Clinical trial results:
Phase II Study of Imatinib Mesylate for Philadelphia-Positive Acute Lymphocytic Leukemia

Summary

EudraCT number	2017-001805-34
Trial protocol	Outside EU/EEA
Global end of trial date	14 February 2007

Results information

Result version number	v1 (current)
This version publication date	26 July 2018
First version publication date	26 July 2018

Trial information

Trial identification

Sponsor protocol code	CSTI571A1203

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

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	14 February 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 February 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy and safety of STI571 in patients diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 May 2004
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	Japan: 8
Worldwide total number of subjects	8
EEA total number of subjects	0

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)	1
Adults (18-64 years)	5
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Treatment initiation day was expressed as Day 1 (the day before the treatment initiation as Day –1). Screening were performed between Day –7 and Day –1 (the day before the treatment initiation).

Period 1

Period 1 title	Core phase
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All subjects - Core phase

Arm description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).
Core phase (up to 12 weeks): a remission induction therapy with STI571 was conducted in this phase.

Arm type	Experimental
Investigational medicinal product name	STI571
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

STI571: 600 mg (oral once daily); a dose may be increased up to 800 mg (400 mg oral twice daily) in patients with an inadequate response

Number of subjects in period 1	All subjects - Core phase
Started	8
Completed	6
Not completed	2
Inadequate response	2

Period 2

Period 2 title	Extension phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All subjects - Extension phase

Arm description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).
Extension phase (until the study completion): treatment with STI571 continues in responders.

Arm type	Experimental
Investigational medicinal product name	STI571
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

STI571: 600 mg (oral once daily); a dose may be increased up to 800 mg (400 mg oral twice daily) in patients with an inadequate response

Number of subjects in period 2	All subjects - Extension phase
Started	6
Completed	1
Not completed	5
Difficulty in making office visits	2
No need to treat with the investigational product	2
Inadequate response	1

Baseline characteristics

Reporting groups	
Reporting group title	Core phase

Reporting group description: -

Reporting group values	Core phase	Total	
Number of subjects	8	8	
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)	1	1	
Adults (18-64 years)	5	5	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	51.6		
standard deviation	± 16.7	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	3	3	

End points

End points reporting groups

Reporting group title	All subjects - Core phase

Reporting group description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).
Core phase (up to 12 weeks): a remission induction therapy with STI571 was conducted in this phase.

Reporting group title	All subjects - Extension phase

Reporting group description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).
Extension phase (until the study completion): treatment with STI571 continues in responders.

Subject analysis set title	Core + Extension phases
Subject analysis set type	Full analysis

Subject analysis set description:

Al patients diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia.
Core phase (up to 12 weeks): a remission induction therapy with STI571 is to be conducted in this phase.
Extension phase (until the study completion): treatment with STI571 continues in responders.

Primary: Percentage of patients with Hematologic response (CHR + Marrow-CR)

End point title	Percentage of patients with Hematologic response (CHR + Marrow-CR)[1]

End point description:

Complete hematologic response (CHR): peripheral blasts = 0%, bone marrow blasts <5%, neutrophils ≥1500/mm^3, and platelets ≥100 000/mm^3 + Complete marrow response (Marrow-CR): peripheral blasts = 0% and bone marrow blasts <5%

End point type	Primary

End point timeframe:

Antileukemic effect of STI571 monotherapy persisted for at least 4 weeks.

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 reported for this primary endpoint.

End point values	All subjects - Core phase			
Subject group type	Reporting group			
Number of subjects analysed	8[2]			
Units: Percentage of patients				
number (confidence interval 95%)				
All Response (n=8)	100 (63.1 to 100.0)			
Sustained Response (n=5)	62.5 (24.5 to 91.5)			

Notes:

[2] - full analysis set (FAS)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with Cytogenetic response

End point title	Percentage of patients with Cytogenetic response

End point description:

Cytogenetic response (CGR):
Complete CGR: At least 1 confirmed elimination of Philadelphia chromosome
Major CGR: At least 1 confirmed suppression of Philadelphia chromosome to between 1% and 35%

End point type	Secondary

End point timeframe:

Antileukemic effect of STI571 monotherapy persisted for at least 4 weeks.

End point values	Core + Extension phases			
Subject group type	Subject analysis set			
Number of subjects analysed	8[3]			
Units: Percentage of patients				
number (confidence interval 95%)	87.5 (47.3 to 99.7)			

Notes:

[3] - full analysis set (FAS); patients who reached the Cytogenetic response : n=7.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	7.0

Reporting groups

Reporting group title	All subjects

Reporting group description:

600 mg oral once daily (400 mg oral twice daily if a daily dose is increased to 800 mg).
Core phase (up to 12 weeks): a remission induction therapy with STI571 was conducted in this phase.
Extension phase (until the study completion): treatment with STI571 continues in responders.

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 8 (50.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Puncture site hemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral hemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin rash			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Sepsis			
subjects affected / exposed	1 / 8 (12.50%)		
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	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor lysis syndrome			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Petechiae			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	5 / 8 (62.50%)		
occurrences (all)	5		
Oedema			
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	5 / 8 (62.50%)		
occurrences (all)	5		
Oedema peripheral			

subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Chest discomfort			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Puncture site haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pharyngolaryngeal pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pharynx discomfort			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pleural effusion			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Upper respiratory tract inflammation			

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	4		
Blood bilirubin increased			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Blood lactate dehydrogenase increased			
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Hemoglobin decreased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Lymphocyte count decreased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Urinary occult blood positive			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Hepatic enzyme increased			

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Blood amylase increased			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Blood creatinine increased			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Blood pressure increased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
PH urine abnormal			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Thermal burn			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Nerve injury			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Nervous system disorders			
Burning sensation			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Dysgeusia			

subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2		
Headache subjects affected / exposed occurrences (all)	5 / 8 (62.50%) 5		
Dizziness subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Hypothymia subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3		
Cerebral haemorrhage subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Dizziness postural subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 4		
Neutropenia subjects affected / exposed occurrences (all)	5 / 8 (62.50%) 5		
Thrombocytopenia subjects affected / exposed occurrences (all)	5 / 8 (62.50%) 5		
Leukopenia subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3		
Myelosuppression subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Febrile neutropenia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		

Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Eye disorders Conjunctival hemorrhage subjects affected / exposed occurrences (all) Conjunctival edema subjects affected / exposed occurrences (all) Blepharitis subjects affected / exposed occurrences (all) Eyelid edema subjects affected / exposed occurrences (all) Lacrimation increased subjects affected / exposed occurrences (all) Photophobia subjects affected / exposed occurrences (all) Retinal haemorrhage subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 4 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain upper	8 / 8 (100.00%) 8 5 / 8 (62.50%) 5		

subjects affected / exposed	5 / 8 (62.50%)			
occurrences (all)	5			
Constipation				
subjects affected / exposed	3 / 8 (37.50%)			
occurrences (all)	3			
Diarrhoea				
subjects affected / exposed	5 / 8 (62.50%)			
occurrences (all)	5			
Stomatitis				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Abdominal distension				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Cheilitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Haemorrhoids				
subjects affected / exposed	4 / 8 (50.00%)			
occurrences (all)	4			
Abdominal pain				
subjects affected / exposed	3 / 8 (37.50%)			
occurrences (all)	3			
Abdominal pain lower				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Gingival bleeding				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Gingivitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Faeces soft				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Oral discomfort				

subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Periodontitis			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Gastrointestinal mucosal disorder			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 8 (87.50%)		
occurrences (all)	7		
Face edema			
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	4		
Eczema			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Erythema			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Keloid scar subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Rash vesicular subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Urticaria subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Renal and urinary disorders Glomerulonephritis chronic subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Cystitis haemorrhagic subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Cystitis-like symptom subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	4 / 8 (50.00%) 4		
Muscular weakness subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Myalgia subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3		
Osteonecrosis subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Infections and infestations			

Neutropenic infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Sepsis				
subjects affected / exposed	4 / 8 (50.00%)			
occurrences (all)	4			
Nasopharyngitis				
subjects affected / exposed	3 / 8 (37.50%)			
occurrences (all)	3			
Dental caries				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Infection				
subjects affected / exposed	2 / 8 (25.00%)			
occurrences (all)	2			
Catheter related infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Herpes simplex				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Herpes virus infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Perianal abscess				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			
Escherichia infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences (all)	1			

Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	5 / 8 (62.50%)		
occurrences (all)	5		
Hypoalbuminemia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Hypokalaemia			
subjects affected / exposed	5 / 8 (62.50%)		
occurrences (all)	5		
Fluid retention			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Hypophosphatemia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 June 2004	Revision to clarify descriptions in inclusion and exclusion criteria and addition of on-site measurement methods to chromosome banding at screening were made.
10 September 2004	Changes in actions to be taken in case of occurrence of serious adverse events (SAE) were made in response to the revision of the clinical study standard operating procedures (SOP) of Novartis Pharma K.K.
30 November 2004	The study period was extended as treatment with the investigational product was likely to continue after April 2005.

Notes:

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.

Data which would be needed to produce non-SAE and SAE tables by programming, does not exist. SAE and non-SAE tables in this document are the data of serious ADR and all AE respectively. For full, disclosure, all data available has been reported.

Notes: