A phase I, first time in human, open-label, dose escalation study to investigate the safety, pharmacokinetics, and pharmacodynamics of anti-HER3 monoclonal antibody GSK2849330 in subjects with advanced HER3-positive solid tumors

Published: 12-02-2015
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Primary: To evaluate the safety of GSK2849330 in a larger population of subjects in molecularly-defined tumor histology groups at the dose regimen(s) recommended for further exploration in Part 1. Secondary: Clinical benefit, pharmacodynamics,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON44080

Source
ToetsingOnline

Brief title
HER117158

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym

1 - A phase I, first time in human, open-label, dose escalation study to investigate ... 26-05-2025

gastric/gastroesophageal cancer, head and neck cancer, or NSCLC, stage III-IV melanoma

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline BV.

Intervention

Keyword: cancer, GSK2849330, phase I, phase IIa

Outcome measures

Primary outcome

Adverse events.

Secondary outcome

Drug plasma concentration, antibodies against GSK2849330, response evaluation

(RESIST 1.1).

Study description

Background summary

The HER family of receptor tyrosine kinases is comprised of HER1 (EGFR), HER2 (ErbB2), HER3 (ErbB3) and HER4 (ErbB4). HER3 is capable of potent signaling through the PI3K pathway leading to proliferation.
Monoclonal antibodies offer an ideal means of blocking both ligand dependent and independent signaling as well as targeting cells over-expressing HER3 for destruction. To this end GSK2849330, a monoclonal antibody specific to HER3, is being developed. This first in human study is designed to assess the safety, tolerability and pharmacokinetics of GSK2849330 as well as looking for preliminary evidence of target engagement in subjects with advanced HER3 positive tumors. An understanding of the distribution of GSK2849330 into tumor tissue and its interaction with HER3 would help to determine an optimal dose level to be taken forward for further clinical development.
Part 1 is the phase I dose-escalation part of the study, which has been performed outside the Netherlands. The Netherlands will participate in Part 2, the phase II part to assess safety and preliminary clinical benefit of the

dose(s) of GSK2849330, selected for phase II based on phase I data.
This ABR form provides information about Part 2 of the study only.

Study objective

Primary: To evaluate the safety of GSK2849330 in a larger population of subjects in molecularly-defined tumor histology groups at the dose regimen(s) recommended for further exploration in Part 1.
Secondary: Clinical benefit, pharmacodynamics, pharmacokinetics, immunogenicity.

Study design

Open-label, non-comparative phase 2 study with 4 groups with different, defined tumor histologies (see protocol page 21). 12-30 subjects per group.
Prescreening of tumor tissue (archival or fresh) for HER3 or HER3 and NRG1.
Treatment until unacceptable side effects or disease progression.
GSK2849330 will be given by IV infusion over 1 hour.

Intervention

Treatment with GSK2849330.

Study burden and risks

Risk: adverse events of study treatment.
Burden: prescreening, screening, 5 visits during 1st treatment month, thereafter every 1-2 weeks (initially infusions every week; later on option to change to every 2 weeks).
Physical examination every 4 weeks.
Blood tests 15-50 mL every visit.
Pregnancy test every 4 weeks.
Scan(s) every 8 weeks.
ECG every 4 weeks.
Optional pharmacogenetic testing (6 mL blood)
2-3 tumor biopsies [screening, treatment day 15 and (optional) at disease progression].

Contacts

Public
GlaxoSmithKline

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NL
Scientific
GlaxoSmithKline

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Written informed consent obtained.
• Males and females >=18 years of age.
• ECOG status 0 or 1.
• Sufficient archival tumor specimen is available for HER3 (± NRG1) analysis or willingness to provide fresh tumor sample.
• Previously treated, unresectable stage III-IV melanoma, gastric/gastroesophageal cancer, head and neck cancer, or non small cell lung cancer, who are HER3 positive or (HN cancer or NSCLC) HER3 and NRG1 positive, see protocol page 23-25 for details.
• Adequate contraception for females of childbearing potential (see protocol page 22-23 for details).
• Men with a female partner of childbearing potential must agree to use effective contraception (see protocol page 23 for details).

Exclusion criteria

• Untreated brain or meningeal metastases or spinal cord compression (see protocol page 25 for details).
• Prior HER3- directed treatment.

• Use of a prohibited medication (see protocol section 10.2).
• Evidence of significant cardiovascular risk (see protocol page 26 for details).
• Pregnancy or lactation.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-06-2015
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GSK2849330
Generic name:	GSK2849330

Ethics review

Approved WMO Date:	12-02-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-03-2015

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-05-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-07-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-07-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-07-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-10-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-02-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-03-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-03-2016

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-03-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-04-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2013-001699-39-NL
Other	gsk-clinicalstudyregister.com; registratienummer 117158
CCMO	NL51818.042.15