# Clinical trial results:
# Cilengitide (EMD121974) in combination with irradiation in children and young adults with newly diagnosed diffuse intrinsic pontine glioma : Phase I study

## Summary

| | |
|---|---|
| EudraCT number | 2009-016870-33 |
| Trial protocol | FR |
| Global end of trial date | 01 March 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 06 August 2025 |
| First version publication date | 06 August 2025 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CILENT-0902 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01165333 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Centre Oscar Lambret |
| Sponsor organisation address | 3 Rue Frédéric Combemale, Lille, France, 59000 |
| Public contact | Marie VANSEYMORTIER, Centre Oscar Lambret, 33 320295918, promotion@o-lambret.fr |
| Scientific contact | Pierre LEBLOND, Centre Oscar Lambret, pierre.leblond@ihope.fr |

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 | 01 March 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 March 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 March 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

- To determine the Maximal Tolerated Dose (MTD) of Cilengitide, administered intravenously over 60 minutes, twice a week, in children and young adults with newly diagnosed diffuse intrinsic pontine glioma, in combination with radiation therapy

Protection of trial subjects:

This clinical trial will be conducted in accordance with the protocol, the ethical principles laid down by the 18th World Medical Assembly (Helsinki, 1964) and all applicable amendments laid down by the World Medical Assemblies, the International Conference on Harmonization (ICH) consolidated Guideline E6 for Good Clinical Practice (CPMP/ICH/135/95), and all applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 September 2010 |
| 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 | France: 32 |
| Worldwide total number of subjects | 32 |
| EEA total number of subjects | 32 |

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) | 28 |
| Adolescents (12-17 years) | 4 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 32 patients were included in the study

### Period 1

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

Blinding implementation details:

This is a phase I trial

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | level 1: 240 mg/m²/infusion |

Arm description: -

| | |
|---|---|
| Arm type | dose escalation |
| Investigational medicinal product name | Cilengitide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Each vial contains 500 mg Cilengitide per 33.3 mL solution (i.e. 15 mg/mL of Cilengitide). Vials have to be carefully inverted 3-5 times before use to ensure a homogenous distribution of Cilengitide in the vial. Cilengitide will be given as an i.v. infusion. It will be diluted with 0.9% isotonic sodium chloride to a final volume of 250 mL in a standard polyvinyl chloride infusion bag (alternatively standard polyethylene or polyethylene/polypropylene bags can be used).

| | |
|---|---|
| **Arm title** | level 2: 480 mg/m²/infusion |

Arm description: -

| | |
|---|---|
| Arm type | dose escalation |
| Investigational medicinal product name | Cilengitide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Each vial contains 500 mg Cilengitide per 33.3 mL solution (i.e. 15 mg/mL of Cilengitide). Vials have to be carefully inverted 3-5 times before use to ensure a homogenous distribution of Cilengitide in the vial. Cilengitide will be given as an i.v. infusion. It will be diluted with 0.9% isotonic sodium chloride to a final volume of 250 mL in a standard polyvinyl chloride infusion bag (alternatively standard polyethylene or polyethylene/polypropylene bags can be used).

| | |
|---|---|
| **Arm title** | level 3: 720 mg/m²/infusion |

Arm description: -

| | |
|---|---|
| Arm type | dose escalation |

| | |
|---|---|
| Investigational medicinal product name | Cilengitide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Each vial contains 500 mg Cilengitide per 33.3 mL solution (i.e. 15 mg/mL of Cilengitide). Vials have to be carefully inverted 3-5 times before use to ensure a homogenous distribution of Cilengitide in the vial. Cilengitide will be given as an i.v. infusion. It will be diluted with 0.9% isotonic sodium chloride to a final volume of 250 mL in a standard polyvinyl chloride infusion bag (alternatively standard polyethylene or polyethylene/polypropylene bags can be used).

| | |
|---|---|
| **Arm title** | level 4: 1200 mg/m²/infusion |

Arm description: -

| | |
|---|---|
| Arm type | dose escalation |
| Investigational medicinal product name | Cilengitide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Each vial contains 500 mg Cilengitide per 33.3 mL solution (i.e. 15 mg/mL of Cilengitide). Vials have to be carefully inverted 3-5 times before use to ensure a homogenous distribution of Cilengitide in the vial. Cilengitide will be given as an i.v. infusion. It will be diluted with 0.9% isotonic sodium chloride to a final volume of 250 mL in a standard polyvinyl chloride infusion bag (alternatively standard polyethylene or polyethylene/polypropylene bags can be used).

| | |
|---|---|
| **Arm title** | level 5: 1800 mg/m²/infusion |

Arm description:

3 patients in escalation phase + 15 patients in extended phase

| | |
|---|---|
| Arm type | dose escalation |
| Investigational medicinal product name | Cilengitide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Each vial contains 500 mg Cilengitide per 33.3 mL solution (i.e. 15 mg/mL of Cilengitide). Vials have to be carefully inverted 3-5 times before use to ensure a homogenous distribution of Cilengitide in the vial. Cilengitide will be given as an i.v. infusion. It will be diluted with 0.9% isotonic sodium chloride to a final volume of 250 mL in a standard polyvinyl chloride infusion bag (alternatively standard polyethylene or polyethylene/polypropylene bags can be used).

| **Number of subjects in period 1** | level 1: 240 mg/m²/infusion | level 2: 480 mg/m²/infusion | level 3: 720 mg/m²/infusion |
|---|---|---|---|
| Started | 3 | 3 | 3 |
| Completed | 3 | 3 | 3 |
| Not completed | 0 | 0 | 0 |
| Adverse event, non-fatal | - | - | - |

| **Number of subjects in period 1** | level 4: 1200 mg/m²/infusion | level 5: 1800 mg/m²/infusion |
|---|---|---|
| Started | 5 | 18 |

| | | |
|---|---|---|
| Completed | 3 | 18 |
| Not completed | 2 | 0 |
| Adverse event, non-fatal | 2 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Overall trial |

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---|---|---|
| Number of subjects | 32 | 32 | |
| Age categorical<br>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<br>Units: years | | | |
| median | 6 | | |
| full range (min-max) | 3 to 15 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 15 | 15 | |
| Male | 17 | 17 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | level 1: 240 mg/m²/infusion |
| Reporting group description: - | |
| Reporting group title | level 2: 480 mg/m²/infusion |
| Reporting group description: - | |
| Reporting group title | level 3: 720 mg/m²/infusion |
| Reporting group description: - | |
| Reporting group title | level 4: 1200 mg/m²/infusion |
| Reporting group description: - | |
| Reporting group title | level 5: 1800 mg/m²/infusion |
| Reporting group description: | |
| 3 patients in escalation phase + 15 patients in extended phase | |

### Primary: MTD (Maximal Tolerated Dose)

| | |
|---|---|
| End point title | MTD (Maximal Tolerated Dose)[1] |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| MTD during the first 6 weeks of study treatment | |

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 is a phase I dose escalation. The main endpoint aims to determine the MDT (maximal dose tolerated). No formal statistical analysis was planned

| End point values | level 1: 240 mg/m²/infusion | level 2: 480 mg/m²/infusion | level 3: 720 mg/m²/infusion | level 4: 1200 mg/m²/infusion |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 3 | 3[2] |
| Units: number of DLT observed | 0 | 0 | 0 | 0 |

Notes:

[2] - 2 patients inevaluable for DLT due to toxicity

| End point values | level 5: 1800 mg/m²/infusion | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: number of DLT observed | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Tumor objective response

| End point title | Tumor objective response |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Over treatment duration

| End point values | level 1: 240 mg/m²/infusion | level 2: 480 mg/m²/infusion | level 3: 720 mg/m²/infusion | level 4: 1200 mg/m²/infusion |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 3 | 4[3] |
| Units: number of patient with objective respons | 1 | 1 | 0 | 0 |

Notes:

[3] - Patient n°11 (level 4) did not complete the first cycle of CT and had no tumor assessment. This pati

| End point values | level 5: 1800 mg/m²/infusion | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: number of patient with objective respons | 4 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy

| End point title | Efficacy |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Rate of overall survival and rate of progression free survival

| End point values | level 1: 240 mg/m²/infusion | level 2: 480 mg/m²/infusion | level 3: 720 mg/m²/infusion | level 4: 1200 mg/m²/infusion |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 3 | 5 |
| Units: median in months | | | | |
| number (confidence interval 95%) | | | | |
| Overall survival | 7.6 (4.1 to 7.6) | 6.2 (4.0 to 6.2) | 5.5 (5.4 to 5.5) | 7.8 (5.7 to 7.8) |
| Progression free survival | 2.9 (1.5 to 2.9) | 3.2 (2.1 to 3.2) | 2.1 (1.9 to 2.1) | 4.4 (2.5 to 4.4) |

| End point values | level 5: 1800 mg/m²/infusion | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: median in months | | | | |
| number (confidence interval 95%) | | | | |
| Overall survival | 9.8 (7.3 to 11.4) | | | |
| Progression free survival | 4.6 (4.3 to 6.6) | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

During the first 6 weeks of study treatment

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 2 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Whole population |

Reporting group description: -

| Serious adverse events | Whole population | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 32 (40.63%) | | |
| number of deaths (all causes) | 31 | | |
| number of deaths resulting from adverse events | 3 | | |
| Investigations | | | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| WOLFF-PARKINSON-WHITE SYNDROME | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| BRAIN OEDEMA | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CEREBELLAR ATAXIA | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| CONVULSION | | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| HEADACHE | | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HYDROCEPHALUS | | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| INTRACRANIAL PRESSURE INCREASED | | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| NERVOUS SYSTEM DISORDER | | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| NEURALGIA | | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| NERVOUS SYSTEM DISORDER (DISEASE PROGRESSION) | | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| General disorders and administration site conditions | | | | |
| FATIGUE / ASTHENIA | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| VOMITING | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| BRONCHIAL OBSTRUCTION | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| DYSPNOEA | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPOXIA | | | |
| subjects affected / exposed | 1 / 32 (3.13%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| 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** | Whole population | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 32 (100.00%) | | |
| Vascular disorders | | | |

| | | | |
|---|---|---|---|
| HAEMATOMA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| HYPERTENSION | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 4 | | |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 24 / 32 (75.00%) | | |
| occurrences (all) | 54 | | |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 6 / 32 (18.75%) | | |
| occurrences (all) | 7 | | |
| PYREXIA | | | |
| subjects affected / exposed | 12 / 32 (37.50%) | | |
| occurrences (all) | 20 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 13 / 32 (40.63%) | | |
| occurrences (all) | 16 | | |
| DYSPNOEA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| EPISTAXIS | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 5 | | |
| RHINORRHOEA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |

| | | | |
|---|---|---|---|
| INSOMNIA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| SLEEP DISORDER | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Investigations | | | |
| BLOOD PHOSPHORUS DECREASED | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| WEIGHT INCREASED | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 5 | | |
| Cardiac disorders | | | |
| SINUS TACHYCARDIA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Nervous system disorders | | | |
| ATAXIA | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | | |
| occurrences (all) | 15 | | |
| CEREBELLAR ATAXIA | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 7 | | |
| CEREBELLAR SYNDROME | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 4 | | |
| CONVULSION | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| DYSARTHRIA | | | |
| subjects affected / exposed | 6 / 32 (18.75%) | | |
| occurrences (all) | 11 | | |
| FACIAL NERVE DISORDER | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 7 / 32 (21.88%) | | | |
| occurrences (all) | 8 | | | |
| GLOSSOPHARYNGEAL NERVE DISORDER | | | | |
| subjects affected / exposed | 5 / 32 (15.63%) | | | |
| occurrences (all) | 7 | | | |
| HEADACHE | | | | |
| subjects affected / exposed | 21 / 32 (65.63%) | | | |
| occurrences (all) | 77 | | | |
| HEMIPARESIS | | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | | | |
| occurrences (all) | 13 | | | |
| HEMIPLEGIA | | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | | |
| occurrences (all) | 3 | | | |
| HYDROCEPHALUS | | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | | |
| occurrences (all) | 5 | | | |
| IIIRD NERVE DISORDER | | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | | |
| occurrences (all) | 6 | | | |
| INTRACRANIAL PRESSURE INCREASED | | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | | |
| occurrences (all) | 2 | | | |
| LANGUAGE DISORDER | | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | | |
| occurrences (all) | 2 | | | |
| MONOPARESIS | | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | | |
| occurrences (all) | 3 | | | |
| MUSCLE SPASTICITY | | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | | |
| occurrences (all) | 6 | | | |
| NERVOUS SYSTEM DISORDER | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all)<br><br>NYSTAGMUS<br>subjects affected / exposed<br>occurrences (all)<br><br>PARAESTHESIA<br>subjects affected / exposed<br>occurrences (all)<br><br>PYRAMIDAL TRACT SYNDROME<br>subjects affected / exposed<br>occurrences (all)<br><br>VIITH NERVE PARALYSIS<br>subjects affected / exposed<br>occurrences (all) | 4 / 32 (12.50%)<br>7<br><br><br>3 / 32 (9.38%)<br>4<br><br><br>2 / 32 (6.25%)<br>3<br><br><br>10 / 32 (31.25%)<br>25<br><br><br>4 / 32 (12.50%)<br>9 | | |
| Blood and lymphatic system disorders<br>LEUKOPENIA<br>subjects affected / exposed<br>occurrences (all)<br><br>LYMPHOPENIA<br>subjects affected / exposed<br>occurrences (all)<br><br>NEUTROPENIA<br>subjects affected / exposed<br>occurrences (all) | <br><br>2 / 32 (6.25%)<br>6<br><br><br>2 / 32 (6.25%)<br>14<br><br><br>2 / 32 (6.25%)<br>3 | | |
| Ear and labyrinth disorders<br>TINNITUS<br>subjects affected / exposed<br>occurrences (all)<br><br>VERTIGO<br>subjects affected / exposed<br>occurrences (all) | <br><br>3 / 32 (9.38%)<br>3<br><br><br>2 / 32 (6.25%)<br>2 | | |
| Eye disorders<br>DIPLOPIA<br>subjects affected / exposed<br>occurrences (all)<br><br>EYELID PTOSIS | <br><br>3 / 32 (9.38%)<br>4<br><br> | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 14 / 32 (43.75%) | | |
| occurrences (all) | 21 | | |
| CHEILITIS | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| CONSTIPATION | | | |
| subjects affected / exposed | 18 / 32 (56.25%) | | |
| occurrences (all) | 32 | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | | |
| occurrences (all) | 7 | | |
| DYSPHAGIA | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 4 | | |
| NAUSEA | | | |
| subjects affected / exposed | 11 / 32 (34.38%) | | |
| occurrences (all) | 13 | | |
| SALIVARY HYPERSECRETION | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| VOMITING | | | |
| subjects affected / exposed | 20 / 32 (62.50%) | | |
| occurrences (all) | 65 | | |
| Skin and subcutaneous tissue disorders | | | |
| ACNE | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| ALOPECIA | | | |
| subjects affected / exposed | 6 / 32 (18.75%) | | |
| occurrences (all) | 6 | | |
| ERYTHEMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| PETECHIAL PURPURA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| PRURITUS | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 5 | | |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| Endocrine disorders | | | |
| CUSHING'S SYNDROME | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| BACK PAIN | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| MYALGIA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 4 / 32 (12.50%) | | |
| occurrences (all) | 4 | | |
| TORTICOLLIS | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| Infections and infestations | | | |
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| DEVICE RELATED INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| GINGIVITIS | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 3 | | |
| INFECTION | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 3 | | |
| INFLUENZA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| ORAL FUNGAL INFECTION | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| RHINITIS | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | | |
| occurrences (all) | 8 | | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 3 / 32 (9.38%) | | |
| occurrences (all) | 7 | | |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 7 / 32 (21.88%) | | |
| occurrences (all) | 12 | | |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 7 | | |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 2 / 32 (6.25%) | | |
| occurrences (all) | 2 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 25 November 2010 | Update of trial site list : addition of a new trial site (CHU de Nantes), and declaration of new investigators among existing trial sites |
| 09 March 2011 | 1. Update of cilengitide's IB<br>2. Update of information consent (for parents of minor patients and adults patients) following new safety features described in cilengitide's IB<br>3. Change of CRA monitor |
| 08 August 2011 | Update of trial site list : declaration of new investigators and removal of participating investigators among existing trial sites |
| 13 February 2012 | Update of trial site list : addition of a new trial site (CHU de Toulouse), |
| 30 October 2012 | 1. Addition of new evaluation criteria (RANO, Revised Assessment in Neuro-Oncology) - as part of the centralized review process - to better assess the anti-tumor efficacy of the experimental treatment<br>2. Addition of cardiological exams for patients currently undergoing treatment and for future patients, following an episode of hypertrophic cardiomyopathy observed in a trial subject |
| 12 February 2013 | Change of IP (CHU de Nantes) |
| 08 March 2013 | Temporary suspension of enrolments following Merck's announcement of the results of the CENTRIC trial (in which cilengitide is being evaluated and for which the primary objective of overall survival was not achieved). Inclusions were suspended until the IDMC committee decided whether the benefit/risk balance was still positive |
| 09 September 2013 | 1. Change of Cilengitide manufacturing site<br>2. Addition of exploratory investigations (mutation studies, etc.) |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported