Chronic stress and Responsiveness to Immunotherapy for Metastasized Melanoma

Published: 31-10-2019
Last updated: 19-08-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Skin neoplasms malignant and unspecified
Study type	Observational non invasive

Summary

ID

NL-OMON55104

Source
ToetsingOnline

Brief title
CRIMM-pilot study

Condition

- Skin neoplasms malignant and unspecified

Synonym
malignant melanoma, skin cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Chronic stress, Immunotherapy, Metastasized Melanoma

Outcome measures

Primary outcome

Main study parameter is whether chronic stress is related to response 3 and 6 months after the start of immunotherapy.

Secondary outcome

Demographic (age, gender, social relational variables) and medical variables (type, duration and doses of immunotherapy, immunotherapy related adverse events, use of immunosuppressive agents, LDH, pain, WHO-performance, location of metastases, oral contraceptive use) will be collected from medical records and by asking some additional questions at baseline.

Study description

Background summary

Immunotherapy with checkpoint inhibitors in metastasized melanoma patients is a relatively new treatment option that is effective in approximately 40% of the cases. Whether people respond to immunotherapy is apparent after three months and, until date, mostly unpredictable although age, gender, lactate dehydrogenase (LDH) and WHO-performance score are found to be associated with overall survival. Identifying additional alterable factors differentiating responders from non-responders after immunotherapy is important as it may direct the development of additional interventions and the allocation of scarce medical and financial resources.
Recently, scholars and researchers have suggested that chronic stress may impact the effectiveness of immunotherapy. The cause for this might be that chronic stress is known to impact the immune system by the release of glucocorticoids which suppresses immune reactions. Consequently, chronic stress may weaken the efficacy of immunotherapy which is aimed at boosting the immune system. Indirect and preliminary evidence supporting the link between chronic stress and the effectiveness of immunotherapy is found in studies investigating

the impact of glucocorticoids on the effectiveness of immunotherapy in mouse as well as in patients.

Study objective

The present pilot study will examine whether chronic stress is related to response to immunotherapy with checkpoint inhibitors for metastasized melanoma. Stress will be assesed by Hair cortisol, Salivary cortisol and some validated questionnaires (Eysenck Personality Questionnaire - Revised Short Scale, stress subscale of the Four-Dimensional Symptom Questionnaire (4DSQ), The Center for Epidemiological Studies Depression Scale (CES-D) and the State-scale of the State Trait Anxiety Index (STAI).

Study design

In this observational cohort study both objective (i.e., hair cortisol and salivary cortisol) and subjective measures (self-report questionnaire) of stress will be assessed in patients with metastasized melanoma. Measurement will take place before start of immunotherapy (baseline, T0) and at three (T1) and six (T2) month after of start immunotherapy. At T1 and T2 responsiveness to the immunotherapy is determined using radiological evaluation as part of standard care. Furthermore, standard baseline characteristics will be analyzed (WHO-score, age, gender, LDH etc).

Study burden and risks

Assessment will take place before start of immunotherapy and at 3 and 6 months after start of immunotherapy. Patients have to donate hair and salivary samples (both non-invasive) for cortisol assessment and complete a short questionnaire at three time points. Time investment per patient will be a maximum of 10 minutes per assessment (30 minutes in total). No risks or adverse events are expected from this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Adults (above 18 years)
Diagnosed with metastasized melanoma
Starting immunotherapy within the next two weeks.
Treatment regimen: pembrolizumab 3 or 6-weekly, nivolumab 4-weekly, ipilimumab/nivolumab 3-weekly.

Exclusion criteria

Age under 18 years
Obvious intellectual impairment
Insufficient knowledge of the Dutch language.
Patients with no or very short hair

Study design

Design

Study type: Observational non invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-01-2020
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	31-10-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	13-01-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	02-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL70304.058.19