



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) | EMA-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/m ² | |
| - 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 occurrences (all) | 3 / 42 (7.14%) 3 | | |
| General disorders and administration site conditions Disease progression subjects affected / exposed occurrences (all) Performance status decreased subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 11 / 42 (26.19%) 11 7 / 42 (16.67%) 7 7 / 42 (16.67%) 10 | | |
| Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) | 4 / 42 (9.52%) 4 | | |
| Eye disorders Conjunctivitis subjects affected / exposed occurrences (all) | 3 / 42 (7.14%) 3 | | |
| Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) | 14 / 42 (33.33%) 23 5 / 42 (11.90%) 7 4 / 42 (9.52%) 5 3 / 42 (7.14%) 6 3 / 42 (7.14%) 3 | | |

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

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: <ul style="list-style-type: none">- 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