Clinical evaluation of the efficacy of methylnaltrexone in resolving constipation induced by different opioid subtypes combined with laboratory analysis of immunomodulatory and antiangiogenic effects of methylnaltrexone

Gepubliceerd: 20-11-2013 Laatst bijgewerkt: 18-08-2022

the efficacy of methylnaltrexone differs between different opioid subtypes

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON27076

Bron
Nationaal Trial Register

Verkorte titel
Methylnaltrexone for opioid induced constipation

Aandoening

constipation
methylnaltrexone
opioid
obstipatie

Ondersteuning

Primaire sponsor: VU University Medical Center

Overige ondersteuning: derde geldstroom (anders dan 1e of 2e geldstroom, zoals collectebusfondsen, Europese Unie, vakministeries of bedrijven), namelijk

Fonds Nuts Ohra

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The proportion of subjects that has a rescue-free laxation response within 4 hours after at least 2 of the first 4 doses (the first week of treatment).

Toelichting onderzoek

Achtergrond van het onderzoek

Opioid-induced constipation (OIC) is one of the major problems in palliative care with a prevalence of 10-50%. Methylnaltrexone for the treatment of OIC is significantly more effective than placebo, but it produces rescue-free laxation only in about fifty percent of the patients regardless of the dose. Because methylnaltrexone is a μ-receptor antagonist and not all opioids are solely μ-receptor agonists, it is likely that the effect of methylnaltrexone is mainly determined by the receptor-profile of each specific opioid. Besides its effect on OIC, methylnaltrexone has also been shown to reduce opioid-induced changes in immune system functioning and angiogenesis in pre-clinical studies.
In this multi-center, prospective, parallel group trial we will evaluate the efficacy of methylnaltrexone in resolving OIC in the most common opioid subtypes: morphine, oxycodone and fentanyl. In total 195 patients with OIC, despite prophylactic laxatives, are prescribed methylnaltrexone every other day up to fourteen days. Participants will report its effect in a laxation diary. Group allocation is based on the opioid type the participant is using. At the start and end of the study period, participants complete the Bowel Function Index questionnaire. A subgroup is invited to donate blood for analysis of immunomodulatory and anti-angiogenic effects of methylnaltrexone.

Doel van het onderzoek

the efficacy of methylnaltrexone differs between different opioid subtypes

Onderzoeksopzet

respons after methylnaltrexone administration day 0 to 14

BFI day 0 and 14

laboratory part day 0, 1, 14 and 42

Onderzoeksproduct en/of interventie

The three study groups (morphine sulphate, oxycodon and fentanyl) will all receive treatment with methylnaltrexone every other day for 14 days (7 doses).

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

. Age >/= 18 years 2. Receiving palliative care 3. Life expectancy > 2 weeks 4. Able to give informed consent 5. Receiving opioid treatment with either morphine sulphate, oxycodone or fentanyl 6. Opioid treatment, both a) On a regular schedule (not just as needed or rescue doses) for the control of pain or dyspnea for at least 2 weeks before the first dose of methylnaltrexone, and b) On a stable opioid regimen for at least 3 days before the first dose of methylnaltrexone. This is defined as no dose reduction of >/= 50%, dose increases are permitted. 7. If a subject uses a combination of short- and long-acting (including continuous administration) opioids, the short-acting opioid should preferably be of the same type as the

long-acting opioid. If the subject uses a different type of short-acting opioid than the long-acting opioid, the subject is allowed to enter the study if he/she has used this short-acting opioid /= 3 days before the first dose of methylnaltrexone. This is defined as at least one type of laxative in an adequate dosing regimen, (e.g. macrogol 2 packets daily, magnesium(hydr)oxide 500 mg three times daily, bisacodyl 10 mg daily or sennoside A+B 10 ml daily) or at least two types of laxatives in a suboptimal dose with patient characteristics hampering optimal treatment. 11. If the subject is a woman with presumed child bearing potential; negative urine pregnancy test at screening 12. Surgically sterile or agrees to use a medically acceptable method of birth control or practice sexual abstinence for the duration of the methylnaltrexone treatment and the following 15 days. ~ * including laxation after rescue laxative or enema ~ not necessary for postmenopausal women

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Previous treatment with methylnaltrexone 2. Known or suspected mechanical gastrointestinal obstruction 3. Presence of an other cause of bowel dysfunction that is considered to be a major contribution to the constipation according to investigator 4. Presence of a peritoneal catheter for intraperitoneal chemotherapy or dialysis 5. Clinically relevant active diverticular disease 6. History of bowel surgery within 10 days before first dose of methylnaltrexone 7. Fecal ostomy 8. Use of vinca alkaloids within previous 4 months 9. Body weight <38 kg 10. Renal failure defined as EGFR <30 ml/min per 1.73m2 or requires dialysis. 11. Known or suspected allergy to methylnaltrexone or similar compounds (e.g. naltrexone or naloxone) 12. Participation in a study with investigational products within 30 days before first dose of methylnaltrexone. 13. Pregnant or nursing 14. Clinically important abnormalities that may interfere with participation or compliance to the study, determined by investigator Additional exclusion criteria for the immunologic and angiogenic analysis part of the study: 15. Chemotherapy or treatment with tyrosine kinase inhibitor during 4 weeks before inclusion or treatment scheduled during participation in this study. 16. Treatment with high dose corticosteroids during 2 weeks before inclusion in this study. This is defined as the equivalent of 30 mg of prednisone per day for >/= 2 consecutive days.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	25-07-2012
Aantal proefpersonen:	195
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	20-11-2013
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
NTR-new	NL4070
NTR-old	NTR4272
Ander register	METC VUmc : 2012/169
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten

N/A