Randomized multicentre phase III study of short course radiation therapy followed by prolonged preoperative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

Leiden University Medical Center
Dept. of Surgery, Datacenter, K6-R
P.O. Box 9600, 2300 RC LEIDEN
E-mail: datacenter@lumc.nl
Phone: +31-71-5263500, Fax: +31-71-5266744

CKS 2011-4997 RAPIDO CRF: F01 (Page 1 of 3), version 2.0 1/08/2014

<table>
<thead>
<tr>
<th>Center Id</th>
<th>Subject Id</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>7-1-19</td>
</tr>
</tbody>
</table>

1. **GENERAL INFORMATION**

1. Physician
   - 1. Speciality
     - [ ] surgeon
     - [ ] oncologist
     - [ ] radiotherapist

2. Surgery and Chemotherapy Center
   - ____________________________

3. Radiation Center
   - ____________________________

2. **INCLUSION CRITERIA:** Main questions must be “Yes”!

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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</table>

1. Biopsy-proven, newly diagnosed primary rectal adenocarcinoma, i.e. with the lowest part of the tumour less than 16 cm from the anal verge using a rigid rectoscope or flexible endoscope
   - [ ]

2. Locally advanced tumour fulfilling at least one of the following criteria on pelvic MRI indicating high risk of failing locally and/or systemically. **Fill out all criteria! At least one should be yes:**
   - 2a. Clinical stage (c) T4a, i.e. overgrowth to an adjacent organ or structure like the prostate, urinary bladder, uterus, sacrum, pelvic floor or side-wall (according to TNM version 5, in version 7 this is T4b)
     - [ ]
   - 2b. cT4b, i.e. peritoneal involvement (TNM5, in version 7 this is T4a)
     - [ ]
   - 2c. Extramural vascular invasion (EMVI+)
     - [ ]
   - 2d. N2, i.e. four or more lymph nodes in the mesorectum showing morphological signs on MRI indicating metastatic disease. Four or more nodes, whether enlarged or not, with a rounded, homogeneous appearance is thus not sufficient
     - [ ]
   - 2e. Positive MRF, i.e. within one mm from the mesorectal fascia
     - [ ]
   - 2f. Metastatic lateral nodes (lat LN+)
     - [ ]

3. Staging done within 5 weeks before randomisation
   - [ ]

4. Age ≥ 18 years
   - [ ]

5. ECOG performance score ≤ 1
   - [ ]

6. No evidence of metastatic disease as determined by CT scan of chest and abdomen or other investigations such as PET scan or biopsy if required
   - [ ]

7. Adequate bone marrow function with platelets ≥ 100 x 10⁹/l; WBC ≥ 4 x 10⁹/l, serum bilirubin < 35 µmol/l, creatinine clearance ≥50ml/min, clinically acceptable haemoglobin levels (max 5 weeks before randomisation)
   - [ ]

8. Mentally and physically fit for chemotherapy as judged by the oncologist
   - [ ]

9. Adequate potential for follow-up
   - [ ]

10. Written informed consent
    - [ ]
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RANDOMISATION FORM

Center Id | Subject Id | Date of Birth
------- | ---------- | -------
          | 7          | 7-1-19

3. EXCLUSION CRITERIA: All must be “No” otherwise patient is not eligible

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Extensive growth into cranial part of the sacrum (above S3) or the lumbosacral nerve roots indicating that surgery will never be possible even if substantial tumour down-sizing is seen</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2. Familial Adenomatosis Polyposis coli (FAP), Hereditary Non-Polyposis Colorectal Cancer (HNPCC), active Crohn's disease or active ulcerative Colitis</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>3. Concomitant malignancies, except for adequately treated basocellular carcinoma of the skin or in situ carcinoma of the cervix uteri. Subjects with prior malignancies must be disease-free for at least 5 years</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>4. Known DPD deficiency</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>5. Any contraindications to MRI (e.g. patients with pacemakers)</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>6. Medical or psychiatric conditions that compromise the patient’s ability to give informed consent</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>7. Presence of metastatic disease or recurrent rectal tumour.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>8. Concurrent uncontrolled medical conditions</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>9. Previous radiotherapy in the pelvic region (e.g. prostate) or previous rectal surgery (e.g. TEM) or any investigational treatment for rectal cancer within the past month.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>10. Pregnancy or breast feeding</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>11. Known malabsorption syndromes or a lack of physical integrity of the upper gastrointestinal tract</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>12. Clinically significant (i.e. active) cardiac disease (e.g. congestive heart failure, symptomatic coronary artery disease and cardiac dysrhythmia, e.g. atrial fibrillation, even if controlled with medication) or myocardial infarction within the past 12 months</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>13. Any symptoms or history of peripheral neuropathy</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
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**RANDOMISATION FORM**

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<td></td>
<td>7</td>
<td>- 1 9</td>
</tr>
</tbody>
</table>

4. **SPECIFIC QUESTIONS**

1. **Written Informed Consent**
   1. Date of Informed Consent: -2012
   2. Consent for Tissue Collection: ☐ no ☐ yes ☐ N.A.

2. **Participation in Side Studies**
   1. Quality of Life (after 3 years): ☐ no ☐ yes ☐ N.A.
   2. Tumour tissue pre and post treatment: ☐ no ☐ yes ☐ N.A.
   3. Serum and Plasma Samples: ☐ no ☐ yes ☐ N.A.

3. **Stratification**
   1. ECOG Performance Status: ☐ 0 ☐ 1
   2. Clinical T-stage: ☐ cT2-3 ☐ cT4
   3. Clinical N-stage: ☐ cN0 ☐ cN+

4. **Gender**
   ☐ male ☐ female

5. **Baseline MRI Scan**
   ☐ no ☐ yes → -2012

6. **Randomisation**
   1. Allocated Treatment
      - Arm A: control: 28 x 1.8 Gy or 25 x 2.0 Gy + CT → surgery → ± CT
      - Arm B: exp.: 5 x 5 Gy → CT → surgery
   2. Date of Randomisation: -2012

**Notes:**

________________________

________________________

________________________

________________________

**Signature**
**Datacenter Name**
**Date**

**Signature**
**Investigator Name**
**Date**
### History and Physical Examination

1. Family History of Bowel Cancer
   - [ ] no
   - [ ] yes

2. History of Ischaemic Heart Disease
   - [ ] no
   - [ ] yes

3. History of Diabetes Mellitus
   - [ ] no
   - [ ] yes

4. ECOG Performance Status
   - [ ]

5. Height [cm]
   - [ ]
   - [ ]
   - [ ]

6. Weight [kg]
   - [ ]
   - [ ]

### Prior Treatment

1. Defunctioning stoma/bypass surgery
   - [ ] no
   - [ ] yes

2. Other surgery
   - [ ] no
   - [ ] yes

### Diagnosis

1. Date of biopsy taken
   - [ ] [ ] [ ] 201

2. Biopsy obtained by
   - endoscopy
   - surgery
   - radiology guided procedure

3. Number Histology Biopsy
   - [ ]

4. Adenocarcinoma
   - [ ] no
   - [ ] yes

### Staging

1. Tumour Palpable by Digital Rectal Examination
   - [ ] no
   - [ ] yes

   1. Distance from Anal Verge [mm]
      - [ ]
      - [ ]

2. Distance from Anal Verge by Endoscopy [mm]
   - [ ]

3. Imaging, Histology, Staging reviewed in Multi Disciplinary Team Meeting
   - [ ] no
   - [ ] yes

   1. Date of MDT
      - [ ] [ ] [ ] 201
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**HISTORY AND STAGING FORM**

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<td>xx 1-9</td>
</tr>
</tbody>
</table>

### 5. Hematology

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Unit</th>
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</thead>
<tbody>
<tr>
<td>1. Date of Hematology Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Hemoglobin</td>
<td></td>
<td>mmol/L mmol/L</td>
</tr>
<tr>
<td>3. Leucocytes</td>
<td></td>
<td>mmol/L mmol/L</td>
</tr>
<tr>
<td>4. Neutrophils</td>
<td></td>
<td>mmol/L mmol/L</td>
</tr>
<tr>
<td>5. Trombocytes</td>
<td></td>
<td>mmol/L mmol/L</td>
</tr>
</tbody>
</table>

### 6. Biochemistry

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Date of Biochemistry Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Creatinin</td>
<td></td>
<td>µmol/L µmol/L</td>
</tr>
<tr>
<td>3. Alkaline Phosphatase</td>
<td></td>
<td>µkat/L µkat/L</td>
</tr>
<tr>
<td>4. ALAT</td>
<td></td>
<td>µkat/L µkat/L</td>
</tr>
<tr>
<td>5. ASAT</td>
<td></td>
<td>µkat/L µkat/L</td>
</tr>
<tr>
<td>6. Total Bilirubin</td>
<td></td>
<td>µmol/L µmol/L</td>
</tr>
<tr>
<td>7. CEA</td>
<td></td>
<td>µg/L µg/L</td>
</tr>
</tbody>
</table>

Notes:

Signature Investigator

Name

Date
## MRI ASSESSMENT

According to the protocol TNM5 has to be used in this trial except for notification of metastatic disease

<table>
<thead>
<tr>
<th>Item</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. MRI Sagittal Assessment</td>
<td>not done</td>
</tr>
<tr>
<td>2. Scan Record Number</td>
<td></td>
</tr>
<tr>
<td>3. Tumour Position in Relation to Peritoneal Reflection</td>
<td>above</td>
</tr>
<tr>
<td>4. Distance from Anal Verge [mm]</td>
<td></td>
</tr>
<tr>
<td>5. Distance from Anorectal junction [mm]</td>
<td></td>
</tr>
<tr>
<td>6. Length (L) of tumour [mm]</td>
<td></td>
</tr>
<tr>
<td>7. Minimum distance to mesorectal fascia [mm]</td>
<td></td>
</tr>
<tr>
<td>8. Location</td>
<td></td>
</tr>
<tr>
<td>9. MRI cT-stage according to TNM5</td>
<td>cT1</td>
</tr>
<tr>
<td></td>
<td>cT3b (&gt;5mm extramural)</td>
</tr>
<tr>
<td>10. Extramural Vascular Invasion</td>
<td>no</td>
</tr>
<tr>
<td>11. Tumours below the level of the levators</td>
<td>no</td>
</tr>
<tr>
<td>12. cN-stage according to TNM5</td>
<td>cN0 (no LN)</td>
</tr>
<tr>
<td>13. Malignant lateral nodes present, &gt; 1cm (lat N+) or morphological features</td>
<td>no</td>
</tr>
<tr>
<td>14. Sites with distant metastases according to TNM7</td>
<td>M0 (no metastases)</td>
</tr>
</tbody>
</table>
### 2. CT ASSESSMENT

1. **CT Assessment**
   - [ ] not done  [ ] done →  [ ] - [ ] - 201

2. **Sites Imaged**  
   - [ ] chest  [ ] abdomen  [ ] pelvis

3. **Positive Lymph Nodes**
   - [ ] no  [ ] yes →
   - 1. Pelvic  [ ] no  [ ] yes  [ ] indeterminate
   - 2. Inguinal  [ ] no  [ ] yes  [ ] indeterminate
   - 3. Abdominal  [ ] no  [ ] yes  [ ] indeterminate
   - 4. Other →  [ ] no  [ ] yes  [ ] indeterminate

4. **Distant Metastasis**
   - [ ] no  [ ] yes →
   - 1. Liver  [ ] no  [ ] yes  [ ] indeterminate
   - 2. Lung  [ ] no  [ ] yes  [ ] indeterminate
   - 3. Other →  [ ] no  [ ] yes  [ ] indeterminate

---

**Notes:**

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**Signature**

**Investigator**

**Name**

**Date**
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RAPIDO CRF: F04 (Page 1 of 1), version 2.1, 15/11/2013

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<td>x x - 1 9</td>
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</tbody>
</table>

1. Radiotherapy Administered
   - □ no → to 1.1
   - □ yes → to 1.2
   - 1. Reason no Radiotherapy
     - □ poor PS
     - □ PD
     - □ dead
     - □ refusal
     - □ adm. difficulty
     - □ immediate surgery
   - 2. Date of Start Radiotherapy: 1-1-2011
   - 3. Date of Stop Radiotherapy: 1-1-2011
   - 4. Technique
     - □ 3D-CRT
     - □ IMRT
     - □ other, specify →
   - 5. Full Bladder
     - □ no
     - □ yes
   - 6. Position
     - □ prone
     - □ supine
   - 7. Belly Board or Similar Device used
     - □ no
     - □ yes
   - 8. Field reduction (arm A)
     - □ no
     - □ yes
     - □ N.A. (arm B:5X5Gy)

2. Schedule
   - 1. Number of fractions
   - 2. Fraction dose [Gy]
   - 3. Boost given
     - □ no
     - □ yes →
   - 3a. Date of boost: 1-1-2011
   - 3b. Number of fractions boost
   - 3c. Fraction dose boost [Gy]
   - 4. Total dose (incl. boost) [Gy]

3. Adverse events (CTC grade ≥ 1)
   - □ no
   - □ yes → fill out AE form

Notes:
________________________________________________________________________
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________________________________________________________________________
________________________________________________________________________

<table>
<thead>
<tr>
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<th>Investigator</th>
<th>Name</th>
<th>Date</th>
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<tbody>
<tr>
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<td></td>
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</table>
### RAPIDO

**Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy**

**PREOPERATIVE CAPECITABINE FORM – ARM A**

CKS 2011-4997

RAPIDO CRF: F05a (Page 1 of 2), version 1.7, 15/01/2014

---

**1. CHEMOTHERAPY**

- [ ] no → [ ] yes go to 2.1

1.1 Reason no chemotherapy

- [ ] not fit for chemotherapy
- [ ] patient refusal
- [ ] other → __________

**2. CAPECITABINE**

<table>
<thead>
<tr>
<th></th>
<th>week 1</th>
<th>week 2</th>
<th>week 3</th>
<th>week 4</th>
<th>week 5</th>
<th>week 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Date of first tablets cycle</td>
<td>-</td>
<td>- 201</td>
<td>-</td>
<td>- 201</td>
<td>-</td>
<td>- 201</td>
</tr>
<tr>
<td>2. Weight at start [kg]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. ECOG Performance at start</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Dose per day [mg]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Cumulative dose per week [mg]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Interruption current week [days]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Dose Modification Relative to Previous week</td>
<td>N.A.</td>
<td>[ ] none</td>
<td>25%</td>
<td>[ ] 50%</td>
<td>stop</td>
<td>25%</td>
</tr>
<tr>
<td>8. Delay next cycle [days] (if no delay, please fill in 0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Reason delay / dose adjustment</td>
<td>[ ] no delay</td>
<td>poor WHO</td>
<td>toxicity</td>
<td>[ ] poor WHO</td>
<td>toxicity</td>
<td>[ ] poor WHO</td>
</tr>
<tr>
<td>10. Date of last tablets</td>
<td>-</td>
<td>- 201</td>
<td>-</td>
<td>- 201</td>
<td>-</td>
<td>- 201</td>
</tr>
</tbody>
</table>
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PREOPERATIVE CAPECITABINE FORM – ARM A

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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>x - 1 9</td>
</tr>
</tbody>
</table>

3. ADVERSE EVENTS

<table>
<thead>
<tr>
<th>1. Toxicity (CTC grade ≥ 1)</th>
<th>week 1</th>
<th>week 2</th>
<th>week 3</th>
<th>week 4</th>
<th>week 5</th>
<th>week 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>yes → AE form</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

4. LAB TESTS

<table>
<thead>
<tr>
<th>1. Date Laboratory Tests</th>
<th>Other unit</th>
<th>before week 1</th>
<th>before week 2</th>
<th>before week 3</th>
<th>before week 4</th>
<th>before week 5</th>
<th>before week 6</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>- 201</td>
<td>- 201</td>
<td>- 201</td>
<td>- 201</td>
<td>- 201</td>
<td>- 201</td>
</tr>
<tr>
<td>2. Hemoglobin</td>
<td>mmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Platelet Count</td>
<td>x 10^9/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. WBC</td>
<td>x 10^9/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Neutrophils</td>
<td>x 10^9/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: ________________________________________________________________
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______________________________________________________________

SIGNATURE
Investigator: ___________________________ NAME: ___________________________ DATE: ___________________________
**PREOPERATIVE CAPOX FORM – ARM B**

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**Center Id**  
**Subject Id**  
**Date of Birth**

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<th>Subject Id</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>x x 1 9</td>
</tr>
</tbody>
</table>

1. **CHEMOTHERAPY**

- [ ] no  
- [x] yes go to 2.1  

1.1 Reason no Chemotherapy  
- [ ] not fit for chemotherapy  
- [ ] patient refusal  
- [ ] other

2. **CAPECITABINE**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Date of first tablets</th>
<th>Weight at start [kg]</th>
<th>ECOG Performance at start</th>
<th>Dose per day [mg]</th>
<th>Cumulative dose per cycle [mg]</th>
<th>Interruption current cycle [days]</th>
<th>Dose Modification Relative to Previous Cycle</th>
<th>Delay next cycle [days]</th>
<th>Reason delay / dose adjustment</th>
<th>Date of last tablets</th>
</tr>
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<tbody>
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9. **Reason delay / dose adjustment**

- [ ] no delay  
- [ ] poor WHO  
- [ ] toxicity  
- [ ] poor compl.  
- [ ] disease rel.  
- [ ] adm. diff.  
- [ ] other

10. **Date of last tablets**

- - 201
## 3. OXALIPLATIN

<table>
<thead>
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<th></th>
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<th>cycle 4</th>
<th>cycle 5</th>
<th>cycle 6</th>
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</thead>
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<td>- - 201</td>
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<td>3. Total Dose [mg]</td>
<td>□□□□□</td>
<td>□□□□□</td>
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<td>5. Dose Modification Relative to Previous Cycle</td>
<td>N.A.</td>
<td>□ none □ 25% □ stop</td>
<td>□ none □ 25% □ stop</td>
<td>□ none □ 25% □ stop</td>
<td>□ none □ 25% □ stop</td>
<td>□ none □ 25% □ stop</td>
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## 4. ADVERSE EVENTS

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<th>cycle 6</th>
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<tr>
<td>1. Toxicity (CTC grade ≥ 1)</td>
<td>□ no □ yes → AE form</td>
<td>□ no □ yes → AE form</td>
<td>□ no □ yes → AE form</td>
<td>□ no □ yes → AE form</td>
<td>□ no □ yes → AE form</td>
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### PREOPERATIVE CAPOX FORM – ARM B

**Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy**

**RAPIDO CRF: F05b (Page 3 of 3), version 1.7, 15/01/2014**

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#### 5. LAB TESTS

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<th>before cycle 5</th>
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<td>- - 201</td>
<td>- - 201</td>
<td>- - 201</td>
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<td>2. Hemoglobin [mmol/L]</td>
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<td>3. Platelet Count [x 10^9/L]</td>
<td>[ ]</td>
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<td>4. WBC [x 10^9/L]</td>
<td>[ ]</td>
<td>[ ]</td>
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<td>5. Neutrophils [x 10^9/L]</td>
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<td>[ ]</td>
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**Notes:**

- 
- 
- 
- 
- 
- 
- 

**SIGNATURE**

**Investigator**

**NAME**

**DATE**
# POSTOPERATIVE CAPOX FORM – ARM A

**RAPIDO**

Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

---

## Center Id | Subject Id | Date of Birth
---|---|---
| | | 7 x x - 1 9 |

### 1. CHEMOTHERAPY

- **no →**
- **yes go to 2.1**

1.1 Reason no Chemotherapy

- not fit for chemotherapy
- patient refusal
- other → __________

### 2. CAPECITABINE

<table>
<thead>
<tr>
<th>cycle 1</th>
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<th>cycle 4 N.A.</th>
<th>cycle 5 N.A.</th>
<th>cycle 6 N.A.</th>
<th>cycle 7 N.A.</th>
<th>cycle 8 N.A.</th>
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<td>-</td>
<td>- 201</td>
<td>-</td>
<td>- 201</td>
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<tr>
<td>Weight at start [kg]</td>
<td></td>
<td></td>
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<td>ECOG Performance at start</td>
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<td>Dose per day [mg]</td>
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<tr>
<td>Cumulative dose per cycle [mg]</td>
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<td>Interruption current cycle [days]</td>
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<td>none 25% 50% stop</td>
<td>none 25% 50% stop</td>
<td>none 25% 50% stop</td>
<td>none 25% 50% stop</td>
<td>none 25% 50% stop</td>
<td>none 25% 50% stop</td>
</tr>
</tbody>
</table>
| Delay next cycle [days] | | | | | | | | (if no delay, please fill in 0)
| Reason delay / dose adjustment | | | | | | | | |
| Date of last tablets | - | - 201 | - | - 201 | - | - 201 | - | - 201 |
### 3. **OXALIPLATIN**

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<th>cycle 3</th>
<th>cycle 4</th>
<th>cycle 5</th>
<th>cycle 6</th>
<th>cycle 7</th>
<th>cycle 8</th>
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<tr>
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<td>-201</td>
<td>-</td>
<td>-201</td>
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<tr>
<td>Total Dose [mg]</td>
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<td>Dose Modification Relative to Previous Cycle</td>
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<td>□none □40% □25% □stop</td>
<td>□none □40% □25% □stop</td>
<td>□none □40% □25% □stop</td>
<td>□none □40% □25% □stop</td>
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<td>□</td>
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### 4. **ADVERSE EVENTS**

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<th>cycle 5</th>
<th>cycle 6</th>
<th>cycle 7</th>
<th>cycle 8</th>
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<tr>
<td>Toxicity (CTC grade ≥ 1)</td>
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<td>□no form</td>
<td>□no form</td>
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<td>□no form</td>
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</table>

**RAPIDO**

*Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy*

**POSTOPERATIVE CAPOX FORM – ARM A**
### POSTOPERATIVE CAPOX FORM – ARM A

**RANDOMIZED MULTICENTRE PHASE III STUDY OF SHORT COURSE RADIATION THERAPY FOLLOWED BY PROLONGED PRE-OPERATIVE CHEMOTHERAPY AND SURGERY IN PATIENTS WITH HIGH RISK PRIMARY RECTAL CANCER COMPARED TO STANDARD PREOPERATIVE CHEMORADIOThERAPY, SURGERY AND OPTIONAL ADJUVANT CHEMOTHERAPY**

**RAPIDO**

Leiden University Medical Center
Dept. of Surgery, Datacenter, K6-R
P.O. Box 9600, 2300 RC LEIDEN
E-mail: datacenter@lumc.nl
Phone: +31-71-5263500, Fax: +31-71-5266744

CKS 2011-4997
RAPIDO CRF: F05c (Page 3 of 3), version 1.7, 15/01/2014

---

**Center Id** | **Subject Id** | **Date of Birth**
--- | --- | ---
7 | x | x-19

---

#### 5. LAB TESTS

<table>
<thead>
<tr>
<th></th>
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<th>cycle 4</th>
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<tr>
<td>Hemoglobin (mmol/L)</td>
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<td>Platelet Count (x10^9/L)</td>
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<td>Neutrophils (x10^9/L)</td>
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Notes:

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**SIGNATURE**

**INVESTIGATOR** | **NAME** | **DATE**
**Center Id** | **Subject Id** | **Date of Birth**
---|---|---
7 | x | x - 19

**1. CHEMOTHERAPY**

- [ ] no → [ ] yes go to 2.1

1.1 Reason no Chemotherapy
- [ ] not fit for chemotherapy
- [ ] patient refusal
- [ ] other →

**2. OXALIPLATIN**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Date of Infusion</th>
<th>Weight at start [kg]</th>
<th>ECOG Performance at start</th>
<th>Total Dose Oxaliplatin [mg]</th>
<th>Dose Modification Relative to Previous Cycle</th>
<th>Reason delay / dose adjustment</th>
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<td>N.A.</td>
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<td>N.A.</td>
<td>N.A.</td>
<td>no delay poor WHO toxicity poor compliance disease related adm. difficulties other</td>
</tr>
<tr>
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<td>N.A.</td>
<td>N.A.</td>
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</tr>
<tr>
<td>cycle 4</td>
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<td>N.A.</td>
<td>N.A.</td>
<td>no delay poor WHO toxicity poor compliance disease related adm. difficulties other</td>
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<td>no delay poor WHO toxicity poor compliance disease related adm. difficulties other</td>
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<td>no delay poor WHO toxicity poor compliance disease related adm. difficulties other</td>
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*Only fill out this form in case FOLFOX4 was given as alternative for CAPOX*
**3. LEUCOVORIN**

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<th>N.A.</th>
<th>6</th>
<th>N.A.</th>
<th>7</th>
<th>N.A.</th>
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<td>201</td>
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<tr>
<td>Dose per day leucovorin [mg]</td>
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<tr>
<td>Interruption current cycle [days]</td>
<td></td>
<td></td>
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<td>25%</td>
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</tbody>
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*Only fill out this form in case FOLFOX4 was given as alternative for CAPOX*
**Only fill out this form in case FOLFOX4 was given as alternative for CAPOX**

<table>
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<tr>
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<th>Subject Id</th>
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<th>4. 5-FU</th>
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</tr>
<tr>
<td>7</td>
<td>x x</td>
<td>19</td>
<td>N.A.</td>
</tr>
</tbody>
</table>

1. Date of Infusion day 1
   - cycle 1: N.A.
   - cycle 2: N.A.
   - cycle 3: N.A.
   - cycle 4: N.A.
   - cycle 5: N.A.
   - cycle 6: N.A.

4. Dose per day 5-FU [mg]
   - cycle 1: N.A.
   - cycle 2: N.A.
   - cycle 3: N.A.
   - cycle 4: N.A.
   - cycle 5: N.A.
   - cycle 6: N.A.

5. Cum. dose per cycle 5-FU [mg]
   - cycle 1: N.A.
   - cycle 2: N.A.
   - cycle 3: N.A.
   - cycle 4: N.A.
   - cycle 5: N.A.
   - cycle 6: N.A.

6. Interruption current cycle [days]
   - none: N.A.
   - 50%: N.A.
   - stop: N.A.

7. Dose Modification Relative to Previous Cycle
   - cycle 1: none
   - cycle 2: 50%
   - cycle 3: stop
   - cycle 4: none
   - cycle 5: 50%
   - cycle 6: stop

8. Delay next cycle [days]
   - no delay: N.A.
   - 25%: N.A.
   - 50%: N.A.

9. Reason delay / dose adjustment
   - no delay: other
   - poor WHO toxicity: other
   - poor compliance disease related adm. difficulties: other

**Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy**
5. ADVERSE EVENTS

<table>
<thead>
<tr>
<th>Cycle</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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</thead>
<tbody>
<tr>
<td>Toxicity (CTC grade ≥ 1)</td>
<td>no</td>
<td>yes → AE form</td>
<td>no</td>
<td>yes → AE form</td>
<td>no</td>
<td>yes → AE form</td>
</tr>
</tbody>
</table>

6. LAB TESTS

<table>
<thead>
<tr>
<th>Test</th>
<th>before cycle 1</th>
<th>before cycle 2</th>
<th>before cycle 3</th>
<th>before cycle 4</th>
<th>before cycle 5</th>
<th>before cycle 6</th>
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<tbody>
<tr>
<td>Date Laboratory Tests</td>
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<td>- 201</td>
<td>- 201</td>
<td>- 201</td>
<td>- 201</td>
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<td>Platelet Count</td>
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<td>N.A.</td>
<td>N.A.</td>
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<tr>
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<td>N.A.</td>
<td>N.A.</td>
<td>N.A.</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
<tr>
<td>Neutrophils</td>
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<td>N.A.</td>
<td>N.A.</td>
<td>N.A.</td>
<td>N.A.</td>
<td>N.A.</td>
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**RAPIDO**

Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

**PREOPERATIVE FOLFOX4 FORM – ARM B**

_Only fill out this form in case FOLFOX4 was given as alternative for CAPOX_

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### 7. OXALIPLATIN

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<th>N.A.</th>
<th>cycle 9</th>
<th>N.A.</th>
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<td>- - 201</td>
<td>- - 201</td>
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<td>3. ECOG Performance at start</td>
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<td>□□□□</td>
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<td>4. Total Dose Oxaliplatin [mg]</td>
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<td>□□□□□</td>
<td>□□□□□</td>
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</tr>
<tr>
<td>5. Dose Modification Relative to Previous Cycle</td>
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<td>□ none □ 25% □ 50% □ stop</td>
<td>□ none □ 25% □ 50% □ stop</td>
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<td>6. Delay next cycle [days] (if no delay, please fill in 0)</td>
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</tr>
<tr>
<td>7. Reason delay / dose adjustment</td>
<td>□ no delay □ poor WHO □ toxicity □ poor compliance □ disease related □ adm. difficulties □ other</td>
<td>□ no delay □ poor WHO □ toxicity □ poor compliance □ disease related □ adm. difficulties □ other</td>
<td>□ no delay □ poor WHO □ toxicity □ poor compliance □ disease related □ adm. difficulties □ other</td>
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8. **LEUCOVORIN**

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<th>cycle 9</th>
<th>Date of Infusion</th>
<th>Dose per day [mg]</th>
<th>Interruption current cycle [days]</th>
<th>Dose Modification Relative to Previous Cycle</th>
<th>Reason delay / dose adjustment</th>
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<td></td>
<td>none</td>
<td>none</td>
<td>poor WHO, toxicity</td>
</tr>
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<td></td>
<td>cycle 8</td>
<td>- 201</td>
<td></td>
<td>none</td>
<td>none</td>
<td>poor compliance, disease related</td>
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<td>cycle 9</td>
<td>- 201</td>
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<td>poor compliance, other</td>
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9. **5-FU**

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<th>Delay next cycle [days]</th>
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**Only fill out this form in case FOLFOX4 was given as alternative for CAPOX**
randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

**PREOPERATIVE FOLFOX4 FORM – ARM B**

Only fill out this form in case FOLFOX4 was given as alternative for CAPOX

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10. **ADVERSE EVENTS**

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<th>cycle 9 N.A</th>
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<td>yes → AE form</td>
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11. **LAB TESTS**

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<th>before cycle 9 N.A</th>
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<tbody>
<tr>
<td>1. Date Laboratory Tests</td>
<td>Other unit</td>
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<td>- 201</td>
</tr>
<tr>
<td>2. Hemoglobin</td>
<td>mmol/L</td>
<td>mg/dL</td>
<td></td>
</tr>
<tr>
<td>3. Platelet Count</td>
<td>x 10⁹/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. WBC</td>
<td>x 10⁹/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Neutrophils</td>
<td>x 10⁹/L</td>
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Notes:

__________________________________________________________

__________________________________________________________

__________________________________________________________

SIGNATURE
Investigator
NAME
DATE
**1. CHEMOTHERAPY**

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<td>□</td>
<td>□</td>
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<td>patient refusal</td>
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<td>other</td>
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**2. OXALIPLATIN**

<table>
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<tr>
<th>Cycle</th>
<th>Date of Infusion</th>
<th>Weight at start</th>
<th>ECOG Performance at start</th>
<th>Total Dose Oxaliplatin [mg]</th>
<th>Delay next cycle [days] (if no delay, please fill in 0)</th>
<th>Reason delay / dose adjustment</th>
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<td>1</td>
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Only fill out this form in case FOLFOX4 was given as alternative for CAPOX
### LEUCOVORIN

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Date of Infusion</th>
<th>Dose per day leucovorin [mg]</th>
<th>Cum. dose leucovorin per cycle [mg]</th>
<th>Interruption current cycle [days]</th>
<th>Dose Modification Relative to Previous Cycle</th>
<th>Delay next cycle [days] (if no delay, please fill in 0)</th>
<th>Reason delay / dose adjustment</th>
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<tr>
<td>1</td>
<td>- 201</td>
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<td>N.A.</td>
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<td>no delay</td>
<td>poor WHO toxicity</td>
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<td>2</td>
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<td>-</td>
<td>-</td>
<td>N.A.</td>
<td>none</td>
<td>no delay</td>
<td>poor WHO toxicity</td>
</tr>
<tr>
<td>3</td>
<td>- 201</td>
<td>-</td>
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<td>N.A.</td>
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<td>no delay</td>
<td>poor WHO toxicity</td>
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<td>no delay</td>
<td>poor WHO toxicity</td>
</tr>
<tr>
<td>5</td>
<td>- 201</td>
<td>-</td>
<td>-</td>
<td>N.A.</td>
<td>none</td>
<td>no delay</td>
<td>poor WHO toxicity</td>
</tr>
<tr>
<td>6</td>
<td>- 201</td>
<td>-</td>
<td>-</td>
<td>N.A.</td>
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<td>no delay</td>
<td>poor WHO toxicity</td>
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<td>no delay</td>
<td>poor WHO toxicity</td>
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<td>no delay</td>
<td>poor WHO toxicity</td>
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<tr>
<td>9</td>
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<td>N.A.</td>
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<td>no delay</td>
<td>poor WHO toxicity</td>
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**Note:** Only fill out this form in case FOLFOX4 was given as alternative for CAPOX
**POSTOPERATIVE FOLFOX4 FORM – ARM A**

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### 5-FU

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<tr>
<td>Dose per day 5-FU [mg]</td>
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<tr>
<td>Cum. dose per cycle 5-FU [mg]</td>
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<td>Interruption current cycle [days]</td>
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<tr>
<td>Dose Modification Relative to Previous Cycle</td>
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*RAPIDO Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy*
5. ADVERSE EVENTS

<table>
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<th></th>
<th>cycle 1</th>
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<th>cycle 3</th>
<th>cycle 4</th>
<th>cycle 5</th>
<th>cycle 6</th>
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<tr>
<td>1. Toxicity (CTC grade ≥ 1)</td>
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<td>yes → AE form</td>
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</table>

6. LAB TESTS

<table>
<thead>
<tr>
<th></th>
<th>before cycle 1</th>
<th>before cycle 2</th>
<th>before cycle 3</th>
<th>before cycle 4</th>
<th>before cycle 5</th>
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</tr>
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<tbody>
<tr>
<td>1. Date Laboratory Tests</td>
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<td>-</td>
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<td>-</td>
<td>- 201</td>
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<tr>
<td>2. Hemoglobin</td>
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<td>mg/dL</td>
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<tr>
<td>3. Platelet Count</td>
<td>x 10^9/L</td>
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<td>4. WBC</td>
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</table>
# Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

**POSTOPERATIVE FOLFOX4 FORM – ARM A**

CKS 2011-4997  
RAPIDO CRF: F05e (Page 5 of 8), version 1.7, 01/07/2014

Only fill out this form in case FOLFOX4 was given as alternative for CAPOX

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<th>Subject Id</th>
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## 7. OXALIPLATIN

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<th>Date of Infusion</th>
<th>Weight at start</th>
<th>ECOG Performance</th>
<th>Total Dose Oxaliplatin</th>
<th>Dose Modification Relative to Previous Cycle</th>
<th>Delay next cycle</th>
<th>Reason delay / dose adjustment</th>
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8. LEUCOVORIN

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Cycle 7</th>
<th>Cycle 8</th>
<th>Cycle 9</th>
<th>Cycle 10</th>
<th>Cycle 11</th>
<th>Cycle 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Infusion day 1</td>
<td>- - 201</td>
<td>- - 201</td>
<td>- - 201</td>
<td>- - 201</td>
<td>- - 201</td>
<td>- - 201</td>
</tr>
<tr>
<td>Dose per day leucovorin [mg]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cum. dose leucovorin per cycle [mg]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interruption current cycle [days]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose Modification Relative to Previous Cycle</td>
<td>none</td>
<td>50%</td>
<td>none</td>
<td>50%</td>
<td>none</td>
<td>50%</td>
</tr>
<tr>
<td>Delay next cycle [days] (if no delay, please fill in 0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reason delay / dose adjustment</td>
<td>no delay</td>
<td>poor WHO toxicity</td>
<td>no delay</td>
<td>poor WHO toxicity</td>
<td>no delay</td>
<td>poor WHO toxicity</td>
</tr>
</tbody>
</table>

Only fill out this form in case FOLFOX4 was given as alternative for CAPOX
## POSTOPERATIVE FOLFOX4 FORM – ARM A

**Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy**

**RAPIDO CRF: F05e (Page 7 of 8), version 1.7, 01/07/2014**

**Only fill out this form in case FOLFOX4 was given as alternative for CAPOX**

<table>
<thead>
<tr>
<th>Center Id</th>
<th>Subject Id</th>
<th>Date of Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>x x - 1 9</td>
<td></td>
</tr>
</tbody>
</table>

9. **5-FU**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Date of Infusion</th>
<th>Dose per day</th>
<th>Cum. dose per cycle</th>
<th>Interruption</th>
<th>Dose Modification</th>
<th>Delay next cycle</th>
<th>Reason delay / dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>1-201</td>
<td>N.A.</td>
<td></td>
<td>none</td>
<td>50%</td>
<td></td>
<td>no delay</td>
</tr>
<tr>
<td>8</td>
<td>1-201</td>
<td>N.A.</td>
<td></td>
<td>none</td>
<td>50%</td>
<td></td>
<td>no delay</td>
</tr>
<tr>
<td>9</td>
<td>1-201</td>
<td>N.A.</td>
<td></td>
<td>none</td>
<td>50%</td>
<td></td>
<td>no delay</td>
</tr>
<tr>
<td>10</td>
<td>1-201</td>
<td>N.A.</td>
<td></td>
<td>none</td>
<td>50%</td>
<td></td>
<td>no delay</td>
</tr>
<tr>
<td>11</td>
<td>1-201</td>
<td>N.A.</td>
<td></td>
<td>none</td>
<td>50%</td>
<td></td>
<td>no delay</td>
</tr>
<tr>
<td>12</td>
<td>1-201</td>
<td>N.A.</td>
<td></td>
<td>none</td>
<td>50%</td>
<td></td>
<td>no delay</td>
</tr>
</tbody>
</table>

- **Dose per day 5-FU [mg]**
  - cycle 7: N.A.
  - cycle 8: N.A.
  - cycle 9: N.A.
  - cycle 10: N.A.
  - cycle 11: N.A.
  - cycle 12: N.A.

- **Cum. dose per cycle 5-FU [mg]**
  - cycle 7: N.A.
  - cycle 8: N.A.
  - cycle 9: N.A.
  - cycle 10: N.A.
  - cycle 11: N.A.
  - cycle 12: N.A.

- **Interruption current cycle [days]**
  - cycle 7: None
  - cycle 8: None
  - cycle 9: None
  - cycle 10: None
  - cycle 11: None
  - cycle 12: None

- **Dose Modification Relative to Previous Cycle**
  - cycle 7: 25%
  - cycle 8: 50%
  - cycle 9: 25%
  - cycle 10: 50%
  - cycle 11: 25%
  - cycle 12: 50%

- **Delay next cycle [days]**
  - cycle 7: N.A.
  - cycle 8: N.A.
  - cycle 9: N.A.
  - cycle 10: N.A.
  - cycle 11: N.A.
  - cycle 12: N.A.

- **Reason delay / dose adjustment**
  - cycle 7: no delay, poor WHO toxicity, poor compliance, disease related, adm. difficulties, other
  - cycle 8: no delay, poor WHO toxicity, poor compliance, disease related, adm. difficulties, other
  - cycle 9: no delay, poor WHO toxicity, poor compliance, disease related, adm. difficulties, other
  - cycle 10: no delay, poor WHO toxicity, poor compliance, disease related, adm. difficulties, other
  - cycle 11: no delay, poor WHO toxicity, poor compliance, disease related, adm. difficulties, other
  - cycle 12: no delay, poor WHO toxicity, poor compliance, disease related, adm. difficulties, other
**POSTOPERATIVE FOLFOX4 FORM – ARM A**

Only fill out this form in case FOLFOX4 was given as alternative for CAPOX

### 10. ADVERSE EVENTS

<table>
<thead>
<tr>
<th>Cycle</th>
<th>N.A.</th>
<th>N.A.</th>
<th>N.A.</th>
<th>N.A.</th>
<th>N.A.</th>
<th>N.A.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Toxicity (CTC grade ≥ 1)</td>
<td>no</td>
<td>yes → AE form</td>
<td>no</td>
<td>yes → AE form</td>
<td>no</td>
<td>yes → AE form</td>
</tr>
</tbody>
</table>

### 11. LAB TESTS

<table>
<thead>
<tr>
<th>Test</th>
<th>before cycle 7 N.A.</th>
<th>before cycle 8 N.A.</th>
<th>before cycle 9 N.A.</th>
<th>before cycle 10 N.A.</th>
<th>before cycle 11 N.A.</th>
<th>before cycle 12 N.A.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Date Laboratory Tests Other unit</td>
<td>-</td>
<td>- 201</td>
<td>-</td>
<td>- 201</td>
<td>-</td>
<td>- 201</td>
</tr>
<tr>
<td>2. Hemoglobin</td>
<td>mmol/L</td>
<td>mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Platelet Count</td>
<td>x 10^9/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. WBC</td>
<td>x 10^9/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Neutrophils</td>
<td>x 10^9/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: _____________________________________________________________

SIGNATURE

Investigator | NAME | DATE
Randomized multicentre phase III study of short course radiation therapy followed by prolonged preoperative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

### RESTAGING RADIOLOGY FORM

<table>
<thead>
<tr>
<th>Center Id</th>
<th>Subject Id</th>
<th>Date of Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>xx - 19xx</td>
</tr>
</tbody>
</table>

#### 1. MRI ASSESSMENT

*According to the protocol TNM5 has to be used in this trial except for notification of metastatic disease*

<p>| | | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. MRI Sagittal Assessment</td>
<td>not done</td>
<td>done →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Scan Record Number</td>
<td></td>
<td></td>
<td>201</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Tumour Position in Relation to Peritoneal Reflection</td>
<td>above</td>
<td>at</td>
<td>below</td>
<td>no tumour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumour / fibrosis</td>
<td>no tumour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Distance from Anal Verge [mm]</td>
<td></td>
<td></td>
<td></td>
<td>no tumour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Distance from Anorectal junction [mm]</td>
<td></td>
<td></td>
<td>no tumour</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Residual tumour visible</td>
<td>no</td>
<td>yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Fibrosis visible</td>
<td>no</td>
<td>yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Length (L) of tumour/fibrosis [mm]</td>
<td></td>
<td></td>
<td>no tumour</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Minimum distance to mesorectal fascia [mm]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Location of tumour from</td>
<td></td>
<td></td>
<td>% of circumference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. MRI cT-stage according to TNM5</td>
<td>cT0</td>
<td>cT1</td>
<td>cT2</td>
<td>cT3ab (≤5mm extramural)</td>
<td>cT3cd (&gt;5mm extramural) organs/structures</td>
<td>cT4a (other)</td>
<td>cT4b (peritoneum)</td>
</tr>
<tr>
<td>12. Extramural Vascular Invasion</td>
<td>no</td>
<td>yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Tumours below the level of the levators</td>
<td>no</td>
<td>yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. cN-stage according to TNM5</td>
<td>cN0 (no LN)</td>
<td>cN0 (benign LN)</td>
<td>cN1 (1 to 3 nodes)</td>
<td>cN2 (4 or more nodes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Malignant lateral nodes present, &gt; 1cm (lat N+) or morphological features</td>
<td>no</td>
<td>yes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sites with distant metastases according to TNM7</td>
<td>M0 (no metastases)</td>
<td>M1a (single metastatic site)</td>
<td>M1b (multiple metastatic sites)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2. CT ASSESSMENT

1. **CT Assessment**
   - not done
   - done →

2. **Sites Imaged** [tick all that apply]
   - chest
   - abdomen
   - pelvis

3. **Positive Lymph Nodes**
   - no
   - yes →
   
   1. Pelvic
   - no
   - yes
   - indeterminate

   2. Inguinal
   - no
   - yes
   - indeterminate

   3. Abdominal
   - no
   - yes
   - indeterminate

   4. Other →
   - no
   - yes
   - indeterminate

4. **Distant Metastasis**
   - no
   - yes →
   
   1. Liver
   - no
   - yes
   - indeterminate

   2. Lung
   - no
   - yes
   - indeterminate

   3. Other →
   - no
   - yes
   - indeterminate

**Notes:**

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

____________________________  __________________________  ______________
Signature                        Name                      Date
1. **PRE-OPERATIVE ASSESSMENTS**

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Center Id</td>
<td>Subject Id</td>
<td>Date of Birth</td>
</tr>
<tr>
<td>7</td>
<td>x x - 1 9</td>
<td></td>
</tr>
</tbody>
</table>

1. **Date of Assessment**

2. **Weight [kg]**

3. **ECOG Performance Status**

4. **Surgery offered**

- no → yes

5. **Reason no Surgery Offered**

- not fit for surgery
- patient refused
- died before surgery
- other →

2. **SURGERY**

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. **Date of Surgery**

2. **Name Surgeon**

3. **Operating Surgeon**

- consultant
- registrar

4. **Assisting Surgeon**

- consultant
- registrar
- robot assistant

5. **Duration Surgery [hrs.min]**

6. **Timing of Surgery**

- elective
- emergency

7. **Metastatic disease at laparotomy**

- no
- yes →

8. **Location Metastatic Disease**

- loco-regional
- distant

9. **Type of Operation**

- laparoscopic complete
- laparoscopic converted to open
- open
- TEM

10. **Type of Resection**

- no resection
- anterior resection, PME
- LAR, TME
- Hartmann
- APR
- local excision
- other →

11. **Intention**

- curative
- palliative

12. **Intra Operative Radio Therapy (IORT)**

- no
- yes →

13. **Stoma**

- no
- yes, defunctioning
- yes, permanent

14. **Mesorectum assessment by surgeon**

- intact
- breached

15. **Margin involvement assessed by surgeon**

- no
- doubtful
- obvious

16. **Blood loss [ml]**

- 0

**Notes:**

**Signature**

**Investigator**

**Name**

**Date**
**Randomized multicentre phase III study of short course radiation therapy followed by prolonged preoperative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy**

**POST SURGERY FORM**

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<tr>
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<th>Subject Id</th>
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</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td></td>
<td>x x - 1 9</td>
</tr>
</tbody>
</table>

### 1. POST-OPERATIVE COMPLICATIONS (according to Clavien)

#### I. Infections within 30 days after Surgery

<table>
<thead>
<tr>
<th>Grade</th>
<th>I</th>
<th>II</th>
<th>IIIa</th>
<th>IIIb</th>
<th>IVa</th>
<th>IVb</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>no</td>
<td>yes →</td>
<td></td>
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</table>

#### II. Cardiovascular

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>IIIa</th>
<th>IIIb</th>
<th>IVa</th>
<th>IVb</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarction</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DVT</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
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</table>

#### III. Neurologic

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>IIIa</th>
<th>IIIb</th>
<th>IVa</th>
<th>IVb</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVL</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

#### IV. Surgical

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>IIIa</th>
<th>IIIb</th>
<th>IVa</th>
<th>IVb</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound Infection</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraabdominal infection</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound Dehiscence</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal Anastomotic Leak</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stoma complication</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileus</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastroparese</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### V. Other

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>IIIa</th>
<th>IIIb</th>
<th>IVa</th>
<th>IVb</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other</td>
<td>no</td>
<td>yes →</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## POST SURGERY FORM

**Center Id**

**Subject Id**

**Date of Birth**

### 2. DISCHARGE / READMISSION / REOPERATION

1. **Date of First Discharge**
   
2. **Unplanned readmission to hospital**
   
3. **Reason(s) Readmission**
   - a. Wound rupture
   - b. Bleeding
   - c. Infection
   - d. Rectal anastomotic leak
   - e. Other →

4. **Date of Second Discharge**

5. **Reoperation during first or second admission**

6. **Reason(s) Reoperation**
   - a. Wound rupture
   - b. Bleeding
   - c. Infection
   - d. Rectal anastomotic leak
   - e. Other →

7. **Post-operative Mortality**

---

**Notes:**

---

**Signature**

**Investigator**

**Name**

**Date**
According to the protocol TNM5 has to be used in this trial. Countries using TNM7 (i.e., Sweden) are asked to answer questions with both TNM5 and TNM7.

1. Macroscopic Assessment
   1. Pathology Number
   2. Surgical plane
      - mesorectal
      - intramural
      - muscularis propria
   3. Anal Canal plane
      - outside levator plane
      - sphincter plane
      - intramuscular/submucosal plane
      - N.A. (no APR)
   4. Tumour to Peritoneal Reflection
      - above
      - at
      - below
      - no tumor
   5. Length of Tumour [mm]
      - no tumor

2. Histology
   1. Tumour Type
      - adenoca
      - no tumor
      - other →
   2. Differentiation Grade
      - well
      - moderate
      - poor
      - no tumor
   3. ypT-stage according to TNM5
      - ypT0
      - ypTis
      - ypT1
      - ypT2
      - ypT3a
      - ypT3b
      - ypT3c
      - ypT3d
      - ypT4a (other organs/structures)
      - ypT4b (peritoneum)
   4. ypT-stage according to TNM7
      - ypT0
      - ypTis
      - ypT1
      - ypT2
      - ypT3a
      - ypT3b
      - ypT3c
      - ypT3d
      - ypT4a (peritoneum)
   5. ypN-stage according to TNM5
      - ypN0 (no LN)
      - ypN0 (benign LN)
      - ypN1 (1 to 3 nodes)
      - ypN2 (4 or more nodes)
   6. ypN-stage according to TNM7
      - ypN0 (no LN)
      - ypN0 (benign LN)
      - ypN1a (1 regional node)
      - ypN1b (2-3 nodes)
      - ypN1c (small tumor deposits)
      - ypN2a (4-6 nodes)
      - ypN2b (7 or more nodes)
Randomized multicentre phase III study of short course radiation therapy followed by prolonged preoperative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

Leiden University Medical Center
Dept. of Surgery, Datacenter, K6-R
P.O. Box 9600, 2300 RC LEIDEN
E-mail: datacenter@lumc.nl
Phone: +31-71-5263500, Fax: +31-71-5266744

PATHOLOGY FORM

<table>
<thead>
<tr>
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<th>Subject Id</th>
<th>Date of Birth</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>19</td>
</tr>
</tbody>
</table>

9. Pathological Response
   - ☐ no regression
   - ☐ regression
   - ☑ pCR

10. Maximum Extramural Spread [mm]
    - ☐ no tumor
    - ☐ no mucin

11. Minimum Distance to distal margin [mm]
    - ☐ no tumor
    - ☐ no mucin

12. Minimum Distance to CRM [mm]
    - ☐ no tumor
    - ☐ no mucin

13. Type of Margin Involvement
    - ☐ none
    - ☐ direct
    - ☐ tumour satellite
    - ☐ nodal
    - ☐ vascular
    - ☐ other →

14. Extramural Vascular Invasion
    - ☐ no
    - ☑ yes

16. Number of Examined Lymph Nodes
    - ☐

17. Number of Positive LN
    - ☐

19. Extranodal deposits < 3 mm
    - ☐ no
    - ☑ yes

20. Macroscopic pictures of tumour
    - ☐ no
    - ☑ yes

21. Tissue fixation
    - ☐ 48 hours
    - ☐ 24 hours
    - ☐ Other:

Notes:

Signature
Investigator

Name

Date
### FOLLOW-UP FORM

<table>
<thead>
<tr>
<th>Center Id</th>
<th>Subject Id</th>
<th>Date of Birth</th>
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<tbody>
<tr>
<td></td>
<td>7</td>
<td>19</td>
</tr>
</tbody>
</table>

#### 1. Visit
- **Weight [kg]**
  - not done
  - done →

#### 2. CEA Measurement
- **Result CEA**
  - not done
  - done →

#### 3. CT or US liver
- **Result CT or US liver**
  - normal
  - suspect
  - metastases

#### 4. X-ray or CT thorax
- **Result thorax investigation**
  - normal
  - suspect
  - metastases

#### 5. Total Colonoscopy
- **Result Colonoscopy**
  - not done
  - done →

#### 6. Adverse Events since previous visit?
- **no**
  - yes → AE form

#### 7. SAE
- **no**
  - yes → SAE form

#### 8. Reoperation
- **no**
  - yes →

#### 9. Overall Assessment
- **disease free**
  - known recurrence
  - new recurrence

### Notes:

- 
- 
- 
- 

### Signature

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Name</th>
<th>Date</th>
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</thead>
</table>
Randomized multicentre phase III study of short course radiation therapy followed by prolonged preoperative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative hemoradiotherapy, surgery and optional adjuvant chemotherapy

**FOLLOW-UP FORM**

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<td>x x - 1 9</td>
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</table>

6 MONTHS POST SURGERY

1. Visit
   - Weight [kg]
   - ECOG Performance Status

2. CEA Measurement
   - Result CEA
     - µg/L=ng/mL

3. Adverse Events since previous visit?
   - no
   - yes → AE form

4. SAE
   - no
   - yes → SAE form

5. Reoperation
   - Reason Reoperation
     - ileus
     - anastomotic leakage
     - tumour recurrence

6. Overall Assessment
   - disease free
   - known recurrence
   - new recurrence

Notes:

Signature
Investigator | Name | Date
Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

FOLLOW-UP FORM

<table>
<thead>
<tr>
<th>Center Id</th>
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</thead>
<tbody>
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</tbody>
</table>

1. Visit

1. Weight [kg]
   - not done
   - done

2. ECOG Performance Status
   - not done
   - done

2. CEA Measurement

1. Result CEA
   - not done
   - done
   - µg/L=ng/mL

3. CT or US liver

1. Result CT or US liver
   - normal
   - suspect
   - metastases

4. X-ray or CT thorax

1. Result thorax investigation
   - normal
   - suspect
   - metastases

5. Total Colonoscopy

1. Result Colonoscopy
   - not done
   - done

6. Adverse Events since previous visit?

   - no
   - yes

7. SAE

   - no
   - yes

8. Reoperation

   1. Reason Reoperation
      - ileus
      - anastomotic leakage
      - tumour recurrence
      - other

9. Overall Assessment

   - disease free
   - known recurrence
   - new recurrence

Notes:

Signature
Investigator Name Date
1. Visit
   - Weight [kg]
   - ECOG Performance Status

2. CEA Measurement
   - Result CEA: µg/L=ng/mL

3. Adverse Events since previous visit?

4. SAE

5. Reoperation
   - Reason Reoperation

6. Overall Assessment
   - Disease free
   - Known recurrence
   - New recurrence

Notes:

Signature
Investigator
Name
Date
Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

FOLLOW-UP FORM

Leiden University Medical Center
Dept. of Surgery, Datacenter, K6-R
P.O. Box 9600, 2300 RC LEIDEN
E-mail: datacenter@lumc.nl
Phone: +31-71-5263500, Fax: +31-71-5266744

CKS 2011-4997
RAPIDO CRF: F11 (Page 1 of 1), version 1.5, 15/11/2013

Center Id
Subject Id
Date of Birth

36 MONTHS POST SURGERY

1. Visit
   - Weight [kg]
   - ECOG Performance Status

2. CEA Measurement
   - Result CEA
   - µg/L=ng/mL

3. CT or US liver
   - Result CT or US liver
   - normal
   - suspect
   - metastases

4. X-ray or CT thorax
   - Result thorax investigation
   - normal
   - suspect
   - metastases

5. Total Colonoscopy
   - Result Colonoscopy

6. Adverse Events since previous visit?
   - no
   - yes → AE form

7. SAE
   - no
   - yes → SAE form

8. Reoperation
   - no
   - yes → ileus
   - anastomotic leakage
   - tumour recurrence
   - other

9. Overall Assessment
   - disease free
   - known recurrence
   - new recurrence → recurrence form

Notes:

_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________

Signature
Investigator
Name
Date
**FOLLOW-UP FORM**

**Leiden University Medical Center**
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P.O. Box 9600, 2300 RC LEIDEN
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CKS 2011-4997
RAPIDO CRF: F11 (Page 1 of 1), version 1.5, 15/11/2013

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<td>xx-19</td>
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</table>

60 MONTHS POST SURGERY

**1. Visit**
- Weight [kg]
- ECOG Performance Status

**2. CEA Measurement**
- Result CEA

**3. Total Colonoscopy**
- Result Colonoscopy

**4. Adverse Events since previous visit?**
- SAE

**5. Reoperation**
- Reason Reoperation

**7. Overall Assessment**
- Disease free

<table>
<thead>
<tr>
<th>Notes:</th>
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**Signature**

**Investigator**

**Name**

**Date**
Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

LOCOREG. RECURRENCE FORM

<table>
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<tbody>
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<td>7</td>
<td>x x - 19</td>
</tr>
</tbody>
</table>

1. Date of LocoRegional Recurrence

2. Location(s) [tick all that apply]
   - at anastomosis
   - regional LN(s)
   - into bladder
   - into prostate
   - into vagina
   - skin in local area
   - other

3. Investigations and Results

   1. Cytology/Histology
      - not done
      - negative
      - positive

   2. CT Scan
      - not done
      - normal
      - suspect

   3. MRI Scan
      - not done
      - normal
      - suspect

   4. PET Scan
      - not done
      - normal
      - suspect

   5. CEA
      - not done
      - normal
      - increased
      - CEA unit: µg/L=ng/mL

   6. Other
      - not done
      - normal
      - suspect

4. Type of Treatment
   - none
   - pall. intent
   - curative intent

   1. Surgery
      - no
      - yes

   2. Radiotherapy
      - no
      - yes

   3. Systemic
      - no
      - yes

   4. Other
      - no
      - yes

Notes:

Signature
Investigator
Name
Date
**Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy**

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Dept. of Surgery, Datacenter, K6-R
P.O. Box 9600, 2300 RC LEIDEN
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Phone: +31-71-5263500, Fax: +31-71-5266744

**DISTANT RECURRENCE FORM**

<table>
<thead>
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<tbody>
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</tr>
</tbody>
</table>

1. Date of Distant Recurrence

2. Location(s) *(tick all that apply)*
   - [ ] bone
   - [ ] brain
   - [ ] liver
   - [ ] lung
   - [ ] skin
   - [ ] peritoneal carcinomatosis
   - [ ] LN para-aortal, retroperitoneal, inguinal, para-iliac etc
   - [ ] other

3. Investigations and Results

   1. Cytology/Histology
      - [ ] not done
      - [ ] negative
      - [ ] positive

   2. Bone Scan
      - [ ] not done
      - [ ] normal
      - [ ] suspect

   3. Chest X Ray
      - [ ] not done
      - [ ] normal
      - [ ] suspect

   4. US Liver
      - [ ] not done
      - [ ] normal
      - [ ] suspect

   5. CT Scan
      - [ ] not done
      - [ ] normal
      - [ ] suspect

   6. MRI Scan
      - [ ] not done
      - [ ] normal
      - [ ] suspect

   7. PET Scan
      - [ ] not done
      - [ ] normal
      - [ ] increased

      CEA unit: [ ] µg/L [ ] ng/mL

   8. CEA
      - [ ] not done
      - [ ] normal
      - [ ] increased

   9. Other
      - [ ] not done
      - [ ] normal
      - [ ] suspect

4. Type of Treatment
   - [ ] none
   - [ ] pall. intent →
   - [ ] curative intent →

   1. Surgery
      - [ ] no
      - [ ] yes

   2. Radiotherapy
      - [ ] no
      - [ ] yes

   3. Systemic
      - [ ] no
      - [ ] yes

   4. Other
      - [ ] no
      - [ ] yes

Notes:

---

Signature
Investigator
Name
Date
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P.O. Box 9600, 2300 RC LEIDEN
E-mail: datacenter@lumc.nl
Phone: +31-71-5263500, Fax: +31-71-5266744

 RK2011-4997 RAPIDO
CRF: F12c (Page 1 of 1), version 1.4, 1/03/2012

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<td>xx-19</td>
</tr>
</tbody>
</table>

1. Date of New Primary Tumour

2. Location(s)
   - bladder
   - breast
   - colon
   - endometrium
   - lung
   - prostate
   - other

3. Investigations and Results
   1. Cytology/Histology
      - not done
      - negative
      - positive
   2. Chest X Ray
      - not done
      - normal
      - suspect
   3. US Liver
      - not done
      - normal
      - suspect
   4. CT Scan
      - not done
      - normal
      - suspect
   5. MRI Scan
      - not done
      - normal
      - suspect
   6. PET Scan
      - not done
      - normal
      - suspect
   7. Other
      - not done
      - normal
      - suspect

4. Type of Treatment
   - none
   - pall. intent
   - curative intent
      1. Surgery
         - no
         - yes
      2. Radiotherapy
         - no
         - yes
      3. Systemic
         - no
         - yes
      4. Other
         - no
         - yes

Notes:

Signature
Investigator
Name
Date
Randomized multicentre phase III study of short course radiation therapy followed by prolonged pre-operative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

END OF TREATMENT FORM

Leiden University Medical Center
Dept. of Surgery, Datacenter, K6-R
P.O. Box 9600, 2300 RC LEIDEN
E-mail: datacenter@lumc.nl
Phone: +31-71-5263500, Fax: +31-71-5266744

CKS 2011-4997 RAPIDO CRF: F13 (Page 1 of 1), version 1.8, 1/07/2014

Center Id | Subject Id | Date of Birth | Date of last Irradiation | Date of last pre-op Capecitabine | Date of last pre-op Oxaliplatin | Date of last pre-op Leucovorin/5-FU | Date of Surgery | Date of last post-op CAPOX or FOLFOX |
---|---|---|---|---|---|---|---|---|
| | 7 | - | - | - | - | - | - | - |

Please fill out this form at start of Follow up

1 Date of last Irradiation
   Date of last pre-op Capecitabine
   Date of last pre-op Oxaliplatin  
   [only arm B]
   Date of last pre-op Leucovorin/5-FU  
   [only arm B if FOLFOX was given]
   Date of Surgery
   Date of last post-op CAPOX or FOLFOX  
   [optional: only arm A in certain centers]

2 Reason for End of Pre-operative Treatment
   [tick only one main category]

   - completed protocol till surgery
   - lack of efficacy [inadequate tumour regression to warrant continuation]
   - disease progression
   - adverse event(s) → unrelated incident
   - intolerable toxicity
   - sudden/toxic death → SAE form + death form
   - self withdrawal → patient refused all treatments
   - Arm A: patient refused CRT: immediate surgery
   - Arm B: patient refused RT: immediate surgery
   - Arm B: patient refused RT: only CT and surgery
   - Arm B: patient refused CT: immediate surgery
   - Arm B: patient refused CT: only RT and surgery
   Other: ________________________________
   Non-compliance → ________________________________
   Other → ________________________________

Notes: __________________________________________
_______________________________________

If chemotherapy was given for recurrent disease, this is outside protocol and must be noted on recurrence forms (F12). Not on this EOT form (F13) and not on post-op CAPOX or FOLFOX form (F05c or F05e)

Signature
Investigator
Name
Date
<table>
<thead>
<tr>
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<th>Date of Birth</th>
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<tbody>
<tr>
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<td>7</td>
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</tr>
</tbody>
</table>

1. Last Date in Study

2. Reason Off Study

- patient wish, specify

- investigator wish, specify

- death → Death Form

Notes:

Signature
Investigator: Name
Date
**DEATH FORM**

Center Id | Subject Id | Date of Birth
---|---|---

1. Date of Death

2. Autopsy

3. Cause of Death

1. Sites of Rectal Disease

[Tick all that apply]

- rectal cancer
- second primary malignancy
- study drug related
- surgery related / postoperative
- other

Notes:

Signature
Investigator

Name

Date
### Randomized multicentre phase III study of short course radiation therapy followed by prolonged preoperative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

**ADVERSE EVENTS FORM**

**Instructions:** Please complete at baseline, after each cycle and during follow-up. Use NCI CTCAE version 4.0 and use 0 in the Grade, if no toxicity was present. Report the worst grading during each cycle.

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</table>

<table>
<thead>
<tr>
<th>1 Modality</th>
<th>Radiation</th>
<th>Chemo-radiation ↓</th>
<th>Preop CAPOX ↓</th>
<th>Preop FOLFOX4 ↓</th>
<th>Postop CAPOX ↓</th>
<th>Postop FOLFOX4 ↓</th>
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<tbody>
<tr>
<td>2 Period</td>
<td>baseline</td>
<td>week</td>
<td>cycle</td>
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<th>Grade</th>
<th>12. RENAL AND URINARY DISORDERS</th>
<th>Grade</th>
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<tbody>
<tr>
<td>Febrile neutropenia</td>
<td></td>
<td>Cystitis noninfective</td>
<td></td>
</tr>
<tr>
<td>5. BLOOD AND LYMPHATIC SYSTEM</td>
<td></td>
<td>13. SKIN AND SUBCUTANEOUS TISSUE</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td></td>
<td>Alopecia</td>
<td></td>
</tr>
<tr>
<td>Colonic obstruction</td>
<td></td>
<td>Palmar-plantar erythro-dysesthesia syndrome</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td>Dermatitis radiation</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td>Rash maculo-papular</td>
<td></td>
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<tr>
<td>Fecal incontinence</td>
<td></td>
<td>14. SEXUAL PROBLEMS</td>
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</tr>
<tr>
<td>Mucositis oral</td>
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<tr>
<td>Nausea</td>
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<td>15. OTHER</td>
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<tr>
<td>Proctitis</td>
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<td>Other toxicity 1</td>
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<tr>
<td>Rectal hemorrhage</td>
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<tr>
<td>Rectal mucositis</td>
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<td>Other toxicity 2</td>
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<tr>
<td>Rectal pain</td>
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<td>→</td>
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</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td>Other toxicity 3</td>
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<td>7. GENERAL</td>
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<tr>
<td>Fatigue</td>
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<td>Other toxicity 4</td>
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<td>8. IMMUNE SYSTEM</td>
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<tr>
<td>Allergic Reaction</td>
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<td>9. INVESTIGATIONS</td>
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<td>10. NERVOUS SYSTEM DISORDERS</td>
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</tr>
<tr>
<td>Lethargy</td>
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<td>Neuralgia</td>
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<tr>
<td>Peripheral sensory neuropathy</td>
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</tr>
<tr>
<td>11. RESPIRATORY, THORACIC AND MEDIASTINAL</td>
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</tr>
<tr>
<td>Laryngopharyngeal dysesthesia</td>
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</table>

16. SAE observed | no | yes → go to SAE form |

Notes: ________________________________

Signature
Investigator
Name
Date
### 1. Reaction Information

- **Report type**: initial, follow-up, final
- **Country**
- **Age [years]**
- **Sex**: male, female
- **Treatment Arm**: Arm A control: 28x1.8 Gy or 25x2.0 Gy + CT → surgery [± optional CT]; Arm B experimental: 5x5 Gy → CT → surgery
- **Date of onset SAE**
- **Onset period of SAE**: during/shortly after 5x5 Gy, during/after pre-op CRT, before treatment
- **Description SAE in a single term**
- **Intensity SAE**: [CTC 4.0] grade 1, grade 2, grade 3, grade 4, grade 5
- **Category of SAE**: patient died → persistent or sign. disability/incapacity, (prolonged) inpatient hospitalisation, life threatening, congenital anomaly or birth defect, other medically important
  - **Date of Death**
  - **Cause of Death**: malignant disease, toxicity, other
- **Outcome SAE**: recovered → sequelae, unchanged, worsened, fatal
  - **Date of recovery SAE**

### 2. Suspect Drug(s) Information Reaction Information

<table>
<thead>
<tr>
<th>Study Drugs /Therapy</th>
<th>Daily dose</th>
<th>Route</th>
<th>First date of administration</th>
<th>Last date of administration</th>
<th>Therapy duration [weeks]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiotherapy [Gy]</strong></td>
<td>N.A. N.A.</td>
<td>N.A. N.A.</td>
<td>- - 201</td>
<td>- - 201</td>
<td>N.A. N.A.</td>
</tr>
<tr>
<td><strong>Capecitabine [Xeloda®] [mg]</strong></td>
<td>N.A. N.A.</td>
<td>oral</td>
<td>- - 201</td>
<td>- - 201</td>
<td>N.A. N.A.</td>
</tr>
<tr>
<td><strong>Oxaliplatin [Eloxatin®] [mg]</strong></td>
<td>N.A. N.A.</td>
<td>i.v.</td>
<td>- - 201</td>
<td>- - 201</td>
<td>N.A. N.A.</td>
</tr>
<tr>
<td><strong>Leucovorin [mg]</strong></td>
<td>N.A. N.A.</td>
<td>i.v.</td>
<td>- - 201</td>
<td>- - 201</td>
<td>N.A. N.A.</td>
</tr>
<tr>
<td><strong>5-FU [mg]</strong></td>
<td>N.A. N.A.</td>
<td>i.v.</td>
<td>- - 201</td>
<td>- - 201</td>
<td>N.A. N.A.</td>
</tr>
</tbody>
</table>
**SERIOUS ADVERSE EVENT FORM**

<table>
<thead>
<tr>
<th>Center Id</th>
<th>Subject Id</th>
<th>Date of Birth</th>
<th>Please add additional / new information to the initial form!</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>xx-19</td>
<td></td>
</tr>
</tbody>
</table>

### Study Drugs /Therapy

<table>
<thead>
<tr>
<th>Study Drugs /Therapy</th>
<th>Causality</th>
<th>Did reaction abate after stopping?</th>
<th>Did reaction reappear after reintroduction?</th>
<th>Action taken?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapy</td>
<td>N.A.</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Capecitabine [Xeloda®]</td>
<td>N.A.</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Oxaliplatin [Eloxatin®]</td>
<td>N.A.</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>N.A.</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>5-FU</td>
<td>N.A.</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>

### Prophylactic Drug(s)

<table>
<thead>
<tr>
<th>Prophylactic Drug(s)</th>
<th>Causality</th>
</tr>
</thead>
<tbody>
<tr>
<td>5HT3 antagonist</td>
<td>unrelated</td>
</tr>
<tr>
<td></td>
<td>unlikely</td>
</tr>
<tr>
<td></td>
<td>possible</td>
</tr>
<tr>
<td></td>
<td>probable</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>unrelated</td>
</tr>
<tr>
<td></td>
<td>unlikely</td>
</tr>
<tr>
<td></td>
<td>possible</td>
</tr>
<tr>
<td></td>
<td>probable</td>
</tr>
<tr>
<td>Trombo-embolic prophylaxis</td>
<td>unrelated</td>
</tr>
<tr>
<td></td>
<td>unlikely</td>
</tr>
<tr>
<td></td>
<td>possible</td>
</tr>
<tr>
<td></td>
<td>probable</td>
</tr>
</tbody>
</table>
### 3. Concomitant medication

**Generic name and dose** | **Start date** | **Stop date**
---|---|---
1. | - - | - - 20
2. | - - | - - 20
3. | - - | - - 20
4. | - - | - - 20
5. | - - | - - 20
6. | - - | - - 20
7. | - - | - - 20
8. | - - | - - 20
9. | - - | - - 20
10. | - - | - - 20

Please add additional / new information to the initial form!

### 4. Relevant Medical History

________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________
### Center Id Subject Id Date of Birth

Please add additional / new information to the initial form!

### 5. Relevant Laboratory Values

1. **Date Laboratory tests**
   - [ ] - [ ] - 20
   - [ ] not done

2. **Hemoglobin**
   - [ ] . [ ]
   - [ ] mmol/L
   - [ ] mg/dL

3. **Platelet Count**
   - [ ] x 10^9/L

4. **WBC**
   - [ ] . [ ]
   - [ ] x 10^9/L

5. **Neutrophils**
   - [ ] . [ ]
   - [ ] x 10^9/L

6. **Other, specify incl unit**
   - [ ] not done

### 6. Manufacturer Information

**Signature:**

1. **Report source**
   - Health professional

2. **Date of initial report**
   - [ ] - [ ] - 20

3. **Date of follow up report**
   - [ ] - [ ] - 20

### 7. Contact details [person who filled out this form and e-mail address]

- 
- 
- 

### Notes:

- 
- 
- 
- 

<table>
<thead>
<tr>
<th>Signature</th>
<th>Name</th>
<th>Date final report</th>
</tr>
</thead>
</table>
Randomized multicentre phase III study of short course radiation therapy followed by prolonged preoperative chemotherapy and surgery in patients with high risk primary rectal cancer compared to standard preoperative chemoradiotherapy, surgery and optional adjuvant chemotherapy

Leiden University Medical Center
Dept. of Surgery, Datacenter, K6-R
P.O. Box 9600, 2300 RC LEIDEN
E-mail: datacenter@lumc.nl
Phone: +31-71-5263500, Fax: +31-71-5266744

COMMENT FORM

<table>
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<tr>
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<th>Page Nr.</th>
<th>Visit Nr.</th>
<th>Date</th>
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Signature
Investigator
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