Randomized phase II trial of cabazitaxel or prolonged infusional ifosfamide in metastatic or inoperable locally advanced dedifferentiated liposarcoma

Published: 06-01-2015
Last updated: 21-04-2024

The main objective is to determine whether cabazitaxel or prolonged infusional ifosfamide demonstrate sufficient antitumor activity (as measured by progression free survival at 12 weeks) in pre-treated patients with metastatic or inoperable locally…

Ethical review	Not approved
Status	Will not start
Health condition type	Soft tissue neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON42166

Source
ToetsingOnline

Brief title
EORTC 1202-STBSG Cabazitaxel/Ifosfamide DD 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

Intervention

Keyword: cabazitaxel, dedifferentiated liposarcoma, ifosfamide

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

Secondary endpoints will include

* 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. Prolonged infusional ifosfamide also shows promise, with a new way of administering an established active drug, supported by encouraging responses and safety data within early case series. 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, or prolonged ifosfamide, as second-line treatment in metastatic or inoperable locally advanced dedifferentiated liposarcoma.

Study objective

The main objective is to determine whether cabazitaxel or prolonged infusional ifosfamide demonstrate 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 of the efficacy of these treatment options 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 randomized between two parallel single agent treatment arms - cabazitaxel or prolonged infusional ifosfamide.
Crossover is not planned.

Intervention

Patients will be randomized in a 1:1 ratio, stratified by institution, performance status (0 vs 1) and prior therapy (ifosfamide vs. molecularly targeted vs. other), to either
* Treatment arm 1: Cabazitaxel will be administered at a dose of 25 mg/m² by intravenous infusion, over 1 hour, on day 1 of each 21 day cycle. Treatment should be administered until disease progression, unacceptable toxicity or patient's refusal.
* Treatment arm 2: Ifosfamide will be administered at a dose of 1 g/m²/day,

along with mesna at 550 mg/m²/day, both as a prolonged intravenous continuous infusion via a central venous catheter and an appropriate ambulatory infusional pump (per local institutional policies) for days 1 to 14 of each 28 day cycle.Treatment will be administered until disease progression, unacceptable toxicity or patient's refusal.

Study burden and risks

300 minutes per cycle in the ifosfamide treatment arm, 450 minutes per cycle in the cabazitaxel treatment arm.

The prolonged infusional ifosfamide will be delivered through an ambulatory pump and central venous catheter in the upper arm for 14 days. This increases changes of infection and thrombosis. The catheter is treated weekly and patients receive instructions to prevent infections. In addition, the ambulatory pump will be changed and turned off during these treatment visits.

Extra blood assessments will be performed compared to regular treatment. This is three times more frequent per cycle in the ifosfamide treatment arm and two times more frequent per cycle in the cabazitaxel treatment arm.

Contacts

Public
European Organisation for Research in Treatment of Cancer (EORTC)

Avenue E. Mounier 83/11
Brussel 1200
BE
Scientific
European Organisation for Research in Treatment of Cancer (EORTC)

Avenue E. Mounier 83/11
Brussel 1200
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Local diagnosis of dedifferentiated liposarcoma
- Mandatory availability for shipment of formalin-fixed, paraffinembedded, tumor-containing tissue blocks from primary tumor and/or metastatic site. Or if not available: 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 (cases to be reviewed in UK), or, 3 x 4 micron sections on unstained (coated) slides for FISH and 15 unstained slides (4 micron) for immunohistochemistry (cases to be reviewed in France)
- 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
- Central pathology confirmation is required before starting the patient screening
- Radiological or histological diagnosis of inoperable locally advanced or metastatic disease, with evidence of disease progression within the past 6 months prior to randomization
- Clinically and/or radiographically documented measurable disease within 21 days prior to randomization. At least one site of disease must be unidimensionally measurable according to RECIST 1.1
- One previous chemotherapy regimen for locally advanced or metastatic dedifferentiated liposarcoma (this could include pre-operative chemotherapy for primary disease if subsequent complete resection was not achieved).
- Not more than 1 prior molecularly targeted therapy (e.g. CDK4 inhibitor). Any such prior therapy must be completed at least 4 weeks prior to randomization.
- Age 18-70 years old
- WHO performance status 0-1
- Adequate haematological, renal and hepatic function within 7 days prior to randomization: Haematology: haemoglobin > 90 g/L or 5.6 mmol/L, absolute granulocytes > 1.5 x 109/L, platelets > 100 x 109/L
Biochemistry: creatinine clearance (CrCl) * > 60 ml/min Hepatic: bilirubin < upper limit of normal (ULN) of institutional limits, ALT and/or AST< 2.5 x ULN, albumin > 30 g/L. If isolated elevated bilirubin < 2 x ULN normal and Gilbert's syndrome suspected, suggest repeating bloods after food. If bilirubin normalizes then this is acceptable.
- 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 birth control is defined as those which result in low failure rate (i.e. less than 1% per year) when used consistently and correctly.
- 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

- Inflammation of the urinary bladder (interstitial cystitis), impaired renal function and/or obstructions of the urine flow.
- Symptomatic CNS metastases. If 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.
- Previous encephalopathy of any cause or other significant neurological condition
- Other invasive malignancy within 5 years, with the exception of nonmelanoma 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 dedifferentiated liposarcoma
- concurrent or planned treatment with strong inhibitors or inducers of cytochrome P450 3A4/5 (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)
- Known hypersensitivity to ifosfamide

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	13
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO

Date:	06-01-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Not approved

Date:	25-08-2015
Application type:	First submission
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	NL51542.091.14