Vincristine-induced peripheral neuropathy in children with childhood cancer: comparing one-hour infusions with short-term infusions (the VINCA-study)

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

Summary

ID

NL-OMON47569

Source
ToetsingOnline

Brief title
The VINCA-study

Condition

- Leukaemias
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
childhood cancer, Pediatric oncology

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Administration method, Neuropathy, Oncology, Vincristine

Outcome measures

Primary outcome

Primary outcome of the study is peripheral neuropathy (PNP). PNP will be evaluated by using the NCI Common Terminology Criteria for Adverse Events (CTCAE), version 4.03. This is a widely-used scoring method for reporting adverse events in clinical trials. PNP will be evaluated by scoring peripheral motor neuropathy, peripheral sensory neuropathy, neuralgia (pain), and constipation.

Secondary outcome

Secondary endpoints include quality of life, costs (direct medical costs, direct non-medical costs, and indirect costs), treatment efficacy, pharmacokinetic measures (claerance, VCR plasma concentrations and the primary metabolite), and genetic polymorphisms known or suspected to be associated with VCR-induced to PNP or VCR resistance. In addition, a recently developed neuropathy measurement tool (ped-mTNS) will be used to assess PNP.

Study description

Background summary

Vincristine (VCR) is a commonly used chemotherapeutic drug in the treatment of

for example pediatric acute lymphoblastic leukemia, nephroblastoma, low-grade glioma, Hodgkin lymphoma and rhabdomyosarcoma. The main dose-limiting side effect of VCR is peripheral neuropathy (PNP). PNP is often seen in the form of weakness of lower limbs, areflexia, neuropathic pain, and/or sensory loss. The quality of life of children who suffer from VCR-induced PNP is severely affected.
There is a lack of information regarding the optimal therapeutic dosing and method of administration of VCR for children with cancer. High peak plasma concentrations seem to be correlated with PNP. However, the exact mechanism underlying VCR-induced PNP is not clear.

Study objective

This study aims to investigate whether the administration of VCR in children with acute lymphoblastic leukemia, nephroblastoma, low-grade glioma, Hodgkin lymphoma and rhabdomyosarcoma by one-hour infusions, resulting in lower peak plasma concentrations, leads to less PNP compared to short-term infusions. In addition, quality of life, (non-)medical costs, and treatment efficacy associated with both administration methods will be evaluated. Moreover, it will be investigated whether other factors, such as pharmacokinetics and genetic susceptibility to drug-induced side-effects, also influence the degree of PNP.

Study design

The study is a clinical intervention study, with a prospective, randomized,controlled design. Participants will receive all VCR administrations of their treatment either by short-term infusions (1-5 minutes) or by one-hour infusions. Study measurements will be performed at 4 - 8 points in time: before the first VCR administration, 1-7 times during treatment, at the end of treatment, and 6 months after end of treatment.

Intervention

Patients will be randomized into two groups. Patients will either receive all VCR administrations during their treatment period by a one-hour infusion, or by means of a short-term infusion of 1-5 minutes (or by injection).

Study burden and risks

The investigational medicinal product (IMP) that is studied is VCR, a drug which is widely used. Moreover, the investigated methods of administration (bolus injection/infusion and one hour infusion) are both being applied in children in daily clinical practice. Which method is being used depends merely on local center*s logistical/ practical considerations. Study measurements will be performed at 7 points in time. At these time points patients are asked to do

the following: 1. undergo a physical neurological examination (3-7 measurements in total, 20 minutes on average per measurement); 2. fill out questionnaires (QoL: 2-6 measurements in total, 15-20 minutes on average per measurement; costs: 0 - 3 measurements in total; 10 minutes on average per measurement); 3. provide blood samples (1-4 pharmacokinetic measurements in total, 8 samples per measurement). Clinical measurements and blood sampling will be performed on days the patient has to visit the clinic for treatment purposes; questionnaires will be given to the patients/guardians and can be filled out at home. Although it is not the primary aim of this study, participants can benefit from the effects of the intervention. The benefit could be less PNP, less use of medication and lower costs, resulting in improved quality of life.

Whenever possible are pharmacokinetic measurements being performed at time points at which the participants undergo general anesthesia, for example for a bone marrow or lumbar puncture according to their treatment protocol. This allows the insertion of an extra intravenous cannula (which is needed for the PK measurements) without any extra burden for the patients. When this is not possible, this part of the study becomes optional. Separate informed consent is asked for participation of this part of the study.

The sampled blood volume is small (7 x 2 ml = 14 ml). As the average blood volume of a 2-year old child weighing 12 kg is around 900 ml, the maximum amount of blood sampled from the smallest eligible study participant concerns 1,6% of the total blood volume.

All in all, the risks associated with participation in the current study can be considered negligible and the patient's and parent's burden can be considered low to moderate. Given this low risk and low-moderate burden, and the fact that this study has the potential to have major consequences for the improvement of quality of life for all childhood acute lymphoblastic leukemia, nephroblastoma, low-grade glioma, Hodgkin lymphoma and rhabdomyosarcoma patients, this study is considered to have a favorable risk-benefit assessment.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
Amsterdam 1081 HV
NL
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
Amsterdam 1081 HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

• age between 2 and 19 years.
• treated for cancer according to a treatment protocol which includes at least 6 administrations of VCR of which 4 are administered within a maximum period of maximum 6 weeks (these are acute lymphoblastic leukemia, nephroblastoma, Hodgkin lymphoma, low-grade glioma, medulloblastoma and rhabdomyosarcoma)
• diagnosed with a cancer diagnosis of which the incidence in the Netherlands is of more than 5 newly diagnosed patients per year; within the Netherlands
• written informed consent.;

Exclusion criteria

• patient or parent refusal
• history of peripheral neuropathy or other pre-existing or disease- related sensory or motor neurologic conditions
• pre-existing severe mental retardation;
• having parents/ guardians who are unable to communicate in the Dutch language.

Study design

Design

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):	18-09-2014
Enrollment:	58
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Vincristine
Generic name:	Vincristine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-06-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-08-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	22-04-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-06-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-08-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2014-001561-27-NL
CCMO	NL49349.029.14