Biomarker blood test shows cancer recurrence months before CT scans

Prospective clinical trial demonstrates that testing for CTCs reveals lung cancer recurrence an average of six months earlier than conventional scans

SAN FRANCISCO, March 16, 2017—Results from a prospective clinical trial showed that a blood test looking at specific biomarkers was able to detect recurrences of lung cancer an average of six months before conventional imaging methods found evidence of recurrence. In the largest prospective clinical trial to date of circulating tumor cells (CTC) as biomarkers for locally advanced lung cancer, the findings indicate that blood tests potentially can be used in conjunction with CT and PET/CT scans to guide personalized treatment planning for patients with non-small cell lung cancer (NSCLC). The study will be presented today at the 2017 Multidisciplinary Thoracic Cancers Symposium.

Lung cancer is known for its aggressive nature and ability to spread throughout a patient’s body. Cancer cells that enter the blood stream are known as circulating tumor cells, or CTCs. While the current standard of care following treatment for locally advanced NSCLC is for patients to get surveillance CT or PET/CT scans to monitor for cancer recurrence, new tests can track elevated CTC counts through a simple blood test, allowing for more frequent and less invasive follow-up. Other biomarkers, such as circulating tumor DNA (ctDNA), also have been studied in lung cancer, although ctDNA trials have been largely restricted to advanced (i.e., metastatic) disease, which is not amenable to curative treatments. By using CTC counts as a biomarker for recurrence in localized disease, treatment teams may be able to diagnose recurrence significantly earlier than they could with imaging scans alone.
“The additional lead time afforded by an earlier diagnosis may enable doctors to better tailor alternative and salvage treatments to improve their patients’ outcomes and quality of life. Earlier detection of recurrence may even translate into an increased likelihood of curing these patients when their tumor burden is lowest and thus more likely to respond to therapy,” said Chimbu Chinniah, lead author of the study and a research fellow in radiation oncology in the Perelman School of Medicine at the University of Pennsylvania in Philadelphia.

A total of 48 patients with stage II-III locally advanced NSCLC were enrolled in the prospective clinical trial. All patients were treated with concurrent chemoradiation. Blood samples were obtained before treatment, during treatment (at weeks 2, 4 and 6) and following treatment (at months 1, 3, 6, 12, 18 and 24). Circulating tumor cells were identified by analyzing the samples with an adenoviral probe that detects elevated activity of a specific enzyme that is produced when cancer cells replicate. Surveillance scans with CT or PET/CT imaging were performed at three-month intervals.

Patients ranged in age from 31 to 84, with a median age of 66 years. No patient had a history of prior malignancy. Researchers also assessed patient gender (54% male), race (69% Caucasian, 21% African American), smoking status (77% former, 21% current), histology (48% squamous cell carcinoma, 46% adenocarcinoma) and primary tumor size (median 3.7 centimeters).

At a median follow-up of 10.9 months following treatment for locally advanced NSCLC, nearly half (46%) of the patients experienced recurrence or progression, as detected by conventional surveillance scans and biopsies. The median time to recurrence was 7.6 months, with a range of 1.3 to 32 months. Blood samples were obtained following chemoradiation therapy for 20 of the 22 recurrent patients.

Fifteen of these 20 patients had elevated CTC counts following treatment, with a median lead time of 4.7 months and a range of 1.2 months to one year. Of these 15 patients, two-thirds demonstrated a rise in CTC counts an average of six months before PET/CT or CT scans detected the recurrence. For many patients, CTC levels were negative immediately following treatment but rose subsequently in the months following treatment. While most of these CTC level rises occurred before disease recurrence was identified on imaging, four of the 20 patients experienced recurrences that were detected with imaging before elevated CTC levels indicated the disease had returned.

“The future use of circulating tumor cells as a diagnostic and prognostic tool for localized NSCLC looks promising. Although imaging remains the cornerstone of post-treatment surveillance for patients, blood tests
could, and perhaps should, be used in conjunction with imaging scans to better monitor patients during their follow-up period after treatment,” said Charles B. Simone, II, MD, the study’s senior author and principal investigator, as well as an associate professor of radiation oncology at the University of Maryland School of Medicine and medical director of the Maryland Proton Treatment Center in Baltimore.

The abstract, “Prospective trial of circulating tumor cells as a biomarker for early detection of recurrence in patients with locally advanced non-small cell lung cancer treated with chemoradiation,” will be presented in detail during the plenary session at the 2017 Multidisciplinary Thoracic Cancers Symposium in San Francisco (full details below). To schedule an interview with Mr. Chinniah or Dr. Simone, 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

- Prospective Trial of Circulating Tumor Cells as a Biomarker for Early Detection of Recurrence in Patients with Locally Advanced Non-small Cell Lung Cancer Treated with Chemoradiation
- Plenary Session, Thursday, March 16, 10:30 a.m. – 12:00 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](http://bit.do/thoracic2)), 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](http://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](http://www.thoracicsymposium.org). For press registration and news briefing information, visit [www.astro.org/thoracicpress](http://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 #3: Prospective Trial of Circulating Tumor Cells as a Biomarker for Early Detection of Recurrence in Patients with Locally Advanced Non-small Cell Lung Cancer Treated with Chemoradiation

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Purpose/Objective(s): Assays identifying circulating tumor cells (CTCs) may allow for noninvasive and sequential monitoring of lung cancer. However, data assessing CTC use for monitoring treatment response and tumor recurrence in non-metastatic lung cancer patients are sparse. We performed a prospective clinical trial in patients with locally advanced non-small cell carcinoma (LA-NSCLC) definitively treated with chemoradiation with primary endpoints to assess CTCs as a biomarker and if CTC trends precede conventional imaging in detecting recurrences.

Materials/Methods: All patients with LA-NSCLC (stage II-III) enrolled in this IRB-approved clinical trial were analyzed. Patients had to receive concurrent chemoradiation and could not have prior active malignancy. CTCs from peripheral blood samples were identified using an adenoviral probe that detects elevated telomerase activity present in nearly all lung cancer cells, but not normal cells. Assay validity was confirmed with secondary tumor-specific markers. Patient samples were obtained before, during (weeks 2, 4, 6), and after (post-RT; months 1, 3, 6, 12, 18, 24) concurrent chemoradiation.

Results: 48 patients were enrolled. Patients were a median of 66 years old (range 31-84), predominantly male (54%), Caucasian (69%) or African American (21%), and former (77%) or current (21%) smokers. They had squamous cell carcinoma (48%) or adenocarcinoma (46%). Median primary tumor size was 3.7 cm (range 1.5-10.0). Patients had stage IIA (54%) or IIIB (33%) NSCLC with cN2 (60%) or cN3 (23%) nodal disease. At a median follow-up of 10.9 months, 22 of 48 patients (46%) recurred at a median time of 7.6 months post-RT (range 1.3-32.0). Post-RT samples were obtained in 20 of 22 recurrent patients. Of these 20 patients, 15 (75%) had a rise in CTC counts post-RT. In 10 of these 15 patients, CTC counts were negative on initial post-RT draw and rose prior to radiographic detection of recurrence, with a median lead time of 4.7 months (range 1.2-12.0) between CTC rise and radiographic evidence of recurrence. One patient with an early recurrence (4.7 months) had persistently elevated CTC levels during and after treatment, and 4 patients had CTC rises after radiographic detection of recurrence.

Conclusion: To our knowledge, this pilot trial is the largest prospective study assessing CTCs in LA-NSCLC. Results indicate that longitudinal CTC monitoring in patients with LA-NSCLC treated with chemoradiation is feasible, and that CTC elevations in many patients meaningfully precede radiologic evidence of disease recurrence. Together, these findings suggest that CTCs may be a promising biomarker of progressive or recurrent disease and may help guide early salvage therapeutic strategies. Additional prospective cohorts are needed to confirm our findings and determine the utility of CTCs following chemoradiation for LA-NSCLC.