Clinical trial results:
ELUXA 2: An international, randomised, multi-centre, active controlled, open-label Phase III study evaluating the efficacy of BI 1482694 versus standard platinum doublet chemotherapy in patients with T790M mutation positive locally advanced or metastatic non-small cell lung cancer (NSCLC) whose disease progressed on one prior epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) treatment

Summary

EudraCT number	2015-005079-26
Trial protocol	ES BE AT
Global end of trial date	11 August 2016

Results information

Result version number	v1 (current)
This version publication date	10 November 2018
First version publication date	10 November 2018
Summary attachment (see zip file)	Statement (1370.2_Statement_Eudract.pdf)

Trial information

Trial identification

Sponsor protocol code	1370.2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim Pharma GmbH & Co KG, +1 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim Pharma GmbH & Co KG, +1 8002430127, clintriage.rdg@boehringer-ingelheim.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	11 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 August 2016
Global end of trial reached?	Yes
Global end of trial date	11 August 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy and safety of BI 1482694 versus standard platinum doublet chemotherapy as a second line treatment for patients with locally advanced or metastatic NSCLC whose disease progressed on or after one prior 1st line EGFR-TKI therapy and whose tumours carry at least one EGFR activating mutation and a T790M mutation versus standard platinum doublet chemotherapy.

Protection of trial subjects:

No patient entered the study, therefore no results data available. 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entering the trial. 199998 number entered in population of trial subjects is "Not applicable", the number is added to match the count in the participant flow which we get after adding the NA value "99999" for each treatment arm.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Portugal: 199998
Worldwide total number of subjects	199998
EEA total number of subjects	199998

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)	199998
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial

Pre-assignment

Screening details:

All subjects had to be screened for eligibility to participate in the trial. Subjects had to attend specialist sites which would then ensure that they (the subjects) met all inclusion/exclusion criteria. Subjects were not to be randomised to trial treatment if any one of the specific entry criteria were violated

Period 1

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

Blinding implementation details:

Open label trial

Arms

Are arms mutually exclusive?	Yes
Arm title	BI 1482694

Arm description:

Subjects were to be orally administered BI 1482694 800 mg once daily as 2 x 400 mg tablets; dose reduction to 600 mg once daily and 400 mg once daily (if applicable) in the presence of drug-related adverse events

Arm type	Experimental
Investigational medicinal product name	BI 1482694
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to be orally administered BI 1482694 800 mg once daily as 2 x 400 mg tablets; dose reduction to 600 mg once daily and 400 mg once daily (if applicable) in the presence of drug-related adverse events

Arm title	Platinum based doublet chemotherapy

Arm description:

Subjects were to be administered intravenous infusion of Chemotherapy once every 3 weeks (21 days) course:
- Cisplatin at 75mg / m2 in combination with Pemetrexed 500 mg / m2 on day 1 of 21 or
- Carboplatin at AUC 5 in combination with Pemetrexed 500 mg / m2 on day 1 of 21
- Pemetrexed 500 mg / m2 on day 1 of 21 as maintenance treatment allowed per SmPC/PI

Arm type	Active comparator
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were to be administered Cisplatin (Solution for infusion) Vials with 200 ml of 0.5 mg/ml solution Up to 6 infusions, each separated by 3 weeks

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were to be administered Carboplatin (Solution for infusion) Vials with 60 ml solution at 10 mg/ml Up to 6 infusions at AUC5, each separated by 3 weeks

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were to be administered Pemetrexed (500 mg powder for reconstitution for infusion) Vials with 500 mg ; after reconstitution each vial contains pemetrexed at 25 mg/ml; infusion at 500 mg/m2 each separated by 3 weeks

Number of subjects in period 1	BI 1482694	Platinum based doublet chemotherapy
Started	99999	99999
Completed	99999	99999

Baseline characteristics

Reporting groups	
Reporting group title	BI 1482694
Reporting group description:	
Subjects were to be orally administered BI 1482694 800 mg once daily as 2 x 400 mg tablets; dose reduction to 600 mg once daily and 400 mg once daily (if applicable) in the presence of drug-related adverse events	
Reporting group title	Platinum based doublet chemotherapy
Reporting group description:	
Subjects were to be administered intravenous infusion of Chemotherapy once every 3 weeks (21 days) course: - Cisplatin at 75mg / m2 in combination with Pemetrexed 500 mg / m2 on day 1 of 21 or - Carboplatin at AUC 5 in combination with Pemetrexed 500 mg / m2 on day 1 of 21 - Pemetrexed 500 mg / m2 on day 1 of 21 as maintenance treatment allowed per SmPC/PI	

Reporting group values	BI 1482694	Platinum based doublet chemotherapy	Total
Number of subjects	99999	99999	199998
Age categorical Units: Subjects			
Age continuous			
All treated patients, those with evidence of receiving one or more doses of either BI 1482694 or standard chemotherapy was to be used for reporting. 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.			
Units: years			
arithmetic mean	0	0	
standard deviation	± 0	± 0	-
Gender categorical			
All treated patients, those with evidence of receiving one or more doses of either BI 1482694 or standard chemotherapy was to be used for reporting. 99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.			
Units: Subjects			
Female	99999	99999	199998
Male	0	0	0

End points

End points reporting groups

Reporting group title	BI 1482694

Reporting group description:

Subjects were to be orally administered BI 1482694 800 mg once daily as 2 x 400 mg tablets; dose reduction to 600 mg once daily and 400 mg once daily (if applicable) in the presence of drug-related adverse events

Reporting group title	Platinum based doublet chemotherapy

Reporting group description:

Subjects were to be administered intravenous infusion of Chemotherapy once every 3 weeks (21 days) course:
- Cisplatin at 75mg / m2 in combination with Pemetrexed 500 mg / m2 on day 1 of 21 or
- Carboplatin at AUC 5 in combination with Pemetrexed 500 mg / m2 on day 1 of 21
- Pemetrexed 500 mg / m2 on day 1 of 21 as maintenance treatment allowed per SmPC/PI

Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)[1]

End point description:

Progression-free survival (PFS) is defined as time from randomisation until disease progression or death from any cause, whichever occurs earlier.

End point type	Primary

End point timeframe:

time from randomisation until disease progression or death

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 subjects entered in the trial hence results are not available.

End point values	BI 1482694	Platinum based doublet chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99999[2]	99999[3]		
Units: years				
median (full range (min-max))	0 (0 to 0)	0 (0 to 0)		

Notes:

[2] - ITT

[3] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Overall survival (OS) is defined as the time from randomisation until death from any cause.
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.

End point type	Secondary

End point timeframe:

time from randomisation until death

End point values	BI 1482694	Platinum based doublet chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99999[4]	99999[5]		
Units: years				
median (full range (min-max))	0 (0 to 0)	0 (0 to 0)		

Notes:

[4] - ITT

[5] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response (OR)

End point title	Objective response (OR)

End point description:

Objective response (OR) is defined as best overall response of complete response (CR) or partial response (PR) from randomisation until the earliest of disease progression, death or last evaluable tumour assessment before start of subsequent anti-cancer therapy, loss to follow-up or withdrawal of consent.
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.

End point type	Secondary

End point timeframe:

time from randomisation until the earliest of disease progression, death or last evaluable tumour assessment

End point values	BI 1482694	Platinum based doublet chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99999[6]	99999[7]		
Units: percentage of participants				
number (not applicable)	99999	99999		

Notes:

[6] - ITT

[7] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Time to OR

End point title	Time to OR

End point description:

Time to OR is defined as the time from randomisation until first documented CR or PR.
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.

End point type	Secondary

End point timeframe:

time from randomisation until first documented CR or PR.

End point values	BI 1482694	Platinum based doublet chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99999[8]	99999[9]		
Units: years				
median (full range (min-max))	0 (0 to 0)	0 (0 to 0)		

Notes:

[8] - ITT

[9] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of OR (DOR)

End point title	Duration of OR (DOR)

End point description:

Duration of OR (DOR) is defined as the time from first documented CR or PR until the earliest of disease progression or death among patients with OR.
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.

End point type	Secondary

End point timeframe:

time from first documented CR or PR until the earliest of disease progression or death

End point values	BI 1482694	Platinum based doublet chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99999[10]	99999[11]		
Units: years				
median (full range (min-max))	0 (0 to 0)	0 (0 to 0)		

Notes:

[10] - ITT

[11] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control (DC)

End point title	Disease control (DC)

End point description:

Disease control (DC) is defined as best overall response of CR, PR or stable disease (SD) from randomisation until the earliest of disease progression, death or last evaluable tumour assessment before start of subsequent anti-cancer therapy, loss to follow-up or withdrawal of consent.
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.

End point type	Secondary

End point timeframe:

from randomisation until the earliest of disease progression, death or last evaluable tumour assessment

End point values	BI 1482694	Platinum based doublet chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99999[12]	99999[13]		
Units: percentage of participants				
number (not applicable)	99999	99999		

Notes:

[12] - ITT

[13] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Tumour shrinkage

End point title	Tumour shrinkage

End point description:

Tumour shrinkage (in millimeters) is defined as the difference between the minimum post-baseline sum of longest diameters of target lesions (longest for non-nodal lesions, short axis for nodal lesions) and the baseline sum of longest diameters of the same set of target lesions.
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.

End point type	Secondary

End point timeframe:

from randomisation until database lock

End point values	BI 1482694	Platinum based doublet chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99999[14]	99999[15]		
Units: millimeters				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Notes:

[14] - ITT

[15] - ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Time to deterioration in Patient Reported Outcomes

End point title	Time to deterioration in Patient Reported Outcomes

End point description:

Time to deterioration in Patient Reported Outcomes (PROs) of:
- cough ((European Organisation for Research and Treatment of Cancer) EORTC QLQ-LC13: Q1)
- dyspnoea (EORTC QLQ-LC13: Q3-5 and EORTC QLQC30: Q8)
- chest pain (EORTC QLQ-LC13: Q10)
- NSCLC specific symptoms of NSCLC SAQ

Deterioration is defined as the time from randomisation until the earliest of a 10-point worsening from baseline score or death.
99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants entered in the trial.

End point type	Secondary

End point timeframe:

time from randomisation until database lock

End point values	BI 1482694	Platinum based doublet chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99999[16]	99999[17]		
Units: percentage of participants				
number (not applicable)	99999	99999		

Notes:

[16] - ITT

[17] - ITT

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All adverse events occurring after first intake of treatment through the Residual effect period.

Adverse event reporting additional description:

99999 is "Not applicable" value or 0 participants, this trial was discontinued with no participants enrolled in the trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No subjects entered in the trial hence results are not available.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 February 2016	The first official version of this clinical trial protocol was version 2.0 (revision 1), Shortly after finalization of CTP version 1.0, additional data became available which had to be included into the document before regulatory and IRB/EC submissions.
06 July 2016	Following sections were changed: - Abbreviations - Drug Profile - Benefit- Risk Assessment - 3.3.4.1 Removal of individual patients - Table of Dose Reduction Scheme for BI 1482694 - Management of dermatological AEs following treatment with BI 1482694 - Definitions of AEs - Published references - Clinical Evaluation of SJS/TEN Description of change:Addition of information on occurrence, grading, management and reporting of serious adverse skin reactions.

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.

Discontinued by Boehringer Ingelheim during preparation of trial. No patient entered the study, therefore no results data available.

Notes: