Clinical trial results:
Phase III Study on the effectiveness of OSAG 101 (Theraloc) in newly diagnosed intrinsic pontine gliomas of children and adolescents

Summary

EudraCT number	2005-003100-11
Trial protocol	DE IT
Global end of trial date	24 July 2009

Results information

Result version number	v1 (current)
This version publication date	23 June 2022
First version publication date	23 June 2022

Trial information

Trial identification

Sponsor protocol code	OSAG 101-BSC-05

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Oncoscience GmbH
Sponsor organisation address	Osterbrooksweg 59, Schenefeld, Germany, 22869
Public contact	Budhi Simon, Oncoscience AG, +65 9633 2476, b.simon@oncoscience.de
Scientific contact	Budhi Simon, Oncoscience AG, +65 9633 2476, b.simon@oncoscience.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000723-PIP01-09
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	24 July 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 July 2009
Global end of trial reached?	Yes
Global end of trial date	24 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the progression-free survival (PFS) of the combination of monoclonal anti-EGFR antibody OSAG 101 and standard local radiotherapy in newly diagnosed intrinsic pontine gliomas

Protection of trial subjects:

Not applicable

Background therapy:

Radiotherapy according to previous HIT GBM D protocol (German Society for Pediatric Haematology and Oncology) in all patients aged >3 years, given as standard fractionated external beam irradiation (5 fractions per week with 1.8 Gy; ICRU 50/62 reference point) up to a total of 54 Gy; target volume dose was given over 6 weeks)

Evidence for comparator:

Not applicable

Actual start date of recruitment	12 April 2006
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	Germany: 15
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Russian Federation: 14
Worldwide total number of subjects	42
EEA total number of subjects	28

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)	7

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Non-randomised study

Pre-assignment

Screening details:

The study was performed in patients aged 3-20 years with newly diagnosed intrinsic pontine glioma documented by MRI and measurable in at least one dimension. Histology was not required; tumour biopsy was not recommended. Minimum life expectancy was 4 weeks.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Arm title	OSAG 101

Arm description:

OSAG 101 given at a dose of 150 mg/m2
- as induction therapy once weekly from Week 0 to 11
- as consolidation therapy I in patients with at least stable disease during induction therapy, once every 2 weeks from Week 13 to 23
- as consolidation therapy II in patients with at least stable disease during consolidation therapy I, once every 2 weeks from Week 25 to 35

Arm type	Experimental
Investigational medicinal product name	Nimtuzumab
Investigational medicinal product code	OSAG 101
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

150 mg/m2 given weekly (during the induction therapy period) and once every 2 weeks during consolidation therapy I and II

Number of subjects in period 1	OSAG 101
Started	42
Completed	3
Not completed	39
Death	39

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	42	42	
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	6.0		
full range (min-max)	3.0 to 15.0	-	
Gender categorical Units: Subjects			
Female	26	26	
Male	16	16	

End points

End points reporting groups

Reporting group title	OSAG 101

Reporting group description:

OSAG 101 given at a dose of 150 mg/m2
- as induction therapy once weekly from Week 0 to 11
- as consolidation therapy I in patients with at least stable disease during induction therapy, once every 2 weeks from Week 13 to 23
- as consolidation therapy II in patients with at least stable disease during consolidation therapy I, once every 2 weeks from Week 25 to 35

Primary: Progression-free survival

End point title	Progression-free survival[1]

End point description:

Progression-free survival was defined as the time from registration to the earliest of: objective tumour progression or death or the end of the observation period or the last date of follow up. Progression was defined based on RECIST criteria.

End point type	Primary

End point timeframe:

3.25 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: This was a single-arm, uncontrolled trial. Inferential testing of the primary endpoint was neither planned nor performed.

End point values	OSAG 101			
Subject group type	Reporting group			
Number of subjects analysed	42[2]			
Units: Days				
median (confidence interval 95%)	175 (145 to 184)			

Notes:

[2] - Full analysis set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were to be reported during the treatment period, i.e. within 36 weeks after inclusion in the study and through follow-up, up to 24 months after the start of study treatment, or until start of new anticancer therapy (whatever happened earlier)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	OSAG 101

Reporting group description:

All patients treated

Serious adverse events	OSAG 101		
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 42 (92.86%)		
number of deaths (all causes)	39		
number of deaths resulting from adverse events	34		
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Injury			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Mechanical ventilation			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Resuscitation			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgery			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventriculo-peritoneal shunt			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Coma			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Convulsions local			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			

subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hydrocephalus				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial pressure increased				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningeal disorder				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
VIIth nerve paralysis				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Medical device complication				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Condition aggravated				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	33 / 42 (78.57%)			
occurrences causally related to treatment / all	0 / 33			
deaths causally related to treatment / all	0 / 33			
General physical health deterioration				

subjects affected / exposed	2 / 42 (4.76%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 42 (4.76%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Deafness unilateral				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Vomiting				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Lung disorder				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Gastroenteritis				
subjects affected / exposed	2 / 42 (4.76%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	OSAG 101		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Investigations			
Urine analysis abnormal			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 42 (33.33%)		
occurrences (all)	18		
Ataxia			
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	9		
Hemiparesis			
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	8		
VIth nerve paralysis			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Neurological decompensation			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Paresis cranial nerve			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
VIIth nerve paralysis			

subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	11		
Performance status decreased			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Pyrexia			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	10		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	14 / 42 (33.33%)		
occurrences (all)	23		
Nausea			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		
Abdominal pain upper			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Constipation			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	6		
Diarrhoea			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Acne			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2007	The following main changes were implemented: - it was clarified that monitoring visits should take place in study centres 3 months after admission of a patient into the study - assessment categories of neuroradiological parameters were clarified - assessment criteria for AEs were clarified

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported