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Oxaliplatin plus S-1 or capecitabine chemotherapy before or after surgery for locally advanced gastric cancer with D2 lymphadenectomy: a phase II-III randomized trial

Submission date
28/02/2018

Recruitment status
No longer recruiting

Registration date
07/03/2018

Overall study status
Completed

Last Edited
05/12/2018

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Gastric cancer is a common cancer worldwide. Surgery is the primary treatment but alone fails to produce satisfactory treatment outcomes. Therefore, chemotherapy (drug treatment) administered after surgery has been used along with surgery to improve patient survival. Recently, preoperative chemotherapy was proposed and has been applied as an alternative to postoperative chemotherapy. Compared with postoperative chemotherapy, preoperative chemotherapy might show patient benefit in terms of fewer adverse effects and higher tolerance of the regimens. However, it is not known whether preoperative chemotherapy is better than postoperative chemotherapy in preventing death. The current study therefore aims to compare pre- and post-operative chemotherapy using oxaliplatin plus S-1 (SOX) or oxaliplatin plus capecitabine (CapeOX) on gastric cancer patients receiving gastrectomy (stomach surgery to remove cancer) with D2 lymphadenectomy (removal of lymph nodes around the stomach).

Who can participate?
Adult patient with gastric cancer.

What does the study involve?
Participants are randomly allocated to one of four groups. Those in the first group receive 2 cycles of SOX before the surgery and 6 cycles after the surgery. Those in the second group receive 2 cycles of CapeOX before the surgery and 6 cycles after the surgery. Those in the third group receive 8 cycles of SOX after the surgery. Those in the last group receive 8 cycles of CapeOX after the surgery. Participants are assessed for adverse effect of chemotherapy and survival status during the study.

What are the possible benefits and risks of participating?
Participants can benefit from improvements in their diseases. Those receiving preoperative chemotherapy may benefit from fewer adverse effects and better tolerance to the regimens. Those receiving postoperative chemotherapy may benefit from early performance of surgery.

There are small risks of surgical complications, adverse effects of chemotherapy, and discomfort and bleeding when providing blood samples.

Where is the study run from?
Peking University Cancer Hospital (Beijing, China)

When is the study starting and how long is it expected to run for?
September 2011 to December 2017

Who is funding the study?
This trial was supported in part by grants from Beijing Municipal Science & Technology Commission (D171100006517002).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
D171100006517002

Study information

Scientific Title
Efficacy and safety of oxaliplatin plus S-1 or capecitabine as neoadjuvant or adjuvant chemotherapy for locally advanced gastric cancer with D2 lymphadenectomy: a phase II-III randomized trial

Study objectives

Neoadjuvant chemotherapy is superior to adjuvant chemotherapy using SOX or CapeOX as the regimen.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Peking University Cancer Hospital Ethical Committee, approval September 2011, approval document issued 2012, 2012101606.

Study design
Single-center open-label randomized controlled phase II/III trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet.

Health condition(s) or problem(s) studied
Locally advanced gastric cancer

Interventions
Eligible patients were randomly assigned to one of the four arms: neoadjuvant SOX (peri-SOX), neoadjuvant CapeOX (peri-CapeOX), adjuvant SOX (post-SOX), and adjuvant CapeOX (post-CapeOX). Patients receiving neoadjuvant chemotherapy started chemotherapy within 3 days after the laparoscopic exploration; and after 2 cycles of chemotherapy, the clinical stage of the tumor was evaluated before the surgery was performed. Radical dissection was aimed in gastrectomy, with standard D2 lymphadenectomy. Patients receiving adjuvant chemotherapy had surgery immediately after the randomization. After the surgery, patients in neoadjuvant chemotherapy arms received 6 cycles of postoperative chemotherapy, whereas 8 cycles were administered to the adjuvant arms. Patients randomized to SOX regimens received oral S-1 (80 mg/m2 twice daily on day 1-14) and intravenous oxaliplatin (130 mg/m2 on day 1) for each cycle, whereas the CapeOX patients received oral capecitabine (1000 mg/m2 twice daily on day 1-14) and intravenous oxaliplatin (130 mg/m2 on day 1). Dose reduction and interruptions were allowed for potentially serious and life-threatening adverse events that were determined by clinicians.

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
S1 (tegafur + gimeracil + oteracil), oxaliplatin, capecitabine

Primary outcome measure
Overall survival (time interval from the time of randomization to the date of all-cause death or last follow-up). Follow-up was conducted by phone call every 6 months after completion or termination of treatment.

Secondary outcome measures
The secondary endpoints included treatment completion rate, surgical complications, chemotherapy adverse events and pathological complete response rate. Treatment completion rate was recorded when the treatment was completed or stopped. Surgical complications were measured during and after surgery. Complete response rate was reported by pathologists after the surgery. Pathological stage was evaluated according to the 7th edition of the American Joint Committee on Cancer TNM Staging Classification for Carcinoma of the Stomach. The clinical response was evaluated by the Response Evaluation Criteria for Solid Tumors (RECIST) in computed tomography and by the downstaging assessed by endoscopic ultrasound using Choi criteria by the end of the second cycle of neoadjuvant chemotherapy (NACT). Pathology response to NACT was evaluated according to the 3rd English edition of the Japanese Classification of Gastric Cancer.

Overall study start date
01/03/2011

Completion date
31/12/2017

Eligibility

Key inclusion criteria
1. Aged between 18 and 80 years
2. Pathologically confirmed gastric adenocarcinoma
3. Disease at the clinical stage of resectable advanced gastric cancer (T2-4NanyM0), without peritoneal metastasis as confirmed by laparoscopy and cytological pathology
4. Eastern Cooperative Oncology Group performance status of 0 or 1
5. No previous treatment history
6. Adequate organ function levels (hematological ANC ≥1.5x10(9)/l, hemoglobin ≥9 g/dl, platelets ≥ 100x10(9)/l, hepatic albumin ≥30 g/l, serum bilirubin ≤1.5x the upper limit of normal [ULN], AST and ALT ≤2.5×ULN, ALP ≤2.5×ULN, TBIL ≤1.5×ULN, renal serum creatinine <1.5xULN)
7. Adequate lung and heart function, without ECG-confirmed ischemic change or ventricular arrhythmias

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
224

Key exclusion criteria
1. Serious comorbidities
2. Distant metastasis
3. Acute inflammation
4. Systematic steroid therapy
5. Pregnant or breast-feeding women or women considering pregnancy
6. Nervous system disorder or psychiatric disease
7. Medical history of allergy or hypersensitivity to any drugs
8. Patient refusal

Date of first enrolment
01/09/2011

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
China

Study participating centre
Peking University Cancer Hospital & Institute
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100142

Sponsor information

Organisation
Peking University Cancer Hospital & Institute

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University/education

ROR
https://ror.org/00nyxxr91

Funder(s)

Funder type
Not defined

Funder Name
Beijing Municipal Science & Technology Commission

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal 6 months after the overall trial end.

Intention to publish date
30/06/2018

Individual participant data (IPD) sharing plan
The data in the current study can be shared on journal editor's request. Please contact Dr. Xue Kan on xuekan213@163.com for details of data sharing.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2018		Yes	No