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-- PRESS BRIEFING SATURDAY, MAY 30, 9:00 AM EDT --

STUDIES ANSWER KEY QUESTIONS ABOUT TREATMENT
OF GASTROINTESTINAL CANCERS

Orlando, FL.—The findings from several large clinical trials of new treatment regimens for gastrointestinal cancers were released today at a press briefing at the 45th Annual Meeting of the American Society of Clinical Oncology (ASCO).

“The studies presented today answer many important questions about the best care for people with gastrointestinal cancers,” said Nicholas Petrelli, MD, medical director of the Helen F. Graham Cancer Center in Wilmington, Delaware, and moderator of the press briefing. “These large, conclusive trials tell us what works, and importantly, tell us what doesn’t work. Some settle long-time debates in the field, others demonstrate that the current standard of care is actually superior to experimental treatments, and others will allow patients to avoid unnecessary side effects or surgery.”

Studies highlighted in the press briefing include:

- *First-ever data on bevacizumab as adjuvant therapy finds no benefit in colon cancer:* A phase III trial finds that adding the targeted therapy bevacizumab (Avastin) to standard adjuvant chemotherapy did not improve disease-free survival for patients with locally advanced colon cancer.
- *Surgery unnecessary for majority of patients with advanced colorectal cancer:* Most patients with metastatic colorectal cancer can safely avoid surgery on their primary tumors.
- *Trial compares common adjuvant treatments for pancreatic cancer:* A phase III trial comparing the adjuvant treatments most commonly used for pancreatic cancer in the United States and Europe (gemcitabine and 5-FU/FA, respectively) found that there is no difference in survival between the two regimens, though gemcitabine was associated with fewer side effects.
- *The largest study to date on anal cancer supports the current standard:* A phase III study finds that the current standard of care for anal cancer should not be changed, and that ongoing maintenance therapy after initial treatment is not effective.
- *Oxaliplatin does not improve outcomes for rectal cancer:* Adding oxaliplatin (Eloxatin) to standard treatment in patients with locally advanced rectal cancer does not improve tumor response. A preliminary analysis suggests the treatment may reduce distant metastases, however.

For consumer-oriented information on these studies and more than 120 cancer types, please refer your readers to ASCO’s patient website, www.Cancer.Net.

**PLENARY PRESENTATION
SUNDAY, MAY 31, 3:15 PM EDT
LEVEL 2, WEST HALL D2
PLENARY SESSION**

**Lead Author: Norman Wolmark, MD
Allegheny General Hospital
Pittsburgh, Pa.**

Adding Bevacizumab to Standard Adjuvant Chemotherapy Does Not Improve Disease-Free Survival for Early-Stage Colon Cancer

The results of a randomized, phase III trial have found that adding bevacizumab (Avastin) to standard adjuvant chemotherapy did not improve disease-free survival (the time that patients are free of tumor recurrence) in early-stage colon cancer.

This was the first study to report results on the use of bevacizumab as an adjuvant treatment. The antibody, which targets the vascular endothelial growth factor (VEGF) receptor, is currently approved for metastatic colorectal, breast, and lung cancers, and other trials are ongoing to evaluate it as an adjuvant treatment for a variety of solid tumors.

The current study enrolled 2,710 patients who were randomized to receive six months of standard adjuvant chemotherapy or six months of adjuvant chemotherapy combined with bevacizumab plus an additional six months of bevacizumab after the chemotherapy had ended. All patients in the study had stage II or stage III disease and first had surgery to remove their tumors. After a median follow-up of three years, the investigators found that 77.4 percent of patients in the experimental group (bevacizumab) were alive and free of disease, compared with 75.5 percent of patients in the control group, a difference that was not statistically significant. There were no unexpected side effects in either arm and the toxicities from bevacizumab were well tolerated.

“One interesting effect was that during the year that patients were receiving bevacizumab we saw a benefit in disease-free survival that subsequently diminished when follow-up was completed,” said Norman Wolmark, MD, chairman of the Department of Human Oncology at Allegheny General Hospital and the study’s lead author. “Our overall conclusion is that bevacizumab was not effective as an adjuvant treatment for early-stage colon cancer, but the transient benefit we saw in patients who received bevacizumab illustrates that we have more to learn about how this reagent works, and we need to design more clinical trials to determine how it can be used most effectively.”

The trial was conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP) group, chaired by Dr. Wolmark, and was funded by the National Cancer Institute.

LBA4

A phase III trial comparing mFolfox6 to mFolfox6 + bevacizumab in stage II or III carcinoma of the colon: Results of NSABP Protocol C-08

N. Wolmark, G. Yothers, M. J. O’Connell, S. Sharif, J. N. Atkins, T. E. Seay, L. Feherenbacher, S. O’Reilly, and C. J. Allegra

Background: The primary aim of this two-arm randomized prospective study was to determine whether mFolfox6 + bevacizumab (mFF6+B) would prolong disease-free survival (DFS) compared to mFolfox6 (mFF6) alone. **Methods:** Between Sept 2004 and Oct 2006, 2,672 patients with follow-up (1338 and 1334 in respective arms) with stage II (24.9%) or III carcinoma of the colon were randomized to receive either mFF6 (oxaliplatin 85 mg/m² IV d1, leucovorin 400 mg/m² IV d1, 5-FU 400 mg/m² IV bolus d1 and 5-FU 2400 mg/ m² CI over 46 hrs (d1+2) q14d x 12 cycles) or mFF6+B (same mFF6 regimen + bevacizumab 5 mg/kg IV q 2 wks x 1 yr). The primary end point was DFS. Events were defined as first recurrence, second primary cancer, or death. **Results:** The median follow-up for patients still alive was 36 months. The hazard ratio (HR: FF6+B vs. mFF6) was 0.89; 95% CI (0.76-1.04); p=0.15. Data censored at intervals disclosed an initial benefit for bevacizumab that diminished over time:

| | N | Ev | 3yDFS | P | Yr | 1 | 1.5 | 2 | 2.5 | 3 |
|--------|------|-----|-------|------|-----------|--------|-------|------|------|------|
| mFF6 | 1338 | 312 | 75.5 | | HR | 0.60 | 0.74 | 0.81 | 0.85 | 0.87 |
| mFF6+B | 1334 | 291 | 77.4 | 0.15 | P | 0.0004 | 0.004 | 0.02 | 0.05 | 0.08 |

The smoothed estimate of the DFS HR over time indicated that bevacizumab significantly reduced the risk of a DFS event during the interval from 0.5 to 1.0 year. There was no evidence that patients receiving bevacizumab had a worse DFS compared to those receiving mFF6 alone following treatment.

Conclusions: The addition of bevacizumab to mFF6 did not result in an overall statistically significant prolongation in DFS. There was a transient benefit in DFS during the one year interval that bevacizumab was utilized. Consideration may be given to clinical trials assessing longer duration of bevacizumab administration.

Disclosures: Norman Wolmark,,Consultant or Advisory Role,GenentechSeamus O’Reilly,,Honoraria,LillySeamus O’Reilly,,Honoraria,Sanofi AventisSeamus O’Reilly,,Honoraria,AmgenSeamus O’Reilly,,Research Funding,Amgen

POSTER DISCUSSION
MONDAY, JUNE 1, 11:00 AM EDT
LEVEL 2, WEST HALL E1
GASTROINTESTINAL (COLORECTAL)
CANCER

Senior Author: Philip B. Paty, MD
Memorial Sloan-Kettering Cancer Center
New York, NY

Most Patients with Metastatic Colorectal Cancer Do Not Need Surgery to Remove their Primary Tumor

New research shows that patients who are newly diagnosed with metastatic, surgically incurable colorectal cancer do not need immediate surgery to remove their primary tumor unless the tumor is causing complications.

Surgical removal of the primary tumor at the time of diagnosis was once standard practice and is still common in patients with metastatic colorectal cancer. Because cancer has already spread to other parts of the body by this stage, the purpose of this surgery is not to extend survival, but to prevent future complications, such as intestinal blockage, perforation of the bowel, and severe bleeding. However, over the past decade several new effective chemotherapy drugs for colorectal cancer have been introduced and until now there has been little data to assess whether this pre-emptive surgery is still warranted.

“In this era of modern chemotherapy, routine surgery to remove the primary tumor in patients with unresectable metastases is no longer supported by the data,” said Philip Paty, MD, an attending surgeon and vice chairman of clinical research at Memorial Sloan-Kettering Cancer Center (MSKCC) and the study’s senior author. “In addition to being an unnecessary procedure that carries its own risks of morbidity and mortality, surgery delays the start of chemotherapy for several weeks, and in some cases may make the patient less fit for and less tolerant of chemotherapy. Unless there is an immediate need for surgery, patients should begin chemotherapy first.”

This retrospective study identified 233 consecutive patients who presented with metastatic colorectal cancer between 2000 and 2006, and were treated with chemotherapy at MSKCC, but had no serious symptoms to prompt immediate surgery. The patients received one of three triple-drug chemotherapy combinations as their initial treatment (the regimens known as FOLFOX, IFL, and FOLFIRI). Some were also treated with the targeted therapy bevacizumab (Avastin).

Investigators determined that 93 percent of patients never developed complications that required removal of their tumor. For the 7 percent who did eventually need surgery, the vast majority (14/16) had successful operations. In addition, the mortality attributable to surgery was very low (0.8 percent), suggesting that this approach, by avoiding unnecessary surgery, improves the overall safety of treatment.

CRA4030

Outcome of primary tumor in patients with synchronous stage IV colorectal cancer receiving combination chemotherapy without surgery as initial treatment

G. A. Poultsides, E. L. Servais, L. B. Saltz, S. Patil, N. E. Kemeny, J. G. Guillem, M. Weiser, L. K. Temple, W. Wong, P. B. Paty

Background: In the absence of symptoms (bleeding, perforation, obstruction) or resectable metastatic disease, primary tumor resection in patients who present with synchronous metastatic colorectal cancer (CRC) is of uncertain benefit. The purpose of this study was to describe the frequency of intervention necessary to palliate the intact primary tumor in patients who present with synchronous stage IV CRC and receive up-front modern combination chemotherapy without prophylactic surgery. **Methods:** Using a prospective institutional database, we identified 233 consecutive patients from 2000 through 2006 with synchronous metastatic CRC and an unresected primary tumor who received oxaliplatin- or irinotecan-based, triple-drug chemotherapy (FOLFOX, IFL, or FOLFIRI) with or without bevacizumab as their initial treatment. The incidence of subsequent use of surgery, radiotherapy, and/or endoluminal stenting to manage primary tumor complications was recorded. **Results:** Of 233 patients, 217 (93%) never required surgical palliation of their primary tumor. Sixteen patients (7%) required emergent surgery for primary tumor obstruction or perforation, 10 patients (4%) required nonoperative intervention (stent or radiotherapy), whereas 213 (89%) never required any direct symptomatic management for their intact primary. Of those, 47 (20%) ultimately underwent elective colon resection at the time of metastasectomy and 8 (3%) during laparotomy for hepatic artery infusion pump placement. Neither use of bevacizumab, location of the primary tumor in the rectum, or metastatic disease burden were associated with increased intervention rate. In addition, when included as a time-varying covariate in a Cox regression model, the need for emergent intervention did not correlate with overall survival. **Conclusions:** Most patients with synchronous stage IV CRC who receive up-front modern combination chemotherapy never require palliative surgery for their intact primary. These data support the use of chemotherapy, without routine prophylactic resection, as the appropriate standard practice for patients with neither obstructed nor hemorrhaging primary colorectal tumors in the setting of metastatic disease.

Disclosures: Leonard Saltz,,Consultant or Advisory Role,PfizerLeonard Saltz,,Consultant or Advisory Role,GenentechLeonard Saltz,,Consultant or Advisory Role,Bristol MyersLeonard Saltz,,Consultant or Advisory Role,ImcloneLeonard Saltz,,Consultant or Advisory Role,AmgenLeonard Saltz,,Research Funding,ImcloneLeonard Saltz,,Consultant or Advisory Role,RocheLeonard Saltz,,Research Funding,GenentechLeonard Saltz,,Research Funding,PfizerLeonard Saltz,,Research Funding,RocheLeonard Saltz,,Research Funding,Bristol MyersLeonard Saltz,,Research Funding,AmgenNancy Kemeny,,Research Funding,Sanofi-AventisNancy Kemeny,,Honoraria,Sanofi-AventisNancy Kemeny,,Research Funding,Pfizer

ORAL PRESENTATION
MONDAY, JUNE 1, 5:00 PM EDT
LEVEL 2, WEST HALL D1
GASTROINTESTINAL
(NONCOLORECTAL) CANCER

Lead Author: John Neoptolemos, MD
University of Liverpool
Liverpool, UK

**No Difference in Survival between Gemcitabine and 5-FU/FA for
 Adjuvant Treatment of Pancreatic Cancer**

The results of an international, multicenter study reports no difference in survival between the adjuvant chemotherapy regimens gemcitabine (Gemzar) and 5-fluorouracil/folinic acid (5-FU/FA) when given after surgery for pancreatic cancer, though gemcitabine was associated with fewer side effects.

5-FU/FA is the current standard adjuvant treatment for pancreatic cancer in parts of Europe, whereas gemcitabine alone or in combination with radiation therapy is more commonly used in the United States. It has not been clear until now whether one was superior. Gemcitabine is also considered the standard treatment in patients with metastatic and locally advanced, inoperable pancreatic cancer. This is the first study to directly compare the two treatments in the adjuvant setting.

In this phase III trial, 1,088 patients were randomized to receive one of the two treatments after surgery. All patients had histologically confirmed disease, 72 percent with metastases to lymph nodes and 35 percent with microscopically involved resected tumor margins. After a median follow up of 34 months, the investigators found that the median overall survival of patients treated with 5-FU/FA was 23 months, compared with 23.6 months in patients treated with gemcitabine. However, patients who received 5-FU/FA reported more toxicities, compared to those treated with gemcitabine, including: grade 3/4 toxicity stomatitis, or inflammation in the mouth (10 percent in the 5-FU/FA group; none in the gemcitabine group); diarrhea (13 percent and 2 percent of patients, respectively); and treatment-related hospitalizations (10 percent and 3.5 percent, respectively).

“This study is important because it shows no difference between these treatments in prolonging survival,” said John P. Neoptolemos, MD, Head of the Division of Surgery and Oncology at the University of Liverpool and the lead author of the study, known as ESPAC-3. “On the basis of the safety profile, however, this trial shows that gemcitabine is likely to be the preferred adjuvant therapy. We are now also looking at combining the two treatments to see if we get a better response, because the drugs have different mechanisms of action.”

LBA4505

ESPAC-3(v2) - A multicentre, international, open label, randomised controlled phase III trial of adjuvant 5-fluorouracil/folinic acid (5-FU/FA) versus gemcitabine (GEM) in patients with resected pancreatic ductal adenocarcinoma

J. Neoptolemos, M. Büchler, D. D. Stocken, P. Ghaneh, D. Smith, C. Bassi, M. Moore, D. Cunningham, C. Dervenis, D. Goldstein, The European Study Group for Pancreatic Cancer (ESPAC)

Background: Adjuvant 5-FU/FA (ESPAC-1 trial) and recently, adjuvant GEM (CONKO-001 trial) have demonstrated improved survival for patients with resected pancreatic cancer. The aim of the ESPAC-3 (v2) trial was to compare 5FU/FA vs GEM to identify if either adjuvant chemotherapy was associated with significantly better survival. **Methods:** Patients with either an R0 or R1 resection for pancreatic ductal adenocarcinoma were randomised (stratified for resection margin status and country) within 8 weeks of surgery to receive either 5FU/FA (FA, 20 mg/m², iv bolus injection followed by 5-FU, 425 mg/m², iv bolus injection given 1-5d every 28 days) or GEM (1000 mg/m² iv infusion 1d, 8d and 15d every 4 weeks) for 6 months. The primary outcome measure was overall survival; the secondary measures were toxicity, progression free survival and quality of life. 1030 patients were needed to detect a 10% difference in 2-year survival rates with 90% power. **Results:** 1088 patients from 16 countries were randomised between 11th July 2000 and 12th Jan 2007 (551 5FU/FA, 537 GEM). Median (range) age was 63 (31-85) years, 598 (55%) were men. Median tumour size was 30 (20-350) mm, 384 (35%) were R1 resections, 777 (72%) were node positive and 263 (25%) were poorly differentiated tumours. Final analysis will be carried out with a minimum of 2 years follow-up (data lock 12th Jan 2009). The current overall number of deaths is 698 (64%). Analysis of the primary outcome will be based on all cause mortality using log-rank analysis on an intention to treat basis. Cox proportional hazards modelling, or alternative, will be used to adjust any treatment effect by stratification factors at randomisation and other known prognostic factors. **Conclusions:** This is the largest adjuvant trial ever conducted for pancreatic ductal adenocarcinoma and the results will be reported in full at the meeting.

Disclosures: John Neoptolemos,,Consultant or Advisory Role,Pfizer,John Neoptolemos,,Research Funding,Pharmexa,John Neoptolemos,,Research Funding,Oxford Biomedica,John Neoptolemos,,Research Funding,Cytimmune

ORAL PRESENTATION
SATURDAY, MAY 30, 5:15 PM EDT
LEVEL 2, WEST HALL D2
GASTROINTESTINAL (COLORECTAL)
CANCER

Lead Author: Roger James, MD
Maidstone Hospital
Kent, UK

UK Study Confirms Standard of Care for Anal Cancer Should Not Be Changed

Findings from the largest trial ever conducted for anal cancer have shown that the current standard of care, using a novel, continuous radiation therapy delivery program combined with 5-fluorouracil (5-FU) and mitomycin-C chemotherapy, results in the best outcomes so far reported for patients with anal cancer, and that cisplatin chemotherapy is not superior to mitomycin-C. The study also showed no evidence of a benefit of adding maintenance chemotherapy to the standard of care.

Anal cancer is rare, with about 5,000 patients diagnosed in the United States each year. Unlike colorectal cancer, the majority of patients with anal cancer do not need surgery, largely because the tumors are the squamous cell type, which are very responsive to chemotherapy and radiation. Cisplatin is commonly used for other squamous cell cancers, but it is less convenient to deliver and is known to have different toxicities from mitomycin-C, such as neurological and renal side effects and hearing loss.

The current study, called ACT II, conducted by the National Cancer Research Institute in the United Kingdom, and funded by Cancer Research UK, randomized 940 patients to receive radiation therapy given at the same time as 5-FU with either mitomycin-C or cisplatin. Patients were also randomized to receive follow-up maintenance therapy with cisplatin and 5-FU after chemoradiation or no maintenance therapy.

After a median follow-up of three years, the investigators found no significant difference in outcome in the two randomized comparisons:

- The complete response rate at 6 months (the number of patients who had all signs of their cancer disappear) was 94 percent in the mitomycin-C group compared with 95 percent in the cisplatin group.
- Recurrence-free survival at 3 years (the number of patients whose tumors did not return) was 75 percent both in patients who got maintenance therapy and in those who did not.
- Overall survival at 3 years was 85 percent in patients who received maintenance therapy and 84 percent in those who did not.

“These findings are good news in spite of the lack of evidence for an improvement in giving either cisplatin or maintenance therapy, since the standard chemoradiation schedule given in this trial was highly effective,” said Roger James, MD, FRCP, FRCR, a radiation oncologist from Maidstone Hospital, Kent, and the study’s lead author. “Although this trial did not show an improvement from adding maintenance therapy, some form of additional treatment will be the subject of future studies, to determine whether some subset of patients might benefit from it.”

LBA4009

A randomised trial of chemoradiation using mitomycin or cisplatin, with or without maintenance cisplatin/5FU in squamous cell carcinoma of the anus (ACT II)

R. James, S. Wan, R. Glynn-Jones, D. Sebag-Montefiore, L. Kadalayil, J. Northover, D. Cunningham, H. Meadows, J. Ledermann, National Cancer Research Institute (NCRI) ACT II Trial Management Group

Background: Chemoradiotherapy (CRT) with 5-fluorouracil (5-FU) and mitomycin-C (MMC) is standard treatment for anal cancer. The ACT II trial addresses two research questions: whether (i) replacing MMC with cisplatin (CDDP) improves the complete response (CR) rate, and (ii) two cycles maintenance chemotherapy (with 5-FU and CDDP) after CRT reduces recurrence. **Methods:** Between 2001 and 2008, 940 patients (pts) were recruited to a multi-centre, randomised factorial trial. They received 5-FU (1000mg/m²/day on days 1-4 and 29-32), radiotherapy (50.4 Gy in 28 fractions), and were randomised to receive in addition either MMC (12 mg/m², day 1; n=471) or CDDP (60 mg/m² on days 1 & 29; n=469). Pts were also randomised to receive maintenance therapy (n=448) 4 weeks after CRT with two cycles of CDDP and 5-FU in weeks 11 and 14, or no maintenance (n=446). Maintenance randomisation was not considered appropriate in 46 pts. The trial was powered to detect a difference in the CR rate of 5% (CDDP vs MMC), and 30% reduction in recurrence (maintenance vs no maintenance); ≥80% power. Clinical response was assessed at 11 & 18 weeks, and by CT at 26 weeks. Median follow-up is currently 2.5 years. **Results:** The median age was 58 yrs; 62% male, 38% female; tumour site - canal (81%), margin (15%), not known (N/K) (4%); stage T1-T2 (50%), T3-T4 (43%), N/K (7%); node negative (62%), positive (30%), N/K (8%). The CR rate was 91% in both CDDP and MMC arms: difference -0.1% (95% CI -4.4, +4.1, p=0.96). CDDP pts had fewer acute grade 3/4 haematological toxicities (12 vs 25%, p<0.001). Follow up data will be mature enough for the maintenance comparison in March 2009 for a logrank analysis of the recurrence rate. Disease-free, colostomy-free and overall survival, and toxicity, will be reported for both comparisons. **Conclusions:** ACT II is the largest trial ever conducted in anal cancer. Very high response rates and

excellent tolerability can be achieved with this CRT schedule.

Disclosures: Rob Glynne-Jones,,Other Remuneration,RocheRob Glynne-Jones,,Honoraria,Merck-SeronoRob Glynne-Jones,,Research Funding,RocheRob Glynne-Jones,,Honoraria,PfizerRob Glynne-Jones,,Other Remuneration,AstraZenecaRob Glynne-Jones,,Other Remuneration,Merck SeronoRob Glynne-Jones,,Research Funding,Merck SeronoRob Glynne-Jones,,Research Funding,Sanofi AventisRob Glynne-Jones,,Honoraria,RocheRob Glynne-Jones,,Other Remuneration,PfizerRob Glynne-Jones,,Honoraria,Sanofi Aventis

ORAL PRESENTATION
SATURDAY, MAY 30, 5:00 PM EDT
LEVEL 2, WEST HALL D2
CANCER

Lead Author: Carlo Aschele, MD, PhD
E.O. Ospedali Galliera
Genoa, Italy

Adding Oxaliplatin to Preoperative Chemoradiotherapy for Locally Advanced Rectal Cancer Does Not Improve Local Tumor Response

[Note: This summary contains updated data not in the abstract]

A large, multicenter Italian study has found that adding oxaliplatin (Eloxatin) to standard preoperative radiochemotherapy in patients with locally advanced rectal cancer does not improve tumor shrinkage. However, preliminary and exploratory data suggest that it may reduce the number of distant metastases.

Chemotherapy and radiation are often administered before surgery for rectal cancer to shrink the tumor and make it easier to remove. Previous results from this study showed that although adding oxaliplatin to standard chemotherapy increased some side effects, especially diarrhea, it did not affect the ability to deliver the full course of radiation therapy or to perform surgery. Oxaliplatin has been found effective and is commonly used in patients with more advanced colon and rectal cancer.

In this phase III trial, 747 patients with locally advanced rectal cancer were randomized to receive standard preoperative chemoradiotherapy or the standard plus oxaliplatin. Researchers found no significant difference between the two groups in terms of tumor reduction: 16 percent of patients in both groups had no tumor present at the time of surgery, and 29 percent in the oxaliplatin group had mildly invasive tumors (T1 or T2) without nodal involvement, compared with 30 percent in the control group. There was also no significant difference in the number of patients who had cancer in the lymph nodes (27 percent in the oxaliplatin group versus 25 percent in the control group). Consistently, the proportions of patients who could have conservative surgery were similar between the two arms.

In an unplanned analysis, when looking at intra-abdominal disease spread at the time of surgical removal of the primary tumor, only 0.5 percent of patients in the oxaliplatin group (2 patients) had distant metastases, versus 3 percent in the control group (11 patients), a difference that was statistically significant.

“Although adding oxaliplatin to the current standard of care did not improve tumor response rates, we found this course of treatment was associated with a reduced number of early distant metastases in the abdomen in a very small number of patients,” said Carlo Aschele, MD, PhD, attending physician and lead clinician in Colorectal/Gastrointestinal Cancer in the Department of Medical Oncology and Cancer Prevention at E.O. Ospedali Galliera in Genoa, Italy, and the study’s first author. “Although the numbers are very small and the analysis of distant metastases was unplanned and exploratory, the difference is significant and indicates that the lack of an effect on local tumor shrinkage does not necessarily imply a lack of effect on micrometastases at distant sites. Longer follow-up is necessary to assess whether treatment with oxaliplatin will have an effect on recurrence rates or survival.”

CRA4008

Preoperative fluorouracil (FU)-based chemoradiation with and without weekly oxaliplatin in locally advanced rectal cancer: Pathologic response analysis of the Studio Terapia Adjuvante Retto (STAR)-01 randomized phase III trial

C. Aschele, C. Pinto, S. Cordio, G. Rosati, A. Tagliagambe, S. Artale, P. Rosetti, S. Lonardi, L. Boni, L. Cionini, on behalf of STAR Network Investigators

Background: Oxaliplatin (OXA) enhances the efficacy of FU-based chemotherapy in colon cancer. This randomized phase III trial investigated the effect of adding OXA to preoperative (preop) FU-based pelvic chemoradiation (CRT) in patients (pts) with locally-advanced rectal cancer. **Methods:** Eligibility required a resectable, biopsy-proven rectal adenocarcinoma within 12 cm from the anal verge with radiological evidence of perirectal fat or lymph node involvement. Randomization was between infused FU (225 mg/msq/day) concomitant to external-beam pelvic radiation (50.4 Gy in 28 daily fractions) (arm A) or the same regimen + weekly OXA (60 mg/msq x 6) (Arm B). Surgery was scheduled 6-8 weeks after completing CRT. Overall survival was the primary endpoint. A protocol-planned analysis of local tumor response to preop treatment (secondary end-point) is the object of this report. **Results:** 747 pts from 41 Italian centers were randomized between 12/2003 and 8/2008 (arm A/B: 379/368). Pretreatment characteristics in arm A/B: median age 63/62 years; male:female 2:1; median distance from anal verge 6 cm; T4 16/14%, N+ 63/65%. Overall grade 3-4 toxicity rates on treated pts (mainly diarrhoea) were 8% and 24% (arm A/B, p<0.001). 96/90% of pts (arm A/B) received > 90% of the planned RT. 82% of Arm B pts had > 5 oxa courses. 358/342 pts (arm A/B) had surgery at a median of 52/53 days from the end of CRT, 14 pts in each arm were not operated (progression 8, death 5, other/unknown 15) and surgery data are not yet available for 19 pts. Pathologic response data analyzed on the randomized population are reported in the table. **Conclusions:** The addition of

weekly OXA to standard FU-based preop CRT significantly increases toxicity without affecting local tumor response. The reduced pathologic M+ rate suggests a potential effect on distant micrometastases. Longer follow-up is needed to assess the impact on efficacy endpoints.

| Pathologic stage | Arm A (N=379) pts (%) | Arm B (N=368) pts (%) | Total (N=747) pts (%) | P value |
|------------------|-----------------------------|-----------------------------|-----------------------------|---------|
| T0N0 | 60 (16) | 57 (15) | 117 (16) | 0.982 |
| T1-2N0 | 104 (27) | 103 (28) | 207 (28) | |
| | | | | |
| N1-2 | 92 (24) | 96 (26) | 188 (25) | 0.568 |
| | | | | |
| M1 | 11 (3) | 2 (0.5) | 13 (2) | 0.014 |

ATTRIBUTION TO THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING IS REQUESTED IN ALL NEWS COVERAGE.

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ASCO is the world's leading professional organization representing physicians who care for people with cancer. With more than 27,000 members, ASCO is committed to improving cancer care through scientific meetings, educational programs and peer-reviewed journals. For ASCO information and resources, visit www.asco.org/presscenter. Patient-oriented cancer information is available at www.cancer.net.