Biomarker blood test predicts survival following localized lung cancer treatment

Presence of circulating tumor DNA during and after treatment is associated with cancer recurrence and worse long-term survival rates

SAN DIEGO, September 24, 2017 – A new study demonstrates that a blood test to detect cancer may predict treatment outcomes for patients with localized non-small cell lung cancer (NSCLC) and afford physicians additional lead time to personalize treatment for recurrent disease. Patients in the study with detectable levels of circulating tumor DNA (ctDNA) shortly after treatment all had recurrences within two years, while all but one of the patients without detectable ctDNA shortly after treatment remained disease-free and survived long-term. Conventional imaging, conversely, was not prognostic for recurrence or survival. Findings will be presented today at the 59th Annual Meeting of the American Society for Radiation Oncology (ASTRO).

The aggressive nature of lung cancer can make long-term management especially challenging. Because NSCLC tends to progress, even following treatment, regular monitoring for recurrence is necessary. The CT scans typically used for monitoring, however, are often unable to detect microscopic tumor deposits or to distinguish normal tissue changes caused by treatment from changes caused by recurrent disease.

“Blood tests that can detect minute traces of cancer that remain after treatment could improve recurrence monitoring and potentially offer physicians months of additional lead time to tailor treatments and improve our patients’ outcomes and quality of life,” said Aadel Chaudhuri, MD, PhD, lead author of the study and a chief resident in radiation oncology at Stanford University in Palo Alto, California.
“Our findings suggest that ctDNA analysis, unlike CT scans, can identify shortly after treatment completion if a patient with localized lung cancer has likely been cured by radiation or surgery or if he or she still has cancer cells present in their body. While we expected that ctDNA detection of molecular residual disease would predict poor clinical outcomes, we were surprised by how strongly predictive the test was for recurrence and survival.”

Presence of ctDNA was measured as a marker of molecular residual disease (MRD) in patients with stage I-III NSCLC immediately before treatment and shortly after treatment was completed. ctDNA levels also were measured mid-treatment (average = 3 weeks, range = 1.4-3.7 weeks) for half of the patients receiving chemoradiation (n = 13 of 27 patients). Cancer Personalized Profiling by Deep Sequencing (CAPP-Seq) was used to assess whether ctDNA was present. Surveillance scans using CT imaging were evaluated using the Response Evaluation Criteria In Solid Tumors (RECIST).

The median patient age was 67 years (range 47-91 years), and most patients (67%) were male. All 41 patients were treated with curative intent, including with chemoradiation therapy (66%), radiation therapy alone (27%) and surgery alone (7%). Median follow-up for the study was 35 months (range 7-56 months).

Researchers detected ctDNA pretreatment in 38 of the 41 patients (93%). Thirty-four of these 38 patients had blood drawn within four months of treatment completion (the prespecified MRD landmark) and were eligible for subsequent analysis.

Among the 34 patients with ctDNA MRD pretreatment, more than half (56%, n = 19) had detectable residual disease after treatment. All of these patients subsequently developed recurrent lung cancer, compared with only one of the 15 patients without detectable ctDNA MRD.

Patients with detectable ctDNA MRD after treatment had worse freedom from progression and survival than patients without detectable ctDNA MRD (freedom from progression Hazard Ratio (HR) = 44.0, p < 0.0001; disease-specific survival HR = 27.7, p < 0.0001). CT imaging at the same time was not prognostic for survival. ctDNA levels before treatment also were not associated with survival outcomes.

In eight of the 13 patients assessed mid-treatment, ctDNA accounted for 0.1 percent or more of all cell-free DNA. For these patients, mid-treatment ctDNA levels predicted eventual disease progression (HR = 2.7, p = 0.006). Sixty percent of the patients with less than 0.1 percent ctDNA mid-treatment were progression-free at two years following treatment, compared to none of the patients with 0.1 percent or higher levels of ctDNA (HR = 4.4, p = 0.037).
“In the future, clinicians may be able to use ctDNA analysis to identify patients who could benefit from additional treatment after first-line therapy,” said Maximilian Diehn, MD, PhD, senior author of the study and an assistant professor of radiation oncology at Stanford.

“In a related study also presented at this year’s ASTRO Annual Meeting, we found that ctDNA analysis detected disease recurrence an average 5.5 months earlier than standard-of-care CT imaging for localized lung cancer and helped with interpretation of equivocal follow-up imaging. This suggests that ctDNA analysis could open a window to treat patients with residual cancer early, while disease burden is minimal.”

The abstract, “Circulating tumor DNA analysis during radiotherapy for localized lung cancer predicts treatment outcome,” will be presented in detail during a news briefing and the clinical trials session at ASTRO’s 59th Annual Meeting in San Diego (full details below). The study is also available beginning today in Cancer Discovery. To schedule an interview with Dr. Diehn, Dr. Chaudhuri and/or outside experts in lung cancer or circulating tumor DNA, contact ASTRO’s media relations team on-site at the San Diego Convention Center September 24 through 27, by phone at 703-286-1600 or by email at press@astro.org.

