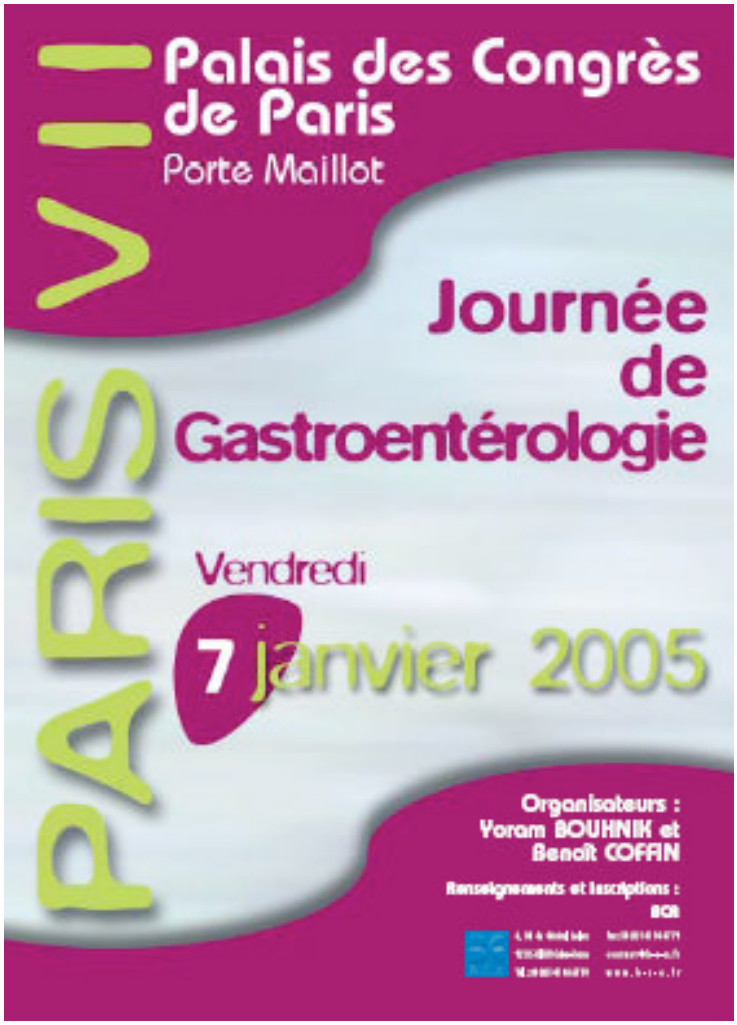

LES 5 ARTICLES 2004 QUI CHANGENT LA PRATIQUE

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Andre T, Boni C, Mounedji-Boudiaf L, Navarro M, Tabernero J, Hickish T, Topham C, Zaninelli M, Clingan P, Bridgewater J, Tabah-Fisch I, de Gramont A; Multicenter International Study of Oxaliplatin/5-Fluorouracil/Leucovorin in the Adjuvant Treatment of Colon Cancer (MOSAIC) Investigators.

Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer.

N Engl J Med. 2004 3;350:2343-51.

BACKGROUND: The standard adjuvant treatment of colon cancer is fluorouracil plus leucovorin (FL). Oxaliplatin improves the efficacy of this combination in patients with metastatic colorectal cancer. We evaluated the efficacy of treatment with FL plus oxaliplatin in the postoperative adjuvant setting.

METHODS: We randomly assigned 2246 patients who had undergone curative resection for stage II or III colon cancer to receive FL alone or with oxaliplatin for six months. The primary end point was disease-free survival.

RESULTS: A total of 1123 patients were randomly assigned to each group. After a median follow-up of 37.9 months, 237 patients in the group given FL plus oxaliplatin had had a cancer-related event, as compared with 293 patients in the FL group (21.1 percent vs. 26.1 percent; hazard ratio for recurrence, 0.77; P=0.002). The rate of disease-free survival at three years was 78.2 percent (95 percent confidence interval, 75.6 to 80.7) in the group given FL plus oxaliplatin and 72.9 percent (95 percent confidence interval, 70.2 to 75.7) in the FL group (P=0.002 by the stratified log-rank test). In the group given FL plus oxaliplatin, the incidence of febrile neutropenia was 1.8 percent, the incidence of gastrointestinal adverse effects was low, and the incidence of grade 3 sensory neuropathy was 12.4 percent during treatment, decreasing to 1.1 percent at one year of follow-up. Six patients in each group died during treatment (death rate, 0.5 percent).

CONCLUSIONS: Adding oxaliplatin to a regimen of fluorouracil and leucovorin improves the adjuvant treatment of colon cancer.

Cunningham D, Humblet Y, Siena S, Khayat D, Bleiberg H, Santoro A, Bets D, Mueser M, Harstrick A, Verslype C, Chau I, Van Cutsem E.

Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer.

N Engl J Med. 2004 22;351:337-45.

BACKGROUND: The epidermal growth factor receptor (EGFR), which participates in signaling pathways that are deregulated in cancer cells, commonly appears on colorectal-cancer cells. Cetuximab is a monoclonal antibody that specifically blocks the EGFR. We compared the efficacy of cetuximab in combination with irinotecan with that of cetuximab alone in metastatic colorectal cancer that was refractory to treatment with irinotecan.
METHODS: We randomly assigned 329 patients whose disease had progressed during or within three months after treatment with an irinotecan-based regimen to receive either cetuximab and irinotecan (at the same dose and schedule as in a prestudy regimen [218 patients]) or cetuximab monotherapy (111 patients). In cases of disease progression, the addition of irinotecan to cetuximab monotherapy was permitted. The patients were evaluated radiologically for tumor response and were also evaluated for the time to tumor progression, survival, and side effects of treatment.
RESULTS: The rate of response in the combination-therapy group was significantly higher than that in the monotherapy group (22.9 percent [95 percent confidence interval, 17.5 to 29.1 percent] vs. 10.8 percent [95 percent confidence interval, 5.7 to 18.1 percent], P=0.007). The median time to progression was significantly greater in the combination-therapy group (4.1 vs. 1.5 months, P<0.001 by the log-rank test). The median survival time was 8.6 months in the combination-therapy group and 6.9 months in the monotherapy group (P=0.48). Toxic effects were more frequent in the combination-therapy group, but their severity and incidence were similar to those that would be expected with irinotecan alone.
CONCLUSIONS: Cetuximab has clinically significant activity when given alone or in combination with irinotecan in patients with irinotecan-refractory colorectal cancer.

Isenmann R, Runzi M, Kron M, Kahl S, Kraus D, Jung N, Maier L, Malfertheiner P, Goebell H, Beger HG; German Antibiotics in Severe Acute Pancreatitis Study Group.

Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: a placebo-controlled, double-blind trial.

Gastroenterology. 2004;126:997-1004.

BACKGROUND & AIMS: Antibiotic prophylaxis in necrotizing pancreatitis remains controversial. Until now, there have been no double-blind studies dealing with this topic. METHODS: A total sample size of 200 patients was calculated to demonstrate with a power of 90% that antibiotic prophylaxis reduces the proportion of patients with infected pancreatic necrosis from 40% placebo (PLA) to 20% ciprofloxacin/metronidazole (CIP/MET). One hundred fourteen patients with acute pancreatitis in combination with a serum C-reactive protein exceeding 150 mg/L and/or necrosis on contrast-enhanced CT scan were enrolled and received either intravenous CIP (2 x 400 mg/day) + MET (2 x 500 mg/day) or PLA. Study medication was discontinued and switched to open antibiotic treatment when infectious complications, multiple organ failure sepsis, or systemic inflammatory response syndrome (SIRS) occurred. After half of the planned sample size was recruited, an adaptive interim analysis was performed, and recruitment was stopped.
RESULTS: Fifty-eight patients received CIP/MET and 56 patients PLA. Twenty-eight percent in the CIP/MET group required open antibiotic treatment vs. 46% with PLA. Twelve percent of the CIP/MET group developed infected pancreatic necrosis compared with 9% of the PLA group (P = 0.585). Mortality was 5% in the CIP/MET and 7% in the PLA group. In 76 patients with pancreatic necrosis on contrast-enhanced CT scan, no differences in the rate of infected pancreatic necrosis, systemic complications, or mortality were observed.
CONCLUSIONS: This study detected no benefit of antibiotic prophylaxis with respect to the risk of developing infected pancreatic necrosis.

Hammer J, Eslick GD, Howell SC, Altiparmak E, Talley NJ.

Diagnostic yield of alarm features in irritable bowel syndrome and functional dyspepsia.

Gut. 2004;53:666-72.

OBJECTIVE: The diagnostic value of the addition of alarm symptoms in distinguishing functional from organic gastrointestinal disease remains uncertain. We aimed to establish the value of alarm features in differentiating between organic disease and irritable bowel syndrome (IBS) and functional dyspepsia (FD).

METHODS: A total of 568 consecutive patients (63% female; mean age 44.7 years) completed a detailed symptom questionnaire and then received a complete diagnostic workup, as required. Questionnaire data were collected prospectively and audited retrospectively; the treating physician was blinded to the results of the questionnaires. Patients were coded and allocated to the following diagnostic groups: IBS, FD, organic diseases of the upper gastrointestinal tract, or organic diseases of the lower gastrointestinal tract. Logistic regression was used to identify the best subset of symptoms that discriminated organic disease from functional illness. Separate models compared IBS (n = 214) with diseases of the lower gastrointestinal tract (n = 66), and FD (n = 70) with diseases of the upper gastrointestinal tract (n = 250).

RESULTS: Age (50 years at symptom onset: odds ratio (OR) 2.65 (95% confidence interval 1.4-5.0); p = 0.002) and blood on the toilet paper (OR 2.7 (1.4-5.1);p = 0.002) emerged as alarm features that discriminated IBS from lower gastrointestinal illness. A diagnosis of IBS was typically associated with female sex (OR2.5 (1.3-4.6); p = 0.004), pain on six or more occasions in the previous year (OR 5.0 (2.2-11.1); p<0.001), pain that radiated outside of the abdomen (OR 2.9 (1.4-6.3); p = 0.006), and pain associated with looser bowel motions (OR 2.1 (1.1-4.2); p = 0.03). A model incorporating three Manning criteria and alarm features yielded a correct diagnosis of IBS in 96% and a correct diagnosis of organic disease in 52% of cases. Alarm features did not discriminate FD from upper gastrointestinal disease. Patients with FD were significantly more likely to report upper abdominal pain (OR 3.7 (1.7-8.3); p = 0.002) and significantly less likely to report aspirin use (OR 0.26 (0.1-0.6); p = 0.001). The predictive value of symptoms in diagnosing FD was only 17%.

CONCLUSIONS: Symptoms plus alarm features have a high predictive value for diagnosing IBS but the predictive value for a diagnosis of FD remains poor. Current criteria for the diagnosis of IBS should incorporate relevant alarm features to improve the diagnostic yield.

Hanauer SB, Korelitz BI, Rutgeerts P, Peppercorn MA, Thisted RA, Cohen RD, Present DH.

Postoperative maintenance of Crohn's disease remission with 6-ercaptopurine, mesalamine, or placebo: a 2-year trial.

Gastroenterology. 2004;127:723-9.

BACKGROUND & AIMS: No therapy has been shown to reliably prevent the evolution of postoperative recurrence of Crohn's disease. The aim of the current trial was to compare 6-mercaptopurine (6-MP) and mesalamine with placebo for the prevention of clinical, endoscopic, and radiographic recurrence of Crohn's disease after resection and ileocolic anastomosis.

METHODS: Five centers randomized 131 patients to receive 6-MP (50 mg), mesalamine (3 g), or placebo daily in a double-blind, double-dummy trial. Patients had clinical assessments at 7 weeks and then every 3 months; colonoscopy at 6, 12, and 24 months; and small bowel series at 12 and 24 months. End points were clinical, endoscopic, and radiographic recurrence rates at 24 months.

RESULTS: Clinical recurrence rates (intent to treat) by life-table analysis at 24 months were 50% (95% confidence interval [CI], 34%-68%), 58% (95% CI, 41%-75%), and 77% (95% CI, 61%-91%) in patients receiving 6-MP, mesalamine, and placebo, respectively. Endoscopic recurrence rates were 43% (95% CI, 28%-63%), 63% (95% CI, 47%-79%), and 64% (95% CI, 46%-81%), and radiographic recurrence rates were 33% (95% CI, 19%-54%), 46% (95% CI, 29%-66%), and 49% (95% CI, 30%-72%), respectively. 6-MP was more effective than placebo ($P < 0.05$) at preventing clinical and endoscopic recurrence over 2 years. Patient withdrawals resulted in 69% of the study population evaluable for the clinical recurrence end point.

CONCLUSIONS: 6-MP, 50 mg daily, was more effective than placebo at preventing postoperative recurrence of Crohn's disease and should be considered as a maintenance therapy after ileocolic resection.

Ardizzone S, Maconi G, Sampietro GM, Russo A, Radice E, Colombo E, Imbesi V, Molteni M, Danelli PG, Taschieri AM, Bianchi Porro G.

Azathioprine and mesalamine for prevention of relapse after conservative surgery for Crohn's disease.

Gastroenterology. 2004;127:730-40

BACKGROUND & AIMS: Because the reoperation rate for Crohn's disease is high after resective surgery, use of conservative surgery has increased. Mesalamine was investigated for the prevention of postoperative relapse, with disappointing results. The role of azathioprine in the postoperative setting is unknown. We aimed to compare the efficacy and safety of azathioprine and mesalamine in the prevention of clinical and surgical relapse in patients who have undergone conservative surgery for Crohn's disease.
METHODS: In a prospective, open-label, randomized study, 142 patients received azathioprine (2 mg. kg -1. day -1) or mesalamine (3 g/day) for 24 months. Clinical relapse was defined as the presence of symptoms with a Crohn's Disease Activity Index score >200 and surgical relapse as the presence of symptoms refractory to medical treatment or complications requiring surgery.
RESULTS: After 24 months, the risk of clinical relapse was comparable in the azathioprine and mesalamine groups, both on intention-to-treat (odds ratio [OR], 2.04; 95% confidence interval [CI], 0.89-4.67) and per-protocol analyses (OR, 1.79; 95% CI, 0.80-3.97). No difference was observed with respect to surgical relapse at 24 months between the 2 groups. In a subgroup analysis, azathioprine was more effective than mesalamine in preventing clinical relapse in patients with previous intestinal resections (OR, 4.83; 95% CI, 1.47-15.8). More patients receiving azathioprine withdrew from treatment due to adverse events than those receiving mesalamine (22% vs. 8%; P = 0.04).
CONCLUSIONS: While no difference was observed in the efficacy of azathioprine and mesalamine in preventing clinical and surgical relapses after conservative surgery, azathioprine is more effective in those patients who have undergone previous intestinal resection.

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