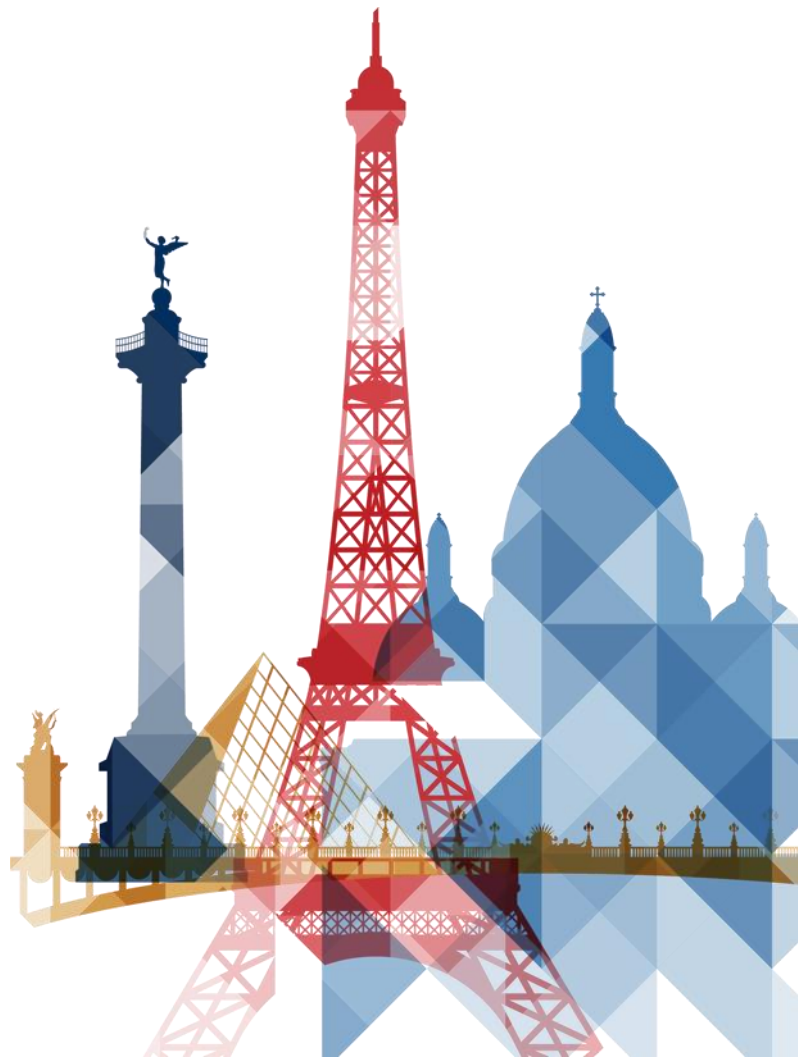


The surgeon's perspective: TME – Local excision – Watch & Wait

Prof Dr Geerard L Beets
The Netherlands Cancer Institute



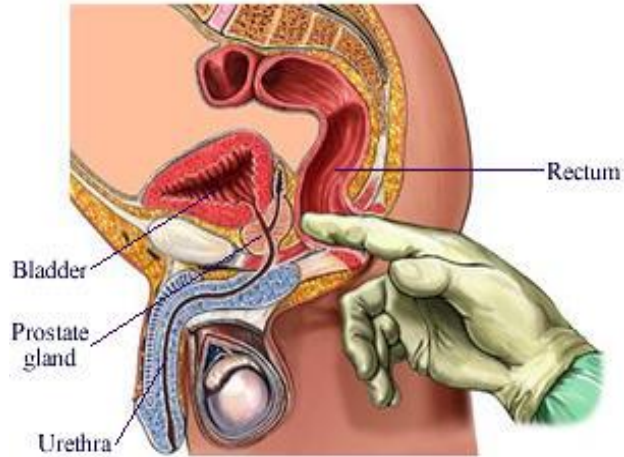
DECLARATION OF INTERESTS

Geerard Beets

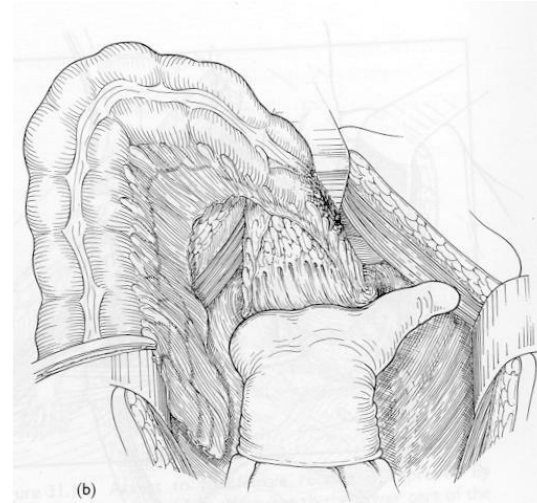
No disclosures

- Very brief history rectal cancer treatment
- Quality of life outcome
- Organ preservation options

Historical approach to rectal cancer

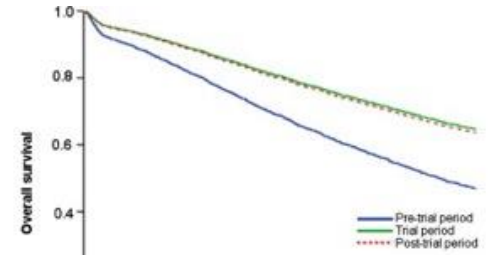
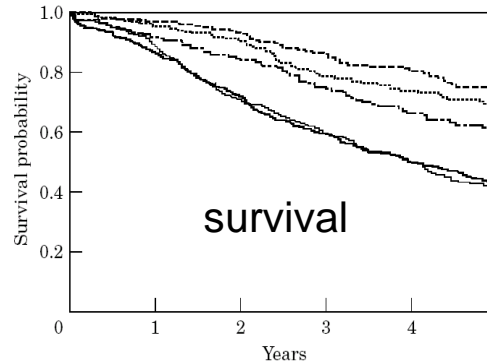
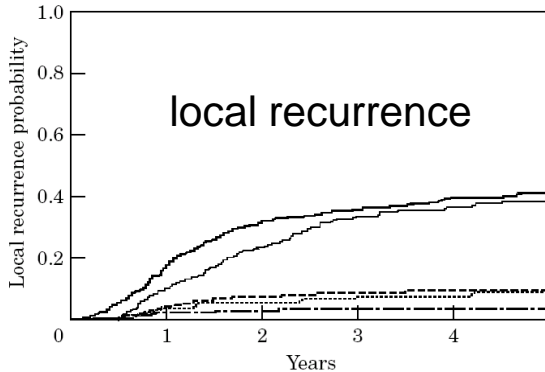
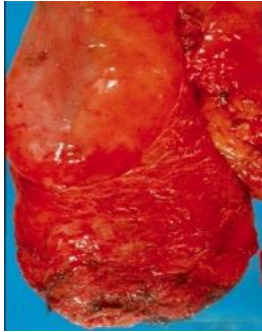
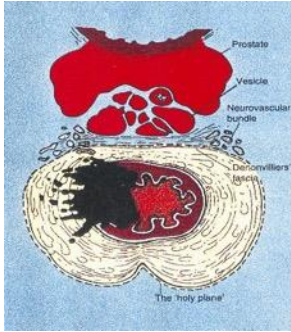


Staging: finger



Operation: hand

Total Mesorectal Excision



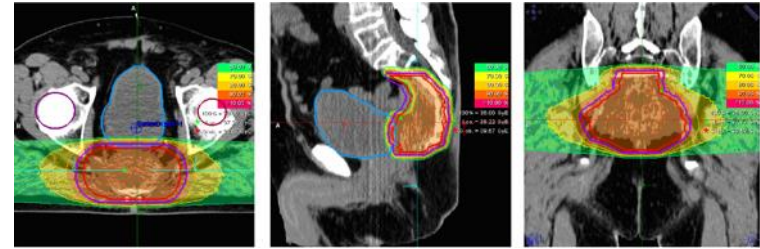
Dutch TME trial

	Time since diagnosis (months)						
Numbers at risk	0	10	20	30	40	50	60
Pre-trial period	1150	1039	938	857	772	707	646
Trial period	1084	978	909	839	767	718	678
Post-trial period	945	867	815	684	478	268	83

Den Dulk et al. EJC 2008

Neo adjuvant radiotherapy

Benefit vs Cost



Local recurrence ↓, Overall survival =

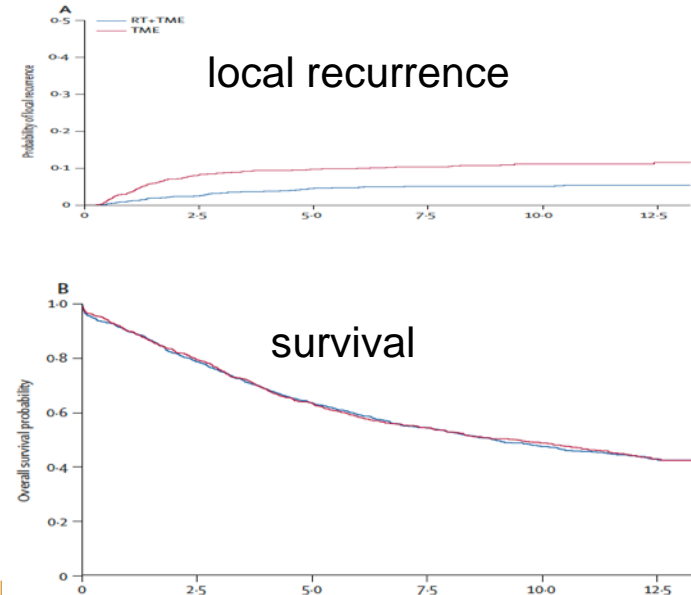
Short term toxicity ↑, Long term toxicity ↑

- ◆ Anorectal and urogenital dysfunction ↑

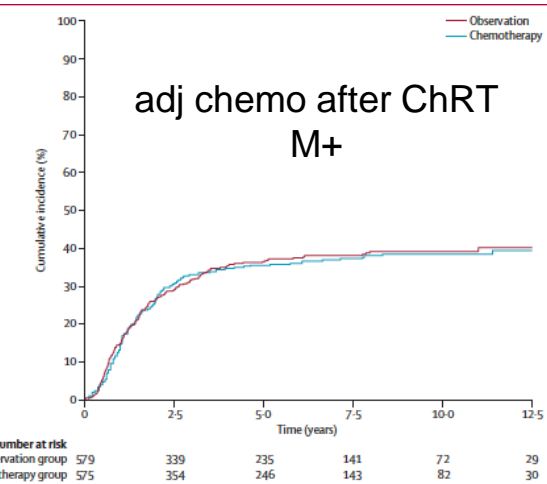
Who benefits most: high risk LR

- ◆ Large tumours: T3cd, T4, MRF+
- ◆ Stage III: extensive N+, extramesorectal N+
- ◆ EMVI+, Distal rectal cancer

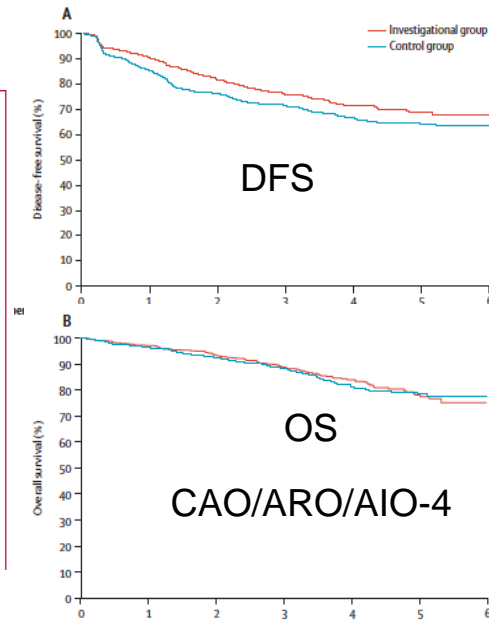
TME surgery +/- neoadj RT



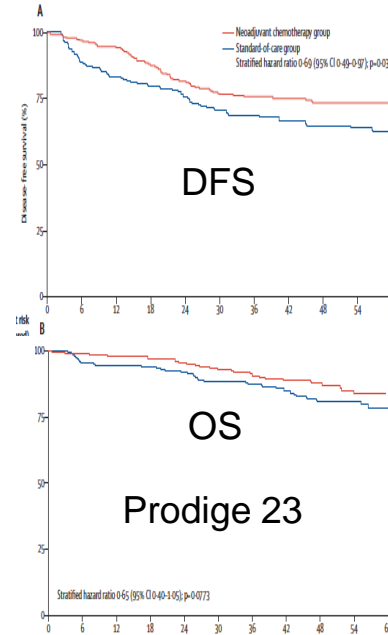
Chemotherapy?



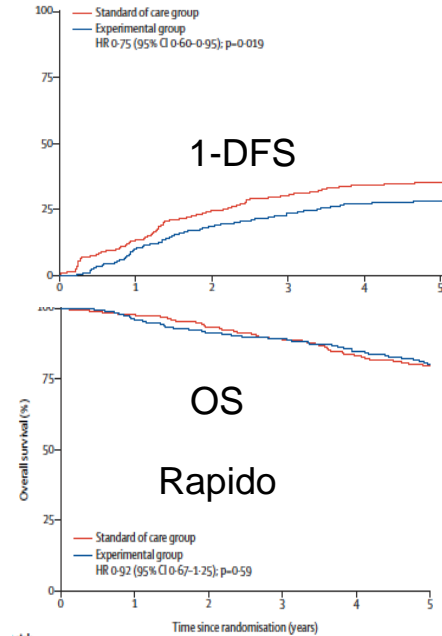
Breugnot, Lancet Oncology 2015



Rodel, Lancet Oncology 2015







Conroy, Lancet Oncology 2021



Bahadoor, Lancet Oncology 2020

Do clinicians know what patients want?

Choice based conjoint experiment

	Patients (n=94)		Clinicians (n=128)		
	1	colostomy	24	worries about cancer recurrence	31 
	2	faecal incontinence	20	fecal incontinence	21
	3	urinary dysfunction	20	sexual dysfunction	15
	4	worries about cancer recurrence	18	urinary dysfunction	12
	5	sexual dysfunction	11	colostomy	11
	6	to live longer	6	to live longer	10

Patients highly value QoL and avoiding a stoma



Improved outcome?

Postop morbidity – mortality

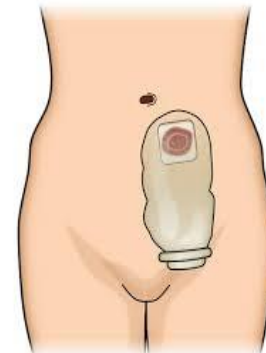
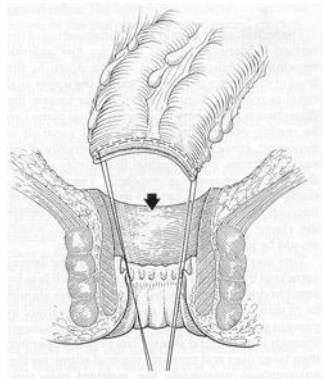
- ◆ Anastomotic leakage

Anorectal/urogenital function?

- ◆ >50% major LARS
- ◆ sexual dysfunction

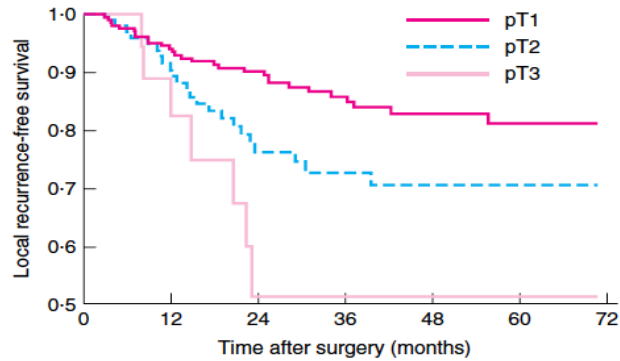
Body image?

Elderly?

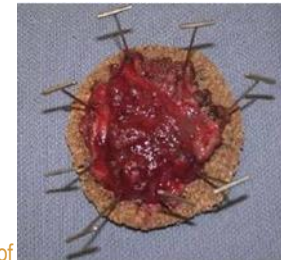
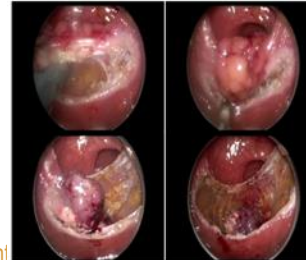
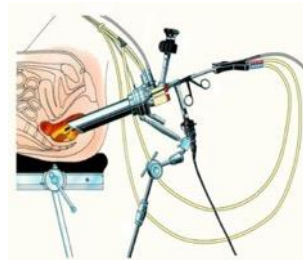
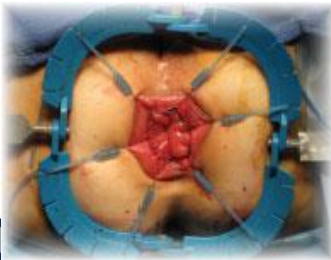


Transanal local excision and early rectal cancer

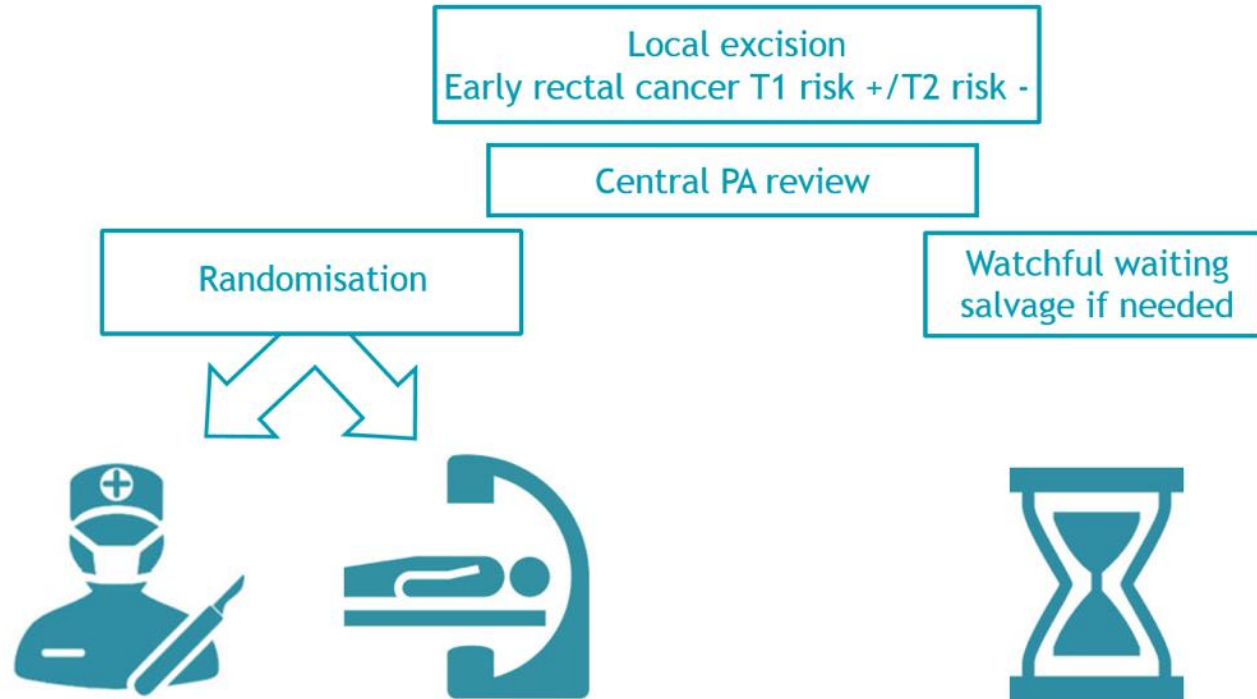
Predictors of local recurrence: T stage, sm subclass, size, LVI



Depth of invasion	Lymphatic invasion	Maximum tumour diameter (cm)					
		≤ 1	1.1-2	2.1-3	3.1-4	4.1-5	≥ 5.1
pT1 sm1	No	3.0	3.6	4.4	5.4	6.6	8.1
	Yes	5.2	6.4	7.7	9.4	11.4	13.7
pT1 sm2-3	No	10.5	12.7	15.5	18.5	22.1	26.4
	Yes	17.8	21.4	25.5	30.3	35.7	41.8
pT2	No	9.8	11.9	14.3	17.3	20.7	24.7
	Yes	16.7	20.0	23.9	28.5	33.7	39.5
pT3	No	19.7	23.6	28.0	33.2	39.0	45.4
	Yes	32.2	37.9	44.1	51.0	58.3	65.7



Radiotherapy after local excision?



Watch and Wait – Organ Preservation

Where do we come from?

Large tumors

- ‘standard RTx’
- oncological indication
- **secondary** organ preservation
- Watch & Wait



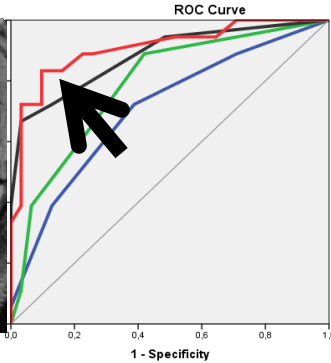
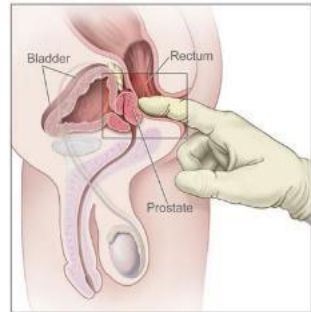
10-25%



Organ Preservation

Assessment – Selection – Follow up

Digital Rectal Examination – Endoscopy - MRI



Year 1	Year 2	Year 3	Year 4	Year 5
4x MRI	2x MRI	1x MRI	1x MRI	1x MRI
4x Endoscopy	4x Endoscopy	2x Endoscopy	1x Endoscopy	1x Endoscopy

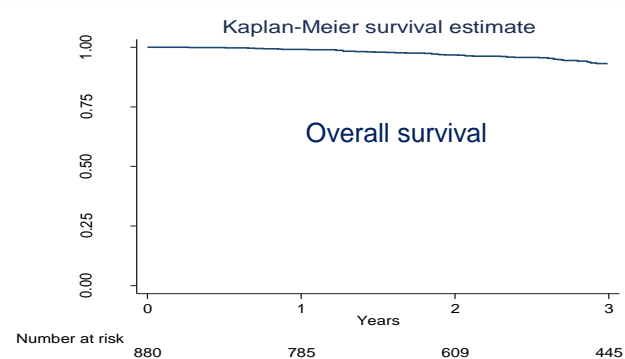
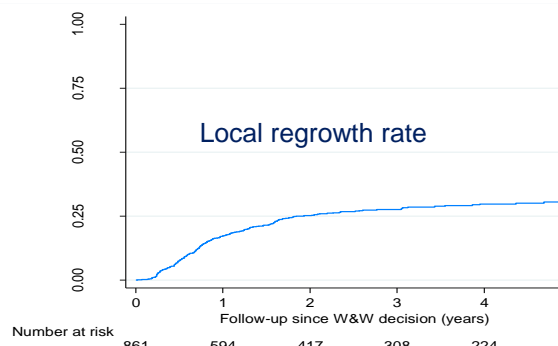


Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study

*Maxime J M van der Valk, Denise E Hilling, Esther Bastiaannet, Elma Meershoek-Klein Kranenborg, Geerard L Beets, Nuno L Figueiredo, Angelita Habr-Gama, Rodrigo O Perez, Andrew G Renehan, Cornelis J H van de Velde, and the IWWD Consortium**

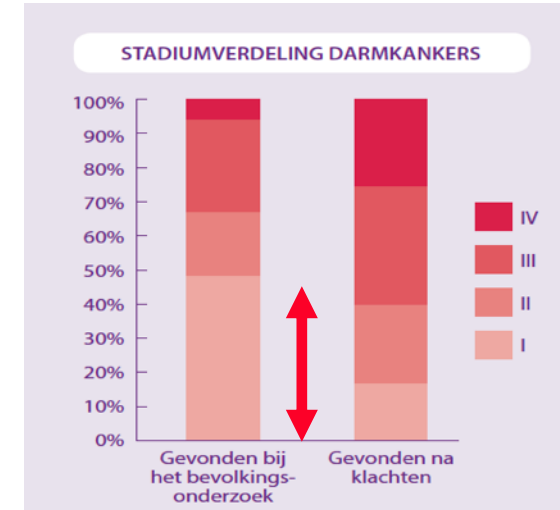
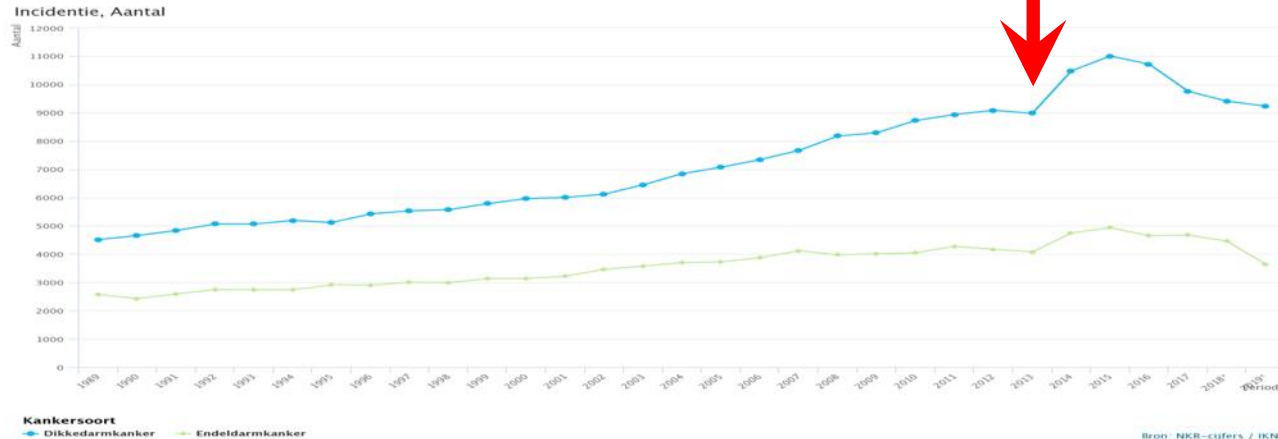
Vd Valk et al. Lancet 2018

- 42 centers: 880 pts cCR, median FU 3.4 yrs
- 2yr local regrowth rate 25% (97% endoluminally)
- Overall Survival 3yr: 93.2%
- Cause of death: rectal cancer 4%



Bowel Cancer Screening

Small asymptomatic tumours



Watch and Wait – Organ Preservation

Where should we go?

Small tumors

- ‘additional RTx’
- functional indication
- **primary** organ preservation
- +/- local excision

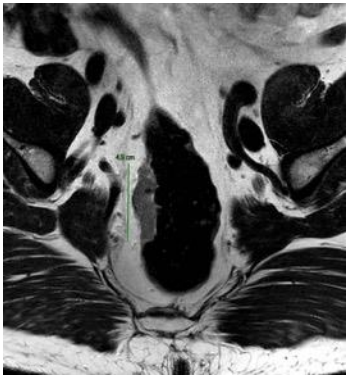
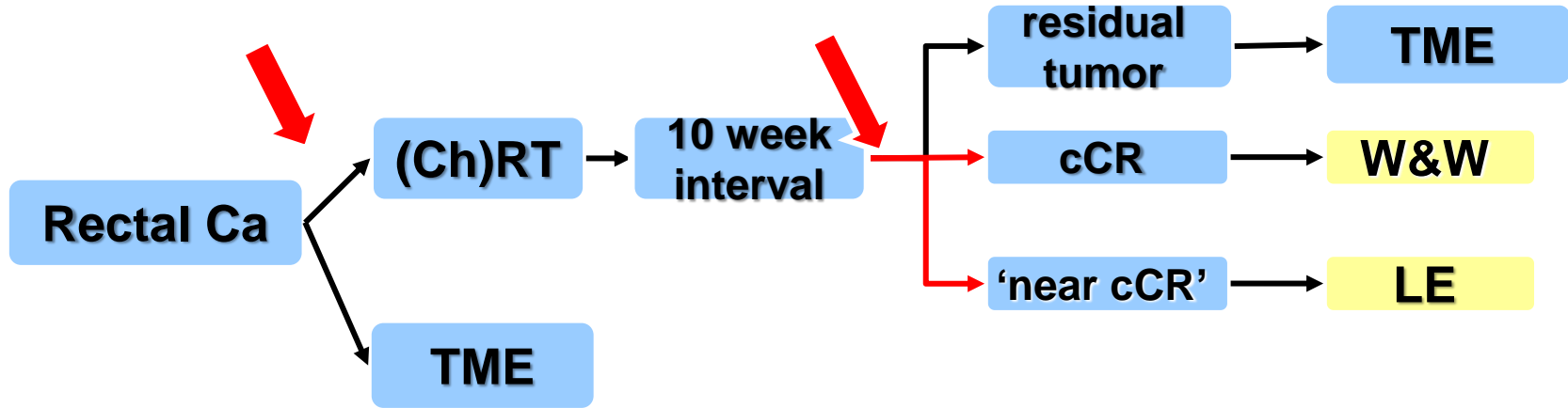
Large tumors

- ‘standard RTx’
- oncological indication
- **secondary** organ preservation
- Watch & Wait



Organ Preservation

Decision making in organ preservation

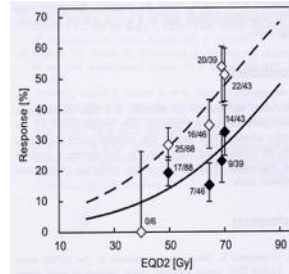


Main goal: improving Quality of Life

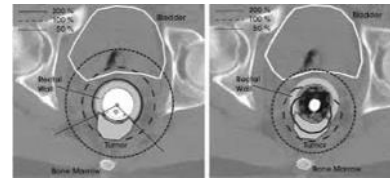


Improving response rates: more RT?

50 Gy: pCR 10-15%
65 Gy: pCR 20-25%
Appelt 2013 IJROBP



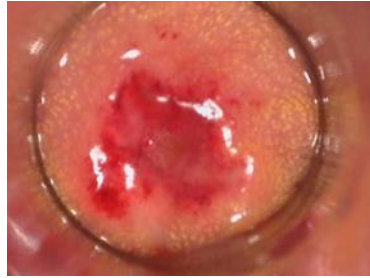
- External RT boost:
 - Habr Gama +, Utrecht boost =
- Endorectal RT boost:
 - brachyRT: Jakobsen =, Appelt +
 - contactRT: Opera +++?



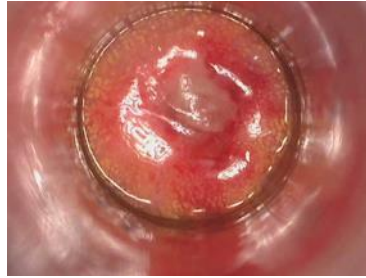
Contact RT boost 3x30Gy



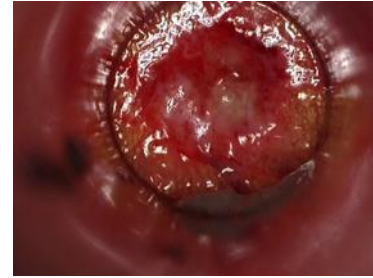
12w post 5x5Gy T3N1



30Gy



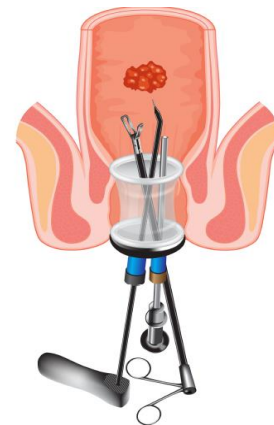
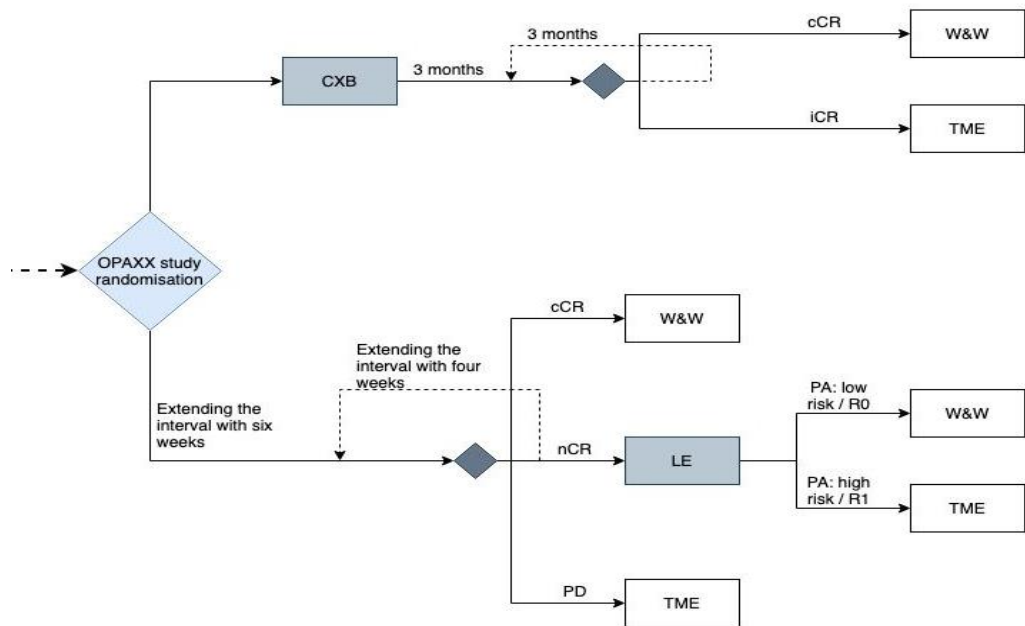
30Gy



30Gy



Contact RT or local excision for small remnant?



Improving response rates: more chemotherapy?



RAPIDO - loc adv rectal cancer

- ◆ pCR : 14% vs 28%

PRODIGE 23 - loc adv rectal cancer

- ◆ pCR : 12% vs 28%

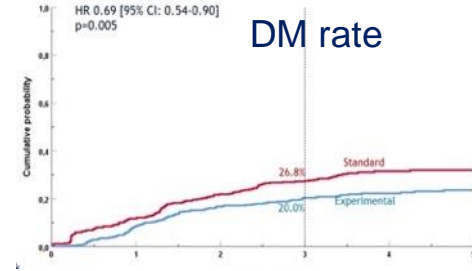
OPRA-TNT - intermediate

- ◆ 3yr organ preservation: 58% vs 43%

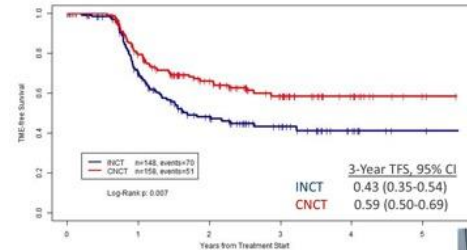
GRECCAR 12 – intermediate:

- ◆ ongoing congress

ChRT vs folfirinox - ChRT



ts: TME-Free by Treatment Group



Immunotherapy?

MSI rectal cancer

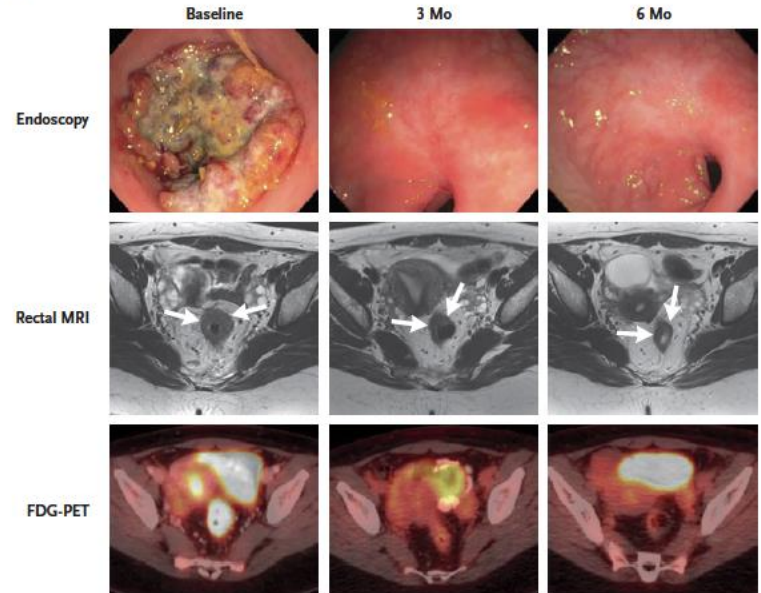
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

PD-1 Blockade in Mismatch Repair– Deficient, Locally Advanced Rectal Cancer

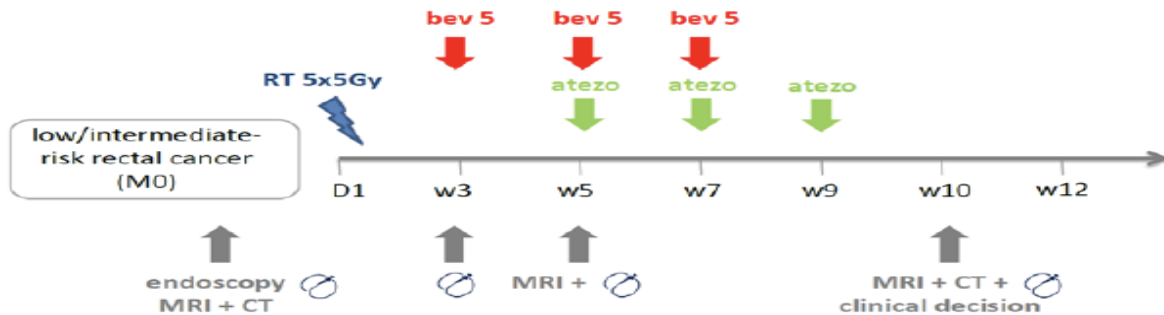
A. Cercek, M. Lumish, J. Sinopoli, J. Weiss, J. Shia, M. Lamendola-Essel, I.H. El Dika, N. Segal, M. Shcherba, R. Sugarman, Z. Stadler, R. Yaeger, J.J. Smith, B. Rousseau, G. Argiles, M. Patel, A. Desai, L.B. Saltz, M. Widmar, K. Iyer, J. Zhang, N. Gianino, C. Crane, P.B. Romesser, E.P. Pappou, P. Paty, J. Garcia-Aguilar, M. Gonen, M. Gollub, M.R. Weiser, K.A. Schalper, and L.A. Diaz, Jr.

A Patient 2



Combined RT and immunotherapy?

single-arm proof-of-concept phase Ib/II study

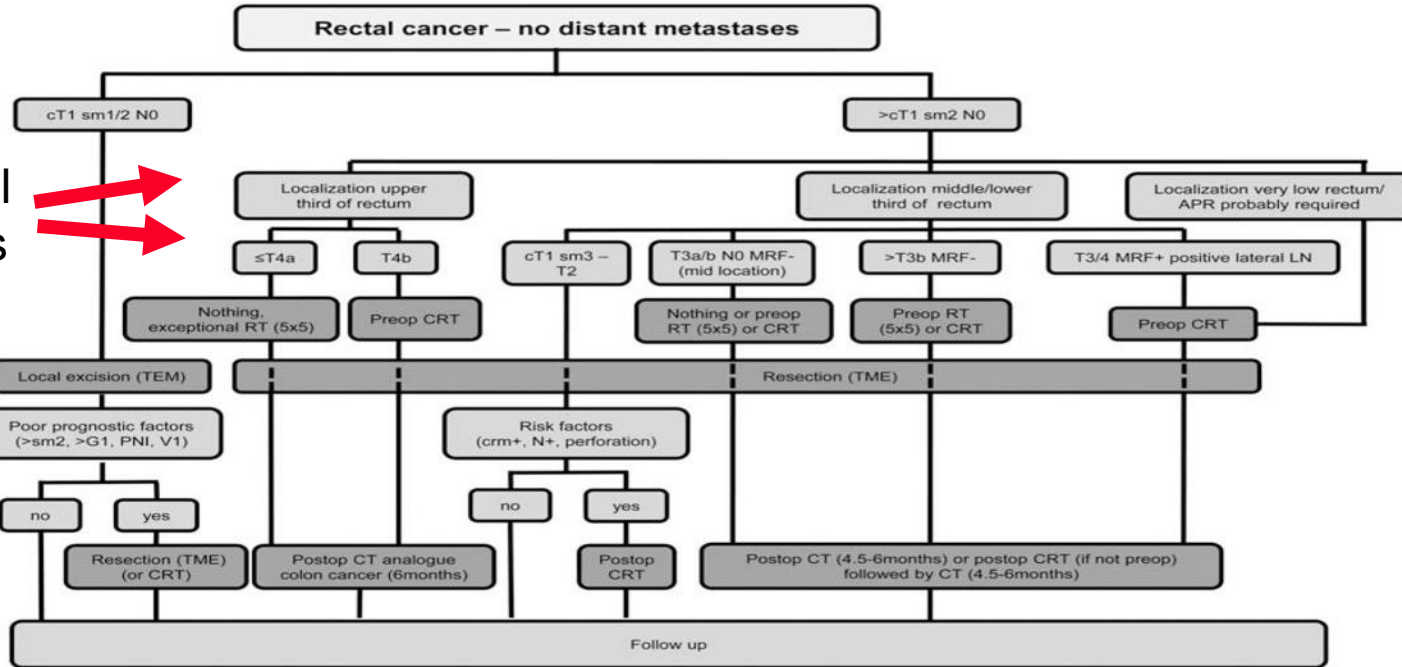
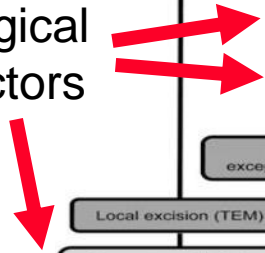


Main goal: improving Quality of Life



Choosing 'the best treatment' with your patient

oncological
risk factors



Rectal Cancer ESMO guideline 2012 – Annals of Oncology



Revised Dutch colorectal cancer guidelines



Secondary organ preservation

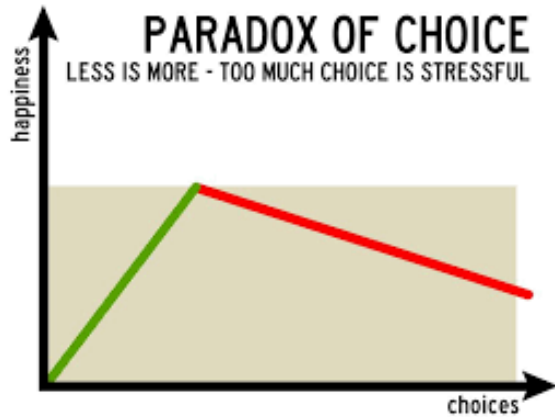
- When a clinical complete response, discuss W&W as alternative to TME, balancing benefits/harms in shared decision making

Primary organ preservation

- cT3abN0: no neoadj therapy before TME
- Induction therapy with explicit aim organ preservation, **preferably** in study setting

Choice overload - Overchoice

“a cognitive impairment in which people have a difficult time making a decision when faced with many options”



Conclusions - 1

Multitude of good treatment options

Oncological point of view

QoL – organ preservation: high interest of patients

Oncological risk very low

High quality program – expertise

Shared decision making

Increasing trend for TNT in loc advanced tumours for oncological reasons
secondary organ preservation in minority of patients

Conclusions - 2

Growing group of early rectal cancer - primary organ preservation

Many questions to solve:

increase responses - toxicity of the treatment

prediction of response - detection of residual disease -

50% of rectal cancers organ preservation?

We will 'rediscover' the value of surgery

Thank you

