An open-label, single arm, multi-centre, Phase II study to evaluate the safety and efficacy of PC-A11 with superficial and interstitial laser light application in patients with recurrent head and neck squamous cell carcinoma unsuitable for surgery and radiotherapy.

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Run-in part: The *run-in part* primary objective:• To determine a safe light dose for PC-A11 with interstitial laser light application in patients with recurrent head and neck squamous cell carcinoma unsuitable for surgery and radiotherapy and...

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

Summary

ID

NL-OMON41537

Source
ToetsingOnline

Brief title
Study investigating efficacy & safety of PC-A11 in head & neck cancer.

Condition

- Skin neoplasms malignant and unspecified

Synonym
Patients with recurrent head and neck squamous cell carcinoma unsuitable for surgery and

radiotherapy

Research involving
Human

Sponsors and support

Primary sponsor: PCI Biotech AS
Source(s) of monetary or material Support: Industry;namely PCI Biotech AS

Intervention

Keyword: - Amphinex, - Bleomycin, - head and neck squamous cell carcinoma, - superficial and interstitial laser light application

Outcome measures

Primary outcome

The *run-in part* primary endpoint:

• Dose-limiting toxicities (DLT) and the safety profile of PC-A11 in patients

undergoing interstitial laser light application

The *expansion part* primary endpoint:

• The proportion of patients with non-progressive local disease 6 months after

start of PC-A11 treatment assessed according to modified RECIST 1.1 criteria

Secondary outcome

The *run-in part* secondary endpoints:

• The proportion of patients with non-progressive local disease 3 months after

start of PC-A11 treatment assessed according to modified RECIST 1.1 criteria.

• PFS defined as the time from start of PC-A11 treatment to the documented

progression or death from any cause.

• Pharmacokinetics of PC-A11 in plasma

• QoL using EORTC QLQ-C30 version 3.0 and QLQ-H&N35

The *expansion part* secondary endpoints:

• The proportion of patients with non-progressive local disease 3 months after start of PC-A11 treatment assessed according to modified RECIST 1.1 criteria.

• ORR calculated as the proportion of patients with a best overall response of confirmed Complete Response (CR) or Partial Response (PR).

• DCR defined as the proportion of patients with best overall response of confirmed CR, PR or Stable Disease (SD).

• PFS defined as the time from start of PC-A11 treatment to the documented progression or death from any cause.

• OS calculated as the time from start of PC-A11 treatment to the date of death due to any cause.

• Pharmacokinetics of PC-A11 in plasma

• QoL using EORTC QLQ-C30 version 3.0 and QLQ-H&N35

Safety endpoints:

• The proportion of patients with adverse events

• Pain scored by a visual analogue scale (VAS) at baseline, after PC-A11 treatment and during follow up visits.

Exploratory endpoints:

• Evaluation of biomarkers obtained from tumour tissue and blood samples;

• Evaluation of local tumour responses by volumetric measurements;

• Evaluation of immune-modulating effects of Amphinex

• Evaluation of skin photosensitivity in a subset of patients;

• Evaluation of fluorescence of tumour tissue in a subset of patients.

Study description

Background summary

This study is an open-label, single arm, multi-centre Phase II study to assess the safety and efficacy of PC-A11 in recurrent SCCHN patients which are unsuitable for surgery and radiotherapy.
Patients will receive one treatment of PC-A11 (Amphinex solution for injection and bleomycin), followed by superficial and/or interstitial laser light application.

The study consists of two parts:
A *run-in part* (for patients eligible for treatment with interstitial laser light application):
• During the *run-in part* a safe light dose for interstitial laser light application with acceptable local toxicity and showing early signs of efficacy should be established in a small number of patients. It is expected that approximately 18-25 evaluable patients will be needed to assess safety and efficacy of PC-A11.
An *expansion part*:
• Patients eligible for superficial laser light application will be enrolled in the *expansion part* of the study. After a light dose is established for interstitial laser light application in the *run-in part* patients eligible for interstitial laser light application will be recruited in the *expansion part* of the study. A total number of 60-68 evaluable patients will be enrolled in the *expansion part*. Patients treated at the established light dose during *run-in part* will be included in the analysis of the *expansion part*.

Patients will be screened during a period of 28 days before study entry. Patients included in the *run-in part* will be followed up to 3 month. Once 12 subjects from the selected dose have provided efficacy data at 3 months, an interim analysis will be conducted. The study may be stopped or modified as described below.

Patients included in the *expansion part* and patients from the *run-in part* treated at the light dose established for interstitial laser light application will be followed until disease progression, but no longer than one year, or until study discontinuation for any other reason. Survival status will be documented in an extended follow up phase until death.

Patients will be monitored for safety at baseline as well as during treatment

and follow up visits until disease progression.

Study objective

Run-in part:
The *run-in part* primary objective:
• To determine a safe light dose for PC-A11 with interstitial laser light application in patients with recurrent head and neck squamous cell carcinoma unsuitable for surgery and radiotherapy and eligible for interstitial laser light application.

The *run-in part* secondary objective:
• To make a preliminary assessment of efficacy at 3 months
• To assess the safety and tolerability;
• To characterize the pharmacokinetics (PK);
• To test the Quality of Life (QoL).

The *run-in part* exploratory objectives;
• To assess possible predictive biomarkers;
• To assess local tumour response by volumetric measurements;
• To assess immune-modulating effects of Amphinex
• To assess skin photosensitivity in a subset of patients;
• To assess fluorescence of tumour tissue in a subset of patients

Expansion part:
The *expansion part* primary objective:
• To assess the efficacy of PC-A11 with superficial and/or interstitial laser light application in patients with recurrent SCCHN by means of local non-progression rates at 6 months.

The *expansion part* secondary objectives:
• To assess efficacy by means of:
- Local non-progression rate at 3 months;
- Objective Overall Response Rate (ORR);
- Disease Control Rate (DCR);
- Progression Free Survival (PFS);
- Overall Survival (OS);
• To assess the safety and tolerability;
• To characterize the pharmacokinetics (PK);
• To test the Quality of Life (QoL).

The *expansion part* exploratory objectives:
• To assess possible predictive biomarkers;
• To assess local tumour response by volumetric measurements;
• To assess immune-modulating effects of Amphinex
• To assess skin photosensitivity in a subset of patients;

• To assess fluorescence of tumour tissue in a subset of patients

Study design

This study is an open-label, single arm, multi-centre Phase II study to assess the safety and efficacy of PC-A11 in recurrent SCCHN patients which are unsuitable for surgery and radiotherapy.
Patients will receive one treatment of PC-A11 (Amphinex solution for injection and bleomycin), followed by superficial and/or interstitial laser light application.

The study consists of two parts:
A *run-in part* (for patients eligible for treatment with interstitial laser light application):
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• Patients eligible for superficial laser light application will be enrolled in the *expansion part* of the study. After a light dose is established for interstitial laser light application in the *run-in part* patients eligible for interstitial laser light application will be recruited in the *expansion part* of the study. A total number of 60-68 evaluable patients will be enrolled in the *expansion part*. Patients treated at the established light dose during *run-in part* will be included in the analysis of the *expansion part*.

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Patients included in the *expansion part* and patients from the *run-in part* treated at the light dose established for interstitial laser light application will be followed until disease progression, but no longer than one year, or until study discontinuation for any other reason. Survival status will be documented in an extended follow up phase until death.

Patients will be monitored for safety at baseline as well as during treatment and follow up visits until disease progression.

Intervention

Amphinex intravenous injection (0.25 mg/kg) at day 0, Bleomycin intravenous

injection (15000 IU/m2) at day 4.
Laser light application within 3 hours after Bleomycin administration, using the PCI-652 nm red light laser.

Study burden and risks

Amphinex is a light sensitive substance. The most common side effect of a similar light sensitive substance that is in clinical use, is that all patients become temporarily light sensitive. The results of the first study in 19 patients who were treated with PC-A11 treatment showed that Amphinex with bleomycin was well tolerated and there were no unexpected safety concerns. There were mild to moderate reactions to skin photosensitivity tests in eight of the nineteen patients treated. The most common side effects of light sensitivity are burns, blistering, redness, changes in pigmentation and sunburn. Some degree of skin photosensitivity is therefore expected, and will probably be the most important side effect of Amphinex.

Patients must take certain precautions to avoid sunlight and strong indoor lighting for a period of time (during the first days after administration until 3 months after administration). These precautions are listed in the Patient Information Form, Patient Leaflet Light Protection and the study protocol.

Other possible side effects that have been seen with similar treatments in the area treated with laser light or in some cased in healthy tissue nearby are typical of for acute tissue inflammation due to light activation and may include: bleeding, swelling, infection, crusting, and skin necrosis. Other possible side effects are fever, constipation, vomiting, anaemia, nausea and dizziness.

Bleomycin is a drug that has been used for a long time to treat different types of cancer and is usually given once or twice per week over a period of several weeks. In the present clinical study bleomycin will only be given once. A known side effect of bleomycin is that it can cause lung problems (symptoms can be difficulty in breathing, shortness of breath, wheezing, fever, or chills). Other common side effects of bleomycin include rise in temperature (on the treatment day), decreased appetite and weight loss, tiredness, nausea, vomiting, rash, hair loss, nail changes, skin changes such as soreness, redness, discoloration of the skin (as after sun exposure), skin thickening, blisters, and inflammation in the mouth.

Patients are informed about the possible side effects and are asked to report these to the investigator.

After light treatment of the cancer lesion some subjects may experience pain at the treatment site. In this clinical study, pain will be assessed on a Visual Analogue Scale (VAS) at all study visits (except for screening and extended follow up visit).

Expected benefit: the results of the Phase I dose-escalating study indicate that PC-A11 treatment may provide considerable benefit to patients in terms of local tumour control.

Contacts

Public
PCI Biotech AS

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NO
Scientific
PCI Biotech AS

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NO

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

To be eligible to participate in this study, patients must meet the following eligibility criteria
1. Study eligibility reviewed and approved by interdisciplinary hospital team.
2. Age >= 18 years.
3. Histologically or cytologically confirmed diagnosis of recurrent SCCHN, with or without metastasis, considered unsuitable for surgery and radiotherapy (patients with distant or regional metastatic disease may be eligible if local palliation is needed).
4. Performance status (ECOG <= 1).

5. At least one measurable target lesion at baseline.
6. Local disease including margins treatable with superficial and/or interstitial laser light application. For superficial lesions: entire tumour accessable for laser light application, treatment margin is 0.5 cm. For interstitial treatment: insertion of implants feasible, treatment margin is 1.0 cm
7. Estimated life expectancy of at least 12 weeks.
8. Written informed consent.

Exclusion criteria

Prior Treatment;
1. Local treatment (e.g. surgery or radiation) of their SCCHN by surgery within the previous 4 weeks or by radiation within the previous 3 months.;
2. Previous treatment with systemic chemotherapy for their SCCHN within the last 4 weeks.;
3. Previous treatment with Photodynamic Therapy within the last 6 months.;
4. Prior treatment with bleomycin.;
5. Prior treatment with PC-A11.;
6. Toxicities incurred as a result of previous anticancer therapy (radiation therapy, chemotherapy, or surgery) which did not resolve to <= grade 2 (as defined by CTCAE version 4.0);
Current Treatment;
7. Current or recent (within 30 days of first study treatment) treatment with another investigational drug or participation in another investigational study.
8. Other concurrent anticancer therapies.
9. Treatment with a medicinal product with known or potential drug-drug interaction with bleomycin or Amphinex.;Haematology, coagulation and biochemistry:
10. Inadequate bone marrow function:
• Absolute Neutrophil Count (ANC): < 1.5 x 109/L, or platelet count <100 x 109/L or haemoglobin < 6 mmol/L.
11. Inadequate liver function, defined as:
• Serum (total) bilirubin > 2 x the Upper Limit of Normal (ULN) for the institution.
• Aspartate Amino Transferase (ASAT) or Alanine Amino Transferase (ALAT) > 2.5 x ULN.
• Alkaline phosphatase levels > 2.5 x ULN.
12. Glomerular filtration rate (GFR) < 30ml/min.
13. Clinical significant electrolyte abnormalities (Potassium, Magnesium, Phosphate that is greater than CTCAE grade 3 for both low and high values)
Other:
14. Tumours known or suspected to be eroding into the dura mater or a major blood vessel, e.g. carotid artery (interna and /or communis) in or adjacent to the illumination site (minimum distance between tumour tissue and critical structure should be 0.5 cm for superficial tumours and 1.0 cm for interstitial tumours).
15. Nasopharyngeal carcinoma.
16. Conditions contraindicated for bleomycin treatment (current lung infection, severely impaired pulmonary function) excluded by lung function test (either formal lung function test for patients able to undertake such assessment, or a suitable opinion by an appropriately

trained Respiratory / Anaesthetic Clinical Specialist).
17. Conditions that worsen when exposed to light (including porphyria).
18. Inability to undergo CT or MRI.
19. Pregnancy or lactation (female patients with childbearing potential). Serum pregnancy test to be performed within 7 days prior to study PC-A11 treatment start, or within 14 days followed by a confirmatory urine pregnancy test within 7 days prior to study treatment start.
20. For female patients of childbearing potential (defined as < 2 years after last menstruation and not surgically sterile) and male patients who are not surgically sterile or with female partners of childbearing potential: absence of highly effective method of contraception resulting in a low failure rate (i.e. less than 1% per year). These methods of contraception according to the note for guidance on non-clinical safety studies for the conduct of human trials for pharmaceuticals (CPMP/ICH/286/95, modification) include consistent and correct use of hormone containing implants and injectables, combined oral contraceptives, hormone containing intrauterine devices, surgical sterilization, sexual abstinence and vasectomy. Note: Abstinence is only acceptable as true abstinence: when this is in line with the preferred and usual lifestyle of the subject, periodic abstinence (eg calender, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.
21. Planned surgery, endoscopic examination or dental treatment in first 30 days after PC-A11 treatment.
22. Co-existing ophthalmic disease likely to require slit-lamp examination within the first 90 days after PC-A11 treatment.
23. Congestive heart failure NYHA Class III and IV. Cardiac arrhythmias (except for atrioventricular block type I, Mobitz type II, and Wenckebach type) signs and symptoms of relevant cardiovascular disease.
24. Known allergy or sensitivity to photosensitisers.
25. Ataxia telangiectasia
26. Concomitant malignant disease, with exception of adequately treated basal cell carcinoma, squamous cell carcinoma or other non-melanomatous skin cancer, or in-situ carcinoma of the uterine cervix.
27. Evidence of any other medical conditions (such as psychiatric illness, infectious diseases, physical examination or laboratory findings) that may interfere with the planned PC-A11 treatment, affect patient compliance or place the patient at high risk from treatment-related complications.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-05-2012
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amphinex
Generic name:	TPCS2a
Product type:	Medicine
Brand name:	Bleomycin
Generic name:	Bleomycin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	24-02-2012
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-07-2012
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-07-2012
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-07-2012
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	09-04-2013
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-07-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-07-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-04-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-04-2015
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2011-003751-19-NL
CCMO	NL38751.031.12

Study results

Results posted: 13-10-2021

First publication
13-10-2021