Clinical trial results:
Induction chemotherapy with Carboplatin and Navelbine Oral® followed by concomitant Navelbine Oral® and irradiation in local-regionally advanced non-small cell lung cancer.
A randomized phase II study.

Summary

EudraCT number	2008-008920-34
Trial protocol	DK
Global end of trial date	21 July 2017
Results information	
Result version number	v1 (current)
This version publication date	27 March 2020
First version publication date	27 March 2020

Trial information

Trial identification	
Sponsor protocol code	09.01
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00887783
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Odense University Hospital
Sponsor organisation address	J. B. Winsløwsvej 2, Indgang 140, kælderen, Odense, Denmark, 5000
Public contact	Olfred Hansen, Odense University Hospital, 0045 24241588, olfred.hansen@rsyd.dk
Scientific contact	Olfred Hansen, Odense University Hospital, 0045 24241588, olfred.hansen@rsyd.dk

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	31 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2016
Global end of trial reached?	Yes
Global end of trial date	21 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial is to test a convenient chemotherapy schedule with an oral formulation of radio-sensitizing Navelbine in concurrent chemo-radiotherapy in radical treatment of inoperable locally advanced non small cell lung cancer (stage IIB-IIIB) with radiotherapy. The trial is a randomized phase II study with two doses of radiotherapy. The primary objective of the study is examine the combination of Navelbine oral 150 mg of Vinorelbine administered in 3 weekly doses a week for 6-6½ weeks concomitant with curatively intended irradiation to 60 Gy (2 Gy x 30, 5 F á weeks) or 66 Gy (2 Gy x 33, 5 F á week) starting 3 weeks after two cycles of inductions chemotherapy with Navelbine oral and Carboplatin.

Primary endpoint:
- Local failure free survival at 9 months after start of radiotherapy

Protection of trial subjects:

Strict planning of radiotherapy observing clear constraints on normal tissue. Frequent clinical follow-up within the trial observing any side adverse effects and risk of relapse.

Background therapy:

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Evidence for comparator:

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Actual start date of recruitment	01 May 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 117
Worldwide total number of subjects	117
EEA total number of subjects	117

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	55
From 65 to 84 years	62
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The inclusion criteria were histologically or cytologically confirmed NSCLC, clinical American Joint Committee of Cancer stage (the seventh edition) IIB–IIIB, performance status (PS) <2 on the ECOG scale, weight

Pre-assignment

Screening details:

Patients refered to the participating centers was screened for the study.

Period 1

Period 1 title	Induction
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Arm title	Induction chemotherapy

Arm description:

All patients were treated with two cycles of carboplatin day 1 and navelbine day 1 and day 8

Arm type	Standard
Investigational medicinal product name	Navelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Navelbine 60 mg m2 - possible to increase dose to 80 mg m2

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

2 cycles of induction therapy - 3 weeks cycles

Number of subjects in period 1	Induction chemotherapy
Started	117
Interim analyses	117
Completed	117

Period 2	
Period 2 title	Randomized
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	60 GY
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Navelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use
Dosage and administration details: Radiotherapy 60 GY, concommittant vinorelbin 50mg Sunday, Tuesday and Thursday	
Arm title	66GY
Arm description: Radiotherapy 60 GY, concommittant vinorelbin 50mg Sunday, Tuesday and Thursday	
Arm type	Experimental
Investigational medicinal product name	Navelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use
Dosage and administration details: 50 mg Sunday, Tuesday and Thursday during RT	

Number of subjects in period 2	60 GY	66GY
Started	59	58
Completed	59	58

Baseline characteristics

Reporting groups	
Reporting group title	Induction

Reporting group description: -

Reporting group values	Induction	Total	
Number of subjects	117	117	
Age categorical			
Overall study population			
Units: Subjects			
Overall study population	117	117	
Age continuous			
Age distribution			
Units: years			
median	65.5		
full range (min-max)	44 to 82	-	
Gender categorical			
Gender distribution			
Units: Subjects			
Female	49	49	
Male	68	68	

End points

End points reporting groups

Reporting group title	Induction chemotherapy
Reporting group description:	
All patients were treated with two cycles of carboplatin day 1 and navelbine day 1 and day 8	
Reporting group title	60 GY
Reporting group description: -	
Reporting group title	66GY
Reporting group description:	
Radiotherapy 60 GY, concommittant vinorelbin 50mg Sunday, Tuesday and Thursday	

Primary: Local progression free interval after start of RT.

End point title	Local progression free interval after start of RT.[1]
End point description:	
Local progression free interval 9 month after start of RT measured on PET CT	
End point type	Primary
End point timeframe:	
Local progression free interval 9 month after start of RT.	

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: Analysis in doi.org/10.1016

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From randomization until EOT	
Adverse event reporting additional description:	
An AE was defined as any adverse medical event in a patient or subject taking a medical treatment regardless of the causal relationship to the trial.	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTC-AE
Dictionary version	3.0

Reporting groups	
Reporting group title	66GY
Reporting group description:	
Study arm	
Reporting group title	60GY
Reporting group description:	
Study arm	

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: Analysis in doi.org/10.1016

Serious adverse events	66GY	60GY	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 58 (8.62%)	3 / 59 (5.08%)	
number of deaths (all causes)	47	50	
number of deaths resulting from adverse events	1	0	
Respiratory, thoracic and mediastinal disorders			
Esophagitis and pneumonitis	Additional description: CTCAE grade 4-5		
subjects affected / exposed	5 / 58 (8.62%)	3 / 59 (5.08%)	
occurrences causally related to treatment / all	5 / 5	3 / 3	
deaths causally related to treatment / all	1 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	66GY	60GY	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 58 (0.00%)	0 / 59 (0.00%)	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was a chemo-radiation study including cancerpatients with an expected 3 years survival 20%.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28410809