Purpose

The purpose of this study is to find out whether either trastuzumab or the combination of trastuzumab and pertuzumab with standard chemotherapy shows more activity against gastro-oesophageal adenocarcinoma than standard chemotherapy given before and after surgery and it can be safely administered.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant Neoplasm of Stomach</td>
<td>Drug: Cisplatin</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Malignant Neoplasm of Cardio-esophageal Junction of Stomach</td>
<td>Drug: 5-fluorouracil or Capecitabine</td>
<td></td>
</tr>
<tr>
<td>Epidermal Growth Factor Receptor (EGFR) Protein Overexpression</td>
<td>Drug: Trastuzumab</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drug: Pertuzumab</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Procedure: gastrectomy</td>
<td></td>
</tr>
</tbody>
</table>

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: INtegratioN of Trastuzumab, With or Without Pertuzumab, Into periOperative chemotherapy of HER-2 poSitive stOmach caNcer: the INNOVATION-TRIAL

Resource links provided by NLM:

MedlinePlus related topics: Stomach Cancer

Drug Information available for: Fluorouracil Cisplatin Capecitabine Trastuzumab Pertuzumab

Genetic and Rare Diseases Information Center resources: Stomach Carcinomas

U.S. FDA Resources

Further study details as provided by European Organisation for Research and Treatment of Cancer - EORTC:

Primary Outcome Measures:
- Near Complete Pathological Response Rate [Time Frame: After 3 cycles (21 days) of neoadjuvant chemotherapy]
To increase the major pathological response rate (< 10% vital tumor cells) to neoadjuvant treatment by integrating both trastuzumab and pertuzumab into perioperative chemotherapy for HER-2 positive, resectable gastric cancer.

Secondary Outcome Measures:
- Locoregional failure [Time Frame: At the time of surgery and at 5 years] [Designated as safety issue: No]
- R0 resection rate [Time Frame: At the time of surgery] [Designated as safety issue: No]
- Distant failure [Time Frame: At the time of surgery and at 5 years] [Designated as safety issue: No]
- Progression-free survival [Time Frame: 5 years after LPI] [Designated as safety issue: No]
- Recurrence-free survival [Time Frame: 5 years after LPI] [Designated as safety issue: No]
- Overall survival [Time Frame: 5 years after LPI] [Designated as safety issue: No]
- Toxicity [Time Frame: 5 years after LPI] [Designated as safety issue: Yes]

Estimated Enrollment: 220
Study Start Date: September 2015
Estimated Study Completion Date: September 2024
Estimated Primary Completion Date: September 2020 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Comparator: Standard chemotherapy</td>
<td>Drug: Cisplatin Drug: 5-fluorouracil or Capecitabine Procedure: gastrectomy</td>
</tr>
<tr>
<td>Cisplatin/capecitabine or cisplatin/5-fluorouracil</td>
<td>D2 gastrectomy</td>
</tr>
<tr>
<td>Experimental: Experimental arm 1</td>
<td>Drug: Cisplatin Drug: 5-fluorouracil or Capecitabine Drug: Trastuzumab Procedure: gastrectomy</td>
</tr>
<tr>
<td>Cisplatin/capecitabine plus trastuzumab or cisplatin/5-fluorouracil plus trastuzumab</td>
<td>D2 gastrectomy</td>
</tr>
<tr>
<td>Experimental: Experimental arm 2</td>
<td>Drug: Cisplatin Drug: 5-fluorouracil or Capecitabine Drug: Trastuzumab Drug: Pertuzumab Procedure: gastrectomy</td>
</tr>
<tr>
<td>cisplatin/capecitabine plus trastuzumab and pertuzumab or cisplatin/5-fluorouracil plus trastuzumab and pertuzumab</td>
<td>D2 gastrectomy</td>
</tr>
</tbody>
</table>

Detailed Description:
This is a randomized phase II trial with an internal control. The randomization will be a 1:2:2 randomization (control: experimental arm 1: experimental arm 2). Potentially eligible patients will be screened centrally for the HER-2 status. After confirmation of HER-2 positive disease, eligible patients will be centrally randomized through the EORTC randomization system. A minimization technique will be used for random treatment allocation between the three treatment arms. Stratification will be done by histological subtype (intestinal/non-intestinal); Korea versus Europe; stage II versus III; node positive versus node negative.

Eligibility
Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria
Inclusion Criteria:
- Histologically proven, gastric or gastroesophageal (GE)-junction adenocarcinoma (Siewert I-III)
- Patient medically fit for gastrectomy/oesophagogastrrectomy as decided by the investigator
- Age ≥ 18 years
- WHO performance status 0 - 1
- HER-2 overexpression
- Amenable to gastrectomy/oesophagogastrectomy
- The cardiac ejection fraction (LVEF), as determined by echocardiography, multiple gated acquisition scan (MUGA) or cardiac MRI should be at least 50%
- Adequate organ function
- Written informed consent
- For women who are not postmenopausal (> 12 months of non-therapy induced amenorrhea) or surgically sterile (absence of ovaries...
and/or uterus): agreement to remain abstinent or use single or combined contraceptive methods that result in a failure rate of < 1% per year during the treatment period and for at least 12 months after the last treatment dose

For men: agreement to remain abstinent or use a condom plus an additional contraceptive method that together result in a failure rate of < 1% per year during the treatment period and for at least 12 months after the last dose of study treatment. Abstinence is only acceptable if it is in line with the preferred and usual lifestyle of the patient. Periodic abstinence (e.g. calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not acceptable methods for contraception.

Exclusion Criteria:

- Absence of distant metastases on CT scan of thorax and abdomen
- prior chemo- or antibody therapy
- history of significant cardiac disease
- current uncontrolled hypertension
- known hypersensitivity to the components of trastuzumab, pertuzumab, cisplatin, 5-fluorouracil or capecitabine
- known dihydropyrimidine dehydrogenase (DPD) deficiency
- ongoing or concomitant use of the antiviral drug sorivudine or its chemically related analogs, such as brivudine
- chronic treatment with high-dose intravenous corticosteroids
- previous malignancy within the last 5 years, with the exception of adequately treated cervical carcinoma in situ, localized non-melanoma skin cancer, or other curatively treated cancer without impact on the patient's overall prognosis according to the judgment of the investigator.
- psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule
- pregnant or breast feeding

▶ Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02205047

Contacts
Contact: Violaine Francois, PhD 0032 2 774 16 72 violaine.francois@eortc.be

Sponsors and Collaborators
European Organisation for Research and Treatment of Cancer - EORTC

Investigators
Study Chair: Anna Dorothea Wagner, MD Centre Hospitalier Universitaire Vaudois - Lausanne

▶ More Information

No publications provided

Responsible Party: European Organisation for Research and Treatment of Cancer - EORTC
ClinicalTrials.gov Identifier: NCT02205047 History of Changes
Other Study ID Numbers: EORTC-1203, 2014-000722-38, MO28922
Study First Received: July 10, 2014
Last Updated: August 3, 2015
Health Authority:
Belgium: Federal Agency for Medicinal Products and Health Products
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Germany: Federal Institute for Drugs and Medical Devices
Italy: Ethics Committee
Estonia: The State Agency of Medicine
Portugal: National Authority of Medicines and Health Products
Spain: Agencia Española de Medicamentos y Productos Sanitarios
Switzerland: Swissmedic
The Netherlands: The Central Committee on Research Involving Human Subjects (CCMO)
United Kingdom: Medicines and Healthcare Products Regulatory Agency
South Korea: Ministry of Food and Drug Safety
Keyw ords provided by European Organisation for Research and Treatment of Cancer - EORTC:
Neoadjuvant chemotherapy

Additional relevant MeSH terms:
- Neoplasms
- Stomach Neoplasms
- Digestive System Diseases
- Digestive System Neoplasms
- Gastrointestinal Diseases
- Gastrointestinal Neoplasms
- Neoplasms by Site
- Stomach Diseases
- Capecitabine
- Cisplatin
- Fluorouracil
- Pertuzumab

- Trastuzumab
- Antimetabolites
- Antimetabolites, Antineoplastic
- Antineoplastic Agents
- Immunologic Factors
- Immunosuppressive Agents
- Molecular Mechanisms of Pharmacological Action
- Pharmacologic Actions
- Physiological Effects of Drugs
- Radiation-Sensitizing Agents
- Therapeutic Uses

ClinicalTrials.gov processed this record on September 03, 2015