



Clinical trial results:

Dose-escalation, PK and safety study with single agent CetuGEXTM in patients with locally advanced and/or metastatic cancer.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2010-019552-50 |
| Trial protocol | DE |
| Global end of trial date | 14 November 2013 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 25 April 2019 |
| First version publication date | 25 April 2019 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | GEXMab52101 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01222637 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Glycotope GmbH |
| Sponsor organisation address | Robert-Roessle-Str. 10, Berlin, Germany, 13125 |
| Public contact | Dr. Alfredo Zurlo, Glycotope GmbH, 030 94892600, alfredo.zurlo@glycotope.com |
| Scientific contact | Dr. Alfredo Zurlo, Glycotope GmbH, 030 94892600, alfredo.zurlo@glycotope.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 | 16 March 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 November 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 November 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

•To evaluate the safety and tolerability profile of CetuGEXTM at various dose levels •To define the recommended phase II dose and regimen

Protection of trial subjects:

The safety data during the study were monitored on a continued basis by an Independent Drug Safety Monitoring Board (DSMB) comprising of 3 experienced physicians. In general, the DSMB provided recommendations if the study could continue as planned in the study protocol, if changes were needed from a safety point of view, or if the maximum tolerated dose (MTD) was reached.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 25 August 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 | Germany: 26 |
| Country: Number of subjects enrolled | Italy: 6 |
| Country: Number of subjects enrolled | Switzerland: 9 |
| Worldwide total number of subjects | 41 |
| 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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 27 |
| From 65 to 84 years | 14 |

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

Subject disposition

Recruitment

Recruitment details:

Date of first enrollment: 25 Aug 2010

Date of last completed: 14 Nov 2013

Pre-assignment

Screening details:

Male or female patients equal or greater 18 years of age with a histologically confirmed locally advanced and/or metastatic solid organ tumor. Patients enrolled in Germany were required to have a positive EGFR overexpression status. Patients must have experienced a failure or non-availability of standard therapy.

Period 1

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

Blinding implementation details:

no blinding

Arms

| | |
|-----------|---------|
| Arm title | CetuGEX |
|-----------|---------|

Arm description:

no other arm

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

Dosage and administration details:

Weekly doses of 12 mg, 60 mg, 120 mg, 240 mg, 480 mg, 720 mg, 990 mg, or 1370 mg CetuGEX™ or dosing every 2 weeks of 990 mg CetuGEX™ administered by an intravenous Infusion.

| Number of subjects in period 1 | CetuGEX |
|--------------------------------|---------|
| Started | 41 |
| Completed | 41 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Intent-to-treat |
|-----------------------|-----------------|

Reporting group description: -

| Reporting group values | Intent-to-treat | Total | |
|------------------------|-----------------|-------|--|
| Number of subjects | 41 | 41 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults >= 18 years | 41 | 41 | |
| Age continuous | | | |
| Adults >= 18 years | | | |
| Units: years | | | |
| arithmetic mean | 59.8 | | |
| standard deviation | ± 10.53 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 12 | 12 | |
| Male | 29 | 29 | |

End points

End points reporting groups

| | |
|--|---------|
| Reporting group title | CetuGEX |
| Reporting group description: no other arm | |

Primary: safety profile adverse event

| | |
|------------------------|---|
| End point title | safety profile adverse event ^[1] |
| End point description: | |

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

End point timeframe:

All adverse events occurring after the patient entered the study until 28+2 days following the last infusion have been reported.

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: The number and percentage of patients with treatment-emergent adverse events (TEAEs) were summarized for each cohort and in total for each dosing scheme by system organ class (SOC) and preferred term (PT).

| End point values | CetuGEX | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: numbers | 41 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics

| | |
|------------------------|------------------|
| End point title | Pharmacokinetics |
| End point description: | |

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

End point timeframe:

2 Treatment Cycles

| End point values | CetuGEX | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: milligram(s) | | | | |
| number (not applicable) | 41 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: preliminary evaluation of anti-tumor activity

| | |
|-----------------|---|
| End point title | preliminary evaluation of anti-tumor activity |
|-----------------|---|

End point description:

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

End point timeframe:

every 8 weeks until tumor progression

| End point values | CetuGEX | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: millimeter(s) | | | | |
| number (not applicable) | 41 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurring after the patient entered the study until 28+2 days following the last infusion have been reported.us

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 13.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | Safety |
|-----------------------|--------|

Reporting group description:

The Intent-to-Treat (ITT) Population included any patient who was enrolled in a cohort and received any amount of study drug.

| Serious adverse events | Safety | | |
|--|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 14 / 41 (34.15%) | | |
| number of deaths (all causes) | 7 | | |
| number of deaths resulting from adverse events | 4 | | |
| Vascular disorders | | | |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vena cava thrombosis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Death | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 1 / 4 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 5 / 41 (12.20%) | | |
| occurrences causally related to treatment / all | 4 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stent malfunction | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Safety | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 41 / 41 (100.00%) | | |
| Investigations | | | |
| Blood magnesium decreased | | | |
| subjects affected / exposed | 5 / 41 (12.20%) | | |
| occurrences (all) | 17 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 5 / 41 (12.20%) | | |
| occurrences (all) | 5 | | |
| Vascular disorders | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 9 / 41 (21.95%) | | |
| occurrences (all) | 13 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | | |
| occurrences (all) | 7 | | |
| General disorders and administration site conditions | | | |
| Nausea | | | |
| subjects affected / exposed | 13 / 41 (31.71%) | | |
| occurrences (all) | 32 | | |
| Vomiting | | | |
| subjects affected / exposed | 12 / 41 (29.27%) | | |
| occurrences (all) | 32 | | |
| ECOG status worsened | | | |
| subjects affected / exposed | 12 / 41 (29.27%) | | |
| occurrences (all) | 22 | | |
| Fatigue | | | |
| subjects affected / exposed | 11 / 41 (26.83%) | | |
| occurrences (all) | 20 | | |
| Asthenia | | | |
| subjects affected / exposed | 9 / 41 (21.95%) | | |
| occurrences (all) | 19 | | |
| Pyrexia | | | |
| subjects affected / exposed | 9 / 41 (21.95%) | | |
| occurrences (all) | 14 | | |

| | | | |
|--|--|--|--|
| General physical health deterioration subjects affected / exposed occurrences (all) | 5 / 41 (12.20%) 6 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 7 / 41 (17.07%) 15 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) | 10 / 41 (24.39%) 14 8 / 41 (19.51%) 10 7 / 41 (17.07%) 8 | | |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) | 10 / 41 (24.39%) 16 10 / 41 (24.39%) 15 | | |
| Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Dermatitis acneiform subjects affected / exposed occurrences (all) dry skin | 10 / 41 (24.39%) 23 12 / 41 (29.27%) 30 10 / 41 (24.39%) 33 | | |

| | | | |
|--|-----------------------|--|--|
| subjects affected / exposed occurrences (all) | 6 / 41 (14.63%) 7 | | |
| Pruritus subjects affected / exposed occurrences (all) | 5 / 41 (12.20%) 9 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 9 / 41 (21.95%) 13 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 7 / 41 (17.07%) 14 | | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 6 / 41 (14.63%) 10 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 6 / 41 (14.63%) 8 | | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 8 / 41 (19.51%) 10 | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 6 / 41 (14.63%) 20 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported