Purpose

The purpose of this study is to determine the safety profile and maximum tolerable dose (MTD) of GBR 1302 monotherapy in subjects with HER2 positive cancers.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 Expressing Solid Tumours</td>
<td>Drug: CD3/HER2 bispecific monoclonal antibody</td>
<td>Phase 1</td>
</tr>
</tbody>
</table>

Study Type: Interventional
Study Design: Endpoint Classification: Safety Study
Primary Purpose: Treatment

Further study details as provided by Glenmark Pharmaceuticals S.A.:

Primary Outcome Measures:
- Maximal Tolerated Dose (MTD) of GBR 1302 [Time Frame: 28 Days] [Designated as safety issue: Yes]
- Number of DLTs (dose limiting toxicities) after the first two administrations of study drug (i.e. Cycle 1) in each cohort
- The relationship of the dose of GBR 1302 with the incidence, nature, and intensity of AEs according to CTCAEv4.03 [Time Frame: 28 Days] [Designated as safety issue: Yes]

Secondary Outcome Measures:
- Objective Response Rate (ORR) for solid tumors [Time Frame: 28 Days] [Designated as safety issue: No]
- Disease control rate (DCR) for solid tumors [Time Frame: 28 Days] [Designated as safety issue: No]
- Duration of disease control (measured from drug start date to the date of disease progression or death for subjects who had CR or PR or SD during treatment). [Time Frame: 28 Days] [Designated as safety issue: No]
- Maximum Concentration (Cmax) of GBR 1302 [Time Frame: 28 Days] [Designated as safety issue: Yes]
- Time to Maximum Concentration (Tmax) of GBR 1302 [Time Frame: 28 Days] [Designated as safety issue: Yes]
- Area Under Curve [AUC0-t and AUC0-tau] of GBR 1302 [Time Frame: 28 Days] [Designated as safety issue: Yes]
- Immunogenicity of GBR 1302 in terms of ADA formation assessed compared to baseline [Time Frame: 28 Days] [Designated as safety issue: Yes]

Estimated Enrollment: 30
Study Start Date: May 2016
Estimated Primary Completion Date: November 2018 (Final data collection date for primary outcome measure)

### Arms

<table>
<thead>
<tr>
<th>Experimental: GBR 1302</th>
<th>Assigned Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drug: CD3/HER2 bispecific monoclonal antibody</td>
</tr>
</tbody>
</table>
Dose escalation
Increasing doses, IV on day 1 and 15 of each 28 day cycle

Eligibility

Ages Eligible for Study: 18 Years and older (Adult, Senior)
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
1. Progressive HER2 positive solid tumours (immunohistochemistry [IHC] positive or equivocal) with no available standard or curative treatment.
2. Eastern Cooperative Oncology Group (ECOG) performance score of 0-2.
3. Subjects who will enter Cohort 1 or 2 need a pre-existing, functioning, central venous access in place for the administration of the study drug.

Exclusion Criteria:
1. Active infectious disease considered by the Investigator to be incompatible with the protocol.
2. Patients not recovered from any therapy-related toxicities from previous therapies to at least CTCAE ≤ Grade 1 except in case of liver metastases or Gilbert's Syndrome or alopecia.
3. Brain metastases that are symptomatic or untreated or that require current therapy.
4. Previous treatment with immunotherapy within 8 weeks of starting study medication, chemotherapy, radiotherapy, molecular-targeted therapy, or biological therapies (including HER2 directed therapies) within 4 weeks of starting study medication, or hormone therapy within 2 weeks of starting study medication.
5. Use of any investigational drug within the past 4 weeks before start of study medication or concomitantly with this study except for investigational immune-stimulatory therapy (e.g. checkpoint-regulator targeted treatment). The minimum washout period should be 8 weeks before starting the study medication.
6. Any history or evidence of clinically significant cardiovascular disease defined as at least one of following criteria:
   1. Baseline Left Ventricular Ejection Fraction (LVEF) < 50% or major wall dyskinesias via echocardiography (ECHO).
   2. History or evidence of poorly controlled arterial hypertension (systolic blood pressure > 180 mmHg or diastolic blood pressure >100 mmHg).
   3. Cardiac arrhythmias requiring anti-arrhythmic therapy, except for betablockers, calcium antagonists and digoxin.
   4. Clinically significant valvular heart disease.
   5. Myocardial infarction or instable angina pectoris within the previous 6 months.
   6. Documented history of congestive heart failure (CHF) of any New York Heart Association (NYHA) criteria.
   7. History of exposure to the cumulative doses of anthracyclines as follows: prior anthracycline cumulative exposure > 360 mg/m2 of doxorubicin or its equivalent.
7. Known allergy to any of the ingredients in the formulation or known allergy to any related class of compounds.

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: NCT02829372

Contacts

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Sponsors and Collaborators

Phase 1 Study of Single Agent GBR 1302 in Subjects With HER2 Positive Cancers ...

Glenmark Pharmaceuticals S.A.

Investigators
Study Director: Eliel Bayever, MBBCh, MRCP  Glenmark Pharmaceutical S.A

More Information

Responsible Party: Glenmark Pharmaceuticals S.A.
ClinicalTrials.gov Identifier: NCT02829372  History of Changes
Other Study ID Numbers: GBR 1302-101  2015-002926-38
Study First Received: July 1, 2016
Last Updated: July 7, 2016
Health Authority: Germany: Paul-Ehrlich-Institut

Additional relevant MeSH terms:
Antibodies
Antibodies, Monoclonal
Antibodies, Bispecific
Immunologic Factors
Physiological Effects of Drugs

ClinicalTrials.gov processed this record on August 03, 2016

https://clinicaltrials.gov/ct2/show/NCT02829372?term=NCT02829372&rank=1
04.08.2016