Management of early rectal cancer: Any role for adjuvant chemotherapy?

Andrés Cervantes
Professor of Medicine
Consulting and advisory services, speaking or writing engagements, public presentations:

Servier, Merck Serono, Amgen, Roche, Lilly, Bayer, Novartis, Takeda, Beigene

Direct research support to the responsible project lead:

Servier, Roche, Genentech, Bayer, Janssen, Merck Serono, Medimmune
CURRENTS CONCEPTS IN RECTAL CANCER DIAGNOSIS AND THERAPY

- TME surgery
- Optimal staging by MRI
- Pathological assessment of the quality of surgery
- Preoperative radiation or chemoradiation
- Integration of knowledge in a multidisciplinary team approach
- Selective approach for preoperative treatment
Distant metastases 4x greater risk than local recurrence

ADJUVANT THERAPY FOR LOCALIZEDRECTAL CANCER

CLINICAL PRACTICE GUIDELINES

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

R. Glynne-Jones¹, L. Wyrwicz², E. Tirt³⁴, G. Brown⁵, C. Rödel⁶, A. Cervantes⁷ & D. Arnold⁸, on behalf of
the ESMO Guidelines Committee*

<table>
<thead>
<tr>
<th>Risk group</th>
<th>TN substage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very early</td>
<td>cT1 sm1 N0 (on ERUS and MRI)</td>
</tr>
<tr>
<td>Early (Good)</td>
<td>cT1-cT2; cT3a/b if middle or high, N0 (or also cN1 if high), MRF clear, no EMVI</td>
</tr>
<tr>
<td>Intermediate</td>
<td>cT3a/b very low, levators clear, MRF clear or cT3a/b in mid- or high rectum, cN1-2 (not extranodal), no EMVI</td>
</tr>
<tr>
<td>Bad</td>
<td>cT3c/d or very low localisation levators threatened, MRF clear cT3c/d mid-rectum, cN1–N2 (extranodal), EMVI+, limited cT4aN0</td>
</tr>
<tr>
<td>Advanced (Ugly)</td>
<td>cT3 with any MRF involved, any cT4a/b, lateral node+</td>
</tr>
</tbody>
</table>
CURRENT APPROACH TO RECTAL CANCER

- MRI Staging
- MDT discussion
- Preoperative treatment if indicated
- TME Surgical resection
- Pathology assessment and estimation of risk
- Postoperative chemotherapy if indicated
THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE?

- The pre-TME/preoperative RT or ChRT data
- The TME/preoperative RT or ChRT data
- How to integrate ChT in patients with locally advanced disease?
THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE IN THE PRE-TME PRE-RT/CHRT PREOPERATIVE ERA?

- American Intergroup
- Quasar
- Japanese Society of Colon and Rectal Meta-analysis on individual data
- Cochrane Meta-analysis on individual data
THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE?

The American Intergroup* Pooled Analysis

* NSABP, NCCTG and US-GI Intergroup

\[ P \text{ value } < .001 \]
**The Role of Adjuvant Chemotherapy in Localised Rectal Cancer: What is the Evidence We Have?**

The QUASAR TRIAL

<table>
<thead>
<tr>
<th>UK QUASAR uncertain indication trial</th>
<th>5yr survival</th>
<th>5 yr recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approx 30% rectal.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chemo (80.3%)</td>
<td>No chemo (77.4%)</td>
</tr>
<tr>
<td>Whole cohort</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal subgroup</td>
<td>p=0.05</td>
<td>19.6%</td>
</tr>
</tbody>
</table>

WHAT IS THE EVIDENCE WE HAVE?

The Quasar trial

WHAT IS THE EVIDENCE WE HAVE?
The Japanese Society of Cancer of Colon and Rectum Meta-analysis on UFT trials

THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE?
The Cochrane Meta-analysis

Postoperative adjuvant chemotherapy in rectal cancer operated for cure. (Review)

Petersen SH, Harling H, Kirkeby LT, Wille-Jørgensen P, Mocellin S

THE COCHRANE COLLABORATION

2012
Figure 8. Forest plot of comparison: 1 Adjuvant vs No Adjuvant ALL, outcome: 1.2 Disease Free Survival (DFS).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[Hazard Ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard Ratio IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grage 1981</td>
<td>-0.562</td>
<td>0.278</td>
<td>2.4%</td>
<td>0.57 [0.33, 0.98]</td>
<td>1981</td>
</tr>
<tr>
<td>Fisher 1988 (NSABP)</td>
<td>-0.342</td>
<td>0.121</td>
<td>7.3%</td>
<td>0.71 [0.56, 0.90]</td>
<td>1988</td>
</tr>
<tr>
<td>Thomas 1988 (GTGR)</td>
<td>-0.198</td>
<td>0.225</td>
<td>3.4%</td>
<td>0.82 [0.53, 1.28]</td>
<td>1988</td>
</tr>
<tr>
<td>Hafström 1990</td>
<td>-0.446</td>
<td>0.236</td>
<td>3.2%</td>
<td>0.64 [0.40, 1.02]</td>
<td>1990</td>
</tr>
<tr>
<td>Krook 1991 (NCCTG)</td>
<td>-0.416</td>
<td>0.144</td>
<td>6.1%</td>
<td>0.66 [0.50, 0.87]</td>
<td>1991</td>
</tr>
<tr>
<td>Matsuda 1991 (SGACCS)</td>
<td>-0.128</td>
<td>0.118</td>
<td>7.4%</td>
<td>0.88 [0.70, 1.11]</td>
<td>1991</td>
</tr>
<tr>
<td>Bosset 2006 (EORTC)</td>
<td>-0.139</td>
<td>0.094</td>
<td>8.9%</td>
<td>0.87 [0.72, 1.05]</td>
<td>1993</td>
</tr>
<tr>
<td>QUASAR 2007</td>
<td>-0.386</td>
<td>0.134</td>
<td>6.6%</td>
<td>0.68 [0.52, 0.88]</td>
<td>1994</td>
</tr>
<tr>
<td>CCCSGJ 1995</td>
<td>-0.462</td>
<td>0.108</td>
<td>8.0%</td>
<td>0.63 [0.51, 0.78]</td>
<td>1995</td>
</tr>
<tr>
<td>Kornek 1996</td>
<td>-0.821</td>
<td>0.4</td>
<td>1.3%</td>
<td>0.44 [0.20, 0.96]</td>
<td>1996</td>
</tr>
<tr>
<td>Ito 1996 (TSHCFU)</td>
<td>-0.105</td>
<td>0.374</td>
<td>1.5%</td>
<td>0.90 [0.43, 1.87]</td>
<td>1996</td>
</tr>
<tr>
<td>Yasutomi 1997 (JFMTC 7-2)</td>
<td>-0.117</td>
<td>0.12</td>
<td>7.3%</td>
<td>0.89 [0.70, 1.13]</td>
<td>1997</td>
</tr>
<tr>
<td>Kodaira 1998 (JFMTC 7-1)</td>
<td>-0.329</td>
<td>0.112</td>
<td>7.8%</td>
<td>0.72 [0.58, 0.90]</td>
<td>1998</td>
</tr>
<tr>
<td>Taal 2001 (NACC)</td>
<td>-0.105</td>
<td>0.165</td>
<td>5.2%</td>
<td>0.90 [0.65, 1.24]</td>
<td>2001</td>
</tr>
<tr>
<td>Kato 2002 (TACSG)</td>
<td>-0.968</td>
<td>0.265</td>
<td>2.6%</td>
<td>0.38 [0.23, 0.64]</td>
<td>2002</td>
</tr>
<tr>
<td>Cafero 2003</td>
<td>0.086</td>
<td>0.14</td>
<td>6.3%</td>
<td>1.09 [0.83, 1.43]</td>
<td>2003</td>
</tr>
<tr>
<td>Watanabe 2004 (JFMTC15-2)</td>
<td>-0.288</td>
<td>0.189</td>
<td>4.4%</td>
<td>0.75 [0.52, 1.09]</td>
<td>2004</td>
</tr>
<tr>
<td>Sakamoto 2007 (JFMTC15-1)</td>
<td>-0.117</td>
<td>0.155</td>
<td>5.6%</td>
<td>0.89 [0.66, 1.21]</td>
<td>2007</td>
</tr>
<tr>
<td>Koda 2009</td>
<td>-1.022</td>
<td>0.528</td>
<td>0.8%</td>
<td>0.36 [0.13, 1.01]</td>
<td>2009</td>
</tr>
<tr>
<td>Hamaguchi 2011</td>
<td>-0.416</td>
<td>0.196</td>
<td>4.1%</td>
<td>0.66 [0.45, 0.97]</td>
<td>2011</td>
</tr>
</tbody>
</table>

Total (95% CI) 100.0% 0.75 [0.68, 0.83]

Heterogeneity: Tau² = 0.02; Chi² = 32.41, df = 19 (P = 0.03); I² = 41%
Test for overall effect: Z = 5.95 (P < 0.00001)
Figure 1. Forest plot of comparison: 1 Adjuvant vs No Adjuvant ALL, outcome: 1.1 Overall Survival

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log[Hazard Ratio]</th>
<th>SE</th>
<th>Weight</th>
<th>Hazard Ratio IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grage 1981</td>
<td>-0.892</td>
<td>0.366</td>
<td>1.4%</td>
<td>0.41 [0.20, 0.84]</td>
<td>1981</td>
</tr>
<tr>
<td>Thomas 1988 (GTSG)</td>
<td>-0.288</td>
<td>0.215</td>
<td>3.5%</td>
<td>0.75 [0.49, 1.14]</td>
<td>1988</td>
</tr>
<tr>
<td>Fisher 1988 (NSABP)</td>
<td>-0.236</td>
<td>0.134</td>
<td>6.8%</td>
<td>0.79 [0.61, 1.03]</td>
<td>1988</td>
</tr>
<tr>
<td>Hafström 1990</td>
<td>-0.342</td>
<td>0.255</td>
<td>2.6%</td>
<td>0.71 [0.43, 1.17]</td>
<td>1990</td>
</tr>
<tr>
<td>Krook 1991 (NCCTG)</td>
<td>-0.342</td>
<td>0.134</td>
<td>6.8%</td>
<td>0.71 [0.55, 0.92]</td>
<td>1991</td>
</tr>
<tr>
<td>Matsuda 1991 (SGACCS)</td>
<td>-0.03</td>
<td>0.119</td>
<td>7.8%</td>
<td>0.97 [0.77, 1.23]</td>
<td>1991</td>
</tr>
<tr>
<td>Bosset 2006 (EORTC)</td>
<td>-0.163</td>
<td>0.105</td>
<td>8.9%</td>
<td>0.85 [0.69, 1.04]</td>
<td>1993</td>
</tr>
<tr>
<td>QUASAR 2007</td>
<td>-0.261</td>
<td>0.13</td>
<td>7.0%</td>
<td>0.77 [0.60, 0.98]</td>
<td>1994</td>
</tr>
<tr>
<td>CCCSGJ 1995</td>
<td>-0.416</td>
<td>0.122</td>
<td>7.6%</td>
<td>0.66 [0.52, 0.84]</td>
<td>1995</td>
</tr>
<tr>
<td>Kornek 1996</td>
<td>-0.868</td>
<td>0.464</td>
<td>0.9%</td>
<td>0.42 [0.17, 1.04]</td>
<td>1996</td>
</tr>
<tr>
<td>Ito 1996 (TSGHCFU)</td>
<td>0.285</td>
<td>0.341</td>
<td>1.6%</td>
<td>1.33 [0.68, 2.59]</td>
<td>1996</td>
</tr>
<tr>
<td>Yasumotomi 1997 (JFMT 7-2)</td>
<td>-0.051</td>
<td>0.133</td>
<td>6.9%</td>
<td>0.95 [0.73, 1.23]</td>
<td>1997</td>
</tr>
<tr>
<td>Kodaira 1998 (JFMT 7-1)</td>
<td>-0.073</td>
<td>0.125</td>
<td>7.4%</td>
<td>0.93 [0.73, 1.19]</td>
<td>1998</td>
</tr>
<tr>
<td>Taal 2001 (NACC)</td>
<td>-0.051</td>
<td>0.184</td>
<td>4.4%</td>
<td>0.95 [0.66, 1.36]</td>
<td>2001</td>
</tr>
<tr>
<td>Kato 2002 (TACSG)</td>
<td>-0.416</td>
<td>0.327</td>
<td>1.7%</td>
<td>0.66 [0.35, 1.25]</td>
<td>2002</td>
</tr>
<tr>
<td>Cafiero 2003</td>
<td>0.285</td>
<td>0.198</td>
<td>4.0%</td>
<td>1.33 [0.90, 1.96]</td>
<td>2003</td>
</tr>
<tr>
<td>Watanabe 2004 (JFMT15-2)</td>
<td>-0.128</td>
<td>0.222</td>
<td>3.3%</td>
<td>0.88 [0.57, 1.36]</td>
<td>2004</td>
</tr>
<tr>
<td>Glimelius 2005 (NGTATG)</td>
<td>-0.1</td>
<td>0.101</td>
<td>9.2%</td>
<td>0.90 [0.74, 1.10]</td>
<td>2005</td>
</tr>
<tr>
<td>Sakamoto 2007 (JFMT15-1)</td>
<td>-0.094</td>
<td>0.165</td>
<td>5.2%</td>
<td>0.91 [0.66, 1.26]</td>
<td>2007</td>
</tr>
<tr>
<td>Koda 2009</td>
<td>-1.309</td>
<td>0.845</td>
<td>0.3%</td>
<td>0.27 [0.05, 1.42]</td>
<td>2009</td>
</tr>
<tr>
<td>Hamaguchi 2011</td>
<td>-0.511</td>
<td>0.239</td>
<td>2.9%</td>
<td>0.60 [0.38, 0.96]</td>
<td>2011</td>
</tr>
</tbody>
</table>

Total (95% CI) 100.0% 0.83 [0.76, 0.91]

Heterogeneity: Tau² = 0.01; Chi² = 28.73, df = 20 (P = 0.09); I² = 30%
Test for overall effect: Z = 4.11 (P < 0.0001)

Petersen et al, Cochrane Data Base of Systematic Rev 2012; CD004078
THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE?

• The pre-TME/preoperative RT or ChRT data
• The TME/preoperative RT or ChRT data
• How to integrate ChT in patients with locally advanced disease?
THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE IN THE TME/PREOPERATIVE RT OR CHRT ERA?

• Chronicle trial
• Proctor/script trial
• Meta-analysis by Breugom on individual data from 4 trials and 1200 pts
• Adore trial
• CAO/ARO/AIO-04 trial
CHRONICLE TRIAL: ASSESSING THE VALUE OF ADJUVANT CHEMOTHERAPY IN THE TREATMENT OF RECTAL CANCER AFTER PREOPERATIVE CHEMORADIATION

Patients with locally advanced rectal cancer

Pre-operative chemoradiation
Min 45Gy and fluoropyrimidine based

RO resection achieved

RANDOMISE

Follow-up only

Capecitabine + Oxaliplatin
6 courses

WHAT IS THE EVIDENCE WE HAVE?

The Chronicle trial

- Target population 800 pts
- Primary end point: DFS at 3 years (HR: 0.75)
- Accrued nr. Patients 113
- Underpowered to detect any potential benefit of Chemotherapy

- HR for DFS: 0.80 (95% CI: 0.38-1.69; p: 0.56)
- HR for OS: 1.18 (95% CI: 0.43-3.26; p: 0.75)

Target population 840 pts
- Primary end point: OS at 5 years improved from 60 to 70%
- Accrued nr. Patients 437 over 14 years
- Underpowered to detect any potential benefit of Chemotherapy
- 5 year OS for observation: 79.2%
- 5 year OS for adj therapy: 80.4%
- HR for DFS: 0.80 (95% CI: 0.60-1.07; p:0.13)
- HR for OS: 0.93 (95% CI: 0.61-1.29; p:0.73)
WHAT IS THE EVIDENCE WE HAVE?
The Breugom’s Meta-analysis

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>MOSAIC¹</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-C07²</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>XELOXA³</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>

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</th>
<th>OS HR</th>
<th>Absolute Gain in OS</th>
<th>G3 Neurtox</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOSAIC¹</td>
<td>224</td>
<td>FULV2</td>
<td>FOLFOX4</td>
<td>II/III</td>
<td>0.80</td>
<td>0.84</td>
<td>4.2% at 6 y stage III</td>
<td>12%</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td></td>
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<td></td>
<td>0.003</td>
<td>0.046</td>
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</tr>
<tr>
<td>NSABP-C07²</td>
<td>240</td>
<td>FULV Roswell</td>
<td>FLOX</td>
<td>II/III</td>
<td>0.80</td>
<td>0.82</td>
<td>2.7 at 5 y Stage III</td>
<td>8.2%</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td>0.0034</td>
<td>0.002</td>
<td></td>
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</tr>
<tr>
<td>XELOXA³</td>
<td>188</td>
<td>FULV Mayo</td>
<td>CAPEOX</td>
<td>III</td>
<td>0.80</td>
<td>0.83</td>
<td>6 % at 7 y</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td>0.0038</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AIO04⁴</td>
<td>123</td>
<td>FU</td>
<td>mFOLFOX6</td>
<td>II/III</td>
<td>0.79</td>
<td>0.96</td>
<td>0.7 at 3 y</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td>0.030</td>
<td>NS</td>
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</tr>
<tr>
<td>NSABP R04⁵</td>
<td>128</td>
<td>FU/Cape + Oxali</td>
<td></td>
<td>II/III</td>
<td>0.94</td>
<td>0.94</td>
<td>NR</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td></td>
<td></td>
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<td>NS</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PETACC6⁶</td>
<td>898</td>
<td>Cape + Oxali</td>
<td></td>
<td>II/III</td>
<td>1.04</td>
<td>NR</td>
<td>NR</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NS</td>
<td>NR</td>
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<td></td>
</tr>
</tbody>
</table>

THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE? THE ADORE TRIAL

Rectal Cancer patients who completed preoperative Long course chemoradiation and Surgery with free margins ypT3-4N0 or anyTN1-2

1:1 Randomization

BOLUS 5FU-LV Mayo Clinic Schedule

FOLFOX

Hong YS et al. Lancet Oncol 2014
THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE? THE ADORE TRIAL

- No observational arm
- Randomised phase II trial 80% Power
- Unilateral hypothesis
- Target population 320 pts
- Primary end point: DFS at 3 years improved by 8% from 70 to 78%
- Accrued nr. Patients 322 over 3.5 years

Hong YS et al. Lancet Oncol 2014
ADORE TRIAL: ADJUVANT CHEMOTHERAPY IN STAGE II/III RECTAL CANCER AFTER PREOPERATIVE CHEMORADIATION
DISEASE FREE AND OVERALL SURVIVAL

Hong YS et al. Lancet Oncol 2014
THE ROLE OF ADJUVANT CHEMOTHERAPY IN LOCALISED RECTAL CANCER: WHAT IS THE EVIDENCE WE HAVE?

- The pre-TME/preoperative RT or ChRT data
- The TME/preoperative RT or ChRT data
- How to integrate ChT in patients with locally advanced disease?
RECTAL CANCER: ESMO CLINICAL PRACTICE GUIDELINES

DOWNSTAGING AFTER NEOADJUVANT TREATMENT: NEOADJUVANT RECTAL SCORE

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

NEoadjuvant Rectal Score
A Series of 158 Locally Advanced Rectal Cancer Patients Treated with CT-RT

Log Rang Test  p: 0.004
(Mantel Cox)

NEOADJUVANT RECTAL SCORE IN CAO/ARO/AIO04 TRIAL

NEOADJUVANT CT PLUS CT-RT VERSUS CT-RT FOLLOWED BY SURGERY AND ADJUVANT CT IN MRI DEFINED HIGH RISK RECTAL CANCER: THE PHASE II RANOMIZED VALENCIAN EXPERIENCE

MRI defined Locally advanced Rectal Cancer patients N=108

1:1 Randomization

Concurrent CRT with CAPOX

S

Adjuvant CAPOX

CAPOX x 4

Concurrent CRT with CAPOX

S

POLISH PHASE III TRIAL CRT VS 5X5 AND FOLFOX

RT+5FU LV wk1,5
Ox weekly

MRI defined 66%
Oxaliplatin became optional
Short duration FOLFOX
Weekly Ox single agent wk 2,3,4

Locally advanced
Unresectable
Locally recurrent

Primary end point R0 resection

Primary end point R0 resection

POLISH TRIAL: OVERALL SURVIVAL FAVORS PREOPERATIVE SCPRT + CHRT VERSUS PREOPERATIVE CHEMORADIATION IN LOCALLY ADVANCED RECTAL CANCER

HR: 0.73 p: 0.046

THE WAY FORWARD: THE PHASE III RANDOMIZED RAPIDO TRIAL

MRI defined Locally advanced Rectal Cancer patients N=920

1:1 Randomization

CRT with CAPECITABINE Week 1-6

Surgery Week 12

Adjuvant CT 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
Adjuvant Chemotherapy is not standard of care for all localized rectal cancer patients

Adjuvant Chemotherapy should be considered for patients at risk after direct surgery without neoadjuvant therapy

Adjuvant Chemotherapy should be also considered after neoadjuvant Chemoradiation for patients with stage ypIII and high risk stage ypII. LoE: II GoR: C

The decision on postoperative Chemotherapy (FU alone or combined with oxaliplatin) should be risk balanced, taking into account both the predicted toxicity for a particular patient and the risk of relapse, and should be made jointly by the individual and the clinician.
Thank you