

peritoneal colorectal carcinomatosis

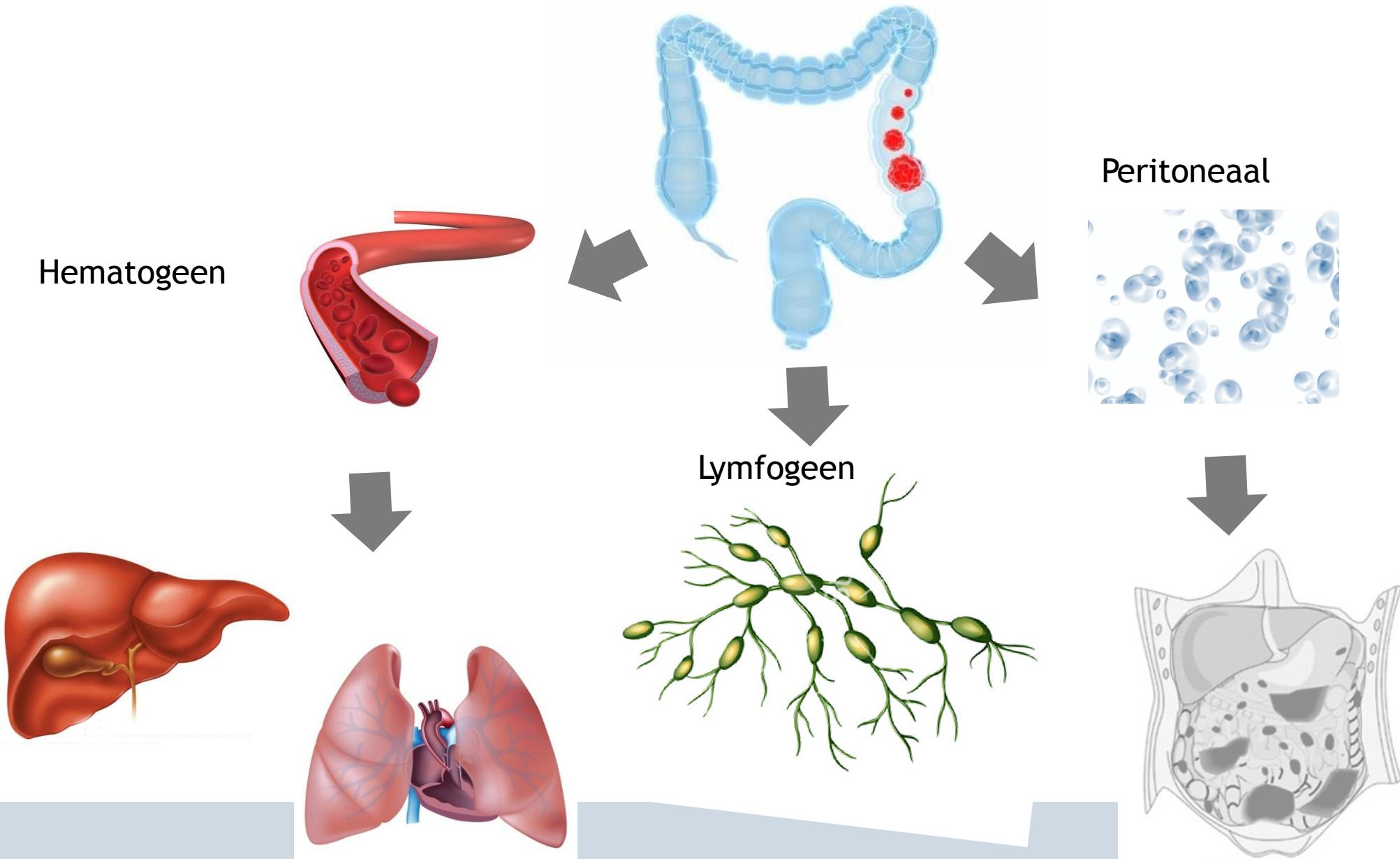
Colorectaal carcinoom en peritonitis carcinomatosa

Wat zijn de behandelopties

Wat is er nog te onderzoeken ?



Colorectaal carcinoom en metastasen





Peritonitis Carcinomatosa CRC

Incidentie

Nederland 14000 colorectale kanker pt / jaar
+/- 500-800 Peritonitis carcinomatosa

25-30 %

van T4 carcinomen ontwikkelt of heeft PC

Overall Survival

Met alleen palliatie overall survival 6-12 mnd



Peritoneal Carcinomatosis

Vaak presentatie met advanced disease

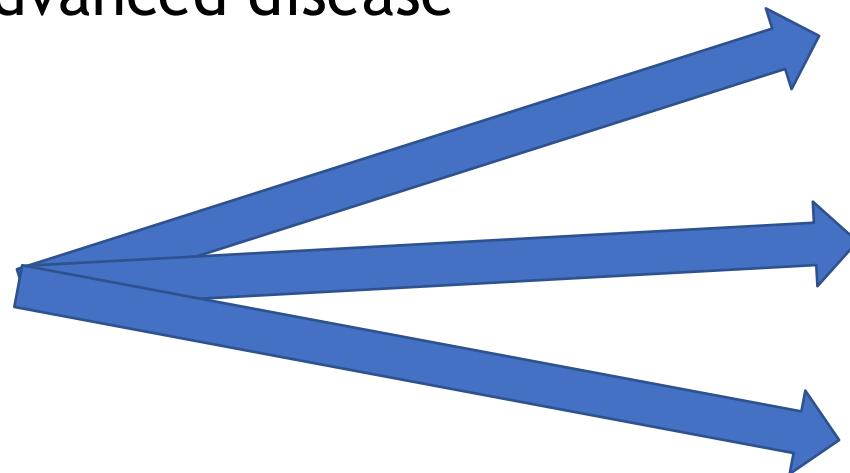
Symptoms ?

Diagnostiek faalt

CEA ?

Vaak bij operatie toch niet zinnig ; Open close up to 10-20%

Imaging





Peritoneal Carcinomatosis - diagnosis

Symptoms

X

CEA

X

CT scan

X

MRI

?

Diagnostic laparoscopy ??



NCPO

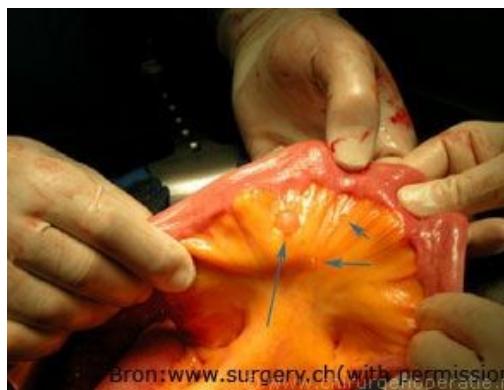
NEDERLANDS CONGRES PERITONEALE ONCOLOGIE

Jurriaan Tuynman Advanced Peritoneal CRC. NCPO 11oct 2019



1. Cytoreductieve chirurgie

- Volledige verwijdering van kanker deposities
- Lever mobilisatie
- Diafragma , milt exploratie
- Maag, bursa omentalis
- Volledige dunne darm
- Colon en rectum
- Bekken; ureterus , blaas, adnexen

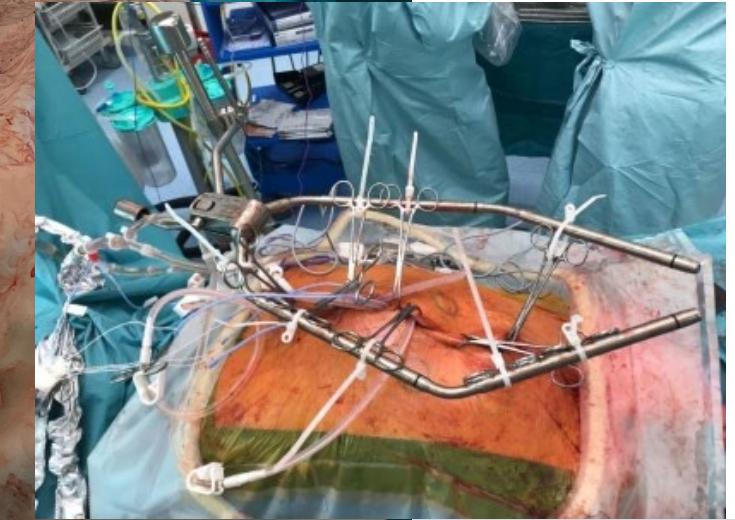
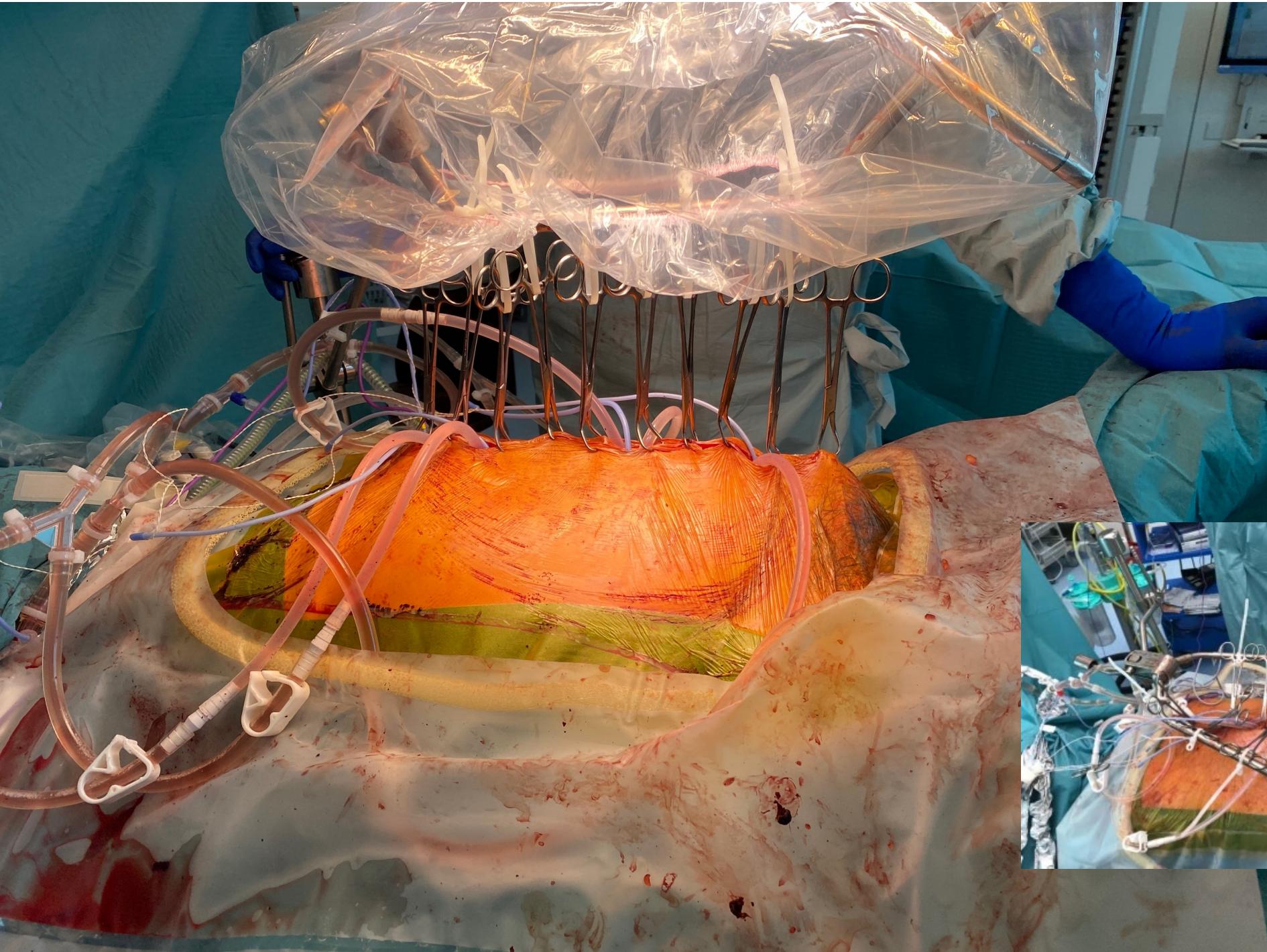




Hypertermische intraperitoneale chemotherapie; HIPEC



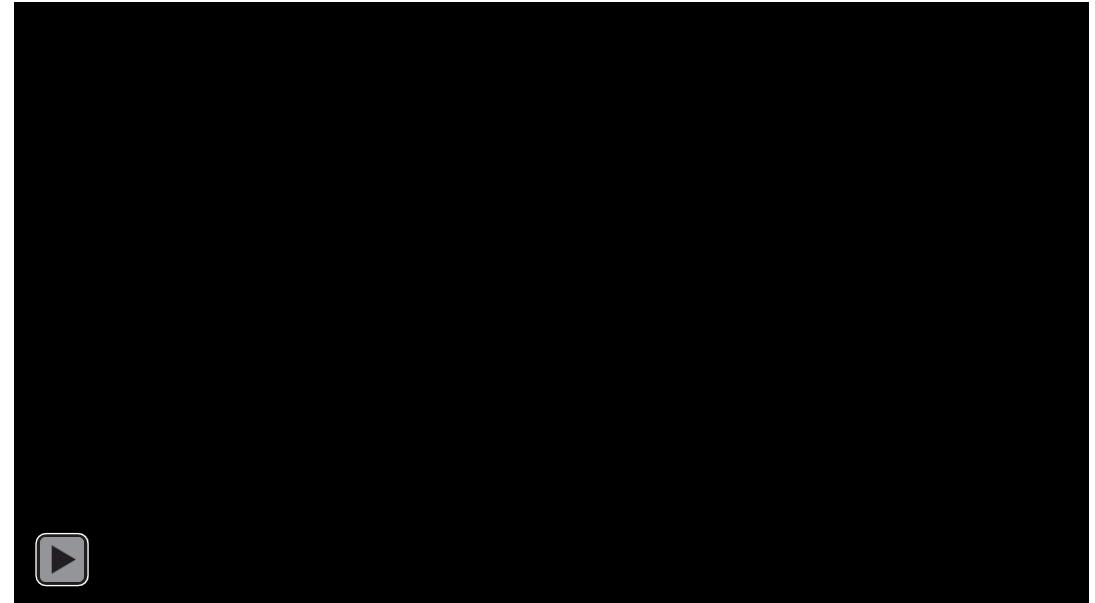
- Spont
- 90 D
- Daar
- Sluit
- Med





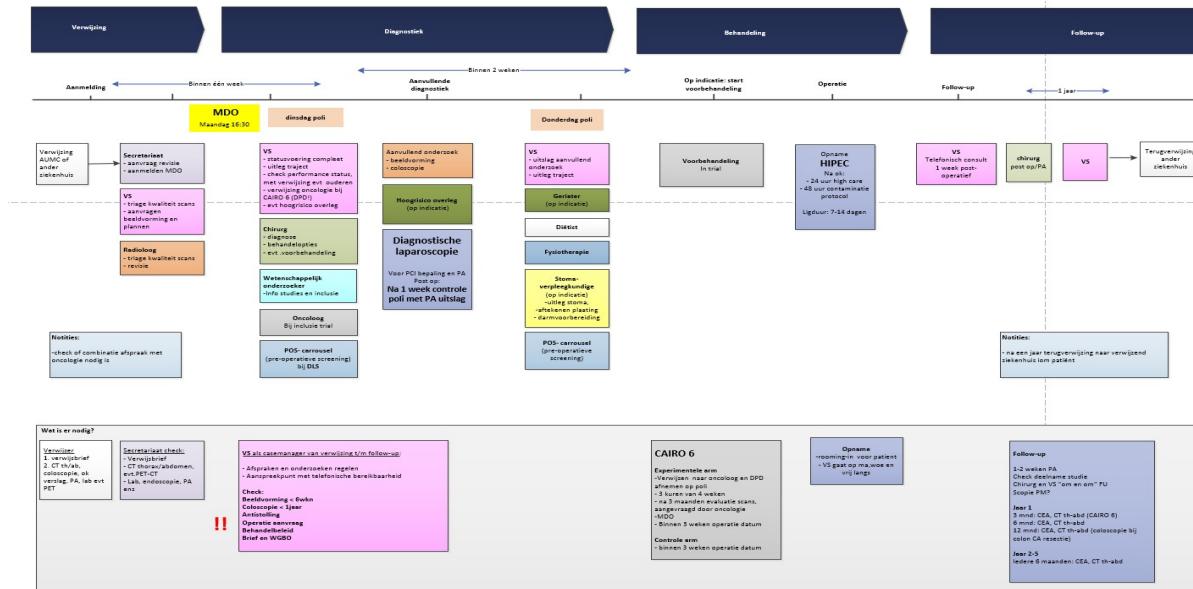
HIPEC en Cytoreductie

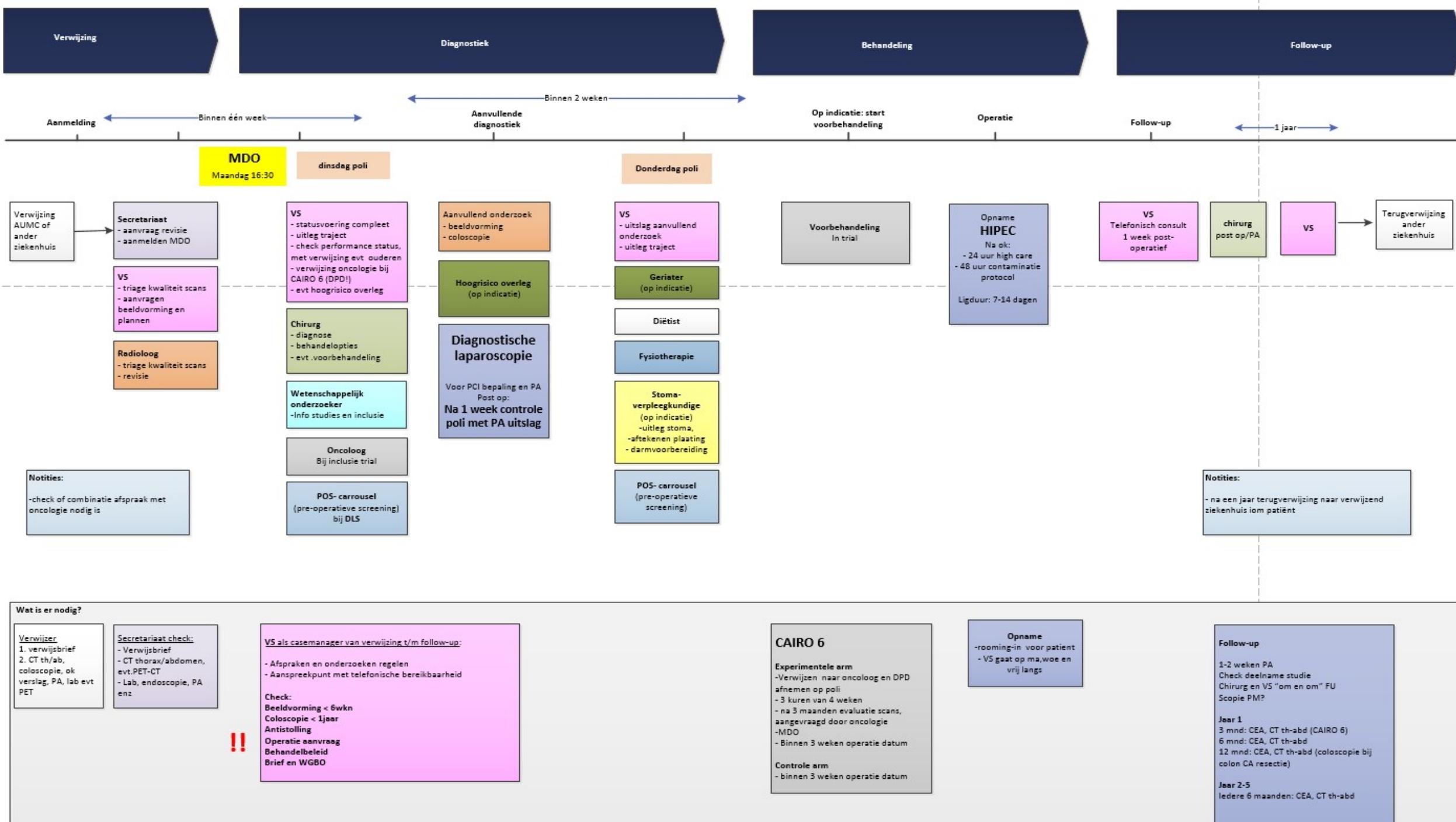
- Spoelen van de buik met Chemotherapie
- 90 minuten
 - Daarna continuiteitsherstel
 - Sluiten buik
- Medium care





Zorgpad Patient met PC







Zorgpad Patient met PC

- Poliklinisch twee gesprekken
- Uitgebreide work - up inclusief diagnostische laparoscopie
- Twee gesprekken chirurg , Verpleegkundig specialist
- Stoma verpleegkundige
- Dietiek
- Fysiotherapie
- Uitleg verpleegkundig
- Anaesthesie
 - Evt - geriater



Postoperatief Herstel

- 24 h contaminatie chemotherapie protocol
- 24 h observatie medium care
 - Vaak overvulling, vochtbalans, noradrenaline behoefte
- Herstel afhankelijk van uitgebreidheid chirurgie
 - Thorax drains bij diaframa opening
 - Drains, ascites
 - epiduraal
 - Voedings problem; langdurige gastroparese



Postoperatief Herstel - complicaties

- 20-30 % langdurige maagparese
- 10 -20% Intraabdominale infecties
- 10-20% Wond infectie

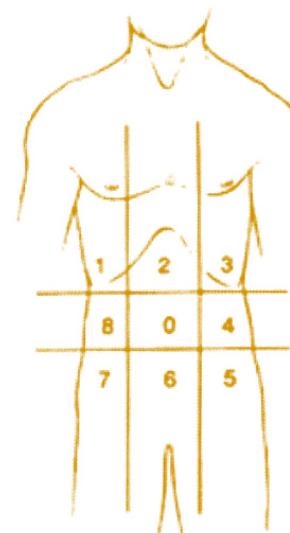
- Hulp bij ADL en Volledige mobilisatie
- Hulp bij stomata

- Mortaliteit 0.5%



HIPEC indicaties

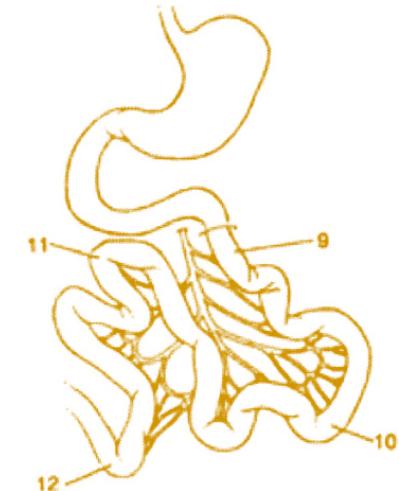
- Colorectal carcinoma / appendix / mesothelioma
- Intra-abdominal metastases
- PCI<20
- Performance status / ASA < 3



Diagnostic laparoscopy

Regions	Lesion Size
0 Central	—
1 Right Upper	—
2 Epigastrium	—
3 Left Upper	—
4 Left Flank	—
5 Left Lower	—
6 Pelvis	—
7 Right Lower	—
8 Right Flank	—
9 Upper Jejunum	—
10 Lower Jejunum	—
11 Upper Ileum	—
12 Lower Ileum	—

Lesion Size Score
LS 0 No tumor seen
LS 1 Tumor up to 0.5 cm
LS 2 Tumor up to 5.0 cm
LS 3 Tumor > 5.0 cm or confluence





Uikomsten HIPEC variable



Morbidity

Gain QoL

OS

- | | | | |
|------------|------------------|-----------------------|-----------|
| • Low PCI | - Low morbidity. | - excellent survival | 5yr > 50% |
| • High PCI | - High Morbidity | - poor survival | 5 Yr <10% |

Alternatives ?



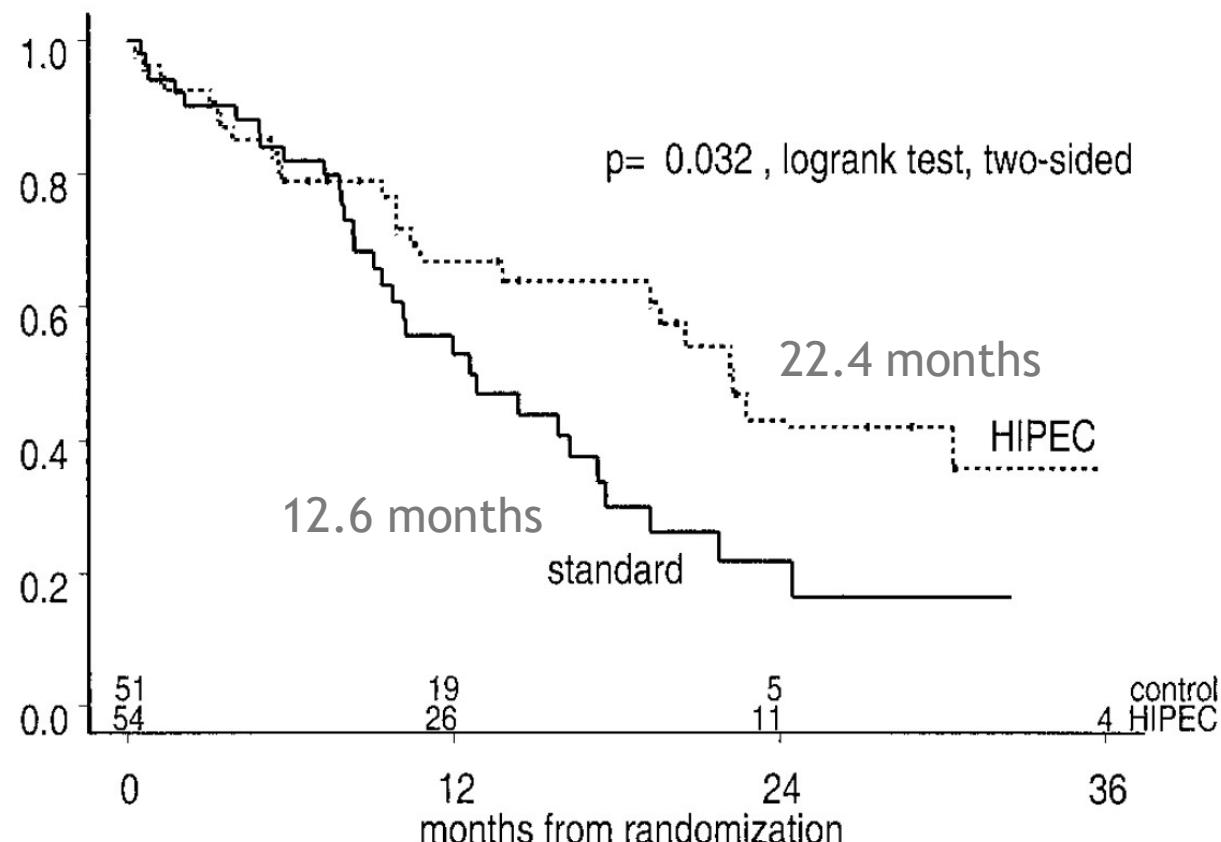
Chemotherapie of HIPEC

NKI-AVL



RTC 2003

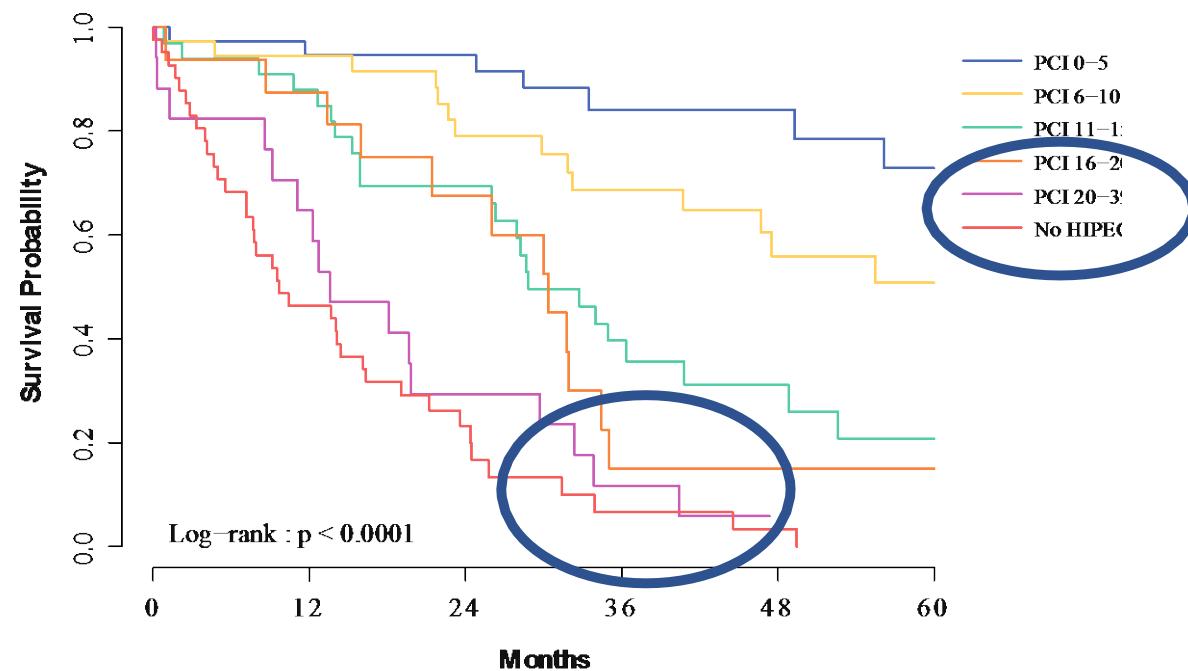
CYTOREDUCTION AND HIPEC VERSUS CHEMOTHERAPY



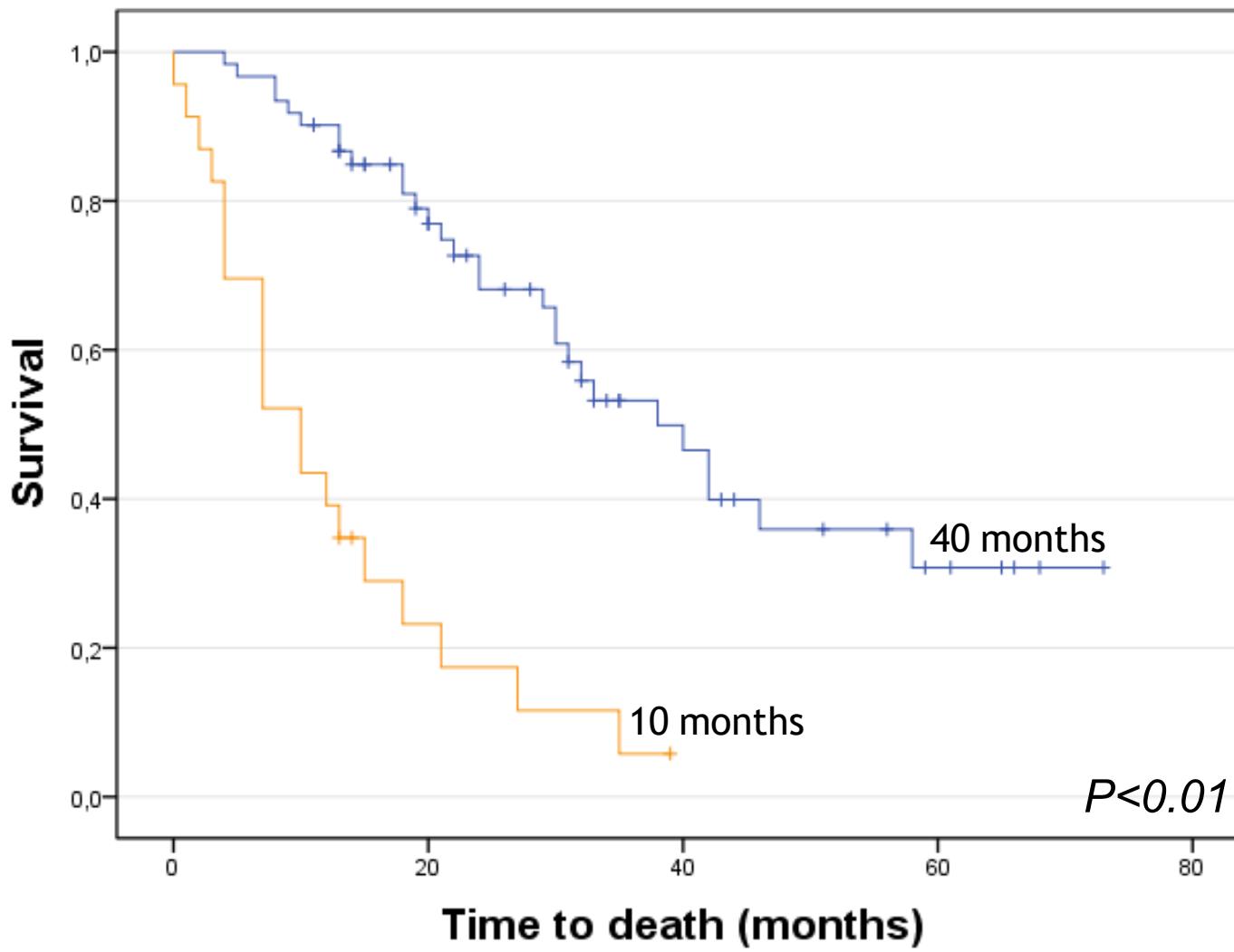


Uitkomsten van HIPEC - overleving

PCI index

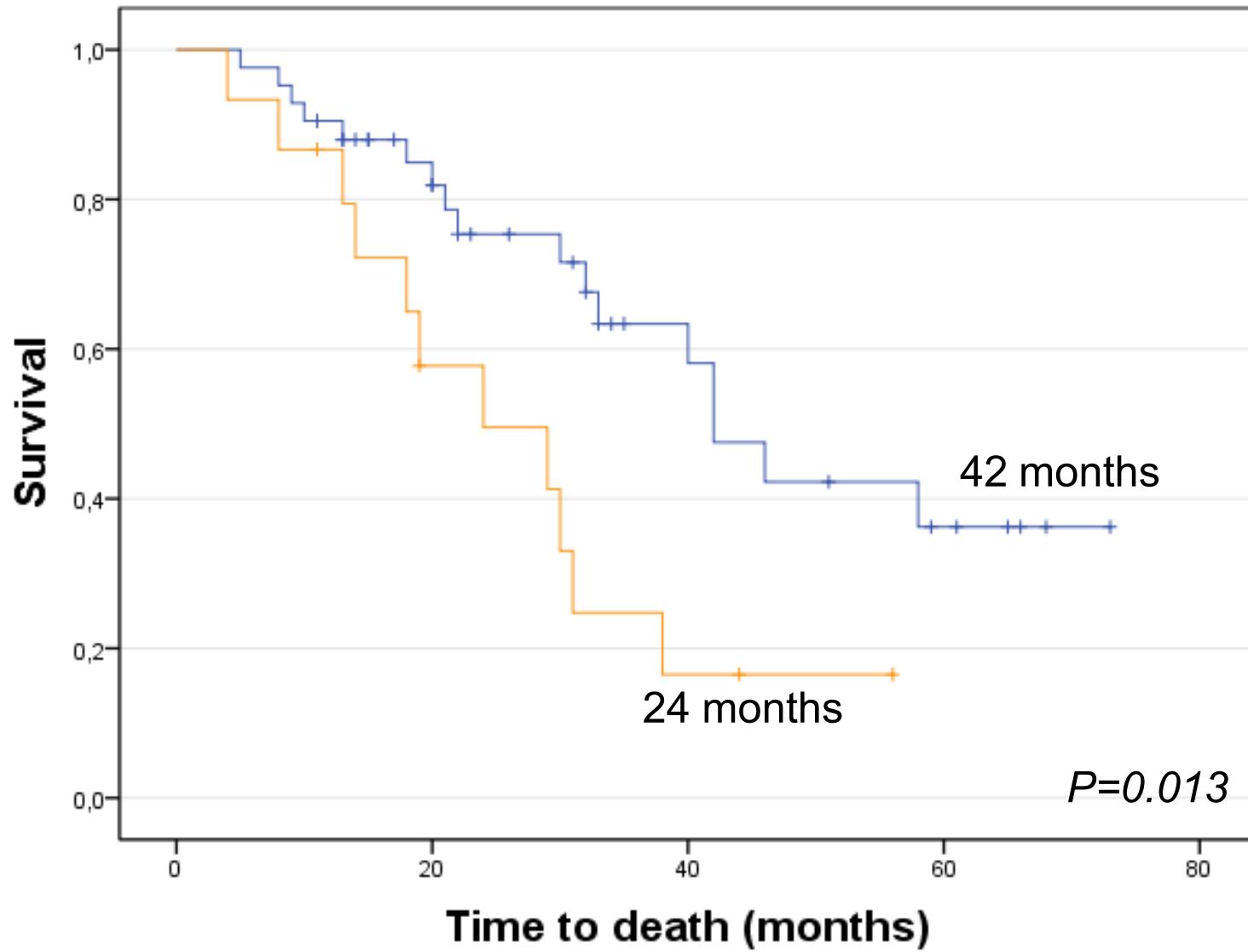


At risk						
37	33	30	18	15	12	PCI 0-5
36	34	24	19	11	9	PCI 6-10
33	29	21	10	6	4	PCI 11-15
16	14	9	1	1	1	PCI 16-20
17	11	5	2			PCI 20-39
41	19	7	2	1		No HIPEC



- CRS+HIPEC
- Open-close (PCI >20)







Wat kan er Beter - challenges

1. Hoge morbiditeit (vooral bij hoge PCI)
2. Betere Diagnostiek / patient selectie
3. Relatief hoge klans op recidief ziekte (up to 70%)



Current challenges

1. Relatively high morbidity
 - Better patient selection
 - Liquid biopsies
 - Diagnostic MRI
 - Diagnostic laparoscopy
2. Diagnostic failure
3. Relatively high recurrence rates
 - Better CRS / chemotherapy
 - Better selection



Ungoing research Amsterdam UMC

LIBEC trial

ctDNA in HIPEC patients

Non coding RNA in HIPEC

iHIPEC

Intra-operative imaging

NET-tumoren

value CRS + HIPEC

Genetic Landscape of pC
(preclinical)

COLOPEC studies

NK cells as targeted
therapy (preclinical)

Cell cultures

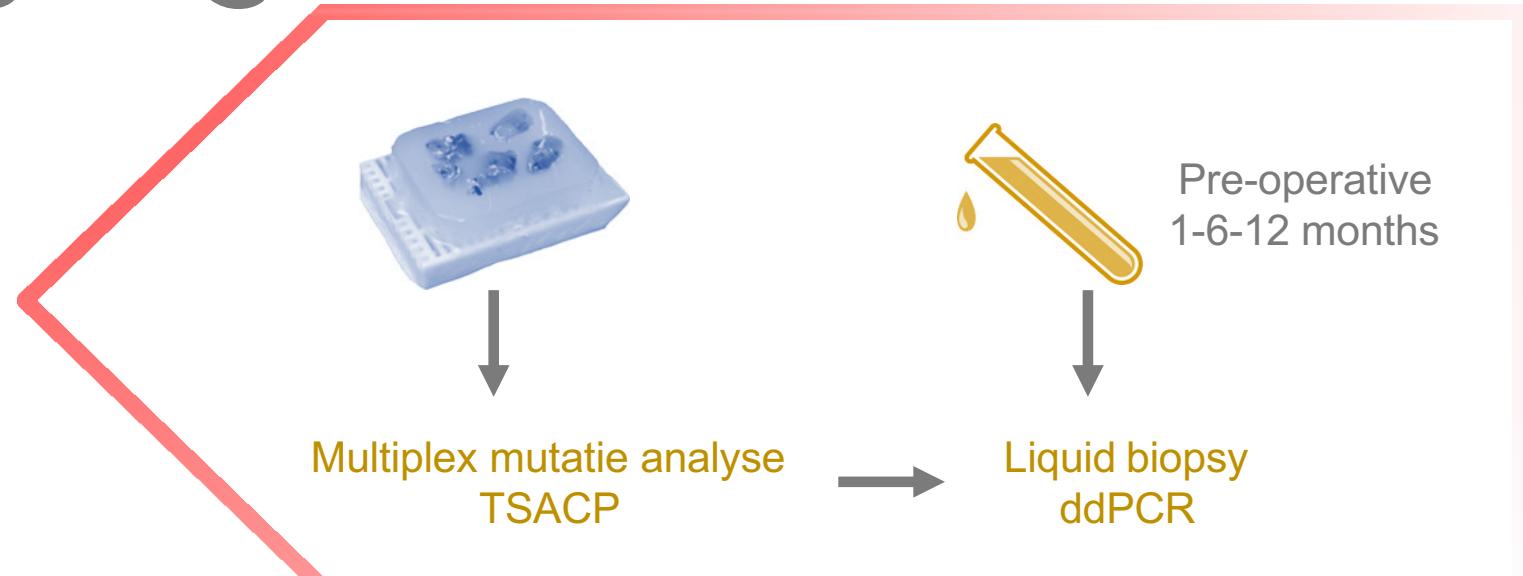


Ungoing research

LIBEC trial
ctDNA in HIPEC patients

iHIPEC
Intraoperative imaging
Toch eraand dat waardeer
tumorcellen in bloed aanwezig
zijn

\geq HIPEC slechte prognose heeft
value CRS + HIPEC



Circulating Tumor DNA as a Preoperative Marker of Recurrence in Patients with Peritoneal Metastases of Colorectal Cancer: A Clinical Feasibility Study.

Beagan JJ, Sluiter NR, Bach S, Eijk PP, Vlek SL, Heideman DAM, Kusters M, Pegtel DM, Kazemier G, van Grieken NCT, Ylstra B, **Tuynman JB**.

J Clin Med. 2020 Jun 4;9(6):E1738. doi: 10.3390/jcm9061738.

Circulating Tumor DNA Analysis: Clinical Implications for Colorectal Cancer Patients. A Systematic Review.

Bach S, Sluiter NR, Beagan JJ, Mekke JM, Ket JCF, van Grieken NCT, Steenbergen RDM, Ylstra B, Kazemier G, **Tuynman JB**.



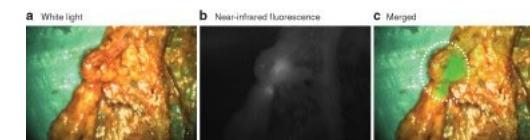
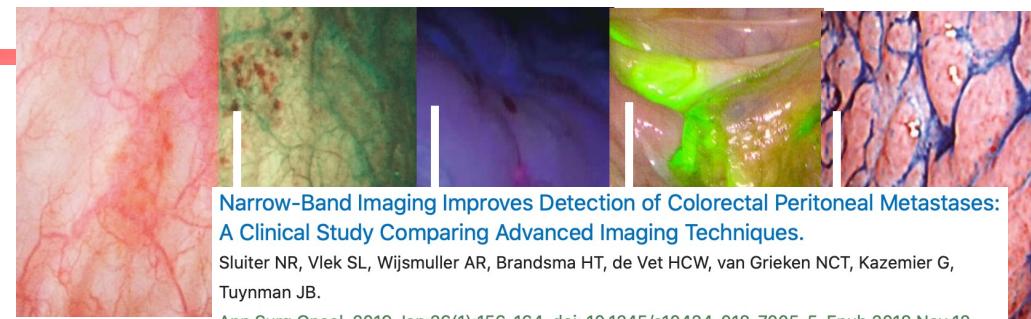
Ungoing research

Tonen aan dat met advanced imaging we meer Peritoneale metastasen aantonen
LIBEC trial
 > ~~BDN~~ Neoadjuvant HIPEC patients

iHIPEC
Intra-operative imaging

NET
value CRS + HIPEC

White light, NBI, 5-ALA, indocyanin green, indigo carmine blue



Carcinoembryonic antigen-specific, fluorescent image-guided cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for metastatic colorectal cancer

D. P. Schaap, K. S. de Valk, M. M. Deken, R. P. J. Meijer, J. Burggraaf, A. L. Vahrmeijer, M. Kusters✉, on behalf of the SGM-101 study group ... See fewer authors ▾



Ungoing research

Tonen aan dat CRS en HIPEC

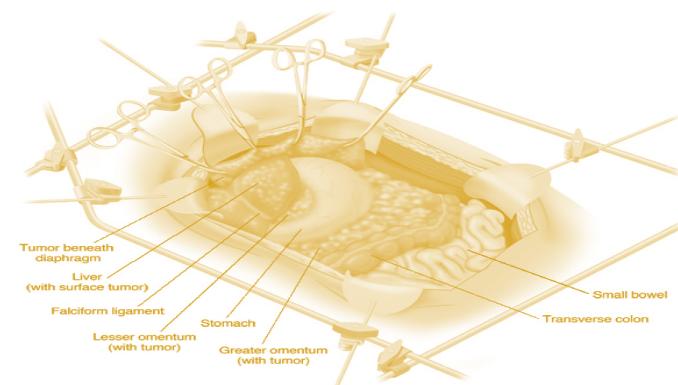
Ook zinvol is bij
LIREC trial
neuroendocriene tumoren en
~~bij DNL in de HIPEC protocols~~

iHIPEC

Intra-operative imaging

NET

value CRS + HIPEC



GE-NET-tumoren
Systematic review + cohort study



Ungoing research

Translational NK cell mediated killing

Toffoli / Vliet / Tuynman

Translational Genetic landscaping PC

Leonos / Vermeulen / Tuynman

Translation ; new drug finding

Vermeulen / Crezee / Tuynman



Ungoing research

Failing diagnostic tools

COLOPEC

T4 colon ca ??

COLOPEC II

**Diagnostic
laparoscopy in
detection PC**

CAIRO 6 trial - chemotherapie combineren met HIPEC



Alléén CRS-HIPEC
179 patiënten

VS

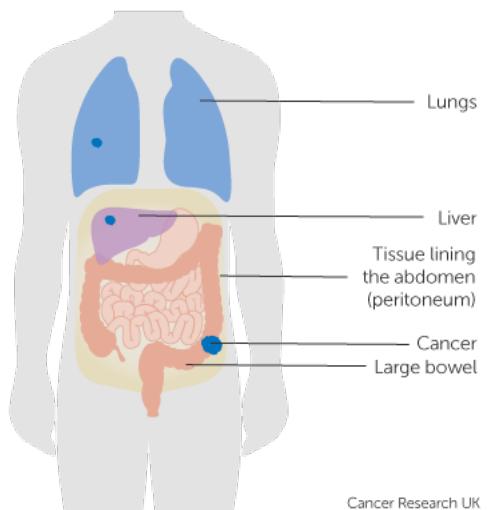
= 358



Chemo-therapie rondom CRS-HIPEC
179 patiënten

Hypothese:
3-year OS van 50% → 65% in de experimentele arm

Nieuwe Amsterdam UMC studie OLIPEC



DPOG/Amsterdam UMC

MCE Polderdijk, DW Sommeijer, PJ Tanis, RJ Swijnenburg, M Meierink, J Waesberge, JB Tuynman



Patient Peritoneal metastasis and oligometastasten

- 2 lever metastasen
- Coloncarcinoom
- Peritonitis carcinomatosa (gelimiteerd)

?



Survival data Peritoneal metastasis and oligometastases

- Option ; Palliative treatment
- Option; Study Orchestra = palliative treatment & palliative +80% debulking
- Option; Systemic and ablative therapy = HIPEC CRS / resection



Survival data Peritoneal metastasis and oligomets

- Option ; Palliative treatment

CAIRO 1 Cairo 2 studies; 10-15 months OS



Survival data Peritoneal metastasis and oligomets

- Option; Study Orchestra = palliative treatment & palliative +80% debulking
 - Patiëntendoelgroep; divers , multiple metastasen
 - Palliatie is insteek / standaard
 - Vraag is of bij oligo metastasen en PC lokale therapie niet voorkeur verdient
 - Studie bijna dicht



Survival data Peritoneal metastasis and oligomets

- Option ; Palliative treatment
- Option; Study Orchestra = palliative treatment & palliative +80% debulking
- Option; Systemic and ablative therapie = HIPEC CRS / resection



Systematic review

- P: PC en hematogene metastasen in 1 orgaan
- I: CRS-HIPEC + lokale therapie
- C: palliatieve chemotherapie/alleen behandeling PC
- O: recurrence-free survival, overall survival
- Zoekstrategie:
 - Colorectal cancer + peritoneal metastasis + hematogenous metastases/oligometastasis/liver metastasis/lung metastasis



Survival data

Peritoneal metastasis and oligomets

- Option ; Palliative treatment CAIRO 1 Cairo 2 studies; 10-15 months OS
ARCAD aanvraag; oligo metastasis lung liver and peritoneal metastasis ; systemic only 10-18 months
- Option; systemic and ablative therapie = HIPEC CRS / resection

Outcome	PM+LM (n=903)	PM (n=1023)
Median OS	30,7 (13-47,6) months	36,6 (20,5-60,1) months
5YS	33,8% (16,5%-48,8%)	39,6% (16%-55,4%)
DFS/PFS	13,3 (6,7-21) months	15,6 (12-24) months



Peritoneal metastasis and oligomets

- STEP 1 Snapshot DPOG uitkomsten
- STEP 2 Prospective study intention to treat
 - Patients with 1 organ oligo mets
 - Systemic induction (triple) therapy 6 months
 - CRS HIPEC / Ablation



HIPEC for PC and liver mets

Metastasis

Curative cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy in patients with peritoneal carcinomatosis and synchronous resectable liver metastases arising from colorectal cancer

G. Lorimier ^a, B. Linot ^{a,*}, N. Paillocher ^a, D. Dupoirion ^a,
V. Verrièle ^a, R. Wernert ^a, A. Hamy ^b, O. Capitain ^a

G. Lorimier et al. / EJSO 43 (2017) 150–158

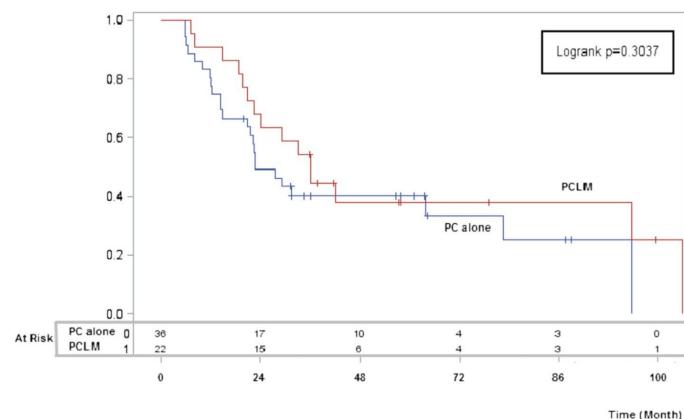
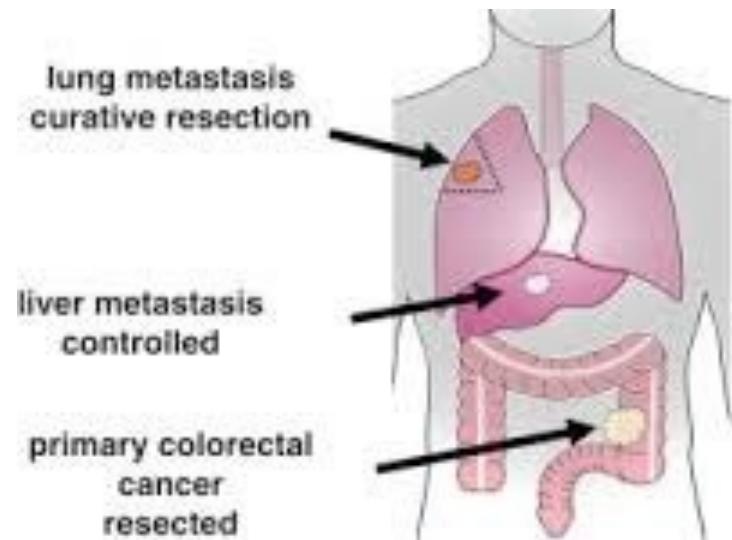


Figure 1. Overall survival of PCLM versus PC alone group.



Systemic therapy

peritoneal colorectal carcinomatosis in Amsterdam UMC

TEAM WORK