Use of involved field irradiation therapy for locally advanced esophageal cancer reduces toxicity without increasing loco-regional lymph nodal recurrence

San Antonio, October 19, 2015—For patients with locally advanced esophageal cancer that has spread to the lymph nodes, radiation therapy (RT) that targets only the involved lymph nodes regions results in less toxicity without causing a statistically significant difference in loco-regional lymph nodal recurrence, distant failure and overall survival rates, according to research presented today at the American Society for Radiation Oncology’s (ASTRO’s) 57th Annual Meeting.

The American Cancer Society estimates that while esophageal cancer makes up approximately one percent of all cancers diagnosed in the U.S., it is far more prevalent in China, with esophageal squamous cell carcinoma (ESCC) being the most common type of esophageal cancer in China. Many patients with ESCC are not diagnosed until the cancer is in an advanced stage.

Chemoradiation (the combination of chemotherapy and radiation therapy) is a standard treatment for locally advanced esophageal cancer (cancer that has spread to the lymph nodes and surrounding tissue). Elective nodal irradiation (ENI)—RT to the tumor and lymph nodes, including uninvolved lymph nodes in the region around the cancerous tumor—is a common form of RT used to
treat ESCC. The use of ENI has been controversial due to increased level of irradiation and possible toxicity. This study evaluated the feasibility of reducing the nodal irradiation volume of RT by comparing ENI to involved-field irradiation (IFI)—RT that involves only the regions where the lymph nodes are located.

The prospective, randomized controlled clinical trial included 110 patients with esophageal cancer enrolled from nine cancer centers across China between April 2012 and November 2014. The patients had inoperable, newly diagnosed stage II – stage III thoracic ESCC.

Patients were treated with concurrent chemoradiotherapy and all of the patients received docetaxel (75 mg/m2 on day one) and CDDP (25 mg/m2 on days one-three) every 21 days for two to four cycles. The patients received image-guided radiation therapy (IGRT) in once-daily fractions of 1.8-2Gy to a total dose of 60-66 Gy to the gross tumor volume (GTV) and 50-54 Gy to the clinical target volume (CTV). The patients were randomly divided into two groups; 56 patients received elective nodal irradiation (the ENI group); and 54 patients received involved-field irradiation (the IFI group).

The primary endpoints of the study were toxicities (side effects) and loco-regional lymph nodal recurrence (indicating the cancer had returned to the area and nearby lymph nodes). The secondary end points were distant failure and overall survival (OS).

At a median follow-up of 20 months, data showed that IFI resulted in significantly decreased radiation pneumonitis (inflammation of the lungs) and radiation esophagitis (inflammation of the lining of the esophagus). Grade ≥ 2 radiation pneumonitis in the ENI group was 26.8 percent, compared to 12.9 percent in the IFI group (p = 0.011); and the rate of radiation esophagitis was 37.5 percent in the ENI group compared to 20.4 percent in the IFI group (p = 0.001).

No significant differences in the loco-regional lymph nodal recurrence rate were observed between the two groups. The ENI group experienced a 17.9 percent loco-regional lymph nodal recurrence, compared to the IFI group, which experienced a 20.4 percent loco-regional lymph nodal recurrence (p = 0.819).
Evaluation of distant failure rates (measurement of whether the cancer appeared in other areas other than the original tumor site), indicated a positive result with no difference between the two groups. The ENI group had a 12.5 percent distant failure rate and the IFI group had a 13 percent distant failure rates (p = 0.465).

The two groups achieved similar one-year and two-year OS rates. The one-year OS rate was 89.2 percent for the ENI group and 88.3 percent for the IFI group (p = 0.431); and the two-year OS rates was 64.2 percent for the ENI group, compared to 55.6 percent for the IFI group (p = 0.857).

“Elective nodal irradiation (ENI) is the most commonly used type of RT for treating esophageal cancer, but its side effects and toxicity have been criticized,” said Tao Li, MD, PhD, lead author of the study and vice chairman of the department of radiation oncology at Sichuan Cancer Hospital and Institute. “Researchers have suggested decreasing the nodal irradiation volume with the use of IFI, yet prior to this study its potential advantages had only been measured in smaller trials. We anticipated that IFI could significantly decrease toxicity such as radiation pneumonitis and radiation esophagitis, but were initially uncertain if IFI might increase the loco-regional lymph nodal recurrence rates, distant failure and overall survival. The mid-term results of our trial show that IFI is an acceptable and toxicity-minimizing method of treatment for thoracic ESCC. This is a significant discovery for future esophageal cancer radiotherapy care.”

The abstract, “Involved-Field Irradiation vs Elective Nodal Irradiation for Locally Advanced Thoracic Esophageal Squamous Cell Carcinoma: A Comparative Interim Analysis of Clinical Outcomes and Toxicities (NCT01551589, CSWOG-RTOG 002),” will be presented in detail during the plenary session at ASTRO’s 57th Annual Meeting at 2:25 p.m. Central time on Monday, October 19, 2015. To speak with Dr. Li, please call Nancy Mayes in ASTRO’s Press Office at the Henry B. González Convention Center, in San Antonio on October 18 – 21, 2015 at 210-258-8104 or 210-258-8105, or email press@astro.org.

ASTRO’s 57th Annual Meeting, being held at the Henry B. González Convention Center in San Antonio, October 18-21, 2015, is the nation’s premier scientific meeting in radiation oncology. The 2015 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 D. Minsky, MD, FASTRO, a radiation oncologist specializing in gastrointestinal cancers, Professor of Radiation Oncology, and the Frank T. McGraw Memorial Chair at The University of Texas MD Anderson Cancer Center, Houston, the theme of the 2015 Meeting is “Technology Meets Patient Care.” Dr. Minsky’s Presidential Symposium, “Multidisciplinary Management of Esophageal and Rectal Cancers,” will feature Leonard L. Gunderson, MD, MS, FASTRO, and Joel E. Tepper, MD, FASTRO, to highlight imaging, staging, genomics and data mining approaches, as well as the latest advances in esophageal and colorectal cancer treatment. ASTRO’s four-day scientific meeting includes presentation of more than 2,100 abstracts: five plenary papers, 351 oral presentations, 1,609 posters and 171 digital posters in more than 53 educational sessions and 26 scientific panels for 20 disease-site tracks. Three keynote speakers will address a range of topics including cancer biology in radiation oncology, the essential roles of a physician, and patient safety: Arul Chinnaiyan, MD, PhD, Professor and Director, Michigan Center for Translational Pathology; Francisco G. Cigarroa, MD, Past President and Chancellor, University of Texas; and Gerald B. Hickson, MD, Senior Vice President and Assistant Vice Chancellor, Vanderbilt University Medical Center.

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 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, www.rtanswers.org; and 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.

###
7 Involved-Field Irradiation vs Elective Nodal Irradiation for Locally Advanced Thoracic Esophageal Squamous Cell Carcinoma: A Comparative Interim Analysis of Clinical Outcomes and Toxicities (NCT01551589, CSWOG-RTOG 002)

**Author Block:** T. Li¹, A. Yisikandraer², X. Zhang³, X. Wang⁴, Y. Ma⁵, L. Chen⁶, B. Lu⁷, H. Chen⁸, J. Yang⁹, J. Lv¹, and J. Lang¹; ¹Sichuan Cancer Hospital and Institute, Chengdu, China, ²The Affiliated Tumor Hospital of Xinjiang Medical University, Xinjiang, China, ³The First Affiliated Hospital of XI’AN Jiaotong University, Xi An, China, ⁴Gansu Cancer Hospital, Lanzhou, China, ⁵Gansu Wu Wei Tumor hospital, Wu Wei, China, ⁶Guangxi Tumor Hospital, The Affiliated Hospital of Guangxi Medical University, Nanning, China, ⁷Guizhou Cancer Hospital, Guiyang, China, ⁸Kunming General Hospital Of Chengdu Military Region, Kunming, China, ⁹Xinjiang Renming Hospital, Xinjiang, China

**Purpose/Objective(s):** Elective nodal irradiation (ENI) and involved-field irradiation (IFI) are definitive radiotherapeutic approaches used to treat patients with locally advanced thoracic esophageal squamous cell carcinoma (ESCC). The necessity of ENI has always been controversial. The aim of this study was to compare the failure patterns, survivals, and toxicities in locally advanced thoracic ESCC treated with ENI and IFI.

**Materials/Methods:** A prospective, multicenter, randomized controlled clinical trial was conducted. Eligible patients were newly diagnosed, untreated, inoperable stages II-III thoracic ESCC. Patients were treated with concurrent chemoradiotherapy and randomized into either an IFI or ENI group. The clinical target volume of regional lymph node (CTVn) of IFI included the nodal region(s) in which the involved lymph node(s) was/were located. The CTVn of ENI included the involved lymph node regions and clinically uninvolved lymph nodal stations according to the location of primary tumor. Image-guided radiation therapy (IGRT) was delivered in once-daily fractions of 1.8-2 Gy to a total dose of 60-66 Gy to the GTV and 50-54 Gy to the CTV. Patients received docetaxel (75 mg/m² on day 1)/CDDP (25 mg/m² on day 1-3) every 21 days for four cycles. The primary end point was loco-regional lymph nodal recurrence. The secondary end points were distant failure, overall survival (OS), and toxicities.

**Results:** Between April 2012 and November 2014, a total of 110 patients were enrolled from nine centers in China. Patients were randomly divided into ENI group (n=56) and IFI group (n=54). At a median follow-up of 20 months, no significant differences were observed in loco-regional lymph nodal recurrence (17.9% vs 20.4%, p = 0.819), distant failure (12.5% vs 13.0%, p = 0.465), 1-year OS rates (89.2% vs 88.3%, p = 0.431) and 2-year OS rates (64.2% vs 55.6%, p = 0.857) between the ENI group and the IFI group. The main pattern of loco-regional lymph nodal failure was in-field lymph node failure (12.5% for group ENI vs 13.0% for group IFI, p = 0.713), while the out-field lymph node failure was rare (5.4% for group ENI vs 7.4% for group IFI, p = 0.335). Grade ≥ 2 radiation pneumonitis and radiation esophagitis in the IFI group were significantly lower than that of the ENI group (12.9% vs 26.8%, p = 0.011; and 20.4% vs 37.5%, p = 0.001).

**Conclusion:** When compared to ENI, the radiation pneumonitis and radiation esophagitis of IFI were significantly decreased, while the loco-regional lymph nodal recurrence rates and distant failure rates were not increased. There were no significant differences in 1- and 2-year overall survival rates between the two groups. IFI is an effective treatment with acceptable toxicity for thoracic ESCC.