Development and clinical activity of low dose metronomic chemotherapy with oral paclitaxel.

Gepubliceerd: 26-09-2012 Laatst bijgewerkt: 13-12-2022

We will develop a bi-daily low-dose metronomic treatment schedule with paclitaxel in a convenient oral formulation and test whether this therapy has significant anti-angiogenic and anti-tumor activity.

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

Samenvatting

ID

NL-OMON21795

Bron
Nationaal Trial Register

Verkorte titel
N10MOP

Aandoening

Cancer, oral, paclitaxel, low dose metronomic, phase 1,
kanker, oraal, laaggedoseerd, metronoom, fase 1

Ondersteuning

Primaire sponsor: The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To determine the safety and feasibility of LDM bi-daily oral paclitaxel (as ModraPac001 capsules) in combination with boosting agent ritonavir.

Toelichting onderzoek

Achtergrond van het onderzoek

Based on preclinical data, the taxane paclitaxel is considered to be an ideal drug to use for the concept of metronomic therapy. In combination with the oral boosting agent ritonavir high apparent bioavailability of oral paclitaxel is achieved when given as a drinking solution, or in a capsule formulation. We will develop a bi-daily low-dose metronomic treatment schedule with paclitaxel in a convenient oral formulation and test whether this therapy has significant anti-angiogenic and anti-tumor activity. The recommended dose of paclitaxel in combination with ritonavir will be determined by dose escalation. Patients with histological or cytological proof of cancer (excluding patients with secondary breast cancer metastasis with only lung metastases and primary brain tumors) for whom no standard treatment options are available, but who might benefit from treatment with paclitaxel and who are in good clinical condition will be eligible. Three patients will be assigned to each dose level. On a predefined day the patient will start receiving oral paclitaxel BID, dosed according to the escalation schedule and 100 mg ritonavir. This regime will be continued until progressive disease or until adverse events, which require dose modifications or discontinuation of therapy, are observed.

Doel van het onderzoek

We will develop a bi-daily low-dose metronomic treatment schedule with paclitaxel in a convenient oral formulation and test whether this therapy has significant anti-angiogenic and anti-tumor activity.

Onderzoeksopzet

Planned start date: Q3 2011;

Planned end date: Q1 2013.

Onderzoeksproduct en/of interventie

Patients with histological or cytological proof of cancer (excluding patients with secondary breast cancer metastasis with only lung metastases and primary brain tumors) for whom no standard treatment options are available, but who might benefit from treatment with paclitaxel and who are in good clinical condition will be eligible. Three patients will be assigned to each dose level. On a predefined day the patient will start receiving oral paclitaxel BID, dosed according to the escalation schedule and 100 mg ritonavir. This regime will be continued until progressive disease or until adverse events, which require dose

modifications or discontinuation of therapy, are observed.

This is a dose escalation study. The starting dose was bi-daily 2.5 mg paclitaxel absolute (as ModraPac001 capsules) and 100 mg ritonavir (as tablets) BID with at least 7, but not more than 12 hours dose interval (intakes around the same time).

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients with histological or cytological proof of cancer who might benefit from treatment with paclitaxel (excluding patients with secondary breast cancer metastasis with only lung metastases and primary brain tumors);

2. Patients for whom no standard therapy of proven benefit exist;

3. Patients have evaluable disease;

4. Age ≥ 18 years;

5. Able and willing to give written informed consent;

6. Able and willing to undergo blood sampling for pharmacokinetics and pharmacodynamics;

7. Life expectancy ≥ 3 months allowing adequate follow up of toxicity evaluation and antitumor activity;

8. Minimal acceptable safety laboratory values:

A. ANC of ≥ 1.5 x 109 /L;

B. Platelet count of ≥ 100 x 109 /L;

C. Hepatic function as defined by serum bilirubin ≤ 1.5 x ULN, ALAT and ASAT ≤ 2.5 x ULN;

D. Renal function as defined by serum creatinine ≤ 1.5 x ULN or creatinine clearance ≤ 50 ml/min (by Cockcroft-Gault formula).

9. WHO performance status of 0, 1 or 2;

10. No radio- or chemotherapy within the last 4 weeks prior to study entry, unless this concerns single dose radiotherapy for pain palliation;

11. Able and willing to swallow oral medication.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Patients with known alcoholism, drug addiction, psychotic disorders in the history and/or other reasons, for which they are not amenable for adequate follow up;

2. Women who are pregnant or breast feeding;

3. Both men and women enrolled in this trial must agree to use a reliable contraceptive method throughout the study (adequate contraceptive methods are: condom, sterilization, other barrier contraceptive measures preferably in combination with condoms);

4. Concomitant use of MDR and CYP3A modulating drugs such as Ca¬¬+-entry blockers (verapamil, dihydropyridines), cyclosporine, (non) nucleoside analoga, St. Johns worth,

macrolide antibiotics as erythromycin and clarithromycin, quinidine, quinine, tamoxifen, megestrol, grapefruit juice, concomitant use of HIV medications or other protease inhibitors;

5. Uncontrolled infectious disease or known HIV-1 or HIV-2 type patients;

6. Unresolved (>grade 1) toxicities of previous chemotherapy, excluding alopecia;

7. Known allergic reaction against contrast agents;

8. Bowel obstructions or motility disorders that may influence the absorption of drugs;

9. Chronic use of H2-receptor antagonists or proton pump inhibitors;

10. Neurologic disease that may render a patient at increased risk for peripheral or central neurotoxicity;

11. Pre-existing neuropathy greater than CTC grade 1;

12. Symptomatic cerebral or leptomeningeal metastases;

13. Evidence of any other disease, neurological or metabolic dysfunction, physical examination finding or laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or puts the patient at high risk for treatment-related complications.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm

Controle: N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	05-09-2011
Aantal proefpersonen:	40
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	26-09-2012
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	NL3339
NTR-old	NTR3632
Ander register	NKI-AVL : N10MOP
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A