p53 immunotherapy in patients treated for metastasised colorectal cancer.

No registrations found.

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

Summary

ID

NL-OMON24376

Source
NTR

Brief title
p53

Health condition

tumour, metastised colorectal cancer

Sponsors and support

Primary sponsor: N/A
Source(s) of monetary or material Support: N/A

Intervention

Outcome measures

Primary outcome

To define safety and immunogenicity of a p53 specific vaccine in combination with a defined adjuvant in patients treated for metastasised colorectal cancer.

Secondary outcome

To study the clinical response to vaccination.

Study description

Background summary

Introduction: Colorectal cancer is the second most frequent cancer in the Netherlands. Despite treatment 45% of all colorectal cancer patients die within 5 years. Efforts to improve survival with advanced colorectal cancer have had only limited success. P53 is a frequently overexpressed and mutated protein in colorectal cancer patients. This overexpression provides an immunological window for immunotherapy of colorectal cancer. It has been shown in animal models that vaccination for p53 specific immune response could eradicate tumours. In humans it has been shown that vaccination can induce a p53 immune response. Our approach is to vaccinate with peptides encoding the p53 protein.
Aim: To define safety and immunogenicity of a p53 specific vaccine in combination with a defined adjuvant. Secondary, to study the clinical response to vaccination.
Population: Patients will be selected from patients treated for colorectal metastases in the liver. Patients will be vaccinated at least three months after last treatment.
Method: A phase I/II study will be carried out. Five patients will be included in a phase I p53 based vaccine study. If in the first five patients no grade 3 or 4 toxicity occurs, we will automatically enter into a phase II study. The five patients of the phase I study will be analyzed in the same way as the next included patients. The phase II study ends if ten patients fully completed vaccination and follow-up.
Intervention: Patients will be vaccinated subcutaneously with a vaccine consisting of 10, overlapping long p53 peptides dissolved in the adjuvant Montanide ISA 51. Patients will be vaccinated two times with an interval of three weeks.
Safety: In a previous clinical study that we performed, in which patients were vaccinated with a canarypoxvirus with a human wildtype p53 inserted, no severe toxicity occurred. Also in a safety study with a HPV peptide vaccine (p 88/89-026) no serious side effects were detected.
Endpoints: Due to the length of the peptides both potential MHC class I and class II epitopes can be processed by antigen presenting cells, therefore both a p53 specific cellular and humoral response can be expected. In order to monitor the immune response, plasma and peripheral blood mononuclear cells will be isolated and tested from patients before and after p53 peptide vaccination. The reactions of the different assays is positive when one of the test is increased twice in the post-vaccination samples compared to the pre-vaccination sample. In all these assays the immune response against p53 will be compared before and after vaccination. To assess a clinical anti tumour response a CT scan will be made and CEA levels will be measured in blood samples before and after vaccination.

Study objective

p53 mutation in colorectal cancer provides an immunological window for immune therapy.

Intervention

Patients will be vaccinated subcutaneously with a vaccine consisting of 10, overlapping long p53 peptides dissolved in the adjuvant Montanide ISA 51. Patients will be vaccinated two times with an interval of three weeks.

Contacts

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Eligibility criteria

Inclusion criteria

1. Stage IV colorectal adenocarcinoma;
2. At least three months after last treatment;
3. Life expectance of more than 6 months;
4. Patients must be 18 years of age or older;
5. Female patients of childbearing potential must be neither pregnant nor breastfeeding and must have a negative serum pregnancy test within 14 days prior to entry. Female patients must agree to use effective contraception (birth control pills, condoms, approved implant, or IUD) during the course of this trial and for at least three months after the last injection;
6. Patients must be ambulatory, with an WHO performance status of 1 to 2;
7. Absence of any psychological, familial, sociological, or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; conditions should be discussed with the patient before registration in the trial;
8. Patient baseline laboratory values must be within the following ranges:Hb>6mmol/l; WBC 3*10e9; serum creatinine <175mmol/l;
9. Before patient registration, written informed consent must be given to the patient, according to Dutch regulations;
10. Patients must sign the written informed consent.

Exclusion criteria

1. History of autoimmune disease or systemic intercurrent disease which might affect immunocompetence;
2. Other malignancies (previous or current), except adequately treated basal or squamous cell carcinoma of the skin;
3.Significant co-morbid medical conditions that in the estimation of the investigator would preclude the patient’s safe participation in the study or may interfere with study objectives;
4. Indication of active infectious disease, including Human Immunodeficiency Virus (HIV) AND Hepatitis B infection;
5. No radiotherapy, chemotherapy or other potentially immunosuppressive therapy administered within 4 weeks prior to vaccination;
6. Receipt of another investigational product within the previous 4 weeks or at any time during the study period;
7. Receipt of prior P53 directed immunotherapy.

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):	01-11-2006
Enrollment:	10
Type:	Anticipated

Ethics review

Positive opinion

Date:	18-10-2006
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	NL793
NTR-old	NTR806
Other	: P06.019
ISRCTN	ISRCTN43704292

Study results

Summary results
N/A