Clinical trial results:
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

Summary

EudraCT number	2011-003751-19
Trial protocol	DE GB NL LT ES
Global end of trial date	27 August 2015

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022
Summary attachment (see zip file)	Clinical Study Report Synopsis PCIA202_10 (PCIA202_10-aCSR-synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	PCIA202/10

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01606566
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PCI BIOTECH AS
Sponsor organisation address	Ullernchausseen 64, Oslo, Norway, 0369
Public contact	Lucy Wabakken , PCI BIOTECH AS, +47 67 11 54 00 , luwa@pcibiotech.no
Scientific contact	Dr. Anders Høgset, PhD – Chief Scientific Officer, PCI BIOTECH AS, +47 67 11 54 00,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 August 2015
Global end of trial reached?	Yes
Global end of trial date	27 August 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

'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
'Run-in part' secondary objective:
To make a preliminary assessment of efficacy at 3 months
To assess the safety and tolerability
To characterize the PK
To test the QoL
'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
'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 PK
To test the QoL

Protection of trial subjects:

Patients will be monitored closely for a minimum of 2 hours following Amphinex and bleomycin administration, and placement of interstitial light applicator fibres and laser light application will be performed under general anaesthesia. Patients will be assessed for safety at baseline, as well as during treatment and follow-up visits until disease progression. Close monitoring for interactions of Amphinex with other medicinal products and other forms of interaction will be considered carefully during patient selection and treatment. Product complaints were reported to the sponsor and are considered any oral or written expression of dissatisfaction related to identity, quality, purity, and safety of the medicinal product.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	15 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Lithuania: 2
Worldwide total number of subjects	24
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	17
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient enrolled: 15 May 2012
Last patient last visit: 27 Aug 2015
Patients recruited at 8 centers

Pre-assignment

Screening details:

Age ≥18 years, histologically or cytological confirmed diagnosis of recurrent SCCHN, with or without metastasis, considered unsuitable for surgery and radiotherapy, a performance status Eastern Cooperative Oncology Group (ECOG) ≤1 and at least 1 measurable target lesion at Baseline

Period 1

Period 1 title	Pre-expansion, Run-in and Expansion (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	'Pre-expansion' Part PC-A11 (Pre Amendment 2)

Arm description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0, followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Laser light application was performed 3 hours (±1 hour) after bleomycin administration. The light source used was a PCI-652 nm laser (CE 0470), emitting red light at 652±2 nm. The laser had 1 channel operating up to 5 W and 6 -+channels operating up to 0.5 W. Superficial laser light applications were performed with a frontal diffuser fiber attached to the 5 W output channel at a light dose of 100 mW and 60 J/cm2. Up to 6 fibers with cylindrical diffuser tips could be connected to the 0.5 W output channels for simultaneous intratumoral laser light application at a light dose of 100 mW and 60 J/cm per fiber.

Arm type	Experimental
Investigational medicinal product name	Amphinex
Investigational medicinal product code	N/A
Other name	Fimaporfin
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Amphinex at a concentration of 0.25 mg/kg was given as a slow intravenous (i.v.) injection over 1-6 minutes, into a vein not distal to the antecubital fossa, on Day 0.

Investigational medicinal product name	Bleomycin
Investigational medicinal product code	N/A
Other name	N/A
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

15,000 IU/m2 was given on Day 4 as an i.v. infusion at a rate of 1,000 to 1,500 IU/minute, i.e. over 10-15 minutes

Arm title	'Run-in' Part: PC-A11 (10 J/cm)

Arm description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 10 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Arm type	Experimental
Investigational medicinal product name	Amphinex
Investigational medicinal product code	N/A
Other name	Fimaporfin
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Amphinex at a concentration of 0.25 mg/kg was given as a slow intravenous (i.v.) injection over 1-6 minutes, into a vein not distal to the antecubital fossa, on Day 0.

Investigational medicinal product name	Bleomycin
Investigational medicinal product code	N/A
Other name	N/A
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

15,000 IU/m2 was given on Day 4 as an i.v. infusion at a rate of 1,000 to 1,500 IU/minute, i.e. over 10-15 minutes

Arm title	'Run-in' Part: PC-A11 (20 J/cm)

Arm description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 20 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Arm type	Experimental
Investigational medicinal product name	Amphinex
Investigational medicinal product code	N/A
Other name	Fimaporfin
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Amphinex at a concentration of 0.25 mg/kg was given as a slow intravenous (i.v.) injection over 1-6 minutes, into a vein not distal to the antecubital fossa, on Day 0.

Investigational medicinal product name	Bleomycin
Investigational medicinal product code	N/A
Other name	N/A
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

15,000 IU/m2 was given on Day 4 as an i.v. infusion at a rate of 1,000 to 1,500 IU/minute, i.e. over 10-15 minutes

Arm title	'Run-in' Part: PC-A11 (30 J/cm)

Arm description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 30 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Arm type	Experimental

Investigational medicinal product name	Amphinex
Investigational medicinal product code	N/A
Other name	Fimaporfin
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Amphinex at a concentration of 0.25 mg/kg was given as a slow intravenous (i.v.) injection over 1-6 minutes, into a vein not distal to the antecubital fossa, on Day 0.

Investigational medicinal product name	Bleomycin
Investigational medicinal product code	N/A
Other name	N/A
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

15,000 IU/m2 was given on Day 4 as an i.v. infusion at a rate of 1,000 to 1,500 IU/minute, i.e. over 10-15 minutes

Arm title	'Expansion' Part: PC-A11

Arm description:

Patients received a single dose of Amphinex 30 mg/mL (at a dose of 0.25 mg/kg) on Day 0. The bleomycin component of PC-A11 was administered intravenously at a dose of 15000 IU/m2 on Day 4. Laser light application was performed 3 hours (±1 hour) after bleomycin administration using the PCI-652 nm red light laser at a light dose of 100 mW and 60 J/cm2, using a single linear diffuser fiber.

Arm type	Experimental
Investigational medicinal product name	Amphinex
Investigational medicinal product code	N/A
Other name	Fimaporfin
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Amphinex at a concentration of 0.25 mg/kg was given as a slow intravenous (i.v.) injection over 1-6 minutes, into a vein not distal to the antecubital fossa, on Day 0.

Investigational medicinal product name	Bleomycin
Investigational medicinal product code	N/A
Other name	N/A
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

15,000 IU/m2 was given on Day 4 as an i.v. infusion at a rate of 1,000 to 1,500 IU/minute, i.e. over 10-15 minutes

Number of subjects in period 1	'Pre-expansion' Part PC-A11 (Pre Amendment 2)	'Run-in' Part: PC-A11 (10 J/cm)	'Run-in' Part: PC-A11 (20 J/cm)
Started	6	3	7
Completed	3	1	5
Not completed	3	2	2
Disease progression	1	-	1
Lost to follow-up	-	-	1
Lack of efficacy	2	2	-

Number of subjects in period 1	'Run-in' Part: PC-A11 (30 J/cm)	'Expansion' Part: PC-A11
Started	1	7
Completed	1	4
Not completed	0	3
Disease progression	-	1
Lost to follow-up	-	-
Lack of efficacy	-	2

Baseline characteristics

Reporting groups

Reporting group title	'Pre-expansion' Part PC-A11 (Pre Amendment 2)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0, followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Laser light application was performed 3 hours (±1 hour) after bleomycin administration. The light source used was a PCI-652 nm laser (CE 0470), emitting red light at 652±2 nm. The laser had 1 channel operating up to 5 W and 6 -+channels operating up to 0.5 W. Superficial laser light applications were performed with a frontal diffuser fiber attached to the 5 W output channel at a light dose of 100 mW and 60 J/cm2. Up to 6 fibers with cylindrical diffuser tips could be connected to the 0.5 W output channels for simultaneous intratumoral laser light application at a light dose of 100 mW and 60 J/cm per fiber.

Reporting group title	'Run-in' Part: PC-A11 (10 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 10 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	'Run-in' Part: PC-A11 (20 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 20 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	'Run-in' Part: PC-A11 (30 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 30 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	'Expansion' Part: PC-A11

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL (at a dose of 0.25 mg/kg) on Day 0. The bleomycin component of PC-A11 was administered intravenously at a dose of 15000 IU/m2 on Day 4. Laser light application was performed 3 hours (±1 hour) after bleomycin administration using the PCI-652 nm red light laser at a light dose of 100 mW and 60 J/cm2, using a single linear diffuser fiber.

Reporting group values	'Pre-expansion' Part PC-A11 (Pre Amendment 2)	'Run-in' Part: PC-A11 (10 J/cm)	'Run-in' Part: PC-A11 (20 J/cm)
Number of subjects	6	3	7
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			

85 years and over			

Age continuous			
Units: years			
arithmetic mean	53.7	52.3	59.7
full range (min-max)	44 to 74	43 to 59	52 to 66
Gender categorical			
Units: Subjects			
Female	2	1	4
Male	4	2	3
Race, n (%)			
Units: Subjects			
White	6	3	7
Fitzpatrick skin type, n (%)			
Units: Subjects			
1.	1	0	0
2.	0	2	2
3.	3	1	5
4.	2	0	0
5.	0	0	0
6.	0	0	0
Tobacco consumption, n (%)			
Units: Subjects			
Has never smoked	2	0	1
Has previously smoked	4	1	0
Patient currently smokes	0	2	6
Alcohol consumption, n (%)			
Units: Subjects			
Has never consumed alcohol	1	0	2
Has previously consumed alcohol	4	2	3
Once a week	0	0	1
Daily	1	1	1
BMI (kg/m^2)			
Units: kg/m^2			
arithmetic mean	22.33	19.29	19.98
full range (min-max)	10.3 to 28.0	16.2 to 21.6	16.5 to 29.2

Reporting group values	'Run-in' Part: PC-A11 (30 J/cm)	'Expansion' Part: PC-A11	Total
Number of subjects	1	7	24
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0

From 65-84 years			0
85 years and over			0

Age continuous Units: years			
arithmetic mean	51.0	70.0	
full range (min-max)	51 to 51	58 to 78	-
Gender categorical Units: Subjects			
Female	0	2	9
Male	1	5	15
Race, n (%) Units: Subjects			
White	1	7	24
Fitzpatrick skin type, n (%) Units: Subjects			
1.	0	1	2
2.	1	4	9
3.	0	1	10
4.	0	0	2
5.	0	1	1
6.	0	0	0
Tobacco consumption, n (%) Units: Subjects			
Has never smoked	0	0	3
Has previously smoked	0	3	8
Patient currently smokes	1	4	13
Alcohol consumption, n (%) Units: Subjects			
Has never consumed alcohol	0	2	5
Has previously consumed alcohol	1	2	12
Once a week	0	1	2
Daily	0	2	5
BMI (kg/m^2) Units: kg/m^2			
arithmetic mean	26.7	22.49	
full range (min-max)	26.7 to 26.7	19.2 to 29.9	-

End points

End points reporting groups

Reporting group title	'Pre-expansion' Part PC-A11 (Pre Amendment 2)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0, followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Laser light application was performed 3 hours (±1 hour) after bleomycin administration. The light source used was a PCI-652 nm laser (CE 0470), emitting red light at 652±2 nm. The laser had 1 channel operating up to 5 W and 6 -+channels operating up to 0.5 W. Superficial laser light applications were performed with a frontal diffuser fiber attached to the 5 W output channel at a light dose of 100 mW and 60 J/cm2. Up to 6 fibers with cylindrical diffuser tips could be connected to the 0.5 W output channels for simultaneous intratumoral laser light application at a light dose of 100 mW and 60 J/cm per fiber.

Reporting group title	'Run-in' Part: PC-A11 (10 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 10 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	'Run-in' Part: PC-A11 (20 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 20 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	'Run-in' Part: PC-A11 (30 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 30 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	'Expansion' Part: PC-A11

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL (at a dose of 0.25 mg/kg) on Day 0. The bleomycin component of PC-A11 was administered intravenously at a dose of 15000 IU/m2 on Day 4. Laser light application was performed 3 hours (±1 hour) after bleomycin administration using the PCI-652 nm red light laser at a light dose of 100 mW and 60 J/cm2, using a single linear diffuser fiber.

Primary: Dose-limiting toxicities (DLTs)

End point title	Dose-limiting toxicities (DLTs)[1][2]

End point description:

Run-In Part: Dose-limiting toxicities (DLT) and the safety profile of PC-A11 in patients undergoing intratumoral laser light application.

End point type	Primary

End point timeframe:

4 weeks after laser light application

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical analyses for this endpoint. No formal statistical analyses were performed due to the study termination resulting in too few patients being eligible for analysis.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the

baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: DLTs were only analysed in the 'run in' cohorts of patients.

End point values	'Run-in' Part: PC-A11 (10 J/cm)	'Run-in' Part: PC-A11 (20 J/cm)	'Run-in' Part: PC-A11 (30 J/cm)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	7	1	
Units: Patients				
DLTs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Endpoint: AEs

End point title	Safety Endpoint: AEs

End point description:

Proportion of patients with adverse events (in the period of observation, as defined above).

End point type	Secondary

End point timeframe:

Period of observation for all AEs: from date of informed consent until 3 months after laser light application.

End point values	'Pre-expansion' Part PC-A11 (Pre Amendment 2)	'Run-in' Part: PC-A11 (10 J/cm)	'Run-in' Part: PC-A11 (20 J/cm)	'Run-in' Part: PC-A11 (30 J/cm)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	7	1
Units: Patients				
TEAEs	6	3	7	1
SAEs	5	1	4	0
Discontinuations due to TEAEs	0	0	0	0

End point values	'Expansion' Part: PC-A11			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Patients				
TEAEs	6			
SAEs	2			
Discontinuations due to TEAEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Safety endpoint: VAS

End point title	Safety endpoint: VAS

End point description:

Pain scored by a visual analogue scale (VAS) Maximal pain was recorded on a 10 centimetre visual analogue scale (VAS) provided in the CRF. The end-points of the VAS were "no pain" and "unbearable pain"

End point type	Secondary

End point timeframe:

At baseline, after PC-A11 treatment and during follow up visits.

End point values	'Pre-expansion' Part PC-A11 (Pre Amendment 2)	'Run-in' Part: PC-A11 (10 J/cm)	'Run-in' Part: PC-A11 (20 J/cm)	'Run-in' Part: PC-A11 (30 J/cm)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	7	1
Units: Patients				
TEAEs related to pain	2	0	6	1
SAEs related to pain	2	0	0	0
Discontinuations due to TEAEs	0	0	0	0

End point values	'Expansion' Part: PC-A11			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Patients				
TEAEs related to pain	4			
SAEs related to pain	0			
Discontinuations due to TEAEs	0			

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Date of informed consent until 3 months after laser light application. After period of observation the adverse event is serious and for which a causal relationship to the study treatment cannot be ruled out and all deaths not due to disease progression.

Adverse event reporting additional description:

An adverse event (AE) is any untoward medical occurrence in a patient administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Pre-expansion’ Part PC-A11 (Pre Amendment 2)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0, followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4.
Laser light application was performed 3 hours (±1 hour) after bleomycin administration .
The light source used was a PCI-652 nm laser (CE 0470), emitting red light at 652±2 nm. The laser had 1 channel operating up to 5 W and 6 -+channels operating up to 0.5 W. Superficial laser light applications were performed with a frontal diffuser fiber attached to the 5 W output channel at a light dose of 100 mW and 60 J/cm2. Up to 6 fibers with cylindrical diffuser tips could be connected to the 0.5 W output channels for simultaneous intratumoral laser light application at a light dose of 100 mW and 60 J/cm per fiber.

Reporting group title	‘Run-in’ Part: PC-A11 (10 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 10 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	Run-in’ Part: PC-A11 (20 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 20 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	‘Run-in’ Part: PC-A11 (30 J/cm)

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL at a fimaporfin (active substance in Amphinex) dose of 0.25 mg/kg on Day 0 followed by bleomycin administration (at a dose of 15000 IU/m2) on Day 4. Tumors were treated with intratumoral light illumination with a light dose of 30 J/cm cylindrical light diffuser fiber, 3 hours (±1 hour) after bleomycin administration.

Reporting group title	‘Expansion’ Part: PC-A11

Reporting group description:

Patients received a single dose of Amphinex 30 mg/mL (at a dose of 0.25 mg/kg) on Day 0.
The bleomycin component of PC-A11 was administered intravenously at a dose of 15000 IU/m2 on Day 4.
Laser light application was performed 3 hours (±1 hour) after bleomycin administration using the PCI-652 nm red light laser at a light dose of 100 mW and 60 J/cm2, using a single linear diffuser fiber.

Serious adverse events	Pre-expansion' Part PC-A11 (Pre Amendment 2)	'Run-in' Part: PC-A11 (10 J/cm)	Run-in' Part: PC-A11 (20 J/cm)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	1 / 3 (33.33%)	4 / 7 (57.14%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Injury, poisoning and procedural complications			
Soft tissue injury			
subjects affected / exposed	3 / 6 (50.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences causally related to treatment / all	3 / 3	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypoperfusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Surgical and medical procedures			
Fistula repair			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrostomy			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain management			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotherapy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Necrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Obstructive airways disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	'Run-in' Part: PC-A11 (30 J/cm)	'Expansion' Part: PC-A11	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Soft tissue injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypoperfusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Fistula repair			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrostomy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain management			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotherapy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Necrosis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Obstructive airways disorder			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Pre-expansion' Part PC-A11 (Pre Amendment 2)	'Run-in' Part: PC-A11 (10 J/cm)	Run-in' Part: PC-A11 (20 J/cm)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 3 (100.00%)	7 / 7 (100.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oncologic complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Tumour haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	6 / 7 (85.71%)
occurrences (all)	4	0	13
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	3 / 7 (42.86%)
occurrences (all)	1	0	3
Swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Application site pain			
subjects affected / exposed	4 / 6 (66.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	7	0	0

Application site scab			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Feeling cold			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	4	0	1
Facial Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Face oedema			
subjects affected / exposed	5 / 6 (83.33%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	9	0	0
General physical health deterioration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Ulcer haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Local Swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	3
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	2
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pharyngeal oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract congestion			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Depression mood			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Hallucination			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	2
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	2
C-reactive protein increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Post procedural swelling			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Excoriation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
VIth nerve paralysis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Amnesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Coordination abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	3	0	2
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	2 / 7 (28.57%)
occurrences (all)	0	2	2
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Eye swelling			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	3 / 7 (42.86%)
occurrences (all)	0	0	4
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	3
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	3 / 7 (42.86%)
occurrences (all)	1	1	6
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Lip pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	2
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tongue oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Swollen tongue			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Tongue ulceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	3 / 6 (50.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Mouth ulceration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Swelling face			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	3 / 7 (42.86%)
occurrences (all)	0	0	6
Photosensitivity reaction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Blister			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Decubitus ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	4 / 6 (66.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	5	0	1
Skin chapped			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Skin burning sensation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Trismus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	9	1
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Exposed bone in jaw			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Soft tissue necrosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			

Localised infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Oral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 7 (28.57%)
occurrences (all)	0	0	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin graft infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	3	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypocalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	'Run-in' Part: PC-A11 (30 J/cm)	'Expansion' Part: PC-A11	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	6 / 7 (85.71%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oncologic complication			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tumour haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Peripheral coldness			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Haemorrhage			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 1 (100.00%)	4 / 7 (57.14%)	
occurrences (all)	3	10	
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	

Fatigue			
subjects affected / exposed	1 / 1 (100.00%)	2 / 7 (28.57%)	
occurrences (all)	1	2	
Swelling			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Application site pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Application site scab			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Feeling hot			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Feeling cold			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Facial Pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Face oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
General physical health deterioration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Ulcer haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Local Swelling			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	3	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Pharyngeal oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract congestion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Depression mood			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hallucination			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Blood phosphorus decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Blood potassium decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Overdose			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Post procedural swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Thermal burn			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Excoriation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
VIth nerve paralysis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Amnesia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Coordination abnormal			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			

subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Eye pruritus			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Eye swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	4 / 7 (57.14%)	
occurrences (all)	0	4	
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Nausea			

subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Lip pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	2	
Oral pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Tongue oedema			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Swollen tongue			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Tongue ulceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Salivary hypersecretion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Mouth ulceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Swelling face			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

Photosensitivity reaction			
subjects affected / exposed	1 / 1 (100.00%)	2 / 7 (28.57%)	
occurrences (all)	3	5	
Blister			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Decubitus ulcer			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin chapped			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin burning sensation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Trismus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Exposed bone in jaw			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Soft tissue necrosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Localised infection			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Postoperative wound infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Oral infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Skin graft infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypercalcaemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2013	UK -Protocol version 2.0 dated 07 Mar 2013 - Changed selected inclusion and exclusion criteria, changed the Coordinating Investigator, changed the number of patients and number and location of participating sites and made various other non-substantial changes. This amendment implemented the 'Run-in' part for intratumoral laser light application.
11 March 2013	France - Protocol version 2.0 dated 31 May 2013 - changed selected inclusion and exclusion criteria, changed the Coordinating Investigator, changed the number of patients and number and location of participating sites and made various other non-substantial changes. This amendment implemented the 'Run-in' part for intratumoral laser light application.
11 March 2013	Netherlands - Protocol version 2.0 dated 15 April 2013 - changed selected inclusion and exclusion criteria, changed the Coordinating Investigator, changed the number of patients and number and location of participating sites and made various other non-substantial changes. This amendment implemented the 'Run-in' part for intratumoral laser light application.
11 March 2013	Netherlands - Protocol version 2.0 dated 07 May 2013 - changed selected inclusion and exclusion criteria, changed the Coordinating Investigator, changed the number of patients and number and location of participating sites and made various other non-substantial changes. This amendment implemented the 'Run-in' part for intratumoral laser light application.
09 June 2014	Protocol version 3.0 dated 09 June 2014 - This amendment changed an exclusion criterion, added determination of human papilloma virus (HPV) status for all patients, and changed the time point for an optional tumor biopsy for biomarker analysis.
16 March 2015	Protocol version 4.0 dated 16 March 2015 - This amendment extended the treatment margin for intra-tumor light application, removed a requirement of a maximum of 10 fibers to be used for intra tumor light application and added an assessment of immune modulating effects of Amphinex.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The dose optimization for intratumoral light application was more complicated than anticipated. Study was terminated due to increased complexity of the treatment with extended treatment margins and the emerging, very promising, immunotherapy data.

Notes: