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# HIPEC therapy and peritoneal carcinomatosis: indications and limitations

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Surgical Oncology

# Conflict of interest

- None

# Summary

- Colorectal peritoneal metastases (PM)
- Prevention of colorectal PM (High risk patients)
- Primary ovarian PM

# Colorectal Cancer PM

# CRC PC: schizophrenia vision

**Arguments pro-HIPEC**

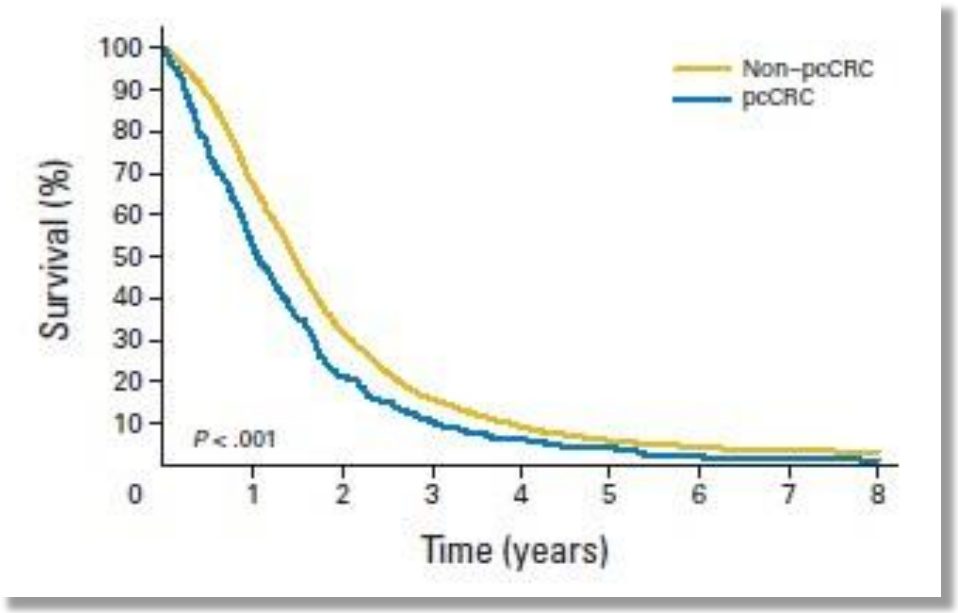
- PC = loco-regional disease
- **Low response rate to systemic chemoT**

**Arguments for systemic Chemotherapy**

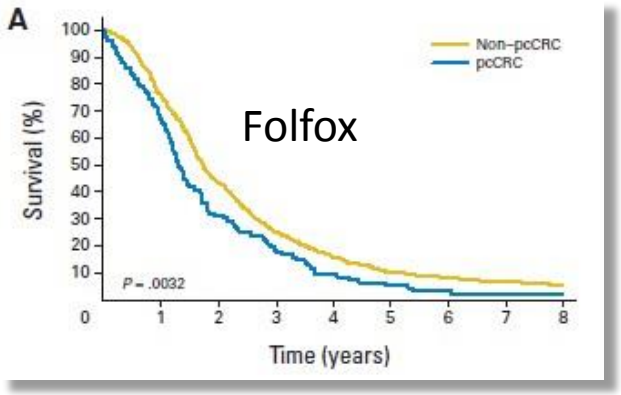
- PC is a systemic disease

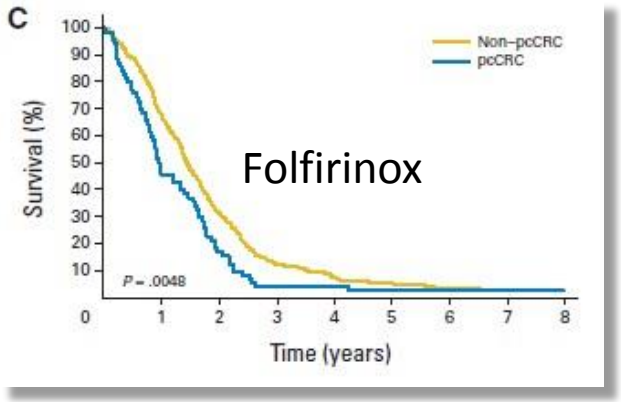
  -treatment of micrometastases

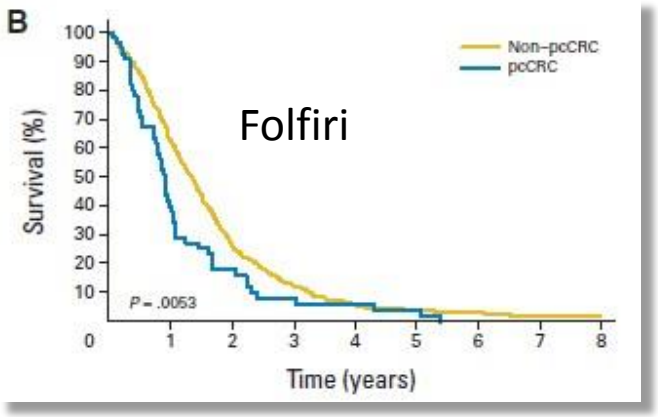
# Are PM more resistant to chemotherapy?




Overall survival by PC CRC status




**CRC PM are less sensitive to IV chemotherapy**

**Franko J Clin Oncol 2012**

# Are there arguments to corroborate the loco-regional disease theory?

- Dutch study*: evaluating ctDNA level in patients with CRC PC:

  -Only 20% of patients with increased blood level !!!

  -100% in ascitis.

  -This represents a major information confirming the hypothesis of loco-regional disease…

  -Could help in selecting patients with systemic infra-clinical multi-metastatic disease who could benefit of systemic chemoT

***In press**

# PRODIGE 7: CRS + systChemoT +/- HIPEC

Peritoneal carcinomatosis of colorectal origin

Surgery: complete surgical resection ≤ 1 mm

**RANDOMIZE** 1:1

- **with HIPEC**
- **without HIPEC**

**For both arms:**

Patients received systemic chemotherapy for 6 months, either pre-operative, post-operative, or both

Inclusion criteria :

- Histologically confirmed colorectal cancer
- Absence of extra peritoneal metastases
- Residual tumor status (R0/R1 vs R2 ≤ 1 mm)
- 6 months systemic chemotherapy
- Patients non previously treated with HIPEC
- Patients aged ≥ 18 and ≤ 70 years old

Stratification :

- Centre
- Residual tumor status (R0/R1 vs R2 ≤ 1 mm)
- Prior regimens of systemic chemotherapy
- Neoadjuvant Chemotherapy

