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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.

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9TH WORLD CONGRESS ON GASTROINTESTINAL CANCER (leggi)

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NEWS DALLA RICERCA

Survival benefits from neoadjuvant chemoradiotherapy or chemotherapy in oesophageal carcinoma: a meta-analysis

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Lancet Oncology 2007; Volume 8: Pages 226 - 234

Background Resectable oesophageal cancer is often treated with surgery alone or with preoperative (neoadjuvant) chemoradiotherapy or chemotherapy. We aimed to clarify the benefits of neoadjuvant chemoradiotherapy or chemotherapy versus surgery alone by a meta-analysis of randomised trial data.

Methods Eligible trials were identified first from earlier published meta-analyses and systematic reviews. We also used MEDLINE, Cancerlit, and EMBASE databases to identify additional studies and published abstracts from major scientific meetings since 1980. Only randomised studies with an analysis by an intention-to-treat principle were included, and searches were restricted to those databases citing articles in English. We used published hazard ratios if available or estimates from other survival data or survival curves. Treatment effects by type of tumour and treatment sequencing were also investigated.

Findings Ten randomised comparisons of neoadjuvant chemoradiotherapy versus surgery alone (n=1209) and eight of neoadjuvant chemotherapy versus surgery alone (n=1724) in patients with local operable oesophageal carcinoma were identified. The hazard ratio for all-cause mortality with neoadjuvant chemoradiotherapy versus surgery alone was 0·81 (95% CI 0·70–0·93; p=0·002), corresponding to a 13% absolute difference in survival at 2 years, with similar results for different histological tumour types: 0·84 (0·71–0·99; p=0·04) for squamous-cell carcinoma (SCC), and 0·75 (0·59–0·95; p=0·02) for adenocarcinoma. The hazard ratio for neoadjuvant chemotherapy was 0·90 (0·81–1·00; p=0·05), which indicates a 2-year absolute survival benefit of 7%. There was no significant effect on all-cause mortality of chemotherapy for patients with SCC (hazard ratio 0·88 [0·75–1·03]; p=0·12), although there was a significant benefit for those with adenocarcinoma (0·78 [0·64–0·95]; p=0·014).

Interpretation A significant survival benefit was evident for preoperative chemoradiotherapy and, to a lesser extent, for chemotherapy in patients with adenocarcinoma of the oesophagus. The findings provide an evidence-based framework for the use of neoadjuvant treatment in management decisions.

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Prospective Multicentric Randomized Phase III Study of Imatinib in Patients With Advanced Gastrointestinal Stromal Tumors Comparing Interruption Versus Continuation of Treatment Beyond 1 Year: The French Sarcoma Group

Jean-Yves Blay, Axel Le Cesne, Isabelle Ray-Coquard, Binh Bui, Florence Duffaud, Catherine Delbaldo, Antoine Adenis, Patrice Viens, Maria Rios, Emmanuelle Bompas, Didier Cupissol, Cecile Guillemet, Pierre Kerbrat, Jérome Fayette, Sylvie Chabaud, Patrice Berthaud, David Perol

Unité INSERM U590 Centre Léon Bérard & Université Claude Bernard Lyon I & Hopital Edouard Herriot; Département de Médecine & UBET, Centre Léon Bérard; Hopital Edouard Herriot, Lyon; Institut Gustave Roussy, Villejuif; Institut Bergonié, Bordeaux; Hopital La Timone, Marseille; Centre Oscar Lambret, Lille; Institut Paoli Calmettes, Marseille; Centre Alexis Vautrin, Nancy; Centre René Gauducheau, Nantes; Centre Val D'Aurelle Montpellier; Centre Henri Becquerel, Rouen; and Novartis Pharma, Rueil Malmaison, France

Journal of Clinical Oncology 2007; Volume 25, Number 9 (March 20): Pages 1107 - 1113

Purpose: Imatinib is the standard treatment of advanced GI stromal tumors (GISTs). It is not known whether imatinib may be stopped in patients in whom disease is controlled.
Methods: This prospective, randomized, multicentric phase III study was designed to compare continuous (CONT) compared with interrupted (INT) imatinib beyond 1 year of treatment in patients with advanced GIST. The primary end point was progression-free survival. Secondary end points included overall survival, response rate after reinitiation of imatinib, and quality of life. Early stopping rules in cases of rapid progression of disease were defined, with preplanned interim analyses.
Results: Between May 2002 and April 2004, 182 patients with advanced GIST were enrolled. Between May 2003 and April 2004, 98 patients in response or stable disease under imatinib reached more than 1 year of follow-up. Forty were not eligible for randomization, and 58 patients were randomly assigned, 32 and 26 patients in the INT and CONT arms, respectively. As of October 15, 2005, eight of 26 patients in the CONT group and 26 of 32 patients in the INT group had documented disease progression ($P < .0001$). Twenty-four of 26 patients with documented progression in the INT arm responded to imatinib reintroduction. No differences in overall survival or imatinib resistance were observed between the two arms. Quality of life evaluated 6 months after random assignment using the 30-item Quality of Life Questionnaire was not significantly different between the two groups of randomly assigned patients.
Conclusion: Imatinib interruption results in rapid progression in most patients with advanced GIST, and cannot be recommended in routine practice unless patient experience significant toxicity.

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Lymph Node Evaluation and Survival After Curative Resection of Colon Cancer: Systematic Review

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Journal of the National Cancer Institute 2007; Volume 99, Number 6, 21 March: Pages 433 - 441

Background: Adequate lymph node evaluation for cancer involvement is important for prognosis and treatment of patients with colon cancer. The number of lymph nodes evaluated may be a measure of quality in colon cancer care and appears to be inadequate in most patients treated for colon cancer. We performed a systematic review of the evidence for the association between lymph node evaluation and oncologic outcomes in patients with colon cancer.

Methods: Medline, Scopus, Cochrane, and the National Guidelines Clearinghouse databases were searched from January 1, 1990, through June 30, 2006, for studies in which survival data as a function of number of lymph nodes evaluated were available. These studies were evaluated for methodologic quality, design, and data source. A total of 61 371 patients were included.

Results: Seventeen studies from nine countries were eligible for systematic review, including two secondary analyses of multicenter randomized trials of adjuvant chemotherapy for colon cancer, five population-based observational studies, and 10 single-institution retrospective cohort studies. Despite heterogeneity in methodology and differences in threshold numbers of lymph nodes evaluated (range = 6–40 lymph nodes), 16 of 17 studies reported that increased survival of patients with stage II colon cancer was associated with increased numbers of lymph nodes evaluated. Four of six studies with data from stage III patients also reported a positive association with survival among patients with stage III colon cancer.

Conclusions: The number of lymph nodes evaluated after surgical resection was positively associated with survival of patients with stage II and stage III colon cancer. These results support consideration of the number of lymph nodes evaluated as a measure of the quality of colon cancer care.

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Development of a risk score for colorectal cancer in men

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American Journal of Medicine 2007 March; Volume 120 (Number 3): Pages 257 - 263

Background: Colorectal cancer is a common and preventable disease for which screening rates remain unacceptably low.
Methods: We developed a risk scoring system for the development of colorectal cancer among participants in the Physician's Health Study, a prospective cohort of 21,581 US male physicians who were all free of cancer. Predictors of colorectal cancer were self-reported and identified from the baseline questionnaire. Logistic regression was used to determine the independent predictors of incident colorectal cancer over the follow-up period. Risk scores were created from the sum of the odds ratios of the final predictors and used to divide the cohort into categories of increasing relative risk.
Results: During 20 years of follow-up, 381 cases of colon cancer and 104 cases of rectal cancer developed in the cohort. Age, alcohol use, smoking status, and body mass index were independent significant predictors of colorectal cancer. The point scores were used to define 10 risk groups. Those in the highest risk group (9-10 points) had an odds ratio of 15.29 (6.19-37.81) for colorectal cancer compared with those with the lowest risk. We further stratified scores into 3 risk classes. Compared with those at the lowest relative risk, the odds ratio for colorectal cancer was 3.07 (2.46-3.83) in the intermediate risk group and 5.75 (4.44-7.44) in the highest risk group.
Conclusions: We developed a simple scoring system for colorectal cancer that identifies men at increased relative risk on the basis of age and modifiable factors. This tool should be validated in other populations.

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FOLFOX-4 regimen as fist-line chemotherapy in elderly patients with advanced gastric cancer: a safety study

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Journal of Chemotherapy 2007 Feb; Volume 19 (Issue 1): Pages 85 - 89

Gastric cancer is often diagnosed in advanced stage (AGC) and in elderly patients. Current chemotherapies induce severe toxicity and are difficult to deliver. Some authors have shown the activity and safety of oxaliplatin with various 5-fluorouracil (FU) and leucovorin (LV) infusions in AGC. The aim of our study was to evaluate the feasibility of the FOLFOX-4 regimen in elderly patients with AGC. From 6/2003 to 7/2005, 33 patients (median age 74 years, range 66-79 years) were enrolled into the study. 31 patients were assessable for the safety analysis and for response. We recorded complete response in 4 patients (13%), partial response in 6 patients (19%), 9 (29%) stable disease and 12 progressive disease for an overall response rate of 32% (95% CI, 16% to 48%). At median follow-up of 20 months the median time to progression was 6.4 months. The therapy was well tolerated, the main G1/2 toxicities were nausea, vomiting and diarrhea. Only 2 patients suffered from severe vomiting. Severe hematologic toxicities were uncommon. Anemia G3 was recorded in 3 patients, neutropenia G3 in 6 patients and febrile neutropenia in 1 patient. G1 and G2 neurotoxicity were a common event while G3 sensorial neuropathy was not reported. We conclude that although our patients were elderly and most had a PS 2, the regimen was manageable, easy to deliver, well accepted by the patients and active.

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Pharmacogenetic Profiling in Patients With Advanced Colorectal Cancer Treated With First-Line FOLFOX-4 Chemotherapy

Annamaria Ruzzo, Francesco Graziano, Fotios Loupakis, Eliana Rulli, Emanuele Canestrari, Daniele Santini, Vincenzo Catalano, Rita Ficarelli, Paolo Maltese, Renato Bisonni, Gianluca Masi, Gaia Schiavon, Paolo Giordani, Lucio Giustini, Alfredo Falcone, Giuseppe Tonini, Rosarita Silva, Rodolfo Mattioli, Irene Floriani, Mauro Magnani

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Journal of Clinical Oncology 2007; Volume 25, Number 10 (April 1): Pages 1247 - 1254

Purpose: The objective is to investigate whether polymorphisms with putative influence on fluorouracil/oxaliplatin activity are associated with clinical outcomes of patients with advanced colorectal cancer treated with first-line oxaliplatin, folinic acid, and fluorouracil palliative chemotherapy.

Materials and Methods: Consecutive patients were prospectively enrolled onto medical oncology units in Central Italy. Patients were required to have cytologically/histologically confirmed metastatic disease with at least one measurable lesion. Peripheral blood samples were used for genotyping 12 polymorphisms in thymidylate synthase, methylenetetrahydrofolate reductase, xeroderma pigmentosum group D (XPD), excision repair cross complementing group 1 (ERCC1), X-ray cross complementing group 1, X-ray cross complementing protein 3, glutathione S-transferases (GSTs) genes. The primary end point of the study was to investigate the association between genotypes and progression-free survival (PFS).

Results: In 166 patients, ERCC1-118 T/T, XPD-751 A/C, and XPD-751 C/C genotypes were independently associated with adverse PFS. The presence of two risk genotypes (ERCC1-118 T/T combined with either XPD-751 A/C or XPD-751 C/C) occurred in 50 patients (31%). This profiling showed an independent role for unfavorable PFS with a hazard ratio of 2.84% and 95% CI of 1.47 to 5.45 (P = .002). Neurotoxicity was significantly associated with GSTP1-105 A/G. Carriers of the GSTP1-105 G/G genotype were more prone to suffer from grade 3 neurotoxicity than carriers of GSTP1-105 A/G and GSTP1-105 A/A genotypes.

Conclusion: A pharmacogenetic approach may be an innovative strategy for optimizing palliative chemotherapy in patients with advanced colorectal cancer. These findings deserve confirmation in additional prospective studies.

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SECONDO CORSO NAZIONALE per il TEAM ONCOLOGICO di APPROFONDIMENTO sugli STRUMENTI ORGANIZZATIVO-GESTIONALI

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