Clinical trial results:
A Phase II, Open-Label Trial of Bortezomib (Velcade®) in Combination with Gemcitabine and Cisplatin in Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer.

Summary

EudraCT number	2006-004963-68
Trial protocol	GR
Global end of trial date	25 October 2013

Results information

Result version number	v1 (current)
This version publication date	10 July 2019
First version publication date	10 July 2019
Summary attachment (see zip file)	Bortezomib Abstract (Abstract bortezomib.pdf)

Trial information

Trial identification

Sponsor protocol code	26866138-LUC-2006

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hellenic Oncology Research Group
Sponsor organisation address	Gr. Theologou 5, Athens, Greece, 11471
Public contact	Evagelia Ageli, Hellenic Oncology Research Group, secretary@horg.gr
Scientific contact	Vasilis Georgoulias, Hellenic Oncology Research Group, georgouliasv@gmail.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	13 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2013
Global end of trial reached?	Yes
Global end of trial date	25 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to establish the objective response rate (complete response [CR] + partial response [PR]) following treatment with VELCADE in combination with cisplatin plus gemcitabine in patients with locally advanced Stage IIIb not amenable to curative treatment or metastatic (stage IV) non-small cell lung cancer (NSCLC) who have not received prior antineoplastic therapy for advanced disease.

Protection of trial subjects:

none

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 July 2009
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	Greece: 53
Worldwide total number of subjects	53
EEA total number of subjects	53

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)	18
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Pts with stage IIIB or metastatic (stage IV) NSCLC , age ≥18 years, measurable disease according to RECIST vrs 1.0, life expectancy >3 months, and ECOG performance status of 0–1.

Pre-assignment

Screening details:

One prior line of anti-neoplastic therapy allowed if given as adjuvant or neo-adjuvant, at least 6 months earlier.

Period 1

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

Arms

Arm title	Intent to treat subjects

Arm description:

One arm with all subjects participating into the Trial and have signed ICF

Arm type	Experimental
Investigational medicinal product name	Bortezomib
Investigational medicinal product code	179324-69-7
Other name	velcade
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 mg/m2 i.v. on days 1 and 8, and starting on day 21 (cycle 2), bortezomib (days 1 and 8) in combination with gemcitabine 1000 mg/m2, (days 1 and 8), and cisplatin 70 mg/m2 (day 1) in cycles of 21 days. Up to 8 cycles of combination therapy could be administered; single-agent bortezomib was continued until disease progression or unacceptable toxicity.

Number of subjects in period 1	Intent to treat subjects
Started	53
Completed	43
Not completed	10
Adverse event, serious fatal	5
Physician decision	2
Consent withdrawn by subject	1
Lost to follow-up	2

Baseline characteristics

Reporting groups

Reporting group title	Entire trial

Reporting group description: -

Reporting group values	Entire trial	Total	
Number of subjects	53	53	
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)	17	17	
From 65-84 years	36	36	
85 years and over	0	0	
Age continuous Units: years			
median	66		
full range (min-max)	49 to 77	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	42	42	

Subject analysis sets

Subject analysis set title	Efficacy of Bortezomib
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pts with histologically or cytologically confirmed, locally advanced (stage IIIB) or metastatic (stage IV) NSCLC. Prior systemic anti-neoplastic therapy for stage IIIB/IV disease was not allowed (one prior line was allowed if given as adjuvant or neo-adjuvant therapy at least 6 months earlier). Age ≥18 years with measurable disease according to RECIST version 1.1 Criteria, life expectancy >3 months, and ECOG performance status of 0–1. All patients treated at least for 1 cycle with the IMP and evaluated according to RECIST criteria version 1.1, were included into this analysis set.

Reporting group values	Efficacy of Bortezomib		
Number of subjects	43		
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)	16		
From 65-84 years	27		
85 years and over	0		
Age continuous			
Units: years			
median	64		
full range (min-max)	49 to 77		
Gender categorical			
Units: Subjects			
Female	9		
Male	34		

End points

End points reporting groups

Reporting group title	Intent to treat subjects

Reporting group description:

One arm with all subjects participating into the Trial and have signed ICF

Subject analysis set title	Efficacy of Bortezomib
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pts with histologically or cytologically confirmed, locally advanced (stage IIIB) or metastatic (stage IV) NSCLC. Prior systemic anti-neoplastic therapy for stage IIIB/IV disease was not allowed (one prior line was allowed if given as adjuvant or neo-adjuvant therapy at least 6 months earlier). Age ≥18 years with measurable disease according to RECIST version 1.1 Criteria, life expectancy >3 months, and ECOG performance status of 0–1. All patients treated at least for 1 cycle with the IMP and evaluated according to RECIST criteria version 1.1, were included into this analysis set.

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[1]

End point description:

Objective response rate (ORR) is defined as the percentage (%) of patients that achieved Complete response (CR) or Partial response (PR) to the treatment, as measured by RECIST 1.1 CRITERIA. ORR= (CR+PR)/total number of patients, expressed as % percentage.

End point type	Primary

End point timeframe:

July 2009 - April 2013

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: The 2 step Simon's design that yields a type I error rate of 0.05 and power of 80% when the true overall response rate is 40% was used. The null hypothesis will be rejected if 12 or more responses are observed in 43 evaluable pts. This is an one arm trial that compares ORR with bibliographic data. The system does keeps asking for comparison group.

End point values	Intent to treat subjects	Efficacy of Bortezomib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	53	43		
Units: % of complete and partial responses	9	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

PFS was measured from the first day of treatment until the day of the first evidence of disease progression or death from any cause.

End point type	Secondary

End point timeframe:

July 2009 - April 2013

End point values	Intent to treat subjects	Efficacy of Bortezomib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	53	43		
Units: months				
median (full range (min-max))	2.5 (0.3 to 48.1)	3.8 (1.1 to 48.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was measured from the first day of treatment until death or last follow-up.

End point type	Secondary

End point timeframe:

July 2009 -April 2013

End point values	Intent to treat subjects	Efficacy of Bortezomib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	53	43		
Units: months				
median (full range (min-max))	10.6 (0.4 to 48.1)	10.8 (1.7 to 48.1)		

Attachments (see zip file)	OS Kaplan Meier/OS Kaplan Meier.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

July 2009 - April 2013

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Bortezomib treated patients

Reporting group description: -

Serious adverse events	Bortezomib treated patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 53 (81.13%)		
number of deaths (all causes)	46		
number of deaths resulting from adverse events	2		
Vascular disorders			
thromboembolism			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	12 / 53 (22.64%)		
occurrences causally related to treatment / all	12 / 12		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	13 / 53 (24.53%)		
occurrences causally related to treatment / all	13 / 13		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia	Additional description: one patient was hospitalized with grade 4 thrombocytopenia after the second cycle, and died due to pulmonary hemorrhage and respiratory failure type II		
subjects affected / exposed	9 / 53 (16.98%)		
occurrences causally related to treatment / all	9 / 9		
deaths causally related to treatment / all	1 / 1		

Febrile neutropenia			
subjects affected / exposed	1 / 53 (1.89%)		
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	3 / 53 (5.66%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
hearing disorders			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
AST/ALT ratio			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis	Additional description: Sepsis and polyorganic failure		
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Frequency threshold for reporting non-serious adverse events: 0.01 %

Non-serious adverse events	Bortezomib treated patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 53 (100.00%)		
Nervous system disorders			
Neurotoxicity			
subjects affected / exposed	8 / 53 (15.09%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	18 / 53 (33.96%)		
occurrences (all)	18		
Leukopenia			
subjects affected / exposed	18 / 53 (33.96%)		
occurrences (all)	18		
Anaemia			
subjects affected / exposed	45 / 53 (84.91%)		
occurrences (all)	45		
Thrombocytopenia			
subjects affected / exposed	19 / 53 (35.85%)		
occurrences (all)	19		
General disorders and administration site conditions			
Nausea			
subjects affected / exposed	19 / 53 (35.85%)		
occurrences (all)	19		
Fatigue			
subjects affected / exposed	31 / 53 (58.49%)		
occurrences (all)	31		
fever			
subjects affected / exposed	13 / 53 (24.53%)		
occurrences (all)	13		
Ear and labyrinth disorders			
hearing disorders			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	5		
Immune system disorders			

allergy subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4		
Eye disorders visual disorders subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 3		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) mucositis subjects affected / exposed occurrences (all)	 7 / 53 (13.21%) 7 6 / 53 (11.32%) 6 1 / 53 (1.89%) 1		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Edema subjects affected / exposed occurrences (all)	 6 / 53 (11.32%) 6 8 / 53 (15.09%) 8		
Renal and urinary disorders nephrotoxicity subjects affected / exposed occurrences (all)	 1 / 53 (1.89%) 1		
Infections and infestations Infection subjects affected / exposed occurrences (all)	 10 / 53 (18.87%) 10		

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/26994909