A phase 2, single arm, multi center trial evaluating the efficacy of the combination of sirolimus and cyclophosphamide in metastatic or unresectable myxoid liposarcoma and chondrosarcoma.

Published: 11-12-2014
Last updated: 07-02-2025

- To evaluate the treatment efficiency by time to progression according to RECIST 1.1

Ethical review	Approved WMO
Status	Completed
Health condition type	Skeletal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON47217

Source
ToetsingOnline

Brief title
COSYMO

Condition

- Skeletal neoplasms malignant and unspecified

Synonym
bone cancer, chondrosarcoma

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Eurosarc en KWF aangevraagd,Pfizer

Intervention

Keyword: chondrosarcoma, liposarcoma, phase II, sirolimus

Outcome measures

Primary outcome

Time to progression after start of treatment according to RECIST 1.1

Secondary outcome

- Translational exploratory tumour pharmacodynamic analysis

- Toxicity according to CTC version 4.0

- Objective response defined as a partial or complete response occurring after start of treatment according to RECIST1.1

- Overall survival from start of treatment until death

- Time to progression during sirolimus/cyclophosphamide treatment (TTP2) divided by time to progression before start of this treatment TTP1 (=growth modulation index)

Study description

Background summary

Chondrosarcoma and liposarcoma consists of different subtypes with a wide range of patient survival. Current treatment options consist of wide surgical resection, however for patients with a local recurrence or metastatic disease the outcome is poor. New treatment options being evaluated and mouse models show in vivo that mTOR inhibition can prevent tumour growth. mTOR is an kinase that is present in two complexes and thereby activates multiple pathways. Aberrant mTOR signalling is known to be involved in cancer cell survival. Several clinical studies for patients with bone or soft tissue sarcoma treated with mTOR inhibitors have been conducted and they show promising results. From these studies we can conclude that the combination of an mTOR inhibitor with cyclophosphamide shows promising results in chondrosarcoma. With the lack of other treatment options for unresectable or metastatic chondrosarcoma or myxoid liposarcoma the Eurosarc consortium decided to treat these patients in a standardised way according to a common protocol with the combination of sirolimus and cyclophosphamide using the growth modulation index for evaluation.

Study objective

- To evaluate the treatment efficiency by time to progression according to RECIST 1.1

Study design

Patients will be treated with the combination of sirolimus and cyclophosphamide. The treatment will be given in a 4 week cycle with cyclophosphamide in a dose of 200mg oral on day 1 to 7 and day 15 to 21. Sirolimus will be given daily at a dose of 4mg oral. Patients will be evaluated according to the growth modulation index on day 0 and after each second cycle. For translational research three core biopsies are taken from the patients maximum 21 days before the start of the treatment unless a paraffin block or 20 unstained slides from the primary tumour are available and after 7-8 weeks of treatment.

Intervention

cyclophosphamide 200mg oral on day 1 to 7 and day 15 to 21.
Sirolimus 4mg oral daily

Study burden and risks

Patient will get one or two extra tumour biopsies with the known risks

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

- Pathologically proven conventional chondrosarcoma
- Or pathologically proven myxoid liposarcoma with PIK3CA mutation or PTEN loss
- Or pathologically proven mesenchymal or dedifferentiated chondrosarcoma
- Or pathologically proven clear cell chondrosarcoma
- Patients of 18 years and up
- Documented radiographic progression of disease according to RECIST 1.1 criteria in last 6 months
- Adequate bone marrow function (Hb >= 6.0 mmol/L, absolute neutrophil count >= 1.5 x 109/L, platelets >= 80 x 109/L)
- Availability of archival tumor material for central review
- Written signed informed consent
- Ability to adhere to the study visits and all protocol requirements

Exclusion criteria

- Previously treated with an mTOR inhibitor
- Known to be allergic to cyclophosphamide
- Life expectancy of less than 3 months
- No measurable lesions according to RECIST 1.1
- ECOG Performance status >2
- Major surgery less than 4 weeks prior to start of treatment
- Known human immunodeficiency virus (HIV) positivity
- A decreased renal function with calculated GFR < 30 ml/min
- Systemic anti-cancer therapy within 28 days prior to the first dose of study drug , or radiotherapy to an index (or target) lesion within 21 days prior to the first dose of study drug
- Pregnant or lactating women
- Other invasive malignancies diagnosed within the last 5 years, except non-melanoma skin cancer and localised cured prostate and cervical cancer

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	15-12-2014
Enrollment:	23
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	endoxan
Generic name:	cyclophosphamide

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

Ethics review

Approved WMO Date:	11-12-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	12-12-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-09-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	08-09-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	05-03-2018
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	03-04-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	23-05-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	15-08-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	03-09-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	22-10-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
Other	COSYMO
EudraCT	EUCTR2013-005155-32-NL
CCMO	NL47304.058.14