# Neoadjuvant chemoradiation for patients with adenocarcinoma of the stomach. A feasibility study.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

## **Summary**

#### ID

NL-OMON24232

**Source** Nationaal Trial Register

**Brief title** N/A

#### **Health condition**

Gastric cancer Neoadjuvant chemotherapy Maagkanker Neoadjuvante chemoradiatie

### **Sponsors and support**

Primary sponsor: University Medical Center Groningen Source(s) of monetary or material Support: University Medical Center Groningen

### Intervention

#### **Outcome measures**

#### **Primary outcome**

The primary endpoint is the possible delay in performing a curative resection due to increased toxicity of more than 10% with a stopping point at a delay in six patients.

#### Secondary outcome

Secondary endpoints are occurrence of downstaging and changes in pathology (pathological responses).

Tissue and serum before and after treatment for genomic profiling, kinome profiling (kinase activity) and protein expression will be collected to determine patterns to predict response to therapy.

- 1. To determine pathological responses;
- 2. To determine genomic profile to predict response to treatment;
- 3. To determine the number of R0 resections;
- 4. To determine progression free survival;
- 5. To detect risk of tumor recurrence patterns.

Furthermore we will assess quality of life (QOL) before, during and after this combined treatment.

## **Study description**

#### **Background summary**

Rationale:

The incidence of gastric cancer has been declining steadily since the 1930s, but it remains a major cause of cancer death in the Western world. The high mortality rate reflects the prevalence of advanced disease at presentation. The five-year survival rate for patients with completely resected early stage gastric cancer is approximately 75%, while it is 30% or less for patients who have extensive lymph node involvement. However, nearly 70-80% of the resected gastric cancer experience a local recurrence at some time in their disease. These sobering results have gathered efforts to improve treatment results for these patients using adjuvant (postoperative) or neoadjuvant (preoperative) radiation therapy (RT) and/or chemotherapy. The rational for chemoradiation is the risk for locoregional recurrence and distant metastases. Radiation with surgery can improve locoregional control while systematic

chemotherapy can eliminate microscopic distant metastases. As limited data that exist, fail to show a survival benefit from the addition of postoperative RT alone in patients with resected gastric cancer, almost all postoperative RT trials have included concurrent chemotherapy to improve the efficacy of RT ("radiation sensitization"). Over time adjuvant chemoradiation is considered as standard of care after curative surgery for adenocarcinoma of stomach cancer in many countries. Preoperative chemoradiotherapy in locally advanced gastric cancer results in significant down staging of the tumor with improved rate of curative resections.

Chemotherapy may also function as a radiosensitiser, improving the effect of radiation by double-stranded DNA breaks and inhibition of DNA repair by blocking the cell cycle at the G2/M phase. Recent studies have shown activity of Paclitaxel in conjunction with radiation in gastric cancer.

Purpose: To evaluate the feasibility and safety of a combination of preoperative chemoradiation of Paclitaxel 50mg/m2 and Carboplatin AUC 2 given intravenously on day 1, 8,15, 22 and 29 in combination with 45 Gy (fractions of 1.8Gy) for locally advanced adenocarcinoma of the stomach.

Type: Interventional

Design:

Non-Randomized, Open Label, Uncontrolled, Single Group Assignment, feasibility study The sample size for this study will be 14 patients in order to determine as <10% delay, defined as surgery after 5 weeks after last course of chemotherapy. The delay of 10% is conform other studies concerning neo-adjuvant treatment. If a delay occurs in more than 5 patients the study will be stopped.

Endpoints:

Primary endpoint: will be feasibility, defined as less than 10% toxicity leading to postponement of surgery.

Secondary endpoints: occurrence of down staging and changes in pathology.

### Study objective

The incidence of gastric cancer has been declining steadily since the 1930s, but it remains a major cause of cancer death in the Western world. The high mortality rate reflects the prevalence of advanced disease at presentation. The five-year survival rate for patients with completely resected early stage gastric cancer is approximately 75%, while it is 30% or less for patients who have extensive lymph node involvement. However, nearly 70-80% of the resected gastric cancer experience a local recurrence at some time in their disease. These sobering results have gathered efforts to improve treatment results for these patients using adjuvant (postoperative) or neoadjuvant (preoperative) radiation therapy (RT) and/or chemotherapy. The rational for chemoradiation is the risk for locoregional recurrence and distant metastases. Radiation with surgery can improve locoregional control while systematic chemotherapy can eliminate microscopic distant metastases. As limited data that exist, fail

to show a survival benefit from the addition of postoperative RT alone in patients with resected gastric cancer, almost all postoperative RT trials have included concurrent chemotherapy to improve the efficacy of RT ("radiation sensitization"). Over time adjuvant chemoradiation is considered as standard of care after curative surgery for adenocarcinoma of stomach cancer in many countries. Preoperative chemoradiotherapy in locally advanced gastric cancer results in significant down staging of the tumor with improved rate of curative resections.

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#### Study design

Surgery will be performed preferably within 4 - 6 weeks after the completion of the chemoradiation.

After completion of the protocol, patients will be followed up every 3 months for the first year, every 6 months for the second year, and then at the end of each year until 5 years after treatment, to document late toxic effects and, if applicable, disease relapse or progression, and death.

#### Intervention

Intervention is the use of chemoradiotherapy as an adjunct to the standard surgical resection. As adjuvant chemoradiation has soms disadvantages such as an improved possibility to abandon chemoradiotherapy because of postoperative complications leading to a too long postoperative course. Therefore neoadjuvant application has several advantages such as good performane status, better response measuring and more curative resections.

## Contacts

#### Public

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## **Eligibility criteria**

## Inclusion criteria

1. Histologically proven and documented adenocarcinoma of the stomach;

2. Surgical resectable gastric cancer stage IB-IVA: T1N1; T2-4, N0-1, M0 (see appendix), as determined by Endoscopic Ultra Sound (EUS), Computed Tomography (CT);

- 3. Age ¡Ý18 and ¡Ü75;
- 4. Ambulatory performance status (WHO scale 0-2(see appendix);
- 5. No prior chemotherapy;
- 6. No prior radiotherapy;

7. If more than 50% of the tumor extends above the gastroesophageal (GE) junction into the esophagus, the bulk of the tumor must involve the stomach. The tumor must not extend more than 2 cm into esophagus;

- 8. Adequate hematological, renal and hepatic functions defined as:
- a. White blood cell count iÝ4.0 x 109/L;
- b. Platelet count ¡Ý100 x 109/L;
- c. Serum bilirubin ¡Ü 1.5 x upper normal limit;
- d. Calculated Creatinine Clearance ¡Ý50 ml/min (cockcroft formula);
- e. Two equally functioning kidneys determined with standard technology(renogram);
- 9. Tumor negative laparoscopy when CT suggests peritoneal carcinomatosis;

10. Written, voluntary informed consent (interval between information and consent at least 7 days);

- 11. Patients must be accessible to follow up and management in the treatment center;
  - 5 Neoadjuvant chemoradiation for patients with a denocarcinoma of the stomach. A fe  $\dots$  13-05-2025

12. Patients must sufficiently understand the Dutch language and must be able to sign the informed consent document.

### **Exclusion criteria**

- 1. T1N0 tumors and in situ carcinoma (endoscopic ultrasound) are not eligible;
- 2. Distant metastases;
- 3. In case of only one functional kidney;

4. Previous or current malignancies at other sites than entry diagnosis except for adequately treated basal or squamous cell carcinoma of the skin, or curatively treated carcinoma in situ of the cervix uteri;

5. Prior chest or upper abdomen radiotherapy, prior systemic chemotherapy, or prior esophageal or gastric surgery;

6. Evidence of serious active infections;

- 7. Severe cardiac and/or pulmonary failure, uncontrolled hypertension, angina pectoris;
- 8. Clinical signs of myocardial ischaemia;

9. Dementia or altered mental status that would prohibit the understanding and giving of informed consent;

10. Pregnant or lactating women. Sexually active patients of childbearing potential must implement effective contraceptive practices during the study when treated with chemotherapy.

## Study design

## Design

Interventional
Other
Non controlled trial
Open (masking not used)
N/A , unknown

## Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2007
Enrollment:	14
Туре:	Actual

## **Ethics review**

Positive opinion	
Date:	30-01-2009
Application type:	First submission

## **Study registrations**

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

Register	ID
NTR-new	NL1564
NTR-old	NTR1644
Other	NL: 18509.042.07
ISRCTN	ISRCTN wordt niet meer aangevraagd

## **Study results**

#### **Summary results**

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