

44. Schweizerische Koloproktologie-Tagung  
44<sup>ème</sup> Journée Suisse de Coloproctologie

11. Januar 2025, Bern | 11 janvier 2025, Berne



# Does Early Onset Colorectal Cancer need to be treated more aggressively ?

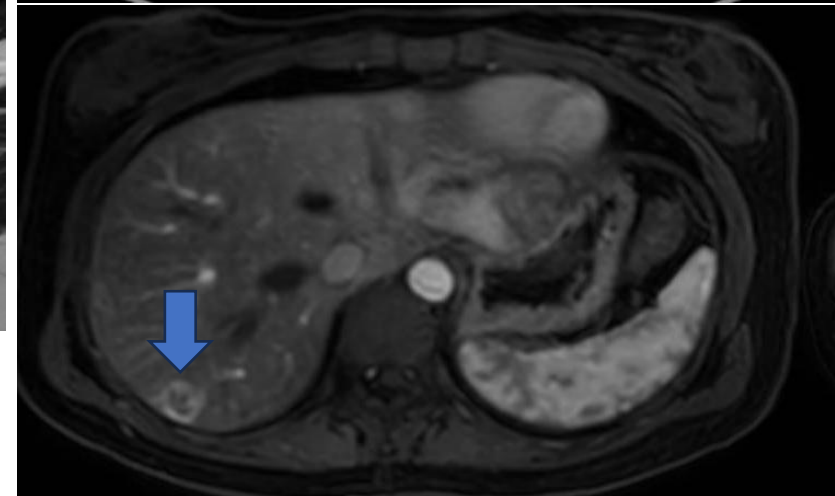
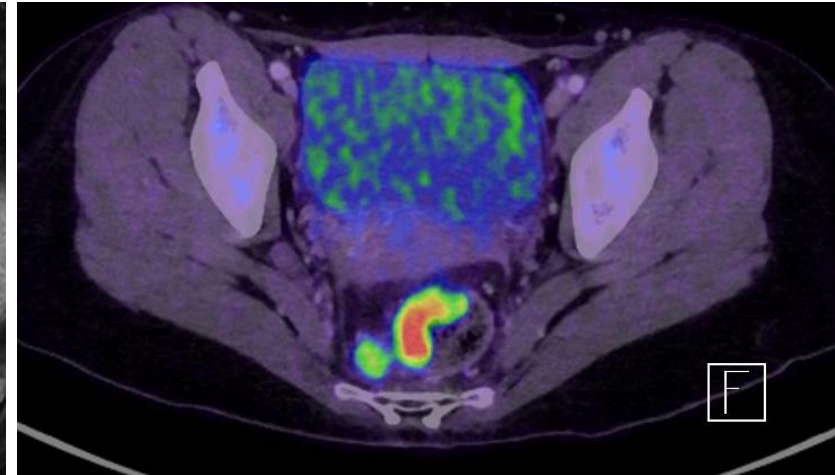
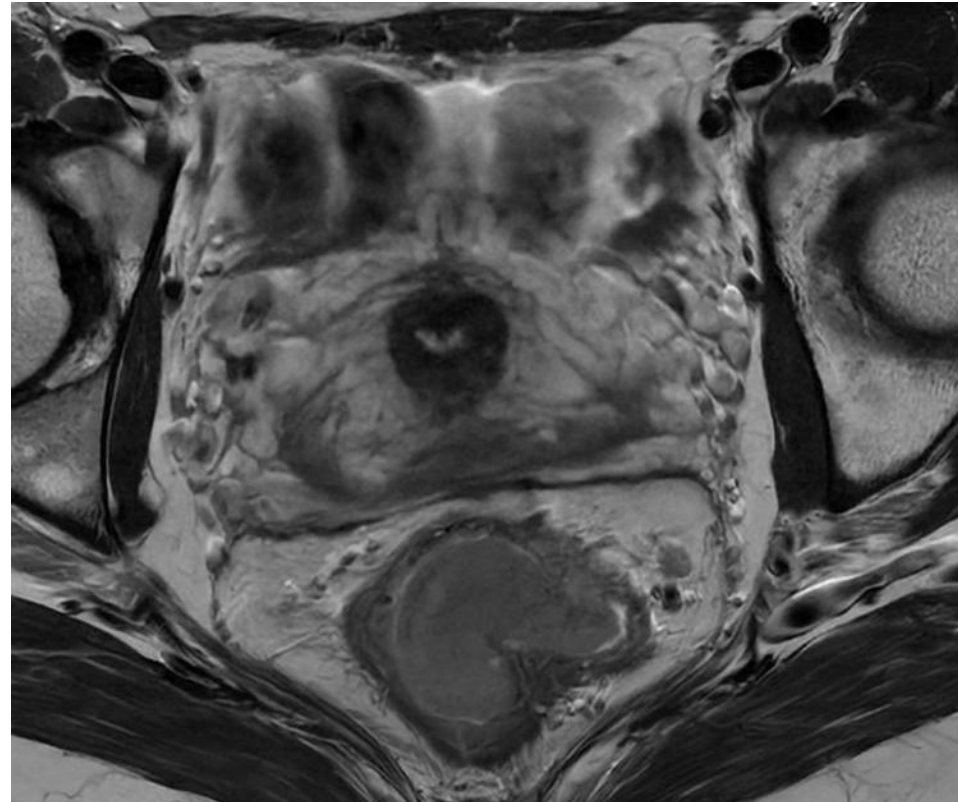
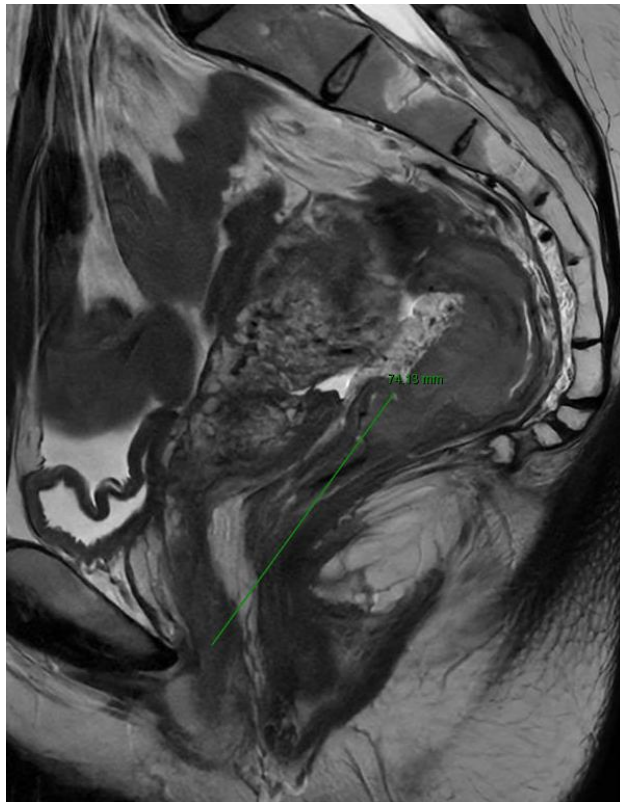
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Department of Visceral Surgery  
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# 32 yo ♀, LAR Dec 9, 2024



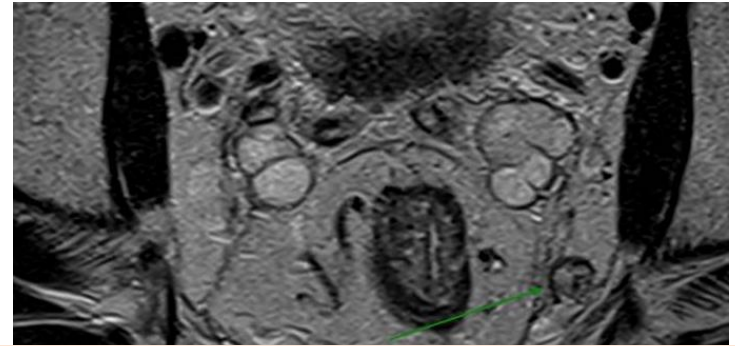
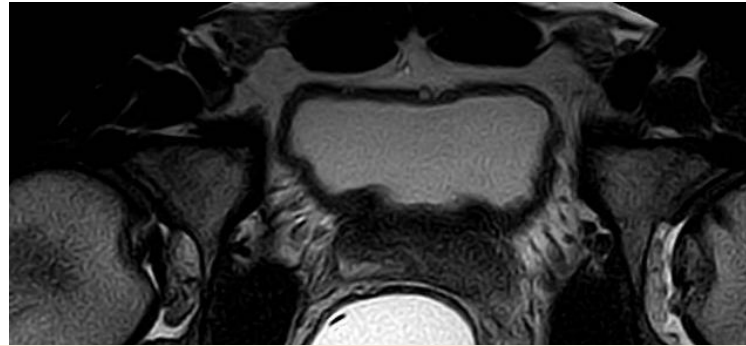
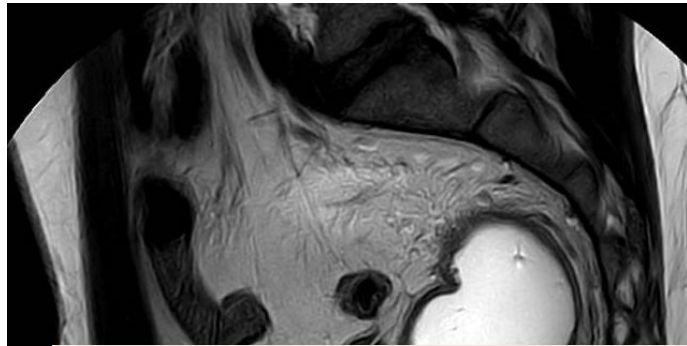
cT3 N1 M1 (liver), pre-ttt sigmoidostomy, liver surgery, SCRT



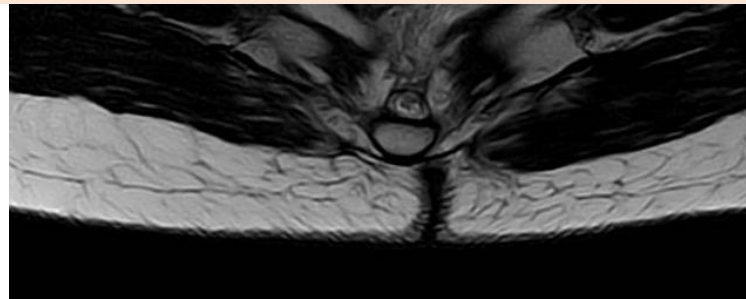
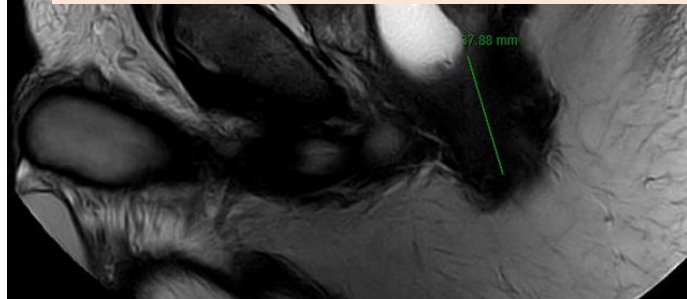
**ypT0 N0 TRG 1/5**

36 yo ♂, LAR Oct 7, 2024

cT3 N1 M1 (lung), lung surgery x 2, long-course CRT

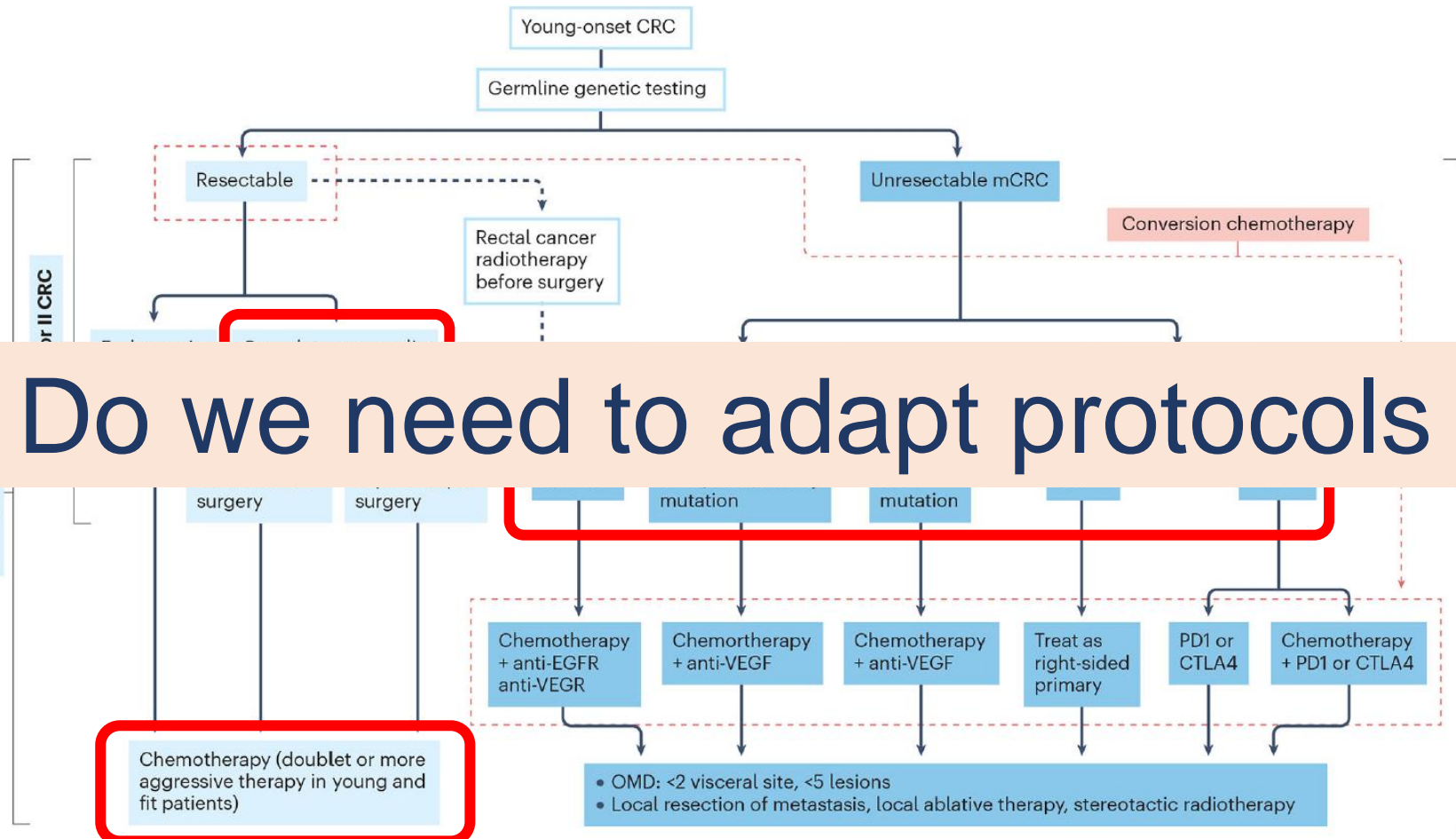


Both of them sporadic



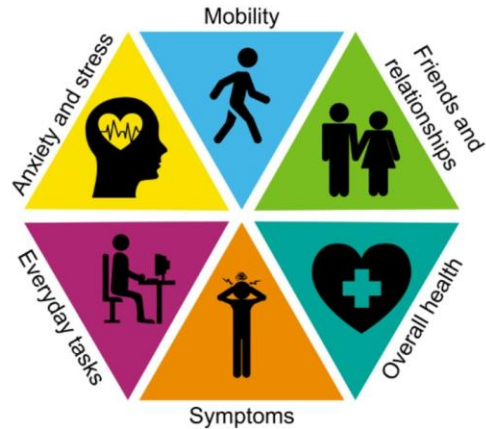
ypT3 ypN2b (15/33), L1 V1 Pn1 R1, TRG 4/5

# Treatment algorithm



Do we need to adapt protocols ?

# What matters ?



QoL: family, work, long life expectancy

Function: best possible functional outcome → highest potential for recovery ?

↓ Toxicity → higher treatment toxicity justified ?

LARS

Sexual  
dysfunction

Radiation  
proctitis

Chemo side  
effects

Urinary  
dysfunction

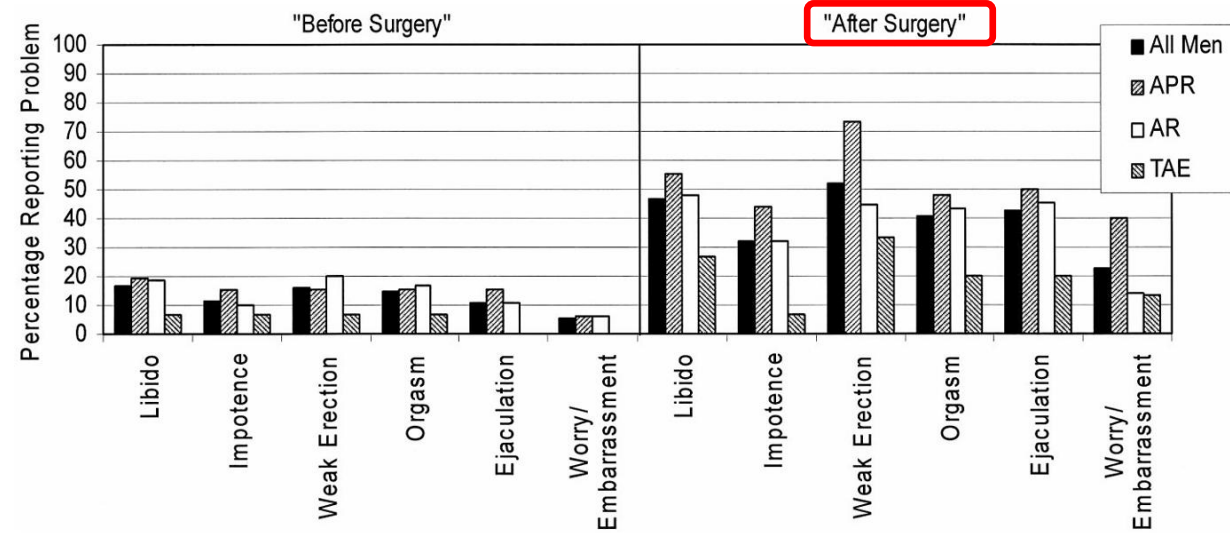
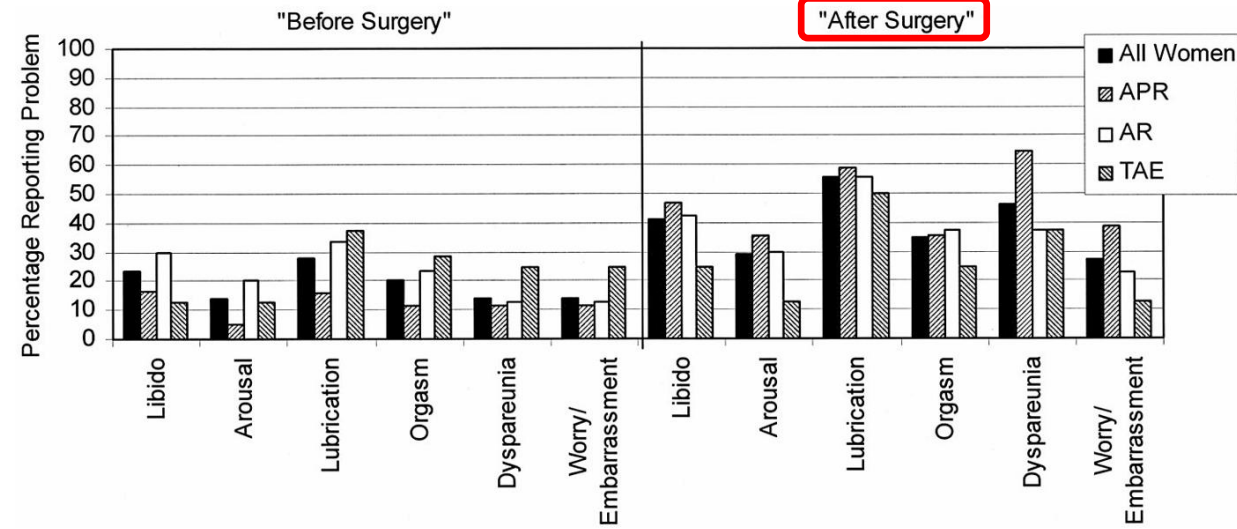
Stoma

Postop  
complication





# Risks in the young... :





# Side effects neoadjuvant ttt



## Risk of permanent amenorrhea

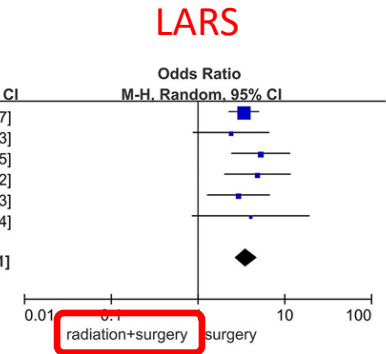


Degree of Risk	Cancer Treatment
High risk (> 80%)	Hematopoietic stem cell transplantation with cyclophosphamide/total body irradiation or cyclophosphamide/busulfan External beam radiation to a field that includes the ovaries CMF, CEF, CAF × 6 cycles in women age 40 and older (adjuvant breast cancer therapy with combinations of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, epirubicin)
Intermediate risk	CMF, CEF, CAF × 6 cycles in women age 30-39 (adjuvant breast cancer therapy with combinations of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, epirubicin) AC × 4 in women age 40 and older (adjuvant breast cancer therapy with doxorubicin/cyclophosphamide)



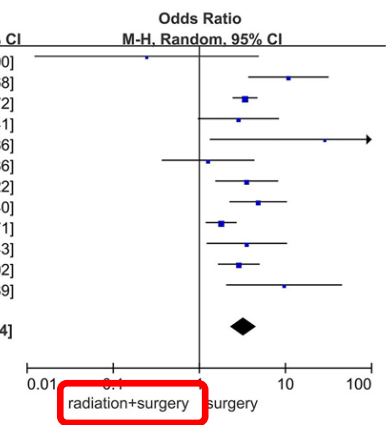
## LARS

Study or Subgroup	radiation+surgery		surgery		Weight	Odds Ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI
Bregendahl, Denmark, 2013	159	191	445	747	51.3%	3.37	[2.24, 5.07]
Emmertsen, Denmark, 2013	26	31	104	152	8.2%	2.40	[0.87, 6.63]
Qin, China, 2017	74	88	27	54	13.9%	5.29	[2.42, 11.55]
Sturiale, Italy, 2017	28	41	16	52	10.9%	4.85	[2.00, 11.72]
Sun, China, 2019	122	132	71	88	12.2%	2.92	[1.27, 6.73]
Theodoropoulos Greece, 2020	18	20	40	58	3.5%	4.05	[0.85, 19.34]
<b>Total (95% CI)</b>		<b>503</b>		<b>1151</b>	<b>100.0%</b>	<b>3.59</b>	<b>[2.68, 4.81]</b>
Total events	427		703				
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.34, df = 5 (P = 0.80); I <sup>2</sup> = 0%							
Test for overall effect: Z = 8.60 (P < 0.00001)							



## Major LARS

Study or Subgroup	radiation+surgery		surgery		Weight	Odds Ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI
Bohlok, Belgium, 2019	27	39	4	4	1.3%	0.24	[0.01, 4.90]
Bondeven, Denmark, 2015	20	25	27	100	7.0%	10.81	[3.69, 31.68]
Bregendahl, Denmark, 2013	123	191	260	747	17.5%	3.39	[2.43, 4.72]
Croese, Australia, 2018	11	21	12	43	6.9%	2.84	[0.96, 8.41]
D'Alba, Italy, 2020	17	17	5	9	1.2%	28.64	[1.32, 619.86]
Dulskas, Lithuania, 2021	8	27	6	24	5.7%	1.26	[0.37, 4.36]
Emmertsen, Denmark, 2013	22	31	62	152	9.4%	3.55	[1.53, 8.22]
Qin, China, 2017	51	88	12	54	10.3%	4.82	[2.24, 10.40]
Sandberg, Sweden, 2020	116	176	109	210	16.1%	1.79	[1.19, 2.71]
Sturiale, Italy, 2017	13	41	6	52	7.0%	3.56	[1.21, 10.43]
Sun, China, 2019	85	132	34	88	13.6%	2.87	[1.64, 5.02]
Theodoropoulos, Greece, 2020	18	20	28	58	4.1%	9.64	[2.05, 45.39]
<b>Total (95% CI)</b>		<b>808</b>		<b>1541</b>	<b>100.0%</b>	<b>3.28</b>	<b>[2.31, 4.64]</b>
Total events	511		565				
Heterogeneity: Tau <sup>2</sup> = 0.15; Chi <sup>2</sup> = 22.55, df = 11 (P = 0.02); I <sup>2</sup> = 51%							
Test for overall effect: Z = 6.68 (P < 0.00001)							



# EOCRC – specific considerations

1. 75% colon cancer, 25% rectal cancer
2. 71% present with stage III or IV
3. 67% saw at least two physicians prior to diagnosis
4. 41% waited at least 6 months after experiencing symptoms





# Symptoms



National Cancer registry 2008-2019  
EOCRC vs. LOCRC  
Symptoms, Survival

characteristics	EOCRC (n = 1240)	LOCRC (n = 4464)	P value
Age, year, median ± IQR	44 ± 8	60 ± 9	<0.001
Gender			
Male	634 (51.1)	2637 (59.1)	<0.001
Female	606 (48.9)	1827 (40.9)	
BMI	23.2 ± 5.1	24.2 ± 4.9	<0.001
Tumor location			0.694
Cecum	47 (3.8)	186 (4.2)	
Ascending colon	109 (8.8)	469 (10.5)	
Transverse colon and hepatic flexure	131 (10.6)	442 (9.9)	
Splenic flexure	18 (1.5)	62 (1.4)	
Descending colon	90 (7.3)	320 (7.2)	
Sigmoid colon	357 (28.8)	1269 (28.4)	
Rectum	488 (39.4)	1716 (38.4)	
Tumor sidedness			0.299
Right-sided	287 (23.1)	1097 (24.6)	
Left-sided	953 (76.9)	3367 (75.4)	
Histology type			<0.001
Adenocarcinoma	1135 (91.5)	4232 (94.8)	
Signet-ring cell adenocarcinoma	22 (1.8)	31 (0.7)	
Mucinous adenocarcinoma	83 (6.7)	201 (4.5)	
Histology grade			

characteristics	EOCRC (n = 1240)	LOCRC (n = 4464)	P value
Family history			
FAP/HNPCC	94 (7.6)	109 (2.4)	0.001
Yes	466 (37.6)	2030 (45.5)	
No	677 (54.6)	2323 (52.0)	
Pre-diagnostic symptoms			
Change in bowel habit	727 (58.6)	2139 (47.9)	<0.001
Frequency	575 (46.4)	1706 (38.2)	<0.001
Stool changes	469 (37.8)	1441 (32.3)	<0.001
Rectal bleeding	728 (58.7)	2175 (48.7)	<0.001
Increased urgency	165 (13.3)	393 (8.8)	<0.001
Abdominal pain	576 (46.5)	1329 (29.8)	<0.001
Abdominal distension	276 (22.3)	668 (15.5)	<0.001
Body weight loss	302 (24.4)	826 (18.5)	<0.001
Tenesmus	255 (20.6)	762 (17.1)	0.004
Anemia	216 (17.4)	570 (12.8)	<0.001
Stool occult blood (+)	92 (7.4)	1436 (32.2)	<0.001
Asymptomatic	59 (4.8)	569 (12.7)	<0.001



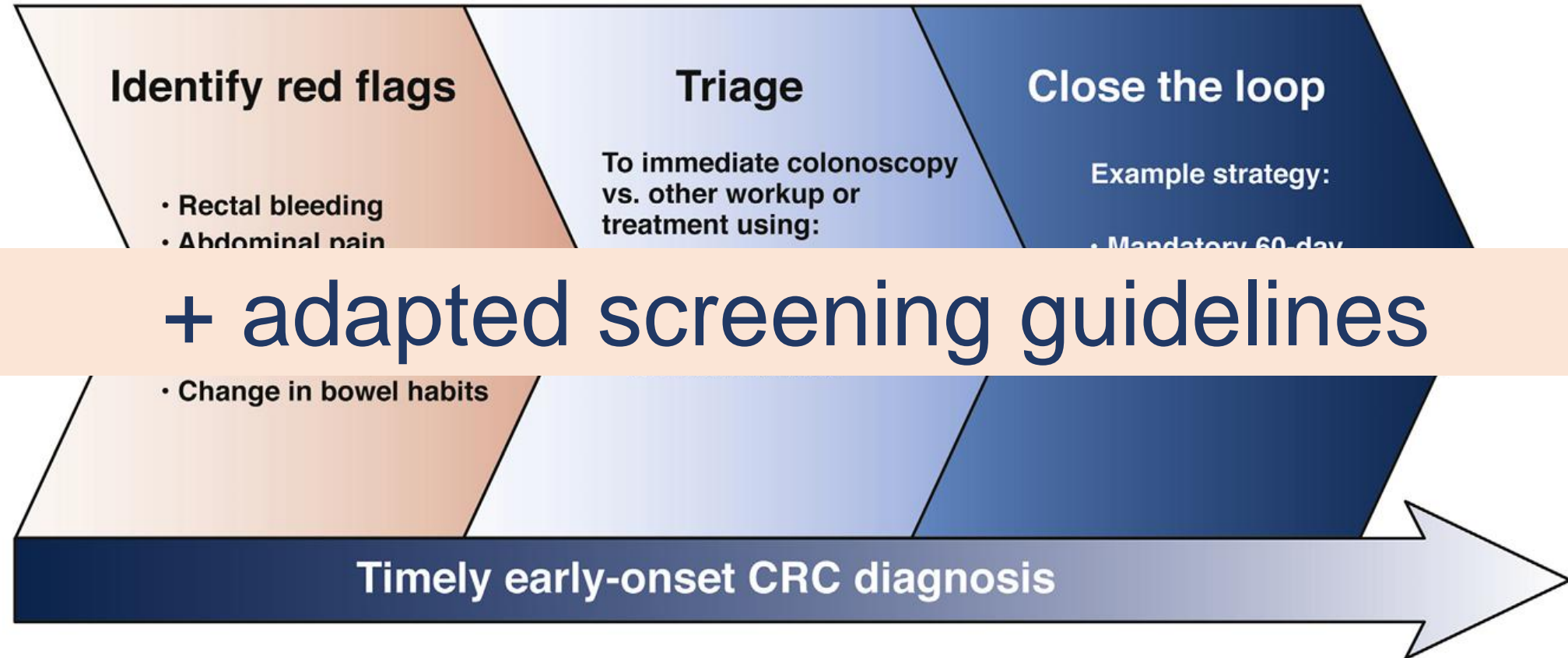
## Rise awareness !

II	207 (20.1)	1170 (26.7)	
III	473 (38.1)	1508 (33.8)	
IV	301 (24.3)	736 (16.5)	
Metastatic organ			
Liver	178 (14.4)	492 (11.0)	0.001
Lung	58 (4.7)	193 (4.3)	0.592
Omentum/peritoneum	116 (9.4)	236 (5.3)	<0.001
Bone	9 (0.7)	14 (0.3)	0.071
Ovary <sup>a</sup>	55 (9.1)	56 (3.1)	<0.001
Systemic LN	54 (4.4)	127 (2.8)	0.007

never	789 (63.7)	2680 (60.0)	
Alcohol			
ever	380 (30.7)	1613 (36.1)	<0.001
never	859 (69.3)	2850 (63.9)	
Coffee			
social	284 (23.0)	770 (16.2)	<0.001
regular	320 (25.9)	793 (17.8)	
never	633 (51.2)	2938 (66.0)	

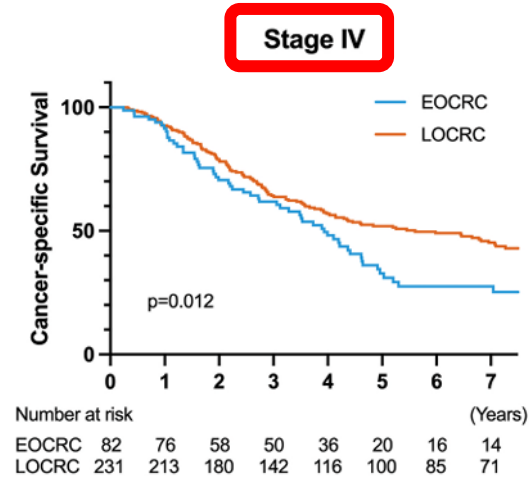
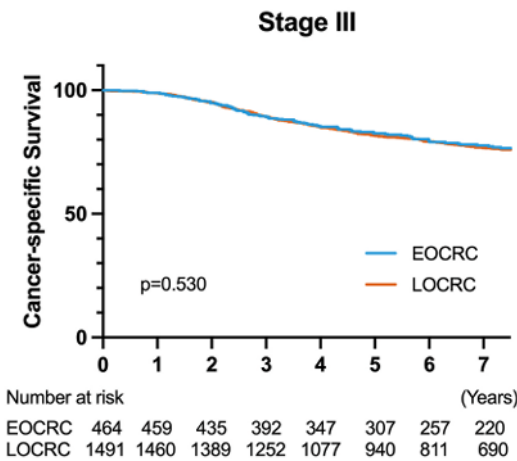
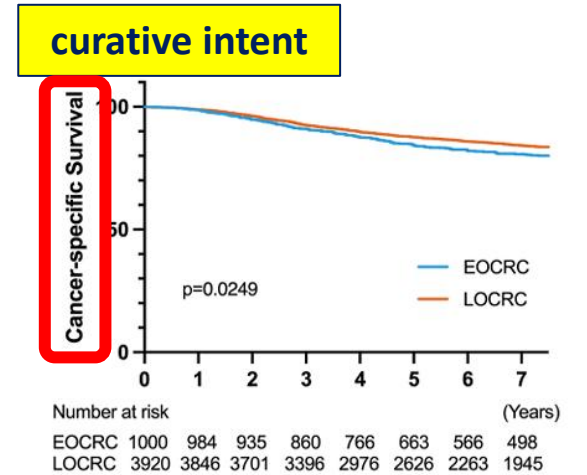
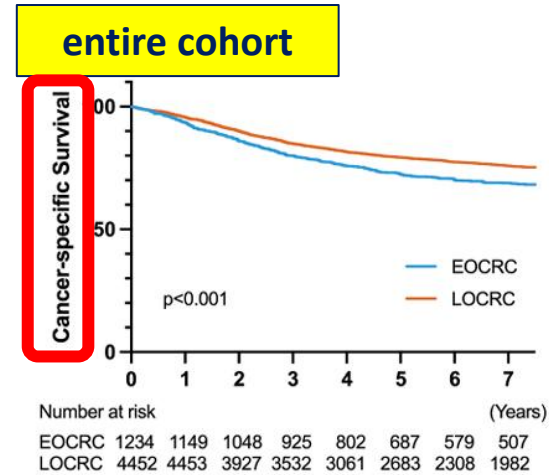
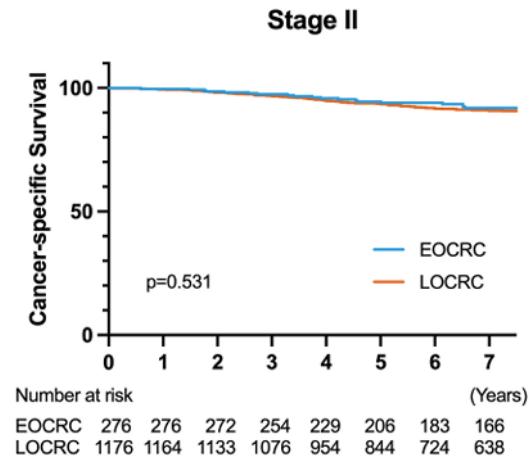
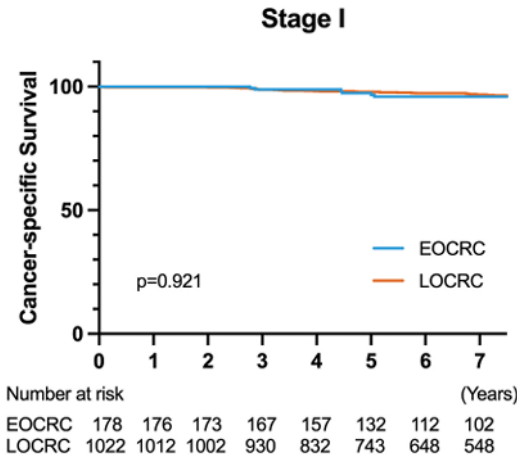


# Workup



# Outcomes by stage

2008-2019  
Clinicopathologic characteristics  
5'700 patients



- Inferior survival (stage IV)
- ↑ symptoms (bleeding, pain)
- Advanced stages at diagnosis
- More aggressive disease characteristics

# How should we treat EOCRC ?

## CLINICAL PRACTICE GUIDELINES

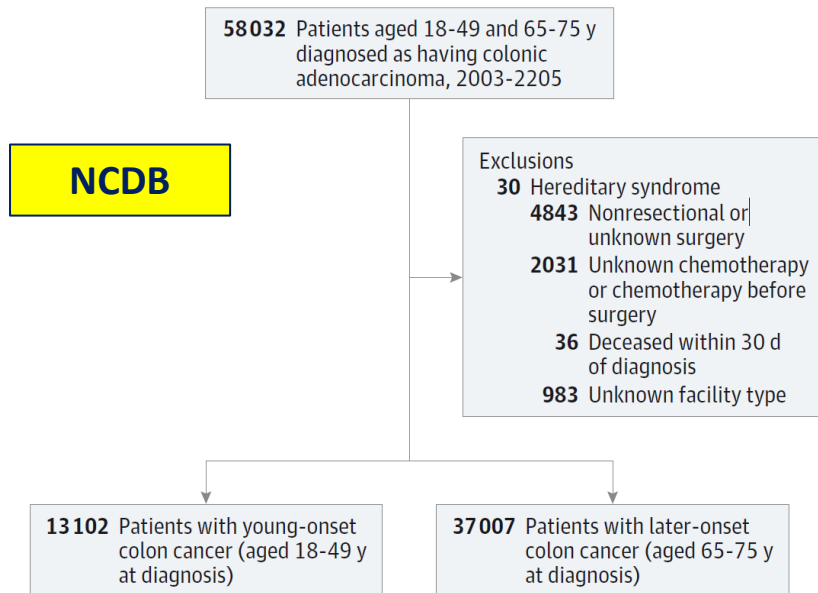
### Delphi Initiative for Early-Onset Colorectal Cancer (DIRECT) International Management Guidelines



Same strategy as for LOCRC

# Same treatment ?

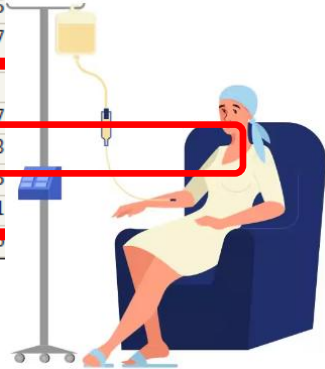
13'000 EOCRC  
National cancer database  
compared to 65-75 yo



Characteristic	Colon Cancer, No. (%)		$\chi^2$ Statistic	P Value
	Young Adults (n = 13 102)	Older Adults (n = 37 007)		
<b>Patient Characteristics</b>				
Sex			3.7	.05
Female	6639 (50.7)	18 389 (49.7)		
Male	6463 (49.3)	18 618 (50.3)		
Race/ethnicity			435.8	<.001
White	10 078 (76.9)	31 423 (84.9)		
African American	2210 (16.9)	4017 (10.9)		
Other	814 (6.2)	1567 (4.2)		
Insurance status			4119.9	<.001
Insured	10 428 (79.6)	35 540 (96.0)		
Medicaid, Medicare, or government	1196 (9.1)	485 (1.3)		
Uninsured	1007 (7.7)	223 (0.6)		
Unknown	471 (3.6)	759 (2.1)		
Median household income quartile, \$			110.9	<.001
<30 000	1837 (14.0)	5212 (14.1)		
30 000 to <35 000	2081 (15.9)	6712 (18.1)		
35 000-45 999	3230 (24.7)	10 106 (27.3)		
≥46 000	5167 (39.4)	12 990 (35.1)		
Unknown	787 (6.0)	1987 (5.4)		
Charles-Deyo Comorbidity Index			2120.6	<.001
0	11 748 (89.7)	25 722 (69.5)		
1	1172 (8.9)	8618 (23.3)		
2	182 (1.4)	2667 (7.2)		

# Colon cancer – adjuvant chemotherapy use

Tumor Characteristics	EOCC	LOCC		
Disease stage at diagnosis			1181.0	<.001
I	1926 (14.7)	8991 (24.3)		
II	3083 (23.5)	11 011 (29.8)		
III	4780 (36.5)	11 202 (30.3)		
IV	3313 (25.3)	5803 (15.7)		
Location			705.8	<.001
Proximal to splenic flexure	5234 (39.9)	19 781 (53.5)		
Distal to splenic flexure	7380 (56.3)	16 163 (43.7)		
Other or unspecified	488 (3.7)	1063 (2.9)		
Pathological stage			104.3	<.001
Well differentiated or moderately differentiated	9576 (73.1)	28 616 (77.3)		
Poorly differentiated or undifferentiated	2869 (21.9)	7005 (18.9)		
Unknown	657 (5.0)	1386 (3.7)		
Histologic grade			116.9	<.001
Nonmucinous adenocarcinoma	11 221 (85.6)	32 433 (87.6)		
Signet ring cell	314 (2.4)	415 (1.1)		
Mucinous	1567 (12.0)	4159 (11.2)		
Overall Treatments				
Treatment facility			358.8	<.001
Community cancer program	2090 (16.0)	7479 (20.2)		
Comprehensive community cancer program	6733 (51.4)	20 451 (55.7)		
Academic or research program, such as comprehensive cancer centers	4279 (32.7)	907 (2.5)		
Use of postoperative systemic chemotherapy				
No	4419 (33.7)	22 277 (60.0)		
Yes	8683 (66.3)	14 731 (40.0)		
Single-agent regimen	2047 (15.0)	495 (1.3)		
Multiagent regimen	5611 (42.8)	781 (2.1)		
Unknown regimen	1025 (7.8)	150 (0.4)		

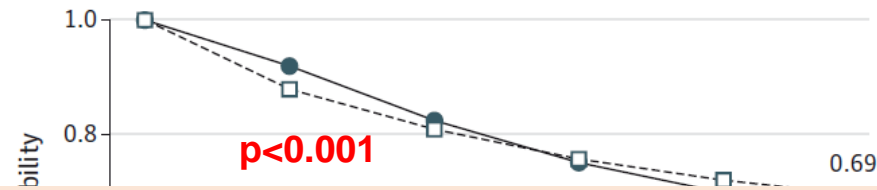


Patients Who Received Chemotherapy	Any Chemotherapy, No. (%)	Odds Ratio for Receiving Chemotherapy (95% CI)	Multiagent Regimens, No. (%)	Odds Ratio for Receiving Multiagent Regimen (95% CI)
<b>Stage I</b>				
Ages 65-75 y (n = 8991)	162 (1.8)	1 [Reference]	52 (43.0)	1 [Reference]
Ages 18-49 y (n = 1926)	109 (5.7)	2.88 (2.21-3.77)	43 (48.3)	1.38 (0.71-2.68)
<b>Stage II Overall</b>				
Ages 65-75 y (n = 11 011)	2748 (25.0)	1 [Reference]	773 (41.7)	1 [Reference]
Ages 18-49 y (n = 3083)	1732 (56.2)	3.93 (3.58-4.31)	670 (54.9)	1.71 (1.48-1.97)
<b>Stage II Low Risk</b>				
Ages 65-75 y (n = 4822)	923 (19.1)	1 [Reference]	313 (39.6)	1 [Reference]
Ages 18-49 y (n = 1636)	826 (50.5)	4.22 (3.70-4.81)	388 (52.5)	1.67 (1.34-2.09)
<b>Stage II High Risk</b>				
Ages 65-75 y (n = 6189)	1825 (29.5)	1 [Reference]	677 (42.7)	1 [Reference]
Ages 18-49 y (n = 1447)	906 (62.6)	3.69 (3.23-4.20)	454 (57.0)	1.77 (1.46-2.14)
<b>Stage III</b>				
Ages 65-75 y (n = 11 202)	8175 (73.0)	1 [Reference]	4209 (59.4)	1 [Reference]
Ages 18-49 y (n = 4780)	4132 (86.4)	2.42 (2.18-2.68)	2590 (71.5)	1.75 (1.58-1.93)
<b>Stage IV</b>				
Ages 65-75 y (n = 5803)	3652 (62.9)	1 [Reference]	2567 (80.4)	1 [Reference]
Ages 18-49 y (n = 3313)	2710 (81.8)	2.74 (2.44-3.07)	2136 (88.6)	1.90 (1.60-2.26)

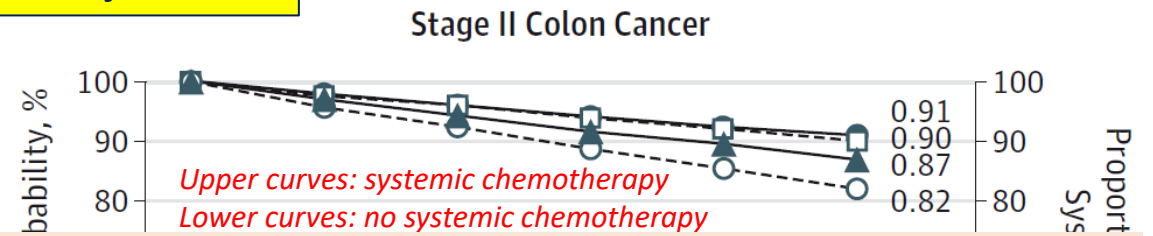
# Colon cancer – adjuvant chemotherapy use



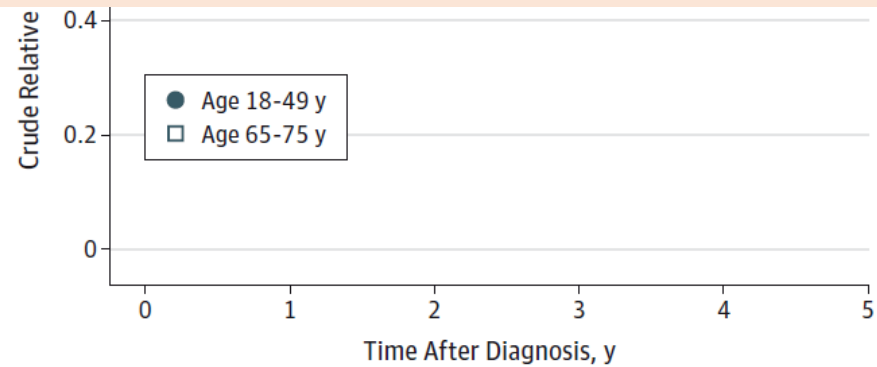
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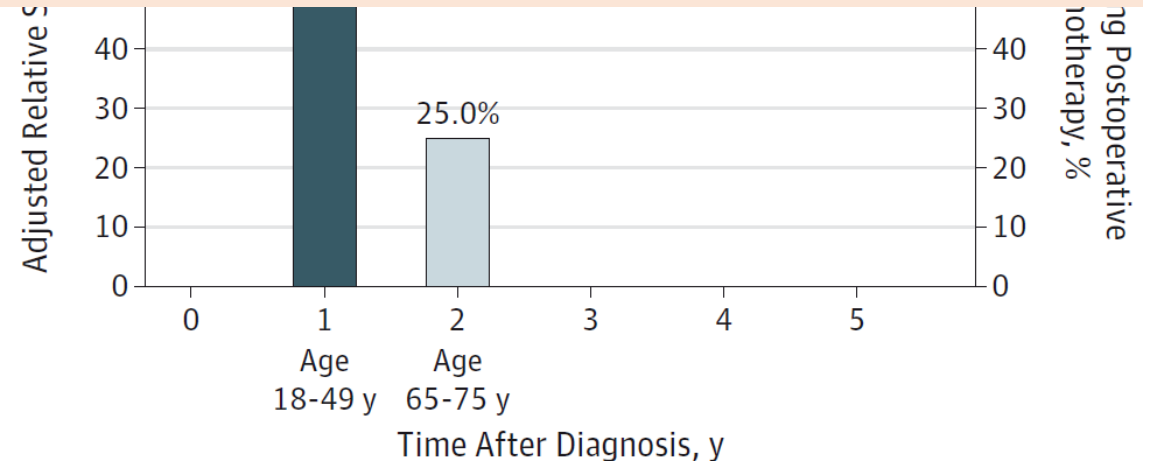
**adjusted**



**No survival benefit !**



Consider more advanced stages !!



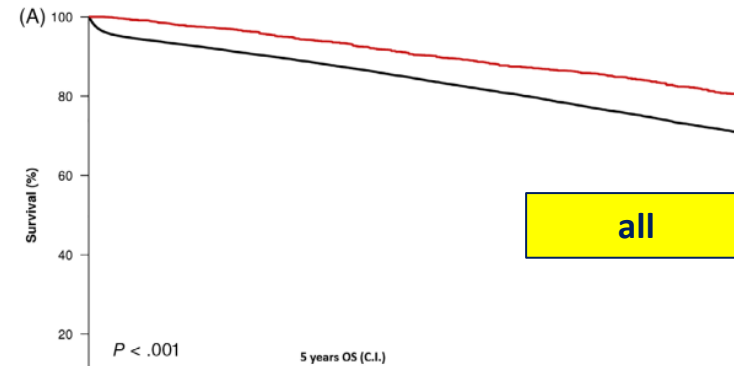
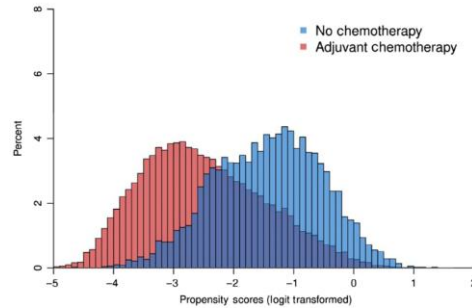
# Survival impact of adjuvant chemotherapy in patients with stage IIA colon cancer: Analysis of the National Cancer Database

T3N0



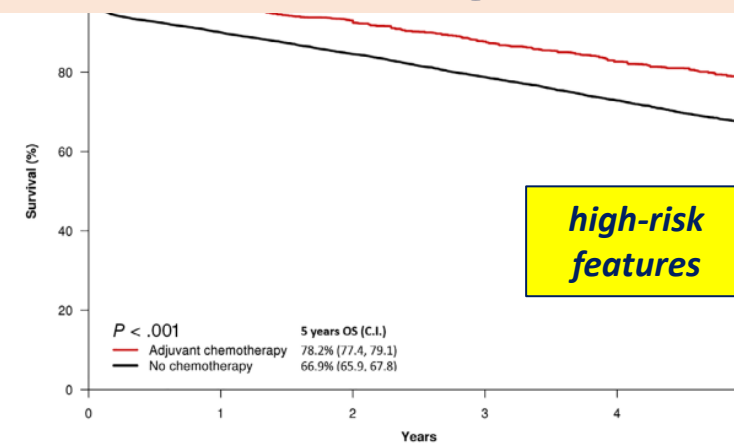
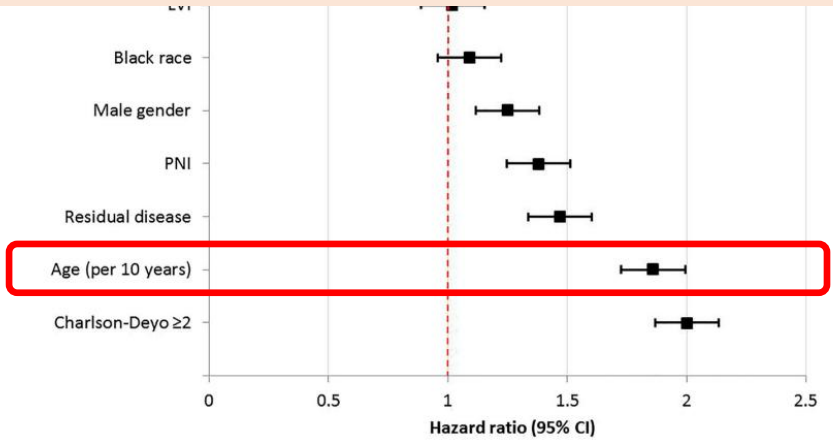
12.7% received adjuvant chemotherapy

IPTW



High risk features:  
IVI

## Benefit in stage IIA with high-risk features ?



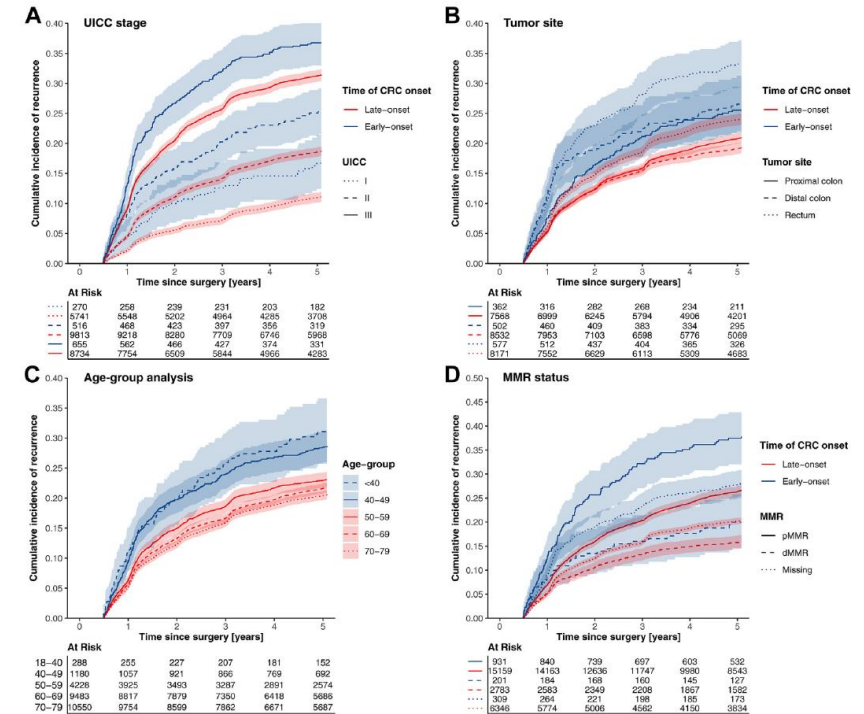
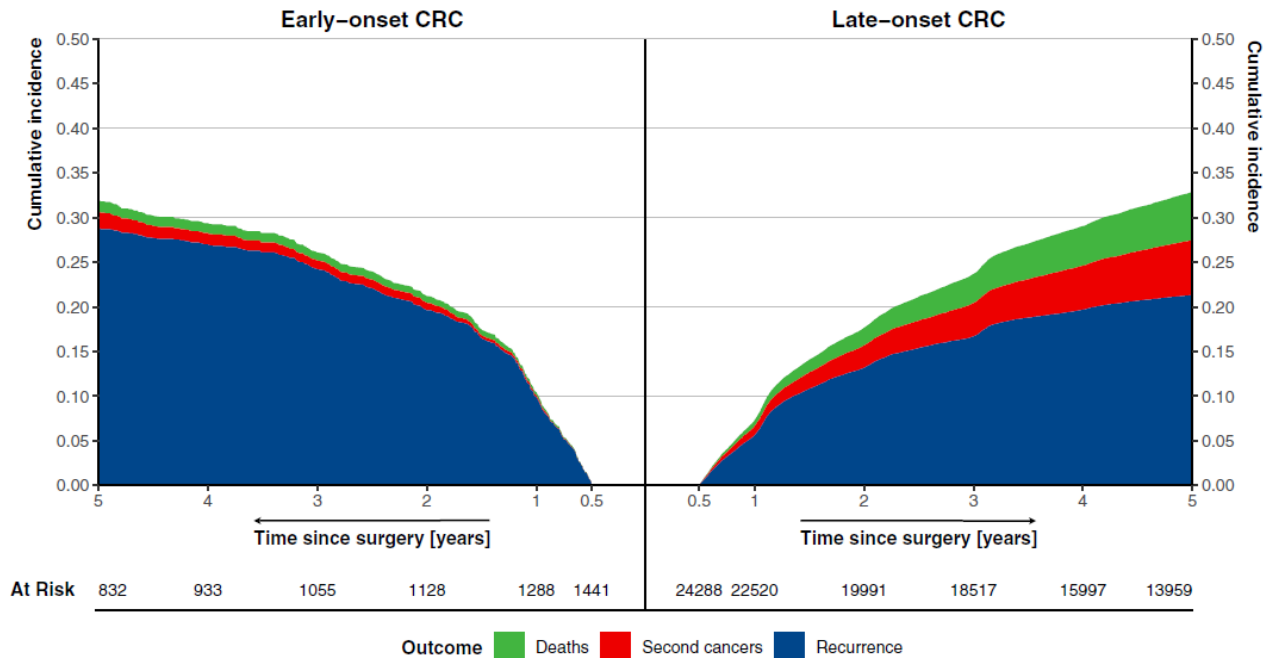


# Recurrence

Risk of recurrence in early-onset versus late-onset non-metastatic colorectal cancer **2004-2019**: a nationwide cohort study



UICC stages I-III CRC  
> 25'000 patients  
5.6% EO CRC

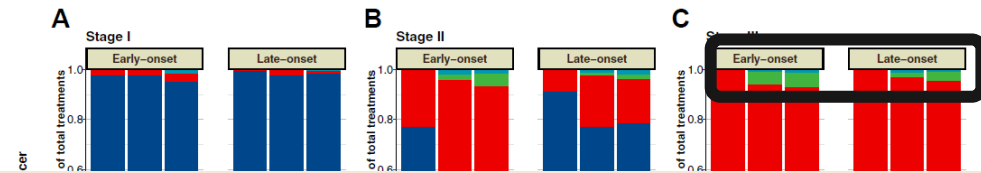


# Recurrence

Risk of recurrence in early-onset versus late-onset non-metastatic colorectal cancer **2004-2019**: a nationwide cohort study

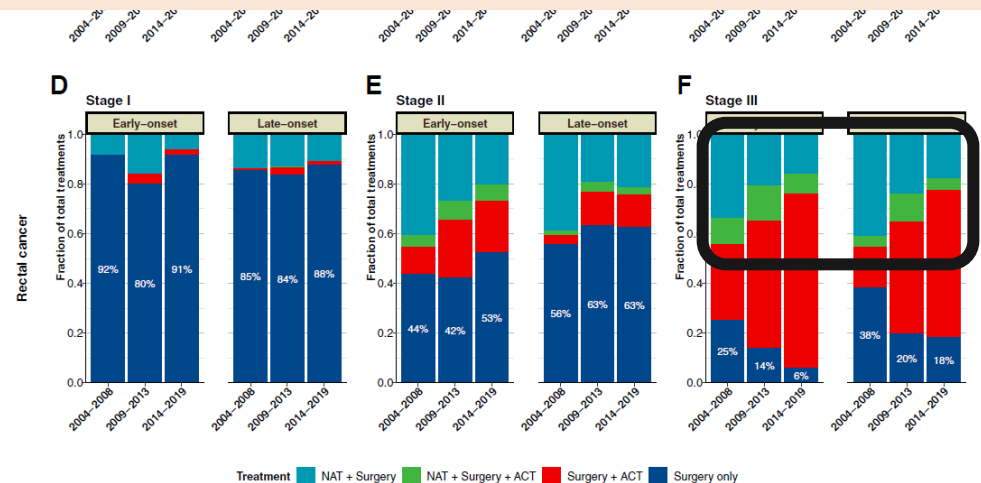


UICC stages I-III CRC  
> 25'000 patients  
5.6% EOCRC



Variable	Cumulative incidence function <sup>a</sup>					Fine-Gray <sup>b</sup>		Cox PH <sup>b</sup>	
	N	N Event	1-year CIF	3-year CIF	5-year CIF	sHR	CI	HR	CI
All									
Early-onset	1441	411	11% (95% CI: 9.9%-13%)	25% (95% CI: 22%-27%)	29% (95% CI: 26%-31%)	1.31	1.18	1.27	1.15

## Recurrence risk decreased in recent years



Treatment: NAT + Surgery (light blue), NAT + Surgery + ACT (green), Surgery + ACT (red), Surgery only (dark blue)

CRC						1.18		1.10	
Late-onset CRC	6584	1851	8.5% (95% CI: 7.8%-9.2%)	22% (95% CI: 21%-23%)	28% (95% CI: 27%-29%)	1	Reference	1	Reference
2009-2013									
Early-onset CRC	449	135	12% (95% CI: 9.2%-15%)	25% (95% CI: 22%-30%)	30% (95% CI: 26%-34%)	1.31	1.10, 1.17	1.28	1.18, 1.13
Late-onset CRC	6829	1564	8.0% (95% CI: 7.3%-8.6%)	19% (95% CI: 18%-20%)	23% (95% CI: 22%-24%)	1	Reference	1	Reference
2014-2019									
Early-onset CRC	554	107	8.3% (95% CI: 6.2%-11%)	18% (95% CI: 15%-21%)	20% (95% CI: 17%-23%)	1.10	0.90, 1.14	1.07	0.88, 1.11
Late-onset CRC	10,875	1735	5.6% (95% CI: 5.2%-6.1%)	14% (95% CI: 13%-14%)	16% (95% CI: 16%-17%)	1	Reference	1	Reference

# De-escalation strategies



## MSS

- IDEA (adjuvant)
- FOxTROT (reports initially reported as negative in ASCO 2019 + 2020)

## MSI

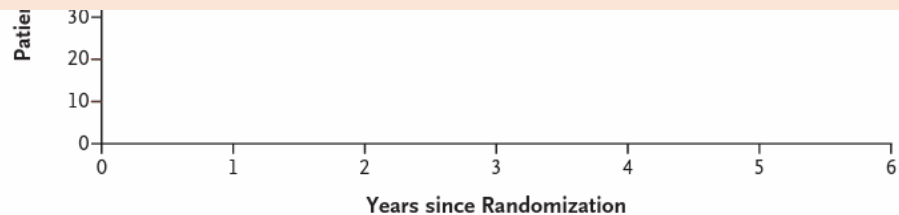
- NICHE II

## Duration of Adjuvant Chemotherapy for Stage III Colon Cancer

Disease-free Survival in Overall Population



Consider 3 months of adjuvant ttt



No. at Risk	0	1	2	3	4	5	6
6 Months	6410	5530	4477	3065	1679	873	334
3 Months	6424	5446	4464	3000	1609	826	321

Stage III colon cancer

✓ CAPOX: 3 months of therapy as effective as 6 months

→ Higher rate of DFS in the 0-6 months group for FOLFOX

Choice of treatment has to be balanced against the substantial risk of increased toxicity (persistent neurotoxicity)

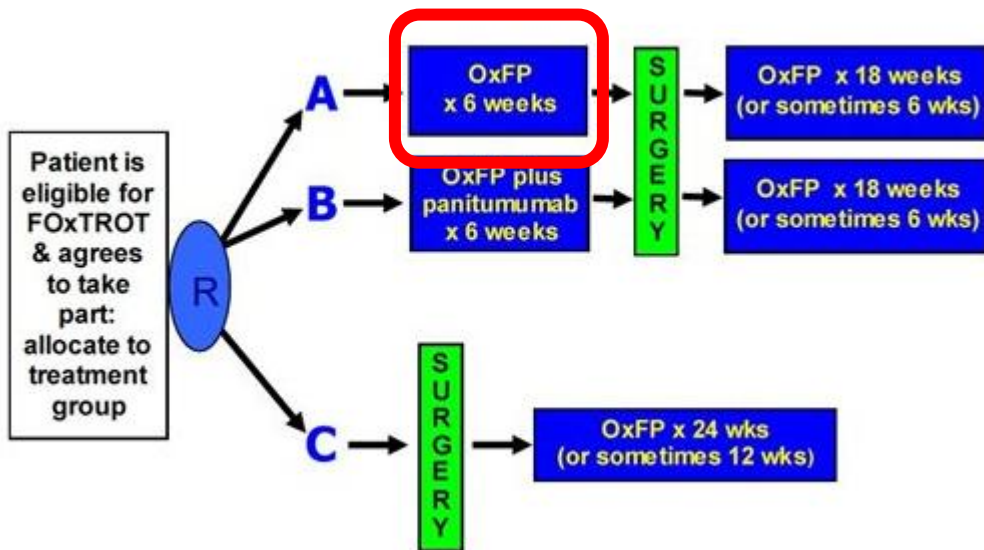
45 yo F

# Scenario 1

cT4 situation



# Preoperative Chemotherapy for Operable Colon Cancer: Mature Results of an International Randomized Controlled Trial



MSS

CT-predicted T3 or T4

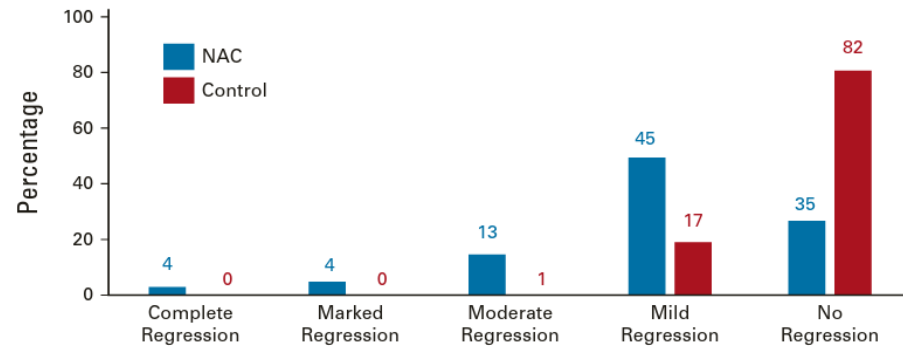
Primary endpoints:

- Freedom from recurrence
- Pathological down-staging

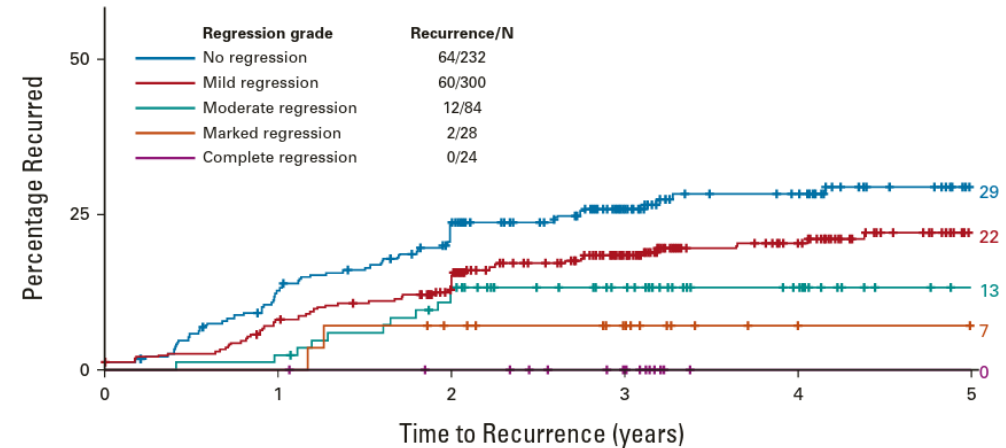
# Preoperative Chemotherapy for Operable Colon Cancer: Mature Results of an International Randomized Controlled Trial



## Pathological down-staging

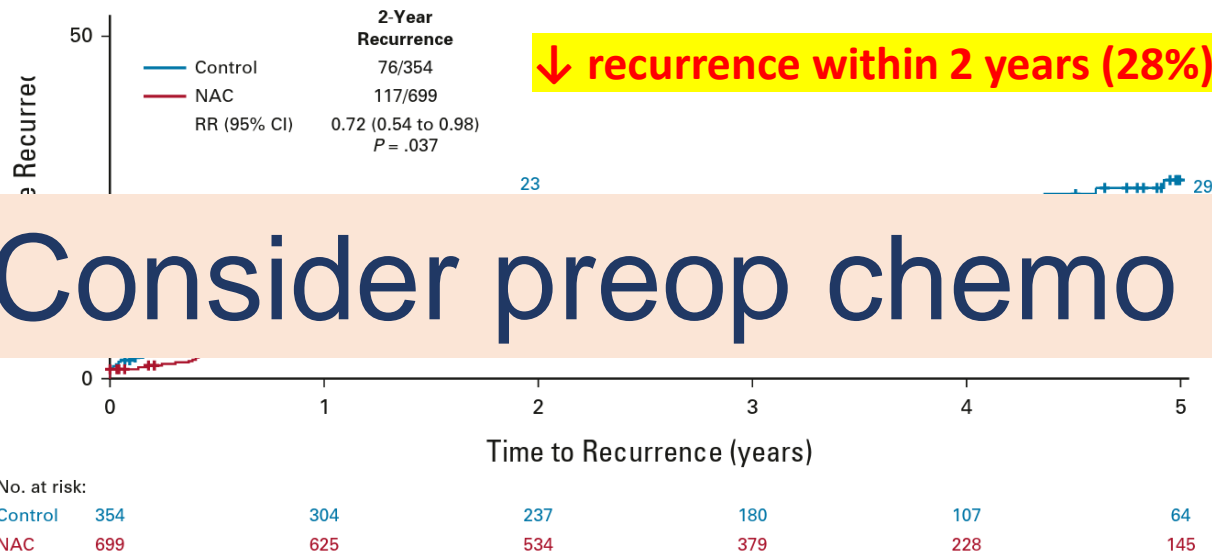


## Freedom from recurrence



No. at risk:	0	1	2	3	4	5
No regression	232	200	167	116	73	48
Mild regression	300	273	236	167	101	58
Moderate regression	84	82	71	56	40	27
Marked regression	28	28	24	17	7	5
Complete regression	24	24	22	15	6	6

# Preoperative Chemotherapy for Operable Colon Cancer: Mature Results of an International Randomized Controlled Trial



Consider preop chemo in MSS colon cancer

downstaging

✓ Reduces likelihood of incomplete resection





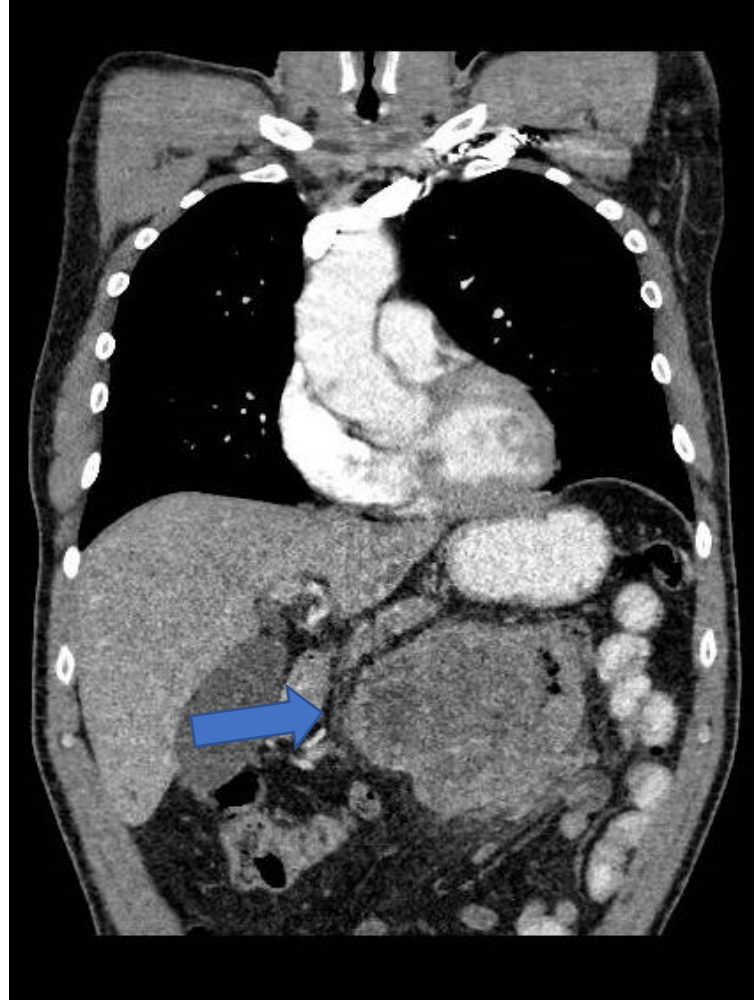
- ✓ Radiological misclassification (low-risk tumors): **24% T3 N0 in FOxTROT**
- ✓ High-risk operable colon cancer: **10 patients to treat to prevent 1 recurrence**
- BUT:** ✓ TRG after neoadjuvant chemotherapy: **may help to tailor adjuvant chemotherapy**

60 yo M

**MSI**

Bulky tumor situation

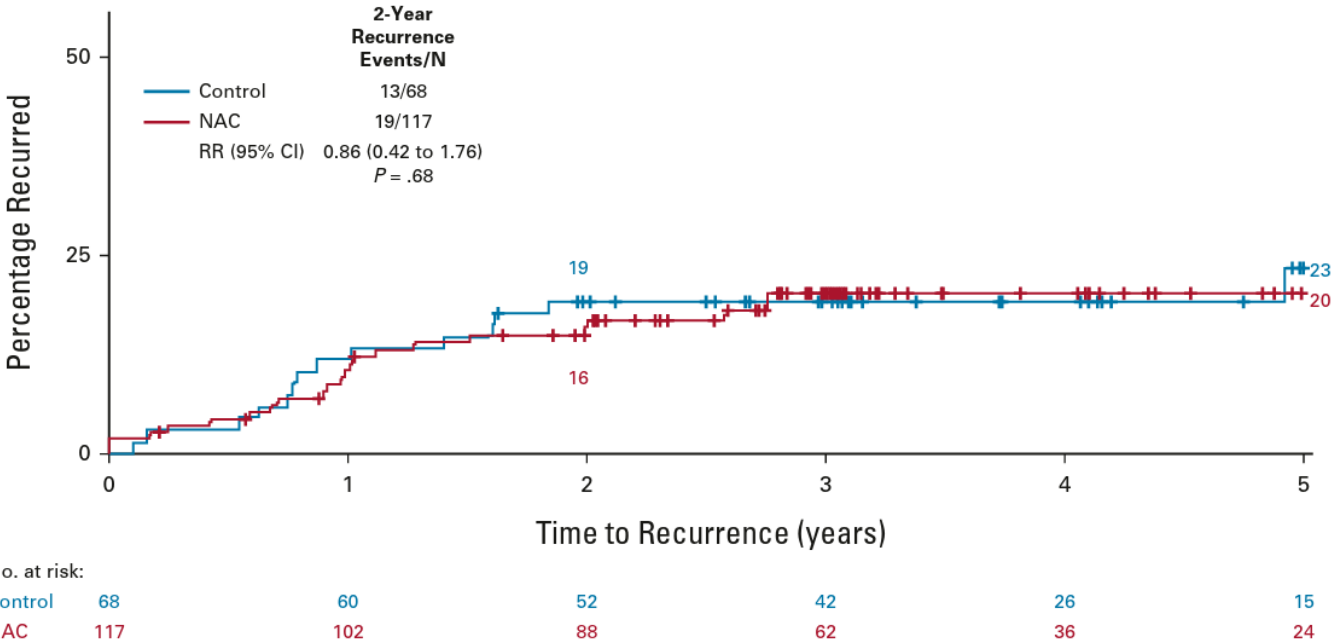
## Scenario 2



# Preoperative Chemotherapy for Operable Colon Cancer: Mature Results of an International Randomized Controlled Trial



## Subgroup MSI patients



## MSI

≈ 15% of all colon cancers

Less chemo-sensitive

- Adjuvant
- neoadjuvant (FOxTROT)
- neoadjuvant rectal (TNT)

Associated with LYNCH syndrome

(rectal > colon)

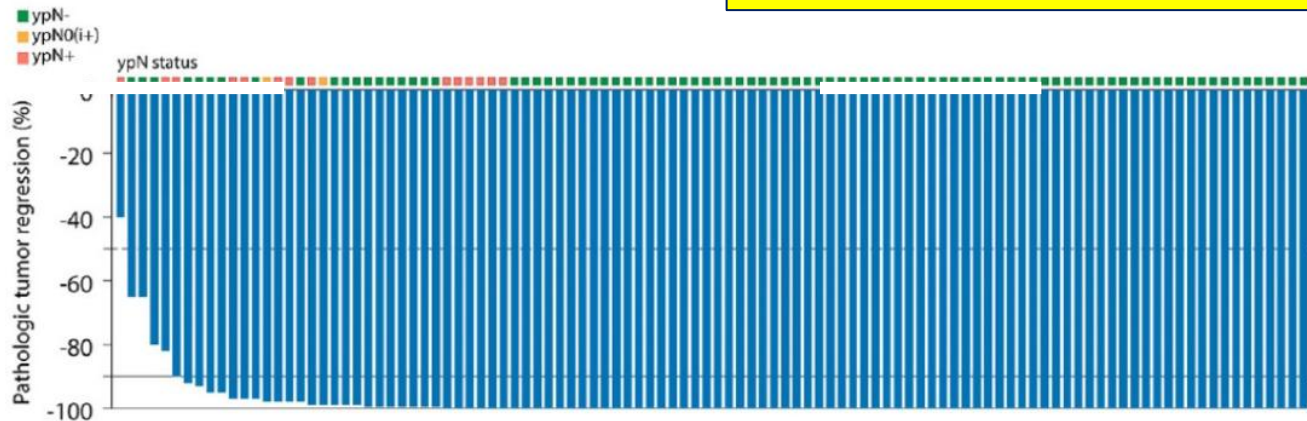
# NICHE-2: 'Unprecedented' Waterfall Plot Achieved With Neoadjuvant Immunotherapy in dMMR Colon Cancer

PARIS 2022 **ESMO** congress

#ESM022

Major PR: 95% / pCR: 67%

MSI



ypN- = post-treatment pathologic lymph nodes tumor-free; ypN+ = post-treatment pathologic lymph nodes with tumor; ypN(i) = post-treatment pathologic lymph nodes with isolated tumor cells. Patients with pathologic complete responses in the primary tumor and viable tumor rest (N+ or N(i+)) in the lymph nodes are considered major pathologic responders.

Non-metastatic, resectable, untreated colon ADK

Original cohort:

30 dMMR vs. 30 pMMR

# NICHE-2: 'Unprecedented' Achieved With Neoadjuvant Immunotherapy in dMMR



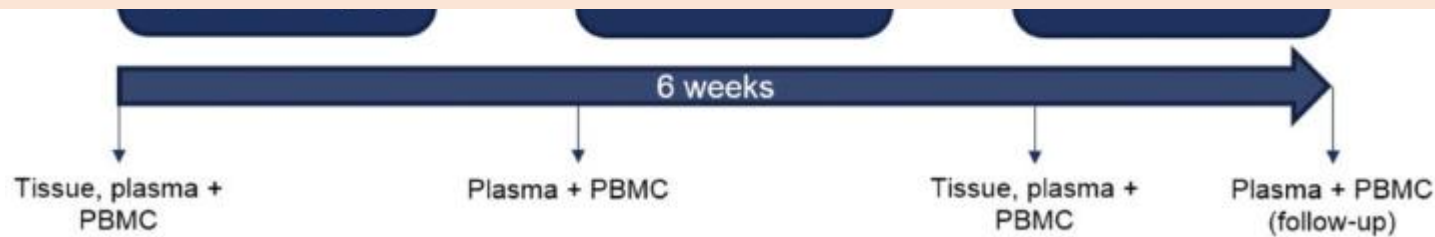
MSI

## NICHE-2 study design

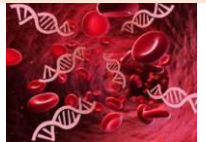
- Investigator-initiated, non-randomized multicenter\*

- Beware of immune-related AE
- Lynch > sporadic dMMR

# MSI and colon cancer = jackpot

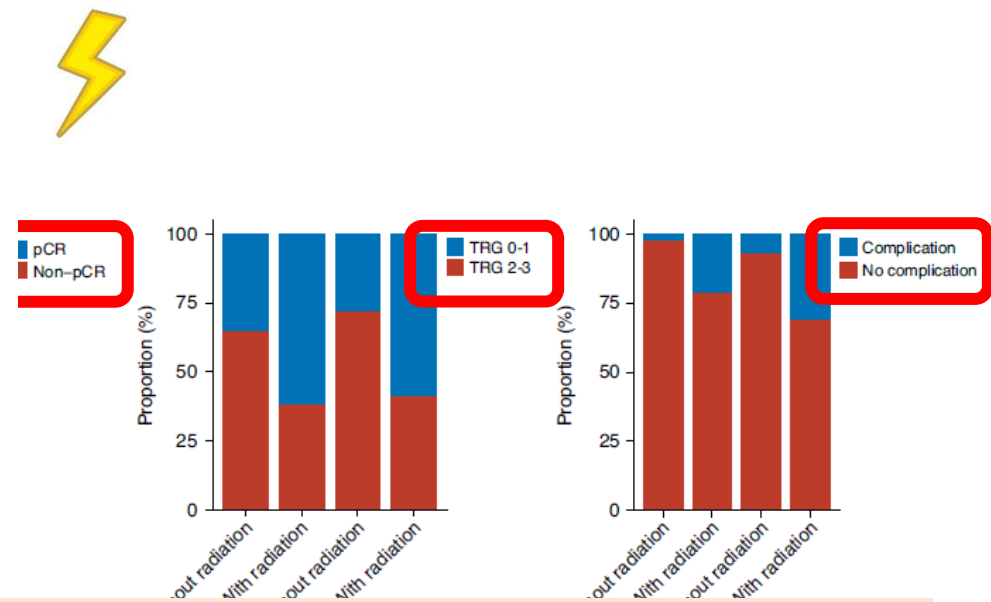
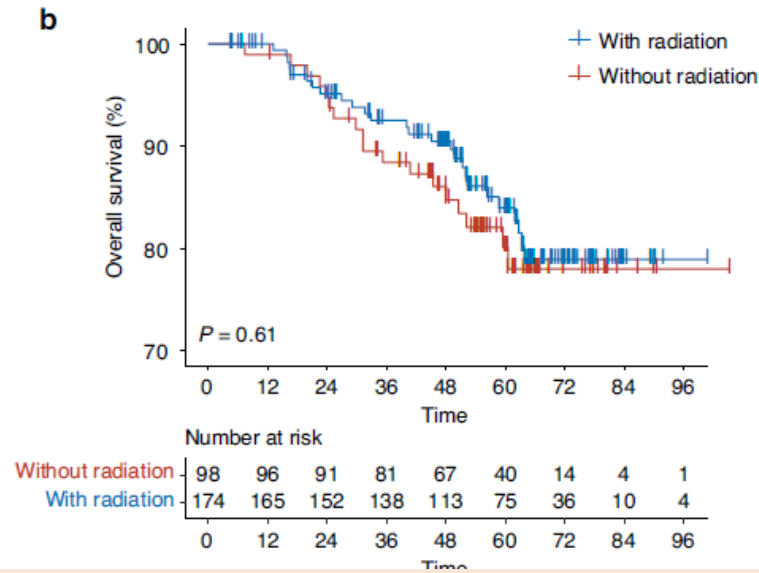
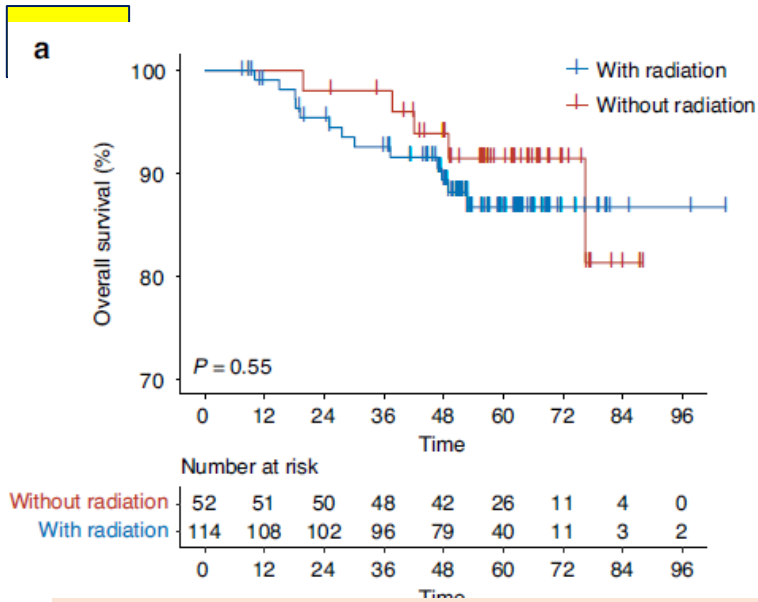


Cancer

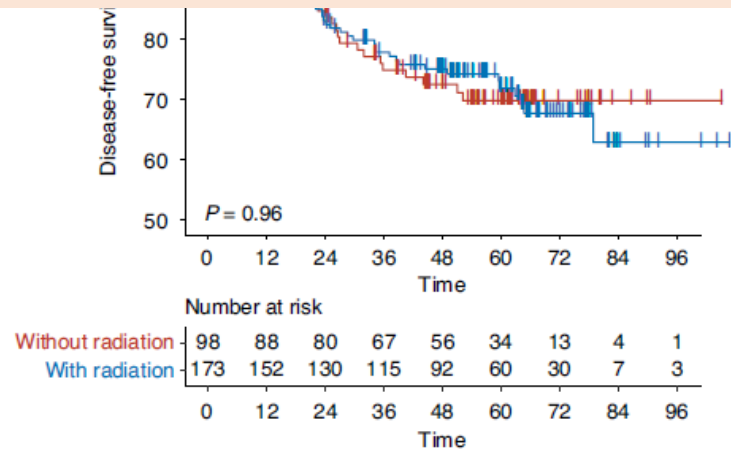
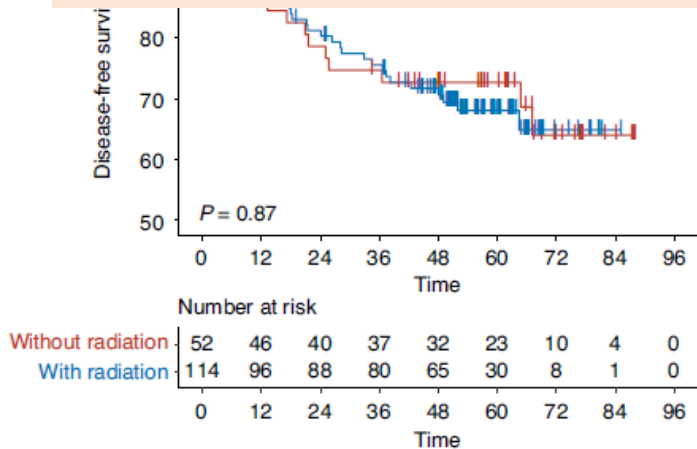


- Strictures !





**Improved TRG, but no survival benefit !**

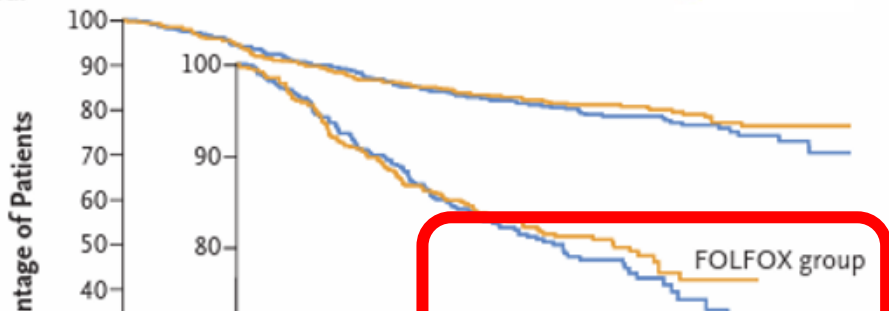


**PROSPECT TRIAL**

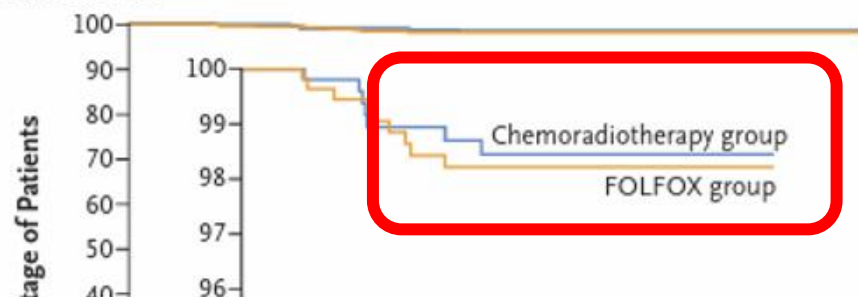


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Disease-free Survival



Freedom from Local Recurrence



**Consider omitting radiotherapy**

Group	No. at Risk								No. of Events/ Total No.	Hazard Ratio (90.2% CI)	5-Year Estimate percent	Stratified P Value for NI
	0	12	24	36	48	60	72	84				
FOLFOX group	585	543	489	443	342	200	97	42	0.92 (0.74–1.14)	80.8 (77.9–83.7)	0.005	
Chemoradiotherapy group	543	500	456	395	295	181	80	37				

Group	No. at Risk								No. of Events/ Total No.	Hazard Ratio (95% CI)	5-Year Estimate percent
	0	12	24	36	48	60	72	84			
FOLFOX group	585	542	483	438	339	195	95	39	9/585	1.18 (0.44–3.16)	98.2 (97.1–99.4)
Chemoradiotherapy group	543	499	455	438	289	175	78	36			

# Early rectal cancer

## Organ Preservation in cT2N0 Rectal Cancer After Neoadjuvant Chemoradiation Therapy

### The Impact of Radiation Therapy Dose-escalation and Consolidation Chemotherapy

Angelita Habr-Gama, MD, PhD,\*†, Guilherme Pagin São Julião, MD,\* Bruna Borba Vailati, MD,\*  
 Jorge Sabbaga, MD, PhD,‡, Patricia Bailão Aguilar, MD,§, Laura Melina Fernandez, MD,\*  
 Sergio Eduardo Alonso Araújo, MD, PhD,† and Rodrigo Oliva Perez, MD, PhD\*†¶

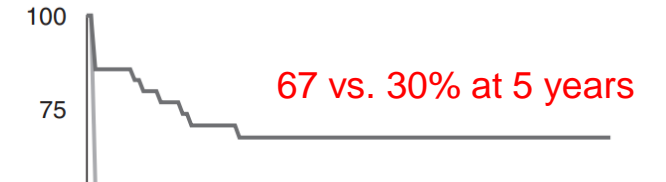


Extended CRT  
 (54 Gy + 6 cycles)

#### T2N0 Patients

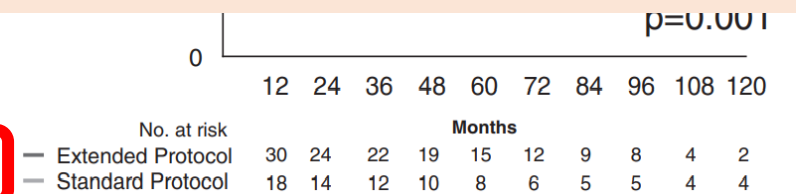
	Extended CRT (n = 35)	Standard CRT (n = 46)	P
Age, yrs	61 (36–82)	61 (30–86)	0.84
Sex (male–female)	24–11 (68.6%–31.4%)	27–19 (58.7%–41.3%)	0.48
Tumor size, mm	40 (15–70)	30 (10–73)	0.36
Distance anal verge, cm	3 (0–7)	3 (0–11)	0.94
Initial CEA level, ng/mL	2 (1–137)	2 (1–18)	0.41
Systemic recurrence	9 (25.7%)	9 (19.6%)	0.33
Death related to cancer	0 (27.3%)	3 (16.3%)	0.55
Initial cCR at 8-10 weeks	30 (85.7%)	26 (56.5%)	<0.001

#### 5-year surgery-free survival



# 67% organ preservation !

	21–9 (70%–30%)	10–10 (61.3%–38.7%)	P
Sex (male–female)	21–9 (70%–30%)	10–10 (61.3%–38.7%)	0.57
Tumor size, mm	40 (15–50)	30 (20–73)	0.48
Distance anal verge, cm	3 (0–7)	3 (0–11)	0.84
Initial CEA level, ng/mL	2 (1–6)	2 (1–4)	0.73
Regrowth (first 12 mos)	1 (2.3%)	4 (15.4%)	0.17
Late recurrence (after 12 mos)*	5/29 (17.2%)	4/22 (18.2%)	1.00
Local recurrence	6 (20%)	8 (30.8%)	0.37
Systemic recurrence	5 (16.1%)	5 (11.3%)	0.71
Death related to cancer	4 (13.3%)	—	0.11





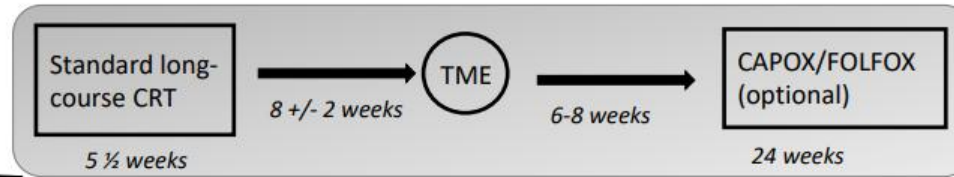
# LARC : RAPIDO vs. PRODIGE 23



## modified RAPIDO

MRI staging  
At least one of:  
cT4a, cT4b, EMVI+,  
N2, positive MRF, lat  
LN+

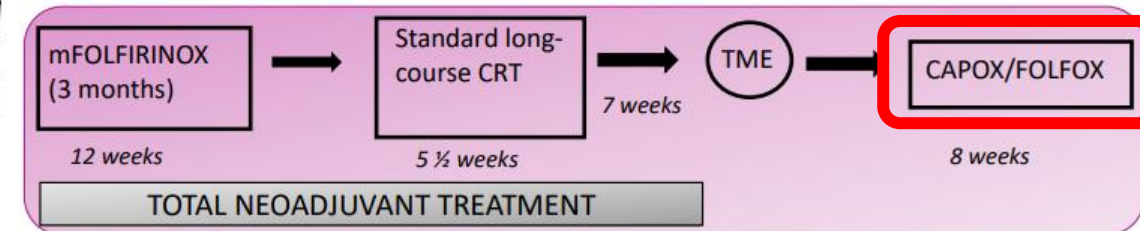
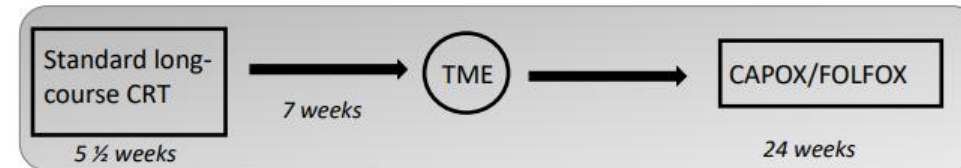
Primary endpoint:  
DrTF



## modified PRODIGE 23

MRI staging  
cT3 with risk of local  
recurrence or cT4,

Primary endpoint:  
DFS

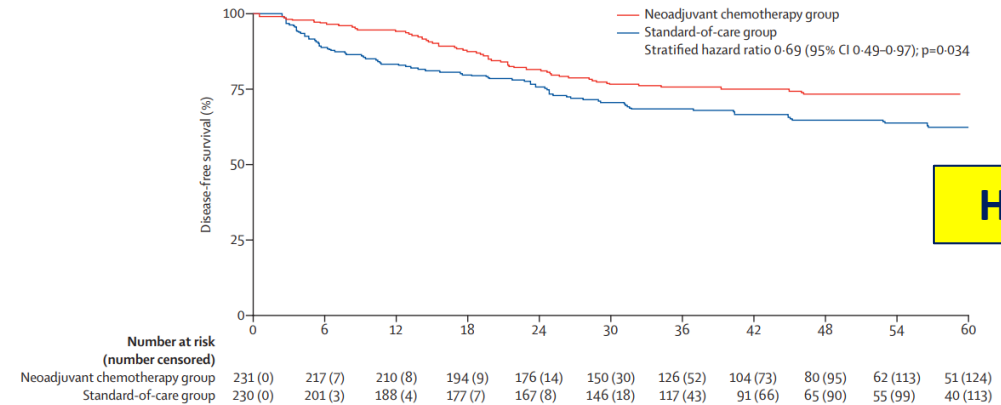


# PRODIGE 23

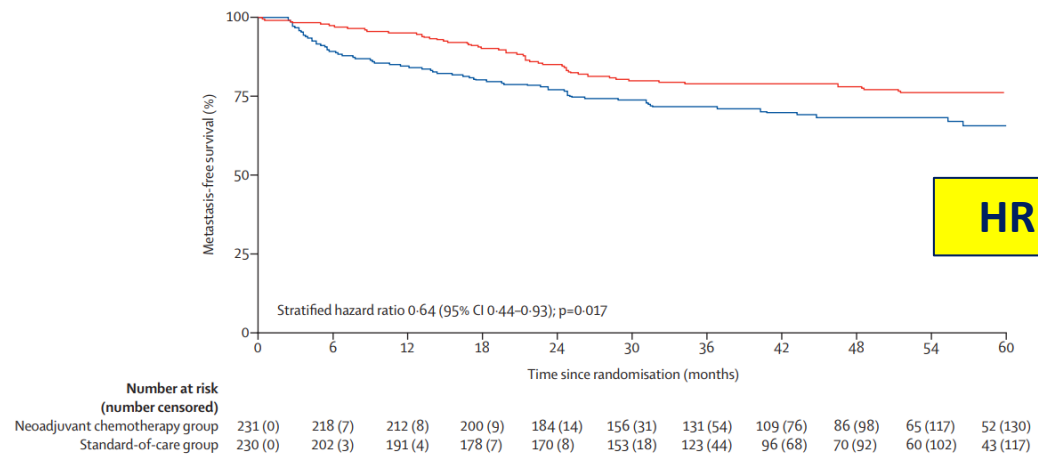


	Neoadjuvant chemotherapy group (n=231)	Standard-of-care group (n=230)
MRI T stage*		
T2	3/225 (1%)	2/225 (1%)
T3	182/225 (81%)	188/225 (84%)
T3a	17/225 (8%)	17/225 (8%)
T3b	77/225 (34%)	92/225 (41%)
T3c	73/225 (32%)	64/225 (28%)
T3d	15/225 (7%)	15/225 (7%)
T4	40/225 (18%)	35/225 (16%)
T4a	3/225 (1%)	4/225 (2%)
T4b	37/225 (16%)	31/225 (14%)
Missing	6	5
cN at inclusion*		
0†	24 (10%)	22 (10%)
1	148 (64%)	155 (67%)
2	59 (26%)	53 (23%)

ypT0N0 rate: 27.5% vs. 11.7%



**HR 0.69**



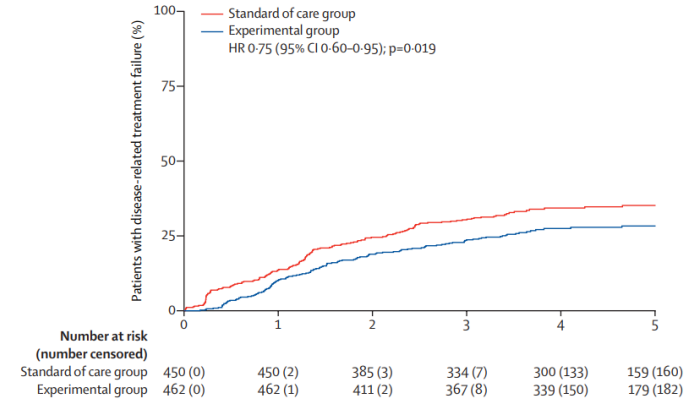
**HR 0.64**

# RAPIDO

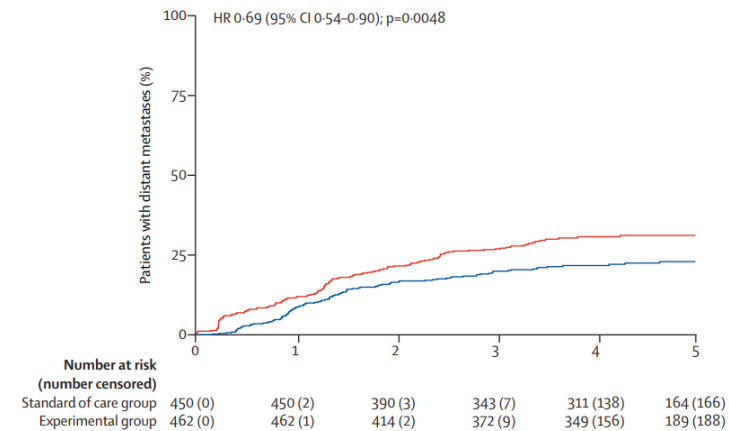


	Experimental group (n=462)	Standard of care group (n=450)
<b>Clinical T stage*†</b>		
cT2	14 (3%)	14 (3%)
cT3	301 (65%)	299 (66%)
cT4	147 (32%)	137 (30%)
<b>Clinical N stage*†</b>		
cN0	42 (9%)	35 (8%)
cN1	118 (26%)	120 (27%)
cN2	302 (65%)	295 (66%)
<b>Other high-risk criteria†</b>		
Enlarged lateral nodes	66 (14%)	69 (15%)
Extramural vascular invasion positive	148 (32%)	125 (28%)
Mesorectal fascia positive	285 (62%)	271 (60%)

ypT0N0 rate: 27.7% vs. 13.8%



**HR 0.75**



**HR 0.69**

# RAPIDO 5-year results

## PATTERNS OF LOCOREGIONAL FAILURE AND DISTANT METASTASES IN PATIENTS TREATED FOR LOCALLY ADVANCED RECTAL CANCER IN THE RAPIDO TRIAL

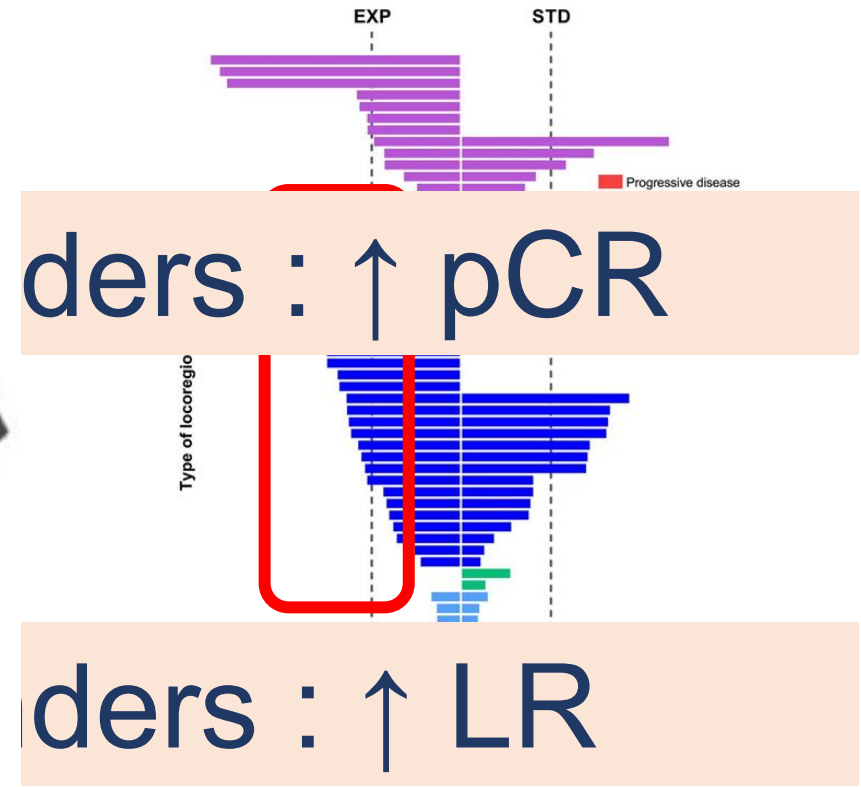
Long delay

➤ Increases



7%

Long delay



# Induction vs. consolidation

## INDUCTION

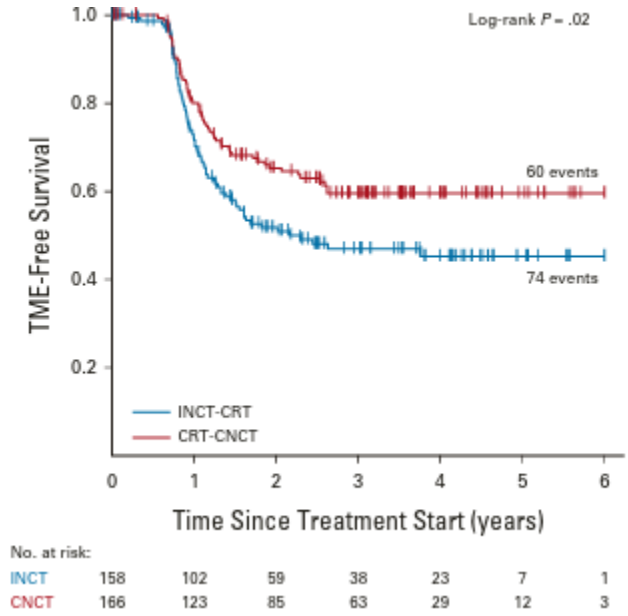
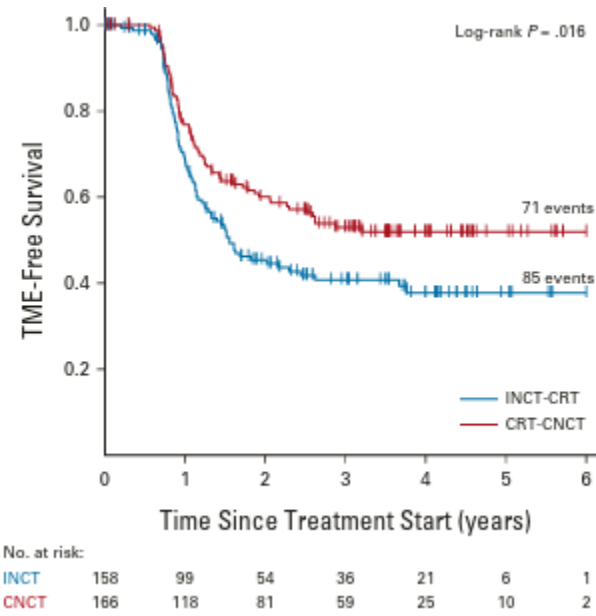
- ✓ Assessing tumor biology
- ✓ High risk factors for distant recurrence (tumor regression, EMVI+, poor TRG)

Selective tool for de-escalation in aggressive tumors (distant mets!!)

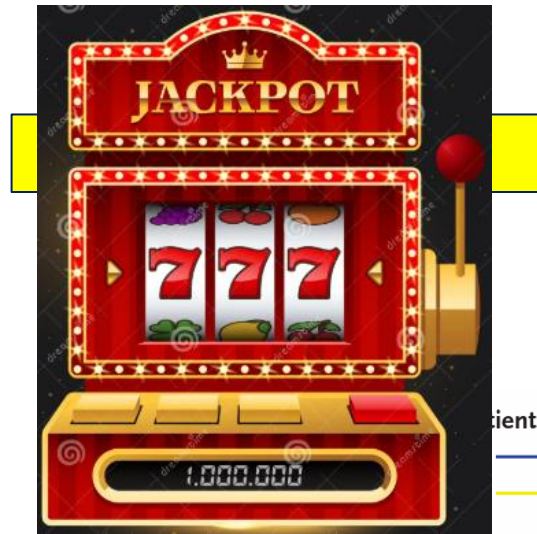
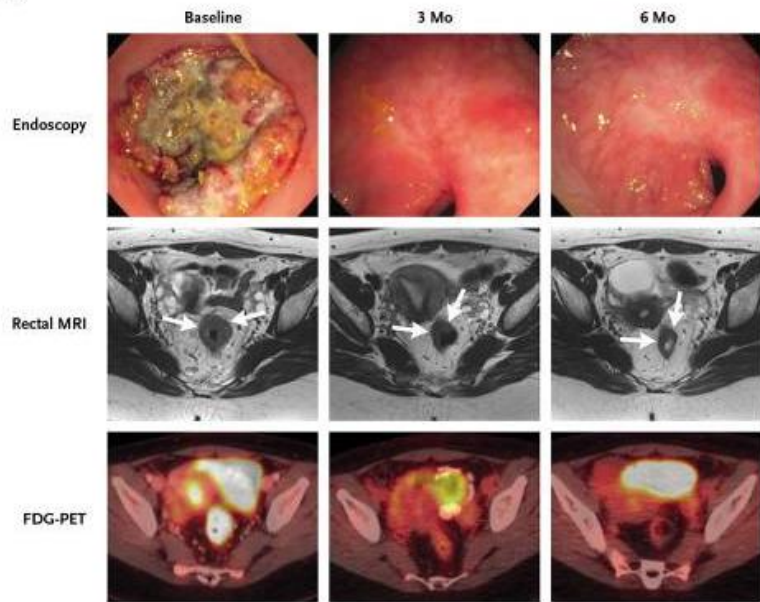
## CONSOLIDATION

- ✓ For low rectal cancers (maximal response!!)

Selective tool for de-escalation in distal tumors (sphincter sparing...)



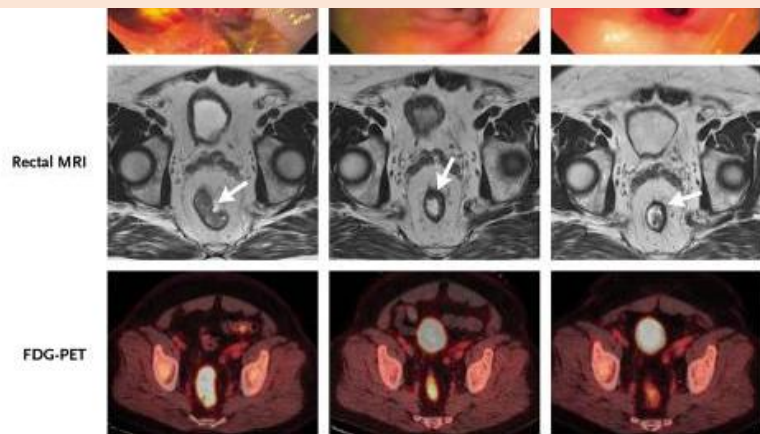
A Patient 2



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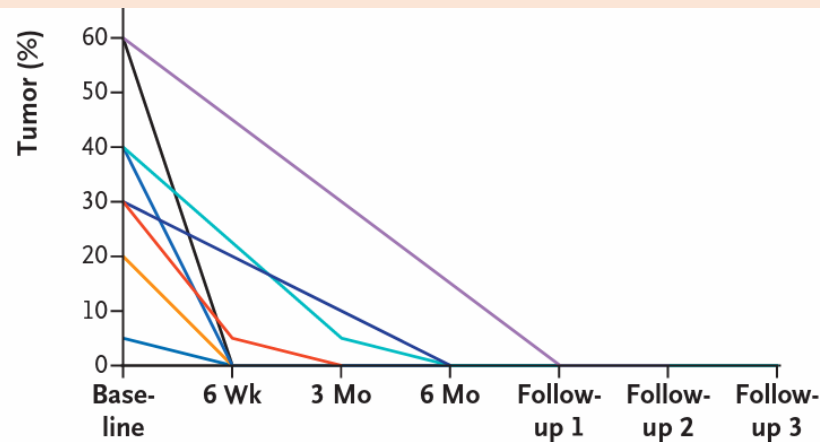
Prospective phase II  
Dostarlimab

B Patient 9



# MSI in rectal cancer: 2<sup>nd</sup> jackpot situation

Then CRT + surgery





# EOCRC

- ✓ symptoms warrant high degree of suspicion
- ✓ better treatment tolerance in young patients but :
- ✓ beware of overtreatment
- ✓ consider de-escalation strategies
- ✓ treat like LOCRC





# Thank you !

