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A research study to investigate the safety of setanaxib and helpfulness in the treatment of recurrent or metastatic squamous cell carcinoma of the head and neck

Submission date
02/02/2022

Recruitment status
No longer recruiting

Registration date
09/05/2022

Overall study status
Completed

Last Edited
02/01/2026

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Squamous cell carcinoma of the head and neck is a type of cancer that occurs in the outermost surface of the skin or in certain tissues within the head and neck region including the throat, mouth, sinuses, and nose. This type of cancer comes from particular cells called squamous cells which are found in the outer layer of skin and in the mucous membranes (the moist lining of digestive, respiratory, reproductive, and urinary tracts). The aim of this study is to evaluate if setanaxib, a test medicine, is safe and will help in the treatment of recurrent or metastatic SCCHN (i.e. cancer that has come back or spread) when combined with another medication, pembrolizumab, which is already approved and used to treat this sort of cancer.

Who can participate?
Patients aged 18 years and over with SCCHN

What does the study involve?
Participants are randomly allocated receive setanaxib or a matching placebo (dummy tablet) in addition to the standard treatment, pembrolizumb. Participants receive pembrolizumab at 3-week intervals as an intravenous infusion (into a vein) together with setanxib or placebo as daily tablets taken by mouth for a maximum of 2 years or until the cancer gets worse or unacceptable side effects from the treatments are seen. Participants will be followed up for side effects and to monitor changes in their cancer with regular tumour scans, and tumour biopsies (samples) will also be performed. The study will consist of an up to 28-day screening period, an up to 24-month treatment period (day 1 to week 105), and a 28-day follow-up period.

What are the possible benefits and risks of participating?
It is hoped that adding setanaxib treatment may be of benefit to the participant by giving better control of the cancer than seen after treatment with the already approved drug, pembrolizumab. However, this cannot be guaranteed. It is possible that the participants' head and neck squamous cell carcinoma may or may not respond at all or may even get worse during

the study. As with any medication, it is possible that the participant could have allergic reactions to study medication, such as itching, skin rash, facial swelling, and/or a severe or sudden drop in blood pressure. A sudden drop in blood pressure could lead to shock with loss of consciousness and/or possible seizures, including the possibility of death. Participants may suffer one or more of the following at the biopsy site: pain and discomfort, tenderness and swelling, risk of bleeding, bruising and infection, or scarring. If a patient takes part in this study (assuming 24 months of treatment), they will have around 15 CT scans, have the possibility of CT-guided biopsies and may undergo other imaging procedures such as bone scans or PET scans where clinically necessary. Some of these will be extra to those that they would have if they did not take part. The radiation dose from each CT scan is about the same as they would receive from 4 to 11 years' natural background radiation. A contrast dye will be injected into their vein and may be administered orally before their CT scan. The injected contrast may cause a slight discomfort, bruising, swelling and sometimes an allergic reaction. Severe allergic reactions (for example, a drop in blood pressure, difficulty in breathing, or kidney problems) are very rare. They may find the CT scanner mildly claustrophobic. The risk of allergic reaction to the bone and PET scan tracers is low. The participant may feel a slight discomfort at the injection site and sitting still during the test can be uncomfortable for some people. The participant will be exposed to a dose of radiation equivalent to around 1 to 7 years of natural background radiation, depending on whether bone or PET scans are necessary. These procedures use ionising radiation to form images of their body and provide their doctor with essential information about their response to treatment. Ionising radiation may cause cancer many years or decades after the exposure. In patients with their current clinical condition, the chance of this happening to them is extremely small. If participants do not like confined spaces being in the MRI scanner may make them feel uncomfortable. The MRI scanner uses strong magnets and they may not be able to have the scan if they have metallic implants. As part of the MRI scan, a contrast agent is injected into their vein. The risks associated with the contrast agent include mild nausea, headache, hives and temporary low blood pressure, although such reactions are very rare. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The participants will be asked questions to ensure that the MRI scan is safe for them. The risks of taking blood include discomfort due to swelling or bruising around the injection site, light-headedness and fainting (uncommon) or a small risk of infection at the injection site. Participants may develop a skin rash or skin irritation where the gel and the electrodes are placed for the electrocardiogram (ECG) testing. In some cases, it may be necessary to have small patches of hair on the chest shaved to properly connect the electrodes for the ECG. There is no data from the use of setanaxib in pregnant women. It is possible that if the medicine is given to a pregnant woman it will harm the unborn child. The potential risk to a human foetus or infants of nursing mothers is unknown. Pregnant or lactating women must not participate in this study, nor should women who plan to become pregnant during the study. Male participants are advised that the effects of the study medicine on the male reproductive system are not known at this time and contraceptive methods should be used throughout the study and for 120 days after completion of the study. The information collected during this study may help the doctors and researchers to learn more about setanaxib that may benefit other people with squamous cell carcinoma of the head and neck.

Where is the study run from?
PRA Health Sciences (Germany)

When is the study starting and how long is it expected to run for?
January 2022 to August 2025

Who is funding the study?
Calliditas Therapeutics Suisse SA (Switzerland)

Who is the main contact?
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Clinical Trials Information System (CTIS)
2021-004627-33

Integrated Research Application System (IRAS)
1004322

Central Portfolio Management System (CPMS)
51108

Protocol serial number
GSN000400

Study information

Scientific Title
A Phase II, randomised, double-blind, placebo-controlled, proof-of-concept study to evaluate the efficacy, safety, and tolerability, and effects on tumour biomarkers of the NOX1/4 inhibitor setanaxib, when administered with the PD-1 inhibitor pembrolizumab, in patients with recurrent or metastatic squamous cell carcinoma of the head and neck

Study objectives
1. To compare the change in tumour size per Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1) in recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) patients treated with setanaxib and pembrolizumab versus patients treated with placebo and pembrolizumab
2. To compare the progression-free survival (PFS) per RECIST v1.1 in recurrent or metastatic SCCHN patients treated with setanaxib and pembrolizumab versus patients treated with placebo and pembrolizumab
3. To compare the change from baseline in cancer-associated fibroblasts (CAFs) level in tumour tissue from recurrent or metastatic SCCHN patients treated with setanaxib and pembrolizumab versus patients treated with placebo and pembrolizumab
4. To compare the change from baseline in CD8+ tumor-infiltrating lymphocytes (TILs) in tumour tissue from recurrent or metastatic SCCHN patients treated with setanaxib and pembrolizumab versus patients treated with placebo and pembrolizumab

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, REC ref: 22/SC/0052

Primary study design
Interventional

Study design
Randomized placebo-controlled double-blind parallel-group trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Recurrent or metastatic squamous cell carcinoma of the head and neck

Interventions
The total duration of the study will be up to 113 weeks for patients remaining until their final follow up assessment, this consists of an up to 28-day Screening Period, an up to 24-month Treatment Period, and a 28-day Follow-up Period. Eligible patients will be randomised to the investigational medicinal product (IMP) oral setanaxib tablets 800 mg BID or placebo, co-administered with pembrolizumab, according to a 1:1 randomisation ratio, stratified by human papillomavirus (HPV) status. Both groups will receive the same instructions. For both setanaxib and placebo, treatment will be initiated on day 1 as the first dose then patients will self-administer two tablets in the morning and two tablets in the evening. Treatment with

pembrolizumab will be initiated on the same day as the first dose of the IMP, and will be administered according to current clinical guidelines and labelling, i.e., 200-mg IV infusion every 3 weeks (q3w).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Setanaxib, pembrolizumb

Primary outcome(s)
Best percentage (%) change in tumour size, defined as the best percentage change from baseline in the sum of diameters (mm) of target lesions, as assessed by Response Evaluation Criteria in Solid Tumours (RECIST v1.1) after 9 weeks of study treatment

Key secondary outcome(s)
1. Progression-free survival (PFS), defined as time from randomisation to the first documented disease progression per RECIST v1.1 or death due to any cause, whichever occurs first. PFS at 3, 6, and 12 months and median PFS will be summarized
2. Cancer-associated fibroblast (CAFs) level in tumour tissue measured using immunohistochemistry at baseline and after 9 weeks of study treatment
3. CD8+ TILs numbers in tumour tissue measured using immunohistochemistry at baseline and after 9 weeks of study treatment

Completion date
21/08/2025

Eligibility

Key inclusion criteria
1. Male or female patients aged ≥18 years, inclusive, at the time of informed consent
2. Willing and able to give informed consent and to comply with the requirements of the study
3. Histologically or cytologically confirmed diagnosis of SCCHN (i.e., primary tumour arising from the oral cavity [including tongue], nasal cavity, paranasal sinuses, oropharynx, hypopharynx, or larynx) that is recurrent or metastatic (including both HPV+ve and HPV-ve SCCHN), with or without nodal involvement, and with or without metastatic spread
4. Candidates for first-line treatment for pembrolizumab for recurrent or metastatic SCCHN, at the discretion of the investigator
5. A positive CAFs level (defined as CAFs level in tumours ≥5%), performed at a central laboratory, with fresh tumour biopsy taken during the Screening Period. Suitable archival tissue, if available, can be used to assess tumour CAFs level and determine patient eligibility
6. Measurable disease, in accordance with RECIST v1.1, and with tumour accessible and of sufficient volume for pre-treatment and on-treatment biopsy
7. Combined positive score (CPS) ≥1, as determined on the archival or fresh tumour biopsy taken at Screening
8. HPV status known at Randomisation
9. Life expectancy of at least 6 months in the judgment of the investigator
10. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1

11. Adequate organ and bone marrow function within 28 days of starting study treatment. Criteria 11.1 to 11.3 cannot be met in patients with ongoing or recent (within 14 days of screening test) transfusions or who require ongoing growth factor support:
11.1. Absolute neutrophil count ≥1,000/mm³ (≥ 1.0×10e9/l)
11.2. Platelet count ≥100,000/mm³ (≥100×10e9/l)
11.3. Haemoglobin ≥9 g/dl, in the absence of transfusions for at least 2 weeks. Patients requiring ongoing transfusions or growth factor support to maintain haemoglobin ≥9 g/dl are not eligible
11.4. Total bilirubin ≤1.5 × upper limit of normal (ULN) (if associated with liver metastases or Gilbert's disease, ≤3 × ULN)
11.5. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤3 × ULN
f. Serum creatinine ≤2.0 mg/dl or creatinine clearance ≥40 ml/min (measured or calculated according to the method of Cockcroft and Gault)
12. Female patients of childbearing potential must use a highly effective method of contraception to prevent pregnancy for ≥4 weeks before randomisation and must agree to continue strict contraception up to 120 days after the last dose of IMP or pembrolizumab, whichever is the later
12.1. For the purposes of this study, women of childbearing potential are defined as all female patients after menarche unless they are postmenopausal for at least 2 years or are surgically sterile
12.2. For female patients ≤55 years of age who are considered postmenopausal and who are not on concomitant oestrogen replacement therapy, confirmation of postmenopausal status will be required with follicle-stimulating hormone (FSH) test results in the postmenopausal range for age at Screening
12.3. Highly effective contraception is defined as the use of two barrier methods (e.g., female diaphragm and male condoms) or the use of at least one barrier method in combination with spermicide, an intrauterine device or hormonal contraceptives (e.g., implant or oral)
13. Female patients of childbearing potential must have a negative serum pregnancy test at Screening and a negative urine pregnancy test at Baseline/Randomisation before dosing
14. Male patients with female partners of childbearing potential must be willing to use a condom and require their partner to use an additional form of adequate contraception as approved by the investigator, such as an established form of hormonal contraceptive, a diaphragm or cervical/vault cap, or intrauterine device. This requirement begins at the time of informed consent and ends 120 days after receiving the last dose of IMP or pembrolizumab, whichever is the later.
15. Male patients must be willing to not donate sperm, and female patients must be willing to not donate eggs, from baseline until 120 days after the last dose of IMP or pembrolizumab, whichever is the later

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit

100 Years

Sex
All

Total final enrolment
55

Key exclusion criteria
1. Diagnosis of immunosuppression or receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of study treatment, with the exception of intranasal and inhaled corticosteroids or systemic corticosteroids at doses not to exceed 10 mg/day of prednisone or equivalent. Steroids as premedication for hypersensitivity reactions due to radiographic contrast agents are allowed.
2. Anti-cancer monoclonal antibody treatment within 4 weeks prior to study Day 1
3. Chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to study Day 1 (radiation therapy can be allowed for palliative therapy of bone metastasis only)
4. Not recovered from AEs Grade 2 or greater (except for alopecia) due to previously administered agents
5. Treatment with any investigational agent within 12 weeks of Screening Visit or 5 half-lives of the IMP (if known), whichever is longer, or current enrolment in an interventional clinical study
6. Prior treatment with setanaxib or participation in a previous setanaxib clinical study
7. Prior treatment with pembrolizumab
8. Known additional malignancy that is progressing or requires active treatment excepting basal cell carcinoma of the skin, squamous cell carcinoma of the skin, in situ cervical cancer that has undergone potentially curative therapy, or malignancy treated with curative intent and with no known active disease ≥2 years before the first dose of IMP and of low potential risk for recurrence.
9. Known active central nervous system metastases and/or carcinomatous meningitis
10. Active autoimmune disease requiring systemic treatment within the past 3 months or documented history of clinically severe autoimmune disease, or syndrome that requires systemic steroids or immunosuppressive agents. The following are exceptions to this criterion:
10.1. Patients with vitiligo or alopecia
10.2. Any chronic skin condition that does not require systemic therapy
10.3. Patients with coeliac disease controlled by diet alone
11. Any evidence of current interstitial lung disease or pneumonitis, or a prior history of interstitial lung disease or non-infectious pneumonitis requiring high-dose glucocorticoids
12. Active infection requiring systemic therapy
13. Known human immunodeficiency virus (HIV) infection or acute or chronic hepatitis B or C infection. Patients with a past or resolved hepatitis B virus infection (defined as the presence of hepatitis B core antibody [HBcAb] and absence of hepatitis B surface antigen [HBsAg]) are eligible provided the hepatitis virus DNA test is negative. Patients positive for hepatitis C antibody are eligible only if polymerase chain reaction (PCR) is negative for hepatitis C virus RNA. Patients with ongoing anti-viral therapy with potent inhibitors of cytochrome P450 (CYP) 3A4 are not eligible. Testing for HIV is only required if clinically indicated and is not mandatory for this study.
14. Serious chronic gastrointestinal conditions associated with diarrhoea
15. History of significant haematological problems, such as blood dyscrasias requiring treatment, aplastic anaemia, myelodysplastic syndrome, or leukaemia
16. Surgery (eg, stomach bypass) or medical condition that might significantly affect the absorption of medicines (as judged by the investigator)

17. A positive pregnancy test or breastfeeding for female patients
18. Evidence of any of the following cardiac conduction abnormalities: a QTc Fredericia interval >450 milliseconds for male patients or >470 milliseconds for female patients. Patients with a second or third degree atrioventricular block are to be excluded.
19. TSH >ULN at Screening
20. Unstable cardiovascular disease as defined in the Protocol
21. Presence of any laboratory abnormality or condition that, in the opinion of the investigator, could interfere with or compromise a patient's treatment, assessment, or compliance with the protocol and/or study procedures
22. Any other condition that, in the opinion of the investigator, constitutes a risk or contraindication for the participation of the patient in the study, or that could interfere with the study objectives, conduct, or evaluation
23. Use of medications known to be potent CYP3A4 inhibitors or inducers, or uridine diphosphate (UDP)-glucuronosyltransferase (UGT) inhibitors or inducers, within 21 days prior to IMP administration
24. Legal incapacity or limited legal capacity
25. Psychiatric illness/social situations that would limit compliance with study requirement, substantially increase risk of incurring AEs or compromise the ability of the patient to give written informed consent
26. Patients who are unable to provide informed consent, are incarcerated or unable to follow protocol requirements`
27. Previous randomisation in this study

Date of first enrolment
13/05/2022

Date of final enrolment
25/10/2023

Locations

Countries of recruitment
United Kingdom

England

France

Germany

Italy

Poland

Spain

United States of America

Study participating centre

The Royal Marsden NHS Foundation Trust
Fulham Road
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SW3 6JJ

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
Clatterbridge Hospital
Clatterbridge Road
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Study participating centre
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The Royal London Hospital
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Study participating centre
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Sponsor information

Organisation
PRA Health Sciences

Funder(s)

Funder type

Industry

Funder Name
Calliditas Therapeutics Suisse SA

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		17/09/2024	02/01/2026	Yes	No
HRA research summary			28/06/2023	No	No
Protocol (other)			02/01/2026	No	No
Statistical Analysis Plan			02/01/2026	No	No