# Clinical trial results:
# An open-label, multicenter rollover study to provide continued treatment with anetumab ravtansine for participants with solid tumors who were enrolled in previous Bayer-sponsored studies

## Summary

| | |
|---|---|
| EudraCT number | 2019-000061-20 |
| Trial protocol | FR BE PL IT |
| Global end of trial date | 18 May 2022 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 14 May 2023 |
| First version publication date | 14 May 2023 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 20322 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03926143 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368 |
| Public contact | Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.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 | 18 May 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 May 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 May 2022 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

This study was a rollover study to permit subjects who received anetumab ravtansine in an applicable Bayer sponsored anetumab ravtansine parent study to continue treatment or follow-up at the time of parent study closure.
Main objective is safety.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 03 June 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Poland: 2 |
| Country: Number of subjects enrolled | United States: 6 |
| Worldwide total number of subjects | 10 |
| EEA total number of subjects | 4 |

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) | 6 |
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 7 study centers in 4 countries worldwide between 03-Jun-2019 (first subject first visit) and 18-May-2022 (last subject last visit).

### Pre-assignment

Screening details:

A total of 10 subjects were screened in this study; of whom 9 subjects started study treatment and 1 subject was a screening failure. Entering subjects had to have been treated with anetumab ravtansine in an applicable Bayer sponsored anetumab ravtansine parent study.

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | Anetumab ravtansine |

Arm description:

Adult subjects with solid tumors who received anetumab-ravtansine treatment as monotherapy, or in combination with gemcitabine in an applicable Bayer-sponsored anetumab ravtansine study.
8 subjects received anetumab ravtansine monotherapy and 1 subject received anetumab ravtansine in combination with gemcitabine. Pooled results were reported.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Gemcitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Gemcitabine as per the dosing instructions from the parent study protocol.

| | |
|---|---|
| Investigational medicinal product name | Anetumab ravtansine |
| Investigational medicinal product code | BAY94-9343 |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Anetumab ravtansine as per the dosing instructions from the parent study protocol in an every 3 weeks (Q3W) schedule.

| **Number of subjects in period 1[1]** | Anetumab ravtansine |
|---|---|
| Started | 9 |
| Completed | 0 |
| Not completed | 9 |
| Physician decision | 3 |
| Adverse event, non-fatal | 2 |

| | |
|---|---|
| Subject decision: Covid-19 Pandemic related | 1 |
| Progressive disease | 3 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: In total, 10 subjects were enrolled and 9 subjects started the treatment.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Anetumab ravtansine |

Reporting group description:

Adult subjects with solid tumors who received anetumab-ravtansine treatment as monotherapy, or in combination with gemcitabine in an applicable Bayer-sponsored anetumab ravtansine study.
8 subjects received anetumab ravtansine monotherapy and 1 subject received anetumab ravtansine in combination with gemcitabine. Pooled results were reported.

| Reporting group values | Anetumab ravtansine | Total | |
|---|---|---|---|
| Number of subjects | 9 | 9 | |
| Age Categorical<br>Units: Subjects | | | |
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | <br><br>50.7<br>± 16.2 | <br><br><br>- | |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 3 | 3 | |
| Male | 6 | 6 | |
| Race<br>Units: Subjects | | | |
| White | 6 | 6 | |
| Asian | 2 | 2 | |
| Not reported | 1 | 1 | |
| Ethnicity<br>Units: Subjects | | | |
| Unknown or Not Reported | 9 | 9 | |

## End points

### End points reporting groups

| Reporting group title | Anetumab ravtansine |
|---|---|

Reporting group description:

Adult subjects with solid tumors who received anetumab-ravtansine treatment as monotherapy, or in combination with gemcitabine in an applicable Bayer-sponsored anetumab ravtansine study.
8 subjects received anetumab ravtansine monotherapy and 1 subject received anetumab ravtansine in combination with gemcitabine. Pooled results were reported.

### Primary: Number of subjects with TEAEs, TESAEs and Drug-related TEAEs and TESAEs

| End point title | Number of subjects with TEAEs, TESAEs and Drug-related TEAEs and TESAEs[1] |
|---|---|

End point description:

Treatment emergent adverse events (TEAEs) were defined as AEs starting or worsening during the treatment period. The treatment period extended from the first date of study treatment in this study until the safety follow-up (30 days after the last administration of study treatment). TESAEs: Treatment emergent serious adverse events.

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

End point timeframe:

Approximately 3 years (from first study treatment until safety follow-up)

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: As study was small and incoming population was heterogeneous and subject to selection bias, no inferential statistical analysis was performed.

| End point values | Anetumab ravtansine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: Subjects | | | | |
| Any TEAE | 9 | | | |
| Serious TEAE | 2 | | | |
| Any study drug-related TEAE | 8 | | | |
| Any study drug-related Serious TEAE | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival

| End point title | Overall survival |
|---|---|

End point description:

Overall survival (OS) defined as the time from first treatment in this study until death from any cause. Data on survival were collected by the site. Time frame was reduced due to early termination of the study. Table reports Kaplan-Meier median with Brookmeyer-Crowley confidence intervals. 99999

indicates value cannot be estimated due to censored data.

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

End point timeframe:

Approximately 3 years (from first study treatment until safety follow-up)

| **End point values** | Anetumab ravtansine | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9[2] | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| 25th percentile | 17.6 (6.9 to 34.1) | | | |
| Median | 34.1 (6.9 to 99999) | | | |
| 75th percentile | 99999 (28.5 to 99999) | | | |

Notes:

[2] - Number of subjects: with event (5) and censored (4)

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

For TEAE: After the first study intervention up to 30 days after the end of study intervention, approximately 2 years. For the deaths (all causes) considers all deaths that occurred at any time during the study before the last contact.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Anetumab ravtansine |

Reporting group description:

Adult patients with solid tumors who received anetumab-ravtansine treatment as monotherapy,or in combination with gemcitabine in an applicable Bayer-sponsored anetumab ravtansine study.
8 subjects received anetumab ravtansine monotherapy and 1 subject received anetumab ravtansine in combination with gemcitabine. Pooled results were reported.

| Serious adverse events | Anetumab ravtansine | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| number of deaths (all causes) | 5 | | |
| number of deaths resulting from adverse events | 0 | | |
| Cardiac disorders | | | |
| Restrictive cardiomyopathy | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Infections and infestations<br>Urosepsis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | <br><br>1 / 9 (11.11%)<br>0 / 1<br>0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | Anetumab ravtansine | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | <br>9 / 9 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>Transitional cell carcinoma<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 9 (11.11%)<br>1 | | |
| Vascular disorders<br>Hypotension<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 9 (11.11%)<br>1 | | |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br>Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)<br>Chest pain<br>subjects affected / exposed<br>occurrences (all)<br>Asthenia<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 9 (11.11%)<br>1<br><br>2 / 9 (22.22%)<br>3<br><br>1 / 9 (11.11%)<br>1<br><br>2 / 9 (22.22%)<br>2 | | |
| Reproductive system and breast disorders<br>Gynaecomastia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 2 | | |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 6 | | |
| Schirmer's test abnormal | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Transaminases increased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Weight decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>4 | | |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>2 | | |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all) | 2 / 9 (22.22%)<br>3 | | |
| Blood thyroid stimulating hormone increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | | |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>2 | | |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | | |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>3 | | |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all) | 2 / 9 (22.22%)<br>3 | | |
| Injury, poisoning and procedural complications | | | |
| Corneal abrasion<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | | |
| Foot fracture<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>1 | | |
| Cardiac disorders | | | |
| Restrictive cardiomyopathy<br>subjects affected / exposed<br>occurrences (all) | 1 / 9 (11.11%)<br>2 | | |
| Pericardial effusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 6 | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 3 | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 3 | | |
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 9 (55.56%) | | |
| occurrences (all) | 10 | | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Keratitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Corneal epithelial microcysts | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Corneal disorder | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Toothache | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 2 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 2 | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Muscle spasms | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 2 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Skin infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | | |
| occurrences (all) | 2 | | |
| Cachexia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | | |
| occurrences (all) | 1 | | |

## 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

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

Due to the small sample size and heterogeneous population, survival distributions and the extent of long-term survival in the applicable populations cannot be reliably estimated from the study results.

Notes: