Clinical trial results:
A Phase 1/2 Study to Evaluate the Safety, Tolerability, Immune Response, and Clinical Efficacy of Cancer Peptide Vaccine S-488210 in Patients with Unresectable Locoregionally Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma (HNSCC)

Summary

EudraCT number	2011-005014-12
Trial protocol	BE DE
Global end of trial date	15 July 2014
Results information	
Result version number	v2 (current)
This version publication date	09 July 2016
First version publication date	01 August 2015
Version creation reason	• Correction of full data set update needed due to EdraCT downtime in the period Jul-2015-Jan2016

Trial information

Trial identification	
Sponsor protocol code	1122P1811
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Shionogi & Co., Ltd.
Sponsor organisation address	1-8 Doshomachi 3-chome Chuo-ku, Osaka/Osaka, Japan, 541-0045
Public contact	Kenji Igarashi, Shionogi & Co., Ltd., +81 664855082, kenji.igarashi@shionogi.co.jp
Scientific contact	Kenji Igarashi, Shionogi & Co., Ltd., +81 664855082, kenji.igarashi@shionogi.co.jp

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	19 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 July 2014
Global end of trial reached?	Yes
Global end of trial date	15 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of S-488210 in human leukocyte antigen (HLA)-A*02:01-positive patients with HNSCC receiving 4 vaccinations of S-488210 at a dose of 1 mg each of the 3 peptides on a weekly basis

Protection of trial subjects:

1st IDMC meeting:21 Oct 2013, Review of safety data for first 6 patients who received 4 weeks of treatment
2nd IDMC meeting: 25 Mar 2014: Review of safety data for first 6 patients and immune response data of those patients. No safety issues were noticed from both meetings.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 January 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Germany: 3
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	4
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First site activated: 25 July 2012. Recruitment stopped 31 December 2013. Type of location was medical hospital.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	28[1]
Number of subjects completed	7

Pre-assignment subject non-completion reasons

Reason: Number of subjects	protocol exclusion criteria met: 21

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Justification: The reported 24 patients were the number of patients planned per protocol. A total of 28 patients were enrolled, and of these patients at least 7 received 1 dose of the study drug. The error in the database occurs because Eudra pulled data from the initial Belgium CT application where the planned number of patients per protocol was filled in (24) and then it compared that number with the actual number of patients screened enrolled in phase 1 (28).

Period 1

Period 1 title	Step 1(Visit 1-4), Step 2(v5-withdrawal) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	S-488210

Arm description:

injection of S-488210 once a week over 4-week treatment period followed by extension period, and every 2 weeks after week 13

Arm type	Experimental
Investigational medicinal product name	not available yet
Investigational medicinal product code	S-488210
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

3 mg per day

Number of subjects in period 1	S-488210
Started	7
4 injections of S-488210	7
Completed	7

Baseline characteristics

Reporting groups	
Reporting group title	Step 1(Visit 1-4), Step 2(v5-withdrawal)
Reporting group description:	
Injection of S-488210 once a week over 4 weeks treatment period followed by extension period	

Reporting group values	Step 1(Visit 1-4), Step 2(v5-withdrawal)	Total	
Number of subjects	7	7	
Age categorical			
injection of S-488210 once a week over a 4-week treatment period followed by extension period.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	3	3	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	60.4		
standard deviation	± 8.66	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	7	7	

Subject analysis sets	
Subject analysis set title	safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least 1 dose of study drug	
Subject analysis set title	full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who received at least 1 dose of study drug	

Reporting group values	safety analysis set	full analysis set	
Number of subjects	7	7	
Age categorical			
injection of S-488210 once a week over a 4-week treatment period followed by extension period.			
Units: Subjects			

In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	3	3	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	60.4	60.4	
standard deviation	± 8.66	± 8.66	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	7	7	

End points

End points reporting groups

Reporting group title	S-488210
Reporting group description:	
injection of S-488210 once a week over 4-week treatment period followed by extension period, and every 2 weeks after week 13	
Subject analysis set title	safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least 1 dose of study drug	
Subject analysis set title	full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who received at least 1 dose of study drug	

Primary: The number and percentage of patients with at least 1 treatment-emergent AEs (TEAE)

End point title	The number and percentage of patients with at least 1 treatment-emergent AEs (TEAE)[1]
End point description:	
Adverse events were assessed from the date the ICF was signed up to 30 days after the last dose of study drug. TEAE was defined as any event not present before exposure to study drug or any event already present that worsened in either intensity or frequency after exposure to study drug.	
End point type	Primary
End point timeframe:	
Duration from the date the ICF was signed up to 30 days after the last dose of study drug	

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: Justification: Shionogi would not perform any statistical analysis as per protocol since Shionogi & Co, Ltd has decided to terminate phase 2 part because of changing the formula of the cancer peptide vaccine S-488210.

End point values	S-488210	safety analysis set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	7[2]	7[3]		
Units: subjects	7	7		

Notes:

[2] - Patients experienced TEAEs

[3] - Patients experienced TEAEs

Statistical analyses

No statistical analyses for this end point

Secondary: Cytotoxic T Lymphocyte Induction Rate

End point title	Cytotoxic T Lymphocyte Induction Rate
End point description:	
Cytotoxic T lymphocyte induction was defined as increased CTL activity compared with baseline	
End point type	Secondary

End point timeframe:
Every 4 week until 12 weeks

End point values	S-488210	full analysis set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	6		
Units: subjects	6	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed from the date the ICF was signed up to 30 days after the last dose of the study drug.

Adverse event reporting additional description:

A treatment-emergent AE (TEAE) was defined as any event not present before exposure to study drug or any event already present that worsened in either intensity or frequency after exposure to study drug. Total No of TEAEs, No and % of patients with at least 1 TEAE were tabulated along with the No and % of patients by system/organ/class and pr term

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	S-488210

Reporting group description:

Injection of S-488210 once a week over 4 week treatment period followed by extension period

Serious adverse events	S-488210		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 7 (42.86%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Disease progression			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Non cardiac chest pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	S-488210		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	7		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	7		
Injection site erythema			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	7		
Asthenia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	7		
Injection site papule			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	7		
Injection site pruritus			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	7		
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	7		
Oropharyngeal pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	7		

Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Confusional state subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 7 1 / 7 (14.29%) 7		
Investigations Weight decreased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 7 1 / 7 (14.29%) 7		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 7 1 / 7 (14.29%) 7		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 7		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Dysphagia subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Diarrhoea	 2 / 7 (28.57%) 7 2 / 7 (28.57%) 7 2 / 7 (28.57%) 7		

subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 7 1 / 7 (14.29%) 7		
Skin and subcutaneous tissue disorders Ecchymosis subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 7 1 / 7 (14.29%) 7		
Musculoskeletal and connective tissue disorders Neck pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	 2 / 7 (28.57%) 7 1 / 7 (14.29%) 7		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 7 1 / 7 (14.29%) 7		
Metabolism and nutrition disorders Hypercalcaemia subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 February 2013	Amendment 3, Protocol version 4.0 - Inclusion criterion 9 was updated to remove the upper age limit. - Exclusion criterion 2 was updated to clarify that only patients with proof or suggestion of active infection will be excluded. - Exclusion criterion 17 was updated to change the allowable time period for previous use of another investigational product from "within 60 days of enrollment" to "within 28 days of enrollment".
21 June 2013	Amendment 4, Protocol version 5.0 • Exclusion criterion 3 was updated to clarify that the exclusion of patients with human papilloma virus-positive tumor applied to patients in the Phase 2 part of the study only.
16 March 2014	Amendment 5, Protocol version 6.0 • It was added that overall survival and progression-free survival will be assessed for the Phase 1 part 6 months after the last patient has completed Step 1 of the Phase 1 part.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported