Clinical trial results:
Phase II pilot, prospective, open label, multicenter Clinical Trial, to evaluate the safety and efficacy of PF299804, a pan-HER irreversible inhibitor, in patients with recurrent glioblastoma with EGFR amplification or presence of EGFRvIII mutation

Summary

EudraCT number	2011-004671-37
Trial protocol	ES
Global end of trial date	09 March 2017

Results information

Result version number	v1 (current)
This version publication date	28 June 2021
First version publication date	28 June 2021
Summary attachment (see zip file)	manuscript (nox105 (1).pdf)

Trial information

Trial identification

Sponsor protocol code	GEINO-11

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01520870
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Grupo Español de Investigacion en NeuroOncología (GEINO)
Sponsor organisation address	C/ Balmes 243 5º 1º, Barcelona, Spain, 08006
Public contact	Pau Doñate, MFAR Clinical Research, investigacion@mfar.net
Scientific contact	Pau Doñate, MFAR Clinical Research, investigacion@mfar.net

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	01 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2017
Global end of trial reached?	Yes
Global end of trial date	09 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess progression-free survival (PFS) at six months (PFS6m) in patients with recurrent glioblastoma with EGFR amplification or presence of EGFRvIII mutation.

Protection of trial subjects:

The protocol included measures to ensure the integrity and safety of all patients and the protection of their data according to the local regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2012
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	Spain: 49
Worldwide total number of subjects	49
EEA total number of subjects	49

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)	29
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with first recurrence were enrolled in 2 cohorts. Cohort A included patients with EGFR gene amplification without EGFRvIII mutation. Cohort B included patients with EGFR gene amplification and EGFRvIII mutation.

Pre-assignment

Screening details:

Patients over 18 years of age who had central review histologically confirmed recurrent GB with EGFR amplification (determined by fluorescence in situ hybridization [FISH] assay), also confirmed by central molecular pathology review, were eligible for the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A

Arm description:

patients with EGFR gene amplification without EGFRvIII mutation.
Dacomitinib was administered (45 mg/day) until disease progression/unacceptable adverse events (AEs).

Arm type	Experimental
Investigational medicinal product name	Dacomintinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

daily dose of 45mg orally

Arm title	Cohort B

Arm description:

Patients with EGFR gene amplification and EGFRvIII mutation.
Dacomitinib was administered (45 mg/day) until disease progression/unacceptable adverse events (AEs).

Arm type	Experimental
Investigational medicinal product name	Dacomintinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

daily dose of 45mg orally

Number of subjects in period 1	Cohort A	Cohort B
Started	30	19
Completed	30	17
Not completed	0	2
Consent withdrawn by subject	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A
Reporting group description:	
patients with EGFR gene amplification without EGFRvIII mutation. Dacomitinib was administered (45 mg/day) until disease progression/unacceptable adverse events (AEs).	
Reporting group title	Cohort B
Reporting group description:	
Patients with EGFR gene amplification and EGFRvIII mutation. Dacomitinib was administered (45 mg/day) until disease progression/unacceptable adverse events (AEs).	

Reporting group values	Cohort A	Cohort B	Total
Number of subjects	30	19	49
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	62.5	52	
full range (min-max)	41 to 81	39 to 72	-
Gender categorical Units: Subjects			
Female	10	7	17
Male	20	12	32
ECOG performance status Units: Subjects			
score 0	3	2	5
score 1	19	13	32
score 2	8	4	12
MGMT methylation Units: Subjects			
unmethylated	7	10	17
Methylated	9	1	10
not determined	14	8	22
IDH mutations Units: Subjects			
IDH1 mutant	2	0	2
IDH2 mutant	0	0	0

IDH1/2 not mutated	19	15	34
not determined	9	4	13

End points

End points reporting groups

Reporting group title	Cohort A

Reporting group description:

patients with EGFR gene amplification without EGFRvIII mutation.
Dacomitinib was administered (45 mg/day) until disease progression/unacceptable adverse events (AEs).

Reporting group title	Cohort B

Reporting group description:

Patients with EGFR gene amplification and EGFRvIII mutation.
Dacomitinib was administered (45 mg/day) until disease progression/unacceptable adverse events (AEs).

Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)[1]

End point description:

End point type	Primary

End point timeframe:

Throughout the study period, 4 years.
MRI was performed every 12 weeks to assess response to treatment according to RANO criteria.

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: This was a single arm open-label phase II trial. All patients received the same treatment despite they were allocated in two arms according to their mutational status. No comparison between arms was planned.

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	17[2]		
Units: Months				
median (confidence interval 95%)	2.7 (2.3 to 3.2)	2.6 (1.8 to 3.4)		

Notes:

[2] - 2 patients were not evaluable due to consent withdrawal

Statistical analyses

No statistical analyses for this end point

Secondary: Best Objective Response

End point title	Best Objective Response

End point description:

End point type	Secondary

End point timeframe:

Throughout the study, 4 years.
MRI was performed every 12 weeks to assess response to treatment according to RANO criteria.

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	19		
Units: Patients				
Complete response	1	0		
Partial response	1	1		
Stable disease	8	4		
Progressive disease	17	13		
not evaluable	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

End point type	Secondary

End point timeframe:

Throughout the study period, 4 years

End point values	Cohort A	Cohort B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	17[3]		
Units: Months				
median (confidence interval 95%)	7.8 (5.6 to 10.1)	6.7 (4.3 to 9.1)		

Notes:

[3] - 2 patients were not evaluable due to consent withdrawal

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Throughout the study, 4 years	
Assessment type	Systematic
Dictionary used	
Dictionary name	NCI CTCAE
Dictionary version	4.0
Reporting groups	
Reporting group title	Safety population
Reporting group description: All patients enrolled in the study and that received at least one dose of study treatment	

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 49 (32.65%)		
number of deaths (all causes)	43		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 49 (6.12%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	11 / 49 (22.45%)		
occurrences causally related to treatment / all	11 / 11		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 49 (95.92%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 49 (22.45%)		
occurrences (all)	11		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	33 / 49 (67.35%)		
occurrences (all)	33		
Vomiting			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	40 / 49 (81.63%)		
occurrences (all)	40		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 October 2013	Change of sites
01 December 2013	Inclusion of a retrospective biological sample substudy

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Important limitations of our study are the small sample size and the nonrandomized design, which preclude drawing firm conclusions.

Notes: