An open-label multicenter phase II study of pazopanib in metastatic and locally advanced hormone-resistant endometrial cancer.

Published: 21-03-2011
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To increase progression-free survival at 3 months.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Uterine, pelvic and broad ligament disorders
Study type	Interventional

Summary

ID

NL-OMON39290

Source
ToetsingOnline

Brief title
PAZEC

Condition

- Uterine, pelvic and broad ligament disorders

Synonym
endometrial cancer, uterine corpus carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,GlaxoSmithKline

Intervention

Keyword: endometrial cancer, hormone-resistant, metastatic, pazopanib

Outcome measures

Primary outcome

Percentage of patients free of progression at 3 months.

Secondary outcome

Response rate, progression free survival, overall survival,

tolerability/toxicity.

Study description

Background summary

Endometrial cancer is mainly diagnosed in the 6th and 7th decade of life, and is often curable by surgery and/or radiotherapy. However, in the approximately 40% of patients with either recurrent or metastatic disease, survival is poor. Although hormonal therapy with progestins is well tolerated, it yields a response rate of only 15-30% overall. These responses occur almost exclusively in well-differentiated, progesterone receptor-positive cancers which show a response rate of 75%, vs. 7% in poorly differentiated tumors. Even well-differentiated tumors become progestin resistant at some point. In hormone resistant tumors, combination chemotherapy with doxorubicin-cisplatin(-paclitaxel) leads to response rates of over 40%, but is generally poorly tolerated in this elderly patient group. Median progression free survival without treatment is 2 months, and with combination chemotherapy 4-8 months. Median overall survival does not exceed 12 months in most series, with maximal OS reported in a randomized trial being 15 months using TAP. Carboplatin-paclitaxel schedules, which are less toxic, are currently being tested, but even this schedule is not always suitable for the endometrial cancer population with frequent comorbidities. There is therefore a pressing need for effective systemic treatment with an acceptable toxicity profile for this patient group.

Angiogenesis inhibition is a novel cancer treatment that has proven efficacy in a variety of tumors, such as colorectal cancer, breast cancer and lung cancer. Angiogenesis plays an important part in the progression of endometrial cancer. VEGF levels in endometrium cancer correlate with established poor prognostic

factors, and VEGF-A is overexpressed in endometrial cancer but not in benign endometrial hyperplasia. The oral small molecule tyrosine kinase inhibitor (TKI) pazopanib targets the ATP-binding site of the VEGF receptor (in addition to the PDGHF and c-kit receptors). There is evidence of single agent activity of pazopanib against renal cell cancer, ovarian cancer and sarcomas. Pazopanib is well tolerated. The main side-effects are hypertension, fatigue and gastro-intestinal symptoms. In view of the importance of angiogenesis in the sustenance of endometrial cancer, pazopanib is an ideal candidate to study in this disease.

Study objective

To increase progression-free survival at 3 months.

Study design

Multi-center open label non-randomized phase II study.

Intervention

Pazopanib 800 mg once daily PO.

Study burden and risks

Patients will visit the outpatient clinic at regular intervals, every 3 weeks for the first 12 weeks, every 4 weeks for the next 12 weeks, and every 6 weeks thereafter. At every visit blood will be drawn. Tumor assessment will take place regularly, every 6 weeks for the first 12 weeks, and every 12 weeks thereafter, for as long as patients continue study treatment. This is in essence not differemnt from the evaluations that would be considered standard in this patient group outside the realm of a study.
All patients will be exposed to pazopanib and therefore all may encounter side-effects. Serious side-effects are fortunately rare. The main side-effects are hypertension, fatigue and gastro-intestinal symptoms.

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. Written informed consent.
2. Age * 18 years
3. Eastern Cooperative Oncology Group (ECOG) performance status of 0-2.
4. Histologically or cytologically confirmed diagnosis of endometrial cancer.
5. Metastatic disease or locally advanced tumor not amenable to local therapy.
6. Documented progressive disease before enrolment.
7. Measurable lesions outside irradiated field or progressive measurable lesions in irradiated area.
8. Not eligible for hormonal therapy (because of negative hormone receptor/poor differentiation, or after failure of hormonal therapy)
9. Previous failure of chemotherapy, or refusal to undergo chemotherapy or chemo-naive patients not suitable for chemotherapy.
10. Adequate organ system function

Exclusion criteria

1. Prior malignancy.
Note: Subjects who have had another malignancy and have been disease-free for 5 years, or subjects with a history of completely resected non-melanomatous skin carcinoma or successfully treated in situ carcinoma are eligible.
2. History or clinical evidence of central nervous system (CNS) metastases or leptomeningeal

carcinomatosis, except for individuals who have previously-treated CNS metastases, are asymptomatic, with no radiological signs of progression and have had no requirement for steroids or anti-seizure medication for 6 months prior to first dose of study drug.
3. Clinically significant gastrointestinal abnormalities that may increase the risk for gastrointestinal bleeding or may affect absorption of investigational product.
4. Presence of uncontrolled infection.
5. Corrected QT interval (QTc) > 480 msecs using Bazett*s formula
6. History of major cardiovascular conditions within the past 6 months or poorly controlled hypertension, history of cerebrovascular accident including transient ischemic attack (TIA), pulmonary embolism or untreated deep venous thrombosis (DVT) within the past 6 months. Note: Subjects with recent DVT who have been treated with therapeutic anti-coagulating agents for at least 6 weeks are eligible.
7. Prior major surgery or trauma within 28 days prior to first dose of study drug and/or presence of any non-healing wound, fracture, or ulcer (procedures such as catheter placement not considered to be major).
8. Evidence of active bleeding or bleeding diathesis.
9. Treatment with any of the following anti-cancer therapies: radiation therapy, surgery or tumor embolization within 14 days prior to the first dose of pazopanib OR chemotherapy, immunotherapy, biologic therapy, investigational therapy or hormonal therapy within 14 days or five half-lives of a drug (whichever is longer) prior to the first dose of pazopanib

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):	09-01-2012
Enrollment:	55
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	21-03-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2013
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	EUCTR2011-000287-99-NL
CCMO	NL35873.018.11