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Analysis finds select group of stage IV lung cancer patient population achieves long-term survival after aggressive treatments

San Francisco, September 16, 2014—A large, international analysis of patients with stage IV non-small cell lung cancer (NSCLC) indicates that a patient's overall survival (OS) rate can be related to factors including the timing of when metastases develop and lymph node involvement, and that aggressive treatment for "low-risk" patients leads to a five-year OS rate of 47.8 percent, according to research presented today at the American Society for Radiation Oncology's (ASTRO's) 56th Annual Meeting.

When lung cancer has spread from an original tumor to other sites of the body, it is classified as metastatic (Stage IV), and the goal of treatment is to slow the cancer down with chemotherapy or radiation, but these treatments are unable to eradicate the cancer and survival is usually in the range of only a few months.

However, when there are only a few locations of metastatic lung cancer (called oligo-metastatic), some studies suggest that by removing or eradicating each of those cancer deposits with aggressive treatments such as surgery or high-dose, precise radiation called stereotactic ablative radiotherapy or SABR, the cancer may be controlled for a long period of time.

In order to further study the possible benefits of aggressive treatments in stage IV lung cancer, researchers completed this meta-analysis which evaluated data of 757 Stage IV NSCLC patients from 20

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hospitals worldwide who had between one and five metastatic deposits that were removed surgically or eradicated with high-dose, precise radiotherapy. Patients in the study also had to have had aggressive treatment of their original lung tumor. The intent of the study was to determine whether long term survivors exist after aggressive treatment of oligo-metastases, and to propose a risk classification scheme that could be used to identify which stage IV patients are most likely to benefit from aggressive treatments.

The analysis determined that the factors that impacted overall survival of the patients included the timing of when the metastases appeared, that is, whether the metastases appeared at the same time as the original lung cancer (synchronous) vs. if they appeared after the original lung cancer (metachronous), whether lymph nodes in the chest were involved (N-stage), and the type of lung cancer (adenocarcinoma vs. other types).

Using these factors, the study identified three risk groups of patients 1) low risk patients (146), or patients who survived the longest, were those with metachronous metastases, with a 5 year OS of 47.8 percent; 2) intermediate-risk patients (201)—those with synchronous metastases and no evidence of involved lymph nodes in the chest, with a 5-year OS of 36.2 percent; and 3) high-risk patients (184), or patients with the poorest survival, were those who had synchronous metastases and evidence of lymph node involvement in the chest; they had a five-year OS of 13.8 percent .

Furthermore, the study found that despite receiving aggressive treatments, more than half of the patients progressed in previously treated areas or developed new sites of disease within one year of treatment.

“Our study finds some stage IV NSCLC patients can achieve long-term survival after aggressive treatments; however, it is important to note that the patients in this study are a very select minority of stage IV patients who are younger, more physically fit, with a lower burden and slower pace of disease than the average stage IV patient,” said lead study author Allison Ashworth, MD, a radiation oncologist who completed the study as part of her training at the London Health Sciences Centre at Western University, in London, Ontario. “We hope our study’s results will help determine which stage IV NSCLC patients are most likely to benefit from aggressive treatments, and equally as important, help identify those patients most likely to fail, thus sparing them from futile and potentially harmful treatments. Our research, however, cannot answer the question of whether the longer survival is due to the treatments or simply because these patients have less aggressive disease. We must await the results of randomized clinical trials to answer this question. In the meantime, it is our hope that our study will help cancer specialists in making treatment decisions and in the development of clinical trials.”

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The abstract, “An Individual Patient Data Meta-Analysis of Outcomes and Prognostic Factors after Treatment of Oligometastatic Non-Small Cell Lung Cancer,” will be presented in detail during a scientific session at ASTRO’s 56th Annual Meeting at 2:45 p.m. Pacific time on Tuesday, September 16, 2014. To speak with Dr. Ashworth, please call Michelle Kirkwood on September 14 – 17, 2014, in the ASTRO Press Office at the Moscone Center in San Francisco Center at 415-978-3503 or 415-978-3504, or email michellek@astro.org.

ASTRO’s 56th Annual Meeting, to be held at the Moscone Center in San Francisco, September 14-17, 2014, is the nation’s premier scientific meeting in radiation oncology. The 2014 Annual Meeting is expected to attract more than 11,000 attendees including oncologists from all disciplines, medical physicists, dosimetrists, radiation therapists, radiation oncology nurses and nurse practitioners, biologists, physician assistants, practice administrators, industry representatives and other health care professionals from around the world. Led by ASTRO President Bruce G. Haffty, MD, FASTRO, a radiation oncologist specializing in breast cancer, the theme of the 2014 Meeting is “Targeting Cancer: Technology and Biology,” and the Presidential Symposium, “Local-regional Management of Breast Cancer: A Changing Paradigm,” will feature Jay R. Harris, MD, FASTRO, and Thomas A. Buchholz, MD, FASTRO, to highlight recent practice-changing, landmark studies and current developments in the local-regional management of breast cancer. ASTRO’s four-day scientific meeting includes presentation of up to four plenary papers, 360 oral presentations, 1,862 posters and 144 digital posters in more than 50 educational sessions and scientific panels for 20 disease-site tracks. Three keynote speakers will address a range of topics including oncologic imaging, biology and targeting in oncology, and human error and safety concerns: Hedvig Hricak, MD, PhD, Chair of the Department of Radiology and the Carroll and Milton Petrie Chair at Memorial Sloan Kettering Cancer Center; Frank McCormick, PhD, FRS, DSc (hon), Professor Emeritus and the David A. Wood Distinguished Professor of Tumor Biology and Cancer Research of the University of California at San Francisco Helen Diller Family Comprehensive Cancer Center; and Sidney Dekker, PhD, MA, MSc, Professor and Director of the Safety Science Innovation Lab at Griffith University, Brisbane, Australia.

ABOUT ASTRO

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 that 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 two medical journals, International Journal of Radiation Oncology • Biology • Physics (www.redjournal.org) and Practical Radiation Oncology (www.practicalradonc.org); developed and maintains an extensive patient website, www.rtanswers.org; and

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created the Radiation Oncology Institute (www.roinstitute.org), a non-profit 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.

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2014 American Society for Radiation Oncology (ASTRO) 56th Annual Meeting
News Briefing, Tuesday, September 16, 2014, 7:00 a.m. Pacific time

Scientific Session: Tuesday, September 16, 2014, 2:45 – 4:15 p.m. PT, the Moscone Center

168 **An Individual Patient Data Meta-Analysis of Outcomes and Prognostic Factors after Treatment of Oligometastatic Non-Small Cell Lung Cancer**

Author Block: A. Ashworth¹, S. Senan², D. A. Palma³, M. Riquet⁴, Y. Ahn⁵, U. Ricardi⁶, M. Congedo⁷, D. R. Gomez⁸, G. Wright⁹, G. Melloni¹⁰, M. T. Milano¹¹, C. V. Sole¹², T. De Pas¹³, D. L. Carter¹⁴, A. Warner³, G. Rodrigues³, ¹Cancer Centre of Southeastern Ontario, Kingston, ON, Canada, ²VU University Medical Center, Amsterdam, Netherlands, ³London Regional Cancer Program, London, ON, Canada, ⁴Georges Pompidou European Hospital, Paris, France, ⁵Samsung Medical Center, Seoul, Korea, Republic of, ⁶University of Turin, Turin, Italy, ⁷Catholic University of Sacred Heart, Rome, Italy, ⁸M.D. Anderson Cancer Center, Houston, TX, ⁹University of Melbourne Department of Surgery, Melbourne, Australia, ¹⁰Department of Thoracic Surgery, San Raffaele Scientific Institute, Milan, Italy, ¹¹University of Rochester, Rochester, NY, ¹²Instituto Madrileño de Oncología, Madrid, Spain, ¹³European Institute of Oncology, Thoracic Oncology Division, Milan, Italy, ¹⁴Rocky Mountain Cancer Centers, Aurora, CO

Purpose/Objective(s): Long-term survival has been observed in patients with oligometastatic NSCLC treated with locally ablative treatments to all sites of metastatic disease. We performed an individual patient data meta-analysis to determine clinical outcomes, and to propose a risk stratification system, related to the comprehensive treatment of patients with oligometastatic non-small cell lung cancer (NSCLC).

Materials/Methods: After a systematic review of the literature, data were obtained on 757 NSCLC patients from 20 hospitals worldwide with 1-5 synchronous or metachronous metastases treated with surgical metastectomy, stereotactic ablative radiotherapy, stereotactic radiosurgery or radical external-beam radiotherapy, and curative-intent treatment of the primary lung cancer. Patients were randomly divided into training and validation sets (two-thirds vs one-third of patients). Cox regression was utilized to identify factors predictive of overall survival (OS) and progression-free survival (PFS). Risk groups were defined by recursive partitioning analysis (RPA).

Results: Median OS was 26 months, 1-year OS 70.2%, and 5-year OS 29.4%. Surgery was the most commonly utilized treatment for the primary tumour (n=635, 83.9%) and metastases (n=339, 62.3%). Median PFS was 11 months. Factors predictive of OS were: synchronous vs. metachronous metastases (p<0.001), N-stage (p=0.002) and adenocarcinoma histology (p=0.036); with the model remaining predictive in the validation set (c-statistic=0.682). Three risk groups were identified on RPA: low-risk: metachronous metastases (5-year OS 47.8%); intermediate risk: synchronous metastases and N0 disease (5-year OS 36.2%); high risk: synchronous metastases and N1/N2 disease (5-year OS 13.8%).

Conclusions: Significant OS differences were observed in oligometastatic patients stratified by type of metastatic presentation, and N-status. Long-term survival is common in selected patients with metachronous oligometastases. We propose this risk classification scheme be utilized in guiding selection of patients for clinical trials of ablative treatment.

Author Disclosure Block: **A. Ashworth:** None. **S. Senan:** None. **D.A. Palma:** None. **M. Riquet:** None. **Y. Ahn:** None. **U. Ricardi:** None. **M. Congedo:** None. **D.R. Gomez:** None. **G. Wright:** None. **G. Melloni:** None. **M.T. Milano:** None. **C.V. Sole:** None. **T. De Pas:** None. **D.L. Carter:** None. **A. Warner:** None. **G. Rodrigues:** None.