RECTAL CANCER
CLINICAL CASE DISCUSSION

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DISCLOSURE

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Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

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†Approved by the ESMO Guidelines Committee: August 2002, last update May 2017. This publication supersedes the previously published version—Ann Oncol 2013; 24 (Suppl. 6): vi81–vi88.
Integration of knowledge in a multidisciplinary team
Optimal staging by MRI
Selective preoperative radiation or chemoradiation
TME surgery
Pathological assessment of the quality of surgery
Non surgical approach for some pCR
Adjuvant chemotherapy for high risk
ESMO Guidelines statement
Rectal MRI for all tumours, including the earliest ones, is required in order to select patients for preoperative treatment and extent of surgery.
ESMO Rectal Cancer Guidelines: Staging

Key Messages

SoC
TME alone
AVOID RT

TME alone if high quality or plus SCPRT/CRT

SCPRT or CRT Then TME

CRT or SCPRT + FOLFOX then TME

**Rectal Cancer: ESMO CPG - Staging**

**Very early**
- cT1-2, sm1, cN0

**Early**
- cT1-2; cT3a/b if middle or high cN0 (cN1 ig high)
- MRF clear; no EMVI

**Intermediate**
- cT3a/b very low, levators clear. MRF clear; cT3a/b in mid or high rectum, cN1-2 (not extranodal), no EMVI

**Locally advanced**
- cT3c/d or very low, levators not threatened, MRF clear. cT3c/d mid rectum, cN1-N2 (extranodal), EMVI +ve

**Advanced**
- cT3 with MRF involved cT4b, levators threatened, lateral node +ve

**Key Messages**
- TME alone
- Avoid RT
- TME alone if high quality or plus SCPRT/CRT
- SCPRT or CRT then TME
- CRT or SCPRT + FOLFOX then TME

CRT, chemoradiotherapy; EMVI, extramural vascular invasion; FOLFOX, leucovorin/fluorouracil/oxaliplatin; MRF, mesorectal fascia; RT, radiotherapy; SCPRT, short-course preoperative radiotherapy; TME, total mesorectal excision; SoC, standard of care
Involvement of mesorectal fascia
Extramural vein invasion
Involvement of puborectal sphincter
High risk features in our case

- Tumour of the upper rectum (11-16 cm from the a.v.)
- Extramural spread: 13 mm T3c
- > 4 heterogeneous/irregular border lymph nodes
- EMVI positive (left middle rectal vein)
- No MRF involvement
- No extramural disease
- No lateral nodes

Stage: cT3cN2M0

a.v., anal verge; EMVI, extramural vascular invasion; MRF mesorectal fascia
SoC
TME alone
AVOID RT

TME alone if high quality or plus SCPRT/CRT

SCPRT or CRT
Then TME

CRT or SCPRT + FOLFOX then TME

Key Messages

Locally advanced disease cT3c/d or very low, levators not threatened, MRF clear cT3c/d mid-rectum, cN1-N2 (extranodal), EMVI+  

SCPRT or CRT  

MRI to re-evaluate tumour  

'Watch-and-wait' may be considered in high-risk patients if cCR achieved with CRT  

TME (plus photographic record of specimen and assessment of TME quality)  


cCR, Clinical complete response; CRT, chemoradiotherapy; EMVI, extramural vascular invasion; MRF, mesorectal fascia; MRI, magnetic resonance imaging; SCPRT, short-course preoperative radiotherapy; TME, total mesorectal excision
Our case treatment

Long-course chemo-radiotherapy
45 Gy in 25 fractions + 9 Gy boost in 5 fractions
Concurrent capecitabine (825 mg/m² twice daily continuously)
Rectal cancer with pre-operative Chemo-RT: OXALIPLATIN NOT RECOMMENDED

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>ChemoRT Regimen</th>
<th>ypCR Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCORD 12 (JCO 2010)</td>
<td>291</td>
<td>Cape+RT</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>293</td>
<td>Cape + Oxali 50mg/m2 wkly+RT</td>
<td>19 (p=0.09)</td>
</tr>
<tr>
<td>STAR-01 (JCO 2011)</td>
<td>379</td>
<td>FU CI+RT</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>368</td>
<td>FU CI + Oxali 60mg/m2 wkly+RT</td>
<td>16</td>
</tr>
<tr>
<td>German AIO-04 (Lancet 2012)</td>
<td>623</td>
<td>FU CI+RT</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>613</td>
<td>FU CI + Oxali 50mg/m2 wkly+RT</td>
<td>17 (p=0.038)</td>
</tr>
<tr>
<td>PETAAC-6 (PASCO, 2013)</td>
<td>547</td>
<td>Cape+RT</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>547</td>
<td>Cape + Oxali 50mg/m2 wkly+RT</td>
<td>13 (p=0.031)</td>
</tr>
<tr>
<td>NSABP R-04 (PASCO, 2012)</td>
<td>636</td>
<td>FU/Cape+RT</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>640</td>
<td>FU/Cape + Oxali 50mg/m2 wkly+RT</td>
<td>20 (p=0.42)</td>
</tr>
</tbody>
</table>

RT, radiotherapy; ypCR, pathological complete response
Locally advanced disease cT3c/d or very low, levators not threatened, MRF clear cT3c/d mid-rectum, cN1–N2 (extranodal), EMVI+

SCPRT or CRT

MRI to re-evaluate tumour

‘Watch-and-wait’ may be considered in high-risk patients if cCR achieved with CRT

TME (plus photographic record of specimen and assessment of TME quality)


cCR, Clinical complete response; CRT, chemoradiotherapy; EMVI, extramural vascular invasion; MRF, mesorectal fascia; MRI, magnetic resonance imaging; SCPRT, short-course preoperative radiotherapy; TME, total mesorectal excision
Our case surgery & pathology

Low anterior resection according to the TME principles and loop ileostomy performed 8 weeks after completion of CRT
No post-operative complications.

Histology
- Resection in the mesorectal plane
- Scanty residual moderately differentiated adenocarcinoma (Dworak’s TRG 3)
- ypT3N0 (0/45)
- No lymphatic or venous invasion

CRT, chemoradiotherapy; TME, total mesorectal excision; TRG, tumour regression grading excision
Macroscopic assessment of mesorectal excision
Downstaging after neoadjuvant treatment: neoadjuvant rectal score

\[ NAR = \frac{[5 \ pN - 3(cT - pT) + 12]^2}{9.61} \]

Our patient NAR score: 14.95
Neoadjuvant rectal score in CAO/ARO/AIO04 trial

Disease-free survival

P < 0.001

Time in years

Neoadjuvant Rectal Score: Low, Intermediate, High

< 8
8-16
>16

Fokas E, et al, Ann Oncol 2018
Our cases decision on adjuvant chemotherapy

4 months (i.e. 6 cycles) of adjuvant chemotherapy with single agent capecitabine
## Adding Oxaliplatin to 5-FU based adjuvant therapy in localised colon/rectal cancer

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Control</th>
<th>Exp.</th>
<th>Stage</th>
<th>DFS HR P value</th>
<th>OS HR P value</th>
<th>Absolute Gain in OS</th>
<th>G3 Neuro Tox</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOSAIC(^1)</td>
<td>2246</td>
<td>FULV2</td>
<td>FOLFOX4</td>
<td>II/III</td>
<td>0.80 0.003</td>
<td>0.84 0.046</td>
<td>4.2% at 6 y stage III</td>
<td>12%</td>
</tr>
<tr>
<td>NSABP-C07(^2)</td>
<td>2407</td>
<td>FULV Roswell</td>
<td>FLOX</td>
<td>II/III</td>
<td>0.80 0.0034</td>
<td>0.82 0.002</td>
<td>2.7 at 5 y Stage III</td>
<td>8.2%</td>
</tr>
<tr>
<td>XELOXA(^3)</td>
<td>1886</td>
<td>FULV Mayo</td>
<td>CAPEOX</td>
<td>III</td>
<td>0.80 0.0038</td>
<td>0.83 0.04</td>
<td>6 % at 7 y</td>
<td>11%</td>
</tr>
</tbody>
</table>

\(^1\)André T et al. J Clin Oncol 2007  
\(^3\)Schmoll HJ et al. J Clin Oncol 2015
# Adding Oxaliplatin to 5-FU based adjuvant therapy in localised colon/rectal cancer

| MOSAIC\(^1\) | 2246 | FULV2 | FOLFOX4 | II/III | 0.80  
|  |  |  |  |  | 0.003  
|  |  |  |  |  | 0.84  
|  |  |  |  |  | 0.046  
|  |  |  |  |  | 4.2% at 6 y stages I-III  
|  |  |  |  |  | 12%  
| NSABP-C07\(^2\) | 2407 | FULV Roswell | FLOX | II/III | 0.80  
|  |  |  |  |  | 0.0034  
|  |  |  |  |  | 0.82  
|  |  |  |  |  | 0.002  
|  |  |  |  |  | 2.7 at 5 y Stage III  
|  |  |  |  |  | 8.2%  
| XELOXA\(^3\) | 1886 | FULV Mayo | CAPEOX | III | 0.80  
|  |  |  |  |  | 0.0038  
|  |  |  |  |  | 0.83  
|  |  |  |  |  | 0.04  
|  |  |  |  |  | 6 % at 7 y  
|  |  |  |  |  | 11%  
| AIO04\(^4\) | 1233 | FU | mFOLFOX | II/III | 0.79  
|  |  |  |  |  | 0.030  
|  |  |  |  |  | 0.96  
|  |  |  |  |  | NS  
|  |  |  |  |  | 0.7 at 3 y  
|  |  |  |  |  | 9%  
| NSABP R04\(^5\) | 1284 | FU/Cape | + Oxali | II/III | 0.94 NS  
|  |  |  |  |  |  
|  |  |  |  |  |  
|  |  |  |  |  | NR  
|  |  |  |  |  | NR  
|  |  |  |  |  | 6%  
| PETACC6\(^6\) | 898 | Cape | + Oxali | II/III | 1.04 NS  
|  |  |  |  |  |  
|  |  |  |  |  |  
|  |  |  |  |  | NR  
|  |  |  |  |  | NR  
|  |  |  |  |  | 8%  

Neoadjuvant ChT plus chemo-RT versus chemo-RT followed by surgery and adjuvant ChT in MRI defined high risk rectal cancer: the Phase II randomised valencian experience

MRI defined Locally advanced Rectal Cancer patients N=108

1:1 Randomisation

Concurrent CRT with CAPOX

Surgery

Adjuvant CAPOX

CAPOX x 4

Concurrent CRT with CAPOX

Surgery


CRT, chemoradiotherapy; MRI, magnetic resonance imaging; RT, radiotherapy
THE WAY FORWARD: THE PHASE III RANDOMIZED RAPIDO TRIAL

MRI defined Locally advanced Rectal Cancer patients N=920

1:1 Randomisation

CRT with capecitabine Week 1-6

Surgery Week 12

Adjuvant ChT OPTIONAL

5x5 RT Week 1

Neoadjuvant XELOX X6 Week 3-16

Surgery Week 24-28

DFS at 3 years improved by 10% from 50% to 60%

PI: Prof. C. van de Velde

CRT, chemoradiotherapy; DFS, disease-free survival; MRI, magnetic resonance imaging; RT, radiotherapy
Integration of knowledge in a multidisciplinary team
LoE: IV GoR: A
Optimal staging by MRI LoE: III GoR: A
Selective preoperative radiation or chemoradiation LoE: I GoR: A
TME surgery LoE: II GoR: A
Adjuvant chemotherapy for high risk patients: LoE II GoR:B

GoR, grade of recommendation; LoE, level of evidence
THANKS