Two-part, Repeated Stepped Infusion Dose Study of the PD of GAL-021 and Opioids

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23830

Source
Nationaal Trial Register

Health condition

Respiratory impairment

Sponsors and support

Primary sponsor: Galleon Pharmaceuticals Inc. 213 Witmer Rd, Horsham, PA 19044, United States.
Source(s) of monetary or material Support: Galleon Pharmaceuticals Inc.

Intervention

Outcome measures

Primary outcome

1. Safety: Safety laboratory tests (hematology, clinical chemistry, and urinalysis), vital signs, ECG parameters, physical examinations, subject sedation scale, BP, HR, adverse events, and CSSRS;

2. Respiratory parameters: Tidal volume (VT) minute ventilation (VE), respiratory rate (RR),

end-tidal CO2 (ETCO2), and transcutaneous hemoglobin saturation (SpO2);

3. Cardiac parameters: Heart rate, systolic and diastolic blood pressure;

4. Pain threshold values (part 2 only);

5. Arterial blood gas values.

Secondary outcome

PK parameters will include but not limited to Cmax, AUCinf, and Tmax, and if possible, t½ for GAL-021 and potentially alfentanil.

Study description

Background summary

A Two-Part, Double Blinded, Placebo Controlled, Crossover Repeated Stepped Infusion Dose Study of Respiratory Pharmacodynamics of GAL-021 and Opioids. GAL-021 is intended to be a first in class, fast acting, and short-duration intravenous agent acting partially through the BK(Ca2+) (Maxi K channels) in the carotid body to stimulate respiration and increase minute ventilation by primarily increasing tidal volume and secondarily through minor increases to respiratory rate.

Study objective

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:

1. To determine the single-dose safety and tolerability of GAL-021 compared to placebo in healthy subjects after intravenous administration;

2. Estimate the reproducibility of sequential treatments under hypercapnic and ambient air conditions.

Study design

Screening (up to -28d), Pre-dose(baseline), Post-dose (up to 24h), Follow-up (8+/-2d).

Intervention

This is a 2 part study design. Subjects will be randomized to two treatments: GAL-021 (1.1 mg/kg/h IV per study day) or placebo (vehicle only), with each subject receiving each treatment once. The treatments will evaluate the effects of GAL-021 on respiratory drive in a model of opioid induced respiratory depression using open-label alfentanil (up to 177 ug/kg IV per study day). Two dose levels of opioid (alfentanil) and two dose levels of respiratory stimulant (GAL-021) are included in each treatment period. Treatments will be conducted under fixed (or clamped) ETCO2 conditions (Part 1) or ambient air (Part 2). The inter-dose interval is at least 3 days.

Contacts

Public
Center for Human Drug Research (CHDR),
Zernikedreef 10
J.M.A. Gerven, van
Zernikedreef 10
Leiden 2333 CL
The Netherlands
+31 (0)71 5246400
Scientific
Center for Human Drug Research (CHDR),
Zernikedreef 10
J.M.A. Gerven, van
Zernikedreef 10
Leiden 2333 CL
The Netherlands
+31 (0)71 5246400

Eligibility criteria

Inclusion criteria

1. Subjects must be willing to give written informed consent for the trial and able to ad-here 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. 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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-11-2012

Enrollment:	36
Type:	Anticipated

Ethics review

Positive opinion Date:	12-11-2012
Application type:	First submission

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
NTR-new	NL3561
NTR-old	NTR3718
Other	Galleon Pharmaceuticals Inc. : GAL-021-104
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A