



# Peritoneal Mesothelioma

## Current standard treatment

**Pr Marc POCARD**

Lariboisière Hospital – Paris - FRANCE

Digestive and oncological surgical Unit

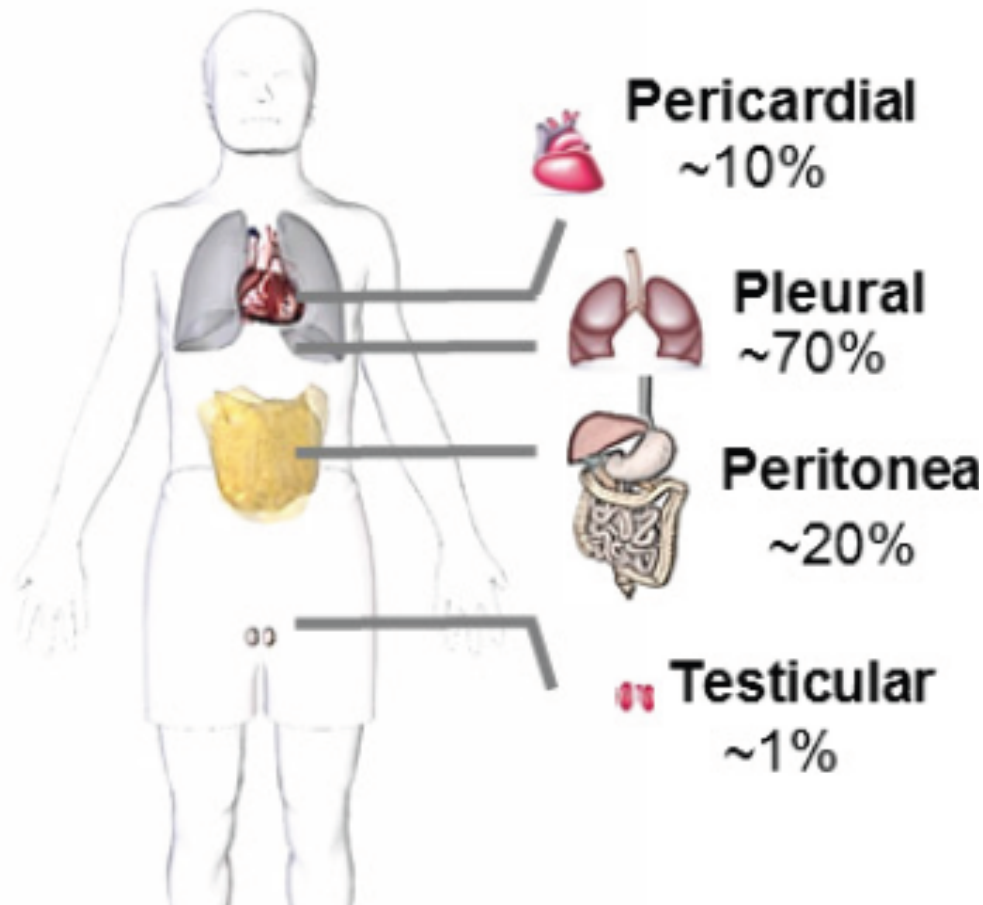
CART Carcinomatosis Research Unit U965 INSERM

## Links of interest – Pr Marc Pocard

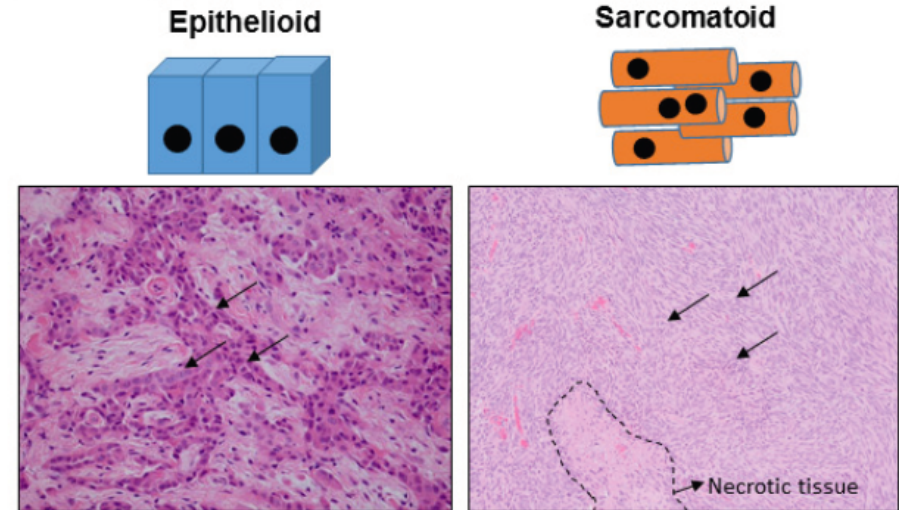
- 2012 – 2017:
- Honorary :
  - Gamida, Léo-Pharm, Pfizer, Novartis, Sanofi, Roche
- Award – congress – laboratory research programme:
  - Capnomed, Clerad, Ethicon, Fujinon, Gamida, INSERMTransfert, Plasma-jet, Roche, Sanofi, Sofra-médical, STAGO, Storz, Rand

# Peritoneal mesothelioma

## (A) Incidence Sites



## (B) Pathology Subtypes



Laparoscopy + histology + MRI

**Figure 1: Common sites of incidence and pathological subtypes of pleural mesothelioma.** (A) Tissues affected by mesothelioma and incidence rates. (B) Hematoxylin and eosin staining of two mesothelioma pathologic subtypes (epithelioid and sarcomatoid). Biphasic phenotype is a mixture of epithelioid and sarcomatoid types. The arrows indicate disorganized neoplastic tumor areas.

# Peritoneal mesothelioma

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ELSEVIER

Contents lists available at [ScienceDirect](#)

## Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: [www.cancerepidemiology.net](http://www.cancerepidemiology.net)



## The next mesothelioma wave: Mortality trends and forecast to 2030 in Brazil



Eduardo Algranti<sup>a,\*</sup>, Cézar Akiyoshi Saito<sup>b</sup>, Ana Paula Scalia Carneiro<sup>c</sup>, Bruno Moreira<sup>c</sup>,  
Elizabethete Medina Coeli Mendonça<sup>a</sup>, Marco Antonio Bussacos<sup>d</sup>

<sup>a</sup> Division of Medicine, FUNDACENTRO, São Paulo, Brazil

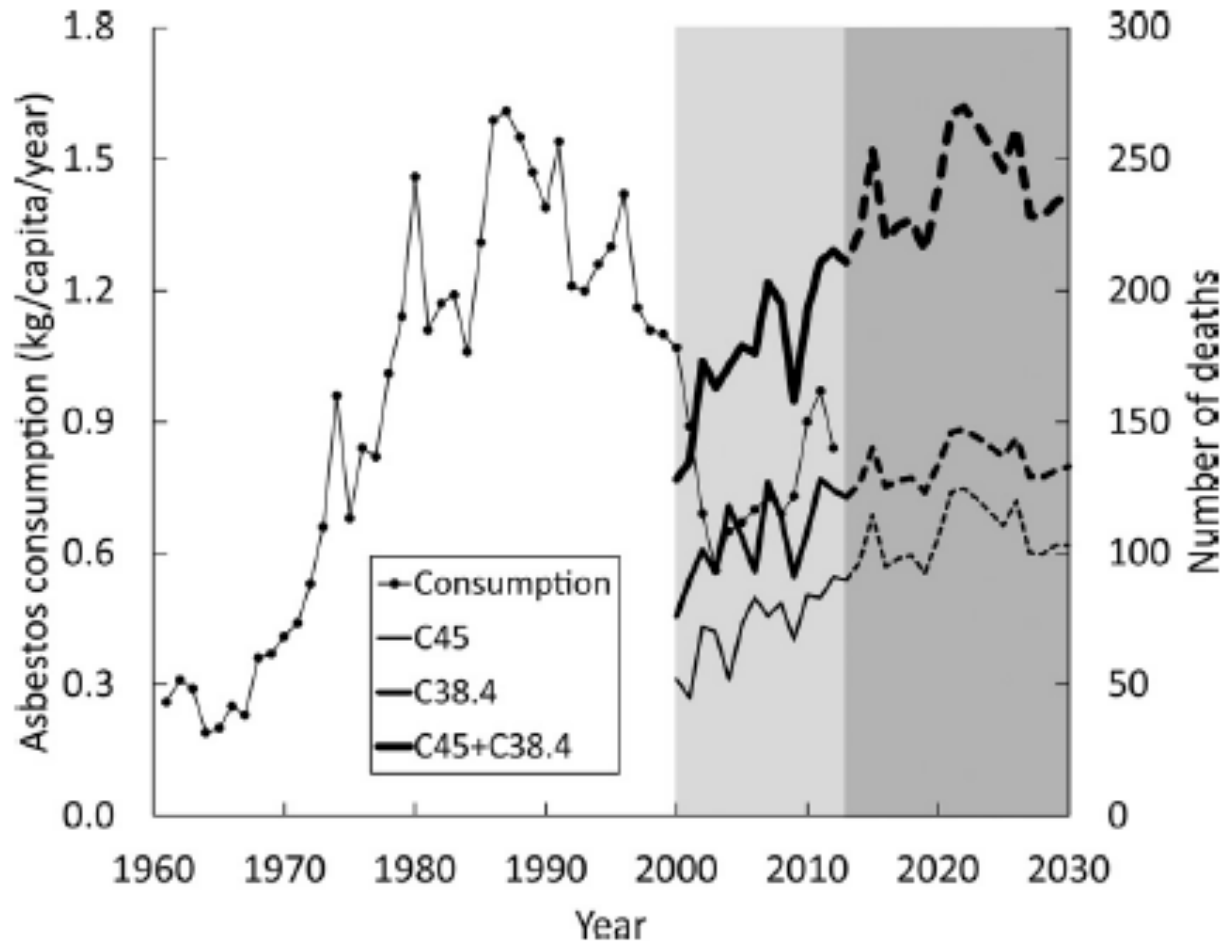
<sup>b</sup> Division of Educative Actions, FUNDACENTRO, São Paulo, Brazil

<sup>c</sup> Workers' Health Service, Hospital das Clínicas, Federal University of Minas Gerais, Brazil

<sup>d</sup> Division of Statistics and Epidemiology, FUNDACENTRO, São Paulo, Brazil

Cancer Epidemiology 39 (2015) 687–692





**Fig 3.** Asbestos consumption in kilograms per capita (solid line with filled circles), 1961–2012. The light shadowed area comprises the 2000–2012 period with observed deaths (solid lines). The dark shadowed area comprises the 2013–2030 period with predicted deaths (traced lines). Number of C45 deaths (thin line), number of C38.4 deaths (medium line) and their sum (thick line), adults aged 30 and over, Brazil.

Peritoneal mesothelioma is not always related with asbestos exposition

Exact incidence in Brazil is unknown

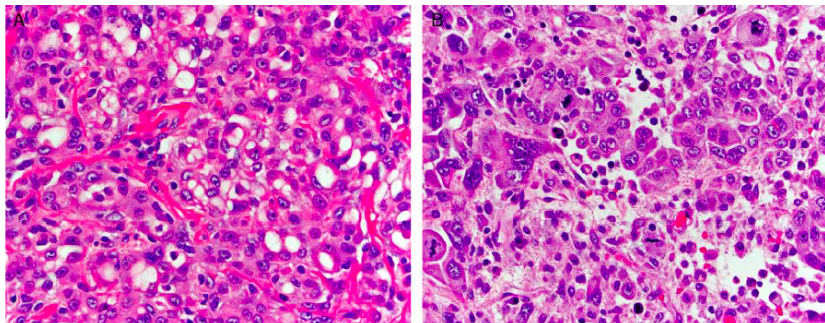
A Regional distribution for pleural mesothelioma exist Southeast

# Peritoneal mesothelioma

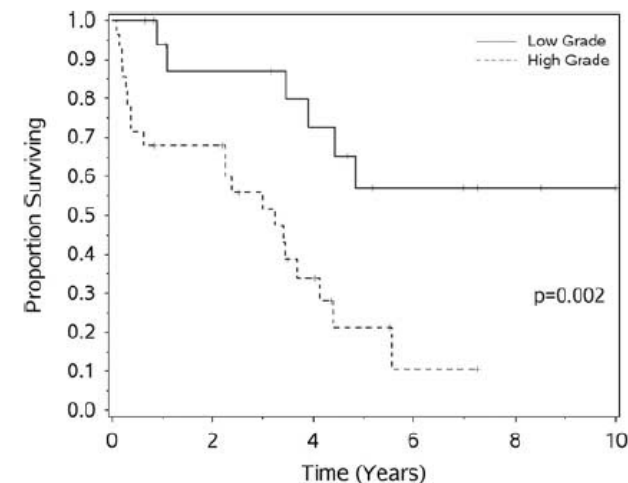
## A Histomorphologic Grading System That Predicts Overall Survival in Diffuse Malignant Peritoneal Mesothelioma With Epithelioid Subtype

*Kari Valente, MD,\* Aaron U. Blackham, MD,† Edward Levine, MD,† Greg Russell, MS,‡  
Konstantinos I. Votanopoulos, MD,† John H. Stewart, MD,† Perry Shen, MD,†  
Kim R. Geisinger, MD,§ and Sahussapont J. Sirintrapun, MD||*

*(Am J Surg Pathol 2016;40:1243–1248)*



**FIGURE 2.** A and B, Representative image of the high-grade tier (hematoxylin and eosin). The tumor cells show severe atypia (score 3) with nuclei that have marked membrane irregularities, bizarre contours, nuclear enlargement, marked variability in size and shape, coarsely granular chromatin pattern, and prominent large nucleoli ( $>3\mu\text{m}$ ). Mitoses are  $>5/10$  HPF (score 3).  $863 \times 677$  mm ( $72 \times 72$  DPI).



**FIGURE 3.** Kaplan-Meier analysis of OS for groups in the low-grade tier and high-grade tier for MPeM with epithelioid subtype. The low-grade tier had the higher OS with a median of 11.9 years and 57% at 5 years when compared with the high-grade tier with a median of 3.3 years and 21% at 5 years. The results did achieve statistical significance ( $P=0.002$ ).  $396 \times 317$  mm ( $96 \times 96$  DPI).

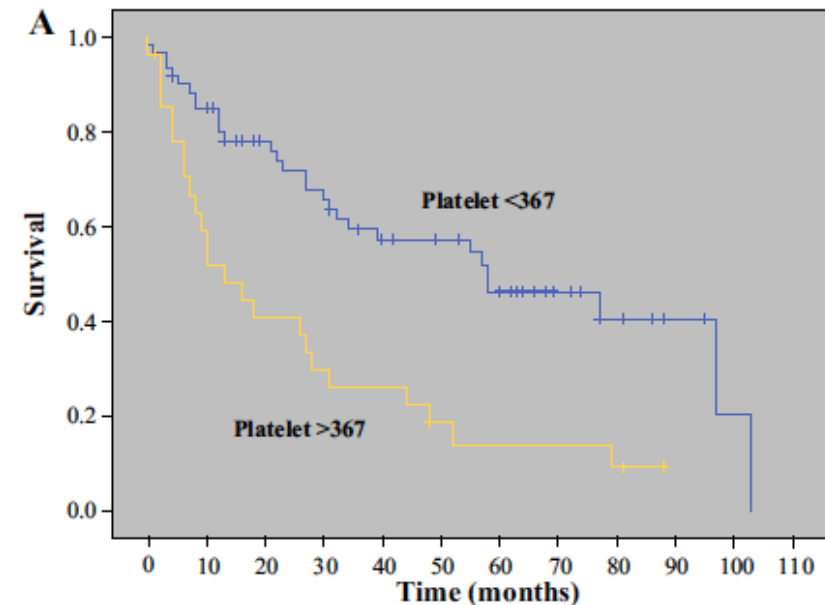
## Preoperative Thrombocytosis Predicts Shortened Survival in Patients with Malignant Peritoneal Mesothelioma Undergoing Operative Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy

Yue C. Li, BS, Tamara Khashab, MD, Julia Terhune, MD, Richard L. Eckert, PhD, Nader Hanna, MD, Allen Burke, MD, and H. Richard Alexander, MD

Annals of

**SURGICAL ONCOLOGY**

OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOG



## **The Challenge of Defining Treatment Standards for a Rare Disease: Malignant Peritoneal Mesothelioma**

*Hedy Lee Kindler, MD*

University of Chicago, Chicago, IL

Volume 12 / Issue 10 / October 2016 • Journal of Oncology Practice



# Peritoneal mesothelioma



Rare disease

Different  
histological  
subtype

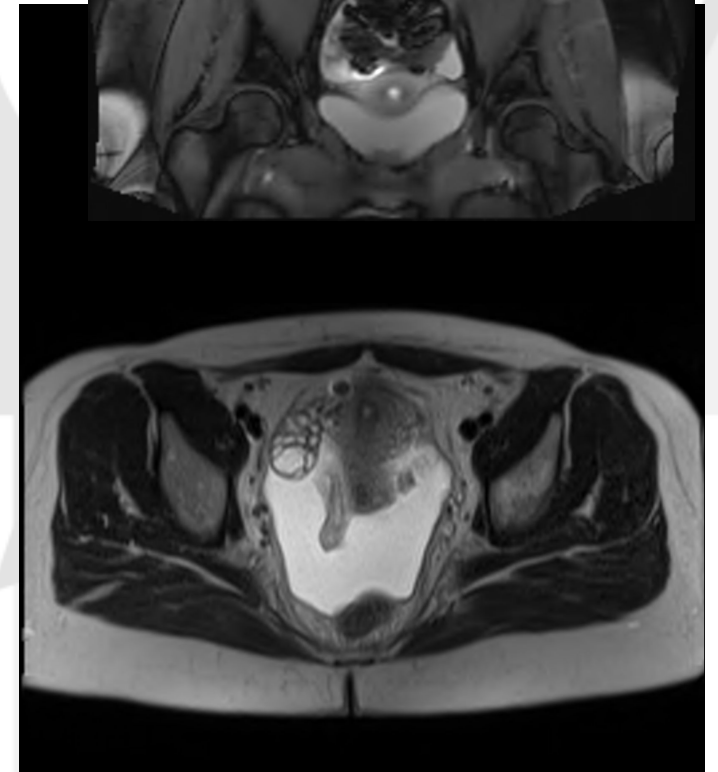
Different  
biological  
predictive  
markers

Different  
aggressivity

# Peritoneal mesothelioma

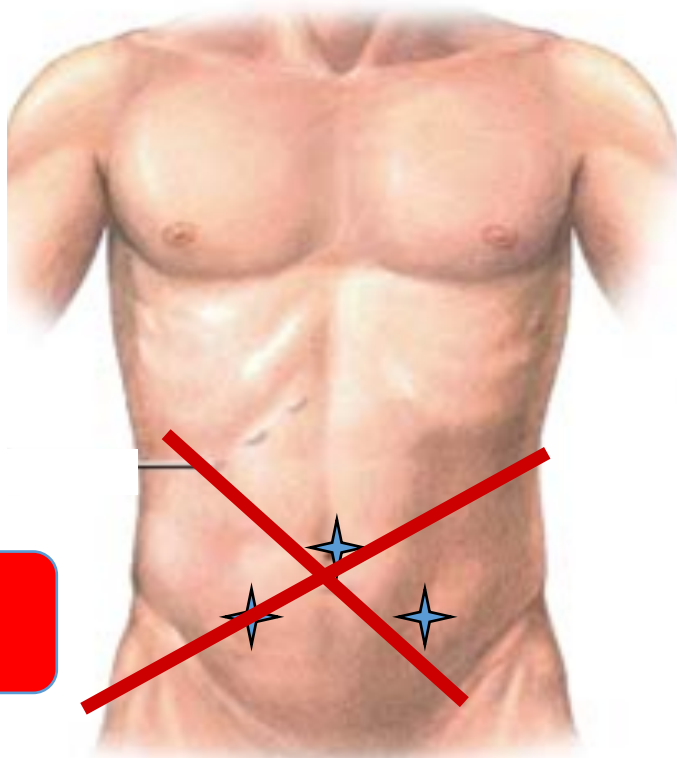
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- Preoperative MRI and CT
  - Cytoreductive surgery
  - Nutrition
  - Thromboembolism prevention
  - Intra peritoneal chemotherapy
  - Intravenous therapy
- 
- Be careful with abdominal wall
  - Think about the family

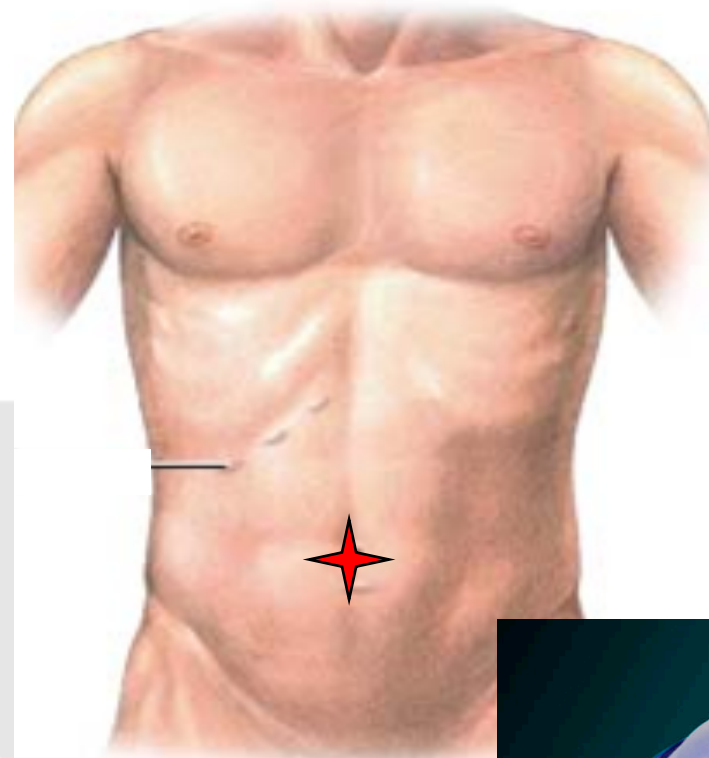




# Peritoneal mesothelioma



NO



YES



# Peritoneal mesothelioma

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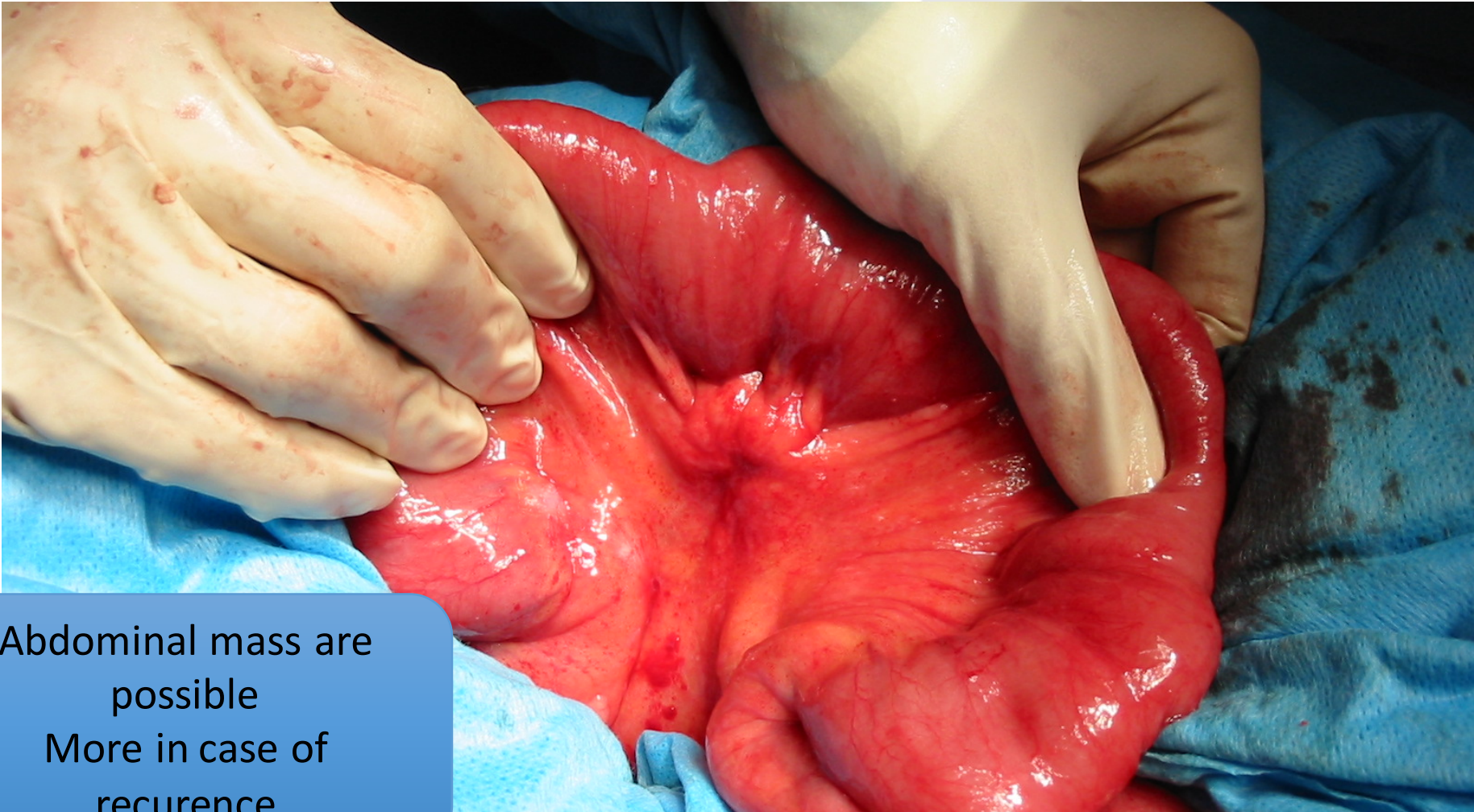
implantation in the lateral abdominal wall along previous laparoscopic trocar tracts. Can kill the patient before the natural course of the disease



Munkholm-Larsen S, Cao CQ, Yan TD. Malignant peritoneal mesothelioma. *World J Gastrointest Surg* 2009; 1(1): 38-48

# Peritoneal mesothelioma : mass

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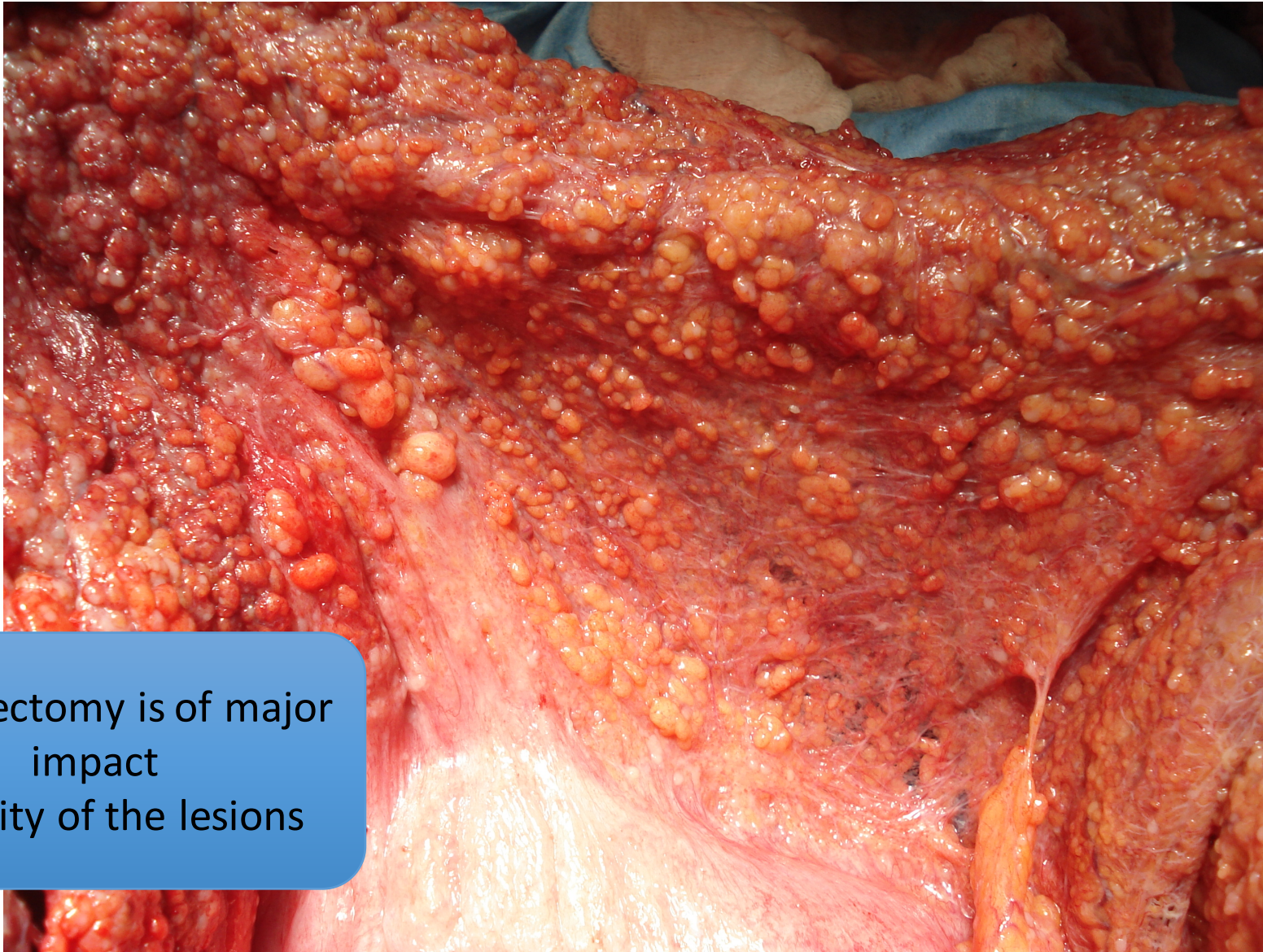


Abdominal mass are possible  
More in case of recurrence



# Peritoneal mesothelioma : CC1 CC2

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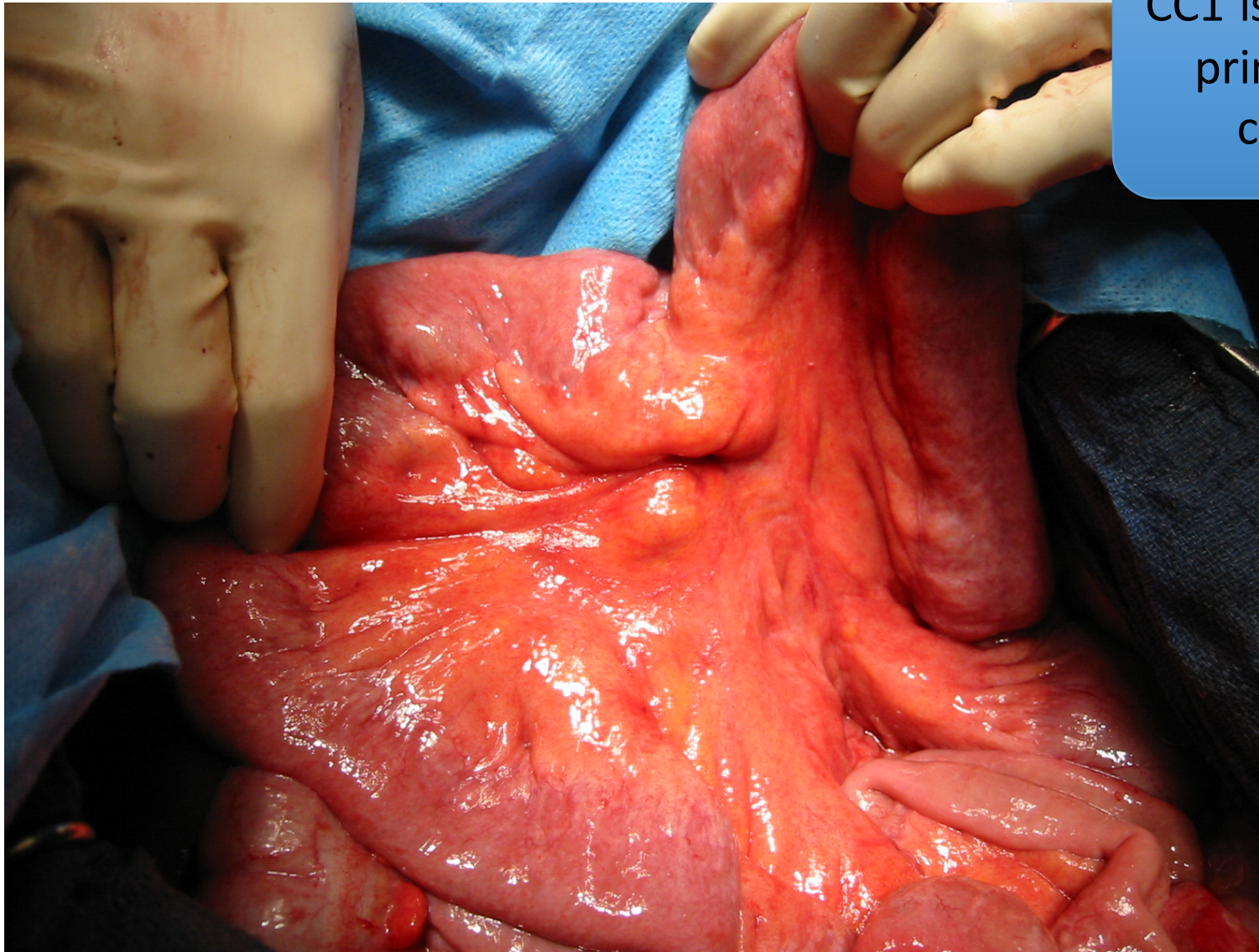
Omentectomy is of major impact  
Majority of the lesions



# Peritoneal mesothelioma : CC1 CC2

HIPEC  
International Meeting  
MCMoving Forward

CC1 is usual because of  
primary peritoneal  
cancer disease



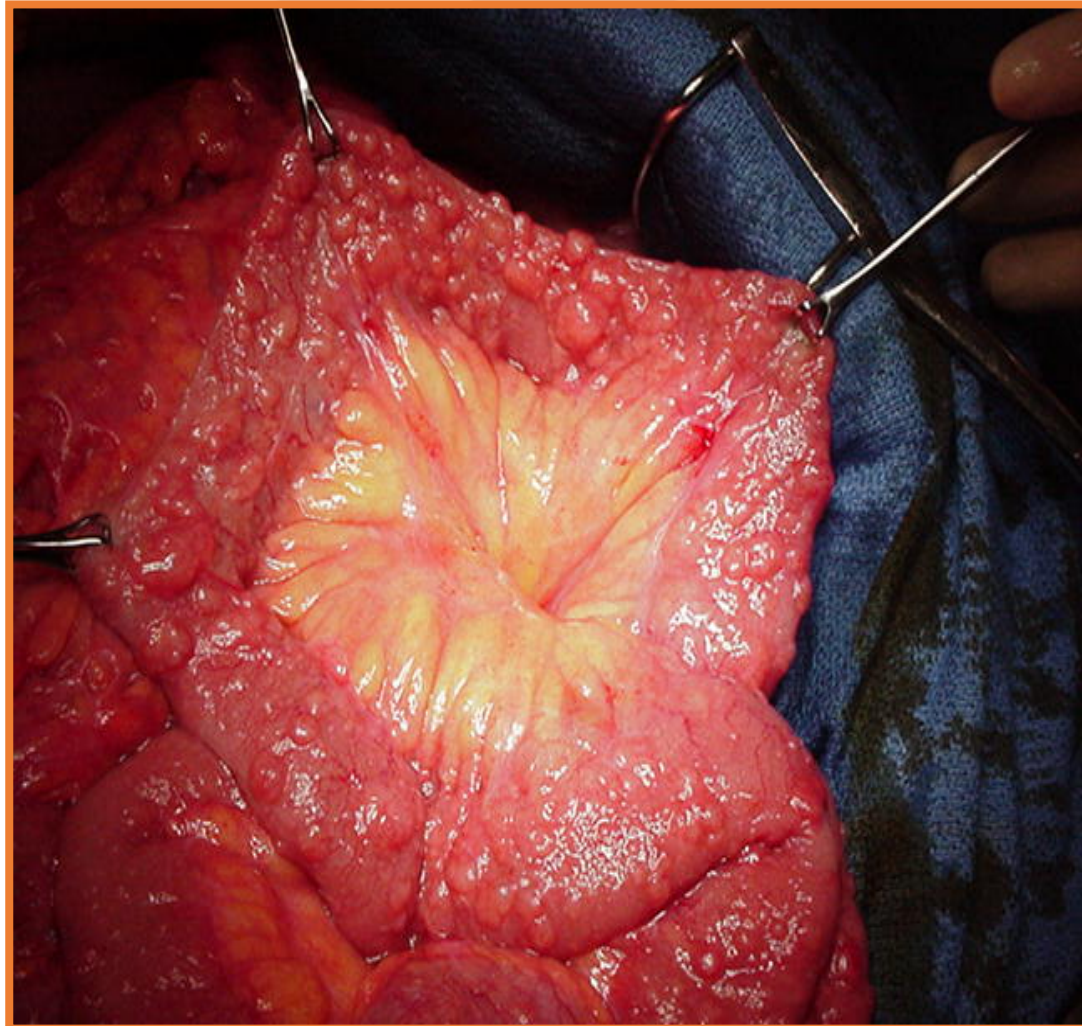


# Peritoneal mesothelioma



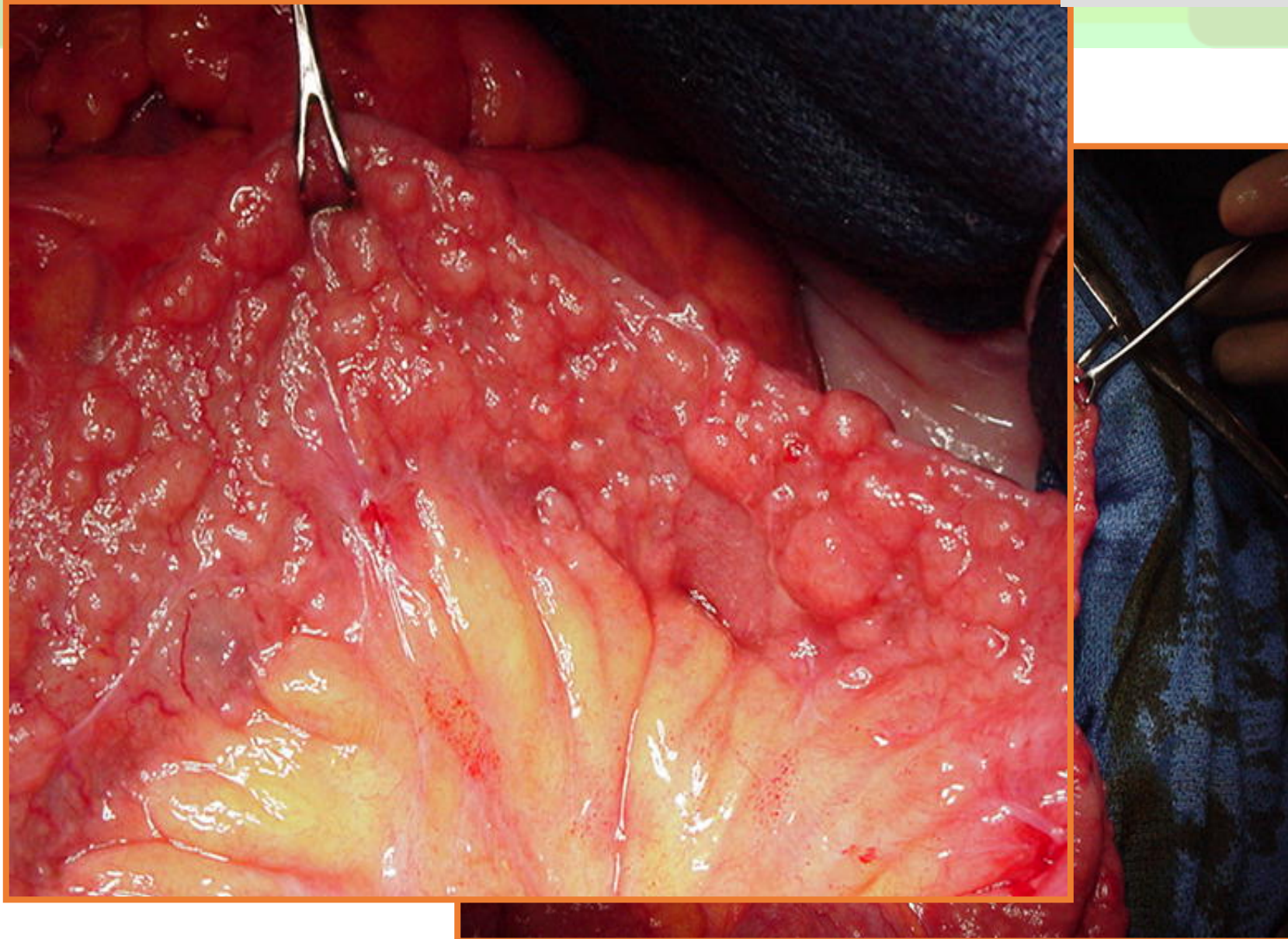


# Peritoneal mesothelioma



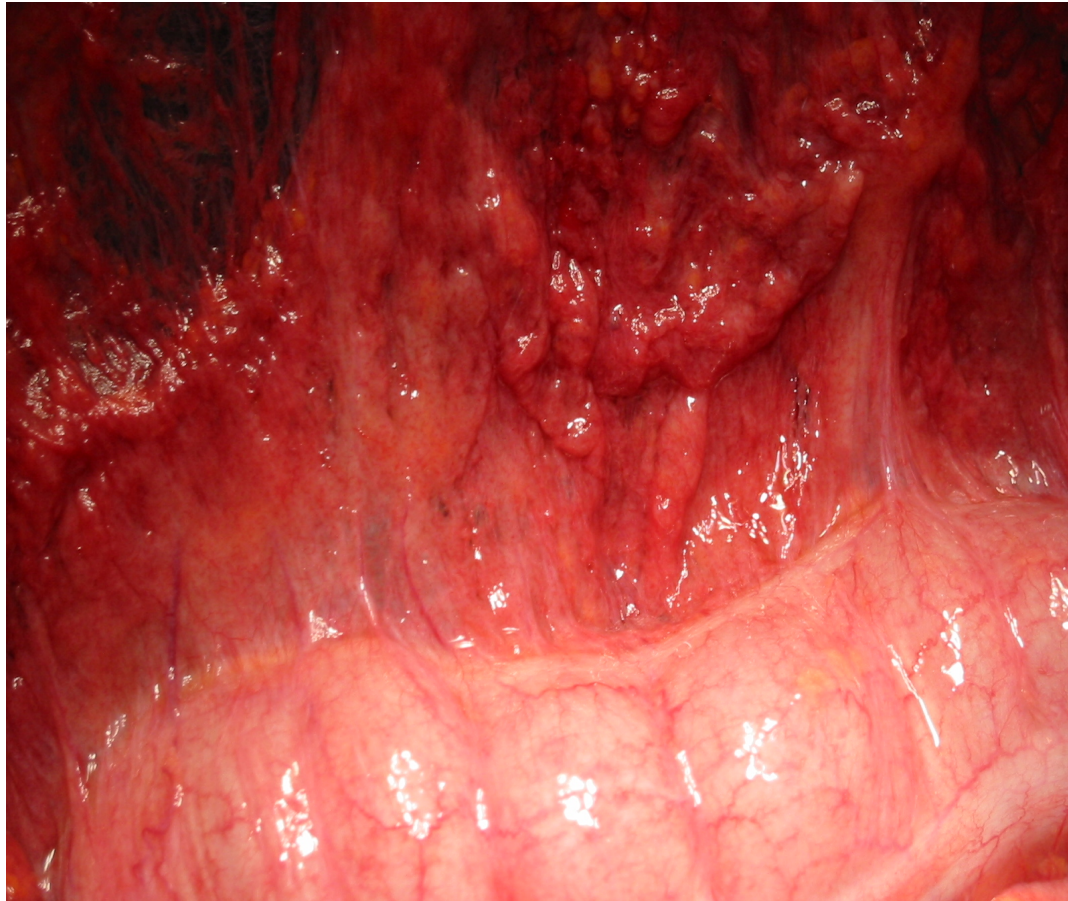
# Peritoneal mesothelioma

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# Peritoneal mesothelioma : specific



Omentectomy +  
CC2 resection with  
HIPEC could control  
part of the disease

# Peritoneal mesothelioma: specific

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Pericardia  
localisation ?

## Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Malignant Peritoneal Mesothelioma: Multi-Institutional Experience

*Tristan D. Yan, Marcello Deraco, Dario Baratti, Shigeki Kusamura, Dominique Elias, Olivier Glehen, François N. Gilly, Edward A. Levine, Perry Shen, Faheez Mohamed, Brendan J. Moran, David L. Morris, Terence C. Chua, Pompiliu Piso, and Paul H. Sugarbaker*

### **Purpose**

This multi-institutional registry study evaluated cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) for diffuse malignant peritoneal mesothelioma (DMPM).

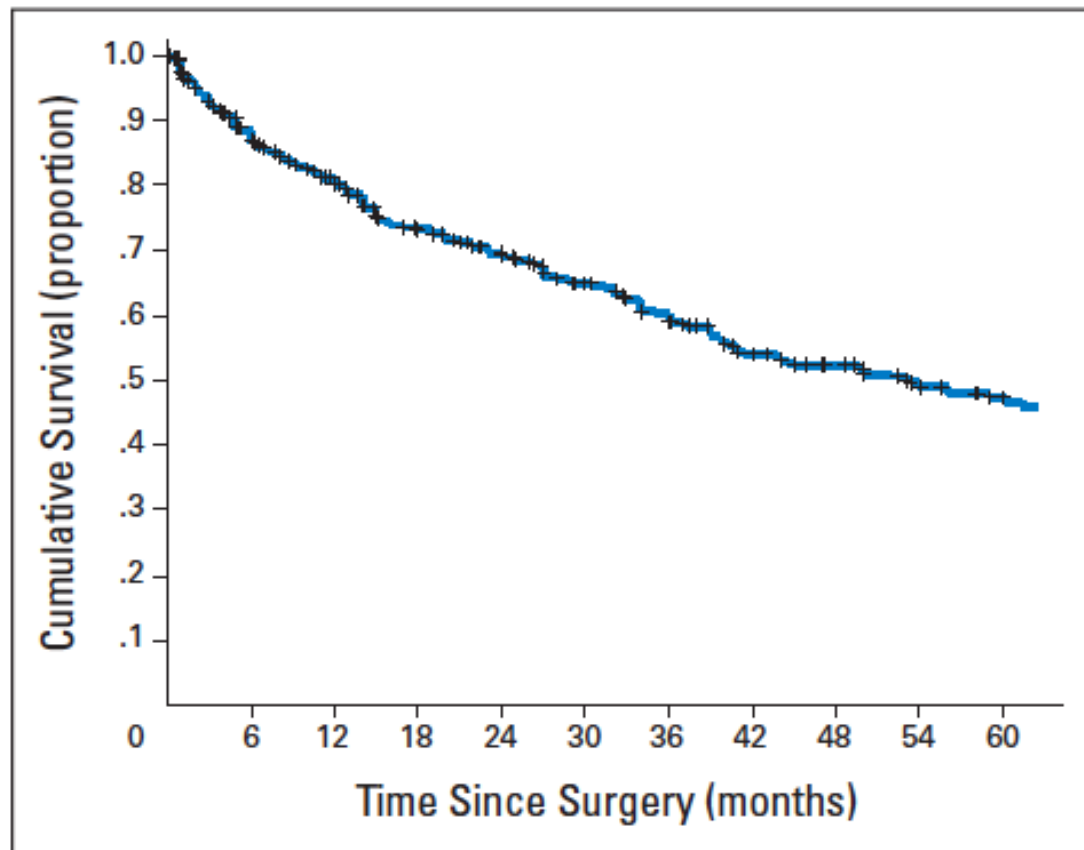
### **Conclusion**

The data suggest that CRS combined with HIPEC achieved prolonged survival in selected patients with DMPM.



# Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Malignant Peritoneal Mesothelioma: Multi-Institutional Experience

*Tristan D. Yan, Marcello Deraco, Dario Baratti, Shigeki Kusamura, Dominique Elias, Olivier Glehen, François N. Gilly, Edward A. Levine, Perry Shen, Faheez Mohamed, Brendan J. Moran, David L. Morris, Terence C. Chua, Pompiliu Piso, and Paul H. Sugarbaker*



**Fig 1.** Overall survival after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal mesothelioma (n = 401). (+) Patients who were alive at the last follow-up.

- 405 patients
- Median follow-up for alive patients = 33 months
  - Mean PCI = 20
- 46% had CC0 or CC1
  - 92% HIPEC
- 31% grade 3 or 4 postoperative complications
- Mean overall survival 53 months
- 3 years survival 60%



# Peritoneal mesothelioma : for all

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- Cytoreductive surgery
- Nutrition
- Thromboembolism prevention
- Intra peritoneal chemotherapy, HIPEC if possible
- Intravenous therapy
  
- Be careful with abdominal wall
- Think about the family
- French : national declaration / 3 national expert center

# Peritoneal mesothelioma - epithelioid

HIPEC  
International Meeting  
M.M. Moving Forward

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## 1. Man of 50 years

- Abdominal pain – moderated ascites
- OMS 1 – normal weight
- MRI / CT : limited disease on the abdomen
- No preoperative treatment
- Cytoreductive surgery + total parietal peritonectomy + HIPEC (2 drugs / 43°C / 60 minutes)
- Cytoreductive to obtain CC0 + Aggressive HIPEC procedure
- Alimta + Cisplatin as adjuvant treatment 3 or 6 months



# Peritoneal mesothelioma - epithelioid

HIPEC  
International Meeting  
M.M. Moving Forward

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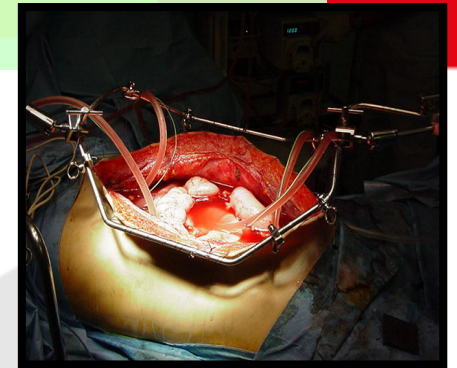
## 1. Women of 60 years

- Abdominal pain – moderated ascites
- OMS 2 – decrease weight of 10%
- MRI / CT : limited disease on the abdomen – legs phlebitis
- Discuss preoperative treatment and nutrition – 2 months, associate heparin treatment
- Cytoreductive surgery + **HIPEC (even if CC2)** mitomycine
- Alimta + Cisplatin as adjuvant treatment 3 or 6 months if possible

# Peritoneal mesothelioma - epithelioid

## 1. Man of 72 years

- Abdominal pain – major ascites
- OMS 2/3 – decrease weight of 15%
- MRI / CT : limited solid disease on the abdomen – phlebitis
- Preoperative treatment for nutrition – 10 days
- Limited Cytoreductive surgery including omentectomy
- HIPEC (even if CC2) with mitomycine and limited hyperthermia 41,5°c for 60 minutes
- Alimta as treatment 3 or 6 months if possible using adapted doses and discuss to associate Bevacizumab or Cisplatin

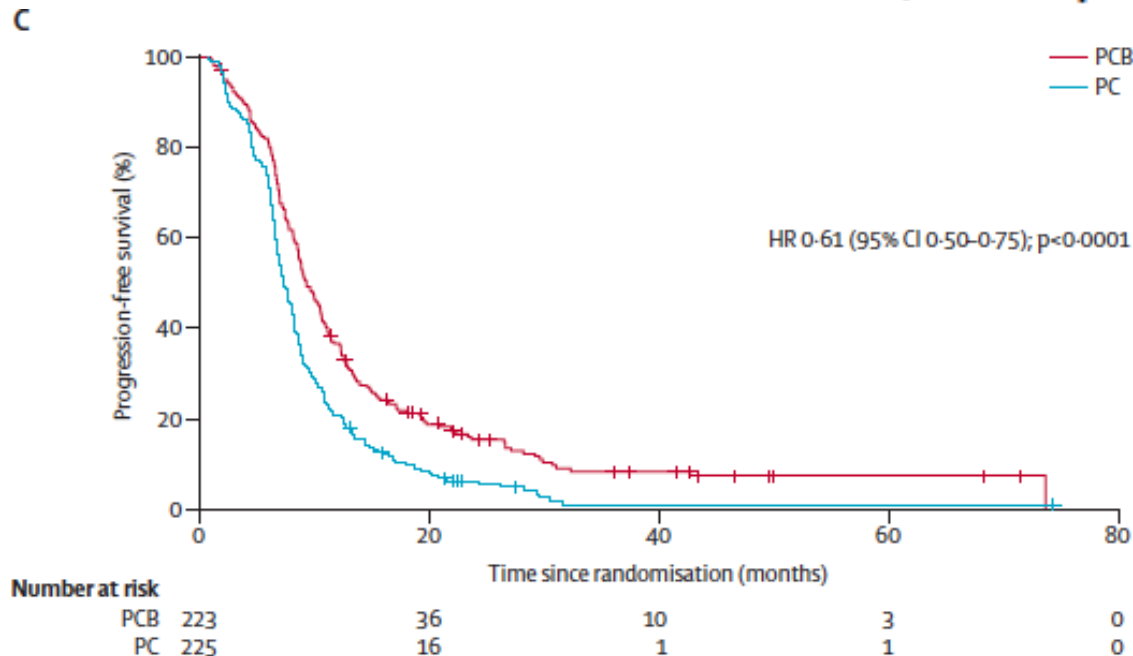


# Mesothelioma non consensus – future?

## Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial

G rard Zalcman, Julien Mazieres, Jacques Margery, Laurent Greillier, Clarisse Audigier-Valette, Denis Moro-Sibilot, Olivier Molinier, Romain Corre, Isabelle Monnet, Val rie Gounant, Fr d ric Riviere, Henri Janicot, Radj Gervais, Chryst le Locher, Bernard Milleron, Quan Tran, Marie-Paule Lebitasy, Franck Morin, Christian Creveuil, Jean-Jacques Parienti, Arnaud Scherpereel, on behalf of the French Cooperative Thoracic Intergroup (IFCT)

www.thelancet.com Published online December 21, 2015 [http://dx.doi.org/10.1016/S0140-6736\(15\)01238-6](http://dx.doi.org/10.1016/S0140-6736(15)01238-6)



Progression  
free survival

# Mesothelioma non consensus – future?



Long-term regional chemotherapy for patients with epithelial malignant peritoneal mesothelioma results in improved survival

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P.H. Sugarbaker<sup>a,\*</sup>, D. Chang<sup>b</sup>

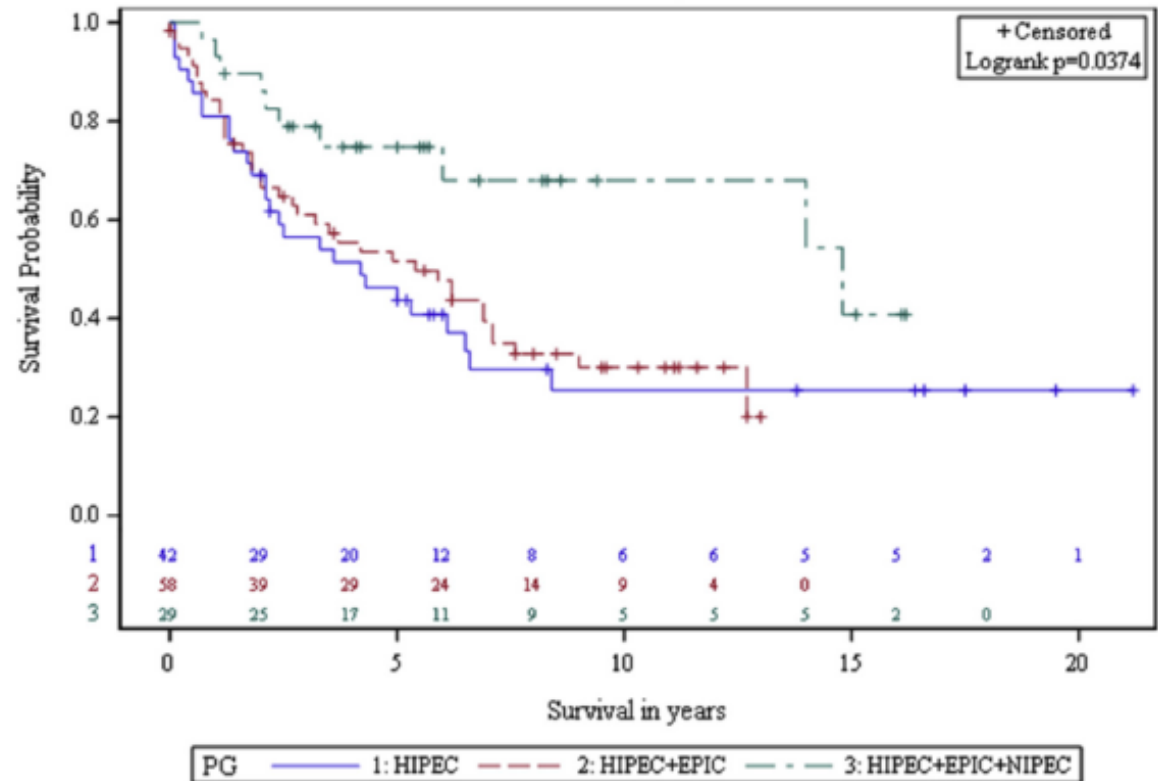
# EJSO

the Journal of Cancer Surgery

Accepted 10 January 2017

Available online ■ ■ ■

Product-Limit Survival Estimates  
With Number of Subjects at Risk





# Mesothelioma non consensus -

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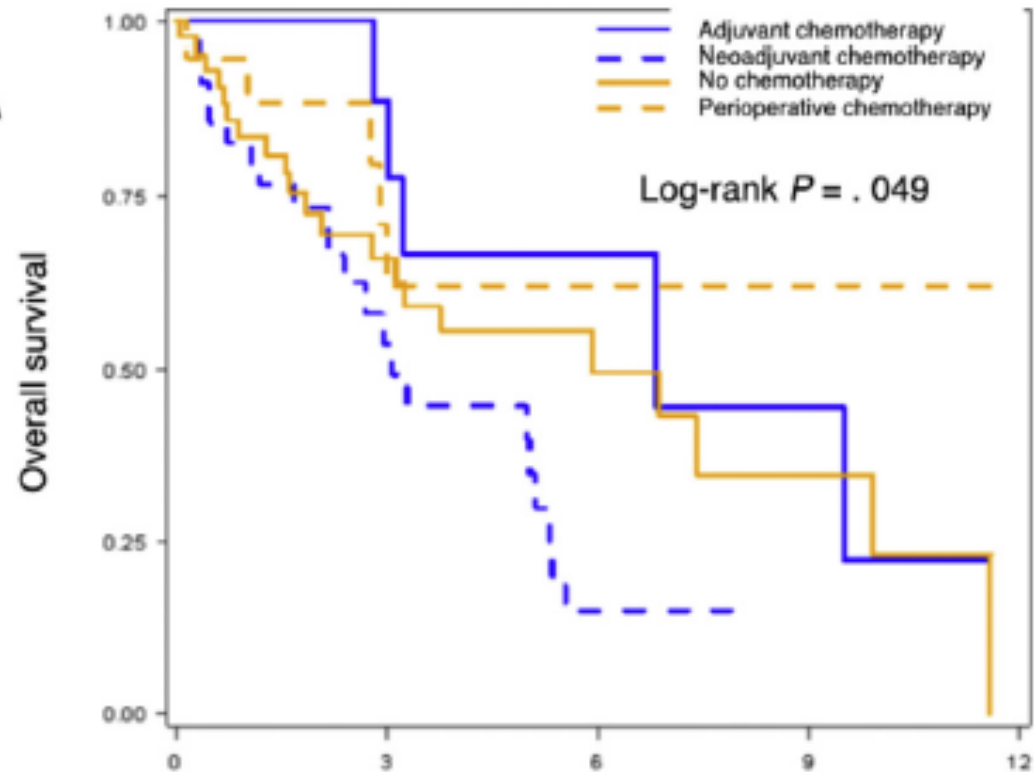


Diffuse malignant peritoneal mesothelioma: Evaluation of systemic chemotherapy with comprehensive treatment through the RENAPE Database Multi-Institutional Retrospective Study<sup>☆</sup>

V. Kepenekian<sup>a</sup>, D. Elias<sup>b</sup>, G. Passot<sup>a</sup>, E. Mery<sup>c</sup>, D. Goere<sup>b</sup>, D. Delroeux<sup>d</sup>, F. Quenet<sup>e</sup>, G. Ferron<sup>f</sup>, D. Pezet<sup>g</sup>, J.M. Guilloit<sup>h</sup>, P. Meeus<sup>i</sup>, M. Pocard<sup>j</sup>, J.M. Bereder<sup>k</sup>, K. Abboud<sup>l</sup>, C. Arvieux<sup>m</sup>, C. Brigand<sup>n</sup>, F. Marchal<sup>o</sup>, J.M. Classe<sup>p</sup>, G. Lorimier<sup>q</sup>, C. De Chaisemartin<sup>r</sup>, F. Guyon<sup>s</sup>, P. Mariani<sup>t</sup>, P. Ortega-Deballon<sup>u</sup>, S. Isaac<sup>v</sup>, C. Maurice<sup>w</sup>, F.N. Gilly<sup>a</sup>, O. Glehen<sup>a,\*</sup>, on behalf of the French Network for Rare Peritoneal Malignancies (RENAPE)<sup>1</sup>

European Journal of Cancer 65 (2016) 69–79

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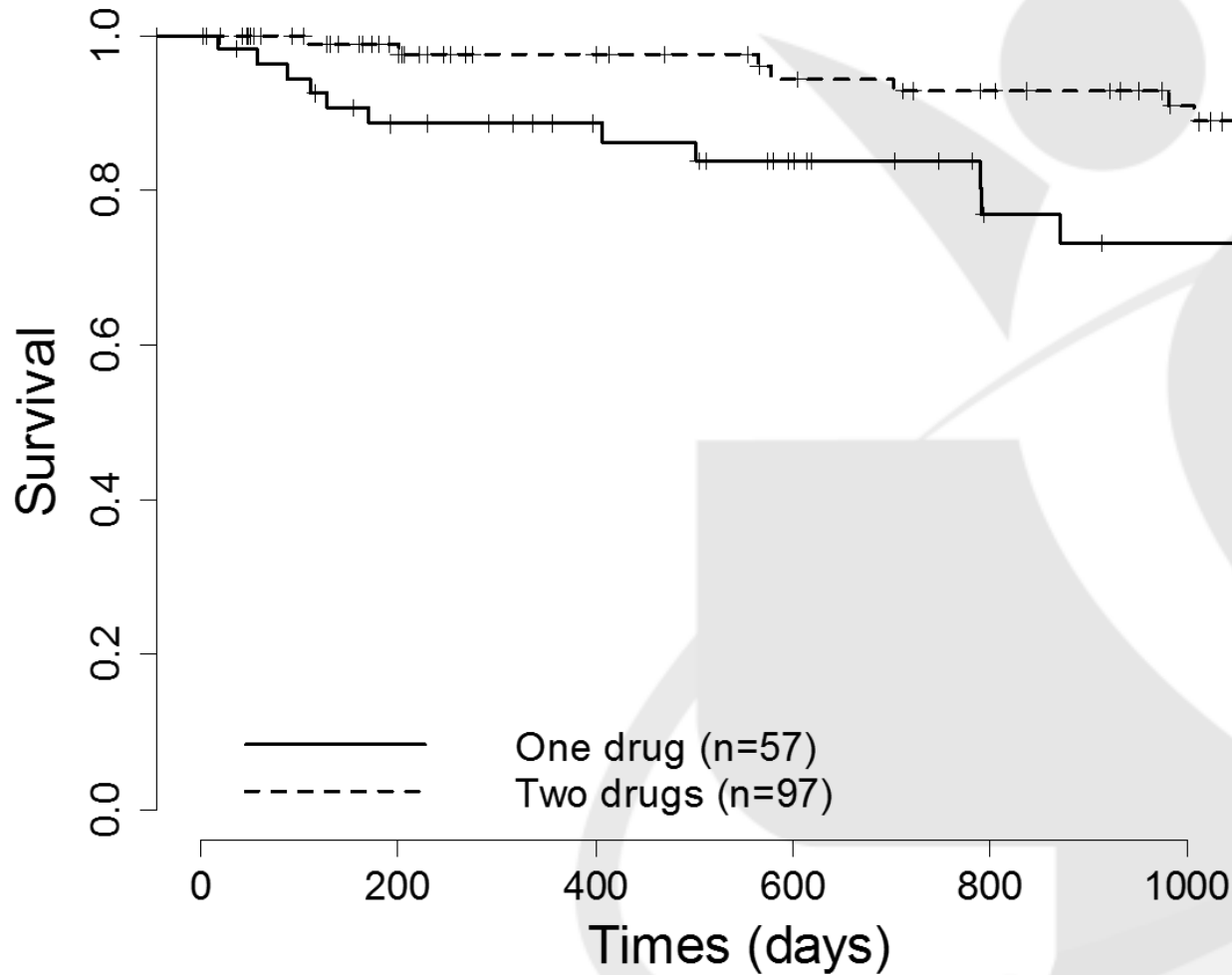
No neo-adjuvant treatment

Adjuvant treatment possible ?

		Time (years)				
No. At risk		0	3	6	9	12
ADJ	Left	13	8	4	2	0
	Failed	0	1	3	4	5
NA	Left	35	12	3	0	0
	Failed	0	14	22	22	22
PO	Left	20	8	2	1	0
	Failed	0	4	5	5	5
NoC	Left	46	19	8	4	0
	Failed	0	13	17	19	21

# Mesothelioma non consensus -

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**French data base  
CC0 resection  
HIPEC  
One drug  
Two drugs  
p= 0.01**

- Future treatments: **Associated treatments**
- Associate two chemotherapy for HIPEC
- Associate EPIC with HIPEC
- Associate antiangiogenic with chemotherapy
- Associate HIPEC and adjuvant chemotherapy

# Peritoneal mesothelioma : Conclusions

- Evaluation of the general status of the patient
- Correct nutrition and detect vascular embolism
- One of the more aggressive peritoneal disease
  
- Propose a cytoreductive surgery + HIPEC
- with ambitious objectives as :
  - CC0
  - 2 drugs for HIPEC and adjuvant IV
  - with 42,5°c and 60 minutes