# Clinical trial results:
# PHASE 1 SAFETY AND TOLERABILITY STUDY OF FIGITUMUMAB COMBINED WITH PEGVISOMANT IN PATIENTS WITH ADVANCED SOLID TUMORS.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

| | |
|---|---|
| EudraCT number | 2009-012769-74 |
| Trial protocol | FI |
| Global end of trial date | 23 October 2012 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 23 March 2016 |
| First version publication date | 01 August 2015 |
| Version creation reason | • New data added to full data set<br>• Correction of full data set<br>reporting periods and duplicate AEs in their data |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | A4021040 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00976508 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 East 42nd Street, New York, United States, 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc, 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |

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 | 12 July 2013 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 23 October 2012 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of figitumumab plus pegvisomant in subjects with advanced solid tumors.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 11 November 2009 |
| 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 | Finland: 4 |
| Country: Number of subjects enrolled | Germany: 5 |
| Country: Number of subjects enrolled | United States: 11 |
| Country: Number of subjects enrolled | Canada: 3 |
| Worldwide total number of subjects | 23 |
| EEA total number of subjects | 9 |

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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 20 |
| From 65 to 84 years | 3 |

| | |
|---|---|
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study was started on 11-November-2009 and ended on 23 October 2012 in Finland, Germany, United States and Canada.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Figitumumab 20mg/kg + Pegvisomant 10 mg |

Arm description:

Figitumumab administered on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year). Pegvisomant administered subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 10 mg subcutaneously once daily, up to a maximum of 17 cycles (corresponding to 1 year). Each cycle was of 21 days. 18 subjects were enrolled; 17 subjects were treated; 1 subject was not eligible. The completed subjects withdrew from last study treatment due to progressive disease.

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

Dosage and administration details:

Figitumumab 20 milligram/kilogram (mg/kg) intravenously over 1 to 2.5 hours on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year).

| | |
|---|---|
| Investigational medicinal product name | Pegvisomant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegvisomant 40 mg subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 10 mg subcutaneously once daily, up to a maximum of 17 cycles (corresponding to 1 year).

| | |
|---|---|
| **Arm title** | Figitumumab 20mg/kg + Pegvisomant 20 mg |

Arm description:

Figitumumab administered on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year). Pegvisomant administered subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 20 mg subcutaneously once daily, up to a maximum of 17 cycles (corresponding to 1 year). Each cycle was of 21 days.

| | |
|---|---|
| Arm type | Experimental |

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

Dosage and administration details:

Figitumumab 20 mg/kg intravenously over 1 to 2.5 hours on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year).

| | |
|---|---|
| Investigational medicinal product name | Pegvisomant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Pegvisomant 40 mg subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 20 mg subcutaneously once daily, up to a maximum of 17 cycles (corresponding to 1 year).

| **Number of subjects in period 1** | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg |
|---|---|---|
| Started | 17 | 6 |
| Completed | 3 | 0 |
| Not completed | 14 | 6 |
| Termination by Sponsor | - | 1 |
| Consent withdrawn by subject | 1 | - |
| Death | 7 | 1 |
| Subject Enrolled in Hospice | 1 | - |
| Lost to follow-up | 1 | - |
| Disease Progression | 4 | 4 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Figitumumab 20mg/kg + Pegvisomant 10 mg |
| Reporting group description: | |
| Figitumumab administered on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year). Pegvisomant administered subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 10 mg subcutaneously once daily, up to a maximum of 17 cycles (corresponding to 1 year). Each cycle was of 21 days. 18 subjects were enrolled; 17 subjects were treated; 1 subject was not eligible. The completed subjects withdrew from last study treatment due to progressive disease. | |
| Reporting group title | Figitumumab 20mg/kg + Pegvisomant 20 mg |
| Reporting group description: | |
| Figitumumab administered on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year). Pegvisomant administered subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 20 mg subcutaneously once daily, up to a maximum of 17 cycles (corresponding to 1 year). Each cycle was of 21 days. | |

| Reporting group values | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | Total |
|---|---|---|---|
| Number of subjects | 17 | 6 | 23 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 49.5 | 32.3 | |
| standard deviation | ± 17.4 | ± 9.8 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 8 | 5 | 13 |
| Male | 9 | 1 | 10 |

## End points

### End points reporting groups

| Reporting group title | Figitumumab 20mg/kg + Pegvisomant 10 mg |
|---|---|

Reporting group description:

Figitumumab administered on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year). Pegvisomant administered subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 10 mg subcutaneously once daily, up to a maximum of 17 cycles (corresponding to 1 year). Each cycle was of 21 days. 18 subjects were enrolled; 17 subjects were treated; 1 subject was not eligible. The completed subjects withdrew from last study treatment due to progressive disease.

| Reporting group title | Figitumumab 20mg/kg + Pegvisomant 20 mg |
|---|---|

Reporting group description:

Figitumumab administered on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year). Pegvisomant administered subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 20 mg subcutaneously once daily, up to a maximum of 17 cycles (corresponding to 1 year). Each cycle was of 21 days.

### Primary: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

| End point title | Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)[1] |
|---|---|

End point description:

Counts of subjects who had treatment-emergent adverse events (TEAEs), defined as newly occurring or worsening after first dose. AEs were graded using National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), version 3.0 (Grade [Gr] 1 = Mild, Gr 2 = Moderate, Gr 3=Severe, Gr 4 = Life-threatening or disabling, Gr 5 = Death). Relatedness to [study drug] was assessed by the investigator (Yes/No). Subjects with multiple occurrences of an AE within a category were counted once within the category. Safety analysis set: all enrolled subjects who received at least 1 dose of either of the study medications.

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

End point timeframe:

From Screening to the follow-up visit (90 days after last dose of figitimumab)

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: Only descriptive data was planned to be reported for this endpoint.

| End point values | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: Subjects | | | | |
| Number of Subjects with AEs | 17 | 6 | | |
| Number of subjects with SAEs | 9 | 4 | | |
| Number of subjects with Gr 3 or Gr 4 AEs | 12 | 4 | | |
| Number of subjects with Gr 5 AEs | 7 | 1 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Dose Limiting Toxicities (DLT)

| End point title | Number of Subjects With Dose Limiting Toxicities (DLT)[2] |
|---|---|

End point description:

DLT was defined as any of the following events occurring during DLT period and considered related to study medication: Gr 4 neutropenia lasting more than or equal to (>=) 7 days, febrile neutropenia (Gr 3 or 4 neutropenia, fever >=38.5 degrees Celsius (°C), lasting over 24 hours), neutropenic infection (Gr >=3 neutropenia infection); Gr 3 or 4 thrombocytopenia associated with bleeding or Gr 4 thrombocytopenia >=7 days; Gr 3 or 4 lymphopenia accompanied by an opportunistic infection; other non-hematologic Gr 4 toxicities or symptomatic Gr 3 toxicities that require medical intervention and 14 days to resolve. Safety analysis set: all enrolled subjects who received at least 1 dose of either of the study medications. N= Number of subjects remained on treatment throughout the required DLT period and included as analyzed for DLT based on the defined DLT evaluability specifications were analyzed for this endpoint.

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

End point timeframe:

From Cycle 2, Day 1 to Cycle 3, Day 8; from Cycle 1, Day 15 to end of Cycle 2

Notes:

[2] - 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: Only descriptive data was planned to be reported for this endpoint.

| **End point values** | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6 | 6 | | |
| Units: Subjects | 1 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Circulating Insulin-like Growth Factor (IGF-1) Levels

| End point title | Serum Circulating Insulin-like Growth Factor (IGF-1) Levels |
|---|---|

End point description:

The effect of the combined therapy with figitumumab and pegvisomant on circulating concentrations of total IGF-1 was assessed. Biomarker analysis set: all enrolled subjects who had at least 1 baseline or on-study sample submitted. N=number of participants who were evaluable for IGF-1 Levels at prespecified time points. For this endpoint "99999" signifies not available (NA). For Figitumumab 20 mg/kg + Pegvisomant 10 mg reporting group in cycle 7 Standard deviation (SD) was not calculated as only 1 out of 17 subjects were evaluable ; In Figitumumab 20 mg/kg + Pegvisomant 10 mg reporting group for Cycle 08 to Cycle 27, Mean and SD were not calculated as the data was not analyzed since no subjects were evaluable; for Figitumumab 20mg/kg + Pegvisomant 20 mg reporting groupMean and SD were not calculated as only 1 out of 6 subjects were evaluable.

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

End point timeframe:

Days 1 and 15 of Cycle 1 (Baseline); Day 1 of subsequent cycles starting from Cycle 2 to Cycle 27; end of treatment (21 days after last dose of figitumumab); follow-up visit (90 days after last dose of figitumumab)

| **End point values** | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: nanogram/milliliter (ng/mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline/Cycle 1 (n = 16, 6) | 150.18 (± 77.06) | 189.17 (± 59.79) | | |
| Cycle 2 (n = 12, 6) | 725.72 (± 497.12) | 498.5 (± 218.28) | | |
| Cycle 3 (n = 6, 5) | 474.53 (± 418.39) | 247.4 (± 147.41) | | |
| Cycle 4 (n = 5, 3) | 542.09 (± 510.84) | 124.67 (± 83.94) | | |
| Cycle 5 (n = 3, 4) | 990.4 (± 542.21) | 248.25 (± 127.43) | | |
| Cycle 6 (n = 2, 2) | 1369.5 (± 161.93) | 122.5 (± 137.89) | | |
| Cycle 7 (n = 1, 2) | 1594 (± 99999) | 272.5 (± 105.36) | | |
| Cycle 8 (n = 0, 2) | 99999 (± 99999) | 501 (± 94.75) | | |
| Cycle 9 (n = 0, 2) | 99999 (± 99999) | 331 (± 229.1) | | |
| Cycle 10 (n = 0, 2) | 99999 (± 99999) | 412.5 (± 185.97) | | |
| Cycle 11 (n = 0, 2) | 99999 (± 99999) | 426.5 (± 119.5) | | |
| Cycle 12 (n = 0, 2) | 99999 (± 99999) | 375.5 (± 350.02) | | |
| Cycle 13 (n = 0, 2) | 99999 (± 99999) | 457.5 (± 36.06) | | |
| Cycle 14 (n = 0, 2) | 99999 (± 99999) | 420 (± 45.25) | | |
| Cycle 15 (n = 0, 2) | 99999 (± 99999) | 444.5 (± 47.38) | | |
| Cycle 16 (n = 0, 2) | 99999 (± 99999) | 443.5 (± 23.33) | | |
| Cycle 17 (n = 0, 2) | 99999 (± 99999) | 426 (± 4.24) | | |
| Cycle 18 (n = 0, 2) | 99999 (± 99999) | 570.5 (± 487.2) | | |
| Cycle 19 (n = 0, 1) | 99999 (± 99999) | 537 (± 99999) | | |
| Cycle 20 (n = 0, 2) | 99999 (± 99999) | 458.5 (± 239.71) | | |
| Cycle 21 (n = 0, 2) | 99999 (± 99999) | 437 (± 21.21) | | |
| Cycle 22 (n = 0, 1) | 99999 (± 99999) | 401 (± 99999) | | |
| Cycle 23 (n = 0, 1) | 99999 (± 99999) | 481 (± 99999) | | |
| Cycle 24 (n = 0, 1) | 99999 (± 99999) | 361 (± 99999) | | |

| | | | | |
|---|---|---|---|---|
| Cycle 25 (n = 0, 1) | 99999 (± 99999) | 424 (± 99999) | | |
| Cycle 26 (n = 0, 1) | 99999 (± 99999) | 366 (± 99999) | | |
| Cycle 27 (n = 0, 0) | 99999 (± 99999) | 99999 (± 99999) | | |
| Follow-Up (n = 2, 1) | 791.5 (± 813.88) | 1285 (± 99999) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Cycle 1: Maximum Observed Plasma Concentration (Cmax) of Figitumumab

| End point title | Cycle 1: Maximum Observed Plasma Concentration (Cmax) of Figitumumab |
|---|---|

End point description:

Pharmacokinetic (PK) samples were not analyzed as the study was terminated prematurely due to lack of operational feasibility and the halt of figitumumab development.

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

End point timeframe:

Cycle 1: Day 1 (within 2 hours before figitumumab infusion), Day 2 (1 hour post figitumumab infusion), Day 8 and Day 15

| End point values | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[3] | 0[4] | | |
| Units: ng\mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[3] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

[4] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Observed Plasma Concentration (Cmax) of Figitumumab

| End point title | Maximum Observed Plasma Concentration (Cmax) of Figitumumab |
|---|---|

End point description:

PK samples were not analyzed as the study was terminated prematurely due to lack of operational feasibility and the halt of figitumumab development.

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

End point timeframe:

Cycle 2: Day 1 (within 2 hours before and 1 hour after figitumumab infusion); Cycle 3 to Cycle 17: Day 1 (within 2 hours before figitumumab infusion); end of treatment; 90-day follow-up visit

| **End point values** | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[5] | 0[6] | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[5] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.
[6] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Cycle 1: Plasma Concentration at the Last Quantifiable Time Point (Clast) of Figitumumab

| End point title | Cycle 1: Plasma Concentration at the Last Quantifiable Time Point (Clast) of Figitumumab |
|---|---|

End point description:

PK samples were not analyzed as the study was terminated prematurely due to lack of operational feasibility and the halt of figitumumab development.

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

End point timeframe:

Cycle 1: Day 1 (within 2 hours before figitumumab infusion), Day 2 (1 hour post figitumumab infusion), Day 8 and Day 15

| **End point values** | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[7] | 0[8] | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[7] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.
[8] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma Concentration at the Last Quantifiable Time Point (Clast) of Figitumumab

| End point title | Plasma Concentration at the Last Quantifiable Time Point (Clast) of Figitumumab |
|---|---|

End point description:

Plasma Concentration at the Last Quantifiable Time Point (Clast) of Figitumumab from Cycle 2 to the end of treatment. PK samples were not analyzed as the study was terminated prematurely due to lack of operational feasibility and the halt of figitumumab development.

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

End point timeframe:

Cycle 2: Day 1 (within 2 hours before and 1 hour after figitumumab infusion); Cycle 3 to Cycle 17: Day 1 (within 2 hours before figitumumab infusion); end of treatment; 90-day follow-up visit.

| **End point values** | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[9] | 0[10] | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[9] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.
[10] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Cycle 1: Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) of Figitumumab

| End point title | Cycle 1: Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) of Figitumumab |
|---|---|

End point description:

Area under the plasma concentration time-curve from zero to the last measured concentration (AUClast) of figitumumab in cycle 1. PK samples were not analyzed as the study was terminated prematurely due to lack of operational feasibility and the halt of figitumumab development.

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

End point timeframe:

Days 1, 2, 8 and 15 of Cycle 1; Day 1 of subsequent cycle starting from Cycle 2 (up to Cycle 17); end of treatment ( 21 days after last dose of figitumumab); follow-up visit (90 days after last dose of figitumumab).

| End point values | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[11] | 0[12] | | |
| Units: nanogram*hours/milliliter (ng*hr/mL) | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[11] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.
[12] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) of Figitumumab

| End point title | Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) of Figitumumab |
|---|---|

End point description:

Area under the plasma concentration time-curve from zero to the last measured concentration (AUClast) of figitumumab after Cycle 1. PK samples were not analyzed as the study was terminated prematurely due to lack of operational feasibility and the halt of figitumumab development.

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

End point timeframe:

Cycle 2: Day 1 (within 2 hours before and 1 hour after figitumumab infusion); Cycle 3 to Cycle 17: Day 1 (within 2 hours before figitumumab infusion); end of treatment; 90-day follow-up visit.

| End point values | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[13] | 0[14] | | |
| Units: ng*hr/mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[13] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.
[14] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Trough Concentrations (AUCtrough)

| End point title | Area Under the Trough Concentrations (AUCtrough) |
|---|---|

End point description:

The trough concentration-time profile (AUCtrough) of pegvisomant was to be analyzed by noncompartmental methods. PK samples were not analyzed as the study was terminated prematurely

due to lack of operational feasibility and the halt of figitumumab development.

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

End point timeframe:

Cycle 1: Day 15 (within 2 hours before loading dose), Day 16 (within 2 hours pre-SC dose); Cycle 2: Days 1, 8 and 15 (within 2 hours pre-SC dose); Cycle 3 up to Cycle 17: Day 1 (within 2 hours pre-SC dose); end of treatment; 90-day follow-up visit.

| **End point values** | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[15] | 0[16] | | |
| Units: ng*hr/mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[15] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.
[16] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change in Glucose Levels Between Fasting and Post Glucose Load

| End point title | Mean Change in Glucose Levels Between Fasting and Post Glucose Load |
|---|---|

End point description:

The effect of combining figitumumab with pegvisomant was analyzed to assess whether pegvisomant reverses figitumumab-induced glucose intolerance at various pegvisomant dose levels. The change in glucose load was assessed by Glucose Tolerance Testing (GTT) at baseline (fasting), during Cycle 1 following administration of figitumumab alone (post load), and near the end of Cycle 2 (post load) following combined therapy with figitumumab and pegvisomant. Glucose tolerance set: All enrolled subjects who started treatment and who had at least one baseline or on-study sample submitted. n=number of subjects with analyzable data for this outcome measure at specific time point.

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

End point timeframe:

Screening; Day 8 of Cycle 1; Day 15 of Cycle 2

| **End point values** | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: milligram/deciliter (mg/dL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Screening (n = 17, 6) | 30.35 (± 34.02) | 4.67 (± 17.6) | | |
| Cycle 1 Day 8 (n = 15, 5) | 37.68 (± 30.95) | 15.4 (± 32.04) | | |

| | | | | |
|---|---|---|---|---|
| Cycle 2 Day 15 (n = 4, 5) | 55.15 (± 49.35) | 13.4 (± 28.35) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects Reporting Positive Anti-Drug Antibodies (ADA) Response for Figitumumab

| End point title | Percentage of Subjects Reporting Positive Anti-Drug Antibodies (ADA) Response for Figitumumab |
|---|---|

End point description:

Percentage of subjects with positive total or neutralizing ADA for figitumumab. ADA samples were not analyzed as the study was terminated prematurely due to lack of operational feasibility and the halt of figitumumab development.

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

End point timeframe:

Day 1 of Cycles 1 and 4; end of treatment (21 days after last dose of figitumumab); follow-up visit (90 days after last dose of figitumumab)

| End point values | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[17] | 0[18] | | |
| Units: percentage of subjects | | | | |

Notes:

[17] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.
[18] - Study was terminated due to lack of operational feasibility and the halt of figitumumab development.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects With Objective Response

| End point title | Number of subjects With Objective Response |
|---|---|

End point description:

Number of subjects with objective response based on assessment of confirmed complete response (CR) or confirmed partial response (PR) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Confirmed CR defined as disappearance of all target lesions. Confirmed PR defined as ≥30% decrease in sum of the longest dimensions (LD) of the target lesions taking as a reference the baseline sum LD according to RECIST version 1.1. Confirmed responses are those that persist on repeat imaging study ≥4 weeks after initial documentation of response. Response-evaluable set: All subjects who started Cycle 1 with an adequate baseline tumor assessment and at least 1 follow up tumor assessment were analysed for this outcome measure.

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

End point timeframe:

From Screening, odd numbered cycles (pre- dose, Cycle 3, 5, 7 etc.) up to Cycle 27 or end of treatment

| End point values | Figitumumab 20mg/kg + Pegvisomant 10 mg | Figitumumab 20mg/kg + Pegvisomant 20 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: subjects | 0 | 3 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AE and SAE were reported from first dose of the study treatment up to 90 -150 days after last dose of study treatment, death were reported from first dose of study treatment up to 28 days after last dose of study treatment

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Figitumumab 20 mg/kg + Pegvisomant 10 mg |

Reporting group description:

Figitumumab 20 mg/kg intravenously over 1 to 2.5 hours on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles, up to a maximum of 17 cycles (corresponding to 1 year). Pegvisomant 40 mg subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 10 mg subcutaneously once daily up to a maximum of 17 cycles (corresponding to 1 year). Each cycle was of 21 days.

| | |
|---|---|
| Reporting group title | Figitumumab 20 mg/kg + Pegvisomant 20 mg |

Reporting group description:

Figitumumab 20 mg/kg intravenously over 1 to 2.5 hours on Day 1 and 2 of Cycle 1 and on Day 1 of subsequent cycles (up to total duration of 27 cycles). Pegvisomant 40 mg subcutaneously on Day 15 of Cycle 1 or Day 1 of Cycle 2 and thereafter pegvisomant 20 mg subcutaneously once daily up to total duration of 27 cycles. Each cycle was of 21 days.

| **Serious adverse events** | Figitumumab 20 mg/kg + Pegvisomant 10 mg | Figitumumab 20 mg/kg + Pegvisomant 20 mg | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 17 (52.94%) | 4 / 6 (66.67%) | |
| number of deaths (all causes) | 2 | 0 | |
| number of deaths resulting from adverse events | 1 | 0 | |
| Investigations | | | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Nervous system disorders | | | |
| Cauda equina syndrome | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Medical device complication | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disease progression | | | |
| subjects affected / exposed | 4 / 17 (23.53%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Flank pain | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pelvic infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Figitumumab 20 mg/kg + Pegvisomant 10 mg | Figitumumab 20 mg/kg + Pegvisomant 20 mg | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 17 (100.00%) | 6 / 6 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Vaginal neoplasm | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Pelvic venous thrombosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Chest pain | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 2 / 6 (33.33%) | |
| occurrences (all) | 4 | 6 | |
| Disease progression | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Exercise tolerance decreased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fatigue | | | |
| subjects affected / exposed | 13 / 17 (76.47%) | 4 / 6 (66.67%) | |
| occurrences (all) | 18 | 8 | |

| | | | |
|---|---|---|---|
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Chills | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Injection site reaction | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Medical device pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Necrosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 2 | |
| Injection site induration | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Thirst | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Pain | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 2 | |

| | | | |
|---|---|---|---|
| Immune system disorders | | | |
| Contrast media allergy | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Reproductive system and breast disorders | | | |
| Vaginal ulceration | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Atrophic vulvovaginitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 4 / 17 (23.53%) | 1 / 6 (16.67%) | |
| occurrences (all) | 7 | 1 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hiccups | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 1 / 6 (16.67%) | |
| occurrences (all) | 4 | 3 | |
| Dysphonia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 2 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pulmonary congestion | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Wheezing | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Depression | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 3 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood creatinine increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 17 (17.65%) | 2 / 6 (33.33%) | |
| occurrences (all) | 5 | 2 | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 10 | 0 | |
| Blood albumin decreased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 1 / 6 (16.67%) | |
| occurrences (all) | 4 | 3 | |
| Insulin-like growth factor increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 2 / 6 (33.33%) | |
| occurrences (all) | 0 | 3 | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Weight decreased | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 3 / 6 (50.00%) | |
| occurrences (all) | 6 | 5 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Weight increased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Contusion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 5 | |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Fall | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Nervous system disorders | | | |
| Dyskinesia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Dysgeusia | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 0 / 6 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Facial nerve disorder | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Convulsion | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Headache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 17 (11.76%) | 2 / 6 (33.33%) | |
| occurrences (all) | 7 | 3 | |
| Intracranial pressure increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Paraesthesia mucosal | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Sensory disturbance | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 2 | |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 2 / 6 (33.33%) | |
| occurrences (all) | 2 | 2 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ear and labyrinth disorders | | | |
| Ear discomfort | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 17 (5.88%) | 2 / 6 (33.33%) | |
| occurrences (all) | 2 | 2 | |
| Hearing impaired | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Sudden hearing loss | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 1 | |
| Dry mouth | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 7 / 17 (41.18%) | 4 / 6 (66.67%) | |
| occurrences (all) | 7 | 5 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 2 / 6 (33.33%) | |
| occurrences (all) | 0 | 3 | |
| Abdominal pain lower | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Constipation | | | |
| subjects affected / exposed | 5 / 17 (29.41%) | 2 / 6 (33.33%) | |
| occurrences (all) | 6 | 5 | |
| Flatulence | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Gastric ulcer | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eructation | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Erosive oesophagitis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 2 / 6 (33.33%) | |
| occurrences (all) | 0 | 2 | |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 3 / 6 (50.00%) | |
| occurrences (all) | 2 | 9 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 17 (52.94%) | 2 / 6 (33.33%) | |
| occurrences (all) | 13 | 3 | |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 17 (23.53%) | 1 / 6 (16.67%) | |
| occurrences (all) | 8 | 1 | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Alopecia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nail disorder | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ecchymosis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Pruritus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Skin disorder | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Pruritus generalised | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal and urinary disorders | | | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Bone swelling | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Back pain | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 3 / 6 (50.00%) | |
| occurrences (all) | 2 | 3 | |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Flank pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Muscle spasms | | | |
| subjects affected / exposed | 5 / 17 (29.41%) | 3 / 6 (50.00%) | |
| occurrences (all) | 6 | 5 | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 6 (16.67%) | |
| occurrences (all) | 6 | 1 | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 3 | |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Infections and infestations | | | |
| Fungal infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 4 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Paronychia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |

| | | | |
|---|---|---|---|
| Pelvic infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 6 (16.67%) | |
| occurrences (all) | 3 | 1 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 2 / 6 (33.33%) | |
| occurrences (all) | 0 | 7 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 5 / 17 (29.41%) | 0 / 6 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Dehydration | | | |
| subjects affected / exposed | 4 / 17 (23.53%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 9 / 17 (52.94%) | 2 / 6 (33.33%) | |
| occurrences (all) | 11 | 3 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Hyperkalaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 25 May 2010 | 1) Gamma-glutamyl transpeptidase (GGT) assessment was added to the Safety Laboratory tests, in addition fasting glucose assessment was modified from 4 hours to 8 hours. |
| 02 May 2011 | Safety Laboratory parameters assessment was modified to be performed and reviewed prior to beginning of each new cycle of therapy. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated prematurely due to lack of operational feasibility and the halt of figitumumab development.

Notes: