An Open-Label, Randomized, Multicenter Phase IIa Study;Evaluating Pertuzumab in Combination with Trastuzumab and;Chemotherapy in Patients with HER2-Positive Advanced;Gastric Cancer

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON35408

Source
ToetsingOnline

Brief title
BP27836 / JOSHUA

Condition

- Other condition

Synonym
adenocarcinoma, gastric cancer

Health condition

gevorderde maligniteiten in gastro-oesopageale overgang of maag

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: F. Hoffmann La Roche Inc.

Intervention

Keyword: HER2-positive advanced gastric cancer, Pertuzumab

Outcome measures

Primary outcome

To estimate the minimum (trough) pertuzumab concentration (Cmin) at Day 43 for two dose levels of pertuzumab in order to identify a dose that produces a steady-state Cmin of *20 *g/mL in 90% of patients receiving pertuzumab and trastuzumab plus chemotherapy as first-line treatment for HER2-positive inoperable locally advanced or recurrent and/or metastatic adenocarcinoma of the stomach or gastroesophageal junction.

To evaluate the safety and tolerability of two dose levels of pertuzumab in combination with trastuzumab and chemotherapy administered every 3 weeks to patients with HER2-positive inoperable locally advanced or recurrent and/or metastatic adenocarcinoma of the stomach or gastroesophageal junction

Secondary outcome

To make an exploratory assessment of the anti-tumor activity of pertuzumab in combination with trastuzumab and chemotherapy in patients with HER2-positive inoperable locally advanced or recurrent and/or metastatic adenocarcinoma of the stomach or gastroesophageal junction.

Study description

Background summary

This is a scientific study investigating pertuzumab combined with trastuzumab plus chemotherapy. Pertuzumab blocks HER2 receptors of the tumor to prevent signal transduction of the tumor cell, thus inhibiting tumorgrowth. Although both drugs bind to the HER2 receptor, they have a different mode of action. Prior studies in HER2 positive breast cancer demonstrated a complementary effect of pertuzumab and trastuzumab.

Study objective

Pertuzumab is an investigational agent being studied for the treatment of HER2-positive gastric cancer. This study intends to provide a dose of pertuzumab to find an acceptable minimum pertuzumabconcentratie pertuzumab effective when administered in combination with trastuzumab and chemotherapy (cisplatin and capecitabine). This minimum pertuzumabconcentratie will help determine the best dose of pertuzumab for administration in advanced gastric cancer.

Study design

This is a randomized, multicenter, open-label study evaluating two different doses of pertuzumab in patients with HER2-positive adenocarcinoma of the stomach or gastroesophageal junction. Patients will be randomized in a 1:1 ratio to two treatment arms. Patients in Arm A will receive a pertuzumab loading dose of 840 mg for Cycle 1 and a dose of 420 mg for Cycles 2*6, and patients in Arm B will receive pertuzumab 840 mg for all six cycles. Patients in both treatment arms will receive trastuzumab, cisplatin, and capecitabine.

Intervention

Patients will receive 6 infusions pertuzumab; Trastuzumab will be administered on the same day and will continue on a 3 week schedule until disease progression.

Study burden and risks

During an infusion, chills, fever, and other flu-like symptoms may occur. These are very common and can affect more than 10 out of 100 patients. Other infusion related symptoms can include the following: feeling sick (nausea), vomiting, pain, increased muscle tension and shaking, headache, dizziness, breathing difficulties, wheezing, high or low blood pressure, heart rhythm disturbances (palpitations, heart fluttering, or irregular heart beat),

swelling of the face and lips, rash, and feeling tired. These effects mainly occur with the first infusion and during the first few hours after the start of the infusion. They are usually temporary.
Heart problems can sometimes occur during treatment and occasionally after treatment has stopped and can be serious. They include weakening of the heart muscle possibly leading to heart failure, inflammation of the lining around the heart, and heart rhythm disturbances.
This can lead to symptoms such as the following: Breathlessness (including breathlessness at night), Cough, Fluid retention (swelling) in the legs or arms, Palpitations.
The following are very common side effects of trastuzumab and pertuzumab (affects more than 10 out of 100 patients): Diarrhea, Weakness, Skin rashes, Chest pain, abdominal pain, joint pain, muscle pain, Febrile neutropenia.
The following are other common side effects of trastuzumab and pertuzumab (affects 1*10 out of 100 patients): Allergic reactions, Itchiness, Abnormal blood counts, Dry mouth and skin, Constipation, Dry or watery eyes, Heartburn, Sweating, Infections, including bladder and skin infections, Feeling weak and unwell, Shingles, Anxiety, Depression, abnormal thinking, Inflammation of the breast, Inflammation of the pancreas or liver, Kidney disorders, Dizziness, Increased muscle tone/tension, Loss of appetite, weight loss, Tremor, Numbness or tingling of the fingers and toes, Altered taste, Nail disorders, hair loss, Asthma, lung disorders, Inability to sleep, sleepiness, Back pain, neck pain, bone pain, Nose bleeds, Bruising, Acne, Hemorrhoids, Leg cramps.
Disadvantages of participation in this study are: extra time investment for this study, additional or prolonged hospitalization (daycare unit), additional blood draws for laboratory tests, additional physical examinations including ECG and CT/MRA scans, biopsies and possible side effects of the new investigational drug pertuzumab.

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

Disease-Specific Inclusion Criteria;* Histologically confirmed adenocarcinoma of the stomach or gastroesophageal junction with inoperable locally advanced or metastatic disease, not amenable to curative therapy. Patients with advanced disease who present with a recurrence post operatively (when intent of surgery was cure) are also eligible for entry.;* Measurable disease, according to the Response Evaluation Criteria in Solid Tumors (RECIST), v1.1, assessed using imaging techniques (CT or MRI), or non-measurable disease that can be followed;* HER2 positive tumor defined as either IHC 3+ or IHC 2+ in combination with ISH +, as assessed by central laboratory on primary or metastatic tumor ISH positivity is defined as a ratio of >< = 2.0 for the number of HER2 gene copies to the number of signals for CEP17.;Availability of formalin-fixed paraffin-embedded (FFPE) tissue with at least 5 mm of invasive tumor for central confirmation of HER2 eligibility is mandatory.;* Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1;* Baseline LVEF >< = 55% (measured by ECHO or MUGA) ;* Life expectancy of at least 3 months.;General Inclusion Criteria;* Male or female;* Age >< = 18 years;* Signed informed consent;* For women of childbearing potential and male participants with partners of childbearing potential: agreement to use a highly effective non-hormonal form of contraception or two effective forms of non-hormonal contraception by the patient and/or partner (see Section 7.2.6 for details). Contraception use must continue for the duration of study treatment and for at least 6 months after the last dose of study medication.

Exclusion criteria

Cancer-Related Exclusion Criteria;* Previous chemotherapy for advanced or metastatic disease, except that prior adjuvant or neoadjuvant therapy is allowed if at least 6 months has elapsed between completion of adjuvant or neoadjuvant therapy and enrollment in the study. Adjuvant or neoadjuvant treatment with platinum-based therapy is not allowed.;* Lack of physical integrity of the upper gastrointestinal tract or malabsorption syndrome (e.g.,

patients with partial or total gastrectomy can enter the study, but not those with a jejunostomy probe);* Active (significant or uncontrolled) gastrointestinal bleeding;* Residual relevant toxicity resulting from previous therapy (e.g., neurological toxicity of >= Grade >= 2 [NCI CTCAE]), with the exception of alopecia;* Other malignancy within the last 5 years, except for carcinoma in situ of the cervix, or basal cell carcinoma.;Exclusion Criteria Related to Hematological, Biochemical, and Organ Function;* Any of the following abnormal laboratory tests immediately prior to randomization: ;Serum total bilirubin > 1.5 times the upper limit of normal (ULN) or, for patients with known Gilberts syndrome, serum total bilirubin > 2 × ULN;For patients with no liver and no bone metastases: ;AST or ALT > 2.5 × ULN, and alkaline phosphatase (ALP) > 2.5 × ULN;In patients with liver metastases and no bone metastases: ;AST or ALT > 5 × ULN, and ALP > 2.5 × ULN;In patients with liver metastases and bone metastases: ;AST or ALT > 5 × ULN, and ALP > 10 × ULN;;In patients with bone metastases and no liver metastases: ;AST or ALT > 2.5 × ULN, and ALP > 10 × ULN ;Albumin < 25 g/L;Creatinine clearance < 60 mL/min;Total WBC count < 2500/*L (< 2.5 × 109/L);Absolute neutrophil count (ANC) < 1500/*L (<1.5 × 109/L);Platelets < 100,000/*L (<100 × 109/L).;Other Study Drug*Related Exclusion Criteria;* Serious cardiac illness or medical conditions including but not confined to:;History of documented heart failure or systolic dysfunction (LVEF < 50%);High-risk uncontrolled arrhythmias, such as atrial tachycardia with a heart rate >= 100/min at rest, significant ventricular arrhythmia (ventricular tachycardia) or higher-grade AV block (second-degree AV block Type 2 [Mobitz II] or third-degree AV block);Angina pectoris requiring anti-anginal medication;Clinically significant valvular heart disease;Evidence of transmural infarction on ECG;Poorly controlled hypertension (e.g., systolic blood pressure > 180 mmHg or diastolic blood pressure > 100 mmHg);* Dyspnea at rest due to complications of advanced malignancy or other disease, or requirement for supportive oxygen therapy;* Treatment with chronic or high-dose corticosteroid therapy.;Inhaled steroids and short courses of oral steroids for anti-emesis or as an appetite stimulant are allowed.;* Clinically significant hearing abnormality;* Known dihydropyrimidine dehydrogenase deficiency.;General Exclusion Criteria;* History or clinical evidence of brain metastases;* Serious uncontrolled systemic intercurrent illness (e.g., infections or poorly controlled diabetes);* Pregnant or lactating. Women of childbearing potential must have a negative serum pregnancy test within 7 days prior to randomization, irrespective of the method of contraception used.;* Radiotherapy within 4 weeks prior to start of study treatment, or within 2 weeks prior to start of study treatment if palliative radiotherapy is given to bone metastatic site peripherally and patient recovers from any acute toxicity;* Major surgery within 4 weeks prior to start of study treatment, without complete recovery;* Known active infection with HIV, hepatitis B virus, or hepatitis C virus;* Known hypersensitivity to any of the study drugs;* Inability to comply with follow-up testing or procedures, as determined by the investigator.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Herceptin
Generic name:	trastuzumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	NVT
Generic name:	pertuzumab

Ethics review

Approved WMO

Date:	19-09-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	19-12-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

Approved WMO Date:	09-01-2012
Application type:	First submission
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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	EUCTR2011-002331-25-NL
CCMO	NL37900.068.11
Other	Onder Eudractnummer 2011002331-25 op www.rochtrials.com zodra de studie is goedgekeurd.