Clinical trial results:
A follow-up study exploring number of cycles for weekly treatment with Paclical® in patients with metastatic breast cancer, previously treated in study OAS-11PAC-W

Summary

EudraCT number	2011-002456-14
Trial protocol	LV
Global end of trial date	25 April 2014

Results information

Result version number	v1 (current)
This version publication date	14 May 2017
First version publication date	14 May 2017

Trial information

Trial identification

Sponsor protocol code	OAS-11PAC-W-fu

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Oasmia Pharmaceutical AB
Sponsor organisation address	Vallongatan 1, Uppsala, Sweden, SE-752 28
Public contact	Nina Heldring, Oasmia Pharmaceutical AB, +46 18 50 54 40, nina.heldring@oasmia.com
Scientific contact	Nina Heldring, Oasmia Pharmaceutical AB, +46 18 50 54 40, nina.heldring@oasmia.com

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	20 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 April 2014
Global end of trial reached?	Yes
Global end of trial date	25 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To explore the number of cycles for weekly treatment with Paclical®

Protection of trial subjects:

Laboratory measurements were assessed to monitor safety of patients (haematology and clinical chemistry). Blood pressure, pulse rate and body temperature were measured prior and during the infusion of IMP. Patients were withdrawn if medically necessary according to investigator.

Background therapy: -

Evidence for comparator:

N.A.

Actual start date of recruitment	28 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Latvia: 7
Worldwide total number of subjects	29
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)	22
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Female patients with histologically confirmed metastatic breast cancer completing the study OAS-11PAC-W were eligible. Patients with progressive disease or unacceptable toxicity at last visit of OAS-11PAC-W or with dose-reduction during OAS-11PAC-W were excluded. Out of 31 screened patients, 22 were included and 2 were screening failures.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Paclical 100 mg/m2

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 110 mg/m2

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 120 mg/m2

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 130 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 140 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 150 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 160 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The

treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 170 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 180 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 190 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 210 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The

treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 230 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Arm title	Paclical 240 mg/m2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Paclical
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclical consists of paclitaxel and XR-17. The powder was reconstituted using Lactated or Acetated Ringer´s solution. The dose was calculated based on body surface area (mg paclitaxel/m2). The treatment was administered over approximately 30 minutes once weekly.

Number of subjects in period 1	Paclical 100 mg/m2	Paclical 110 mg/m2	Paclical 120 mg/m2
Started	3	3	2
Completed	2	1	1
Not completed	1	2	1
Adverse event, serious fatal	-	1	-
Physician decision	-	1	-
Consent withdrawn by subject	-	-	-
Protocol violation, fulfilling exclusion criteria	-	-	-
Adverse event, non-fatal	1	-	1

Number of subjects in period 1	Paclical 130 mg/m2	Paclical 140 mg/m2	Paclical 150 mg/m2
Started	3	2	2
Completed	2	0	0
Not completed	1	2	2
Adverse event, serious fatal	-	-	-

Physician decision	-	-	-
Consent withdrawn by subject	1	-	1
Protocol violation, fulfilling exclusion criteria	-	1	-
Adverse event, non-fatal	-	1	1

Number of subjects in period 1	Paclical 160 mg/m2	Paclical 170 mg/m2	Paclical 180 mg/m2
Started	3	3	2
Completed	1	0	0
Not completed	2	3	2
Adverse event, serious fatal	1	-	-
Physician decision	-	-	-
Consent withdrawn by subject	1	3	1
Protocol violation, fulfilling exclusion criteria	-	-	-
Adverse event, non-fatal	-	-	1

Number of subjects in period 1	Paclical 190 mg/m2	Paclical 210 mg/m2	Paclical 230 mg/m2
Started	1	1	2
Completed	0	0	0
Not completed	1	1	2
Adverse event, serious fatal	-	-	-
Physician decision	-	-	1
Consent withdrawn by subject	-	1	1
Protocol violation, fulfilling exclusion criteria	-	-	-
Adverse event, non-fatal	1	-	-

Number of subjects in period 1	Paclical 240 mg/m2
Started	2
Completed	0
Not completed	2
Adverse event, serious fatal	-
Physician decision	1
Consent withdrawn by subject	1
Protocol violation, fulfilling exclusion criteria	-
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	29	29	
Age categorical Units: Subjects			
Adults (18-64 years)	22	22	
From 65-84 years	7	7	
Age continuous Units: years			
arithmetic mean	54.1		
standard deviation	± 10.6	-	
Gender categorical Units: Subjects			
Female	29	29	
Male	0	0	
Child bearing potential Units: Subjects			
Yes	9	9	
No	20	20	
HER2 assessment Units: Subjects			
HER2 positive	8	8	
HER2 negative	21	21	
ECOG status			
ECOG = Eastern Cooperative Oncology Group performance status			
Units: Subjects			
Status 0	26	26	
Status 1	3	3	
Status 2	0	0	
Status 3	0	0	
Status 4	0	0	
Status 5	0	0	

End points

End points reporting groups

Reporting group title	Paclical 100 mg/m2
Reporting group description: -	
Reporting group title	Paclical 110 mg/m2
Reporting group description: -	
Reporting group title	Paclical 120 mg/m2
Reporting group description: -	
Reporting group title	Paclical 130 mg/m2
Reporting group description: -	
Reporting group title	Paclical 140 mg/m2
Reporting group description: -	
Reporting group title	Paclical 150 mg/m2
Reporting group description: -	
Reporting group title	Paclical 160 mg/m2
Reporting group description: -	
Reporting group title	Paclical 170 mg/m2
Reporting group description: -	
Reporting group title	Paclical 180 mg/m2
Reporting group description: -	
Reporting group title	Paclical 190 mg/m2
Reporting group description: -	
Reporting group title	Paclical 210 mg/m2
Reporting group description: -	
Reporting group title	Paclical 230 mg/m2
Reporting group description: -	
Reporting group title	Paclical 240 mg/m2
Reporting group description: -	
Subject analysis set title	Entire study population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All included patients, irrespective of treatment dose

Subject analysis set title	Completers
Subject analysis set type	Per protocol

Subject analysis set description:

This data set includes the patients reaching an endpoint (i.e. complete response, disease progression, unacceptable toxicity). The 22 withdrawn patients are not included in this data set.

Primary: Number of cycles for weekly treatment of Paclical

End point title	Number of cycles for weekly treatment of Paclical[1][2]

End point description:

The number of treatment cycles for Paclical weekly treatment could not be obtained.

End point type	Primary

End point timeframe:

Assessment was made until a reason for completion (complete response, unacceptable toxicity or progressive disease).

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: Given the exploratory nature (i.e. to determine the number of cycles for weekly administration), no statistical hypothesis testing was performed.

[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: Due to withdrawal primary endpoint data were not available for all treatment arms.

End point values	Paclical 100 mg/m2	Paclical 110 mg/m2	Paclical 120 mg/m2	Paclical 130 mg/m2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	1	1	2
Units: Treatment cycles				
median (full range (min-max))	8 (8 to 8)	10 (10 to 10)	13 (13 to 13)	14 (8 to 20)

End point values	Paclical 160 mg/m2			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Treatment cycles				
median (full range (min-max))	15 (15 to 15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reason for completion due to endpoint

End point title	Reason for completion due to endpoint

End point description:

End point type	Secondary

End point timeframe:

From start of study (5th treatment cycle) until the patient discontinued the study due to any of the three pre-defined endpoints.

End point values	Completers			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Patients				
Complete response	1			
Disease progression	2			
Unacceptable toxicity	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Tumour response

End point title	Tumour response

End point description:

Tumour response was assessed by CT evaluated according to RECIST 1.1 at the radiology department of the sites. The patient´s last assessment is presented. The reason is that a limited number of patients were treated more than 8 cycles and that not all patients had an end of treatment assessment due to short interval between last scheduled CT and study withdrawal.

End point type	Secondary

End point timeframe:

Tumour response was assessed at entry into the present follow-up study (treatment cycle 5) and every 8th week and at end of study.

End point values	Entire study population			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: Patients				
Complete response	1			
Partial response	9			
Stable disease	16			
Progressive disease	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first treatment administration in the follow-up study (cycle 5) until one week (7-9 days) after the last treatment or withdrawal.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Entire study population

Reporting group description:

All patients included in the study (one patient never received any treatment in this follow-up study but is still included in this safety data set).

Serious adverse events	Entire study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 28 (10.71%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression	Additional description: Relation to treatment assessed by investigator		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Cardiopulmonary failure	Additional description: Relation to treatment assessed by investigator		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Administration site abscess	Additional description: Relation to treatment assessed by investigator		
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Entire study population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 28 (67.86%)		
Vascular disorders			
Phlebitis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		
Neuropathy peripheral			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Leukocytosis			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		

Neutropenia subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 6		
Neutrophilia subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	7 / 28 (25.00%) 8		
Infusion site phlebitis subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 6		
Injection site extravasation subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Spinal pain subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Visual acuity reduced subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Gastrointestinal disorders Stomatitis			

subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Hepatobiliary disorders Hepatotoxicity subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all) Pneumothorax subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Skin and subcutaneous tissue disorders Nail discolouration subjects affected / exposed occurrences (all) Nail disorder subjects affected / exposed occurrences (all) Onychoclasis subjects affected / exposed occurrences (all) Skin erosion subjects affected / exposed occurrences (all) Skin ulcer subjects affected / exposed occurrences (all) Onychomadesis subjects affected / exposed occurrences (all)	 2 / 28 (7.14%) 2 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1		
Renal and urinary disorders Enuresis subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1		

Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 August 2012	This is a follow-up of a study intended to be a phase I/II (OAS-11PAC-W). When the phase II part of the main study was removed this also warranted changes in the present follow-up study.

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.

Since no MTD was established in OAS-11PAC-W, patients in the present follow-up were treated with different doses. A high withdrawal rate resulting in a small sample size limits the possibility to draw conclusions regarding number of treatment cycles.

Notes: