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	v2 (current)
This version publication date	28 June 2023
First version publication date	14 May 2023
Version creation reason	• Correction of full data set Correction for AE timeframe is needed.

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 Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 50.7 ± 16.2	 -	
Gender Categorical Units: Subjects			
Female	3	3	
Male	6	6	
Race Units: Subjects			
White	6	6	
Asian	2	2	
Not reported	1	1	
Ethnicity 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 3 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 Urosepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 9 (11.11%) 0 / 1 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 subjects affected / exposed	 9 / 9 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Transitional cell carcinoma subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1		
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1		
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all)	 2 / 9 (22.22%) 3 1 / 9 (11.11%) 1 2 / 9 (22.22%) 2 1 / 9 (11.11%) 1		
Reproductive system and breast disorders Gynaecomastia			

subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pleural effusion			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Investigations			
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	1 / 9 (11.11%)		
occurrences (all)	4		
Neutrophil count decreased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Lipase increased			

subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Blood bilirubin increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	3		
Amylase increased			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
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		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Corneal abrasion			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

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

subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	2 / 9 (22.22%) 2 1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Infections and infestations Skin infection subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1 1 / 9 (11.11%) 2 1 / 9 (11.11%) 1		
Metabolism and nutrition disorders Cachexia subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all)	 1 / 9 (11.11%) 1 2 / 9 (22.22%) 2 1 / 9 (11.11%) 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: