Clinical trial results:
Multi-centric randomized phase II study of pre-operative Afatinib (BIBW2992) aiming at identifying predictive and pharmacodynamic biomarkers of biological activity and efficacy in untreated non-metastatic head and neck squamous cell carcinoma patients

Summary

EudraCT number	2010-024046-29
Trial protocol	FR
Global end of trial date	06 January 2016

Results information

Result version number	v1 (current)
This version publication date	24 April 2021
First version publication date	24 April 2021

Trial information

Trial identification

Sponsor protocol code	GEP 11/1010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01415674
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 RUE DE TOLBIAC, PARIS, France, 75013
Public contact	N. AIT RAHMOUNE, UNICANCER, 33 (0) 1 71 93 67 04, n.ait-rahmoune@unicancer.fr
Scientific contact	N. AIT RAHMOUNE, UNICANCER, 33 (0)171936704, n.ait-rahmoune@unicancer.fr

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 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 January 2016
Global end of trial reached?	Yes
Global end of trial date	06 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To identify potential predictive biomarkers of efficacy by exploring correlation between baseline potential biomarkers and:
a. radiological response to Afatinib
b. FDG-PET response to Afatinib

Protection of trial subjects:

In order to ensure the protection of the rights, safety and well-being of trial subjects, this clinical trial was performed in compliance with the principles laid down in the declaration of Helsinki, good Clinical Practice and European regulation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 January 2012
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	France: 61
Worldwide total number of subjects	61
EEA total number of subjects	61

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)	42
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with untreated, operable, non-metastatic squamous cell carcinoma of the head and neck

Pre-assignment

Screening details:

Histologically or cytologically confirmed squamous cell carcinoma of the oral cavity, paranasal sinus and nasal cavity, oropharynx, larynx or hypopharynx, previously untreated, amenable to curative treatment with surgery. Patients with a diagnosis of SCCHN of occult primary may be enrolled only with the agreement of the lead investigator upon revie

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Afatinib

Arm description:

Afatinib will be administered orally at the dose of 40 mg per day on a continuous schedule for 14 to 28 days, depending on the date of surgery.

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:

Afatinib will be administered orally at the dose of 40 mg per day on a continuous schedule for 14 to 28 days, depending on the date of surgery.

Arm title	No treatment

Arm description:

No treatment

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Afatinib	No treatment
Started	41	20
Completed	41	18
Not completed	0	2
Consent withdrawn by subject	-	1
SURGERY NOT PERFORMED	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Afatinib
Reporting group description:	
Afatinib will be administered orally at the dose of 40 mg per day on a continuous schedule for 14 to 28 days, depending on the date of surgery.	
Reporting group title	No treatment
Reporting group description:	
No treatment	

Reporting group values	Afatinib	No treatment	Total
Number of subjects	41	20	61
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	31	14	45
From 65-84 years	10	6	16
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	9	14	23
Male	32	6	38

End points

End points reporting groups

Reporting group title	Afatinib
Reporting group description:	
Afatinib will be administered orally at the dose of 40 mg per day on a continuous schedule for 14 to 28 days, depending on the date of surgery.	
Reporting group title	No treatment
Reporting group description:	
No treatment	

Primary: EFFICACY ON FDG-PET PER PERCIST

End point title	EFFICACY ON FDG-PET PER PERCIST
End point description:	
Number of patients with response to treatment excluding lymph nodes	
End point type	Primary
End point timeframe:	
Efficacy will be defined as the tumour reduction between baseline and surgery (end of treatment).	

End point values	Afatinib	No treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	20		
Units: number	24	0		

Statistical analyses

Statistical analysis title	EFFICACY ON FDG-PET PER PERCIST
Statistical analysis description:	
EFFICACY ON FDG-PET PER PERCIST	
Comparison groups	Afatinib v No treatment
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Mean difference (final values)

Secondary: EFFICACY ON CT/MRI PER RECIST 1.1

End point title	EFFICACY ON CT/MRI PER RECIST 1.1

End point description:

Number of patients with response to treatment

End point type	Secondary

End point timeframe:

CT Scan or MRI must be done within one week prior surgery

End point values	Afatinib	No treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	20		
Units: Number	2	0		

Statistical analyses

Statistical analysis title	EFFICACY ON CT/MRI PER RECIST
Comparison groups	Afatinib v No treatment
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events were reported during all the period of the trial

Adverse event reporting additional description:

Adverse events (not serious) are not available and not reported here

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	Arm A (with afatinib)
Reporting group description: -	
Reporting group title	Arm B (without afatinib)
Reporting group description: -	

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 adverse events not available

Serious adverse events	Arm A (with afatinib)	Arm B (without afatinib)	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 41 (24.39%)	5 / 20 (25.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Bleeding postoperative			
subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft ischemia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative bleeding			

subjects affected / exposed	0 / 41 (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	
Vascular disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 41 (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	
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 41 (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	
Mucositis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphocele			
subjects affected / exposed	0 / 41 (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	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	2 / 41 (4.88%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucositis oral			

subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral cavity fistula			
subjects affected / exposed	1 / 41 (2.44%)	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			
Pneumonitis			
subjects affected / exposed	0 / 41 (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	
Pneumopathy			
subjects affected / exposed	0 / 41 (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	
Skin and subcutaneous tissue disorders			
Necrosis skin			
subjects affected / exposed	0 / 41 (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	
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 41 (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	
Infections and infestations			
Folliculitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative infection			

subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purulent discharge			
subjects affected / exposed	1 / 41 (2.44%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A (with afatinib)	Arm B (without afatinib)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 20 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 January 2012	New name of the sponsor
31 January 2012	protocol was updated (modification of 2 inclusion criteria)
02 April 2012	Submission of new IB
19 July 2012	Protocole updated (precision concerning inclusion criteria)
03 September 2012	submission of new IB
27 May 2013	inclusion period extended
03 October 2013	Submission of new IB
07 April 2014	IMPD was updated
23 May 2014	Protocol updated and inclusion period extended
21 October 2014	Submission of new IB

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported