Clinical trial results:
HOMERUS: A Local, Open Label, Multicentre, Phase IIIB Study, Investigating Subcutaneous Trastuzumab Administered at Home With Single Injection Device in Patients With HER2-Positive Early Breast Cancer

Summary

EudraCT number	2013-000829-31
Trial protocol	NL
Global end of trial date	14 September 2018

Results information

Result version number	v2
This version publication date	18 December 2019
First version publication date	04 October 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	ML28878

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +4161 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +4161 6878333, 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	14 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A study to investigate subcutaneous trastuzumab administration at home with a Single Injection Device in subjects with HER2-positive early breast cancer.

Protection of trial subjects:

Each subject or legally authorized representative signed an Informed Consent Form (ICF) before participating in this study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 125
Worldwide total number of subjects	125
EEA total number of subjects	125

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)	115
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult subjects With HER2-Positive Early Breast Cancer were included in this study.

Period 1

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

Arms

Arm title	Trastuzumab

Arm description:

Participants will receive 600 milligrams (mg) trastuzumab SC by single-use injection device (SID) every 3 weeks (Q3W) for up to a total of 1 year, unless disease recurrence, unacceptable toxicity or participant withdrawal occurs. The first 3 administrations will be done at hospital, after that participants will be permitted to self-administer under the supervision of a healthcare professional (HCP).

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

Dosage and administration details:

Participants received 600 milligrams (mg) trastuzumab subcutaneously (SC) by a single-use injection device (SID) every 3 weeks (Q3W) for up to a total of 1 year, unless disease recurrence, unacceptable toxicity or participant withdrawal occurred. The first 3 administrations were done at hospital, after that participants were permitted to self administer under the supervision of a healthcare professional (HCP).

Number of subjects in period 1	Trastuzumab
Started	125
Completed	108
Not completed	17
Consent withdrawn by subject	2
Recurrence of disease	1
Adverse event, non-fatal	9
Administrative/other	1
Violation of selection criteria	2
Refused treatment/did not cooperate	2

Baseline characteristics

Reporting groups	
Reporting group title	Trastuzumab
Reporting group description:	
Participants will receive 600 milligrams (mg) trastuzumab SC by single-use injection device (SID) every 3 weeks (Q3W) for up to a total of 1 year, unless disease recurrence, unacceptable toxicity or participant withdrawal occurs. The first 3 administrations will be done at hospital, after that participants will be permitted to self-administer under the supervision of a healthcare professional (HCP).	

Reporting group values	Trastuzumab	Total	
Number of subjects	125	125	
Age categorical 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)	115	115	
From 65-84 years	10	10	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	50.7		
standard deviation	± 9.91	-	
Gender categorical Units: Subjects			
Female	124	124	
Male	1	1	

End points

End points reporting groups

Reporting group title	Trastuzumab

Reporting group description:

Participants will receive 600 milligrams (mg) trastuzumab SC by single-use injection device (SID) every 3 weeks (Q3W) for up to a total of 1 year, unless disease recurrence, unacceptable toxicity or participant withdrawal occurs. The first 3 administrations will be done at hospital, after that participants will be permitted to self-administer under the supervision of a healthcare professional (HCP).

Primary: Percentage of Participants With Adverse Events (AEs) and Serious AEs (SAEs)

End point title	Percentage of Participants With Adverse Events (AEs) and Serious AEs (SAEs)[1]

End point description:

End point type	Primary

End point timeframe:

From Baseline up to approximately 4 years

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

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: percentage of subjects				
number (not applicable)				
Treatment-Emergent AEs	96.8			
Treatment-Emergent SAEs	8.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics Trough Concentrations (Ctrough) of Trastuzumab

End point title	Pharmacokinetics Trough Concentrations (Ctrough) of Trastuzumab

End point description:

End point type	Secondary

End point timeframe:

Pre-dose (within 1 day before trastuzumab administration) at Cycles 2, 3, 9, 10, 12, 13 (cycle length=21 days)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: ug/mL				
arithmetic mean (standard deviation)	()			

Notes:

[2] - Data has not been analysed for reporting purposes

Statistical analyses

No statistical analyses for this end point

Secondary: Health Survey Short Form-36 (SF-36) Score

End point title	Health Survey Short Form-36 (SF-36) Score

End point description:

SF-36 to assess Physical component score (PCS) and mental component score (MCS)

End point type	Secondary

End point timeframe:

Cycles 3 and 9 (cycle length=21 days)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: Score on a scale				
arithmetic mean (standard deviation)				
SF-36 PCS, Cycle 3 (n=109)	59.4 (± 18.90)			
SF-36 PCS, Cycle 9 (n=98)	+6.9 (± 19.38)			
SF-36 MCS, Cycle 3 (n=106)	71.5 (± 18.88)			
SF-36 MCS, Cycle 9 (n=95)	-0.3 (± 17.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mood and Anxiety Questionnaire (MASQ) Score

End point title	Mood and Anxiety Questionnaire (MASQ) Score

End point description:

End point type	Secondary

End point timeframe:

Cycles 3 and 9 (cycle length=21 days)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Anhedonic Depression, Cycle 9 (n=100)	+0.2 (± 9.30)			
Anxious Arousal, Cycle 9 (n=100)	+1.1 (± 7.83)			
General Distress Depression, Cycle 9 (n=100)	-0.1 (± 7.12)			
General Distress Anxiety, Cycle 9 (n=100)	+0.4 (± 5.68)			
General Distress Mixed, Cycle 9 (n=100)	-0.0 (± 6.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Choosing to Return to Hospital Administration

End point title	Percentage of Subjects Choosing to Return to Hospital Administration

End point description:

According to protocol, patients should have been given the choice to return to in-hospital administration at cycle 6, however the patients deciding to do so made that decision later on during the study. Due to ethical considerations (patient well-fare), this could not be refused. Analysing according to original endpoint would not reflect the actual course of the decision of patients to return to hospital administration. Therefore it was decided to analyse at later timepoints, deviating from the original endpoint.

End point type	Secondary

End point timeframe:

Cycle 7 to Cycle 18 (cycle length=21 days)

End point values	Trastuzumab			
Subject group type	Reporting group			
Number of subjects analysed	114			
Units: Percentage of subjects				
number (not applicable)				
Cycle 7 (n=114)	3.5			
Cycle 8 (n=114)	0.0			
Cycle 9 (n=112)	2.7			
Cycle 10 (n=112)	1.8			
Cycle 11 (n=109)	0.0			
Cycle 12 (n=108)	1.9			
Cycle 13 (n=100)	3.0			
Cycle 14 (n=99)	0.0			

Cycle 15 (n=6)	0.0			
Cycle 16 (n=6)	0.0			
Cycle 17 (n=6)	0.0			
Cycle 18 (n=6)	0.0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to approximately 4 years

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Trastuzumab

Reporting group description:

Participants will receive 600 milligrams (mg) trastuzumab SC by SID every 3 weeks (Q3W) for up to a total of 1 year, unless disease recurrence, unacceptable toxicity or participant withdrawal occurs. The first 3 administrations will be done at hospital, after that participants will be permitted to self-administer under the supervision of a healthcare professional (HCP).

Serious adverse events	Trastuzumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 125 (8.00%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Wound necrosis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			

Rectocele			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mastitis			
subjects affected / exposed	2 / 125 (1.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 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	119 / 125 (95.20%)		
Vascular disorders			
Hot flush			

subjects affected / exposed	40 / 125 (32.00%)		
occurrences (all)	41		
Hypertension			
subjects affected / exposed	26 / 125 (20.80%)		
occurrences (all)	32		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	8 / 125 (6.40%)		
occurrences (all)	8		
Influenza type illness			
subjects affected / exposed	18 / 125 (14.40%)		
occurrences (all)	21		
Fatigue			
subjects affected / exposed	40 / 125 (32.00%)		
occurrences (all)	43		
Injection site haematoma			
subjects affected / exposed	6 / 125 (4.80%)		
occurrences (all)	7		
Injection site pain			
subjects affected / exposed	14 / 125 (11.20%)		
occurrences (all)	16		
Injection site erythema			
subjects affected / exposed	12 / 125 (9.60%)		
occurrences (all)	30		
Injection site reaction			
subjects affected / exposed	10 / 125 (8.00%)		
occurrences (all)	11		
Oedema peripheral			
subjects affected / exposed	14 / 125 (11.20%)		
occurrences (all)	15		
Uncoded	Additional description: Uncoded		
alternative dictionary used: Other Other			
subjects affected / exposed	16 / 125 (12.80%)		
occurrences (all)	18		
Reproductive system and breast disorders			

Breast oedema subjects affected / exposed occurrences (all) Breast pain subjects affected / exposed occurrences (all)	7 / 125 (5.60%) 7 7 / 125 (5.60%) 7		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	13 / 125 (10.40%) 13 10 / 125 (8.00%) 10		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	7 / 125 (5.60%) 7 7 / 125 (5.60%) 7		
Investigations Ejection fraction decreased subjects affected / exposed occurrences (all)	14 / 125 (11.20%) 15		
Injury, poisoning and procedural complications Radiation skin injury subjects affected / exposed occurrences (all)	6 / 125 (4.80%) 9		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	9 / 125 (7.20%) 9		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness	11 / 125 (8.80%) 13		

subjects affected / exposed	14 / 125 (11.20%)		
occurrences (all)	14		
Neuropathy peripheral			
subjects affected / exposed	7 / 125 (5.60%)		
occurrences (all)	7		
Paraesthesia			
subjects affected / exposed	14 / 125 (11.20%)		
occurrences (all)	17		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	16 / 125 (12.80%)		
occurrences (all)	18		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	7 / 125 (5.60%)		
occurrences (all)	7		
Rash			
subjects affected / exposed	4 / 125 (3.20%)		
occurrences (all)	7		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	24 / 125 (19.20%)		
occurrences (all)	24		
Back pain			
subjects affected / exposed	8 / 125 (6.40%)		
occurrences (all)	8		
Muscle spasms			
subjects affected / exposed	7 / 125 (5.60%)		
occurrences (all)	7		
Musculoskeletal Stiffness			
subjects affected / exposed	8 / 125 (6.40%)		
occurrences (all)	8		
Myalgia			
subjects affected / exposed	25 / 125 (20.00%)		
occurrences (all)	25		
Musculoskeletal chest pain			

subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	8 / 125 (6.40%) 8 9 / 125 (7.20%) 10		
Infections and infestations Cystitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 8 / 125 (6.40%) 9 30 / 125 (24.00%) 34		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2014	Exclusion criterion 10 (inadequate bone marrow function) was deleted. This criterion is used for (dis)continuation of chemotherapy, not for (dis)continuation of trastuzumab. Safety lab was determined at screening, but bone marrow function was not used for in/exclusion. The sample size was corrected from 150 to 128. Trastuzumab SC vials were added as IMP because vials were used as back-up in case of SID failure. Furthermore, a description on how to handle SID failure was added. Text was added to indicate that also HCP could return the SID to the hospital. Text was added to indicate that the ICF had to be signed within 28 days to first dose. Visit windows were added to Protocol Section 4.4.2.1, and the time point for completion of the questionnaires was clarified and a time window was added to Protocol Section 4.4.7. The option of paper questionnaires was added to Protocol Section 7.3. MRI was deleted as a method for left ventricular ejection fraction (LVEF) measurement because this is only done by echocardiography (ECHO) or multiple gated acquisition (MUGA). Time points for cardiac safety assessments were added to Protocol Section 5.1.2 following addition of an extra schedule of assessments (see below). A schedule of assessment for patients that received 6 cycles of trastuzumab prior to the study was added and time of assessments were corrected throughout the protocol. Further revisions to the schedule of assessments were made to clarify which assessments needed to be done at which time point, and a time window for PK sampling "within 1 day before administration" and a note [t] concerning hematology and chemistry were added.
29 April 2014	The time point for completion of the questionnaires was clarified and a time window was added in Protocol Section 3.9.4. In inclusion criterion 6, the text 'except for patients in the neo-adjuvant setting' was deleted because this study only included patients in the adjuvant setting, and the text ‘in combination with chemotherapy’ was added to be compliant with the guidelines for breast cancer therapy. In inclusion criterion 7, LVEF was adjusted from ≥55% to ≥50% in line with the Dutch guidelines for mamma care "mammacarcinoom richtlijn, 2.0", which states that LVEF needs to be 50%-55% shortly before start of trastuzumab. In inclusion 7 criterion, the text ‘Except in case patient received anthracycline treatment previously then documented results within an acceptable limit from a cardiac assessment within 14 days prior to enrolment.’ was added. A section on Adverse Events of Special Interest (AESI) was added. In the schedule of assessment, LVEF at Cycle 1 Day 1 was deleted due to the change in inclusion criterion 7; the LVEF occurred at screening within 14 days prior to enrolment for all patients that received anthracycline treatment previously and did not need to be repeated at Cycle 1 Day 1.
21 May 2015	The Multiplex Ligation-dependent Probe Amplification (MLPA) method was added as an additional test to determine HER2 status. The use of hormonal auterine devices (IUDs) was clarified in exclusion criterion 6. The time window for completion of the SF-36 en MASQ questionnaires was clarified (within one week after dosing at Cycles 3 and 9).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported