A phase I study of the combination of daily oral pazopanib with intravenous ifosfamide in patients with advanced solid malignancies.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28441

Source
Nationaal Trial Register

Brief title
Pazi

Health condition

advanced solid malignancy; sarcoma; phase I; pazopanib; ifosfamide

gevorderde solide tumor; sarcoom; fase I; pazopanib; ifosfamide

Sponsors and support

Primary sponsor: Erasmus University Medical center
Source(s) of monetary or material Support: Glaxo Smith Kline

Intervention

Outcome measures

Primary outcome

To determine the MTD of pazopanib in combination with standard doses of ifosfamide, dosed according to two regimens (continuous ifosfamide infusion [Arm A]; short ifosfamide infusion [Arm B]), in subjects with solid malignancies.

Secondary outcome

1. To assess the safety and tolerability of the investigational combination of pazopanib and ifosfamide;

2. To characterize the PK of pazopanib when administered alone and with ifosfamide, and of ifosfamide and its metabolites when administered alone and with pazopanib (with continuous and short ifosfamide regimens);

3. To analyze biomarkers in blood associated with clinical outcome to treatment to allow identification of markers useful for selecting subjects likely to benefit from therapy;

4. To explore the anti-tumor activity of the combination of pazopanib and ifosfamide (continuous and short ifosfamide regimens) in solid tumors.

Study description

Background summary

This is a dose-finding (phase I) study on the combination of pazopanib and ifosfamide. Ifosfamide (standard dose) will be combined with escalating doses of pazopanib. No intrapatient escalation will take place. The highest dosing combination with as Dose-limiting toxicity occurring in less then 1/3 of patients in the first treatment cycle will be the maximally tolerated dose. Potential drug-drug interaction will be studied bij pharmacokinetic analysis. Efficacy will be routinely assessed by CT-scan.

Study objective

To determine the MTD of pazopanib in combination with standard doses of ifosfamide, dosed according to two regimens (continuous ifosfamide infusion [Arm A]; short ifosfamide infusion [Arm B]), in subjects with solid malignancies.

Study design

Adverse event observation during first or first 2 cycles.

Intervention

Combination therapy will consist out of daily pazopanib and 3-weekly infusion of ifosfamide. Up to 6 courses of ifosfamide will be administered.

Contacts

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Eligibility criteria

Inclusion criteria

1. Subjects must provide written informed consent prior to performance of study specific procedures or assessments, and must be willing to comply with treatment and follow up assessments and procedures;

2. Histologically or cytologically confirmed diagnosis of advanced solid tumor for which ifosfamide-based systemic therapy is considered appropriate or for which there is no standard therapy;

3. Age >18 years;

4. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1;

5. Adequate organ function;

6. There must be measurable disease or evaluable disease (according to RECIST v1.1 criteria) for subjects to be included in the cohort expansion phase. Measurable disease is not a criterion for subjects enrolling in the dose escalation phase;

7. Able to swallow and retain oral medication;

8. A life expectancy of at least 12 weeks.

Exclusion criteria

1. Unable to discontinue prohibited medications, as listed in Section 5.5.2, 14 days or five half-lives (whichever is longer) of the drug prior to Visit 1 and for the duration of the study;

2. Clinically significant gastrointestinal abnormalities which might interfere with oral dosing;

3. Any unstable or serious concurrent condition (e.g., active infection requiring systemic therapy);

4. Poorly controlled hypertension (SBP of ³160 mmHg, or DBP of ³90 mmHg).
Note: Initiation or adjustment of blood pressure medication is permitted prior to study entry provided the subject has 2 consecutive blood pressure readings less than 160/90 mmHg, each separated by a minimum of 1 hour. These readings need to be collected prior to the first dose. See Appendix 2 for details on blood pressure control and reassessment prior to study enrollment;

5. Prolongation of corrected QT interval (QTc) >480 msecs;

6. History of any one of more of the following cardiovascular conditions within the past 6 months:

A. Cardiac angioplasty or stenting;

B. Myocardial infarction;

C. Unstable angina;

D. Symptomatic peripheral vascular disease;

E. Class II, III or IV congestive heart failure as defined by the New York Heart Association (NYHA).

7. History of cerebrovascular accident, 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-coagulant agents (excluding therapeutic warfarin) for at least 6 weeks are eligible;

8. Macroscopic hematuria;

9. Hemoptysis that is clinically relevant within 4 weeks of first dose of study drug;

10. 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;

11. Chemotherapy or radiation therapy within 2 weeks prior to the first dose of study drug;

12. Biological therapy, hormonal therapy or treatment with an investigational agent within 28 days (for bevacizumab, 60 days) prior to the first dose of study drug;

13. Has not recovered from toxicities associated with prior anti-cancer therapy;

14. Metastatic disease to the brain or leptomeninges (of note: radiologic assessment of the brain is only needed in those subjects with clinical symptoms suspicious for brain metastases);

15. Psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol;

16. Clinically assessed as having inadequate venous access for PK sampling;

17. Is pregnant or lactating.
Note: 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.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	10-06-2009
Enrollment:	80
Type:	Anticipated

Ethics review

Positive opinion Date:	16-10-2009
Application type:	First submission

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
NTR-new	NL1946
NTR-old	NTR2063
Other	EMC : 2008-245
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A