Clinical trial results:
Phase 1 Study of SRC, ABL Tyrosine Kinase Inhibitor Dasatinib (BMS-354825) in Children and Adolescents with Relapsed or Refractory Leukemia

Summary

EudraCT number	2005-002882-35
Trial protocol	DE AT GB IT BE
Global end of trial date	22 May 2019

Results information

Result version number	v1 (current)
This version publication date	21 November 2020
First version publication date	21 November 2020

Trial information

Trial identification

Sponsor protocol code	CA180-018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000567-PIP01-09
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	02 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 May 2011
Global end of trial reached?	Yes
Global end of trial date	22 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish, by stratum using a dose-finding design, a recommended Phase 2 dose of dasatinib (BMS-354825) in children and adolescents with relapsed or refractory leukemia.

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 Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 January 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	United Kingdom: 11
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	2
Children (2-11 years)	32
Adolescents (12-17 years)	23

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Stratum 1 - 18 were enrolled; 1 no longer met study criteria and was never treated Stratum 2/3 - 20 were enrolled;3 never treated(2 no longer met study criteria;1 withdrew consent) Stratum 4 - 25 were enrolled; 1 no longer met study criteria and was never treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose

Arm description:

Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Starting Dose Level of 60 mg/m^2; Escalated/Dose Level 2 of 80 mg/m^2. Once daily (QD), as long as clinical benefit was maintained.

Arm type	Experimental
Investigational medicinal product name	Dasatinib
Investigational medicinal product code	
Other name	BMS-354825-03
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

5mg, 20mg and 50mg tablets

Arm title	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose

Arm description:

Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in accelerated phase (AP), or in myeloid blast phase (MBP), or in lymphoid blast phase (LBP); or relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL) after imatinib use; or second or subsequent relapse of Ph+ acute myeloid leukemia (AML). Starting Dose Level of 60 mg/m^2; Escalated/Dose level 2 of 80 mg/m^2. QD, as long as clinical benefit was maintained.

Arm type	Experimental
Investigational medicinal product name	Dasatinib
Investigational medicinal product code	
Other name	BMS-354825-03
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

5mg, 20mg and 50mg tablets

Arm title	Stratum4 Ph- ALL/AML; Dasatinib 60 mg/m^2 Starting Dose

Arm description:

Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Starting Dose Level of 60 mg/m^2; Escalated/Dose level 2 of 80 mg/m^2, Escalated/Dose level 3 of 100 mg/m^2, and Escalated/Dose level 4 of 120 mg/m^2. QD, as long as clinical benefit was maintained.

Arm type	Experimental

Investigational medicinal product name	Dasatinib
Investigational medicinal product code	
Other name	BMS-354825-03
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

5mg, 20mg and 50mg tablets

Number of subjects in period 1	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose	Stratum4 Ph-ALL/AML; Dasatinib 60 mg/m^2 Starting Dose
Started	17	17	24
Completed	17	17	24

Baseline characteristics

Reporting groups	
Reporting group title	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose
Reporting group description:	
Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Starting Dose Level of 60 mg/m^2; Escalated/Dose Level 2 of 80 mg/m^2. Once daily (QD), as long as clinical benefit was maintained.	
Reporting group title	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose
Reporting group description:	
Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in accelerated phase (AP), or in myeloid blast phase (MBP), or in lymphoid blast phase (LBP); or relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL) after imatinib use; or second or subsequent relapse of Ph+ acute myeloid leukemia (AML). Starting Dose Level of 60 mg/m^2; Escalated/Dose level 2 of 80 mg/m^2. QD, as long as clinical benefit was maintained.	
Reporting group title	Stratum4 Ph- ALL/AML; Dasatinib 60 mg/m^2 Starting Dose
Reporting group description:	
Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Starting Dose Level of 60 mg/m^2; Escalated/Dose level 2 of 80 mg/m^2, Escalated/Dose level 3 of 100 mg/m^2, and Escalated/Dose level 4 of 120 mg/m^2. QD, as long as clinical benefit was maintained.	

Reporting group values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose	Stratum4 Ph- ALL/AML; Dasatinib 60 mg/m^2 Starting Dose
Number of subjects	17	17	24
Age Categorical Units: Participants			
< 2 years	0	0	2
Between 2 and 6 years	2	5	7
Between 7 and 11 years	6	5	7
Between 12 and 18 years	9	7	7
> 18 years	0	0	1
Age Continuous Units: years			
arithmetic mean	12.4	9.7	8.6
standard deviation	± 4.1	± 4.3	± 5.6
Sex: Female, Male Units:			
Female	6	5	8
Male	11	12	16
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White	16	15	21
Black/African American	0	0	1
Asian	1	1	1
Other	0	1	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	0	1	0

Unknown or Not Reported	17	16	24

Reporting group values	Total		
Number of subjects	58		
Age Categorical Units: Participants			
< 2 years	2		
Between 2 and 6 years	14		
Between 7 and 11 years	18		
Between 12 and 18 years	23		
> 18 years	1		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units:			
Female	19		
Male	39		
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White	52		
Black/African American	1		
Asian	3		
Other	2		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	1		
Unknown or Not Reported	57		

Subject analysis sets

Subject analysis set title	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in accelerated phase (AP), or in myeloid blast phase (MBP), or in lymphoid blast phase (LBP); or relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL) after imatinib use; or second or subsequent relapse of Ph+ acute myeloid

leukemia (AML). Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in accelerated phase (AP), or in myeloid blast phase (MBP), or in lymphoid blast phase (LBP); or relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL) after imatinib use; or second or subsequent relapse of Ph+ acute myeloid leukemia (AML). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 4 Ph- ALL/AML (Dasatinib 60 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 4 Ph- ALL/AML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 4 Ph- ALL/AML (Dasatinib 100 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 4 Ph- ALL/AML (Dasatinib 120 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 80 mg/m^2, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant Ph+ chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum1 Ph+ CP-CML (Dasatinib 60 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2 QD Starting Dose
Subject analysis set type	Full analysis

Subject analysis set description:

Stratum 1 (Ph+ CP-CML): Participants with imatinib-resistant Ph+ CML in CP; Stratum 2/3 (PH+ ALL OR AP/BP-CML): Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in AP, or in MBP, or in LBP; or relapsed or refractory Ph+ ALL after imatinib use; or second or subsequent relapse of Ph+ AML; Stratum 4 (PH- ALL/AML): Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Strata 1, 2/3, and 4: 60 mg/m^2 starting dose; 80 mg/m^2 escalated/dose level 2; Stratum 4: 100 mg/m^2 escalated/dose level 3 and 120 mg/m^2 escalated/dose level 4. QD, as long as clinical benefit was observed.

Subject analysis set title	Dasatinib 60 mg/m^2 QD Starting Dose
Subject analysis set type	Full analysis

Subject analysis set description:

Stratum 1 (Ph+ CP-CML): Participants with imatinib-resistant Ph+ CML in CP; Stratum 2/3 (PH+ ALL OR

AP/BP-CML): Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in AP, or in MBP, or in LBP; or relapsed or refractory Ph+ ALL after imatinib use; or second or subsequent relapse of Ph+ AML; Stratum 4 (PH- ALL/AML): Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Strata 1, 2/3, and 4: 60 mg/m^2 starting dose; 80 mg/m^2 escalated/dose level 2; Stratum 4: 100 mg/m^2 escalated/dose level 3 and 120 mg/m^2 escalated/dose level 4. QD, as long as clinical benefit was observed.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 80 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 80 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2

Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 80 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 80 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Reporting group values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)
Number of subjects	11	6	8
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units:			
Female Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian Other			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 60 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 80 mg/m^2)
Number of subjects	9	6	6
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units:			
Female Male			

Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian Other			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Stratum 4 Ph- ALL/AML (Dasatinib 100 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 120 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)
Number of subjects	6	6	6
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units:			
Female Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian Other			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Dasatinib 60 mg/m^2 QD Starting Dose
Number of subjects	6	11	53
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years			

Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	6 ±	90.9 ±	 ±
Sex: Female, Male Units:			
Female Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian Other			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Dasatinib 60 mg/m^2 QD Starting Dose	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2
Number of subjects	53	20	25
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	 ±	 ±	 ±
Sex: Female, Male Units:			
Female Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian Other			
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2	Dasatinib 60 mg/m^2
Number of subjects	19	10	19
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units:			
Female Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian Other			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2	Dasatinib 60 mg/m^2
Number of subjects	18	9	18
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units:			
Female			

Male			

Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White			
Black/African American			
Asian			
Other			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			

Reporting group values	Dasatinib 80 mg/m^2	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2
Number of subjects	20	15	8
Age Categorical			
Units: Participants			
< 2 years			
Between 2 and 6 years			
Between 7 and 11 years			
Between 12 and 18 years			
> 18 years			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Units:			
Female			
Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White			
Black/African American			
Asian			
Other			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			

Reporting group values	Dasatinib 100 mg/m^2	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2
Number of subjects	16	13	21

Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	± 	± 	±
Sex: Female, Male Units:			
Female Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian Other			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Dasatinib 100 mg/m^2	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2
Number of subjects	14	4	10
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	± 	± 	±
Sex: Female, Male Units:			
Female Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian			

Other			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

Reporting group values	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2	
Number of subjects	6	1	
Age Categorical Units: Participants			
< 2 years Between 2 and 6 years Between 7 and 11 years Between 12 and 18 years > 18 years			
Age Continuous Units: years arithmetic mean standard deviation	±	±	
Sex: Female, Male Units:			
Female Male			
Race/Ethnicity, Customized			
Race only			
Units: Subjects			
White Black/African American Asian Other			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

End points reporting groups

Reporting group title	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose
Reporting group description:	
Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Starting Dose Level of 60 mg/m^2; Escalated/Dose Level 2 of 80 mg/m^2. Once daily (QD), as long as clinical benefit was maintained.	
Reporting group title	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose
Reporting group description:	
Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in accelerated phase (AP), or in myeloid blast phase (MBP), or in lymphoid blast phase (LBP); or relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL) after imatinib use; or second or subsequent relapse of Ph+ acute myeloid leukemia (AML). Starting Dose Level of 60 mg/m^2; Escalated/Dose level 2 of 80 mg/m^2. QD, as long as clinical benefit was maintained.	
Reporting group title	Stratum4 Ph- ALL/AML; Dasatinib 60 mg/m^2 Starting Dose
Reporting group description:	
Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Starting Dose Level of 60 mg/m^2; Escalated/Dose level 2 of 80 mg/m^2, Escalated/Dose level 3 of 100 mg/m^2, and Escalated/Dose level 4 of 120 mg/m^2. QD, as long as clinical benefit was maintained.	
Subject analysis set title	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.	
Subject analysis set title	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.	
Subject analysis set title	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in accelerated phase (AP), or in myeloid blast phase (MBP), or in lymphoid blast phase (LBP); or relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL) after imatinib use; or second or subsequent relapse of Ph+ acute myeloid leukemia (AML). Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.	
Subject analysis set title	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in accelerated phase (AP), or in myeloid blast phase (MBP), or in lymphoid blast phase (LBP); or relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL) after imatinib use; or second or subsequent relapse of Ph+ acute myeloid leukemia (AML). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.	
Subject analysis set title	Stratum 4 Ph- ALL/AML (Dasatinib 60 mg/m^2)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.	
Subject analysis set title	Stratum 4 Ph- ALL/AML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.	
Subject analysis set title	Stratum 4 Ph- ALL/AML (Dasatinib 100 mg/m^2)

Subject analysis set type	Full analysis

Subject analysis set description:

Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 4 Ph- ALL/AML (Dasatinib 120 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 80 mg/m^2, as long as clinical benefit was maintained.

Subject analysis set title	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant Ph+ chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Stratum1 Ph+ CP-CML (Dasatinib 60 mg/m^2)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants with imatinib-resistant Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP). Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2 QD Starting Dose
Subject analysis set type	Full analysis

Subject analysis set description:

Stratum 1 (Ph+ CP-CML): Participants with imatinib-resistant Ph+ CML in CP; Stratum 2/3 (PH+ ALL OR AP/BP-CML): Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in AP, or in MBP, or in LBP; or relapsed or refractory Ph+ ALL after imatinib use; or second or subsequent relapse of Ph+ AML; Stratum 4 (PH- ALL/AML): Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Strata 1, 2/3, and 4: 60 mg/m^2 starting dose; 80 mg/m^2 escalated/dose level 2; Stratum 4: 100 mg/m^2 escalated/dose level 3 and 120 mg/m^2 escalated/dose level 4. QD, as long as clinical benefit was observed.

Subject analysis set title	Dasatinib 60 mg/m^2 QD Starting Dose
Subject analysis set type	Full analysis

Subject analysis set description:

Stratum 1 (Ph+ CP-CML): Participants with imatinib-resistant Ph+ CML in CP; Stratum 2/3 (PH+ ALL OR AP/BP-CML): Participants with imatinib-resistant or imatinib-intolerant Ph+ CML in AP, or in MBP, or in LBP; or relapsed or refractory Ph+ ALL after imatinib use; or second or subsequent relapse of Ph+ AML; Stratum 4 (PH- ALL/AML): Participants with second or subsequent relapse of Ph- ALL or Ph- AML. Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Strata 1, 2/3, and 4: 60 mg/m^2 starting dose; 80 mg/m^2 escalated/dose level 2; Stratum 4: 100 mg/m^2 escalated/dose level 3 and 120 mg/m^2 escalated/dose level 4. QD, as long as clinical benefit was observed.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 80 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 80 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 80 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 60 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Dasatinib 60 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 80 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 80 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 100 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 100 mg/m^2 QD, as long as clinical benefit was maintained.

Subject analysis set title	Dasatinib 120 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Tablets, Oral; If necessary in participants who could not swallow, tablets were dispersed into 30 cc of 100% fruit juice with no preservatives (minute maid lemonade or orange juice or apple juice). Dasatinib 120 mg/m^2 QD, as long as clinical benefit was maintained.

Primary: Recommended Phase II Dose of Dasatinib in Children and Adolescents with Relapsed or Refractory Leukemia

End point title	Recommended Phase II Dose of Dasatinib in Children and Adolescents with Relapsed or Refractory Leukemia[1]

End point description:

The recommended phase 2 dasatinib dose was determined based on efficacy, safety, and pharmacokinetic data obtained at the prespecified dose levels. Note: 9999 = NA (not available)

End point type	Primary

End point timeframe:

From the date of first dose to end-of-treatment (EOT) (Median duration of therapy in months: Stratum 1=24.11 [Range:2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

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 summary statistics were planned for this endpoint

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose	Stratum4 Ph- ALL/AML; Dasatinib 60 mg/m^2 Starting Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	17	24	
Units: mg/m^2 QD	60	80	9999	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Related Deaths, Serious Adverse Events (SAEs), and Adverse Events (AEs) by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 3.0.

End point title	Number of Participants with Related Deaths, Serious Adverse Events (SAEs), and Adverse Events (AEs) by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 3.0.

End point description:

AE: New untoward medical occurrence or worsening of a preexisting medical condition that does not have causal relationship with this treatment. SAE: Untoward medical event that at any dose: results in death, persistent or significant disability/incapacity, drug dependency/abuse; life-threatening, an important medical event, a congenital anomaly/birth defect; requires inpatient hospitalization/prolongs existing hospitalization. Grade 3 = Severe; Grade 4 = Life-threatening or disabling.

End point type	Secondary

End point timeframe:

From the date of first dose until at least 30 days after the last dose of study drug (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	6	8	9
Units: participants				
Drug-Related Deaths	0	0	0	0
Drug-Related SAEs	1	1	2	3
Drug-Related AEs Leading to Discontinuation	0	0	0	0
Grade 3/4 AEs	5	3	4	3

End point values	Stratum 4 Ph- ALL/AML (Dasatinib 60	Stratum 4 Ph- ALL/AML (Dasatinib 80	Stratum 4 Ph- ALL/AML (Dasatinib 100	Stratum 4 Ph- ALL/AML (Dasatinib 120

	mg/m^2)	mg/m^2)	mg/m^2)	mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: participants				
Drug-Related Deaths	0	0	0	0
Drug-Related SAEs	2	2	2	2
Drug-Related AEs Leading to Discontinuation	1	0	1	0
Grade 3/4 AEs	3	4	3	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Dose-limiting Toxicity (DLT)

End point title	Number of Participants with Dose-limiting Toxicity (DLT)

End point description:

DLTs: AEs which were at least possibly drug-related occurring within first 3 weeks of dasatinib therapy (toxicities occurring after 21 days were also considered) and are:- --Any nonhematologic clinically-apparent toxicity of Grade(GR)≥3 occurring despite appropriate medical management and GR4 laboratory abnormality/GR3 lasting ≥7 days --GR4 neutropenia or thrombocytopenia lasting ≥7 days and not explained by the presence of leukemia after hematopoietic reconstitution --Any clinically important toxicity of GR≥2 requiring treatment discontinuation or interruption ≥7 days.

End point type	Secondary

End point timeframe:

From the date of first dose until at least 30 days after the last dose of study drug (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	6	8	9
Units: participants	0	0	0	0

End point values	Stratum 4 Ph- ALL/AML (Dasatinib 60 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 80 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 100 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 120 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: participants	1	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Hematology Abnormalities by NCI CTCAE Version 3.0

End point title	Number of Participants with Hematology Abnormalities by NCI CTCAE Version 3.0

End point description:

GR1=Mild; GR2=Moderate; GR3=Severe; GR4=Life-threatening or disabling. Normal ranges provided by local laboratory and may also vary from site to site. WBC: GR1=<LLN-3.0*10^9/L; GR2=<3.0-2.0*10^9/L; GR3=<2.0-1.0*10^9/L; GR4=<1.0*10^9/L. ANC: GR1=<LLN-1.5*10^9 /L; GR2=<1.5-1.0*10^9/L; GR3=<1.0-0.5*10^9/L; GR4=<0.5*10^9/L. Hemoglobin: GR1=<LLN-10.0g/dL; GR2=<10.0-8.0g/dL; GR3=<8.0-6.5g/dL; GR4=<6.5g/dL. Platelets: GR1=<LLN-75.0*10^9/L; GR2=<75.0-50.0*10^9/L; GR3=<50.0-25.0*10^9/L; GR4=<25.0*10^9/L.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43, then every 3 weeks, then every 3 months after 1 Year, EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	6	8	9
Units: participants				
WBC GR1	6	4	2	1
WBC GR2	0	1	3	3
WBC GR3	0	0	0	1
WBC GR4	0	0	1	3
ANC GR1	3	3	1	1
ANC GR2	4	0	2	2
ANC GR3	1	2	2	0
ANC GR4	0	1	3	4
Platelet GR1	4	4	0	2
Platelet GR2	0	1	0	2
Platelet GR3	2	0	4	1
Platelet GR4	0	0	4	3
Hemoglobin GR1	3	4	1	0
Hemoglobin GR2	4	1	5	3
Hemoglobin GR3	0	0	1	4
Hemoglobin GR4	0	0	1	0

End point values	Stratum 4 Ph-ALL/AML (Dasatinib 60 mg/m^2)	Stratum 4 Ph-ALL/AML (Dasatinib 80 mg/m^2)	Stratum 4 Ph-ALL/AML (Dasatinib 100 mg/m^2)	Stratum 4 Ph-ALL/AML (Dasatinib 120 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: participants				
WBC GR1	1	1	0	0
WBC GR2	0	1	1	1
WBC GR3	0	2	1	0
WBC GR4	2	2	3	1
ANC GR1	0	0	0	0
ANC GR2	1	0	0	0
ANC GR3	0	2	0	2
ANC GR4	4	4	6	3
Platelet GR1	0	0	0	0
Platelet GR2	1	0	0	0
Platelet GR3	0	1	1	1
Platelet GR4	4	5	5	5
Hemoglobin GR1	0	0	0	0
Hemoglobin GR2	2	3	3	3
Hemoglobin GR3	3	1	3	2
Hemoglobin GR4	0	2	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Serum Chemistry Abnormalities (calcium, magnesium, and phosphate) by NCI CTCAE Version 3.0

End point title	Number of Participants with Serum Chemistry Abnormalities (calcium, magnesium, and phosphate) by NCI CTCAE Version 3.0

End point description:

GR1=Mild; GR2=Moderate; GR3=Severe; GR4=Life-threatening or disabling. Normal ranges provided by local laboratory and may also vary from site to site. Low calcium: GR1=<LLN–8.0 mg/dL, GR2=<8.0–7.0 mg/dL, GR3=<7.0–6.0 mg/dL, GR4=<6.0 mg/dL; Low magnesium: GR1=<LLN–1.2 mg/dL, GR2=<1.2–0.9 mg/dL, GR3=<0.9–0.7 mg/dL, GR4=<0.7 mg/dL; Low phosphate: GR1=<LLN – 2.5 mg/dL, GR2=<2.5 – 2.0 mg/dL, GR3=<2.0 – 1.0 mg/dL, GR4=<1.0 mg/dL.

End point type	Secondary

End point timeframe:

Days 22 and 43, then every 12 weeks, then every 24 weeks after 24 months of treatment, EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	6	8	9
Units: participants				
Low Calcium GR1	3	0	2	2
Low Calcium GR2	0	0	1	1
Low Calcium GR3	0	0	0	0
Low Calcium GR4	0	0	0	0
Low magnesium GR1	1	1	5	0
Low Magnesium GR2	0	0	0	0
Low Magnesium GR3	0	0	0	0
Low Magnesium GR4	0	0	0	0
Low Phosphate GR1	2	1	2	2
Low Phosphate GR2	1	0	0	1
Low Phosphate GR3	0	0	0	0
Low Phosphate GR4	0	0	0	0

End point values	Stratum 4 Ph- ALL/AML (Dasatinib 60 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 80 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 100 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 120 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: participants				
Low Calcium GR1	2	0	1	0
Low Calcium GR2	0	2	2	1
Low Calcium GR3	0	0	1	0
Low Calcium GR4	0	0	0	0
Low magnesium GR1	1	0	4	1
Low Magnesium GR2	0	0	0	0
Low Magnesium GR3	0	0	0	0
Low Magnesium GR4	0	0	0	0
Low Phosphate GR1	0	2	2	1
Low Phosphate GR2	0	2	1	1
Low Phosphate GR3	1	0	1	1
Low Phosphate GR4	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Serum Chemistry Abnormalities (Liver and Renal Function) by NCI CTCAE Version 3.0

End point title	Number of Participants with Serum Chemistry Abnormalities (Liver and Renal Function) by NCI CTCAE Version 3.0

End point description:

GR1=Mild; GR2=Moderate; GR3=Severe; GR4=Life-threatening or disabling. Normal ranges provided by local laboratory and may also vary from site to site. AST and ALT: GR1=>ULN-2.5*ULN; GR2=>2.5-5.0*ULN; GR3=>5.0-20.0*ULN; GR4:>20.0*ULN. Total bilirubin:GR1=>ULN-1.5*ULN, GR2=>1.5-3.0*ULN, GR3=>3-10*ULN, GR4=>10*ULN. Creatinine: GR1=>ULN-1.5*ULN, GR2=>1.5-3.0*ULN, GR3=>3.0-6.0*ULN, GR4=>6.0*ULN.

End point type	Secondary

End point timeframe:

Days 22 and 43, then every 12 weeks, then every 24 weeks after 24 months of treatment, EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	6	8	9
Units: participants				
AST GR1	1	3	5	3
AST GR2	0	0	2	1
AST GR3	0	0	1	2
AST GR4	0	0	0	0
High ALT GR1	4	4	4	2
High ALT GR2	0	0	2	1
High ALT GR3	0	0	1	0
High ALT GR4	0	0	0	2
Total Bilirubin GR1	2	0	1	1
Total Bilirubin GR2	0	1	0	0
Total Bilirubin GR3	1	0	0	0
Total Bilirubin GR4	0	0	0	0
High Serum Creatinine GR1	1	1	1	1
High Serum Creatinine GR2	0	0	1	0
High Serum Creatinine GR3	0	0	0	0
High Serum Creatinine GR4	0	0	0	0

End point values	Stratum 4 Ph- ALL/AML (Dasatinib 60 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 80 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 100 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 120 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: participants				
AST GR1	1	4	2	2
AST GR2	1	1	1	1
AST GR3	1	1	0	0
AST GR4	0	0	0	0
High ALT GR1	0	2	3	2
High ALT GR2	1	2	1	0

High ALT GR3	1	2	0	1
High ALT GR4	0	0	0	0
Total Bilirubin GR1	0	1	2	0
Total Bilirubin GR2	1	2	1	1
Total Bilirubin GR3	0	0	0	0
Total Bilirubin GR4	0	0	0	0
High Serum Creatinine GR1	1	0	0	0
High Serum Creatinine GR2	0	0	1	0
High Serum Creatinine GR3	0	0	0	0
High Serum Creatinine GR4	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Major Cytogenetic Response (MCyR) at Any Time in Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point title	Number of Participants with Major Cytogenetic Response (MCyR) at Any Time in Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point description:

Cytogenetic responses were based on the karyotype analysis of the percentage of Ph+ metaphases among cells in metaphase on a BM sample. At least 20 metaphase cells from a BM sample were evaluated. MCyR: A cytogenetic response that is either complete cytogenetic response (CCyR) or partial cytogenetic response (PCyR). CCyR: 0% Ph+ cells in metaphase in BM. PCyR: >0% to 35% Ph+ cells in metaphase in BM.

End point type	Secondary

End point timeframe:

Strata 1 and 2/3: At Week 7, 13, then every 12 weeks, and EOT; Stratum 2/3: Additionally at Week 4, 19, 31 (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	6	8	9
Units: participants	9	6	4	7

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Major Cytogenetic Response (MCyR) in Stratum 1 (Ph+ CP-CML) Within First 12 and 24 Weeks

End point title	Number of Participants with Major Cytogenetic Response

	(MCyR) in Stratum 1 (Ph+ CP-CML) Within First 12 and 24 Weeks

End point description:

Cytogenetic responses were based on the karyotype analysis of the percentage of Ph+ metaphases among cells in metaphase on a BM sample. At least 20 metaphase cells from a BM sample were evaluated. MCyR: A cytogenetic response that was either CCyR or PCyR. CCyR: 0% Ph+ cells in metaphase in BM. PCyR: >0% to 35% Ph+ cells in metaphase in BM.

End point type	Secondary

End point timeframe:

After completion of Week 12 and 24 (measured at Weeks 13 and 25)

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	6		
Units: participants				
MCyR within first 12 weeks	6	2		
MCyR within first 24 weeks	9	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Cytogenetic Response (CyR) in Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point title	Best Cytogenetic Response (CyR) in Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point description:

Best CyR was assessed based on the percentages of Ph+ metaphases of ≥20 analyzed metaphases in BM sample. Participants with complete, partial, minor, minimal, or no CyR. Refer to Outcome Measure 7 for definitions of CCyR and PCyR. Minor CyR:>35%-65% Ph+ cells in metaphase in BM. Minimal CyR:>65%-95% Ph+ cells in metaphase in BM. No CyR:>95%-100% Ph+ cells in metaphase in BM. Unable to determine:Participants without valid cytogenetic assessment (i.e., at least 1 metaphase observed and number of Ph+ metaphases smaller than total number of metaphases [%Ph+ <100%]).

End point type	Secondary

End point timeframe:

Strata 1 and 2/3: At Weeks 7, 13, then every 12 weeks, and EOT; Stratum 2/3: Additionally at Weeks 4, 19, 25, 31 (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	6	8	9
Units: participants				
No Response (>95% - 100%)	1	0	0	1
Minimal (>65% - 95%)	0	0	0	0
Minor (>35% - 65%)	1	0	0	0
Partial (>0% - 35%)	1	0	0	0
Complete (0%)	8	6	4	8
Unable to determine	0	0	4	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Complete Cytogenetic Response (CCyR) or Major Cytogenetic Response (MCyR) at Recommended Phase II Dose

End point title	Percentage of Participants with Complete Cytogenetic Response (CCyR) or Major Cytogenetic Response (MCyR) at Recommended Phase II Dose

End point description:

Cytogenetic responses were based on the karyotype analysis of the percentage of Ph+ metaphases among cells in metaphase on a BM sample. At least 20 metaphase cells from a BM sample were evaluated. MCyR: A cytogenetic response that was either CCyR or PCyR. CCyR: 0% Ph+ cells in metaphase in BM. PCyR: >0% to 35% Ph+ cells in metaphase in BM.

End point type	Secondary

End point timeframe:

Strata 1 and 2/3: At Week 7, 13, then every 12 weeks, and EOT; Stratum 2/3: Additionally at Week 4, 19, 31 (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	9		
Units: percentage of participants				
number (confidence interval 95%)				
CCyR	72.7 (39.0 to 94.0)	88.9 (51.8 to 99.7)		
MCyR	81.8 (48.2 to 97.7)	88.9 (51.8 to 99.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Major Cytogenetic Response (MCyR) in Responders: Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point title	Time to Major Cytogenetic Response (MCyR) in Responders: Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ ALL or AP/BP-CML)[2]

End point description:

Defined as time (in days) from the first dose of dasatinib until criteria were first met for MCyR. MCyR: A CyR that was either CCyR or PCyR. CCyR: 0% Ph+ cells in metaphase in BM. PCyR: >0% to 35% Ph+ cells in metaphase in BM. The Kaplan-Meier plot was used. A 2-sided, 95% confidence interval (CI) for the median was computed using the Brookmeyer and Crowley method.

End point type	Secondary

End point timeframe:

Strata 1 and 2/3: At Weeks 7, 13, 25, 37, then every 12 weeks; Stratum 2/3: Additionally at Weeks 4, 19, 31; until first MCyR (maximum participant time to first MCyR of 92 days).

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	12		
Units: days				
median (confidence interval 95%)	75.0 (43.0 to 92.0)	33.5 (22.0 to 43.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Major Cytogenetic Response (MCyR) in Responders (Stratum 1 [Ph+ CP-CML] and Stratum 2/3 [Ph+ ALL or AP/BP-CML])

End point title	Duration of Major Cytogenetic Response (MCyR) in Responders (Stratum 1 [Ph+ CP-CML] and Stratum 2/3 [Ph+ ALL or AP/BP-CML])[3]

End point description:

Defined as the time (in months) from the first day that all criteria were met for MCyR until the date of progression (based on the Investigator's assessment) or death (for participants whose best responses were MCyR and CCyR respectively). MCyR: A cytogenetic response that was either CCyR or PCyR. CCyR: 0% Ph+ cells in metaphase in BM. PCyR: >0% to 35% Ph+ cells in metaphase in BM. The Kaplan-Meier plot was used. A 2-sided, 95% CI for the median was computed using the Brookmeyer and Crowley method.

End point type	Secondary

End point timeframe:

From the date of first MCyR assessment to date of progression, death, or last tumor assessment (maximum participant duration of response of 48.6 months)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	12		
Units: months				
median (confidence interval 95%)	52.2 (10.0 to 56.1)	4.6 (1.2 to 17.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Complete Cytogenetic Response (CCyR) in Responders: Stratum 1 [Ph+ CP-CML] and Stratum 2/3 [Ph+ ALL or AP/BP-CML]

End point title	Duration of Complete Cytogenetic Response (CCyR) in Responders: Stratum 1 [Ph+ CP-CML] and Stratum 2/3 [Ph+ ALL or AP/BP-CML][4]

End point description:

Defined as time (in months) from the first day that all criteria were met for CCyR until the date of progression (based on the Investigator's assessment) or death (for participants whose best response was CCyR). CCyR = 0% Ph+ metaphases of ≥ 20 analyzed metaphases in BM aspiration. The Kaplan-Meier plot was used. A 2-sided, 95% CI for the median was computed using the Brookmeyer and Crowley method.

End point type	Secondary

End point timeframe:

From the date of first CCyR assessment to date of progression, death, or last tumor assessment (maximum participant duration of response of 45.1 months)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	12		
Units: months				
median (confidence interval 95%)	48.1 (10.0 to 56.1)	4.6 (1.2 to 17.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Major Hematologic Response (MaHR) at Any Time in Stratum 2/3 (Ph+ ALL or AP/BP-CML) and Stratum 4 (Ph- ALL/AML)

End point title	Number of Participants with Major Hematologic Response (MaHR) at Any Time in Stratum 2/3 (Ph+ ALL or AP/BP-CML) and Stratum 4 (Ph- ALL/AML)

End point description:

Defined as participants having as best response complete hematologic response (CHR) or CHR with incomplete platelet recovery (CHRp). Criteria: CHR-WBC in Peripheral Blood (PB):≤ULN; Immature cells in PB:No blasts, promyelocytes, myelocytes, metamyelocytes; Platelet count (untransfused):≥100,000/mm^3 and ≤450,000/mm^3; ANC:≥ 1000/mm^3; Blasts in BM:<5%; Extra medullary disease:No extramedullary leukemia, including no hepato or splenomegaly (regardless of CNS involvement). CHRp-CHR except platelet count (untransfused) & ANC:20,000/mm^3 ≤platelet <100,000/mm^3 & /or 500/mm^3 ≤ANC ≤1000/mm^3.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43; Weeks 4, 7, 13, 19, 25, 31, 37; at Week 10 (only stratum 4); then every 12 weeks upto 24 months; then once/year; EOT(Median duration of therapy in months: Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 60 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 80 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	9	6	6
Units: participants	2	6	0	0

End point values	Stratum 4 Ph- ALL/AML (Dasatinib 100 mg/m^2)	Stratum 4 Ph- ALL/AML (Dasatinib 120 mg/m^2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Major Hematologic Response (MaHR) in Stratum 2/3 (Ph+ ALL or AP/BP-CML) Within First 6 and 24 Weeks

End point title	Number of Participants with Major Hematologic Response (MaHR) in Stratum 2/3 (Ph+ ALL or AP/BP-CML) Within First 6 and 24 Weeks

End point description:

Defined as participants having as best response a CHR or CHRp. Criteria: CHR-WBC in PB:≤ULN; Immature cells in PB:No blasts, promyelocytes, myelocytes, metamyelocytes; Platelet count (untransfused):≥100,000/mm^3 and ≤450,000/mm^3; ANC:≥ 1000/mm^3; Blasts in BM:<5%; Extra medullary disease:No extramedullary leukemia, including no hepato or splenomegaly (regardless of CNS involvement). CHRp-CHR except platelet count (untransfused) and ANC:20,000/mm^3 ≤platelet <100,000/mm^3 and /or 500/mm^3 ≤ANC ≤1000/mm^3.

End point type	Secondary

End point timeframe:

After completion of Week 6 and 24 (measured at weeks 7 and 25)

End point values	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	9		
Units: participants				
MaHR within first 6 weeks	2	5		
MaHR within first 24 weeks	2	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Hematologic Response (HR) At Any Time: Stratum 1 (Ph+ CP-CML)

End point title	Best Hematologic Response (HR) At Any Time: Stratum 1 (Ph+ CP-CML)

End point description:

HR: Determined by complete blood count (CBC), differential, and platelet count (PLT). Criteria for complete hematologic response (CHR): WBC in PB: <10,000/mm^3; Immature cells in PB: No blasts or promyelocytes (myelocytes + metamyelocytes) <5%; Basophils in PB: <5%; Platelet count (untransfused): <450,000/mm^3; Extra medullary disease: No extramedullary leukemia, including no splenomegaly. Unconfirmed HR = All criteria met. Confirmed HR = Criteria for HR fulfilled again at least 28 days after they first met with no concomitant use of anagrelide or hydroxyurea during this interval.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43; Weeks 7, 13, 25, 37; then every 12 weeks upto 24 months; then once/year; EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	6		
Units: participants				
Best Confirmed HR-Complete	10	6		

Best Confirmed HR-No Response	1	0		
Best Unconfirmed Hematologic Response-Complete	10	6		
Best Unconfirmed Hematologic Response-No Response	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Hematologic Response (HR) At Any Time: Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point title	Best Hematologic Response (HR) At Any Time: Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point description:

HR was determined by CBC, differential, and platelet count. Refer to outcome measure 15 for criteria for CHR and CHRp. Criteria for minor hematologic response (MiHR): CHRp except blasts in BM-≥5% and ≤15% blasts in BM. Unconfirmed HR = All criteria met. periph=peripheral. Confirmed HR = Criteria for HR fulfilled again at least 28 days after they first met with no concomitant use of anagrelide or hydroxyurea during this interval.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43; Weeks 4, 7, 13, 19, 25, 31, 37; then every 12 weeks up to 24 months; then once/year; EOT (Median duration of therapy in months: Stratum 2/3=3.02 [Range: 0.53-37.72])

End point values	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	9		
Units: participants				
Best Confirmed HR-Complete	1	5		
Best Confirmed HR-Complete except periph. recovery	1	1		
Best Confirmed HR-No Response	6	3		
Best Unconfirmed HR-Complete	3	7		
Best Unconfirmed HR-Minor	0	1		
Best Unconfirmed HR-No Response	5	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Hematologic Response (HR) At Any Time: Stratum 4 (Ph- ALL/AML)

End point title	Best Hematologic Response (HR) At Any Time: Stratum 4 (Ph-ALL/AML)

End point description:

HR was determined by CBC, differential, and platelet count. Unable to determine = Participants without any valid hematologic assessments.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43; Weeks 4, 7, 10, 13, 19, 25, 31, 37; then every 12 weeks upto 24 months; then once/year; EOT (Median duration of therapy in months: Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum 4 Ph-ALL/AML (Dasatinib 60 mg/m^2)	Stratum 4 Ph-ALL/AML (Dasatinib 80 mg/m^2)	Stratum 4 Ph-ALL/AML (Dasatinib 100 mg/m^2)	Stratum 4 Ph-ALL/AML (Dasatinib 120 mg/m^2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	6	6
Units: participants				
Best Confirmed HR-No Response	5	6	6	6
Best Confirmed HR-Unable to Determine	1	0	0	0
Best Unconfirmed HR-No Response	5	6	6	6
Best Unconfirmed HR-Unable to Determine	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Major Hematologic Response (MaHR): Stratum 2/3 (PH+ ALL or AP/BP-CML)

End point title	Time to Major Hematologic Response (MaHR): Stratum 2/3 (PH+ ALL or AP/BP-CML)[5]

End point description:

Defined as time (in days) from first dose of dasatinib until the first day MaHR criteria were met, provided they were confirmed later (after 28 days) with no concomitant use of anagrelide or hydroxyurea during this interval. MaHR: Defined as participants having as best response a CHR or CHRp. Refer to Outcome Measure 15 for criteria for CHR and CHRp. Estimated by the Kaplan-Meier method and a 2-sided, 95% CI for the median was computed using the Brookmeyer and Crowley method.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43; Weeks 4, 7, 13, 19, 25, 31, 37; then every 12 weeks upto 24 months; then once/year; until confirmed MaHR (maximum participant time to first MaHR of 44 days).

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: days				
median (confidence interval 95%)	36.0 (29.0 to 42.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Complete Hematologic Response (CHR): Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ALL or AP/BP-CML)

End point title	Time to Complete Hematologic Response (CHR): Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ALL or AP/BP-CML)[6]

End point description:

Time to CHR is the time (in days) from first dose of dasatinib until the first day CHR criteria were met, provided they were confirmed later after 28 days with no concomitant use of anagrelide or hydroxyurea during this interval. Refer to Outcome Measure 16 for criteria to CHR in Stratum 1 and to Outcome Measure 15 for criteria for CHR in Stratum 2/3. Estimated by the Kaplan-Meier method and a 2-sided 95% CI for median was computed using the Brookmeyer and Crowley method.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43; Weeks 7, 13, 25, 37; at Week 4, 19, 31 (only stratum 2/3); then every 12 weeks upto 24 months; then once/year; until criteria was first met for CHR (maximum participant time to first CHR of 65 days).

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: days				
median (confidence interval 95%)	21.5 (16.0 to 23.0)	39.5 (36.0 to 44.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Major Hematologic Response (MaHR): Stratum 2/3 (Ph+ALL

or AP/BP-CML)

End point title	Duration of Major Hematologic Response (MaHR): Stratum 2/3 (Ph+ALL or AP/BP-CML)[7]

End point description:

Duration of MaHR is the time (in months) from the first day criteria were met for MaHR, provided they were confirmed later at least after 28 days with no concomitant use of anagrelide or hydroxyurea during this interval, until death or progression was first observed. MaHR: Defined as participants having as best response a CHR or CHRp. Refer to outcome measure 20 for criteria for CHR or CHRp. The Kaplan-Meier plot was used. A 2-sided, 95% CI for the median was computed using the Brookmeyer and Crowley method. Note: 9999 = NA (not available)

End point type	Secondary

End point timeframe:

From the date of first confirmed MaHR to date of progression, death, or last tumor assessment (maximum participant duration of response of 37 months).

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: months				
median (confidence interval 95%)	4.4 (3.5 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Complete Hematologic Response (CHR): Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ALL or AP/BP-CML)

End point title	Duration of Complete Hematologic Response (CHR): Stratum 1 (Ph+ CP-CML) and Stratum 2/3 (Ph+ALL or AP/BP-CML)[8]

End point description:

Duration of CHR is the time (in months) from the first day criteria were met for CHR, provided they were confirmed later (after 28 days) with no concomitant use of anagrelide or hydroxyurea during this interval until death or progression was first observed. Refer to Outcome Measure 20 for criteria for CHR (Stratum 1) and Outcome Measure 19 for CHR (Stratum 2/3). The Kaplan-Meier plot was used. A 2-sided, 95% CI for the median was computed using the Brookmeyer and Crowley method.

End point type	Secondary

End point timeframe:

From the date of first confirmed CHR to date of progression, death, or last tumor assessment (maximum participant duration of response of 50 months).

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: months				
median (confidence interval 95%)	9999 (14.3 to 9999)	7.3 (3.5 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Confirmed Hematologic Response (HR) at Recommended Phase II Dose: Stratum 1 (Ph+ CP-CML)

End point title	Percentage of Participants with Confirmed Hematologic Response (HR) at Recommended Phase II Dose: Stratum 1 (Ph+ CP-CML)

End point description:

A participant was said to have a confirmed HR if all the criteria for HR were fulfilled again at least 28 days after they first met with no concomitant use of anagrelide or hydroxyurea during this interval. HR observed in stratum 1 was CHR. Refer to Outcome Measure 20 for criteria for CHR. The Clopper and Pearson method was used to compute 95% exact CIs.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43; Weeks 7, 13, 25, 37; then every 12 weeks upto 24 months; then once/year; EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63])

End point values	Stratum1 Ph+ CP-CML (Dasatinib 60 mg/m^2)			
Subject group type	Subject analysis set			
Number of subjects analysed	11			
Units: percentage of participants				
number (confidence interval 95%)	90.9 (58.7 to 99.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Confirmed Hematologic Response (HR) at Recommended Phase II Dose: Stratum 2/3 (Ph+ALL or AP/BP-CML)

End point title	Percentage of Participants with Confirmed Hematologic Response (HR) at Recommended Phase II Dose: Stratum 2/3

	(Ph+ALL or AP/BP-CML)

End point description:

A participant is said to have a confirmed HR if criteria for HR were fulfilled again at least 28 days after they first met with no concomitant use of anagrelide or hydroxyurea during this interval. Confirmed HR observed in stratum 2/3 was either CHR or MaHR or overall hematologic response (OHR). Refer to Outcome Measure 19 for criteria for CHR and MaHR. OHR is defined as MaHR or MiHR. MiHR=CHRp except blasts in BM (≥ 5% and ≤ 15% blasts in BM). The Clopper and Pearson method was used to compute 95% exact CIs.

End point type	Secondary

End point timeframe:

Days 8, 15, 22, 29, 36, 43; Weeks 4, 7, 13, 19, 25, 31, 37; then every 12 weeks upto 24 months; then once/year; EOT (Median duration of therapy in months: Stratum 2/3=3.02 [Range: 0.53-37.72])

End point values	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percentage of participants				
number (confidence interval 95%)				
CHR	55.6 (21.2 to 86.3)			
MaHR	66.7 (29.9 to 92.5)			
OHR	66.7 (29.9 to 92.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Molecular Responses in Stratum 1 (Ph+ CP-CML)

End point title	Number of Participants with Molecular Responses in Stratum 1 (Ph+ CP-CML)

End point description:

Molecular response was calculated by measuring p210 variant of BCR-ABL transcripts in blood during treatment using quantitative polymerase chain reaction (qPCR) assay. Major molecular response (MMR): Ratio of the BCR-ABL to ABL <10^-3 or 0.1% on the international scale. Complete molecular response (CMR): Complete absence of BCR-ABL or the ratio is <10^-4.5 or 0.00316% on the international scale. Confirmed MMR or CMR = Criteria met again >6 weeks. BCR-ABL=the fused gene found in participants with this type of CML.

End point type	Secondary

End point timeframe:

At baseline (within 3 weeks before initiation of study therapy), After hematologic response, EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63])

End point values	Stratum 1 Ph+ CP-CML (Dasatinib 60 mg/m^2)	Stratum 1 Ph+ CP-CML (Dasatinib 80 mg/m^2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	6		
Units: participants				
MMR (Overall)	6	2		
CMR (Unconfirmed)	3	1		
CMR (Confirmed)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Major Molecular Response (MMR) in Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point title	Number of Participants with Major Molecular Response (MMR) in Stratum 2/3 (Ph+ ALL or AP/BP-CML)

End point description:

Molecular response was calculated by measuring BCR-ABL transcripts in blood during treatment using qPCR assay. MMR: Ratio of the BCR-ABL to ABL <10^-3 or a ≥3 log reduction from baseline in participants with p190 variant; ratio of the BCR-ABL to ABL <10^-3 on the international scale in participants with p210 variant. BCR-ABL=the fused gene found in participants with this type of CML.

End point type	Secondary

End point timeframe:

At baseline (within 3 weeks before initiation of study therapy), After hematologic response, EOT (Median duration of therapy in months: Stratum 2/3=3.02 [Range: 0.53-37.72])

End point values	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 60 mg/m^2)	Stratum 2/3 Ph+ ALL or AP/BP-CML (Dasatinib 80 mg/m^2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	9		
Units: participants	2	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Time in months from 1st first dose until progression (resistance or refractory disease) or death was first documented by investigator. Progressive disease: Resistant disease for which investigator may electively stop treatment or refractory disease requiring cessation of study treatment. The PFS was estimated

using the Kaplan-Meier product-limit method, and a two-sided 95% CI for the median PFS time was computed using the method of Brookmeyer and Crowley.

End point type	Secondary

End point timeframe:

From the date of randomization to date of progression, death, last tumor assessment, or 5 years after EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose	Stratum4 Ph-ALL/AML; Dasatinib 60 mg/m^2 Starting Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	17	24	
Units: months				
median (confidence interval 95%)	53.6 (11.4 to 9999)	4.9 (0.5 to 8.4)	1.4 (0.4 to 1.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Defined as time in months from start of study therapy to death. The OS was estimated using the Kaplan-Meier product-limit method, and a two-sided 95% CI for the median OS time was computed using the Brookmeyer and Crowley method.

End point type	Secondary

End point timeframe:

From start of study therapy until death or 5 years after EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72]; Stratum 4=1.14 [Range: 0.03-3.38])

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose	Stratum4 Ph-ALL/AML; Dasatinib 60 mg/m^2 Starting Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	17	24	
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	8.6 (3.2 to 9999)	3.0 (1.7 to 4.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic (PK) Parameter: Time to Achieve the Observed Maximum Plasma Concentration (Tmax) by Age Group

End point title	Dasatinib Plasma Pharmacokinetic (PK) Parameter: Time to Achieve the Observed Maximum Plasma Concentration (Tmax) by Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. Tmax is the time taken to reach the maximum observed plasma concentration.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2 QD Starting Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: hours				
median (full range (min-max))				
Infants and Toddlers (age<2 years old; n=2)	0.5 (0.5 to 0.5)			
Children (age>=2 and <12 years old; n=43)	1.1 (0.5 to 4.1)			
Adolescents (age>=12 and <18 years old; n=28)	1.0 (0.5 to 6.0)			
Above 18 Years (n=1)	0.9 (0.9 to 0.9)			
Total (n=74)	1.0 (0.5 to 6.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic Parameter: Terminal Half-life (T 1/2) by Age Group

End point title	Dasatinib Plasma Pharmacokinetic Parameter: Terminal Half-life (T 1/2) by Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. T 1/2 is the time required for the concentration of the drug to reach half of its original value in plasma.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2 QD Starting Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: hours				
geometric mean (geometric coefficient of variation)				
Infants and Toddlers (age<2 years old; n=2)	2.1 (± 24.0)			
Children (age>=2 and <12 years old; n=36)	3.0 (± 62.8)			
Adolescents (age>=12 and <18 years old; n=22)	3.8 (± 43.9)			
Above 18 years (n=1)	7.3 (± 9999)			
Total (n=61)	3.3 (± 55.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic Parameter: Dose Normalized Observed Maximum Plasma Concentration (Cmax) by Age Group

End point title	Dasatinib Plasma Pharmacokinetic Parameter: Dose Normalized Observed Maximum Plasma Concentration (Cmax) by Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. Dose Normalized Cmax is the maximum observed concentration of drug substance in plasma normalized for different dasatinib dose levels.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2 QD Starting Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: ng/mL/mg/m^2				
geometric mean (geometric coefficient of variation)				

Infants and Toddlers (age<2 years old; n=2)	1.0 (± 15.2)			
Children (age>=2 and <12 years old; n=43)	1.9 (± 79.9)			
Adolescents (age>=12 and <18 years old; n=28)	1.0 (± 69.7)			
Above 18 Years (n=1)	0.9 (± 9999)			
Total (n=74)	1.5 (± 86.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic Parameter: Dose Normalized Area Under the Plasma Concentration Versus Time Curve From Time 0 to the time of the last quantifiable concentration (AUC[0-T]) by Age Group

End point title	Dasatinib Plasma Pharmacokinetic Parameter: Dose Normalized Area Under the Plasma Concentration Versus Time Curve From Time 0 to the time of the last quantifiable concentration (AUC[0-T]) by Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. AUC[0-T] is the area under the plasma concentration-time curve from time zero to time of last quantifiable concentration, normalized by dasatinib dose level.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2 QD Starting Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: ng.h/mL/mg/m^2				
geometric mean (geometric coefficient of variation)				
Infants and Toddlers (age<2 years old; n=2)	2.8 (± 4.6)			
Children (age>=2 and <12 years old; n=40)	6.1 (± 95.7)			
Adolescents (age>=12 and <18 years old; n=28)	3.8 (± 66.8)			
Above 18 Years (n=1)	2.2 (± 9999)			
Total (n=71)	4.9 (± 98.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic Parameter: Dose Normalized Area Under the Plasma Concentration Versus Time Curve From Time Zero Extrapolated to Infinite Time (AUC[INF]) by Age Group

End point title	Dasatinib Plasma Pharmacokinetic Parameter: Dose Normalized Area Under the Plasma Concentration Versus Time Curve From Time Zero Extrapolated to Infinite Time (AUC[INF]) by Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. AUC (0-inf) is the area under the plasma concentration-time curve from time zero extrapolated to infinite time, normalized by dasatinib dose level.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2 QD Starting Dose			
Subject group type	Subject analysis set			
Number of subjects analysed	53			
Units: ng.h/mL/mg/m^2				
geometric mean (geometric coefficient of variation)				
Infants and Toddlers (age<2 years old; n=2)	3.2 (± 17.7)			
Children (age>=2 and <12 years old; n=36)	6.7 (± 95.0)			
Adolescents (age>=12 and <18 years old; n=22)	4.2 (± 67.6)			
Above 18 Years (n=1)	2.4 (± 9999)			
Total (n=61)	5.4 (± 97.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic Parameter: Observed Maximum Plasma Concentration (Cmax) by Dose Level and Age Group

End point title	Dasatinib Plasma Pharmacokinetic Parameter: Observed Maximum Plasma Concentration (Cmax) by Dose Level and Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. Cmax is the maximum observed concentration of drug substance in plasma.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	25	19	10
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Infants and Toddlers (age>2yr; n=0; n=0; n=1; n=1)	9999 (± 9999)	9999 (± 9999)	30.6 (± 9999)	53.8 (± 9999)
Children (age>=2 and <12yr; n=11; n=16; n=9; n=7)	110.6 (± 61.8)	142.5 (± 80.2)	111.2 (± 82.6)	208.4 (± 78.5)
Adolescents (age>=12; n=9; n=8; n=9; n=2)	92.6 (± 50.6)	116.5 (± 73.0)	235.1 (± 59.0)	123.3 (± 68.3)
Above 18 years (n=0; n=1; n=0; n=0)	9999 (± 9999)	143.2 (± 9999)	9999 (± 9999)	9999 (± 9999)
Total	102.1 (± 58.0)	133.6 (± 77.6)	148.1 (± 75.0)	163.9 (± 87.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic (PK) Parameter: Time to Achieve the Observed Maximum Plasma Concentration (Tmax) By Dose Level and Age Group

End point title	Dasatinib Plasma Pharmacokinetic (PK) Parameter: Time to Achieve the Observed Maximum Plasma Concentration (Tmax) By Dose Level and Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. Tmax is the time taken to reach the maximum observed plasma concentration.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	25	19	10
Units: hour				
median (full range (min-max))				
Infants and Toddlers (age<2yr; n=0; n=0; n=1; n=1)	9999 (9999 to 9999)	9999 (9999 to 9999)	0.5 (0.5 to 0.5)	0.5 (0.5 to 0.5)
Children (age>=2 and <12yr; n=11; n=16; n=9; n=7)	1.1 (0.5 to 2.1)	1.5 (0.5 to 3.2)	1.1 (0.6 to 4.1)	1.0 (0.9 to 2.2)
Adolescents(age>=12 and <12yr; n=9; n=8; n=9; n=2)	1.0 (0.5 to 4.0)	1.1 (0.5 to 4.0)	1.0 (0.5 to 6.0)	1.6 (1.0 to 2.1)
Above 18 years (n=0; n=1; n=0; n=0)	9999 (9999 to 9999)	0.9 (0.9 to 0.9)	9999 (9999 to 9999)	9999 (9999 to 9999)

Total	1.0 (0.5 to 4.0)	1.1 (0.5 to 4.0)	1.0 (0.5 to 6.0)	1.0 (0.5 to 2.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic Parameter: Area Under the Plasma Concentration Versus Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUC[0-T]) by Dose Level and Age Group

End point title	Dasatinib Plasma Pharmacokinetic Parameter: Area Under the Plasma Concentration Versus Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUC[0-T]) by Dose Level and Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. AUC(0-T) is the area under the plasma concentration-time curve from time zero to time of last quantifiable concentration.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 80 mg/m^2	Dasatinib 60 mg/m^2	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	19	18	9
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Infants and Toddlers (age<2yr; n=0; n=0; n=1; n=1)	9999 (± 9999)	9999 (± 9999)	100.8 (± 9999)	134.9 (± 9999)
Children (age>=2 and <12yr; n=10; n=16; n=8; n=6)	490.8 (± 96.7)	295.0 (± 63.5)	373.5 (± 82.0)	676.7 (± 99.9)
Adolescents(age>=12 and <18yr; n=9; n=8; n=9; n=2)	488.1 (± 35.0)	320.8 (± 59.1)	787.0 (± 76.2)	526.1 (± 56.6)
Above 18 years (n=0; n=1; n=0; n=0)	367.2 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Total	484.3 (± 88.9)	307.0 (± 60.2)	504.1 (± 89.6)	534.9 (± 103.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic Parameter: Area Under the Plasma Concentration Versus Time Curve From Time Zero Extrapolated to Infinite Time (AUC[INF]) by Dose Level and Age Group

End point title	Dasatinib Plasma Pharmacokinetic Parameter: Area Under the Plasma Concentration Versus Time Curve From Time Zero Extrapolated to Infinite Time (AUC[INF]) by Dose Level and Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. AUC(INF) is the area under the plasma concentration-time curve from time zero extrapolated to infinite time.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	20	15	8
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Infants and Toddlers (age<2yr; n=0; n=0; n=1; n=1)	0 (± 0)	0 (± 0)	127.7 (± 9999)	142.1 (± 9999)
Children (age>=2 and <12yr; n=10; n=14; n=7; n=5)	313.9 (± 59.8)	513.6 (± 99.2)	429.1 (± 76.8)	817.6 (± 93.7)
Adolescents(age>=12 and <18yr; n=8; n=5; n=7; n=2)	305.8 (± 60.9)	605.1 (± 25.3)	1008.9 (± 69.4)	547.8 (± 58.2)
Above 18 years (n=0; n=1; n=0; n=0)	0 (± 0)	390.0 (± 9999)	0 (± 0)	0 (± 0)
Total	310.3 (± 58.6)	527.8 (± 90.4)	589.8 (± 86.2)	594.4 (± 101.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Plasma Pharmacokinetic Parameter: Terminal Half-life (T 1/2) by Dose Level and Age Group

End point title	Dasatinib Plasma Pharmacokinetic Parameter: Terminal Half-life (T 1/2) by Dose Level and Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. T 1/2 is the time required for the concentration of the drug to reach half of its original value in plasma.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	20	15	8
Units: hour				
arithmetic mean (standard deviation)				
Infants and Toddlers (age<2yr; n=0; n=0; n=1; n=1)	9999 (± 9999)	9999 (± 9999)	2.5 (± 9999)	1.8 (± 9999)
Children (age>=2 and <12yr; n=10; n=14; n=7; n=5)	2.4 (± 1.0)	3.9 (± 1.9)	4.6 (± 3.5)	3.2 (± 1.9)
Adolescents(age>=12 and <18yr; n=8; n=5; n=7; n=2)	3.7 (± 1.6)	5.1 (± 0.5)	4.5 (± 2.5)	3.5 (± 2.9)
Above 18 years (n=0; n=1; n=0; n=0)	9999 (± 9999)	7.3 (± 9999)	9999 (± 9999)	9999 (± 9999)
Total	3.0 (± 1.4)	4.4 (± 1.8)	4.4 (± 2.9)	3.1 (± 1.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Metabolite (BMS-582691) Plasma Pharmacokinetic Parameter: Observed Maximum Plasma Concentration (Cmax) by Dose Level and Age Group

End point title	Dasatinib Metabolite (BMS-582691) Plasma Pharmacokinetic Parameter: Observed Maximum Plasma Concentration (Cmax) by Dose Level and Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. Cmax is the maximum observed concentration of drug substance in plasma.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 80 mg/m^2	Dasatinib 120 mg/m^2	Dasatinib 60 mg/m^2	Dasatinib 100 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	10	18	16
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Infants and Toddlers (age<2yr; n=0; n=0; n=0; n=1)	9999 (± 9999)	1.2 (± 9999)	9999 (± 9999)	9999 (± 9999)
Children (age>=2 and <12yr; n=10; n=16; n=7; n=7)	3.4 (± 82.0)	4.8 (± 65.3)	3.6 (± 46.4)	6.0 (± 69.3)
Adolescents(age>=12 and <18yr; n=8; n=8; n=9; n=2)	3.6 (± 56.7)	4.3 (± 77.9)	3.1 (± 40.3)	6.9 (± 75.0)
Above 18 years (n=0; n=1; n=0; n=0)	2.2 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Total	3.4 (± 74.4)	4.1 (± 70.8)	3.4 (± 43.7)	6.5 (± 72.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Metabolite (BMS-582691) Plasma Pharmacokinetic (PK) Parameter: Time to Achieve the Observed Maximum Plasma Concentration (Tmax) By Dose Level and Age Group

End point title	Dasatinib Metabolite (BMS-582691) Plasma Pharmacokinetic (PK) Parameter: Time to Achieve the Observed Maximum Plasma Concentration (Tmax) By Dose Level and Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. Tmax is the time taken to reach the maximum observed plasma concentration.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at 0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 80 mg/m^2	Dasatinib 120 mg/m^2	Dasatinib 60 mg/m^2	Dasatinib 100 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	25	10	18	16
Units: hour				
median (full range (min-max))				
Infants and Toddlers (age<2yr; n=0; n=0; n=0; n=1)	9999 (9999 to 9999)	0.9 (0.9 to 0.9)	9999 (9999 to 9999)	9999 (9999 to 9999)
Children (age>=2 and <12yr; n=10; n=16; n=7; n=7)	2.0 (0.5 to 6.0)	2.0 (1.0 to 2.2)	2.0 (1.0 to 4.5)	2.1 (1.0 to 4.1)
Adolescents(age>=12 and <18yr; n=8; n=8; n=9; n=2)	2.0 (1.0 to 4.0)	2.1 (2.0 to 2.1)	2.0 (1.0 to 4.0)	2.0 (1.0 to 8.1)
Above 18 years (n=0; n=1; n=0; n=0)	0.9 (0.9 to 0.9)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)
Total	2.0 (0.5 to 6.0)	2.0 (0.9 to 2.2)	2.0 (1.0 to 4.5)	2.0 (1.0 to 8.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Dasatinib Metabolite (BMS-582691) Plasma Pharmacokinetic Parameter: Area Under the Plasma Concentration Versus Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUC[0-T]) by Dose Level and Age Group

End point title	Dasatinib Metabolite (BMS-582691) Plasma Pharmacokinetic Parameter: Area Under the Plasma Concentration Versus Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUC[0-T]) by Dose Level and Age Group

End point description:

PK is the process by which a drug is absorbed, distributed, metabolized, and eliminated by the body. AUC(0-T) is the area under the plasma concentration-time curve from time zero to time of last quantifiable concentration.

End point type	Secondary

End point timeframe:

During Week 1 of Course 1, and any course in which dose escalation was performed (at pre-dose, and at

0.5, 1, 2, 4, 6, 8 and 24 hours).

End point values	Dasatinib 120 mg/m^2	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2	Dasatinib 100 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	13	21	14
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
Infants and Toddlers (age<2yr; n=0; n=0; n=0; n=1)	1.9 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Children (age>=2 and <12yr; n=7; n=12; n=5; n=6)	23.6 (± 102.2)	8.8 (± 50.4)	16.6 (± 145.2)	25.4 (± 71.1)
Adolescents(age>=12 and <12yr; n=6; n=8; n=9; n=2)	15.8 (± 105.5)	12.3 (± 38.4)	13.5 (± 54.4)	20.0 (± 112.3)
Above 18 years (n=0; n=1; n=0; n=0)	9999 (± 9999)	9999 (± 9999)	6.6 (± 9999)	9999 (± 9999)
Total	16.3 (± 110.3)	10.3 (± 44.9)	14.7 (± 141.1)	21.8 (± 100.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of Dasatinib in Cerebrospinal Fluid (CSF) by Dose Level and Age Group

End point title	Concentration of Dasatinib in Cerebrospinal Fluid (CSF) by Dose Level and Age Group

End point description:

Concentration of dasatinib in CSF was assessed only in participants who had lumbar puncture during the treatment. y=years

End point type	Secondary

End point timeframe:

4 hours after oral dose

End point values	Dasatinib 60 mg/m^2	Dasatinib 80 mg/m^2	Dasatinib 100 mg/m^2	Dasatinib 120 mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	10	6	1
Units: ng/mL				
arithmetic mean (standard deviation)				
Children (age>=2 and <12 y; n=3, n=9, n=3, n=1)	1.1 (± 0.2)	1.5 (± 0.6)	1.7 (± 0.4)	3.8 (± 9999)
Adolescents(age>=12 and <18 y; n=1; n=1; n=3; n=0)	1.1 (± 9999)	1.0 (± 9999)	2.6 (± 0.6)	9999 (± 9999)
Total (Children + Adolescents;n=4; n=10; n=6; n=1)	1.1 (± 0.1)	1.4 (± 0.6)	2.1 (± 0.7)	3.8 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with BCR-ABL Mutations at Baseline: Stratum1 Ph+ CP-CML and Stratum 2/3 Ph+ALL or AP/BP-CML

End point title	Number of Participants with BCR-ABL Mutations at Baseline: Stratum1 Ph+ CP-CML and Stratum 2/3 Ph+ALL or AP/BP-CML[9]

End point description:

BCR-ABL, also referred to as the Philadelphia chromosome, is formed from the fusion of the BCR gene on chromosome 22 with the ABL gene on chromosome 9.

End point type	Secondary

End point timeframe:

At baseline (within 3 weeks before initiation of study therapy)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: participants				
L384M	1	0		
G250E	1	0		
T315I	0	1		
Y253H	0	1		
Y253F	0	1		
No Mutation	15	11		
No Data	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with BCR-ABL Mutations at End-of-Treatment: Stratum1 Ph+ CP-CML and Stratum2/3 Ph+ ALL or AP/BP-CML

End point title	Number of Participants with BCR-ABL Mutations at End-of-Treatment: Stratum1 Ph+ CP-CML and Stratum2/3 Ph+ ALL or AP/BP-CML[10]

End point description:

BCR-ABL = These are fused genes found in participants with this type of leukemia.

End point type	Secondary

End point timeframe:

At EOT (Median duration of therapy in months: Stratum 1=24.11 [Range: 2.27-50.63]; Stratum 2/3=3.02 [Range: 0.53-37.72])

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: participants				
T315I	0	4		
No Mutation	8	9		
No Data	9	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with FLT3 and KIT Mutations in Stratum4 Ph- ALL/AML at Baseline

End point title	Number of Participants with FLT3 and KIT Mutations in Stratum4 Ph- ALL/AML at Baseline[11]

End point description:

FLT3 and KIT = These are fused genes found in participants with this type of leukemia.

End point type	Secondary

End point timeframe:

At baseline (within 3 weeks before initiation of study therapy)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum4 Ph- ALL/AML; Dasatinib 60 mg/m^2 Starting Dose			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: participants				
FLT3 Absent	20			
FLT3 Present	1			

FLT3 No Data	3			
KIT Absent	21			
KIT Present	0			
KIT No Data	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with FLT3 and KIT Mutations in Stratum4 Ph- ALL/AML at End-Of-Treatment

End point title	Number of Participants with FLT3 and KIT Mutations in Stratum4 Ph- ALL/AML at End-Of-Treatment[12]

End point description:

FLT3 and KIT = These are fused genes found in participants with this type of leukemia.

End point type	Secondary

End point timeframe:

At EOT (Median duration of therapy in months: Stratum 4=1.14 [Range: 0.03-3.38])

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is specific to Stratum 1 and Stratum 2/3 arms only

End point values	Stratum4 Ph- ALL/AML; Dasatinib 60 mg/m^2 Starting Dose			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: participants				
FLT3 Absent	6			
FLT3 Present	0			
FLT3 No Data	18			
KIT Absent	6			
KIT Present	0			
KIT No Data	18			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants With Hematologic Toxicity at Baseline by NCI CTCAE Version 3.0

End point title	Number of Participants With Hematologic Toxicity at Baseline by NCI CTCAE Version 3.0

End point description:

GR1=Mild; GR2=Moderate; GR3=Severe; GR4=Life-threatening or disabling. Normal ranges provided by local laboratory and may also vary from site to site. White Blood Cell (WBC):GR1=<LLN-3.0*10^9/L;

GR2=<3.0-2.0*10^9/L; GR3=<2.0-1.0*10^9/L; GR4=<1.0*10^9/L. Absolute Neutrophil Count (ANC): GR1=<LLN-1.5*10^9 /L; GR2=<1.5-1.0*10^9/L; GR3=<1.0-0.5*10^9/L; GR4=<0.5*10^9/L. Hemoglobin: GR1=<LLN-10.0g/dL; GR2=<10.0-8.0g/dL; GR3=<8.0-6.5g/dL; GR4=<6.5g/dL. Platelets: GR1=<LLN-75.0*10^9/L; GR2=<75.0-50.0*10^9/L; GR3=<50.0-25.0*10^9/L; GR4=<25.0*10^9/L. LLN=lower limit of normal.

End point type	Other pre-specified

End point timeframe:

At baseline (within 1 week before initiation of study therapy)

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose	Stratum4 Ph-ALL/AML; Dasatinib 60 mg/m^2 Starting Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	17	24	
Units: participants				
WBC GR1	1	2	3	
WBC GR2	0	2	2	
WBC GR3	0	0	6	
WBC GR4	0	1	4	
ANC GR1	1	2	3	
ANC GR2	1	1	0	
ANC GR3	0	2	3	
ANC GR4	0	2	13	
Platelet GR1	1	5	5	
Platelet GR2	0	2	3	
Platelet GR3	0	3	8	
Platelet GR4	0	2	6	
Hemoglobin GR1	7	7	7	
Hemoglobin GR2	1	7	7	
Hemoglobin GR3	0	1	3	
Hemoglobin GR4	0	0	0	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants With Serum Chemistry Abnormalities (Liver and Renal Function) at Baseline by NCI CTCAE Version 3.0

End point title	Number of Participants With Serum Chemistry Abnormalities (Liver and Renal Function) at Baseline by NCI CTCAE Version 3.0

End point description:

GR1=Mild; GR2=Moderate; GR3=Severe; GR4=Life-threatening or disabling. Normal ranges provided by local laboratory and may also vary from site to site. Aspartate aminotransferase (AST) and alanine aminotransferase(ALT): GR1=>ULN-2.5*ULN; GR2=>2.5-5.0*ULN; GR3=>5.0-20.0*ULN; GR4=>20.0*ULN. Total bilirubin:GR1=>ULN-1.5*ULN, GR2=>1.5-3.0*ULN, GR3=>3-10*ULN, GR4=>10*ULN. Creatinine: GR1=>ULN-1.5*ULN, GR2=>1.5-3.0*ULN, GR3=>3.0-6.0*ULN, GR4=>6.0*ULN. ULN=upper limit of normal.

End point type	Other pre-specified

End point timeframe:

At baseline (within 1 week before initiation of study therapy)

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose	Stratum4 Ph-ALL/AML; Dasatinib 60 mg/m^2 Starting Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	17	24	
Units: participants				
AST GR1	1	3	8	
AST GR2	0	2	1	
AST GR3	0	1	0	
AST GR4	0	0	0	
AST GR Not Reported	1	3	2	
High ALT GR1	2	6	6	
High ALT GR2	0	2	5	
High ALT GR3	0	0	0	
High ALT GR4	0	0	0	
High ALT GR Not Reported	0	0	0	
High Total Bilirubin GR1	3	0	1	
High Total Bilirubin GR2	0	1	0	
High Total Bilirubin GR3	0	0	0	
High Total Bilirubin G4	0	0	0	
High Total Bilirubin GR Not Reported	0	0	1	
High Serum Creatinine GR1	2	0	4	
High Serum Creatinine GR2	0	1	0	
High Serum Creatinine GR3	0	0	0	
High Serum Creatinine GR4	0	0	0	
High Serum Creatinine GR Not Reported	0	0	1	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants With Serum Chemistry Abnormalities (Calcium, Magnesium, and Phosphate) at Baseline by NCI CTCAE Version 3.0

End point title	Number of Participants With Serum Chemistry Abnormalities (Calcium, Magnesium, and Phosphate) at Baseline by NCI CTCAE Version 3.0

End point description:

GR1=Mild; GR2=Moderate; GR3=Severe; GR4=Life-threatening or disabling. Normal ranges provided by local laboratory and may also vary from site to site. Low calcium: GR1=<LLN–8.0 mg/dL, GR2=<8.0–7.0 mg/dL, GR3=<7.0–6.0 mg/dL, GR4=<6.0 mg/dL; Low magnesium: GR1=<LLN–1.2 mg/dL, GR2=<1.2–0.9 mg/dL, GR3=<0.9–0.7 mg/dL, GR4=<0.7 mg/dL; Low phosphate: GR1=<LLN – 2.5 mg/dL, GR2=<2.5 – 2.0 mg/dL, GR3=<2.0 – 1.0 mg/dL, GR4=<1.0 mg/dL.

End point type	Other pre-specified

End point timeframe:

At baseline (within 1 week before initiation of study therapy)

End point values	Stratum1 Ph+ CP-CML; Dasatinib 60 mg/m^2 Starting Dose	Stratum2/3 Ph+ALL or AP/BP-CML;Dasatinib60mg/m^2 Starting Dose	Stratum4 Ph-ALL/AML; Dasatinib 60 mg/m^2 Starting Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	17	24	
Units: participants				
Low Calcium GR1	0	0	1	
Low Calcium GR2	0	0	0	
Low Calcium GR3	0	0	0	
Low Calcium GR4	0	0	0	
Low Calcium GR Not Reported	0	0	2	
Low Magnesium GR1	0	6	0	
Low Magnesium GR2	0	0	0	
Low Magnesium GR3	0	0	0	
Low Magnesium GR4	0	0	0	
Low Magnesium GR Not Reported	0	0	2	
Low Phosphate GR1	0	1	0	
Low Phosphate GR2	0	0	0	
Low Phosphate GR3	0	1	0	
Low Phosphate GR4	0	0	0	
Low Phosphate GR Not Reported	2	0	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Time frame for AE reporting	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1
Reporting groups	
Reporting group title	CP-CML
Reporting group description:	
CP-CML	
Reporting group title	Ph-ALL/AML
Reporting group description:	
Ph-ALL/AML	
Reporting group title	Ph+ALL or AP/BP-CML
Reporting group description:	
Ph+ALL or AP/BP-CML	

Serious adverse events	CP-CML	Ph-ALL/AML	Ph+ALL or AP/BP-CML
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 17 (47.06%)	22 / 24 (91.67%)	14 / 17 (82.35%)
number of deaths (all causes)	3	23	12
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 17 (0.00%)	7 / 24 (29.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 6	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)	4 / 24 (16.67%)	3 / 17 (17.65%)
occurrences causally related to treatment / all	1 / 1	1 / 8	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			

subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Thrombosis in device			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Ammonia increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Coma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial nerve disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 17 (0.00%)	5 / 24 (20.83%)	3 / 17 (17.65%)
occurrences causally related to treatment / all	0 / 0	2 / 5	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			

subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Exfoliative rash			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash macular			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bone pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 17 (5.88%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			

subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	CP-CML	Ph-ALL/AML	Ph+ALL or AP/BP-CML
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)	24 / 24 (100.00%)	16 / 17 (94.12%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chloroma			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Skin papilloma			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Hot flush			
subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Hypertension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Catheter site erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Catheter site haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Catheter site pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	2
Chills			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	7 / 17 (41.18%)	4 / 24 (16.67%)	4 / 17 (23.53%)
occurrences (all)	15	5	5
Influenza like illness			
subjects affected / exposed	2 / 17 (11.76%)	1 / 24 (4.17%)	2 / 17 (11.76%)
occurrences (all)	10	1	10
Injection site pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	2
Malaise			
subjects affected / exposed	3 / 17 (17.65%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	4	0	0

Mucosal inflammation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
Pain			
subjects affected / exposed	3 / 17 (17.65%)	0 / 24 (0.00%)	3 / 17 (17.65%)
occurrences (all)	3	0	4
Peripheral swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	5 / 17 (29.41%)	8 / 24 (33.33%)	8 / 17 (47.06%)
occurrences (all)	13	10	9
Swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Ovarian failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	11 / 17 (64.71%)	2 / 24 (8.33%)	5 / 17 (29.41%)
occurrences (all)	30	3	16
Dry throat			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	3 / 17 (17.65%)
occurrences (all)	3	0	3
Nasal congestion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
subjects affected / exposed	5 / 17 (29.41%)	1 / 24 (4.17%)	2 / 17 (11.76%)
occurrences (all)	18	1	20
Pleural effusion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	1 / 17 (5.88%)
occurrences (all)	0	2	1
Pulmonary oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Anxiety			

subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Depressed mood			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Enuresis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	1 / 17 (5.88%)
occurrences (all)	1	1	1
Sleep disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Suicidal ideation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Investigations			
Body temperature			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	2 / 17 (11.76%)
occurrences (all)	0	3	2
Heart rate increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	3
Neutrophil count decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	1 / 17 (5.88%)	4 / 24 (16.67%)	0 / 17 (0.00%)
occurrences (all)	1	5	0

Weight increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Clavicle fracture			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	3 / 17 (17.65%)
occurrences (all)	3	0	3
Fall			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Head injury			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Joint injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	3 / 17 (17.65%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Mouth injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Skin abrasion			

subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Skin laceration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Sunburn			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Wound			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Post-Traumatic pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 17 (17.65%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	5	0	1
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	3 / 17 (17.65%)	1 / 24 (4.17%)	1 / 17 (5.88%)
occurrences (all)	5	1	1
Facial paralysis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	11 / 17 (64.71%)	6 / 24 (25.00%)	5 / 17 (29.41%)
occurrences (all)	83	10	6
Intracranial pressure increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Neuralgia			

subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Post-Traumatic headache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Pancytopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Splenomegaly			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Thrombocytopenia			
subjects affected / exposed	1 / 17 (5.88%)	3 / 24 (12.50%)	3 / 17 (17.65%)
occurrences (all)	1	4	4
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Ear pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	3 / 17 (17.65%)
occurrences (all)	6	0	4
Middle ear effusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	4	0	0
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dacryoadenitis acquired			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dry eye			

subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Erythema of eyelid			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Eye discharge			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	2 / 17 (11.76%)
occurrences (all)	1	0	2
Eye pruritus			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Eye swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eyelid oedema			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	1 / 17 (5.88%)
occurrences (all)	0	3	1
Eyelid ptosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Orbital oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
Swelling of eyelid			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0

Abdominal distension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	9 / 17 (52.94%)	3 / 24 (12.50%)	2 / 17 (11.76%)
occurrences (all)	33	3	8
Abdominal pain lower			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	3 / 17 (17.65%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	7	0	4
Aphthous ulcer			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Colitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	3 / 17 (17.65%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
Dental caries			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	11 / 17 (64.71%)	6 / 24 (25.00%)	7 / 17 (41.18%)
occurrences (all)	28	7	18
Dyspepsia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Flatulence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	1 / 17 (5.88%)
occurrences (all)	0	2	1

Irritable bowel syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	3 / 17 (17.65%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	11	0	0
Nausea			
subjects affected / exposed	7 / 17 (41.18%)	13 / 24 (54.17%)	6 / 17 (35.29%)
occurrences (all)	18	15	10
Oral mucosal blistering			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	3
Periodontal disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Tongue disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Tongue ulceration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Tooth loss			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	5	0	0
Vomiting			
subjects affected / exposed	9 / 17 (52.94%)	11 / 24 (45.83%)	7 / 17 (41.18%)
occurrences (all)	25	12	19
Hepatobiliary disorders			
Hepatomegaly			

subjects affected / exposed	0 / 17 (0.00%)	2 / 24 (8.33%)	0 / 17 (0.00%)
occurrences (all)	0	3	0
Hepatotoxicity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hyperbilirubinaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	3
Alopecia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	2 / 17 (11.76%)
occurrences (all)	1	1	3
Dermatitis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Dry skin			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
Erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Hair colour changes			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	1 / 17 (5.88%)
occurrences (all)	0	1	2

Miliaria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Nail disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Petechiae			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	3 / 17 (17.65%)
occurrences (all)	0	1	3
Pigmentation disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	7 / 17 (41.18%)	3 / 24 (12.50%)	6 / 17 (35.29%)
occurrences (all)	9	4	9
Rash macular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	3
Skin disorder			
subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Urticaria			
subjects affected / exposed	3 / 17 (17.65%)	2 / 24 (8.33%)	1 / 17 (5.88%)
occurrences (all)	5	2	1
Musculoskeletal and connective tissue disorders			
Aneurysmal bone cyst			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Arthralgia			

subjects affected / exposed	6 / 17 (35.29%)	4 / 24 (16.67%)	3 / 17 (17.65%)
occurrences (all)	21	6	4
Back pain			
subjects affected / exposed	5 / 17 (29.41%)	1 / 24 (4.17%)	4 / 17 (23.53%)
occurrences (all)	11	1	6
Bone pain			
subjects affected / exposed	1 / 17 (5.88%)	4 / 24 (16.67%)	1 / 17 (5.88%)
occurrences (all)	2	4	1
Epiphyses delayed fusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Growth retardation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Hypermobility syndrome			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	4 / 17 (23.53%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	7	0	1
Muscle tightness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Musculoskeletal disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	2 / 17 (11.76%)	2 / 24 (8.33%)	1 / 17 (5.88%)
occurrences (all)	3	2	1
Myalgia			

subjects affected / exposed	4 / 17 (23.53%)	1 / 24 (4.17%)	1 / 17 (5.88%)
occurrences (all)	5	1	2
Neck pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Osteoporosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	9 / 17 (52.94%)	2 / 24 (8.33%)	5 / 17 (29.41%)
occurrences (all)	25	2	9
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
Conjunctivitis bacterial			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Device related infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 24 (4.17%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Epididymitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2

Gastrointestinal infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Herpes simplex			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Infection			
subjects affected / exposed	2 / 17 (11.76%)	2 / 24 (8.33%)	1 / 17 (5.88%)
occurrences (all)	3	2	1
Lice infestation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Molluscum contagiosum			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	8 / 17 (47.06%)	0 / 24 (0.00%)	2 / 17 (11.76%)
occurrences (all)	21	0	14
Oral fungal infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	1 / 17 (5.88%)	1 / 24 (4.17%)	2 / 17 (11.76%)
occurrences (all)	1	1	2
Otitis externa			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1

Pharyngitis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Rhinitis			
subjects affected / exposed	3 / 17 (17.65%)	1 / 24 (4.17%)	1 / 17 (5.88%)
occurrences (all)	4	2	1
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Tinea cruris			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 17 (17.65%)	0 / 24 (0.00%)	3 / 17 (17.65%)
occurrences (all)	7	0	4
Urinary tract infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Varicella			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Viral rhinitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 17 (5.88%)	0 / 24 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	2
Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	3 / 24 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	5	0
Tumour lysis syndrome			
subjects affected / exposed	0 / 17 (0.00%)	0 / 24 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2006	The purpose of this amendment is to make numerous corrections which arose during review process: 1) Delete references throughout protocol to Pharmacodynamic assays and to central morphology review of BM smears, which will not be performed in this trial. Reason: Analysis will not be performed. 2) Correct primary efficacy endpoint from CHR to MaHR in Strata 2- 4. 3) Specify that Mutation analysis will be done in all Strata (mutations of Abl in Strata 1 - 3 and of Flt3 & Kit in Stratum 4). 4) Add moderate neutropenia (i.e. ANC 500 - 1,000) to the definition of CHRp Reason: bring definition into consistency with previous dasatinib studies. 5) Specify definitions of imatinib-resistance and imatinib-intolerance by stratum. Reason: Definitions were unclear in previous protocols. 6) Removed requirement for baseline lumbar puncture (LP) in Stratum 1 (chronic phase). Reason: Not considered indicated in chronic phase population. 7) Modifications in eligibility criteria a. Clearly state that search for an identical HLA donor must be ongoing for subjects included in Stratum 1. Reason: French regulatory request. b. Permit Grade 1 electrolyte abnormalities and Grade 2 renal insufficiency. Reason: Numerous exceptions have been issued for Grade 1 electrolyte abnormalities of no clinical significance (note: serum Ca will still be required to e ≥LLN). Moderate renal insufficiency (Grade 2) emitted because drug is not excreted significantly via urine. 8) Changed certain anticoagulants from prohibited to "used as indicated" in absence of hrombopenia. Reason: Hemorrhage is typically associated with thrombopenia and numerous exceptions have been issued for concomitant anticoagulants in absence of thrombopenia. 9) Moved strong CYP3A4 inhibitors from restricted to prohibited Reason: Data are available showing 5 - 6 fold increase in dasatinib exposure in presence of strong 3A4 inhibitor, consistent with safety risk.
06 July 2006	10) Changed on-treatment CXR to "at Investigator discretion" Reason: German regulatory request. 11) Allowed multiple-gated acquisition scan (MUGA) or echocardiogram for cardiac assessment to be consistent with prior evaluations per institutional choice. Reason: Many subjects will have had prior cardiac evaluation; the same method should be used for accuracy. 12) Echocardiograms (or MUGA scans) will be performed within the first month, after course 4, and then every 8 courses (6 months) while on study, and in case of heart failure. Additionally added echocardiogram or MUGA at end of treatment visit. Reason: French regulatory request. 13) Added that BM aspirates are NOT required to document progressive disease IF there is an increase in the white blood cell with blasts in the peripheral blood. Reason: flow cytometry can be performed on peripheral blood, so BM is unnecessary.
06 July 2006	14) Increased 'window' for baseline BM and LP to 3 weeks prior to treatment. Reason: It proved to be impractical to require that baseline procedures be within 1 week. 15) Increased 'window' for initiation of treatment after enrollment for Stratum 1 from 3 to 10 days and for Strata 2 - 4 from 3 to 5 days. Reason: It proved to be impractical to require that treatment start within 3 days. 16) Added orange or apple juice as vehicles for dispersion of tablets if necessary, including revised Appendix 3: Reason: Apple and orange juices were shown to be adequate vehicles for dasatinib tablet dispersion. 17) Correct inconsistencies in eligibility criteria, specifically in definition of primary cytogenetic resistance, minimum accepted age, Karnofsky/Lansky score. Reason: Typographical inconsistencies were found between Synopsis and Protocol text. 18) State that effect of dasatinib on spermatogenesis and fertility have not been studied. Reason: German regulatory request. 19) Reduce the washout period of imatinib before treatment start. Reason: Specifically in advanced stages of disease, patients can progress very rapidly, and remain on imatinib until alternative therapies are available, therefore a 2 week washout was impractical.

06 December 2007	Amendment Rationale: The purpose of this amendment is to make changes to the protocol based on slower than excepted accrual rates and recent findings in the ongoing adult Phase II program. 1) Update the Study Medical Monitor and Director. 2) Elimination of the previous stratum 3 (accelerated or myeloid blast phase CML, or Ph+ AML in ≥ 2nd relapse), and incorporate previous strata 2 and 3 into a newly called stratum "2/3". Reason: (a) the accelerated or myeloid blast phase CML or Ph+AML in ≥ 2nd relapse are rare which resulted in too slow an enrollment. Consolidating the strata will allow for faster enrollment within one group (stratum "2/3") and diseases are very similar based on adult CML data; (b) the name stratum "2/3" is chosen for it accurately indicates the 'historical' composition of this stratum. 3) The stratum 4 remains and keeps its original name. Reason: despite that there will only be 3 separate strata, it was felt to be less confusing going forward to keep the name for Stratum 4. 4) Hence, upon implementation of this amendment the 3 strata will be as follows: Stratum 1: unchanged, i.e., Ph+ CML in chronic phase with resistant or progressive disease during, or intolerance to, imatinib; Stratum 2/3: consolidation of old stratum 2 and 3 into a single stratum, i.e., Ph+ leukemia (ALL, AML) in first or subsequent relapse [≥ 25% blasts in bone marrow] after prior imatinib and/or Ph+ CML in accelerated, myeloid or lymphoid blast phase with resistant or progressive disease during, or intolerance to, imatinib; Stratum 4: unchanged Ph-negative acute leukemia, any cytopathologic subtype, in second or subsequent relapse [≥ 25% blasts in bone marrow] or refractory after 2 or more induction regimens and for whom no therapy of greater curative potential is available
06 December 2007	5) Add additional data from an ongoing phase I study in pedatric patients with refractory/relapsed solid tumors or imatinib resistant Ph+ leukemias and an adult Phase II breast cancer trial to provide an update when using dasatinib doses at or above 120 mg/m2 QD. Given our limited pediatric data we will accrue a total of 6 patients at the 120 mg/m2 starting dose level if the first 3 patients at the 120 starting mg/m2 QD dose level do not show excessive toxicity. Based on the safety data obtained in these 6 patients enrolled at 120 mg/m2 QD starting dose level decisions will be made regarding future enrollment of patients at the 150 mg/m2 QD starting dose levels. 6) In accordance with the above, in each of strata 2/3 and 4, a maximum of 6 subjects will be accrued per dose level in the Phase I portion of the study. Intra-patient dose escalation for lack of efficacy in case of proven safety in a subject will be allowed and will be based on the tolerability and the clinical efficacy at any given dose. Regardless of efficacy data, no patients will be treated at a dose higher than 150 mg/m2.
06 December 2007	7) Additional enrollment at the recommended Phase II dose for strata 1, 2/3, and 4, (i.e., 'expansion of the cohorts at the recommended Phase II dose') will be discussed at a later stage when the 'expansion' cohorts will be discussed. The final recommended Phase II dose level and the numbers of patients to enroll in the expansion phase for each cohort will be decided based on the forthcoming safety and observed efficacy data for each stratum. Reason: based on ongoing discussions with worldwide regulatory authorities regarding the use of dasatinib in a pediatric population. 8) Allow extramedullary disease. Reason: stratum 2 currently has allowed patients with isolated asymptomatic CNS disease (with previous enrollment exceptions) and the patients have responded well without toxicity. 9) Clarify the pharmacodynamic secondary objectives. 10) Clarify that confirmation of hematologic response must occur at least 4 weeks after it is first documented and clarify complete hematological response. 11) Since interphase FISH will be used in subjects with unsuccessful cytogenetic analysis, it is recommended that FISH analysis is systematically conducted when a cytogenetic analysis is performed 12) Clarification of the preparation of an oral solution of dasatinib. 13) Clarification of the "Handling and Dispensing of Investigational Product"

24 June 2008	Amendment Rationale: The purpose of this amendment is to open the study to participation of clinical sites outside of the ITCC consortium. This revision will not impact study conduct or data analysis, it applies to all future enrolled patients. Other changes incorporated in this amendment are: 1) Updated Medical Monitor. 2) Updated contact details of coordinating investigator. 3) Updated description of investigational product. 4) Removed inconsistencies in description of duration of treatment. 5) Added additional detail regarding collection of peripheral blood and bone marrow aspirate samples. 6) Inserted a new mandatory paragraph pertaining to serious breaches of GCP. 7) Removed typographical errors and any references to pharmacodynamic tests. 8) Added clarification regarding collection of samples for mutation analysis. 9) Updated protocol language to comply with current model document
18 November 2008	Amendment 4 will clarify that study CA 180018 will not proceed to its phase II component. It will also lead to the timely completion of CA180018 and transitioning to the phase II trial. Other changes incorporated in this amendment are: 1) Clarification of per-stratum use of dose levels both for starting doses and for intra-patient dose escalations. 2) Adjustment of patient numbers that will be accrued per stratum. 3) Change of study phase from Phase I/II to Phase I. 4) Change in duration and content of follow-up period. 5) Added precision to requirements for SAE collection post study drug treatment period. 6) Removal of typos.
08 December 2009	Amendment 05 will add tests to monitor growth & development and bone metabolism both during the treatment period and also for up to 5 years of follow-up after study drug administration. Amendment 05 will also implement a modified visit schedule for study participants who are on treatment for more than 12 months. Other changes incorporated in this amendment are: Update of Central Medical Monitor and emergency telephone number Updated maximum treatment duration Amended visit schedule for study subjects after 12 months of treatment Included language to expand on regulation of access to study drug after the end of the study Updated tables in the section "Flow Chart/Time and Events Schedules" Added paragraph, providing rationale for radiograph and DXAscan. Handling of Serious Adverse Events: updated standard language to describe change in the SAE submission process (hardcopies no longer required); updated SAE telephone contacts. References: added references 56 and 57 Appendix 3: added a new version; clarified that only glass containers can be used for preparation of oral drug solution; added safety recommendations and clean-up instructions; added precision to the language throughout the document. Appendix 4: newly added appendix (The Tanner Stages). Change of emergency telephone number. Change of SAE submission process (mailing of hardcopies is no longer a requirement).
02 December 2011	The purpose of the amendment is to modify the frequency of the follow-up visits from quarterly visits to annual visits, as the conduct of quarterly follow-up visit is no longer required to meet the study objectives. In addition, the conduct of procedures to monitor growth and development will be requested for all study subjects, the current limitation for some procedures to only "subjects with a significant growth deceleration" will be removed to ensure complete alignment with Pediatric Investigational Plan. Change in the assignment of the Central Medical Monitor and an update of the SAE contact details. PK sample collection for study participants that are on treatment and may have dose escalations in the future is no longer a protocol requirement and such samples should neither be collected nor shipped

06 February 2014	The main purpose of this amendment is to extend the maximum treatment duration from 6 years to 10 years to allow participants who are still on treatment and benefitting continued access to the study drug. Dasatinib has not been formally studied in pregnant women. However, the dasatinib team has recently completed a comprehensive review of the BMS Dasatinib safety database (CARES) for all pregnancies in female patients or female partners of male patients in order to reassess the risk of use of dasatinib during pregnancy. Pregnancies in female patients on dasatinib sometimes resulted in spontaneous abortions or infant and fetal anomalies. Based on this analysis and a revision to an internal BMS directive related to "Women of Childbearing Potential (WOCBP) in clinical trials", protocols in the dasatinib program are being amended to: 1) update language related to WOCBP to harmonize with the new BMS directive including requiring 2 highly effective forms of birth control 2) define highly effective forms of birth control 3) adjust language related to sexually active fertile men with WOCBP partners and adapt the length of birth control to be used after the last dose of investigational product (90 days). In the study under discussion only male subjects were on treatment when the amendment was authored. The amendment will hence implement changes to the rules governing pregnancy prevention for sexually active fertile men and their partners, as referenced in items 2 and 3 above.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported