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

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26122

Source
Nationaal Trial Register

Brief title
SECIRA-UM

Health condition

uveal melanoma
liver metastases
oog melanoom
lever metastasen

Sponsors and support

Primary sponsor: NKI-AVL
Source(s) of monetary or material Support: BMS

Intervention

Outcome measures

Primary outcome

Phase Ib: Toxicity and safety of treatment:

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.

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).

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.

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

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

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

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

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.

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:

1. Non-hematological toxicity ¡Ý grade 3;

2. irAE ¡Ý grade 3;

3. Dosing delay ¡Ý 3 weeks due to toxicity;

4. Hepatic bleeding grade 3 or 4;

5. Treatment related hepatic failure grade 3 or 4.

Grade and type of adverse events in all patients.

Phase II extension: Efficacy and safety.

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.

Secondary outcome

Efficacy:

1. OS;

2. irPFS;

3. Clinical response benefit (CR, irPR, and irSD as defined by irRC criteria);

4. Immune-related duration of response (for patients achieving an objective response);

5. Response according to MHC expression on the melanoma cells.

Analysis of immunological and genetic changes in the tumor and peripheral blood pre and post- treatment.

Collection of PBMC pre, on day 1, 22, 43, 64, week 12, 16, 28, and every threemonths, and tumor biopsy mandatory day 1 and week 6, and optional in week 12.

Study description

Background summary

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.

Study objective

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.

Study design

N/A

Intervention

Radiofrequent ablation combined with intravenous ipilimumab 3 weekly.

Contacts

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Eligibility criteria

Inclusion criteria

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 progresses 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 ¡Ý 2.0x109/L, Neutrophils ¡Ý1.0x109/L, Platelets ¡Ý100 x109/L, Hemoglobin ¡Ý5.5 mmol/L, Creatinine ¡Ü2x ULN, AST ¡Ü 5 x ULN, ALT ¡Ü5 x ULN, Total bilirubin ¡Ü3 X ULN, INR and PTT in normal range, LDH ¡Ü 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 eradicative intent for which the patient has been continuously disease free for > 2 years.

Exclusion criteria

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.

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:	Recruitment stopped
Start date (anticipated):	01-04-2012
Enrollment:	44
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	18-06-2012
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	NL3327
NTR-old	NTR3488
Other	NKI-AVL / CCMO : N11RFA / NL37985.031.11;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A