Clinical trial results:
A phase II open-label study to determine the safety and anti-leukemic effects of STI571 in patients with Philadelphia chromosome-positive chronic myeloid leukemia in myeloid blast crisis extended for in total of 11 years (Extension 1: 2002-2004 and Extension 2: 2004- 2013)

Summary

EudraCT number	2005-001380-61
Trial protocol	IT
Global end of trial date	22 April 2013

Results information

Result version number	v1
This version publication date	28 July 2018
First version publication date	28 July 2018

Trial information

Trial identification

Sponsor protocol code	CSTI571A0102E2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00171158
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	22 April 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 April 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To enable patients to have access to study drug, continue study treatment and to decrease data collection to include overall survival and serious adverse events.

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	26 March 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	France: 17
Country: Number of subjects enrolled	Germany: 62
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	United Kingdom: 35
Country: Number of subjects enrolled	United States: 126
Country: Number of subjects enrolled	Italy: 15
Worldwide total number of subjects	260
EEA total number of subjects	129

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)	199
From 65 to 84 years	61
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients recruited were adults with Philadelphia chromosome-positive (Ph+) CML transformed into myeloid BC. Patients that completed extension study #1 could enter into the extension study #2.

Period 1

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

Arms

Arm title	All subjects

Arm description:

STI571 was originally provided in capsule form in 100 mg strength. STI571 will be supplied as tablets instead of capsules. Patients will continue to use capsules until the supply of capsules is finished and are supplied with tablets. The capsules and tablets are bioequivalent. The initial dose was either 400 mg once daily or 600 mg once daily. Dosage increase from 400 mg once daily to 600 mg once daily and from 600 mg once daily to 800 mg once daily was permitted in all patients for improved therapeutic effect.

Arm type	Experimental
Investigational medicinal product name	STI571
Investigational medicinal product code	
Other name	imatinib, Glivec®, Gleevec®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

STI571 was supplied as 25 mg, 50 mg and 100 mg tablets, taken orally, once a day with 250 ml of water after breakfast for 400 mg/day and 600 mg/day doses, or twice a day after breakfast and the evening meal for 800 mg/day (2 x 400 mg/day) dose.

Number of subjects in period 1	All subjects
Started	260
Still on treatment	21
Completed	21
Not completed	239
No longer required drug (BMT)	14
Consent withdrawn by subject	6
Adverse event, non-fatal	21
Protocol violation	4
Death	27
Unsatisfactory therapeutic effect	163

Administrative problems	1
Abnormal laboratory values	2
Lost to follow-up	1

Period 2

Period 2 title	Overall Trial - E2 extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All subjects - Extension phase

Arm description:

STI571 was provided in capsule form in 100 mg strength. STI571 will be supplied as tablets instead of capsules. Patients will continue to use capsules until the supply of capsules is finished and are supplied with tablets. The capsules and tablets are bioequivalent. The initial dose was either 400 mg once daily or 600 mg once daily. Dosage increase from 400 mg once daily to 600 mg once daily and from 600 mg once daily to 800 mg once daily was permitted in all patients for improved therapeutic effect.

Arm type	Experimental
Investigational medicinal product name	STI571
Investigational medicinal product code	imatinib mesylate
Other name	imatinib, Glivec®, Gleevec®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

STI571 was supplied as 25 mg, 50 mg and 100 mg tablets, taken orally, once a day with 250 ml of water after breakfast for 400 mg/day and 600 mg/day doses, or twice a day after breakfast and the evening meal for 800 mg/day (2 x 400 mg/day) dose.

Number of subjects in period 2[1]	All subjects - Extension phase
Started	8
Completed	1
Not completed	7
Unknown reason	7

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: In Extension 1 (E1) of the study, 13 subjects discontinued. Reasons are unknown.

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	260	260	
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)	199	199	
From 65-84 years	61	61	
85 years and over	0	0	
Age continuous Units: years			
median	56		
full range (min-max)	19 to 81	-	
Gender categorical Units: Subjects			
Female	124	124	
Male	136	136	

End points

End points reporting groups

Reporting group title	All subjects

Reporting group description:

STI571 was originally provided in capsule form in 100 mg strength. STI571 will be supplied as tablets instead of capsules. Patients will continue to use capsules until the supply of capsules is finished and are supplied with tablets. The capsules and tablets are bioequivalent. The initial dose was either 400 mg once daily or 600 mg once daily. Dosage increase from 400 mg once daily to 600 mg once daily and from 600 mg once daily to 800 mg once daily was permitted in all patients for improved therapeutic effect.

Reporting group title	All subjects - Extension phase

Reporting group description:

STI571 was provided in capsule form in 100 mg strength. STI571 will be supplied as tablets instead of capsules. Patients will continue to use capsules until the supply of capsules is finished and are supplied with tablets. The capsules and tablets are bioequivalent. The initial dose was either 400 mg once daily or 600 mg once daily. Dosage increase from 400 mg once daily to 600 mg once daily and from 600 mg once daily to 800 mg once daily was permitted in all patients for improved therapeutic effect.

Primary: Summary overall survival (ITT)

End point title	Summary overall survival (ITT)[1]

End point description:

Overall survival was defined as the time from first dose of STI571 to death of the patient.

End point type	Primary

End point timeframe:

From first dose until death of the patient, up to 11 years.

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 end point

End point values	All subjects			
Subject group type	Reporting group			
Number of subjects analysed	260[2]			
Units: Number of events (%)				
number (not applicable)				
All patients	89.2			

Notes:

[2] - Intent-to-treat (ITT) population.

Statistical analyses

No statistical analyses for this end point

Primary: Summary of overall survival (by month)

End point title	Summary of overall survival (by month)[3]

End point description:

Kaplan-Meier estimates per month.

End point type	Primary

End point timeframe:

From first dose until death of the patient, up to 11 years.

Notes:

[3] - 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 end point

End point values	All subjects			
Subject group type	Reporting group			
Number of subjects analysed	260[4]			
Units: percentage f participants				
number (confidence interval 95%)				
12 months	32.7 (27.0 to 38.5)			
24 months	18.7 (14.2 to 23.8)			
36 months	15.4 (11.2 to 20.2)			
48 months	14.5 (10.4 to 19.2)			
60 months	9.1 (5.7 to 13.4)			
72 months	8.4 (5.2 to 12.7)			
84 months	7.5 (4.3 to 11.8)			
96 months	7.5 (4.3 to 11.8)			
108 months	7.5 (4.3 to 11.8)			
120 months	6.6 (3.5 to 11.0)			
132 months	5.5 (2.6 to 10.0)			

Notes:

[4] - Intent-to-treat (ITT) population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

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.

Adverse event reporting additional description:

After 31-Jul-2002 no safety data was collected in the clinical database and Serious adverse events (SAEs) were reported in the safety database. No drug-related SAEs leading to discontinuation or drug-related deaths were reported after 31-Jul-2002 in the safety database.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	All subjects

Reporting group description:

STI571 was originally provided in capsule form in 100 mg strength. STI571 will be supplied as tablets instead of capsules. Patients will continue to use capsules until the supply of capsules is finished and are supplied with tablets. The capsules and tablets are bioequivalent. The initial dose was either 400 mg once daily or 600 mg once daily. Dosage increase from 400 mg once daily to 600 mg once daily and from 600 mg once daily to 800 mg once daily was permitted in all patients for improved therapeutic effect.

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	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	0 / 8 (0.00%)		

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: After 31-Jul-2002 no safety data was collected in the clinical database and Serious adverse events (SAEs) were reported in the safety database.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2004	To allow patients to receive study drug for as long as the patient should require it. Also, it changed the frequency of bone marrow cytogenetics for those patients maintaining a complete cytogenetic response to annually from twice yearly until the patient reached month 48 of the extension or 31-July-2006, whichever date came first.
01 March 2008	To accommodate patient site visits on a yearly (±3 months) basis rather than every six months. In addition, a new section was added to include new protocol deviation language which stated that under no circumstances were protocol deviations allowed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported