“Perioperative radio/chemoradiotherapy for rectal cancer”
T-staging for rectal cancer

T1: Invades submucosa (sm).
T2: Invades muscularis propria (mp).
T3: Through mp into subserosa or peri-rectal tissues.
T4: Invades other organs / structures and/or perforates visceral peritoneum.

<table>
<thead>
<tr>
<th>Tx</th>
<th>Primary tumor cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades submucosa but does not extend into circular muscle layer</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades but does not penetrate MP</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades subserosa through MP</td>
</tr>
<tr>
<td>T3a</td>
<td>Tumor extends &lt;1mm beyond MP</td>
</tr>
<tr>
<td>T3b</td>
<td>Tumor extends ≥1-5mm beyond MP</td>
</tr>
<tr>
<td>T3c</td>
<td>Tumor extends &gt;5-15mm beyond MP</td>
</tr>
<tr>
<td>T3d</td>
<td>Tumor extends &gt;15mm beyond MP</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades:</td>
</tr>
<tr>
<td>T4a</td>
<td>Peritoneal reflection</td>
</tr>
<tr>
<td>T4b</td>
<td>Others organs</td>
</tr>
</tbody>
</table>
MRI high risk features

- Tumour within 1mm or beyond MR fascia
- T3 low lying tumour at/or below levators
- Tumour extending 5mm or more into peri-rectal fat (T3c)
- T4 tumours
- N2 tumours

Gina Brown
Treatment algorithm for localised rectal cancer

Figure 1. Treatment algorithm for localized rectal cancer. (Lateral LN: drainage of the a rectalis media (if present) or along the obturatorius or internal iliac vessels).
Pre-operative RT – short or long course?

Operable tumours

Surgery or SCRT

“potentially” operable tumours

LCRT
### T-stage and Rectal Pre-op RT

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T2</th>
<th>T3 &gt;1mm*</th>
<th>T3 &lt;1mm*</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upper</strong></td>
<td>-</td>
<td>-</td>
<td>- / S\textsubscript{(T3c/d)}</td>
<td>L**</td>
<td>L**</td>
</tr>
<tr>
<td><strong>Mid</strong></td>
<td>-</td>
<td>-</td>
<td>S</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td><strong>Low</strong></td>
<td>-</td>
<td>-</td>
<td>/ S??</td>
<td>L</td>
<td>L</td>
</tr>
</tbody>
</table>

* Distance from tumour to CRM

S: Short; L: Long course of RT

** ESMO: “Intensive chemotherapy might be an option, which however has not yet systematically been proved”

13 years follow-up
1168 patients
Surgery v Surgery after pre-op RT (25Gy / 5 fractions)

<table>
<thead>
<tr>
<th></th>
<th>S + RT</th>
<th>S</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence</td>
<td>9%</td>
<td>26%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cancer specific survival</td>
<td>72%</td>
<td>62%</td>
<td>0.03</td>
</tr>
<tr>
<td>Overall survival</td>
<td>38%</td>
<td>30%</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Benefits to all Dukes stages

(Folkesson et al, JCO 23, 24: 5644 - 5650)
The “Dutch” study (2001)

1861 patients
Operable rectal cancer
TME + RT (25 Gy in 5 fractions)

Local recurrence at 5 years

- TME: 11.4%
- TME + RT: 5.8% (p<0.001)

No survival benefit

(Kapiteijn et al, NEJM, 345 (9), 638-646, 2001)
Recurrence and distance from anal verge

<table>
<thead>
<tr>
<th>(At 2 years)</th>
<th>TME</th>
<th>RT/TME</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 - 15cm</td>
<td>3.8%</td>
<td>1.3%</td>
</tr>
<tr>
<td>5 - 10cm</td>
<td>10.1%</td>
<td>1.0%</td>
</tr>
<tr>
<td>&lt; 5cm</td>
<td>10.0%</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

(Kapiteijn et al, NEJM, 345 (9), 638-646, 2001)
<table>
<thead>
<tr>
<th>Trial</th>
<th>Date</th>
<th>Local recurrence Surgery alone</th>
<th>Local recurrence Surgery + DXT</th>
<th>p value</th>
<th>Length of follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR02</td>
<td>1996</td>
<td>46%</td>
<td>36%</td>
<td>=0.04</td>
<td>5 years</td>
</tr>
<tr>
<td>CR03</td>
<td>1996</td>
<td>34%</td>
<td>21%</td>
<td>=0.001</td>
<td>5 years</td>
</tr>
<tr>
<td>North West</td>
<td>1994</td>
<td>36.5%</td>
<td>12.8%</td>
<td>=0.0001</td>
<td>8 years</td>
</tr>
<tr>
<td>Swedish</td>
<td>1997</td>
<td>27%</td>
<td>11%</td>
<td>&lt;0.001</td>
<td>5 years</td>
</tr>
<tr>
<td></td>
<td>2002</td>
<td>26%</td>
<td>9%</td>
<td>&lt;0.001</td>
<td>13 years</td>
</tr>
<tr>
<td>Dutch</td>
<td>2001</td>
<td>8.2%</td>
<td>2.4%</td>
<td>&lt;0.01</td>
<td>2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11.4%</td>
<td>5.8%</td>
<td></td>
<td>5 years</td>
</tr>
</tbody>
</table>
Toxicity ?
BACKGROUND: We investigated very long-term bowel function after total mesorectal excision (TME) with or without preoperative short-course radiotherapy (PRT).

PATIENTS AND METHODS:
- TME trial (1996-1999),
- 1530 Dutch patients with rectal cancer were randomized to PRT/TME or TME alone.
- A set of questionnaires was sent to the surviving patients (n = 583) in 2012.
- The questionnaires included the Low Anterior Resection Syndrome Score (LARS score),
- Split into "no LARS," "minor LARS," and "major LARS" in ascending severity of bowel dysfunction.

RESULTS:
- 478 respondents (242 non-stoma patients were included in the present analysis)
- The median interval since treatment was 14.6 years
- Major LARS was reported by 46% of all patients (56% PRT plus TME vs. 35% TME).
- PRT (odds ratio [OR], 3.0; 99% confidence interval [CI], 1.3-6.9) and age ≤ 75 years at the follow-up point (OR, 2.4; 99% CI, 1.1-5.5) increased the risk of major LARS.

CONCLUSION:
A considerable proportion of non-stoma patients endured major LARS years after TME. PRT and age ≤ 75 years at follow-up pose additional risks of major LARS in addition to surgery.
Do we need to give RT?

Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial.

David Sebag-Montefiore et al...........
CRO7

Pre-op 25Gy in 5 fractions

V

Selected* post-op CRT (45Gy in 25#)

(* If tumour within 1mm of CRM)
CRO7

1350 pts

80 centre (UK, Canada, S.Africa, NZ)

Operable rectal cancer

674 / 676 in each arm
## Local recurrence (LR)

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>3yrs</td>
<td>5%</td>
<td>11%</td>
</tr>
</tbody>
</table>
| 5yrs  | 5%  | 17%  | \( p < 0.0001 \)

- LR less in the pre-op group
- LR less at all stages in pre-op group
- DFS better in the pre-op group
So, we can reduce LR but can we improve survival?
UK “Operable” trials (NCRN)

.........can we improve survival?

COPPERNICUS (Simon Gollins)

62 pts
OxMdG x4........25Gy/5#........op........OxMdG x8

BACCHUS (Rob Glynne-Jones)

30 + 30 pts
FOLFOX+Av x3.....PET..... FOLFOX+Av x3.....Op
FOLFOXIRI+Av x3.....PET..... FOLFOXIRI+Av x3.....Op
Short-course radiotherapy followed by neo-adjuvant chemotherapy in locally advanced rectal cancer--the RAPIDO trial.


? DFS / OS improved
Adjuvant chemotherapy for rectal cancer?
Adjuvant chemotherapy for rectal cancer patients treated with preoperative (chemo)radiotherapy and total mesorectal excision: a Dutch Colorectal Cancer Group (DCCG) randomized phase III trial


BACKGROUND:
A multicentre, randomised phase III trial, PROCTOR-SCRIPT, was conducted to compare adjuvant chemotherapy with observation for rectal cancer patients treated with pre-op ChemoRT and TME.

PATIENTS AND METHODS:
Radiotherapy consisted of 5 × 5 Gy.
Chemoradiotherapy consisted of 25 × 1.8-2 Gy combined with 5FU-based chemotherapy.
Adjuvant chemotherapy consisted of 5FU (PROCTOR) or capecitabine (SCRIPT).

RESULTS:
470 enrolled patients, 437 were eligible.
The trial closed prematurely because of slow patient accrual.
After a median follow-up of 5.0 years, 5-year OS was 79.2% in the observation group and 80.4% in the chemotherapy group [hazard ratio (HR) 0.93, 95% confidence interval (CI) 0.62-1.39; P = 0.73].

CONCLUSION:
The PROCTOR-SCRIPT trial could not demonstrate a significant benefit of adjuvant chemotherapy with fluoropyrimidine monotherapy after pre-op ChemoRT and TME on OS.
Chronicle: results of a randomised phase III trial in locally advanced rectal cancer after neoadjuvant chemoradiation randomising postoperative adjuvant capecitabine plus oxaliplatin (XELOX) versus control.
Glynne-Jones R, Counsell N, Quirke P, Mortensen N, Maraveyas A, Meadows HM, Ledermann J, Sebag-Montefiore D.

BACKGROUND:
We examined the benefit of postoperative adjuvant capecitabine and oxaliplatin (XELOX) chemotherapy in rectal adenocarcinoma following neoadjuvant chemoradiation (CRT)

METHODS:
• Eligible patients were randomly assigned following fluoropyrimidine-based CRT and curative resection to observation or six cycles of XELOX
• The primary end point was DFS
• 390 patients were required in each arm

RESULTS/ CONCLUSIONS:
• The study closed prematurely in 2008 because of poor accrual
• Only 113 patients were assigned to either observation (n = 59) or XELOX (n = 54).
• Compliance was poor, 93% allocated chemo started and 48% completed six cycles.
• The 3-year DFS rate was 78% with XELOX and 71% with observation (NS) [hazard ratio (HR) for DFS = 0.80; 95% confidence interval (CI) 0.38-1.69; P = 0.56].
• Our findings support the need for trials that test the role of neoadjuvant chemotherapy.

Does adjuvant fluoropyrimidine-based chemotherapy provide a benefit for patients with resected rectal cancer who have already received neoadjuvant radiochemotherapy? A systematic review of randomised trials.

Bujko K, Glynne-Jones R, Bujko M
Poland

NO

Nomograms for predicting local recurrence, distant metastases, and overall survival for patients with locally advanced rectal cancer on the basis of European randomized clinical trials.

Italy

YES
Adjuvant chemotherapy after preoperative (chemo)radiotherapy and surgery for patients with rectal cancer: a systematic review and meta-analysis of individual patient data.


BACKGROUND:
We did a meta-analysis of individual patient data to compare adjuvant chemotherapy with observation for patients with rectal cancer

METHODS:
We analysed data from four eligible trials, including data from 1196 patients with stage II or III disease, who had an R0 resection and had a tumour located within 15 cm of the anal verge

FINDINGS:
• No significant differences in OS between patients who received adjuvant chemotherapy and those who underwent observation (hazard ratio [HR] 0.97, 95% CI 0.81-1.17; p=0.775)
• However, in subgroup analyses, patients with a tumour 10-15 cm from the anal verge had improved DFS (0.59, 0.40-0.85; p=0.005, p(interaction)=0.107) and fewer distant recurrences (0.61, 0.40-0.94; p=0.025, p(interaction)=0.126) when treated with adjuvant chemotherapy

INTERPRETATION:
• Adjuvant 5FU-based chemotherapy did not improve OS, DFS or distant recurrences
• However, adjuvant chemotherapy might benefit patients with a tumour 10-15 cm from the anal verge

Lancet Oncol. 2015 Feb;16(2):200-7
ESMO

“The majority of consensus participants recommended adjuvant 5FU/Cap with or without oxaliplatin based on data from colon cancer”

..................Lancet Oncology May 14 articles

YES !
Timing of surgery after SCRT?

ESMO: “2-3 days after END of SCRT”
Patients > 75 years

Dutch data van den Broek et al (EJC 2013)

TME trial - 600 pts (median age 67 years)

Patients > 75 years old operated 4-7 days post last # RT had a higher chance of dying compared to surgery 0-3 days post last # RT (4.7 v 2.1%).

Stockholm III (Petterson BJS 2010) also showed an increase in post-op complications for those treated 11-17 days post starting RT.

Hartley et al, BJS 2002 – reduced risk of complications if overall treatment time < 10 days.

operate early after SCRT especially in elderly

or ? Delayed surgery
Short course and delayed surgery?
<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>Patients</th>
<th>Operative Rate</th>
<th>Pathologic Complete Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK (Hatfield)</td>
<td>2009</td>
<td>43 pts</td>
<td>61%</td>
<td>85%</td>
</tr>
<tr>
<td>Sweden (Radu)</td>
<td>2008</td>
<td>46 pts</td>
<td>80%</td>
<td>11%</td>
</tr>
<tr>
<td>Pettersson (Sweden)</td>
<td>2012</td>
<td>112 pts</td>
<td></td>
<td>8%</td>
</tr>
<tr>
<td>Canada (Faria)</td>
<td>2014</td>
<td>52 pts</td>
<td>100%</td>
<td>10%</td>
</tr>
</tbody>
</table>
Conventional European CRT

- 3 or 4 field CT planned volume (MLC)

Capecitabine 825mg/m² bd for 7/7 per week

Radiotherapy 45 GY in 25# *

(* to 5040Gy/28#...........and up to 54gy boost)
Chemoradiotherapy

- 4732 pts
- 77 phase II and III trials
- pCR 13.5%
- Adding 2nd drug to 5FU and total radiation dose were associated with higher pCR (small studies 20-30%)

Timing of surgery after LCRT?

ESMO: "4-8 weeks after END of LCRT"
Regression of Rectal Cancer with Radiotherapy with or without Concurrent Capecitabine d Optimising the Timing of Surgical Resection

A. S. Dhadda*, A. M. Zaitouny, E. M. Bessell

Aims: To determine tumour regression (volume-halving time) obtained after chemo/radiotherapy, and thereby the ideal interval between the start of treatment and surgery in order to obtain a high rate of complete response.

Materials and methods: In total, 106 patients with cT3,4 rectal cancer who received preoperative radiotherapy alone or concurrently with capecitabine chemotherapy at Nottingham City Hospital, UK were studied. The rectal tumour volume visible on the computed tomography planning scan was compared with the residual pathological volume and the tumour volume-halving time calculated. The radiotherapy response was graded according to the Mandard system.

Results: Fifty-three patients had radiotherapy alone, with 53 patients having concurrent chemoradiotherapy. The median tumour volume-halving time was found to be 14 days and not influenced by the addition of chemotherapy. The Mandard score, the interval from the start of treatment to surgery and the tumour volume-halving time were statistically associated with tumour regression. The median tumour volume in our series of 54 cm³ would require an interval of 20 weeks after the start of treatment to surgery to regress to 0.1 cm³ (10 volume-halving times; 140 days).

Conclusions: The initial tumour volume and median volume-halving time provide the best estimates for determining the optimum length of interval between the completion of preoperative chemo/ Probably need to wait longer than the standard 8 weeks................maybe even longer for larger tumours
Optimal time interval between neoadjuvant chemoradiotherapy and surgery for rectal cancer.


Source: The Netherlands.

All evaluable patients who underwent preoperative CRT for rectal cancer between 2009 and 2011 were selected from the Dutch Surgical Colorectal Audit. The interval between radiotherapy and surgery was calculated from the start of radiotherapy. The primary endpoint was pathological complete response (pCR).

1593 patients.
The median interval between radiotherapy and surgery was 14 (range 6-85, interquartile range 12-16) weeks.

Outcome measures were calculated for intervals of less than 13 weeks (312 patients), 13-14 weeks (511 patients), 15-16 weeks (406 patients) and more than 16 weeks (364 patients). Age, tumour location and R0 resection rate were distributed equally between the four groups. Significant differences were found for clinical tumour category (cT4: 17·3, 18·4, 24·5 and 26·6 per cent respectively; P = 0·010) and clinical metastasis category (cM1: 4·4, 4·8, 8·9 and 14·9 per cent respectively; P < 0·001).

Resection 15-16 weeks after the start of CRT resulted in the highest pCR rate (18·0%; P = 0·013), with an independent association (hazard ratio 1·63, 95 per cent confidence interval 1·20 to 2·23).

CONCLUSION:
Delaying surgery until the 15th or 16th week after the start of CRT (10-11 weeks from the end of CRT) seemed to result in the highest chance of a pCR.
IMRT for rectal cancer?
Efficacy and safety of neoadjuvant intensity-modulated radiotherapy with concurrent capecitabine for locally advanced rectal cancer

Wang L, Li ZY, Li ZW, Li YH, Sun YS, Ji JF, Gu J, Cai Y (BEIJING, CHINA)

OBJECTIVE:
The objective of this study was to retrospectively review the efficacy, toxicity, and surgical complications following IMRT in patients who have rectal cancer.

PATIENTS:
This study included patients who underwent IMRT with gross tumor volume/clinical target volume of 50.6/41.8 Gy in 22 fractions with concurrent capecitabine.

RESULTS:
• 260 patients
• pCR 18.5%
• The grade 3 toxicity rate was 5.8% and there were no grade 4 toxicity and perioperative mortality
• The 30-day post-op and severe complication (≥grade 3) rates were 23.1% and 2.7%.
• The anastomotic leakage rate was 3.3% (5/152).

CONCLUSION:
IMRT-Cap regimen used to treat rectal cancer in this study has a high efficacy rate and a low toxicity rate.
CAPIRI-IMRT

Cai G et al, 2015

**AIM:**
To evaluate the efficacy and toxicity of CAPIRI-IMRT

**METHOD:**
71 patients
Recurrent rectal cancer (no previous RT)
IMRT 45/25 + 10-16Gy boost
Ir 50mg/m2 weekly; Cap 625mg/m2 daily (M-F)

**RESULTS:**
4 patients (5.6%) had a cCR
14 patents (19.7%) underwent a R0 resection
53 patents were symptomatic – 88% gained partial or complete benefit
Diarrhoea was as expected the most common toxicity (G3 in 16 patients (22.5%)

**CONCLUSION:**
Promising efficacy in terms of clinical and pathological response
Good symptomatic relief provided
“manageable” toxicities

Radiat Oncol 10(1); 360, 2015
CRT with Irinotecan
Irinotecan+5-fluorouracil with concomitant pre-operative radiotherapy in locally advanced non-resectable rectal cancer: a phase I/II study.


31 patients

MRI: 19/24 (79%) reduction in T-stage, 7pts cCR

OP: 28pts – 81% clear CRM

Ir: Irinotecan 60mg/m² wk1-4

5FU 200mg/m²/day for 5 weeks

Radiotherapy 45 GY in 25# *
Preoperative chemoradiotherapy using concurrent capecitabine and irinotecan in magnetic resonance imaging-defined locally advanced rectal cancer: impact on long-term clinical outcomes.


Capecitabine 650mg/m² bd for 7/7 per week

Radiotherapy 45 GY in 25# *

Ir: Irinotecan 60mg/m² wk1-4

110 patients (MRI demonstration of tumour threatening (≤ 2 mm) or involving mesorectal fascia)

MRI: 72pts (67%) reduction in T-stage

OP: 107pts – 95 (89%) clear CRM (>2mm)

pCR: 22%

Capecitabine 650mg/m² bd for 5/7 per week

Radiotherapy 45 GY in 25# *

Ir: Irinotecan 60mg/m² wk1-4

Randomise

Tumour ≤ 1mm from CRM

Capecitabine 900mg/m² bd for 5/7 per week

Radiotherapy 45 GY in 25# *
CRT with Irinotecan....?

...............under investigation
CRT with Oxaliplatin
CRT with Oxaliplatin

CAO/ARO/AIO-04 (1)
Ox5FU
1265pts, pCR 17 v 13% p=0.038
Increased toxicity with oxaliplatin arm

ACCORD 12/0405-Prodige 2 (2)
OxCap
598pts, pCR 19.2 v 13.9% NS
Increased toxicity with oxaliplatin arm

STAR-01 (3)
Ox5FU
747pts, pCR 16 v 16% NS
Increased toxicity with oxaliplatin arm

( NSABP) R-04 (4)
OxCap
1608pts
No sig diff in pCR
Increased toxicity with oxaliplatin arm

PETACC6 (5)
RCT Cap v OxCap with RT and adjuvant
1094pts
Reduced treatment compliance
(>90% dose: 91 v 63%)
Increased toxicity
(G3/4: 15.1 v 36.7%)
pCR 11.3 v 13.3% (p=0.31)
CRT with VEGF inhibitors
<table>
<thead>
<tr>
<th>AVASTIN studies</th>
<th>Treatment</th>
<th>Number pts</th>
<th>pCR</th>
<th>Markers/Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gasparini 2012</td>
<td>RT + C + BVZ</td>
<td>43</td>
<td>14% (51% few cells)</td>
<td>CD34, Ki67, VEGFR-2</td>
</tr>
<tr>
<td>Volenik 2011</td>
<td>RT + C + BVZ</td>
<td>61</td>
<td>13%</td>
<td>62% developed peri-operative complications</td>
</tr>
<tr>
<td>Resch 2012</td>
<td>RT + C + BVZ</td>
<td>8</td>
<td>25%</td>
<td>Intestinal bleed, Diarrhoea STOPPED</td>
</tr>
<tr>
<td>Crane 2010</td>
<td>RT + C + BVZ</td>
<td>25</td>
<td>32%</td>
<td>3 wound complications requiring surgical intervention</td>
</tr>
<tr>
<td>Spigel 2012</td>
<td>RT + 5FU + BVZ</td>
<td>32</td>
<td>Regression in all pts (mean 5.0 – 2.4cm)</td>
<td>VEGF, IL-6, sVEGFR1, PIGF, CECs (post-op complications)</td>
</tr>
<tr>
<td>Willett 2009</td>
<td>RT + 5FU + BVZ</td>
<td>32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kennecke 2012</td>
<td>RT + C + BVZ + Ox</td>
<td>42</td>
<td>16%</td>
<td></td>
</tr>
</tbody>
</table>
Diagnostic biopsy

Bx

Capecitabine 825mg/m² bd for 7/7 per week

Radiotherapy 45 GY in 25#

AZD 2171 or AZD6244

DCE-MRI: √√ √

FLT-PET: √ √

Blood: √ √ √ √ √ √ √
Clinical / Pathological response
(VEGFi 2171)

9 out of 17 patients have had an ECPR* (1: exc – NET)

- cCR: 4
- pCR: 2 (TRG 1)
- Microfoci: 2 (TRG 2)
- cCR relapse: 1 (10 months after RT completed)

Minimal toxicity

53%
41% cCR/pCR

ECPR: Excellent Clinical or Pathological Response
Assessing response to treatment

- MRI response
  - Tumour regression grade (TRG)
  - DWI-MRI
  - Tumour thickness
  - Tumour length / volume

- Tumour regression (TRG1 (pCR) - TRG5)
- pCR (cCR/ECPR)
- DFS
pCR or DFS?

PURPOSE:
- To evaluate pathologic complete response (pCR) and two-year disease-free survival (2yr DFS) for overall survival (OS) and their potential to be relevant intermediate endpoints to predict.

METHODS:
- 5 large European rectal cancer trials (2795 patients),
- All received long-course radiotherapy with or without concomitant and/or adjuvant chemotherapy.
- The ratio of distant metastasis (DM) and local recurrence (LR) rates was used to identify patient characteristics that increase the risk of recurrences.

FINDINGS / INTERPRETATION:
- The DM/LR ratio decreased to a plateau in the first 2 years, revealing it to be a critical follow-up period.
- Compared with pCR, 2yr DFS is a stronger predictor of OS.
- To adapt treatment most efficiently, accurate prediction models should be developed for pCR to select patients for organ preservation and for 2yDFS to select patients for more intensified treatment strategies.
No Increased Risk of Second Cancer After Radiotherapy in Patients Treated for Rectal or Endometrial Cancer in the Randomized TME, PORTEC-1, and PORTEC-2 Trials.


PURPOSE:
This study investigated the long-term probability of developing a second cancer in a large pooled cohort of patients treated with surgery with or without radiotherapy (RT).

PATIENTS AND METHODS:
All second cancers diagnosed in patients included in the TME (Rectal), PORTEC-1, and PORTEC-2 trials (Endometrial) were analysed.

RESULTS / CONCLUSION:
2,554 patients
All cancer survivors had a higher risk of developing a second cancer compared with an age- and sex-matched general population
The standardized incidence ratio for any second cancer was 2.98 (95% CI, 2.82 to 3.14)
No differences were found in second cancer probability between patients who were treated without RT (10- and 15-year rates, 15.8% and 26.5%, respectively) and those treated with RT (10- and 15-year rates, 15.4% and 25.6%, respectively)
Follow ESMO guidelines for SCRT and LCRT!!

Adjuvant chemo for rectal cancer..................yes?
If operable disease and need RT...........SCRT and not LCRT
Timing after SCRT.........2-3 days (ASAP in elderly)
Timing after LCRT..........4-8 wks (?) longer
SCRT and delayed op............interesting

LCRT and fluoropyrimidine is standard
  + oxaliplatin.....no
  + irinotecan......under investigation
  + VEGFi............under investigation.........? No BVZ

Assessment of response..................path and MRI