Clinical trial results:
A Phase II Study of Sunitinib (NSC# 736511, IND# 74019) in Recurrent, Refractory or Progressive High Grade Glioma (HGG) And Ependymoma Tumors in Pediatric And Young Adult Patients

Summary

EudraCT number	2018-004520-10
Trial protocol	Outside EU/EEA
Global end of trial date	24 June 2013

Results information

Result version number	v1 (current)
This version publication date	22 September 2019
First version publication date	22 September 2019

Trial information

Trial identification

Sponsor protocol code	ACNS1021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01462695
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	National Cancer Institute, National Institutes of Health
Sponsor organisation address	BG 9609 MSC 9760, 9609 Medical Center Drive, Bethesda, United States,
Public contact	National Cancer Institute, National Cancer Institute, National Institutes of Health, 001 1-800-422-6237, NCIinfo@nih.gov
Scientific contact	National Cancer Institute, National Cancer Institute, National Institutes of Health, 001 1-800-422-6237, NCIinfo@nih.gov

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000147-PIP20-18
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	31 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2013
Global end of trial reached?	Yes
Global end of trial date	24 June 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To estimate the objective response rate (ORR [partial response {PR} or complete response {CR} greater than or equal to 8 weeks]) to sunitinib in 2 strata of recurrent or progressive brain tumors in pediatric and young adult patients. The target tumors were:
•Stratum A: Recurrent/progressive/refractory high-grade glioma (excluding diffuse intrinsic pontine glioma).
•Stratum B: Recurrent/progressive/refractory ependymoma

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 Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	United States: 26
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Saudi Arabia: 1
Worldwide total number of subjects	29
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	13
Adolescents (12-17 years)	14
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

National Cancer Institute (NCI) was the trial sponsor and Children's Oncology Group (COG) conducted the study on behalf of NCI. Pfizer performed the data analysis based on the data transferred from COG.

Pre-assignment

Screening details:

The study was conducted in 4 countries at multiple sites.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Stratum A: Recurrent High Grade Glioma

Arm description:

Subjects with recurrent/progressive/refractory HGG received sunitinib, starting dose of 15 milligram per square meter (15 mg/m^2) on basis of body surface area, orally once daily for a 6-week cycle. Each cycle consisted of treatment period of 28 days and a 14 days rest period without sunitinib. Treatment continued for a maximum of 18 cycles in the absence of disease progression or unacceptable toxicity.

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

Dosage and administration details:

In each cycle subjects received sunitinib, starting dose of 15 mg/m^2 orally once daily for 28 days followed by 14 days without sunitinib.

Arm title	Stratum B: Recurrent Ependymoma

Arm description:

Subjects with recurrent/progressive/refractory ependymoma received sunitinib, starting dose of 15 mg/m^2 on basis of body surface area, orally once daily for a 6-week cycle. Each cycle consisted of treatment period of 28 days and a 14 days rest period without sunitinib. Treatment continued for a maximum of 18 cycles in the absence of disease progression or unacceptable toxicity.

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

Dosage and administration details:

In each cycle subjects received sunitinib, starting dose of 15 mg/m^2 orally once daily for 28 days followed by 14 days without sunitinib.

Number of subjects in period 1	Stratum A: Recurrent High Grade Glioma	Stratum B: Recurrent Ependymoma
Started	16	13
Completed	0	0
Not completed	16	13
Progressive disease represents >25% increase	6	11
Occurrence of new/worsening hemorrhage	1	1
Physician decision	5	1
Consent withdrawn by subject	2	-
Death	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Stratum A: Recurrent High Grade Glioma
Reporting group description:	
Subjects with recurrent/progressive/refractory HGG received sunitinib, starting dose of 15 milligram per square meter (15 mg/m^2) on basis of body surface area, orally once daily for a 6-week cycle. Each cycle consisted of treatment period of 28 days and a 14 days rest period without sunitinib. Treatment continued for a maximum of 18 cycles in the absence of disease progression or unacceptable toxicity.	
Reporting group title	Stratum B: Recurrent Ependymoma
Reporting group description:	
Subjects with recurrent/progressive/refractory ependymoma received sunitinib, starting dose of 15 mg/m^2 on basis of body surface area, orally once daily for a 6-week cycle. Each cycle consisted of treatment period of 28 days and a 14 days rest period without sunitinib. Treatment continued for a maximum of 18 cycles in the absence of disease progression or unacceptable toxicity.	

Reporting group values	Stratum A: Recurrent High Grade Glioma	Stratum B: Recurrent Ependymoma	Total
Number of subjects	16	13	29
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)	6	7	13
Adolescents (12-17 years)	8	6	14
Adults (18-64 years)	2	0	2
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	12.5	10.3	
standard deviation	± 4.5	± 4.5	-
Gender categorical Units: Subjects			
Female	4	7	11
Male	12	6	18

End points

End points reporting groups

Reporting group title	Stratum A: Recurrent High Grade Glioma

Reporting group description:

Subjects with recurrent/progressive/refractory HGG received sunitinib, starting dose of 15 milligram per square meter (15 mg/m^2) on basis of body surface area, orally once daily for a 6-week cycle. Each cycle consisted of treatment period of 28 days and a 14 days rest period without sunitinib. Treatment continued for a maximum of 18 cycles in the absence of disease progression or unacceptable toxicity.

Reporting group title	Stratum B: Recurrent Ependymoma

Reporting group description:

Subjects with recurrent/progressive/refractory ependymoma received sunitinib, starting dose of 15 mg/m^2 on basis of body surface area, orally once daily for a 6-week cycle. Each cycle consisted of treatment period of 28 days and a 14 days rest period without sunitinib. Treatment continued for a maximum of 18 cycles in the absence of disease progression or unacceptable toxicity.

Primary: Sustained Objective Response Rate

End point title	Sustained Objective Response Rate[1]

End point description:

Sustained objective response was defined as a partial response (PR) or complete response (CR) lasting at least 8 weeks. PR: greater than or equal to 50 percent decrease in the sum of the products of the 2 perpendicular diameters of all target lesions (up to 5), taking as reference the initial baseline measurements. CR: disappearance of all target lesions.

End point type	Primary

End point timeframe:

Up to 2 years

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: Descriptive statistics (percentage and its 95% confidence interval) were calculated.

End point values	Stratum A: Recurrent High Grade Glioma	Stratum B: Recurrent Ependymoma		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	13		
Units: percentage of subjects				
number (confidence interval 95%)	0 (0.0 to 20.6)	0 (0.0 to 24.7)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 30 days after the last dose (up to 2 years)

Adverse event reporting additional description:

The same events may occur as both an adverse event (AE) and a serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Stratum A: Recurrent High Grade Glioma

Reporting group description:

Subjects with recurrent/progressive/refractory HGG received sunitinib, starting dose of 15 mg/m^2 on basis of body surface area, orally once daily for a 6-week cycle. Each cycle consisted of treatment period of 28 days and a 14 days rest period without sunitinib. Treatment continued for a maximum of 18 cycles in the absence of disease progression or unacceptable toxicity.

Reporting group title	Stratum B: Recurrent Ependymoma

Reporting group description:

Subjects with recurrent/progressive/refractory ependymoma received sunitinib, starting dose of 15 mg/m^2 on basis of body surface area, orally once daily for a 6-week cycle. Each cycle consisted of treatment period of 28 days and a 14 days rest period without sunitinib. Treatment continued for a maximum of 18 cycles in the absence of disease progression or unacceptable toxicity.

Serious adverse events	Stratum A: Recurrent High Grade Glioma	Stratum B: Recurrent Ependymoma	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 16 (68.75%)	3 / 13 (23.08%)	
number of deaths (all causes)	4	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioblastoma multiforme			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neoplasm			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neoplasm progression			
subjects affected / exposed	4 / 16 (25.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dysarthria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial nerve disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	2 / 16 (12.50%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	2 / 16 (12.50%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			

subjects affected / exposed	3 / 16 (18.75%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Stratum A: Recurrent High Grade Glioma	Stratum B: Recurrent Ependymoma	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 16 (56.25%)	8 / 13 (61.54%)	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Amylase increased			
subjects affected / exposed	1 / 16 (6.25%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Aspartate aminotransferase			

increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	1	
Lipase increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	1 / 16 (6.25%)	5 / 13 (38.46%)	
occurrences (all)	1	5	
White blood cell count decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Hemiparesis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 16 (12.50%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Eye disorders			

Extraocular muscle paresis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Skin striae			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported