



Systemic treatment of peritoneal carcinomatosis from colorectal cancer

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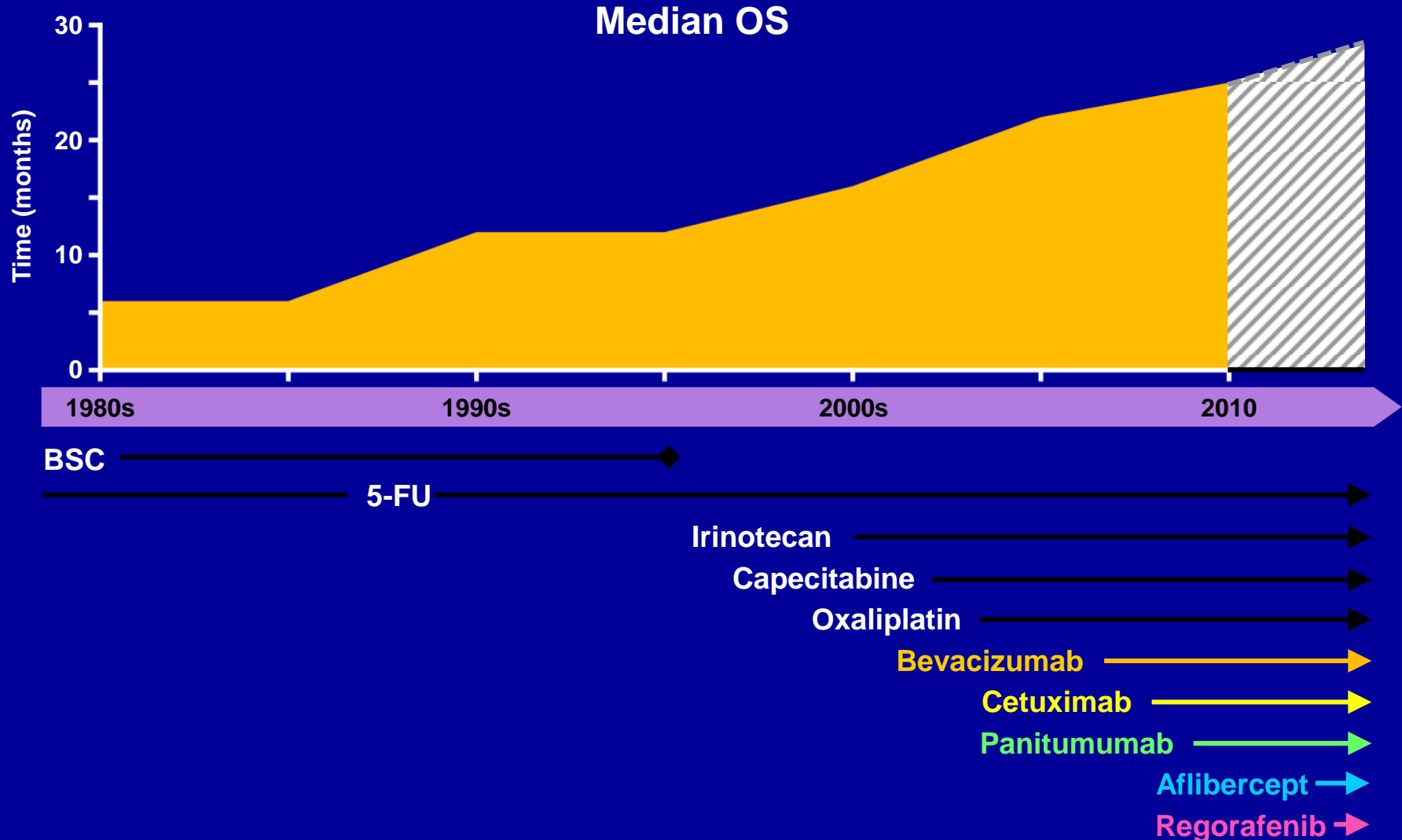
The Netherlands

Disclosures

Advisor for

Roche, Amgen, Merck-Serono, Sanofi, Bayer, Nordic Pharma

In the past 3 decades, advances in the treatment of mCRC have led to improved OS



Peritoneal carcinomatosis of CRC

- incidence -



- Data are scarce!
- PC in 4%-8% in synchronous disease and 4%-19% in metachronous disease
- In autopsy series, PC is found in up to 40%

Jayne et al. Br J Surg 2002
Lemmens et al. Int J Cancer 2011
Segelman et al. Br J Surg 2012
Koppe et al. Ann Surg 2006
Gilbert et al. Br J Surg 1984

Peritoneal carcinomatosis of CRC

- risk factors -



- Right-sided tumor
- Stage T4 and/or N+
- Poor differentiation grade
- Young age
- Initial emergency procedures
- Non-radical resection of primary

Peritoneal carcinomatosis of CRC - prognosis -



- PC is a poor prognostic feature
- Value of systemic therapy has been questioned
- This subset of patients is rarely analyzed in phase 3 studies
- Published series are prone to selection bias

Peritoneal carcinomatosis (PC) of CRC

Q:

- So if the prognosis of PC is poor, why don't we stratify for this in randomised clinical trials?

A:

- Extent of PC is frequently underestimated by imaging modalities, and, if visible, usually non-measurable¹

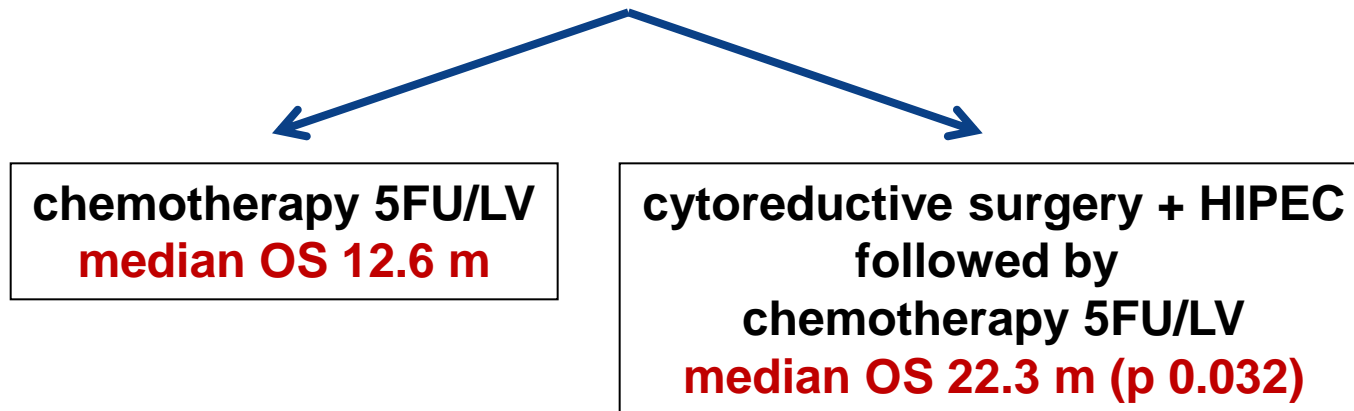
This obviously complicates the interpretation of retrospective series!

Peritoneal carcinomatosis (PC) of CRC

- pivotal trial -



Fase 3 randomised trial, n = 105



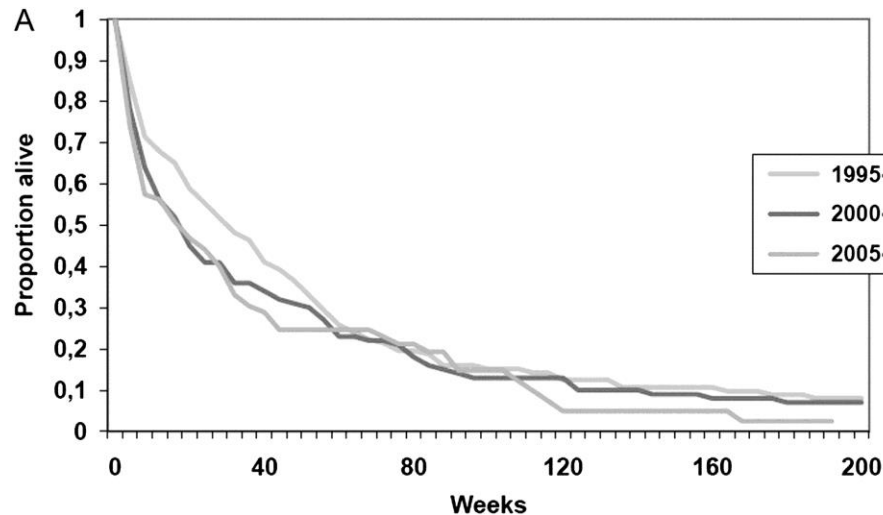
Comments:

- low number of patients
- some imbalances in treatment groups
- outdated systemic therapy

Peritoneal carcinomatosis (PC) of CRC

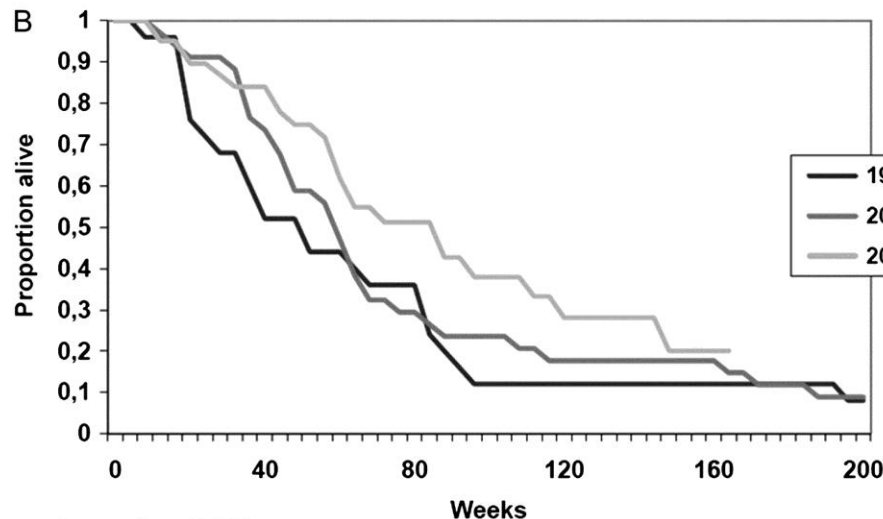
- Retrospective survey in local Dutch registry, 1995 - 2008
- Synchronous cancer with PC, n = 904
- Over time, there was an increased use of chemotherapy
- Trend towards an improved overall survival after 2005
- No data on use of targeted therapies
- Only 10 pts received cytoreductive surgery+HIPEC (>2005)

Population-based survival of patients with peritoneal carcinomatosis of CRC



Not treated with chemotherapy

> 2005: n=180
median OS 11 weeks



Treated with chemotherapy

> 2005: n=136¹
median OS 66 weeks

¹10 patients treated with HIPEC

Log-rank, p=0.064

Peritoneal carcinomatosis (PC) of CRC

- single center retrospective analysis -



	Chemotherapy	Chemotherapy + targeted therapy in any line	Chemotherapy + targeted therapy in 1st line
n	38	22	14
Median OS	12.5 m	18.5 m	22.4 m

These data suggest a benefit of the addition of targeted therapies, however the retrospective nature and small numbers do not allow definite conclusions

Peritoneal carcinomatosis (PC) of CRC

- subset analysis of CAIRO/CAIRO2 studies -



- CAIRO: sequential versus combination chemotherapy¹
- CAIRO2: CAPOX+bevacizumab +/- cetuximab²

Median overall survival³

	PC	No PC	P value
CAIRO n = 803, PC n = 34	10.4 m	17.3 m	≤ 0.001
CAIRO2 n = 736, PC n = 47	15.2 m	20.7 m	< 0.001

These data suggest a benefit of the addition of targeted therapies, however cross-study comparisons are hazardous!

¹Koopman et al. *Lancet* 2007

²Tol et al. *NEJM* 2009

³Klaver et al. *Eur J Surg Oncol* 2012

Peritoneal carcinomatosis (PC) of CRC

- pathological response of systemic therapy -

- Single-center retrospective review 2005-2012 of patients with PC who underwent neoadjuvant chemotherapy followed by cytoreductive surgery +/- HIPEC
- Irinotecan- or oxaliplatin-based chemotherapy, n = 115
- Pathological response: 9.7% complete, 20.2% major
- Conclusion: pathological response in PC can be achieved with systemic therapy, and was the only independent predictor for survival

Peritoneal carcinomatosis (PC) of CRC

- conclusions -



- Lack of prospective data on modern systemic treatment
- Published retrospective series may be biased
- Data suggest efficacy for chemotherapy + targeted therapy
- Role of systemic therapy in relation to cytoreductive surgery/HIPEC is not clear