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MULTIDISCIPLINARY HEAD and NECK CANCER SYMPOSIUM EXPANDING TREATMENT HORIZONS

News Release

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Induction chemotherapy does not predict survival advantage over concurrent chemoradiation for locally advanced head and neck cancer

Patients receiving induction chemotherapy less likely to receive definitive course of radiation treatment

SCOTTSDALE, Ariz., February 18, 2016—Head and neck cancer patients who receive induction chemotherapy (IC; chemotherapy administered prior to radiation therapy) rather than the standard treatment of concurrent chemoradiation (CRT) do not benefit from increased survival rates and are less likely to receive a full course of radiation, according to research presented at the 2016 Multidisciplinary Head and Neck Cancer Symposium. The study, which examined more than 8,000 patient records in the National Cancer Data Base, represents the largest comparative analysis of IC and CRT in head and neck cancer to date.

The role of IC remains controversial in locally advanced head and neck squamous cell carcinoma (HNSCC). "Most randomized trials designed to address whether induction chemotherapy improves outcomes by enhancing local control and minimizing distant metastases have failed to demonstrate an increased overall survival benefit," explained study co-author Daniel W. Bowles,

MD, an assistant professor in the department of medical oncology at the University of Colorado School of Medicine and director of cancer research and staff physician at the Denver VA Medical Center. "Those findings, however, typically were based on study designs that enrolled too few patients or too few patients with advanced cancers, thereby diluting the possible benefit of IC."

Dr. Bowles and colleagues extended the question of whether IC improves survival in HNSCC to the 8,003 records in the National Cancer Data Base (NCDB) of patients diagnosed with T(any) N2b-3 M0 oropharyngeal, laryngeal and hypopharyngeal cancers between 2003 and 2011. The NCDB is a jointly-sponsored project of the American College of Surgeons and the American Cancer Society based on patient records from more than 1,500 Commission on Cancer-accredited facilities.

Cases were classified into two cohorts based on the type of treatment delivered. Patients in the induction chemotherapy (IC) group (n = 1,917) began chemotherapy 43 to 98 days before starting radiation therapy (RT); this time frame allowed for two to three cycles of IC, which is the common protocol in recent clinical trials. Patients in the concurrent chemoradiation (CRT) group (n = 6,086) began chemotherapy within seven days of RT start and did not receive IC. Of the two groups, the IC cohort tended to be younger and presented with more advanced disease, as well as more hypopharyngeal cancer.

Patients in the IC group were less likely to receive a full course of RT following administration of induction therapy. Twenty-one percent of the IC patients received less-than-definitive doses of RT (i.e., < 66 Gy), compared to 15 percent of the CRT patients ($p < 0.01$). Multivariate analyses adjusting for age, sex, race, income, location, year, comorbidities, primary disease site, T-status and N-status confirmed the increased odds among the induction cohort of receiving non-guideline-concordant RT doses (Odds Ratio (OR), 1.42; $p < 0.01$).

Comparative analysis using Cox regression also indicated shorter median survival following IC compared to CRT, with a median overall survival (OS) of 52 months for IC patients compared to 65 months for CRT patients ($p < 0.01$), though this difference did not persist on multivariate (Hazard Ratio (HR) for mortality, 1.04; $p = 0.28$) or propensity score matched analysis ($p = 0.18$).

Subgroup analyses further divided the treatment cohorts by disease stage to assess possible benefits of IC for advanced cases of HNSCC. Induction chemotherapy did not improve OS even for patients with the most advanced disease, including T4 or N3 status (HR, 0.99; $p = 0.81$), N3 status (HR, 0.98; $p = 0.84$), and T4N3 status (HR, 0.91; $p = 0.53$).

"While we suspected that induction chemotherapy would not have an impact on our entire study population, we thought it might prolong survival for the most advanced cancers," said Dr. Bowles. "Our finding from this large database that IC is not associated with improved overall survival over CRT, even for these patients, will continue to dampen enthusiasm for routine use of induction therapy. In cancer care, sometimes more is less. If adding induction chemotherapy fails to improve survival over the current standard of care, then we should reconsider its use."

The abstract, "Induction Chemotherapy Predicts Cumulative Radiation Dose and Fails to Improve Survival in Advanced Head and Neck Cancer, a National Cancer Database Analysis," will be presented in detail as a poster presentation at the 2016 Multidisciplinary Head and Neck Cancer Symposium in Scottsdale, Arizona. To speak with Dr. Bowles, contact the ASTRO media relations team at 480-905-7935 (February 18-19 only), 703-286-1600 or press@astro.org.

The 2016 Multidisciplinary Head and Neck Cancer Symposium is sponsored by the American Society for Radiation Oncology (ASTRO), the American Society of Clinical Oncology (ASCO) and the American Head & Neck Society (AHNS). The two-and-a-half day meeting includes interactive educational sessions focused on topics such as novel multidisciplinary therapies, directed therapy, treatment guidelines, prevention, surveillance and supportive care, as well as 13 oral abstract presentations of the current science of relevance to the head and neck cancer community. A total of 262 abstracts will be presented, including 249 posters. Keynote speakers include Tanguy Seiwert, MD, of the University of Chicago, to present "Immunotherapy for Head and Neck Cancer;" Robert I. Haddad, MD, of Brigham and Women's Hospital, to present "Personalized Treatment for Head and Neck Cancer -- The Time is Now;" Quynh-Thu Le, MD, FASTRO, of the Stanford School of Medicine, to present "Precision Therapy in Head and Neck Cancer -- From Technology to Biomarker-based Risk

Stratification;" and Neil Hayes, MD, MPH, of the UNC School of Medicine, to present "Genome Atlas and Sequencing Data: How We Use This Going Forward."

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 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 (http://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 the world's leading professional organization representing physicians who care for people with cancer. With nearly 40,000 members, ASCO is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation, which funds ground-breaking research and programs that make a tangible difference in the lives of people with cancer. For ASCO information and resources, visit www.asco.org. Patient-oriented cancer information is available at www.cancer.net.

ABOUT AHNS

The American Head & Neck Society (AHNS) is the single largest organization in North America for the advancement of research and education in head and neck oncology. The mission of the American Head and Neck Society is: to promote and advance the knowledge of prevention, diagnosis, treatment, and rehabilitation of neoplasms and other diseases of the head and neck; to promote and advance research in diseases of the head and neck, and; to promote and advance the highest professional and ethical standards. For more information, visit www.ahns.info.

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2016 Multidisciplinary Head and Neck Cancer Symposium
News Briefing, Friday, February 19, 2016, 7:00 a.m., MT

Poster Session: Thursday, February 18, 2016, 5:30 – 6:30 p.m., MT, Arizona Ballroom H-N, JW Marriott Camelback Resort and Spa

109 Induction Chemotherapy Predicts Cumulative Radiation Dose and Fails to Improve Survival in Advanced Head and Neck Cancer, a National Cancer Database Analysis

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Purpose/Objective(s): The role of induction chemotherapy (IC) in advanced head and neck squamous cell carcinoma (HNSCC) remains controversial. In recent randomized trials, the addition of IC to concurrent chemoradiation (CRT) failed to improve overall survival (OS). This failure may stem from the studies' lack of power due to slow accrual and/or from their inclusion of patients with less-advanced nodal disease, prompting the present analysis of the National Cancer Database (NCDB).

Materials/Methods: NCDB was queried for subjects diagnosed from 2003-2011 with T(any) N2b-3 M0 cancers of the oropharynx, hypopharynx, and larynx, who underwent external-beam radiation without surgery. We defined 2 analytic cohorts based on the sequencing of chemotherapy (CT) and radiotherapy (RT): an IC cohort with start of CT preceding RT by 43-98 days (thus allowing 2-3 cycles of IC as used in recent trials), and a CRT alone cohort with CT starting within 7 days of RT start. Logistic regression was used to identify factors associated with non-guideline-concordant RT dose (i.e. <66Gy), and Cox regression was used to assess the association of CT sequence on OS.

Results: 6086 CRT and 1917 IC subjects were evaluable. As compared to the CRT group, the IC cohort tended to be younger and to have more advanced T- and N-status and more hypopharynx cancer, were more likely to receive <66Gy of RT (20.9% vs 14.9%; p<0.01), and displayed worse OS (median 52.1 vs 64.9 months, p<0.01). After adjusting for age, year, sex, race, location, income, comorbidities, primary site, and T- and N-status with multivariate analysis, the IC cohort had increased odds of receiving <66Gy (OR 1.42; 95%CI 1.24-1.63; p<0.01), but their OS did not significantly differ from that of the CRT cohort (HR for mortality 1.07; 95%CI 0.99-1.16; p=0.08). On subgroup analysis, IC status was not associated with improved OS among the 2809 subjects with T4 or N3 disease (HR 1.02; 95%CI 0.92-1.13; p=0.72), the 1107 patients with N3 disease (HR 1.02 (0.86-1.22; p=0.82), or the 351 subjects with T4N3 disease (HR 0.97; 95%CI 0.73-1.28; p=0.81). Among the 5194 patients without T4 or N3 disease, IC status predicted a slight increase in mortality (HR 1.12; 95%CI 1.00-1.25; p=0.046).

Conclusion: In this large group of HNSCC patients with advanced nodal disease from the NCDB, IC subjects were more likely to receive less-than-definitive doses of radiotherapy, and OS was not significantly different from that of CRT subjects, even on subgroup analyses of increasingly advanced disease. Failure of prior studies to demonstrate an OS benefit with IC may have less to do with statistical power or patient selection and more to do with difficulty completing guideline-concordant care following IC.

Author Disclosures: W. Stokes: Employee; University of Colorado Denver GME. A. Amini: None. J. McDermott: None. A. Jimeno: None. D. Raben: None. D.W. Bowles: None. S. Karam: None.