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

Gepubliceerd: 16-10-2009 Laatst bijgewerkt: 18-08-2022

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.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28441

Bron
Nationaal Trial Register

Verkorte titel
Pazi

Aandoening

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

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

Ondersteuning

Primaire sponsor: Erasmus University Medical center
Overige ondersteuning: Glaxo Smith Kline

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

Adverse event observation during first or first 2 cycles.

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	10-06-2009
Aantal proefpersonen:	80
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	16-10-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1946
NTR-old	NTR2063
Ander register	EMC : 2008-245
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A