The effects of an oncology tailored nutritional intervention on the bioavailability and immune-activity of PD-1 immune checkpoint inhibitors in patients with lung cancer: *Nutritional intervention in cancer immunotherapy (NutriCim) *

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON51244

Source
ToetsingOnline

Brief title
NutriCim

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Efficacy of nutritional supplement on efficacy of immunotherapy in lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Nutricia

Intervention

Keyword: Immune checkpoint inhibitors, Nutritional supplement support, treatment of non-small-cell lung cancer

Outcome measures

Primary outcome

The main endpoint is the recruitment rate: how many patients can be recruited in 1 year? Secundary endpoints are the rate of compliance to the study procedures including the intake of the nutritional intervention and the rate of data collection (blood samples, fecal samples, diaries). In order to study feasibility of an nutritional intervention study in NSCLC patients receiving anti PDL-1 treatment, the primary objective is to assess whether it is possible to recruit 50 patients in 1.5 year for this study. The secondary objective is to assess whether it is feasible for the subjects to comply with the study protocol (i.e. undergo study assessments and collect blood and faecal samples at the indicated time points). Lastly, exploratory objectives are to study the effect of the nutritional intervention on anti-PD-1 drug clearance, immune activation status, nutritional status, microbiome status, and clinical response.

Secondary outcome

not applicable

Study description

Background summary

Several studies in cancer patients receiving chemotherapy have shown that nutritional supplements influences catabolism. We hypothesize that high energy/high protein nutritional supplements decrease protein clearance including drug clearance in NSCLC patients reveiving anti-PD-1 ICIs, which on its turn would positively affect anti-PD-1 drug bioavailability, leading to activation of the immune system and thereby an increased response to PD-1 ICIs. An increased clearance of anti-PD-1 ICI may also represent a general dysfunctioning of the immune system, because immune cell activation, proliferation, migration and tumor cell killing may all be influenced by cachexia. Enrichment of nutritional supplements with specific nutrients known to have immune-modulating properties, may further balance immune responses supportive of ICI efficacy.
In conclusion, nutrional intervention with high energy/high protein nutritional supplements, especially if enriched with nutrients known for their immune- or microbiome-modulation properties, may have a positive impact on several mechanisms underlying cachexia-induced PD-1 ICI efficacy impairment. Lung cancer (NSCLC) patients are a relevant target population to investigate the clinical relevance of a nutritional intervention on anti-PD-1 ICI, because NSCLC is one of the cancer types with highest prevalence of cancer-induced cachexia amongst patients and PD-1 ICI is a standard of care treatment for these patients. However, nutritional intervention studies in a vulnerable patient population, such as patients with cancer, can be perceived as a burden, especially when there are a lot of additional assessments (e.g. questionnaires, diaries, blood sampling, fecal sampling). Therefore, the recruitment of sufficient representative patients within a certain time period can be challenging.

Study objective

The aim is to investigate whether it is feasible to perform a 12-weeks nutritional intervention study in NSCLC patients on PD-1 ICI, and to effectively assess their nutritional, immune, and microbial status, with the intention to use this information for designing an efficacy study to effectively show the added value of a nutritional intervention in cancer patients undergoing immunotherapy.

Study design

NutriCim is a feasibility study specifically designed to gather information on: (i) the rate of NSCLC patient recruitment,(ii) the feasibility of collecting relevant data (compliance to protocol), and (iii) the effects of nutritional

intervention on a number of parameters representing the patients* nutritional, immune, and microbiomal status.
Patients will start with the daily nutritional intervention prior to start of the first infusion of anti-PD-1 ICI immunotherapy and will continue this nutritional support for 4 treatment cycles, corresponding with 12 weeks of treatment. Blood samples, questionnaires and faecal specimens will be collected on several time points during this treatment. Changes from baseline for the different parameters on an individual patient level will, taking into account nutritional supplements compliance, be compared to patient outcomes, as well as with a historical cohort of NSCLC patients on similar treatment not receiving nutritional supplements.

Intervention

Patients will start with 2 times daily nutritional intervention preferably 5 days (with a minum of 3 days) prior to start the first infusion of immunotherapy, and remain on treatment and nutritional intervention for the period of 4 cycles of q3week treatment.

Study burden and risks

In the studyprocedures the only intervention is the drawal of blood sampes, which is accompanied by a negligible addition risk of complications.

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

Participants are eligible to be included in the study if the following criteria apply:
• Age > 18 years
• Patient must be willing and capable of giving written Informed Consent, and meeting all study requirements
• Capable of oral intake and digestion of the nutritional test product
• Subjects with cytologically confirmed Stage IV or recurrent NSCLC, who have not received prior systemic therapy treatment for their advanced NSCLC. Completion of treatment with cytotoxic chemotherapy, biological therapy, and/or radiation as part of neoadjuvant/adjuvant therapy is allowed as long as therapy was completed at least 6 months prior to the diagnosis of metastatic disease.

Exclusion criteria

• Subject with an active auto-immune disease requiring systemic treatment
• Lung disease requiring systemic steroids in doses of >10 mg prednisolone (or equivalent dose of other steroid)
• Previous allogeneic or organ transplant
• Serious concomitant systemic disorders (for example active infection, unstable cardiovascular disease) which in the opinion of the investigator would compromise the patient's ability to complete the study, or would interfere with the evaluation of the efficacy and safety of the study treatment
• Known positive test for hepatitis B virus or hepatitis C virus or human immunodeficiency virus (HIV) indicating acute or chronic infection
• Allergy to cow*s milk protein, soy or fish, requiring a fibre-free diet or suffering galactosemia or lactose intolerance
• Moderate to severe hypercalcemia, i.e. total calcium level corrected for albumin >=142.0 mg/dL (3.05 mmol/L)
• Patient has had other malignancies within the past 3 years , except for stable non-melanoma skin cancer, fully treated and stable early stage prostate cancer or carcinoma in situ of the cervix or breast without need of treatment

• Simultaneous participation in other clinical trial
• Pregnant or lactating women

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-07-2021
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	01-07-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL76015.078.21