A Double Blind, Ascending Multiple Dose Study to Evaluate the Safety and Tolerability of GAL-021 in Healthy Volunteers.

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Primary objectives:1) To evaluate the safety and tolerability of multiple doses GAL-021 in healthy volunteers.2) To evaluate the pharmacokinetic profile of multiple doses of GAL-021 in healthy volunteers.3) To evaluate the pharmacodynamic effects at...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON41554

Source
ToetsingOnline

Brief title
An Ascending Multiple Dose Study of GAL-021.

Condition

- Respiratory disorders NEC

Synonym
Breathing problems, Respiratory impairment

Research involving
Human

Sponsors and support

Primary sponsor: Galleon Pharmaceuticals, Inc

Source(s) of monetary or material Support: Galleon Pharmceuticals Inc

Intervention

Keyword: Drug interaction, Pharmacodynamics, Pharmacokinetics, Respiratory stimulation

Outcome measures

Primary outcome

Safety: Safety laboratory tests (hematology, clinical chemistry, and

urinalysis), vital signs, ECG parameters, physical examinations, Subject

Sedation Scale, BP, HR, adverse events, and CSSRS.

Secondary outcome

PK: PK parameters will include but not limited to Cmax, AUCinf, and Tmax, and

if possible, t* for GAL-021 and CYP probes.

PD: Will include tidal volume (TV), respiratory rate, minute ventilation (MV),

end-tidal CO2, and transcutaneous hemoglobin saturation (SpO2). NOX-T3 EEG

and/or EMG analysis may be explored .

Study description

Background summary

This study is for GAL-021 (a BK channel antagonist) , which is being developed as an intravenous therapeutic agent for short-term use
to stimulate ventilation in patients with respiratory insufficiency. This multiple dose study would serve as first step in exploring the safety and tolerability of GAL-021 use in the inpatient surgical setting.
Repeated dosing with GAL-021 in combination with bupropion (CYP2B6) or midazolam should be sufficient to permit understanding of its potential to cause induction of CYP enzymes enabling appropriate clinical use of the drug in a poly-pharmacy environment.

Study objective

Primary objectives:
1) To evaluate the safety and tolerability of multiple doses GAL-021 in healthy volunteers.
2) To evaluate the pharmacokinetic profile of multiple doses of GAL-021 in healthy volunteers.
3) To evaluate the pharmacodynamic effects at fixed intervals of multiple doses of GAL-021 in healthy volun-teers.

Secondary objectives:
1) To evaluate the potential for GAL-021 to cause metabolic induction of a coadministered CYP2B6 substrate.
2) To evaluate the potential for GAL-021 to cause metabolic induction of a coadministered CYP3A4 substrate.

Exploratory Objective:
To explore the data collection method of monitoring sleep with a NOX-T3 polysomnographic system in a co-residence environment.

Study design

A double blind, ascending multiple dose study to evaluate the safety and tolerability of GAL-021 in healthy volunteers.

Intervention

Bupropion, midazolam and GAL-021

Study burden and risks

Bupropion dosing: the adverse events associated with this drug are insomnia, headache, dizziness, tremor, disturbance of concentration, depression, excitement, agitation, anxiety, gastro-intestinal disease (like nausea, vomiting, stomach ache, obstipation), dry mounth, disturbance of taste, fever, transpiration, acute exanthema, itch, urticaria and anorexia (symptom).

Midazolam dosing: the adverse events associated with this drug are sleepiness, muscle weakness, dizziness, confusion, fatigue, double vision, gastro-intestinal side-effects, increased appetite, skin reaction.

GAL-021 dosing: From previous studies in healthy subjects the follwing adverse events were infusion related reactions (burning sensation), headache, nasopharyngitis (common cold symptoms), nausea, and catheter site pain (pain from the site of pharmacokinetic sample collection), dizziness, vomiting, abdominal pain, hyperventilation, diarrhoea. All of the AEs were reported as mild to moderate in severity.

Sometimes people may have allergic reaction to drugs (e.g. rash, shortness of breath, sudden drop in blood pressure, fast pulse and sweating).

Venapuncture: Inserting a catheter for the administration the study drugs and for taking blood for testing may cause pain and discomfort such as bleeding, bruising, dizziness, fainting, inflammation of the vein and infection.

No benefit ofr the subjects is expected. Development of GAL-021 could constitute an additional pharmacotherapy for the treatment of respiratory insufficiency.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Subjects must be willing to give written informed consent for the trial and able to adhere to dose and visit schedules.
2. The subject is female or male >=30 to <=60 years of age.
3. Subject must weigh >=70 to <=120 kg.
4. Subjects must have Body Mass Index [weight/height^2 (kg/m^2)] between 25 to 35 kg/m2.
5. Female subjects must be:
a. Postmenopausal (defined as 12 months with no menses, with an estradiol < 30 pmol/L) and FSH concentrations compatible with being postmenopausal.
b. Surgically sterilized at least 3 months prior to baseline (e.g., documented hysterec-tomy or tubal ligation) with a negative serum β-hCG.Non-lactating and non-breastfeeding prior to and 1 year following study completion.
c. Premenopausal and if unsterilized must have used a medically accepted method of contraception for 3 months (or abstained from sexual intercourse) prior to the screening period, and agree to use a medically accepted method of contraception during the trial (including the screening period prior to receiving trial medication) and for 2 months after stopping the trial medication. An acceptable method of contraception includes one of the following:
I. stable oral, transdermal, injectable, or sustained-release vaginal hormonal contraceptive regimen without breakthrough uterine bleeding for 3 months prior to screening; in addition, during the study use of condom and/or spermacide (when marketed within the country).
II. intrauterine device (inserted at least 2 months prior to Screening visit); in addition, during study use of condom and/or spermacide (when marketed within country).
NOTE: vasectomy of the partner is not considered sufficient contraception and one of the 2 methods listed above must be used.
III. Condom (male or female) with spermacide (when marketed within the country).
IV. diaphargm or cervical cap with spermacide (when marketed within the country) and condom (male).
7. Have no clinical or electrocardiographic signs of ischemic heart disease as determined by the Investigator with normal cardiac intervals appropriate for their gender. The Screening 12 lead ECG conduction intervals must be within gender specific normal range (e.g., QTcF males <= 450 msec, PR interval <= 220 msec females QTcF <= 450 msec, PR interval <= 200 msec). ECGs are to be judged by the investigator or subinvestigator as per standardized procedures.
8. Subjects* clinical laboratory tests (CBC, blood chemistry, coagulation and urinalysis) must be within normal limits or clinically acceptable to the investigator and within an allowed expanded range supplied by sponsor (Appendix 2). However, subject*s liver function test results (e.g.., AST, ALT) must not be elevated above the normal limits at Screening and on Day -1. No rescreening of liver function tests will be allowed.
9. Vital sign measurements must be within the following ranges: (Individuals with values outside of these ranges may be enrolled if clinically acceptable to the investigator and sponsor.
a. body temperature, between 35.5°C and 37.5°C
b. systolic blood pressure, 90 to 150 mm Hg

c. diastolic blood pressure, 40 to 100 mm Hg
d. pulse rate, 50 to 100 bpm
10. Non-vasectomized men must agree to use a condom with spermicide (when marketed in the country), double-barrier contraception, or abstain from sexual intercourse, during the trial and for 3 months after stopping the medication.
11. Subjects must be free of any clinically significant disease that would interfere with the study evaluations.

Exclusion criteria

1. Current diagnosis of psychiatric disease requiring daily medication, including controlled or uncontrolled schizophrenia, current or recently treated depressive disorders, or Columbia-Suicide Severity Rating Scale (C-SSRS) indicative of suicidal ideation or behavior at screening.
2. Past history of the anxiety disorder including panic attack, depression, obsessive compulsive disorder, phobias restricting normal daily function, social anxiety, and paranoia.
3. History of alcohol abuse (more than an average of 2-drinks per day) within the past 2 years.
4. History of smoking within the past year.
5. Failure of the drug of abuse tests at screening or check-in.
6. Positive for HIV, or Hepatitis B or C at screening.
7. Blood donation or blood loss within 60 days of screening or plasma donation within 7 days of screening.
8. Subjects with a history of bleeding disorders or coagulopathies.
9. History of dyspnea, asthma, tuberculosis, chronic obstructive pulmonary disease, sleep apnea or any other ventilatory / lung disease.
10. Treatment with another investigational drug within 3 months prior to dosing or having participated in more than four investigational drug studies within 1 year prior to screening.
11. Inability to perform acceptable, quality spirometry, and FEV1 <80% of predicted for age, sex and height according to standard criteria, e.g., ATS, ECCS.
12. History of drug abuse within 3 years.
13. Subjects with excessive facial hair preventing sealing of the occlusive face mask for ventilatory monitoring.
14). Any surgical or medical condition which might significantly alter the distribution, metabolism or excretion of any drug. The investigator should be guided by evidence of any of the following, and be discussed with the sponsor prior to enrollment into the trial:
a. history of pancreatic injury or pancreatitis;
b. history or presence of liver disease or liver injury;
c. history or presence of impaired renal function as indicated by clinically significant elevation in creatinine, BUN/urea, urinary albumin, or clinically significant urinary cellular constituents ; or
d. history of urinary obstruction or difficulty in voiding.
15. Subject who has a history of any infectious disease within 4 weeks prior to drug administration that in the opinion of the investigator, affects the subject*s ability to participate in the trial.
16. Subjects who are part of the study staff personnel or family members of the study staff

personnel.
17. Subjects who have demonstrated allergic reactions (e.g., food, drug, atopic reactions or asthmatic episodes) which, in the opinion of the investigator and sponsor, interfere with their ability to participate in the trial.
18. Subjects who have a history of malignancy.
19. Personal or family history of malignant hyperthermia.
20. Personal or family history of arrhythmias or ECG conductance abnormalities.
21. Subjects with a history of daily consumption of caffeine greater than 6 servings (40 mL each) from beverages (e.g., coffee, tea, soft drinks) and food stuffs (e.g., chocolate, ice cream, cookies) (45 gm each).
22. Subjects who have used any drugs or substances known to inhibit (within 10 days) or induce (within 28 days) CYP450 enzymes prior to the first dose.
23. Subjects who have received monoamine oxidase inhibitors within 28 days of starting the study.
24. Subjects who are taking hormone replacement therapy or have known sensitivities to benzodiazepines, midazolam or bupropion.
25. Subjects who, in the opinion of the investigator, will not be able to participate optimally in the study.
26. Female subjects who are pregnant, intent to become pregnant (within 3 months of ending the study), or are breastfeeding.

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):	01-10-2013
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bupropion
Generic name:	Bupropion
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Dormicum
Generic name:	Midazolam
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	GAL-021
Generic name:	GAL-021

Ethics review

Approved WMO Date:	19-06-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-07-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-03-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-03-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	22-04-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-05-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-05-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-06-2015
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	EUCTR2013-002427-41-NL
CCMO	NL45121.056.13