Trial Description

Title

Randomised trial comparing completeness of adjuvant chemotherapy after early vs. late diverting stoma closure in low anterior resection for rectal cancer

Trial Acronym

CoCStom

URL of the trial

http://www.cocstom.de

Brief Summary in Lay Language

The purpose of the CoCStom trial is to determine the optimal timing for closure of a colostomy (stoma = “artificial anus”) that was temporarily created as part of the surgical removal of the rectum, operation performed for locally advanced rectal cancer.

In these patients a temporary stoma is recommended in order to prevent a so called anastomotic leakage – i.e. to prevent that contents of the bowel enters the abdominal cavity. Usually, the stoma will be closed after the subsequent chemotherapy. But having a stoma means for the patients an additional limitation of the quality of life to the already stressful surgery and to the side effects of chemotherapy. This study will examine whether an earlier closure of the stoma - before the start of chemotherapy - is possible without an increase of the incidence of complications.

The primary objective of the study is to determine whether the timing of the reversal of the stoma affects the completeness and therefore the effectiveness of the chemotherapy administrated after tumor removal. Other outcomes will be assessed e.g. how effective are the different methods in terms of oncological issues, the quality of life of patients with early compared to late stoma closure. This study will include more than 250 patients in around 30 German Centres randomised in two groups: early closure (8-10 days after tumor resection = experimental group) and late closure (25 weeks after randomisation= control group).

Brief Summary in Scientific Language

Current evidence supports creation of a diverting stoma in patients undergoing low anterior resection (LAR) for locally advanced rectal cancer. The current standard of care is stoma closure after completion of adjuvant chemotherapy. Evidence from one RCT and other non-randomized studies shows that early closure (EC), before starting adjuvant chemotherapy, is feasible without a major increase of the complication rate, but does not provide information on the influence of EC on completeness of chemotherapy (CoC). Besides surgery, adjuvant chemotherapy represents a cornerstone in the treatment of locally advanced cancer. Data from an exploratory analysis of a multicentre phase III study suggest that CoC is associated with better oncological outcome. Timing of stoma closure is assumed

to influence administration and CoC but in which direction is unclear. Early stoma closure may improve CoC because stoma related morbidity is avoided. But on the other hand complications after early closure may have a negative impact on CoC. CoCStom is a randomised multicentre trial comparing completeness of adjuvant chemotherapy as primary endpoint after early (8-10 days after tumor resection, before starting adjuvant therapy - experimental group) vs. late (26 weeks after tumor resection after completion of adjuvant therapy - control group) stoma closure in patients with locally advanced rectal cancer undergoing low anterior resection after neoadjuvant chemoradiation. An increase of 20% for the rate of completely administered adjuvant chemotherapy is regarded as a clinically meaningful step forward and serves as basis for the sample size calculation. Quality of life and oncological outcome will be explored as patient-relevant key secondary endpoints.
CoCStom's objective is to clarify the optimal timing of stoma closure in the context of adjuvant chemotherapy.

Organizational Data

- DRKS-ID: **DRKS00005113**
- Date of Registration in DRKS: **2013/08/28**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **2011-271N-MA , Medizinische Ethik-Kommission II Medizinische Fakultät Mannheim der Universität Heidelberg**

Secondary IDs

Health condition or Problem studied

- ICD10: **C20 - Malignant neoplasm of rectum**

Interventions/Observational Groups

- Arm 1: **Early stoma closure (experimental group): 8-10 days after tumor resection (LAR) followed by chemotherapy**
- Arm 2: **Late stoma closure (control group): 25 weeks after randomisation and after receiving the planned chemotherapy.**

Characteristics

- Study Type: **Interventional**
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Study Type Non-Interventional: **[---]***

- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Active control (effective treament of control group)**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

Completness of Chemotherapy [CoC = the proportion of the randomised patients which complete all planned cycles of adjuvant chemotherapy (4 Cy. 5-FU or 5-FU plus folinic acid, or 5 Cy. Capecitabine or 5 Zy. XELOX or 8 Zy. de Gramont regimen or 8 Zy. FOLFOX6)] measured at 28 weeks after randomisation. Additional administration of folic acid is allowed.

Secondary Outcome

a) Quality of life: QoL baseline will be measured (EORTC QLQ-C30 and the CR 29, in German) at randomisation (baseline), before starting chemotherapy and 12 and 18 weeks after the start of chemotherapy. During the course of the trial, QoL will be determined 7 and 24 months after randomisation;
b) rate of stoma related complications: percentage of patients developing stoma related complications over a period of 28 weeks after randomisation in relation to all patients;
c) number of re-operations: the number of additional operations performed because of complications related to the stoma itself or the stoma closure procedure;
d) individual CoC rate: the proportion of completed chemotherapy cycles calculated for each patient in relation to the planned number of cycles determined 7 months after randomisation;
e) dose modification or delay: measured 7 months after randomisation, the proportion of randomised patients receiving a dose modification or delay in relation to the total number of patients receiving adjuvant chemotherapy;
f) disease-free survival: determined from the date of randomisation to the date of diagnosis of recurrence or death during the 24 months follow-up period;
g) local recurrence-free survival and distant recurrence-free survival: determined from the date of randomisation to the date of the respective recurrence event or death during the 24 months follow-up period;
h) rate of symptomatic rectal anastomotic leaks: proportion of anastomotic leakages clinically symptomatic in relation to the total number of stoma closures within 30 days after the procedure;
i) cumulative days of hospitalisation: additional days in hospital in both groups over a period of 28 weeks after randomisation;
j) cumulative readmissions: number of readmissions due to complications related

to the stoma closure operation or stoma related complications over a period of 28 weeks after randomisation.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Chirurgische Klinik und III. Medizinische Klinik, Mannheim**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2013/12/27**
- Target Sample Size: **257**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

a) temporary diverting stoma (independent from the stoma type);
b) curative resection;
c) elective LAR with TME (laparoscopic, open or converted) for UICC II – III rectal cancer;
d) no anastomotic leakage (endoscopic or contrast enema assessment of the anastomosis around day 7 after LAR);
e) indication to undergo adjuvant chemotherapy;
f) female or male with an age ≥18 years;
g) written informed consent;
h) patient is able to cooperate.

Exclusion criteria

a) immunocompromised patients (HIV positive, patients under chemotherapy or under immunosuppressive therapy, e.g. prednisolone >= 10 mg);
b) ASA > 3;
c) inflammatory bowel disease;

**d) contraindication to adjuvant chemotherapy arising after rectal cancer resection;
e) participation in another intervention-trial with interference of intervention and outcome of this study.**

Addresses

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Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

  Deutsche Forschungsgemeinschaft
  Kennedyallee 40

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Status

- Recruitment Status: **Recruiting complete, follow-up continuing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

- Further trial documents **Studienprotokoll / study protocol doi: 10.1186/s12885-015-1838-0**

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