A phase I clinical trial, evaluating the therapeutic vaccine hVEGF26-104/RFASE in patients with advanced cancer

No registrations found.

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

Summary

ID

NL-OMON20622

Source
NTR

Health condition

cancer, advanced solid tumors
kanker, gemetastaseerde solide tumor

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: Divisie I Beheer BV

Intervention

Outcome measures

Primary outcome

1. To investigate the safety and tolerability profile of the therapeutic vaccine hVEGF26-104/RFASE;

2. To determine the effective dose of hVEGF26-104/RFASE required to neutralize VEGF in serum, defined as a VEGF level below 9,0 pg/mL.

Secondary outcome

1. The anti-VEGF antibody titer, induced by hVEGF26-104/RFASE administration;

2. To determine the effective dose of hVEGF26-104/RFASE required to neutralize VEGF in plasma and in a platelet sample;

3. The effect of VEGF neutralization in a functional Ba/F3-R2 cell proliferation assay.

Study description

Background summary

Angiogenesis (the formation of new blood vessels from pre-existing blood vessels) plays an important role in the growth and spread of tumors. Angiogenesis is regulated by a balance of activators and inhibitors. One of the angiogenic activators is the vascular endothelial growth factor (VEGF, also referred to as VEGF-A). Over the past decade, several angiogenesis inhibitors have been discovered and implemented in the therapy of cancer patients. Bevacizumab (a humanized monoclonal antibody that inhibits VEGF-A) has been shown to improve survival in different tumor types in first and second line therapy when given in various chemotherapy combinations. Furthermore, research has shown a survival benefit of continued VEGF suppression with bevacizumab beyond first progression in metastatic colorectal cancer. So although repeated use of bevacizumab as a chronic therapy is much desired, currently this is not feasible because of substantial disadvantages of bevacizumab therapy. First, since bevacizumab only offers temporary VEGF neutralization, it needs frequent repeated administration. Secondly, bevacizumab is an intravenous therapy, which requires hospitalization on each administration. Third, bevacizumab has very high production costs.
These specific drawbacks of longer term monoclonal antibody therapy could be circumvented by the use of a therapeutic cancer vaccine targeting VEGF. A vaccine is able to induce sustained VEGF suppression and can be administered via an intramuscular (IM) injection. In addition, a vaccine will likely inhibit VEGF more effectively as compared to bevacizumab, because a vaccine induces a polyclonal antibody response, resulting in higher avidity binding. Furthermore, it is believed that endogenous antibodies have a better tumor penetrating capacity, as compared to exogenously administered antibodies.
The vaccine hVEGF26-104 is a truncated synthetic peptide mimic of the VEGF protein and consists of 79 amino acids (residue 26-104). The vaccine contains an antigen that directs the body’s own polyclonal antibody response towards the active site of the endogenous VEGF molecule. After binding of the antibodies to endogenous VEGF this hormone will no longer be able to bind to its receptors (VEGFR1 and VEGFR2) and consequently will no longer exert its pro-angiogenic effect. To enhance the immune response, RFASE, which belongs to the adjuvant group of sulpholipopolysaccharides, will be used as an adjuvant.

Study objective

The hypothesis is that immunization against VEGF will circumvent the specific drawbacks of the current anti-VEGF treatment modalities. The primary objectives of this study are to investigate the safety and tolerability of hVEGF26-104/RFASE and to assess whether hVEGF26-104/RFASE immunization induces VEGF neutralization.

Study design

Primary endpoints

1. Safety and tolerance is at each study visit
reviewed. DLT is defined as the period of 10 weeks.

2. VEGF concentration in serum will be determined after every examination.

Intervention

Patients participating in the study will receive a total of 3 IM injections with hVEGF26-104/RFASE.

Contacts

Public
De Boelelaan 1117
H.M.W. Verheul
Amsterdam 1081 HV
The Netherlands
+31 (0)20 4444321/300
Scientific
De Boelelaan 1117
H.M.W. Verheul
Amsterdam 1081 HV
The Netherlands
+31 (0)20 4444321/300

Eligibility criteria

Inclusion criteria

1. Histologically confirmed advanced, solid malignancy;

2. Refractory or not amenable to standard therapy;

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

4. Willing and able to give written informed consent;

5. Patient is > 18 years of age at the time of signature of the informed consent;

6. Adequate hematological function: Absolute neutrophil count (ANC) > 1.5 x 109/L, platelets > 100 x 109/L, Hemoglobin > 6.0 mmol/L;

7. Adequate hepatic function: serum bilirubin < 1.5 times the upper limit of normal (ULN), ALT and AST < 2.5 x ULN (or < 5 times ULN if liver metastases are present);

8. Adequate renal function: eGFR > 50ml/min;

9. Female patients of childbearing potential may be enrolled in the study, if the patient has practiced adequate contraception for 30 days prior to first hVEGF26-104/RFASE administration, has a negative pregnancy test and has agreed to continue adequate contraception for as long as VEGF is neutralized;

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

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

Exclusion criteria

1. Major surgery within 28 days before the initiation of study treatment;

2. Any serious non-healing wounds, ulcers, or bone fractures within 28 days prior to the initiation of study treatment;

3. Deep venous thrombosis (DVT) or pulmonary embolus (PE) within 1 year prior to the initiation of study treatment;

4. Uncontrolled hypertension (systolic > 150 mmHg and/or diastolic > 100 mmHg);

5. The patient is scheduled to receive another vaccination during the DLT period;

6. A previous serious allergic reaction to a vaccine such as angioedema and anaphylaxis;

7. Treatment with bevacizumab within 6 weeks prior to the initiation of study treatment;

8. Primary or secondary immunodeficiency;

9. Treatment with a glucocorticoid derivative in an equivalent dose of ¡Ý 10mg prednisone a day;

10. Female patients: the patient is pregnant or lactating;

11. Uncontrolled auto-immune diseases

12. Primary or secondary immunodeficiency, including HIV

13. When the patient is scheduled to receive any other anticancer treatments.

14. Chemotherapy within 28 days prior to the initiation of study treatment.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2014
Enrollment:	15
Type:	Anticipated

Ethics review

Positive opinion

Date:	12-06-2013

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	NL3766
NTR-old	NTR4031
Other	VEGFVAX : VU University Medical Center
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A