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 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. 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 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 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