

# Patient Selection and Work up for CRS and HIPEC

## Management of Peritoneal Surface Malignancy

**Irkutsk, Sibiria**


F.Quénet  
ICM Montpellier  
France

# CRS & HIPEC



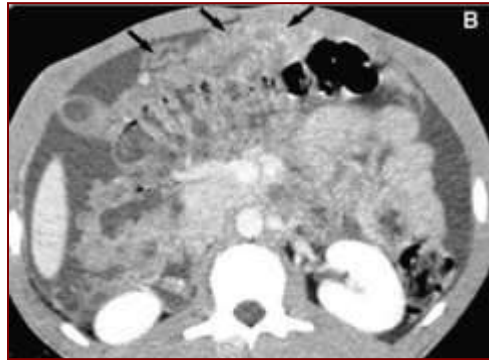
## General Contra-Indications

- Absolute
  - Age > 75
  - Poor general status
  - Co-morbidities
- Relative
  - Bowel obstruction by more than one stenosis



There is not any example of a peritoneal malignancy in which  
completeness of cytoreduction  
is not  
the strongest prognostic factor

# Preoperative assessment



**CT scan : Sensitivity: 60-79%**

**Pet-Scan : Se 57%**

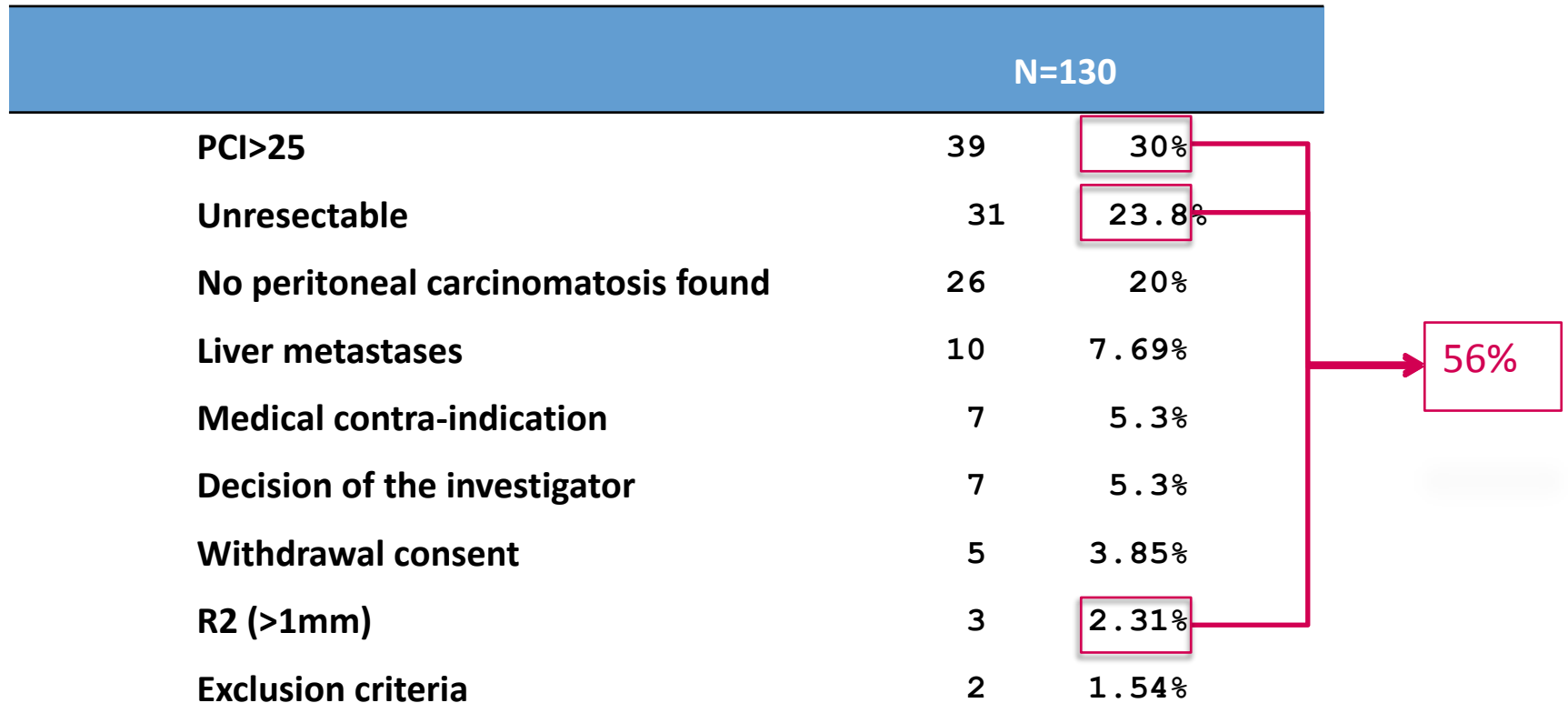


Under-estimation of the extent of disease  
Sensitivity < 30% if < 0,5mm

PC diagnosed preoperatively in 55% of cases

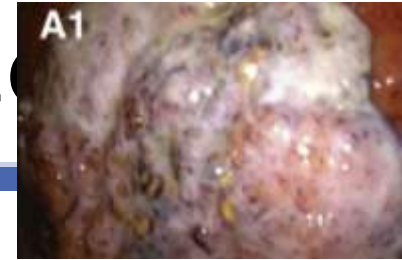
# PRODIGE 7: Non Randomized Patients

(population 264)



Non randomization rate : 33%

# Evaluation laparosc



**TABLE 2**

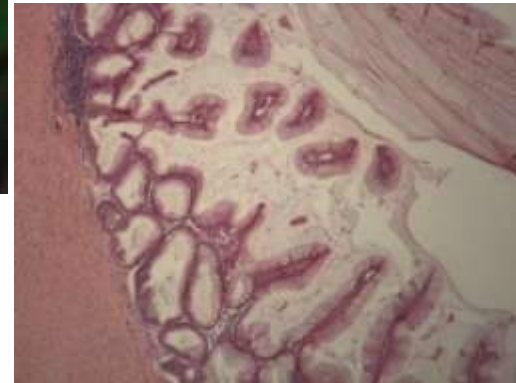
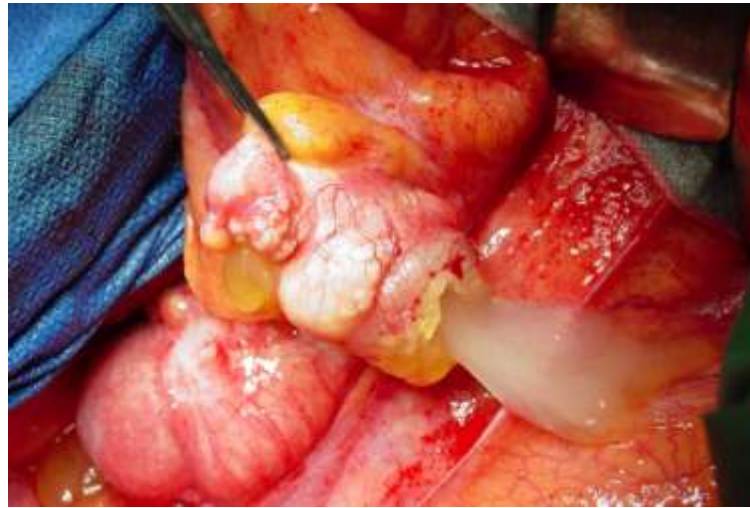
**Accuracy of laparoscopic assessment for each parameter (per-protocol analysis)**

Parameter	Not evaluable, n (%)	False positive, n (%)	False negative, n (%)	NPV, %	PPV, %	Specificity, %	Accuracy, n (%)	Cohen's kappa
Omental cake	3 (2.5)	5 (4.2)	2 (1.7)	95.8	92.8	90.2	110 (94.0)	0.878
Peritoneal carcinomatosis	1 (0.8)	15 (12.6)	1(0.8)	97.9	78.9	75.8	103 (86.5)	0.733
Diaphragmatic carcinomatosis	2 (1.6)	8 (6.7)	3 (2.5)	92.9	89.6	83.0	107 (90.7)	0.802
Mesenteral retraction	31 (25.8)	4 (4.4)	4 (4.4)	94.0	82.6	94.0	81 (91.0)	0.766
Bowel infiltration	12 (10.0)	8 (7.4)	11(10.1)	81.7	83.3	86.0	89 (82.4)	0.646
Stomach infiltration	8 (6.6)	4 (3.5)	3 (2.6)	97.0	63.6	96.1	105 (93.7)	0.632
Superficial liver metastasis	4 (3.3)	5 (4.3)	4 (3.4)	95.7	78.3	94.7	107 (92.2)	0.752

NPV, negative predictive value; PPV, positive predictive value.

Fagotti. Diagnostic accuracy of laparoscopy in advanced ovarian cancer. *Am J Obstet Gynecol* 2013.

# Pseudomyxoma peritonei



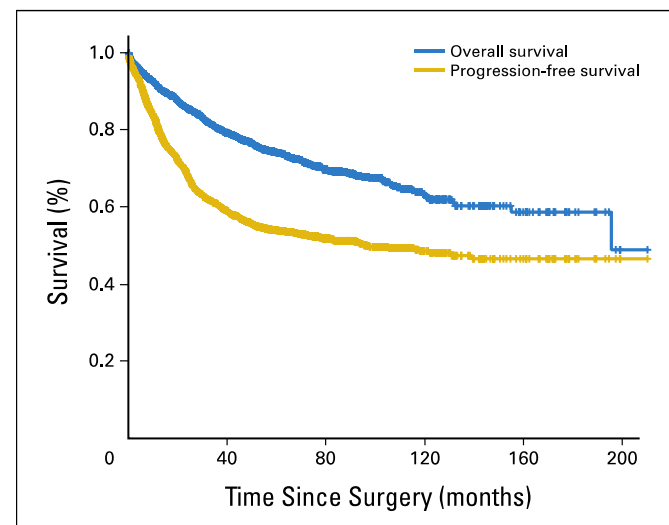
# Early- and Long-Term Outcome Data of Patients With Pseudomyxoma Peritonei From Appendiceal Origin Treated by a Strategy of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

Terence C. Chua, Brendan J. Moran, Paul H. Sugarbaker, Edward A. Levine, Olivier Glehen, François N. Gilly, Dario Baratti, Marcello Deraco, Dominique Elias, Armando Sardi, Winston Liauw, Tristan D. Yan, Pedro Barrios, Alberto Gómez Portilla, Ignace H.J.T. de Hingh, Wim P. Ceelen, Joerg O. Pelz, Pompiliu Piso, Santiago González-Moreno, Kurt Van Der Speeten, and David L. Morris

2298 patients from 16 specialized centres

- ☐ The median survival rate was 196 months (16.3 years)
- ☐ the median PFS rate was 98 months (8.2 years).
- ☐ The overall 5-, 10-, and 15-year survival rates were 74%, 63%, and 59%,

In Univariate & multivariate analysis, the use of HIPEC was associated with PFS (HR, 0.65;  $P < .030$ )

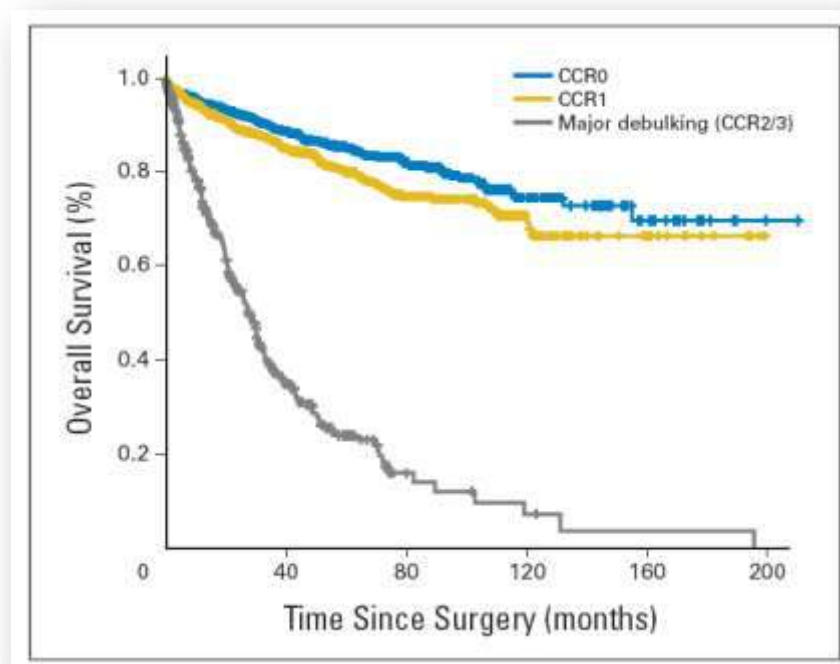


**Fig 1.** Overall survival and progression-free survival rates of 2,298 patients with appendiceal pseudomyxoma treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy.



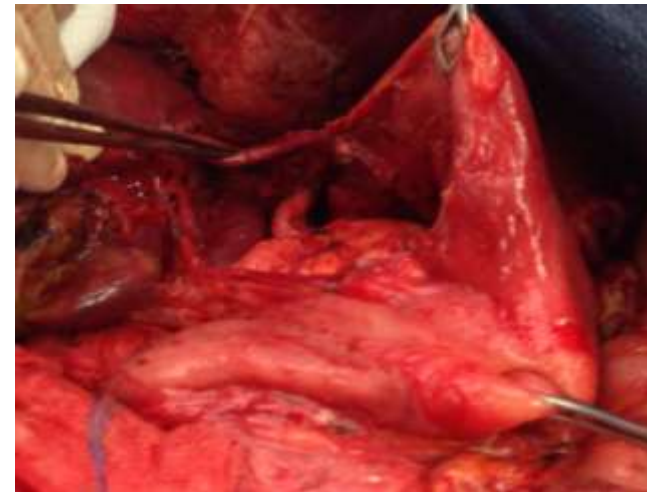
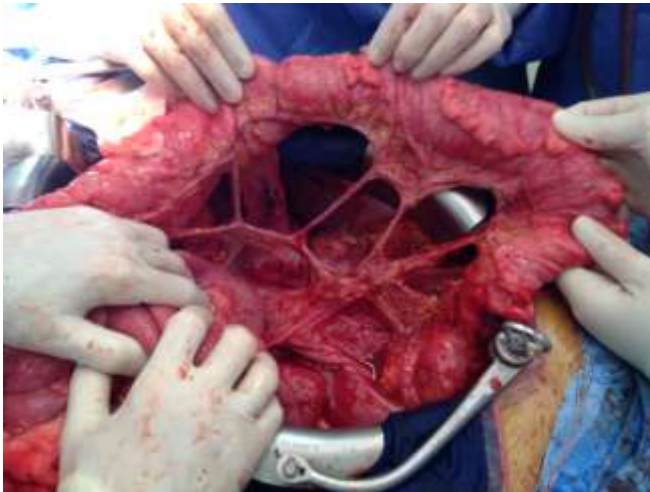
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# Visceral Preservation

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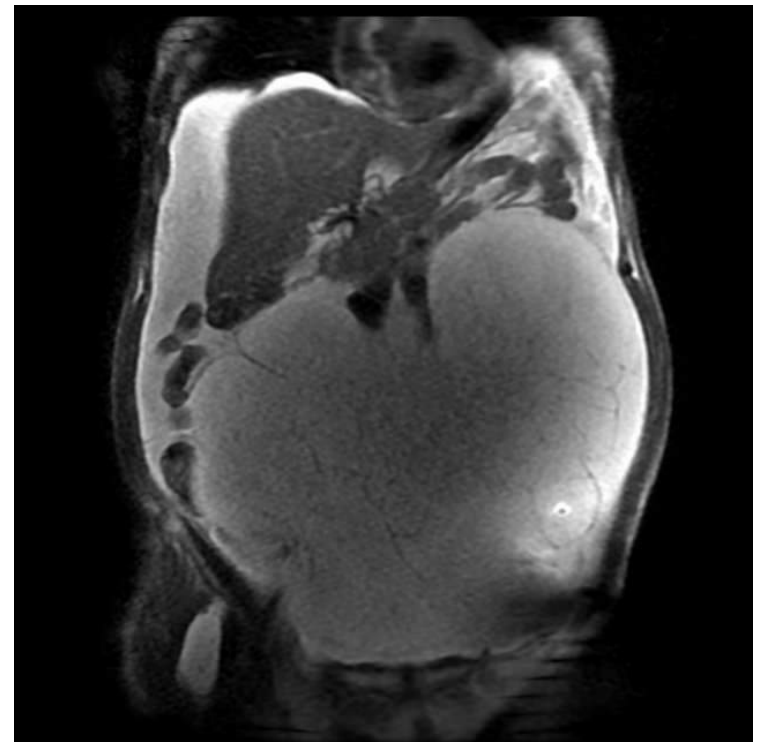


# Transplantation

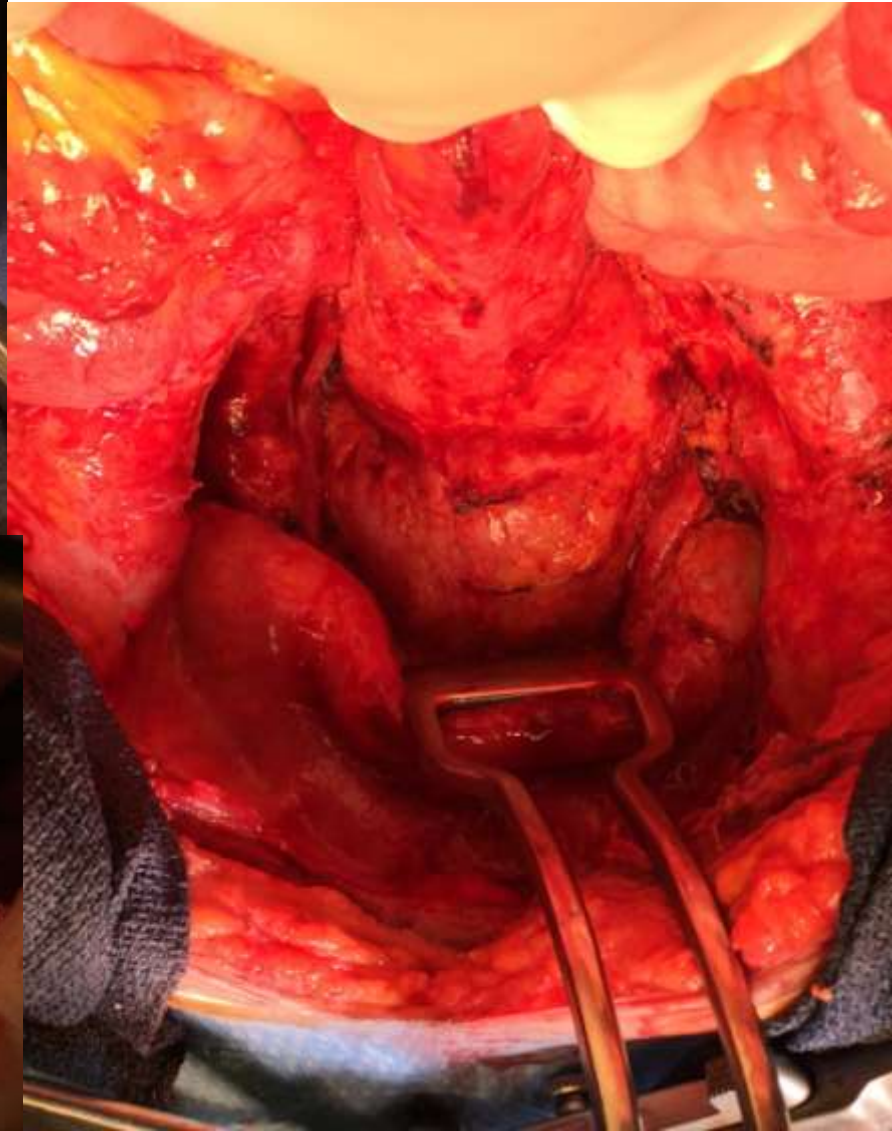


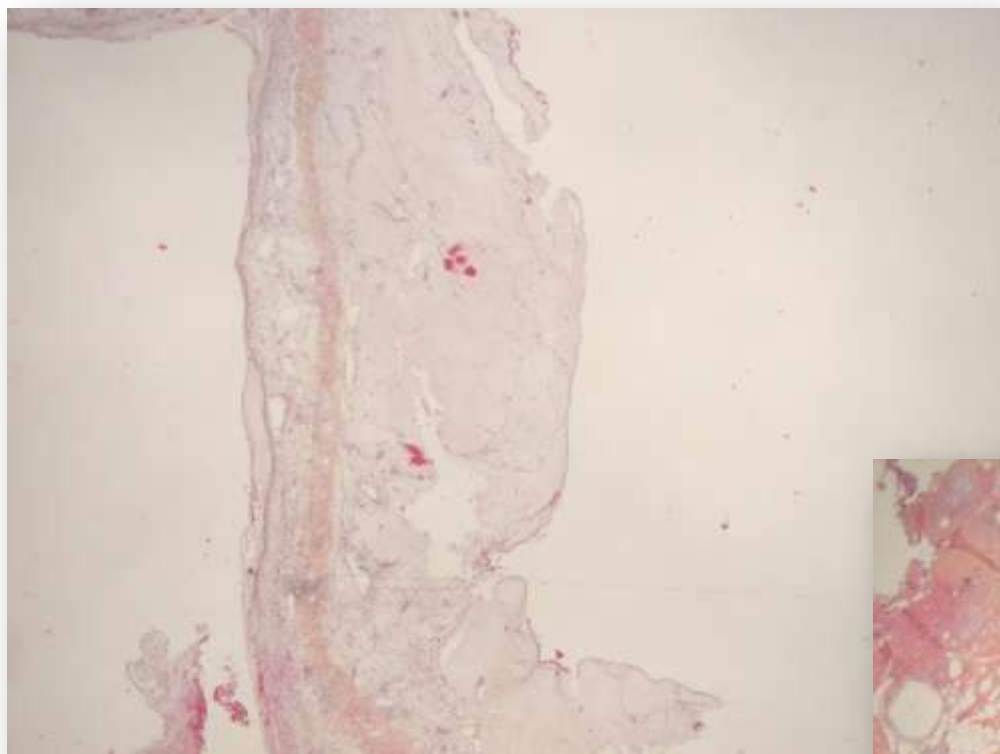
# PMP 2 Stage Resection

- JR, 62 ans
  - ♀
  - 06/2012: appendicectomie + résection bas fond caecal
  - Anapath: lésion mucineuse de bas grade
  - 12/2013: TDM ascite mucineuse
  - Evolution clinique: périmètre abdominal; compression veineuse; dénutrition, FEV 55%
  - 01/2014: évaluation pré CHIP

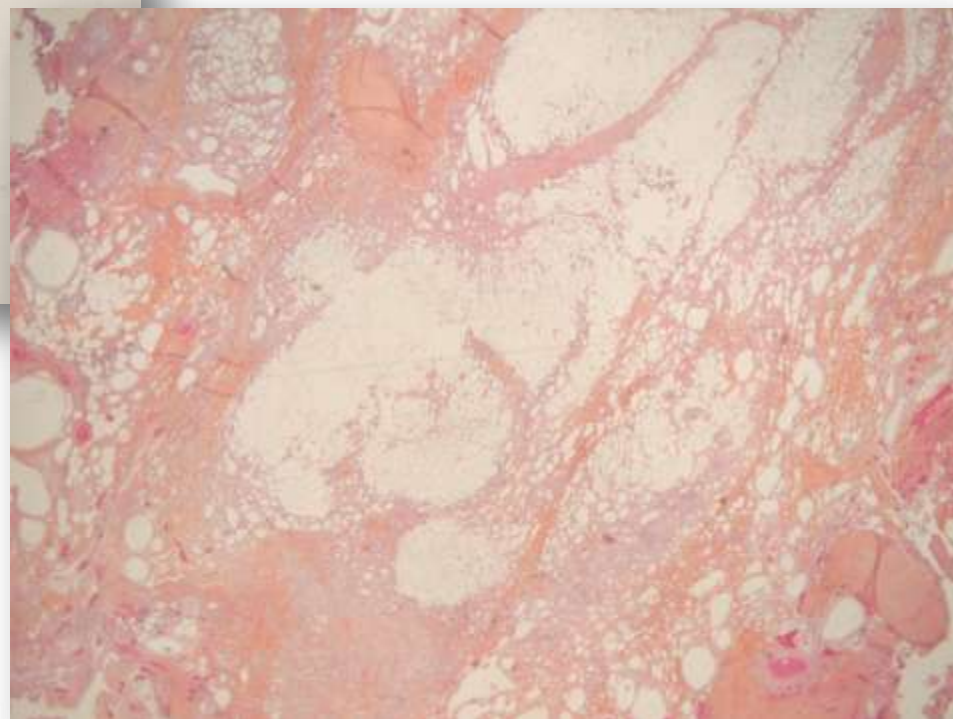








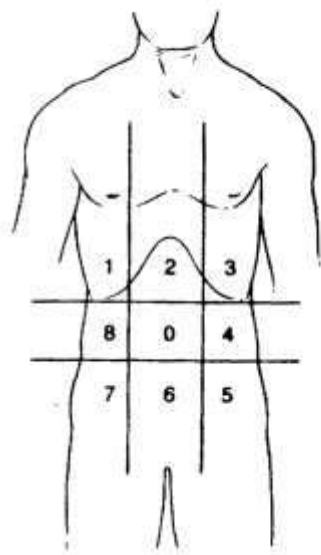
1<sup>st</sup> Stage



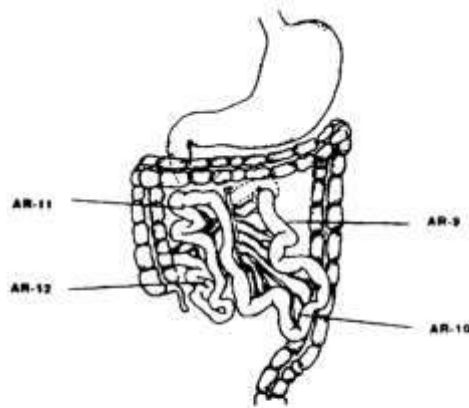
2<sup>d</sup> Stage



# Colo-rectal Carcinomatosis



- 0 Central
- 1 Right upper
- 2 Epigastrium
- 3 Left upper
- 4 Left flank
- 5 Left lower
- 6 Pelvis
- 7 Right lower
- 8 Right flank



# Survival Results

CRS & HIPEC is no Longer an Experimental Treatment

## ➤ Dutch Trial : 105 patients

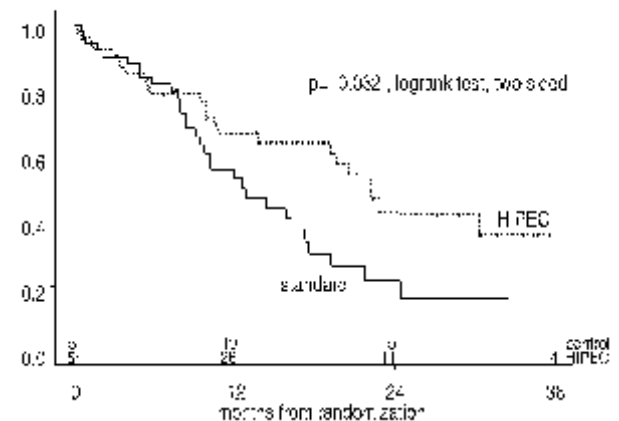
### ➤ Survival

- Standard arm: 12.6 months
- HIPEC : 22.4 months

### ➤ After a 8-year follow up : for R1,

- median OS 48 months
- 5-year survival rate 45%

CYTOREDUCTION AND HIPEC VERSUS CHEMOTHERAPY



## Median OS from 33 to 60 months

- Verwaal & al, JCO. 2005 / Ann. Surg. Oncol 2008)
- Elias & al, JCO. 2010 / JCO 2008
- Quénet & al, Ann Surg 2011
- Prada-Villaverde & al, Ann Surg Oncol 2014



# PRODIGE 7 : Mortality

30 days

Group	Days after resection	Cause of death
HIPEC	26	Pneumonia
HIPEC	10	Intra-peritoneal hæmorrhage
Non HIPEC	21	Sepsis + renal failure
Non HIPEC	12	Multivisceral failure

Mortality rate at 30 days : 1.5%

60 days

Group	Days after resection	Cause of death
HIPEC	37	Pulmonary embolism
Non HIPEC	60	Acute respiratory distress
HIPEC	61	Septic shock

Total mortality rate : 2.6%

# PRODIGE 7 : Morbidity at 30 days

Post-operative complications	HIPEC		No HIPEC		Total		p
	n	(%)	n	(%)	n	(%)	
All grades	87	65.4	73	55.3	160	60.4	0.092
Grades 3-4-5	54	40.6	41	31.1	95	35.9	NS

Global morbidity grade 3-5 : 35%

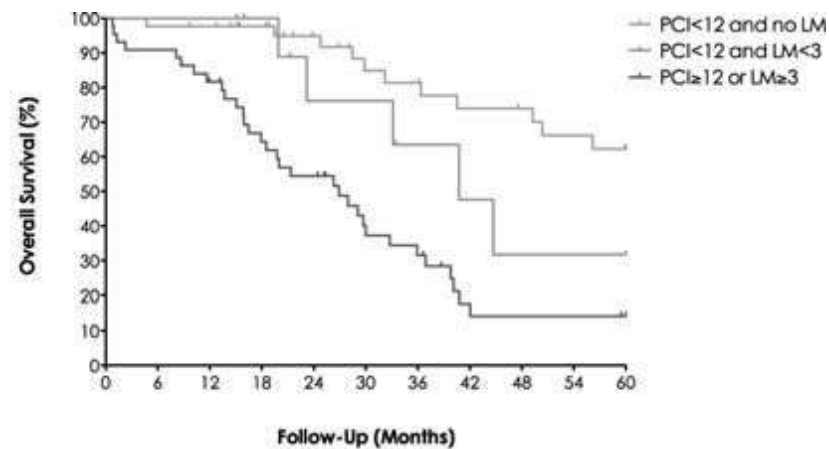
# Oncologic Contra-Indications...



- Retro-peritoneal involvement
  - One ureteral stenosis is not a CI
- Extra-abdominal Metastasis
  - PET-CT
  - Discussion métastase pulmonaire
  - Problème des métastases ganglionnaires rétropéritonéales

# Liver metastases

Groupe	Median OS (month)
PCI<12 no LM	76
PCI<12 1 or 2 LM	40
PCI<12 >3 LM	27



# Ovarian Metastasis



- Frequent
- Often resistant to systemic chemo
- Retro-peritoneal lymph node dissemination

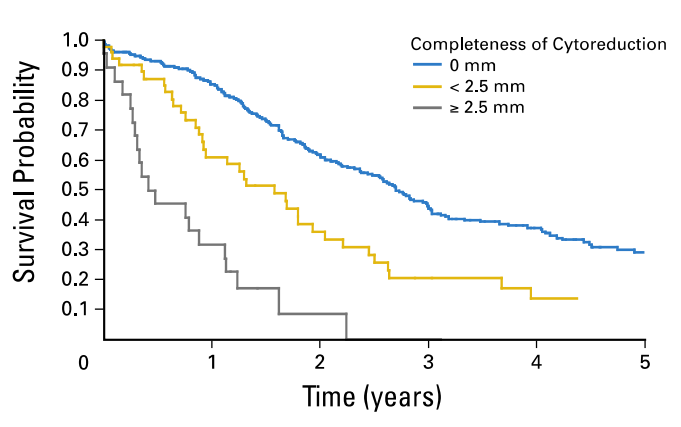
**Never a contra indication**

**Need to be resected before neoadjuvant chemo**

# In HIPEC Procedures, Which are the determining factors in improving survival ?

Complete CRS is probably the most important factor

## Completeness of cytoreduction



French Multicentric Study 523 patients



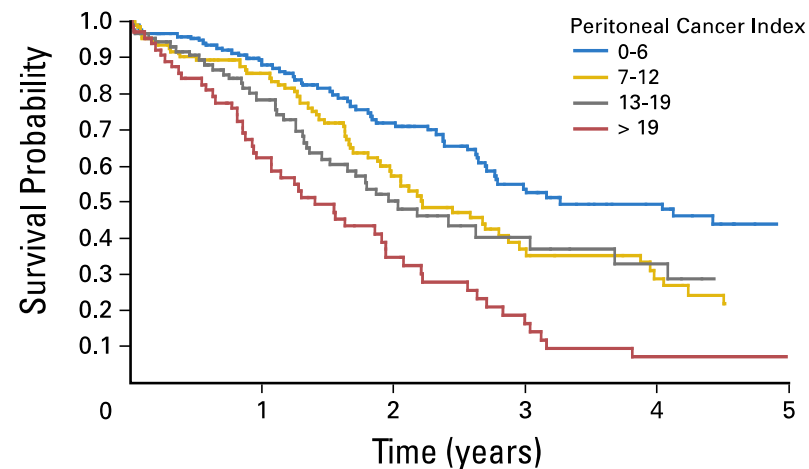
(D.Elias & al JCO 2010)

# In HIPEC Procedures,

Which are the determining factors in improving survival ?

PCI	5 years OS (%)
1-6	44
7-12	22
13-19	29
>19	7

Extent of peritoneal disease

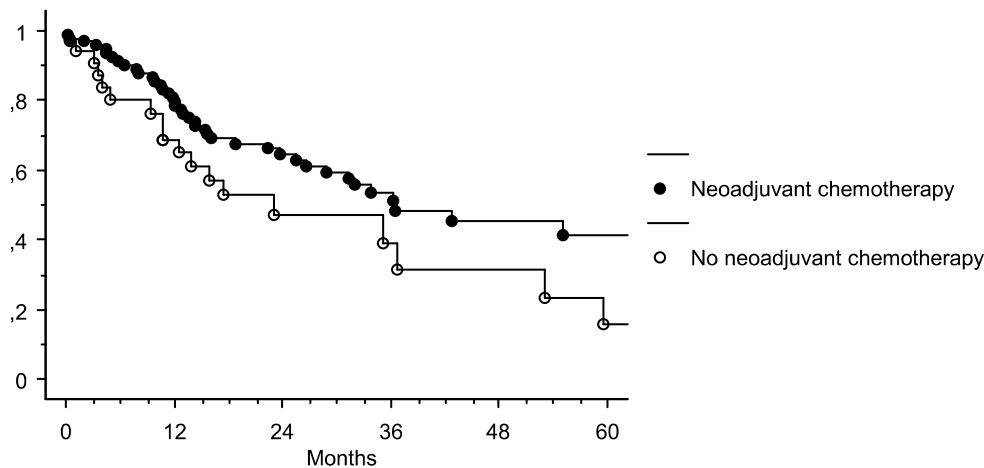


(D.Elias & al JCO 2010)

French Multicentric Study 523 patients

# Use of neoadjuvant chemotherapy

The use of neoadjuvant systemic chemotherapy was found to be a positive prognostic indicator ( $p=0.040$ )



Kaplan Meier survival distribution based on the use of neoadjuvant systemic chemotherapy



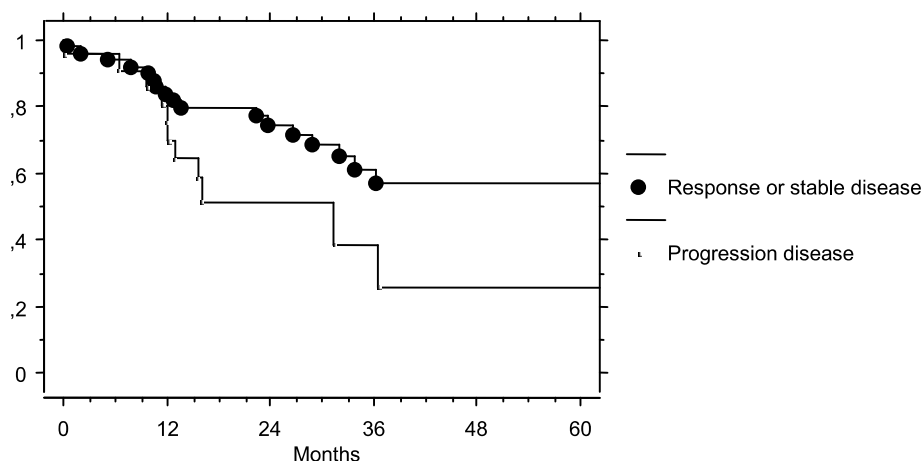
Impact on a microscopic metastatic dissemination ?



# Progression Following Neoadjuvant Systemic Chemotherapy May Not Be a Contraindication to a Curative Approach for Colorectal Carcinomatosis



120 patients



Kaplan Meier survival distribution based on the response to neoadjuvant systemic chemotherapy

Median OS : 36.2 mois

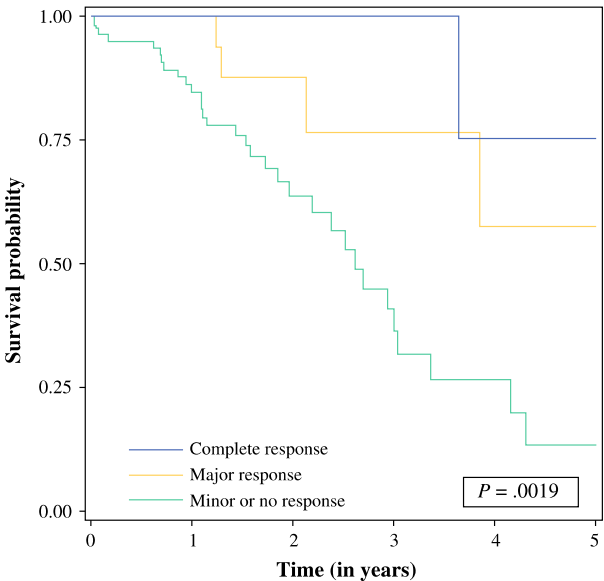
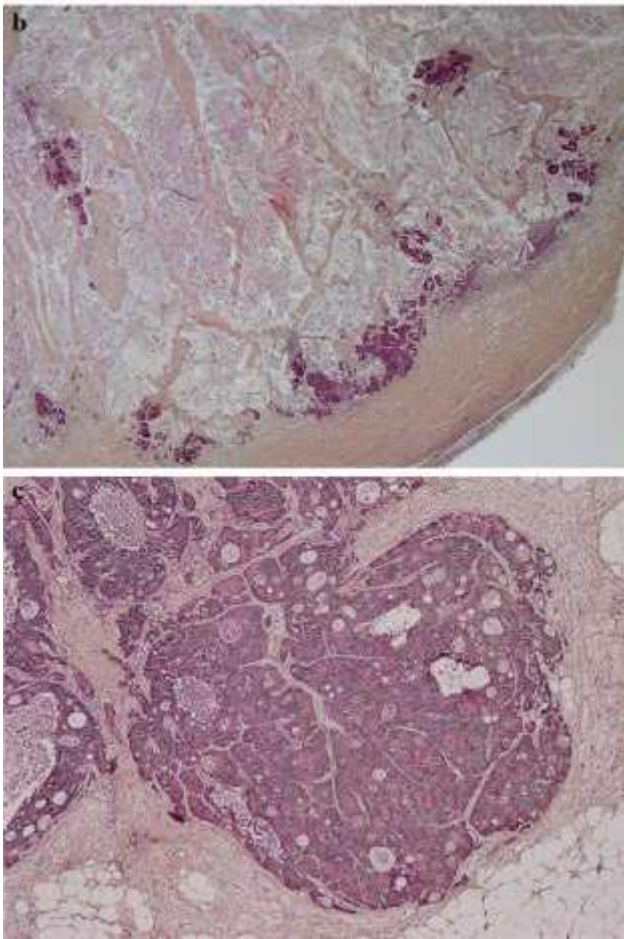
- 1-year survival rates 77%
- 2-year survival rates 51%
- 5-year survival rates 33%

Patients non répondeurs  
Median OS 31.4 mois

- 1-year survival rates 75%
- 2-year survival rates 51%
- 5-year survival rates 26%

# Pathological Response to Neoadjuvant Chemotherapy: A New Prognosis Tool for the Curative Management of Peritoneal Colorectal Carcinomatosis

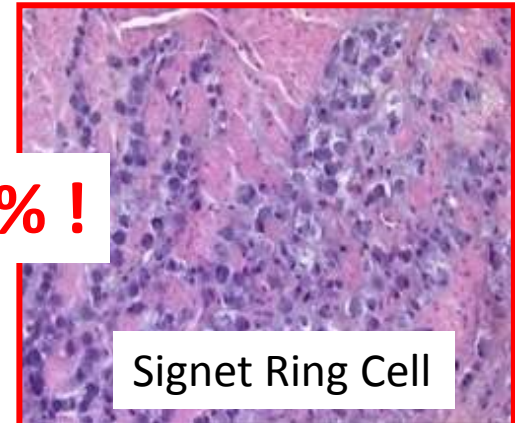
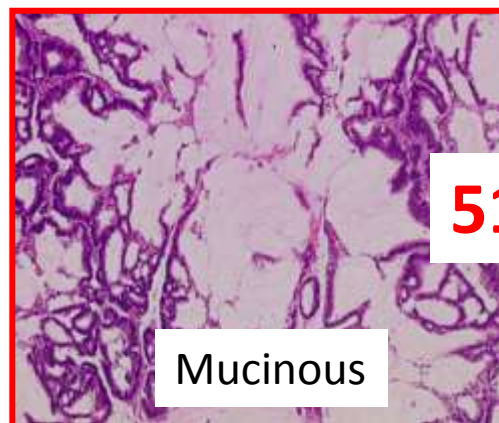
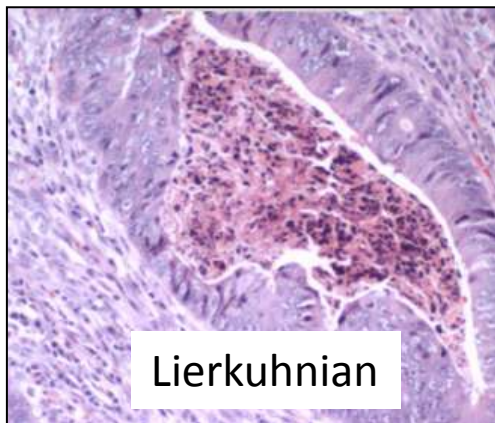
Guillaume Passot<sup>1,2</sup>, Benoît You<sup>2,3</sup>, Gilles Boschetti<sup>4</sup>, Juliette Fontaine<sup>5</sup>, Sylvie Isaac<sup>5</sup>, Evelyne Decullier<sup>6,7</sup>,  
 Christele Maurice<sup>6,7</sup>, Delphine Vaudoyer<sup>1,2</sup>, François-Noël Gilly<sup>1,2</sup>, Eddy Cotte<sup>1,2</sup>, and Olivier Glehen<sup>1,2,8</sup>



Patients at risk	0	1	2	3	4	5
<b>Complete response</b>	12	10	7	5	2	2
<b>Major response</b>	23	16	11	5	3	2
<b>Minor or no response</b>	80	54	21	9	4	1

# Colorectal Cancer (CCR) peritoneal carcinomatosis

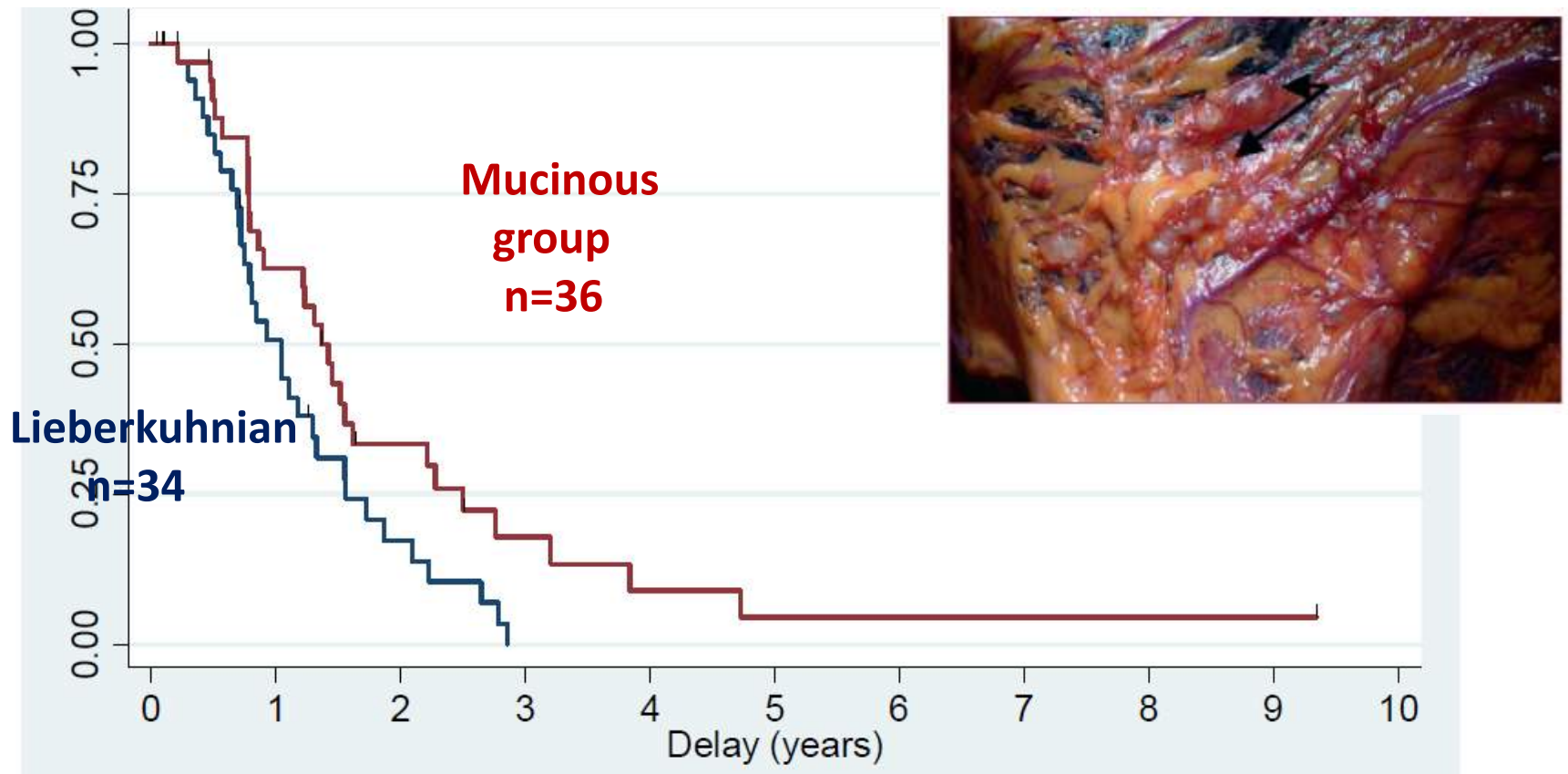
## Frequency of histologic subtypes



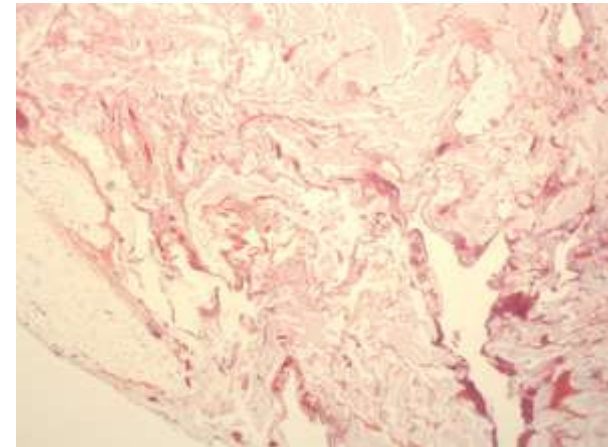
**51% !**

# Impact of histologic subtypes

Relapse Free Survival ( $p=0.04$ )

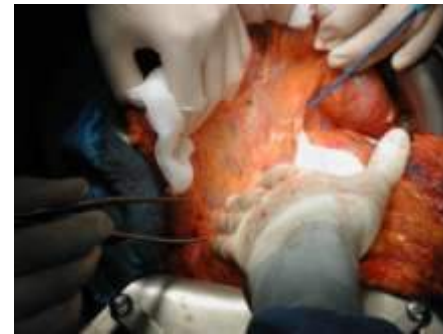
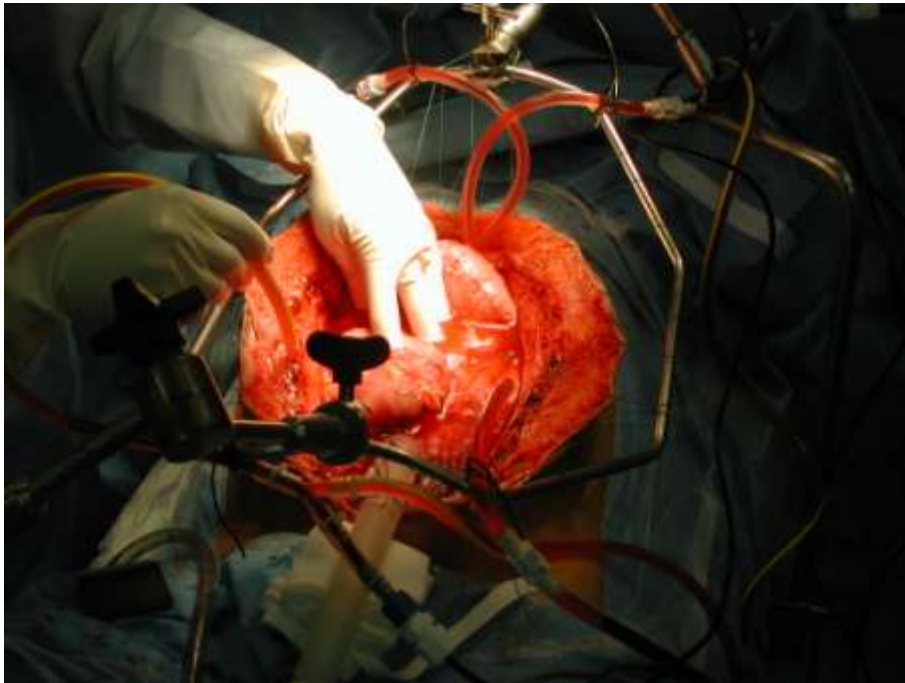


# Mucinous colorectal peritoneal carcinomatosis





# 4- Gastric Adenocarcinoma



# Peritoneal Carcinomatosis from Gastric Cancer: A Multi-Institutional Study of 159 Patients Treated by Cytoreductive Surgery Combined with Perioperative Intraperitoneal Chemotherapy

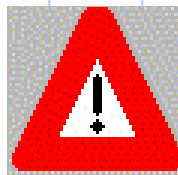
Olivier Glehen, MD, PhD<sup>1</sup>, François Noel Gilly, MD, PhD<sup>1</sup>, Catherine Arvieux, MD, PhD<sup>2</sup>, Eddy Cotte, MD<sup>1</sup>,  
Florent Boutitie<sup>3</sup>, Baudouin Mansvelt, MD, PhD<sup>4</sup>, Jean Marc Bereder, MD<sup>5</sup>, Gérard Lorimier, MD<sup>6</sup>,  
François Quenet, MD<sup>7</sup>, Dominique Elias, MD, PhD<sup>8</sup> and Association Française de Chirurgie



## Mortality-Morbidity

### Gastric

- Mortality: 10cases **(6,5%)**
- Morbidity grade 3-4:
  - 38 cases (27,8%)
    - Digestive fistula : 16%
    - Reoperation: 14%
- • Mean post-operative stay : 24,2±19 days



### Overall (n=1344)

- Mortality : 4,1%
- Morbidity gr. 3-4:
  - 33,8%
    - Dig. fistula : 9,6%
    - Reoperation: 14%
- • Mean post-operative stay : 24,1±18 day

# Selection criterias



## **Age, co-morbidities and general status**

- More strict than for other peritoneal surface malignancies
- Specialized Institutions in gastric cancer and/or peritoneal surface malignancies management



# Prognostic factors

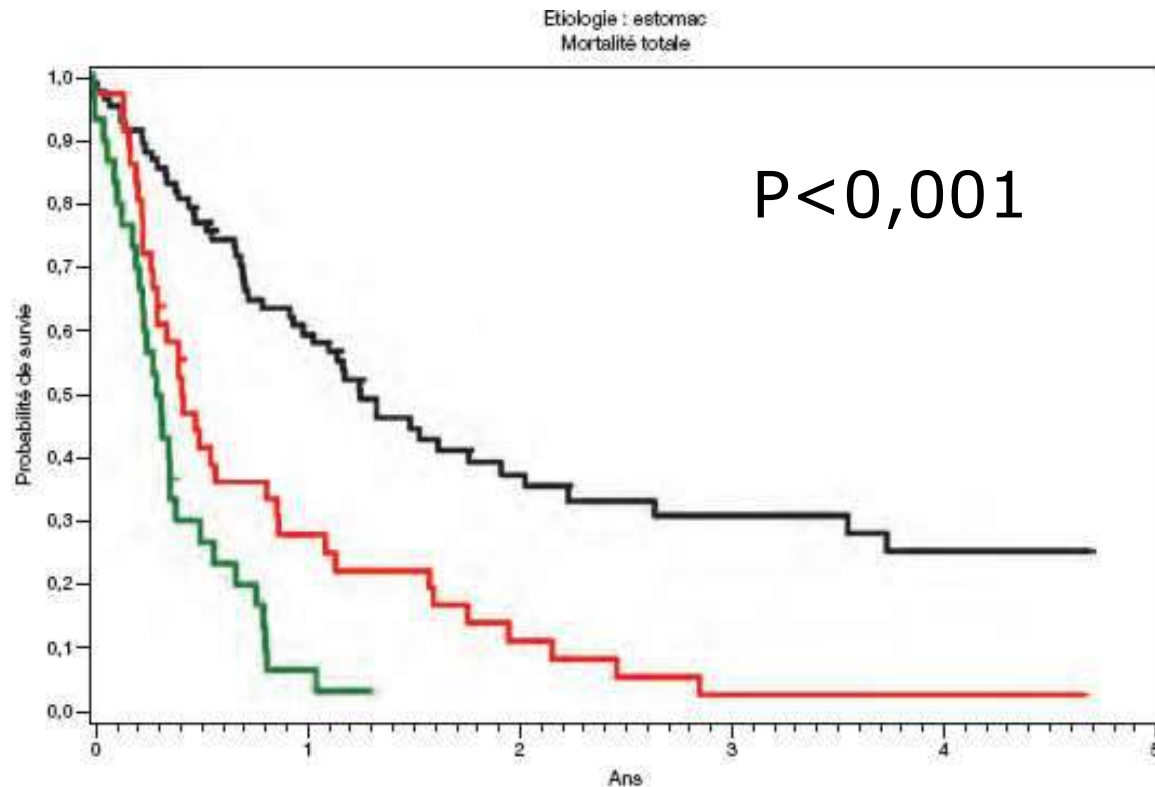
## Completeness of cytoreductive surgery

### Patients CC-0:

- Median 15 months
- 5 year survival: 25%

### Patients CC-2 or 3

- Median 4 months
- 2 years survival: 0%



# Selection criterias

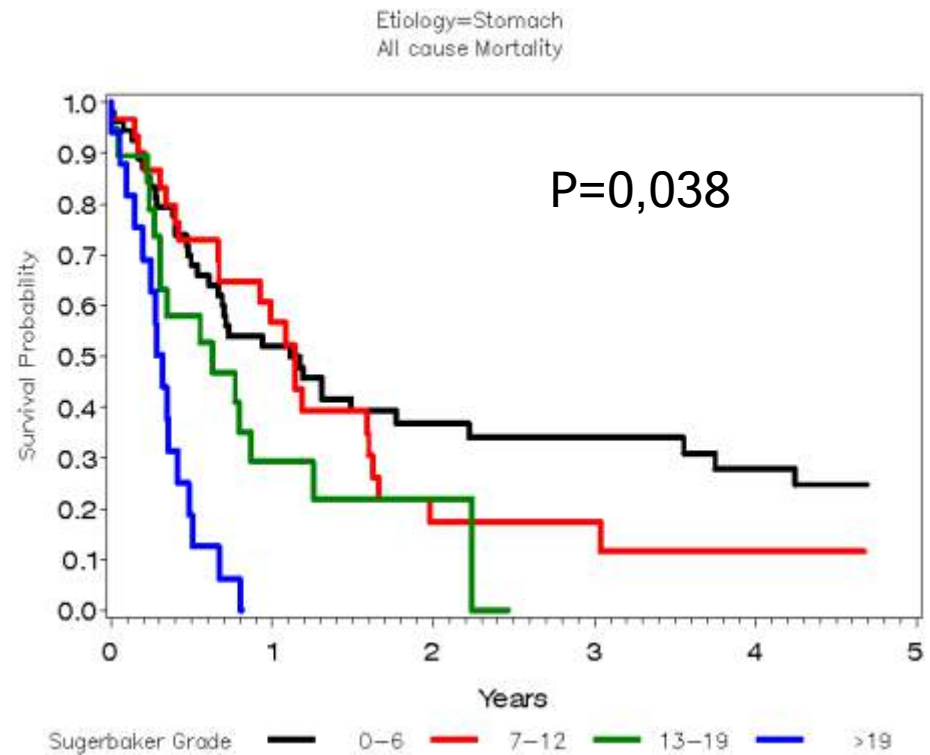


- CC-0 (complete cytoreductive surgery) should be imperative for curative procedure in gastric carcinomatosis

# Pronoctic Factors

## Influence of disease extension in patients treated by complete cytoreductive surgery

- No patient alive at 2 years for PCI > 13
- No patient alive at 1 year for PCI > 19



# Selection criterias



- **Low PCI are recommended**
- **PCI less than 12 and may be less than 10**



**How to detect these kind of indications?  
PCI less than 10 often not visible on  
morphologic exams**

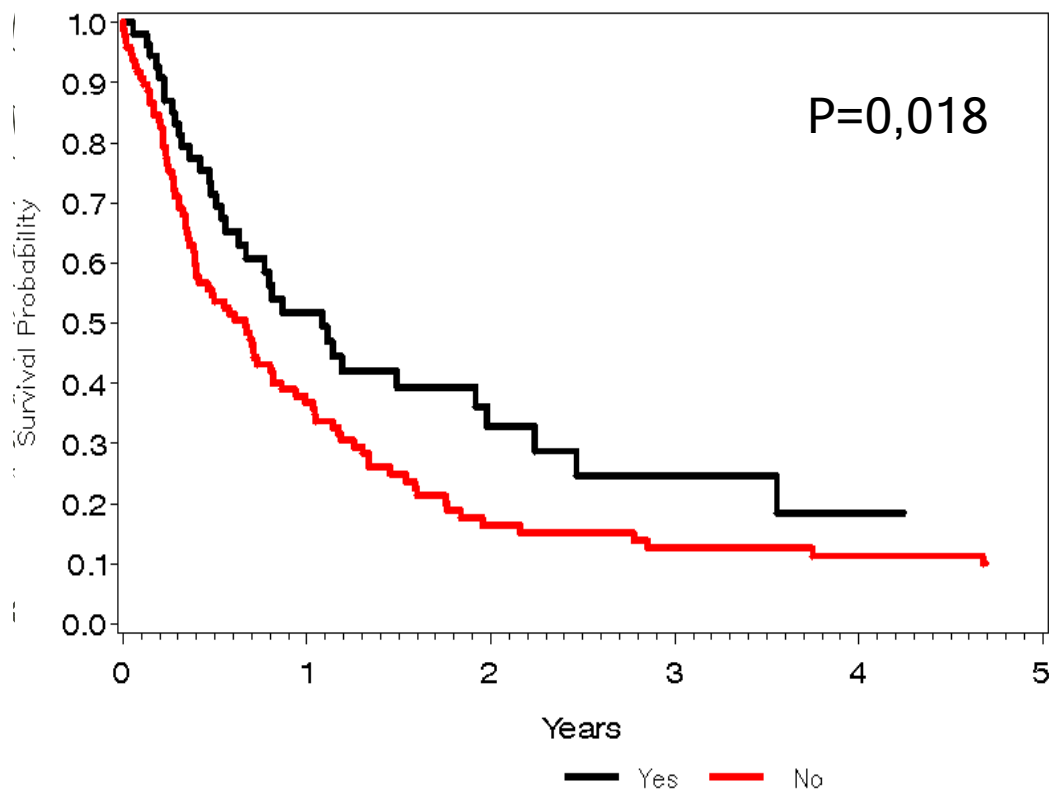
# LAPAROSCOPY should be performed systematically in case of advanced gastric

- One day surgery
- Veinous access under GA
- Early diagnosis of limited carcinomatosis non visible on morphologic exams
- Diagnosis of diffuse carcinomatosis non amenable to complete cytoreductive surgery



# Prognostic factors

## ➤ Neoadjuvant systemic chemotherapy



# Summary and Conclusion



- Age, co-morbidities and general status
- Extent of peritoneal disease
- Extra peritoneal metastases
- Histology, tumour response
- RAS mutation, BRAF