A randomised controlled trial in the palliative setting regarding off-label medication: investigating the efficiency of amitriptyline versus pregabalin from a societal perspective

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To compare efficiency, side effects and costs of a strategy with amitriptyline as drug of first choice versus a strategy with pregabalin as drug of first choice.

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

Summary

ID

NL-OMON31425

Source
ToetsingOnline

Brief title
Amitriptyline or Pregabalin to treat neuropathic pain in incurable cancer

Condition

- Other condition

Synonym
neuropathic pain

Health condition

neuropathische pijn

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: cost-effectiveness, neuropathic pain, off-label, palliative care

Outcome measures

Primary outcome

Mean current pain intensity self-rated by the patients with a 11-scale NRS ranged from no pain at all to the worst pain ever experienced, measured one time a day with the help of a pain diary. NRS ratings have been shown to be valid and reliable for measuring pain intensity.

Secondary outcome

- Costs (of medication and health care consumption)

- Sort of pain and intensity (McGill Pain Questionnaire)

- Mean number of episodes with breakthrough pain or pain attacks (pain diary)

- Number of patients for whom the drug of first choice is not effective enough and therefere are given a prescription of the drug of the other arm (add-on)

- Number of patients that stop to take the drug of first choice as a consequence of side-effects (switching, ADR)

- Side-effects (EORTC QLQC30

- Number of different drugs prescribed for pain relief (using prescribed daily dose methodology, ATC/PDD)

- Patient Global Impression of Change (PGIc)

- Clinical Global Impression of Change (CGIC)

- Presence of depression (BDI-PC)

- Quality of Life (EORTC QLQC30; EQ-5D)

- Costs (of all medications, consultations, home care, hospital care)

Study description

Background summary

As a consequence of recent changes in the Dutch law about prescribing medication, off-label use of drugs is allowed only based upon evidence, or using standards or protocol. This study deals with neuropathic pain in incurable cancer patients. The drug pregabalin has been registered for neuropathic non-cancer pain. Amitriptyline is not registered for neuropathic pain but is recommended as the drug of first choice in the Dutch handbooks of palliative care. So far clinical trials for this patient group are lacking.
This study will show what stategy is appropriate for this patientpopulation.

Study objective

To compare efficiency, side effects and costs of a strategy with amitriptyline as drug of first choice versus a strategy with pregabalin as drug of first choice.

Study design

An open-label, randomised non-inferiority trial

Intervention

When a patient agrees to take part in the study and has given informed consent, he will be allocated randomly to one of the two treatment groups. Each drug will be dosed in a step up titration procedure. Patients will be followed during 8 weeks.
Arm 1: amitriptyline will be prescribed in a step-up procedure. Starting dose 25 mg before the night, if not effective enough (less than 2 points improvement on a NRS compared to the previous titration or NRS>3) and acceptable or no side-effects, step up every 48 hours (till a maximum of 75 mg).
Arm 2: pregabalin will be prescribed, also in a step-up procedure. Starting dose 2 dd 75 mg, if not effective enough (less than 2 points improvement on a NRS compared to the previous titration or NRS>3) and acceptable or no side

effects, step up every 48 hours until a maximum dose of 2 dd 300 mg. If the prescribed drug does not have the desierd effect:
- too less pain reduction on maximum daily dose: add drug of other arm in step up procedure as described in protocol;
- major side-effects (meaning that the patient wants to stop the drug as a result of the side-effects): stop drug that causes side-effects and start drug of other arm in step up procedure as described above.
Additional drugs (e.g. PCM, opioids, NSAID, benzodiazepines) that the patient already used or needs to start during the study period are allowed, except for other TADs and AEDs. Palliative chemotherapy and radiotherapy are also allowed. All medication will be recorded, including daily dose and route of administration. All drug us is recorded.

Study burden and risks

Burden:
To distinguish neuropathic pain from other sorts of pain, the assessment of 2 assessors will be used. Next, patients suffering from neuropathic pain will be asked to score a NRS.
When included, they will be asked to fill in a pain diary (NRS once a day, number of episodes of break through pain once a day). The oncologist will be asked to write down an overview of all medications and alternations at T0, T4 and T8. The research nurse keeps this information with him.
At T0, four weeks and eight weeks, the patient will be asked to fill in the QLQc30, the Euroqol, BDI-PC and the McGill pain questionnaire, as well at the moment he changes to the other arm of the study. At 4 and 8 weeks, the patient will be asked to fill in the PGIC, and the oncologist to fill in the CGIC.

Risks:
We have chosen a design with hardly any or no risks for the patient. The drugs in both arms already are usual care for the target population. If there is no or just a too small effect, the drug of the other arm will be added, which strategy also is already usual care. If the drug of the first arm causes to many or to large side-effects, the drug will be stopped and we wil offer the drug of the other arm. Finally, all other medication, except for TADs and AEDs, as well as radiotherapy and chemotherapy are allowed.

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

All patients, belonging to the above mentioned target group, that have a rating of 4 or higher on a NRS
Recently diagnosed
18+

Exclusion criteria

Curable cancer
jonger dan 18 jaar
Already using tricyclic antidepressive agents or anti-epileptic drugs
Pregnant women

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2007
Enrollment:	130
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lyrica
Generic name:	pregabalin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	tryptizol
Generic name:	amitriptyline
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	31-07-2008
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2007-003961-42-NL
CCMO	NL18892.091.07