A randomized, double-blind, placebo-controlled first time into human study to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of intranasal dosing with GSK2245035, a TLR7 agonist, in healthy volunteers and allergic rhinitics

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Part 1Primary:- to evaluate the safety and nasal tolerability of single escalating i.n. GSK2245035 doses in HVSecondary:- to evaluate the systemic PK of single i.n. GSK2245035 administration in HV- to evaluate the induction of TLR7-associated PD...

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

Summary

ID

NL-OMON36044

Source
ToetsingOnline

Brief title
GSK2245035 SAD study in HV and rhinitis patients

Condition

- Respiratory tract infections

Synonym
Allergic reaction; hay fever

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: GlaxoSmithKline Research & Development Limited Brentford Middlesex UK

Intervention

Keyword: Allergic rhinitis, GSK2245035, Healthy subjects

Outcome measures

Primary outcome

Safety: adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination

Pharmacodynamics

Pharmacokinetics

Secondary outcome

Not applicable

Study description

Background summary

The drug to be given, GSK2245035, is a new, investigational compound that may eventually be used for the treatment of allergic rhinitis (for example with hay fever) and potentially other allergic disorders, such as asthma. Of GSK2245035 is expected that, when administered in the nose, it alters the immune environment of the airways in a way that results in long-lasting control of allergic rhinitis symptoms. The study medication will be administered as a nasal spray and will cause a local inflammatory reaction in the nose. This new compound is not registered as a drug. This is the first time that this compound is being given to humans.

Study objective

Part 1
Primary:
- to evaluate the safety and nasal tolerability of single escalating i.n. GSK2245035 doses in HV
Secondary:
- to evaluate the systemic PK of single i.n. GSK2245035 administration in HV
- to evaluate the induction of TLR7-associated PD blood biomarkers following single i.n. GSK2245035 administration in HV
- to evaluate the induction of TLR7-associated PD biomarkers in nasal lavage
- to evaluate the correlation between i.n. GSK2245035 dose - systemic PK - PD blood biomarkers * PD nasal biomarkers in HV

Part 2
Primary:
- to evaluate the safety and nasal tolerability of single escalating i.n. GSK2245035 doses in individuals with AR
- to evaluate the induction of TLR7-associated PD biomarkers i) in nasal lavage, and ii) in nasal tissues following single i.n. GSK2245035 administration versus placebo in individuals with AR

Secondary:
- to evaluate the systemic PK of single i.n. GSK2245035 administration in individuals with AR
- to evaluate the induction of TLR7-associated blood PD biomarkers following single i.n. GSK2245035 administration in individuals with AR
- to evaluate the correlation between i.n. GSK2245035 dose - systemic PK - PD blood biomarkers - PD nasal biomarkers in individuals with AR

Study design

Part 1:
a randomized, double-blind, placebo-controlled, parallel group, single-ascending dose study in one cohort of five healthy male subjects and seven cohorts of seven healthy male subjects each receiving a single intranasal dose of GSK2245035 or placebo (three active and two placebo on Cohort 1 and five active and two placebo in Cohorts 2-8); each cohort will be staggered over three days; two subjects (one active and one placebo) will be dosed and monitored for 24 h on day 1, two subjects (active or placebo) will be dosed and monitored for 24 h on day 2 and the remaining subjects will be dosed on day 3 (active or placebo)

Part 2:
a randomized, double-blind, parallel group study with three cohorts of seven allergic rhinitis (AR) patients each receiving a single intranasal dose of GSK2245035 or placebo (five active and two placebo)

Intervention

Study Medication
Active substance: GSK2245035
Activity: TLR7 agonist
Indication: allergic rhinitis
Strength: 0.01, 0.1, 1, 10 and 100 *g/mL
Dosage form: nasal spray solution

Treatments
Part 1
Cohort 1: a single intranasal dose of 2 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 2: a single intranasal dose of 20 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 3: a single intranasal dose of 100 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 4: a single intranasal dose of 200 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 5: a single intranasal dose of 400 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 6: a single intranasal dose of 1000 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 7: a single intranasal dose of 2000 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 8: a single intranasal dose of 4000 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)

Part 2
Cohort 9: a single intranasal dose of 20 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 10: a single intranasal dose of 200 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)
Cohort 11: a single intranasal dose of 4000 ng GSK2245035 or placebo on Day 1 (split into the two nostrils)

Study burden and risks

Not applicable

Contacts

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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

Part 1:
healthy male volunteers
18 - 55 years of age
BMI 19 - 29.9 kg/m2;Part 2:
male volunteers with a pollen allergy
18 - 55 years of age
BMI 19 - 29.9 kg/m2
positive RAST test for pollen allergy

Exclusion criteria

- Suffering from: hepatitis B, cancer or HIV/AIDS
- Participation in another drug study within 3 months prior to dosing in this study
- Blood donation within 3 months prior to dosing in this study of donated more than 1.5 liters of blood in the 10 months prior to dosing in this study

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-06-2011
Enrollment:	75
Type:	Actual

Ethics review

Approved WMO Date:	02-05-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-05-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-08-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	01-09-2011
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
EudraCT	EUCTR2011-023795-78-NL
CCMO	NL36605.056.11