Clinical trial results:
A Two-Part Phase 1/2 Study to Determine Safety, Tolerability, Pharmacokinetics, and Activity of K0706, a Novel Tyrosine Kinase Inhibitor (TKI), in Healthy Subjects and in Subjects with Chronic Myeloid Leukemia (CML) or Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia (Ph+ ALL)

Summary

EudraCT number	2016-001754-18
Trial protocol	CZ GB BE PL ES HU RO
Global end of trial date	03 January 2025

Results information

Result version number	v1 (current)
This version publication date	18 December 2025
First version publication date	18 December 2025

Trial information

Trial identification

Sponsor protocol code	CLR_15_03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02629692
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 127347

Notes:

Sponsors

Sponsor organisation name	Sun Pharma Advanced Research Company (SPARC) Limited
Sponsor organisation address	17/B Mahal Industrial Estate, Mahakali Caves Road Andheri (E), Mumbai , India, 400093
Public contact	Sponsor representative - Dr. Sandeep Inamdar, Sun Pharma Advanced Research Company (SPARC) Limited, 022 66455876, clinical.trials@sparcmail.com
Scientific contact	Sponsor representative - Dr. Sandeep Inamdar, Sun Pharma Advanced Research Company (SPARC) Limited, 022 66455876, clinical.trials@sparcmail.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 January 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 January 2025
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Part A of the study is to:
• Examine the safety and tolerability of single oral doses of K0706 in healthy male subjects

The primary objectives of Part B of the study are to:
• Determine the MTD (or RP2D) of K0706 administered orally in subjects with the selected BCR::ABL1-associated hematologic malignancies who have resistance or intolerance to the local Standard of Care CML therapy
• Evaluate the safety of K0706 in subjects with BCR::ABL1-associated hematologic malignancies listed in the entry criteria

The primary objectives of Part C of the study are to:
• Evaluate the anti-leukemic efficacy of K0706 in subjects with CML-CP by cytogenetic outcomes and in subjects with CML-AP & BP by hematologic outcomes who have failed ≥ 3 TKIs, one of which includes ponatinib

Protection of trial subjects:

The trial and site activities were monitored according to the ICH-GCP guidelines considering every aspect of the trial, ensuring that the rights, safety and well-being of patients are protected and consistent with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2016
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	Romania: 5
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	India: 20
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 15

Country: Number of subjects enrolled	United States: 54
Worldwide total number of subjects	124
EEA total number of subjects	29

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)	98
From 65 to 84 years	26
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Part A: The screening must be completed within 28 days prior to the first dose of the study drug.
Part B: The screening must be performed within 21 days prior to the first dose of the study drug (i.e. Cycle 1 Day 1).
Part C: The screening must be performed within 24 days prior to first dose of the study drug (i.e.: Cycle 1 Day 1).

Period 1

Period 1 title	K0706 (Vodobatinib) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	K0706 Part B+C

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Vodobatinib
Investigational medicinal product code	K0706
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Part B: K0706 capsules will be self-administered. The initial administered dose will be the dose from Part A where acceptable safety was observed.

Part C: K0706 capsules will be self-administered once daily at dose of 174 mg.

Arm title	K0706 Part A

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Vodobatinib
Investigational medicinal product code	K0706
Other name	Vodobatinib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Part A: K0706 capsules were administered orally (in an upright position) after an overnight fast of at least 8 hours. For the food effect study, the 6 mg and 24 mg doses were evaluated.

Number of subjects in period 1	K0706 Part B+C	K0706 Part A
Started	84	40
Completed	44	39
Not completed	40	1
Increased worsening of memory impairment grade 2	1	-
Adverse event, non-fatal	13	-
Death	1	-
Patient chose to come off trial	1	-
Subject change treatment plan	1	-
Progression of disease	18	-
Lost to follow-up	1	1
Missing	1	-
Transitioning to alternate therapy	1	-
Consent withdrawal and lack of compliance	1	-
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	K0706 Part B+C
Reporting group description: -	
Reporting group title	K0706 Part A
Reporting group description: -	

Reporting group values	K0706 Part B+C	K0706 Part A	Total
Number of subjects	84	40	124
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	58	40	98
From 65-84 years	26	0	26
85 years and over	0	0	0
Gender categorical Units: Subjects			
Male	46	40	86
Female	38	0	38

End points

End points reporting groups

Reporting group title	K0706 Part B+C
Reporting group description: -	
Reporting group title	K0706 Part A
Reporting group description: -	

Primary: To Determine the Maximum Tolerated Dose (MTD) as Determined by Frequency of Dose Limiting Toxicities

End point title	To Determine the Maximum Tolerated Dose (MTD) as Determined by Frequency of Dose Limiting Toxicities[1]
End point description:	
Part B	
End point type	Primary
End point timeframe:	
Dose Limiting toxicities observed over a 4 week 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: Analysis Population Description: Safety Analysis Set

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	0[2]		
Units: Count of participants	4			

Notes:

[2] - This parameter is only applicable to Part B

Statistical analyses

No statistical analyses for this end point

Primary: Incidence and severity of treatment emergent AEs (PART B)

End point title	Incidence and severity of treatment emergent AEs (PART B)[3]
End point description:	
Part B	
End point type	Primary
End point timeframe:	
All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)	

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Analysis Population Description: Safety Analysis Set

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	0[4]		
Units: Number of participants	57			

Notes:

[4] - This parameter is only applicable to Part B

Statistical analyses

No statistical analyses for this end point

Primary: For CML subjects in CP at study entry

End point title	For CML subjects in CP at study entry[5]

End point description:

PART C: Proportion of subjects achieving Major Cytogenetic Response [defined as complete cytogenetic response (CCyR; 0% Ph+metaphases) or partial cytogenetic response (PCyR; 1-35% Ph+ metaphases)] as assessed by conventional Karyotyping of Bone marrow aspirate

End point type	Primary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

Notes:

[5] - 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: Analysis Population Description: Efficacy Analysis Set

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	0[6]		
Units: Count of participants	13			

Notes:

[6] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Primary: For CML subjects in AP at study entry

End point title	For CML subjects in AP at study entry[7]

End point description:

PART C: Proportion of subjects achieving Major Hematologic Response [defined as complete hematologic response (CHR) or no evidence of leukemia (NEL)] as assessed by complete blood count of peripheral blood sample

End point type	Primary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

Notes:

[7] - 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: Analysis Population Description: Efficacy Analysis Set

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	0[8]		
Units: Number of participants	1			

Notes:

[8] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Primary: For CML subjects in BP at study entry

End point title	For CML subjects in BP at study entry[9]

End point description:

PART C: Proportion of subjects achieving Major Hematologic Response [defined as complete hematologic response (CHR) or no evidence of leukemia (NEL)] as assessed by complete blood count of peripheral blood sample

End point type	Primary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

Notes:

[9] - 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: Analysis Population Description: Efficacy Analysis Set

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: Count of participants				

Notes:

[10] - No subjects in this group

[11] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Primary: Examination of the Safety and Tolerability of Single Oral Doses of K0706

End point title	Examination of the Safety and Tolerability of Single Oral Doses of K0706[12]

End point description:

Part A

End point type	Primary

End point timeframe:

Approximately 56 ± 2 days

Notes:

[12] - 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: Analysis Population Description: Safety Analysis Set

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	40		
Units: Number of participants		40		

Notes:

[13] - This end point is only applicable to Part A

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Profile of K0706 - Cmax [The Maximum (Peak) Observed Drug Concentration After Dose Administration]

End point title	Pharmacokinetic Profile of K0706 - Cmax [The Maximum (Peak) Observed Drug Concentration After Dose Administration]

End point description:

Part B and Part C

End point type	Secondary

End point timeframe:

All subjects will be followed for up to approximately 60 months after the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	0[14]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	3217.7 (± 83.5)	()		

Notes:

[14] - This parameter is only applicable to Parts B and C

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Profile of Vodobatinib (K0706) - Tmax [The Time to Reach Maximum (Peak) Drug Concentration After Dose Administration]

End point title	Pharmacokinetic Profile of Vodobatinib (K0706) - Tmax [The Time to Reach Maximum (Peak) Drug Concentration After Dose Administration]

End point description:

Part B and Part C

End point type	Secondary

End point timeframe:

All subjects will be followed for up to approximately 60 months after the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	0[15]		
Units: hours				
median (full range (min-max))	2 (0 to 8)	(to)		

Notes:

[15] - This parameter is only applicable to Parts B and C

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic Profile of Vodobatinib (K0706) - Cmin [Minimum Observed Drug Concentration After Dose Administration]

