

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

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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...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23830

Bron

Nationaal Trial Register

Aandoening

Respiratory impairment

Ondersteuning

Primaire sponsor: Galleon Pharmaceuticals Inc. 213 Witmer Rd, Horsham, PA 19044, United States.

Overige ondersteuning: Galleon Pharmaceuticals Inc.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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. 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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).

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	05-11-2012
Aantal proefpersonen:	36
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum: 12-11-2012

Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3561
NTR-old	NTR3718
Ander register	Galleon Pharmaceuticals Inc. : GAL-021-104
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten

N/A