Progression-free survival triples in select metastatic lung cancer patients with surgery or radiation after chemotherapy

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Lung cancer patients with oligometastases, defined as three or fewer sites of metastasis, may benefit from aggressive local therapy, surgery or radiation, after standard chemotherapy, according to research led by The University of Texas MD Anderson Cancer Center. If validated in larger studies, the findings could represent a dramatic shift in clinical care for thousands of lung cancer patients.

Daniel Gomez, M.D., associate professor, Radiation Oncology, will present the results June 6 in an oral presentation at the 2016 American Society of Clinical Oncology Annual Meeting. He and his colleagues found an eight month progression free survival benefit (PFS) in patients treated with local consolidative therapy (LCT).

According to the American Cancer Society, 224,390 people will be diagnosed with lung cancer and 158,080 will die from the disease in the U.S. this year. Of those diagnosed, says Gomez, approximately 50 percent have metastatic disease, and it has estimated that about 20-50 percent present with three or fewer metastases.

Historically, explains Gomez, all metastatic lung cancer patients have been treated with chemotherapy and thought to have incurable disease. With treatment advances over the past decade, however, a number of retrospective studies have suggested that in those lung cancer patients with minimal metastases, theoretically, the disease could be better

controlled long-term by LCT.

"With recent advances in radiation delivery, targeted agents and systemic and maintenance therapy, some research has suggested it's possible to control the disease. Yet those studies have inherent bias because patients treated with local consolidative therapy were selected due to favorable risk factors," explains Gomez, the study's corresponding author.

"Our research is the first randomized prospective study of oligometastases in lung cancer to look at treating patients aggressively and comparing results to standard therapy, which typically is maintenance therapy or observation."

The prospective Phase II study was planned for 94 patients; however, because of the benefit seen in the study arm, the trial was stopped early. In total, the study enrolled and evaluated 49 non-small cell lung cancer patients from three participating centers, with MD Anderson serving as the lead site. All patients had: Stage IV disease; three or fewer metastases and no progression after initial treatment with chemotherapy. The study's primary endpoint was PFS.

Half of the patients were randomized to the experimental arm of LCT ¬¬— radiation or surgical resection of all metastases, with or without chemotherapy; the other half received standard-of-care chemotherapy (no-LCT). Radiation or surgery was determined by a multidisciplinary team based on metastasis presentation, and all variations of both modalities were permissible.

"With this study, we wanted to be pragmatic and allow the breadth of treatments that are now available to patients in general practice," says Gomez.

The study was powered for a three month PFS benefit. The median PFS

time was 11.9 months in the LCT arm, compared to 3.9 months in the no-LCT arm.

Seventeen patients in the no-LCT group crossed over to the LCT arm, 14 due to progression.

Overall, of the 28 patients that progressed (12 in the LCT and 16 in the no-LCT) seven had progression in the primary site; three in a known site of metastasis; seven in a different metastasis and 11 in a combination of sites. Because the study was stopped early, overall survival is not yet mature.

The significance of the PFS findings surprised the researchers, says Gomez.

"For some time, there's been a push from this patient population as well as a provider trend to treat with additional therapy," says Gomez. "These findings provide evidence and enthusiasm to offer aggressive local treatment and, with validation, could pave the way to treat tens of thousands of lung cancer patients with curative intent."

Further research will report on both overall survival and quality of life, and follow up studies are being designed to include immunotherapy, making future findings more applicable to the current treatment options available to patients.

Limitations of the research include the heterogeneity of the patient population and the overall small size of the study. The study also was not powered to detect an overall survival benefit, and crossover between arms may dilute this effect.

Provided by University of Texas M. D. Anderson Cancer Center