# A study examining the interaction between buprenorphine and fentanyl

No registrations found.

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

## Summary

### ID

NL-OMON25893

**Source**
NTR

**Brief title**
Buprenorphine-Fentanyl Interaction Study

**Health condition**

• Opioid Use Disorder, Respiratory depression

### Sponsors and support

**Primary sponsor:** Indivior UK Ltd
**Source(s) of monetary or material Support:** Indivior UK Ltd

### Intervention

### Outcome measures

**Primary outcome**

• Minute ventilation (L/min), respiratory rate (/min), oxygen saturation (SpO2), tidal volume (L), end-tidal PCO2 (kPa; PEiCO2) and end-tidal PO2 (kPa; PEiO2) are measured for each breath during the Baseline period and during infusion of study drugs.

Peak ventilatory depression (change in minute ventilation) will be calculated based on a 1-

minute average of the ventilation data of each individual subject/patient. For buprenorphine or placebo, absolute changes and percentage changes are calculated from the Baseline value. For fentanyl, absolute changes and percentage changes for each bolus are calculated from the
Baseline value and from the pre-fentanyl baseline value immediately before the first fentanyl bolus. The Baseline value is the minute ventilation value when a stable ventilation pattern is established for at least 2 minutes prior to the infusion of buprenorphine/placebo. The pre-fentanyl baseline value is defined as the minute ventilation value averaged between the timepoint when a stable ventilation pattern is established for at least 2 minutes after start buprenorphine/placebo infusion and the timepoint before the first fentanyl bolus.

**Secondary outcome**

For Part A (Healthy Subjects):

Number (percentage) of subjects who experience apnoea for each fentanyl dose during the placebo treatment vs. the buprenorphine treatment. Apnoea is defined as a 20 second pause in respiration. If apnoea is observed at any fentanyl dose for a subject, that subject will be classified as ‘experienced apnoea’ for that dose, and any higher fentanyl dose planned in the study (the next higher fentanyl dose or doses will be withheld); Number (percentage) of subjects who require stimulation for breathing for each fentanyl dose during the placebo treatment vs. the buprenorphine treatment. If a subject required stimulation for breathing at a fentanyl dose and the next higher fentanyl dose or doses was withhold, the subject will also be classified as requiring breath stimulation for the withheld higher fentanyl.

For Part B (Opioid experienced patients):

Whether the subject experiences apnoea during buprenorphine treatment at the fentanyl dose, at which the subject had apnoea during the placebo treatment.

Fentanyl dose corresponding to the occurrence of apnoea during placebo and buprenorphine infusion periods (if applicable)

# Study description

**Background summary**

This is a study examining the pharmacodynamic interaction between buprenorphine and fentanyl.

Many patients are not aware that addiction is a disease that can be medically treated. The goals of MAT are to reduce substance use and risk of relapse or overdose, to reduce harm

from sequelae of substance abuse and to help patients return to a healthy, functional life. Buprenorphine, a partial agonist at the MOR is used for the MAT of OUD. Buprenorphine has high affinity for the MOR and therapeutic plasma concentrations achieve ≥70% receptor occupancy. As a partial agonist, buprenorphine has a ceiling effect on respiratory depression such that it does not cause apnoea when administered alone and minute ventilation is not suppressed beyond 50 to 60%. It is hypothesised that buprenorphine will competitively inhibit the effects of potent, short-acting MOR agonists like fentanyl and carfentanil that can result in apnoea and death. The objective of this trial is to determine if MOR blockade with buprenorphine can shift the respiratory depression response to intravenous (IV) fentanyl injection to the right, thereby reducing the potency of fentanyl in causing respiratory depression - the usual fatal precipitant associated with IV fentanyl/heroin overdose. Subjects will be recruited in the Netherlands.

### Study objective

• To determine if buprenorphine action at the MOR receptor can inhibit the respiratory depression response to IV fentanyl injection in healthy subjects and patients with chronic opioid use;

• To determine if therapeutic concentrations achieved with administration of buprenorphine in chronic opioid experienced patients protect against respiratory depression associated with high concentrations of fentanyl.

### Study design

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### Intervention

• Buprenorfine

• Fentanyl

## Contacts

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# Eligibility criteria

## Inclusion criteria

Part A:

1. Signed the informed consent form (ICF) and able to comply with the study requirements and restrictions listed there in;

2. Male and female subjects, age 18 to 45 years, inclusive;

3. Women of childbearing potential (defined as all women who are not surgically sterile or postmenopausal for at least 1 year prior to informed consent) must have a negative serum pregnancy test prior to enrollment and must agree to use a medically acceptable means of contraception from screening through at least 3 months after the last dose of study drug;

4. Body Mass Index (BMI) 18 to 30 kg/m2, inclusive

5. Healthy as defined by the Investigator, based on a medical evaluation that includes the subject's medical and surgical history, physical examination, vital signs, 12-lead electrocardiogram (ECG), hematology, blood chemistry, and urinalysis;

6. No history of substance use disorder;

7. No current use of any central nervous system (CNS) depressants prescribed or otherwise.

Part B:

1. Signed the ICF and able to comply with the requirements and restrictions listed therein;

2. Males or females age 18 to 55 years, inclusive;

3. Women of childbearing potential (defined as all women who are not surgically sterile or postmenopausal for at least 1 year prior to informed consent) must have a negative serum pregnancy test prior to enrollment and must agree to use a medically acceptable means of contraception from screening through at least 3 months after the last dose of study drug.

4. BMI 18 to 32 kg/m2, inclusive;

5. Patients administered prescription opioids or heroin obtained through a medical heroin dispensation program) at daily doses ≥ 90 mg

6. Stable as defined by the Investigator, based on a medical evaluation that includes the subject's medical and surgical history, physical examination, vital signs, 12-lead ECG, haematology, blood chemistry, and urinalysis;

7. No current use of any CNS depressants, besides opioids, prescribed or otherwise for 5 half-lives of the product before first study drug administration.

## Exclusion criteria

Part A :

1. Currently meet the criteria for diagnosis of substance use disorder according to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 criteria on any substance;

2. Any other active medical condition, organ disease or concurrent medication or treatment that may either compromise subject safety or interfere with study endpoints;(including sleep apnoea, other significant respiratory illness, history or risk of difficult intubation, limited cervical spine mobility or limited oral excursion);

3. Current smokers and those who have smoked within the last 6 months;

4. Current users of e-cigarettes and nicotine replacement products and those who have used these products within the last 6 months;

5. Consume, on average, >20 units/week of alcohol in men and >13 units/week of alcohol in women (1 unit = 1 glass (250 mL) beer, 125 mL glass of wine or 25 mL of 40% spirit);

6. Previous treatment with any prescribed medications (including all type of vaccines) or over-the-counter (OTC) medications (including homeopathic preparations, vitamins, and minerals) within 14 days or 5 half-lives (whichever is longer) prior to first study treatment administration;

7. Previous or current treatment with opioid agonist, partial agonist, or antagonist treatment within 30 days prior to the first study drug administration;

8. Require on-going prescription or OTC medications that are clinically relevant CYP P450 3A4 or CYP P450 2C8 inducers or inhibitors (e.g., rifampicin, azole antifungals [e.g., ketoconazole], macrolide antibiotics [e.g., erythromycin]);

9. History or presence of allergic response to buprenorphine or fentanyl;

Part B:

1. Currently meet the criteria for diagnosis of moderate or severe substance use disorder according to the DSM-5 criteria on any substances other than opioids, caffeine, or nicotine;

2. Any active medical condition, organ disease or concurrent medication or treatment that may either compromise subject safety or interfere with study endpoints;including sleep apnoea, other significant respiratory illness, history or risk of difficult intubation, limited cervical spine mobility or limited oral excursion);

3. Smoking of >10 cigarettes/day or equivalent and not able to abstain from smoking cigarettes during each dose administration day;

4. Consume, on average, >27 units/week of alcohol in men and >20 units/week of alcohol in women (1 unit = 1 glass (250 mL) beer, 125 mL glass of wine or 25 mL of 40% spirit);

5. Use of buprenorphine within 10 days of the first study drug administration;

6. Currently receiving Medication-Assissted Therapy (MAT) for the treatment of Opioid Use Disorder (OUD);

7. History or presence of allergic response to buprenorphine or fentanyl;

# Study design

## Design

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| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Single blinded (masking used) |
| Control: | Placebo |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 19-03-2018 |
| Enrollment: | 26 |
| Type: | Anticipated |

## Ethics review

Positive opinion

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|---|---|
| Date: | 28-05-2018 |
| 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 | NL7028 |
| NTR-old | NTR7233 |
| Other | • CHDR1754, NL6426.056.18, 2017-04858-42, INDV-6000-101 : CHDR1754, |

## Study results

**Summary results**

NA