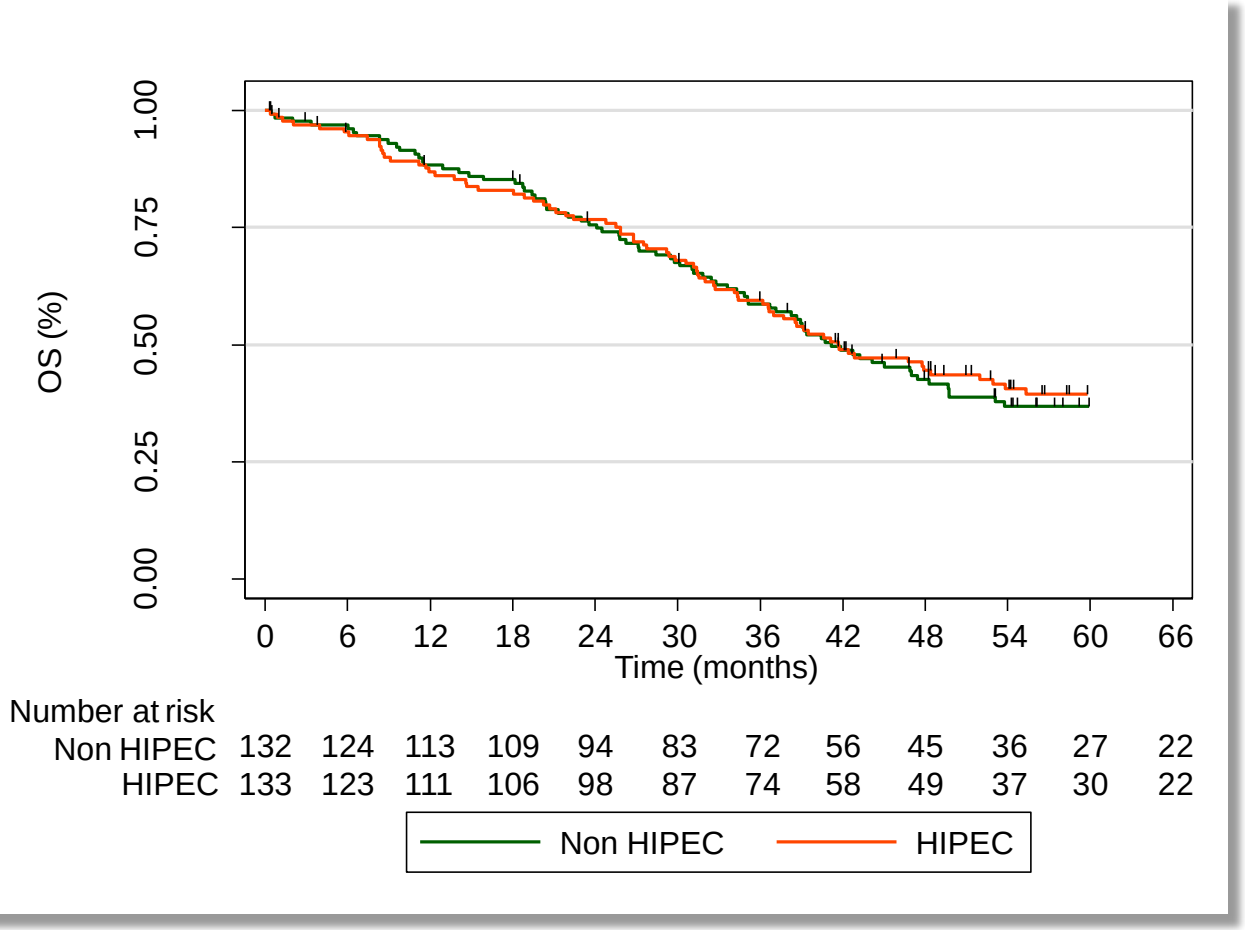
Primary endpoint: Overall survival

**Quenet et al. ASCO 2018**

# PRODIGE 7: CRS + systChemoT +/- HIPEC

| | HIPEC | Non-HIPEC | P-value |
|---|---|---|---|
| Median Survival (months) [95% CI] | 41.7 [36.2-52.8] | 41.2 [35.1-49.7] | 0.995 |
| 1-year Survival | 86.9% | 88.3% | |
| 5-year Survival | 39.4% | 36.7% | |

**HR=1.00: 95%CI [0.73 - 1.37] p=0.995**




**Quenet et al. ASCO 2018**

# PRODIGE 7: some personnel criticism

- Standard **6 months chemotherapy in** both groups
- Inclusion of patients with **PCI>16** (till 25)
- Not clear if some patients with extent PC were included after response to systemic chemotherapy (different populations)

**so adding HIPEC for 30' could be miraculous**

**Liberale et al. ACB 2019**

# PRODIGE 7: some personnel criticism

- Standard **6 months chemotherapy in** both groups
- Inclusion of patients with **PCI>16** (till 25)
- Not clear if some patients with extent PC were included after response to systemic chemotherapy (different populations)

NO solid data to support that in the literature*

**Maillet et al. Ann Surg Oncol 2015; Repullo et al. manuscript in preparation**

# HIPEC in CRC PM?

- Complete abdominal exploration with **COMPLETE MACROSCOPIC resection is the mainstain treatment of CRC PM**
  -problem: in practice, CRS and HIPEC always combined

- **NO HIPEC in patients treated by 6mo chemoT** and/or if major risk of complications

- **Role of HIPEC remains undetermined in chemoT naive patients**

# Colorectal Cancer:
# prevention of PM in high risk patients

# Locally advanced CR cancer: PM prevention

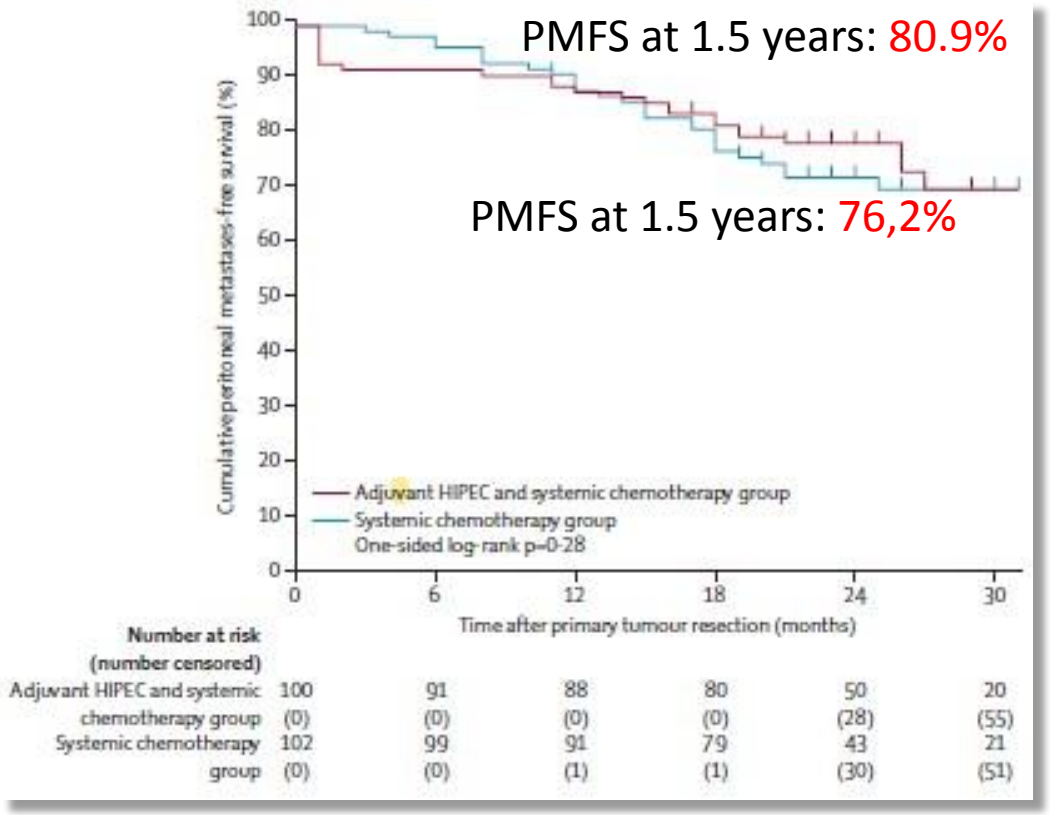
**Adjuvant hyperthermic intraperitoneal chemotherapy in patients with locally advanced colon cancer (COLOPEC): a multicentre, open-label, randomised trial**

*Charlotte E L Klaver, Daniel D Wisselink, Cornelis J A Punt, Petur Snaebjornsson, Johannes Grezee, Arend G J Aalbers, Alexandra Brandt, Andre J A Bremers, Jacobus W A Burger, Hans F J Fabry, Floris Ferenschild, Sebastiaan Festen, Wilhelmina M U van Grevenstein, Patrick H J Hemmer, Ignace H J T de Hingh, Niels F M Kok, Gijsbert D Musters, Lotte Schoonderwoerd, Jurriaan B Tuynman, Anthony W H van de Ven, Henderik L van Westreenen, Marinus J Wiezer, David D E Zimmerman, Annette A van Zweeden, Marcel G W Dijkgraaf, Pieter J Tanis, on behalf of the COLOPEC collaborators group**

Multi-centric Dutch Prospective RCT
204p patients: 2015-2017
High risk PM: pT4-N0-2, peforated T+

HIPEC: 400mg/m2 Oxaliplatin, 30min, 42°.

Primary EP: Peritoneal M+ Free survival at 18m (explorative laparoscopy at 18m)



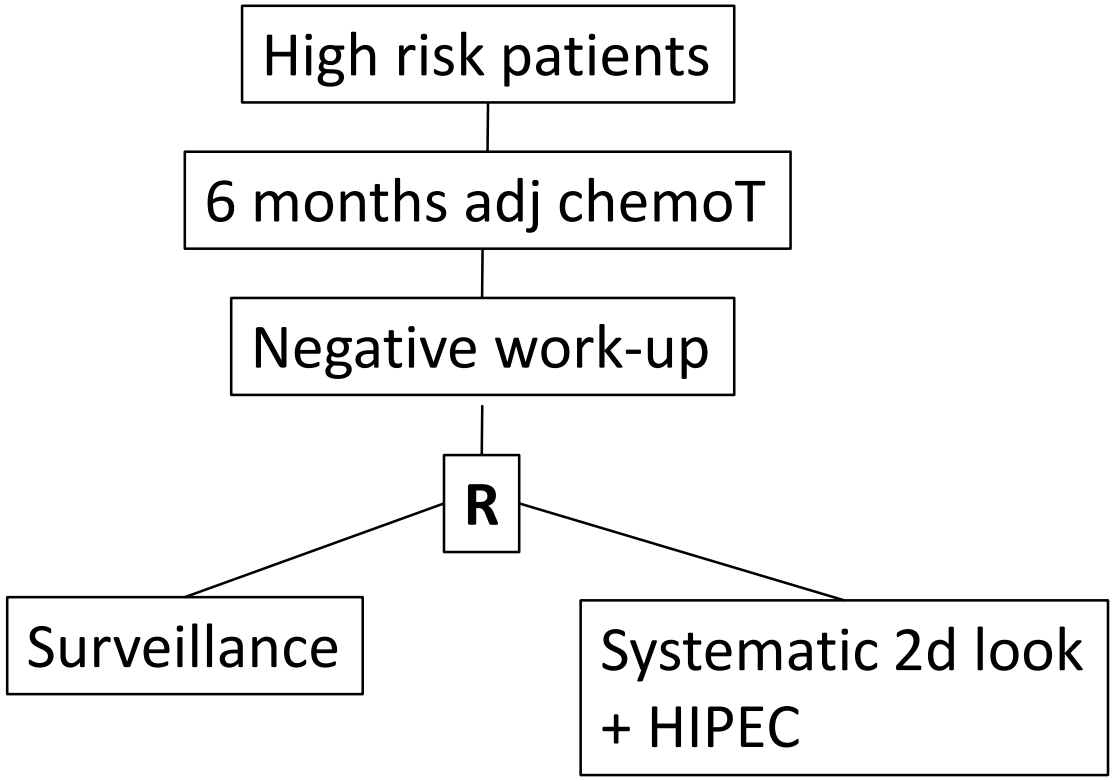

**Peritoneal M+ FS: no difference**

Klaver et al. Lancet Gastroenterol Hepatol 2019

# PROPHYLOCHIP: CR resection + systChemoT +/- second look and HIPEC

Inclusion criteria :

- Histologically confirmed CRC
- **High risk for PM: ovarian mets, perforated T+, limited PM resected**
- 6 months systemic adjuvant chemoT
- Patients aged ≥ 18 and ≤ 70 years old




First endpoint: 3-y DFS

**Goéré et al. ASCO 2018**

# PROPHYLOCHIP: CR resection + systChemoT +/- second look and HIPEC

Résultats:

- 150 patients; 2012-2015
- **Group 2d look (71p): 52% PM; median PCI 4 (0-26)**
- **Mortalité: 0%;** complications grade 3-4: 41%
- Median follow-up 51m (47-55)

3-y DFS: 44% (2d look) vs 51% (surveillance) (p=0.75)
No significant difference

**Goéré et al. ASCO 2018**

# HIPEC in High risk CRC patients?

- Criteria to define High risk patients are strong
- **NO role of proactive CRS/HIPEC**

# Ovarian Cancer PM: first line

# Ovarian Ca PM: HIPEC in first line

The NEW ENGLAND JOURNAL of MEDICINE

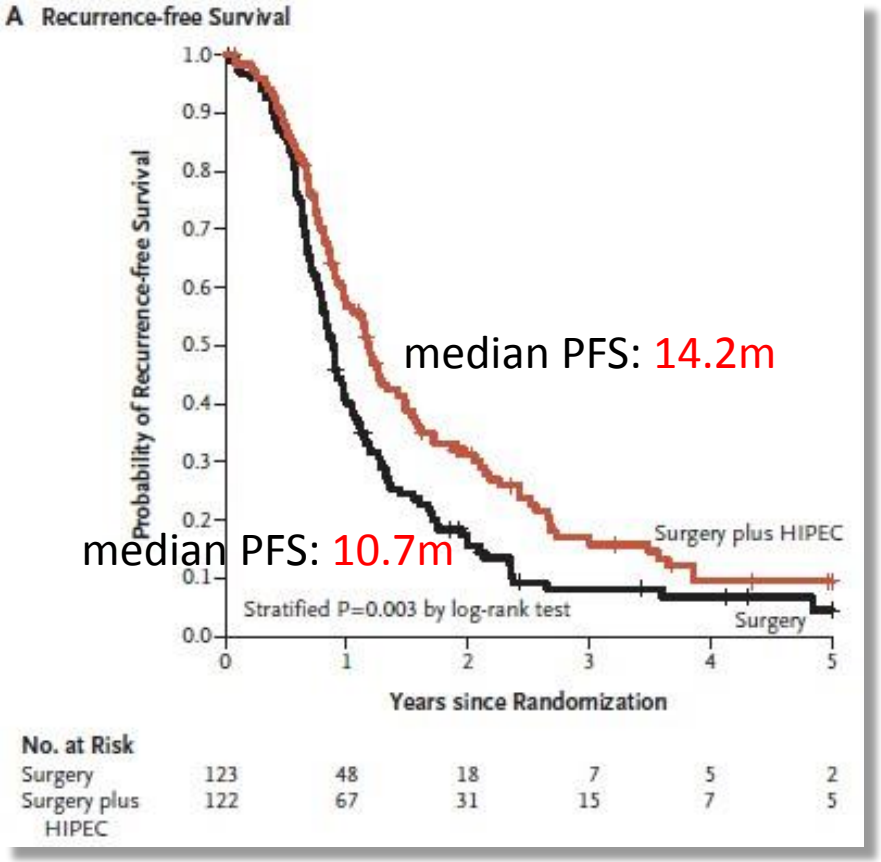
ORIGINAL ARTICLE

## Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer

W.J. van Driel, S.N. Koole, K. Sikorska, J.H. Schagen van Leeuwen, H.W.R. Schreuder, R.H.M. Hermans, I.H.J.T. de Hingh, J. van der Velden, H.J. Arts, L.F.A.G. Massuger, A.G.J. Aalbers, V.J. Verwaal, J.M. Kieffer, K.K. Van de Vijver, H. van Tinteren, N.K. Aaronson, and G.S. Sonke

Multi-centric Dutch Prospective RCT
245p Stage III patients: 2007-2016
Interval surgery
HIPEC: 100mg/m2 Cisplatin, 90min, 40°.
Primary EP: RFS (↑50%DFS)

Median Follow-up: 4.7years




**Van Driel et al. NEJM 2018**

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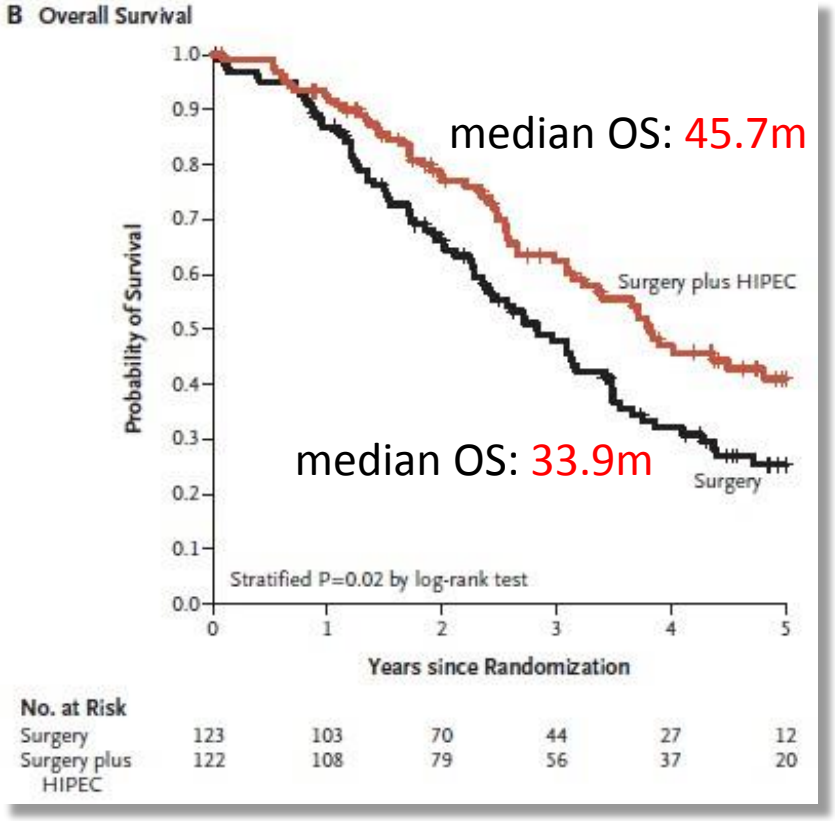
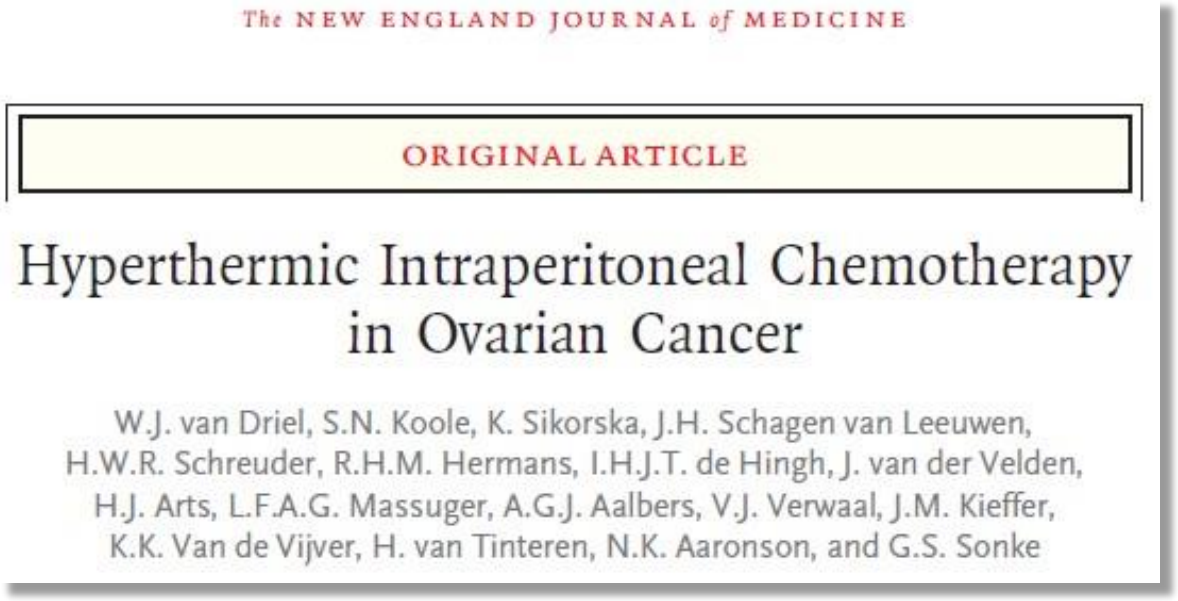



**Van Driel et al. NEJM 2018**

# Ovarian Ca PM: HIPEC in first line



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**PRO**

First step!!
Similar side effect.
No delay adjuvant chemoT
Several questions remaining: T°, IPC?, cost-benefit

**CON**

No BRCA status stratification, Histologic type, centers, toxic effects
Corean trial: no difference but stage III/IV

**Spriggs et al. NEJM 2018; Vergote et al. NEJM 2018**

# HIPEC in ovarian PM?

- Role of HIPEC remains undetermined in patients treated by upfront surgery (results of OVHIPEC-2)
- HIPEC is an **option** in France in **interval debulking** and recommended (**standard**) in Netherland
- **Encouraging but not yet accepted as a standard treatment** by the majority of country → more trials needed!!!

Thank you for your attention

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