Clinical trial results:
A non-randomized, open-label study to characterize the pharmacokinetics of Glivec/Gleevec® (imatinib mesylate) in pediatric (age range 1 to less than 4 years) patients with chronic myeloid leukemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)

Summary

EudraCT number	2010-018418-53
Trial protocol	FR NL HU DE
Global end of trial date	07 May 2011

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	CSTI571A2110

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01066468
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000463-PIP01-08
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 May 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 May 2011
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to characterize the pharmacokinetics (PK) of imatinib in pediatric subjects of age 1 to less than (<) 4 years using appropriate integrated physiologically-based pharmacokinetic (PBPK) and population PK approaches.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all 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	27 October 2010
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	Canada: 1
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	3
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)	3
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 3 centres in 3 countries.

Pre-assignment

Screening details:

Only 3 subjects were enrolled into the study.

Period 1

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

Blinding implementation details:

This was a non-randomized, open-label study, hence no blinding was performed.

Arms

Arm title	Imatinib

Arm description:

Subjects received imatinib once daily orally in dose ranging from 260 milligrams per square metre (mg/m^2) to 340 mg/m^2. Lower dose of imatinib (60 mg/m^2/day) was allowed at the discretion of investigator.

Arm type	Experimental
Investigational medicinal product name	Imatinib
Investigational medicinal product code	STI571
Other name	
Pharmaceutical forms	Coated tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Imatinib mesylate oral suspension (260-320 mg/m^2) was administered once daily

Number of subjects in period 1	Imatinib
Started	3
Completed	3

Baseline characteristics

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	3	3	
Age categorical Units: Subjects			
Children (2-11 years)	3	3	
Age continuous Units: years			
arithmetic mean	2.7		
standard deviation	± 0.58	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	2	2	

End points

End points reporting groups

Reporting group title	Imatinib

Reporting group description:

Subjects received imatinib once daily orally in dose ranging from 260 milligrams per square metre (mg/m^2) to 340 mg/m^2. Lower dose of imatinib (60 mg/m^2/day) was allowed at the discretion of investigator.

Primary: Pharmacokinetic parameters of Imatinib

End point title	Pharmacokinetic parameters of Imatinib[1]

End point description:

This study was discontinued early due to the lack of patient population and accrual. Due to scarcity of PK data, planned non-compartmental analysis was not done. Only listings on 3 patients were completed.

End point type	Primary

End point timeframe:

Predose (0 hour), 1-2 hours, 2-4 hours, 6-24 hours post-dose at steady state

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: Only descriptive summary statistics was planned for this outcome measure for each subject.

End point values	Imatinib			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Not Applicable				
number (not applicable)				

Notes:

[2] - Lack of data from incomplete enrollment prevents the representation of any summary statistics

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV). All other adverse events are monitored from First Subject First Treatment until Last Subject Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Imatinib

Reporting group description:

Subjects received imatinib once daily orally in dose ranging from 260 mg/m^2 to 340 mg/m^2. Lower dose of imatinib (60 mg/m^2/day) was allowed at the discretion of investigator.

Serious adverse events	Imatinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (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	Imatinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 1 / 3 (33.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2010	Study inclusion criteria was broadened to allow subjects with other imatinib indicated hematological disorders (i.e. myelodysplastic/myeloproliferative neoplasms, hypereosinophilic syndrome and chronic eosinophilic leukemia). This amendment also allowed the imatinib dose as low as 60 mg/m^2/day below the dose range of 260 mg/m^2 to 340 mg/m^2 (as defined in the original protocol) to ensure an acceptable safety profile and clinical benefit at the treating physician's discretion and with approval by the Novartis clinical trial team.

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.

The study was discontinued early due to the lack of subject population and accrual. Due to the rarity of the disease in children (1-4 years), minimum enrollment (10 subjects) was not met.

Notes: