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Can within-patient controlled trials help to personalize the treatment of chronic pain?

Submission date
22/11/2018

Recruitment status
Stopped

Registration date
10/12/2018

Overall study status
Stopped

Last Edited
17/07/2023

Condition category
Nervous System Diseases

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
How well medication for chronic (long-lasting) pain works varies from person to person and it is hard to predict how well a drug will work in an individual patient. There are also many external factors that might affect a person's pain and response to medication, including psychological and family situations. N-of-1 or within-subject trials are studies performed in a single patient, comparing a treatment to a dummy treatment (placebo) during several randomly alternated time periods.
This study aims to investigate the usefulness of N-of-1 trials in chronic pain management to select effective drugs and to support stopping the prescription of ineffective ones.

Who can participate?
Adult patients, suffering from pain of any origin lasting for at least 3 months, being treated with a medication that the patient or doctor has doubts will work, either before or during treatment.

What does the study involve?
The patients will be seen for a screening visit to collect medical history, fill in different types of questionnaires and undergo a physical examination. At the end of this visit, participants will be randomly allocated to one of the two trial groups.
Those in the intervention group will be offered an N-of-1 trial. During 6 alternate periods of typically 2 weeks, they will receive either the medication or a placebo. Neither the participants nor the study team will know whether they are receiving medication and placebo. Participants will fill in a diary recording how well they think the treatment is working and whether they have any side effects. At the end of the N-of-1 trial, during a feedback visit, a report summarizing the results of the test will be shown to every participant and sent to his/her pain specialist.
Participants will be seen one last time at 6 months from inclusion to record their current treatment and collect final questionnaires.
Those in the control group will be treated and followed up as usual by the pain center. They will also be asked to fill in a diary on a daily basis.
In addition, six sessions of psychological treatment will be offered to patients of both groups.

What are the possible benefits and risks of participating?
Each participant in the N-of-1 group will benefit from a personalized evaluation of how well his

/her medication is working. If the N-of-1 test reveals that the medication does not work well, it would avoid pointless prescription and potential side-effects. This evaluation could also increase the understanding, awareness and knowledge of the patient's condition and medication. Patients in both groups might also benefit from psychological training sessions, in that they might cope better with their pain.
Risks from the N-of-1 trial are similar to those related to standard practice, because the medications prescribed will be those which are or would have been prescribed anyway. The participants will receive medications that are commonly used and generally safe. Rapid changeover from active medication to placebo could lead to withdrawal symptoms, but gradual increase and decrease of doses will be carefully evaluated case by case, in order to minimize this risk. The patients in whom the medication is effective could feel a worsening of pain during the placebo weeks. On-demand medication will be prescribed to overcome this risk.

Where is the study run from?
University Hospital of Lausanne

When is the study starting and how long is it expected to run for?
December 2018 to February 2021

Who is funding the study?
The trial is supported by the Swiss National Science Foundation through the Investigator Initiated Clinical Trials program.

Who is the main contact?
Prof Thierry Buclin
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Study website
https://www.chuv.ch/fr/pcl/pcl-home/recherche/n-of-1/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N-of-1 CER-VD-2018-01843

Study information

Scientific Title
N-of-1 within-patient trials to improve the rational use of therapeutic drugs: Evaluation of their contribution in personalizing the treatment of chronic pain

Acronym
N-of-1

Study objectives
The study hypothesis is that N-of-1 (within-subject) trials are more successful in detecting medication inefficacy or efficacy than standard practice (definition of success: deprescription or decrease of pain by at least 30%, respectively).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee Vaud on clinical research (member of the Swissethics joint working group), 24 /10/2018, ref: 2018-01843

Study design
Randomized parallel multi-centered open-label controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Available on request through the trial website

Health condition(s) or problem(s) studied
Chronic pain

Interventions
Patients with chronic pain, in whom doubts emanate from the patient or the practitioner about the efficacy of a given medication, will be separated in two arms after their inclusion:
Intervention: Patients allocated to the N-of-1 trial arm will be offered a within-subject, randomized, double-blind, crossover trial comparing the medication to evaluate with a placebo. A treatment comparison plan will be constructed in six periods, with three periods of active drug and three periods of placebo assigned in a random order. The duration of each period will typically be 2 weeks, but could slightly differ depending on the drug's pharmacological properties (e.g time to reach full pharmaco-dynamic effect, time required for titration, wash-out period needed). Daily pain and adverse effects evaluation on a visual analog scale (VAS) by the patient will allow a comparison between active treatment and placebo.
Control: Patients in the control group will be offered the standard management of chronic pain currently offered in pain centers.
All participants: In addition, patients from both arms will benefit from a psychological intervention of cognitive-behavioral inspiration aimed to improve their coping skills facing chronic pain.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Any medicinal drug potentially usable to treat chronic pain conditions and testable in a N-of-1 trial

Primary outcome measure
1. Number of pain medications assessed by reviewing patient medical records at baseline and at 6 months.
2. Average pain intensity as recorded by the patient on a 2-week visual analogue scale (VAS) at baseline and at 6 months.

Secondary outcome measures
1. Quality of life assessed using the Short Form Health Survey SF-36 at inclusion and at 6 months
2. Estimation of the cost of N-of-1 trials taking into account the difference in financial burden of pain treatment
3. Consumption of analgesic medications and of other interventions against pain throughout the study, assessed by reviewing patient medical records.
4. Patient's emotional state assessed by the psychologist using a Clinical Global Impression (CGI) scale at baseline and at 4 months
5. Patient's daily-life functioning assessed by the psychologist using the Hospital Anxiety and Depression Scale (HADS) questionnaire at baseline and at 4 months
6. Qualitative evaluation of patients' and physician's reactions towards the N-of-1 approach (respectively at 6 months and at the end of the whole trial), based on interviews

Overall study start date
01/11/2016

Completion date

30/06/2022

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Aged over 18 years
2. Experiencing pain of any origin for at least 3 months and followed in one of the pain centers included in the trial
3. Patient or the practitioner has doubts about the efficacy of a given medication, either before initiation or during treatment
4. Informed consent form signed

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
240

Key exclusion criteria
1. Contraindication to the class of drugs to be tested, e.g. known hypersensitivity or allergy
2. Specific disease or organ dysfunction, which would contraindicate the prescription of the planned medication
3. Evolving major comorbidity likely to worsen during the trial
4. Any situation where carrying out N-of-1 trial would put the patient at risk of side effects or withdrawal (e.g. high doses opiates)
5. Women who are pregnant or breast feeding
6. Intention to become pregnant during the course of the study
7. Lack of safe contraception, defined as: female participants of childbearing potential, not using and not willing to continue using a medically reliable method of contraception for the entire study duration, such as oral, injectable, or implantable contraceptives, or intrauterine contraceptive devices, or who are not using any other method considered sufficiently reliable by the investigator in individual cases. (Female participants who are surgically sterilised /hysterectomised or post-menopausal for longer than 2 years are not considered as being of child bearing potential.)
8. Inability to give informed consent
9. Inability to follow the procedures of the study, e.g. due to language problems, psychological disorders, dementia, etc. of the participant
10. Known or suspected non-compliance

11. Drug or alcohol abuse
12. Previous enrolment into the current trial

Date of first enrolment
01/01/2019

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
Switzerland

Study participating centre
University Hospital CHUV
Lausanne
Switzerland
1011

Study participating centre
Geneva University Hospitals
Geneva
Switzerland
1211

Sponsor information

Organisation
University Hospital Lausanne (CHUV)

Sponsor details
Bugnon 17
Lausanne
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1011

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05a353079

Funder(s)

Funder type
Government

Funder Name
Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung

Alternative Name(s)
Schweizerischer Nationalfonds, Swiss National Science Foundation, Fonds National Suisse de la Recherche Scientifique, Fondo Nazionale Svizzero per la Ricerca Scientifica, Fonds National Suisse, Fondo Nazionale Svizzero, Schweizerische Nationalfonds, SNF, SNSF, FNS

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Each patient will receive the result of his/her individual N-of-1 trial within 4 weeks of the end of the trial (efforts would be made to keep this time lag as short as possible).
At the end of the study, the investigators will be responsible for preparing a Clinical Study Report in accordance with applicable requirements. The main clinical study report describes the results of all primary and secondary endpoints, including tolerability and safety assessments.
The Investigator will also be responsible for sending a Summary Report on safety and essential study findings to the Ethics Committee in a reasonable time after study completion.
The Investigators shall present and publish the scientific findings from the study within a reasonable time after termination of the study and availability of clinical study report. Results will also be presented at academic meetings and scientific conferences. Subsequent sub-analysis may be presented as well (e.g. aggregated N-of-1 trial results concerning specific analgesic agent).

Intention to publish date
30/09/2022

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date