Clinical trial results:
A Randomized, Phase 2 Study of INCB039110 or Placebo in Combination With Docetaxel in Subjects With Previously Treated Stage IIIb, IV, or Recurrent Non-Small Cell Lung Cancer

Summary

EudraCT number	2013-004812-24
Trial protocol	IE IT DE ES HU
Global end of trial date	05 April 2016

Results information

Result version number	v1 (current)
This version publication date	28 September 2017
First version publication date	28 September 2017

Trial information

Trial identification

Sponsor protocol code	INCB 39110-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02257619
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cut-Off, Wilmington, DE, United States, 19803
Public contact	Incyte Corporation, Incyte Corporation Call Centre, +44 (0)330 100 3677, globalmedinfo@incyte.com
Scientific contact	Incyte Corporation, Incyte Corporation Call Centre, +44 (0)330 100 3677, globalmedinfo@incyte.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	05 April 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study were to evaluate the safety and tolerability of itacitinib in combination with docetaxel and to select doses for further evaluation (Part 1, safety run-in portion), and to evaluate and compare the overall survival of subjects with previously treated advanced or metastatic non-small cell lung cancer (NSCLC) when treated with itacitinib in combination with docetaxel versus docetaxel alone (Part 2, randomized portion).
The secondary objectives of this study (Part 2) were to evaluate and compare the efficacy of the 2 treatment groups with respect to progression-free survival, overall tumor response, and duration of response, and to evaluate and compare disease control, safety, and tolerability of itacitinib in combination with docetaxel versus docetaxel alone.
Part 2 of the study was not conducted.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonisation Guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2014
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	United States: 7
Country: Number of subjects enrolled	Spain: 2
Worldwide total number of subjects	9
EEA total number of subjects	2

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)	4
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study enrolled subjects in 7 study centers: 6 in the United States and 1 in Spain.

Pre-assignment

Screening details:

Duration of treatment for an individual subject was expected to average approximately 5 months: up to 28 days for screening and baseline, followed by 3-week and up to 5 weeks for safety follow-up.

Period 1

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

Arms

Arm title	itacitinib plus docetaxel

Arm description:

itacitinib 400 mg QD administered orally in combination with docetaxel 75 mg/m^2 once every 3 weeks (q3w) administered intravenously

Arm type	Experimental
Investigational medicinal product name	itacitinib
Investigational medicinal product code	
Other name	INCB039110
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Itacitinib tablets administered orally at 400 mg QD for Part 1 of the study.

Investigational medicinal product name	docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as an intravenous infusion in the clinic at 75 mg/m^2 Q3W for Part 1 of the study.

Number of subjects in period 1	itacitinib plus docetaxel
Started	9
Completed	0
Not completed	9
Disease progression	6
Subject decision	1
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	itacitinib plus docetaxel
Reporting group description:	
itacitinib 400 mg QD administered orally in combination with docetaxel 75 mg/m^2 once every 3 weeks (q3w) administered intravenously	

Reporting group values	itacitinib plus docetaxel	Total	
Number of subjects	9	9	
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)	4	4	
From 65-84 years	5	5	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	66.1		
standard deviation	± 7.17	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	7	7	

End points

End points reporting groups

Reporting group title	itacitinib plus docetaxel

Reporting group description:

itacitinib 400 mg QD administered orally in combination with docetaxel 75 mg/m^2 once every 3 weeks (q3w) administered intravenously

Primary: Number of Participants With Dose Limiting Toxicities (DLTs)

End point title	Number of Participants With Dose Limiting Toxicities (DLTs)[1]

End point description:

Number of participants with DLT for the determination of the Maximum Tolerated Dose (MTD).

End point type	Primary

End point timeframe:

Baseline through 21 days; the end of cycle 1.

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: No statistical analyses have been performed for this primary end point.

End point values	itacitinib plus docetaxel			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study medication through approximately 30 days post treatment discontinuation; up to 05 APR 2016.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	itacitinib plus docetaxel

Reporting group description:

itacitinib 400 mg QD administered orally in combination with docetaxel 75 mg/m^2 once every 3 weeks (q3w) administered intravenously

Serious adverse events	itacitinib plus docetaxel		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial tachycardia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia bacterial			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	itacitinib plus docetaxel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		

Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	9		
Fatigue			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	5		
Oedema peripheral			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Reproductive system and breast disorders			
Vaginal inflammation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	4		
Haemoptysis			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	4		
Oropharyngeal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pulmonary embolism			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hallucination			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Irritability			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Weight decreased			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
White blood cell count decreased			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Tachycardia			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	11		
Febrile neutropenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	9		
Dyspepsia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	5		
Oesophagitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Stomatitis			

subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin ulcer			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Renal failure acute			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Bone pain			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	5		
Dehydration			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Hypokalaemia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2014	The primary purpose of the amendment was to change the itacitinib tablet sustained release (SR) formulation to be administered during the study. The clinically important changes included: • Administration of a 100 mg SR tablet instead of 200 or 300 mg tablets as stated in Section 10.1 of the original Protocol.
04 August 2014	The primary purpose of the amendment was to clarify the study design and reduce the number of planned cohorts and subjects within the study. The clinically important changes included: • Number of cohorts reduced from 3 and 4 in Regimens A and B, respectively (Part 1) to 2 cohorts per regimen. • 600 mg QD dose removed. • Subjects with a known sensitivity to any of the active substances or excipients excluded.
29 August 2014	The primary purpose of the amendment was to revise inclusion and exclusion criteria to provide flexibility for recruitment. The clinically important changes included: • Exclusion criterion of prior taxane use was removed and replaced with prior docetaxel use only. • Measurable lesions caveat regarding the field of prior radiation and 4-week timeframe between treatment and progression was removed. • Corticosteroid use added to allow subjects with known and stable central nervous system metastases eligibility for the study. • Mandatory withdrawal of subjects who must increase their corticosteroid use. • Aspartate transaminase/alanine transaminase and alkaline phosphatase criterion amended to match docetaxel prescriber’s information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 May 2015	The sponsor elected to terminate the study and not open enrollment to Part 2 due to slow enrollment into Part 1 and ongoing competing trials in similar subject populations. Subjects in Part 1 were allowed to continue receiving study treatment and were followed until discontinuation criteria were met.	-

Notes:

Limitations and caveats

None reported