Phase II trial of cabazitaxel in metastatic or inoperable locally advanced dedifferentiated liposarcoma

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Soft tissue neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON45497

Source
ToetsingOnline

Brief title
EORTC 1202-STBSG Cabazitaxel / liposarcoma

Condition

- Soft tissue neoplasms malignant and unspecified

Synonym
locally advanced liposarcoma

Research involving
Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: EORTC Soft Tissue and Bone Sarcoma group,Sanofi-aventis

Intervention

Keyword: cabazitaxel, dedifferentiated liposarcoma

Outcome measures

Primary outcome

The primary endpoint will be progression free survival, assessed at 12 weeks after start of treatment. Progression will be defined according to RECIST 1.1.

Secondary outcome

-Time to progression

- Progression free survival

-Overall survival

-Objective tumor response as defined by RECIST 1.1 (Ref. 20) where the dedifferentiated component is targeted for measurements of local disease (section 7.5,1 .1)

-Objective tumor response as defined by RECIST 1.1 where both well differentiated and dedifferentiated components are included in measurements of local disease (measurements to be performed by central review only)

-Time to onset of response (for patients achieving an objective response)

- Duration of response (for patients achieving an objective response)

- Safety (CTCAE Version 4.0)

Study description

Background summary

Soft tissue sarcomas have a historical lack of investment in research due to their rarity but there is a recognized need to improve treatment options

through clinical trials tailored to individual subtypes. In the case of dedifferentiated liposarcoma, anti-microtubular agents show promise and the aforementioned index patient's experience suggests that cabazitaxel, for which extensive safety data is available, should be formally assessed. The relative paucity of alternative treatment options with clinically meaningful benefit for this group of patients, who are often young and fit,
has led to the development of this phase II study, assessing progression-free survival rates at 12 weeks with cabazitaxel as second-line treatment in metastatic or inoperable locally advanced dedifferentiated liposarcoma.

Study objective

The main objective is to determine whether cabazitaxel demonstrates sufficient antitumor activity (as measured by progression free survival at 12 weeks) in pre-treated patients with metastatic or inoperable locally advanced DD liposarcoma to justify further investigation in the phase III setting.

Study design

This trial will be an international, multi-center, open label phase II trial where patients with metastatic or locally advanced DD liposarcoma will be treated with cabazitaxel.

Intervention

not applicable

Study burden and risks

60 min.

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

Registration step 1
-Local diagnosis of DD liposarcoma.
-Mandatory availability for shipment of formalin-fixed, paraffin-embedded, tumor-containing tissue blocks from primary tumor and/or metastatic site. Information on previous histopathology reports and previous molecular analysis will be entered in an electronic CRF, to accompany the tissue sample(s).
-If a block cannot be provided, the following should be submitted:
EORTC-1202-STBSG Ph II Cabazitaxel DD liposarcoma Version 3.0 22/75 May 10, 2016
-For cases that will be reviewed in UK (refer to chapter 15.3): 4 x 1 micron sections on coated slides, one thin H&E stained section and 20 unstained sections of usual thickness (2-4 micron) on coated slides.
-For cases that will be reviewed in France (refer to chapter 15.3): 3 x 4 micron sections on unstained (coated) slides for FISH and 15 unstained slides (4 micron) for immunohistochemistry.
-Before patient registration step 1, written informed consent for central collection of tissue block or slides and any other trial-specific procedures must be obtained from the patient according to ICH/GCP, and national/local regulations, allowing for collection, storage and analysis of tissue and screening procedures.;Registration step 2
-Central pathology confirmation of DD liposarcoma within 3 weeks after registration step 1.
-Radiological or histological diagnosis of inoperable locally advanced or metastatic disease, with evidence of disease progression within the past 6 months prior to registration step 2.
-Clinically and/or radiographically documented measurable disease within 28 days prior to registration step 2.
At least one site of disease must be unidimensionally measurable according to RECIST 1.1
-Note: as DD liposarcoma commonly arises on a background of well differentiated liposarcoma, and as the latter well differentiated element can remain stable for prolonged

periods without therapy, we recommend that when defining radiological measurable or target lesions per RECIST 1.1, specially in the region of the primary tumor mass if present, these should be chosen to include specifically the solid or higher density elements of the disease (which tend to correlate pathologically with the DD element), and not the low density fatty elements of the disease, which tend to correlate with the well differentiated element.
-One previous chemotherapy regimen for locally advanced or metastatic DD liposarcoma (this could include pre-operative chemotherapy for primary disease).
-Age 18-75 years old
-WHO performance status 0-1
-Adequate haematological, renal and hepatic function
-Estimated life expectancy > 3 months
-All related adverse events from previous therapies must have recovered to * Grade 1 (except alopecia).
-Women of child bearing potential must have a negative serum pregnancy test within 72 hours prior to the first dose of study treatment.
-Patients of childbearing / reproductive potential should use adequate birth control measures, as defined by the investigator. A highly effective method of birlh control is defined as those which result in low failure rate (i.e. less than 1% per year) when used consistently and correctly.
-lt is recommended that patients do not attempt to become pregnant or to breast feed after exposure to these chemotherapy agents, as there is no available data on safety. lf despite this advice patients wish to do so, then it is recommended a minimum of 6 months should first be allowed to elapse from the last received dose.
-Men should use reliable contraception throughout treatment and are recommended to continue this for up to 6 months after the last dose of cabazitaxel.
-Absence of any psychological, familial, sociological or geographical condition potentially hampering
compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial.

Exclusion criteria

Registration step 2
-more than 1 prior molecularly targeted therapy (e.9. CDK4 inhibitor). Any such prior therapy must be completed at least 2-4 weeks prior to registration step 2.
-inflammation of the urinary bladder (cystitis)
-symptomatic CNS metastases. lf asymptomatic CNS metastases are present these should have been previously treated and stable for at least 3 months and patient should not require maintenance steroids.
-other invasive malignancy within 5 years, with the exception of non-melanoma skin cancer, localized cervical cancer, localized and presumably cured prostate cancer or adequately treated basal or squamous cell skin carcinoma.
-significant cardiac disease: i.e. active ischaemic heart disease or cardiac failure (NYHA (Appendix D) > class 1)
-uncontrolled severe illness or medical condition (including acute infection, uncontrolled

diabetes), other than the DD liposarcoma
-concurrent or planned treatment with strong inhibitors or inducers of cytochrome P450 3A415 (a -one week wash-out period is necessary for patients who are already on these treatments)
known hypersensitivity to taxanes or their excipients (cabazitaxel, like docetaxel, is solubilized in polysorbate 80 and ethanol)

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-09-2018
Enrollment:	9
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	14-02-2017
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-03-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-05-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-05-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-05-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-05-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-06-2020
Application type:	Amendment
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	EUCTR2012-003672-39-NL
ClinicalTrials.gov	NCT01913652
CCMO	NL60717.091.17