

A Two-Part, Double Blinded, Placebo Controlled, Crossover Repeated Stepped Infusion Dose Study of Respiratory Pharmacodynamics of GAL- 021 and Opioids (Protocol - GAL-021-104).

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PrimaryPart 1: - To determine the respiratory response of low and high doses of GAL-021 in conjunction with a low dose of opioids and hypercapnia in healthy subjects. Part 2: - To determine the respiratory response of low and high doses of GAL-021...

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

Summary

ID

NL-OMON37240

Source

ToetsingOnline

Brief title

A two-part study of the effects of GAL-021 and opioids.

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 Pharmaceuticals Inc

Intervention

Keyword: hypercapnia., 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.
- Respiratory parameters: tidal volume (VT) minute ventilation (VE), respiratory rate (RR), end-tidal CO₂ (ETCO₂), and transcutaneous hemoglobin saturation (SpO₂).
- Cardiac parameters: Heart rate, systolic and diastolic blood pressure.
- Pain threshold values (part 2 only).
- Arterial blood gas values.

Secondary outcome

PK parameters will include but not limited to C_{max}, AUC_{inf}, and T_{max}, and if possible, t* for GAL-021 and potentially alfentanil.

Study description

Background summary

This study is for GAL-021 (a BK channel agonist) , which is being developed as an intravenous therapeutic agent for short-term use to stimulate ventilation in patients with respiratory insufficiency. This study is a proof-of concept study

to investigate if GAL-021 can reverse opioid-induced respiratory depression in healthy male subjects.

Study objective

Primary

Part 1:

- To determine the respiratory response of low and high doses of GAL-021 in conjunction with a low dose of opioids and hypercapnia in healthy subjects.

Part 2:

- To determine the respiratory response of low and high doses of GAL-021 in conjunction with a low dose of opioids in healthy subjects.

Parts 1 and 2:

- To determine the single-dose safety and tolerability of GAL-021 compared to placebo in healthy subjects after intravenous administration.
- Estimate the reproducibility of sequential treatments under hypercapnic and ambient air conditions.

Secondary

Part 1:

- To determine the respiratory response of a high dose of GAL-021 in conjunction with a high dose of opioids in healthy subjects.
- To evaluate the tolerability of GAL-021 in conjunction with a low and high dose of opioids in healthy subjects.

Parts 1 and 2:

- To determine the PK parameters of GAL-021 and opioids in healthy volunteers.

Exploratory

Part 1:

- To evaluate PK-PD relationship of the respiratory responses of GAL-021 in conjunction with a low and high dose of opioids in healthy subjects.
- To estimate the reproducibility of PD effects during repeated exposure of alfentanil in Part 1, Segment 2 and 3.
- To evaluate the effect of GAL-021 on the change in the responsiveness to CO₂ with and without opioids.

Part 2:

- To evaluate the effect of respiratory stimulants on pain intensity and threshold during a transient experimental pain model in healthy subjects

Study design

A Two-Part, Double Blinded, Placebo Controlled, Crossover Repeated Stepped Infusion Dose Study of Respiratory Pharmacodynamics of GAL- 021 and alfentanil.

Intervention

Study burden and risks

Alfentanil dosing: The adverse events associated with this drug are nausea and vomiting, slow heart rate, high blood pressure, low blood pressure, fast heart rate, muscle stiffness, respiratory depression, stopping breathing, blurred vision, dizziness, sleepiness, severe allergic reactions, headaches, involuntary muscle movements, shivering, itching, redness to skin, high levels of carbon dioxide and spasms in the bronchia and larynx.

GAL-021 dosing: From previous studies in healthy subjects the following 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).

Arterial/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.

Carbon dioxide clamp (method described in section J, additional comments): will cause hyperventilation and may cause headache and dry mouth.

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

Contacts

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US

Scientific

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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 male >18 to ≤45 years of age.
3. Subject must weigh ≥60 to ≤90 kg .
4. Subjects must have Body Mass Index [weight/height² (kg/m²)] between 18 to 30 kg/m².
5. 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 ≤ 430 msec, PR interval ≤ 220 msec). ECGs are to be judged by the investigator or subinvestigator as per standardized procedures.
6. 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 (i.e., 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.
7. Vital sign measurements must be within the following ranges: (Individuals with values outside (or indicate lower or higher) of these ranges may be enrolled if clinically acceptable to the investigator and sponsor.
 - a. body temperature, between 35.5 oC and 37.5 oC
 - b. systolic blood pressure, 90 to 150 mm Hg
 - c. diastolic blood pressure, 40 to 95 mm Hg
 - d. pulse rate, 40 to 100 bpm
8. 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.

9. Subjects must be free of any clinically significant disease that would interfere with the study evaluations.

Subjects presenting out of range values of lab/ECG/vital signs compatible with normal variation of the normal healthy subject can be included in the study at the investigator's discretion and sponsor written approval.

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 screening 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 ECCS criteria.
12. History of any abuse of or sensitivity (allergies, gastrointestinal adverse effects) to opioids.
13. History of motion sickness.
14. Subjects with excessive facial hair preventing sealing of the occlusive face mask.
15. Subjects who, in the opinion of the investigator, will not be able to participate optimally in the study.
16. 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.
17. 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.

18. Subjects who are part of the study staff personnel or family members of the study staff personnel.
19. 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.
20. Subjects who have a history of malignancy.
21. Personal or family history of malignant hyperthermia.
22. Personal or family history of arrhythmias or ECG conductance abnormalities.
23. 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).

Study design

Design

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

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	29-10-2012
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GAL-021
Generic name:	GAL-021
Product type:	Medicine
Brand name:	Rapifen

Generic name:	Alfentanil
Registration:	Yes - NL intended use

Ethics review

Approved WMO	
Date:	11-10-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	25-10-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	
Date:	19-12-2012
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	EUCTR2012-004363-50-NL

Register

CCMO

ID

NL42256.056.12