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A clinical phase I study on GIC-1001 in healthy volunteers

Submission date 26/11/2012	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 11/12/2012	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 26/04/2017	**Condition category** Digestive System	[_] Individual participant data

Plain English summary of protocol

Background and study aims
GIC-1001 is a drug that is intended to provide analgesia (pain relief) for patients undergoing colonoscopy, where a thin flexible tube with a tiny camera on the end (colonoscope) is used to look inside the bowel. It may later be used for pain management in colonic diseases such as irritable bowel syndrome and ulcerative colitis. The aim of this study is to assess the safety, tolerability (side effects) and pharmacokinetic profile (movement of the drug into, through, and out of the body) of GIC-1001 in healthy volunteers.

Who can participate?
Healthy volunteers aged 18 to 50

What does the study involve?
In Part 1 participants are randomly allocated to take GIC-1001 tablets at one of five doses or placebo (dummy) tablets once a day for 7 days. Up to 21 blood samples are taken over a 36-hour period. In Part 2 participants are randomly allocated to take GIC-1001 tablets at one of four doses or placebo (dummy) tablets three times a day for 7 days. Up to 18 blood samples are taken over a 7-day period. In Part 3 participants take a single dose of GIC-1001 in two periods with and without food to assess the effects of food intake on GIC-1001. A total of 16 blood samples are taken over a 36-hour period. Physical examinations, 24-hour cardiac (heart) monitoring and lab tests are carried out to assess the safety and tolerability of GIC-1001 in all groups.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Algorithme Pharma (Canada)

When is the study starting and how long is it expected to run for?
November 2012 to March 2013

Who is funding the study?
gIcare Pharma Inc (Canada)

Who is the main contact?
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Contact information

Type(s)
Scientific

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ClinicalTrials.gov (NCT)
NCT01738425

Protocol serial number
GIC-P2-458

Study information

Scientific Title
A double-blind, placebo controlled, phase I study to assess safety, tolerability and pharmacokinetics of single and multiple ascending oral doses of GIC-1001 in normal healthy volunteers

Acronym
GIC-1001

Study objectives
GIC-1001 is a non-centrally-acting, orally-administered, hydrogen sulfide releasing opioid agonist, which intends to provide adequate colonic analgesia to patients undergoing sedation-free colonoscopy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Board Review Services, 09/11/2012, ref: IBRS-GIC-1001-09-NOV-2012

Primary study design
Interventional

Study design
Randomized controlled phase I trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Gastroenterology/pain management/management of visceral pain during sedation-free colonoscopy

Interventions
Experimental: GIC-1001 oral tablets
GIC-1001; 125 mg oral tablets; Single ascending doses (SAD) from 125 mg to 1000 mg; multiple ascending dose (MAD) from 125 mg to 500 mg TID over 7 successive days

Part 1: Single Doses Cohort A: Single dose of 125 mg of GIC-1001 or placebo; Cohort B: Single dose of 250 mg of GIC-1001 or placebo; Cohort C: Single dose of 375 mg of GIC-1001 or placebo; Cohort D: Single dose of 500 mg of GIC-1001 or placebo; and Cohort E: Single dose of 1000 mg of GIC-1001 or placebo. Up to 21 blood samples will be obtained over a 36 hour period.

Part 2: Multiple Doses, three times a day (TID) during 7 consecutive days; Cohort F: Multiple doses of 125 mg of GIC-1001 or placebo; Cohort G: Multiple doses of 250 mg of GIC-1001 or placebo; Cohort H: Multiple doses of 375 mg of GIC-1001 or placebo; and Cohort I: Multiple doses of 500 mg of GIC-1001 or placebo. Up to 18 blood samples will be obtained over a 7 day period.

Part 3: one single dose of GIC-1001 to be selected for the Food Effect cross-over evaluation. A total of 16 blood samples will be obtained over a 36 hour period.

Placebo Comparator: GIC-1001 matching placebo
Matching placebo, single or multiple dosing

Physical exams, 24 hour cardiac monitoring, and a complete battery of biochemical and hematological lab tests will be done to assess the safety and tolerability of GIC-1001 in all dosing cohorts.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
GIC-1001

Primary outcome(s)
Safety and Tolerability: Single and multiple (7 consecutive days) doses
In this Phase I study, 5 single ascending doses of GIC-1001 will be studied, as well as 4 multiple

doses administered during 7 consecutive days (TID regimen). As well, one single dose will be administered with and without food to assess the effect of food intake on the PK of the study drug. Safety issues monitored.

Key secondary outcome(s)
Pharmacokinetics: Up to 36 hours for single ascending doses; every day and up to 8 hour post last dose for multiple ascending doses
Blood samples will be obtained over a 36 hour period in the single dose portion of the study and over 7 days, every morning prior to GIC-1001, as well as 8 hours post-last dose in the multiple dosing phase. Main absorption and disposition parameters using a non-compartmental approach will be measured.

For GIC-1001 and its metabolites, the pharmacokinetic parameters of interest for the single dose regimens will be Cmax, AUC0-8, AUCT, AUC∞, Tmax, AUCT/∞, Kel, T½el, Cl/F and Vd/F. The parameters Cmax, AUC0-8, AUCT and AUC∞ will be dose-normalized, and their natural logarithm will be calculated. The pharmacokinetic parameters of interest for the multiple dose regimens will be Cmax, Tmax, AUCτ, Cmin, Cpds, Fluctuation and Swing. The parameters Cmax, AUCτ and Cmin will be dose-normalized, and the natural logarithm of Cmax, AUCτ, Cmin and Cpds of will be calculated. For hydrogen sulfide and thiosulfate, the pharmacokinetic parameters of interest will be Cmax, Tmax and AUC0-4.

Completion date
08/03/2013

Eligibility

Key inclusion criteria
1. Male or female volunteer
2. A female volunteer must meet one of the following criteria:
2.1. Participant is of childbearing potential and agrees to use one of the accepted contraceptive regimens from the screening visit until 2 months after the last drug administration. Additionally, if the participant is using systemic contraceptives, she must use an additional form of acceptable contraception from first drug administration until 2 months after the last drug administration.
OR
2.2. Participant is of non-childbearing potential, defined as a female who had had a hysterectomy or tubal ligation, is clinically considered infertile or is in a menopausal state (at least 1 year without menses)
3. A male volunteer with sexual partners who are pregnant, possibly pregnant, or who could become pregnant must meet the following criterion: Participant agrees to use one of the accepted contraceptive regimens from first drug administration until 3 months after the last drug administration. An acceptable method of contraception includes one of the following: Abstinence from heterosexual intercourse or condom with spermicide
4. Volunteer aged of at least 18 years but not older than 50 years
5. Volunteer with a body mass index (BMI) greater than or equal to 18.50 and below 30 kg/m2
6. Non- or ex-smokers. An ex-smoker is defined as someone who completely stopped smoking for at least 6 months before day 1 of this study
7. Clinical laboratory values within the laboratory's stated normal range; if not within this range, they must be without any clinical significance
8. Have no clinically significant diseases captured in the medical history or evidence of clinically significant findings on physical examination and/or clinical laboratory evaluations (hematology, biochemistry, ECG and urinalysis)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. History of significant hypersensitivity to trimebutine, to sulfur containing drugs (e.g. Captopril) or any related products (including excipients of the formulation) as well as severe hypersensitivity reactions (like angioedema) to any drugs
2. Presence of significant gastrointestinal, liver/kidney disease, or any other conditions known to interfere with the absorption, distribution, metabolism or excretion of drugs or known to potentiate or predispose to undesired effects
3. History of significant gastrointestinal, liver or kidney disease that may affect drug bioavailability
4. Presence of significant cardiovascular, pulmonary, hematologic, neurological, psychiatric, endocrine, immunologic or dermatologic disease
5. Suicidal tendency, history of or disposition to seizures, state of confusion, clinically relevant psychiatric diseases
6. Presence of out-of-range cardiac interval (PR < 110 msec, PR > 200 msec, QRS <60 msec, QRS >110 msec and QTc > 440 msec) on the screening ECG or other clinically significant ECG abnormalities
7. Known presence of rare hereditary problems of galactose and /or lactose intolerance
8. Use of cysteine, methionine, and other sulfur containing amino acid supplements in the previous 7 days before day 1 of this study
9. Maintenance therapy with any drug, or significant history of drug dependency or alcohol abuse (> 3 units of alcohol per day, intake of excessive alcohol, acute or chronic)
10. Any clinically significant illness in the previous 28 days before day 1 of this study
11. Use of any enzyme-modifying drugs, including strong inhibitors of cytochrome P450 (CYP) enzymes (such as cimetidine, fluoxetine, quinidine, erythromycin, ciprofloxacin, fluconazole, ketoconazole, diltiazem and HIV antivirals) and strong inducers of CYP enzymes (such as barbiturates, carbamazepine, glucocorticoids, phenytoin, rifampin and St John's Wort), in the previous 28 days before day 1 of this study
12. Any history of tuberculosis and/or prophylaxis for tuberculosis
13. Positive urine screening of ethanol and/or drugs of abuse
14. Positive results to HIV, HBsAg or anti-HCV tests
15. Females who are pregnant according to a positive serum pregnancy test
16. Volunteers who took an Investigational Product (in another clinical trial) or donated 50 mL or more of blood in the previous 28 days before day 1 of this study

Date of first enrolment

14/11/2012

Date of final enrolment
08/03/2013

Locations

Countries of recruitment
Canada

Study participating centre
Algorithme Pharma Inc.
Montreal
Canada
H7V 4B3

Sponsor information

Organisation
gIcare Pharma Inc (Canada)

Funder(s)

Funder type
Industry

Funder Name
gIcare Pharma Inc (Canada)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
	results				

Results article	01/11/2014	Yes	No