A Phase 3 Efficacy, Safety and Tolerability Study of Zolbetuximab (Experimental Drug) Plus mFOLFOX6 Chemotherapy Compared to Placebo Plus mFOLFOX6 as Treatment for Gastric and Gastroesophageal Junction (GEJ) Cancer (Spotlight)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03504397

Recruitment Status: Recruiting
First Posted: April 20, 2018
Last Update Posted: January 18, 2020

See Contacts and Locations

Sponsor:
Astellas Pharma Global Development, Inc.

Information provided by (Responsible Party):
Astellas Pharma Inc (Astellas Pharma Global Development, Inc.)
Brief Summary:

A study of zolbetuximab (IMAB362) plus mFOLFOX6 versus placebo plus mFOLFOX6 in subjects with Claudin 18.2 positive, HER2-negative, locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma.

Why is this study being done?

SPOTLIGHT is a new clinical study for adult patients who have any of:

- advanced unresectable gastric or GEJ cancer
- metastatic gastric or GEJ cancer

These types of cancers have a unique set of proteins (called Claudin 18.2). We may be able to use a treatment that targets the proteins to kill the cancer cells.

For patients with one of the types of cancer listed above, mFOLFOX6 (a combination of three chemotherapies known as Oxaliplatin, Leucovorin, and Fluorouracil) is a current treatment option. This study is testing an experimental medicine called zolbetuximab (IMAB362). Zolbetuximab attaches itself to Claudin 18.2 on the cancer cells causing cancer cell death.

Patients will be assigned to one of two groups by chance and given either:

- zolbetuximab with mFOLFOX6; or
- a placebo with mFOLFOX6

A placebo is a treatment that looks like the experimental medicine, but contains no medicine.

The goal of the study is to find out if zolbetuximab with mFOLFOX6 helps patients to live longer by stopping the cancer from getting worse.

<table>
<thead>
<tr>
<th>Condition or disease</th>
<th>Intervention/treatment</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locally Advanced Unresectable Gastroesophageal Junction (GEJ) Adenocarcinoma or Cancer</td>
<td>Drug: zolbetuximab</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Locally Advanced Unresectable Gastric Adenocarcinoma or Cancer</td>
<td>Drug: placebo</td>
<td></td>
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<tr>
<td>Metastatic Gastric Adenocarcinoma or Cancer</td>
<td>Drug: oxaliplatin</td>
<td></td>
</tr>
<tr>
<td>Metastatic Gastroesophageal Junction (GEJ) Adenocarcinoma</td>
<td>Drug: folinic acid</td>
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<tr>
<td></td>
<td>Drug: fluorouracil</td>
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</tbody>
</table>

Detailed Description:

The study consists of the following periods: screening; treatment; post-treatment follow up, safety follow up,
Study Design

**Study Type**: Intervventional (Clinical Trial)
**Estimated Enrollment**: 550 participants
**Allocation**: Randomized
**Intervention Model**: Parallel Assignment
**Masking**: Double (Participant, Investigator)
**Primary Purpose**: Treatment

**Official Title**: A Phase 3, Global, Multi-Center, Double-Blind, Randomized, Efficacy Study of Zolbetuximab (IMAB362) Plus mFOLFOX6 Compared With Placebo Plus mFOLFOX6 as First-line Treatment of Subjects With Claudin (CLDN)18.2-Positive, HER2-Negative, Locally Advanced Unresectable or Metastatic Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma

**Actual Study Start Date**: June 21, 2018
**Estimated Primary Completion Date**: February 2021
**Estimated Study Completion Date**: September 2022

Arms and Interventions

<table>
<thead>
<tr>
<th>Arm 1</th>
<th>Intervention/treatment 1</th>
</tr>
</thead>
</table>
| **Experimental: Arm A (zolbetuximab plus mFOLFOX6)** | **Drug: zolbetuximab**<br>Zolbetuximab will be administered as a minimum 2-hour IV infusion.<br>**Other Name: IMAB362**
| Participants will receive a loading dose of zolbetuximab at Cycle 1 Day 1 followed by a lower dose in subsequent cycles every 3 weeks. Additionally, participants will receive up to 12 treatments of mFOLFOX6 (or components of mFOLFOX6 if some components are discontinued due to toxicity) over 4 or more cycles (each cycle is | **Drug: oxaliplatin**<br>Oxaliplatin will be administered as a 2-hour IV infusion |

Resource links provided by the National Library of Medicine

Genetic and Rare Diseases Information Center resources: Stomach Cancer

U.S. FDA Resources

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long term and survival follow-up.
### Arm

approximately 42 days) in which mFOLFOX6 is administered on Days 1, 15 and 29. After 12 mFOLFOX6 treatments, participants may continue to receive fluorouracil (5-FU) and folinic acid at the investigator's discretion until the subject meets study treatment discontinuation criteria.

### Intervention/treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>folinic acid</td>
<td>Folinic acid will be administered as a 2-hour IV infusion.</td>
</tr>
<tr>
<td>fluorouracil</td>
<td>Fluorouracil will be administered as IV bolus over 5-15 minutes and continuous IV infusion over 46-48 hours.</td>
</tr>
<tr>
<td>placebo</td>
<td>Placebo will be administered as a minimum 2-hour IV infusion.</td>
</tr>
<tr>
<td>oxaliplatin</td>
<td>Oxaliplatin will be administered as a 2-hour IV infusion</td>
</tr>
<tr>
<td>folinic acid</td>
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</table>

### Placebo Comparator: Arm B (Placebo plus mFOLFOX6)

Participants will receive placebo starting at Cycle 1 Day 1 and every 3 weeks thereafter. Additionally, participants will receive up to 12 treatments of mFOLFOX6 (or components of mFOLFOX6 if some components are discontinued due to toxicity) over 4 or more cycles (each cycle is approximately 42 days) in which mFOLFOX6 is administered on Days 1, 15 and 29. After 12 mFOLFOX6 treatments, participants may continue to receive fluorouracil (5-FU) and folinic acid at the investigator's discretion until the subject meets study treatment discontinuation criteria.

### Outcome Measures

**Primary Outcome Measures**

1. Progression Free Survival (PFS) [ Time Frame: Up to 13 months ]

   PFS is defined as the time from the date of randomization until the date of radiological progressive disease (per Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 by Independent Review Committee (IRC)) or death from any cause, whichever is earliest.
Secondary Outcome Measures:

1. Overall Survival (OS) [Time Frame: Up to 23 months]  
   OS is defined as the time from the date of randomization until the date of death from any cause.

2. Objective Response Rate (ORR) [Time Frame: Up to 13 months]  
   ORR is defined as the proportion of participants who have a best overall response of Complete Response (CR) or Partial Response (PR) as assessed by Independent Review Committee (IRC) per RECIST 1.1.

3. Duration Of Response (DOR) [Time Frame: Up to 13 months]  
   DOR, defined as the time from the date of the first response (CR/PR) until the date of progressive disease as assessed by IRC per RECIST 1.1 or date of death from any cause, whichever is earliest.

4. Safety and tolerability assessed by adverse events (AEs) [Time Frame: Up to 16 months]  
   An AE is any untoward medical occurrence in a subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

5. Number of participants with laboratory assessments abnormalities and or adverse events [Time Frame: Up to 14 months]  
   Number of participants with potentially clinically significant laboratory values.

6. Number of participants with vital signs abnormalities and or adverse events [Time Frame: Up to 14 months]  
   Number of participants with potentially clinically significant vital sign values.

7. Number of participants with electrocardiograms (ECG) abnormalities and or adverse events [Time Frame: Up to 14 months]  
   Number of participants with potentially clinically significant ECG values.

8. Number of participants with Eastern Cooperative Oncology Group (ECOG) performance status abnormalities and or adverse events [Time Frame: Up to 13 months]  
   Number of participants with potentially clinically significant ECOG performance status.
values. ECOG grades 0-5, where 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work; 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours; 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours; 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair and 5 = Dead.

9. Health Related Quality of Life (HRQoL) measured by the European Organization for Research and Treatment of Cancer (EORTC-QLQ-C30) questionnaire [ Time Frame: Up to 16 months ]

The EORTC-QLQ-C30 is a cancer-specific instrument consisting of 5 functional domain scales: physical, role, emotional, social and cognitive.

10. HRQoL measured by the QLQ-OG25 questionnaire [ Time Frame: Up to 16 months ]

The EORTC-QLQ-OG25 instrument evaluates Gastric and GEJ cancer-specific symptoms such as stomach discomfort, difficulties eating and swallowing and indigestion.

11. HRQoL measured by the Global Pain (GP) questionnaire [ Time Frame: Up to 16 months ]

The GP instrument is a single assessment of overall pain.

12. HRQoL measured by the EuroQOL Five Dimensions Questionnaire 5L (EQ-5D-5L) questionnaire [ Time Frame: Up to 16 months ]

The EQ-5D-5L is a standardized instrument developed by the EuroQol Group for use as a generic, preference-based measure of health outcomes. The EQ-5D-5L is a 5-item self-reported measure of functioning and wellbeing, which assesses 5 dimensions of health, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension comprises 5 levels (no problems, slight problems, moderate problems, severe problems, extreme problems). A unique EQ-5D-5L health state is defined by combining 1 level from each of the 5 dimensions. This questionnaire also records the respondent's self-rated health status on a vertical graduated (0 = the worst health a participant can imagine to 100 = the best health a participant can imagine) visual analogue scale. Responses to the 5 items will also be converted to a weighted health state index (utility score) based on values derived from general population samples.

13. PK of zolbetuximab: Concentration Immediately Prior to Dosing at multiple dosing (C\text{trough}) [ Time Frame: Up to 16 months ]

C\text{trough} will be derived from the PK serum samples collected.
14. Number of anti-drug antibody (ADA) Positive Participants [ Time Frame: Up to 16 months ]

Immunogenicity will be measured by the number of participants that are ADA positive.

Eligibility Criteria

Information from the National Library of Medicine

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, Learn About Clinical Studies.

- Ages Eligible for Study: 18 Years and older (Adult, Older Adult)
- Sexes Eligible for Study: All
- Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Female subject eligible to participate if she is not pregnant (negative serum pregnancy test at screening; female subjects with elevated serum beta human chorionic gonadotropin and a demonstrated non-pregnant status through additional testing are eligible) and at least one of the following conditions applies:
  - Not a woman of child-bearing potential (WOCBP) OR
  - WOCBP who agrees to follow the contraceptive guidance throughout the treatment period and for at least 6 months after the final study drug administration
- Female subject must agree not to breastfeed starting at screening and throughout the study period, and for 6 months after the final study drug administration.
- Female subject must agree not to donate ova starting at screening and throughout the study period, and for 6 months after the final study drug administration.
- A sexually active male subject with a female partner(s) who is of child-bearing potential must agree to use contraception during the treatment period and for at least 6 months after the final...
study drug administration.

- Male subject must agree not to donate sperm starting at screening and throughout the study period, and for 6 months after the final study drug administration.

- Male subject with a pregnant or breastfeeding partner(s) must agree to remain abstinent or use a condom for the duration of the pregnancy or time partner is breastfeeding throughout the study period and for 6 months after the final study drug administration.

- Subject has histologically confirmed diagnosis of Gastric or GEJ adenocarcinoma.

- Subject has radiologically confirmed locally advanced unresectable or metastatic disease within 28 days prior to randomization.

- Subject has radiologically evaluable disease (measurable and/or non-measurable disease according to RECIST 1.1), per local assessment, ≤ 28 days prior to randomization. For subjects with only 1 evaluable lesion and prior radiotherapy ≤ 3 months before randomization, the lesion must either be outside the field of prior radiotherapy or have documented progression following radiation therapy.

- Subject's tumor expresses CLDN18.2 in ≥ 75% of tumor cells demonstrating moderate to strong membranous staining as determined by central immunohistochemistry (IHC) testing.

- Subject has a HER2-Negative tumor as determined by local or central testing on a gastric or GEJ tumor specimen.

- Subject has ECOG performance status 0 to 1.

- Subject has predicted life expectancy ≥ 12 weeks.

- Subject must meet all of the following criteria based on the centrally or locally analyzed laboratory tests collected within 14 days prior to randomization. In case of multiple laboratory data within this period, the most recent data should be used to determine eligibility.
  
  o Hemoglobin (Hgb) ≥ 9 g/dL. Subjects requiring transfusions are eligible if they have a post-transfusion Hgb ≥ 9 g/dL.
  
  o Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L
  
  o Platelets ≥ 100 x 10^9/L
  
  o Albumin ≥ 2.5 g/dL
  
  o Total bilirubin ≤ 1.5 x upper limit of normal (ULN) without liver metastases (or < 3.0 x ULN if liver metastases are present)
  
  o Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 2.5 x ULN without liver metastases (or ≤ 5 x ULN if liver metastases are present)
  
  o Estimated creatinine clearance ≥ 30 mL/min
  
  o Prothrombin time (PT)/international normalized ratio (INR) and partial thromboplastin time (PTT) ≤ 1.5 x ULN (except for subjects receiving anticoagulation therapy)
Exclusion Criteria:

- Subject has received prior systemic chemotherapy for locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma. However, subject may have received either neo-adjuvant or adjuvant chemotherapy as long as it was completed at least 6 months prior to randomization. Subject may have received treatment with herbal medications that have known antitumor activity > 28 days prior to randomization.

- Subject has received radiotherapy for locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma ≤ 14 days prior to randomization and has not recovered from any related toxicity.

- Subject has received systemic immunosuppressive therapy, including systemic corticosteroids within 14 days prior to randomization. Subjects using a physiologic replacement dose of hydrocortisone or its equivalent (defined as up to 30 mg per day of hydrocortisone or up to 10 mg per day of prednisone), receiving a single dose of systemic corticosteroids or receiving systemic corticosteroids as premedication for radiologic imaging contrast use are allowed.

- Subject has received other investigational agents or devices within 28 days prior to randomization.

- Subject has prior severe allergic reaction or intolerance to known ingredients of zolbetuximab or other monoclonal antibodies, including humanized or chimeric antibodies.

- Subject has known immediate or delayed hypersensitivity, intolerance or contraindication to any component of study treatment.

- Subject has prior severe allergic reaction or intolerance to any component of mFOLFOX6.

- Subject has known dihydropyrimidine dehydrogenase deficiency.

- Subject has a complete gastric outlet syndrome or a partial gastric outlet syndrome with persistent/recurrent vomiting.

- Subject has significant gastric bleeding and/or untreated gastric ulcers that would exclude the subject from participation.

- Subject has a known history of a positive test for human immunodeficiency virus (HIV) infection or known active hepatitis B (positive hepatitis B surface antigen (HBs Ag)) or C infection. NOTE: Screening for these infections should be conducted per local requirements.
  
  o For subjects who are negative for HBs Ag, but hepatitis B core antibody (HBC Ab) positive, an HB deoxyribonucleic acid (DNA) test will be performed and if positive, the subject will be excluded.

  o Subjects with positive hepatitis C virus (HCV) serology, but negative HCV ribonucleic acid (RNA) test are eligible.

  o Subjects treated for HCV with undetectable viral load results are eligible.

- Subject has an active autoimmune disease that has required systemic treatment within the past 3
months prior to randomization.

- Subject has active infection requiring systemic therapy that has not completely resolved within 7 days prior to randomization.

- Subject has significant cardiovascular disease, including any of the following:
  - Congestive heart failure (defined as New York Heart Association Class III or IV), myocardial infarction, unstable angina, coronary angioplasty, stenting, coronary artery bypass graft, cerebrovascular accident (CVA) or hypertensive crisis within 6 months prior to randomization.
  - History of clinically significant ventricular arrhythmias (i.e., sustained ventricular tachycardia, ventricular fibrillation or Torsades de Pointes)
  - QTc interval > 450 msec for male subjects; QTc interval > 470 msec for female subjects
  - History or family history of congenital long QT syndrome
  - Cardiac arrhythmias requiring anti-arrhythmic medications (Subject with rate controlled atrial fibrillation for > 1 month prior to randomization are eligible).

- Subject has a history of central nervous system metastases and/or carcinomatous meningitis from gastric/GEJ cancer.

- Subject has known peripheral sensory neuropathy > Grade 1 unless the absence of deep tendon reflexes is the sole neurological abnormality.

- Subject has had a major surgical procedure ≤ 28 days prior to randomization.
  - Subject is without complete recovery from a major surgical procedure ≤ 14 days prior to randomization.

- Subject has psychiatric illness or social situations that would preclude study compliance.

- Subject has another malignancy for which treatment is required.

- Subject has any concurrent disease, infection or comorbid condition that interferes with the ability of the subject to participate in the study, which places the subject at undue risk or complicates the interpretation of data.

Contacts and Locations

Go to
Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number):
NCT03504397

Contacts

Contact: Astellas Pharma Global Development  800-888-7704  astellas.registration@astellas.com

Locations

Show 170 study locations

Sponsors and Collaborators

Astellas Pharma Global Development, Inc.

Investigators

Study Director:  Global Medical Lead  Astellas Pharma Global Development, Inc.

More Information

Responsible Party:  Astellas Pharma Global Development, Inc.
ClinicalTrials.gov Identifier:  NCT03504397  History of Changes
Other Study ID Numbers:  8951-CL-0301
2017-002567-17 ( EudraCT Number )
First Posted:  April 20, 2018  Key Record Dates
Last Update Posted:  January 18, 2020
Last Verified:  January 2020

Individual Participant Data (IPD) Sharing Statement:
Plan to Share IPD:  Undecided

Studies a U.S. FDA-regulated Drug Product:  Yes
Studies a U.S. FDA-regulated Device Product:  No

Keywords provided by Astellas Pharma Inc ( Astellas Pharma Global Development, Inc. ):

https://clinicaltrials.gov/ct2/show/NCT03504397
HER2  
zolbetuximab
IMAB362  
oxaliplatin
leucovorin  
adenocarcinoma
fluorouracil  
Gastro-Esophageal Junction cancer
Gastric cancer  
HER2 Negative mFOLFOX6
claudiximab

Additional relevant MeSH terms:
Adenocarcinoma  
Antimetabolites, Antineoplastic
Carcinoma  
Immunosuppressive Agents
Neoplasms, Glandular and Epithelial  
Immunologic Factors
Neoplasms by Histologic Type  
Physiological Effects of Drugs
Neoplasms  
Antidotes
Leucovorin  
Protective Agents
Folic Acid  
Vitamin B Complex
Oxaliplatin  
Vitamins
Fluorouracil  
Micronutrients
Levoleucovorin  
Nutrients
Antineoplastic Agents  
Growth Substances
Antimetabolites  
Hematinics
Molecular Mechanisms of Pharmacological Action

A Phase 3 Efficacy, Safety and Tolerability Study of Zolbetuximab (Exp... https://clinicaltrials.gov/ct2/show/NCT03504397
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