Trabectedin for recurrent grade II or III meningioma: a randomized phase II study of the EORTC Brain Tumor Group.

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

Summary

ID

NL-OMON44858

Source
ToetsingOnline

Brief title
EORTC 1320

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
meningioma

Research involving
Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: bedrijf,Pharma Mar

Intervention

Keyword: meningioma, recurrent, trabectedin

Outcome measures

Primary outcome

* Progression Free Survival (PFS)

Secondary outcome

* Progression Free Survival at 6 months (PFS-6), median PFS (mPFS)

* Best overall response (BOR). Objective response (CR/PR), rate and median

duration. Complete response (CR), rate and median duration.

* Overall survival (OS), OS probability at 6 (OS6) and 12 months (OS12), median

OS (mOS)

* Safety (CTCAE v.4.0)

* Health-related Quality of life (Qol)

Study description

Background summary

There is no proven effective or standard treatment for recurrent grade II or III meningioma after maximal treatment with surgery and radiotherapy. Trabectedin is an anti-cancer agent which has been registered for treatment of recurrent or extensive soft-tissue sarcoma and is currntly under investigation for mesothelioma and other sarcoma types. Meningiomas are considered to be related to sarcomas. In a recent study strong activity of trabectedin has been seen on meningioma cell lines. Furhtermore, meningiomas frequently show extensive infiltration of macrofages and strong angiogenesis. Both macrophages and angogenesis are therapeutic targets of trabectedin.

Study objective

The objective of the study is to investigate whether trabectedin demonstrates sufficient antitumor activity against recurrent grade II or III to justify

further investigation in phase III or as adjuvant therapy for newly diagnosed disease after resection and radiotherapy.

Study design

This is a randomized open label multicenter comparative phase II trial. The Korn design will be applied.
Patients will be randomized at the EORTC headquarters after verification of the eligibility criteria to receive one of the following:
* Arm 1 (treatment): Trabectedin delivered as a 24-hour infusion every 3 weeks (day 1 of each 21-day cycle) at a starting dose of 1.5 mg/m2 body surface area (BSA), until one of the treatment withdrawal criteria has been met.
* Arm 2 (control): Best investigators` choice.
There will be a 2:1 randomisation of trabectedin vs control

Intervention

treatment with intravenous trabectedin every 3 weeks until progression or unacceptable toxicity

Study burden and risks

Before inclusion into the study standard blood tests need to be performed, as well as an ECG, investigation of left ventricular ejection fraction, tumor evaluation by cranial MRI or, if applicable, CT of thorax and abdomen, and pregnancy test in women of reproductive potential. Patients must be examined by a neurologist and an oncologist and must fill out quality of life forms. this does not entail a significant risk.

Trabectedin is administered as a 24-hour infusion for which patients should be admitted to hospital and preferably have a central venous access device. The central venous device carries a small risk of infection, thrombosis or hemorrhage. Trabectedin is generally well tolerated with mostly treatable and reversible side-effects such as increased hepatic enzymes, myelosuppression, nausea, vomiting and fatigue. Occasionally increased creatin phosphokinase and rhabdomyolysis has been observed.

Trabectidin is administered in in-patient setting once every 3 weeks as long as it is tolerated and no tumor progression occurs. Prior to each cycle standard laboratory tests are performed. additionally once every 3 cycles tumor imaging is performed, quality of life questionnaires must be filled out 5 times during the whole study and 2 further pregnancy tests must be done in females of reproductive potential.

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

*Age 18 or older;
*Histological diagnosis of WHO grade II (chordoid meningioma, clear cell meningioma, atypical meningioma) or WHO grade III (papillary meningioma, rhabdoid meningioma, anaplastic/malignant meningioma) according to WHO 2007 classification;
*Radiologically documented progression of any existing tumor (growth 25% in the last year) or appearance of new lesions (including intra- and extracranial manifestations);
*Measurable disease (10 x10 mm) on cranial MRI or CT thorax/abdomen no more than 2 weeks prior to randomization;
*WHO performance status 0-2;
*Adequate liver, renal and hematological function within 2 weeks prior to randomization, defined as:
*Neutrophils * 1.5 x 109/L, hemoglobin * 9 g/dL or hemoglobin * 5.6 mmol/L, platelets * 100 x

109/L;
*Total Bilirubin * ULN, SGPT/ALT and SGOT/AST * 2.5 x ULN;
*Alkaline phosphatase * 2.5 x ULN; if alkaline phosphatase 2.5 ULN, hepatic isoenzymes 5-nucleotidase or gamma glutyamyltransferase (GGT) must be within the normal range;
*Albumin * 30 g/L;
*Serum creatinine * 1.5 x ULN;
*Creatinine clearance 30 ml/min as calculated by Cockcroft and Gault formula (see Appendix E)
*Creatine phosphokinase (CPK) * 2.5 x ULN
*Normal cardiac function (LVEF assessed by MUGA or ECHO within normal range of the institution), normal 12 lead ECG (without clinically significant abnormalities). The following unstable cardiac conditions are not allowed:
*Congestive heart failure
*Angina pectoris
*Myocardial infarction within 1 year before registration/randomization
*Uncontrolled arterial hypertension defined as blood pressure * 150/100 mm Hg despite optimal medical therapy
*Arrhythmias clinically significant
*Life expectancy of at least 9 weeks
*Women of child bearing potential (WOCBP) must have a negative serum (or urine) pregnancy test within 72 hours prior to randomization and again 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, during the study treatment period and for at least 3 months after the last study treatment. Men who are fertile must use effective contraception during treatment with trabectedin and for 5 months thereafter. A highly effective method of birth control is defined as one which results in low failure rate, i.e. less than 1% per year, when used consistently and correctly.
*Female subjects who are breast feeding should discontinue nursing prior to the first dose of study treatment and until 3 months after the last study treatment.
*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
*Patients with a buffer range from the normal values of +/- 5 % for hematology and +/- 10% for biochemistry are acceptable. A maximum of +/- 2 days for timelines may be acceptable
*Before patient randomization, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion criteria

*More option for local therapy (resection or radiotherapy) after maximal feasible surgery and radiotherapy.;*Prior systemic anti-neoplastic therapy for meningioma (patient may have received prior radionuclide therapy).;*History of any other invasive malignancy within the last 5 years (except adequately treated non-melanoma skin cancer, clinicaly localized and very low risk prostate cancer, and adequately treated cervical intraepithelial neoplasia).;*Serious illness or medical conditions, specifically: active infectious process; chronic active liver

disease, including chronic hepatitis B, C or cirrhosis.;*Concomitant use of any other investigational agent or phenytoin.;*Known MRI or CT, including contrast media, contraindications.

Study design

Design

Study phase:	2
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):	27-11-2015
Enrollment:	3
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	06-05-2015
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-09-2015
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-05-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2014-002446-47-NL
ClinicalTrials.gov	NCT02234050
CCMO	NL51924.078.15