Clinical trial results:
A randomized, double-blind, placebo-controlled, phase III study to evaluate the efficacy of afatinib (BIBW 2992) in maintenance therapy after postoperative concurrent radiotherapy and chemotherapy for squamous-cell carcinoma of the head and neck : a GORTEC collaborative group study 2010-02

Summary

EudraCT number	2010-023265-22
Trial protocol	FR
Global end of trial date	30 November 2020

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022
Summary attachment (see zip file)	RRF (2010-023265-22_Updated_BIBW2992.pdf)

Trial information

Trial identification

Sponsor protocol code	ET2010-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01427478
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre Léon Bérard
Sponsor organisation address	28 rue Laennec, Lyon, France, 69008
Public contact	DRCI Séverine METZGER, Centre Léon Bérard, 00 334 78 78 28 28,
Scientific contact	Centre Léon Bérard Dr Séverine RACADOT Dr Pascal POMMIER, Centre Léon Bérard, 00 334 78 78 28 28,

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	22 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Démontrer la supériorité d'un traitement de maintenance de 12 mois par afatinib par rapport à un placebo, après une radiothérapie et chimiothérapie concomitante par cisplatine, sur l'amélioration du taux de survie sans maladie (DFS) à 2 ans

Protection of trial subjects:

The investigator will have to proceed to the following information/procedures during the screening visit:
- Fully inform the patient of the study treatments, the objectives and the design of the study, answer to any questions that the patient may have and ensure that the patient understands the potential risks and benefits of participating in the study before signing the informed consent form. None study-related procedure can be started before ICF is signed and dated by both the patient (and impartial witness, if applicable) and the investigator
- Check the eligibility criteria list and perform the exams

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 September 2011
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	France: 134
Worldwide total number of subjects	134
EEA total number of subjects	134

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)	107

From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at the time of enrolment at the participating sites. The declared investigator, after having identified a potential candidate for the study, informed her orally of the terms of the study and provide her with : an information note, An informed consent form that has been dated and signed by the patient and the investigator.

Pre-assignment

Screening details:

None study-related procedure can be started before ICF was signed and dated by both the patient (and impartial witness, if applicable) and the investigator - Checked the eligibility criteria list and perform the exams.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	BIBW

Arm description: -

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

Dosage and administration details:

Maintenance treatment with afatinib (GIOTRIF®) for 1 year: at a dose of 40 mg/day for one month, then 50 mg/day for the following 11 months.

Arm title	Placebo

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Afatinib placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Afatinib placebo maintenance for 1 year: 40 mg/day for one month, then 50 mg/day for the next 11 months.

Number of subjects in period 1	BIBW	Placebo
Started	67	67
Completed	67	67

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	134	134	
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)	107	107	
From 65-84 years	27	27	
85 years and over	0	0	
Age continuous Units: years			
median	57.2		
full range (min-max)	27 to 74	-	
Gender categorical Units: Subjects			
Female	19	19	
Male	115	115	

Subject analysis sets

Subject analysis set title	Analysis population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intention-to-treat (ITT) population includes all randomised patients.

Reporting group values	Analysis population		
Number of subjects	134		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	107		

From 65-84 years	27		
85 years and over	0		

Age continuous			
Units: years			
median	57.2		
full range (min-max)	27 to 74		
Gender categorical			
Units: Subjects			
Female	19		
Male	115		

End points

End points reporting groups

Reporting group title	BIBW
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	Analysis population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The intention-to-treat (ITT) population includes all randomised patients.	

Primary: Disease free survival

End point title	Disease free survival
End point description:	
End point type	Primary
End point timeframe:	
2 years	

End point values	BIBW	Placebo	Analysis population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	67	67	134	
Units: 15	67	67	134	

Statistical analyses

Statistical analysis title	Overall survival
Comparison groups	BIBW v Placebo
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.9553
Method	Logrank
Parameter estimate	Log hazard ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.65

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The investigator collects (spontaneous patient report or questionning) and immediately notifies the sponsor of all SAEs, in a written report, wether or not theay are deemed to be attributable to research and wich occur during the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 134 (0.00%)		
number of deaths (all causes)	58		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 134 (0.00%)		

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: Non-serious events were collected and not specifically reported.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2012	- Updated the newsletter following the change in the BI. - Increased the time to start radiation therapy from 6 to 8 weeks after surgery. - Added criteria for non-randomization. - Updated the list of participating centers
24 September 2012	- Transmit the new Afatinib Investigator Brochure. - Make changes regarding prohibited treatments during maintenance therapy. - Adapt patient information letter. - Update the list of investigators.
03 February 2014	- Modification of the study design (simultaneous inclusion and randomization). Adjuvant radiochemotherapy with cisplatin (is removed from the study procedures and the inclusion and non-inclusion criteria as well as the treatment, procedures and follow-up before randomization are modified accordingly. - Modification of the post-maintenance follow-up by decreasing the frequency of visits (cardiac follow-up frequency unchanged): at M1, M3 and M12 (instead of every 2 months) and then every year (instead of every 3 months) until the end of the 5th year. - BI update impacting patient safety and determination of expected or unexpected nature of a suspected SAE (impact on anticipated protocol with liver follow-up): modification of the section regarding potential risks in the information note. - Modification of the contact person with the sponsor: Séverine METZGER replaces Sophie DUSSART as project manager. - Update of the investigators list.
30 June 2014	- Modification of the IMPD submitted at the time of the initial application by the Boehringer laboratory, owner of the data relating to IMP (afatinib), which obtained a marketing authorization (centralized procedure) on 2013/09/25 under the name of GIOTRIF in another indication (treatment of adult patients naïve to anti EGFR TKIs with locally advanced or metastatic non-small cell bronchial cancer NSCLC) that presents an activating mutation(s) of EGFR). The supply of the IMP will be done accordingly either with the tablets already used in this trial or with those that conform to the product that has obtained the standard IMP : only the color may vary, the packaging and labeling remain identical. - Update of the investigator list.
03 September 2020	- Update of the list of investigators.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported