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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

Venous thromboembolism predicts poor prognosis in irresectable pancreatic cancer patients - Annals of Oncology 2007; Volume 18, Number 10, October: Pages 1660-1665 (abstract)

Phase II trial of docetaxel and oxaliplatin in patients with advanced gastric cancer and/or adenocarcinoma of the gastroesophageal junction - Annals Oncology 2007 Sep 25; [Epub ahead of print] (abstract)

Phase I study of S-1, docetaxel and cisplatin combination chemotherapy in patients with unresectable metastatic gastric cancer - British Journal of Cancer 2007; Volume 97, Number 7, October 8: Pages 851-856 (abstract)

Increased survival using platinum analog combined with gemcitabine as compared to single-agent gemcitabine in advanced pancreatic cancer: pooled analysis of two randomized trials, the GERCOR /GISCAD intergroup study and a German multicenter study - Annals of Oncology 2007; Volume 18, Number 10, October: Pages 1652-1659 (abstract)

Patients With Curative Resection of cT3-4 Rectal Cancer After Preoperative Radiotherapy or Radiochemotherapy: Does Anybody Benefit From Adjuvant Fluorouracil-Based Chemotherapy? A Trial of the European Organisation for Research and Treatment of Cancer Radiation Oncology Group - Journal of Clinical Oncology 2007; Volume 25, Number 28, October 1: Pages 4379-4386 (abstract)

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NEWS DALLA RICERCA

Venous thromboembolism predicts poor prognosis in irresectable pancreatic cancer patients

M. Mandalà[1], M. Reni[2], S. Cascinu[3], S. Barni[4], I. Floriani[5], S. Cereda[2], R. Berardi[3], S. Mosconi[1], V. Torri[5] and R. Labianca[1]

[1] Unit of Medical Oncology, Ospedali Riuniti, Bergamo [2] Division of Medical Oncology, San Raffaele Hospital, Milan [3] Clinica di Oncologia Medica, Università Politecnica delle Marche; Azienda Ospedaliero-Universitaria, Ospedali Riuniti di Ancona, Umberto I, Lancisi, Salesi, Ancona [4] Division of Medical Oncology, Treviglio Hospital, Treviglio [5] Department of Oncology, Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

Annals of Oncology 2007; Volume 18, Number 10, October: Pages 1660-1665

Background: The aim was to investigate the outcomes associated with venous thromboembolism (VTE) among irresectable pancreatic cancer patients.

Methods: This is a follow-up study of consecutive irresectable cancer patients, treated and followed up in clinical trials between December 2001 and December 2004 in order to evaluate the prognostic impact of symptomatic VTE on clinical outcomes, such as response to treatment, progression-free survival (PFS) and overall survival (OS).

Results: Among 227 irresectable pancreatic cancer patients, with Eastern Cooperative Oncology Group performance status (ECOG-PS) $\leq$ 2, 59 (26.0%) patients developed a VTE. A synchronous VTE occurred in 28 (12.3%) patients, while a VTE during chemotherapy was observed in 15 (6.6%) patients, and 16 (7.0%) patients experienced both events. Presence of synchronous VTE was associated with a higher probability of not responding to treatment (odds ratio 2.98, 95% CI 1.42–6.27, $P = 0.004$), but showed no effect on both PFS and OS at least at multivariate analysis. Occurrence of a VTE during chemotherapy showed a statistically significant effect on PFS (hazard ratio [HR] 2.59, 95% CI 1.69–3.97, $P < 0.0001$) and OS (HR 1.64, 95%CI 1.04–2.58, $P = 0.032$).

Conclusions: Our data suggest that the occurrence of VTE may be associated with a reduced response rate and a shorter PFS and OS among patients with irresectable pancreatic cancer. In these patients the development of VTE may reflect the presence of a biologically more aggressive cancer that in turn leads to a worse prognosis.

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Phase II trial of docetaxel and oxaliplatin in patients with advanced gastric cancer and/or adenocarcinoma of the gastroesophageal junction

Richards D, McCollum D, Wilfong L, Sborov M, Boehm KA, Zhan F, Asmar L
US Oncology Research, Inc., Houston

Annals of Oncology 2007 Sep 25; [Epub ahead of print]

Background: Platinum-based chemotherapy is the standard treatment for advanced gastric cancer (GC). This trial explored the efficacy and tolerability of combined docetaxel (Taxotere) + oxaliplatin (DOCOX) in GC patients.
Patients and Methods: Patients with untreated stage IV GC or adenocarcinoma of the gastroesophageal junction (AGEJ) received docetaxel 60 mg/m(2) followed by oxaliplatin 130 mg/m(2) on day 1 of each 21-day cycle until progression or unacceptable toxicity. The primary end points were response rate (RR), toxicity, progression-free survival (PFS), and overall survival (OS).
Results: Baseline characteristics (N = 71): median age 59 years, 72% male, 51% esophagogastric junction cancer, and Eastern Cooperative Oncology Group performance status of zero, one, two were 42%, 51%, 7%, respectively. The median number of cycles was 6 (range, 1-19). Grades 3-4 toxic effects: neutropenia (70%); vomiting (17%); nausea (16%); dehydration, fatigue, or diarrhea (13%, each); and thrombocytopenia or febrile neutropenia (7%, each). Sixty-six patients completed >/=2 cycles. The RR was 36% with 25 partial response (PR) and no complete responses (CRs); stable disease (SD) was 49%. Clinical benefit rate (CBR = CR + PR + SD >/=6 months) was 40%; median PFS was 4.3 months, and OS was 8.5 months.
Conclusions: DOCOX produced manageable toxicity in patients with advanced GC and AGEJ. The confirmed RR of 36%, CBR of 40%, and median survival of 8.5 months are encouraging and comparable to standard front-line regimens.

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Phase I study of S-1, docetaxel and cisplatin combination chemotherapy in patients with unresectable metastatic gastric cancer

T Takayama[1], Y Sato[1], T Sagawa[1], T Okamoto[1], H Nagashima[1], Y Takahashi[2], H Ohnuma[2], G Kuroiwa[3], K Miyanishi[1], R Takimoto[1], T Matsunaga[1], J Kato[1], K Yamaguchi[4], K Hirata[4] and Y Niitsu[1]

[1]Fourth Department of Internal Medicine, Sapporo Medical University, School of Medicine, [2]Department of Gastroenterology, Hokkaido Cancer Center, [3]Department of Internal Medicine, Higashi Sapporo Hospital [4]First Department of Surgery, Sapporo Medical University, School of Medicine, Sapporo, Japan

British Journal of Cancer 2007; Volume 97, Number 7, October 8: Pages 851-856

The aim of this dose escalation study was to determine the maximum-tolerated dose (MTD), dose-limiting toxicities (DLTs) and preliminary efficacy of docetaxel, S-1 and cisplatin combination chemotherapy in patients with unresectable metastatic gastric cancer. Seventeen patients received oral S-1 (40 mg m^{-2} bid) on days 1-14, intravenous cisplatin (60 mg m^{-2}) and docetaxel (60, 70 or 80 mg m^{-2} depending on DLT) on day 8 every 3 weeks. The MTD of this combination was presumed to be docetaxel 70 mg m^{-2}. At this dose level, 40% of the patients (two of five) developed grade 4 neutropenia and 20% (one of five) exhibited grade 3 nausea during the first course. Therefore, the recommended dose of docetaxel was defined as 60 mg m^{-2}. The DLT was neutropenia. The response rate (RR) was 88.2% (15 of 17), consisting of one complete response and 14 partial responses. There were two stable diseases but no progressive disease. Of these 15 responders, four (23.5%) with high VEGF expression showed rapid tumour regression and achieved downstaging, leading to subsequent curative gastrectomy. Three of these have been disease free for about 3 years, suggesting a complete cure. In conclusion, this regimen was tolerable and showed a quite high RR, with an appreciable downstaging rate in metastatic gastric cancer.

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Increased survival using platinum analog combined with gemcitabine as compared to single-agent gemcitabine in advanced pancreatic cancer: pooled analysis of two randomized trials, the GERCOR/GISCAD intergroup study and a German multicenter study

V. Heinemann[1,*], R. Labianca[2], A. Hinke[3] and C. Louvet[4]

[1] Medical Clinic III, Klinikum Grosshadern, Munich, Germany [2] Ospedali Riuniti, Bergamo, Italy [3] Wissenschaftlicher Service Pharma, Langenfeld, Germany [4] Service d'Oncologie, Médecine Interne, Hôpital St. Antoine, Paris, France

Annals of Oncology 2007; Volume 18, Number 10, October: Pages 1652-1659

Background: The aim was to evaluate the efficacy of gemcitabine combined with a platinum agent compared to single-agent gemcitabine in a pooled analysis of two randomized trials.

Methods: The French Multidisciplinary Clinical Research Group (GERCOR)/Italian Group for the Study of Gastrointestinal Tract Cancer (GISCAD) intergroup study comparing gemcitabine plus oxaliplatin to gemcitabine and a German multicenter trial comparing gemcitabine plus cisplatin versus gemcitabine were included in a pooled analysis based on individual patient data.

Results: Among 503 evaluable patients, 252 received gemcitabine plus a platinum analog (GP), while 251 patients were treated with gemcitabine alone. For progression-free survival (PFS), the pooled univariate analysis indicated a hazard ratio (HR) of 0.75 (P = 0.0030) in favour of the GP combination. The benefit from the GP combination was greatest in the subgroup of patients with performance status (PS) = 0 (HR = 0.64; P = 0.013). Also overall survival was significantly superior in patients receiving the GP combination (HR = 0.81; P = 0.031). Again, patients with PS = 0 appeared to have a greater benefit from treatment intensification (HR = 0.72; P = 0.063).

Conclusion: The pooled analysis of the GERCOR/GISCAD intergroup study and the German multicenter study indicates that the combination of gemcitabine with a platinum analog such as oxaliplatin or cisplatin significantly improves progression-free survival and overall survival as compared to single-agent gemcitabine in advanced pancreatic cancer. The benefit seems to prevail in patients with a good performance status.

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Patients With Curative Resection of cT3-4 Rectal Cancer After Preoperative Radiotherapy or Radiochemotherapy: Does Anybody Benefit From Adjuvant Fluorouracil-Based Chemotherapy? A Trial of the European Organisation for Research and Treatment of Cancer Radiation Oncology Group

Laurence Collette, Jean-Francois Bosset, Marcel den Dulk, France Nguyen, Laurent Mineur, Philippe Maingon, Ljiljana Radosevic-Jelic, Marianne Piérart, Gilles Calais

Statistics Department, European Organisation for Research and Treatment of Cancer Data Center, Brussels, Belgium; Department of Radiation Therapy, University of Franche-Comté, Besançon; Department of Radiation Therapy, Clinic Sainte-Catherine, Avignon; Department of Radiation Therapy, Cancer Center Dijon, Dijon; Department of Radiation Therapy, University François Rabelais, Tours, France; Department of Surgery, Leiden University Medical Center, Leiden, the Netherlands; and Institute for Oncology and Radiology, Belgrad, Serbia

Journal of Clinical Oncology 2007; Volume 25, Number 28, October 1: Pages 4379-4386

Purpose: European Organisation for Research and Treatment of Cancer (EORTC) trial 22921 compared adjuvant fluorouracil-based chemotherapy (CT) to no adjuvant treatment in a 2 x 2 factorial trial with randomization for preoperative (chemo)radiotherapy in patients with resectable T3-4 rectal cancer. The results showed no significant impact of adjuvant CT on progression-free or overall survival, although a difference seemed to emerge at approximately, respectively, 2 and 5 years after the start of preoperative treatment. We further explored the data with the aim of refining our understanding of the long-term results.

Patients and Methods: Data of 785 of the 1,011 randomly assigned patients who whose disease was M0 at curative surgery were used. Using meta-analytic methods, we investigated the homogeneity of the effect of adjuvant CT on the time to relapse or death after surgery (disease-free survival [DFS]) and survival in patient subgroups.

Results: Although there was no statistically significant impact of adjuvant CT on DFS for the whole group ($P > .5$), the treatment effect differed significantly between the ypT0-2 and the ypT3-4 patients (heterogeneity $P = .009$): only the ypT0-2 patients seemed to benefit from adjuvant CT ($P = .011$). The same pattern was observed for overall survival.

Conclusion: Exploratory analyses suggest that only good-prognosis patients (ypT0-2) benefit from adjuvant CT. This could explain why, in the whole group, the progression-free and overall survival diverged only after the poor-prognosis patients (ypT3-4) had experienced treatment failure. Patients in whom no downstaging was achieved did not benefit. This also suggests that the same prognostic factors may drive both tumor sensitivity for the primary treatment and long-term clinical benefit from further adjuvant CT.

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APPUNTAMENTI

FOCUS IN ONCOLOGIA
Dagli Off label alla gestione del File F in oncologia
Melegnano, 22 novembre 2007 - Azienda Ospedaliera Melegnano
Per scaricare il programma consulta il sito web: www.medinews.it (Società Scientifiche-AIOM-Appuntamenti)

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X INTERNATIONAL SYMPOSIUM ON PLATINUM COORDINATION COMPOUNDS IN CANCER CHEMOTHERAPY
Verona, 30 novembre-3 dicembre 2007 - Palazzo della Gran Guardia, Piazza Brà
Organizzazione: Department of Oncology Mater Salutis Hospital Legnago, Department of Medicine and Public Health, Section of Pharmacology University of Verona, *in collaborazione con* Sendo, South Europe New Drug Organization
Segreteria Scientifica: infotiscali@ispcc2007.org
Per scaricare il programma consulta il sito web: www.ispcc2007.org

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1° CONVEGNO NAZIONALE MULTIDISCIPLINARE DI MEDICINA
Convegno di Oncologia: "Prevenzione, Diagnosi, Stadiazione, Terapia e Supporto Psicologico al malato e ai parenti per tumori del Colon Rettale, Polmoni e Mammella"
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