



## 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:

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**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:

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**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:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Spain: 49 |
| Worldwide total number of subjects   | 49        |
| EEA total number of subjects         | 49        |

Notes:

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**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      |
| <b>Arm title</b>             | 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 | Dacomitinib  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

daily dose of 45mg orally

|                  |          |
|------------------|----------|
| <b>Arm title</b> | 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 | Dacomitinib  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

daily dose of 45mg orally

| <b>Number of subjects in period 1</b> | 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:<br>patients with EGFR gene amplification without EGFRvIII mutation.<br>Dacomitinib was administered (45 mg/day) until disease progression/unacceptable adverse events (AEs). |          |
| Reporting group title   | Cohort B |
| Reporting group description:<br>Patients with EGFR gene amplification and EGFRvIII mutation.<br>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<br>Units: Subjects                    |          |          |       |
| In utero  |          |          | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) |          |          | 0     |
| Newborns (0-27 days)                                  |          |          | 0     |
| Infants and toddlers (28 days-23<br>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<br>Units: years                        |          |          |       |
| median  | 62.5     | 52       |       |
| full range (min-max)                                  | 41 to 81 | 39 to 72 | -     |
| Gender categorical<br>Units: Subjects                 |          |          |       |
| Female  | 10       | 7        | 17    |
| Male  | 20       | 12       | 32    |
| ECOG performance status<br>Units: Subjects            |          |          |       |
| score 0   | 3        | 2        | 5     |
| score 1   | 19       | 13       | 32    |
| score 2   | 8        | 4        | 12    |
| MGMT methylation<br>Units: Subjects                   |          |          |       |
| unmethylated  | 7        | 10       | 17    |
| Methylated  | 9        | 1        | 10    |
| not determined  | 14       | 8        | 22    |
| IDH mutations<br>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:<br>patients with EGFR gene amplification without EGFRvIII mutation.<br>Dacomitinib was administered (45 mg/day) until disease progression/unacceptable adverse events (AEs). |          |
| Reporting group title   | Cohort B |
| Reporting group description:<br>Patients with EGFR gene amplification and EGFRvIII mutation.<br>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) <sup>[1]</sup> |
| End point description:  |  |
| End point type  | Primary  |
| End point timeframe:<br>Throughout the study period, 4 years.<br>MRI was performed every 12 weeks to assess response to treatment according to RANO criteria.   |  |
| Notes:<br>[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.<br>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 <sup>[2]</sup> |  |  |
| 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:<br>Throughout the study, 4 years.<br>MRI was performed every 12 weeks to assess response to treatment according to RANO criteria. |                         |

| <b>End point values</b>     | 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

| <b>End point values</b>          | Cohort A          | Cohort B          |  |  |
|----------------------------------|-------------------|-------------------|--|--|
| Subject group type               | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed      | 30                | 17 <sup>[3]</sup> |  |  |
| 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 %

|   |                   |  |  |
|---|-------------------|--|--|
| <b>Non-serious adverse events</b>                     | 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:

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### 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: