

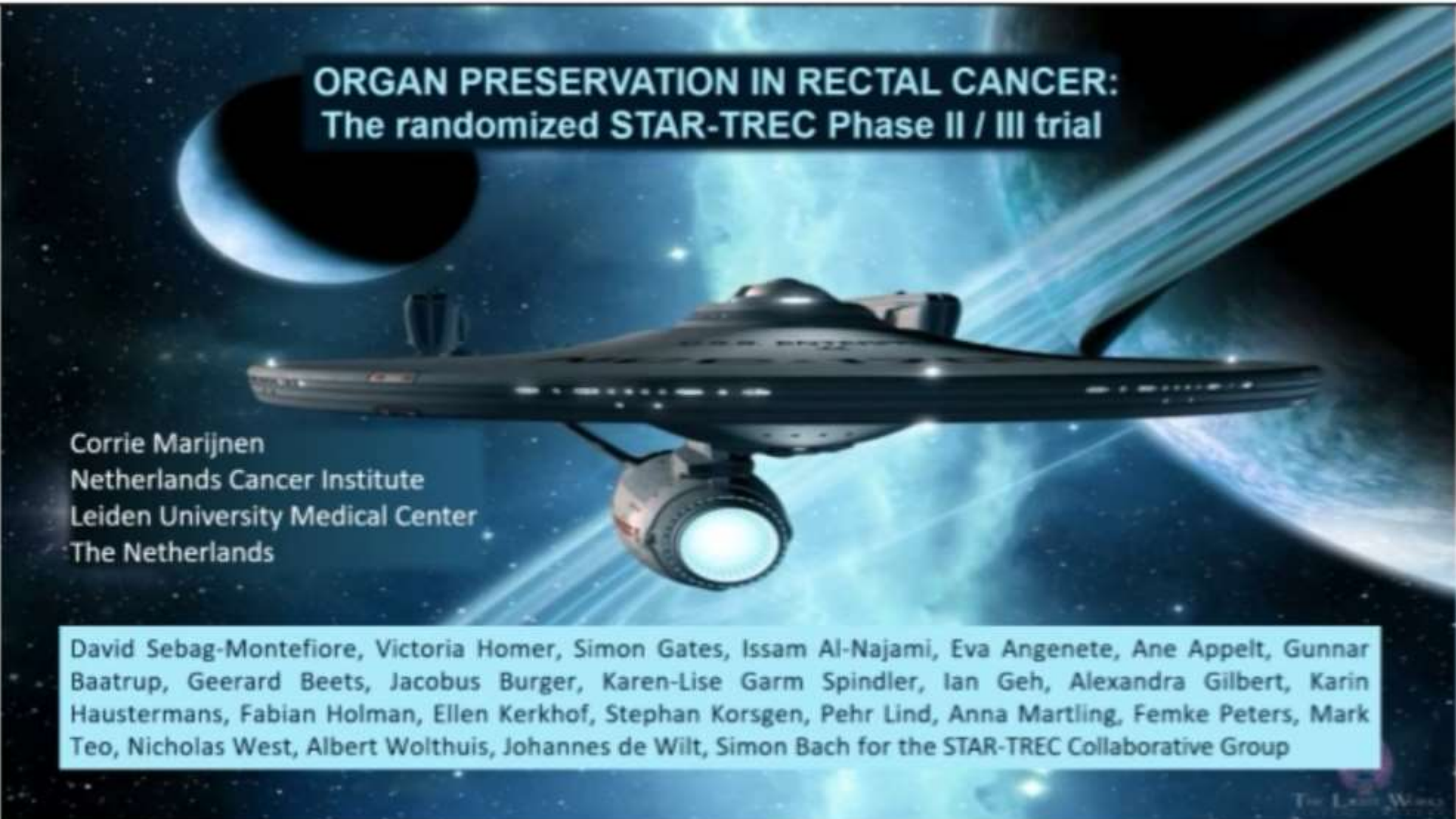
Post
ESTRO
2025
AFRIQUE DU NORD



BY SMC/STOR
LE 28 MAI 2025 À 18H00 (GMT+1)
Evenement VIRTUEL

CANCERS
DIGESTIFS

Zenab ALAMI



ORGAN PRESERVATION IN RECTAL CANCER: The randomized STAR-TREC Phase II / III trial

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Corrie Marijnen
Netherlands

STUDY DESIGN PHASE III

R



LCCRT

25x2 Gy + capecitabine

SCRT

5x5 Gy

Pt prefers surgery

AIMS:

Compare effectiveness of 2 radiotherapy schedules

PRIMARY ENDPOINT:

The proportion of patients with successful organ preservation at 30 months

TRIAL STEERING GROUP: ADVISED TO REPORT 12 MONTHS OUTCOMES

CURRENT ANALYSES ADVISED BY TRIAL STEERING GROUP



Only patients with 12 months* follow-up (or more) are included

TME free survival at 12 months

Post hoc analyses

- phase II and III separately
- tumors ≤ 3 cm vs > 3 cm

Acute toxicity

R

LCCRT

25x2 Gy + capecitabine

SCRT

5x5 Gy

TME

1st assessment2nd assessmentLocal excision
histopathology

TME surgery

INCLUSION CRITERIA

Biopsy proven adenocarcinoma

mrT1-T3b (≤ 5 mm extramural spread) N0 CRM-ve

ECOG 0-1

Multidisciplinary team considers all treatment arms feasible

Minimum follow-up 12 months: 424/503 included*

Responder:
2nd assessmentcCR:
Watch & WaitNo cCR:
Local excisionNo HR features:
Observation1 HR feature:
TME or observation>1 HR feature:
TME advisedNon responder:
TME11-13 weeks after
start treatment16-20 weeks after
start treatment



INCLUSION OF PATIENTS: M-ITT

LCCRT
25x2 Gy + capecitabine

Did not start any trial treatment: 9

Started trial treatment: 163

- Received LCCRT: 161
- Received SCRT: 1
- Received TME: 1

Included in analyses: 163

SCRT
5x5 Gy

Did not start any trial treatment: 4

Started trial treatment: 168

- Received LCCRT: 0
- Received SCRT: 167
- Received TME: 1

Included in analyses: 168

TME

Did not start any trial treatment: 4

Started trial treatment: 78

- Received LCCRT: 0
- Received SCRT: 0
- Received TME: 78

Included in analyses: 78

PATHOLOGY RESULTS TME PATIENTS

Indication for the “real staging” of our organ preservation patients

	MR-based (N=78)		Pathology (N=78)	
T-stage				
Tx	2	3%	1	1%
T1	2	3%	18	23%
T2	49	63%	39	50%
T3	25	32%	20	26%
N-stage				
N0	78	100%	58	74%
N+	0		18	23%
missing	0		2	3%

PATIENT CHARACTERISTICS

	LCCRT (N=163)		SCRT (N=168)		TME (N=78)	
Recruitment phase						
Phase II (N)	38		40		36	
Phase III (N)	125		128		42	
Sex						
Male	115	71%	125	74%	53	68%
Median age (years)	67		67		67	
Tumor stage						
mrTX	2	1%	3	2%	2	3%
mrT1	15	9%	11	7%	2	3%
mrT2	114	70%	128	76%	49	63%
mrT3a	25	15%	18	11%	15	19%
mrT3b	7	4%	7	4%	10	13%
Tumor length (mm)	28		28		30	
Distance to anal verge (mm)	60		53		54	

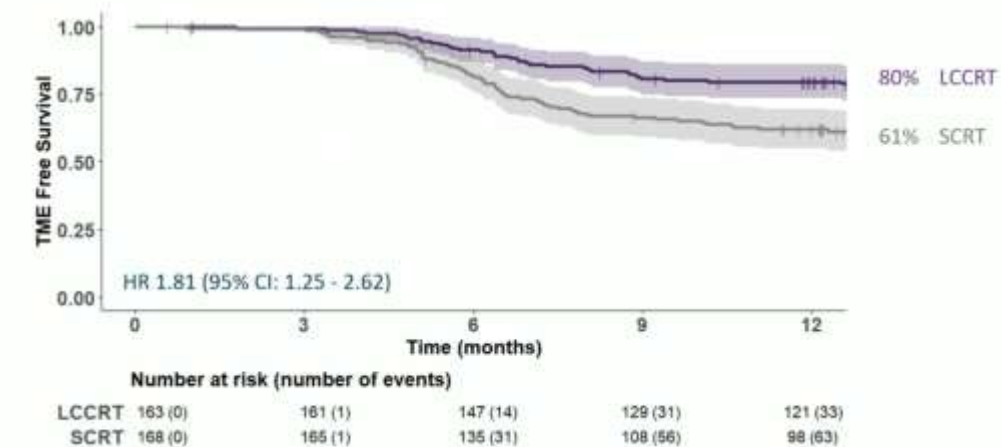
TOXICITY

No treatment-related deaths

	LCCRT (N=163)		SCRT (N=168)	
SAE (including surgery)				
Number of SAEs	23		30	
Number of patients	21	12%	26	15%
Toxicity (only (C)RT)*				
None	12	7%	36	22%
Grade 1	89	55%	69	41%
Grade 2	55	34%	48	29%
Grade 3	6	4%	12	7%
Grade 4	0		0	
Grade 5	0		0	

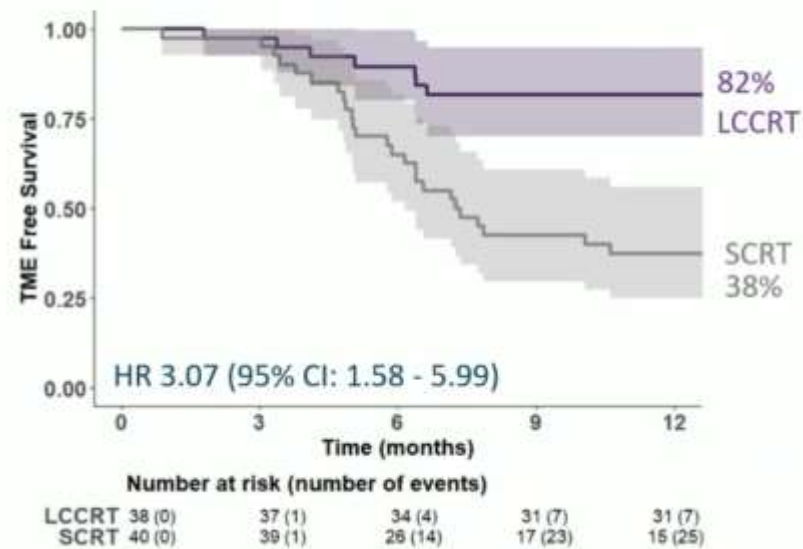
TME FREE SURVIVAL AT 12 MONTHS

Better TME free survival after LCCRT

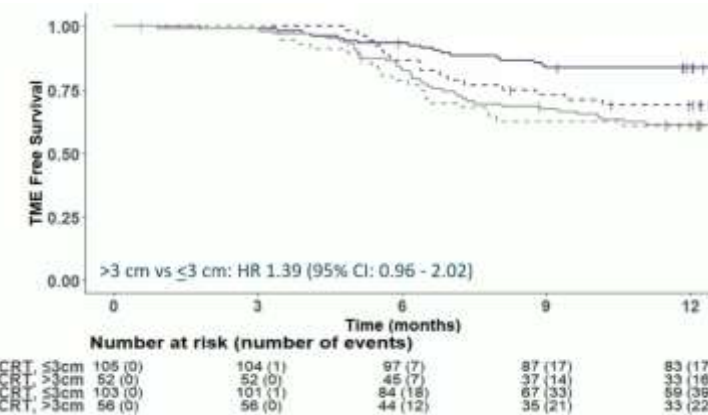


TME FREE SURVIVAL AT 12 MONTHS: TRIAL PHASE
Difference mainly seen in phase II

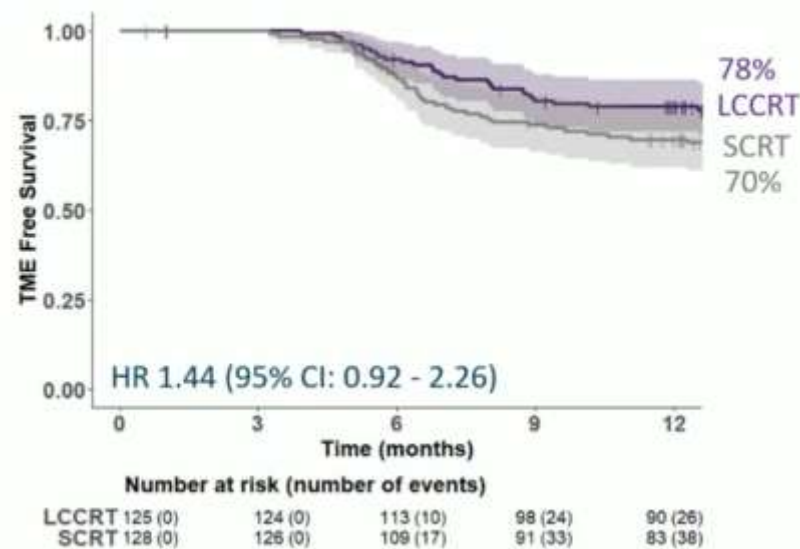
Phase II patients



TME FREE SURVIVAL AT 12 MONTHS: TUMOR SIZE
No difference in SCRT arm



Phase III patients



— LCCRT ≤ 3cm 84%
 - - - LCCRT > 3cm 69%
 — SCRT ≤ 3cm 61%
 - - - SCRT > 3cm 60%

DISCUSSION

For cT1-3b N0 rectal cancer

First study to include TME arm and compare two radiotherapy strategies

First study to include mesorectal-only target volume

Difference in phase II and III difficult to explain

SCRT dose may be less effective to achieve ypT0/1

Proof durability of outcomes with 30 months primary endpoint

Impact on HRQL evaluated at 24 months

IN CONCLUSION

For cT1-3b N0 rectal cancer

Excellent one year organ preservation rates

80% for LCCRT and 61% for SCRT

Little radiotherapy-associated toxicity with mesorectum only target volume

Organ preservation a very good option for early-intermediate risk rectal cancer

Short-term radiotherapy plus chemotherapy for locally advanced rectal cancer: 5-year outcomes of the phase III clinical trial

Presenter: Yuan Tang¹

Co-first Authors: Yuan Tang¹, Haitao Zhou², Tongzhen Xu¹, Ning Li³

Corresponding Authors: Jing Jin^{4,1}, Chen Hu⁵, Ye-Xiong Li¹, Yuan-Hong Gao⁶, Shi-Xin Liu⁷, Li-Chun Wei⁸

On behalf of the STELLAR study group

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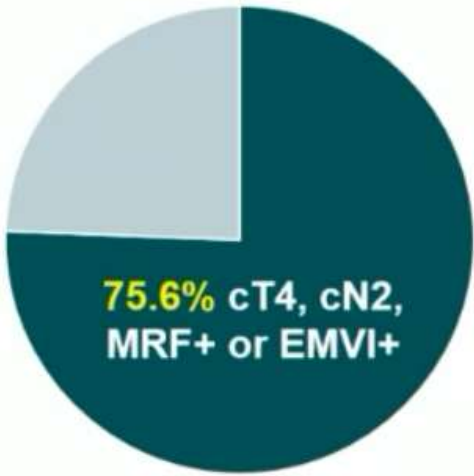
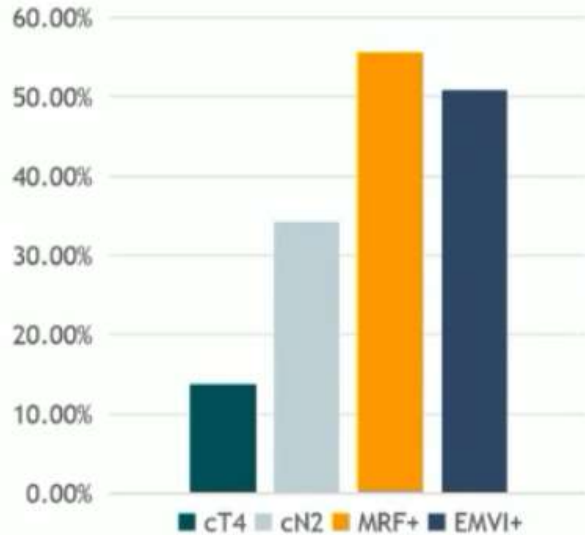
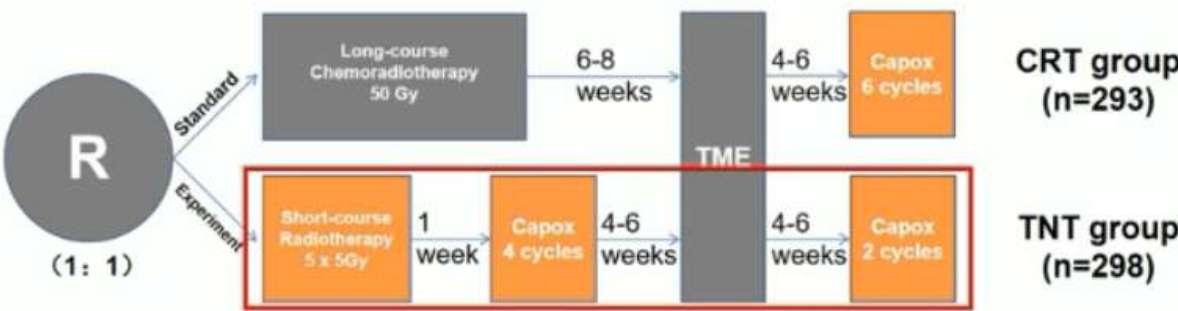
Yuan Tang
China

Background

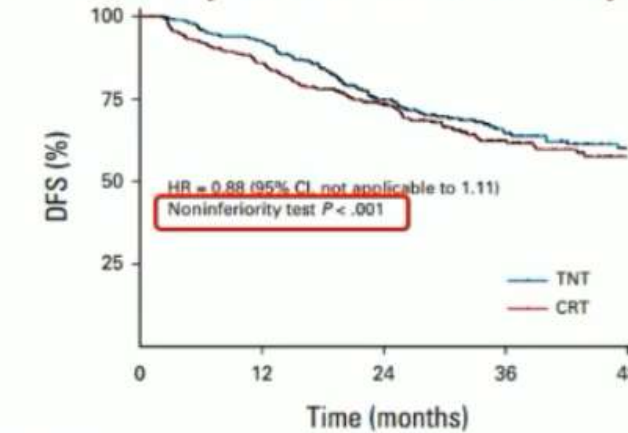
Primary endpoint: 3-year DFS

Primary hypothesis:

TNT is non-inferior to CRT in 3-year DFS



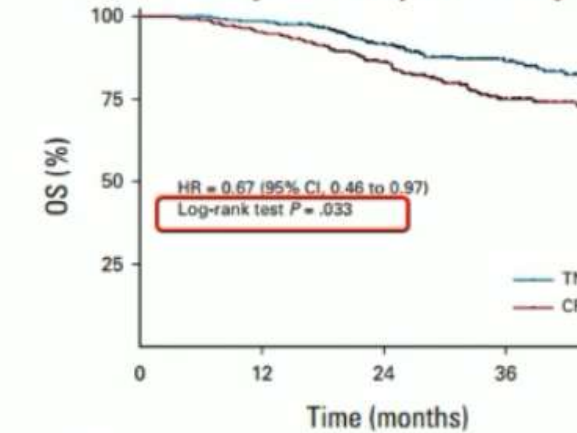
A 3y DFS non-inferiority



No. at risk:

	0	12	24	36	48
TNT	302	275	183	92	49
CRT	297	249	165	86	40

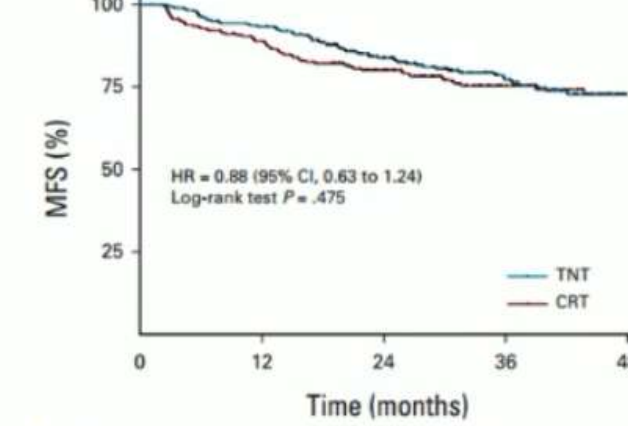
B 3y OS superiority



No. at risk:

	0	12	24	36
TNT	302	292	231	123
CRT	297	274	204	105

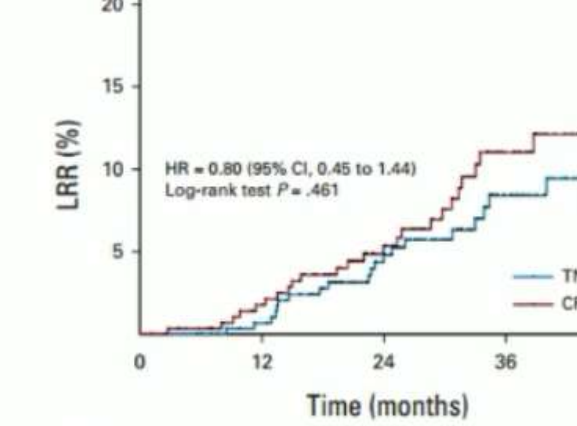
C



No. at risk:

	0	12	24	36	48
TNT	302	270	198	103	52
CRT	297	247	177	93	40

D



No. at risk:

	0	12	24	36
TNT	302	287	221	113
CRT	297	270	195	102

Objectives

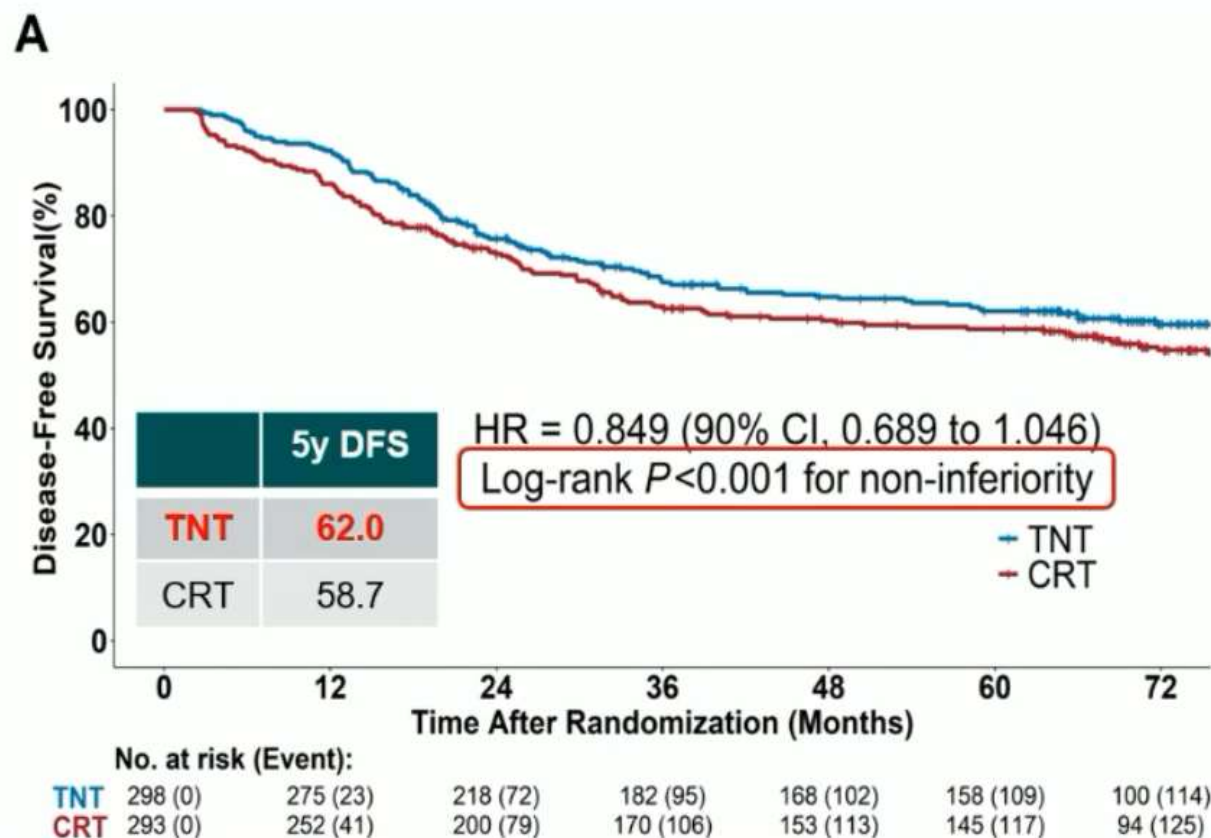
The STELLAR trial previously demonstrated that preoperative SCRT followed by chemotherapy (TNT) was **non-inferior** to standard CRT in terms of **3-year DFS** in LARC patients, and showed a **superior OS**.

This presentation reports the **updated 5-year follow-up results**, including

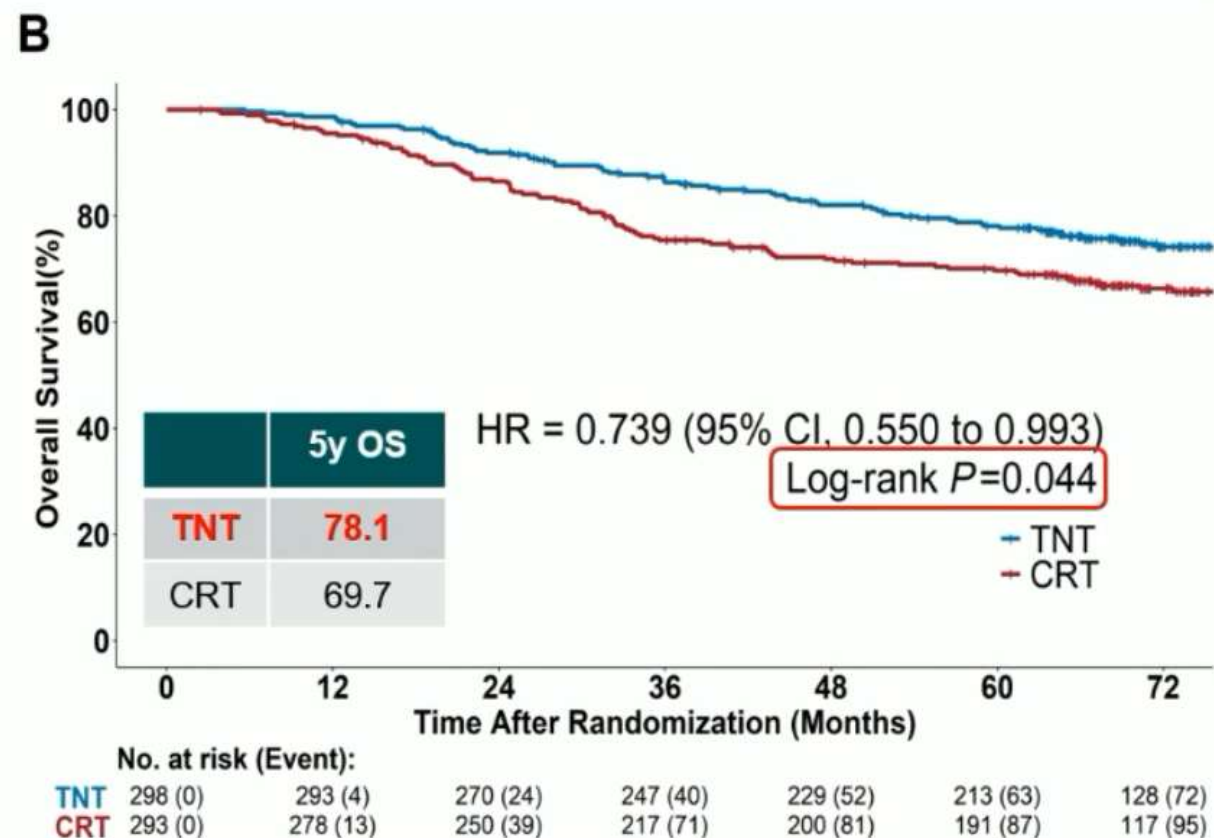
- **DFS** and **OS**
- Distant metastasis (**DM**) and Locoregional Recurrence (**LRR**)
- **QoL** and **anorectal function** (EORTC QLQ-C30, Wexner fecal incontinence score)

5-year DFS and OS

Median follow-up of 68.7 months



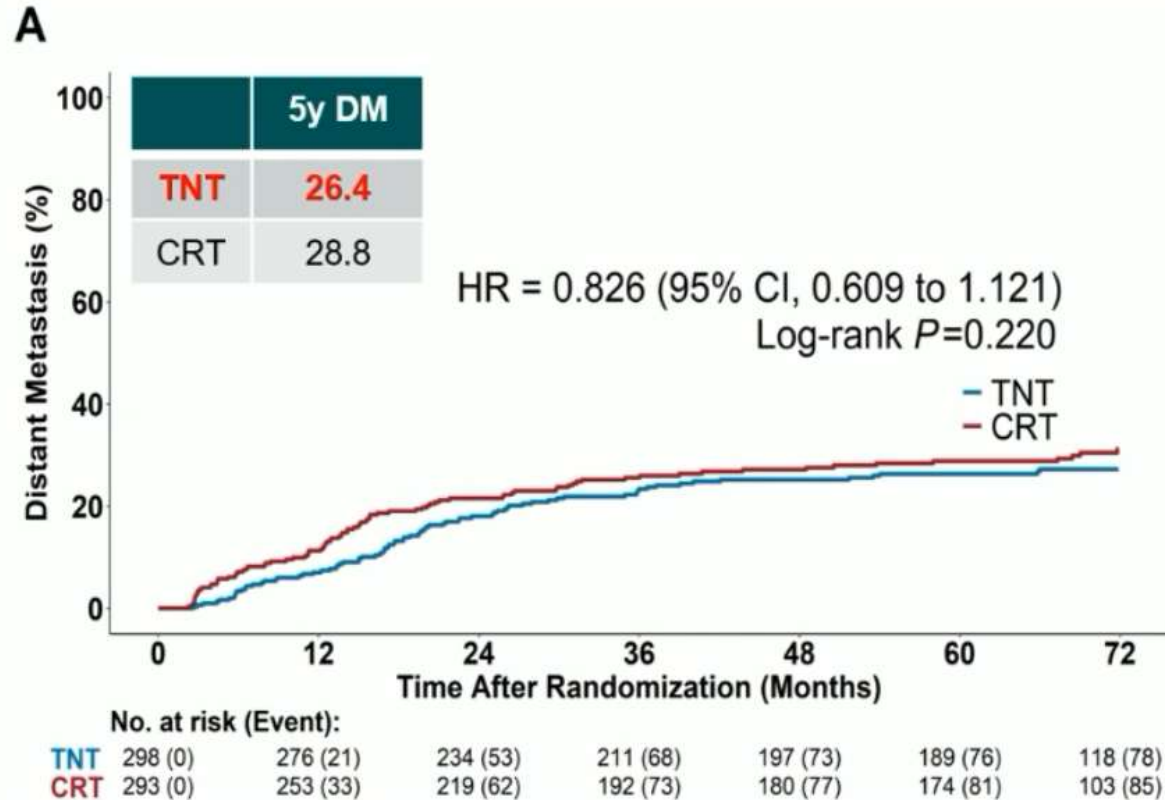
Absolute 5-year DFS difference: 3.3%



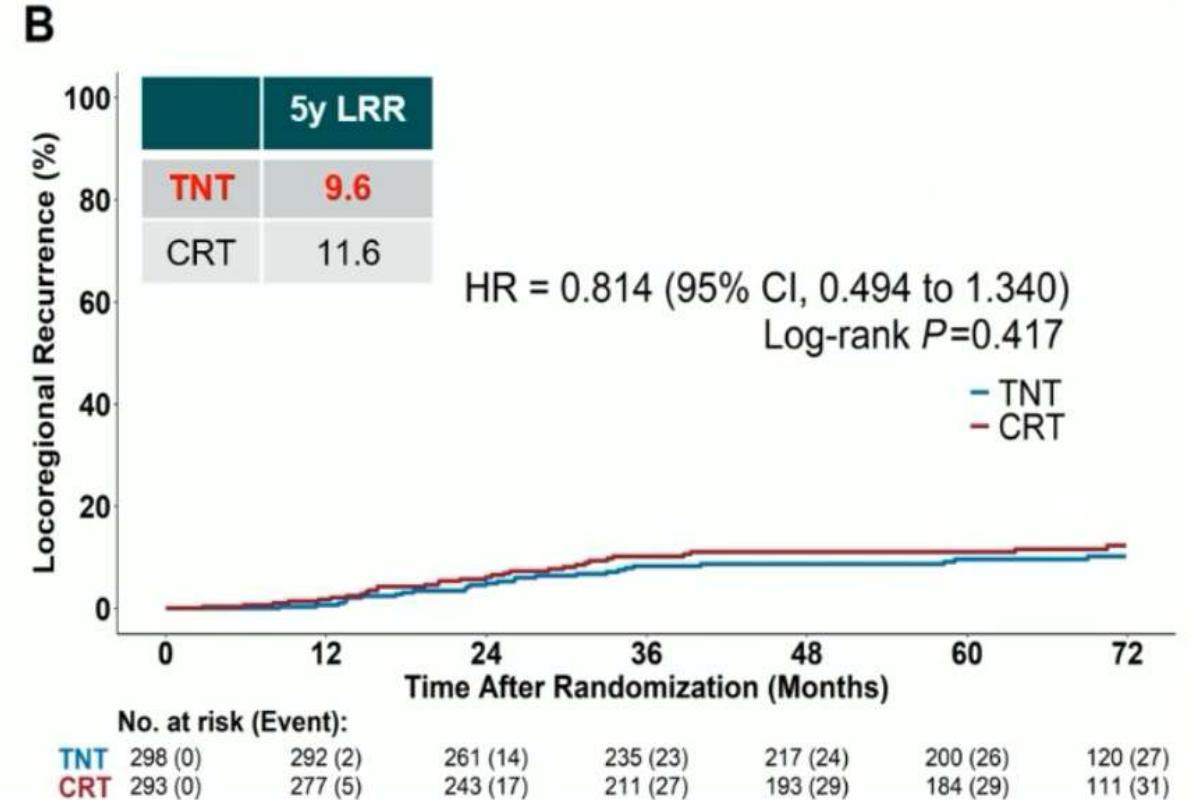
Absolute 5-year OS benefit: 8.4%

5-year DM and LRR

Median follow-up of 68.7 months



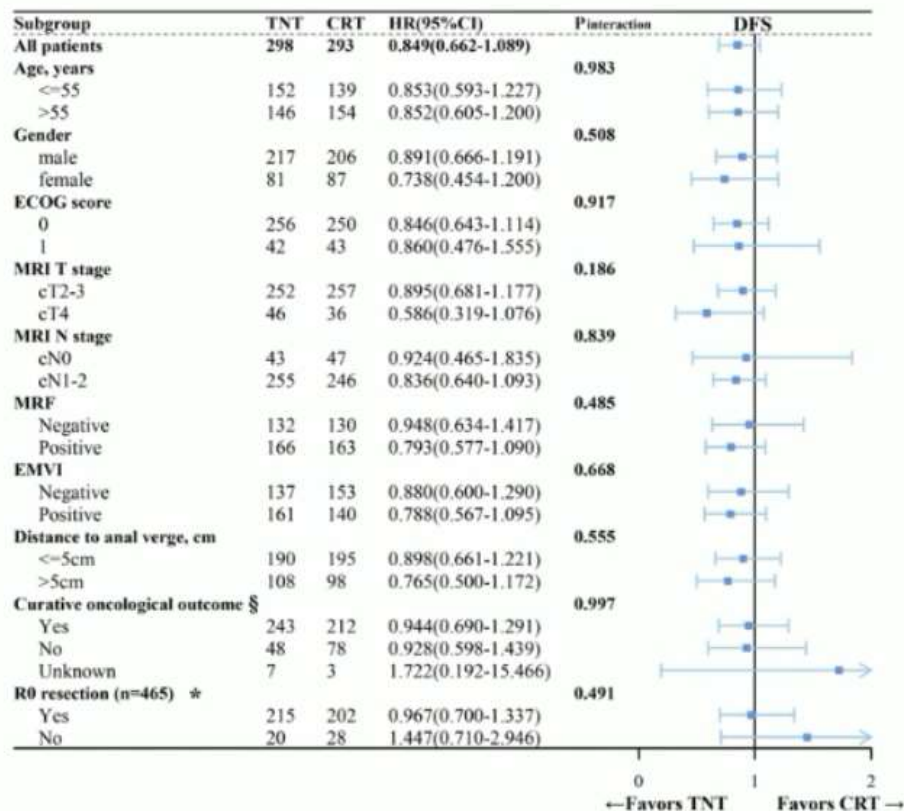
Absolute 5-year DM difference: 2.4%



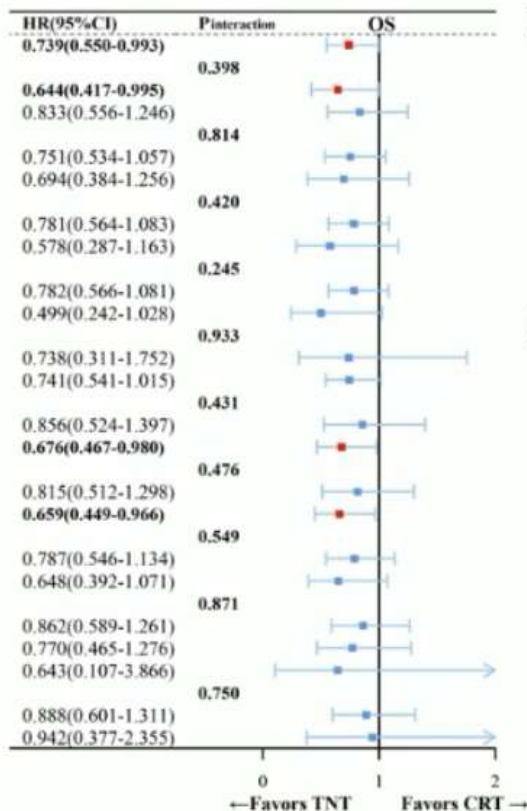
Absolute 5-year LRR difference: 2.0%

Forest Plots of DFS and OS across Subgroups

DFS



OS



➤ 5y DFS (TNT vs. CRT)

TNT did not show a clear DFS advantage in any specific subgroup.

➤ 5y OS (TNT vs. CRT)

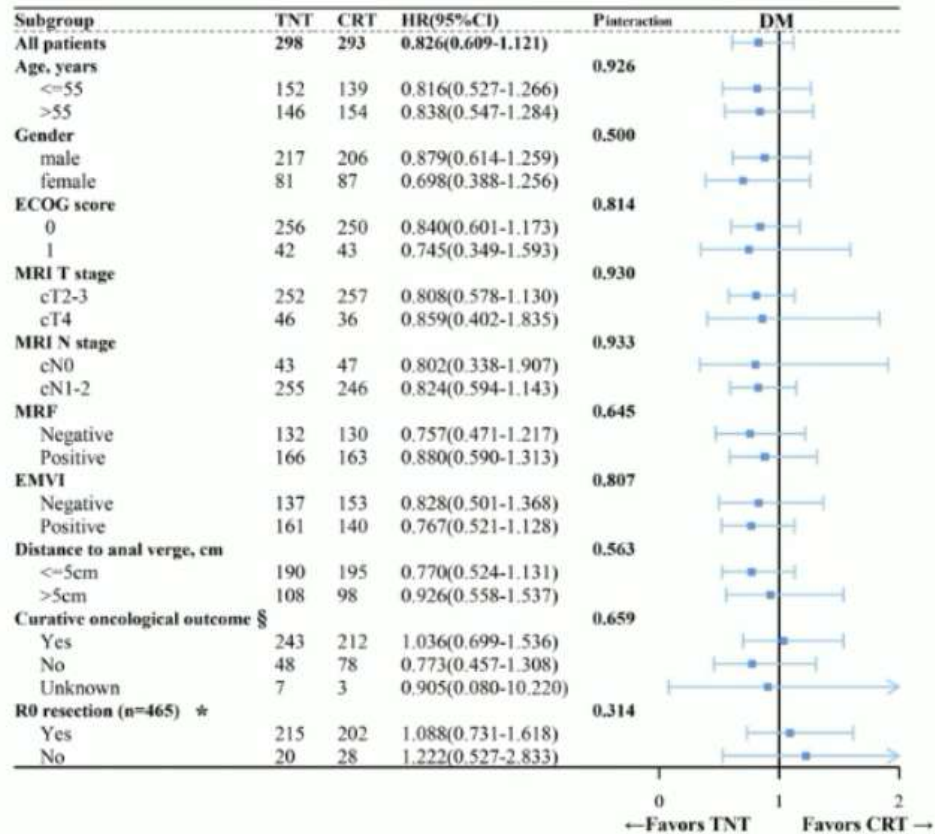
TNT was superior to CRT in some subgroups.

- Aged ≤55 years:** 77.9% vs. 68.5%
- MRF involvement:** 76.8% vs. 63.2%
- EMVI positive:** 75.5% vs. 63.1%

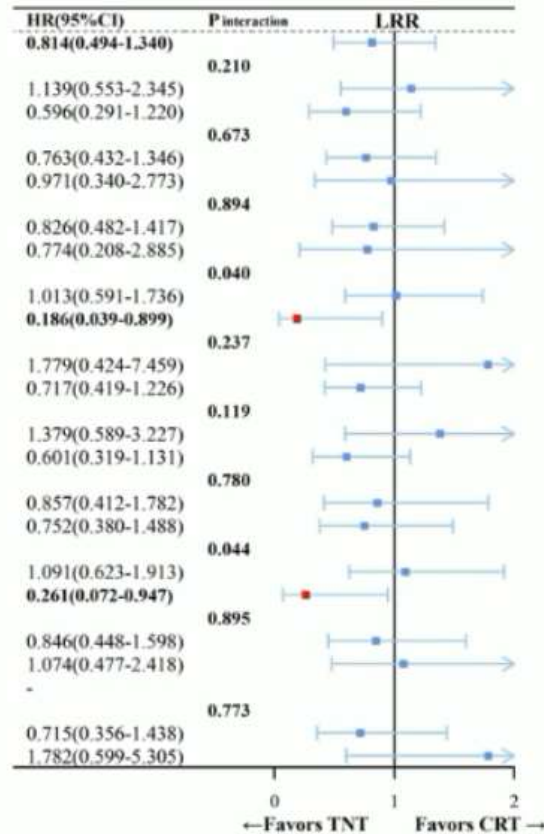
However, the interaction *P*-value was not significant.

Forest Plots of DM and LRR across Subgroups

DM



LRR



➤ 5y DM (TNT vs. CRT)
TNT did not reduce 5y DM compared with CRT in any subgroup.

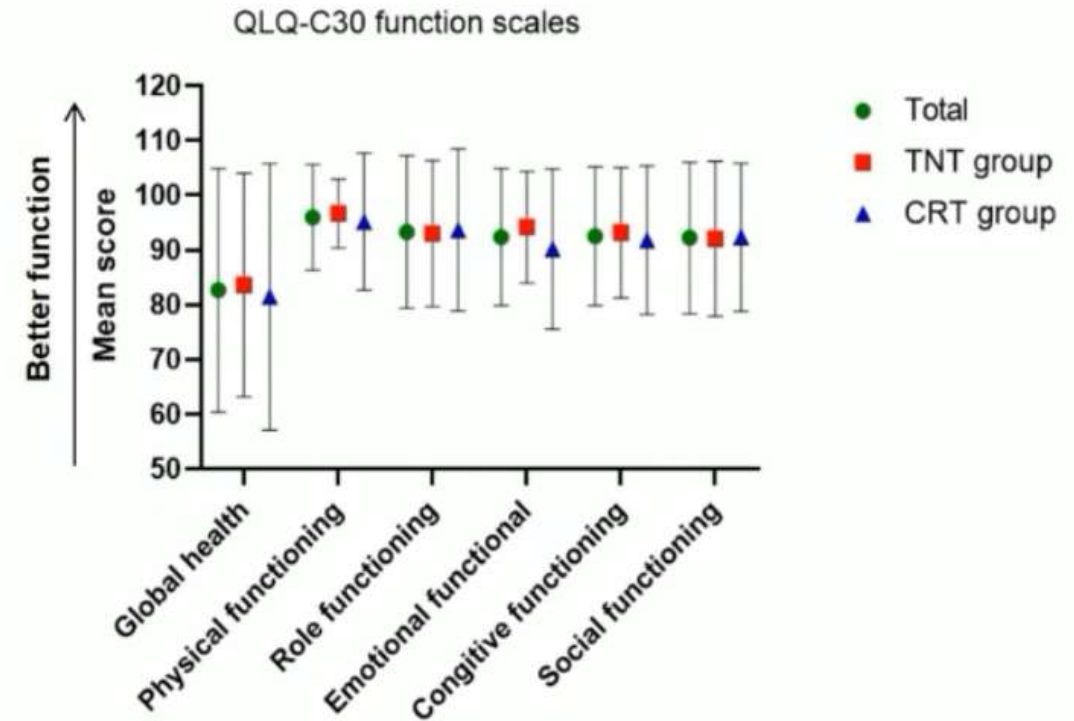
➤ 5y LRR (TNT vs. CRT)
TNT was superior to CRT in some subgroups.

- cT4 stage: 5.6% vs. 23.6%
- >5 cm to anal verge: 1.9% vs. 9.1%

The interaction *P*-value was statistically significant in the above subgroups.

Quality of Life and Anorectal Function

	TNT	CRT	P
Surviving patients median follow-up (months)	77.1	77.6	-
rate of questionnaires completion	49.5	44.9	0.350
QLQ-C30			
Global health	83.5	81.4	0.511
Physical functioning	96.6	95.1	0.304
Role functioning	92.9	93.6	0.750
Emotional functioning	94.1	90.1	0.031
Cognitive functioning	93.1	91.7	0.447
Social functioning	92.0	92.3	0.894
Wexner Score			
Wexner incontinence score	5	3	0.357



Comparable QoL and anorectal function

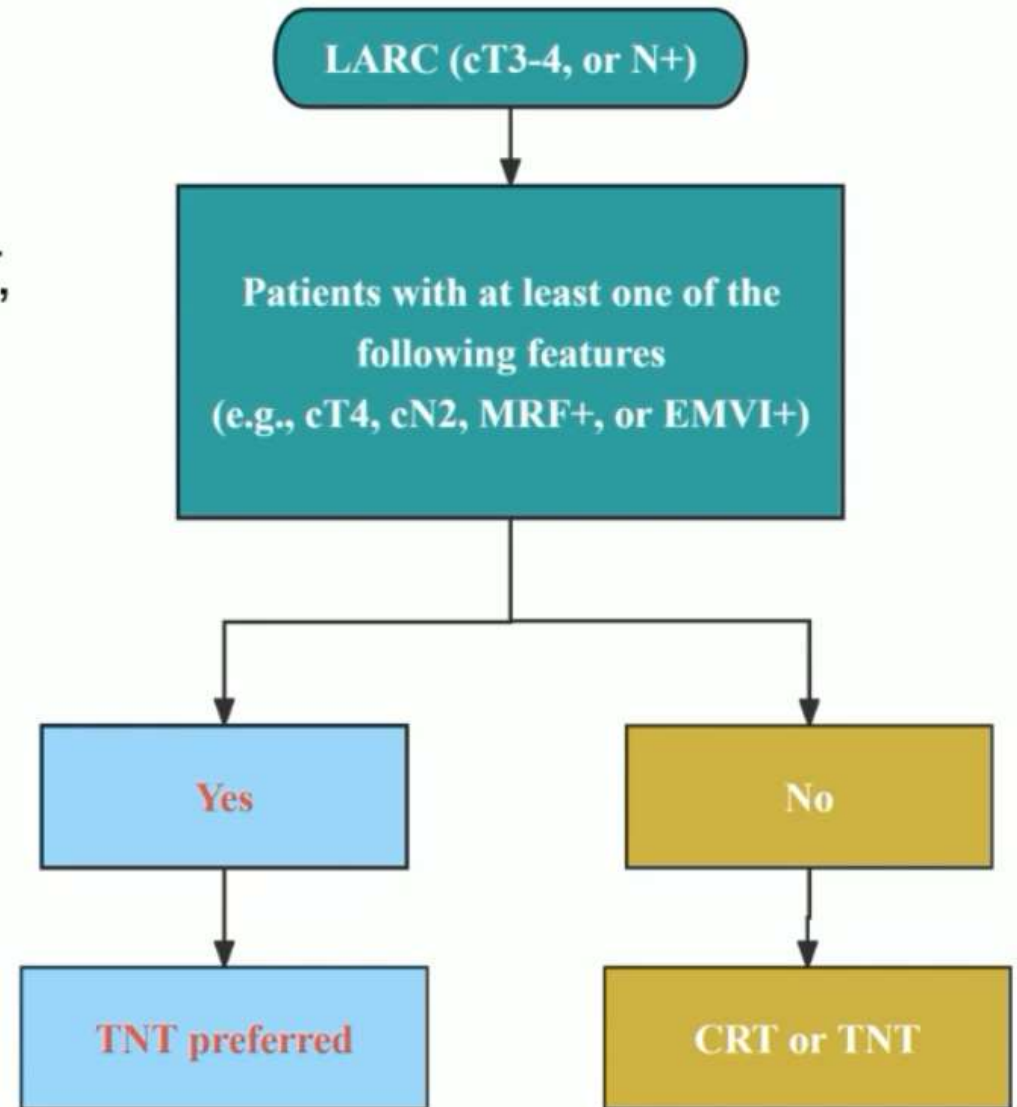
Treatment failure locations

Fewer regional-only recurrences
in TNT group.

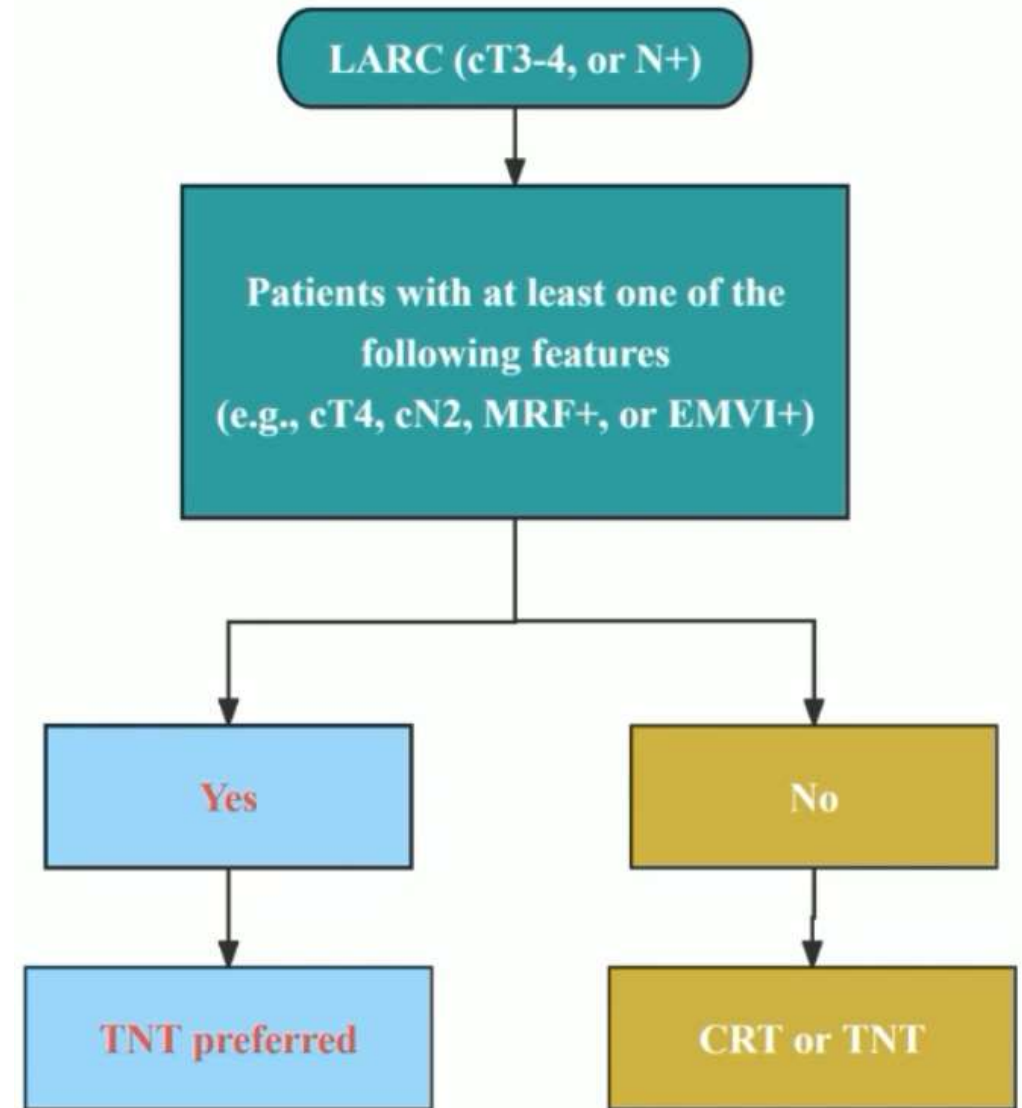
	TNT N=98 (%)	CRT N=104 (%)	P
LRR lesion			
Primary location alone	27 (27.6)	20 (19.2)	0.187
Regional lymphatic drainage area alone	1 (1.0)	10 (9.6)	0.010
Primary location together with Regional lymphatic drainage area	1 (1.0)	3 (2.9)	0.621
DM lesion			
Liver alone	19 (19.4)	24 (23.1)	0.607
Lung alone	24 (24.5)	21 (20.2)	0.502
Liver	35 (35.7)	45 (43.3)	0.314
Lung	37 (37.8)	39 (37.5)	0.999
Other distant organ (except for lung and liver)	17 (17.3)	9 (8.7)	0.092
Peritoneal metastasis	7 (7.1)	12 (11.5)	0.339
Non-regional lymphatic drainage area	3 (3.1)	5 (4.8)	0.721

Key Findings

- **TNT maintains DFS non-inferiority and provides a sustained OS benefit over CRT, solidifying its long-term efficacy**
--5y OS **improved by 8.4%** in the TNT group
- **No difference in QoL and anorectal function**
- **TNT should be recommended as a neoadjuvant option for LARC**



- Le TNT maintient la non-infériorité en termes de survie sans maladie (DFS) et offre un bénéfice durable en termes SG par rapport à la CRT, renforçant ainsi son efficacité à long terme.
 - SG à 5 ans améliorée de 8,4 % dans le groupe TNT
- Aucune différence dans la qualité de vie et la fonction anorectale
- Le TNT devrait être recommandé comme option néoadjuvante pour les LARC



Preoperative Short-course Radiotherapy Followed by Chemotherapy and PD-1 Inhibitor for Locally Advanced Rectal Cancer: Phase II Results of STELLAR II

Yuan Tang, Hao-Yue Li, Li-Chun We, Ning Li, Wen-Jue Zhang, Yu-Fei Lu, Fei-Yan Deng, Tong-Zhen Xu, Jia-Cheng Shuai, Zi-Fa Lei, Xian-Yu Meng, Shu-Nan Qi, Yong-Wen Song, Wen-Wen Zhang, Hao Jing, Gong Li, Shi-Xin Liu, Ying-Jie Wang, Zheng Liu, Hui-Ying Ma, Ning-Yu Wang, Bo Chen, Shu-Lian Wang, Ye-Xiong Li, Li-Na Zhao, Jian-Qiang Tang, Zheng Jiang, Ying-Gang Chen, Hai-Tao Zhou, Chen Hu, and **Jing Jin**

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Cancer Hospital Chinese Academy of Medical Sciences



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CANCER HOSPITAL CHINESE ACADEMY OF MEDICAL SCIENCES, SHENZHEN CENTER

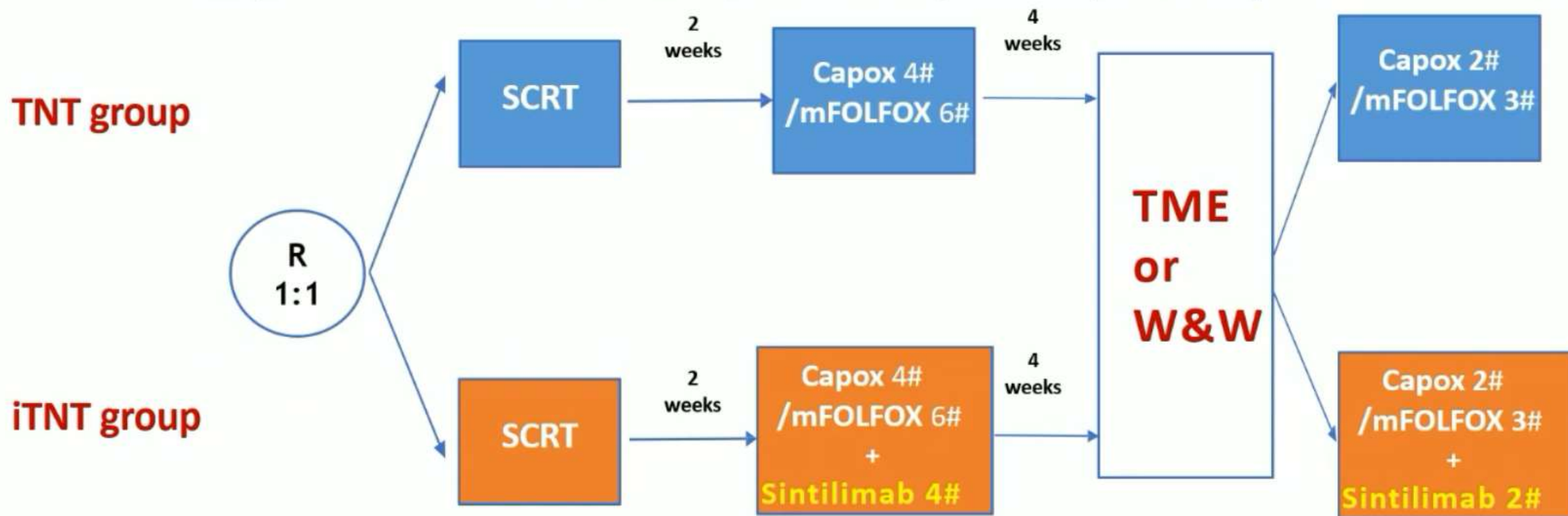
Presented by : Jing Jin, email: jinjing@esco.org.cn



Jing Jin
China

Study design

- Multi-center, randomized controlled, seamless phase II/III study (NCT05484024)



W&W

a watch-and-wait (W&W) strategy was implemented if patients achieved cCR

SCRT

Pelvic radiotherapy, IMRT/VMAT 5Gy*5f

Sintilimab

Sintilimab 200mg, d1
Q21d*4

Capox

Capecitabine 2000 mg/m², d1-14
Oxaliplatin 130mg/m², d1
Q21d*4

**mFOLFOX
(selectable)**

Oxaliplatin 100 mg/m² ivgtt(2h) d1
Calcium folinate 400 mg/m² ivgtt (2h) d1
Fluorouracil 400 mg/m² iv d1, 2400 mg/m² ivgtt(46h) d1
Q14d*6

Key eligibility criteria

- Patients aged from 18 to 75 years
- ECOG 0-1
- Rectal adenocarcinoma
- pMMR/MSS
- MRI-staged II-III: cT3-4N0 or cT2-4N+, M0
- ≤10cm from the anal verge

Endpoints

■ Primary endpoints:

Phase II—complete response rate (CR, cCR+pCR)

Phase III—3-year disease free survival (DFS)

■ Secondary endpoints:

Grade 3–5 acute adverse events

3-year local recurrence free survival

3-year overall survival (OS)

Surgical complications

Quality of life (QoL)

Patients baseline characteristics

- ◆ Between August 2022 and November 2023, 218 patients were enrolled
- ◆ The median follow-up duration was 19.6 months (January 23, 2025)

	iTNT Group (n=110)	TNT Group (n=108)
Age, years, median (range)	59 (21-74)	59.5 (32-73)
Sex		
Male	81 (73·6)	72 (66·7)
Female	29 (26·4)	36 (33·3)
ECOG score		
0	40 (36·4)	41 (38·0)
1	70 (63·6)	67 (62·0)

Tumor characteristics



	iTNT Group (n=110)	TNT Group (n=108)
Clinical T category		
T2	5 (4·5)	6 (5·6)
T3	85 (77·3)	85 (78·7)
T4	20 (18·2)	17 (15·7)
T4a	11 (10·0)	12 (11·1)
T4b	9 (8·2)	5 (4·6)
Clinical N category		
N0	8 (7·3)	6 (5·5)
N1	33 (30·0)	30 (27·8)
N2	69 (62·7)	72 (66·7)
Clinical stage		
II	8 (7·3)	6 (5·6)
III	102 (92·7)	102 (94·4)

	iTNT Group (n=110)	TNT Group (n=108)
Distance to anal verge, cm		
≤ 5	83 (75·5)	81 (75·0)
5.1-10	27 (24·5)	27 (25·0)
MRF		
Positive	58 (52·7)	57 (52·8)
Negative	52 (47·3)	51 (47·2)
EMVI		
Positive	53 (48·2)	44 (40·7)
Negative	57 (51·8)	64 (59·3)
Risk group*		
Low-risk	18 (16·4)	19 (17·6)
High-risk	92 (83·6)	89 (82·4)

* Patients meeting any of the following criteria were defined as high-risk: cT4a/b, cN2, EMVI+, MRF+

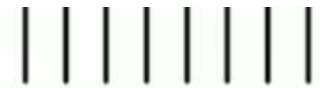
Treatment compliance

	iTNT Group (n=110)	TNT Group (n=108)	<i>P</i>
Compliance with neoadjuvant therapy			
4 cycles of chemotherapy	97 (88.2)	101 (93.5)	0.269
Full-dose of chemotherapy	85 (77.3)	90 (83.3)	0.261
Sintilimab			
≥2 cycles	109 (99.1)	-	
≥3 cycles	107 (97.3)	-	
≥4 cycles	97 (88.2)	-	
Compliance with adjuvant therapy			
full-cycle of chemotherapy	33 (45.8)	46 (56.1)	0.204
2 cycles of sintilimab	19 (26.4)	-	-

Toxicities

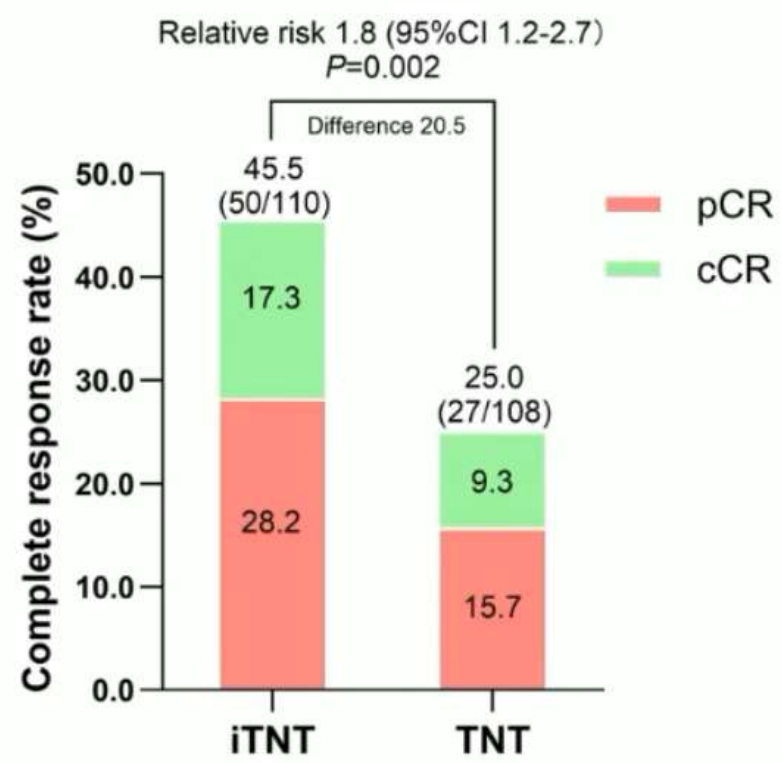


iTNT Group			TNT Group			
Acute toxicity during SCRT						
Total No. of evaluable patients	110			108		
Overall grade 3 to 4 adverse events during SCRT	14 (12.7)			8 (7.4)		
Acute toxicity during chemotherapy ± PD-1 inhibitor						
Total No. of evaluable patients	109			105		
Overall grade 3 to 4 adverse events during chemotherapy ± PD-1 inhibitor*	30 (27.5)			14 (13.3)		
Overall grade 3 to 4 adverse events during neoadjuvant therapy*	38 (34.5)			21 (19.4)		
Postoperative complications						
	Grades 1-2	Grade 3	Grade 4	Grades 1-2	Grade 3	Grade 4
Total No. of evaluable patients	72			82		
Overall postoperative complications	18 (25.0)	6 (8.3)	0 (0)	16 (19.5)	2 (2.4)	0 (0)

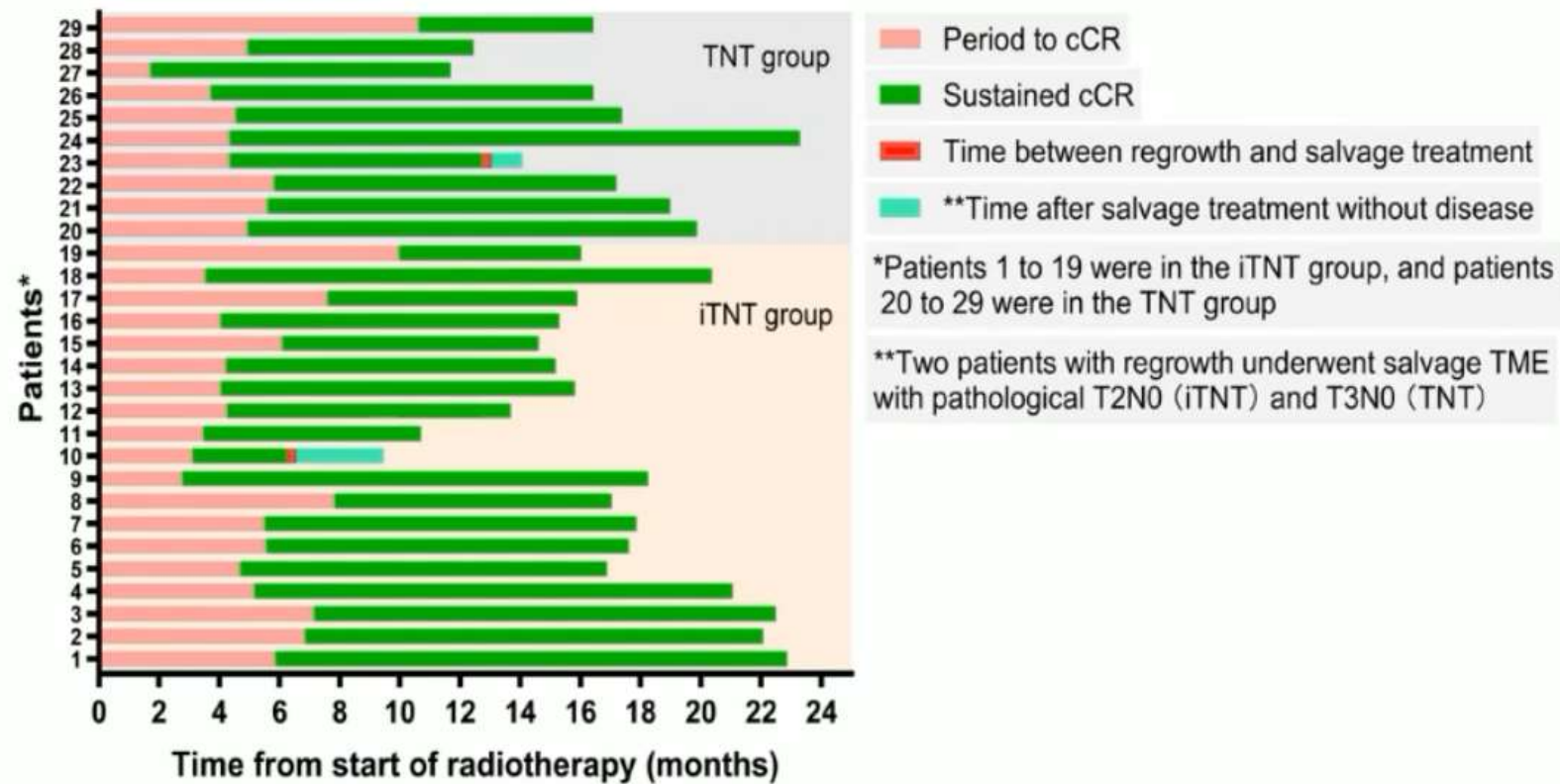


CR rate

- The iTNT regimen significantly improved CR rate: 45.5% versus 25.0% (difference 20.5%, 95%CI 12.4-28.6; P=0.002)



The primary endpoint (CR rate)



Swimmer plot of twenty-nine patients who achieved cCR, and adopted W&W strategy

Univariate and multivariate analyses



Univariate Analyses			Multivariate Analyses		
	CR rate (%)	OR (95% CI)	P	OR (95% CI)	P
Group			0.002		0.000
iTNT (n=110)	45.5	2.500 (1.407 to 4.443)		4.194 (2.100 to 8.376)	
TNT (n=108)	25.0	Referent		Referent	
Age group, years			0.953		0.123
<60 (n=111)	35.1	0.984 (0.564 to 1.714)		0.588 (0.300 to 1.155)	
≥60 (n=107)	35.5	Referent		Referent	
Sex			0.120		0.102
Male (153)	32.0	0.623 (0.343 to 1.131)		0.552 (0.270 to 1.125)	
Female (n=65)	43.1	Referent		Referent	
ECOG score			0.115		0.058
0 (n=81)	42.0	1.581 (0.894 to 2.796)		1.971 (0.978 to 3.973)	
1 (n=137)	31.4	Referent		Referent	
Clinical T category			< 0.001		0.000
T2-3 (n=181)	41.4	12.382 (2.889 to 53.068)		19.328 (4.013 to 93.098)	
T4 (n=37)	5.4	Referent		Referent	
Clinical N category			0.544		0.721
N0 (n=14)	42.9	1.405 (0.469 to 4.208)		1.290 (0.318 to 5.233)	
N1-2 (n=204)	34.8	Referent		Referent	

Univariate Analyses			Multivariate Analyses		
	CR rate (%)	OR (95% CI)	P	OR (95% CI)	P
Distance to anal verge, cm			0.338		0.094
≤ 5 (n=164)	33.5	0.734 (0.390 to 1.381)		0.514 (0.236 to 1.121)	
5.1-10 (n=54)	40.7	Referent		Referent	
MRF			0.112		0.266
Positive (n=115)	30.4	0.635 (0.363 to 1.111)		1.571 (0.709 to 3.484)	
Negative (n=103)	40.8	Referent		Referent	
EMVI			0.002		0.024
Positive (n=97)	23.7	Referent		Referent	
Negative (n=121)	44.6	2.593 (1.438 to 4.675)		2.414 (1.122 to 5.190)	
CEA, ng/ml			0.003		0.003
≤5 (n=123)	43.9	Referent		Referent	
>5 (n=95)	24.2	0.408 (0.226 to 0.736)		0.347 (0.171 to 0.704)	
Risk degree*			0.048		0.539
Low-risk (n=37)	48.6	Referent		Referent	
High-risk (n=181)	31.5	0.485 (0.237 to 0.994)		0.728 (0.264 to 2.006)	

STELLAR2: Conclusion

- Pour le traitement par LARC pMMR/MSS, l'association SCRT suivie de quatre cycles de chimiothérapie plus un inhibiteur de PD-1 (sintilimab) a été bien tolérée, sans événements indésirables graves inattendus.
- Le taux de réponse complète a été significativement amélioré dans la stratégie iTNT (45,5 %).
- L'étude de phase III approche de la fin du recrutement et les résultats finaux de la survie sans maladie sont attendus

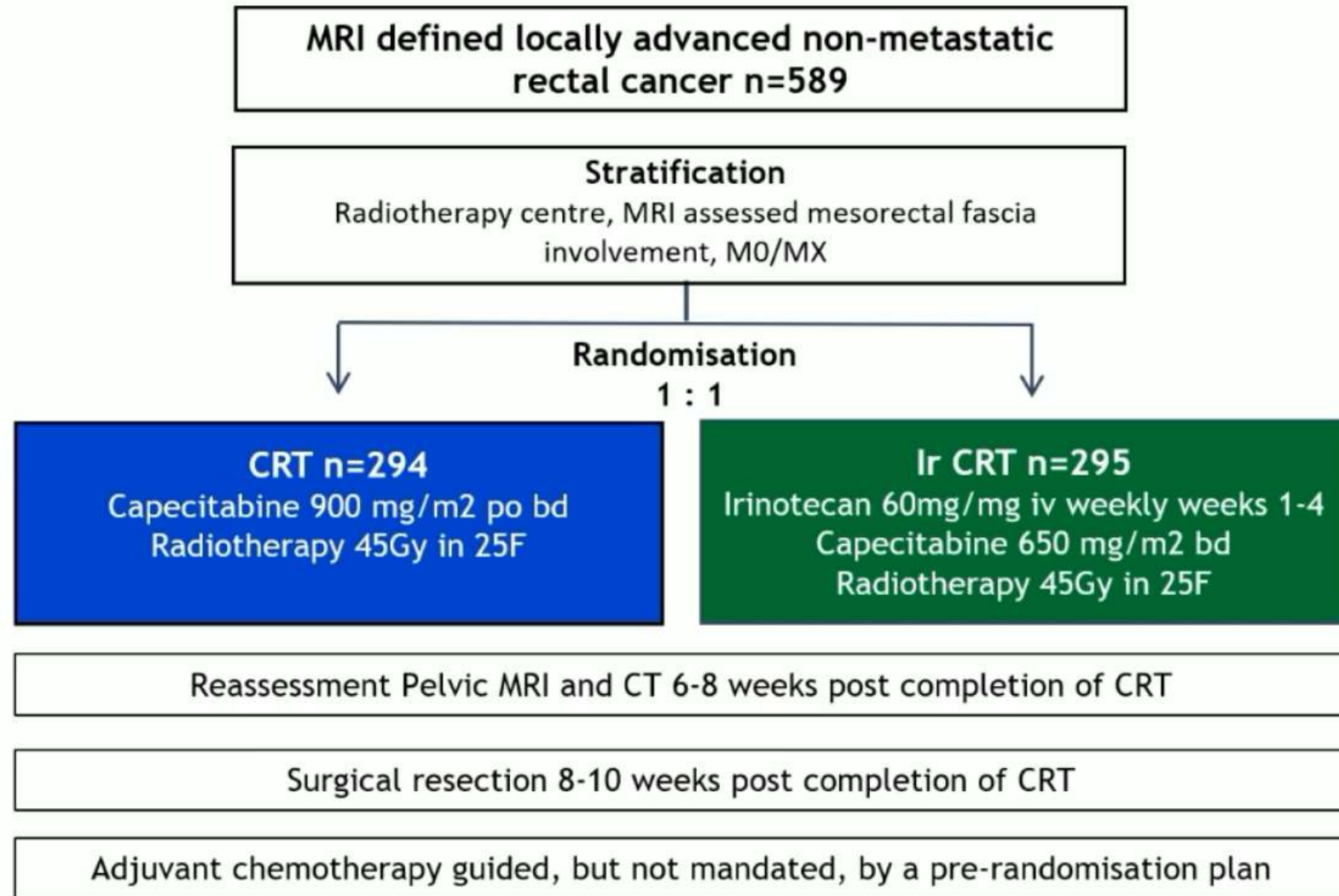
Background

- The addition of neoadjuvant radiotherapy prior to surgical resection reduces local recurrence in rectal cancer
- Randomised phase III trials demonstrate that concurrent chemotherapy (CRT) is superior to long course radiotherapy alone, and is more effective and less toxic, when given pre-operatively
- Phase II, mainly single arm, clinical trials using doublet concurrent chemotherapy (oxaliplatin or irinotecan) with radiotherapy report higher pathological complete response rates (pCR) than using fluoropyrimidine CRT
- The phase II UK RICE study using concurrent irinotecan, capecitabine CRT reported 22% pCR, 64% three-year disease free and 88% overall survival with acceptable toxicity
- We planned a randomised phase III trial to evaluate the benefit of adding concurrent irinotecan and capecitabine to radiotherapy in MRI-defined locally advanced rectal cancer considered at high risk of loco-regional failure and distant relapse



David Sebag-Montefiore
United Kingdom

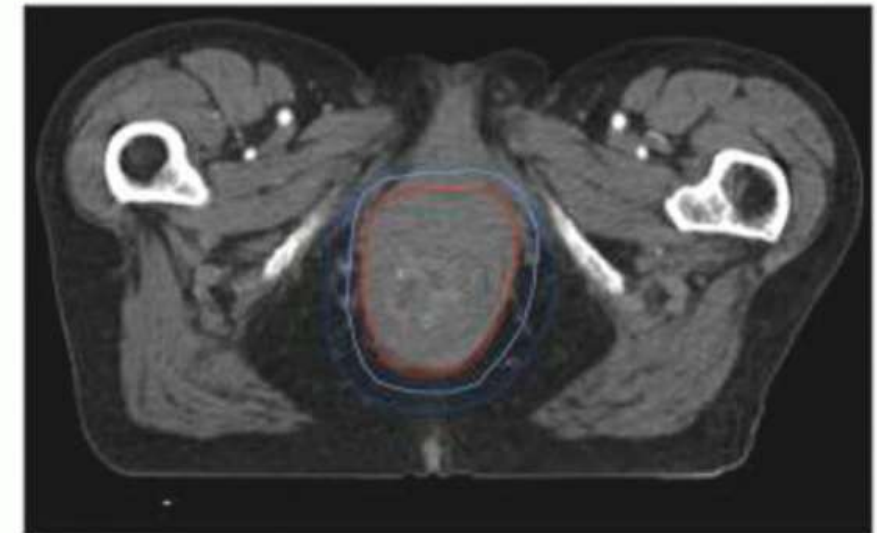
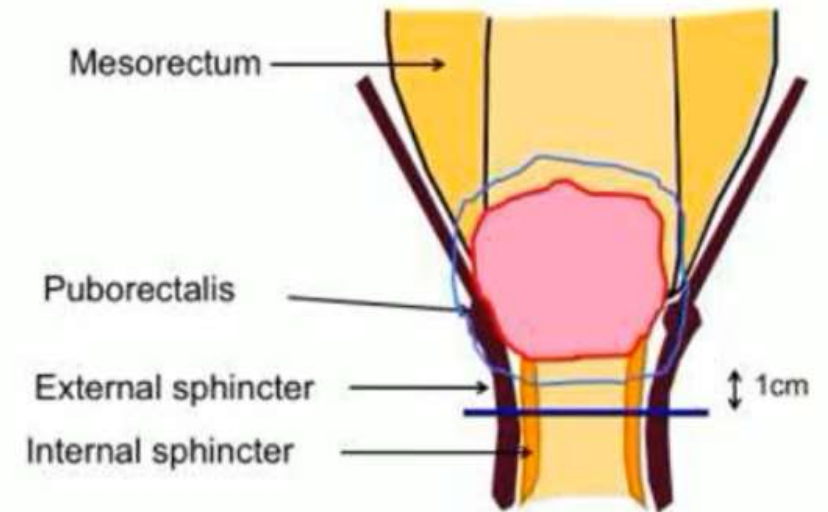
ARISTOLE Study Design



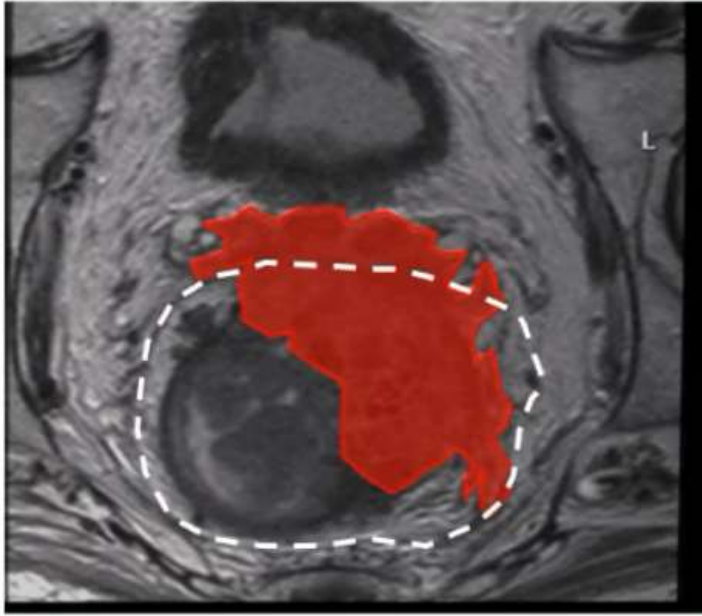
Primary end point: 3-year Disease Free Survival

Trial conduct

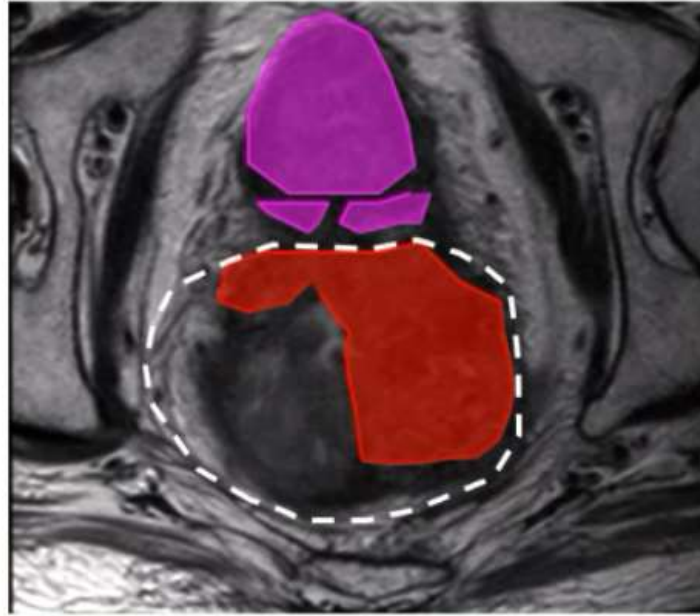
- 75 UK sites - radiotherapy and surgery centres
- Pre-trial
 - Eight regional radiotherapy workshops
 - Detailed RT protocol
 - Real-time review first patient and review of 10% radiotherapy outlines and plans
- Recruitment
 - Oct 2011- July 2018
- Median follow-up
 - 76.4 months (95% CI 70.8-81.2)



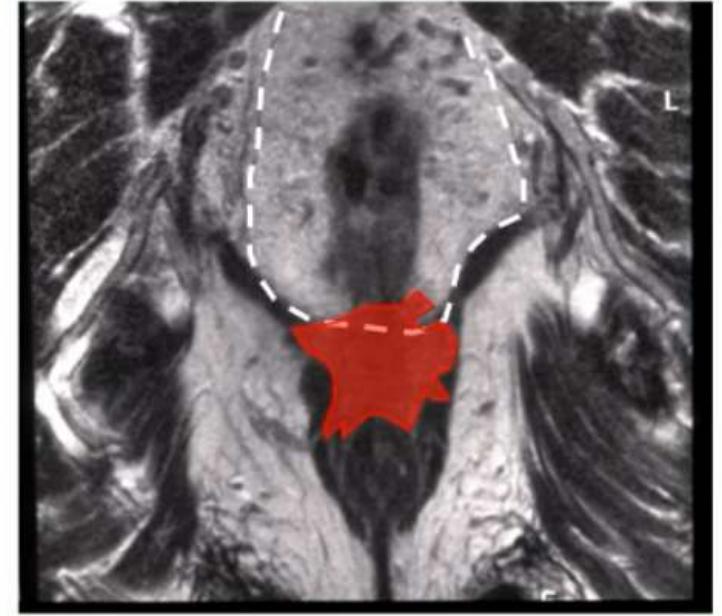
MRI defined locally advanced rectal cancer



Mesorectal fascia (MRF) involved
or breached



MRF threatened:
tumour $\leq 1\text{mm}$ from MRF



Low tumours $\leq 1\text{mm}$ from the
levator on two imaging planes; or
full thickness of muscularis propria
at the level of puborectalis or below;
or tumour involving the inter-
sphincteric plane or external anal
sphincter

Patients with involved pelvic side wall nodes were only eligible if the primary tumour
assessment met the above inclusion criteria

Patient Characteristics

	Ir CRT n=280*		CRT n=284*	
Age, years				
Median age (range)	60.5 (24.0-82.8)		60.9 (28.5-77.7)	
Sex				
Male	173	61.8	197	69.4
Female	107	38.2	87	30.6%
ECOG				
Fully active	217	77.5%	226	79.6%
Ambulatory (work able)	63	22.5%	58	20.4%
mrCRM				
Involved (0mm)	139	49.6%	138	48.6%
Threatened (</=1mm)	108	38.6%	109	38.4%
T stage (MRI defined)				
T2	17	6.1%	16	5.6%
T3	212	75.7%	223	78.5%
T4	45	16.1%	44	15.5%
N stage (MRI defined)				
N0	50	17.9%	81	28.5%
N1	141	50.4%	119	41.9%
N2	82	29.3%	83	29.2%
N3	1	0.4%	0	0%
Pre-treatment stoma				
No	174	62.1%	194	68.3%
Yes	39	13.9%	22	7.7%

Chemoradiotherapy compliance

Radiotherapy compliance

	Ir CRT n=276		CRT n=283	
Radiotherapy dose delivered				
RT as scheduled (45Gy/25fractions)	208	75.4%	251	88.7%
RT delivered >45Gy	15	5.4%	3	1.1%
Proportion of intended RT received				
Received ≥90% intended RT	260	94.2%	279	98.6%
Received <90% intended RT	16	5.8%	4	1.4%

Chemotherapy compliance

	Ir CRT n=276		CRT n=283	
Days on capecitabine				
Median (range)	35	4-58	35	7-47
Total % capecitabine dose delivered				
Median (range)	98	14-112	100	20-106
Capecitabine dose delivered				
Capecitabine as scheduled (100%)	129	46.7%	196	69.3%
Capecitabine delivered >100%	6	2.2%	7	2.5%
Received ≥90% intended capecitabine dose	187	67.8%	253	89.4%
Received <90% intended capecitabine dose	89	32.2%	30	10.6%
Irinotecan Compliance				
Received ≥90% intended irinotecan dose	205	74.3%		
Received <90% intended irinotecan dose	71	25.7%		

Worst Grade 3-5 acute adverse events

o	Ir CRT n=280*		CRT n=284*	
Blood disorders				
Anaemia	8	2.9%	4	1.4%
Lymphocytes decreased	181	65.6%	100	35.3%
Neutrophils decreased	27	9.8%	3	1.1%
Febrile neutropaenia	3	1.1%	1	0.4%
Platelets decreased	1	0.4%	1	0.4%
Infections and infestations				
Any infections	29	10.5%	27	9.5%
Gastrointestinal disorders				
Diarrhoea	38	13.8%	10	3.5%
Abdominal pain	13	4.7%	2	0.7%
Proctitis	8	2.9%	7	2.5%
General disorders				
Fatigue	17	6.2%	8	2.8%
Renal and urinary disorders				
Any renal and urinary disorders	5	1.8%	4	1.4%
Vascular disorders				
Any vascular disorders	13	4.7%	8	2.8%
Metabolism and nutrition				
Other metabolism and nutrition disorders	34	12.3%	9	3.2%
Dehydration	10	3.6%	1	0.4%
Anorexia	6	2.2%	2	0.7%

* Eligible patients

5 patients had a Gd 5 AE - 3 IrCRT and 2 CRT

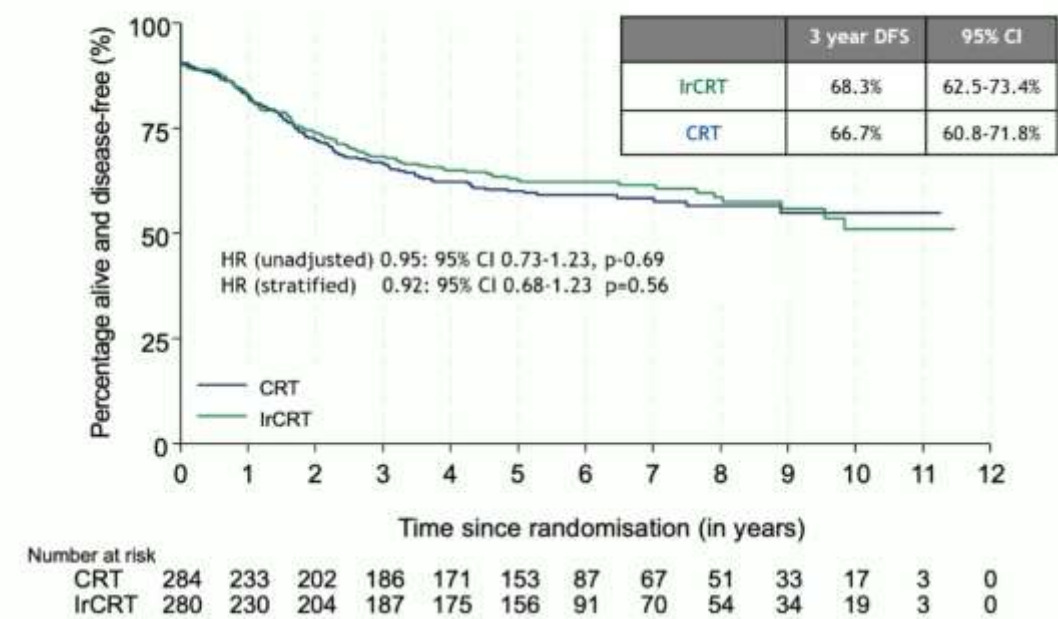
Radiological, pathological and surgical outcomes

	Ir CRT n=280*		CRT n=284*	
MRI Tumour Regression Grade (mrTRG)				
TRG1	38	13.6%	39	13.7%
TRG2	90	32.1%	86	30.3%
TRG3	63	22.5%	68	23.9%
TRG4	49	17.5%	51	18.0%
TRG5	19	6.8%	24	8.5%
Time from CRT to surgical resection				
Median Weeks (Range)	10.6	(7.0 to 33.3)	10.6	(7.4 to 68.4)
Pathological TNM Stage	n=238^		n=243^	
Stage 0 (ypT0N0) - pCR	46	19.3%	42	17.3%
Stage I	63	27.3%	49	20.2%
Stage IIA	46	19.9%	64	26.3%
Stage IIB/C	8	3.5%	7	2.9%
Stage IIIA	12	5.2%	16	6.6%
Stage IIIB	55	23.8%	60	24.7%
Stage IIIB	1	0.4%	1	0.4%
Pathological Resection Status	1			
R0 (>1mm)	207	87.0%	212	87.2%
R1 (0mm)	13	5.5%	13	5.3%
R1 (<+1mm)	10	4.2%	11	4.5%
R2	1	0.4%	2	0.8%

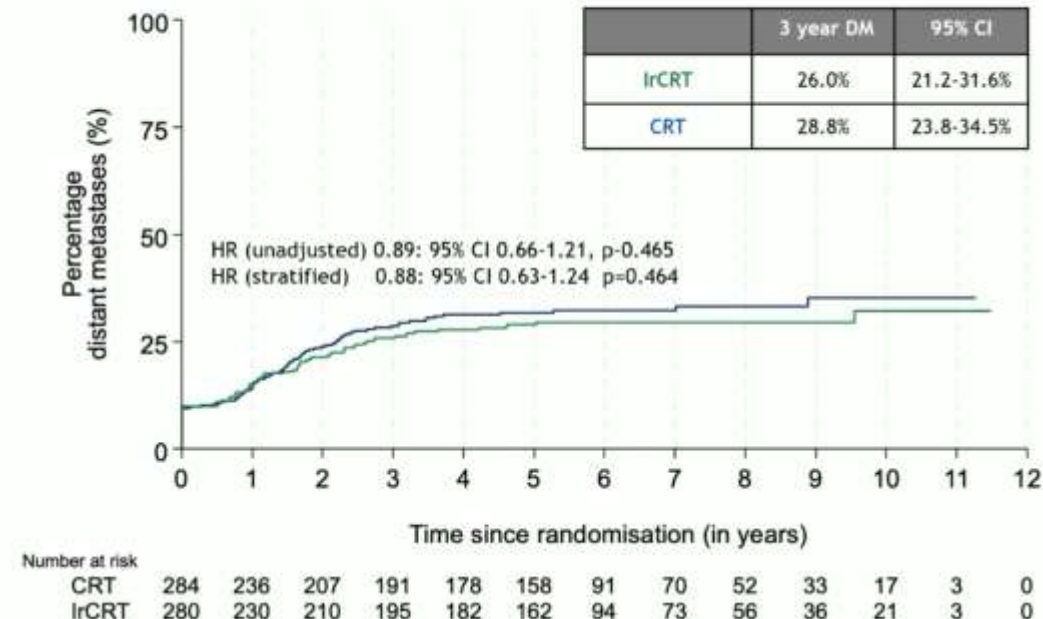
* Eligible patients
^ Patients who had surgery

>90% of the patients underwent surgical resection: APER 134 (55.1%) CRT and 130 (54.6%) IrCRT
or anterior resection 94 (38.7%) CRT and 100 (42.0%) IrCRT

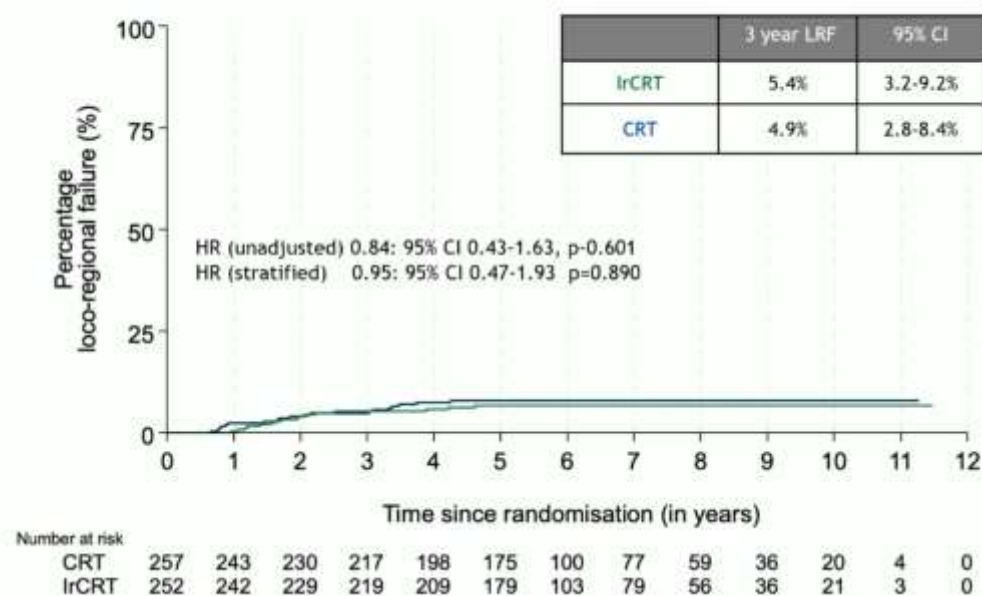
Primary end point: Disease-free survival



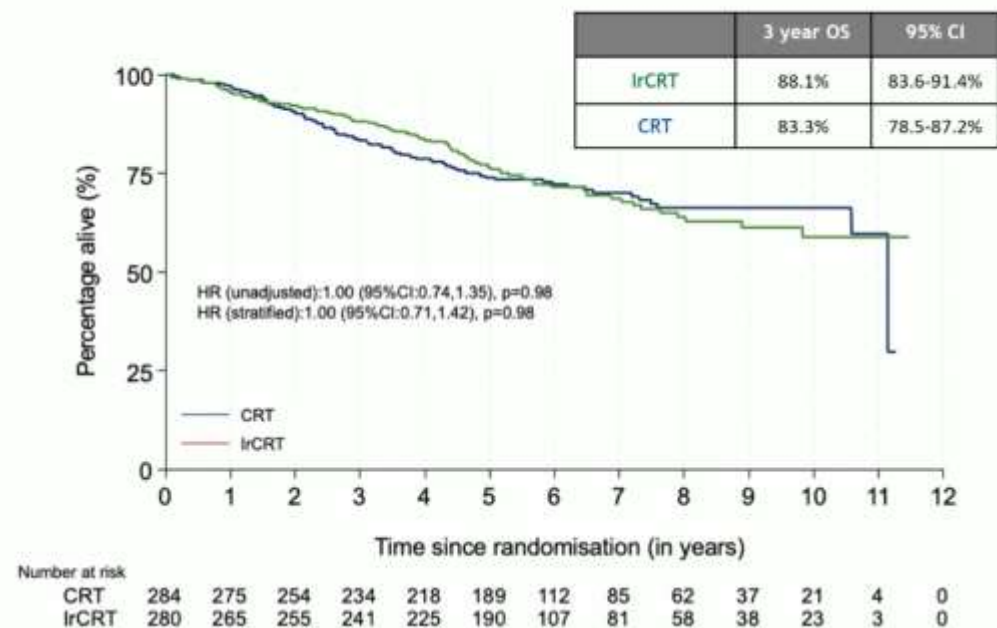
Distant Metastases



Loco-regional failure



Overall Survival



ARISTOTLE: CONCLUSION

- Il n'existe aucune différence en termes de pCR ou de DFS lorsque l'irinotécan concomitant est ajouté à la CRT par capécitabine en préopératoire.
- L'ajout d'irinotécan concomitant a entraîné un taux plus élevé de toxicité aiguë et une réduction de l'observance de la radiothérapie.

Cihan Gani
University Hospital Tübingen

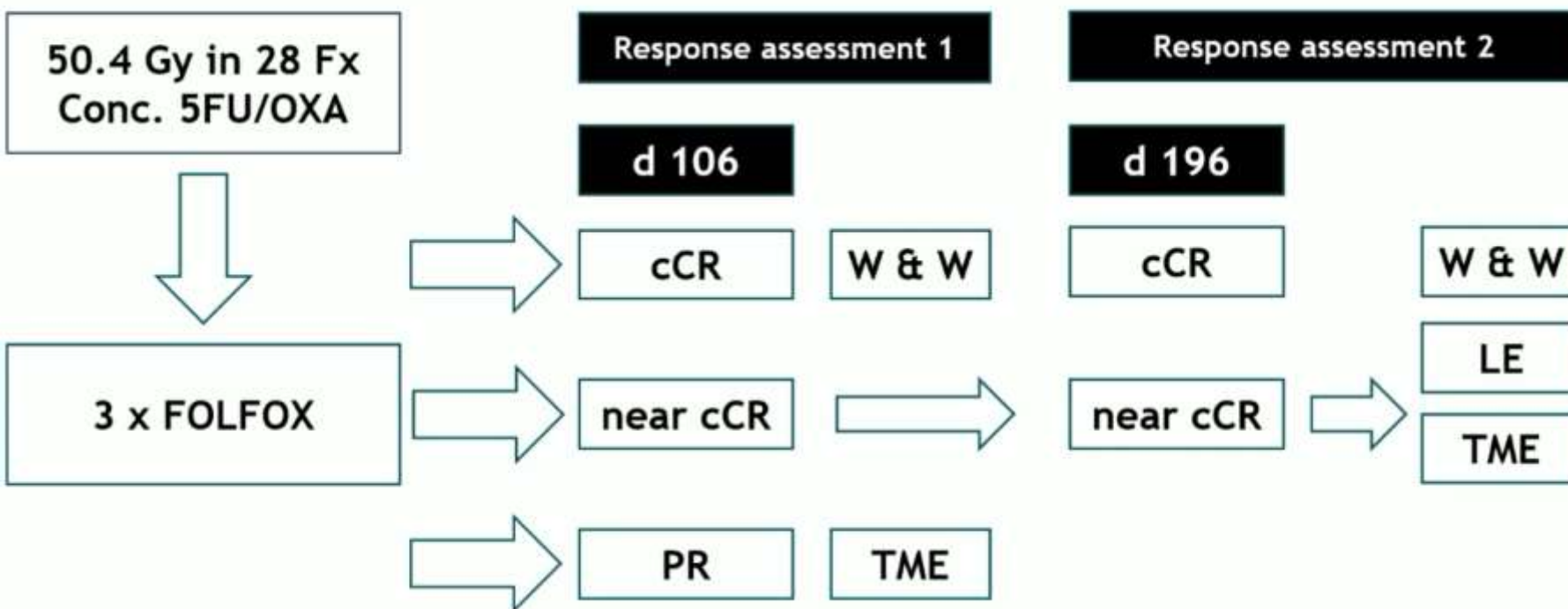
**Organ preservation and quality of life after
TNT for locally advanced rectal cancer:
A study of the German Rectal Cancer Study
Group (CAO/ARO/AIO-16)**

ESTRO Vienna - May 5th 2025

Methods - Study flowchart

CAO-ARO-AIO-16

Protocol v. 1.0 03.04.2017



Examples for a clinical complete response:



Examples for a near clinical complete response:



Examples for residual tumor:



Methods

- **Single arm multicenter phase II trial** conducted at 4 centers in Germany (Tübingen, Frankfurt, Würzburg, Erlangen).
- **Primary endpoint:** clinical complete response rate on d106/196.
Simon's optimal 2 stage design
Goal: cCR rate 20% - 89 patients needed.
- Patients with **cT1-cT2 cN+** or **any cT3 tumor** of the mid and distal rectum were eligible (T4 excluded!)

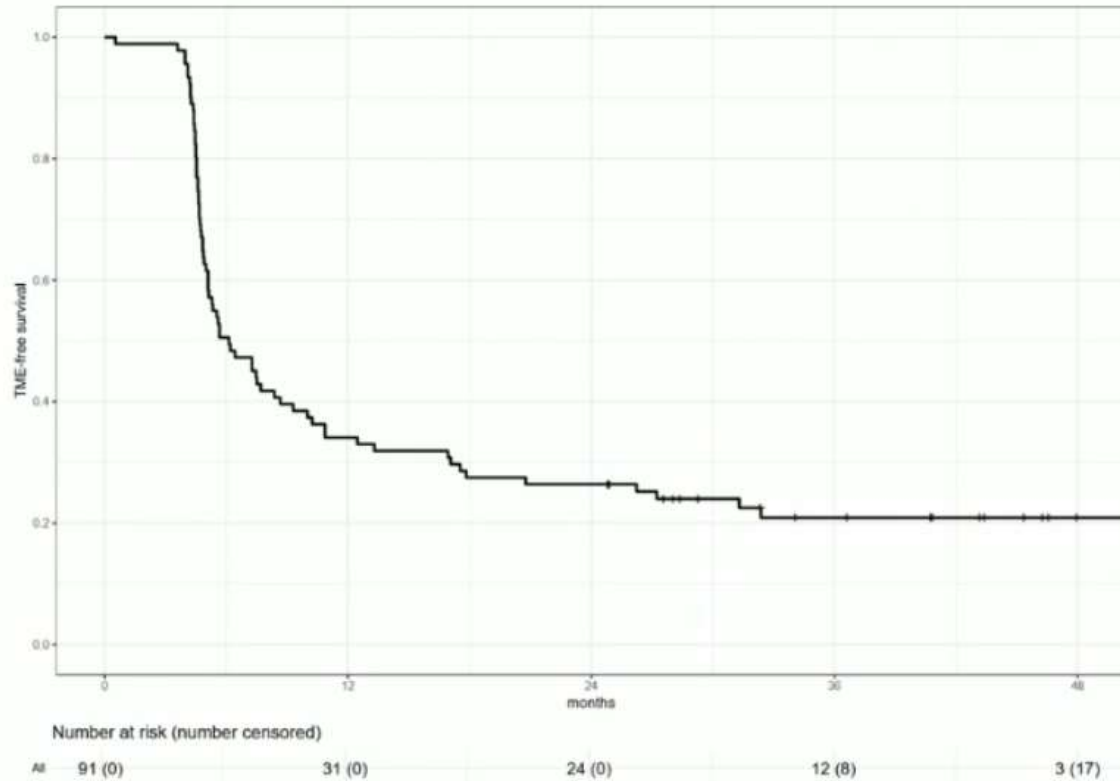
Results - Cohort

- 91 patients recruited between 2018 and 2020

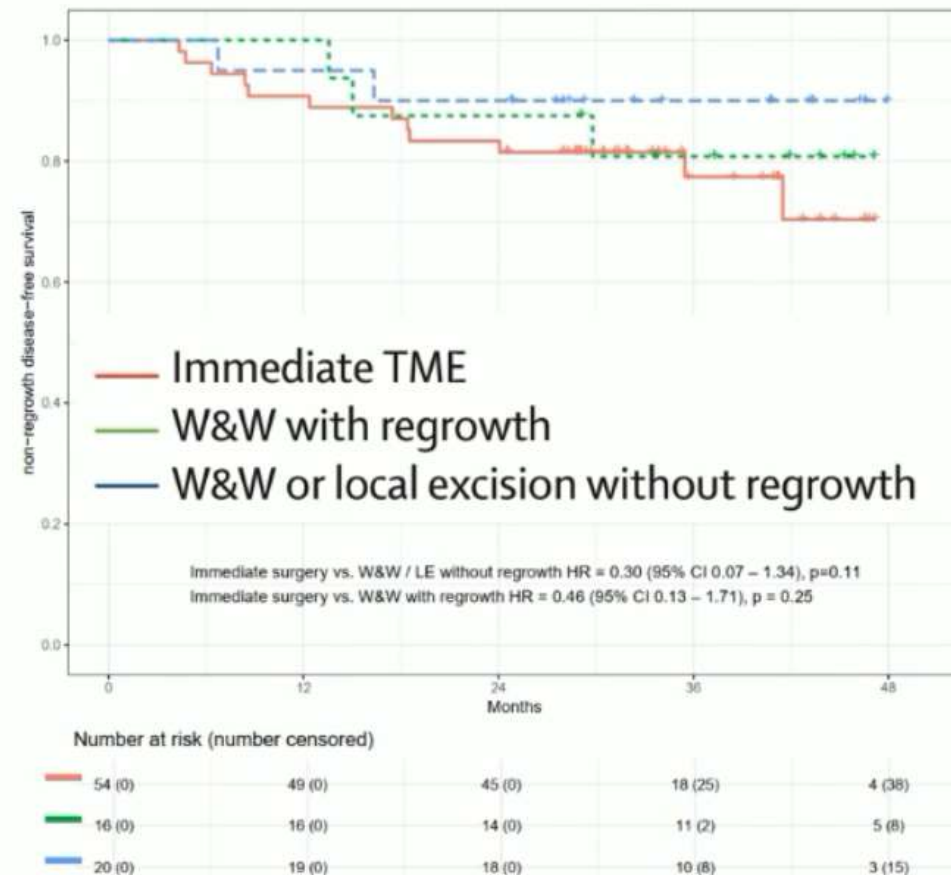
		n	%
T-Stage	cTx	1	1%
	cT2	5	5%
	cT3a	28	31%
	cT3b	27	30%
	cT3c	24	26%
	cT3d	6	7%
MRF-status	MRF+	51	56%
	MRF-	38	42%
EMVI	EMVI negative	62	68%
	EMVI (minor vessels)	23	25%
	EMVI (large vessels)	2	2%
N-Stage	cN0	12	13%
	cN1	34	37%
	cN2	44	48%
	cNx	1	1%

Results - events during follow-up (median 39 months) ^{|||||}

- During follow-up 16 / 36 patients had local regrowth (all intraluminal)
- R0 salvage surgery in all instances

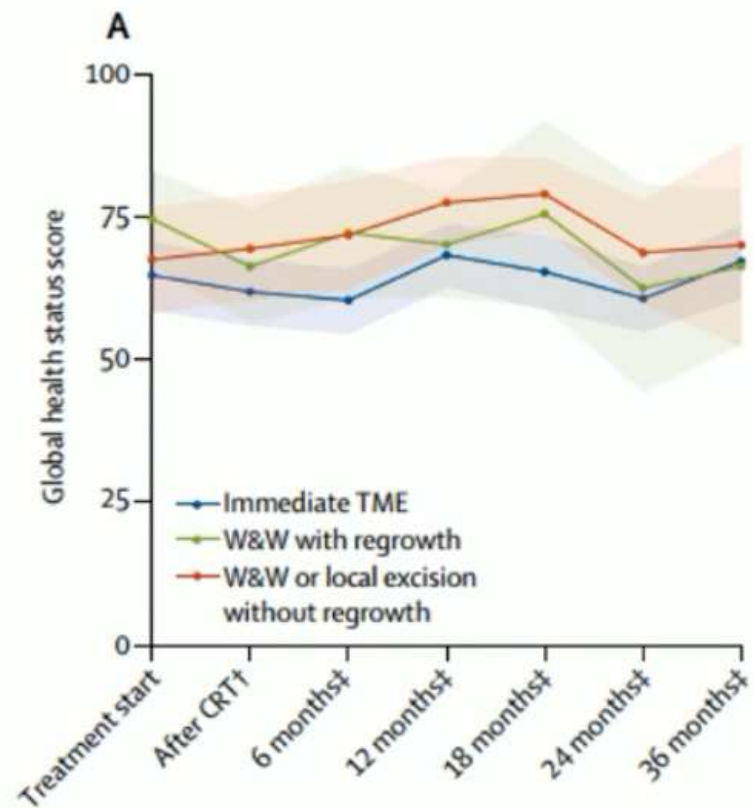


3y- TME-free survival: 21%

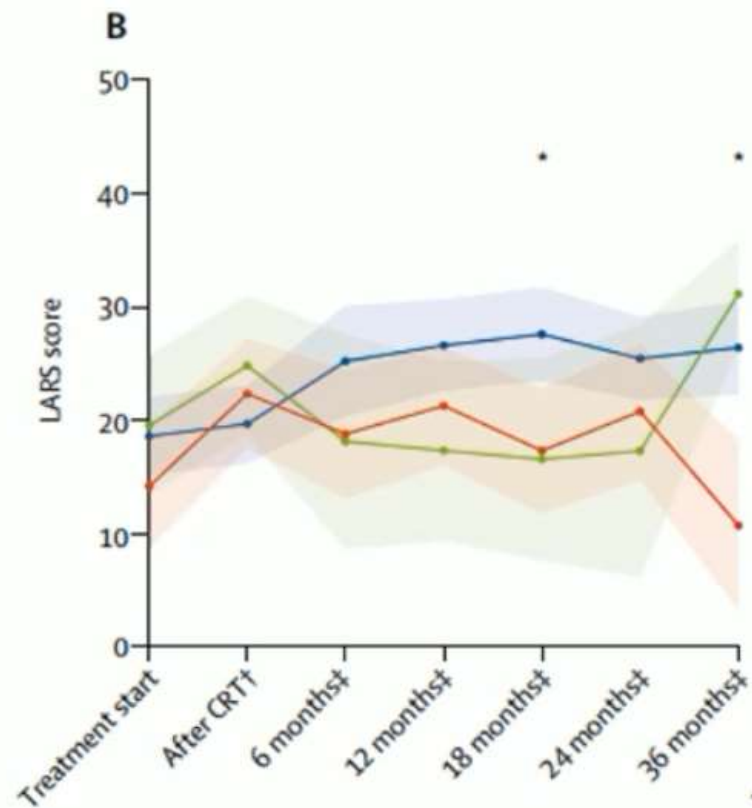


Results - Quality of life and organ function

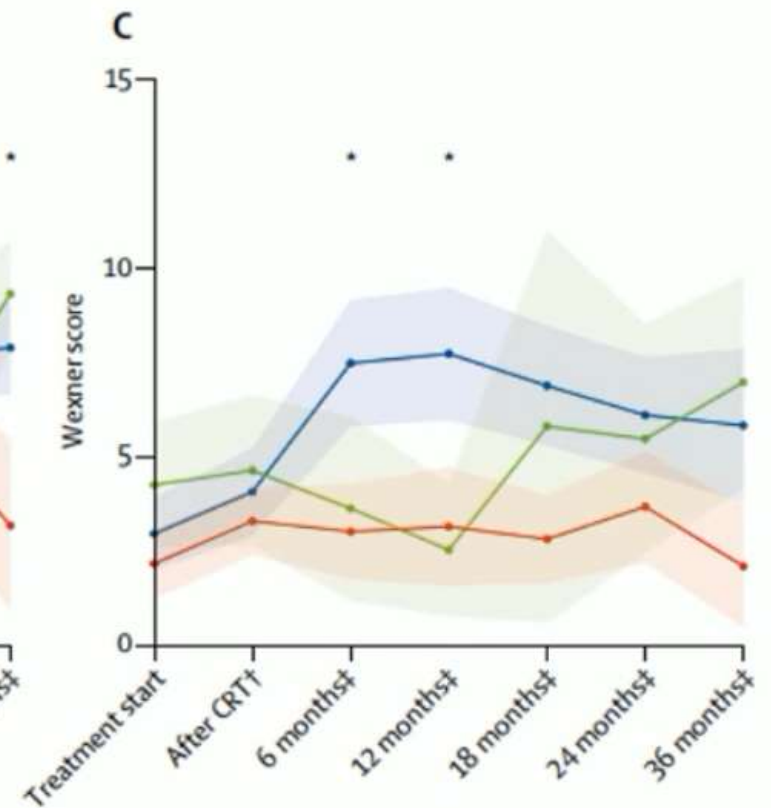
Global health



LARS score



Incontinence



Conclusion

- Les patients dont l'organe a été préservé avec succès ont une fonction rectale supérieure à celle des patients ayant subi une TME.
- La régression tumorale peut prendre du temps, comme en témoigne le fait qu'environ 2/3 des patients obtiennent une CCR après une deuxième évaluation de la réponse après une cCR initiale quasi complète.
- Les patients ayant eu une repousse locale et une chirurgie de sauvetage n'ont pas eu de résultats inférieurs en termes de survie sans maladie (DFS) par rapport aux patients ayant subi une chirurgie TME immédiate.

Conclusion - What we still don't know

- TME-free survival in CAO/ARO/AIO-16 (21%) is lower than in OPRA (54%)



Extensive biomaterial collection in CAO/ARO/AIO-16 (RNAseq, sequential MRI imaging, liquid biopsies)

Study accepted for publication in Lancet Gastroenterology Hepatology and to appear online on May 8th 2025.

Factors influencing locoregional recurrences in the RAPIDO trial



Presenter
I. Prata, MD

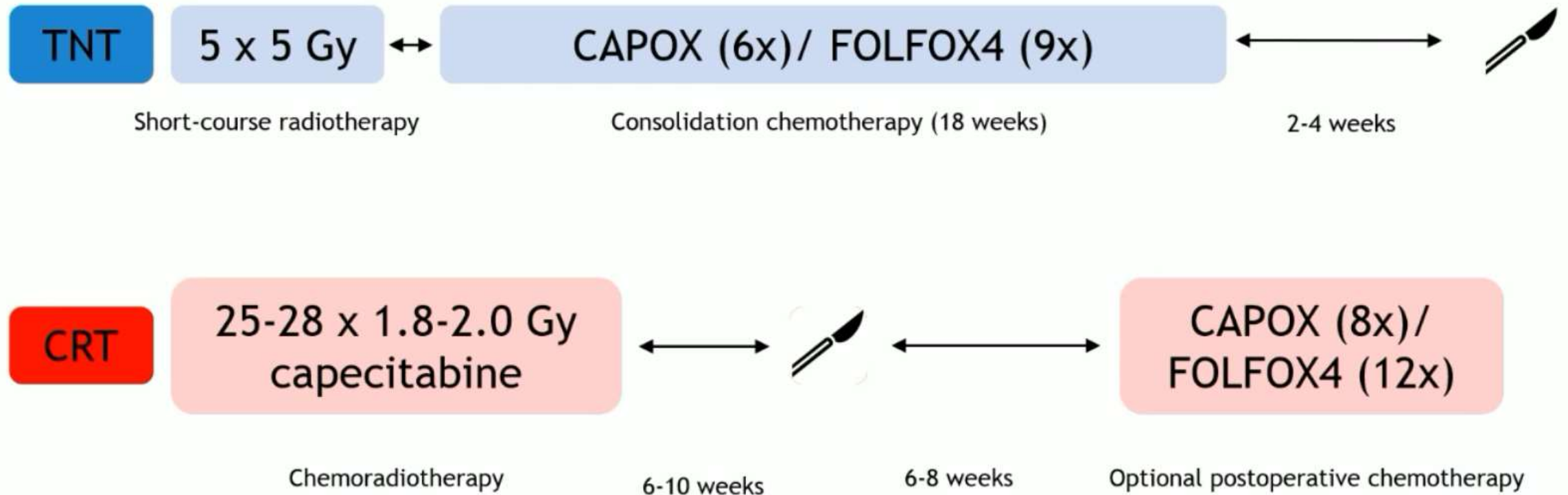
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Prof. C.A.M. Marijnen, MD, PhD
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M.D. Tanaka, MD
and collaborative investigators.

Ilaria Prata
Netherlands



RAPIDO TRIAL



5-YEAR OUTCOMES



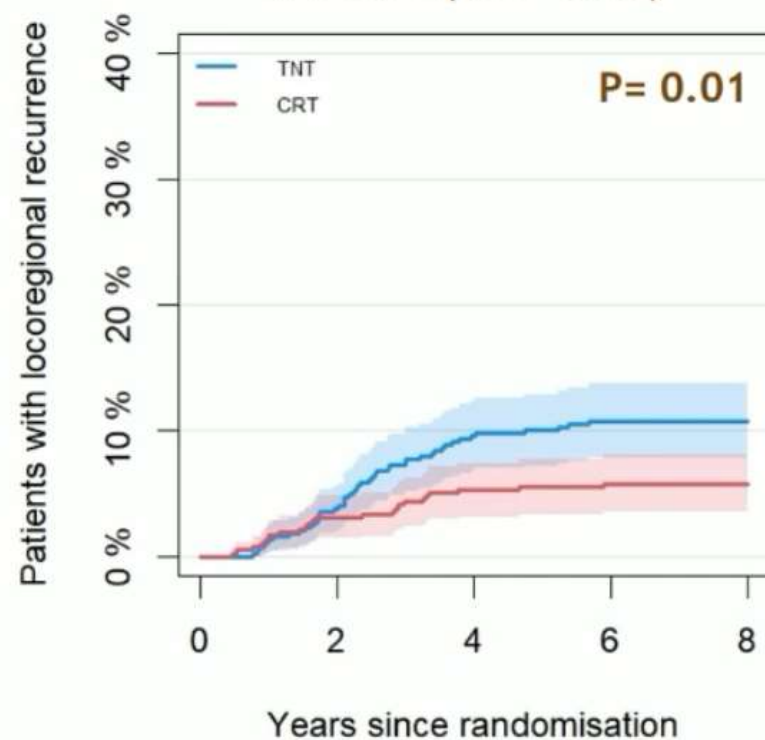
Outcome	TNT	CRT	
Disease-related Treatment Failure	28%	34%	P=0.048
Distant metastases	23%	30%	P=0.011
Pathological Complete response	28%	14%	P<0.0001

MORE LOCOREGIONAL RECURRENCES



Locoregional recurrences (LRR)

HR 1.91 (1.17-3.13)



11% TNT
6% CRT

Which factors contributed to the difference in locoregional recurrences rates between TNT and CRT?

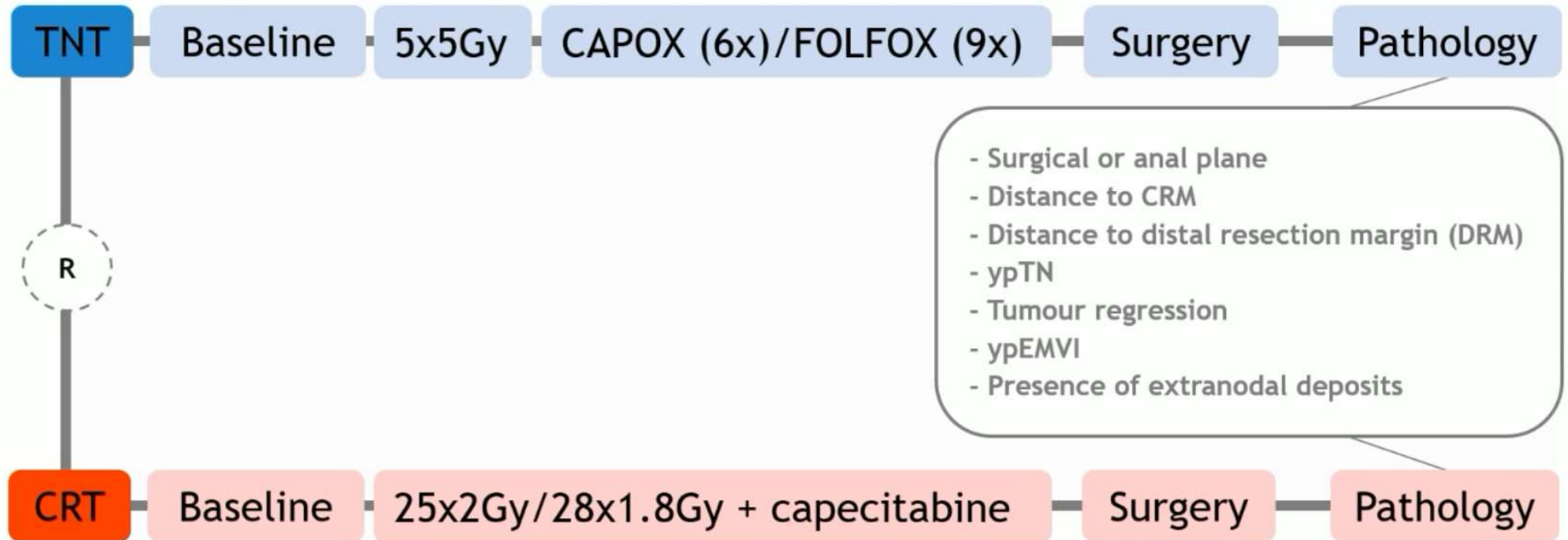
Inclusion criteria:
local R0 or R1 surgery

N=829

Number at risk

TNT	430	392	350	278	189
CRT	419	391	348	282	153

EVALUATED FACTORS



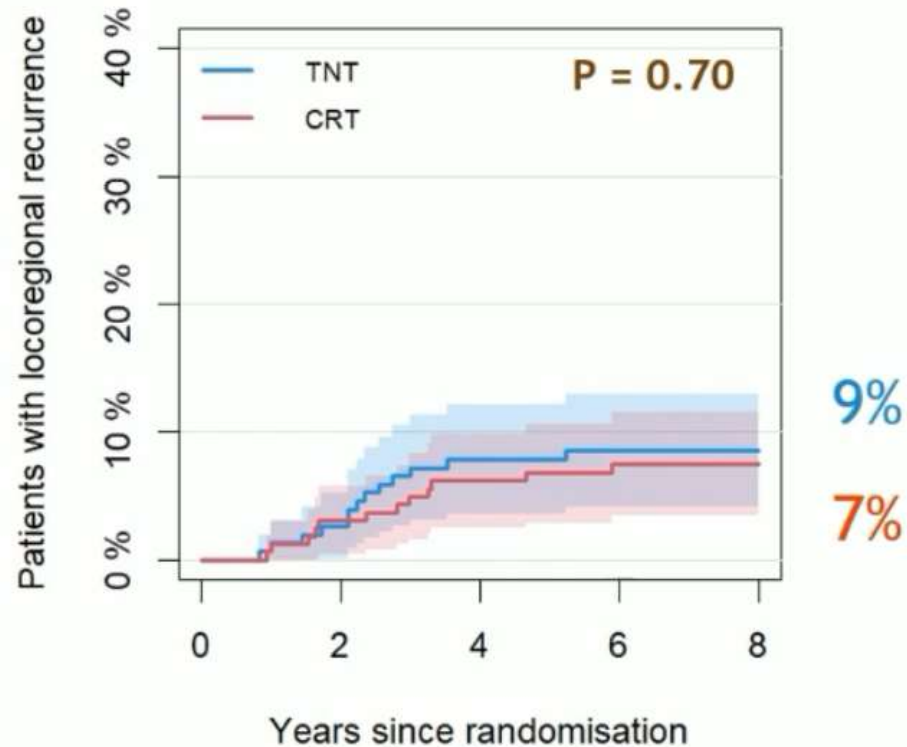
DIFFERENCE AFTER SPHINCTER PRESERVATION



Abdominoperineal resection

N = 316

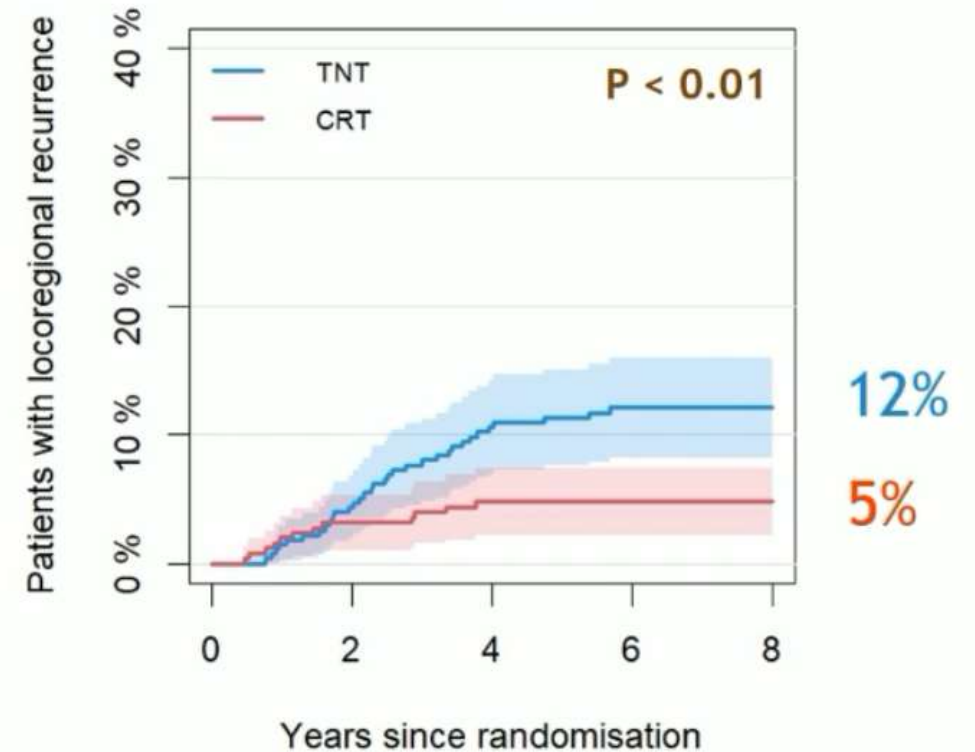
HR 1.17 (0.53-2.56)



Sphincter preserving surgery

N = 528

HR 2.60 (1.34-5.04)



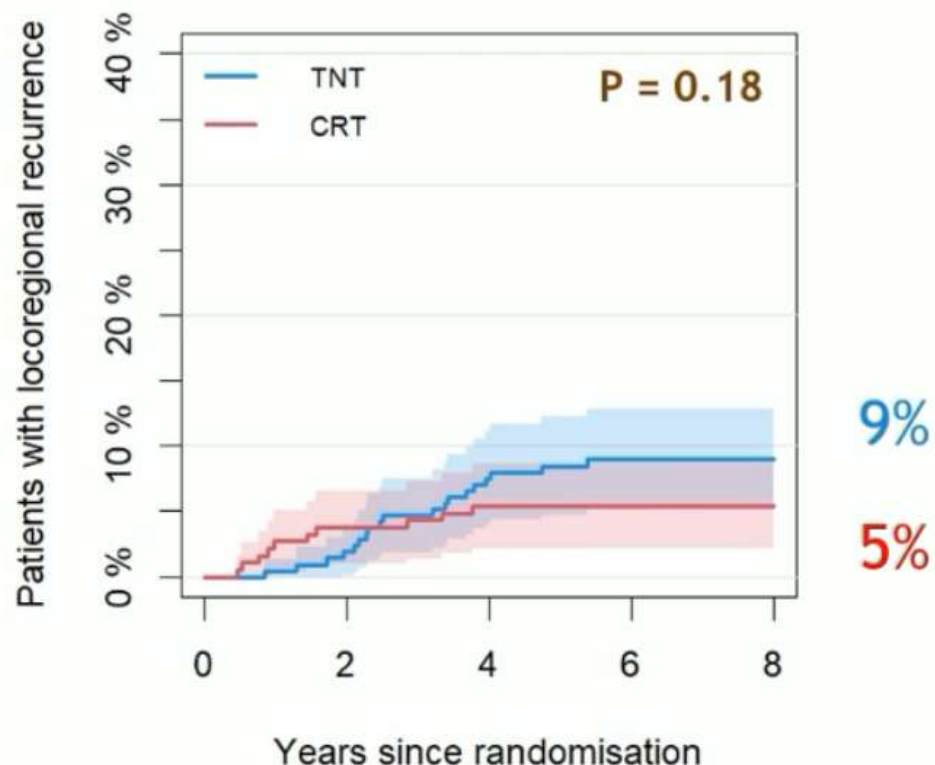
DIFFERENCE WITH DISTAL MARGIN ≤ 10 MM



DRM > 10 mm or pCR

N = 400

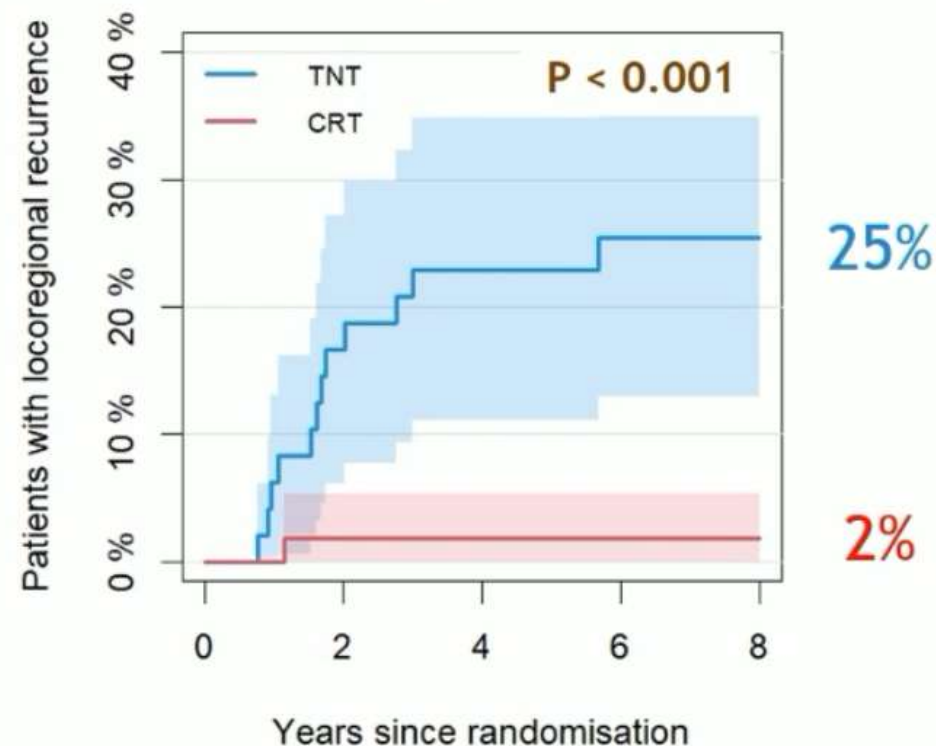
HR 1.67 (0.78-3.59)



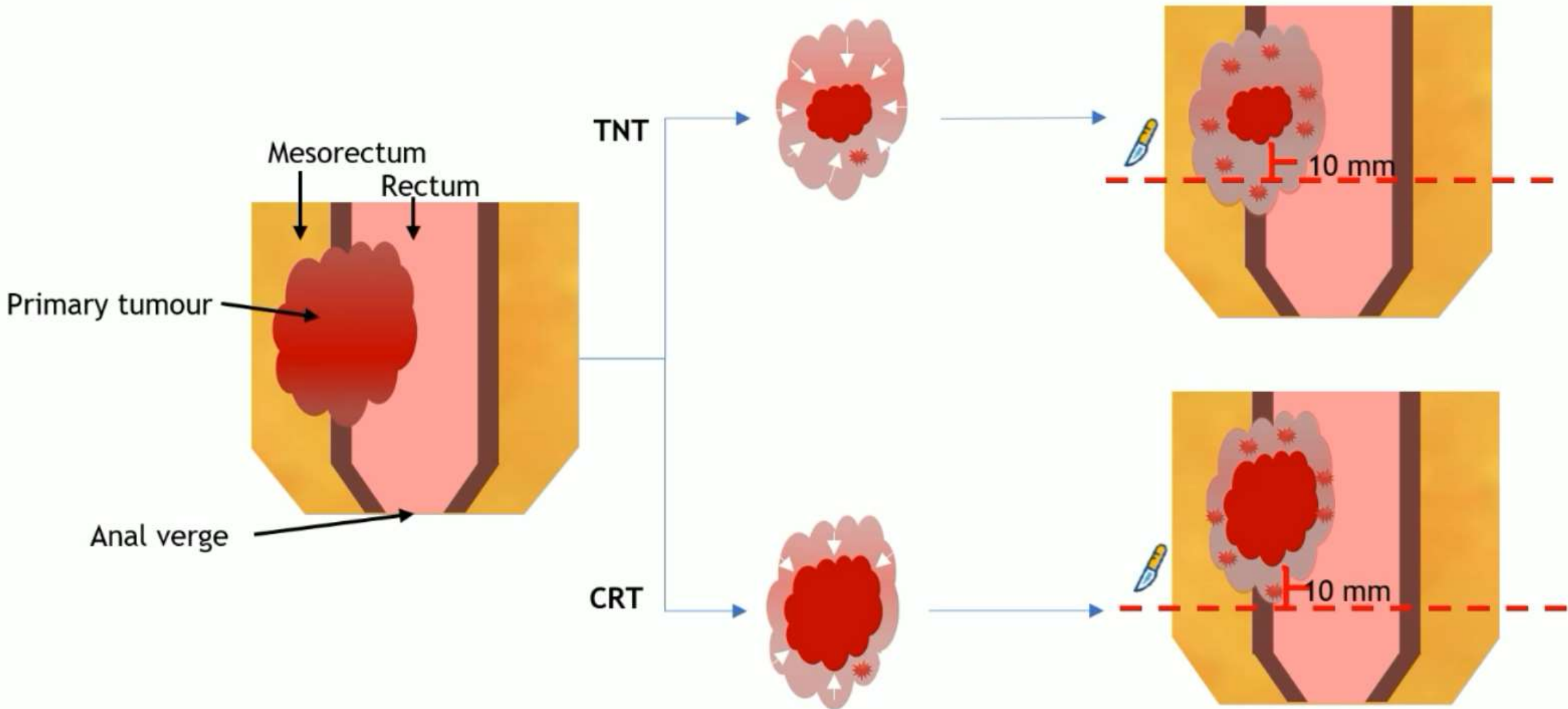
DRM ≤ 10 mm

N = 104

HR 15.51 (2.02 -119.35)



DRM ≤ 10 mm IS NOT SUFFICIENT AFTER TNT



TAKE HOME MESSAGES



- ☐ More locoregional recurrences after sphincter-preserving surgery with TNT
- ☐ A distal resection margin of 10 mm might not be sufficient after TNT
- ☐ DRM is probably important with all TNT schedules

07h00 – 07h40

 Strauss 1-2

PANEL DISCUSSION

Rectal cancer is the new anal cancer: Organ preservation in focus

Clinical

Organ preservation in rectal cancer:

For some, or will it be for all?

State-of-the-art and future perspectives

Emmanouil Fokas

Department of Radiotherapy, Cyberknife and Radiation Oncology
University of Cologne

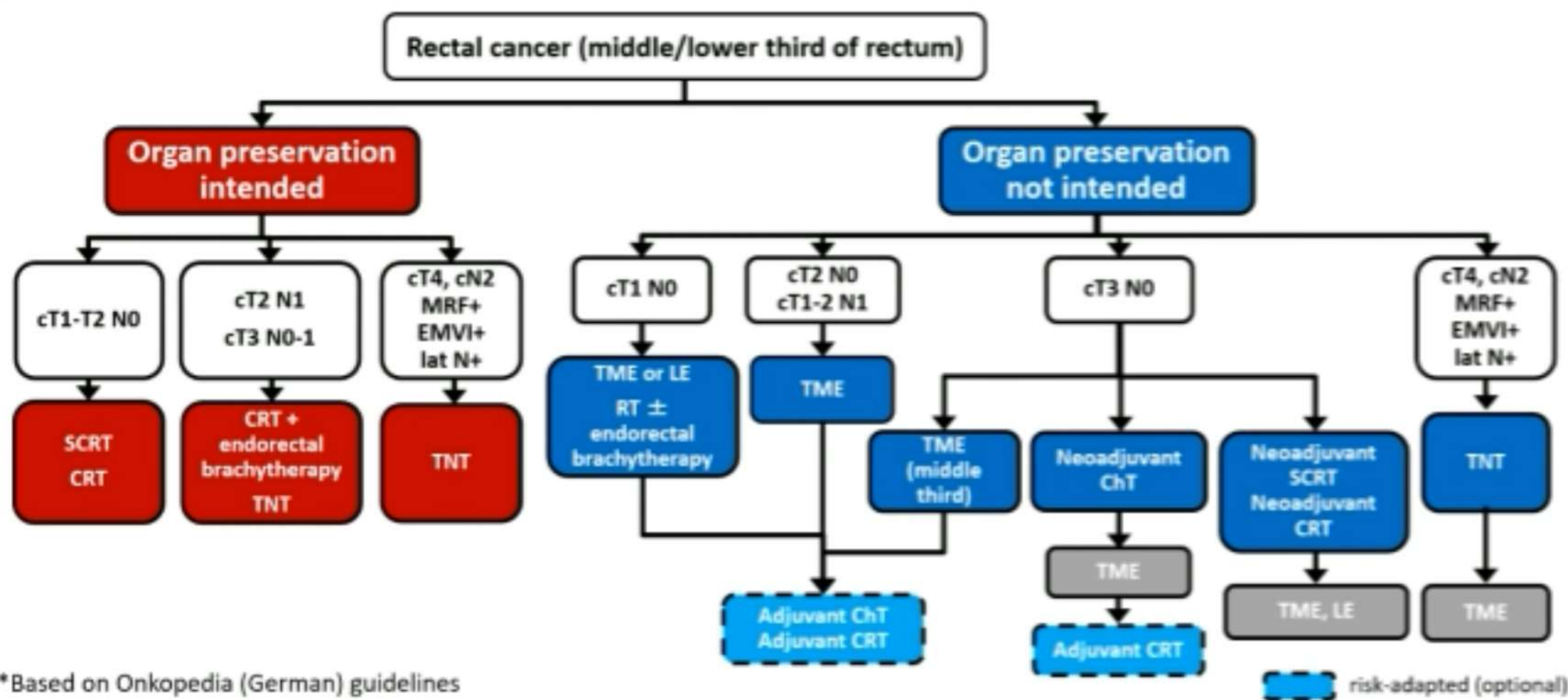
the-art and future p...

Strauss 1-2



Emmanouil Fokas
Germany

New oncology guidelines - new era



*Based on Onkopedia (German) guidelines

Treatment options for organ preservation

Rectal cancer (middle/lower third of rectum)

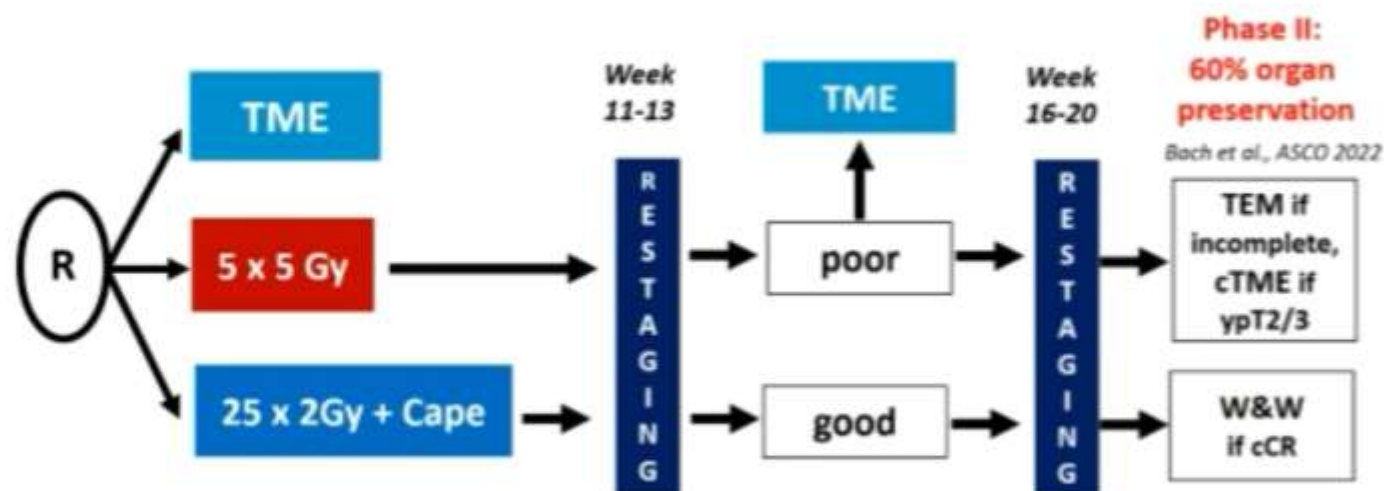
Organ preservation
intended

cT1-T2 N0

SCRT
CRT

STAR-TREC phase II/III trial

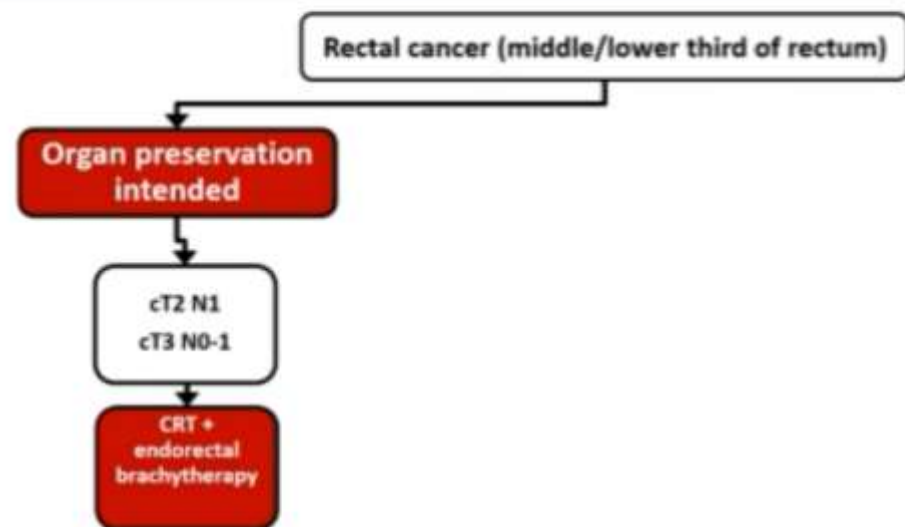
Inclusion: cT1-3b N0M0, < 4 cm



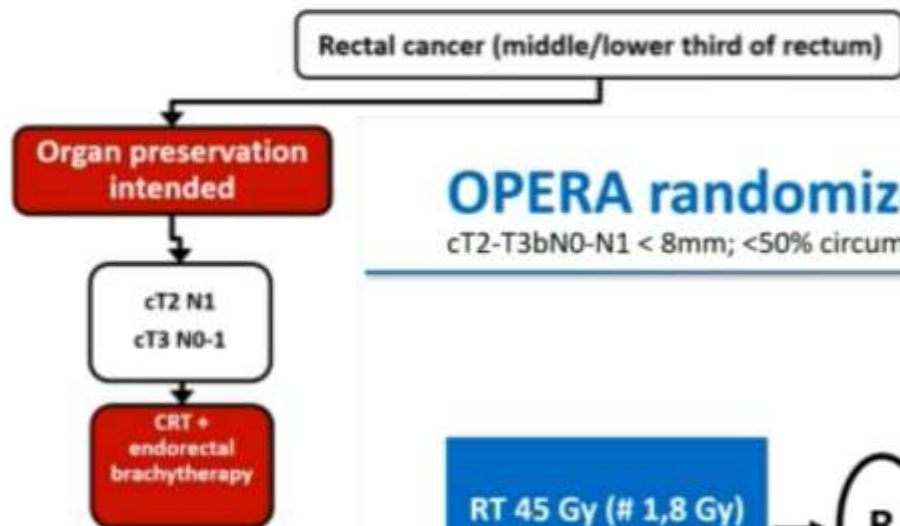
Primary endpoint: recruitment (n=120, phase II), organ preservation (n=380, phase III; TME arm omitted)

Marijnen et al. ESTRO2025 - Top clinical trials
Sunday, May 04, 11:40 - 12:45, Plenary Hall

Treatment options for organ preservation

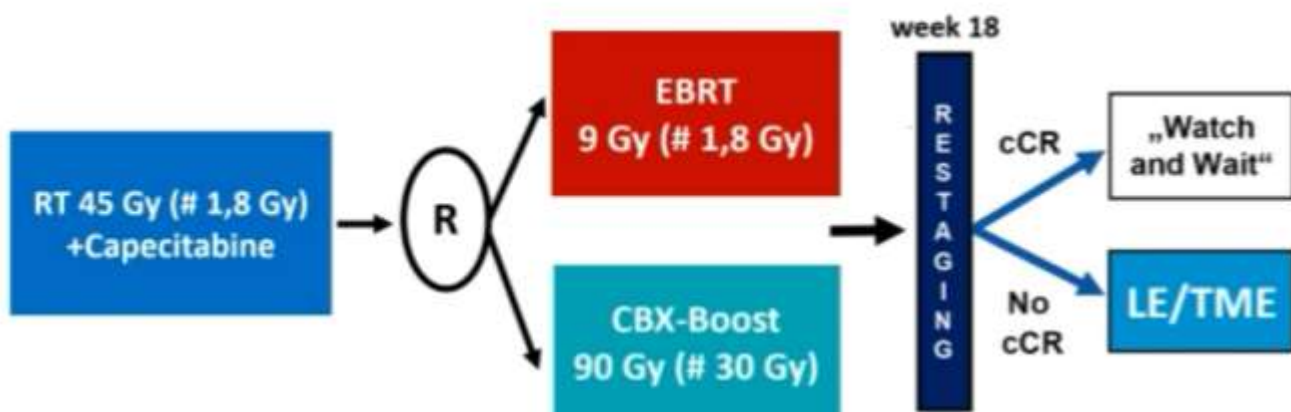


Treatment options for organ preservation



OPERA randomized phase III trial

cT2-T3bN0-N1 < 8mm; <50% circumference, <5 cm, < 10 cm from AV

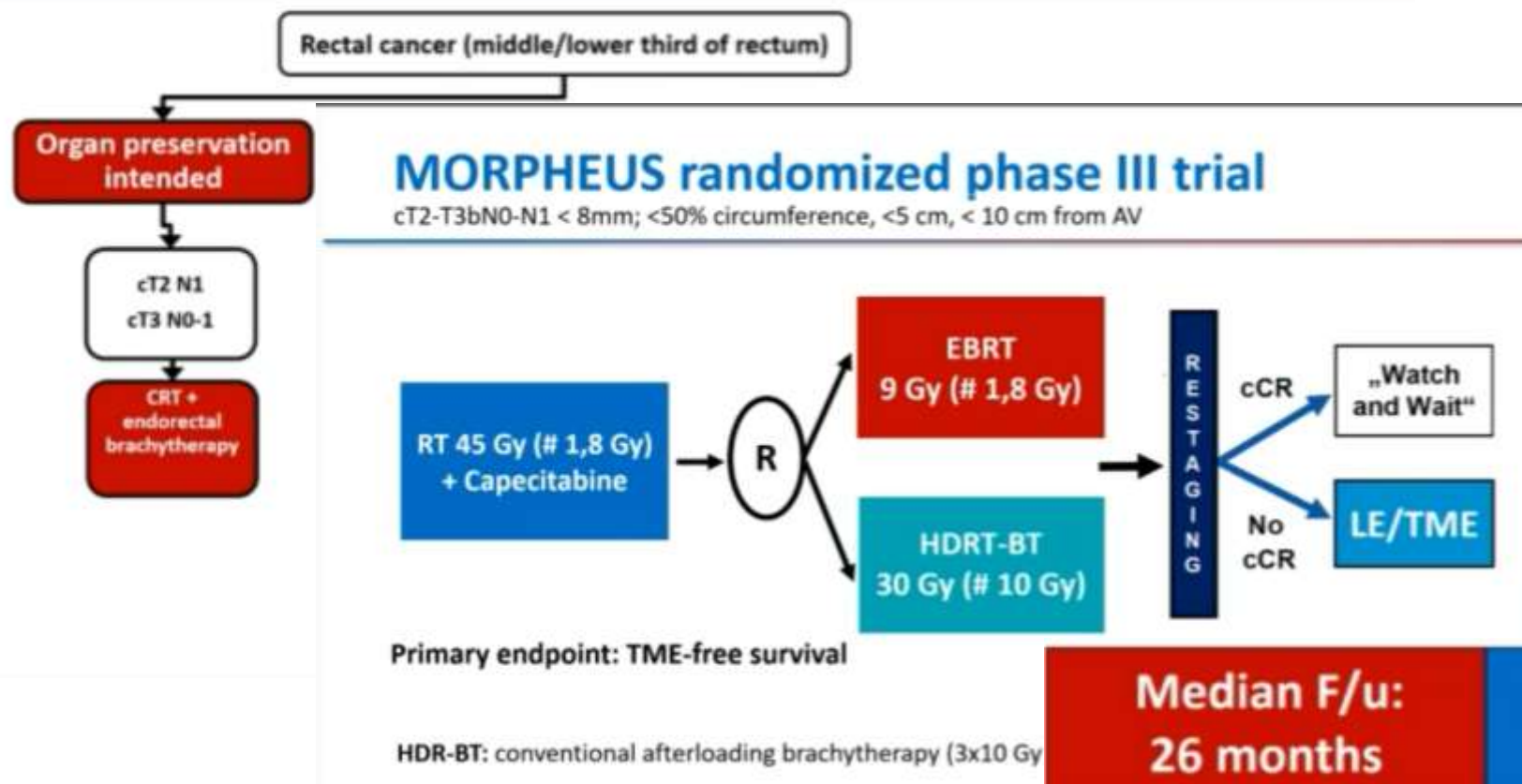


Primary endpoint: Organ preservation

CXB: Papillon 50 KV contact brachytherapy (3x30 Gy, s

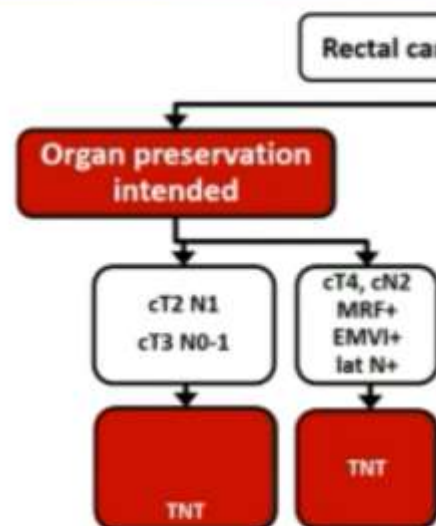
Median F/u: 61.1 months	CRT+EBRT N=69	CRT+CBX N=72	p-value
5-year organ preservation (all pts)	56%	79%	0.004
5-year organ preservation(T<3cm)	54%	93%	0.006
Acute proctitis Grade II-III	6%	13%	-
Poor LARS (incontinence score >30)	24%	17%	NS
Rectal bleeding (telangiectasia)	17%	64%	<0.001

Treatment options for organ preservation



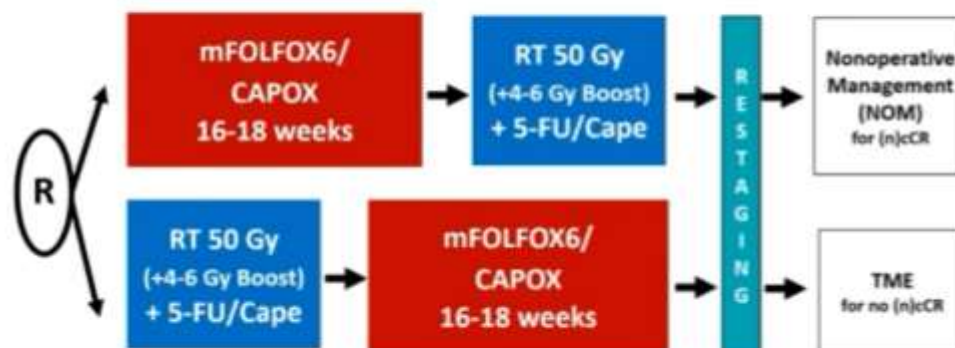
Median F/u: 26 months	CRT+EBRT N=20	CRT+Brachy N=20	p-value
2-year TME-free Survival	40%	85%	0.006
cCR	10/20 (50%)	18/20 (90%)	-
Local regrowth at 2 years	3/10 (30%)	3/18 (17%)	-
G3 proctitis	-	10%	-

TNT when organ preservation is the main aim



OPRA phase II

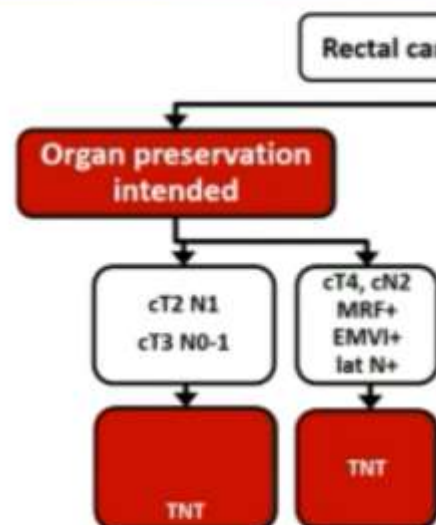
UICC stage II and III, distal RC (requiring APR or coloanal anastomosis)



Primary Endpoint: 3y-DFS, n=322

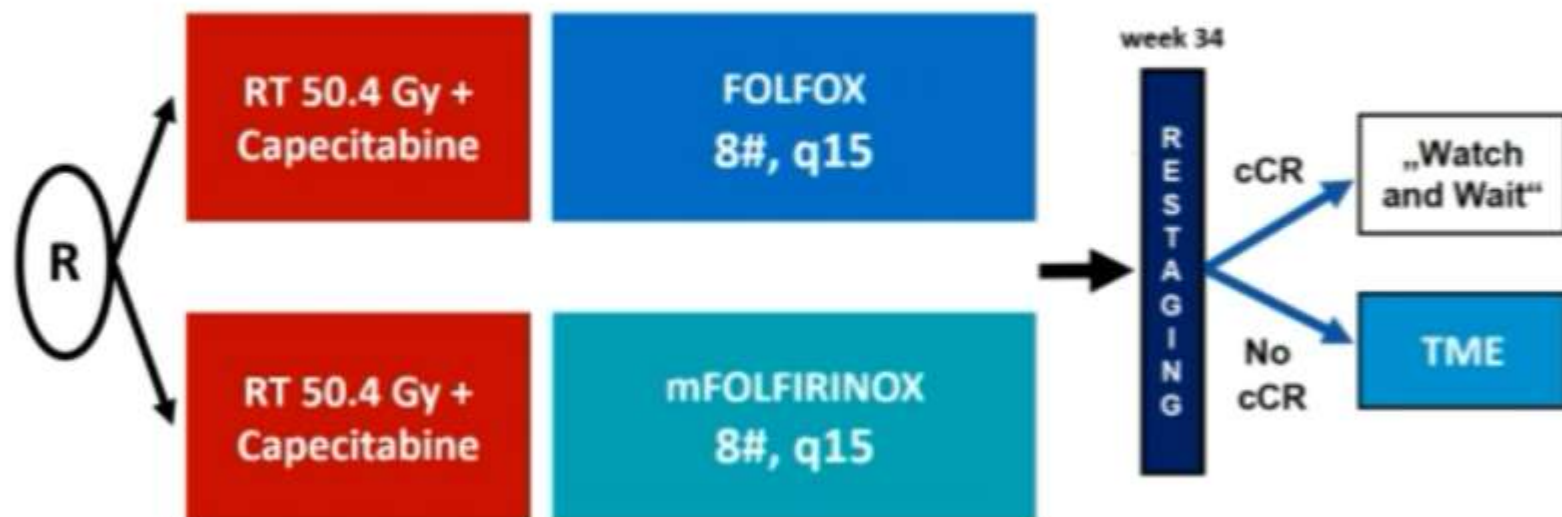
5-year F/U	Induction chemo/CRT (N=158)	CRT/consolid chemo (N=166)	p-value
DFS	71 %	69 %	0.68
TME-free survival	39%	54%	0.01
G3/4 toxicity	34% / 11%	31% / 7%	0.18
DFS	TME after restaging:	TME after regrowth:	0.94
	64%	64%	

TNT when organ preservation is the main aim



JANUS/NRG GI010 phase II/III

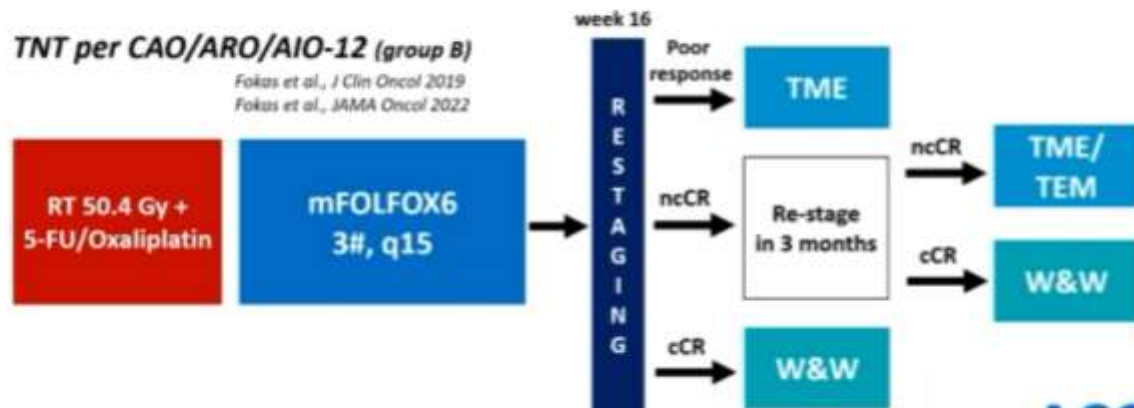
Inclusion: cT4; N+; any T3N0 requiring APR



Primary Endpoints: phase II cCR (n=312); phase III organ preservation-adapted DFS (n=700)

CAO/ARO/AIO-16 phase II

Inclusion: MRF+, EMVI+, any cT3 if low rectal third, cT3c/d, N+, mid rectal third



Primary endpoint: **cCR**, n=89

NCT03561142

ACO/ARO/AIO-18.1 phase III

Inclusion: MRF+, EMVI+, any cT3 if low rectal third, cT3c/d, N+, T4 mid rectal third

Gani et al.
Monday, M



Primary endpoint: 3-year organ preservation (OP) rate, N=702

Hypothesis: improvement in 3y-OP rate from **30%** (SCRT - TNT) to **40%** (LCRT - TNT)

Accrual completed September 2023; report scheduled for Q1/2026

NCT04230759

Definition of tumor response



cCR: clinical complete remission
ncCR: near cCR

Smith et al., BMC Cancer 2015
Martens et al. JNCI 2021
Fokas et al., Nature Rev Clin Oncol 2021

Follow-up methods and intervals for organ preservation

Year	Serum carcino-embryonic antigen	DRE	Endoscopy	Pelvic MRI	Chest and/or abdominal CT
1	4 months	3–4 months	3–4 months	3–4 months	6 months
2	4 months	3–4 months	3–4 months	3–4 months	Annually
3	4 months	6 months	6 months	6 months	Annually
4	6 months	6 months	6 months	6 months	Annually
5	6 months	6 months	6 months	6 months	Annually

Patients should be informed in advance by the physician about the surveillance programme for organ preservation strategies

Fokas et al., Nat Rev Clin Oncol 2021

Benefits of organ preservation compared to surgery

- high priority for patients
- avoidance of colostomy (deeply seated tumors)
- better physical and cognitive function
- better physical and emotional resilience
- better global state of health
- fewer problems with bowel movements
- fewer problems with sexual and urinary function

Hupkens B et al., Dis Colon Rectum 2017
Van de Sande M et al., Radiother Oncol 2019

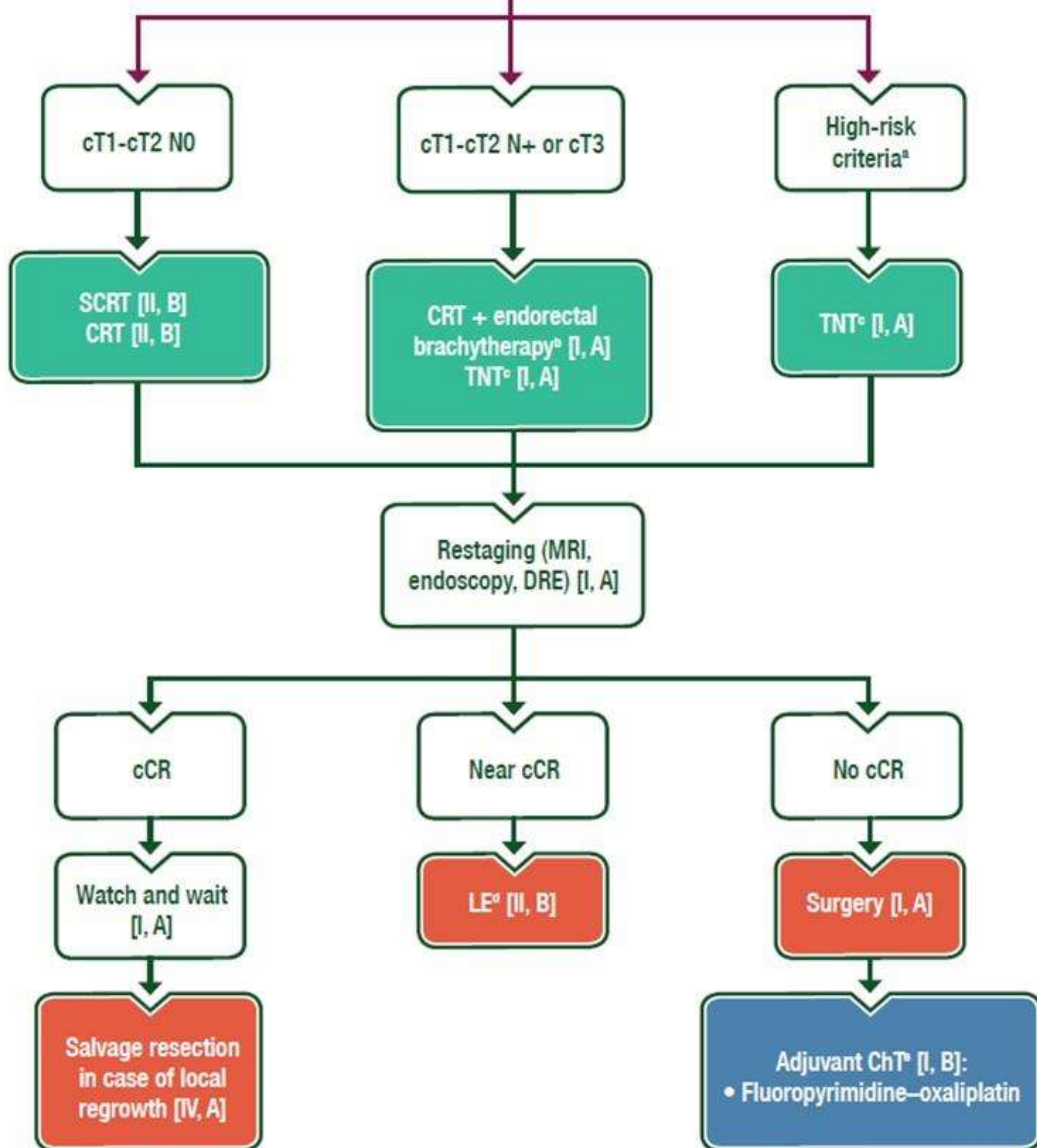
Gani C et al., Front Oncol 2019
Van der Valk et al., EJSO 2019

Bach S et al., Lancet Gastro Hep 2021
Fokas et al., Nat Rev Clin Oncol 2021

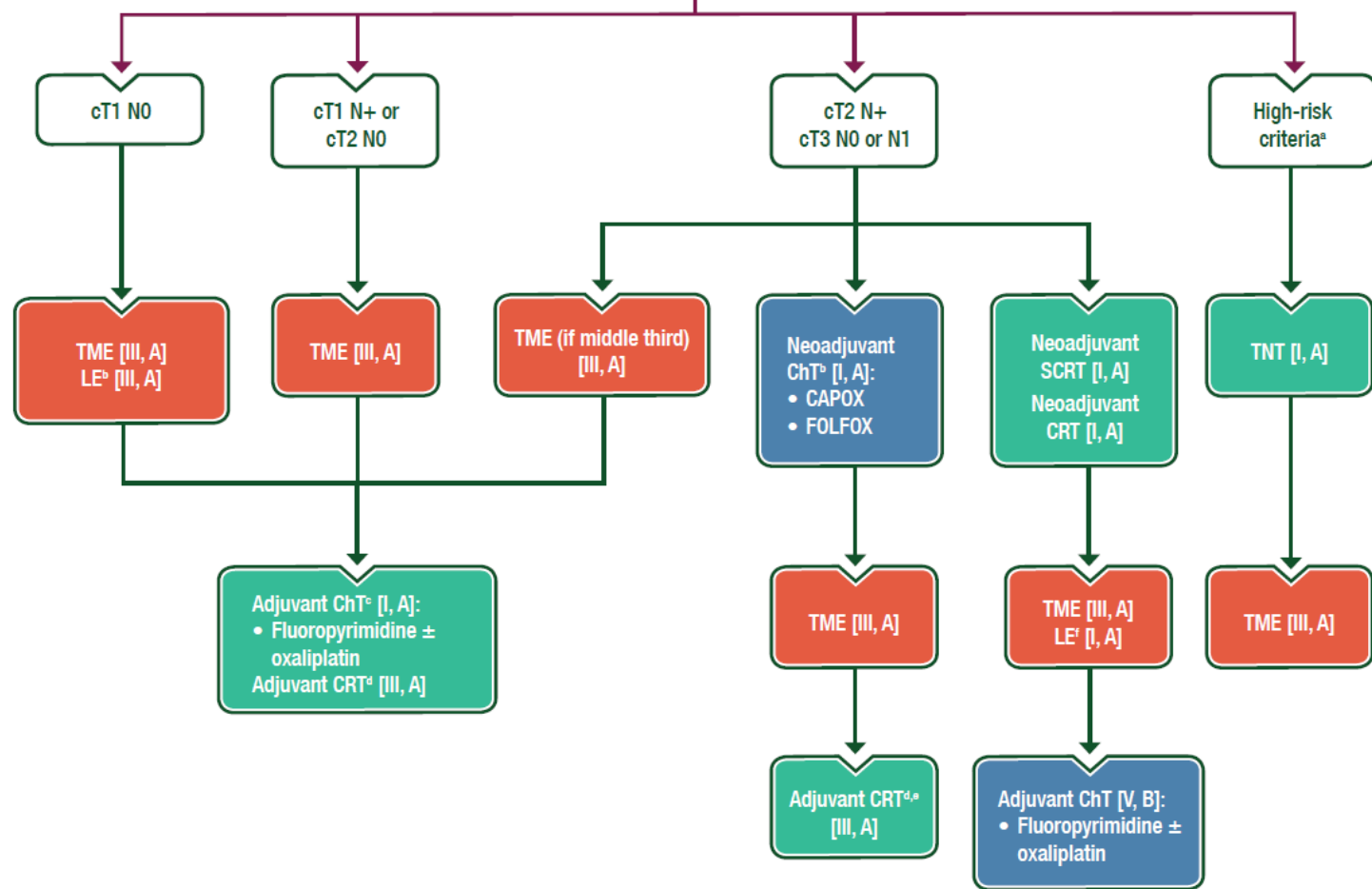
Préservation rectal: Conclusion

- La prise en charge du cancer du rectum s'est orientée vers la préservation d'organe : nouvelle ère, nouvelles lignes directrices ; **nécessité de développer une expertise nationale**
- Quelques points clés :
 - IRM de haute qualité pour une stratification précise du traitement basée sur le risque à l'inclusion
 - définition de la réponse tumorale ;
 - programme de surveillance intensif
- Le traitement multidisciplinaire intégrant la RT a placé la barre très haut en termes de taux de préservation des organes au stade précoce/intermédiaire
 - (par exemple, essais OPERA, STAR-TREC : 60-80 %)
 - et au stade avancé de la maladie (par exemple, essai OPRA : 50 %)
- La prise de décision partagée s'imposera progressivement comme un élément clé, en raison de la complexité accrue des stratégies thérapeutiques dans le cancer du rectum.

Localised rectal cancer in lower or middle third of rectum when organ preservation is intended



Localised rectal cancer in lower or middle third of rectum when surgery is intended





Leeds
Clinical Trials Unit



PLATO ACT 4

Long term results of a randomised trial evaluating reduced dose and standard dose chemoradiotherapy in early-stage anal cancer

Sebag-Montefiore D¹, Harrison M², Gilbert A¹, Abbott N³, Berkman L⁴, Copeland J¹, Gilbert D⁵, Gaul C¹, Glynne-Jones R², Goh V⁶, Hawkins M⁷, Muirhead R⁸, Rao S⁹, Renehan A¹⁰, Ruddock S¹, Smith A¹, Webster J¹, Brown S¹, Adams R¹¹
on behalf the PLATO Trial Management Group

¹University of Leeds, ²Mount Vernon Hospital, ³RTTQA Group, ⁴Patient advocate

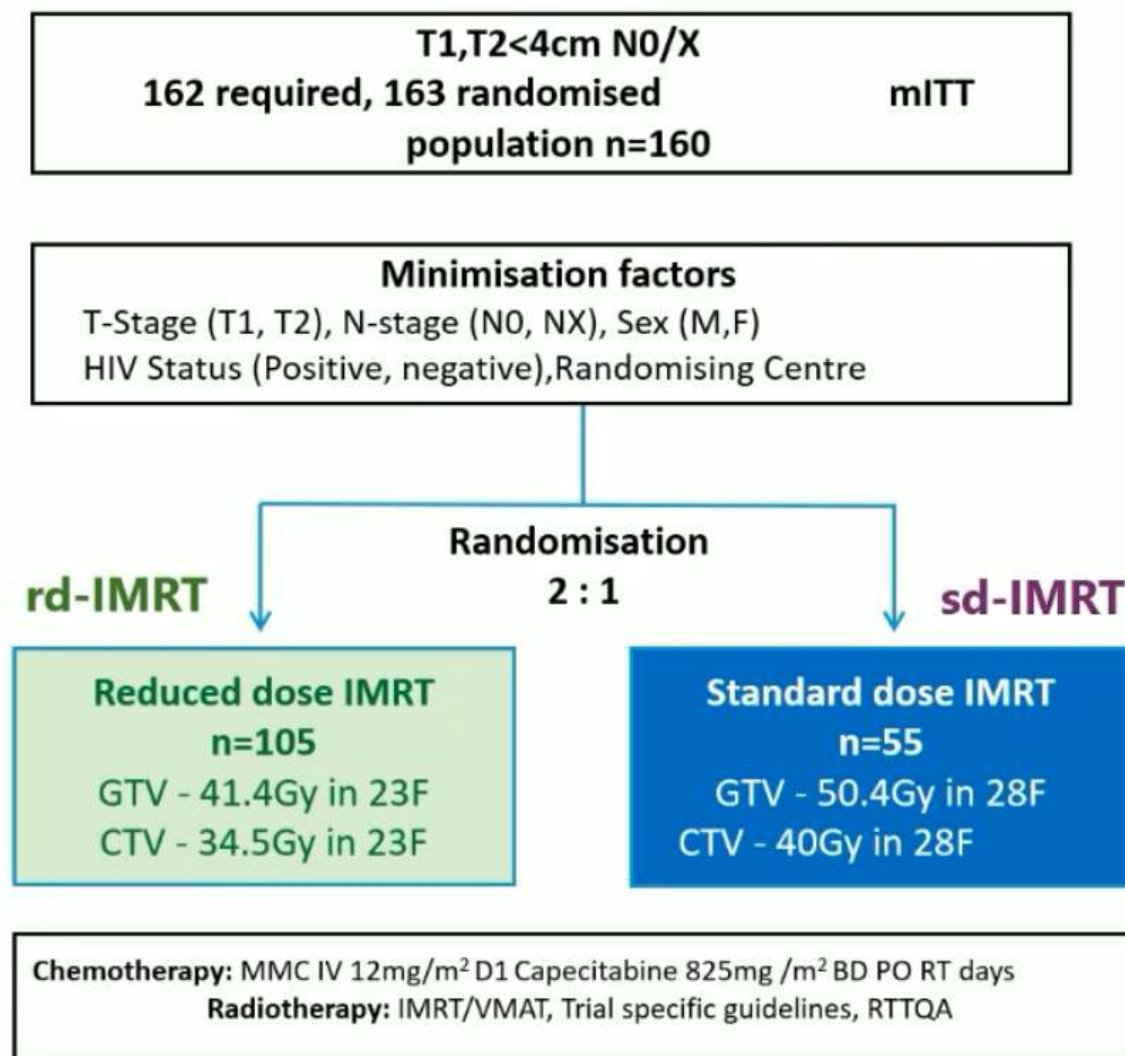
⁵Royal Sussex County Hospital, ⁶Kings College London, ⁷University College London, ⁸Churchill Hospital Oxford,

⁹Institute of Cancer Research, Royal Marsden London, ¹⁰University of Manchester, ¹¹Cardiff University



David Sebag-Montefiore
United Kingdom

ACT4 Study Design



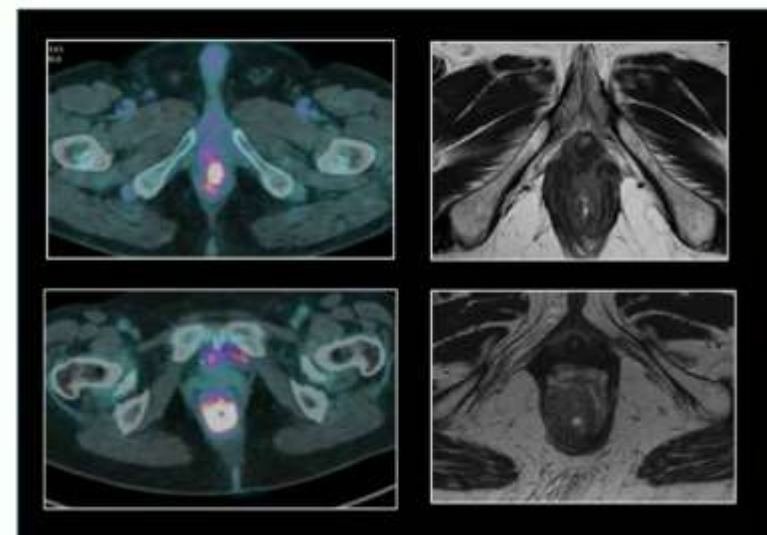
STUDY AIM

to determine if rd-IMRT results in an acceptably **low rate of LRF** and **reduced toxicity**

rd-IMRT

lower limit of 90% CI >80% for 3-year LRF free rate with rd-IMRT

T1,T2<4cm N0/X



Patient Characteristics

	Standard dose IMRT N (%) n=55		Reduced dose IMRT N (%) N=105		Total N (%) n=160	
Gender						
Male	14	25.5%	29	27.6%	43	26.9%
Female	41	74.5%	76	72.4%	117	73.1%
Age (years)						
Median (Range)	64.0 (38.0 - 87.0)		68.0 (35.0 - 84.0)		66.0 (35.0 - 87.0)	
Tumour site						
Anal margin	11	20.0%	24	22.9%	35	21.9%
Anal canal	44	80.0%	81	77.1%	125	78.1%
T stage						
T1	10	18.2%	19	18.1%	29	18.1%
T2	45	81.8%	86	81.9%	131	81.9%
N Stage						
N0	55	100.0%	104	99.0%	159	99.4%
Nx	0	0.0%	1	1.0%	1	0.6%
ECOG						
0	48	87.3%	90	85.7%	138	86.3%
1	7	12.7%	15	14.3%	22	13.8%
HIV status						
Positive	1	1.8%	4	3.8%	5	3.1%
Negative	54	98.2%	101	96.2%	155	96.9%
p16 Status						
Positive	45	90%	84	95.5%	129	93.5%
Negative	5	10%	4	4.5%	9	6.5%

Treatment Compliance

	Standard dose IMRT N=55		Reduced dose IMRT N=105		Total N=160	
RADIOTHERAPY						
Total radiotherapy dose received	50.4Gy	28.8-50.4	41.4GY	23.4-50.4		
Median Treatment duration (days, range)	38 days	30-40	31 days	17-30		
Radiotherapy Interruption*	14	25.5%	16	15.2%	30	18.8%
CHEMOTHERAPY						
Chemotherapy as per protocol	28	50.9%	66	62.9%	94	58.8%
Capecitabine delay	3	5.5%	5	4.8%	8	5.0%
Capecitabine reduction	4	7.3%	12	11.4%	16	10.0%
Capecitabine omission	25	45.5%	33	31.4%	58	36.3%

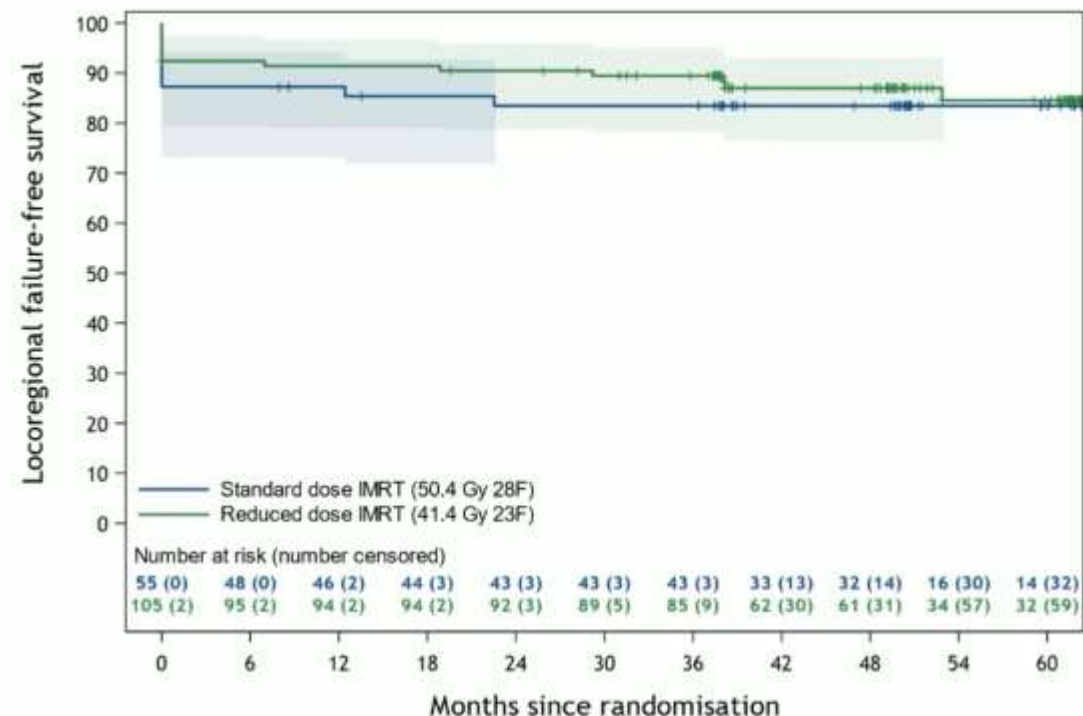
*All participants adhered to the radiotherapy schedule and completed the scheduled course without more than 3 days delay due to toxicity

Primary end point - 3-year loco-regional failure rate

|||||

- The 3-year locoregional failure-free rate is:
 - **Reduced dose IMRT** 87.6% (90% CI 81.04-92.52)
 - **Standard dose IMRT** 83.6% (90% CI 73.18-91.19)
- We reject the null hypothesis as the lower bound of the 90% confidence interval in the reduced dose arm is above 80%
- **The primary end-point is met**

Primary end point: 3 year loco-regional failure free rate

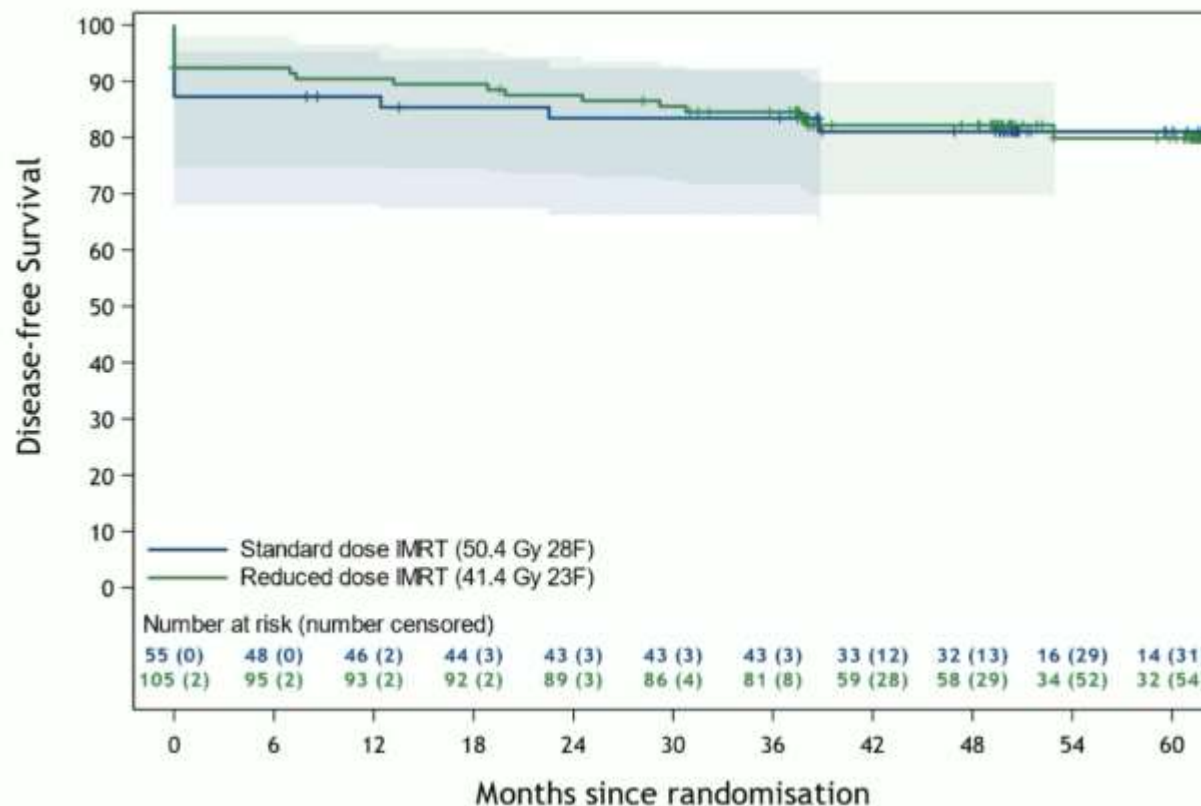


	3-year LRFF	90% CI
Reduced dose IMRT	89.4%	78.19-95.06
Standard dose IMRT	83.4%	70.58-91.02

Pattern of loco-regional failure

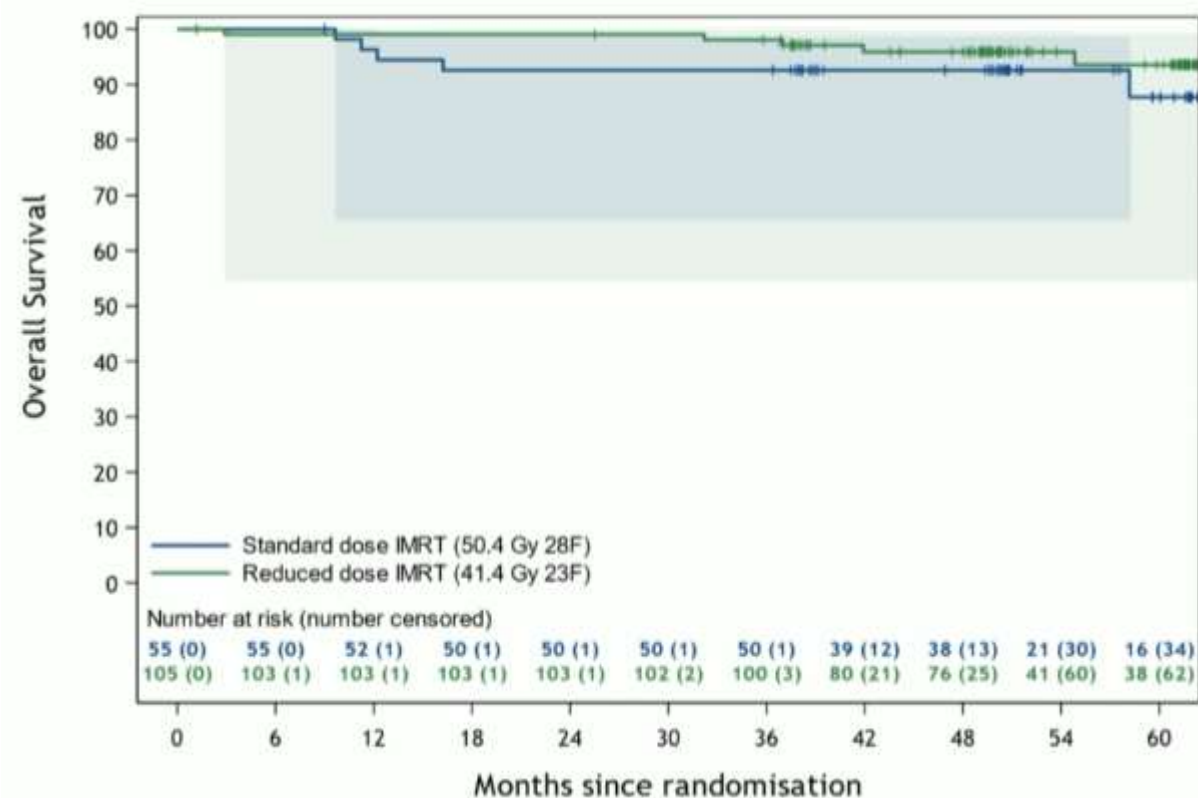
	Standard dose IMRT N=55		Reduced dose IMRT N=105		Total N=160	
Complete response at 6 months						
Primary site only	2	3.6%	4	3.7%	6	3.7%
Primary and nodal	0	0%	1	0.9%	1	0.09%
Nodal only	0	0%	0	0%	0	0%
Incomplete response at 6 months						
Primary site only	2	3.6%	4	3.7%	6	3.7%
Primary and nodal	1	1.8%	0	0%	1	0.06%
Nodal only	0	0%	0	0%	0	0%
Total	5	9.0%	9	8.3%	14	8.6%

Disease-Free Survival



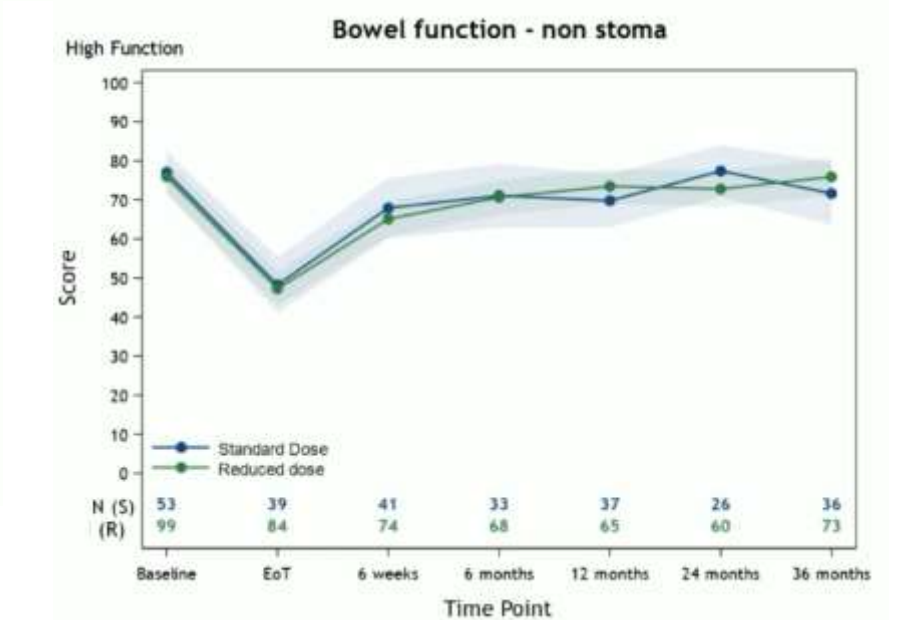
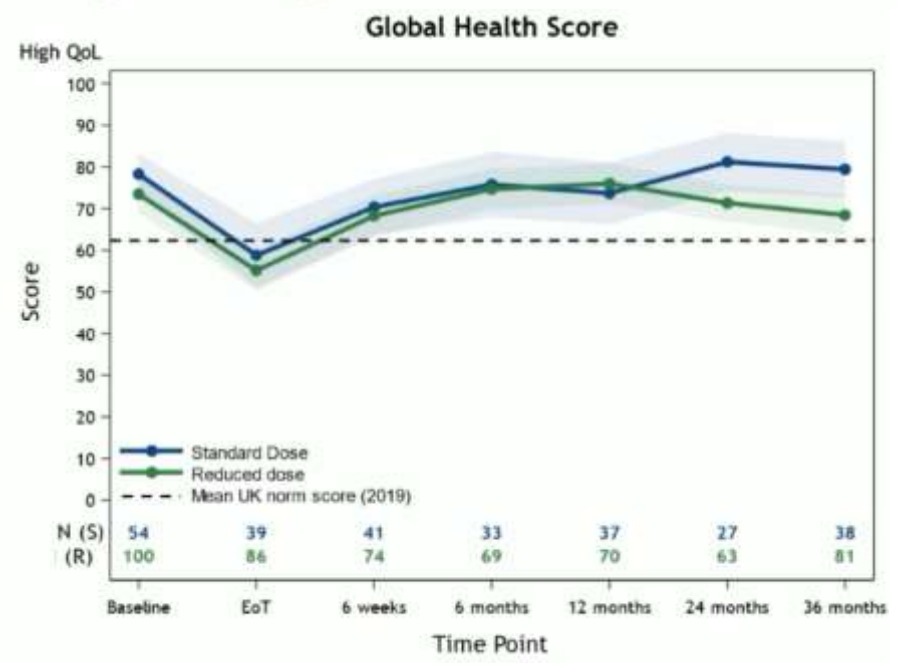
	3-year DFS	95% CI
Reduced dose IMRT	84.5%	71.66-91.88
Standard dose IMRT	83.4%	66.31-92.33

Overall Survival

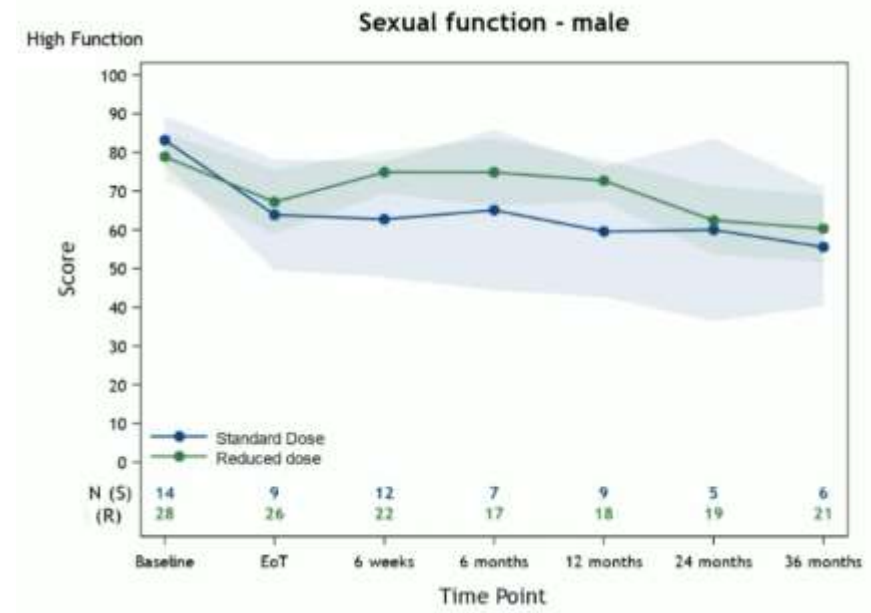
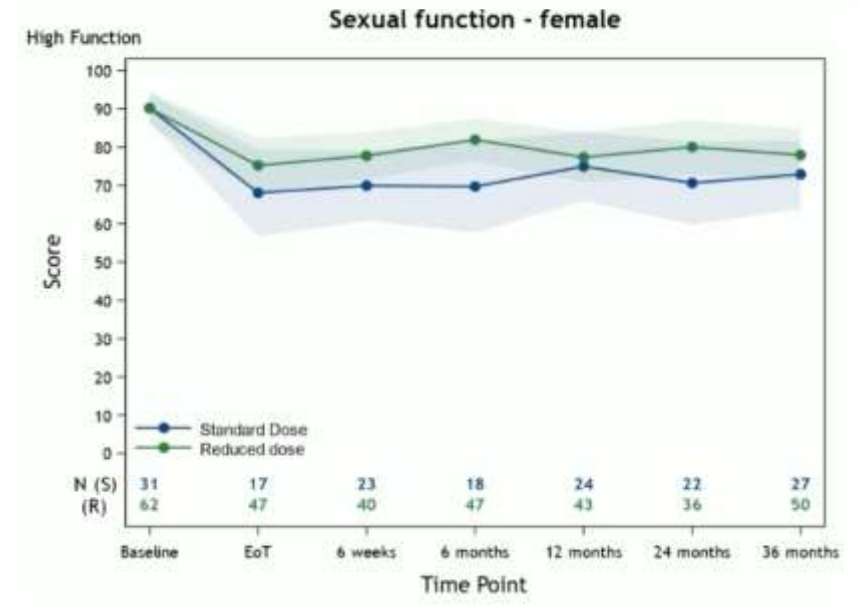


	3-year OS	90% CI
Reduced dose IMRT	98.1%	54.57-100
Standard dose IMRT	92.6%	65.49-98.66

EORTC QLQ Patient Reported Outcomes



EORTC QLQ-ANL27 Patient Reported Outcomes - Sexual Function



Conclusions

- Reduced dose IMRT with concurrent MMC and capecitabine resulted in a:
 - **87.6% loco-regional failure free rate at 3 years - the primary end point is met**
 - 84.5% disease free survival at 3 years
 - 98.1% overall survival at 3 years
- There were no isolated nodal failures
- Patient reported outcomes measuring late toxicity were similar
- **The shorter, reduced dose IMRT regimen offers major advantages to patients, their carers, and health care systems and should be considered as a new treatment option for patients with early-stage anal cancer**



Société Marocaine de Cancérologie
الجمعية المغربية لداء السرطان



الجمعية التونسية للأمراض الورمية والعلاج بالإشعاع
Société Tunisienne d'Oncologie Radiothérapie

Post
ESTRO
2025
AFRIQUE DU NORD

BY SMC/STOR
LE 28 MAI 2025 À 18H00 (GMT+1)
Evenement VIRTUEL

MARRAKECH