Clinical trial results:
Continuing Access to the Tyrosine Kinase Inhibitor of VEGFR-2, AG-013736 (A406) for Patients Previously Receiving AG-013736 in Clinical Trials

Summary

EudraCT number	2005-000051-15
Trial protocol	DE CZ IT HU
Global end of trial date	14 August 2023

Results information

Result version number	v1 (current)
This version publication date	01 August 2024
First version publication date	01 August 2024

Trial information

Trial identification

Sponsor protocol code	A4061008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00828919
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 East Hudson boulevard, New York, United States, NY 1001
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	25 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the trial was to provide continued access to axitinib tablets and to the study drugs given in combination (if applicable) to participants who had completed their participation in a prior axitinib monotherapy or combination study and who had documented stable disease, responding disease or clinical benefit at the time they discontinued from the previous trial.

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 Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 2003
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	Czechia: 2
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	United States: 30
Worldwide total number of subjects	49
EEA total number of subjects	9

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)	35
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 52 participants were enrolled in this study, out of which 49 participants were treated. 3 enrolled participants had unreported dosing information.

Pre-assignment

Screening details:

This study was conducted in participants with solid tumors who had completed their participation in prior axitinib monotherapy or combination therapy clinical trial and who had documented stable disease, responding disease or clinical benefit at the time of prior clinical trial closure. No participant enrolled in axitinib combination therapy group.

Period 1

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

Arms

Arm title	Axitinib Monotherapy

Arm description:

Participants under current study (A4061008) received oral dose of Axitinib alone twice daily as they were taking in the previous clinical trial. Maximum treatment duration was of 119.56 months.

Arm type	Experimental
Investigational medicinal product name	Axitinib
Investigational medicinal product code	AG-013736
Other name	Inlyta
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received oral dose of Axitinib, starting dose from 1 to 8 milligram twice a day

Number of subjects in period 1	Axitinib Monotherapy
Started	49
Completed	0
Not completed	49
Adverse events	10
Death	3
No longer willing to participate in study	2
Insufficient Clinical Response	3
Unspecified	2
Alternative source of treatment	1
Lost to follow-up	1
Objective progression or relapse	24

Discontinued for reason other than adverse event	3

Baseline characteristics

Reporting groups	
Reporting group title	Axitinib Monotherapy
Reporting group description:	
Participants under current study (A4061008) received oral dose of Axitinib alone twice daily as they were taking in the previous clinical trial. Maximum treatment duration was of 119.56 months.	

Reporting group values	Axitinib Monotherapy	Total	
Number of subjects	49	49	
Age categorical Units: Participants			
Adults (18-64 years)	35	35	
From 65-84 years	14	14	
Age Continuous Units: years			
arithmetic mean	60.4		
standard deviation	± 9.0	-	
Sex: Female, Male Units: Participants			
Female	14	14	
Male	35	35	
Race (NIH/OMB) Units: Subjects			
Asian	11	11	
Black or African American	1	1	
White	32	32	
Unknown or Not Reported	5	5	

End points

End points reporting groups

Reporting group title	Axitinib Monotherapy

Reporting group description:

Participants under current study (A4061008) received oral dose of Axitinib alone twice daily as they were taking in the previous clinical trial. Maximum treatment duration was of 119.56 months.

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, Treatment Related TEAEs and Treatment Related Serious TEAEs

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, Treatment Related TEAEs and Treatment Related Serious TEAEs[1]

End point description:

An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between first dose of study drug and up to 28 days after last dose that were absent before treatment or that worsened relative to pretreatment state. Relatedness of an AE to study drug was based on investigator's assessment. AEs included both serious and all non-serious AEs. Safety population included all participants who received at least 1 dose of Axitinib under A4061008 protocol.

End point type	Primary

End point timeframe:

Day 1 up to 28 days after last dose of study drug (maximum treatment exposure was 119.56 months; maximum follow up to approximately 120.56 months)

Notes:

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

End point values	Axitinib Monotherapy			
Subject group type	Reporting group			
Number of subjects analysed	49			
Units: Participants				
TEAEs	49			
Serious TEAEs	21			
Treatment Related TEAEs	47			
Treatment Related Serious TEAEs	15			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to 28 days after last dose of study drug (maximum treatment exposure was 119.56 months; maximum follow up to approximately 120.56 months)

Adverse event reporting additional description:

Same event may appear as both non-SAE and SAE but what is presented are distinct events. An event may be categorised as serious in one participant and nonserious in another participant or one participant may have experienced both serious and non-serious event. Safety population was analysed.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Axitinib Monotherapy

Reporting group description:

Participants under current study (A4061008) received oral dose of Axitinib alone twice daily as they were taking in the previous clinical trial. Maximum treatment duration was of 119.56 months.

Serious adverse events	Axitinib Monotherapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 49 (42.86%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphocytic leukaemia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diffuse large B-cell lymphoma			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			

Cholecystectomy				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disease progression				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal disorders				
Pneumothorax				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary toxicity				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 2		
Acute coronary syndrome			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Intracardiac thrombus			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	6 / 49 (12.24%)		
occurrences causally related to treatment / all	5 / 6		
deaths causally related to treatment / all	0 / 0		

Arrhythmia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Transient global amnesia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	2 / 49 (4.08%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 49 (4.08%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 49 (2.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer haemorrhage				

subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Proteinuria			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			

subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Axitinib Monotherapy		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 49 (97.96%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	28 / 49 (57.14%)		
occurrences (all)	36		
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	5		
Influenza like illness			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	21 / 49 (42.86%)		
occurrences (all)	32		
Chills			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Chest pain			
subjects affected / exposed	6 / 49 (12.24%)		
occurrences (all)	7		
Asthenia			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	6		

Oedema peripheral subjects affected / exposed occurrences (all)	7 / 49 (14.29%) 8		
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	4 / 49 (8.16%) 4		
Respiratory, thoracic and mediastinal disorders Dysphonia subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	9 / 49 (18.37%) 10 8 / 49 (16.33%) 10 3 / 49 (6.12%) 3 3 / 49 (6.12%) 6 6 / 49 (12.24%) 8		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	5 / 49 (10.20%) 10		
Investigations Blood cholesterol increased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all) Blood creatinine increased	3 / 49 (6.12%) 3 17 / 49 (34.69%) 28		

subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Nervous system disorders			
Taste disorder			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	4		
Paraesthesia			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	12 / 49 (24.49%)		
occurrences (all)	13		
Dizziness			
subjects affected / exposed	6 / 49 (12.24%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Anaemia			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	6		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	17		
Stomatitis			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	10		
Nausea			
subjects affected / exposed	11 / 49 (22.45%)		
occurrences (all)	28		
Gastrooesophageal reflux disease			

subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Dyspepsia			
subjects affected / exposed	7 / 49 (14.29%)		
occurrences (all)	9		
Diarrhoea			
subjects affected / exposed	30 / 49 (61.22%)		
occurrences (all)	63		
Constipation			
subjects affected / exposed	6 / 49 (12.24%)		
occurrences (all)	8		
Abdominal pain upper			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Hyperkeratosis			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	8		
Dry skin			
subjects affected / exposed	6 / 49 (12.24%)		
occurrences (all)	6		
Alopecia			
subjects affected / exposed	5 / 49 (10.20%)		
occurrences (all)	5		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	19 / 49 (38.78%)		
occurrences (all)	31		
Rash			
subjects affected / exposed	5 / 49 (10.20%)		
occurrences (all)	6		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	14 / 49 (28.57%)		
occurrences (all)	114		
Dysuria			

subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	16 / 49 (32.65%)		
occurrences (all)	17		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	9 / 49 (18.37%)		
occurrences (all)	13		
Myalgia			
subjects affected / exposed	6 / 49 (12.24%)		
occurrences (all)	6		
Musculoskeletal stiffness			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	4		
Arthralgia			
subjects affected / exposed	11 / 49 (22.45%)		
occurrences (all)	11		
Back pain			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	8		
Infections and infestations			
Tooth infection			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Sinusitis			
subjects affected / exposed	6 / 49 (12.24%)		
occurrences (all)	7		
Rhinitis			
subjects affected / exposed	5 / 49 (10.20%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Urinary tract infection			

subjects affected / exposed	3 / 49 (6.12%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	9 / 49 (18.37%)		
occurrences (all)	19		
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	5		
Hyperglycaemia			
subjects affected / exposed	6 / 49 (12.24%)		
occurrences (all)	7		
Dehydration			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Decreased appetite			
subjects affected / exposed	8 / 49 (16.33%)		
occurrences (all)	13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2004	The drug formulations were updated to include a 1-mg and 5-mg tablet. The 10-mg tablet was no longer available. The adverse event reporting section (Section 8) was updated to reflect Pfizer's current safety reporting procedures.
17 October 2006	Trail treatment section was updated. Safety assessment section was updated.
06 February 2008	Trail Design section was updated. Safety assessment section was updated.
15 December 2008	Trail Design section was updated. Safety assessment section was updated.
05 December 2012	Update of safety information to align with most recent version of Investigator Brochure (IB). Update AE and safety wording, including pregnancy and Hy's law, to align with current Pfizer SOP (Standard Operating Procedures).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported