Role of RT Rectal Cancer

COLORECTA2024L SYMPOSIUM 2024

Role of RT

- Early Stage –T1,T2, N0
- Locally Advanced (≥T3 , ≥N: Locally Advanced -operable)
- Inoperable/Unresectable

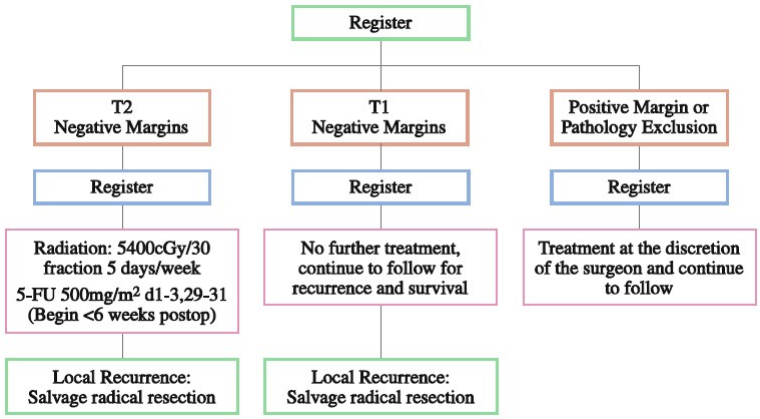
Role of RT- T1,T2,N0

Surgery Alone- Total Mesorectal Excision(TME) –No role of RT

Trans Anal Local Excision Criteria:

- <3cm
- <30% of circumference
- within 8 cm from anal verge
- Mobile, not fixed
- W.D to M.D.
- No PNI or LVI

CALGB Trial 8984



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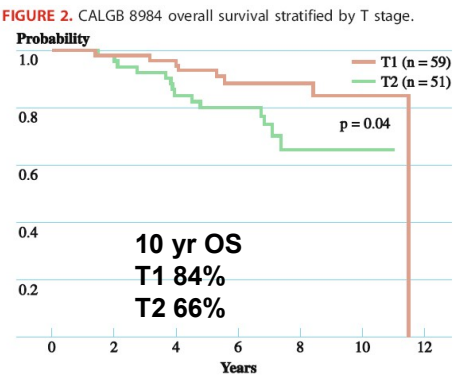
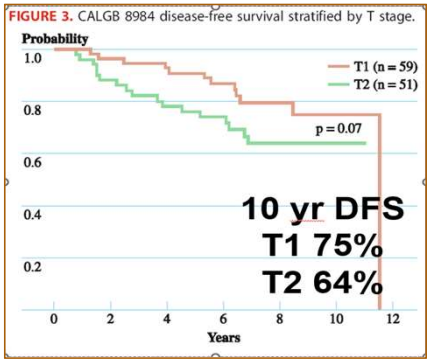
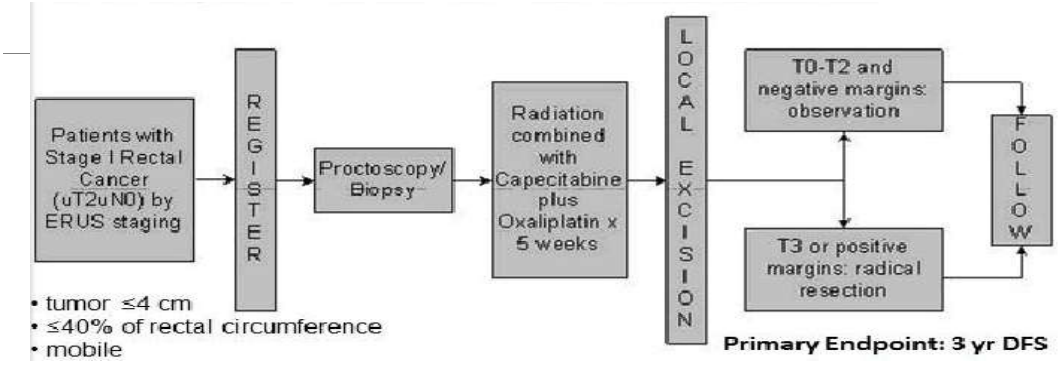
CALGB 8984





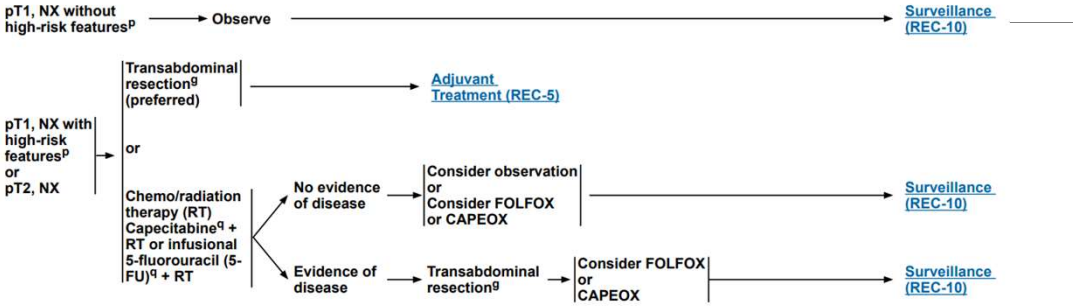
T2 lesions treated via local excision and adjuvant therapy are associated with higher recurrence rates

ACOSOG Z6041: Ph II



-3-year disease-free survival LESS than anticipated
-Consider, who "refuse", or are "not candidates for transabdominal resection"

Early Stage: NCCN Guidelines



- **High-risk features:**
  - Positive margins (+ve)
  - Lymphovascular invasion (LVI)
  - Poorly differentiated tumors (PD)
  - sm3 invasion (submucosal invasion to the lower third of the submucosal level).

Why RT in Locally advanced, operable rectal cancer?

Pre op RT

SWEDISH	DUTCH
(25Gy/5fx)→ surgery vs. surgery (non-TME) alone	25Gy/5fx→TME vs. TME alone
Local Control: 11% vs. 27%	Local Control: 6% vs 12%
Preop RT improved overall survival (58% vs. 48% at 5 years and 38% vs. 30% at 13 years)	OS: No difference

Pre-op RT vs. Pre op ChemoRT

- **French FFCD 9203**
- **EORTC 22921**

FFCD 9203

733 Patients T3-4 Nx M0 rectal adenoca accessible to DRE

2 arms: Preop RT vs. Preop ChemoRT

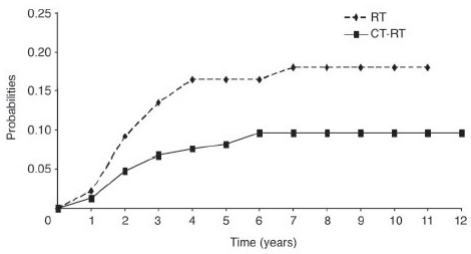
RT – 45 Gy in 1.8 Gy per fraction

Concurrent chemo w/ RT: bolus 5-FU/LV x 2

Adjuvant chemo: 5 FU/LV x 4

Surgery – within 2 weeks after preoperative treatment

FFCD 9203 -- Results



5 yrs Follow Up:

LR: 16.5% vs 8.1% , P=0.04

pCR: 3.6% vs. 11.4% p<0.0001

Grade 3/4 toxicities: 2.7% vs. 14.6% p<0.05

5-yr OS: 67.9% vs 67.4% p=0.684

5-yr PFS: 55.5% vs. 59.4% CI 0.77-1.20

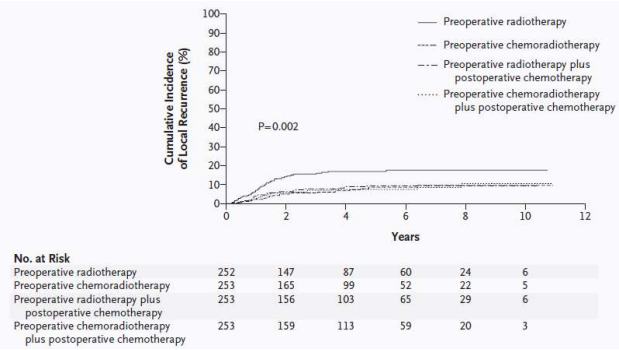
No difference in rate of sphincter-saving surgery

EORTC 22921

4 arms:
- Preop RT
- Preop ChemoRT
- Preop RT + Postop Chemo
- Preop ChemoRT + Postop Chemo

Preop RT – 45 Gy @1.8 Gy

ChemoRT increased pCR 5→14%



No. at Risk						
Preoperative radiotherapy	252	147	87	60	24	6
Preoperative chemoradiotherapy	253	165	99	52	22	5
Preoperative radiotherapy plus postoperative chemotherapy	253	156	103	65	29	6
Preoperative chemoradiotherapy plus postoperative chemotherapy	253	159	113	59	20	3

5 years LR
17.1%
8.7%
9.6%
7.6%
P=0.002

No difference in OS

Pre-op vs. Post-op ChemoRT

German rectal Cancer Study group

MRC CR07 / NCIC-CTG C016

German Rectal Cancer Study Group

823 pts, <16 cm anal verge, no T1 or M1.

Surgery
- TME – 6 weeks after preop CHT/RT

Radiation
- 50.4Gy in 28 fx
- 5.4Gy boost to tumor bed in post op group

PMID: 15496622

German Rectal Cancer Study Group

Increased rate of sphincter sparing surgery in pre-op group

Table 4. Rates of Sphincter-Sparing Surgery in 194 Patients Determined by the Surgeon before Randomization to Require Abdominoperineal Resection, According to Actual Treatment Given.

Variable	Preoperative Chemoradiotherapy (N=415)	Postoperative Chemoradiotherapy (N=384)	P Value
Abdominoperineal resection deemed necessary — no. (%)	116 (28)	78 (20)	
Sphincter-preserving surgery performed — no./total no. (%)	45/116 (39)	15/78 (19)	0.004

PMID: 15496622

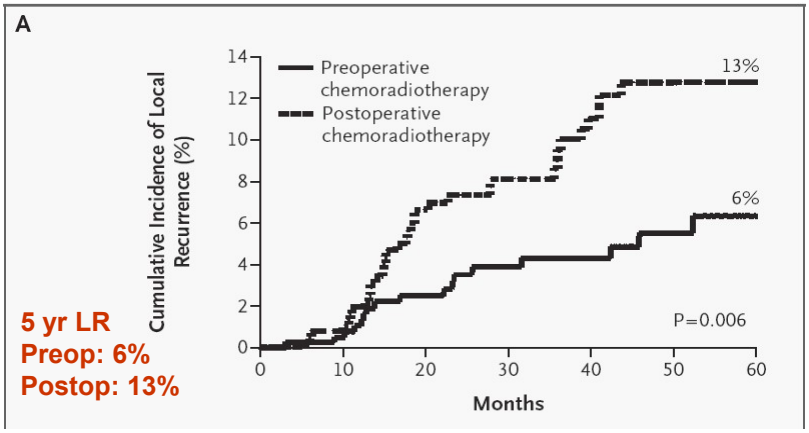
German Rectal Cancer Study Group

Table 5. Grade 3 or 4 Toxic Effects of Chemoradiotherapy, According to Actual Treatment Given.*

Type of Toxic Effect	Preoperative Chemoradiotherapy (N=399)	Postoperative Chemoradiotherapy (N=237)	P Value
	% of patients		
Acute			
Diarrhea	12	18	0.04
Hematologic effects	6	8	0.27
Dermatologic effects	11	15	0.09
Any grade 3 or 4 toxic effect	27	40	0.001
Long-term			
Gastrointestinal effects†	9	15	0.07
Strictures at anastomotic site	4	12	0.003
Bladder problems	2	4	0.21
Any grade 3 or 4 toxic effect	14	24	0.01

PMID: 15496622

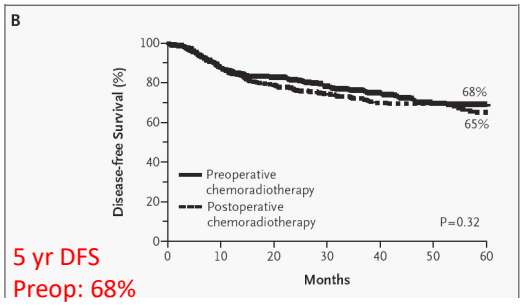
German Rectal Cancer Study Group



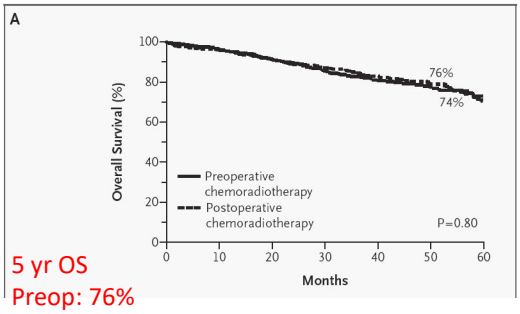
5 yr LR
Preop: 6%
Postop: 13%

PMID: 15496622

German Rectal Cancer Study Group



5 yr DFS
Preop: 68%
Postop: 65%



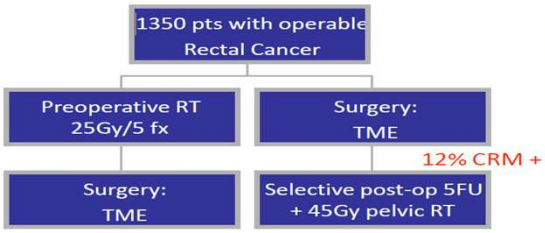
5 yr OS
Preop: 76%
Postop: 74%

German Study Conclusion

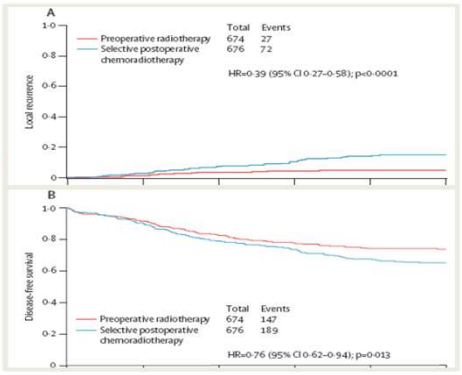
Pre-op as compared with post-op chemoRT

- Improved local control
- Increase rate of sphincter-preserving surgery
- Associated with reduced toxicity
- No improvement in overall survival.

MRC CR07



	Pre-op RT	Selective post-op CRT	
3 yr LR	4.4%	10.6%	p<0.0001
3 yr DFS	77.5%	71.5%	p=0.013
3 yr OS	80.3%	78.6%	p=0.40



Sebag-Montefiore, Lancet;2009

PROSPECT

PROSPECT: A randomized phase III trial of neoadjuvant chemoradiation versus neoadjuvant FOLFOX chemotherapy with selective use of chemoradiation, followed by total mesorectal excision (TME) for treatment of locally advanced rectal cancer (LARC) (Alliance N1048)

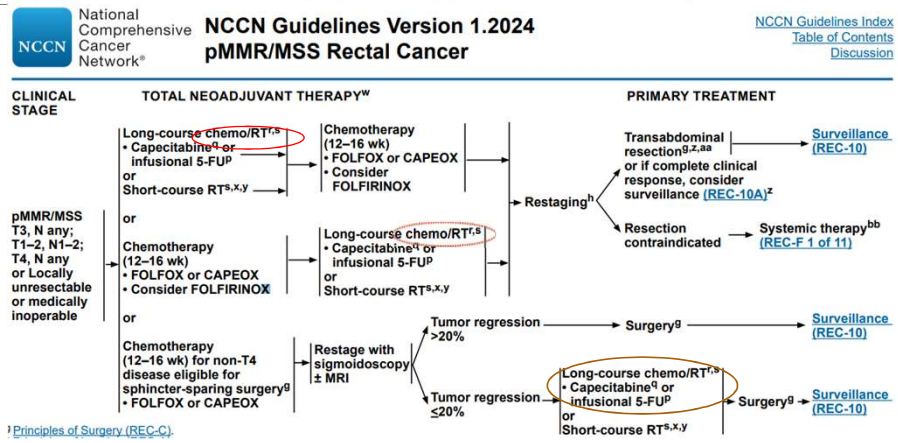
- - *Control group:* Neoadjuvant chemoradiotherapy with fluorouracil or capecitabine and 5,040 cGy over 5.5 weeks (28 fractions)
- *Intervention group:* Six cycles of modified FOLFOX, followed by restaging with pelvic imaging and rectal endoscopy. The addition of neoadjuvant pelvic chemoradiation was contingent upon response.

- -- A total of 9% of patients required pelvic radiation therapy based on poor response to neoadjuvant chemotherapy, meaning that 91% of patients in the intervention group were spared radiation

PROSPECT

Table. Summary of Efficacy Results

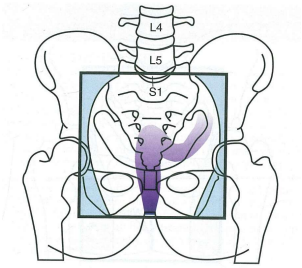
Outcomes	FOLFOX with selective 5-FU CRT (585 patients)	5-FU CRT, (543 patients)
5-year disease-free survival, % (90.2% CI)	80.8 [77.9, 83.7]	78.6 [75.4, 81.8]
	HR 0.92 [0.74, 1.14] stratified noninferiority $P = .0051$	
5-year overall survival, % (95% CI)	89.5 [87.0, 92.2]	90.2 ([87.6, 92.9]
	HR 1.04 [0.74, 1.44]	
5-year local recurrence-free survival, % (95% CI)	9 events	7 events
	98.2 [97.1, 99.4]	98.4 [97.3, 99.6]
	HR 1.18 [0.44, 3.16]	
Surgical and pathological endpoints		
Number completing surgery	535	510
Complete (R0) rectal resection	98.9%	97.1%
Pathologic complete response	21.9%	24.3%
Low anterior resection rate	97.6%	98.0%
Positive radial margin	1.2%	1.5%

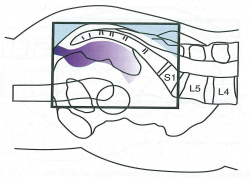


RT Technique-3D Conformal

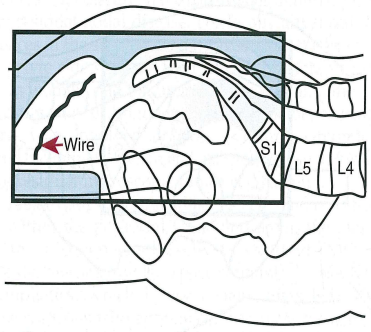
- CT Simulation
- Prone or Supine position
- Belly Board –Prone position

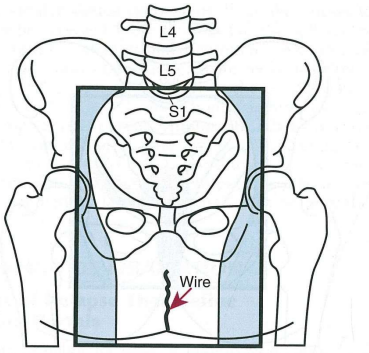
- Oral contrast for Small Bowel
- Wire perineal scar if present
- Vac Lok





Post APR





Following APR use a wire to designate resection scar

GUNDERSON & TEPPER - CLINICAL RADIATION ONCOLOGY, 2ND ED. 2007

IMRT

Lowered the incidence of grade ≥2 acute toxicity for overall gastrointestinal toxicity, as well for diarrhea and proctitis

Japanese journal of clinical oncology. 2018;48(5):458-466.

CTVA: internal iliac, pre-sacral and peri-rectal nodal regions for both anal and rectal case planning; CTVB: external iliac nodal region for anal case planning and for selected rectal cases; CTVC: inguinal nodal region for anal case planning and for select rectal cases),