Safety and Activity of IMAB362 in Combination With Zoledronic Acid and Interleukin-2 in CLDN18.2-positive Gastric Cancer (PILOT)

**Purpose**

The purpose of the trial is to assess the immunological effects and their kinetics, the safety and activity of IMAB362 plus Zoledronic acid with/without low to intermediate doses of Interleukin-2 in subjects with advanced gastroesophageal cancer. In case favorable effects of adding Zoledronic acid/Interleukin-2 are observed a third arm featuring IMAB362, EOX and Zoledronic Acid/Interleukin-2 may be started in a concomitant Phase II FAST trial (EudraCT 2011-005285-38) will start. The sponsor will provide an amended protocol including dosing details of IL-2 in case of a positive decision to start arm 3.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLDN18.2-positive Gastric Adenocarcinoma</td>
<td>Drug: IMAB362</td>
<td>Phase 1</td>
</tr>
<tr>
<td>CLDN18.2-positive Adenocarcinoma of Esophagus</td>
<td>Drug: Zoledronic acid</td>
<td></td>
</tr>
<tr>
<td>CLDN18.2-positive Adenocarcinoma of the Gastroesophageal Junction</td>
<td>Drug: Interleukin-2 (1 million IU)</td>
<td></td>
</tr>
<tr>
<td>CLDN18.2-positive Adenocarcinoma of the Gastroesophageal Junction</td>
<td>Drug: Interleukin-2 (3 million IU)</td>
<td></td>
</tr>
</tbody>
</table>

**Condition Intervention Phase**

- CLDN18.2-positive Gastric Adenocarcinoma
- CLDN18.2-positive Adenocarcinoma of Esophagus
- CLDN18.2-positive Adenocarcinoma of the Gastroesophageal Junction

**Study Type:** Interventional

- **Allocation:** Non-Randomized
- **Endpoint Classification:** Safety Study
- **Intervention Model:** Parallel Assignment
- **Masking:** Open Label
- **Primary Purpose:** Treatment

**Official Title:** Multicenter, Open-label, Exploratory Phase I Pilot Study to Investigate Safety, Pharmacodynamics and Pharmacokinetics of Immunological Effects and Activity of Combining Multiple Doses of IMAB362 With Immunomodulation (Zoledronic Acid, Interleukin-2) in Patients With Advanced Adenocarcinoma of the Stomach, the Lower Esophagus or the Gastro-esophageal Junction.

**Resource links provided by NLM:**

- MedlinePlus related topics: Cancer, Stomach Cancer
- Drug Information available for: Zoledronic acid
- U.S. FDA Resources

**Further study details as provided by Ganymed Pharmaceuticals AG:**

**Primary Outcome Measures:**

- **Safety and Tolerability** [Time Frame: at least 18 months] [Designated as safety issue: Yes]
  - Descriptive statistics for treatments will be given on the number of patients whose treatment had to be reduced, delayed or permanently stopped.

- **Immune cell profile and kinetics** [Time Frame: at least 18 months] [Designated as safety issue: No]
  - Descriptive statistics for treatments will be given on the number and activity of immune cells in peripheral blood of patients.
Secondary Outcome Measures:

- **Progression-free survival (PFS)** [Time Frame: at least 18 months] [Designated as safety issue: No]
  
  PFS is defined as the time from registration of therapy to the first observation of disease progression or death from any cause or last tumor evaluation if free of progression. For patients who have not progressed either clinically or on the last scan, they will be censured as of the last tumor evaluation.

- **Objective tumor response rate (ORR)** [Time Frame: at least 18 months] [Designated as safety issue: No]
  
  ORR comprises the fraction of patients with CR, PR according to RECIST v1.1. It is set in relation to the ITT population and PP population.

- **Disease control rate (DCR)** [Time Frame: at least 18 months] [Designated as safety issue: No]
  
  DCR is defined as the fraction of patients with CR or PR or SD according to RECIST v1.1. It is set in relation to the ITT population and PP population.

- **Duration of response (DOR)** [Time Frame: at least 18 months] [Designated as safety issue: No]
  
  Duration of response is determined as the time when criteria for CR, PR, and SD are first met until the first date that recurrent or progressive disease or death occurs.

**Estimated Enrollment:** 20

**Study Start Date:** August 2012

**Estimated Study Completion Date:** February 2014

**Estimated Primary Completion Date:** August 2013 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental: IMAB362 + ZA</td>
<td>Drug: IMAB362 800 mg/m2 on d 1 of cycle 1. 600 mg/m2 on d 1 of every other cycle Drug: Zoledronic acid 4 mg on d 1 of cycle 1 and cycle 3</td>
</tr>
<tr>
<td>Experimental: IMAB362 + ZA + IL-2 (1 million IU)</td>
<td>Drug: IMAB362 800 mg/m2 on d 1 of cycle 1. 600 mg/m2 on d 1 of every other cycle Drug: Zoledronic acid 4 mg on d 1 of cycle 1 and cycle 3 Drug: Interleukin-2 (1 million IU) 1 million IU on day 1, 2 and 3 of cycles 1 and 3.</td>
</tr>
<tr>
<td>Experimental: IMAB362 + ZA + IL-2 (3 million IU)</td>
<td>Drug: IMAB362 800 mg/m2 on d 1 of cycle 1. 600 mg/m2 on d 1 of every other cycle Drug: Zoledronic acid 4 mg on d 1 of cycle 1 and cycle 3 Drug: Interleukin-2 (3 million IU) 3 million IU on day 1, 2 and 3 of cycles 1 and 3.</td>
</tr>
<tr>
<td>Active Comparator: IMAB362</td>
<td>Drug: IMAB362 800 mg/m2 on d 1 of cycle 1. 600 mg/m2 on d 1 of every other cycle</td>
</tr>
</tbody>
</table>

**Eligibility**

Ages Eligible for Study: 18 Years and older

Genders Eligible for Study: Both

Accepts Healthy Volunteers: No

**Criteria**

Inclusion Criteria:

- Histologically confirmed adenocarcinoma of the stomach, the esophagus or the gastroesophageal junction
- Inoperable locally advanced disease, resections with R0, R1 or R2 outcome or metastatic disease.
- CLDN18.2 expression confirmed by immunohistochemistry in paraffin embedded tumor tissue sample.
- Measurable and/or non-measurable disease as defined according to RECIST v1.1
- Age ≥ 18 years
- Written informed consent
- ECOG performance status (PS) 0-1
- Life expectancy > 3 months

http://clinicaltrials.gov/ct2/show/NCT01671774?term=gm+imab+001...
Exclusion Criteria:

- Prior hypersensitivity reaction or intolerance to one of the compounds of the study treatment
- Known HIV infection or known symptomatic hepatitis (A, B, C)
- Clinical symptoms of cerebral metastases
- Pregnancy or breastfeeding
- Patients treated with any bisphosphonate-based therapeutic for any indication during the previous year
- Hypocalcemia that requires medication. Corrected (adjusted for serum albumin) serum calcium < 8 mg/dl (2 mmol/L) or > 12 mg/dL (3.0 mmol/L)

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01671774

Locations

Germany

Institut für Klinische Forschung, Krankenhaus Nordwest GmbH
Frankfurt, Hessen, Germany, 60488
Contact: Salah-Eddin Al-Batran, PD Dr. med. +49 69 7601 4420 albatran@khnw.de
Principal Investigator: Salah-Eddin Al-Batran, PD Dr. med.

Onkologische Schwerpunktpraxis Bielefeld
Bielefeld, Nordrhein-Westfalen, Germany, 33604
Contact: Marianne Just, Dr. med. +49 521 988 777 19 studien@onkologie-bielefeld.de
Principal Investigator: Marianne Just, Dr. med.

Universitätsklinikum Halle/Saale; Poliklinik für innere Medizin IV
Halle/Saale, Sachsen-Anhalt, Germany, 06120
Contact: Jörn Rüssel, Dr. med. +49 345 557 7224 joern.ruessel@medizin.uni-halle.de
Principal Investigator: Jörn Rüssel, Dr. med.

BAG / Onkologische Schwerpunktpraxis
Dresden, Sachsen, Germany, 01307
Contact: Jens Freiberg-Richter, Dr. med. +49 351 4400022 freiberg-richter@onkologie-dresden.net
Principal Investigator: Jens Freiberg-Richter, Dr. med.

Charité Universitätsmedizin Berlin - CVK, Med. Klinik m.S. Hämatologie und Onkologie
Berlin, Germany, 13353
Contact: Peter Thuss-Patience, Dr. med. +49 30 450 553 699 magenkarzinom@charite.de
Principal Investigator: Peter Thuss-Patience, Dr. med.

Sponsors and Collaborators
Ganymed Pharmaceuticals AG

More Information

No publications provided

ClinicalTrials.gov Identifier: NCT01671774
Other Study ID Numbers: GM-IMAB-001-04, 2011-005509-64
Study First Received: August 21, 2012
Last Updated: August 21, 2012
Health Authority: Germany: Paul-Ehrlich-Institut

Additional relevant MeSH terms:

- Adenocarcinoma
- Stomach Neoplasms
- Carcinoma
- Neoplasms, Glandular and Epithelial
- Neoplasms by Histologic Type
- Neoplasms
- Gastrointestinal Neoplasms
- Digestive System Neoplasms
- Neoplasms by Site
- Digestive System Diseases
- Gastrointestinal Diseases
- Stomach Diseases
- Interleukin-2
- Zoledronic acid
- Diphosphonates
- Antineoplastic Agents
- Therapeutic Uses
- Pharmacologic Actions
- Analgesics, Non-Narcotic
- Analgesics
- Sensory System Agents
- Peripheral Nervous System Agents
- Physiological Effects of Drugs
- Central Nervous System Agents
- Bone Density Conservation Agents

ClinicalTrials.gov processed this record on November 06, 2012