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Maximal induction chemotherapy followed by Chemoradiation in order to improve resection margins

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Inclusion:
cT4a "ugly" (with EMVI and N2)
cT4b
Locally recurrent rectal cancer

Work-up MRI and PET/CT
Treatable oligo metastatic disease allowed
Endpoint pCR and R0 resection rate stratified for T4a/b and LRRC

Optimal treatment decision is tailored to the patient:

- Good responders to ICT will continue with consolidation therapy
- Poor responders will have no therapy or depending on condition with intensification.

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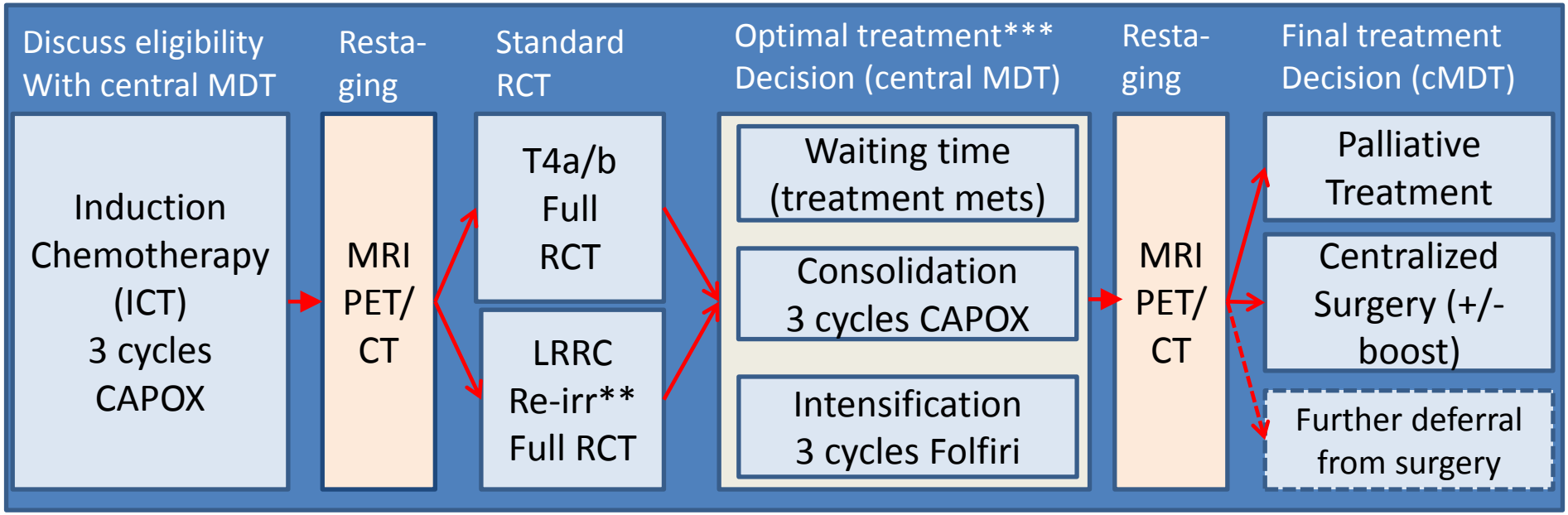
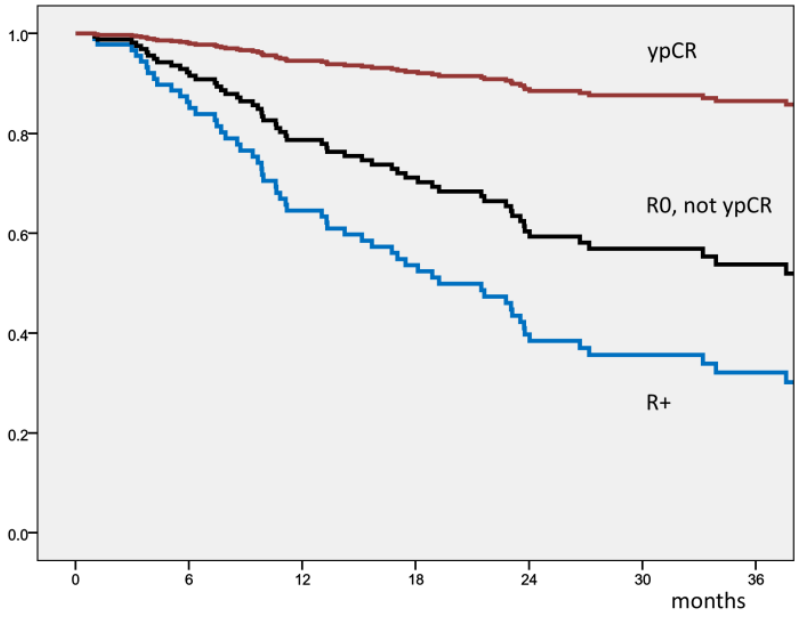


Feasibility trial

Comparison (ypCR, R0) with best regimen of RAPIDO study

Preliminary results LRRC, Eindhoven series. Only patients with re-irradiation M0

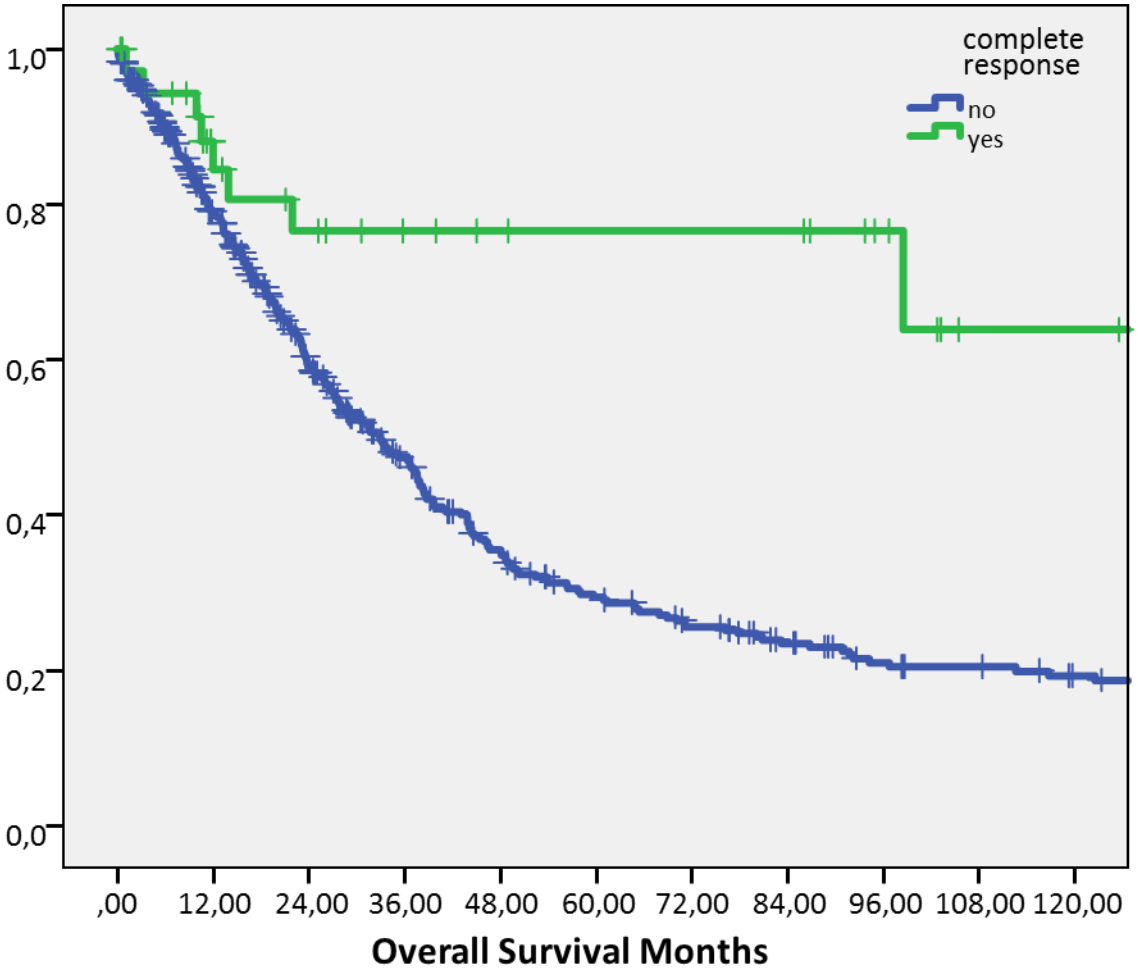
	ICT + CRRT	CRRT only	p-value
	No. of patients (n=58)	No. of patients (n=71)	
R0	32 (55)	35 (49)	0.506
pCR	10 (17)	3 (4)	0.015



ICT group:
Significant higher pCR rate,
higher R0 resection rate (NS),
ypCR significant better survival

Submitted, revisions under review in BJS

Importance of complete response for overall survival in LRRC patients (including all Patients with long course preop treatment, reirradiation, treatable metastases n=506)
5 year OS pCR 77%, vs non-pCR 30%



In this group, 6% pCR
Without Induction CT vs .
13% with induction CT

Unpublished data Catharina Hospital

Hypotheses

- Induction chemotherapy is a strong facilitator of pCR
- Good response will lead to higher rate of R0 resections
- R0 resections leads to better oncological outcome

Questions

- Systemic effect of induction chemotherapy likely (more intense) ?
- Role of consolidation therapy?
- Is there a place for dose intensification in poor responders to CT?
- Role of imaging in response assessment?
- In selected patients role for deferral of surgery?

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Maximal induction chemotherapy followed by Chemoradiation

- Participation of whole country (DCCG)
- Only limited number of centers
- Experience with beyond TME surgery
- MDT decision centralized between centers

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Neoadjuvant chemotherapy in MRI-staged high-risk rectal cancer in addition to or as an alternative to preoperative chemoradiation?

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Background: For patients with resectable rectal cancer chemoradiation (CRT) or short-course preoperative radiotherapy (SCPRT) reduces locoregional failure, without extending disease-free survival (DFS) or overall survival (OS). Compliance to postoperative adjuvant chemotherapy is poor. Neoadjuvant chemotherapy (NACT) offers an alternative strategy.

Methods: A systematic computerised database search identified studies exploring NACT alone or NACT preceding/succeeding radiation. The primary outcome measure was pathological complete response (pCR). Secondary outcome measures included acute toxicity, surgical morbidity, circumferential resection margin, locoregional failure, DFS and OS.

Results: Four case reports, 12 phase I/II studies, 4 randomised phase II and one randomised phase III study evaluated chemotherapy before CRT. Four prospective studies reviewed chemotherapy after CRT. Three phase II studies investigated chemotherapy using FOLFOX plus bevacizumab without radiotherapy. In 24 studies of 1271 patients, pCR varied from 7% to 36%, but with no impact on metastatic disease.

Conclusions: NACT before CRT delivers does not compromise CRT but has not increased pCR rates, R0 resection rate, improved DFS or reduced metastases. NACT following CRT is an interesting strategy, and the utility of NACT alone could be explored compared with SCPRT or CRT in selected patients with rectal cancer where the impact of radiotherapy on DFS and OS is marginal.