Study of high-dose sunitinib in patients with solid tumors.

No registrations found.

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

Summary

ID

NL-OMON20988

Source
NTR

Brief title
SUNRISE

Health condition

Adult patients with locally advanced or metastatic solid tumors for which no standard therapy exists.

Sponsors and support

Primary sponsor: VU Medical Center
Amsterdam
Source(s) of monetary or material Support: Divisie I beheer B.V.

Intervention

Outcome measures

Primary outcome

To determine the maximum tolerated dose (MTD) of sunitinib when administered once a week or once every two weeks.

- To assess the safety and tolerability of sunitinib in a once weekly or once every two weeks dose schedule

Secondary outcome

- To determine the pharmacokinetic (PK) behaviour of the parent compound sunitinib and the primary, active, metabolite SU12662.

- Preliminary assessment of the efficacy of sunitinib intermittent treatment, administered at the MTD determined for each of the time schedules of the study (once weekly or once every two weeks).

- To determine a recommended phase II dose (RP2D) and the optimal dose schedule

- To determine the skin and intratumoral concentration of sunitinib and their correlation with the plasma concentration.

- To assess immune/angiogenesis modulating systemic and local effects such as MDSC, Tregs and DC subset frequencies and tumor infiltrating leukocytes

Study description

Background summary

Study design: Single center, open-label, phase I dose-finding study of a once weekly and a once every two weeks schedule of high-dose sunitinib.

Hypothesis: Sunitinib, when given in a high-dose, intermittent schedule, may exhibit improved efficacy with an acceptable toxicity profile.

Study population: Adult patients with locally advanced or metastatic solid tumors for which no standard therapy exists.

Primary objectives:

- To determine the maximum tolerated dose (MTD) of sunitinib when administered once a week or once every two weeks.

- To assess the safety and tolerability of sunitinib in a once weekly or once every two weeks dose schedule

Secondary objectives:

- To determine the pharmacokinetic (PK) behaviour of the parent compound sunitinib and the

primary, active, metabolite SU12662.

- Preliminary assessment of the efficacy of sunitinib intermittent treatment, administered at the MTD determined for each of the time schedules of the study (once weekly or once every two weeks).

- To determine a recommended phase II dose (RP2D) and the optimal dose schedule

- To determine the skin and intratumoral concentration of sunitinib and their correlation with the plasma concentration.

- To assess immune/angiogenesis modulating systemic and local effects such as MDSC, Tregs and DC subset frequencies and tumor infiltrating leukocytes

Treatment: The initial dose of sunitinib is set at 200 mg once weekly; sunitinib is to be administered p.o. Dose escalation cohorts consist of 3-6 patients per dose level. After determination of the MTD for the once weekly schedule, patients will be enrolled in a once every 2 weeks schedule until the MTD for this schedule is reached. At the MTD level for both schedules, patients will be entered into expansion cohorts; the expansion cohorts will not be opened until at least 42 days after the last patient in the escalation phase received his/her first study treatment. In the expansion cohorts a minimum of 10 patients will be treated per schedule (once weekly and once every 2 weeks).

Pharmacokinetic studies: Plasma pharmacokinetic parameters of sunitinib and its active metabolite SU012662 will be assessed.

Correlative studies: A pre-treatment and an on-treatment biopsy will be performed, the second along with a skin biopsy on Day 17, for patients entering both the escalation and the expansion cohort in order to gain more insight into the biological effects of the drug. This biopsy is essential for 5 out of the 10 patients entering the expansion cohort.

Study objective

Sunitinib, when given in a high-dose, intermittent schedule, may exhibit improved efficacy with an acceptable toxicity profile.

Study design

Primary outcome:

After 4 or 6 weeks of treatment (for the once-weekly vs once-every 2 weeks schedule, respectively), while patients will be followed until progression for the expansion cohort.

Secondary outcome:

After 4 or 6 weeks of treatment (for the once-weekly vs once-every 2 weeks schedule, respectively),
Evaluation by CT scan(s) every 8 weeks

Intervention

Sunitinib once every week or once every 2 weeks, at a starting dose of 200 mg

Contacts

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Eligibility criteria

Inclusion criteria

1. Signed (by the patient or legally acceptable representative) and dated Informed Consent Form

2. Histological or cytological documentation of incurable locally advanced or metastatic solid malignancy for which no standard therapy exists.

3. Primary tumor or metastatic site must be accessible for biopsy. Patients eligible for the expansion cohort must be willing to undergo tumor biopsies, while tumor biopsy remains optional for patients enrolled in the escalation cohort. Bone metastases are excluded as a biopsy site.

4. Evaluable disease by RECIST version 1.1 criteria (see appendix III; at least 1 target or non-target lesion for dose escalation cohorts; at least 1 target lesion for dose expansion cohort).

5. Patients must have documented radiographic or clinical progressive disease.

6. Age ≥ 18 years.

7. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1.

8. Normal 12-lead ECG (clinically insignificant abnormalities permitted), and Left Ventricular Ejection Fraction (LVEF) > 50% by multigated acquisition (MUGA) scan or echocardiogram.

9. Normal regulated thyroid function- suppletion or blocking drugs permitted.

10. Urinalysis: no clinically significant abnormalities.

11. Adequate bone marrow, liver and renal function as assessed by the following laboratory requirements to be conducted within 14 days prior to screening:

a. Hemoglobin > 5.6 mmol/l

b. Absolute neutrophil count (ANC) >1,5 x 10*9/l

c. Platelet count 100 x 10*9/l

d. Total bilirubin < 1.5 times the upper limit of normal (ULN)

e. ALT and AST 2.5 x ULN (In case of liver metastases: < 5 x ULN)

f. Alkaline phosphatase < 4 x ULN

g. Serum creatinine <= 1.5 x ULN Creatinine clearance >=50 ml/min (based on MDRD)

h. PT-INR/PTT < 1.5 x ULN, unless coumarin derivatives are used

i. Activated partial thromboplastin time < 1.25 x ULN (therapeutic anticoagulation therapy is allowed, if this treatment can be interrupted for a biopsy as judged by the treating physician)

Patients with known Gilbert’s disease who have serum bilirubin < x ULN may be enrolled.

Pregnant or breast-feeding subjects: Women of childbearing potential must have a negative pregnancy test performed within 7 days of the start of treatment. For fertile men or women of childbearing potential: documented willingness to use a highly effective means of contraception (e.g., hormonal methods [implants, injectables, or combined oral contraceptives], intrauterine devices, sexual abstinence, or vasectomized or surgically sterilized partner).
Contraception is necessary for at least 6 months after receiving the study kinase inhibitor.

Exclusion criteria

1. Evidence of a significant uncontrolled concomitant disease, such as cardiovascular disease (including stroke, New York Heart Association Class III or IV cardiac disease or myocardial infarction within 6 months prior to screening, unstable arrhythmia, clinically significant valvular heart disease and unstable angina); nervous system, pulmonary (including obstructive pulmonary disease and history of symptomatic bronchospasm), renal, hepatic, endocrine, or gastrointestinal disorders; or a serious non-healing wound or fracture.

2. Poorly controlled hypertension despite adequate blood pressure medication. Blood pressure must be ≤160/95 mmHg at the time of screening on a stable antihypertensive regimen. Blood pressure must be stable on at least 2 separate measurements.

3. Seizure disorders requiring anticonvulsant therapy.

4. Major surgery, other than diagnostic surgery, within 4 weeks prior to Day 1, without complete recovery.

5. Known active bacterial, viral, fungal, mycobacterial, or other infection (including HIV and atypical mycobacterial disease, but excluding fungal infection of the nail beds.)
6. Known hypersensitivity to sunitinib or to its excipients.

7. Presence of any significant central nervous system or psychiatric disorder(s) that would interfere with the patient’s compliance.

8. Drug or alcohol abuse.

9. Females who are pregnant or breast-feeding.

10. Any evidence of a disease or condition that might affect compliance with the protocol or interpretation of the study results or render the patient at high risk from treatment complications.

11. Unwillingness or inability to comply with study and follow-up procedures.

12. No chemotherapy, radiotherapy, or biologic therapy within the previous 4 weeks; no nitrosoureas or mitomycin C within the previous 6 weeks; no investigational agents within the previous 4 weeks.

13. Clinically significant history of liver disease, including viral or other hepatitis, current alcohol abuse, or cirrhosis.

14. Untreated or active central nervous system (CNS) metastases (progressing or requiring anticonvulsants or corticosteroids for symptomatic control);

15. Patients with a history of treated CNS metastases are eligible, provided that all of the

following criteria are met:

 Presence of evaluable or measurable disease outside the CNS

 Radiographic demonstration of improvement upon completion of
CNS-directed therapy and no evidence of interim progression between completion of CNS-directed therapy and the screening radiographic study

 Completion of radiotherapy ≥ 8 weeks prior to the screening radiographic study

 Discontinuation of corticosteroids and anticonvulsants ≥ 4 weeks prior to the screening radiographic study.
Note: Prior sunitinib therapy does not constitute an exclusion criterion.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-07-2013
Enrollment:	40
Type:	Anticipated

Ethics review

Positive opinion

Date:	10-09-2013
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	NL3995
NTR-old	NTR4167
Other	METC VUmedical Center : 2013/75
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A