

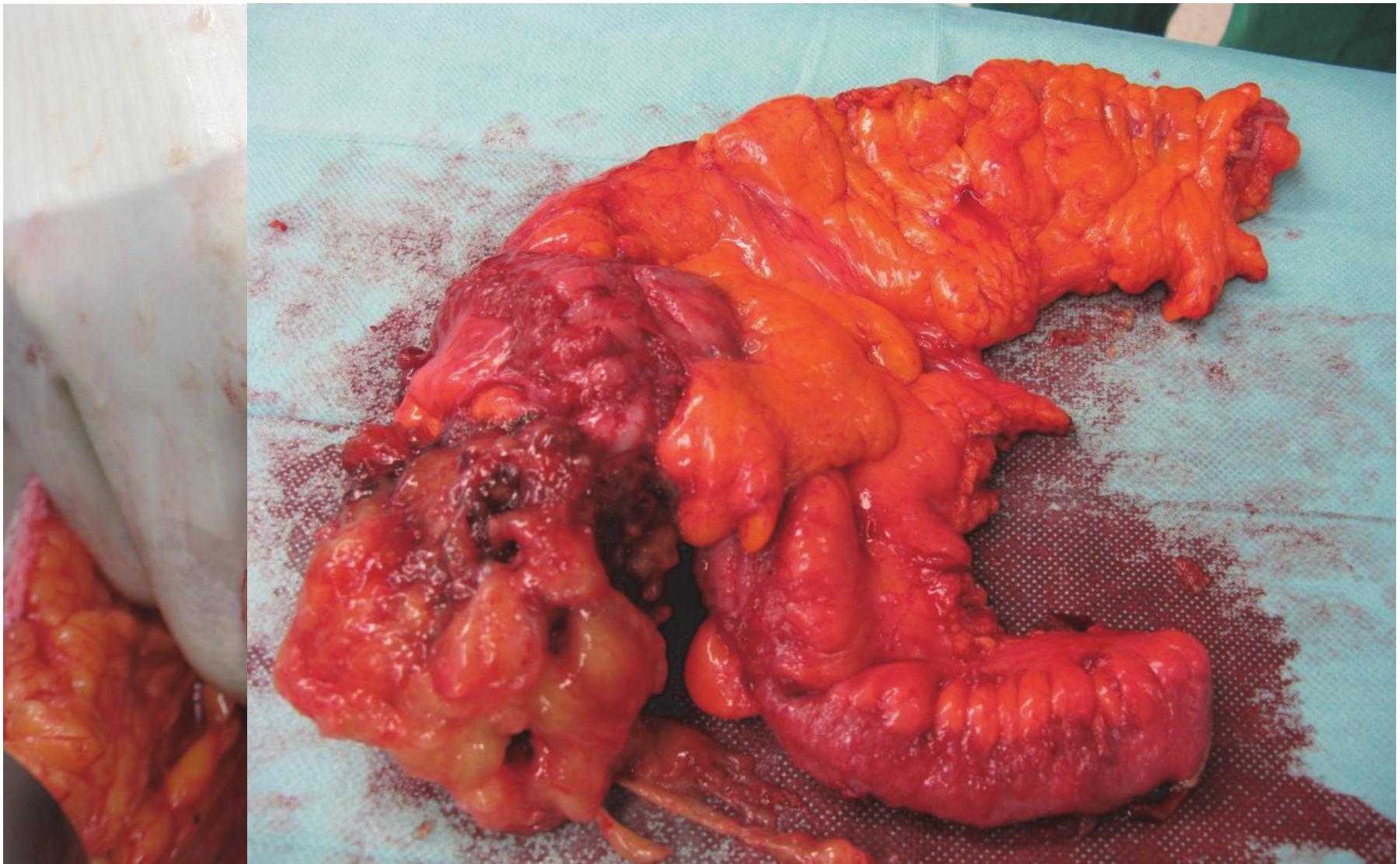


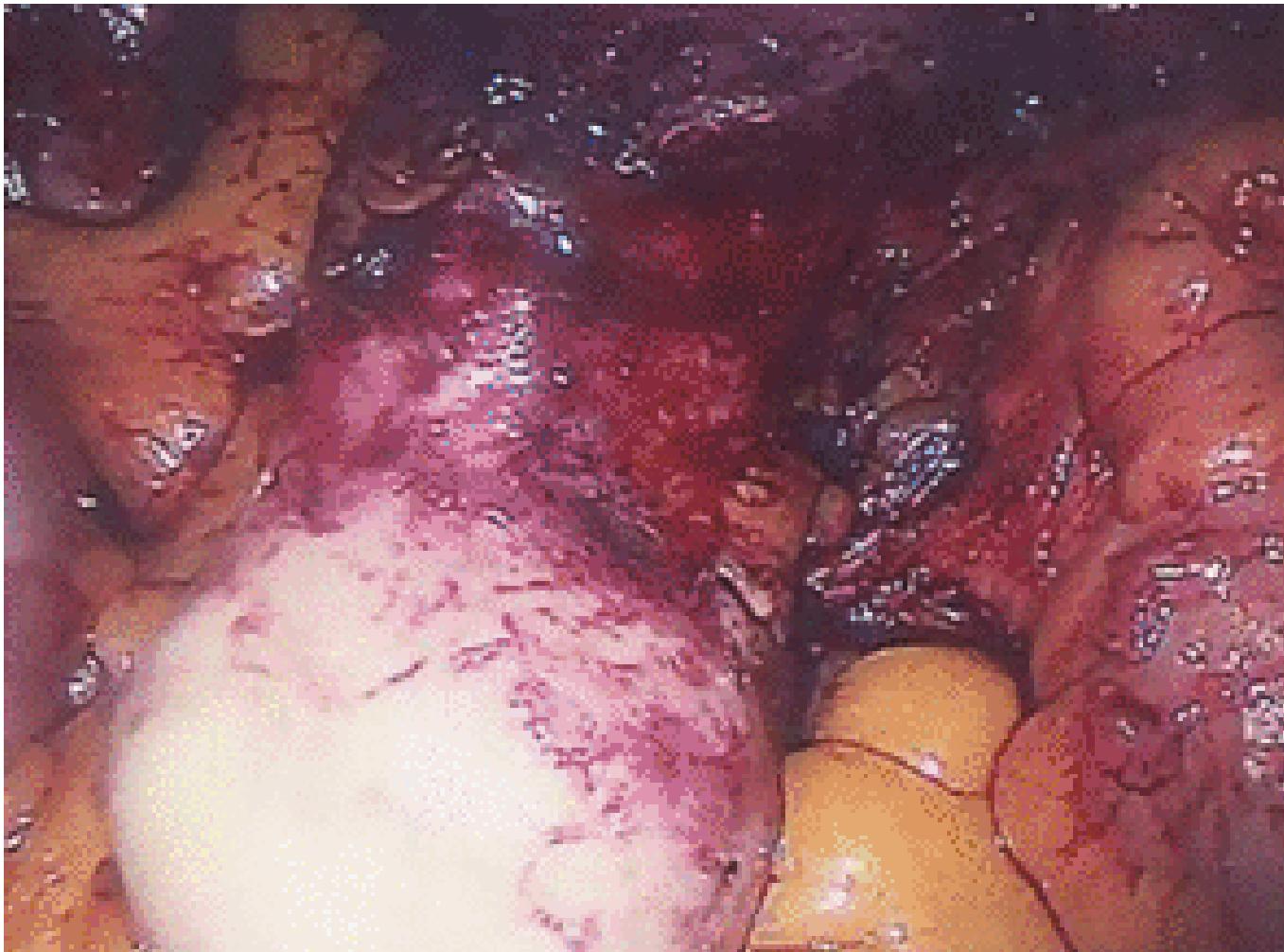
Suspicious appendiceal findings & adenocarcinoma of appendix

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Stapel A, Chirurg 2013

Problems with historical data

“Natural history studies show that peritoneal carcinomatosis (PC) is uniformly fatal, with median survival attaining 6-9 months (1)”

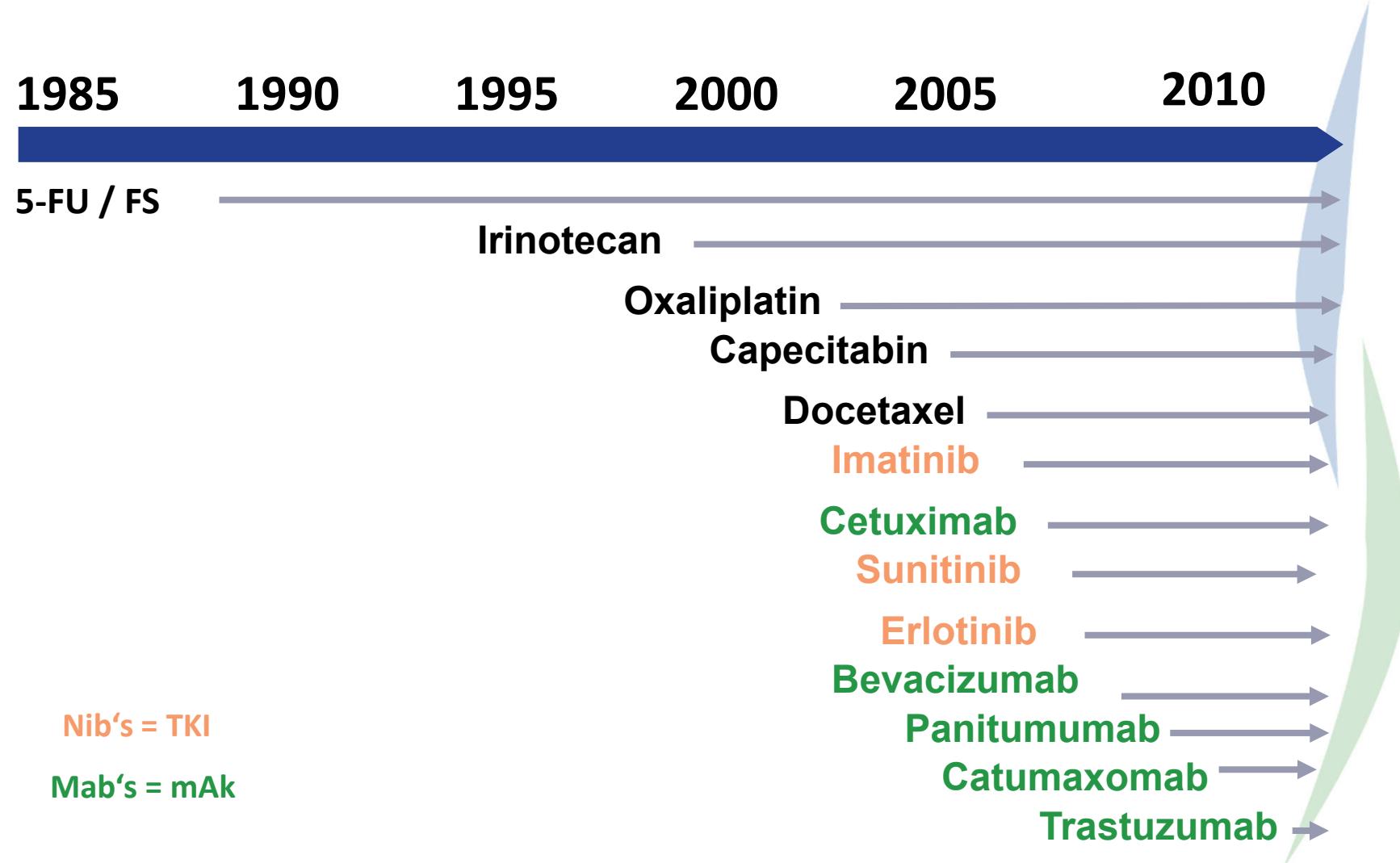
Publication JCO 2010

(1) Sadeghi B et al.

(2000) Peritoneal carcinomatosis from non-gynecologic malignancies: Results of EVOCAPE 1 multicentric prospective study. Cancer 88:358–363

(5 FU)

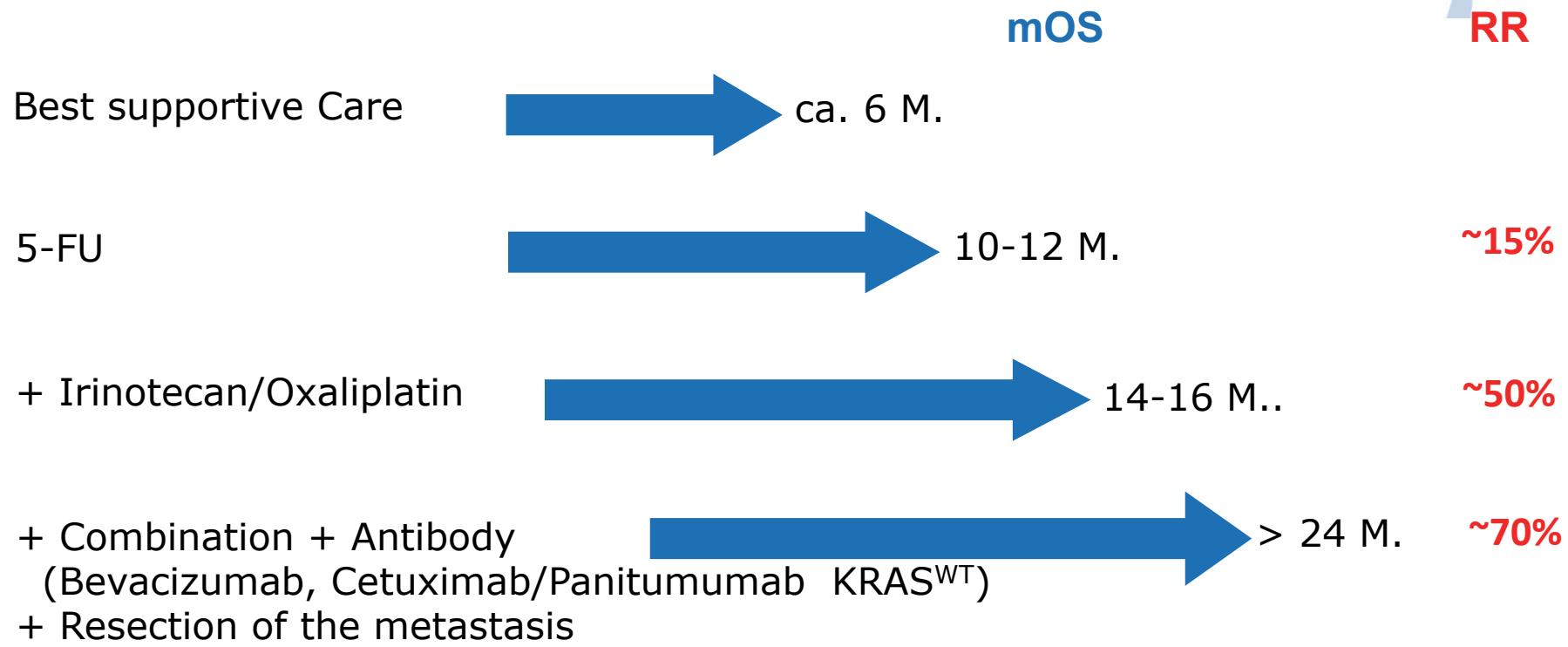
New Chemo in GI Tumoren



Nib's = TKI

Mab's = mAk

Survival in metastatic CRC



mOS = median Survival

RR = Response (n. RECIST-Criteria)

Randomized Trial of Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy Versus Systemic Chemotherapy and Palliative Surgery in Patients With Peritoneal Carcinomatosis of Colorectal Cancer

By Vic J. Verwaal, Serge van Ruth, Eelco de Bree, Gooike W. van Slooten, Harm van Tinteren, Henk Boot, and Frans A.N. Zoetmulder

J Clin Oncol 2003, 21: 3737-3743

n = 105, Appendix n=18, Colon n=75, Rectum n=12

Surgery + HIPEC + Ctx

n=54

MS 22,3 months

(Surgery) + Ctx

n=51

MS 12,6 months

p=0.032

HIPEC: 35 mg/m² MMC, 40-41°C

Ctx: 5FU 400 mg/m², LV 80 mg/m²

Complete Cytoreductive Surgery Plus Intraperitoneal Chemohyperthermia With Oxaliplatin for Peritoneal Carcinomatosis of Colorectal Origin

Dominique Elias, Jérémie H. Lefevre, Julie Chevalier, Antoine Brouquet, Frédéric Marchal, Jean-Marc Classe, Gwenaël Ferron, Jean-Marc Guilloit, Pierre Meeus, Diane Goéré, and Julia Bonastre

J Clin Oncol; 27:681-685 2009

n = 96, Colorectal

Surgery + HIPEC + Ctx

n=48

(prospectiv)

MS 62,7 months

(Surgery) + Ctx

n=48

(retrospectiv)

MS 23,9 months

P<0.05

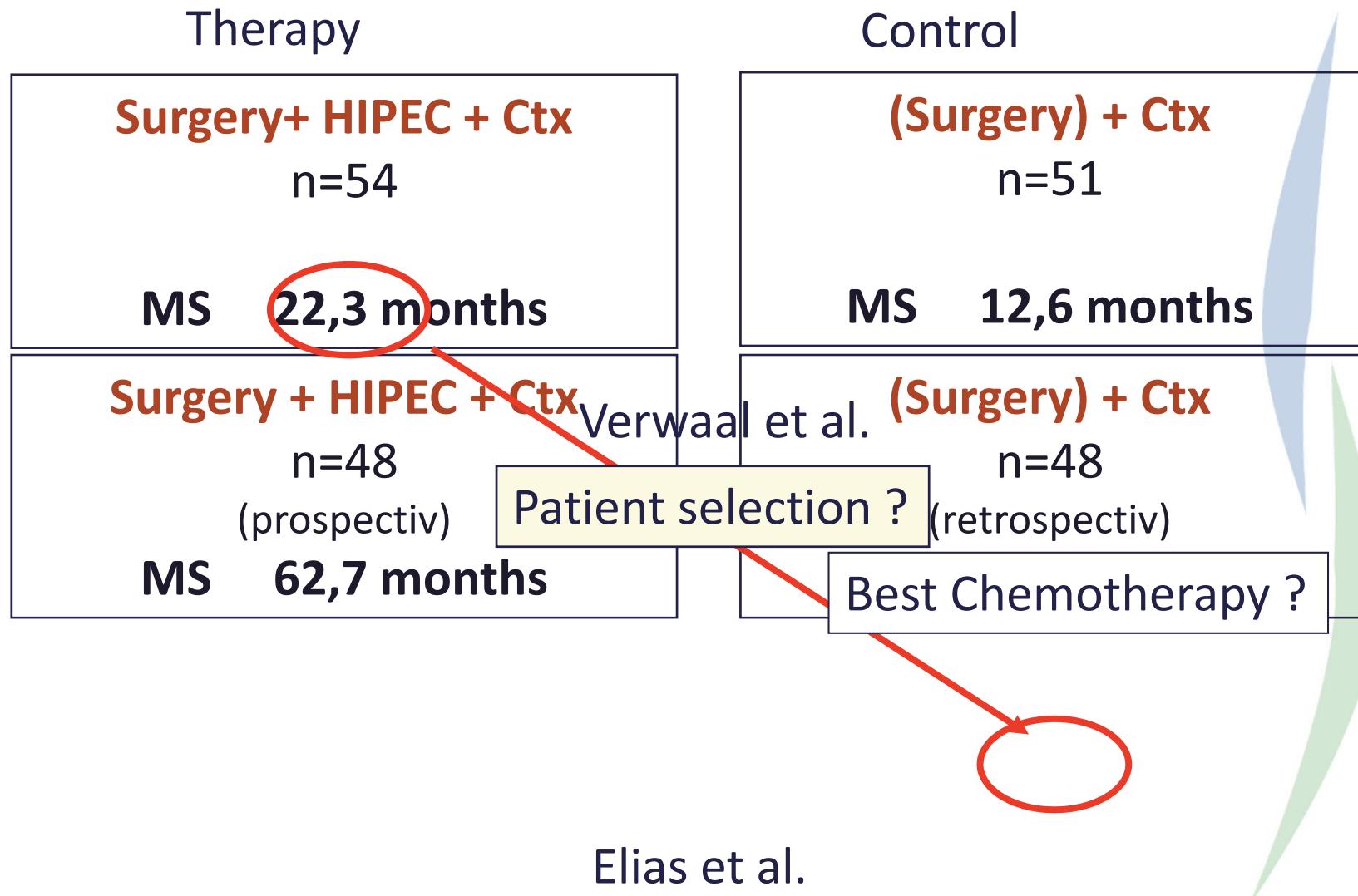
HIPEC: 460 mg/m² Oxaliplatin

43°C for 30 minutes; synchron iv. 5FU 400

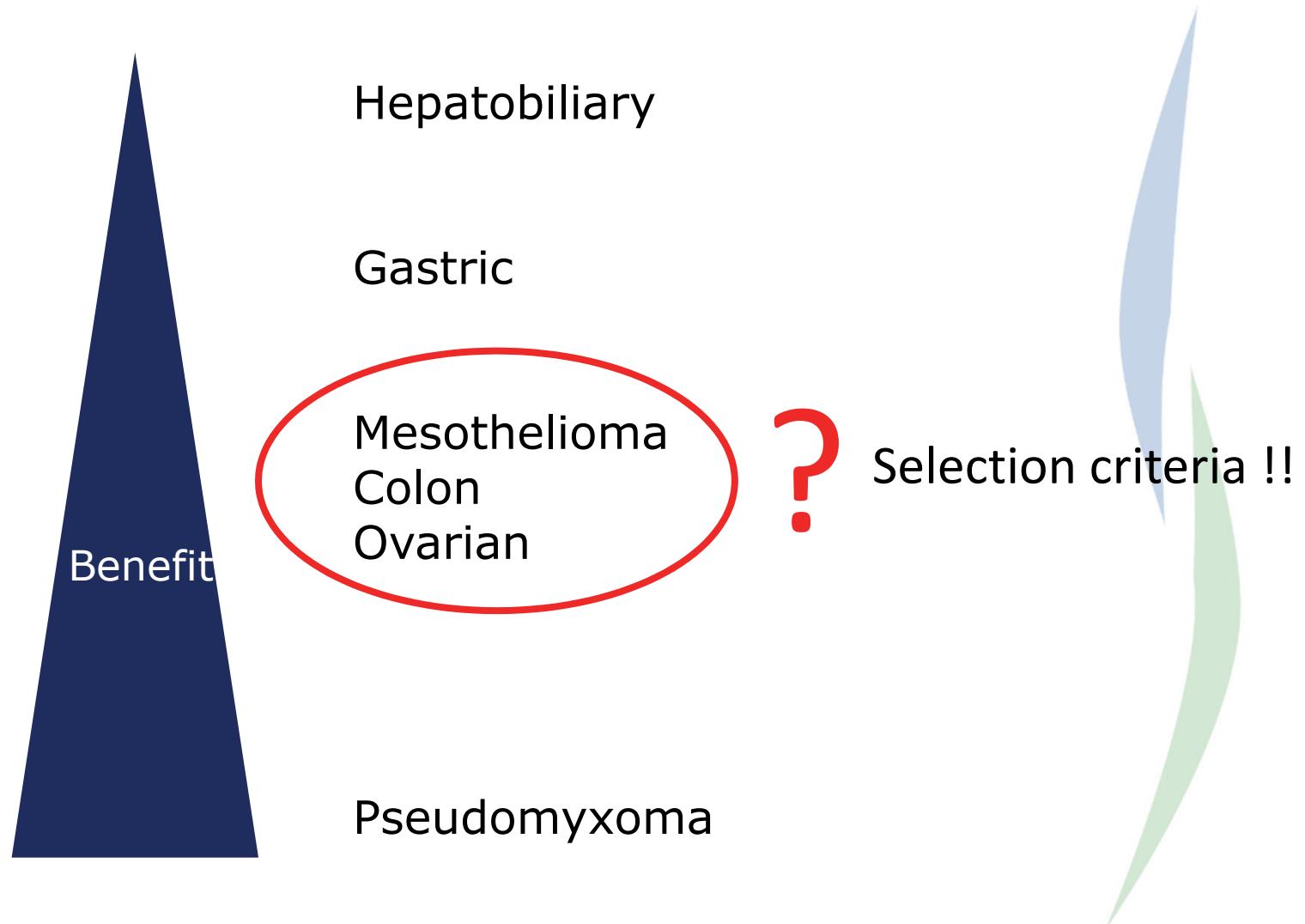
mg/m², LV 80 mg/m²

Ctx:best systemic chemotherapy

Ctx:best systemic chemotherapy



Benefit in multimodal treatment for peritoneal carcinomatosis



Problems in comparing

Problems in comparing patients with peritoneal carcinomatosis

- Different tumors (Histology, PCI)
- Different Therapies (Surgery, Chemo, HIPEC)
- Different Chemo (BSC, 5FU/L, combination)

Apples and oranges

Cave: don't compare apples and oranges !!



Evaluation of a Peritoneal Surface Disease Severity Score in Patients With Colon Cancer With Peritoneal Carcinomatosis

Pelz, Esquivel et al. Journal of Surgical Oncology 2009; 99:9-15

Key factors:

Histology

Peritoneal carcinomatosis index (PCI)

Clinical Symptoms



Symptoms	PCI	Histology
no	PCI < 10 0 point	G1, G2 N- 1 point
mild	PCI 10-20 1 point	G2 N+ 3 points
severe	PCI > 20 6 points	every G3 Signet ring 9 points

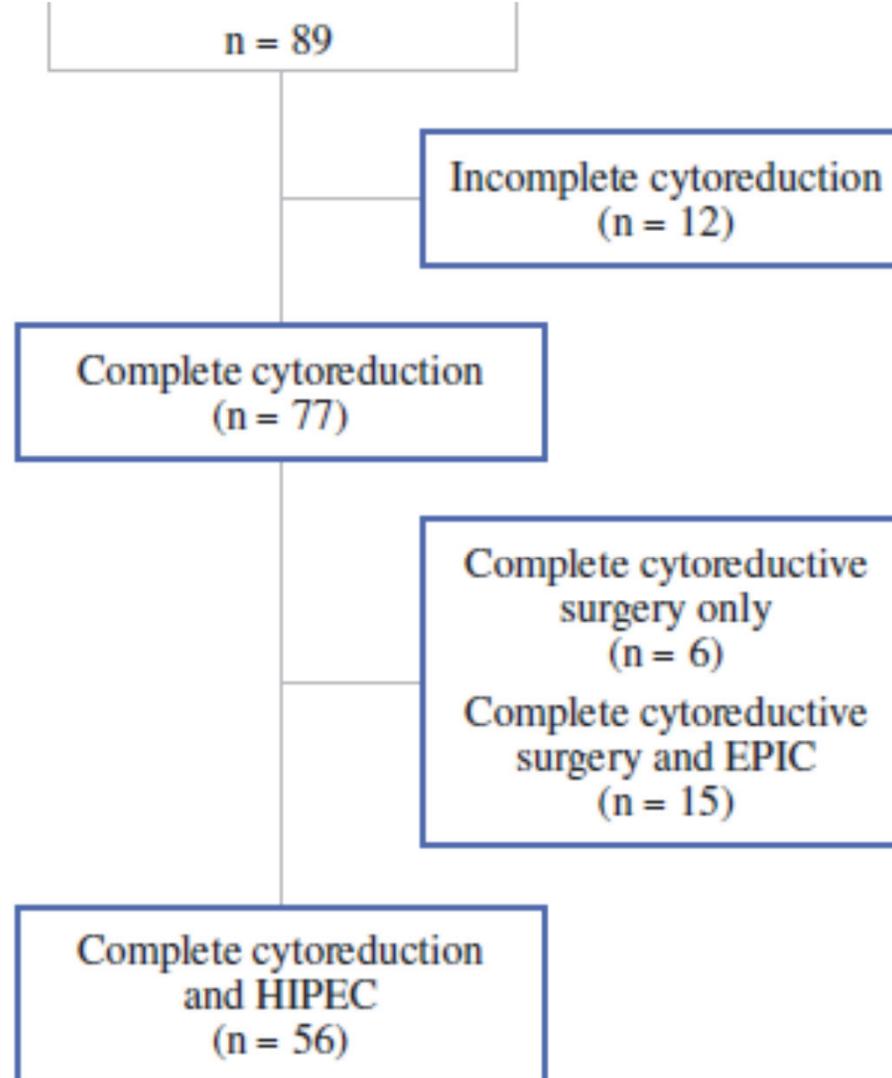


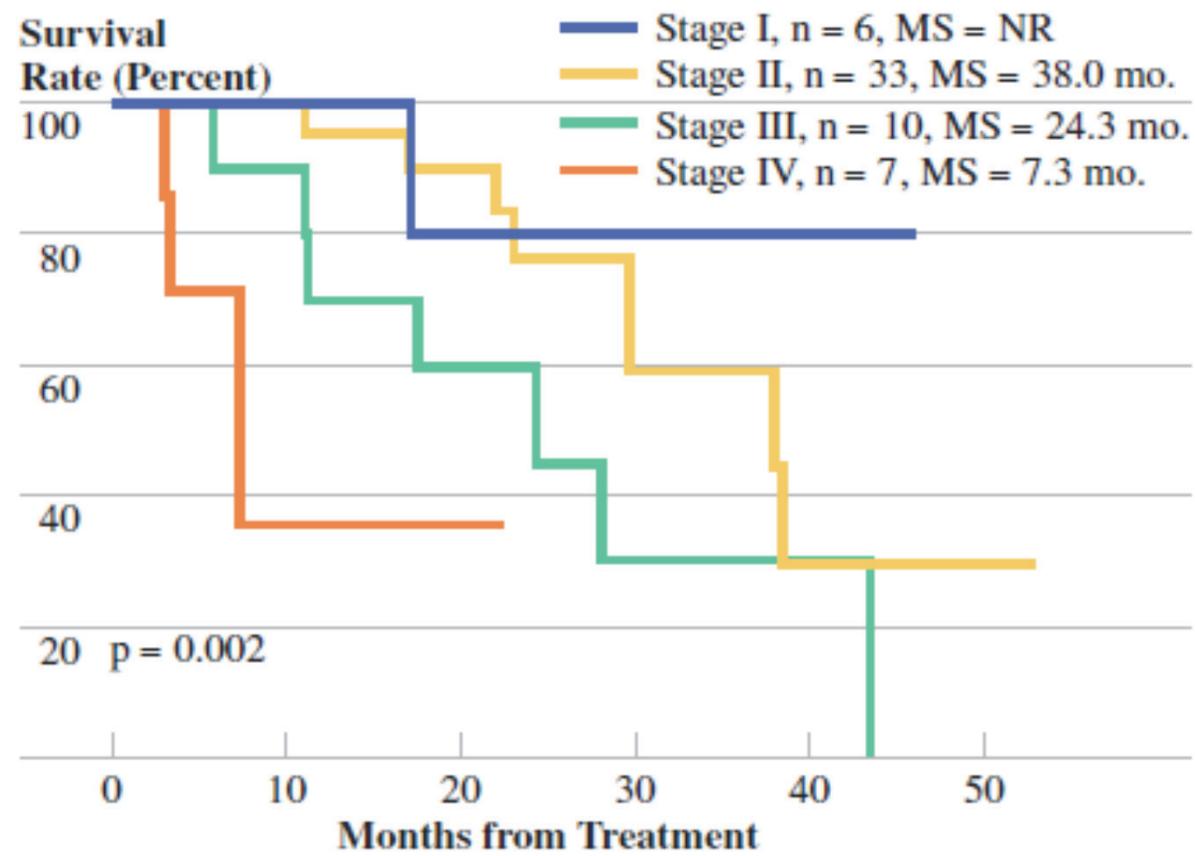
Proposed PSDS-Stage-depending Therapy

Score	PSDS	Proposed Therapy
2-3	Stage I	CRS/HIPEC
4-7	Stage II	Neo-adjuvant Rx for 3 months, then CRS/HIPEC
8-10	Stage III	Protocol
>10	Stage IV	Palliativ (no CRS/HIPEC)

Impact of Cytoreductive Surgery on Survival in Peritoneal Carcinomatosis and Hyperthermic Intraperitoneal Chemotherapy

Terence C. Chua





Easy !?



Case report I

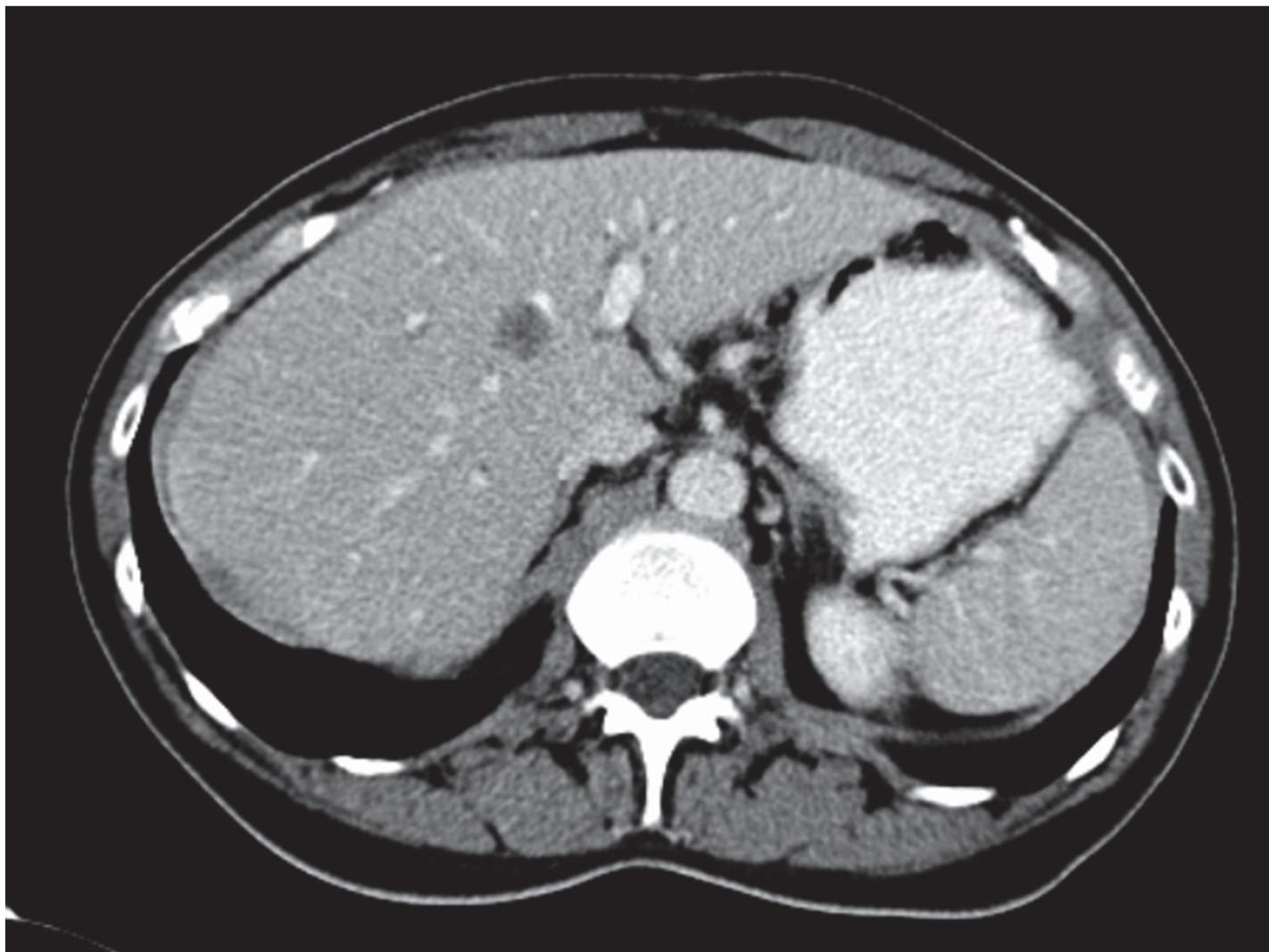
M.F. female, 43 years

Appendixcarcinoma (pT2, pN1 (1/35), G2) DD:07/10
Synchronous Peritoneal carcinomatosis (PCI 6) **PSDSS II**

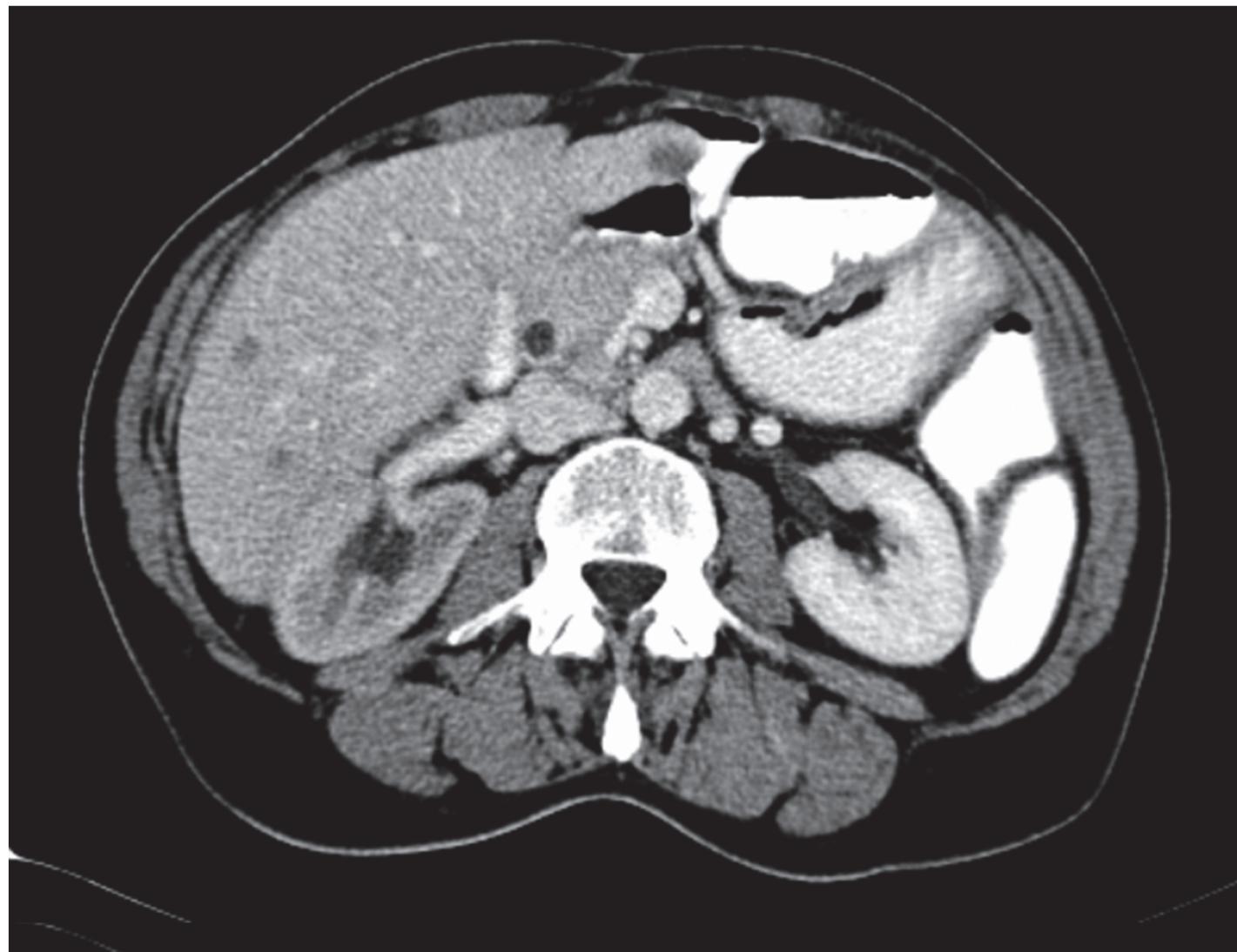
08-11/2010
Neoadjuvante/palliative Chemotherapy FOLFOX
CRS (CC-0) and HIPEC (Oxaliplatin ip and 5FU/L iv)
and adjuvant systemic chemo (FOLFOX)

Peritoneal recurrence and multiple Livermetastasis
3 month after adjuvant Chemotherapy
DOD 22 months after HIPEC

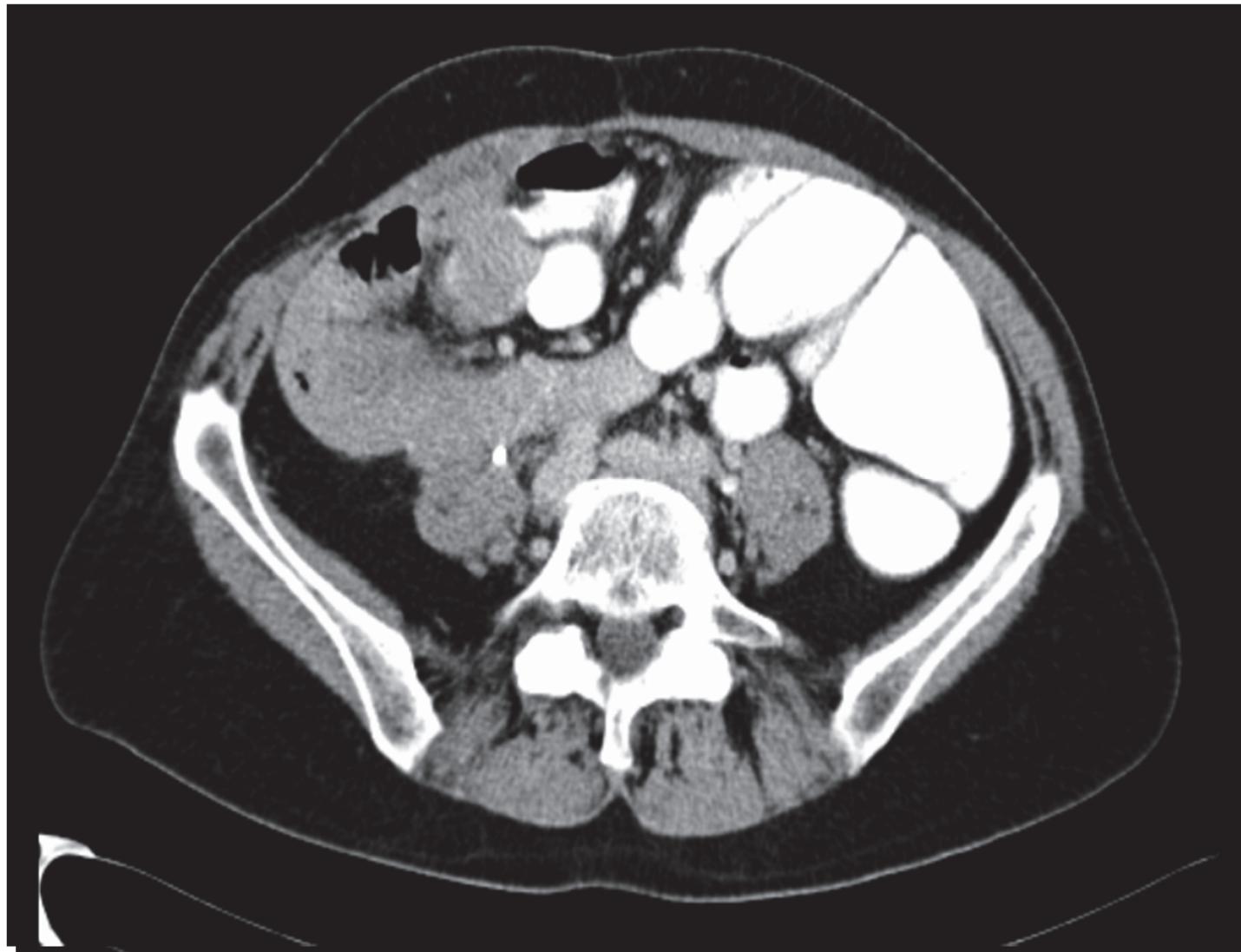
Case report I



Case report I



Case report I



Case report II

R.B. female 65 years

Appendixcarcinoma (pT4, pN2 (7/30), signet ring PD:07/09
Synchronous Peritonealcarzinomatosis

Involvement of the small bowel (PCI 20) **PSDSS IV**

Since 08/09 palliative Chemotherapy (FOLFOX)

CT-morphologic Stable Disease for 2 years in good quality of life. Since 08/11 progression, DOD 01/13

Survival 36 months ! ???

Individual (bad)success

Different outcome within same groups
Do we need other selection factors ?

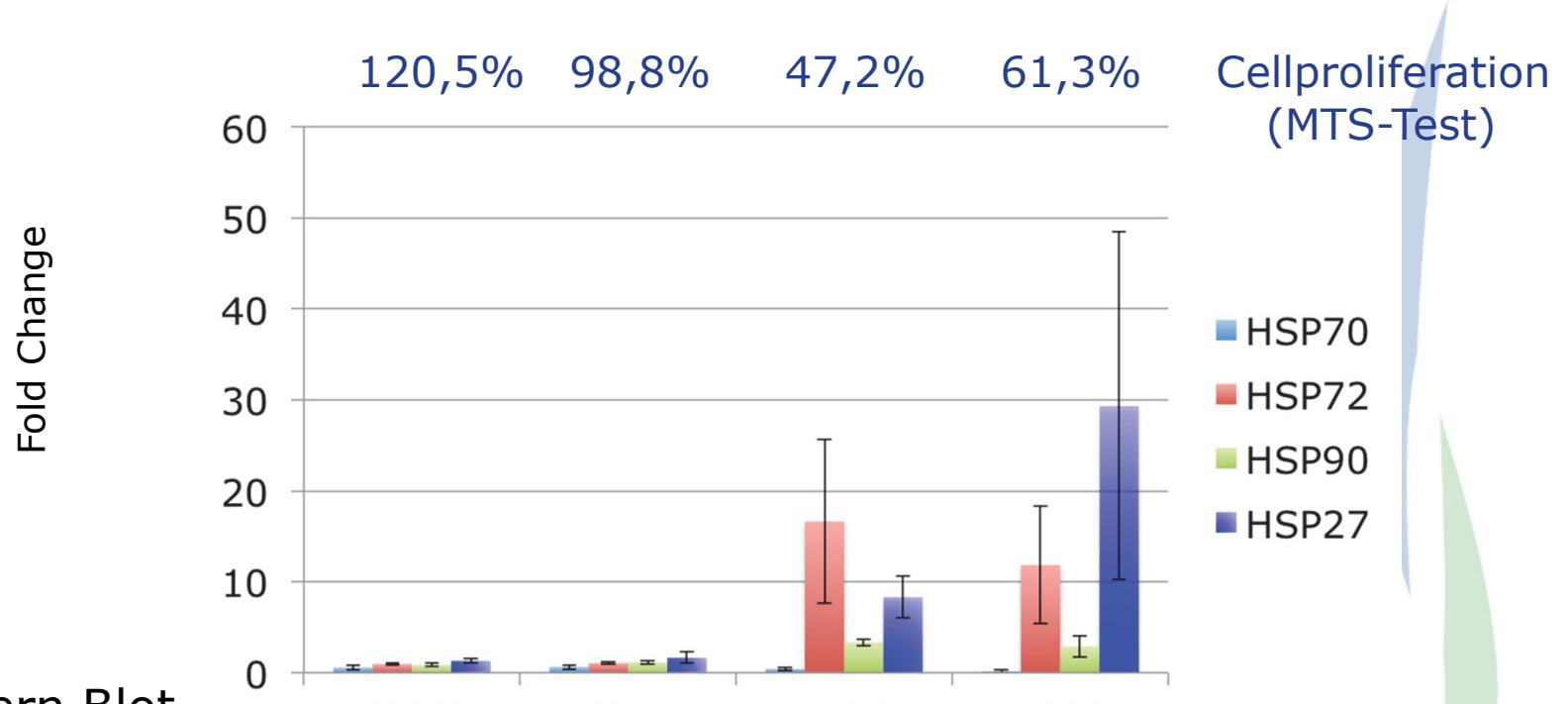


Role of Resistencemechanisms in different Tumors ?



HSP-Expression depends on Temperatur (Hyperthermia-Model: In vitro – Expression after 30 min. Regeneration)

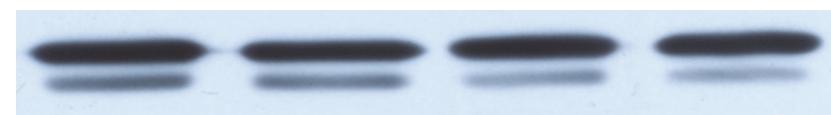
RT-qPCR



Western Blot



Beta-Aktin



Hyperthermia and intraperitoneal chemotherapy for the treatment of peritoneal carcinomatosis: an experimental study.

Treatment:	Median survival
CS only,	63 d
CS + HIPEC (MMC at 41° C),	121 d
CS + ip MMC at 37° C,	n.r. (126 d follow up)
CS + ip saline perfusion at 41° C.	57 d

The effectiveness of intraoperative intraperitoneal perfusion after CS is highly dependent on the presence of chemotherapeutic agents in the perfusate but not on hyperthermia

Ann Surg. 2011 Jul;254(1):125-30.

Summary

A trend towards improved outcomes is demonstrated from treatment of patients with PC from colorectal cancer using modern systemic chemotherapy (up to 36 months)

Cytoreductive Surgery+ HIPEC improved outcomes compared to systemic chemotherapy alone.

The PSDSS appears to be a useful tool in patient selection and prognostication in PC of colorectal origin

Repair mechanisms (HSPs) and induced chemotherapy-resistance (ABC-transporter) inhibit the HIPEC-induced tumorcellapoptosis



Thank you!

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