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

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON27076

Source
Nationaal Trial Register

Brief title
Methylnaltrexone for opioid induced constipation

Health condition

constipation
methylnaltrexone
opioid
obstipatie

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: derde geldstroom (anders dan 1e of 2e

geldstroom, zoals collectebusfondsen, Europese Unie, vakministeries of bedrijven), namelijk

Fonds Nuts Ohra

Intervention

Outcome measures

Primary outcome

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).

Secondary outcome

- Time to first laxation

- Laxation within 4 hours after the first dose of study drug

- Laxation within 4 or 24 hours after each dose

- Laxation within 4 hours after at least 4 of the maximum 7 doses

- Number of laxations per week

- Change in BFI score between day 0 and 14

- changes in immunologic and angiogenic markers

Study description

Background summary

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.

Study objective

the efficacy of methylnaltrexone differs between different opioid subtypes

Study design

respons after methylnaltrexone administration day 0 to 14

BFI day 0 and 14

laboratory part day 0, 1, 14 and 42

Intervention

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

Contacts

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Eligibility criteria

Inclusion criteria

. 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

Exclusion criteria

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.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-07-2012
Enrollment:	195
Type:	Anticipated

Ethics review

Positive opinion

Date:	20-11-2013
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	NL4070
NTR-old	NTR4272
Other	METC VUmc : 2012/169
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A