Anno II, n. 9 - 30 giugno 2007

GASTROINTESTINAL NEWS

Newsletter di aggiornamento sui tumori gastrointestinali

GASTROINTESTINAL NEWS nel 2007 si presenta rinnovato sia nella veste che nel contenuto. Nato per iniziativa del comitato scientifico e coordinato da Intermedia, mantiene la pubblicazione quindicinale e continua ad occuparsi di cancro gastrointestinale. Le news non verranno più tradotte in italiano, ma pubblicate in lingua inglese e, una volta al mese, verrà proposto un commento su un particolare articolo, preparato da un componente del comitato scientifico.

NEWS DALLA RICERCA

Oxaliplatin/5FU/LV in adjuvant colon cancer: Updated efficacy results of the MOSAIC trial, including survival, with a median follow-up of six years - Journal of Clinical Oncology 2007; ASCO Annual Meeting Proceedings (abstract)

Final results of the EORTC Intergroup randomized phase III study 40983 [EPOC] evaluating the benefit of peri-operative FOLFOX4 chemotherapy for patients with potentially resectable colorectal cancer liver metastases - Journal of Clinical Oncology 2007; ASCO Annual Meeting Proceedings (abstract)

ATTAX: Randomised phase II study evaluating weekly docetaxel-based chemotherapy combinations in advanced esophago- gastric cancer, final results of an AGITG trial - Journal of Clinical Oncology 2007; ASCO Annual Meeting Proceedings (abstract)

Outcome of distal gastric cancer with pyloric stenosis after curative resection - European Journal of Surgical Oncology 2007; Volume 33, Issue 5, June, Pages 556 - 560 (abstract)

Oxaliplatin Combined With Weekly Bolus Fluorouracil and Leucovorin As Surgical Adjuvant Chemotherapy for Stage II and III Colon Cancer: Results From NSABP C-07 - Journal of Clinical Oncology 2007; Volume 25, Number 16 (June 1): Pages 2198 - 2204 (abstract)

Neurotoxicity From Oxaliplatin Combined With Weekly Bolus Fluorouracil and Leucovorin As Surgical Adjuvant Chemotherapy for Stage II and III Colon Cancer: NSABP C-07 - Journal of Clinical Oncology 2007; Volume 25, Number 16 (June 1): Pages 2205 - 2211 (abstract)

APPUNTAMENTI

I TUMORI NEUROENDOCRINI DEL PANCREAS (info)

Per contattare la redazione scrivi a: newsletters@intermedianews.it
Per i numeri arretrati di Gastrointestinal News consulta il sito web: www.medinews.it

NEWS DALLA RICERCA

Oxaliplatin/5FU/LV in adjuvant colon cancer: Updated efficacy results of the MOSAIC trial, including survival, with a median follow-up of six years

A. de Gramont, C. Boni, M. Navarro, J. Tabernero, T. Hickish, C. Topham, A. Bonetti, P. Clingan, C. Lorenzato, T. André

Journal of Clinical Oncology 2007; ASCO Annual Meeting Proceedings Part I, Volume 25, Number 18S (June 20 Supplement): 4007

Background: The MOSAIC study was designed to evaluate the effects of the FOLFOX4 regimen (5-FU/LV + oxaliplatin) on 3- year disease free survival (DFS) probability in patients with stage II and III colon cancer.
Methods: Patients (n = 2246) with completely resected stage II (40%) or III (60%) colon cancer were randomly assigned to receive 5-FU/LV (LV5FU2) or FOLFOX4 every 2 weeks for 12 cycles.
Results: Results for the primary endpoint of the study (for the overall population, with a median follow-up [FU] of 3 years), showed a significant benefit in DFS for the FOLFOX4-treated patients (78.2% vs 72.9%; HR: 0.77, p = 0.002) (André et al, NEJM, 2004). Patients were followed beyond the 3-year cut-off for DFS and overall survival (OS) updates. Final DFS, at 5 years FU, are consistent with earlier results (HR: 0.80, p = 0.003). In addition, at a median FU of 6 years, the study demonstrates a significant benefit in OS for the stage III patients. Summary of OS results (median FU 6 years) Long-term safety update shows no increase in the rate of secondary cancer (5.0% in both treatment arms).
Conclusions: These results confirm the benefit of the FOLFOX4 regimen in adjuvant colon cancer patients.

Probability of surviving at 6 years

	LV5FU2	FOLFOX4	HR
Overall population	75.8%	78.5%	0.85 [0.71, 1.01]
Stage III	68.3%	72.9%	0.80 [0.66, 0.98]
Stage II	86.8%	86.8%	1.00 [0.70, 1.43]

TOP

Final results of the EORTC Intergroup randomized phase III study 40983 [EPOC] evaluating the benefit of peri-operative FOLFOX4 chemotherapy for patients with potentially resectable colorectal cancer liver metastases

B. Nordlinger, H. Sorbye, L. Collette, B. Glimelius, G. J. Poston, P. M. Schlag, P. Rougier, W. Bechstein, E. Walpole, T. Gruenberger

Journal of Clinical Oncology 2007; ASCO Annual Meeting Proceedings Part I, Volume 25, Number 18S (June 20 Supplement): LBA5

Background: The 5-year survival after resection of colorectal cancer liver metastases is 30% but recurrence is common. This study evaluates the benefit of combining peri-operative chemotherapy and surgery for patients with initially resectable liver only metastases from colorectal cancer (LM).

Methods: Between September 2000 and July 2004, 364 pts with up to 4 LM were randomized between peri-operative FOLFOX4 (oxaliplatin 85mg/m² and LV5FU2), 6 cycles before and 6 cycles after surgery, (CT), and surgery alone (S). The primary endpoint was progression free survival (PFS) with the goal to increase median PFS by 40% (HR = 0.71). Safety was a secondary endpoint (already reported at ASCO 2005). PFS results are reported at the 2-sided 0.0434 significance level (adjusting for one interim analysis).

Results: Baseline characteristics were similar in both arms. Eleven of 182 pts were ineligible in each arm, mostly for more advanced disease. In the CT arm, a median of 6 pre-op cycles were delivered and 151 patients were resected. 115 pts (63%) received post-op CT, with a median number of 6 cycles and a relative dose intensity of 79% to 86%. In the S arm, 152 pts were resected. Due to the nature of the trial, evaluation of resectability (relevant for eligibility) was based on pre-op imaging, but 31/182 pts (CT arm) and 30/182 pt (S arm) could not undergo resection. There were 2 (S arm) and 1 (CT arm) deaths after surgery. At a median follow-up of 3.9 years, 254 PFS events were reported (240 in eligible pts) and the results are as follows:

	N pts CT	N pts Surgery	% abs difference in 3-y PFS	HR (CI)	P-value
All patients	182	182	+7.2% (28.1% to 35.4%)	0.79 (0.62-1.02)	p = 0.058
All eligible	171	171	+8.1% (28.1% to 36.2%)	0.77 (0.60-1.00)	p = 0.041
All resected	151	152	+9.2% (33.2% to 42.4%)	0.73 (0.55-0.97)	p = 0.025

Conclusions: Peri-operative FOLFOX4 chemotherapy improved PFS over surgery alone in patients whose metastases were actually resected. The benefit was slightly diluted when also pts considered resectable on imaging but eventually not resected were taken into account. FOLFOX4 given peri-operatively is safe and does not prevent the pts from undergoing surgery.

TOP

ATTAX: Randomised phase II study evaluating weekly docetaxel-based chemotherapy combinations in advanced esophago- gastric cancer, final results of an AGITG trial

N. Tebbutt, T. Sourjina, A. Strickland, G. Van Hazel, V. Ganju, D. Gibbs, V. Gebski, S. Munro, M. Cummins

Journal of Clinical Oncology 2007; ASCO Annual Meeting Proceedings Part I, Volume 25, Number 18S (June 20 Supplement): 4528

Background: Docetaxel (T), cisplatin (C) and 5FU(F) are active agents in esophago-gastric cancer. A recent phase III study evaluating 3-weekly TCF demonstrated a survival advantage over standard therapy, but TCF was associated with high rates of hematological toxicity (30% incidence of febrile neutropenia/neutropenic infection) as well as non-hematological side effects (Van Cutsem et al, J. Clin Oncol.; 24: 4991-4997, 2006). Weekly docetaxel is associated with a lower incidence of hematological toxicity. This randomized phase II study aimed to test weekly docetaxel based combination chemotherapy regimens with the aim of maintaining the activity of such regimens but reducing toxicity.

Methods: Eligibility included; histologically confirmed, metastatic esophageal or gastric (OG) carcinoma, measurable disease, PS0-2, adequate organ function, no prior treatment, informed consent. Patients (Pts) were randomized to receive weekly (w) T 30 mg/m^2 d1,8 C 60 mg/m2 d1 F 200 mg/m^2/d continuously q 3w or wT 30 mg/m^2 d1,d8 and capecitabine (X) 1,600 mg/m^2/d d1-14 q3w. The primary endpoint is confirmed response rate (RR), with each arm analyzed independently. Simon's 2-stage design was used, with 5/21 responses required in the first stage to allow continuation to 50 pts per arm.

Results: Response rates in each arm satisfied the first stage, and complete accrual of 106 pts was completed in May 2006. Demographics, toxicity and response rates are shown in the table. With a median follow-up of 14.6 months, progression free and overall survival times are 5.9 m and 12.8 m, and 4.2m and 10.1 m for wTCF and wTX, respectively.

Conclusions: wTCF and wTX have encouraging activity and a far more favorable toxicity profile than TCF administered 3-weekly. Weekly docetaxel-based combination regimens should be evaluated further in this disease.

	wTCF n = 50	wTX n = 56
Age Median (range)	62 (36-83)	60 (33-79)
PS0-1 (%)	98	97
Male sex (%)	84	75
Confirmed PR+CR (%) (95% CI)	49 (35 - 63)	26 (16 - 39)
Febrile neutropenia/neutropenic infection (%)	4	2
Gr 3/4 lethargy (%)	10	4
Gr 3/4 diarrhea (%)	10	7
Gr 3/4 stomatitis (%)	22	2
Gr 3 hand-foot syndrome (%)	4	2

TOP

Outcome of distal gastric cancer with pyloric stenosis after curative resection

J.-H. Chen[a], C.-W. Wu[a], S.-S. Lo[a], A.F.-Y. Li[b], M.-C. Hsieh[a], K.-H. Shen[a] and W.-Y. Lui[a]
[a]Department of Surgery, Taipei Veterans General Hospital and National Yang-Ming University, Section 2, Taipei, [b]Department of Pathology, Taipei Veterans General Hospital and National Yang-Ming University, Taipei 11217, Taiwan

European Journal of Surgical Oncology 2007; Volume 33, Issue 5, June: Pages 556 - 560

Aims Pyloric stenosis usually presents with symptoms, and this may lead patients to consult their physician. We evaluate whether distal gastric cancer patients with pyloric stenosis had a better outcome than those without.
Methods A total of 551 distal gastric cancer patients who received curative subtotal gastrectomy between January 1988 and December 2003 at Taipei Veterans General Hospital were analyzed. Among them, 174 patients were sorted into the pyloric stenosis group according to obstructive symptoms. Their clinicopathological features, survival and prognostic factors were evaluated.
Results The 5-year overall and disease-free survival rate of distal third gastric adenocarcinoma for the pyloric stenosis group was significantly lower than those without pyloric stenosis. Multivariate analysis revealed the pyloric stenosis group had deeper cancer invasion (relative to pT_1, RR of pT_2 3.1, $p = 0.009$; pT_3 6.1, $p < 0.001$; pT_4 16.5, $p < 0.001$), and more lymph node metastasis (RR 3.6; $p = 0.001$). The pyloric stenosis group had a tendency to lymph node metastasis toward the hepatoduodenal ligament, but this did not reach statistical difference. However, the pyloric stenosis group had significantly higher lymph node metastasis in the retropancreatic region (5.17% vs. 0.53%; $p = 0.001$).
Conclusions Distal gastric cancers with pyloric stenosis have worse biological behavior than those without, and consequently have a poor outcome.

TOP

Oxaliplatin Combined With Weekly Bolus Fluorouracil and Leucovorin As Surgical Adjuvant Chemotherapy for Stage II and III Colon Cancer: Results From NSABP C-07

J. Philip Kuebler, H. Samuel Wieand†, Michael J. O'Connell, Roy E. Smith, Linda H. Colangelo, Greg Yothers, Nicholas J. Petrelli, Michael P. Findlay, Thomas E. Seay, James N. Atkins, John L. Zapas, J. Wendall Goodwin, Louis Fehrenbacher, Ramesh K. Ramanathan, Barbara A. Conley, Patrick J. Flynn, Gamini Soori, Lauren K. Colman, Edward A. Levine, Keith S. Lanier, Norman Wolmark

National Surgical Adjuvant Breast and Bowel Project Operations Office and Biostatistical Center; Department of Biostatistics, University of Pittsburgh, Graduate School of Public Health; Allegheny General Hospital; Division of Hematology/Oncology, University of Pittsburgh, Cancer Institute; Department of Medicine, University of Pittsburgh, Pittsburgh, PA; Columbus Community Clinical Oncology Program (CCOP), Columbus, OH; Department of Surgery, Helen F. Graham Cancer Center, Newark, DE; Australasian Gastro-Intestinal Trials Group, University of Sydney, Sydney, Australia; Atlanta Cancer Care, Atlanta, GA; Southeast Cancer Control Consortium, Goldsboro; Surgical Oncology Service, Wake Forest University, Winston-Salem, NC; Division of Surgical Oncology, Harry and Jeanette Weinberg Cancer Institute at Franklin Square Hospital Center, Baltimore, MD; Cancer Research for the Ozarks (CCOP), Springfield, MO; Hematology/Oncology Department, Kaiser Permanente, Northern California, Vallejo, CA; Division Hematology/Oncology, Department of Medicine, Michigan State University, East Lansing, MI; Metro-Minnesota CCOP, Minneapolis, MN; CCOP Missouri Valley Cancer Consortium, Omaha, NE; Northwest CCOP, Tacoma, WA; and the Columbia River Oncology Program, Portland, OR †*Deceased*

Journal of Clinical Oncology 2007; Volume 25, Number 16, June 1: Pages 2198 - 2204

Purpose: This phase III clinical trial evaluated the impact on disease-free survival (DFS) of adding oxaliplatin to bolus weekly fluorouracil (FU) combined with leucovorin as surgical adjuvant therapy for stage II and III colon cancer.

Patients and Methods: Patients who had undergone a potentially curative resection were randomly assigned to either FU 500 mg/m^2 intravenous (IV) bolus weekly for 6 weeks plus leucovorin 500 mg/m^2 IV weekly for 6 weeks during each 8-week cycle for three cycles (FULV), or the same FULV regimen with oxaliplatin 85 mg/m^2 IV administered on weeks 1, 3, and 5 of each 8-week cycle for three cycles (FLOX).

Results: A total of 2,407 patients (96.6%) of the 2,492 patients randomly assigned were eligible. Median follow-up for patients still alive is 42.5 months. The hazard ratio (FLOX *v* FULV) is 0.80 (95% CI, 0.69 to 0.93), a 20% risk reduction in favor of FLOX ($P < .004$). The 3- and 4-year disease-free survival (DFS) rates were 71.8% and 67.0% for FULV and 76.1% and 73.2% for FLOX, respectively. Grade 3 neurosensory toxicity was noted in 8.2% of patients receiving FLOX and in 0.7% of those receiving FULV ($P < .001$). Hospitalization for diarrhea associated with bowel wall thickening occurred in 5.5% of the patients receiving FLOX and in 3.0% of the patients receiving FULV ($P < .01$). A total of 1.2% of patients died as a result of any cause within 60 days of receiving chemotherapy, with no significant difference between regimens.

Conclusion: The addition of oxaliplatin to weekly FULV significantly improved DFS in patients with stage II and III colon cancer. FLOX can be recommended as an effective option in clinical practice.

TOP

Neurotoxicity From Oxaliplatin Combined With Weekly Bolus Fluorouracil and Leucovorin As Surgical Adjuvant Chemotherapy for Stage II and III Colon Cancer: NSABP C-07

Stephanie R. Land, Jacek A. Kopec, Reena S. Cecchini, Patricia A. Ganz, H. Samuel Wieand†, Linda H. Colangelo, Kate Murphy, J. Philip Kuebler, Thomas E. Seay, Burton M. Needles, James D. Bearden, III, Lauren K. Colman, Keith S. Lanier, Eduardo R. Pajon, Jr, David Cella, Roy E. Smith, Michael J. O'Connell, Joseph P. Costantino, Norman Wolmark

National Surgical Adjuvant Breast and Bowel Project Operations Office and Biostatistical Center; University of Pittsburgh Graduate School of Public Health, Department of Biostatistics, Pittsburgh; The Regional Cancer Center, Erie; and Allegheny General Hospital, Pittsburgh, PA; Department of Health Care and Epidemiology, University of British Columbia, Vancouver, BC, Canada; University of California, Los Angeles, Schools of Medicine and Public Health, and the Jonsson Comprehensive Cancer Center, Los Angeles, CA; Colorectal Cancer Coalition, Skaneateles, NY; Clinical Community Oncology Program, Columbus, OH; Atlanta Regional Community Clinical Oncology Program (CCOP), Atlanta, GA; St John's Mercy Medical Center, St Louis, MO; Upstate Carolina CCOP, Spartanburg, SC; Northwest CCOP, Tacoma, WA; Columbia River Oncology Program, Portland, OR; Colorado Cancer Research Program, Denver Veterans Medical Center, Denver, CO; and the Evanston Northwestern Healthcare, Evanston, IL †*Deceased*

Journal of Clinical Oncology 2007; Volume 25, Number 16, June 1: Pages 2205 - 2211

Purpose: The randomized, multicenter, phase III protocol C-07 compared the efficacy of adjuvant bolus fluorouracil and leucovorin (FULV) versus FULV with oxaliplatin (FLOX) in stage II or III colon cancer. Definitive analysis revealed an increase in 4-year disease-free survival from 67.0% to 73.2% in favor of FLOX. This study compares neurotoxicity between the treatments.

Patients and Methods: Neurotoxicity was recorded for all patients using standard adverse event reporting. Patients at select institutions completed a neurotoxicity questionnaire through 18 months of follow-up.

Results: A total of 2,492 patients enrolled onto C-07 and 400 patients enrolled onto the patient-reported substudy. Mean patient-reported neurotoxicity was higher with oxaliplatin throughout the 18 months of study ($P < .0001$). During therapy, patients receiving oxaliplatin experienced significantly more hand/foot toxicity (eg, "quite a bit" of cold-induced hand/foot pain 26% FLOX *v* 2.6% FULV) and overall weakness (eg, moderate weakness in 27.4% FLOX *v* 16.2% FULV). At 18 months, hand neuropathy had diminished, but patients who received oxaliplatin experienced continued foot discomfort (eg, moderate foot numbness and tingling for 22.1% FLOX *v* 4.6% FULV). Observer-reported neurotoxicity was low grade and primarily neurosensory rather than neuromotor. Sixty-eight percent in the FLOX group *v* 8% in the FULV group had neurotoxicity at their first on-treatment assessment. Time to resolution was significantly longer for those receiving oxaliplatin, and continued beyond 2 years for more than 10% in the oxaliplatin group.

Conclusion: Oxaliplatin causes significant neurotoxicity. It is experienced primarily in the hands during therapy and in the feet during follow-up. In a minority of patients the neurotoxicity is long lasting.

TOP

I TUMORI NEUROENDOCRINI DEL PANCREAS
Padova, 17 settembre 2007
Aula Ramazzini, Policlinico
Università di Padova, Via Giustiniani 2
Per scaricare il programma collegati al sito: www.medinews.it
(Società Scientifiche - Aiom - Appuntamenti)

TOP