**Combination of radiation and immune checkpoint therapy holds potential for lung cancer**

*Retrospective analysis finds acceptable rates of severe treatment-related toxicity following combined treatment for metastatic disease*

SAN FRANCISCO, March 16, 2017 — An emerging approach for cancer treatment seeks to combine radiation therapy with immune checkpoint inhibitors (ICPIs) to more effectively control tumors in the chest with an acceptable risk of severe treatment-related side effects. Ten percent of patients in a retrospective analysis of metastatic lung cancer experienced severe toxicity as a result of the combination therapy. Findings will be presented tomorrow at the 2017 Multidisciplinary Thoracic Cancers Symposium.

Cancer cells produce proteins that are designed to stop the body’s natural immune response to overtake the disease. One type of targeted therapy uses immune checkpoint inhibitors to stop cancer growth by blocking these proteins, which allows the immune system to remain active and attack malignant cells more successfully. A potential downside to this form of immunotherapy, however, is that the immune system may also target healthy cells and cause serious treatment-related side effects for some patients. Moreover, research on the potential of immune checkpoint inhibitors used in conjunction with traditional therapies, such as thoracic radiation therapy (RT), is still relatively new.

“In previous analyses, our team found that a combination of radiation therapy and anti-PD-1 therapy was safe and effective in treating melanoma-related brain metastases,” said Kamran A. Ahmed, MD, lead author of the study and a resident in radiation oncology at the Moffitt Cancer Center in Tampa, Florida. “The
current findings show potential for the tolerability and efficacy of this combined approach for treating thoracic tumors, as well.”

Findings are based on a retrospective analysis of 29 metastatic lung cancer patients treated with thoracic RT and immune checkpoint inhibitors at a single institution between February 2012 and May 2016. Patients received RT within the six months preceding or six months following initiation of ICPIs, given as anti-PD-1 therapy or anti-PD-L1 therapy alone or in combination with anti-CTLA-4 therapy. Seventeen patients (59%) received a single-agent ICPI, and 12 patients received combination ICPIs. All patients received ICPIs until their disease progressed.

The median patient age at the time of study enrollment was 64 years, and 55 percent of patients were female. Most patients presented with non-small cell lung cancer (79%) and ECOG 1 performance status (69%). The number of metastatic sites ranged from two to eight, with a median of three sites.

The primary outcome was treatment-related toxicity, namely pneumonitis and other types of lung damage; occurrence and severity were assessed qualitatively from patients’ clinical records. Median follow-up was 6.6 months following treatment. The Kaplan-Meier method was used to determine estimates of progression free survival (PFS) and overall survival (OS) from the date that ICPI therapy began.

Roughly half of the patients (52%) received thoracic RT concurrent with or after ICPI therapy. The other 14 patients were administered radiation two weeks to 5.5 months before they began ICPI therapy, with a median interval of 2.2 months between RT and ICPI. Total radiation doses ranged from 10 to 70 Gray (Gy), delivered in one to 35 fractions.

For the patients in this study, median PFS was 3.8 months, and median OS was 9.2 months following initiation of ICPI therapy. These cancer control rates are similar to other prospective studies that used ICPIs to treat NSCLC.

Three patients (10%) experienced severe possible treatment-related toxicity, including one grade 5 toxicity two weeks following radiation treatment and two cases of grade 3 pneumonitis at two and four months post-radiation treatment, respectively. For all three of these patients, thoracic RT was administered following ICPI therapy. None of the patients who received RT prior to ICPI therapy experienced severe treatment-related toxicity as a result of radiation therapy.
Two additional cases of pneumonitis, one grade 2 and one grade 3, were noted following anti-PD-1 therapy but before radiation treatments began. Both of these patients subsequently received thoracic RT without any additional pulmonary toxicity.

“Our results suggest that a treatment regimen combining thoracic radiation therapy and immune checkpoint inhibitors may carry a modest risk of severe side effects,” said Dr. Ahmed. “These findings should be evaluated further within the context of prospective clinical trials, particularly those that examine the risk of lung toxicity and the potential opportunity to improve outcomes with this emerging form of combination therapy.”

The abstract, “Tolerability and safety of thoracic radiation and immune checkpoint inhibitors among patients with lung cancer,” will be presented in detail during the oral abstract session at the 2017 Multidisciplinary Thoracic Cancers Symposium in San Francisco (full details below). To schedule an interview with Dr. Ahmed or an outside expert, contact the ASTRO media relations team at press@astro.org or 703-286-1600.

ATTRIBUTION TO THE 2017 MULTIDISCIPLINARY THORACIC CANCERS SYMPOSIUM REQUESTED IN ALL NEWS COVERAGE.

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Abstract and Presentation Details

- Tolerability and Safety of Thoracic Radiation and Immune Checkpoint Inhibitors among Patients with Lung Cancer
- Oral Abstract Session, Friday, March 17, 11:00 a.m. – 12:30 p.m. Pacific time, Yerba Buena Salon 9
- This news release contains additional and/or updated information from the study author(s). Full original abstract and author disclosures available on the final page of this release.

Resources on Lung Cancer and Radiation Therapy

- Digital brochures: Radiation Therapy for Lung Cancer (Spanish version), Plain Talk about Stereotactic Radiation, Understanding Clinical Trials
- Videos: Radiation Therapy for Lung Cancer, An Introduction to Radiation Therapy
- Additional brochures, videos and information on radiation therapy from RTAnswers.org
ABOUT THE SYMPOSIUM

The 2017 Multidisciplinary Thoracic Cancers Symposium, co-sponsored by the American Society for Radiation Oncology (ASTRO), the American Society of Clinical Oncology (ASCO) and The Society of Thoracic Surgeons (STS), features the latest advances in surgery, radiation therapy, chemotherapy and novel molecular biologic therapies for thoracic malignancies such as lung cancer. The symposium will be held March 16-18, 2017, at the San Francisco Marriott Marquis. For more information about the symposium, visit www.thoracicsymposium.org. For press registration and news briefing information, visit www.astro.org/thoracicpress.

ABOUT ASTRO

The American Society for Radiation Oncology (ASTRO) is the premier radiation oncology society in the world, 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. As the leading organization in radiation oncology, 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 (www.redjournal.org), Practical Radiation Oncology (www.practicalradonc.org) and Advances in Radiation Oncology (www.advancesradonc.org); developed and maintains an extensive patient website, RT Answers (www.rtanswers.org); and created the Radiation Oncology Institute (www.roinstitute.org), a nonprofit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit www.astro.org.

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 #10: Tolerability and Safety of Thoracic Radiation and Immune Checkpoint Inhibitors among Patients with Lung Cancer


Purpose/Objective(s): Immune checkpoint inhibitors (ICPIs) are changing systemic management of lung cancer. Pneumonitis can lead to dose limiting toxicity. There are limited published data on the use of thoracic radiation therapy (TRT) before, during or after administration of these agents. The goal of this study was to assess safety and tolerability among patients receiving TRT within 6 months before or after receipt of ICPIs.

Materials/Methods: For all patients, ICPIs were delivered until disease progression. We identified 29 patients who received TRT between February 2012 and May 2016 to 29 unique intrathoracic sites within 6 months of either single agent ICPI (n=14 anti-PD-1, n=3 anti-PD-L1) or combined ICPIs (n=7 anti-PD-1/CTLA-4, n= 5 anti-PD-L1/CTLA-4). TRT associated toxicities were defined qualitatively based on careful review of the clinical chart. Kaplan-Meier (KM) estimates of progression free survival (PFS) and overall survival (OS) were calculated from the date of ICPI initiation.

Results: The median age at time of ICPI study enrollment was 64 years (range 41-77) with 16 females (55%). The majority of patients had an ECOG 1 performance status (69%), were of NSCLC histology (79%), with a median of 3 metastatic sites (range 2-8). Fifteen lesions (52%) were treated with TRT concurrent with or after ICPI therapy. The median interval between ICPI and TRT administration was 2.2 months (range 0.4-5.5 month) in lesions treated with TRT before or after ICPI. Median PFS and OS was 3.8 months (1.9, 8-95% CI) and 9.2 months (5.1, not reached-95% CI), respectively with a median PFS/toxicity follow-up of 6.6 months (range: 0.5-40.4 months). TRT doses ranged between 10 to 70 Gy in 1 to 35 fractions. One patient experienced possible TRT/ICPI related grade 5 pulmonary toxicity 2 weeks following completion of TRT (4 Gy x 5 to right hilum/lung), which was initiated 1 month after the last dose of anti-PD-1 therapy. Two cases of possible grade 3 TRT/ICPI related pneumonitis were noted approximately 2 and 4 months following palliative TRT to the mediastinum and right lower lobe, respectively. In these cases, anti-PD-L1/CTLA-4 and anti-PD-L1 therapy were completed approximately 1 and 2 months before starting RT. Additionally, two cases of grade 2 and grade 3 pneumonitis related to anti-PD-1 agent alone were noted prior to initiation of TRT. In both cases, patients were treated with steroid therapy and subsequently received TRT without additional pulmonary toxicity.

Conclusion: In this analysis of TRT delivered among lung cancer patients treated with ICPIs, 3 of 29 patients experienced possible grade ≥3 pneumonitis, which may have been related to TRT while two patients developed pneumonitis from ICPIs alone and were subsequently treated with TRT without increased toxicity. Further prospective safety data is necessary with combination TRT and ICPI therapy.