A PHASE Ia/b, OPEN-LABEL, DOSE-ESCALATION STUDY OF THE SAFETY AND PHARMACOKINETICS OF RUNIMOTAMAB ADMINISTERED INTRAVENOUSLY AS A SINGLE AGENT AND IN COMBINATION WITH TRASTUZUAMB IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC HER2-EXPRESSING CANCERS

Published: 10-03-2021
Last updated: 07-09-2024

This study has been transitioned to CTIS with ID 2023-504491-15-00 check the CTIS register for the current data. • To evaluate the safety and tolerability of Runimotamab when administered as a single agent (Phase Ia) and in combination with...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON54065

Source
ToetsingOnline

Brief title
GO40311

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Breast cancer, cancer

Research involving
Human

Sponsors and support

Primary sponsor: Genentech Inc.
Source(s) of monetary or material Support: Genentech Inc.

Intervention

Keyword: First in human, Metastatic Cancer

Outcome measures

Primary outcome

1. Occurrence, nature, and severity of adverse events graded according to NCI

CTCAE v5.0 and the Modified Cytokine Release Syndrome Grading System

2. Changes from baseline in LVEF as assessed by ECHO/MUGA scans

3. Change from baseline in targeted vital signs

4. Change from baseline in targeted clinical laboratory test results, including

ECGs

5. Number of cycles received and dose intensity

6. Occurrence and nature of DLTs

Secondary outcome

1. Area Under the Serum Concentration vs. Time Curve (AUC) of Runimotamab

2. Maximum Observed Serum Concentration (Cmax) of Runimotamab

3. Minimum Observed Serum Concentration (Cmin) of Runimotamab

4. Clearance (CL)

5. Volume of Distribution at Steady State (Vss) of Runimotamab

6. Objective response

7. Duration of response

8. Presence of anti-drug antibodies (ADAs) during the study relative to the

presence of ADAs at baseline

Study description

Background summary

Locally advanced and metastatic HER2-positive breast and gastric cancers largely remain incurable diseases, with most patients progressing after receiving HER2-targeted therapies. T cell-recruiting bispecific agents represent an alternative mechanism to induce T cell-mediated killing of HER2-expressing cancer cells. While there are limited clinical data with these agents in HER2-expressing cancers to date, these agents have shown evidence of clinical activity in hematologic malignancies, as exemplified by clinical activity observed with the CD19-directed bispecific molecule blinatumomab in both B-cell acute lymphoblastic leukemia (ALL; Blincyto USPI) and non-Hodgkin lymphoma (NHL; Topp et al. 2015; Viardot et al. 2016).

Although the rationale for molecular-targeted therapies is well established, the use of anti-HER2 therapies, outside of BC and gastric/GEJ cancer, has been limited. HER2 overexpression and gene amplification has been described in several different tumor types, including NSCLC, pancreatic cancer, colorectal cancer, bladder cancer, salivary duct carcinoma, epithelial ovarian cancer, and endometrial cancer (Omar et al. 2015; Yan et al. 2015). Currently there are several ongoing studies investigating HER2-targeted therapies in a broad range of tumor types (Parakh et al. 2017).
Runimotamab*s novel mechanism of action has the potential to provide clinical benefit and another therapeutic option for patients with HER2-positive solid tumors.

Study objective

This study has been transitioned to CTIS with ID 2023-504491-15-00 check the CTIS register for the current data.

• To evaluate the safety and tolerability of Runimotamab when administered as a single agent (Phase Ia) and in combination with trastuzumab (Phase Ib)
• To determine the maximum tolerated dose (MTD), to identify the recommended phase II dose (RP2D), and to characterize the dose-limiting toxicities (DLTs)

associated with Runimotamab as a single agent (Phase Ia) and in combination with trastuzumab (Phase Ib)

Study design

This Phase Ia/b, open-label, multicenter, dose-escalation study designed to evaluate the safety, tolerability, and pharmacokinetics of Runimotamab, to make a preliminary assessment of antitumor activity of Runimotamab, administered as a single agent and in combination with trastuzumab, and to identify recommended Phase II doses (RP2D) for Runimotamab as a single agent and in combination with trastuzumab in patients with locally advanced or metastatic HER2-expressing cancers for which standard therapy does not exist, has proven to be ineffective or intolerable, or is considered inappropriate.

Patients will be enrolled in two stages: a dose-escalation stage (Phase Ia/b) and a dose-expansion stage. The safety, pharmacokinetics, pharmacodynamics, and preliminary anti-tumor activity data in the Phase Ia and Ib dose escalation stages will be evaluated, in order to select the dose(s) and schedule(s) for the planned expansion stages (Runimotamab as a single agent and/or in combination with trastuzumab). Approximately 213-521 patients may be enrolled in this global study, at approximately 35 investigative sites.

Intervention

- Intravenous infusion of Runimotamab
- Intravenous infusion of trastuzumab (in phase 1b only)
- Intravenous infusion of tocilizumab (in patients experiencing Cytokine release syndrome as a side-effect)

Study burden and risks

This is a phase 1 first in human study of Runimotamab as a single agent and in combination with Trastuzumab for people with HER2 positive breast cancer and gastro-esophageal junction cancer. Approximately 231-521 participants are enrolled in either a dose-escalation or dose-expansion stage to assess the safety, tolerability and preliminary efficacy of the study drug. Patients will undergo tumor assessments, physical examinations, pregnancy tests, blood draws for laboratory analysis, liver function tests, scans and biopsies (both mandatory and optional).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

General inclusion criteria:
* ECOG Performance Status of 0 or 1
* Life expectancy of at least 12 weeks
* Adequate hematologic and end-organ function
* LVEF equal to or over 50% by either ECHO or MUGA scan
* All acute, clinically significant treatment-related toxicity from prior therapy, except for alopecia and G2 anemia (Hb 9.0 g/dL), must have resolved to grade equal to or under 1 prior to study entry

HER2-Positive Breast Cancer-Specific Inclusion Criteria:
* Locally tested, HER2 BC
* Locally advanced or metastatic BC that has relapsed or is refractory to established therapies

HER2-Positive gastric/gej cancer-specific inclusion criteria:
* Histologically or cytologically documented adenocarcinoma of the stomach or GEJ with inoperable locally advanced or recurrent and/or metastatic disease, not amenable to curative therapy.
* HER2 tumor (primary tumor or metastasis) as assessed by local (non-central)

laboratory testing
* Must have received prior trastuzumab, cisplatin (or carboplatin or oxaliplatin or investigational platinum agent) and 5-FU/capecitabine

For more specific inclusion criteria, please refer to p.104-106 of the protocol

Exclusion criteria

Patients who meet any of the following criteria will be excluded from study entry. Unless specified, all exclusion criteria listed apply to both the Phase Ia and Ib:

* Pregnant or breastfeeding, or intending to become pregnant during the study or within 140 days after the last dose of Runimotamab or tocilizumab, and within 7 months after the last dose of trastuzumab (for the Phase Ib).
* Significant cardiopulmonary dysfunction
* Known clinically significant liver disease
* Positive serologic or PCR test results for acute or chronic HBV infection
* Acute or chronic HCV infection
* HIV seropositivity
* Poorly controlled Type 2 diabetes mellitus
* History of ventricular dysrhythmias or risk factors for ventricular dysrhythmias
* Current treatment with medications that are well known to prolong the QT interval
* Primary CNS malignancy, untreated CNS metastases, or active CNS metastases (progressing or requiring corticosteroids for symptomatic control)
* Leptomeningeal disease
* Spinal cord compression that has not definitively treated with surgery and/or radiation
* History of autoimmune disease
* Prior allogeneic stem cell or solid organ transplantation

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-04-2022
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Herceptin
Generic name:	Trastuzumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	RoActemra
Generic name:	Tocilizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	RUNIMOTAMAB
Generic name:	RUNIMOTAMAB

Ethics review

Approved WMO Date:	10-03-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-08-2021
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	02-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EU-CTR	CTIS2023-504491-15-00
EudraCT	EUCTR2019-004596-39-NL
ClinicalTrials.gov	NCT03448042
CCMO	NL76482.056.21