Individualizing Pazopanib therapy by exploRing the role of Early metabolic responsE and drug exposure as a preDICTor for treatment outcome in patients with STS

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Primary Objectives:- To evaluate whether early metabolic response is correlated to clinical benefit (defined as PFS).- To evaluate the effect of age (>= 70 years) on pazopanib pharmacokinetics (AUC0-24hr).Secondary Objectives:- To evaluate...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Soft tissue neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON41252

Source
ToetsingOnline

Brief title
PREDICT

Condition

- Soft tissue neoplasms malignant and unspecified

Synonym
Soft tissue sarcom

Research involving
Human

Sponsors and support

Primary sponsor: Medische Oncologie
Source(s) of monetary or material Support: GlaxoSmithKline

Intervention

Keyword: FDG-PET, Pazopanib, Pharmacokinetics, Soft tissue sarcoma

Outcome measures

Primary outcome

- The aim of this study is to show distinction between the PFS curves between the patients who have a more or less pronounced metabolic response.

- The aim of this study is to show a difference in pazopanib exposure (AUC0-24hr) between elderly (>= 70 years) compared to younger (<= 65 years) patients. The difference in exposure should at least be 15% to consider expansion of the study to a larger cohort.

Secondary outcome

- To explore, quantify and describe the correlation between early metabolic response and pazopanib exposure (AUC) on steady-state pharmacokinetics

- To explore, quantify and describe the correlation between tumor histology and early metabolic response

- To explore, quantify and describe the correlation between pazopanib exposure and the frequency of adverse events as graded by CTCAE v4.0

Study description

Background summary

The ability to target mutated oncogenes has led to significant therapeutic

advance in oncology. Recently, based on the outcome of the PALETTE-study, the FDA approved pazopanib for the treatment of patients with non-adipocytic soft-tissue sarcoma. However, with these new targeted therapies new problems arise. Reliable imaging to observe early response is required to minimize unnecessary toxicity and to avoid underestimations of initial responses as traditional methods like radiological responses has a large delay between treatment onset and evaluation of treatment benefit. FDG-PET imaging after a single cycle of neoadjuvant therapy appeared to be predictive for survival in patients with high-grade soft tissue sarcomas. Absolutely no information is available on the diagnostic value of FDG-PET in patients with Soft Tissue Sarcoma (STS) treated with pazopanib. In the proposed study we would therefore like to investigate what the relation is between: 1. tumor histology, 2. metabolic response (FDG-PET), 3. pazopanib exposure(AUC0-24hr) and 4. clinical benefit in patients with STS who are treated with pazopanib. This approach could facilitate future early clinical decision making (dose personalization / altering therapy) in patients with soft tissue sarcoma.
With an increasing number of elderly patients with cancer the geriatric patients will be encountered frequently in the clinical practice. However little information is available whether and how the dose of pazopanib should be adjusted in this substantial subgroup of patients, while it is evident that multiple factors influencing pazopanib pharmacokinetics (PK) are altered with increased age: the absorption is decreased due to reduced gastric acid secretion, reduced gastrointestinal motility, reduced splanchnic blood flow and potentially loss of absorption surface. The volume of distribution is altered due to decreased plasma albumin content and decreased total body water with increased fat content. Finally, the hepatic metabolism is changed due to decreased concentration and activity of cytochrome P450 enzymes. Therefore we would like to study pazopanib pharmacokinetics in the elderly patient.

Study objective

Primary Objectives:
- To evaluate whether early metabolic response is correlated to clinical benefit (defined as PFS).
- To evaluate the effect of age (>= 70 years) on pazopanib pharmacokinetics (AUC0-24hr).

Secondary Objectives:
- To evaluate whether early metabolic response (% decrease in FDG uptake (SUVmax) due to pazopanib therapy) is correlated with pazopanib exposure (AUC0-24hr)
- To evaluate whether early metabolic response (% decrease in FDG uptake (SUVmax) due to pazopanib therapy) is correlated with the histological subtypes.

Study design

Phase IV post registration prospective observational feasibility study in patients with metastatic STS.

Study burden and risks

Patients have to fill in a diary during the 8 weeks of the study, in which they have to record their time of taking their medication. Patients will spend two days in the hospital where blood will be taken at nine different time points from a peripheral vein. Patients will get 3 PETscans, where they will receive a dose of FDG. The total radiation dose is weight dependent, but is estimated at 4 millisievert (mSv) per PET, resulting in 12 mSv cumulatively.

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) 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.
2) Age >= 18 years or legal age of consent if greater than 18 years.
3) Histological confirmed diagnosis of selective subtypes of advanced soft tissue sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy.
4) Eastern Cooperative Oncology Group (ECOG) performance status of 0-2.
5) Measurable disease criteria (RECIST 1.1).
6) No radio-, chemo- or tumor specific targeted therapy within the last 4 weeks prior to study entry.
7) Adequate organ system function.
8) Minimal evaluable laesion of >= 15mm.

Exclusion criteria

1) Prior malignancy.
2) Central nervous system (CNS) metastases at baseline
3) Clinically significant gastrointestinal abnormalities that may increase the risk for gastrointestinal bleeding
4) Clinically significant gastrointestinal abnormalities that may affect absorption of investigational product
5) Corrected QT interval (QTc) > 480msecs

Study design

Design

Study phase:	4
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	09-12-2013
Enrollment:	30
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	23-09-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-11-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-12-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-01-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2013-003533-16-NL
CCMO	NL46119.091.13