Clinical trial results:
A Phase 1, Open-Label, Randomized, 2-Period, 2-Sequence, Crossover Study to Evaluate the Bioequivalence of Bosutinib Pediatric Capsule and the Commercial Tablet Formulations in Healthy Participants Under Fed Condition

Summary

EudraCT number	2020-002782-34
Trial protocol	NL
Global end of trial date	15 January 2021

Results information

Result version number	v1 (current)
This version publication date	29 January 2022
First version publication date	29 January 2022

Trial information

Trial identification

Sponsor protocol code	B1871061

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000727-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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2021
Global end of trial reached?	Yes
Global end of trial date	15 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this pivotal bioequivalence study was to support the bridging of the approved immediate release film coated tablet to the proposed age-appropriate capsule formulation in healthy subjects.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	66
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 66 subjects were enrolled and treated in this study. There were 2 periods in this study, which were separated by at least 14 days washout. No subjects discontinued in Period 1, 5 subjects discontinued during washout period, and 3 subjects discontinued in Period 2. A total of 58 subjects completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet

Arm description:

Subjects received PF-05208763 capsule 100 mg single dose (SD) on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 2.

Arm type	Experimental
Investigational medicinal product name	PF-05208763
Investigational medicinal product code	
Other name	Bosutinib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

100 mg single dose

Arm title	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule

Arm description:

Subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 2.

Arm type	Experimental
Investigational medicinal product name	PF-05208763
Investigational medicinal product code	
Other name	Bosutinib
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg single dose

Number of subjects in period 1	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule
Started	33	33
Completed	33	33

Period 2	
Period 2 title	Washout Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet

Arm description:

Subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 2.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule

Arm description:

Subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 2.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule
Started	33	33
Completed	30	31
Not completed	3	2
Consent withdrawn by subject	-	1
Adverse event, non-fatal	2	-
Unspecified	1	1

Period 3

Period 3 title	Period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet

Arm description:

Subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 2.

Arm type	Experimental
Investigational medicinal product name	PF-05208763
Investigational medicinal product code	
Other name	Bosutinib
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg single dose

Arm title	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule

Arm description:

Subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 2.

Arm type	Experimental
Investigational medicinal product name	PF-05208763
Investigational medicinal product code	
Other name	Bosutinib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

100 mg single dose

Number of subjects in period 3	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule
Started	30	31
Completed	30	28
Not completed	0	3
Adverse event, non-fatal	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Period 1
Reporting group description:	
A total of 33 subjects who were assigned to Treatment Sequence 1 received PF-05208763 capsule 100 mg SD on Day 1 in Period 1. A total of 33 subjects who were assigned to Treatment Sequence 2 received PF-05208763 tablet 100 mg SD on Day 1 in Period 1.	

Reporting group values	Period 1	Total	
Number of subjects	66	66	
Age Categorical Units: Subjects			
Adults (18-64 years)	66	66	
Age Continuous Units: years			
median	27.0		
full range (min-max)	18 to 54	-	
Gender Categorical Units: Subjects			
Female	5	5	
Male	61	61	
Race Units: Subjects			
White	54	54	
Black or African American	3	3	
Asian	5	5	
American Indian or Alaska Native	1	1	
Multiracial	3	3	
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	65	65	

End points

End points reporting groups

Reporting group title	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet
Reporting group description:	
Subjects received PF-05208763 capsule 100 mg single dose (SD) on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 2.	
Reporting group title	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule
Reporting group description:	
Subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 2.	
Reporting group title	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet
Reporting group description:	
Subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 2.	
Reporting group title	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule
Reporting group description:	
Subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 2.	
Reporting group title	Treatment Sequence 1: PF-05208763 Capsule First Then Tablet
Reporting group description:	
Subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 2.	
Reporting group title	Treatment Sequence 2: PF-05208763 Tablet First Then Capsule
Reporting group description:	
Subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 1, following by a washout period of at least 14 days. Then subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 2.	
Subject analysis set title	Treatment A: PF-05208763 100 mg SD Capsule
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects received PF-05208763 capsule 100 mg SD on Day 1 in Period 1 or 2.	
Subject analysis set title	Treatment B: PF-05208763 100 mg SD Tablet
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects received PF-05208763 tablet 100 mg SD on Day 1 in Period 1 or 2.	

Primary: Area Under the Plasma Concentration-Time Profile From Time 0 Extrapolated to Infinite Time (AUCinf) of Bosutinib

End point title	Area Under the Plasma Concentration-Time Profile From Time 0 Extrapolated to Infinite Time (AUCinf) of Bosutinib[1]
End point description:	
AUCinf of bosutinib 100 mg SD when administered as a capsule and tablet formulation under fed condition. The analysis population for this endpoint included all subjects randomized and treated who had at least 1 of the pharmacokinetics (PK) parameters of primary interest in at least 1 treatment period.	
End point type	Primary
End point timeframe:	
Pre-dose, 1, 2, 3, 4, 6, 8, 12, 24, 36, 48, 60, 72, 96, and 144 hours post dose on Day 1 in each treatment period	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	56		
Units: nanogram*hour per milliliter (ng*hr/mL)				
geometric mean (geometric coefficient of variation)	432.7 (± 32)	457.1 (± 33)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax) of Bosutinib

End point title	Maximum Plasma Concentration (Cmax) of Bosutinib[2]

End point description:

Cmax of bosutinib 100 mg SD when administered as a capsule and tablet formulation under fed condition. The analysis population for this endpoint included all subjects randomized and treated who had at least 1 of the PK parameters of primary interest in at least 1 treatment period.

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 3, 4, 6, 8, 12, 24, 36, 48, 60, 72, 96, and 144 hours post dose on Day 1 in each treatment period

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	16.47 (± 39)	17.08 (± 34)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Profile From Time 0 to the Time of the Last Quantifiable Concentration (AUClast) of Bosutinib

End point title	Area Under the Plasma Concentration Time Profile From Time 0 to the Time of the Last Quantifiable Concentration (AUClast) of Bosutinib

End point description:

AUClast of bosutinib 100 mg SD administered as capsule and tablet formulation under fed condition. The analysis population for this endpoint included all subjects randomized and treated who had at least 1 of

the PK parameters of primary interest in at least 1 treatment period.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4, 6, 8, 12, 24, 36, 48, 60, 72, 96, and 144 hours post dose on Day 1 in each treatment period

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)	371.5 (± 41)	389.7 (± 38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time for Cmax (Tmax) of Bosutinib

End point title	Time for Cmax (Tmax) of Bosutinib

End point description:

Tmax of bosutinib 100 mg SD administered as capsule and table formulation under fed condition. The analysis population for this endpoint included all subjects randomized and treated who had at least 1 of the PK parameters of primary interest in at least 1 treatment period.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4, 6, 8, 12, 24, 36, 48, 60, 72, 96, and 144 hours post dose on Day 1 in each treatment period

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	63	62		
Units: Hours (hrs)				
median (full range (min-max))	6.00 (1.00 to 12.0)	6.00 (1.00 to 8.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance After Oral Dose (CL/F) of Bosutinib

End point title	Apparent Clearance After Oral Dose (CL/F) of Bosutinib

End point description:

CL/F of bosutinib 100 mg SD administered as capsule and table formulation under fed condition. CL/F was calculated as Dose/AUCinf after oral dose. AUCinf was defined as area under the plasma concentration-time profile from time 0 extrapolated to infinite time. The analysis population for this endpoint included all subjects randomized and treated who had at least 1 of the PK parameters of primary interest in at least 1 treatment period.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4, 6, 8, 12, 24, 36, 48, 60, 72, 96, and 144 hours post dose on Day 1 in each treatment period

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	56		
Units: litre per hour (L/hr)				
geometric mean (geometric coefficient of variation)	231.1 (± 32)	218.8 (± 33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution After Oral Dose (Vz/F) of Bosutinib

End point title	Apparent Volume of Distribution After Oral Dose (Vz/F) of Bosutinib

End point description:

Vz/F of bosutinib 100 mg SD administered as capsule and table formulation under fed condition. Vz/F was calculated as Dose/(AUCinf*kel) after oral dose. AUCinf was defined as area under the plasma concentration-time profile from time 0 extrapolated to infinite time. kel was defined as the terminal phase rate constant calculated by a linear regression through at least 3 data points in the terminal phase of the log-linear concentration-time curve. The analysis population for this endpoint included all subjects randomized and treated who had at least 1 of the PK parameters of primary interest in at least 1 treatment period.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4, 6, 8, 12, 24, 36, 48, 60, 72, 96, and 144 hours post dose on Day 1 in each treatment period

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	56		
Units: Litre (L)				
geometric mean (geometric coefficient of variation)	10160 (± 25)	10320 (± 27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-Life (t1/2) of Bosutinib

End point title	Terminal Elimination Half-Life (t1/2) of Bosutinib

End point description:

t1/2 of bosutinib 100 mg SD administered as capsule and table formulation under fed condition. t1/2 was calculated as Log e(2)/kel. kel was defined as the terminal phase rate constant calculated by a linear regression through at least 3 data points in the terminal phase of the log-linear concentration-time curve. The analysis population for this endpoint included all subjects randomized and treated who had at least 1 of the PK parameters of primary interest in at least 1 treatment period.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 4, 6, 8, 12, 24, 36, 48, 60, 72, 96, and 144 hours post dose on Day 1 in each treatment period

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	56		
Units: hrs				
arithmetic mean (standard deviation)	31.43 (± 8.2561)	33.81 (± 9.1516)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Abnormalities

End point title	Number of Subjects With Laboratory Abnormalities

End point description:

Evaluated laboratory parameters included hematology (lymphocytes < 0.8*lower limit of normal [LLN] or >1.2*upper limit of normal [ULN], neutrophils <0.8*LLN, and eosinophils >1.2*ULN), clinical chemistry (bilirubin >1.5*ULN and urate >1.2*ULN), and urinalysis (ketones >=1, urine hemoglobin >=1, and leukocyte esterase >=1). The analysis population for this endpoint included all subjects randomly assigned to study intervention and who have taken at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Post first dose up to Day 7 in Period 2 or early termination (maximum of 22 days)

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	63		
Units: Subjects				
Lymphocytes <0.8*LLN	1	0		
Lymphocytes >1.2*ULN	2	0		
Neutrophils <0.8*LLN	2	2		
Eosinophils >1.2*ULN	0	2		
Bilirubin >1.5*ULN	1	1		
Urate >1.2*ULN	1	1		
Ketones >=1	9	2		
Urine Hemoglobin >=1	2	4		
Leukocyte Esterase >=1	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point description:

AE = any untoward medical occurrence in subject who received study treatment without regard to possibility of causal relationship. Treatment-emergent events = between first dose of study treatment and up to 28 days after last dose that were absent before treatment or that worsened relative to pretreatment state. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. SAEs were adjudicated according to the investigator's assessment. Treatment-related AEs and SAEs were determined by the investigator. The analysis population for this endpoint included all subjects randomly assigned to study intervention and who have taken at least 1 dose of study intervention.

End point type	Secondary

End point timeframe:

Post first dose up to 28 days after end of treatment (maximum of 43 days)

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	63		
Units: Subjects				
Subjects with all-causality TEAEs	30	26		
Subjects with treatment-related TEAEs	6	9		
Subjects with all-causality SAEs	0	0		
Subjects with treatment-related SAEs	0	0		
Subjects with severe all-causality TEAEs	0	0		
Subjects with severe treatment-related TEAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Electrocardiograms (ECGs) Meeting Categorical Criteria

End point title	Number of Subjects With Electrocardiograms (ECGs) Meeting Categorical Criteria

End point description:

Categorical criteria included PR interval >=300 msec, percent change (Pctchg) of PR interval >=25% for baseline value of >200 msec and >=50% for baseline value of <=200 msec; QRS interval >=140 msec, Pctchg of QRS interval >=50%; maximum of QT interval of >= 500 msec; maximum QTcB interval (Bazett's Correction) of 450 msec to <480 msec, 480 msec to <500 msec, >=500 msec, and a maximum change of <=30change<60 or >=60 msec from baseline; maximum QTcF interval (Friderecia's Correction) of 450 msec to <480 msec, 480 msec to <500 msec, >=500 msec, and a maximum change of <=30change<60 or >=60 msec from baseline. The analysis population for this endpoint included all subjects randomly assigned to study intervention and who had taken at least 1 dose of study intervention and had at least 1 ECG assessment undertaken post dose.