End point title	Pharmacokinetic Profile of Vodobatinib (K0706) - Cmin [Minimum Observed Drug Concentration After Dose Administration]

End point description:

Part B and Part C

End point type	Secondary

End point timeframe:

All subjects will be followed for up to approximately 60 months after the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	0[16]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	720.1 (± 133.6)	()		

Notes:

[16] - This parameter is only applicable to Parts B and C

Statistical analyses

No statistical analyses for this end point

Secondary: In Subjects With CML- CP:Proportion of Subjects Achieving Complete Hematological Response as Assessed by Complete Blood Count of Peripheral Blood Sample

End point title	In Subjects With CML- CP:Proportion of Subjects Achieving Complete Hematological Response as Assessed by Complete Blood Count of Peripheral Blood Sample

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	0[17]		
Units: NA	4			

Notes:

[17] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: In Subjects With CML- CP:Proportion of Subjects Achieving Complete Cytogenetic Response as Assessed by Conventional Karyotyping of Bone Marrow Aspirate

End point title	In Subjects With CML- CP:Proportion of Subjects Achieving Complete Cytogenetic Response as Assessed by Conventional Karyotyping of Bone Marrow Aspirate

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	0[18]		
Units: NA	10			

Notes:

[18] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: In Subjects With CML- CP:Proportion of Subjects Achieving Major Molecular Response as Assessed by BCR-ABL Transcript Levels (BCR-ABL1 Ratio of ≤ 0.1%) in Peripheral Blood Using PCR (Polymerase Chain Reaction)

End point title	In Subjects With CML- CP:Proportion of Subjects Achieving Major Molecular Response as Assessed by BCR-ABL Transcript Levels (BCR-ABL1 Ratio of ≤ 0.1%) in Peripheral Blood Using PCR (Polymerase Chain Reaction)

End point description: Part C	
End point type	Secondary
End point timeframe: All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)	

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	0[19]		
Units: NA	7			

Notes:

[19] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: In Subjects With CML-AP & BP: Proportion of Subjects Achieving Complete Cytogenetic Response as Assessed by Conventional Karyotyping of Bone Marrow Aspirate

End point title	In Subjects With CML-AP & BP: Proportion of Subjects Achieving Complete Cytogenetic Response as Assessed by Conventional Karyotyping of Bone Marrow Aspirate
End point description: Part C	
End point type	Secondary
End point timeframe: All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)	

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	0[20]		
Units: NA	2			

Notes:

[20] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: In Subjects With CML-AP & BP: Proportion of Subjects Achieving Partial Cytogenetic Response (PCyR) as Assessed by Conventional Karyotyping of Bone Marrow Aspirate

End point title	In Subjects With CML-AP & BP: Proportion of Subjects Achieving Partial Cytogenetic Response (PCyR) as Assessed by

	Conventional Karyotyping of Bone Marrow Aspirate

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of K0706

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	0[21]		
Units: NA	0			

Notes:

[21] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: In Subjects With CML-AP & BP: Proportion of Subjects Achieving Major Molecular Response as Assessed by BCR-ABL Transcript Levels (BCR-ABL1 Ratio of ≤ 0.1%) in Peripheral Blood Using PCR (Polymerase Chain Reaction)

End point title	In Subjects With CML-AP & BP: Proportion of Subjects Achieving Major Molecular Response as Assessed by BCR-ABL Transcript Levels (BCR-ABL1 Ratio of ≤ 0.1%) in Peripheral Blood Using PCR (Polymerase Chain Reaction)

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	0[22]		
Units: NA	1			

Notes:

[22] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Major Cytogenetic Response (MCyR): Time to MCyR is the Time From First Dose to First MCyR (0-35% Ph+ Metaphases) ; Computed Only for Subjects Who Achieved MCyR

End point title	Time to Major Cytogenetic Response (MCyR): Time to MCyR is the Time From First Dose to First MCyR (0-35% Ph+ Metaphases) ; Computed Only for Subjects Who Achieved MCyR

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	0[23]		
Units: months				
arithmetic mean (standard deviation)	3.9 (± 2.53)	()		

Notes:

[23] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Major Molecular Response : Time to MMR is the Time From First Dose to First MMR (BCR-ABL1 Ratio of ≤ 0.1%) Computed Only for Subjects Who Achieved MMR

End point title	Time to Major Molecular Response : Time to MMR is the Time From First Dose to First MMR (BCR-ABL1 Ratio of ≤ 0.1%) Computed Only for Subjects Who Achieved MMR

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	0[24]		
Units: months				
arithmetic mean (standard deviation)	5.0 (± 4.71)	()		

Notes:

[24] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: In All Subjects Progression Free Survival (PFS)

End point title	In All Subjects Progression Free Survival (PFS)

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[25]	0[26]		
Units: Months				
number (confidence interval 95%)	81.2 (57.2 to 92.5)	(to)		

Notes:

[25] - Timepoint: At 12 months

[26] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: In All Subjects Overall Survival (OS)

End point title	In All Subjects Overall Survival (OS)

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[27]	0[28]		
Units: Months				
number (confidence interval 95%)	95.7 (72.9 to 99.4)	(to)		

Notes:

[27] - Timepoint: At 12 months

[28] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and Severity of Treatment Emergent AEs (PART C)

End point title	Incidence and Severity of Treatment Emergent AEs (PART C)

End point description:

Part C

End point type	Secondary

End point timeframe:

All subjects will be followed up for 60 months from the first dose of Vodobatinib (K0706)

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	0[29]		
Units: NA	21			

Notes:

[29] - This parameter is only applicable to Part C

Statistical analyses

No statistical analyses for this end point

Secondary: To Characterize the Pharmacokinetics (Cmax) of K0706 After Single Oral Doses in Healthy Male Subjects

End point title	To Characterize the Pharmacokinetics (Cmax) of K0706 After Single Oral Doses in Healthy Male Subjects

End point description:

Part A

End point type	Secondary

End point timeframe:

Approximately 28 ± 2 days

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	6[31]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	866.5 (± 35.9)		

Notes:

[30] - This end point is only applicable to Part A

[31] - PK Analysis Set (SAD study; 24 mg cohort)

Statistical analyses

No statistical analyses for this end point

Secondary: To Characterize the Pharmacokinetics (Cmax) of K0706 After Single Oral Doses in Fasted and Fed State in Healthy Male Subjects

End point title	To Characterize the Pharmacokinetics (Cmax) of K0706 After Single Oral Doses in Fasted and Fed State in Healthy Male

	Subjects
End point description:	
Part A	
End point type	Secondary
End point timeframe:	
Approximately 28 ± 2 days	

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[32]	8[33]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	642 (± 54.6)		

Notes:

[32] - This endpoint is only applicable to Part A

[33] - PK Analysis Set (24 mg cohort); Cmax (fasted state)

Statistical analyses

No statistical analyses for this end point

Secondary: To Characterize the Pharmacokinetics (AUC(0-inf)) of K0706 After Single Oral Doses in Healthy Male Subjects

End point title	To Characterize the Pharmacokinetics (AUC(0-inf)) of K0706 After Single Oral Doses in Healthy Male Subjects
End point description:	
Part A	
End point type	Secondary
End point timeframe:	
Approximately 28 ± 2 days	

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[34]	6[35]		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)	()	6322 (± 32.6)		

Notes:

[34] - This parameter is only applicable to Part A

[35] - PK Analysis Set (SAD study; 24 mg cohort)

Statistical analyses

No statistical analyses for this end point

Secondary: To Characterize the Pharmacokinetics (Cmax) of K0706 After Single Oral

Doses in Fasted and Fed State in Healthy Male Subjects	
End point title	To Characterize the Pharmacokinetics (Cmax) of K0706 After Single Oral Doses in Fasted and Fed State in Healthy Male Subjects
End point description: Part A	
End point type	Secondary
End point timeframe: Approximately 28 ± 2 days	

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[36]	8[37]		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	()	323.7 (± 26.3)		

Notes:

[36] - This end point is only applicable to Part A

[37] - PK Analysis Set (24 mg cohort); Cmax (fed state)

Statistical analyses

No statistical analyses for this end point

Secondary: To Characterize the Pharmacokinetics of K0706 (AUC(0-inf)) After Single Oral Doses in Fasted and Fed State in Healthy Male Subjects	
End point title	To Characterize the Pharmacokinetics of K0706 (AUC(0-inf)) After Single Oral Doses in Fasted and Fed State in Healthy Male Subjects
End point description: Part A	
End point type	Secondary
End point timeframe: Approximately 28 ± 2 days	

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[38]	8[39]		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)	()	5739 (± 26.2)		

Notes:

[38] - This end point is only applicable to Part A

[39] - PK Analysis Set (24 mg cohort); AUC(0-inf) (fasted state)

Statistical analyses

No statistical analyses for this end point

Secondary: To Characterize the Pharmacokinetics of K0706 (AUC(0-inf)) After Single Oral Doses in Fasted and Fed State in Healthy Male Subjects

End point title	To Characterize the Pharmacokinetics of K0706 (AUC(0-inf)) After Single Oral Doses in Fasted and Fed State in Healthy Male Subjects

End point description:

Part A

End point type	Secondary

End point timeframe:

Approximately 28 ± 2 days

End point values	K0706 Part B+C	K0706 Part A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[40]	8[41]		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)	()	4521 (± 28.8)		

Notes:

[40] - This end point is only applicable to Part A

[41] - PK Analysis Set (24 mg cohort); AUC(0-inf) (fed state)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE reporting period for safety surveillance begins after subject is randomized into the study and receives at least 1 dose of drug for treatment emergent adverse events (TEAEs) and continues until 30 days from end of treatment visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	K0706

Reporting group description:

Parts B+C

Serious adverse events	K0706		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 124 (21.77%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	7		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung neoplasm malignant			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Hypertension			

subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Deep vein thrombosis				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Disease progression				
subjects affected / exposed	2 / 124 (1.61%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pyrexia				
subjects affected / exposed	2 / 124 (1.61%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Immune system disorders				
Swollen tongue				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				

subjects affected / exposed	2 / 124 (1.61%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary toxicity				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fall				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skull fracture				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Pericardial effusion				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acute myocardial infarction				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Amnesia				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Cerebral haemorrhage				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dementia				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Hypoxic-ischaemic encephalopathy				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Transient ischaemic attack				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	2 / 124 (1.61%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	1 / 124 (0.81%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leukocytosis				

subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Varices oesophageal			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 124 (2.42%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 124 (1.61%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

COVID-19			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia fungal			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia viral			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suspected COVID-19			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 124 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	K0706		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 124 (75.00%)		
Investigations			
Lipase increased			
subjects affected / exposed	12 / 124 (9.68%)		
occurrences (all)	12		
Amylase increased			

subjects affected / exposed occurrences (all)	7 / 124 (5.65%) 7		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	 11 / 124 (8.87%) 11		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 15 / 124 (12.10%) 15 8 / 124 (6.45%) 8		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all)	 28 / 124 (22.58%) 28 16 / 124 (12.90%) 16 12 / 124 (9.68%) 12 7 / 124 (5.65%) 7		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 16 / 124 (12.90%) 16 9 / 124 (7.26%) 9		
Gastrointestinal disorders Diarrhoea			

subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all)	19 / 124 (15.32%) 19 15 / 124 (12.10%) 15 13 / 124 (10.48%) 13 10 / 124 (8.06%) 10 10 / 124 (8.06%) 10 8 / 124 (6.45%) 8		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	 16 / 124 (12.90%) 16 12 / 124 (9.68%) 12		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 13 / 124 (10.48%) 13 10 / 124 (8.06%) 10 8 / 124 (6.45%) 8		
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	10 / 124 (8.06%) 10		
Back pain subjects affected / exposed occurrences (all)	10 / 124 (8.06%) 10		
Myalgia subjects affected / exposed occurrences (all)	10 / 124 (8.06%) 10		
Pain in extremity subjects affected / exposed occurrences (all)	9 / 124 (7.26%) 9		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	12 / 124 (9.68%) 12		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	11 / 124 (8.87%) 11		
COVID-19 subjects affected / exposed occurrences (all)	10 / 124 (8.06%) 10		
Rhinitis subjects affected / exposed occurrences (all)	7 / 124 (5.65%) 7		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	8 / 124 (6.45%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 September 2019	The total number of sites participating in Part C was changed from 80 to 90. The study population was specified and Ph+ ALL was excluded from the pivotal study after consideration of FDA comments and the lack of sufficient data in Ph+ALL of Part B. Additional secondary objectives were added in alignment with the endpoints. The objectives were modified in alignment with endpoints. The duration of study treatment was extended to 60 months as per FDA's recommendations. Primary endpoints changed as per FDA recommendation to not consider maintenance of response as an efficacy endpoint. Inclusion and Exclusion criteria updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported