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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.

NEWS DALLA RICERCA

Prognostic model to predict survival following first-line chemotherapy in patients with metastatic gastric adenocarcinoma Annals of Oncology 2007; Volume 18 (issue 5): Pages 886 - 891 (abstract)

Thymidylate synthase polymorphisms and colon cancer: Associations with tumor stage, tumor characteristics and survival International Journal of Cancer 2007; Volume 120, Issue 10, (15 May): Pages 2226 - 2232 (abstract)

Phase III Trial of Infusional Fluorouracil, Leucovorin, Oxaliplatin, and Irinotecan (FOLFOXIRI) Compared With Infusional Fluorouracil, Leucovorin, and Irinotecan (FOLFIRI) As First-Line Treatment for Metastatic Colorectal Cancer: The Gruppo Oncologico Nord-Ovest Journal of Clinical Oncology 2007; Volume 25, Number 13 (May 1): Pages 1670 - 1676 (abstract)

The impact on survival of thromboembolic phenomena occurring before and during protocol chemotherapy in patients with advanced gastroesophageal adenocarcinoma Cancer2007; Volume 109, Issue 10, 15 May: Pages 1989 - 1995 (abstract)

Hereditary diffuse gastric cancer and E-cadherin: Description of the first germline mutation in an Italian family European Journal of Surgical Oncology 2007; Volume 33, Issue 4, May: Pages 448 - 451 (abstract)

Prognostic influence of multiple hepatic metastases from colorectal cancer European Journal of Surgical Oncology 2007; Volume 33, Issue 4, May: Pages 468-473 (abstract)

APPUNTAMENTI

9TH WORLD CONGRESS ON GASTROINTESTINAL CANCER (info)

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NEWS DALLA RICERCA

Prognostic model to predict survival following first-line chemotherapy in patients with metastatic gastric adenocarcinoma

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Background: This study was to devise a prognostic model for metastatic gastric cancer patients undergoing first-line chemotherapy.

Patients and methods: A retrospective analysis was carried out on 1455 gastric cancer patients, who received first-line chemotherapy from September 1994 to February 2005.

Results: At multivariate level, poor prognostic factors were no previous gastrectomy [*P* = 0.003; relative risk (RR), 1.191; 95% confidence interval (CI) 1.061–1.338], albumin <3.6 g/dl (*P* = <0.001; RR, 1.245; 95% CI 1.106–1.402), alkaline phosphatase >85 U/l (*P* = <0.001; RR, 1.224; 95% CI 1.092–1.371), Eastern Cooperative Oncology Group performance status of two or more (*P* = <0.001; RR, 1.690; 95% CI 1.458–1.959), the presence of bone metastases (*P* = 0.001; RR, 1.460; 95% CI 1.616–1.836), and the presence of ascites (*P* = <0.001; RR, 1.452; 95% CI 1.295–1.628). Of 1434 patients, 489 patients (34.1%) were categorized as low-risk group (zero to one factors), 889 patients (62.0%) as intermediate-risk group (two to four factors), and 56 patients (3.9%) as high-risk group (five to six factors). Median survival durations for low, intermediate, and high-risk groups were 12.5 months, 7.0 months, and 2.7 months, respectively.

Conclusions: This model should facilitate the individual patient risk stratification and thus, more appropriate therapies for each metastatic gastric cancer patient.

TOP

Thymidylate synthase polymorphisms and colon cancer: Associations with tumor stage, tumor characteristics and survival

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Abstract Thymidylate synthase (TS) is a key enzyme in folate metabolism, a pathway that is important in colorectal carcinogenesis. We investigated the role of functional polymorphisms in the TS 5'-UTR promoter enhancer region (TSER, 3 or 2 repeats of a 28-bp sequence) and the 3'-UTR (1494delTTAAAG) and their association with colon tumor characteristics, including tumor stage and acquired mutations in p53, Ki-ras and microsatellite instability. Data from a population-based incident case-control colon cancer study in northern California, Utah and Minnesota (1,206 cases, 1,962 controls) was analyzed using unordered polytomous logistic regression models. In both men and women, individuals with variant TS alleles were at reduced risk of having an advanced stage tumor (metastatic disease: OR = 0.35, 95% CI: 0.2-0.6 vs. wildtype TSER and 3'-UTR). Stage-adjusted survival did not differ by genotype. Men with 1 or 2 variant alleles in both the TSER and 3'-UTR genotypes had a 50% reduced risk of a p53-positive tumor (OR = 0.5, 95% CI: 0.3-0.9 vs. homozygous wildtype TSER and 3'-UTR). Women with 1 or 2 variant alleles for either the TSER or 3'-UTR polymorphism had reduced risk of having any colon tumor that did not vary by mutation status. This study provides some support for associations between TS genotype and colon cancer tumor characteristics.

TOP

Phase III Trial of Infusional Fluorouracil, Leucovorin, Oxaliplatin, and Irinotecan (FOLFOXIRI) Compared With Infusional Fluorouracil, Leucovorin, and Irinotecan (FOLFIRI) As First-Line Treatment for Metastatic Colorectal Cancer: The Gruppo Oncologico Nord-Ovest

Alfredo Falcone, Sergio Ricci, Isa Brunetti, Elisabetta Pfanner, Giacomo Allegrini, Cecilia Barbara, Lucio Crinò, Giovanni Benedetti, Walter Evangelista, Laura Fanchini, Enrico Cortesi, Vincenzo Picone, Stefano Vitello, Silvana Chiara, Cristina Granetto, Gianfranco Porcile, Luisa Fioretto, Cinzia Orlandini, Michele Andreuccetti, Gianluca Masi

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Journal of Clinical Oncology 2007; Volume 25, Number 13 (May 1): Pages 1670 - 1676

Purpose: The Gruppo Oncologico Nord Ovest (GONO) conducted a phase III study comparing fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI [irinotecan 165 mg/m^2 day 1, oxaliplatin 85 mg/m^2 day 1, leucovorin 200 mg/m^2 day 1, fluorouracil 3,200 mg/m^2 48-hour continuous infusion starting on day 1, every 2 weeks]) with infusional fluorouracil, leucovorin, and irinotecan (FOLFIRI).

Methods: Selection criteria included unresectable metastatic colorectal cancer, age 18 to 75 years, and no prior chemotherapy for advanced disease. The primary end point was response rate (RR).

Results: A total of 244 patients were randomly assigned. An increase of grade 2 to 3 peripheral neurotoxicity (0% v 19%; P < .001), and grade 3 to 4 neutropenia (28% v 50%; P < .001) were observed in the FOLFOXIRI arm. The incidence of febrile neutropenia (3% v 5%) and grade 3 to 4 diarrhea (12% v 20%) were not significantly different. Responses, as assessed by investigators, were, for FOLFIRI and FOLFOXIRI, respectively, complete, 6% and 8%; and partial, 35% and 58%, (RR, 41% v 66%; P = .0002). RR confirmed by an external panel was 34% versus 60% (P < .0001). The R0 secondary resection rate of metastases was greater in the FOLFOXIRI arm (6% v 15%; P = .033, among all 244 patients; and 12% v 36%; P = .017 among patients with liver metastases only). Progression-free survival (PFS) and overall survival (OS) were both significantly improved in the FOLFOXIRI arm (median PFS, 6.9 v 9.8 months; hazard ratio [HR], 0.63; P = .0006; median OS, 16.7 v 22.6 months; HR, 0.70; P = .032).

Conclusion: The FOLFOXIRI regimen improves RR, PFS, and OS compared with FOLFIRI, with an increased, but manageable, toxicity in patients with metastatic colorectal cancer with favorable prognostic characteristics. Further studies of FOLFOXIRI in combination with targeted agents and in the neoadjuvant setting are warranted.

TOP

The impact on survival of thromboembolic phenomena occurring before and during protocol chemotherapy in patients with advanced gastroesophageal adenocarcinoma

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Cancer 2007; Volume 109, Issue 10, 15 May: Pages 1989 - 1995

Background: Thromboembolic events (TEEs) are considered common in patients with gastroesophageal carcinoma, but their frequency at baseline and during chemotherapy is not known. Because prophylactic anticoagulation results in improved overall survival (OS) of solid tumor patients, the authors hypothesized that TEEs at baseline and during chemotherapy would have an adverse effect on OS.

Methods: The authors analyzed patients with advanced gastroesophageal carcinoma who were treated on 4 prospective chemotherapy Phase II/III trials. Baseline and subsequent TEEs were documented and correlated with OS.

Results: On the 4 trials, 191 patients received single-agent or a combination of a taxane, camptothecin, platinum, or fluoropyrimidine. At baseline, TEEs occurred in 5.3% of untreated patients compared with 8.5% of previously treated patients (who had received prior treatment for metastatic disease). The median OS was only 3.9 months for patients who had a TEE at any time versus 8.7 months for patients who never developed a TEE (P = .007). TEEs at baseline were correlated with poor median OS in untreated patients (4.9 months vs 8.9 months for patients without a TEE; P = .014). There was no associated between TEEs and the type of chemotherapy used.

Conclusions: The current results established that TEEs at baseline and/or during chemotherapy are frequent and result in poor OS for patients with advanced gastroesophageal carcinoma. Aggressive methods to treat or prevent TEEs are warranted.

TOP

Hereditary diffuse gastric cancer and E-cadherin: Description of the first germline mutation in an Italian family

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European Journal of Surgical Oncology 2007; Volume 33, Issue 4, May: Pages 448 - 451

Aims: Germline mutation of the E-cadherin gene (*CDH1*) accounts for the Hereditary Diffuse Gastric Cancer (HDGC) syndrome. Fourteen pedigrees with Diffuse Gastric Cancer that fulfilled the International Gastric Cancer Linkage Consortium (IGCLC) criteria were selected and screened for *CDH1* germline mutations.

Methods: The entire coding region of the *CDH1* gene and all intron–exon boundaries were analyzed by direct sequencing in the 14 families fulfilling the IGCLC criteria. E-cadherin immunohistochemical expression was evaluated on tumour as well as normal formalin-fixed paraffin embedded tissues.

Results: A novel germline missense mutation was found. It was a single C → T substitution in exon 8, resulting in a transition of CCG → CTG (C1118T; Pro373Leu) demonstrated in the proband and her brother. At immunohistochemical analysis, the staining intensity was reduced and considered weakly positive (15%).

Conclusions: The first *CDH1* germline mutation of an Italian family is herein reported. The present missense mutation has never been described so far.

TOP

Prognostic influence of multiple hepatic metastases from colorectal cancer

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European Journal of Surgical Oncology 2007; Volume 33, Issue 4, May: Pages 468-473

Aims: The aim of this study was to report the results of surgery for multiple colorectal liver metastases on patient outcome.
Methods: This was a review of 484 consecutive patients who underwent liver resection for colorectal liver metastases between 1993 and 2003. The cohort was divided into 2 groups, those with 1–3 metastases and those with "multiple" metastases, namely 4 or more lesions. The later group was subdivided into those with less than 8 ("several") or 8 or more ("numerous") separate lesions. Main outcome measures: the post-operative hospital stay was calculated and morbidity and mortality were assessed.
Results: On multivariate analysis the presence of multiple metastases was the only predictor for both poorer overall survival ($p = 0.007$) and disease-free survival ($p = 0.031$). However, when patients with multiple metastases are analysed in detail this survival disadvantage appears to be only present in patients with numerous (8 or more) lesions.
Conclusion: Although patients with multiple metastases appear to have a poorer outcome, significant number of patients with multiple metastases survive to 5 years or more and should not be denied surgery. Patients with numerous (8 or more) metastases showed a poorer survival disadvantage. These patients need alternative treatment speculatives.

TOP

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TOP