Clinical trial results:
A Phase 2, Multicenter, Single-Arm Study of Trastuzumab Emtansine in Patients With HER2 IHC-Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer Who Have Received At Least One Prior Chemotherapy Regimen

Summary

EudraCT number	2014-001237-83
Trial protocol	DE ES IT PL
Global end of trial date	

Results information

Result version number	v1
This version publication date	09 November 2017
First version publication date	09 November 2017

Trial information

Trial identification

Sponsor protocol code	BO29389

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02289833
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-LaRoche
Sponsor organisation address	Grenzacherstrasse 124, CH, Basel, Basel, Switzerland, 4070
Public contact	Medical Communications, Hoffmann-LaRoche, +41 8008218590, genentech@druginfo.com
Scientific contact	Medical Communications, Hoffmann-LaRoche, +41 8008218590, genentech@druginfo.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	Interim
Date of interim/final analysis	26 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 October 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the efficacy of single-agent trastuzumab emtansine in subjects with centrally confirmed human epidermal growth factor receptor (HER2) immunohistochemistry (IHC)-positive (IHC2+ or IHC3+) locally advanced or metastatic non-small cell lung cancer (NSCLC) who had received at least one prior chemotherapy regimen, as measured by confirmed objective response rate (ORR).

Protection of trial subjects:

All subjects signed an informed consent form before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2014
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	Spain: 12
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	49
EEA total number of subjects	29

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)	27

From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were screened centrally for HER2 status, using archived tumor specimens from previously collected tissue, if available.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort IHC2+

Arm description:

Subjects with HER2 IHC2-positive (IHC 2+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.

Arm type	Experimental
Investigational medicinal product name	Trastuzumab emtansine
Investigational medicinal product code	
Other name	Kadcyla, T-DM1
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Trastuzumab emtansine will be administered intravenously (IV) at a dose of 3.6 milligrams/kilogram (mg/kg) on Day 1 of every 21-day cycle until disease progression (as assessed by the investigator), unmanageable toxicity, or study termination by the sponsor, whichever occurs first.

Arm title	Cohort IHC3+

Arm description:

Subjects with HER2 IHC3-positive (IHC 3+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.

Arm type	Experimental
Investigational medicinal product name	Trastuzumab emtansine
Investigational medicinal product code	
Other name	Kadcyla, T-DM1
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Trastuzumab emtansine will be administered intravenously (IV) at a dose of 3.6 mg/kg on Day 1 of every 21-day cycle until disease progression (as assessed by the investigator), unmanageable toxicity, or study termination by the sponsor, whichever occurs first.

Number of subjects in period 1	Cohort IHC2+	Cohort IHC3+
Started	29	20
Completed	0	0
Not completed	29	20
Death	15	8
Continued Participation in Study	12	8
Lost to follow-up	2	-
Clinical Progression	-	1
Disease Progression	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Cohort IHC2+
Reporting group description:	
Subjects with HER2 IHC2-positive (IHC 2+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.	
Reporting group title	Cohort IHC3+
Reporting group description:	
Subjects with HER2 IHC3-positive (IHC 3+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.	

Reporting group values	Cohort IHC2+	Cohort IHC3+	Total
Number of subjects	29	20	49
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	63.0	61.3	
standard deviation	± 10.3	± 8.5	-
Gender, Male/Female Units: Subjects			
Female	13	7	20
Male	16	13	29

End points

End points reporting groups

Reporting group title	Cohort IHC2+
Reporting group description:	
Subjects with HER2 IHC2-positive (IHC 2+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.	
Reporting group title	Cohort IHC3+
Reporting group description:	
Subjects with HER2 IHC3-positive (IHC 3+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.	
Subject analysis set title	PK Analyses for Trastuzumab Emtansine and Total Trastuzumab
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects with HER2 IHC2 or IHC3-positive (IHC 2+ or IHC 3+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.	
Subject analysis set title	Cmax Analysis for DM1
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects with HER2 IHC2 or IHC3-positive (IHC 2+ or IHC 3+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.	
Subject analysis set title	Anti-drug Antibody Analysis Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects with HER2 IHC2 or IHC3-positive (IHC 2+ or IHC 3+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine. Treated subjects with post-dose sample available for ADA analysis.	

Primary: Percentage of Subjects With Objective Response as per Investigator Assessment According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v. 1.1)

End point title	Percentage of Subjects With Objective Response as per Investigator Assessment According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v. 1.1)[1]
End point description:	
Objective response is defined as a complete response (CR) or partial response (PR) determined on two consecutive assessments ≥ 4 weeks apart, based on investigator assessment according to RECIST, Version 1.1. CR: disappearance of all target lesions; and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 millimeters (mm). PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. The efficacy-evaluable population included subjects who received at least one dose of study drug.	
End point type	Primary
End point timeframe:	
From Day 1 to disease progression (PD) or death from any cause, up to the clinical cutoff date (approximately 22 months)	

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: Descriptive analysis only.

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	20		
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 11.9)	20.0 (5.7 to 43.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from first study drug administration to death from any cause. The efficacy-evaluable population included subjects who received at least one dose of study drug. 9999 indicates that the upper limit confidence interval was not calculable due to the low number subjects with events.

End point type	Secondary

End point timeframe:

From Day 1 to death from any cause, up to the clinical cutoff date (approximately 22 months)

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	20		
Units: months				
median (confidence interval 95%)	12.2 (3.8 to 9999)	15.3 (9.3 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) as per Investigator Assessment According to RECIST v. 1.1

End point title	Progression-Free Survival (PFS) as per Investigator Assessment According to RECIST v. 1.1

End point description:

PFS is defined as the time from first study drug administration to first documented disease progression, based on investigator assessment using RECIST, v1.1, or death from any cause during the study, whichever occurs first. Disease progression is defined as: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, including baseline; an absolute increase of at least 5 mm in the sum of diameters of target lesions; the appearance of one or more new lesions. The efficacy-evaluable population included subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Day 1 to PD or death from any cause, up to the clinical cutoff date (approximately 22 months)

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	20		
Units: months				
median (confidence interval 95%)	2.6 (1.4 to 2.8)	2.7 (1.4 to 8.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response (DOR) Assessed According to RECIST v1.1

End point title	Duration of Objective Response (DOR) Assessed According to RECIST v1.1

End point description:

DOR is defined as the time from the initial documentation of response (CR or PR using RECIST, v1.1) to documented disease progression using RECIST v1.1 or death from any cause during the study. CR: disappearance of all target lesions; and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Disease progression: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, including baseline; an absolute increase of at least 5 mm in the sum of diameters of target lesions; the appearance of one or more new lesions. The efficacy-evaluable population included subjects who received at least one dose of study drug. Data are reported for subjects with response.

End point type	Secondary

End point timeframe:

From first documented objective response to PD or death from any cause, up to the clinical cutoff date (approximately 22 months)

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	4		
Units: months				
median (confidence interval 95%)	(to)	7.3 (2.9 to 8.3)		

Notes:

[2] - No subjects had response.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Benefit as per Investigator

Assessment According to RECIST, v1.1

End point title	Percentage of Subjects With Clinical Benefit as per Investigator Assessment According to RECIST, v1.1

End point description:

Clinical benefit is defined as having a CR or PR or stable disease (using RECIST, v1.1) at 6 months. Subjects with no post-baseline response assessment are considered as experiencing no clinical benefit. CR: disappearance of all target lesions; and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Stable disease: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum while in the study. PD: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, including baseline; an absolute increase of at least 5 mm in the sum of diameters of target lesions; the appearance of one or more new lesions. The efficacy-evaluable population included subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Day 1 to PD or death from any cause, up to the clinical cutoff date (approximately 22 months)

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	20		
Units: percentage of subjects				
number (confidence interval 95%)	6.9 (0.9 to 22.8)	30.0 (11.9 to 54.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Adverse Events (AEs) and Serious AEs (SAEs)

End point title	Percentage of Subjects With Adverse Events (AEs) and Serious AEs (SAEs)

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product, whether or not considered related to the study drug. A SAE is any experience that: results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is medically significant. The safety-evaluable population included subjects who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

From Day 1 to 30 days after last dose of study drug, up to the clinical cutoff date (approximately 22 months)

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	20		
Units: percentage of subjects				
number (not applicable)				
AEs	89.7	95.0		
SAEs	17.2	25.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) for Trastuzumab Emtansine and Total Trastuzumab

End point title	Maximum Observed Concentration (Cmax) for Trastuzumab Emtansine and Total Trastuzumab

End point description:

Cmax is the maximum observed concentration of a drug and was measured in blood serum. The pharmacokinetic (PK) population included subjects who had received at least one dose of study treatment and had at least one serum or plasma concentration result available at clinical data cut-off. Data are reported for evaluable subjects.

End point type	Secondary

End point timeframe:

Pre-dose (within 2 days) and 30 minutes (min) after end of infusion (infusion length= 100 min or less) on Day 1 of Cycles 1 and 3 (one cycle=21 days); at treatment discontinuation/early termination, up to the clinical cutoff date (approximately 22 months)

End point values	PK Analyses for Trastuzumab Emtansine and Total Trastuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: micrograms per milliliter (ug/mL)				
arithmetic mean (standard deviation)				
Trastuzumab Emtansine	78.7 (± 19.6)			
Total Trastuzumab	79.9 (± 21.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUCinf for Trastuzumab Emtansine and Total Trastuzumab

End point title	AUCinf for Trastuzumab Emtansine and Total Trastuzumab

End point description:

AUC (from zero to infinity) represents the total drug exposure over time in blood serum. The pharmacokinetic (PK) population included subjects who had received at least one dose of study treatment and had at least one serum or plasma concentration result available at clinical data cut-off. Data are reported for evaluable participants who consented to intense sampling.

End point type	Secondary

End point timeframe:

Pre-dose and 30 minutes (min) post-infusion (inf.) on Day 1 of Cycles 1 and 3; post- inf. on Days 2, 3, 4 or 5, 8, and 15 of Cycle 1, and pre- inf. on Day 1 of Cycle 2 and Day 1 of Cycle 4 (cycle=21 days); discontin./termination, up to approx. 22 months

End point values	PK Analyses for Trastuzumab Emtansine and Total Trastuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	4[3]			
Units: days times ug/mL				
arithmetic mean (standard deviation)				
Trastuzumab Emtansine	324 (± 49.9)			
Total Trastuzumab	436 (± 83.4)			

Notes:

[3] - 4 subjects had valid intense sampling data.

Statistical analyses

No statistical analyses for this end point

Secondary: Elimination Half-Life (t1/2) for Trastuzumab Emtansine and Total Trastuzumab

End point title	Elimination Half-Life (t1/2) for Trastuzumab Emtansine and Total Trastuzumab

End point description:

t1/2 is the time required for the drug serum concentration to be reduced to half. The pharmacokinetic (PK) population included subjects who had received at least one dose of study treatment and had at least one serum or plasma concentration result available at clinical data cut-off. Data are reported for evaluable participants who consented to intense sampling.

End point type	Secondary

End point timeframe:

Pre-dose and 30 minutes (min) post-infusion (inf.) on Day 1 of Cycles 1 and 3; post- inf. on Days 2, 3, 4 or 5, 8, and 15 of Cycle 1, and pre- inf. on Day 1 of Cycle 2 and Day 1 of Cycle 4 (cycle=21 days); discontin./termination, up to approx. 22 months

End point values	PK Analyses for Trastuzumab Emtansine and Total Trastuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	4[4]			
Units: days				
arithmetic mean (standard deviation)				
Trastuzumab Emtansine	3.2 (± 0.51)			
Total Trastuzumab	5.6 (± 1.14)			

Notes:

[4] - 4 subjects had valid intense sampling data.

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution (Vss) for Trastuzumab Emtansine and Total Trastuzumab

End point title	Volume of Distribution (Vss) for Trastuzumab Emtansine and Total Trastuzumab

End point description:

Vss is the volume of distribution of study drug at steady state. The pharmacokinetic (PK) population included subjects who had received at least one dose of study treatment and had at least one serum or plasma concentration result available at clinical data cut-off. Data are reported for evaluable participants who consented to intense sampling.

End point type	Secondary

End point timeframe:

Pre-dose and 30 minutes (min) post-infusion (inf.) on Day 1 of Cycles 1 and 3; post- inf. on Days 2, 3, 4 or 5, 8, and 15 of Cycle 1, and pre- inf. on Day 1 of Cycle 2 and Day 1 of Cycle 4 (cycle=21 days); discontin./termination, up to approx. 22 months

End point values	PK Analyses for Trastuzumab Emtansine and Total Trastuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	4[5]			
Units: milligrams per kilogram (mL/kg)				
arithmetic mean (standard deviation)				
Trastuzumab Emtansine	51.1 (± 1.81)			
Total Trastuzumab	60.7 (± 4.23)			

Notes:

[5] - 4 subjects had valid intense sampling data.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) for Trastuzumab Emtansine and Total Trastuzumab

End point title	Clearance (CL) for Trastuzumab Emtansine and Total Trastuzumab

End point description:

CL is a measure of the body’s elimination of a drug from blood serum over time. The pharmacokinetic (PK) population included subjects who had received at least one dose of study treatment and had at least one serum or plasma concentration result available at clinical data cut-off. Data are reported for evaluable participants who consented to intense sampling.

End point type	Secondary

End point timeframe:

Pre-dose and 30 minutes (min) post-infusion (inf.) on Day 1 of Cycles 1 and 3; post- inf. on Days 2, 3, 4 or 5, 8, and 15 of Cycle 1, and pre- inf. on Day 1 of Cycle 2 and Day 1 of Cycle 4 (cycle=21 days); discontin./termination, up to approx. 22 months

End point values	PK Analyses for Trastuzumab Emtansine and Total Trastuzumab			
Subject group type	Subject analysis set			
Number of subjects analysed	4[6]			
Units: mL/day/kg				
arithmetic mean (standard deviation)				
Trastuzumab Emtansine	11.35 (± 1.99)			
Total Trastuzumab	8.54 (± 1.99)			

Notes:

[6] - 4 subjects had valid intense sampling data.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) for N2'- deacetyl-N2'-(3-mercapto-1-oxopropyl)-maytansine (DM1)

End point title	Maximum Observed Concentration (Cmax) for N2'- deacetyl-N2'-(3-mercapto-1-oxopropyl)-maytansine (DM1)

End point description:

Cmax is the maximum observed concentration of a drug and was measured in blood plasma. The pharmacokinetic (PK) population included subjects who had received at least one dose of study treatment and had at least one serum or plasma concentration result available at clinical data cut-off. Data are reported for evaluable subjects.

End point type	Secondary

End point timeframe:

Pre-dose (within 2 days) and 30 minutes (min) after end of infusion (infusion length= 100 min or less) on Day 1 of Cycle 1 (one cycle=21 days); at treatment discontinuation/early termination, up to the clinical cutoff date (approximately 22 months)

End point values	Cmax Analysis for DM1			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	4.3 (± 3.36)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment-Emergent Anti-Drug Antibodies (ADAs)

End point title	Percentage of Subjects With Treatment-Emergent Anti-Drug Antibodies (ADAs)

End point description:

The presence of ADAs in blood serum is an indication of the body's immune response to a drug. The pharmacokinetic (PK) population included subjects who had received at least one dose of study treatment and had at least one serum or plasma concentration result available at clinical data cut-off. Data are reported for evaluable subjects.

End point type	Secondary

End point timeframe:

Pre-dose (within 2 days) on Day 1 of Cycles 1 and 3; at treatment discontinuation/early termination, up to the clinical cutoff date (approximately 22 months)

End point values	Anti-drug Antibody Analysis Group			
Subject group type	Subject analysis set			
Number of subjects analysed	39[7]			
Units: percentage of subjects	0			

Notes:

[7] - Treated subjects with post-dose sample available for ADA analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of HER2 Extracellular Domain (ECD)

End point title	Serum Concentration of HER2 Extracellular Domain (ECD)

End point description:

This outcome measure was not assessed at the time of the primary analysis (data cutoff 26-Oct-2016).

End point type	Secondary

End point timeframe:

Pre-dose (within 2 days) on Day 1

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	()	()		

Notes:

[8] - This endpoint was not assessed at the time of the primary analysis (data cutoff 26-Oct-2016).

[9] - This endpoint was not assessed at the time of the primary analysis (data cutoff 26-Oct-2016).

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Died

End point title	Percentage of Subjects who Died

End point description:

The efficacy-evaluable population included subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Day 1 to death from any cause, up to the clinical cutoff date (approximately 22 months)

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	20		
Units: percentage of subjects				
number (not applicable)	51.7	40.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with PFS Event of Disease Progression, as per Investigator Assessment According to RECIST v. 1.1, or Death

End point title	Percentage of Subjects with PFS Event of Disease Progression, as per Investigator Assessment According to RECIST v. 1.1, or Death

End point description:

PFS is defined as the time from first study drug administration to first documented disease progression, based on investigator assessment using RECIST, v1.1, or death from any cause during the study, whichever occurs first. Disease progression is defined as: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, including baseline; an absolute increase of at least 5 mm in the sum of diameters of target lesions; the appearance of one or more new lesions. The efficacy-evaluable population included subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From Day 1 to PD or death from any cause, up to the clinical cutoff date (approximately 22 months)

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	20		
Units: percentage of subjects				
number (not applicable)	96.6	85.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with DOR Event of Disease Progression, Assessed According to RECIST v1.1

End point title	Percentage of Subjects with DOR Event of Disease Progression, Assessed According to RECIST v1.1

End point description:

DOR is defined as the time from the initial documentation of response (CR or PR using RECIST, v1.1) to documented disease progression using RECIST v1.1 or death from any cause during the study. CR: disappearance of all target lesions; and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Disease progression: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, including baseline; an absolute increase of at least 5 mm in the sum of diameters of target lesions; the appearance of one or more new lesions. The efficacy-evaluable population included subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From first documented objective response to PD or death from any cause, up to the clinical cutoff date (approximately 22 months)

End point values	Cohort IHC2+	Cohort IHC3+		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	4		
Units: percentage of subjects				
number (not applicable)		75.0		

Notes:

[10] - No subjects had response.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 to 30 days after last dose of study drug, up to the clinical cutoff date (approximately 22 months).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Cohort IHC2+

Reporting group description:

Subjects with HER2 IHC2-positive (IHC 2+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.

Reporting group title	Cohort IHC3+

Reporting group description:

Subjects with HER2 IHC3-positive (IHC 3+) locally advanced or metastatic NSCLC, who had received at least one prior platinum-based chemotherapy regimen, will receive trastuzumab emtansine.

Serious adverse events	Cohort IHC2+	Cohort IHC3+	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 29 (17.24%)	5 / 20 (25.00%)	
number of deaths (all causes)	15	8	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 29 (3.45%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 29 (3.45%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 29 (3.45%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 29 (3.45%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 29 (3.45%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	1 / 29 (3.45%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
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	Cohort IHC2+	Cohort IHC3+	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 29 (79.31%)	19 / 20 (95.00%)	
Vascular disorders			
Poor venous access			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 29 (34.48%)	3 / 20 (15.00%)	
occurrences (all)	13	5	
Asthenia			
subjects affected / exposed	4 / 29 (13.79%)	4 / 20 (20.00%)	
occurrences (all)	5	5	
Chills			
subjects affected / exposed	1 / 29 (3.45%)	4 / 20 (20.00%)	
occurrences (all)	1	4	
Pyrexia			
subjects affected / exposed	2 / 29 (6.90%)	2 / 20 (10.00%)	
occurrences (all)	2	2	
Chest pain			

subjects affected / exposed	0 / 29 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	3	
Mucosal inflammation			
subjects affected / exposed	2 / 29 (6.90%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Malaise			
subjects affected / exposed	2 / 29 (6.90%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	1 / 29 (3.45%)	1 / 20 (5.00%)	
occurrences (all)	1	3	
Influenza like illness			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Vaginal haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 29 (27.59%)	5 / 20 (25.00%)	
occurrences (all)	10	6	
Dyspnoea			
subjects affected / exposed	7 / 29 (24.14%)	2 / 20 (10.00%)	
occurrences (all)	7	3	
Epistaxis			

subjects affected / exposed	0 / 29 (0.00%)	4 / 20 (20.00%)	
occurrences (all)	0	6	
Pleural effusion			
subjects affected / exposed	2 / 29 (6.90%)	1 / 20 (5.00%)	
occurrences (all)	2	2	
Dysphonia			
subjects affected / exposed	1 / 29 (3.45%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Nasal congestion			
subjects affected / exposed	1 / 29 (3.45%)	1 / 20 (5.00%)	
occurrences (all)	1	2	
Dyspnoea exertional			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pulmonary pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Depressive symptom			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 29 (3.45%)	3 / 20 (15.00%)	
occurrences (all)	1	3	
Platelet count decreased			

subjects affected / exposed	2 / 29 (6.90%)	2 / 20 (10.00%)	
occurrences (all)	3	2	
Weight decreased			
subjects affected / exposed	3 / 29 (10.34%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Blood bilirubin increased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Lymphocyte count decreased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	3 / 29 (10.34%)	4 / 20 (20.00%)	
occurrences (all)	3	4	
Wound			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 29 (3.45%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	4 / 29 (13.79%)	1 / 20 (5.00%)	
occurrences (all)	5	2	
Headache			

subjects affected / exposed	3 / 29 (10.34%)	1 / 20 (5.00%)	
occurrences (all)	4	1	
Cerebrovascular accident			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 29 (3.45%)	3 / 20 (15.00%)	
occurrences (all)	1	3	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 29 (20.69%)	3 / 20 (15.00%)	
occurrences (all)	8	6	
Vomiting			
subjects affected / exposed	3 / 29 (10.34%)	2 / 20 (10.00%)	
occurrences (all)	7	4	
Dry mouth			
subjects affected / exposed	4 / 29 (13.79%)	0 / 20 (0.00%)	
occurrences (all)	4	0	
Constipation			
subjects affected / exposed	1 / 29 (3.45%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	2 / 29 (6.90%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Dyspepsia			

subjects affected / exposed	1 / 29 (3.45%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Abdominal pain			
subjects affected / exposed	2 / 29 (6.90%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Abdominal pain upper			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Mouth ulceration			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Stomatitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 29 (6.90%)	1 / 20 (5.00%)	
occurrences (all)	2	2	
Rash maculo-papular			
subjects affected / exposed	0 / 29 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	3	
Dermatitis acneiform			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Petechiae			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	4 / 29 (13.79%)	4 / 20 (20.00%)	
occurrences (all)	4	6	
Muscle spasms			
subjects affected / exposed	1 / 29 (3.45%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Muscular weakness			
subjects affected / exposed	1 / 29 (3.45%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 29 (3.45%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 29 (3.45%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Myalgia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	3 / 29 (10.34%)	0 / 20 (0.00%)	
occurrences (all)	4	0	
Urinary tract infection			
subjects affected / exposed	1 / 29 (3.45%)	2 / 20 (10.00%)	
occurrences (all)	2	3	
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Paronychia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 29 (34.48%)	3 / 20 (15.00%)	
occurrences (all)	10	3	
Hypokalaemia			

subjects affected / exposed	2 / 29 (6.90%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Hyperglycaemia			
subjects affected / exposed	2 / 29 (6.90%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	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