Dendritic cell-based immunotherapy in mesothelioma.

No registrations found.

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

Summary

ID

NL-OMON22849

Source
NTR

Brief title
DC-immunotherapy

Health condition

For this phase I study, patients with end-stage malignant mesothelioma and who are deemed to be fit enough to be treated with chemotherapy will be asked to participate in this study. Patients will first be treated with 4 courses of chemotherapy (standard treatment[Alimta/cisplatin]). After this chemotherapy a leukapherese is performed of which the monocytes are used for differentiation to dendritic cells. The procedure to grow these dendritic cells in vitro (culture) and pulse them with tumor lysate is performed in a cleanroom environment. Several quality control tests will be performed before the dendritic cells are ready for re-injection. Three doses of properly pulsed autologous dendritic cells are then re-injected every two weeks.

Sponsors and support

Primary sponsor: Erasmus Medical Center Rotterdam
Stichting Asbestkanker Rotterdam
Source(s) of monetary or material Support: Mesothelioma Applied Research Foundation (MARF)

Intervention

Outcome measures

Primary outcome

1. Safety;
2. Tolerability.

Secondary outcome

1. Anti-tumor responses in vitro and in vivo;
2. Clinical response evaluation.

Study description

Background summary

Dendritic cells are extremely potent antigen presenting cells and vital in inducing activation and proliferation of CD8+ cytotoxic T-lymphocytes. Exploiting the immunostimulatory capacities of these cells holds great promise for cancer immunotherapy. 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 malignant mesothelioma, it now seems feasible and warranted to introduce dendritic cell based-immunotherapy for mesothelioma patients. This study will test the feasibility and safety of a clinical trial using autologous dendritic cells as a therapeutic adjuvant for the treatment of mesothelioma. It can be expected that using the proper procedure in mesothelioma patients, a beneficial effect of immunotherapy can be obtained without major side effects.

Study objective

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 malignant mesothelioma (MM), it now seems feasible and warranted to introduce dendritic cell (DC)-immunotherapy for human mesothelioma. It can be expected that using the proper procedure in mesothelioma patients, a beneficial effect of immunotherapy can be obtained without major side effects. The objectives of this phase I study are:
1. To define the safety and toxicity of tumor lysate-pulsed DCs injected in patients with mesothelioma;
2. To determine if vaccination with tumor lysate-pulsed DCs results in a detectable immune response by skin delayed type hypersensitivity (DTH) reactions on mesothelioma crude antigen and KLH and by in vitro laboratory analysis.

- To observe and document anti-cancer activity by clinival evaluation.

Intervention

Formulation: autologous monocyte-derived dendritic cells (DCs) pulsed with autologous tumor lysate, Dose: > 5x10e6 DCs,
Route of administration: 1/3 intraveneously and 2/3 intradermally
Number of doses: 3
Schedule of doses: every 2 weeks

Contacts

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

Eligibility criteria

Inclusion criteria

1. Patients with clinically and histological or cytological confirmed newly diagnosed mesothelioma, 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 ³ 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*109/l, platelet count > 100*109/l, and Hb > 6.0 mmol/l;
5. Positive DTH skin test (induration > 2mm after 48hrs) against at least one positive control

antigen of MULTITEST CMI (Pasteur merieux);
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.

Exclusion criteria

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 coordinators to constitute an unwarranted high risk for investigational DC treatment;
8. Patients with a known allergy to shell fish (contains 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.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Masking:	Open (masking not used)

Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2006
Enrollment:	10
Type:	Anticipated

Ethics review

Positive opinion

Date:	07-02-2006
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	NL545
NTR-old	NTR600
Other	: MEC-2005-269
ISRCTN	ISRCTN66517336

Study results

Summary results
Immunotherapy of murine malignant mesothelioma using tumor lysate-pulsed dendritic cells

http://ajrccm.atsjournals.org/cgi/reprint/171/10/1168

Am J Respir Crit Care Med
Vol 171, pp 1168 – 1177
2005.