

# A study to detect the effect of radiofrequent ablation in combination with ipilimumab in patients with eye melanoma that spread out to the liver.

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Uveal melanoma is an uncommon malignancy (0.6-0.7 cases/100.000/year) that, in the case of metastatic stage, has a poor prognosis for response to treatment and survival. It is remarkable for its purely hematogenous pattern of dissemination, most...

<b>Ethische beoordeling</b>	Positief advies
<b>Status</b>	Werving gestopt
<b>Type aandoening</b>	-
<b>Onderzoekstype</b>	Interventie onderzoek

## Samenvatting

### ID

NL-OMON26122

### Bron

Nationaal Trial Register

### Verkorte titel

SECIRA-UM

### Aandoening

uveal melanoma  
liver metastases  
oog melanoom  
lever metastasen

### Ondersteuning

**Primaire sponsor:** NKI-AVL

**Overige ondersteuning:** BMS

## Onderzoeksproduct en/of interventie

### Uitkomstmaten

#### Primaire uitkomstmaten

Phase Ib: Toxicity and safety of treatment:<br>

DLT toxicities will be any unexpected SAE and AE deemed related to the investigational treatment. DLT observation period ranges from week 1 to week +10 after last Ipilimumab infusion into third patient of cohort.<br>

The phase 1b part of the study will test the safety of the combination of RFA and ipilimumab in a 3+3 design, and an expansion phase II cohort (consisting of 38 patients).<br>

The study will consist of 3 cohorts of each 3 patients, with an interval of 10 weeks before opening the next dose escalation cohort after the last patient having received the last ipilimumab treatment. The identified MTDL will be extended to 6 patients.<br>

The uveal melanoma patients will be treated in the phase Ib part with RFA + ipilimumab in three dose escalation cohorts:<br>

Cohort 1: RFA + ipilimumab 0.3 mg/kg, 4x, q3wk;<br>

Cohort 2: RFA + ipilimumab 3 mg/kg, 4x, q3wk;<br>

Cohort 3: RFA + ipilimumab 10 mg/kg, 4x, q3wk.<br>

Cohort 1 consists of three patients. If 1 DLT is observed then a cohort 2 consisting of additional 3 patients is opened. If 2 DLT of the 6 patients is observed then the discontinuation of the study will be discussed with the ethics committee and BMS.

In the case of no or only 1 DLT among the 6 patients included in the DLT cohort the study will continue to accrue to a total of 38 patients at that dosis level.<br>

DLT is also defined as the following treatment-related adverse events or laboratory abnormalities, graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.0:<br>

1. Non-hematological toxicity ;Ý grade 3;<br>
2. irAE ;Ý grade 3;<br>
3. Dosing delay ;Ý 3 weeks due to toxicity;<br>
4. Hepatic bleeding grade 3 or 4;<br>
5. Treatment related hepatic failure grade 3 or 4.<br>

Grade and type of adverse events in all patients.

<br><br>

Phase II extension: Efficacy and safety.<br>

Response rate as measured by irRC of intra- and extrahepatic lesions, excluding the metastasis that is treated by RFA) at week 12 from the start of RFA and ipilimumab treatment. Response as well as progression will require confirmation through a subsequent scan at least 4 weeks apart.

# Toelichting onderzoek

## Achtergrond van het onderzoek

This is an open label, non-randomized, single centre, mono-arm phase II trial, evaluating the efficacy (as measured by irRC) and safety of the combination of RFA and Ipilimumab in patients with at least two unresectable hepatic metastases of uveal melanoma in first line systemic treatment. This study will include patients >18 years, with histologically or cytologically confirmed unresectable metastatic uveal melanoma, who have a performance status of 0-1.

## Doel van het onderzoek

Uveal melanoma is an uncommon malignancy (0.6-0.7 cases/100.000/year) that, in the case of metastatic stage, has a poor prognosis for response to treatment and survival. It is remarkable for its purely hematogenous pattern of dissemination, most commonly to the liver (60%) and lungs (25%). Only 28 phase I-II studies were performed in uveal melanoma patients between 1980 and 2008, none of them showing convincing improvements of overall survival rates. Current approaches using chemoembolization with cisplatin-based regimens or intrahepatic artery administration of fotemustin resulted in response rates of up to 40% without increasing the overall survival rates beyond 12 months. Ipilimumab has been shown to improve OS in cutaneous melanoma in two phase III studies and seems to have activity in uveal melanoma, based on own experience from another group. Based on preclinical data and the observed activity of ipilimumab monotherapy in uveal melanoma this study will test the safety and efficacy of a combination of RFA and ipilimumab in uveal melanoma patients that have unresectable liver metastases.

## Onderzoeksopzet

N/A

## Onderzoeksproduct en/of interventie

Radiofrequent ablation combined with intravenous ipilimumab 3 weekly.

# Contactpersonen

## Publiek

NKI-AVL<br>  
Department of Medical Oncology/Immunology<br>  
Plesmanlaan 121

Christian Blank  
Amsterdam 1066 CX  
The Netherlands  
+31 (0)20 512 2570

## Wetenschappelijk

NKI-AVL  
Department of Medical Oncology/Immunology  
Plesmanlaan 121  
Christian Blank  
Amsterdam 1066 CX  
The Netherlands  
+31 (0)20 512 2570

## Deelname eisen

### Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Changed 8-jun-2015:

1. Adults at least 18 years of age;
2. World Health Organization (WHO) Performance Status 0 or I;
3. Histologically or cytologically confirmed unresectable metastatic uveal melanoma (as confirmed by multidisciplinary opinion, including liver surgeon);
4. Subjects must have at least two liver metastases (both > 1 cm in diameter) and one of them feasible for RFA
5. No prior systemic treatment (including chemotherapy, vaccine therapy, monoclonal Ab-treatment, IL-2);
6. Local pretreatment of uveal melanoma metastases is allowed, except for chemotherapy containing procedures (e.g. chemoembolisation), and as long patients have progressed with at least two measurable lesions now;
7. No concurrent immunosuppressive medications (including dexamethason, prednisolon, azathioprin);
8. Screening laboratory values must meet the following criteria: WBC  $\geq 2.0 \times 10^9/L$ , Neutrophils  $\geq 1.0 \times 10^9/L$ , Platelets  $\geq 100 \times 10^9/L$ , Hemoglobin  $\geq 5.5 \text{ mmol/L}$ , Creatinine  $\leq 2 \times \text{ULN}$ , AST  $\leq 5 \times \text{ULN}$ , ALT  $\leq 5 \times \text{ULN}$ , Total bilirubin  $\leq 3 \times \text{ULN}$ , INR and PTT in normal range,

LDH  $\leq$  2x ULN;

9. Women of child bearing potential (WOCBP) must agree to use a reliable form of contraceptive during the study treatment period and for at least 180 days following the last dose of study drug;

10. Men must agree to the use of male contraception during the study treatment period and for at least 180 days after the last dose of study drug;

11. Absence of additional severe and/or uncontrolled concurrent disease;

12. No prior, or ongoing other malignancy, except adequately treated basal cell or squamous cell skin cancer, cervical cancer in situ or adequately treated other cancer with eradicated intent for which the patient has been continuously disease free for > 2 years.

### **Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)**

1. Cerebral or meningeal metastasized uveal melanoma;

2. Subjects with any active autoimmune disease or a documented history of autoimmune disease, or history of syndrome that required systemic steroids or immunosuppressive medications, except for subjects with vitiligo or resolved childhood asthma/atopy;

3. Prior immunotherapy (tumor vaccine, cytokine, or growth factor);

4. Known history of infection with Human Immunodeficiency Virus;

5. Active infection requiring therapy, positive serology for Hepatitis B surface antigen or Hepatitis C ribonucleic acid (RNA);

6. Underlying medical conditions that, in the Investigator's opinion, will make the administration of study treatment hazardous or obscure the interpretation of toxicity determination or adverse events;

7. Concurrent medical condition requiring the use of immunosuppressive medications, or immunosuppressive doses of systemic or absorbable topical corticosteroids;

8. History of or current immunodeficiency disease, splenectomy or splenic irradiation; Prior allogeneic stem cell transplantation;

9. Use of other investigational drugs before study drug administration for systemic malignancy;

10. Pregnancy or nursing.

## Onderzoeksopzet

### Opzet

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

### Deelname

Nederland	
Status:	Werving gestopt
(Verwachte) startdatum:	01-04-2012
Aantal proefpersonen:	44
Type:	Werkelijke startdatum

### Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Nog niet bepaald

## Ethische beoordeling

Positief advies	
Datum:	18-06-2012
Soort:	Eerste indiening

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

Register	ID
NTR-new	NL3327
NTR-old	NTR3488
Ander register	NKI-AVL / CCMO : N11RFA / NL37985.031.11;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

## Resultaten

### Samenvatting resultaten

N/A