A Randomized, Open-label, Multicenter, Phase 3 Study to Compare the Efficacy and Safety of Eribulin with Dacarbazine in Subjects with Soft Tissue Sarcoma.

Published: 12-05-2011
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Primary:* To compare overall survival (OS) in subjects with advanced soft tissue sarcoma ([STS], one of two subtypes: adipocytic [ADI] or leiomyosarcoma [LMS]) when treated with eribulin (Arm A) or dacarbazine (Arm B).Secondary:* To compare...

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

Summary

ID

NL-OMON35766

Source
ToetsingOnline

Brief title
E7389-G000-309

Condition

- Soft tissue neoplasms malignant and unspecified

Synonym
soft tissue sarcoma

Research involving
Human

Sponsors and support

Primary sponsor: Eisai

Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: adipocytic, eribulin, leiomyosarcoma, soft tissue sarcoma

Outcome measures

Primary outcome

Overall survival, measured from the date of randomization until date of death from any cause. Subjects who are lost to follow-up and the subjects who are alive at the date of data cut-off will be censored at the date the subject was last known alive.

Secondary outcome

Secondary Endpoints:

* Progression-free survival, defined as the time from the date of randomization to the date of first documentation of disease progression, or date of death (whichever occurs first). Progression free survival censoring rules will apply, and will be defined in the SAP.
* Progression-free rate at Week 12, defined as the proportion of subjects alive and progression-free at 12 weeks from the date of randomization.
* Clinical Benefit Rate, the proportion of subjects who have best overall response of CR + PR + dSD.

Exploratory Endpoints:

* Objective response rate, the proportion of subjects who have overall response of CR and PR.
* Disease control rate, the proportion of subjects who have best overall

response of CR + PR + SD.

* Durable Stable Disease, defined as the proportion of subjects who have the

duration of SD *11 weeks.

* Quality of Life Scores, measured using the QLQ C30 and EQ-5D questionnaires.

Overige evaluatiecriteria:

* Pharmacokinetic

* Pharmacodynamic

* Relationship between pharmacokinetic and pharmacodynamic

* Safety

* Assessment of quality of life

Study description

Background summary

Approximately half of all STS subjects with intermediate or high-grade tumors develop metastatic disease requiring systemic treatment. The median survival of subjects that develop metastases is approximately 12 months, and only a small subgroup of these subjects achieve long term survival.

Anthracyclines are the first-line therapy for advanced disease. Response rates of * 20% has been reported with doxorubicin alone or in combination with ifosfamide, however the median overall survival of patients with metastatic STS has not improved beyond 12 months. While the majority of patients receive first line chemotherapy for advanced STS, the rate of delivery of later lines of therapy falls quickly after failure of first line therapy. Of those patients receiving adjuvant or first line chemotherapy, approximately half will receive a 2nd line regimen. There is limited clinical data to support the selection of the best treatment options in second-line.

Eribulin has demonstrated activity in advanced STS in an EORTC Phase 2 study. In this trial the Efficacy and Safety of Eribulin is studied, compared with

Dacarbazine.

Study objective

Primary:
* To compare overall survival (OS) in subjects with advanced soft tissue sarcoma ([STS], one of two subtypes: adipocytic [ADI] or leiomyosarcoma [LMS]) when treated with eribulin (Arm A) or dacarbazine (Arm B).

Secondary:
* To compare progression-free survival (PFS) between Arm A and Arm B.
* To compare progression-free rate at Week 12 (PFR12wks) between Arm A and Arm B.
* To compare the clinical benefit rate ([CBR], complete response (CR), partial response (PR) + durable stable disease ([dSD], duration of stable disease (SD)
* 11 weeks) between Arm A and Arm B.
* To compare the safety and tolerability between Arm A and Arm B.
* To characterize the population pharmacokinetics (PK) of eribulin in subjects with STS.

Exploratory:
* To compare:
- Overall response rate ([ORR] CR and PR),
- Disease control rate ([DCR], CR + PR + stable disease [SD]),
- dSD,
between Arm A and Arm B.
* To explore the relationship between exposure to eribulin and pharmacodynamic biomarkers and efficacy.
* To explore the relationship between exposure to eribulin and adverse events.
* To investigate and identify blood and tumor biomarkers which can be correlated with safety and efficacy endpoints.
* To compare quality of life (QoL) scores between Arm A and Arm B.

Study design

This is a Randomized, Open-label, Multicenter, Phase 3 Study

Intervention

Arm A: eribulin mesylate 1.4 mg/m2, as an IV bolus infusion over 2-5 minutes on Days 1 and 8 of every cycle, where the duration of each cycle is 21 days.
Arm B: dacarbazine 850 mg/m2, or 1,000 mg/m2, or 1,200 mg/m2 (depending on the subject*s clinical status), IV infusion over 15-30 minutes on Day 1 of every cycle, where the duration of each cycle is 21 days.

Study burden and risks

Assuming a maximum estimated participation period of approximately 10 months (screening, baseline, 14 cycles & end of treatment):

- 14x comprehensive physical examination (incl. neurological examination)
- 5x symptom-directed physical exam
- 22x vital signs
- 16x weight
- 1x length
- 30x ECG
- 20x blood sample
- 15x urine collection
- 6x tumour assessment (MRI/CT)
- 2x bone scan
- 17x quality-of-life questionnaires

Also refer to table 2 and 3 of the protocol for a complete overview of the study visits and procedures.

The most common side effects and risks of Eribulin are: leucopenia, neutropenia, anemia, thrombocytopenia, periferal neuropathy, nausea, vomiting, diarrhea, constipation, headache, joint pain and muscle pain, hair loss, loss of appetite, elevated temperature.
Less common side effects of Eribulin are: gastrointestinal problems, respiratory problems, infections, depression and insomnia, elevated liver function test, decrease of potassium, magnesium and phosphate, dehydration, increase of glucose, increased heart rate, dry mouth, eyes watering, nose bleed, fluid retention, weight loss and dizziness, tinnitus, interstitial lung disease, angioedema, kidney failure, dysuria, haematuria, proteinuria, deep vein thrombosis and pulmonary embolism, allergic reactions.

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

1. Histologically confirmed diagnosis of soft tissue sarcoma of high or intermediate grade with one of the following histological subtypes: Adipocytic sarcoma (including Dedifferentiated, Myxoid, Round Cell, Pleomorphic), Leiomyosarcoma.
2. Documented evidence of advanced adipocytic or leiomyosarcoma, incurable by surgery and/or radiotherapy.
3. Subjects should have received standard therapies for advanced soft tissue sarcoma which must have included an anthracycline (unless contraindicated) with or without ifosfamide and then at least one additional regimen after failure of the anthracycline.
4. Radiographic evidence of disease progression by RECIST criteria on or after the last anti-cancer therapy within the 6 months prior to randomization.
5. Presence of measurable disease meeting the following criteria:
a. At least one lesion of * 1.0 cm in long-axis diameter for non lymph nodes or * 1.5 cm in short-axis diameter for lymph nodes which is serially measurable according to RECIST 1.1 using either computerized tomography or magnetic resonance imaging or panoramic and close-up color photography.
b. Lesions that have had radiotherapy must show evidence of progressive disease based on RECIST 1.1 to be deemed a target lesion.

Exclusion criteria

1. Subjects who have received any anti-cancer therapy, including radiotherapy, cytotoxic, hormonal, biological (including humanized antibodies) and targeted agents within 21 days, or any investigational agent within 30 days, prior to randomization.
2. Subjects who have not recovered from acute toxicities as a result of prior anti-cancer therapy to * Grade 1, according to Common Terminology Criteria for Adverse Events (CTCAE), except for peripheral neuropathy (see Exclusion 6) and alopecia.
3. Subjects that have previously been treated with dacarbazine or participated in a study with

eribulin (whether treated with eribulin or not).
4. Radiation therapy encompassing > 30% of bone marrow.

Study design

Design

Study phase:	3
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):	08-12-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	eribulin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	dacarbazine medac
Generic name:	dacarbazine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	12-05-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2014
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	EUCTR2010-024483-17-NL
ClinicalTrials.gov	NCT01327885
CCMO	NL36010.018.11