# A randomized, single center, 2-way crossover, comparator controlled Phase I trial to evaluate the effect of a new analgesic on ventilation in healthy subjects

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON32792

**Source**
ToetsingOnline

**Brief title**
A study to investigate the effect of GRT6005 on ventilation.

### Condition

- Other condition

**Synonym**
nociceptive pain, pain

**Health condition**

pijn

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Grunenthal
**Source(s) of monetary or material Support:** Industrie

## Intervention

**Keyword:** analgesic, ventilation

## Outcome measures

### Primary outcome

Respiratory function (respiratory rate and oxygen saturation) using the dynamic

end-tidal forcing technique (model for respiratory depression).

### Secondary outcome

Pain test (pain detection threshold and pain tolerance) using an electrical

pain test (transcutaneous electrical stimulation).

Static pupillometry (pupil diameter).

Ventilation (i.e., inspiratory volume per minute) using the dynamic end-tidal

forcing technique.

# Study description

### Background summary

GRT6005 is a highly potent mixed opioid receptor agonist with central antinociceptive activity. GRT6005 hemi-citrate is highly effective in animal models of
acute pain, visceral and inflammatory pain as well as chronic mono- and poly-neuropathic and bone cancer pain. In acute pain models, GRT6005 hemi-citrate is approximately equi-potent to the strong opioid fentanyl citrate. Whereas classical opioids generally have the same potency in acute pain and neuropathic pain models, GRT6005 hemi-citrate was found to be *10-

times more potent in neuropathic pain when compared to acute pain models. The respiratory depressant effects were markedly lower than those of equi-antinociceptive doses of oxycodone hydrochloride (HCl). Earlier research in humans shows that GRT6005 is well tolerated up to doses of 800 microgram.

## Study objective

This trial assesses the safety profile of GRT6005 in terms of its effect on respiratory function. Data on its effect on ventilation in a model of respiratory depression will be obtained and compared to fentanyl (a strong opioid with comparable potency in acute pain). Non-clinical data suggest that GRT6005 might have an advantage regarding respiratory depression compared to other classical opioids (e.g., oxycodone). To further investigate this possibility in
humans, this trial has been set up. In the past, the ventilation model chosen for this trial was shown to be accurate and specialized in showing differences between opioids (Dahan et al. 2005). A comparator was chosen to enable the obtained data to be compared with a known substance yielding
a comparable antinociceptive potency in a non-clinical acute pain model.

## Study design

A randomized, single center, 2-way crossover, comparator controlled study. The study consists of 3 periods of 2 or 3 days (per period 2-3 night(s) at CHDR) with a period of at least 2 weeks between study dosings.

## Intervention

period 1: GRT6005 600 microgram oral solution,
period 2: Fentanyl 3.5 microgram per kg bodyweight - Schedule A,
period 3: Fentanyl 3.5 microgram per kg bodyweight - Schedule B.

## Study burden and risks

This trial will be performed in healthy male subjects who will receive no medical benefit from participation in the trial. Potential subjects will be fully informed about the risks and requirements of the trial and, during the trial, subjects will be given any new information that may affect their decision to continue participation. They will be told that their consent to participate in the trial may be withdrawn at any time with no reason given and without penalty. Only subjects who are fully able to understand the risks, benefits, and potential adverse events of the trial, and provide their consent voluntarily will be enrolled. No undue incentives will be provided. The potential risks to subjects in this trial include exposure to IMP, with a potential for side effects,
and the inherent risks associated with venipuncture and the use of an arterial

line for blood sample collection.

# 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

1. White male subjects aged 18 years to 45 years inclusive.
2. Body mass index between 20 kg/m2 and 28 kg/m2 inclusive, with a body weight of not less than 50 kg.
3. Subjects must be in good health as determined by medical history, physical examination, 12-lead ECG, oxygen saturation, vital signs, and clinical laboratory parameters.
4. Subjects willing to use barrier contraception (condom) during sexual intercourse with women, and no sexual intercourse with women who are pregnant or lactating is allowed from dosing of GRT6005 until 1 month after the Final Examination. Subjects willing to ensure that their female sexual partner uses medically acceptable contraception during this time frame

(e.g., oral contraceptive).
5. Subjects giving written informed consent to participate in the trial.

## Exclusion criteria

1. Resting pulse rate is <45 bpm or >100 bpm after 5 min rest in semi-recumbent position.
2. Resting blood pressure after 5 min rest in semi-recumbent position:
a. Systolic blood pressure is <100 mmHg or >150 mmHg.
b. Diastolic blood pressure is <50 mmHg or >90 mmHg.
3. History of orthostatic hypotension. Standardization of trial population and safety.
4. Positive or missing test for human immunodeficiency virus antibodies (Type 1 and Type 2), hepatitis B surface antigens, hepatitis B core antigen antibodies, or hepatitis C virus antibodies.
5. Participation in another clinical trial within 90 days prior to enrollment into this trial.
6. Positive or missing drugs of abuse screening (alcohol breath test, urine screening test for drugs of abuse).
7. Diseases or condition known to interfere with the absorption, distribution, metabolism, or excretion of drugs.
8. Marked repolarization abnormality (e.g., suspected or definite congenital long QT syndrome with QT and/or QTcB >500 ms or prolonged QTcB, i.e., >450 ms).
9. Bronchial asthma or other respiratory diseases.
10. Definite or suspected history of drug allergy or hypersensitivity.
11. Regular use of any medication at the time of enrollment and anticipated further use until first administration of IMP.
12. History of alcohol or drug abuse.
13. History of neurotic personality, psychiatric illness, or suicide risk.
14. Not able to abstain from consumption of:
a. Beverages or food containing caffeine (tea, coffee, cola, chocolate, etc.) from 48 h prior to each dosing until discharge from the ward.
b. Beverages or food containing quinine (bitter lemon, tonic water) from 2 weeks before dosing and during the whole trial.
c. Grapefruit juice (sweet or sour) or alcohol from 48 h prior to each dosing until discharge from the ward.
d. Poppy seed-containing beverages or food, from 72 h prior to enrollment and each dosing.
15. Blood loss of 500 mL within 3 months before enrollment into this trial, including blood donation.
16. History of or at risk of seizures (i.e., head trauma, epilepsy in family history, unclear loss of consciousness).
17. Known or suspected of not being able to comply with procedures described in the trial protocol.
18. Not able to communicate meaningfully with the Investigator
and staff.
19. Smoking of >10 cigarettes/day or equivalent.

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 04-03-2010 |
| Enrollment: | 12 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | fentanyl citrate |
| Generic name: | fentanyl citrate |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | GRT6005 |
| Generic name: | GRT6005 |

# Ethics review

Approved WMO

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| Date: | 17-12-2009 |
| Application type: | First submission |
| Review commission: | METC Leids Universitair Medisch Centrum (Leiden) |

Approved WMO

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|---|---|
| Date: | 25-02-2010 |
| Application type: | First submission |
| Review commission: | METC Leids Universitair Medisch Centrum (Leiden) |

# 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 | EUCTR2009-010893-39-NL |
| CCMO | NL30817.058.09 |