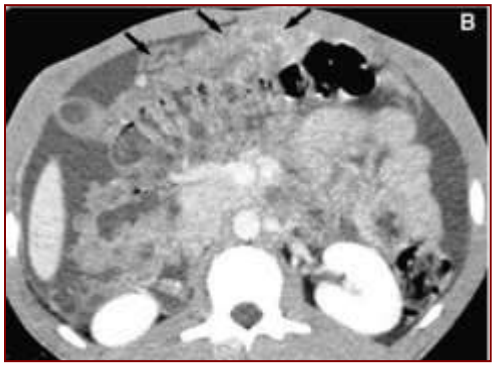
Is prophylactic HIPEC after colorectal cancer surgery the right strategy?

Management of Peritoneal Surface Malignancy

Irkutsk, Sibiria

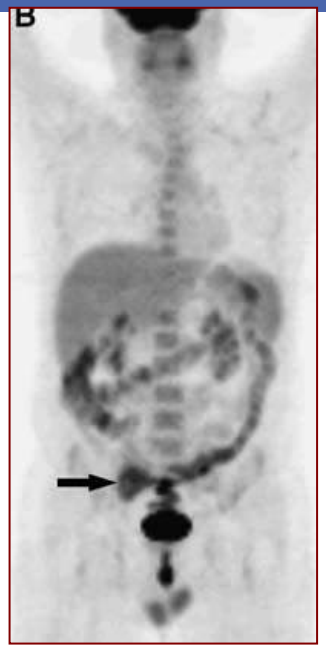
F.Quénet
ICM Montpellier
France

Preoperative assesment of PC



CT scan : Sensitivity: 60-79%

Pet-Scan : Se 57%



Under-estimation of the extent of desease
Sensitivity < 30% if < 0,5mm

PC diagnosed preoperatively in 55% of cases

Jacquet et al. Cancer 1993
De Bree et al. J S urg Oncol 2004
Dromain et al. Abdom Imaging 2008

Results of Systematic Second-look Surgery Plus HIPEC in Asymptomatic Patients Presenting a High Risk of Developing Colorectal Peritoneal Carcinomatosis

D Elias, MD, PhD, C Honoré, MD,* F Dumont, MD,* M. Ducreux, MD, PhD,† V. Boige, MD, PhD,† D. Malka, MD, PhD,† P. Burtin, MD,† C. Dromain, MD,‡ and D. Goéré, MD**

Ann Surg 2011;254:289–293

A macroscopic PC was found and treated in 23/41 patients, **(56%)**

Initial PC (n=25)	Ovarian Metastasis (n=8)	Perforation (n=8)
62%	60%	37%

- Mortality 2%
- Morbidity (grade III/IV) 10%.
- Mean hospital stay 21days

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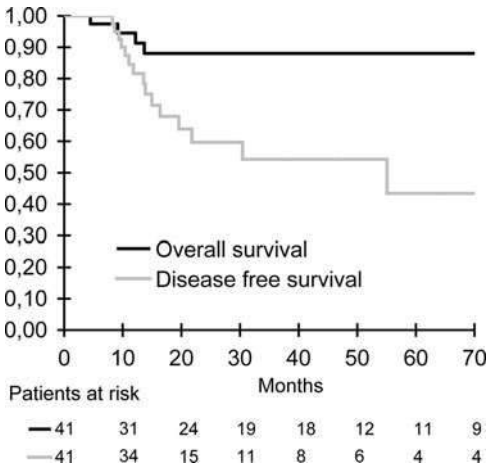
Annals of Surgery • Volume 254, Number 2, August 2011

- Median OS was not reached
- 5-year OS rate : 90%
- 5-year RFS rate : 44%
- 7 out of the 41 patients (17%) relapsed in the peritoneum
  - 1 patient in the PC0 group (6%)
  - 6 in the PC + group (26%) (*P* = 0.006).



Median follow up : 30 months

Ninety percent of the adverse outcomes occur in 10% of patients: can we identify the populations at high risk of developing peritoneal metastases after curative surgery for colorectal cancer?

Charles Honoré, Maximiliano Gelli, Julie Francoual, Léonor Benhaim, Dominique Elias & Diane Goéré

The search strategy identified 259 new articles to add to the 6522 articles initially analysed…

Synchronous peritoneal metastases
(completely resected during the primary tumour surgery)

- Unexpected synchronous PM are discovered peroperatively in 4.8 –7.3% of patients with colorectal cancer scheduled for surgery.
- Recurrent PM rate is estimated between 54% and 71% at 1year with a high level of evidence

Ch Honoré 2017

Synchronous ovarian metastasis

- Unexpected synchronous ovarian metastases are synchronously found in 0.8–7.4%
- But are associated with synchronous PM in 29–72% of the cases
- the rate of recurrent PM in patients with isolated synchronous ovarian metastases is estimated between 62% and 71% at 1year with a high level of evidence (2b).

Perforated primary tumour

- The incidence of colorectal cancer presenting with a perforated primary tumour is ranging from 1.6% to 5.4%
- The incidence of recurrent PM after surgery for a perforated primary tumour is 27% at one year with a low level of evidence

Primary tumour with serosa and/or adjacent organ invasion

- T4 is found in 13.7% of all colorectal cancer

- The incidence of recurrent PM after surgery for a pT4 tumour is 15.6% at 1 year and 36.7% at 3 years with a low level of evidence (3a).

Mucinous histological subtype

- Mucinous adenocarcinoma and signet ring cell carcinoma (SRC) account, respectively, for 3–15% and for 0.1–2.4%

- Recurrent PM in patients with MA or with a mucinous/SRC component is estimated between 11% and 36% with a low level of evidence (3b).

Positive peritoneal cytology

- The incidence of positive peritoneal cytology, without distinguishing tumour stages and detecting methods, ranges between 2.2% and 52%

- The incidence of recurrent PM after surgery for colorectal cancer with positive peritoneal cytology is estimated between 0% and 36% with a very poor level of evidence (3b–4).

Original article

doi:10.1111/codi.12552

Individualized prediction of risk of metachronous peritoneal carcinomatosis from colorectal cancer

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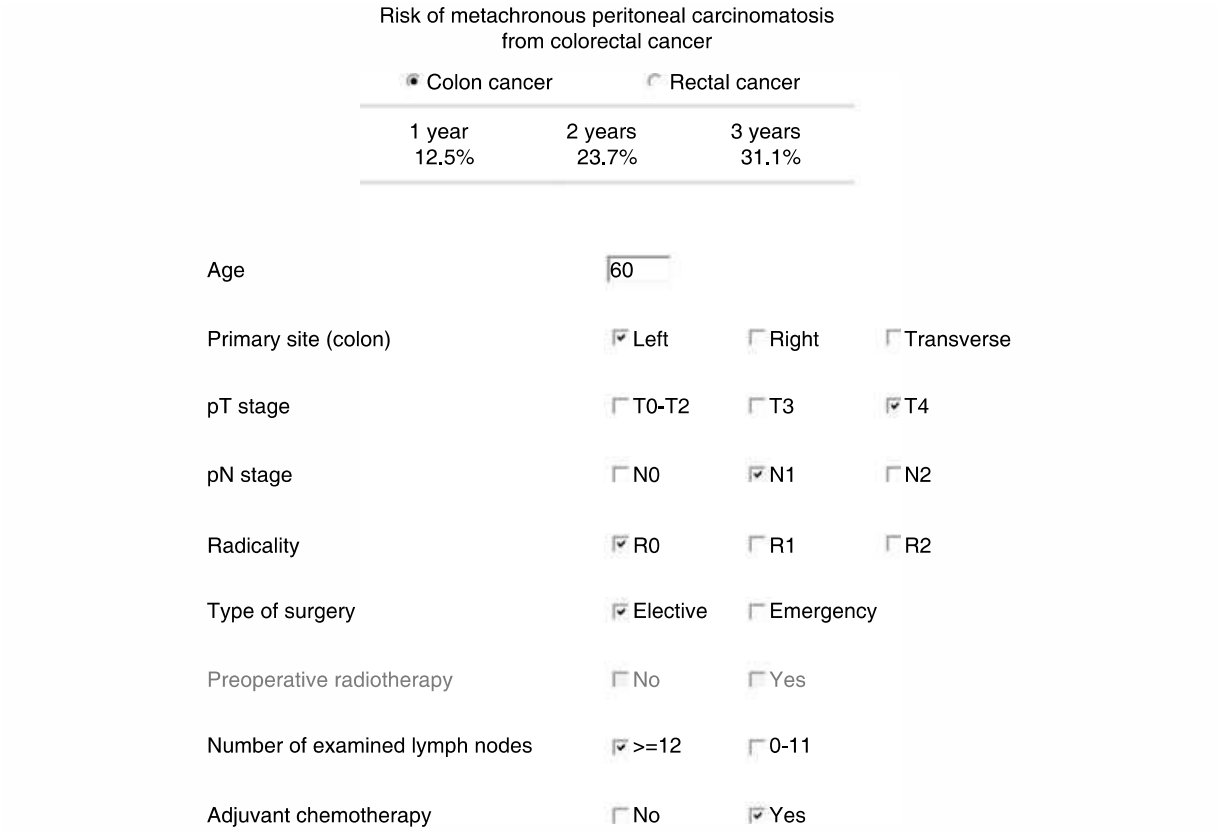


Figure 2 The web-calculator, equivalent to Tables 3 and 4, presents predicted probabilities of peritoneal recurrence after resection of Stage I–III colorectal cancer. http://www.imm.ki.se/biostatistics/calculators/pcrisk/.

Patients at risk

More than 40%

- Ovarian metastasis
- Resected localized PC
- Perforated tumors

8 to 30%

- T4 tumors
- Positive peritoneal cytology
- Obstructive or bleeding tumors
- Mucinous tumors

Honoré Ann Surg Oncol 2013

Standard risk patients

- No evidence of an increased incidence of recurrent PM was found in patient with
  - Bleeding primary tumours
  - occlusive primary tumours
  - invaded lymph node
  - after laparoscopic resection
- The running risk of PM is evaluated in this category between 3.4% and 6.3%

Clinical Study

Adjuvant Perioperative Intraperitoneal Chemotherapy in Locally Advanced Colorectal Carcinoma: Preliminary Results

A. A. K. Tentes,[1] I. D. Spiliotis,[2] O. S. Korakianitis,[3] A. Vaxevanidou,[4] and D. Kyziridis[1]

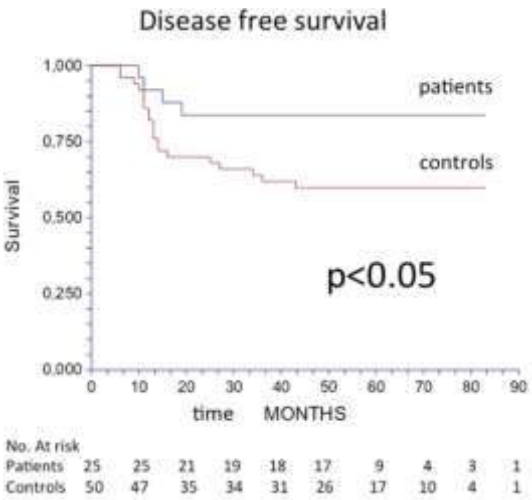
- HIPEC in 40 patients with a T3/T4 tumour without synchronous PM
- Recurrent PM rate of 0% after 17 months of median follow-up.

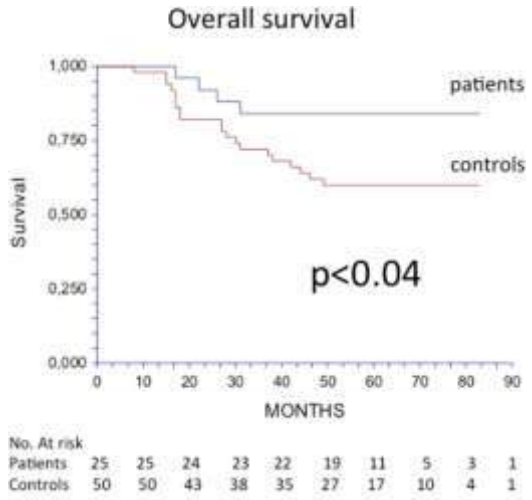
ISRN Surgery 2011

Long-term results after proactive management for locoregional control in patients with colonic cancer at high risk of peritoneal metastases

P. Sammartino · S. Sibio · D. Biacchi · M. Cardi · P. Mingazzini · M. S. Rosati · T. Cornali · B. Sollazzo · J. Maherfouad Atta · A. Di Giorgio

- 25 patients with a mucinous T3/T4 tumour without synchronous PM who underwent HIPEC were compared with 50 patients treated with standard surgical resection
- The peritoneal recurrence rate was significantly lower in the group that received HIPEC (4% vs. 22%)
- with similar overall recurrence rates (28% vs. 32%)





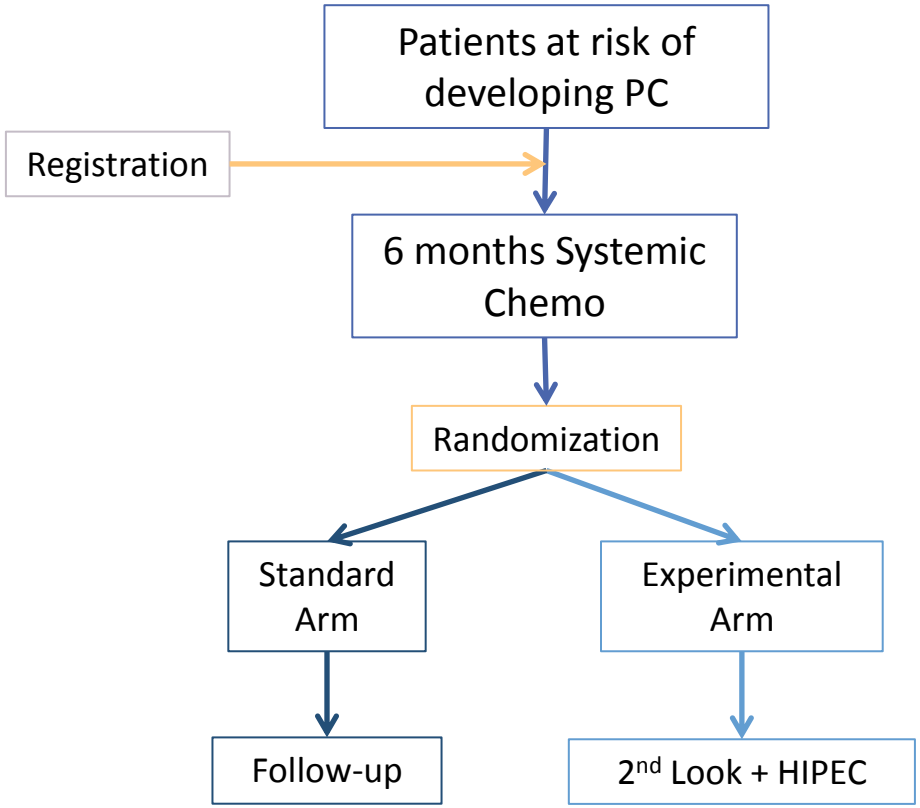
Int J Colorectal Dis (2014) 29:1081–1089

ProphyloCHIP TRIAL

Multicentric Phase III Trial Comparing
Simple Follow-up to Exploratory Laparotomy Plus "in Principle" HIPEC in Colorectal Patients Initially Treated With Surgery and Adjuvant Chemotherapy at High Risk of Developing Colorectal Peritoneal Carcinomatosis

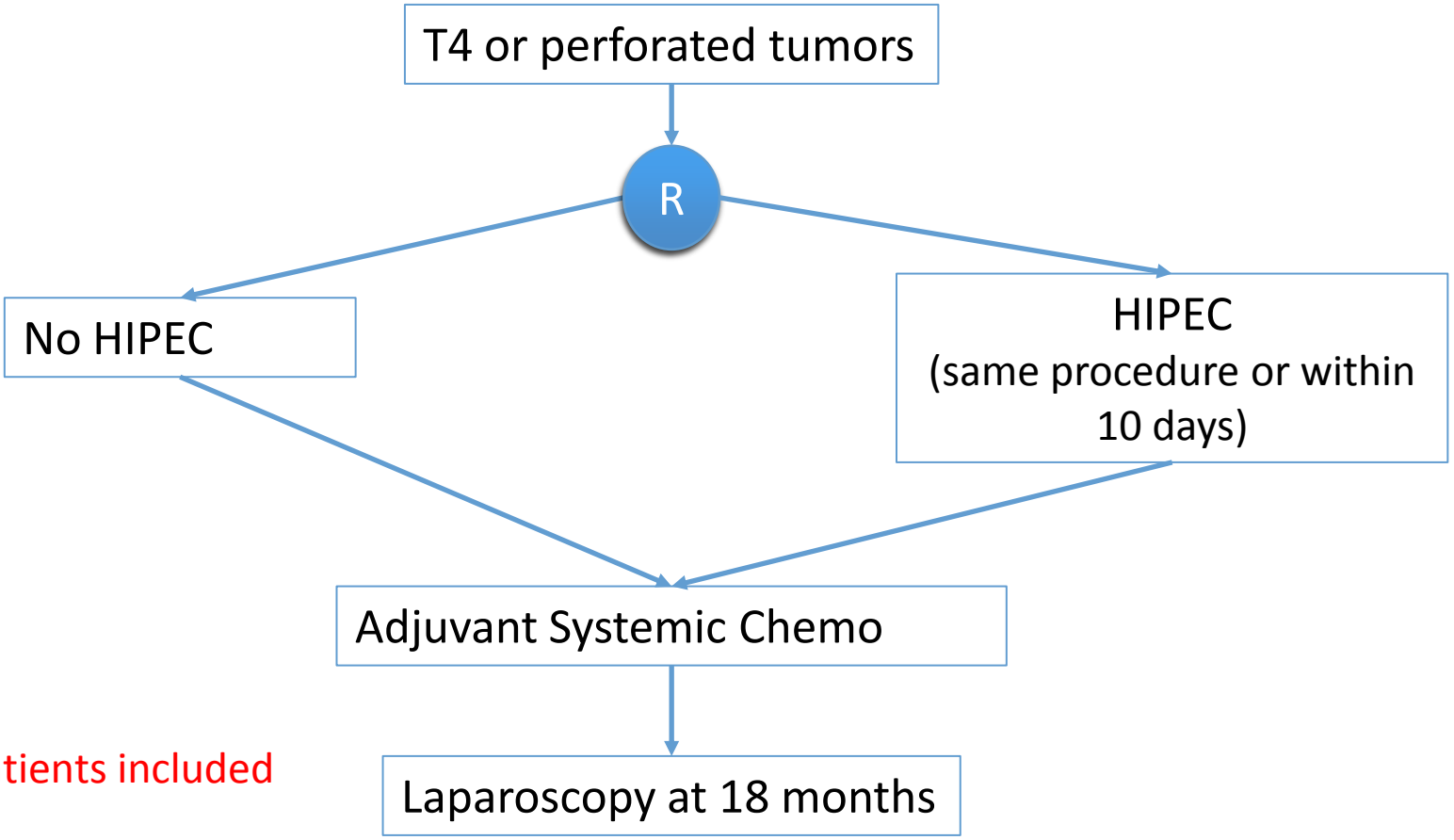
PI: D.Elias

ProphyloCHIP Trial Design



The Dutch Study: COLOPEC

PI: IH de Hingh



56/173 patients included

Conclusions

- Situations at higher risk of recurrent PM are
  - synchronous PM
  - synchronous isolated ovarian metastases
  - perforated primary tumour
  - tumour with serosa invasion
  - mucinous histological subtype

- Further studies are now required to evaluate effective means to prevent PC occurrence