Bioimmunoradiotherapy (BIR) with concurrent Avelumab, Cetuximab and Radiotherapy as first line treatment in patients with locally advanced squamous cell carcinoma of the head and neck. A feasibility study in patients unfit for cisplatin

Published: 05-10-2016
Last updated: 16-04-2024

Feasibility

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON46250

Source
ToetsingOnline

Brief title
N16BIR

Condition

- Other condition

Synonym
head and neck cancer, squamous cell carcinoma

Health condition

neoplasms squamous cell carcinoma head and neck

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Merck,Merck bv

Intervention

Keyword: anti-EGFR, anti-PD-L1, avelumab, bioimmunoradiotherapy, locally advanced, squamous cell carcinoma of the head and neck

Outcome measures

Primary outcome

Toxicity measured according to CTC 4.03

Secondary outcome

Response Rates (i.e. CR, PR, SD, PD)

Differences in tumor microenvironment in biopsies of the primary tumor site

obtained prior and at day +14 of treatment.

Study description

Background summary

To date in humans no toxicity data are present for BioImmunoRadiotherapy. In patients with locally advanced SCCHN unfit for cisplatin treatment with Bioradiation, i.e. concurrent radiotherapy and anti-EGFR (i.e. cetuximab) the 5-years overall survival is 45.6%. The five-year survival of the current standard, i.e. chemoradiation, a combined treatment not applicable in this patientgroup is 50%. Addition of immune checkpoint inhibitors, e.g. anti-PD1 or anti-PD-L1 monoclonal antibodies to Bioradiation might ameliorate treatment outcome in SCCHN via specific T-cell responses raised against viral antigens (i.e. in case of HPV positive SCCHN) or neo-antigens (i.e. HPV negative SCCHN). Longer exposure to an immunecheckpoint inhibitor may maximize the effect and

therefore may increase the efficacy.

Study objective

Feasibility

Study design

open-label phase 1b study with concurrent Avelumab, Cetuximab and Radiotherapy followed by avelumab maintenance therapy

Intervention

Concurrent Radiation therapy (i.e. 5 times a week, 7 weeks, total dose 70 Gy) with cetuximab (loading dose 400 mg/m2 i.v. day -7, 250 mg/m2 i.v weekly wk 1-6) and Avelumab10 mg/kg i.v. at day -7, 7, 21,35 + maintenance therapy i.e avelumab10 mg/kg i.v. every 2 weeks for 6 months (wk 8,10, 12, 14, 16, 18, 20, 22, 24, 26.

Study burden and risks

The following side effects (related to avelumab) have been observed in more than 5% of the 717 patients treated with the study drug: infusion-related reactions, fatigue (tiredness), nausea, diarrhea, chills (feeling cold), and decreased appetite.
Other side effects (less often) for avelumab as well as side effects for cetuximab and radiotherapy are described in the patient informed consent form. Besides, side effects can occur as a consequence of study procedures.

Contacts

Public
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066CX
NL
Scientific
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
Amsterdam 1066CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Be willing and able to provide written informed consent for the trial.
2. Be *18 years of age on day of signing informed consent.
3. WHO Performance Status 0-2
4. Histologically confirmed Locally Advanced (i.e. stage III or IV) head and neck squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx and larynx.
5. Unfit for concurrent chemoradiation with cisplatin, e.g. GFR < 60 ml/min, cardiovascular co-morbidity, hearing loss or polyneuropathy or written confirmed unwillingness for treatment with chemotherapy
6. Willingness to provide tissue for tumor microenvironment analysis from archival tumor material or newly obtained core or excisional biopsy and willingness to provide a core or excisional biopsy at day 14 (±2 days) after start of treatment.
7. At least one measurable lesion as defined by RECIST 1.1.
8. Patients who are willing and able to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures.
9. Adequate bone marrow, renal and liver function.
10. Serum pregnancy test (for females of childbearing potential) negative at screening.
11. Highly effective contraception for both male and female subjects if the risk of conception exists.

Exclusion criteria

1. The following prior therapies are excluded:
* Prior systemic therapy, radiotherapy or surgery directed at locally advanced SCCHN.
* Prior immunotherapy with IL-2, IFN-*, or anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody (including ipilimumab), or any other antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways.

2. A diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of trial treatment.
3. Current or prior use of immunosuppressive medication within 7 days prior to randomization, (see protocol for exceptions)
4. Known severe hypersensitivity reactions to monoclonal antibodies (Grade *3), any history of anaphylaxis, or uncontrolled asthma (ie, 3 or more features of partially controlled asthma).
5. Known prior or suspected hypersensitivity to study drugs or any component in their formulations.
6. Diagnosis of any other malignancy within 5 years prior to randomization, except for adequately treated basal cell or squamous cell skin cancer, or carcinoma in situ of the breast or of the cervix, or low-grade (Gleason 6 or below) prostate cancer on surveillance with no plans for treatment intervention (eg, surgery, radiation, or castration).
7. Significant acute or chronic infections.
8. Prior organ transplantation, including allogeneic stem cell transplantation
9. Active autoimmune disease that might deteriorate when receiving an immunostimulatory agent, but
a. Subjects with diabetes type I, vitiligo, psoriasis, hypo- or hyperthyroid disease not requiring immunosuppressive treatment are eligible
b. Subjects requiring hormone replacement with corticosteroids are eligible if the steroids are administered only for the purpose of hormonal replacement and at doses * 10 mg or 10 mg equivalent prednisone per day
c. Administration of steroids through a route known to result in a minimal systemic exposure (topical, intranasal, intro-ocular, or inhalation) are acceptable
10. Persisting toxicity related to prior therapy of Grade >1 NCI-CTCAE v 4.03; however, alopecia and sensory neuropathy Grade * 2 is acceptable
11. Pregnancy or lactation
12. Known alcohol or drug abuse
13. All other significant diseases, which, in the opinion of the Investigator, might impair the subject*s tolerance of trial treatment
14. Any psychiatric condition that would prohibit the understanding or rendering of informed consent
15. Vaccination within 4 weeks of the first dose of avelumab and while on trial is prohibited except for administration of inactivated vaccines (for example, inactivated influenza vaccines).
16. Any of the following in the previous 6 months: myocardial infarction, severe/unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure, cerebrovascular accident, transient ischemic attack, deep vein thrombosis or symptomatic pulmonary embolism.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-02-2017
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	avelumab
Generic name:	avelumab
Product type:	Medicine
Brand name:	cetuximab
Generic name:	cetuximab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	05-10-2016
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	13-10-2016
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO

Date:	24-02-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-06-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2016-001524-54-NL
CCMO	NL57770.031.16