EVALUATION OF SAFETY, TOLERABILITY AND PHARMACOKINETIC CHARACTERISTICS OF MULTIPLE-ASCENDING DOSES OF CG400549 IN HEALTHY VOLUNTEERS

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON34490

Source
ToetsingOnline

Brief title
CG400549 Multiple ascending dose study

Condition

- Bacterial infectious disorders

Synonym
MRSA

Research involving
Human

Sponsors and support

Primary sponsor: Crystal Genomics
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: (FAbl) inhibitor, CG400549, MRSA

Outcome measures

Primary outcome

Pharmacokinetics: plasma and urine CG400549 concentrations, pharmacokinetic

parameters

Safety : adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination,

Secondary outcome

N/A

Study description

Background summary

The study medication to be administered, CG400549 is a new, investigational compound that may eventually be used for the treatment of infections caused by methicillin-resistant Staphylococcus aureus (MRSA). MRSA is a microbe, which is resitent for most of the common antibiotics. Because of this resistance, MRSA is difficult to treat.

For survival, microbes (bacteria) need an intact cell wall. CG400549 specifically inhibits the synthesis of the cell wall for all kinds of bacteria; as a consequence, bacteria will not survive. As CG400549 differentiates itself from other antibacterial agents through its novel mechanism of action, it may eventually be used to treat infections cuased by resistant bacteria, such as MSRA

Study objective

The purpose of the study is to investigate how safe the compound is and how well the compound is tolerated. The study will also investigate how quickly and to what extent the compound is absorbed and eliminated from the body (this is called pharmacokinetics).

Study design

Design
This is a Phase 1, 3 cohorts study consisting of a randomised, double-blind, and placebo-controlled design., each cohort will consist of 8 healthy male subjects., Subjects in Group 1 will receive an oral dose of CG400549 or placebo (six verum and two placebo) twice daily on Days 1-5 and a final oral morning dose of CG400549 or placebo on Day 6; subjects in Groups 2 and 3 will receive a single oral dose of CG400549 or placebo (six verum and two placebo) on Day 1, an oral dose of CG400549 or placebo twice daily on Days 3-7 and a final oral morning dose of CG400549 or placebo on Day 8. The safety and PK data from each cohort will be reviewed before advancing to the next cohort.

Screening and Follow up
physical examination, 12-lead electrocardiogram (ECG), clinical laboratory (clinical chemistry, haematology, coagulation, thyroid function and urinalysis), vital signs (including supine systolic and diastolic blood pressure, pulse rate and oral body temperature), adverse event (AE) assessments and previous and concomitant medication at eligibility screening only: informed consent; inclusion/exclusion criteria; demographics; medical history; height and weight; drug, alcohol, and nicotine screen; testing for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) 1/2. On admission: physical examination, vital signs, 12-lead ECG, clinical laboratory (clinical chemistry, haematology, coagulation, thyroid function and urinalysis) and alcohol, drug, and nicotine screen.

Observation period

Blood sampling
For PK of CG400549 in plasma:
Cohort 1 : pre-dose (D1), 12 h (D1), 24 h (D2), 36 h (D2), 48 h (D3), 60 h (D3), 72 h (D4), 84 h (D4), 96 h (D5), 108 h (D5), 120 h (D6), 120.25h (D6), 120.5 h (D6), 121 h (D6), 121.5 h (D6), 122 h (D6), 122.5 h(D6), 123 h (D6), 124 h (D6), 125 h (D6), 126 h (D6), 128 h (D6), 130 h (D6), 132 h (D6), 144 h (D7), 156 h (D7), 168 h (D8),

Cohort 2 and 3 : pre-dose and 0.25 h, 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h, 3 h, 4 h, 5 h, 6 h, 8 h, 10 h, 12 h, 24 h (D2), 36 h (D2), 48 h (D3), 60 h (D3), 72 h (D4), 84 h (D4), 96 h (D5), 108 h (D5), 120 h (D6), 132 h (D6), 144 h (D7), 156

h (D7), 168 h (D8), 168.25h (D8), 168.5 h (D8), 169 h (D8), 169.5 h (D8), 170 h (D8), 170.5 h(D8), 171 h (D8), 172 h (D8), 173 h (D8), 174 h (D8), 176 h (D8), 178 h (D8), 180 h (D8), 192 h (D9), 204 h (D9), 216 h (D10).

Urine sampling
For PK of CG400549 in urine
Cohort 1: pre-dose (point sample) and in intervals of 120-124, 124-128, 128 132, 132 144, 144 156 and 156-168 h post-dose

Cohort 2 and 3: pre-dose (point sample) and in intervals of 0-4, 4-8, 8 12, 12 24, 24 36, 36-48, 168-172, 172-176, 176-180, 180-192, 192-204 and 204-216 h

Safety assessments
AEs: recorded from the time the Informed Consent Form is signed until completion of the follow up visit;
Cohort 1 : physical examination: Day -1~8 and D15; clinical laboratory (clinical chemistry, haematology, coagulation, thyroid function and urinalysis): once on Days -1, 3, 5, 8 and 15; 12 lead ECG: On Day 1, at 30 min pre-dose and 4, 8, 12, and 24 h, On Day 2~5 at 4, 8, 12 and 24h. On Day 6 at 1, 4, 8, 12, 24 and 48h and Day 15; weight: Days -1; vital signs: On Day 1, at pre-dose and 4, 8, 12 and 24h. On Day 2~5 at 4, 8, 12 and 24h. On Day 6, at 0.5, 1, 2, 4, 8, 12, 24, 28, 32, 36 and 48 h and Day 15,

Cohort 2 and 3 : physical examination: Day -1~10; clinical laboratory (clinical chemistry, haematology, coagulation, thyroid function and urinalysis): once on Days -1, 3, 5, 8 and 10; 12 lead ECG: On Day 1, at 30 min pre-dose and 1, 4, 8, 12, 24 and 48h, On Day 3~7 at 4, 8, 12 and 24h. On Day 8 at 1, 4, 8, 12, 24 and 48h and Day 17; weight: Days -1; vital signs: On Day 1, at pre-dose and 0.5, 1, 2, 4, 8, 12, 24, 28, 32, 36 and 48 h, On Day 3~7 at 4, 8, 12 and 24h. On Day 8 at 0.5, 1, 2, 4, 8, 12, 24, 28, 32, 36 and 48 h and Day 17

Intervention

Active medication
Active substance: CG400549
Activity: enoyl-acyl-carrier-protein reductase (Fabl) inhibitor
Indication: methicillin-resistant Staphylococcus aureus
Strength: 160mg
Dosage form: oral capsule

Placebo
Substance: microcrystalline cellulose, sodium stearyl fumarate
Activity: none
Indication: not applicable
Strength: not applicable (to appear identical to 160mg active capsules)
Dosage form: oral capsule

Study burden and risks

Procedures: pain, light bleeding, haematoma and infection

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

Sex: male
Age: 18-55 years, inclusive
BMI: 19-30 kg/m2
No relevant deviations at screening

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS.
In case of participation in another drug study within 60 days before the start of this study or being a blood donor (50 mL or more) within 60 days from the start of the study. In case of donating more than 1.5 liters of blood (for men) / more than 1.0 liters of blood (for women) in the 10 months preceding the start of this study.

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):	11-05-2010
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	28-04-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-05-2010

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-10-2010
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	EUCTR2010-020011-37-NL
CCMO	NL32350.056.10