

A study examining the interaction between buprenorphine and fentanyl

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- 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...

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

Samenvatting

ID

NL-OMON25893

Bron

NTR

Verkorte titel

Buprenorphine-Fentanyl Interaction Study

Aandoening

- Opioid Use Disorder, Respiratory depression

Ondersteuning

Primaire sponsor: Indivior UK Ltd

Overige ondersteuning: Indivior UK Ltd

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- 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.

Toelichting onderzoek

Achtergrond van het onderzoek

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 $\geq 70\%$ 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.

Doel van het onderzoek

- 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.

Onderzoeksopzet

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Onderzoeksproduct en/of interventie

- Buprenorfine
- Fentanyl

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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 \geq 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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-Assisted Therapy (MAT) for the treatment of Opioid Use Disorder (OUD);
7. History or presence of allergic response to buprenorphine or fentanyl;

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blinding:	Enkelblind
Controle:	Placebo

Deelname

Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	19-03-2018
Aantal proefpersonen:	26
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies	
Datum:	28-05-2018
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
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NTR-new	NL7028
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NTR-old	NTR7233
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Ander register • CHDR1754, NL6426.056.18, 2017-04858-42, INDV-6000-101 : CHDR1754,

Resultaten

Samenvatting resultaten

NA