An open-label, single-arm study to determine the excretion balance and metabolic disposition of [14C]GW642444 administered as a single dose of an oral solution to healthy male volunteers

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Primary:To compare total radioactivity (drug-related material) in plasma relative to parent plasma GW642444 concentration following a single oral dose (200µg) of [14C]-GW642444 in healthy male subjects.To determine the rate and extent of excretion...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON34294

Source
ToetsingOnline

Brief title
[14C]-GW642444 ADME study

Condition

- Respiratory tract infections

Synonym
Asthma, COPD

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Asthma, COPD, GW642444

Outcome measures

Primary outcome

Pharmacokinetics

Safety

Secondary outcome

n.a.

Study description

Background summary

The drug to be given GW642444 is a new, investigational compound that may eventually be used in the treatment of asthma and Chronic Obstructive Pulmonary Disease (COPD).

In asthma and COPD, difficulty in breathing results from one or more different processes including spasm of the bronchial tubes, swelling of the bronchial tubes, mucus that is difficult to clear from the bronchial tubes, and thickening of the bronchial wall.
The compound GW642444 is expected to be a long acting bronchodilator and as such will make it easier to breath for people suffering from asthma and COPD. Currently available medications require twice-daily administration. GW642444 should have the advantage of requiring only once-daily administration in the treatment of asthma and COPD. This new compound is not registered as a drug but has been given to humans before.

Study objective

Primary:
To compare total radioactivity (drug-related material) in plasma relative to

parent plasma GW642444 concentration following a single oral dose (200µg) of [14C]-GW642444 in healthy male subjects.
To determine the rate and extent of excretion of total radioactivity in urine and faeces and the total recovery of radioactivity, after a single oral dose (200µg) of [14C]-GW642444 to healthy male subjects.

Secondary:
To generate samples with which to characterise and quantify the metabolic profile of GW642444 in plasma, urine, duodenal bile and faeces following administration of a single oral dose (200µg) of [14C]GW642444 to healthy male subjects. These investigations will be conducted as a separate study.
To generate samples with which to provide a relative estimate of GW642444 metabolites in human bile, following administration of a single oral dose (200µg) of [14C]GW642444 to healthy male subjects. These investigations will be conducted as a separate study.
To evaluate the safety and tolerability of a single oral dose (200µg) of [14C]-GW642444 in healthy male subjects.

Study design

Design:
An open-label ADME study in six healthy male subjects receiving a single oral dose of GW642444 containing 2 *Ci (0.074 MBq) of [14C]-GW642444.

Procedures and assessments
Screening and follow-up:
Clinical laboratory, vital signs, physical examination, 12-lead ECG; at eligibility screening: medical history, 12-hour Holter, alcohol urine test, drug screen, HBsAg, anti HCV, anti-HIV 1/2; brief physical examination, alcohol urine test, drug screen and clinical laboratory to be repeated upon admission.

Observation period:
One period in clinic from -17 h up to 168 h (Day 8) after drug administration with possible extension to Day 11 if discharge criteria (less than 1% of total dose excreted in urine and faeces combined for 2 consecutive 24 h periods) are not met. If discharge criteria are still not met on Day 11, collection of urine and or faeces at home until Day 14 will be requested.

Blood sampling:
For pharmacokinetics of GW642444 and total radioactivity: once at screening and on Day -1 and pre-dose and 0.25, 0.5, 0.75, 1, 1.25, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 12, 24, 48, 72, 96, 120, 144 and 168 h post-dose. For metabolite profiling: pre-dose and 0.5, 1.5, 3 and 24 h post-dose.
For genotyping: once on Day -1.

Urine sampling:
For pharmacokinetics: pre-dose and 24 h intervals until discharge (one aliquot

of each urine collection will be taken for metabolite profiling).

Faeces sampling:
For pharmacokinetics: pre-dose and 24 h intervals until discharge (one aliquot of each faeces collection will be taken for metabolite profiling).

Entero test (bile sampling):
For bile sampling: from 2 h post dose until 6.5 h post dose.

Safety assessments:
Adverse events: throughout the study; vital signs and 12-lead ECG: pre-dose (in triplicate) and 0.5, 1, 2, 6 and 12 h post-dose.

Bioanalysis:
Analysis of plasma GW642444 samples using validated methods by Sponsor, analysis of total radioactivity in urine and faeces using validated methods by PRA, analysis of total radioactivity in plasma by Sponsor, quick counts by PRA, metabolite profiling by Sponsor,
genotyping by Sponsor.

Intervention

Active substance: GW642444 and [14C]-GW642444

Study burden and risks

Procedures:
Pain, light bleeding, haematoma, possible an infection.

Contacts

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Scientific
GlaxoSmithKline

New Frontiers Science Park South
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United Kingdom

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.Healthy male aged between 30 and 55 years inclusive, at the time of signing the informed consent.
2.Body Mass Index (BMI) within the range 18.5-29.0 kg/m2.
3.Subjects who are current non-smokers, who have not used any tobacco products in the 12 month period preceding the screening visit, and have a pack history of * 5 pack years.

Exclusion criteria

1.Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study.

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):	18-05-2010
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO Date:	29-04-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-05-2010
Application type:	First submission
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
EudraCT	EUCTR2009-017948-14-NL
CCMO	NL32313.056.10