Purpose

This clinical trial shall clarify the efficacy and safety of pazopanib in combination with weekly topotecan in patients with platinum-resistant or intermediate platinum-sensitive recurrent epithelial ovarian cancer, fallopian and peritoneal carcinoma.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Cancer</td>
<td>Drug: pazopanib in combination with weekly topotecan</td>
<td>Phase 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phase 2</td>
</tr>
</tbody>
</table>

Study Type: Interventional

Study Design:
- Endpoint Classification: Safety/Efficacy Study
- Intervention Model: Single Group Assignment
- Masking: Open Label
- Primary Purpose: Treatment

Official Title: A Phase I/II Study of Pazopanib and Weekly Topotecan in Patients With Platinum-resistant or Intermediate-sensitive Recurrent Ovarian Cancer

Resource links provided by NLM:

MedlinePlus related topics: Cancer Ovarian Cancer

Drug Information available for: Topotecan hydrochloride Topotecan Pazopanib

U.S. FDA Resources

Further study details as provided by Charite University, Berlin, Germany:

Primary Outcome Measures:

- Phase I: Assessment of dose-limiting toxicity in order to determine the maximum tolerated dose (MTD) of pazopanib in combination with weekly topotecan [ Time Frame: after 4 weeks ] [ Designated as safety issue: Yes ]
  
  Dose-limiting toxicities are defined as follows:
  - grade 3 or 4 non-hematologic toxicity other than nausea or vomiting
  - grade 3 or 4 thrombocytopenia (platelet count less than 50000/µl)
  - grade 4 neutropenia lasting ≥ 7 days or febrile neutropenia defined as ANC <1000 /µl concurrent with fever
  - Any grade 2 and more toxicity of cycle 1 other than nausea, vomiting, rash, alopecia or anemia, that persisted over 35 days.

- Phase II: Progression-free survival according to RECIST criteria [ Time Frame: up to 3.5 years ] [ Designated as safety issue: No ]
  - Phase II: Progression-free survival according to RECIST criteria

ClinicalTrials.gov Identifier: NCT01600573

First received: May 9, 2012
Last updated: May 16, 2012
Last verified: May 2012
History of Changes

How to Read a Study Record

A service of the U.S. National Institutes of Health

Trial record 4 of 16 for: TOPAZ

Previous Study | Return to List | Next Study

Pazopanib and Weekly Topotecan in Patients Recurrent Ovarian Cancer (TOPAZ)
Secondary Outcome Measures:

- Overall survival [Time Frame: up to 3.5 years] [Designated as safety issue: No]
  - Overall survival

- Response rate (CR, PR) according to RECIST criteria [Time Frame: up to 3.5 years] [Designated as safety issue: No]
  - Response rate (CR, PR) according to RECIST criteria

- Clinical benefit rate (CR, PR, SD) [Time Frame: up to 3.5 years] [Designated as safety issue: No]
  - Clinical benefit rate (CR, PR, SD)

- Duration of response [Time Frame: up to 3.5 years] [Designated as safety issue: No]
  - Duration of response

- Time to progression (TTP) [Time Frame: up to 3.5 years] [Designated as safety issue: No]
  - Time to progression (TTP)

- Evaluation of CA-125 tumour response [Time Frame: up to 3.5 years] [Designated as safety issue: No]
  - Evaluation of CA-125 tumour response

- Safety and tolerability of pazopanib in combination with weekly topotecan [Time Frame: up to 3.5 years] [Designated as safety issue: No]

  Incidence and type of AE in terms of:
  - All AE,
  - Related AE,
  - SAE,
  - Related SAE,
  - NCI-CTC (version 4.0) grade 3 and 4 AE,
  - Related NCI-CTC (version 4.0) grade 3 and 4 AE,
  - AE leading to treatment discontinuation,
  - Incidence of, and reason for, deaths.

- Quality of life as defined by EORTC-QLQ C 30 and Ovar 28 questionnaire [Time Frame: up to 3.5 years] [Designated as safety issue: No]
  - Quality of life as defined by EORTC-QLQ C 30 and Ovar 28 questionnaire

Estimated Enrollment: 68
Study Start Date: May 2012
Estimated Study Completion Date: June 2015
Estimated Primary Completion Date: June 2015 (Final data collection date for primary outcome measure)

### Arms

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental: pazopanib in combination with weekly topotecan</td>
<td>Drug: pazopanib in combination with weekly topotecan</td>
</tr>
<tr>
<td>pazopanib in combination with weekly topotecan</td>
<td>+ Topotecan as an IV infusion over 30 minutes on days 1, 8, and 15 of a 28 day cycle and</td>
</tr>
<tr>
<td></td>
<td>+ Pazopanib orally once daily continuous dosing in the following dose levels:</td>
</tr>
<tr>
<td></td>
<td>Phase I Trial:</td>
</tr>
<tr>
<td></td>
<td>Dose level -I: Topotecan weekly 3mg/m2, Pazopanib 400 mg Dose level I: Topotecan weekly 4mg/m2, Pazopanib 400 mg Dose level II: Topotecan weekly 4mg/m2, Pazopanib 600 mg Dose level III: Topotecan weekly 4mg/m2, Pazopanib 800 mg</td>
</tr>
<tr>
<td></td>
<td>Phase II Trial:</td>
</tr>
<tr>
<td></td>
<td>Phase II will either use the MTD as determined in Phase I or a lower dose if deemed necessary.</td>
</tr>
<tr>
<td></td>
<td>Other Name: pazopanib in combination with weekly topotecan</td>
</tr>
</tbody>
</table>

### Detailed Description:

This study is a prospective single-arm, open-label, multicenter phase I/II trial. The phase I-trial is a dose-escalation trial to determine the maximum tolerated dose (MTD) of pazopanib in combination with weekly topotecan. The phase II-trial is a single arm open-label trial to further assess the safety and the efficacy of this combination of treatment.

### Eligibility


2 von 4 25.02.2013 13:19
Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Female
Accepts Healthy Volunteers: No

Criteria
Inclusion Criteria:
- written informed consent
- histologically confirmed diagnosis of epithelial ovarian cancer, primary peritoneal carcinoma or fallopian tube cancer
- platinum resistant (recurrence within 6 months of a platinum-containing regimen) or platinum refractory (progression during platinum treatment) or intermediate platinum-sensitive (recurrence within 12 months after a platinum-based primary therapy) disease
- no more than 2 prior treatment regimens for epithelial ovarian cancer
- Age more than 18 years
- ECOG of 0 or 1
- adequate organ function
- measurable disease or evaluable disease according to RECIST criteria
- able to swallow and retain oral medication
- life expectancy of at least 12 weeks
- non-childbearing potential or negative serum pregnancy test of women of childbearing potential and agrees to use adequate contraception for 14 days before exposure to investigational product, through the dosing period, and for at least 6 months after the last dose of investigational product. Female subjects who are lactating should discontinue nursing prior to the first dose of study drug and should refrain from nursing throughout the treatment period and for 14 days following the last dose of study drug.

Exclusion Criteria:
- prior malignancies; subject who have had another malignancy and have been disease-free for 5 years which effect progression free survival, or subject with a history of completely resected non-melanomatous skin carcinoma or successfully treated in situ carcinoma are eligible
- History or clinical evidence of central nervous system (CNS) metastases or leptomeningeal carcinomatosis, except for individuals who have previously-treated CNS metastases, are asymptomatic, and have had no requirement for steroids or anti-seizure medication for 6 months prior to first dose of study drug. Screening with CNS imaging studies (computed tomography [CT] or magnetic resonance imaging [MRI]) is required only if clinically indicated or if the subject has a history of CNS metastases.
- clinically significant gastrointestinal abnormalities that might interfere with oral dosing or that may increase the risk for gastrointestinal bleeding
- Grade 3 or 4 diarrhea
- Any unstable or serious concurrent condition (e.g., active infection requiring systemic therapy)
- poorly controlled hypertension [defined as systolic blood pressure (SBP) of ≥140 mmHg or diastolic blood pressure (DBP) of ≥90 mmHg]
- Prolongation of corrected QT interval (QTc) >450 milliseconds using Bazett's formula
- History of any one or more of the following cardiovascular conditions within the past 6 months: Cardiac angioplasty or stenting; myocardial infarction; unstable angina; symptomatic peripheral vascular disease; coronary artery by-pass graft surgery
- Class III or IV congestive heart failure as defined by the New York Heart Association (NYHA)
- History of cerebrovascular accident including transient ischemic attack (TIA), pulmonary embolism or untreated deep venous thrombosis (DVT) within the past 6 months
- Macroscopic hematuria
- Hemoptysis in excess of 2.5 mL (or one half teaspoon) within 8 weeks of first dose of study drug
- Evidence of active bleeding or bleeding diathesis
- known endobronchial lesions and/or lesions infiltrating major pulmonary vessels and/or involvement of large pulmonary vessels by tumor
- prior major surgery or trauma within 14 days prior to first dose of study drug and/or presence of any non-healing wound, fracture, or ulcer
- Chemotherapy or radiation therapy or tumour embolization within 2 weeks prior to the first dose of study drug
- biological therapy, immunotherapy, hormonal therapy or treatment with an investigational agent within 14 days (for bevacizumab, 60 days) or 5 half-lives, whichever is longer prior to the first dose of study drug
- is unable or unwilling to discontinue predefined prohibited medications listed in the protocol (refer to section 4.2.3) for 14 days or five half-lives of a drug (whichever is longer) prior to first dose of study drug and for the duration of the study
- any ongoing toxicity from prior anti-cancer therapy that is >Grade 1 and/or that is progressing in severity, except alopecia
- known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to pazopanib
- psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol
- clinically assessed as having inadequate venous access for PK sampling
- any condition that is unstable or could jeopardize the safety of the patient and their compliance in the study
- legal incapacity or limited legal capacity
- Participation in another clinical study with experimental therapy within the 30 days before start of treatment
- Subjects housed in an institution on official or legal orders
- Pregnancy or lactation period

Contacts and Locations

3 von 4
25.02.2013 13:19
Please refer to this study by its ClinicalTrials.gov identifier: NCT01600573

Contacts

Contact: Jalid Sehouli, Prof. Dr.  +49 (0) 30 450 ext 564002  jalid.sehouli@charite.de
Contact: Radoslav Chekerov, Dr.  030/450 ext 664399  radoslav.chekerov@charite.de

Locations

Germany
Charité Campus Virchow-Klinikum
Not yet recruiting
Berlin, Germany, 13353
Contact: Jalid Sehouli, Prof. Dr.  +49 (0) 30 450 ext 564002  jalid.sehouli@charite.de
Contact: Radoslav Chekerov, Dr.  +49 (0) 30/450 ext 664399  radoslav.chekerov@charite.de
Principal Investigator: Jalid Sehouli, Prof. Dr.
Sub-Investigator: Radoslav Chekerov, Dr.

Sponsors and Collaborators

JSehouli
GlaxoSmithKline

Investigators

Principal Investigator: jalid Sehouli, Prof. Dr.  Charité Campus Virchow-Klinikum

More Information

No publications provided

Responsible Party: JSehouli, Prof. Dr. Jalid Sehouli, Charite University, Berlin, Germany
ClinicalTrials.gov Identifier: NCT01600573  History of Changes
Other Study ID Numbers: PazTo, 2010
Study First Received: May 9, 2012
Last Updated: May 16, 2012
Health Authority: Germany: Federal Institute for Drugs and Medical Devices

Keywords provided by Charite University, Berlin, Germany:
- ovarian cancer

Additional relevant MeSH terms:
- Ovarian Neoplasms
- Endocrine Gland Neoplasms
- Neoplasms by Site
- Neoplasms
- Ovarian Diseases
- Adnexal Diseases
- Genital Diseases, Female
- Genital Neoplasms, Female
- Urogenital Neoplasms
- Endocrine System Diseases

Gonadal Disorders
Topotecan
Topoisomerase I Inhibitors
Topoisomerase Inhibitors
Enzyme Inhibitors
Molecular Mechanisms of Pharmacological Action
Pharmacologic Actions
Antineoplastic Agents
Therapeutic Uses

ClinicalTrials.gov processed this record on February 21, 2013