patients with synchronous oligometastatic NSCLC. These results support ongoing prospective efforts to fully characterize the therapeutic benefits associated with this management strategy.

Author Disclosure: **K.G. Mitchell:** None. **A. Farooqi:** None. **E.B. Ludmir:** None. **E.M. Corsini:** None. **A.A. Vaporciyan:** None. **S.G. Swisher:** Consultant; GlaxoSmithKline. **J. Heymach:** None. **J. Zhang:** None. **D.R. Gomez:** Research Grant; Merck, AstraZeneca. Honoraria; BMS. Speaker's Bureau; Merck, Varian. Advisory Board; AstraZeneca. **M. Antonoff:** None.

Abstract 3: The Impact of the Stage III Randomized Trial by Takahashi et al. on the Use of Prophylactic Cranial Irradiation (PCI) in Patients with Extensive-Stage Small-Cell Lung Cancer (ES-SCLC)

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Purpose/Objective(s): While controversial, the EORTC phase III PCI trial in ES-SCLC (Slotman *et al.*, NEJM 2007) demonstrated an overall survival (OS) advantage of PCI. This drastically altered the practice pattern in the US such that most radiation oncologists had come to accept the practice of PCI as standard of care for ES-SCLC patients. Recently, however, Takahashi *et al.*, (NEJM 2017) reported a contemporary phase III clinical trial that demonstrated no OS advantage of PCI when compared to observation with close MRI surveillance, although it did reduce the incidence of intracranial metastases. The impact of this recent trial on clinical practice in the US is unknown.

Materials/Methods: Over a two-week period in September 2018, a total of 205 attending radiation oncologists who specialize in the treatment of thoracic malignancies from 105 academic centers in the US were contacted *via* email to participate in an anonymous 24-question survey regarding the use of PCI in ES-SCLC pre- and post-publication of the Takahashi *et al.* study.

Results: A total of 49 (24%) radiation oncologists responded to the survey. Responders were evenly distributed geographically within the US. The majority of the responders were from large academic centers (>10 radiation oncologists) (67%), and 42% of them had lung cancer cases constitute >50% of their practices. All respondents were aware of the Takahashi *et al.* trial. While 78% routinely offered PCI for ES-SCLC prior to the publication, only 38% of them continued to do so after its publication ($p < 0.01$, Fisher's exact test). A majority of respondents (67%) had altered their practice patterns in response to the Takahashi, *et al.* trial. Subset analyses showed no significant trends in post-Takahashi PCI usage pattern based on physicians' geographic location, years of practice or volume of SCLC cases treated (all $p > 0.1$). Individual responder comments indicate that close MRI surveillance is often being utilized as an alternative to PCI and that medical oncologists had significantly reduced referrals in this patient population since the publication of Takahashi *et al.*

Conclusion: The study by Takahashi *et al.* has markedly impacted current practice patterns in the US by reducing PCI use for ES-SCLC among academic radiation oncologists. We observed a decrease in PCI utilization for ES-SCLC from 78% to 38% following publication of this trial. The lack of equipoise in practice approaches and a reduction in clinical referral may negatively impact physician participation in similar randomized clinical trials regarding PCI being planned in the US and Europe.

Author Disclosure: O. Gjyshi: None. E.B. Ludmir: None. A. Dursteler: None. S.H. Lin: Research Grant; STCube Pharmaceuticals, Inc, Roche/Genentech, Hitachi Chemical, Inc, New River Labs, Beyond Spring Pharmaceuticals, Inc. Advisory Board; AstraZeneca Inc.

Abstract 5: The Impact of Structured, Prospective Exposure to the NCCN Guidelines when Making Treatment Decisions: Improved Metrics of Guideline-Concordant Care for Patients with Non-Small Cell Lung Cancer

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Purpose/Objective(s): A structured, interactive web-based tool was designed to present the NCCN guidelines to non-small cell lung cancer (NSCLC) patients, tailored to their individual clinical and pathologic features. We evaluated differences in guideline concordance according to 6 metrics assessed before and after implementation of the tool.

Materials/Methods: This was an IRB-approved, prospective clinical trial assessing feasibility, acceptability, and clinical impact. We enrolled 76 patients with NSCLC, newly diagnosed or at the time of new disease progression. Patients were introduced to the web-based tool by a trained coordinator and were assisted in accessing it during and after their initial consultation. Guideline concordance was evaluated in a binary (yes/no) fashion for 6 metrics: 1) smoking cessation/intervention; 2) adjuvant chemotherapy for stage IB-IIB patients undergoing surgery; pathologic mediastinal staging in stage III patients prior to 3) surgery or 4) nonsurgical treatment; 5) upfront definitive chemoradiation for stage III patients; and 6) molecular testing for EGFR and ALK mutations prior to systemic therapy for stage IV disease. Baseline level of guideline concordance was evaluated in a series of 159 patients seen before the tool was available and results were compared to concordance when the tool was available.

Results: Median age at the time of study was 67.5 years (interquartile range, 14 years). The most common histologies were adenocarcinoma and squamous cell carcinoma in the study group (78% and 18%, respectively) and the retrospective cohort (67%, 18%) ($p = 0.10$). Among patients exposed to the tool, there was an increase in smoking cessation counseling/intervention in active smokers (80% vs. 4%, $p < 0.001$). There was a decrease in use of adjuvant chemotherapy following surgery for stage IB-IIB disease (0/8 (0%) vs. 6/12 (50%), $p = 0.02$). This decrease was mostly driven by decreased use of adjuvant chemotherapy for stage IB NSCLC resected with negative margins (0/6 vs. 4/4 in the comparison group, $p = 0.04$). There was an increase in molecular testing prior to initiation of systemic therapy in patients with metastatic NSCLC experiencing the tool (96% vs. 68%, $p = 0.01$). In patients with stage III NSCLC, there were no differences in the frequency of pathologic mediastinal staging performed prior to surgery ($p = 0.70$) or nonsurgical treatment ($p = 0.55$). Likewise, the use of upfront chemoradiation in non-operative candidates was not different between study patients and the comparator cohort ($p = 0.55$).

Conclusion: Structured exposure to the NCCN guidelines during and after oncology consultation improved guideline concordance in smoking cessation, testing for molecular markers, and more judicious use of adjuvant chemotherapy. These findings add further support that evidence-based decision and communication aids can improve cancer care.

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