An open label positron emission tomography (PET) imaging study using 89Zirconium to investigate the biodistribution of anti-HER3 monoclonal antibody (mAb) GSK2849330 and characterize its dose receptor occupancy relationship in subjects with advanced HER3-positive solid tumors

Published: 11-12-2014
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To measure in vivo biodistribution of 89Zirconium labeled GSK2849330 and characterize its dose receptor occupancy relationship in subjects with advanced HER3 positive solid malignancies.

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

Summary

ID

NL-OMON44283

Source
ToetsingOnline

Brief title
study 200980

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
tumors; advanced solid tumors

Research involving
Human

Sponsors and support

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

Intervention

Keyword: biodistribution, GSK2849330, HER3, PET

Outcome measures

Primary outcome

• Quantitative parameters derived from PET-CT images to assess uptake in tumor

tissue and normal tissues.

• SUV (peak, mean) for each region of interest and Volume of region of interest

Secondary outcome

• PET-CT images showing anatomical localization of radiolabel

• Blood radioactivity concentration

• PK parameters

• Organ dose and total effective dose

• Adverse events

• Antibodies to GSK2849330 in serum

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. A FTIH study is being undertaken 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.
PET scanning is both quantitative and capable of assessing sites throughout the body. Labeling antibodies with the radionuclide 89Zr allows them to be tracked by PET scanning. The half-life of 89Zr is 3.3 days. The information from the PET scanning will help to select a suitable dose to take forward for further development of GSK2849330.

Study objective

To measure in vivo biodistribution of 89Zirconium labeled GSK2849330 and characterize its dose receptor occupancy relationship in subjects with advanced HER3 positive solid malignancies.

Study design

Open label imaging study. Subjects will be screened for HER3 status. Only HER3 positive patients will be eligible.
Part 1: primarily in vivo biodistribution (3 weeks; 89 Zirconium labeling of GSK2849330 to enable PET-CT scanning); Part 2: primarily to assess safety (infusions with GSK2849330 every 1, 2 or 3 weeks). Treatment until disease progression or severe toxicity (which ever comes first).
15 subjects.
Study in NL only.

Intervention

Two doses 89Zr labeled GSK2849330 and unlabelled GSK2849330.

Study burden and risks

Risk: adverse events of study treatment.
Burden:
Visits: prescreening (0-1), screening (1), part 1 (4, 2-13 h), part 2 every 1, 2 of 3 weeks (until progression, 2-6 h), final visits (2, 1-5 h).
Infusions:
Labeled (2, during part 1), not labeled (0-2 during part 1, every 1, 2 or 3

weeks during part 2).
Tests:
Possibly tumor biopsy during prescreening (in case no/not enough archived tumor material present).
Physical examination screening, every 3-4 weeks during part 2.
Blood tests during every visit (approx. 2-50 ml per visit).
ECG screening, part 1 2 visits, part 2 every 3-4 weeks.
Echocardiogram/MUGA-scan screening, part 2 every 8-10 weeks.
PET-CT scan max. 5 during part 1.
Scan for tumor measurements screening, 1 during part 1 and every 8-12 weeks during part 2.
Optional: extra PET-scan during part 1.

The subject may be asked for permission that one or some employees from or on behalf of the sponsor may attend some tests and procedures for monitoring purposes. The subject is free to consent or to refuse.

Regimen for scans with 89 zirconium:
In principle the best measures during the first week after administration are keeping at a distance and having physical contact as briefly as possible.
- Children under the age of 10 years should be kept at a distance as much as possible and hugging (physical contact) should be limited to 3 times 30 minutes per day *).
- Pregnant women should stay at a distance (> 1 meter).
- With regard to sleeping with the partner: keep as much distance as possible.
- Practice adequate hygiene: e.g. males should urinate when being seated, wash your hands etc.
*) At 50 MBq: max 4 times 30 minutes, at 37 MBq max 5 times 30 minutes.

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

• Males and females, 18 years and above.
• Tumors with HER3 expression.
• No standard therapeutic alternatives.
• ECOG Performance Status 0-1.
• Measurable disease suitable for PET imaging.
• Females of childbearing potential: adequate method of contraception during study.
• Men must use adequate contraception during study.

Exclusion criteria

• Active central nervous system metastases.
• Prior HER3- directed treatment.
• Recent anti-cancer therapy or major surgery.
• Allergic reaction to previous biological therapy.
• Prohibited medications during study including immunesuppressants.
• Significant CV risk, see protocol page 42 for details.
• Pregnancy or breastfeeding

Study design

Design

Study type: Interventional
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-03-2015
Enrollment:	15
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	11-12-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-03-2016

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
Other	Clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2013-004546-42-NL
CCMO	NL49326.029.14