Immunotherapy in mesothelioma patients.

Gepubliceerd: 09-10-2009 Laatst bijgewerkt: 15-05-2024

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

Samenvatting

ID

NL-OMON24867

Bron
NTR

Verkorte titel
DC=dendritic cell; CTX=cyclophosphamide

Aandoening

mesothelioma
mesothelioom
asbestkanker
borstvlieskanker

Ondersteuning

Primaire sponsor: Erasmus Medical Center
Department of Pulmonary Medicine
Rotterdam
Overige ondersteuning: Stichting Asbestkanker

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The aim of this new phase I protocol is to study the toxicity and safety of low dose CTX in combination with DC-based immunotherapy in MM patients.

Toelichting onderzoek

Achtergrond van het onderzoek

N/A

Doel van het onderzoek

Currently there is no satisfactory low-toxicity treatment for patients with MM. Based on studies in other types of cancer in humans where beneficial effects were obtained, and based on our pre-clinical data in a mouse model for MM, led to the introduction of DC-immunotherapy for human MM in 2005. A beneficial effect of immunotherapy in MM patients without major side effects was found, however, research has shown that DC immunotherapy might be further improved. The objectives of the here proposed phase study are:

1. To define the safety and toxicity of low dose CTX in combination with MesoCancerVac in patients with MM;

2. To determine if vaccination with low dose CTX in combination with MesoCancerVac results in a detectable immune response by skin DTH reactions on MM crude antigen and KLH and by in vitro laboratory analysis;

3. To observe and document anti-cancer activity by laboratory evaluation (e.g. decrease in Tregs, increase in CTLs using 51Cr release and IFN-gamma ELISPOT);

4. To observe and document anti-cancer activity by clinical evaluation (e.g. CT scan).

Onderzoeksopzet

After 4 cycles of chemotherapy a leukapheresis is performed of which the monocytes are used for differentiation to DCs using different cytokines. Three doses of properly pulsed autologous DCs (MesoCancerVac) are then re-injected every two weeks. Quality control tests will be performed before the cellular vaccine is released. Six and twelve months after the third injection with MesoCancerVac, a revaccination to boost the immunsystem might be given (if enough MesoCancerVac is available [4^th /

5^th vaccination]). Patients will be treated with a low dose of CTX for seven day in a row the week before the 1^st vaccination, the weeks in between the 2^nd , and for one week after the 3^rd vaccination.

Onderzoeksproduct en/of interventie

1. Formulation: Cyclophosphamide (Endoxan)

Dose: 100 mg daily dose (dd) : 2 tablets

Route of administration: oral

Number of doses: 28

Schedule of doses: 7 days followed by a week interval repeated for 3 times .

2. Formulation: autologous monocyte-derived DCs pulsed with autologous tumor lysate [MesoCancerVac]

Dose: > 50x106 DCs

Route of administration: 1/3 intravenously and 2/3 intradermal

Number of doses: 3

Schedule of doses: every 2 weeks.

Contactpersonen

Publiek

Erasmus Medical Center, Department of Pulmonary Medicine,
Dr. Molewaterplein 50
J. Hegmans
Dr. Molewaterplein 50
Rotterdam 3015 GE
The Netherlands
+31 (0)10 4087703

Wetenschappelijk

Erasmus Medical Center, Department of Pulmonary Medicine,

Dr. Molewaterplein 50
J. Hegmans
Dr. Molewaterplein 50
Rotterdam 3015 GE
The Netherlands
+31 (0)10 4087703

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients with clinically and histological or cytological confirmed newly diagnosed MM, that can be measured in two dimensions by a radiologic imaging study;

2. Patients must be at least 18 years old and must be able to give written informed consent;

3. Patients must be ambulatory (Karnofsky scale > 70, or WHO-ECOG performance status 0,1, or 2) and in stable medical condition. The expected survival must be at least 4 months;

4. Patients must have normal organ function and adequate bone marrow reserve: absolute neutrophil count > 1.5 x 109/l, platelet count > 100 x 109/l, and Hb > 6.0 mmol/l;

5. Positive DTH skin test (induration > 2mm after 48 hrs) against at least one positive control antigen tetanus toxoid;

6. Stable disease or response after chemotherapy;

7. Availability of sufficient tumor material of the patient;

8. Ability to return to the Erasmus MC for adequate follow-up as required by this protocol;

9. Able to tolerate oral therapy;

10. No impairment of gastrointestinal (GI) function or GI disease that may affect or alter absorption of CTX (e.g., mal-absorption syndrome, history of total gastrectomy/significant small bowel resection);

11. No history of allergic reactions (¡Ý grade 3 or 4) to compounds of similar chemical or biologic composition to CTX (i.e., alkylating agents);

12. No known intolerance or hypersensitivity reaction to CTX.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Conditions that make the patient unfit for chemotherapy or progressive disease after 4 cycles of chemotherapy;

2. Pleurodesis at the affected side before the pleural fluid is obtained;

3. Medical or psychological impediment to probable compliance with the protocol;

4. Patients on steroid (or other immunosuppressive agents) are excluded on the basis of potential immune suppression. Patients must have had 6 weeks of discontinuation and must stop of any such treatment during the time of the study;

5. No prior malignancy is allowed except for adequately treated basal cell or squamous cell skin cancer, superficial or in-situ cancer of the bladder or other cancer for which the patient has been disease-free for five years;

6. Serious concomitant disease, no active infections. Patients with a history of autoimmune disease or organ allografts, or with active acute or chronic infection, including HIV (as determined by ELISA and confirmed by Western Blot) and viral hepatitis (as determined by HBsAg and Hepatitis C serology);

7. Patients with serious intercurrent chronic or acute illness such as pulmonary (asthma or COPD) or cardiac (NYHA class III or IV) or hepatic disease or other illness considered by the study coordinator to constitute an unwarranted high risk for investigational DC treatment;

8. Patients with a known allergy to shell fish (may contain KLH);

9. Pregnant or lactating women;

10. Patients with inadequate peripheral vein access to perform leukapheresis;

11. Concomitant participation in another clinical trial;

12. An organic brain syndrome or other significant psychiatric abnormality which would comprise the ability to give informed consent, and preclude participation in the full protocol and follow-up;

13. Absence of assurance of compliance with the protocol. Lack of availability for follow-up assessment.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	10-01-2009
Aantal proefpersonen:	10
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	09-10-2009
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 32554
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1932
NTR-old	NTR2049
CCMO	NL24050.000.08
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON32554

Resultaten

Samenvatting resultaten

Hegmans JP, Hemmes A, Aerts JG, Hoogsteden HC, Lambrecht BN. Immunotherapy of murine malignant mesothelioma using tumor lysate-pulsed dendritic cells. Am J Respir Crit Care Med 2005; 171:1168-77.

Hegmans JP, Hemmes A, Hammad H, Boon L, Hoogsteden HC, Lambrecht BN. Mesothelioma environment comprises cytokines and T-regulatory cells that suppress immune responses. Eur Respir J 2006; 27:1086-95.