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

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Purpose: To evaluate the feasibility and efficacy 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...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON33628

Source
ToetsingOnline

Brief title
Gastric Cancer: neoadjuvant treatment

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
gastric cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: gastric cancer, neoadjuvant chemotherapy

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 :

- efficacy

- occurence of downstaging and changes in pathology

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 carcinoma specimens have regional lymph nodes and over 80% of patients who die from 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.

Study objective

Purpose: To evaluate the feasibility and efficacy 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.

Study design

Type: Interventional
Design: Non-Randomized, Open Label, Uncontrolled, Multi Group Assignment study

Intervention

Intervention is the use of chemoradiotherapy as an adjunct to the standard surgical resectioen. As adjuvant chemoradiation has some disadvantages such as an improved possibilty to abandon chemoradiotherapy because of postoperative complications leading to a to long postoperative course. Therefore neoadjuvant application has several advantages such as good performance status, better response measuring and more curative resections (R0).

Study burden and risks

The burden or risk associated with this study is considered to be low and will be subject of this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Histologically proven and documented adenocarcinoma of the stomach
- 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).
- Age >= 18 and <= 75
- Ambulatory performance status (WHO scale 0 - 2; see appendix)
- No prior chemotherapy
- No prior radiotherapy
- If the tumor extends above the gastroesophageal (GE) junction into the esophagus, the bulk of the tumor(therefore more than 50%)must involve the stomach. The tumor must not extend more than 2 cm into esophagus.
- Adequate hematological, renal and hepatic functions defined as:
- White blood cell count >= 4.0 x 109/L
- Platelet count >= 100 x 109/L
- Serum bilirubin <= 1.5 x upper normal limit
- Calculated Creatinine Clearance >=50 ml/min (cockcroft formula)
-Two equally functioning kidneys determined with standard technology (renogram)
- Tumor negative laparoscopy when CT suggests peritoneal carcinomatosis
- Written, voluntary informed consent (interval between information and consent at least 7 days)
- Patients must be accessible to follow up and management in the treatment center
- Patients must sufficiently understand the Dutch language and must be able to sign the informed consent document.

Exclusion criteria

- T1N0 tumors and in situ carcinoma (endoscopic ultrasound) are not eligible
- Distant metastases
- In case of only one functional kidney
- 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
- Prior chest or upper abdomen radiotherapy, prior systemic chemotherapy, or prior esophageal or gastric surgery.
- Evidence of serious active infections
- Severe cardiac and/or pulmonary failure, uncontrolled hypertension, angina pectoris
- Clinical signs of myocardial ischaemia
- Dementia or altered mental status that would prohibit the understanding and giving of informed consent
- 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

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2007
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Carboplatin
Generic name:	Carboplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Paclitaxel
Generic name:	Paclitaxel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2007-003669-41-NL
CCMO	NL18509.042.07