Clinical trial results:
A prospective phase II study on dose escalation using PET based adaptive IMRT stage II-III non small lung cancer

Summary

EudraCT number	2011-003124-12
Trial protocol	BE
Global end of trial date	28 February 2017

Results information

Result version number	v1 (current)
This version publication date	20 March 2023
First version publication date	20 March 2023

Trial information

Trial identification

Sponsor protocol code	B-40320109424

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Cliniques Universitaires Saint Luc
Sponsor organisation address	Avenue Hippocrate, 10, Bruxelles, Belgium, 1200
Public contact	GEETS, Xavier, Cliniques Universitaires Saint Luc, xavier.geets@saintluc.uclouvain.be
Scientific contact	GEETS, Xavier, Cliniques Universitaires Saint Luc, xavier.geets@saintluc.uclouvain.be

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	28 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the impact of individualized and escalated dose prescription based on FDG-PET on the tumor local control, the local progression-free survival and overall survival.
- To secondarily assess early and late radio-induced toxicities

Protection of trial subjects:

Not specified

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	6
From 65 to 84 years	7

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients enrolled from Novembre 2010 till February 2013, at the Belgian hospitals
Inclusion:
- Patients with histolagically proven stage II-III NSCLC
- FDG-PET positive primary tumor > 3 cm
- Patient considered fit for sequential or concomitant CRT (i.e. ECOG performance status < or =2)

Pre-assignment

Screening details:

Exclusion:
- No Bulky lymph node (LN) involvement (==> average LN diameter of 13.3 +/- 5.5 mm)
- Prior thoracic radiation
- Poor lung

Period 1

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

Blinding implementation details:

Not applicable

Arms

Arm title	Radiotherapy

Arm description: -

Arm type	Experimental
Investigational medicinal product name	18F fluorodeoxyglucose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

18F fluorodeoxyglucose was administred as per standard of care.

The dose prescription for Radiotherapy :
o The treatment total dose (TTD) will be based on normal tissue constraints instead of a classic fixed prescribed dose. Actually, the radiation dose will be individually escalated until a dose-limiting normal tissue constraint is reached.
o The radiation treatment will begin at day 22 of chemotherapy (corresponding to the first day of the cycle 2 chemotherapy) based on cisplatin/etoposide or cisplatin/vinorelbine regimens.
o Prescribed dose on PTV1 : 25x2.3Gy once daily
o Prescribed dose on PTV2: dose escalation with Simultaneous Integrated Boost (SIB) based on the tolerance of the organs at risk (OARs) until a maximal dose per fraction of 3Gy once daily, corresponding to a maximal total dose of 75Gy (physical dose).

Number of subjects in period 1	Radiotherapy
Started	13
Radiotherapy	13
Follow-up	13
Completed	7
Not completed	6
Adverse event, serious fatal	2
Death - related to patient's condition	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	13	13	
Age categorical Units: Subjects			
Adults (18-64 years)	6	6	
From 65-84 years	7	7	
Age continuous Units: years			
arithmetic mean	63.3		
standard deviation	± 8.9	-	
Gender categorical Units: Subjects			
Gender Not Reported	13	13	

End points

End points reporting groups

Reporting group title	Radiotherapy

Reporting group description: -

Primary: Overall survival - at 36 month

End point title	Overall survival - at 36 month[1]

End point description:

Survival was determined using the Kaplan-Meier method, the results were presented with median and CI at 95% - there were 7 patients who were still alive after followup.
The result of the overall survival with Kaplan-Meier estimate (in months) was NE with IC95% (13.85 - NE).

End point type	Primary

End point timeframe:

Entire study - follow-up included

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: Kaplan Meier was performed - however, as some patients survived after follow-up, some results are showing "NE" as the number of survival months is not evaluable. And EudraCT doesn't allow to add "NE" instead of a number.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall study

Assessment type	Systematic

Dictionary used

Dictionary name	ICD 10 - English
Dictionary version	2010

Reporting groups

Reporting group title	Experimental

Reporting group description: -

Serious adverse events	Experimental		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)		
number of deaths (all causes)	6		
number of deaths resulting from adverse events	2		
Cardiac disorders			
Pericarditis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 13 (30.77%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Retrosternal pain			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Leucocytopenia				
subjects affected / exposed	3 / 13 (23.08%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Lymphopenia				
subjects affected / exposed	13 / 13 (100.00%)			
occurrences causally related to treatment / all	16 / 16			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	5 / 13 (38.46%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Thrombopenia				
subjects affected / exposed	2 / 13 (15.38%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Oesophagitis				
subjects affected / exposed	3 / 13 (23.08%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal stenosis				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 13 (7.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal				

disorders			
Dyspnea			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Bronchial fistula			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hemoptysis			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	2 / 2		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)		
Investigations			
Weight Loss			
subjects affected / exposed	9 / 13 (69.23%)		
occurrences (all)	13		
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	13 / 13 (100.00%)		
occurrences (all)	22		
Retrosternal pain			
subjects affected / exposed	13 / 13 (100.00%)		
occurrences (all)	13		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	13 / 13 (100.00%)		
occurrences (all)	20		
Leucocytopenia			
subjects affected / exposed	13 / 13 (100.00%)		
occurrences (all)	15		
Lymphopenia			
subjects affected / exposed	13 / 13 (100.00%)		
occurrences (all)	16		
Neutropenia			
subjects affected / exposed	9 / 13 (69.23%)		
occurrences (all)	9		
Thrombopenia			
subjects affected / exposed	9 / 13 (69.23%)		
occurrences (all)	9		
Gastrointestinal disorders			
Oesophagitis			
subjects affected / exposed	13 / 13 (100.00%)		
occurrences (all)	19		
Nausea			
subjects affected / exposed	9 / 13 (69.23%)		
occurrences (all)	9		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 13 (100.00%)		
occurrences (all)	14		
Dyspnea			
subjects affected / exposed	12 / 13 (92.31%)		
occurrences (all)	18		

Pneumonitis subjects affected / exposed occurrences (all) Hemoptysis subjects affected / exposed occurrences (all) Pulmonary fibrosis subjects affected / exposed occurrences (all)	6 / 13 (46.15%) 6 2 / 13 (15.38%) 2 5 / 13 (38.46%) 5		
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all)	13 / 13 (100.00%) 13		
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all)	7 / 13 (53.85%) 7		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28733723