# Clinical trial results:
# A Phase II Multi-Centre Study of Concomitant and Prolonged Adjuvant Temozolomide with Radiotherapy in Diffuse Pontine Gliomas

## Summary

| | |
|---|---|
| EudraCT number | 2007-001768-60 |
| Trial protocol | GB |
| Global end of trial date | 24 January 2014 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 18 December 2019 |
| First version publication date | 17 February 2019 |
| Version creation reason | • Changes to summary attachments<br>Wrong upload provided |
| Summary attachment (see zip file) | BS TEM ESR 17Feb2014 (BSG_Final Study Report_Signed_Scanned_17Feb2014.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CNS 2007 04 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Sponsor ID : RG_09-200 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | University of Birmingham |
| Sponsor organisation address | Edgbaston , Birmingham , United Kingdom, B15 2TT |
| Public contact | Nicola Fenwick , University of Birmingham , reg@trials.bham.ac.uk |
| Scientific contact | Nicola Fenwick , University of Birmingham , reg@trials.bham.ac.uk |

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 | 17 February 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 24 January 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 January 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

• To evaluate the time to death in patients with newly diagnosed diffuse pontine gliomas, when treated with the combination of concomitant low dose oral Temozolomide and radiation therapy, followed by up to 12 months maintenance therapy with extended low dose Temozolomide. • To assess the quality of life in patients with diffuse pontine gliomas during and after the above treatment.

Protection of trial subjects:

The study was reviewed and approved by East Midlands Research Ethics Committee (REC) 07/MRE04/38

The patients and/or parents provided written consent to participate in the study after a full explanation was been given of the treatment options. If the patient was a minor, the treatment was explained to, and consent received from, his or her parent or guardian. Additionally the child received an age appropriate explanation and could give assent as well if he/she was able to do so. The right of a patient or parents/guardian to refuse to participate without giving reasons was respected.

Background therapy:

Radiotherapy

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 07 January 2008 |
| 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 | United Kingdom: 43 |
| Worldwide total number of subjects | 43 |
| EEA total number of subjects | 43 |

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) | 35 |
| Adolescents (12-17 years) | 6 |
| Adults (18-64 years) | 2 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

43 patients were recruited between 07-Feb-2008 and 07-Jul-2010 from 16 UK centres.

### Pre-assignment

Screening details:

Inclusion Criteria
a) Newly diagnosed diffuse intrinsic lesion centred in the pons on MRI imaging. No requirement for histological diagnosis.
b) Age between 2 and 21 years
c)Karnofsky Performance Status (KPS) or a Lansky play score of 60
d) Adequate neutrophil and platelet count

### Period 1

| | |
|---|---|
| Period 1 title | Registration (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | BSG Treatment: Temozolomide with radiotherapy |

Arm description:

Temozolomide at a low dose of 75 mg/m2 administered daily for 6 weeks during radiotherapy (7 days per week), starting up to 72 hours prior to the first dose of radiotherapy.
Temozolomide administered at 75 mg/m2/day for 6 weeks

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Temozolomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Temozolomide be administered at 75 mg/m2/day for 6 weeks. All doses rounded up to the nearest 5mg to accommodate capsule strength, and given with a glass of water after a minimum 2 hour fast. If the child was unable to swallow capsules then the capsules may be opened and diluted in apple juice prior to swallowing.

| **Number of subjects in period 1** | BSG Treatment: Temozolomide with radiotherapy |
|---|---|
| Started | 43 |
| Completed | 43 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | BSG Treatment: Temozolomide with radiotherapy |
| Reporting group description: | |
| Temozolomide at a low dose of 75 mg/m2 administered daily for 6 weeks during radiotherapy (7 days per week), starting up to 72 hours prior to the first dose of radiotherapy.<br>Temozolomide administered at 75 mg/m2/day for 6 weeks | |

| Reporting group values | BSG Treatment: Temozolomide with radiotherapy | Total | |
|---|---|---|---|
| Number of subjects | 43 | 43 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 35 | 35 | |
| Adolescents (12-17 years) | 6 | 6 | |
| Adults (18-64 years) | 2 | 2 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 19 | 19 | |
| Male | 24 | 24 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | BSG Treatment: Temozolomide with radiotherapy |

Reporting group description:

Temozolomide at a low dose of 75 mg/m2 administered daily for 6 weeks during radiotherapy (7 days per week), starting up to 72 hours prior to the first dose of radiotherapy.
Temozolomide administered at 75 mg/m2/day for 6 weeks

| | |
|---|---|
| Subject analysis set title | Treatment Analysis Set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

All patients entered in to the study.

### Primary: Overall Survival

| | |
|---|---|
| End point title | Overall Survival |

End point description:

Median survival times to tumour progression and to death after study entry. The response rate will be summarised and compared to historical controls treated with standard radiotherapy alone.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Until death

| End point values | BSG Treatment: Temozolomide with radiotherapy | Treatment Analysis Set | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: patient | | | | |
| number (not applicable) | 43 | 43 | | |

### Statistical analyses

| Statistical analysis title | Overall survival |
|---|---|
| Comparison groups | BSG Treatment: Temozolomide with radiotherapy v Treatment Analysis Set |
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| P-value | = 0.23 |
| Method | likelihood Bayesian |

Notes:

[1] - Study design: This trial was originally designed as a Case-Morgan design. This method was chosen to allow the trial to stop early for futility. It was a single arm study, testing a null hypothesis of 50% overall survival at 9 months against an alternate hypothesis of 70%. The level of significance for the study was set at a 1-tailed alpha of 0.05. There was one intermediate analysis for futility, which did not result in the trial stopping. The primary hypothesis test in the study was a 1-ta

## Adverse events

| Adverse events information[1] | |
|---|---|
| Timeframe for reporting adverse events: | |
| Patients were observed for safety for 30 days following the last dose of temozolomide | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | CTACE |
| Dictionary version | 4 |

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: 43 patients were registered in to the study - for all of which non-serious adverse events were recorded. See attached publication and end of study report for further information.

19 Serious Adverse Reactions were recorded for 17 patients. See attached publication and end of study report for further information.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 01 March 2008 | Treatment updated from 12 months to 12 cycles. Duration of follow-up amended. QOL elements updated. Change in timing of start of radiotherapy. |
| 01 May 2010 | Contact details updated to the Cancer Research UK Clinical Trials Unit. Change to SAE reporting contact details. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/24011536