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ATTRIBUTION TO THE AMERICAN SOCIETY OF RADIATION ONCOLOGY (ASTRO) ANNUAL MEETING REQUESTED IN ALL COVERAGE.

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.

Study Presentation Details

- News Briefing: Sunday, September 24, 1:00 – 2:00 p.m. Pacific time, San Diego Convention Center, room 24C, webcast: http://www.bit.do/astro17-1
- Scientific Session: Clinical Trials, Sunday, September 24, 3:15 – 4:45 p.m. Pacific time, San Diego Convention Center, Ballroom 20

Resources on Lung Cancer and Radiation Therapy

- Digital brochure: Radiation Therapy for Lung Cancer (Spanish version)
- Videos: Radiation Therapy for Lung Cancer (Spanish version), An Introduction to Radiation Therapy (Spanish version)
- Additional brochures, videos and information on radiation therapy from ASTRO’s patient site, RTAnswers.org
- ASTRO’s clinical practice statements and guidelines

ABOUT ASTRO’S ANNUAL MEETING

ASTRO’s 59th Annual Meeting, the world’s largest scientific meeting in radiation oncology, will be held September 24-27, 2017, at the San Diego Convention Center. The 2017 Annual Meeting is expected to attract more than 11,000
attendees from across the globe, including oncologists from all disciplines and members of the entire radiation oncology team. More than 2,800 abstracts sharing results from clinical trials and other research studies will be presented in conjunction with educational sessions and keynote addresses that underscore the meeting’s theme, “The Healing Art and Science of Radiation Oncology.” Led by ASTRO President Brian Kavanagh, MD, MPH, FASTRO, the 2017 meeting will feature keynote addresses from Richard D. Zane, MD, FAAEM, Chief Innovation Officer for the University of Colorado Health System; Lucy Kalanithi, MD, FACP, widow of Paul Kalanithi, MD, the best-selling author of “When Breath Becomes Air,” with Heather Wakelee, MD, Paul’s oncologist; and Vinay K. Prasad, MD, MPH, an assistant professor of medicine at the Oregon Health & Science University. During the four-day meeting, more than 200 exhibitors will demonstrate cutting-edge technology and medical device innovations for radiation oncology. Visit us online for more information about ASTRO’s 59th Annual Meeting or press opportunities at the meeting.

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 (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 and follow us on our blog, Facebook and Twitter.
Abstract 2: Circulating tumor DNA analysis during radiotherapy for localized lung cancer predicts treatment outcome

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Purpose/Objective(s): Identifying lung cancer patients with residual disease following curative intent radiotherapy (RT) or surgery is difficult due to normal tissue changes and inability to detect microscopic disease. Cancer Personalized Profiling by deep Sequencing (CAPP-Seq) is an ultra-sensitive blood-based assay that uses next-generating sequencing to quantitate circulating tumor DNA (ctDNA). We performed a prospective study to determine the prognostic value of CAPP-Seq molecular residual disease (MRD) detection during and after treatment of localized lung cancer patients.

Materials/Methods: We applied CAPP-Seq to pre- and post-treatment blood samples from 41 patients treated with chemoRT (n=27, 66%), RT (n=11, 27%) or surgery (n=3, 7%) for stage I-III lung cancer. Detection of ctDNA at a single MRD time-point within 4 months of treatment completion was compared with long-term clinical and radiographic outcomes. For a subset of patients treated with chemoRT (n=13), we also performed CAPP-Seq at a mid-treatment time point (average=3 weeks, range 1.4-3.7).

Results: Median follow-up was 35 months. There was no correlation between pre-treatment ctDNA levels and clinical outcomes. Among 38 patients with detectable pre-treatment ctDNA, 19 (50%) had detectable post-treatment ctDNA at the MRD time-point. Patients with detectable post-treatment MRD had significantly worse freedom from progression (HR 37Chaud.7; P<0.0001) and overall survival (HR 12.3; P<0.0001) than patients with undetectable post-treatment MRD. In contrast, CT imaging scored by RECIST criteria at the MRD time-point was not prognostic. Among the 19 MRD+ patients, ratio of post-treatment to pre-treatment ctDNA level was associated with overall survival (HR 1.2, P=0.008). In patients with mid-treatment blood samples (n=13), mid-treatment ctDNA levels were associated with eventual disease progression (HR 2.7; P=0.006). Patients with >0.1% ctDNA at the mid-treatment time point displayed significantly inferior 2-year freedom from progression than patients with <0.1% mid-treatment ctDNA (0% vs. 60%; HR 4.4; P=0.037).

Conclusion: Our results suggest that mid-treatment ctDNA levels during chemoRT predict treatment outcomes in patients treated with chemoRT for localized lung cancer. If confirmed, ctDNA analysis may facilitate response-adapted radiotherapy and/or systemic therapy.

Lymphoma Research Foundation. M. Diehn: Employee; Kaiser Permanente. Consultant; Roche Sequencing, Stock; CiberMed. Stock Options; Quanticel Pharmaceuticals.