International cooperative prospective study for children and adolescents with standard risk ALK-positive anaplastic large cell lymphoma (ALCL) estimating the efficacy of Vinblastine.

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This study has been transitioned to CTIS with ID 2022-501454-11-00 check the CTIS register for the current data. PRIMARY OBJECTIVE:- To show that it is possible to cure at least 75% of patients belonging to the SR group with Vinblastine-monotherapy…

Ethical review	Approved WMO
Status	Pending
Health condition type	Lymphomas non-Hodgkin's unspecified histology
Study type	Interventional

Summary

ID

NL-OMON51961

Source
ToetsingOnline

Brief title
ALCL-VBL

Condition

- Lymphomas non-Hodgkin's unspecified histology

Synonym
Anaplastic large-cell lymphoma (ALCL), lymphnode cancer

Research involving
Human

Sponsors and support

Primary sponsor: German Pediatric Oncology Group (GPOH) gGmbH
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: ALCL, Childhood, Lymphoma, Vinblastin

Outcome measures

Primary outcome

- Probability of event-free-survival (pEFS) at 3 years, with EFS defined as the

time of diagnosis to the first event (progressive disease, nonresponse,

secondary malignancy or death due to any cause) or last follow-up.

Secondary outcome

- Overall survival

- Treatment related mortality

- Time from diagnosis to progressive disease /event

- Toxicity

- Response

Study description

Background summary

The development of standard multi-agent chemotherapy has reached its limits for the treatment of ALK-positive ALCL: intensification did not increase survival but the risk of late effects. In ALCL patients a 5-year EFS rate of 70% is achieved independently of the chemotherapy regimen. Vinblastine monotherapy reaches more than 80% remission-rates and long-term survival in relapsed patients. The experiences with Vinblastine in relapse therapy suggest that a low-dose long-term therapy could be as effective as standard short-term multi-agent therapy.

Patients who can be cured by Vinblastine are spared both acute and late toxicity of the multi-agent chemotherapy including Etoposide, alkylators and anthracyclines. Further advantages for single drug Vinblastine therapy are that patients can be treated as outpatients. They can go to school / work and have no major restrictions in daily live in contrast to standard intensive multi-agent chemotherapy. A distinct disadvantage is the duration of treatment and the associated frequent outpatient visits and vinblastine administration.

Since safety is not an issue with Vinblastine monotherapy, its efficacy in relapsed patients has been shown, and overall survival is foreseeable not reduced by Vinblastine, this study forms the basis towards establishing a low toxicity new chemotherapy backbone substituting multi-agent chemotherapy. This would provide a new basis to study the addition of targeted therapies like ALK-inhibitors.

Study objective

This study has been transitioned to CTIS with ID 2022-501454-11-00 check the CTIS register for the current data.

PRIMARY OBJECTIVE:
- To show that it is possible to cure at least 75% of patients belonging to the SR group with Vinblastine-monotherapy for 24 months.

SECONDARY OBJECTIVE:
- To describe overall survival and treatment related mortality of 24 months Vinblastine monotherapy.
- To identify clinical, pathological and biological factors predictive of progressive disease during / after VBL therapy.
- To estimate the rate of SR patients requiring multi-agent chemotherapy
- To describe the toxicity of Vinblastine given for 24 months rated with CTCAE v4.03.
- To describe the response after 3 weeks (between day 17-22), 3 months and 6 months of treatment (including a possible pre-phase) assessed by appropriate imaging methods

Study design

ALCL-VBL is a collaborative multi-centre, open-label non-randomized study of international groups with the intention of optimizing the treatment results in children and adolescents with standard risk ALK-positive ALCL by assessing the efficacy of a 24-months Vinblastine monotherapy after a screening phase for stratification.

Intervention

Vinblastine monotherapy: 6 mg/m2 (max 10 mg) intravenous (i.v.) for a total treatment duration of 24 months, weekly for 18 months and bi-weekly for the final 6 months

Study burden and risks

Although the treatment within this protocol takes longer than the current standard therapy, it is anticipated that the toxicity and burden are lower. Patients who can be cured by Vinblastine are spared both acute and late toxicity of the standard multi-agent chemotherapy including Etoposide, alkylators and anthracyclines. During the treatment they can go to school / work and have no major restrictions in daily live in contrast to standard intensive multi-agent chemotherapy.

All diagnostic assessments are comparable to the standard of care assessments. When participants consent to add-on studies, we will draw extra blood (max. 15x 10 ml) and ask them to complete Quality of Life questionnaires (5 timepoints).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

* Stratification into the standard risk group (SR):
-Newly diagnosed ALK-positive ALCL
-Stage I not completely resected, or stage II or stage III
-MDD negative
* Age < 18 years
* Informed consent of the parents/legal guardians (and assent of the competent child) for study participation and data collection, storage and handling given before study entry
* Participation in national / study group's reference pathology
* Follow-up for at least 3 years after enrolment is expected
* Application of a highly effective contraceptive method (Pearl index <1) in sexually active patients
* Application of one intrathecal triple therapy with Methotrexate, Cytarabine and Prednisolone (or Hydrocortisone respectively)

Exclusion criteria

* Progressive disease during a possible clinically indicated pre-phase treatment before inclusion in the study
* Steroids for more than 2 days or chemotherapy pre-treatment before taking the screening sample for MDD
* Chemotherapy pre-treatment before start of the study treatment except for
-the obligatory initial intrathecal triple therapy with Methotrexate, Cytarabine and Prednisolone (or Hydrocortisone respectively)
-a possible clinically indicated pre-phase including up to 5 days of steroids combined with up to 3 doses of Vinblastine (or up to 2 doses of Cyclophosphamide)
* Pregnancy or lactation period
* Contraindications for the treatment with Vinblastine:
-hypersensitivity against VBL or other vinca-alkaloids
-leukopenia, other than in the context of the ALCL
-severe uncontrolled infection
* Other medical, psychiatric, familial or social condition prohibiting

treatment according to the protocol

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2022
Enrollment:	10
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	21-04-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	29-07-2022
Application type:	First submission

Review commission:	METC NedMec
Approved WMO Date:	30-09-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-11-2022
Application type:	Amendment
Review commission:	METC NedMec

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
EU-CTR	CTIS2022-501454-11-00
EudraCT	EUCTR2017-002935-40-NL
CCMO	NL78684.041.21