End point type	Secondary

End point timeframe:

Post first dose up to Day 7 in Period 2 or early termination (maximum of 22 days)

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	31	31		
Units: Subjects				
PR interval >=300 msec	0	0		
PR interval Pctchg >=25%/50%	0	0		
QRS interval >=140 msec	0	0		
QRS interval Pctchg >=50%	0	0		
QT interval >=500 msec	0	0		
450 msec <= QTcB interval <480 msec	1	0		
480 msec<= QTcB interval <500 msec	0	0		

QTcB interval >= 500 msec	0	0		
30 msec <= QTcB interval change <60 msec	2	2		
QTcB interval change >=60 msec	1	0		
450 msec <= QTcF interval <480 msec	0	0		
480 msec<= QTcF interval <500 msec	0	0		
QTcF interval >= 500 msec	0	0		
30 msec <= QTcF interval change <60 msec	0	0		
QTcF interval change >=60 msec	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Vital Signs Meeting Categorical Criteria

End point title	Number of Subjects With Vital Signs Meeting Categorical Criteria

End point description:

Categorical criteria were defined as diastolic blood pressure (mm Hg): value <50 mm Hg, increase >=20 mm Hg, or decrease >=20 mm Hg; pulse rate(bpm): value <40 bpm and value>120 bpm; systolic blood pressure (mm Hg): value <90 mm Hg, increase >=30 mm Hg, or decrease >=30 mm Hg. The analysis population for this endpoint included all subjects randomly assigned to study intervention and who had taken at least 1 dose of study intervention and had at least 1 assessment undertaken post treatment.

End point type	Secondary

End point timeframe:

Post first dose up to Day 7 in Period 2 or early termination (maximum of 22 days)

End point values	Treatment A: PF-05208763 100 mg SD Capsule	Treatment B: PF-05208763 100 mg SD Tablet		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	31		
Units: Subjects				
Diastolic blood pressure <50 mm Hg	0	0		
Diastolic blood pressure increase >= 20 mm Hg	0	0		
Diastolic blood pressure decrease >=20 mm Hg	0	0		
Pulse rate <40 bpm	0	0		
Pulse rate >120 bpm	0	0		
Systolic blood pressure <90 mm Hg	0	0		
Systolic blood pressure increase >=30 mm Hg	0	1		
Systolic blood pressure decrease >=30 mm Hg	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Post first dose up to 28 days after last dose of study intervention (maximum of 43 days)

Adverse event reporting additional description:

Each AE was to be assessed to determine if it met the criteria for SAEs. If an SAE occurred, expedited reporting followed local and international regulations, as appropriate.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Treatment B: PF-05208763 100 mg SD Tablet

Reporting group description:

Subject received PF-05208763 tablet 100 mg SD on Day 1 in Period 1 or 2.

Reporting group title	Treatment A: PF-05208763 100 mg SD Capsule

Reporting group description:

Subject received PF-05208763 capsule 100 mg SD on Day 1 in Period 1 or 2.

Serious adverse events	Treatment B: PF-05208763 100 mg SD Tablet	Treatment A: PF-05208763 100 mg SD Capsule	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 63 (0.00%)	0 / 64 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Treatment B: PF-05208763 100 mg SD Tablet	Treatment A: PF-05208763 100 mg SD Capsule	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 63 (23.81%)	13 / 64 (20.31%)	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 63 (14.29%)	7 / 64 (10.94%)	
occurrences (all)	10	7	
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	5 / 63 (7.94%) 5	4 / 64 (6.25%) 4	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	5 / 63 (7.94%) 5	3 / 64 (4.69%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 August 2020	An additional PK sampling time at 144 hours postdose was added to cover at least 3 terminal half-lives of bosutinib in healthy subjects. This sample will be collected as an outpatient visit on Day 7. In addition, the PK sampling time at 16 hours post dose was removed as there are adequate number of PK samples collected to fully characterize the PK of bosutinib. Accordingly, the following sections were updated in the protocol: Section 1.1, Section 1.3, Section 4.1, and Section 8.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported