A study to investigate the psychomotor and cognitive effects of alcohol when co-administered with GSK 1144814 or matching placebo in healthy subjects

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To investigate whether the psychomotor and cognitive effects of alcohol are exacerbated by GSK1144814 in healthy subjects.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON32631

Source
ToetsingOnline

Brief title
GSK1144814 and ethanol interaction study

Condition

- Other condition
- Schizophrenia and other psychotic disorders

Synonym
substance dependence

Health condition

Alcoholverslaving

Research involving

Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: Farrnaceutische industrie (GSK)

Intervention

Keyword: alcohol interaction, GSK1144814, neurokinin, NK1/NK3 receptor antagonist

Outcome measures

Primary outcome

Pharmacodynamic:

• Saccadic eye movements (saccadic reaction time, saccadic peak velocity and saccadic accuracy): to assess sedation.

• Smooth pursuit eye movements (percentage of time the eyes are in smooth pursuit of the target): to assess attention and eye movement coordination.

• Body sway (antero-posteral sway in mm/2min): to assess body movements in a single plane, providing a measure of postural (in)stability. During sway measurements, subjects will be instructed to keep their eyes closed for two minutes.

• Adaptive tracking (average performance %): to assess visuo-motor control and vigilance.

• Visual Verbal Learning Test (VVLT) for the assessment of cognition.

• Visual Analogue Scale (VAS) for subjective effects of alcohol.

• Epworth Sleepiness Scale to assess change in sedation

• Bond and Lader VAS for alertness, calmness and contentedness.

Secondary outcome

• Vital signs, 12-lead ECGs, clinical laboratory and AEs

Pharmacokinetics:

• Breath ethanol (EtOH) concentrations (BrAC)

• PK parameters of GSK1144814 (in the presence of blood alcohol): AUC (0-24h),

Cmax, Tmax.

Study description

Background summary

GSK1144814 is a potent, insurmountable antagonist at human neurokinin 1 (NK1) and neurokinin 3 (NK3) receptors that is under development as a novel treatment for schizophrenia, depression and substance dependence disorders.

Since GSK1144814 is being developed for use in schizophrenia, depression and substance dependence disorder (including alcohol dependence) it is important to understand the effects of GSK114814 and alcohol when taken together.

Study objective

To investigate whether the psychomotor and cognitive effects of alcohol are exacerbated by GSK1144814 in healthy subjects.

Study design

This is a single-blind, randomized, placebo-controlled, 2-period crossover, single dose study

Intervention

20 subjects will participate in 2 treatment periods, and will be administered each of the following treatments:
• Treatment A: 5- hour alcohol-clamp at a level of 0.6 g•L-1 in combination with matched GSK1144814 placebo
• Treatment B: 5- hour alcohol-clamp at a level of 0.6 g•L-1 in combination with GSK1144814 200 mg

Study burden and risks

The risks are occurence of adverse drug reactions resulting from GSK1144814 usage.
The burden for the subjects consists of: residing at the facility, venous bloodsampling, infusion needle insertion.
All subjects will be closely monitored for possible adverse drug reactions by experienced personel and doctors.

Contacts

Public
GlaxoSmithKline

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RTP, NC 27709
USA
Scientific
GlaxoSmithKline

5 Moore Drive
RTP, NC 27709
USA

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Healthy as determined by a responsible and experienced physician, based on a medical evaluation including medical history, physical examination, laboratory tests and cardiac monitoring. A subject with a clinical abnormality or laboratory parameters significantly outside the reference range for the population being studied may be included only if the

Investigator and the GSK Medical Monitor agree that the finding is unlikely to introduce additional risk factors and will not interfere with the study procedures.
2. Male or female between 18 and 65 years of age inclusive, at the time of signing the informed consent.
3. A female subject is eligible to participate if she is of:
• Non-childbearing potential defined as pre-menopausal females with a documented tubal ligation or hysterectomy; or postmenopausal defined as 12 months of spontaneous amenorrhea [in questionable cases a blood sample with simultaneous follicle stimulating hormone (FSH) > 40 MIU/ml and estradiol < 40 pg/ml (<140 pmol/L) is confirmatory].
• Females on hormone replacement therapy (HRT) and whose menopausal status is in doubt will be required to discontinue HRT to allow confirmation of post-menopausal status prior to study enrollment. For most forms of HRT, at least 2-4 weeks will elapse between the cessation of therapy and the blood draw; this interval depends on the type and dosage of HRT. Following confirmation of their post-menopausal status, they can resume use of HRT during the study without use of a contraceptive method.
4. Male subjects must agree to use one of the contraception methods listed in Section 8.1. This criterion must be followed from the time of the first dose of study medication until 3 months after the last dose.
5. Body weight > 50 kg and BMI within the range 19 - 29.9 kg/m2 (inclusive).
6. Capable of giving written informed consent, which includes compliance with the requirements and restrictions listed in the consent form.
7. Average QTcB or QTcF < 450 msec.
8. Demonstrates no evidence of mental impairment or co-morbid psychiatric disorders

Exclusion criteria

1. A positive pre-study Hepatitis B surface antigen or positive Hepatitis C antibody result within 3 months of screening.
2. Current or chronic history of liver disease, or known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones).
3. History or presence of clinically significant cardiac arrhythmias, or other clinically significant cardiac disease.
4. Subjects, who in the investigator's judgement, pose a significant suicide risk. Evidence of serious suicide risk may include any history of suicidal behaviour and/or any suicidal ideation of type 4 or 5 on the C-SSRS in the last 6 months.
5. Significant renal abnormality (from medical history or as indicated by laboratory investigations). Additionally subjects with idiopathic haematuria or proteinuria or conditions such as benign orthostatic proteinuria and benign familial haematuria should be excluded from the study)
6. Subjects with LFT >1.5 ULN
7. Subjects, who in the investigator's judgement, pose a significant homicidal risk or have ever been homicidal.
8. A positive pre-study drug/alcohol screen.
9. A positive test for HIV antibody.
10. History of regular alcohol consumption within 6 months of the study defined as:

• an average weekly intake of >21 units for males or >14 units for females. One unit is equivalent to 8 g of alcohol: a half-pint (~240 ml) of beer, 1 glass (125 ml) of wine or 1 (25 ml) measure of spirits.
11. Past history of alcohol dependence or abuse.
12. History of increased sensitivity to the effects of alcohol or violent behaviour/aggression when intoxicated.
13. Inability to adequately perform pharmacodynamic testing during the training session.
14. The subject has participated in a clinical trial and has received an investigational product within the following time period prior to the first dosing day in the current study: 30 days, 5 half-lives or twice the duration of the biological effect of the investigational product (whichever is longer).
15. Exposure to more than four new chemical entities within 12 months prior to the first dosing day.
16. Use of prescription or non-prescription drugs, including vitamins, herbal and dietary supplements (including St John*s Wort) within 7 days (or 14 days if the drug is a potential enzyme inducer) or 5 half-lives (whichever is longer) prior to the first dose of study medication, unless in the opinion of the Investigator and GSK Medical Monitor the medication will not interfere with the study procedures or compromise subject safety.
17. History of sensitivity to any of the study medications, or components thereof or a history of drug or other allergy that, in the opinion of the investigator or GSK Medical Monitor, contraindicates their participation.
18. Where participation in the study would result in donation of blood or blood products in excess of 500 mL within a 56 day period.
19. Unwillingness or inability to follow the procedures outlined in the protocol.
20. Urinary cotinine levels indicative of smoking or history or regular use of tobacco- or nicotine-containing products within 6 months prior to screening.
21. Consumption of red wine, seville oranges, grapefruit or grapefruit juice and/or Chinese grapefruit (pomelo), exotic citrus fruits, grapefruit hybrids or fruit juices from 7 days prior to the first dose of study medication.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-11-2009
Enrollment:	20
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	GSK1144814
Generic name:	GSK1144814

Ethics review

Approved WMO Date:	01-10-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	06-11-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	23-11-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2009-014587-19-NL
CCMO	NL29666.058.09