PD-L1 PET/CT to predict durvalumab treatment response in HNSCC

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON48737

Source
ToetsingOnline

Brief title
PD-L1 imaging in HNSCC

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
head and neck cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: Astra Zeneca,Farmaceutische industrie

Intervention

Keyword: Durvalumab, HNSCC, imaging, PD-L1

Outcome measures

Primary outcome

Assess the potential of PD-L1 PET/CT to image PD-L1 expression in tumour lesions and to predict disease control rate for durvalumab in patients with advanced head and neck cancer

Secondary outcome

1. Assess the heterogeneity of 89Zr-durvalumab uptake within and between tumour lesions

2. Asses the correlation between tumour uptake of 89Zr-durvalumab and PD-L1 expression as determined immunohistochemically

3. Asses the correlation between tumour uptake of 89Zr-durvalumab in the individual tumor lesions and tumour response

4. Assess the correlation between PD-L1 expression as measured immunohistochemically and response to durvalumab

5. Assess the correlation between tumour uptake of 89Zr-durvalumab and overall survival

Study description

Background summary

Novel immune therapies with anti-PD-1 and PD-L1 immune checkpoint inhibitors (ICI) have shown impressive and durable antitumor responses. However, only 15-20% of patients respond to these drugs. This means that nonresponders are exposed to expensive, ineffective treatment, and its associated side effects,

while alternative treatment is delayed.
Durvalumab is an ICI shown to be effective in patients with advanced head and neck cancer (HNSCC).To predict its effect, there is an urgent need for a predictive biomarker to select patients which could benefit from ICI therapy.
The aim of the study is to develop PD-L1 PET/CT imaging in patients with an advanced stage HNSCC to noninvasively image PD-L1 expression in tumors and to determine the correlation with response to durvalumab

Study objective

The aim of the study is to develop PD-L1 PET/CT imaging in patients with advanced HNSCC to non-invasively image PD-L1 expression in tumours and to determine the correlation with response to durvalumab. The studie will be divided into 2 parts:
1: Determine the optimal 89Zr-durvalumab dose to image HNSCC lesions and
2: Assess the potential of PD-L1 PET/CT to image PD-L1 expression in tumour lesions, and predict disease control rate for durvalumab in patients with advances HNSCC.

Study design

non-randomized, non-blinded, prospective multi-centre study among 58 patients; 15 (part 1) and 43 (part 2) patients with advanced HNSCC

Intervention

Part 1: Dose optimization for PD-L1 PET/CT
15 patients receive sequentially 2,10 or 50mg iv 89Zr-Durvalumab followed by a PET/CT scan 5 days later.

Part 2: Predictive value of PD-L1 PET/CT
43 patients receive the dose selected from part 1 (best tumor-to-normal tissue-ratio) and a PET/CT 5 days later.

Afterwards all patients will receive intravenous Durvalumab treatment 4-weekly, with an evaluation CT/MRI-scan every 8 weeks.

Study burden and risks

All patients will receive an intravenous injection of 89Zr-durvalumab followed by a PET/CT scan five days later. After de PET/CT scan a tumor biopsy will be performed.
After the PET/CT scan, patients will initiate Durvalumab treatment which is administered IV every 4 weeks (q4w, 1500mg) with a duration up till 12 months or until progressive disease. Tumour evaluation will be assessed by CT or MRI scan at baseline and at every 8 weeks. All hospital visits will be accompanied

by laboratory (blood and urine) analysis and controle of vital signs.

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

1. Written informed consent and any locally-required authorization (e.g., HIPAA in the USA, EU Data Privacy Directive in the EU) obtained from the subject prior to performing any protocol-related procedures, including screening evaluations ;2. Age > 18 years at time of study entry, age > 20 years for Japanese subjects.;3. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 ;4. Life expectancy of > 12 weeks;5. Adequate normal organ and marrow function as defined below: ;6. Haemoglobin * 9.0 g/dL;7. Absolute neutrophil count (ANC) * 1.5 x 109/L (> 1500 per mm3);8. Platelet count * 100 x 109/L (>100,000 per mm3);9. Serum bilirubin * 1.5 x institutional upper limit of normal (ULN). (This will not apply to subjects with confirmed Gilbert*s syndrome (persistent or recurrent

hyperbilirubinemia that is predominantly unconjugated in the absence of hemolysis or hepatic pathology), who will be allowed only in consultation with their physician);10. AST (SGOT)/ALT (SGPT) * 2.5 x institutional upper limit of normal unless liver metastases are present, in which case it must be * 5x ULN;11. Serum creatinine CL>40 mL/min by the Cockcroft-Gault formula (Cockcroft and Gault 1976) or by 24-hour urine collection for determination of creatinine clearance:;12. Female subjects must either be of non-reproductive potential (ie, post-menopausal by history: *60 years old and no menses for *1 year without an alternative medical cause; OR history of hysterectomy, OR history of bilateral tubal ligation, OR history of bilateral oophorectomy) or must have a negative serum pregnancy test upon study entry. ;13. Subject is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up.;14. Histological proven recurrent or metastatic squamous cell cancer of the head and neck ;15. At least one lesion with a tumor size * 1 cm

Exclusion criteria

1. Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site). Previous enrollment in the present study;2. Participation in another clinical study with an investigational product during the last 4 weeks;3. Any previous treatment with a PD1 or PD-L1 inhibitor, including durvalumab ;4. History of another primary malignancy except for:;a. Malignancy treated with curative intent and with no known active disease *5 years before the first dose of study drug and of low potential risk for recurrence;b. Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease;c. Adequately treated carcinoma in situ without evidence of disease eg, cervical cancer in situ;5. Receipt of the last dose of anti-cancer therapy (chemotherapy, immunotherapy, endocrine therapy, targeted therapy, biologic therapy, tumor embolization, monoclonal antibodies, other investigational agent) 28 days prior to the first dose of study drug 28 days prior to the first dose of study drug for subjects who have received prior TKIs [e.g., erlotinib, gefitinib and crizotinib] and within 6 weeks for nitrosourea or mitomycin C). ;6. Mean QT interval corrected for heart rate (QTc) *470 ms calculated from 3 electrocardiograms (ECGs) using Fredericia*s Correction;7. Current or prior use of immunosuppressive medication within 28 days before the first dose of durvalumab, with the exceptions of intranasal and inhaled corticosteroids or systemic corticosteroids at physiological doses, which are not to exceed 10 mg/day of prednisone, or an equivalent corticosteroid;8. Any unresolved toxicity (>CTCAE grade 2) from previous anti-cancer therapy. Subjects with irreversible toxicity that is not reasonably expected to be exacerbated by the investigational product may be included (e.g., hearing loss, peripherally neuropathy) ;9. Any prior Grade *3 immune-related adverse event (irAE) while receiving any previous immunotherapy agent, or any unresolved irAE >Grade 1 ;10. Active or prior documented autoimmune disease within the past 2 years NOTE: Subjects with vitiligo, Grave*s disease, or psoriasis not requiring systemic treatment (within the past 2 years) are not excluded.;11. Active or prior documented inflammatory bowel disease (e.g., Crohn*s disease, ulcerative colitis);12. History of primary immunodeficiency;13. History of allogeneic organ transplant ;14. History of hypersensitivity to durvalumab or any comparable agent;15. Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic

congestive heart failure, uncontrolled hypertension, unstable angina pectoris, cardiac arrhythmia, active peptic ulcer disease or gastritis, active bleeding diatheses including any subject known to have evidence of acute or chronic hepatitis B, hepatitis C or human immunodeficiency virus (HIV), or psychiatric illness/social situations that would limit compliance with study requirements or compromise the ability of the subject to give written informed consent;16. Known history of previous clinical diagnosis of tuberculosis;17. History of leptomeningeal carcinomatosis;18. Receipt of live attenuated vaccination within 30 days prior to study entry or within 30 days of receiving durvalumab;19. Female subjects who are pregnant, breast-feeding or male or female patients of reproductive potential who are not employing an effective method of birth control;20. Any condition that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of patient safety or study results;21. Symptomatic or uncontrolled brain metastases requiring concurrent treatment, inclusive of but not limited to surgery, radiation and/or corticosteroids. ;22. Subjects with uncontrolled seizures

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-12-2018
Enrollment:	58
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Durvalumab
Generic name:	MEDI4736

Ethics review

Approved WMO Date:	21-08-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-12-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-02-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2017-003447-37-NL
CCMO	NL63062.091.17