Clinical trial results:
A Phase 2, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of IPI-926 in Patients with Metastatic or Locally Advanced (Unresectable) Chondrosarcoma

Summary

EudraCT number	2010-024518-74
Trial protocol	GB SE DE NO NL AT IT ES
Global end of trial date	15 October 2013

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	09 August 2015

Trial information

Trial identification

Sponsor protocol code	IPI-926-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 78,428

Notes:

Sponsors

Sponsor organisation name	Infinity Pharmaceuticals, Inc.
Sponsor organisation address	780 Memorial Drive , Cambridge, MA, United States, 02139
Public contact	IPI-926-04 Trial Information, Infinity Pharmaceuticals, Inc., +1 617 453 1000,
Scientific contact	David A. Roth, MD, Infinity Pharmaceuticals, Inc., +1 617 453 1412,

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	Interim
Date of interim/final analysis	12 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 October 2012
Global end of trial reached?	Yes
Global end of trial date	15 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- Compare progression-free survival (PFS) in patients with metastatic or locally advanced (unresectable) chondrosarcoma administered IPI-926 or placebo.
- Evaluate the safety of IPI-926 in patients with metastatic or locally advanced(unresectable) chondrosarcoma

Protection of trial subjects:

Independent Data Monitoring Committee initiated for IPI-145-04. Agroup of individuals with pertinent expertise that regularly reviews accumulating data from an ongoing clinical study. The iDMC advises the Sponsor regarding the continuing safety of trial subjects, as well as the continuing validity and scientific merit of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 38
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 3
Worldwide total number of subjects	105
EEA total number of subjects	59

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)	82
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	152[1]
Number of subjects completed	105

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening failure: 47

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of screened patients (152) per country and per age group has been collected but has not been prespecified in the Statistical Analysis Plan. Therefore, the number of randomized patients (105) per country and per age group is indicated in the Trial information section.

Period 1

Period 1 title	Double-blind (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	IPI-926

Arm description: -

Arm type	Experimental
Investigational medicinal product name	IPI-926
Investigational medicinal product code	PR1
Other name	2',3a,3',4,4',4a',5,5',6,6',6a',6b',7,7a,7',8',10',12',12a',12b'-icosahydro-1'H,3Hspiro[furo[3,2-b]pyridine-2,9'-naphtho[2,1-a]azulene]-3'-yl)methanesulfonamide
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

IPI-926 will be administered at a dose of 160 mg/day, as one dose per day.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	PL1
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Doses of placebo are to be taken as one dose per day.

Number of subjects in period 1	IPI-926	Placebo
Started	71	34
Completed	0	0
Not completed	71	34
RECIST confirmed Disease Progression	37	19
Study termination by Sponsor	13	-
Terminated by Sponsor	-	8
Physician decision	1	-
Consent withdrawn by subject	1	1
'Clinical disease progression '	8	-
Other	7	1
Adverse event	4	2
Clinical or symptomatic disease progression	-	2
'Non-compliance with study drug '	-	1

Baseline characteristics

Reporting groups

Reporting group title	Double-blind

Reporting group description:

For each cycle during the double-blind portion of the study, 160 mg oral IPI-926 or placebo was administered daily for 28 days.
For the 71 subjects treated with IPI-926 in the double-blind phase, the median (range) duration of exposure was 10.1 (2 to 52.6) weeks. The median (range) total dose of IPI-926 received was 11360 (2240 to 49100) mg.

Reporting group values	Double-blind	Total	
Number of subjects	105	105	
Age categorical Units: Subjects			
Adults (18-64 years)	82	82	
From 65-84 years	23	23	
Age continuous Units: years			
arithmetic mean	52.8		
full range (min-max)	24 to 82	-	
Gender categorical Units: Subjects			
Female	31	31	
Male	74	74	

Subject analysis sets

Subject analysis set title	IPI-926
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) includes all randomized patients in the treatment group assigned by randomization. The FAS is used for all efficacy analyses. The principle of an intent-to-treat analysis will be used to define the FAS population.

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) includes all randomized patients in the treatment group assigned by randomization. The FAS is used for all efficacy analyses. The principle of an intent-to-treat analysis will be used to define the FAS population.

Reporting group values	IPI-926	Placebo	
Number of subjects	71	34	
Age categorical Units: Subjects			
Adults (18-64 years)	53	29	
From 65-84 years	18	5	
Age continuous Units: years			
arithmetic mean	53.7	50.9	
full range (min-max)	24 to 82	25 to 70	

Gender categorical Units: Subjects			
Female	20	11	
Male	51	23	

End points

End points reporting groups	
Reporting group title	IPI-926
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	IPI-926
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set (FAS) includes all randomized patients in the treatment group assigned by randomization. The FAS is used for all efficacy analyses. The principle of an intent-to-treat analysis will be used to define the FAS population.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
The full analysis set (FAS) includes all randomized patients in the treatment group assigned by randomization. The FAS is used for all efficacy analyses. The principle of an intent-to-treat analysis will be used to define the FAS population.	

Primary: PFS	
End point title	PFS
End point description:	
End point type	Primary
End point timeframe:	
CT scan or MRI on Day 27 (± 2 days) of Cycles 1, 2, 4, 6, and 8, and every third cycle thereafter on Day 27 (±2 days), as well as at the end of treatment.	

End point values	IPI-926	Placebo	IPI-926	Placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	71	34	71	34
Units: months				
number (confidence interval 95%)	3.7 (1.87 to 3.71)	2.9 (1.84 to 4.04)	3.7 (1.87 to 3.71)	2.9 (1.84 to 4.04)

Statistical analyses

Statistical analysis title	Kaplan Meyer estimate
Comparison groups	IPI-926 v Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.792
Method	Logrank

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were recorded from the time of informed consent until 30 days after the last dose of study treatment.

Adverse event reporting additional description:

Patients were instructed to report all AEs and were asked a general health status question at each study visit. All adverse events, whether volunteered or elicited, were recorded on the eCRF. An adverse event was followed until it was either resolved, had returned to baseline, or was determined to be a stable or chronic condition.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	IPI-926
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	IPI-926	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 71 (30.99%)	8 / 34 (23.53%)	
number of deaths (all causes)	5	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to neck			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	1 / 71 (1.41%)	2 / 34 (5.88%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural			

complications			
Periprosthetic fracture			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	2 / 71 (2.82%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	3 / 71 (4.23%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 3	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 71 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enterocutaneous fistula			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	2 / 71 (2.82%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 71 (2.82%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 71 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 71 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary hesitation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 71 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 71 (2.82%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 22	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	IPI-926	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 71 (94.37%)	29 / 34 (85.29%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	28 / 71 (39.44%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Aspartate aminotransferase increased			
subjects affected / exposed	22 / 71 (30.99%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Blood alkaline phosphatase increased			
subjects affected / exposed	12 / 71 (16.90%)	1 / 34 (2.94%)	
occurrences (all)	67	29	
Blood bilirubin increased			
subjects affected / exposed	5 / 71 (7.04%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	8 / 71 (11.27%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Headache			
subjects affected / exposed	6 / 71 (8.45%)	1 / 34 (2.94%)	
occurrences (all)	67	29	
Dizziness			
subjects affected / exposed	5 / 71 (7.04%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	21 / 71 (29.58%)	2 / 34 (5.88%)	
occurrences (all)	67	29	
Constipation			
subjects affected / exposed	21 / 71 (29.58%)	2 / 34 (5.88%)	
occurrences (all)	67	29	
Vomiting			

subjects affected / exposed	11 / 71 (15.49%)	2 / 34 (5.88%)	
occurrences (all)	67	29	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	9 / 71 (12.68%)	2 / 34 (5.88%)	
occurrences (all)	67	29	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	6 / 71 (8.45%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Rash			
subjects affected / exposed	4 / 71 (5.63%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	12 / 71 (16.90%)	4 / 34 (11.76%)	
occurrences (all)	67	29	
Back pain			
subjects affected / exposed	4 / 71 (5.63%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 71 (5.63%)	0 / 34 (0.00%)	
occurrences (all)	67	29	
Nasopharyngitis			
subjects affected / exposed	1 / 71 (1.41%)	3 / 34 (8.82%)	
occurrences (all)	67	29	
Clostridium difficile colitis			
subjects affected / exposed	0 / 71 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	67	29	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	14 / 71 (19.72%)	3 / 34 (8.82%)	
occurrences (all)	67	29	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 January 2011	Protocol Amendment 1
07 April 2011	IMPD Amendment
19 April 2011	IB Edition 04
19 August 2011	IB Edition 05
07 September 2011	Protocol Amendment 2
09 September 2011	IMPD Amendment
23 December 2011	IMPD Amendment
27 March 2012	Protocol Amendment 3
27 March 2012	IB Edition 06

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 June 2012	On 14 June 2012, a planned futility analysis of data from the study concluded that treatment with IPI-926 was similar to placebo and, therefore, the trial would not meet its primary endpoint. Based on this interim analysis, Infinity announced on 18 June 2012 it was stopping the trial. No formal efficacy or exploratory analyses were performed.	-

Notes:

Limitations and caveats

None reported