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Radiktherapie
Medische Oncologie
Hematologie




Universiteit
Antwerpen

Orgaansparende behandeling voor rectumkanker

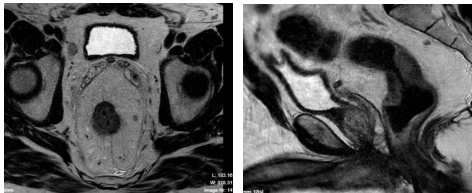
Postgraduaat Iridium 12/06/2019

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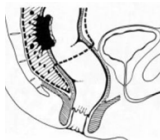
Klassieke behandeling LARC (cT3/4, N+)




chemoradiotherapie **TME** **chemotherapie**



6-8w



chemotherapie



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Heterogene respons op CRT

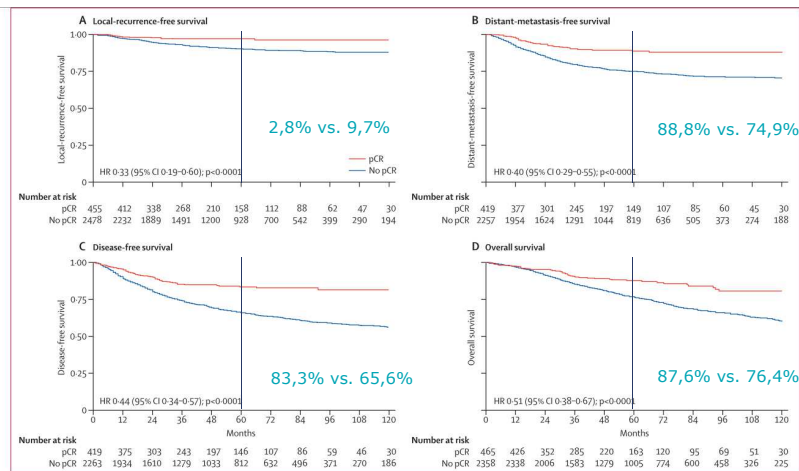


15-27% pCR
54-75% partiële respons
Geen respons

Maas et al. Lancet Oncol 2010, Maas et al. JCO 2011

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Heterogene respons op CRT



Maas et al. Lancet Oncol 2010

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Heelkunde komt met een kost...

Heelkundige complicaties

TABLE 3. Complication Rates of Rectal Cancer Surgery

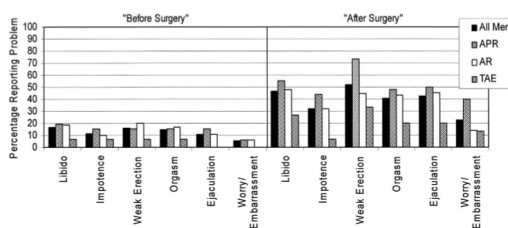
Complication	Rate*	95% CI	No. Studies
Wound infection	0.07	0.05-0.08	50
Anastomotic leak	0.11	0.10-0.12	84
Pelvic sepsis	0.12	0.09-0.16	29
Postoperative death	0.02	0.02-0.03	75

Chirurgische mortaliteit: 3-4% in Dutch TME trial

Tijdelijk/definitief stoma

Late nevenwerkingen

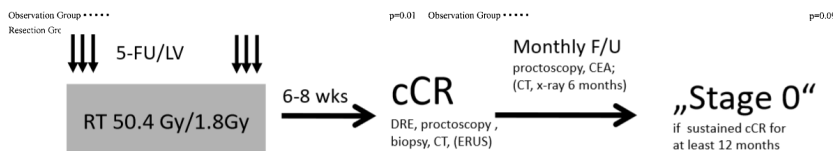
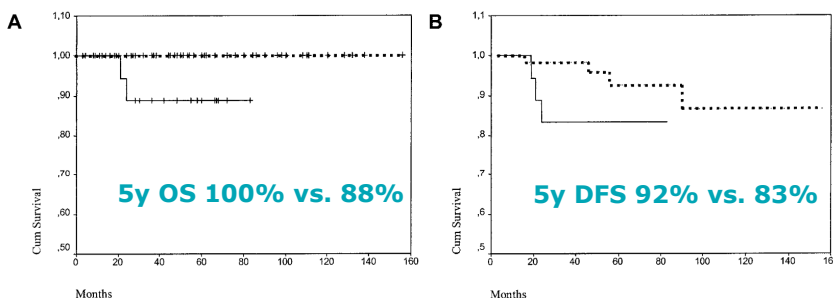
- urinaire
- gastrointestinale
- seksuele dysfunctie



Paun et al. Ann Surg 2010, Marijnen et al JCO 2002, Hendren Ann Surg 2005

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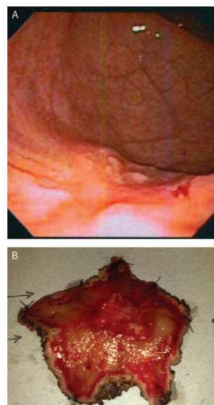
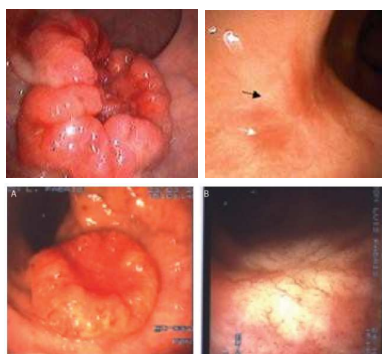
Orgaansparende behandeling



Habr-Gama et al. Ann Surg 2004

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Hoe klinische respons beoordelen?

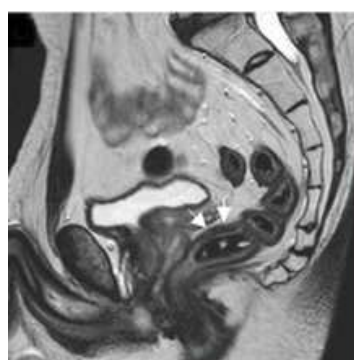


cCR: afwezigheid van residuele ulceratie, onregelmatigheid of nodule in het rectum op klinisch en endoscopisch onderzoek

Maas et al. JCO 2011, Habr-Gama et al. Dis Colon Rectum 2010

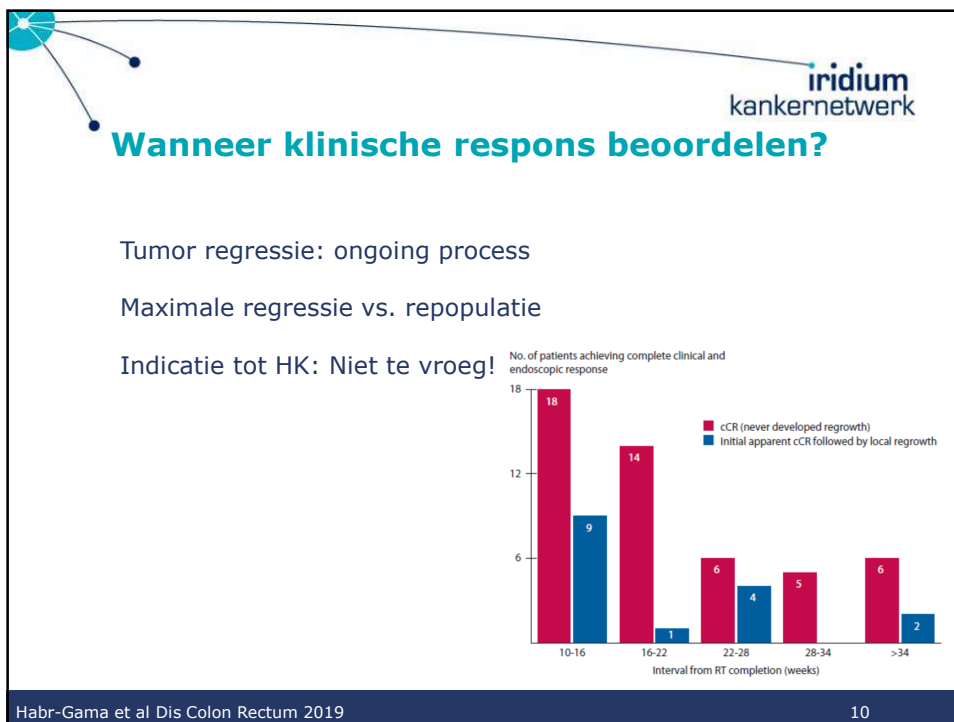
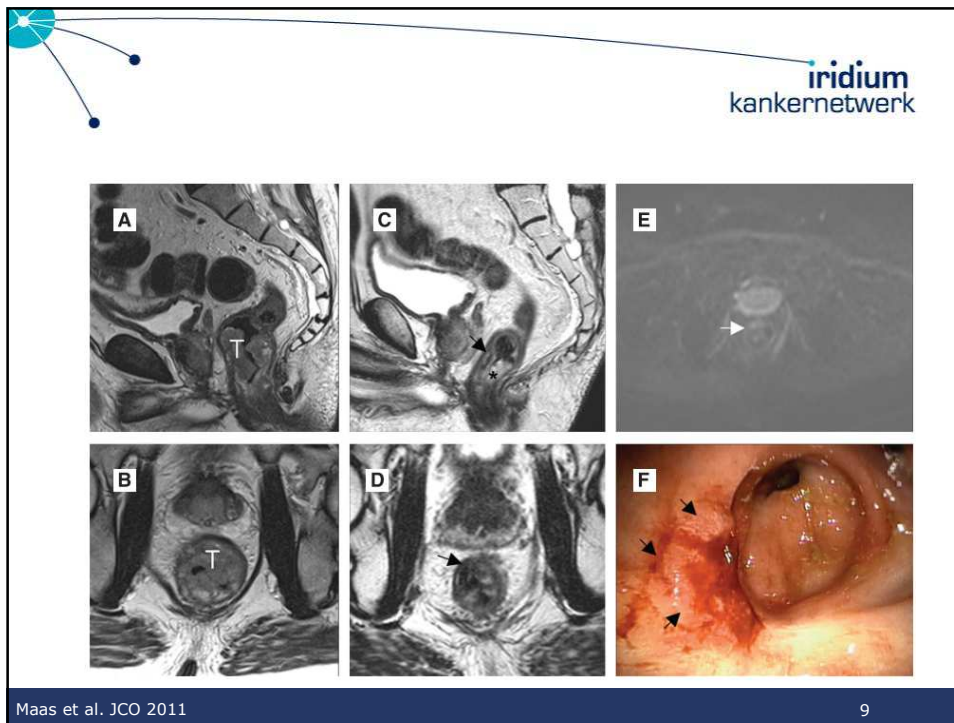
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Beyond the Wall



Maas et al. JCO 2011

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Watchful waiting

Idealiter hebben patiënten met cCR en W&W **minstens dezelfde of betere outcome** (oncologische en functioneel) tov patiënten die radicale heekunde ondergaan.

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Wat zijn de data?

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 Kranenbarg, Geerard L Beets, Nuno L Figueiredo, Anaelita Hahr-Gama, Rodriao O Perez, Andrew G Renehan, Cornelis J H van de Velde, and the IWWD Consortium*

Lancet 2018; 391: 2537-45

- Pooled individuele data, rectumcarcinoom
- 50% unpublished
- 880 patiënten met cCR na CRT, in watch and wait
- 4/2015-06/2017
- Mediane follow-up 3,3 jaar

van der Valk et al. Lancet 2018

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Veilig?


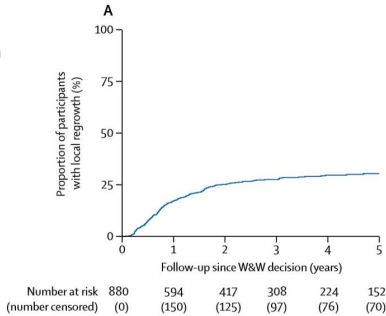
Lokaal herval

2j lokaal herval 25,2% (213/880)

- 97% darmwand
- 5% locoregionale klieren

Salvage heelkunde

- lokale excisie 46/148
- TME 115/148

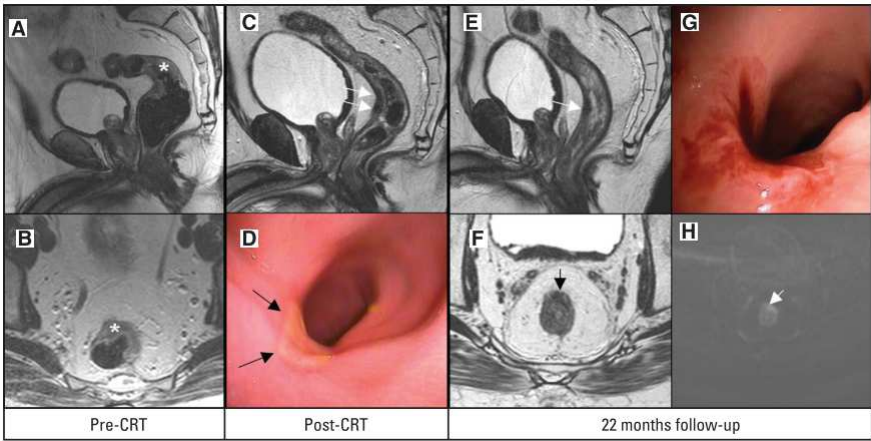
Follow-up since W&W decision (years)	Number at risk	(number censored)
0	880	(0)
1	594	(150)
2	417	(125)
3	308	(97)
4	224	(76)
5	152	(70)

van der Valk et al. Lancet 2018

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Lokaal herval

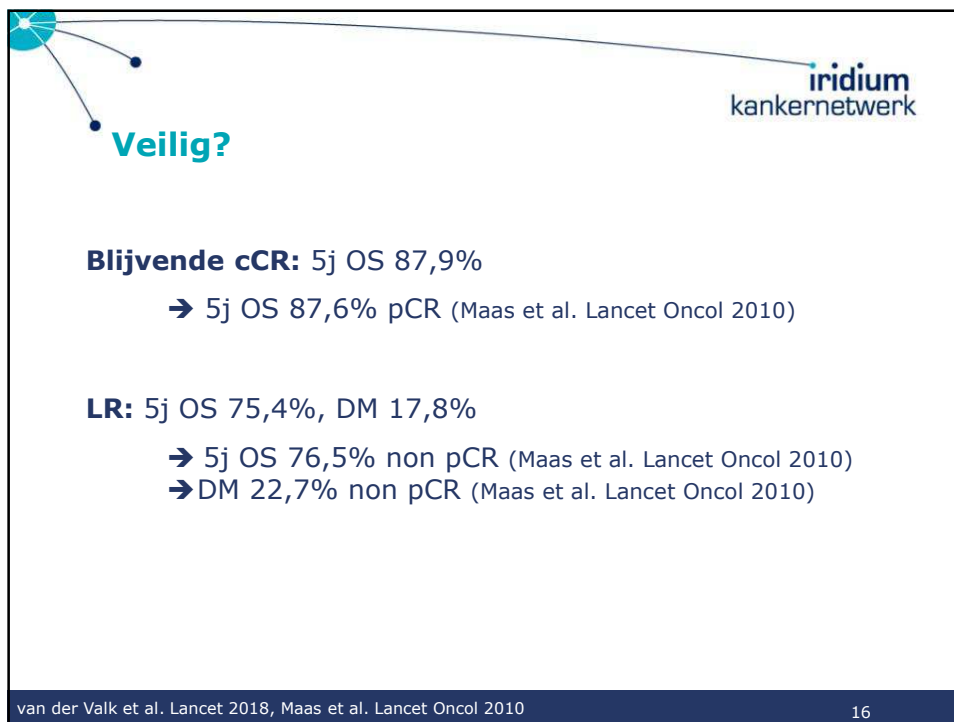
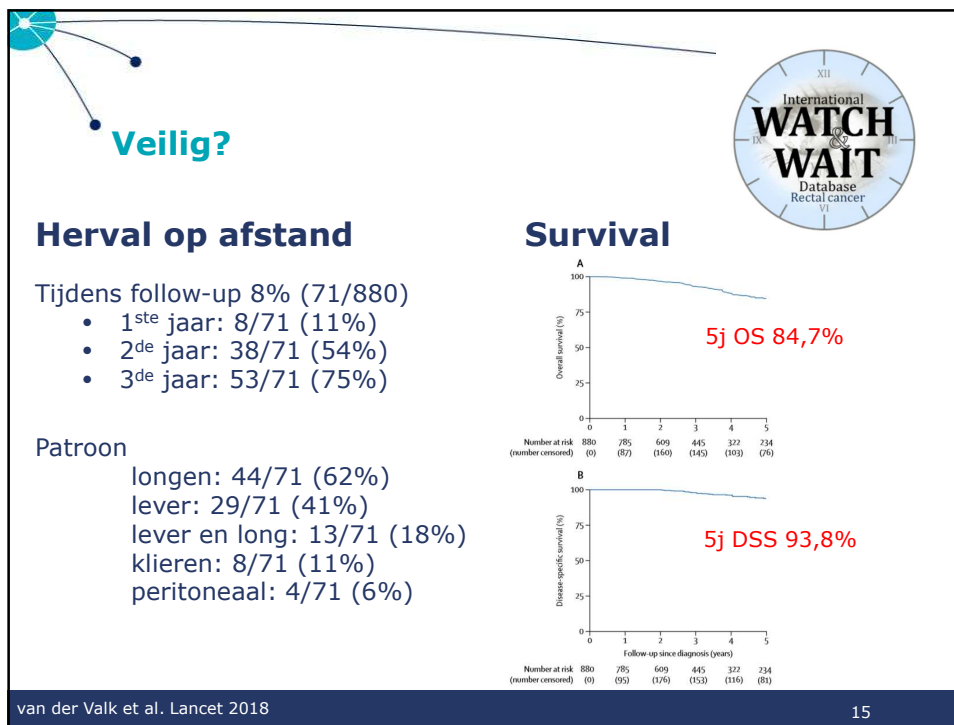
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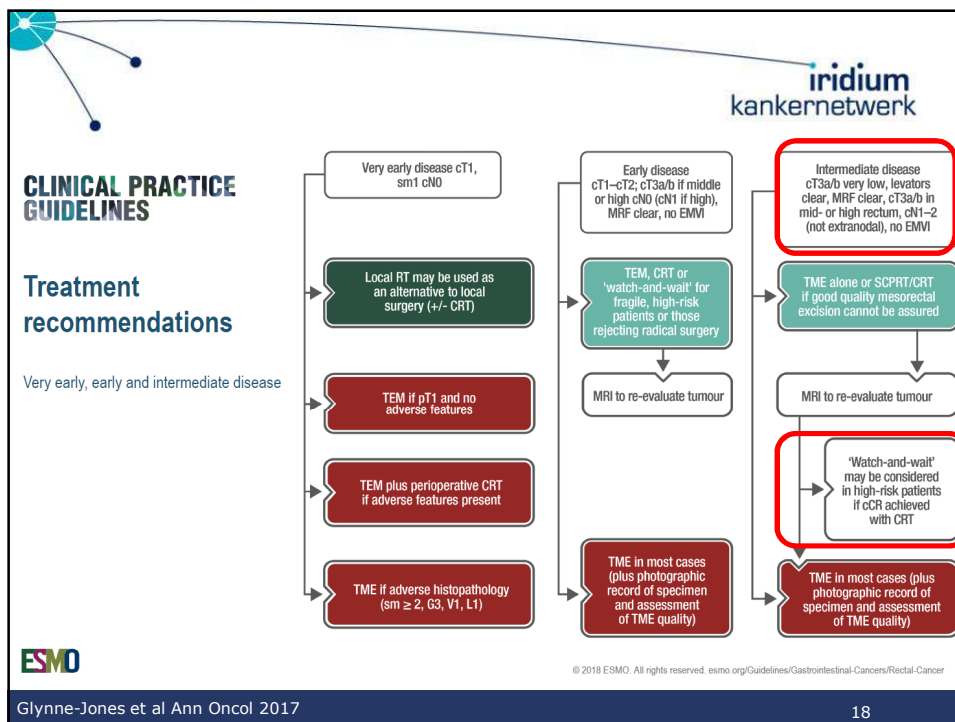
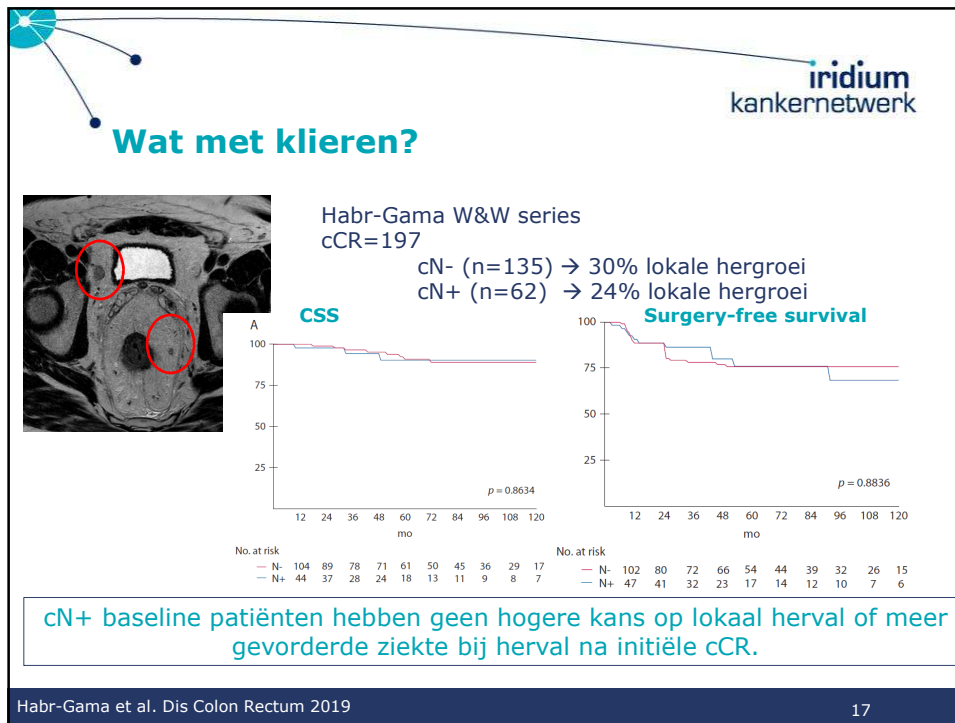


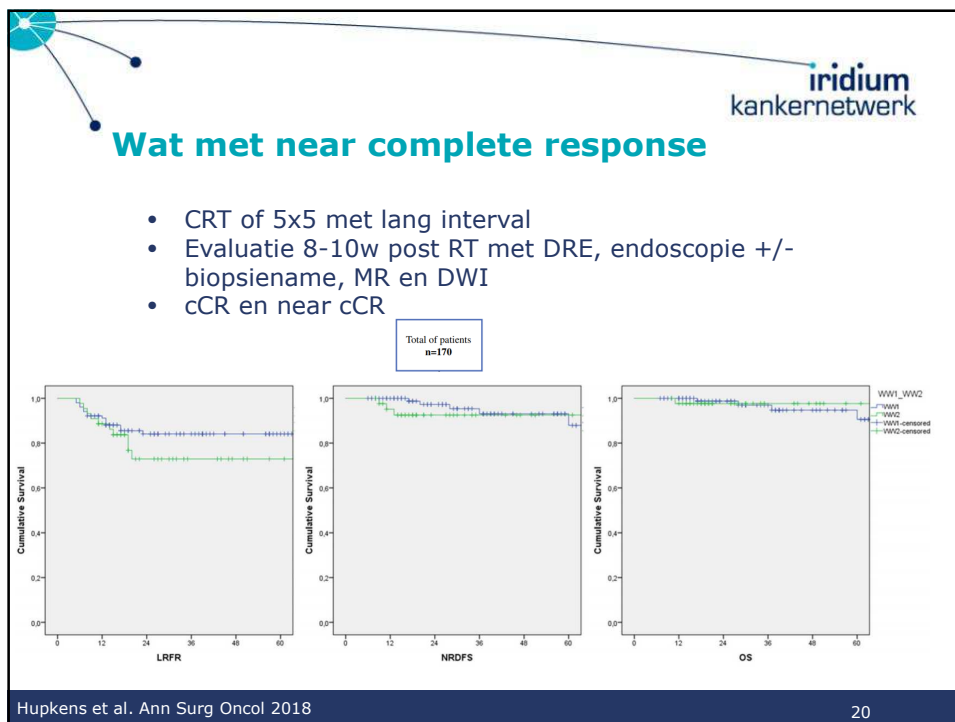
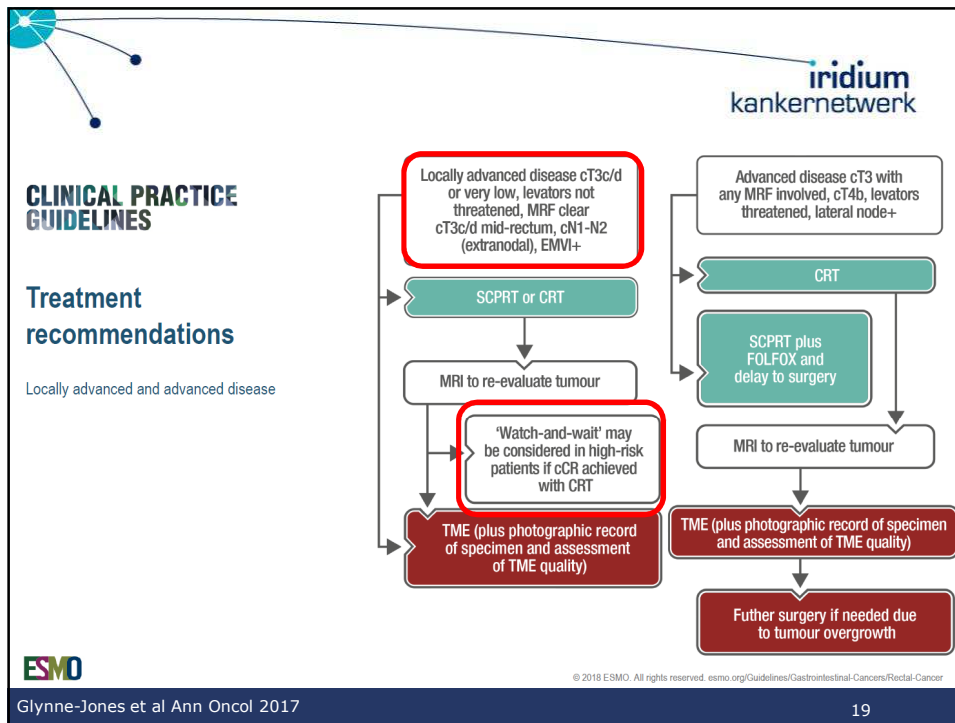
Pre-CRT Post-CRT 22 months follow-up

Maas et al. JCO 2011

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Follow-up

- Geen uniform protocol
- Combinatie van
 - PPA
 - Endoscopie
 - MRI
- Biopten en PET: nut is onduidelijk

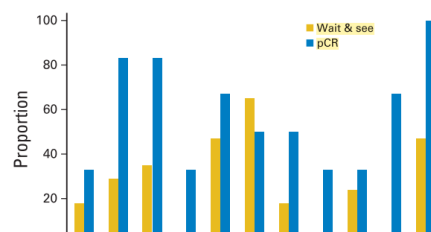
Year	CEA	DRE	CT for distant staging	Endoscopy*	MRI*
1	4x	4x	2x	4x	4x
2	4x	2x	1x	2x	2x
3	4x	2x	1x	2x	2x
4	2x	2x	1x	2x	2x
5	2x	2x	1x	2x	2x

Martens et al. JNCI 2016

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Quality of life

- n=21 cCR (1 LR @22m), n=20 controle groep pCR
- MSKCC bowel function questionnaire



- Mean Wexner score: 0,8 vs. 3,5 (cCR vs. pCR, $p=0.182$)
- Mean defaecation frequency 1,8 vs. 2,8 (cCR vs. pCR, $p=0.323$)

Maas et al. JCO 2011

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Quality of life

- N=100 (61 cCR, 39 near cCR)
- 3 jaars colostomie vrije overleving: 94,8%
- Vaizey score 3,4 W&W vs. 9,7 TEM

Metric	W&W (%)	TEM (%)
Solid stool incontinence	~10	~25
Liquid stool incontinence	~10	~50*
Gas incontinence	~15	~55*
Alteration in lifestyle	~5	~30
Need for pad or plug	~5	~60*
Constipation medicine	~30	~60
Defter defecation for 15 min	~10	~45*
Total	~3.4	~9.7

Martens et al. JNCI 2016

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Ready for prime time?


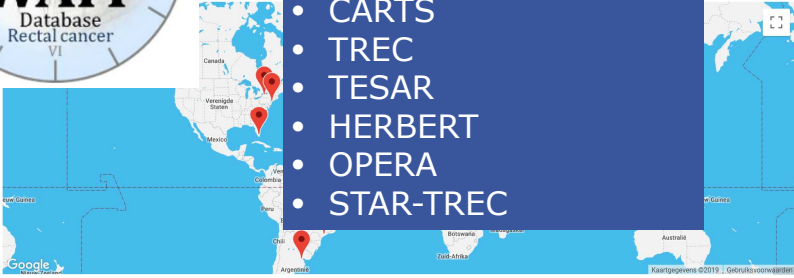
- Evidentie gebaseerd op **kleine cohortes**
- **Heterogeniteit** mbt patiëntenkarakteristieken alsook mbt CT schema en RT dosis (cfr cCR rates 10%-78%)
- Geen internationale **consensus** ivm timing en modaliteit van **responsevaluatie**, alsook wat betreft **follow-up**
- Weinig data mbt **long-term survival, functionele outcome en QoL**

RCT?

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Ongoing studies and future prospects

Prospective clinical trials

- GRECCAR 2
- MSKCC
- CARTS
- TREC
- TESAR
- HERBERT
- OPERA
- STAR-TREC

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Take home messages

- Orgaansparende behandeling met **dedicated follow-up programma en ervaring** in endoscopie en MRI.
- **Klinische en MR evaluatie** correleert niet perfect met echte **pathologische respons** gezien 2jaars lokaal herhaal 25%, maar ook dan is salvage resectie vaak mogelijk.
- Niet duidelijk of CRT en zo mogelijk W&W een valabel alternatief is voor TME bij **vroegtijdige tumoren**.
- W&W: altijd **shared decision making** met patiënt.

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Is pCR gelijk aan cCR?

Glynne Jones Critical appraisal Br J Surg 2012

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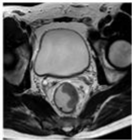



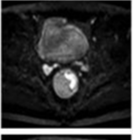




Hoe kunnen we de respons verhogen?

- Interval? Niet zeker
 - Sloothaak Br J Surg 2013
 - Perez IJROBP 2012
 - Lefevre J Clin Oncol GRECCAR-6: 7 vs. 11 weken niet duidelijk
 - Evans Ann Oncol 2016: 6 vs. 12 w
- Dose: Habr-Gama Ann Surg 2019, Appelt IJROBP 2013: minder reproductie
- FOLFOX (cfr CAOARO AIO, metformine)

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pCR predictie?

	T2-MRI	DWI	¹⁸ F-FDG PET
pre CRT			
during CRT			
post CRT			

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Lokale hergroei

≠ lokaal hervul na TME
goede prognose, salvageable

= alle lokale hergroei thv tumor locatie of regionale klieren

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