Clinical trial results:
LISAH: AN OPEN-LABEL, RANDOMISED PHASE II STUDY ASSESSING QUALITY OF LIFE ASSOCIATED WITH SUBCUTANEOUS TRASTUZUMAB INJECTED INTO THE THIGH OR UPPER ARM IN PATIENTS WITH HER2-POSITIVE EARLY BREAST CANCER

Summary

EudraCT number	2013-001023-39
Trial protocol	AT
Global end of trial date	18 October 2013

Results information

Result version number	v1 (current)
This version publication date	04 May 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	ML28786

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01928615
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	18 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the Quality of Life in Human Epidermal Growth Factor 2 (HER2) - positive early breast cancer patients treated with trastuzumab solution injected subcutaneously into the thigh versus upper arm.

Protection of trial subjects:

This study will be conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research is conducted, whichever affords the greater protection to the individual.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 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	Austria: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

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)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Neither of the 2 enrolled participants were randomized to 1 of the 2 crossover treatment arms. Randomization would not have occurred until after Cycle 6. Both participants only received 1 cycle of treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Trastuzumab

Arm description:

In the run-in phase, participants received trastuzumab intravenously every 3 weeks for 18 weeks (Cycles 1-6). They first received trastuzumab 8 mg/kg once (Cycle 1) followed by trastuzumab 6 mg/kg 5 times for 15 weeks (Cycles 2-6). Following the run-in phase, participants were randomized to receive trastuzumab 600 mg subcutaneously every 3 weeks in the thigh and upper arm in a cross-over design for a total of 24 weeks (Cycles 7-14). They received trastuzumab either in the thigh first for 4 cycles (Cycles 7-10) followed by trastuzumab in the upper arm for 4 cycles (Cycles 11-14) or the upper arm first (Cycles 7-10) followed by the thigh (Cycles 11-14). In Cycles 15-18, participants received trastuzumab 600 mg SC every 3 weeks into either the thigh or the upper arm (participant’s choice) for 12 weeks (Cycles 15-18).

Arm type	Experimental
Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion, Solution for injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

8 mg/kg loading dose in Cycle1 followed by 6 mg/kg maintenance dose from Cycle 2 to Cycle 6 (3-week cycles) administered intravenously. A 600 mg subcutaneous injection from Cycle 7 to Cycle 18.

Number of subjects in period 1	Trastuzumab
Started	2
Completed	0
Not completed	2
Study terminated by Sponsor	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description:

In the run-in phase, participants received trastuzumab intravenously every 3 weeks for 18 weeks (Cycles 1-6). They first received trastuzumab 8 mg/kg once (Cycle 1) followed by trastuzumab 6 mg/kg 5 times for 15 weeks (Cycles 2-6). Following the run-in phase, participants were randomized to receive trastuzumab 600 mg subcutaneously every 3 weeks in the thigh and upper arm in a cross-over design for a total of 24 weeks (Cycles 7-14). They received trastuzumab either in the thigh first for 4 cycles (Cycles 7-10) followed by trastuzumab in the upper arm for 4 cycles (Cycles 11-14) or the upper arm first (Cycles 7-10) followed by the thigh (Cycles 11-14). In Cycles 15-18, participants received trastuzumab 600 mg SC every 3 weeks into either the thigh or the upper arm (participant's choice) for 12 weeks (Cycles 15-18).

Reporting group values	Overall Study	Total	
Number of subjects	2	2	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 38 ± 14.14	 -	
Gender categorical Units: Subjects			
Female	2	2	
Male	0	0	

End points

End points reporting groups

Reporting group title	Trastuzumab

Reporting group description:

In the run-in phase, participants received trastuzumab intravenously every 3 weeks for 18 weeks (Cycles 1-6). They first received trastuzumab 8 mg/kg once (Cycle 1) followed by trastuzumab 6 mg/kg 5 times for 15 weeks (Cycles 2-6). Following the run-in phase, participants were randomized to receive trastuzumab 600 mg subcutaneously every 3 weeks in the thigh and upper arm in a cross-over design for a total of 24 weeks (Cycles 7-14). They received trastuzumab either in the thigh first for 4 cycles (Cycles 7-10) followed by trastuzumab in the upper arm for 4 cycles (Cycles 11-14) or the upper arm first (Cycles 7-10) followed by the thigh (Cycles 11-14). In Cycles 15-18, participants received trastuzumab 600 mg SC every 3 weeks into either the thigh or the upper arm (participant's choice) for 12 weeks (Cycles 15-18).

Primary: Quality of Life Score

End point title	Quality of Life Score[1]

End point description:

Participants rated their quality of life on a visual analog scale (VAS) at the end of each cycle for Cycles 7-14. The left-end of the VAS represented the lowest-rated quality of life and the right-end of the VAS represented the highest-rated quality of life. Both the mean ratings for injections into the thigh and the upper arm and the minimum ratings for during injections into the thigh and the upper arm are reported. Quality of life scores ranged from 1 to 100 with a higher score indicating a better rated quality of life.

End point type	Primary

End point timeframe:

Cycles 7-14 (Weeks 19-42, 24 weeks total)

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: Since the study was terminated by the sponsor, endpoints were not analyzed and no statistical analyses were performed.

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: participants				
number (not applicable)				

Notes:

[2] - Due to premature termination of the study, the Outcome Measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time in months from Baseline to death from any cause.

End point type	Secondary

End point timeframe:

Baseline to the end of the study (up to 54 weeks)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: participants				
number (not applicable)				

Notes:

[3] - Due to premature termination of the study, the Outcome Measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease-free Survival

End point title	Disease-free Survival

End point description:

Disease-free survival was defined as the time in months from Baseline to disease recurrence or death, whichever occurred first.

End point type	Secondary

End point timeframe:

Baseline to the end of the study (up to 54 weeks)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: participants				
number (not applicable)				

Notes:

[4] - Due to premature termination of the study, the Outcome Measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Health Care Provider’s Satisfaction With the Injection Site

End point title	Health Care Provider’s Satisfaction With the Injection Site

End point description:

The health care provider for each participant was asked to rate their satisfaction with the 2 injection sites, thigh and upper arm, on a scale of 1 to 10, where 10 represents greater satisfaction. Ratings were made at the end of Cycles 10 and 14.

End point type	Secondary

End point timeframe:

End of Cycles 10 and 14 (Weeks 30 and 42)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: participants				
number (not applicable)				

Notes:

[5] - Due to premature termination of the study, the Outcome Measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Participant's Satisfaction With the Injection Site

End point title	Participant's Satisfaction With the Injection Site

End point description:

Each participant was asked to rate their satisfaction with the 2 injection sites, thigh and upper arm, on a scale of 1 to 10, where 10 represents greater satisfaction. Ratings were made at the end of Cycles 10 and 14.

End point type	Secondary

End point timeframe:

End of Cycles 10 and 14 (Weeks 30 and 42)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: participants				
number (not applicable)				

Notes:

[6] - Due to premature termination of the study, the Outcome Measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Preferring Each Injection Site

End point title	Percentage of Participants Preferring Each Injection Site

End point description:

Participants were asked which of the 2 injection sites was their preferred site at the end of Cycle 14.

End point type	Secondary

End point timeframe:

End of Cycle 14 (Week 42)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: participants				
number (not applicable)				

Notes:

[7] - Due to premature termination of the study, the Outcome Measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first dose of study drug administration until study termination.

Adverse event reporting additional description:

Intent-to-treat population: All participants who received at least 1 dose of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	Trastuzumab

Reporting group description:

In the run-in phase, participants received trastuzumab intravenously every 3 weeks for 18 weeks (Cycles 1-6). They first received trastuzumab 8 mg/kg once (Cycle 1) followed by trastuzumab 6 mg/kg 5 times for 15 weeks (Cycles 2-6). Following the run-in phase, participants were randomized to receive trastuzumab 600 mg subcutaneously every 3 weeks in the thigh and upper arm in a cross-over design for a total of 24 weeks (Cycles 7-14). They received trastuzumab either in the thigh first for 4 cycles (Cycles 7-10) followed by trastuzumab in the upper arm for 4 cycles (Cycles 11-14) or the upper arm first (Cycles 7-10) followed by the thigh (Cycles 11-14). In Cycles 15-18, participants received trastuzumab 600 mg SC every 3 weeks into either the thigh or the upper arm (participant's choice) for 12 weeks (Cycles 15-18).

Serious adverse events	Trastuzumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Trastuzumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)		
Respiratory, thoracic and mediastinal disorders			
Common cold			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported