



**EMBARGOED FOR RELEASE UNTIL  
Friday, January 19, 2007, 7:30 AM (EST)**

**CONTACT: Heather Goethe  
703-299-1016  
Onsite:  
407-238-4050**

**-- PRESS BRIEFING FRIDAY, JANUARY 19, 7:30 AM (EST) --**

**ADVANCES IN THE TREATMENT OF ESOPHAGEAL AND STOMACH CANCERS**

**-- Single Chemotherapy Agent after Surgery Extends Survival in Stomach Cancer;  
Important Findings on Adjuvant Radiation for Stomach Cancer  
Are Being Put into Practice, But Rates Still Need to Increase --**

*Orlando, FL*—New research on the treatment of esophageal and stomach cancers was discussed today at a press briefing at the 2007 Gastrointestinal Cancers Symposium, co-sponsored by the American Gastroenterological Association (AGA), the American Society of Clinical Oncology (ASCO), the American Society for Therapeutic Radiology and Oncology (ASTRO), and the Society of Surgical Oncology (SSO). The fourth annual symposium is being held at the Orlando World Center Marriott in Orlando, Florida, from Friday, January 19 to Sunday, January 21.

“Preoperative therapy and therapy after surgery are becoming increasingly important elements of the arsenal for treating cancers of the esophagus and stomach,” said A. William Blackstock, MD, Associate Professor of Radiation Oncology and Attending Physician at North Carolina Baptist Hospital in Winston-Salem and moderator of the briefing. “A significant area of investigation in esophageal and stomach cancer is to determine the best ways to administer these treatments and to discover who will benefit from them most.”

Nearly 37,000 people in the United States were diagnosed with esophageal and stomach cancers in 2006, and more than 25,000 died from these diseases.

Studies include:

- A phase III Japanese trial showing that administration of a single drug—an experimental chemotherapy agent called S-1—following surgery in patients with stomach cancer improves overall survival when compared with surgery alone.
- A study showing that the proportion of patients with stomach cancer who receive radiation therapy following surgery more than doubled between 2000 and 2003—after a trial in 2000 showed that patients who received such therapy survived longer than those treated with surgery alone—but that rates still need to increase.

**EMBARGOED until Friday, January 19, 2007, 7:30 AM (EST)**

**January 19, 1:00 – 2:15 PM  
Palms Ballroom**

**Lead Author: Mitsuri Sasako, MD  
National Cancer Center Hospital  
Tokyo, Japan**

**New Single Chemotherapy Agent Following Surgery for Stomach Cancer  
Improves Survival Compared with Surgery Alone**

*Note: This summary contains updated data not in the abstract.*

A phase III Japanese trial has found that administration of an experimental chemotherapy agent called S-1 following surgery in patients with stomach cancer improves overall survival when compared with surgery alone.

“This is the first phase III study to compare S-1 chemotherapy following surgery to surgery alone,” said Mitsuro Sasako, MD, Professor of Surgery and Deputy Director of the National Cancer Center Hospital in Tokyo, Japan and the study’s lead author. “The findings are significant because they showed improved survival with a single chemotherapy agent—one that is cheaper and has lower toxicity than adjuvant chemotherapy regimens commonly used in North America and Europe.”

Standard treatment for gastric cancer, or cancer of the stomach, is surgery to remove the tumor, part or all of the stomach, and the affected lymph nodes, sometimes followed by chemotherapy, radiation, or a combination of the two. Although chemotherapy following surgery has shown benefit in some patients, it is unclear which chemotherapy drugs are the most effective.

In the current study, 1,059 patients were randomized to receive S-1 chemotherapy following surgery (529 patients) or surgery alone (530 patients), the current standard treatment in Japan. All patients had stage II or III disease, meaning that the tumors had spread locally, but had not spread to other parts of the body. At three years, the overall survival for patients who received S-1 was 80.5%, compared with 70.1% of patients who received surgery alone. Side effects were rare and included anorexia (6.0% in the S-1 group had severe symptoms, versus 2.1% in the surgery group) and some blood-related toxicities.

S-1 belongs to a class of drugs called oral fluoropyrimidines. It is also being evaluated in clinical trials as a treatment for other gastrointestinal cancers including colorectal and pancreatic tumors.

**Abstract #8**

**Randomized phase III trial comparing S-1 monotherapy versus surgery alone for stage II/III gastric cancer patients (pts) after curative D2 gastrectomy (ACTS-GC study)**

M. Sasako, T. Yamaguchi, T. Kinoshita, M. Fujii, A. Nashimoto, H. Furukawa, T. Nakajima, Y. Ohashi, S. Sakuramoto, H. Imamura

**Introduction:** Although a RCT (INT-0116) proved the efficacy of postoperative chemoradiotherapy after limited surgery (D0/1) for curable gastric cancer, the role of radiotherapy is uncertain after D2 dissection. S-1 showed high activity as a single agent for gastric cancer in phase II trials for metastatic disease. Effect of adjuvant chemotherapy with S-1 was tested for pts after curative D2 dissection.

**Methods:** Eligibility included R0 resection, pathological stage II/III (Japanese Classification), 80 $\geq$ age $\geq$  20, no prior adjuvant treatment, adequate organ function. Pts were randomized to S-1 (80-120mg/day according to the body surface, 4 weeks administration with 2 weeks off in each course, starting within 45 days of surgery till 1 year after surgery,) or surgery alone (C). Primary end point was overall survival (OS). Assuming 500 pts in each, the study had 80% power to detect 0.70 HR for S-1 to C in OS at 0.05 two-sided  $\alpha$ . Two interim analyses were planned at 1 & 3 years after completing enrollment.

**Results:** Between 10/2001 & 12/2004, 1059 pts were randomized (529 to S-1 & 530 to C). 25 pts were ineligible. There was no background difference between the groups. 474, 409, 175 pts were stage II, IIIA, IIIB respectively. Because the first interim analysis in 06/2006 using the survival data of 12/2005 showed that HR of death for S-1 to C was 0.57 (95%CI, 0.40-0.81, p=0.0016), the data & safety monitoring committee recommended the investigators to stop the trial. As of 09/2006, when the final analysis was conducted using the data of 06/2006, OS at 3-years for all randomized pts was 80.5% (95% CI, 76.6%-84.4%) for S-1 & 70.1% (65.5%-74.6%) for C. HR of death for S-1 was 0.68 (0.52-0.87, p=0.0024). Among all eligible pts, HR was 0.66 (0.51-0.85, p=0.0015). The proportion of pts who could complete the S-1 therapy was 65.8% (340/517). Grade 3/4 toxicity was rare (max 6.0% in anorexia) including hematological toxicity.

**Conclusions:** Adjuvant chemotherapy with S-1 for gastric cancer is feasible and effective. This regimen can be the standard treatment for stage II/III gastric cancer pts after curative D2 dissection.

**EMBARGOED until Friday, January 19, 2007, 7:30 AM (EST)**

**January 19, 11:30 AM – 1:00 PM**  
**Crystal Ballroom G, H, J**

**Lead Author: Ulrich Guller, MD, MHS**  
**University of Toronto**  
**Toronto, Canada**

**Study Shows New Stomach Cancer Findings Are Being Put into Practice—  
Rates of Radiation Therapy after Surgery Are Increasing, but Should Be Higher**

*Note: This summary contains updated data not in the abstract.*

A new study shows that the proportion of patients with stomach cancer who receive radiation therapy after surgery more than doubled after results from the Intergroup 0116 trial were presented at the 2000 American Society of Clinical Oncology (ASCO) Annual Meeting. The Intergroup trial showed that patients receiving radiation treatment following surgery (“adjuvant” therapy) had significantly better overall survival (36 months versus 27 months) and disease-free survival (30 months versus 19 months) compared with those treated with surgery alone. The findings were important for patients, since five-year survival rate across all stages of stomach cancer is low, at approximately 23%.

The current study examined records from 9,528 patients who underwent surgery for stomach cancer between 1996 and 2003, divided into two groups: those treated before and after the presentation of the Intergroup study results at the 2000 ASCO Annual Meeting. Patients were identified using the Surveillance Epidemiology and End Results (SEER) cancer registry, a National Cancer Institute-sponsored population-based database that provides detailed information on cancer statistics.

The study found that prior to the presentation of the 0116 results, only 15% of gastric cancer patients received adjuvant radiation therapy, compared with 30.4% of patients in the three years following presentation of the study. Researchers reviewed several demographic categories (such as age, gender, race, and marital status), finding increases of at least 10% in the rate of adjuvant therapy in each of these groups in the three years following the presentation of the 0116 data. However, younger patients, married patients, patients with higher tumor stage and higher grade, and patients from whom more lymph nodes were assessed were significantly more likely to receive radiation therapy after surgery. Moreover, there were important variations in the use of adjuvant radiation therapy between different regions of the United States.

“The increasing use of radiation treatment following surgery for gastric cancer is highly significant. However, the percentage of patients getting such treatment is still low, and further efforts are needed to ensure that the results of the Intergroup 0116 trial are put into practice for the appropriate patients,” said Ulrich Guller, MD, MHS, a Surgical Oncology Fellow at the University of Toronto and the study’s lead author.

**Abstract #34**

**Trends in adjuvant treatment of gastric cancer: An analysis of 9,528 patients**

U. Guller, N. N. Baxter, C. H. Law, C. J. Swallow, N. Coburn

**Introduction:** The Intergroup 0116 trial (0116) showed that adjuvant chemoradiotherapy (ADJTX) improves survival in patients with gastric adenocarcinoma. Our objective of this study is to evaluate the impact of 0116 on the use of ADJTX and the variables that influence this decision.

**Methods:** From 1996-2003, patients aged 18-85 yrs who underwent curative resection of gastric adenocarcinoma were identified in the Surveillance Epidemiology and End Results (SEER) database. Patients were classified into two subsets: those resected prior to presentation of 0116 results at ASCO (Jan 1996 - April 2000 = PRE) vs after (May 2000 - Dec 2003 = POST). Univariate and multivariable models were used to determine factors associated with use of ADJTX in patients diagnosed from May 2000 - December 2003. **Results:** Overall, 9,528 patients were included, with a median age of 70 yrs. The percentage of patients given ADJTX in the PRE group was 15%, rising to 24% POST ( $p < 0.001$ ), with the most significant increase in the months surrounding the ASCO meeting. Significant increases in ADJTX usage from PRE to POST were seen in all demographic categories studied. In the POST group, patients aged 18-59 yrs were significantly more likely to receive ADJTX (46%) vs those 60-74 yrs (32%) and 75 yrs and older (13%,  $p < 0.0001$ ). Higher tumor stage was associated with greater use of ADJTX ( $p < 0.0001$ ). Patients having total gastrectomy were more likely to receive ADJTX (32.5%) than those having proximal (27%) or distal gastrectomy (29%,  $p = 0.048$ ). Married patients were significantly more likely to receive ADJTX (31.8%) than unmarried patients (24.9%,  $p < 0.001$ ). The rate of ADJTX ranged from 24% to 45% ( $p < 0.001$ ) in the SEER regions. In multivariable analysis, age, SEER region, type of surgery, marital status, and tumor stage were all found to be significant predictors of receiving ADJTX. **Conclusions:** Use of ADJTX for gastric cancer significantly increased following 0116. However, the fraction of patients receiving ADJTX is still low, with significant variability according to patient demographics, resection type, and SEER region. The causes of this variability must be explored and continued educational efforts are required.