A Double-Blind, Randomized, Two Arm Phase 2 Study of Nivolumab in Combination with Ipilimumab versus Nivolumab in combination with Ipilimumab placebo in Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck (SCCHN)

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON47328

Source
ToetsingOnline

Brief title
CheckMate 714

Condition

- Other condition

Synonym
Head and Neck Cancer, SCCHN

Health condition

Neoplasms - Squamous Cell Carcinoma of the Head and Neck

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Ipilimumab, Nivolumab, SCCHN

Outcome measures

Primary outcome

To compare the Objective Response Rate (ORR) and Duration of Response (DoR) of the treatment of nivolumab in combination with ipilumumab vs. nivolumab in combination with ipilimumab placebo, as determined by a blinded independent central review (BICR) using RECIST 1.1 criteria, for first line treatment of recurrent or metastatic SCCHN in the platinum refractory setting.

Secondary outcome

Secondary Objectives:

- To compare the ORR and DoR of the treatment of nivolumab in combination with ipilimumab vs nivolumab in combination with ipilimumab placebo in the platinum eligible setting

- To assess progression-free survival (PFS) and overall survival (OS) of nivolumab in combination with ipilimumab vs. nivolumab in combination with ipilimumab placebo in the platinum eligible and platinum refractory settings,

separately and overall

- To assess efficacy (ORR, PFS and OS) by PD-L1 expression and HPV p-16 status of nivolumab in combination with ipilumumab compared to nivolumab in combination with ipilimumab placebo in the platinum eligible and platinum refractory settings, separately and overall

Exploratory Objectives

- To assess the ORR, PFS and disease control rate (DCR) of the treatment of nivolumab in combination with ipilimumab vs nivolumab in combination with ipilimumab placebo, as determined by the investigator using RECIST 1.1 criteria in the platinum eligible and platinum refractory settings, separately and overall
- To assess safety and tolerability nivolumab in combination with ipilimumab/ipilimumab placebo
- To assess the subject's overall health status and health utility using the 3-level version of the EQ-5D (EQ-5D-3L) visual analog scale (VAS) and utility index, respectively
- To assess the subject's cancer-related symptoms and quality of life using components of the Functional Assessment of Cancer Therapy Head and Neck (FACT-HN) cancer questionnaire
- To evaluate differences in subject-reported symptomatic adverse events using selected items from the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)
- To investigate the immunomodulatory properties of nivolumab in combination

with ipilimumab or with ipilimumab placebo, and to evaluate potential baseline

and on-treatment biomarkers for association with efficacy

- To characterize the pharmacokinetics and immunogenicity of nivolumab in

combination with ipilimumab or with ipilimumab placebo

Study description

Background summary

CA209-714 is a multi-centre, phase 2 study involving adult patients with untreated metastatic or recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN). The study will compare nivolumab combined with ipilimumab vs. nivolumab alone as first line treatment in this population. Approximately 396 patients will take part in this study, approximately 15 of those will be from the Netherlands.

Metastatic and recurrent SCCHN causes substantial morbidity and high mortality and has a median overall survival of less than 12 months with the current available treatments. In a sub-set of patients that progress after platinum based therapy (referred to as platinum refractory), the median overall survival is about 6 months and there are no well-defined treatment options. As such, there is high unmet medical need in improving upon the established standard of care in recurrent and metastatic SCCHN, in both the platinum eligible and platinum refractory populations.

Cancer immunotherapy is based on the knowledge that tumours can be recognized as foreign rather than as self and can be effectively attacked by an activated immune system. Nivolumab and ipilimumab are types of immunotherapy drugs called monoclonal antibodies that work by blocking inhibitory signalling pathways in the immune response. This results in stimulation of the body*s own immune system to help attack the cancer cells.

Nivolumab has demonstrated clinical activity and been approved for the treatment of several tumour types, including melanoma, renal cell cancer and NSCLC. Furthermore, it has demonstrated a survival benefit in second line platinum refractory recurrent and metastatic SCCHN (when compared to investigators choice single agent chemotherapy). Ipilimumab is approved for the treatment of melanoma (alone or in combination with nivolumab). There is a sound biological rationale for the combination of nivolumab and ipilimumab, with existing pre-clinical data suggestive of a synergistic effect.

The aim of this study is to determine if the combination of nivolumab and ipilimumab represents an improvement in response compared to current treatment options for platinum refractory recurrent or metastatic SCCHN patients, a group in which there is currently a high level of unmet need. The study will also investigate the combination therapy compared to nivolumab alone in a smaller sub-group of platinum eligible patients, and these results will complement a concurrent study (CA209-651) which is assessing the efficacy of the combination compared to current standard of care in platinum eligible patients.

Study objective

The aim of the study is to compare the Overall Response Rate (ORR) and assess Duration of Response (DoR) of the treatment of nivolumab in combination with ipilumumab vs. nivolumab in combination with ipilimumab placebo, as determined by a blinded independent central review (BICR) using Response Evaluation Criteria In Solid Tumors (RECIST 1.1) criteria, for first line treatment of recurrent or metastatic SCCHN in the platinum refractory setting.

Study design

This is a randomized, double blinded, two-arm Phase 2 trial in adult subjects with untreated metastatic SCCHN or recurrent SCCHN that is not amenable to curative therapy.

Subjects will undergo screening tests to determine eligibility and, those eligible for the study will be randomized to a treatment arm in a 2:1 ratio:
Arm A: Nivolumab and Ipilimumab
Arm B: Nivolumab and Ipilimumab-Placebo

Randomization will be done by an automated sorting process through IVRS (a telephone based computer system) which will assign subjects to a treatment based on platinum sub-group and their PD-L1 and HPV p16 status. This ensures that both Arms are equally balanced with subject numbers for comparison at time of analysis, but also ensures the integrity of the randomization itself.

Subjects must receive their treatment within 3 days of randomization. Dose reductions will be not be allowed for nivolumab, ipilumumab or ipilumumab-placebo. Treatment will continue until disease progression, discontinuation due to toxicity, withdrawal of consent, or the study ends. Continuation of treatment beyond initial investigator-assessed progression (either clinical or radiographical) will be permitted if the subject has an investigator-assessed clinical benefit and is tolerating study drug.

A Data Monitoring Committee (DMC) will be established and meet regularly during the study to ensure that subject safety is carefully monitored and to provide oversight regarding safety and efficacy considerations.

The total duration of the study from start of randomization to final analysis of ORR is expected to be approximately 19 months, assuming 13 months accrual duration. Survival follow-up may continue for up to 5 years from the time of this analysis. The study will end once survival follow-up has concluded.

Intervention

Subjects will be randomly assigned to a treatment arm in a 2:1 ratio, allocation will be double-blinded.

Arm A:
* Nivolumab 3 mg/kg IV will be administered every 2 weeks
* Ipilimumab 1 mg/kg IV will be administered every 6 weeks

Arm B:
* Nivolumab 3 mg/kg IV will be administered every 2 weeks
* Ipilimumab-Placebo IV will be administered every 6 weeks

Both nivolumab and ipilimumab will be provided by the sponsor.

Treatment with nivolumab and ipilimumab will be given for up to 24 months in the absence of disease progression or unacceptable toxicity. Subjects who complete 24 months of nivolumab with ipilimumab and have subsequent disease progression may reinitiate nivolumab with ipilimumab at the same dose and schedule given previously on study and continue such treatment for up to 1 additional year.

Study burden and risks

As part of the trial, patients will be expected to attend multiple clinic visits where they will undergo physical examinations, vital sign measurements, blood tests for safety assessment, pregnancy testing (for females of child bearing potential) and monitoring for adverse events. Blood will also be collected at certain visits for research purposes (PK, immunogenicity and biomarker studies).
If there is no archive tumour tissue available or the sample was taken too long ago (more than 6 months), patients will be required to have a biopsy in order to participate. A biopsy of tumour tissue will also be collected at the time of disease progression.
In addition, every 6 weeks, patients will undergo radiographic assessment of their tumours (by CT or MRI) for the first 48 weeks, and then every 12 weeks thereafter. These assessments will continue until disease progression or initiation of subsequent therapy. The frequency of visits and number of procedures carried out during this trial would typically be considered over and above standard of care. The procedures are carried out by trained medical professionals and every effort will be made to minimise any risks or discomfort

to the patient.

Treatment for cancer often has side effects, including some that are life threatening. An independent Data Monitoring Committee (DMC) will be utilized in this trial to ensure that the safety data is reviewed during the study. New Immune system targeted therapy (immunotherapies) such as Nivolumab and Ipilimumab could potentially provide clinical benefit and improvement in the outcome for patients with this disease (disease improvement and improvement in survival). However, with all experimental drugs and clinical trials, there are known and unknown risks. Study medication and procedure related risks are outlined in the patient information sheet in detail to ensure the patients are fully informed before agreeing to take part in the 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

Confirmed squamous cell head and neck cancer
Widespread (metastatic) disease, or returned after previous treatment (recurrent)
No previous treatment for metastatic or recurrent disease
Tumor sample must be available for analysis of PDL1 and HPV (oropharynx only)
Performance status (ECOG 0-1)

Exclusion criteria

Cancer arising from one of the following primary sites: paranasal sinus, nasopharynx, salivary gland, skin
Any non-squamous subtype
Active autoimmune disease
Positive test for hepatitis B, C or HIV virus
Previous treatment with checkpoint inhibitor drugs
Active CNS metastases or carcinomatous meningitis

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	14-12-2016
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Opdivo
Generic name:	Nivolumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Yervoy
Generic name:	Ipilimumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	20-09-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-11-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-02-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-05-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-06-2017
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-08-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-03-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-05-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-08-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-10-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-06-2019
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-08-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-09-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-05-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-08-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-09-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
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Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2021
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-06-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-09-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2016-001645-64-NL
ClinicalTrials.gov	NCT02823574
CCMO	NL58491.042.16

Study results

Date completed:	05-10-2021
Results posted:	14-03-2023

First publication
01-01-1900