Clinical trial results:
A Phase II Study of Cabazitaxel for Patients with Breast or Lung Cancer and Recurrent or Progressive Brain Metastases - Cabazitaxel for Brain Metastases

Summary

EudraCT number	2013-005545-37
Trial protocol	DE
Global end of trial date	27 January 2017

Results information

Result version number	v1 (current)
This version publication date	24 October 2021
First version publication date	24 October 2021

Trial information

Trial identification

Sponsor protocol code	AIO-ZNS-0113 (CaBaMet)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02166658
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AIO-Studien-gGmbH
Sponsor organisation address	Kuno-Fischer-Str. 8, Berlin, Germany, 14057
Public contact	Sponsor, AIO-Studien-gGmbH, 0049 30814534431, info@aio-studien-ggmbh.de
Scientific contact	Sponsor, AIO-Studien-gGmbH, 0049 30814534431, info@aio-studien-ggmbh.de

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	06 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 January 2017
Global end of trial reached?	Yes
Global end of trial date	27 January 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Objective tumor response of brain metastases (BM)

Protection of trial subjects:

This study was planned, analyzed and conducted according to the study protocol and in accordance with the International Conference on Harmonization (ICH) ‚Guideline for Good Clinical Practice E6(R1)', CPMP/ICH/135/95, based on the principles of the Declaration of Helsinki (1964) and its October 1996 amendment (Somerset West, South Africa), as well as the German Arzneimittelgesetz (AMG; German Drug Law), and the corresponding Directive 2001/20/EC. Subjects were fully informed regarding all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 September 2015
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	Germany: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	2
From 65 to 84 years	6

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited between September 2015 and January 2017 at six different sites in Germany. Planned sample size, using a two-stage trial design, was 29 or 63 patients. Recruitment was low, leading to early trial termination.

Pre-assignment

Screening details:

Selected inclusion criteria: Adult patients (≥ 18 years of age), Histologically or cytologically confirmed stage IV lung or breast cancer with progressive or recurrent brain metastases, ECOG status 0-2, At least one two-dimensional measurable lesion on brain MRI

Period 1

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

Arms

Arm title	Overall trial

Arm description:

Cabazitaxel 25 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle until disease progression (PD) or discontinuation due to AE or death (from any cause).

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

Dosage and administration details:

Cabazitaxel 25 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle

Number of subjects in period 1	Overall trial
Started	8
Completed	8

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description:

Cabazitaxel 25 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle until disease progression (PD) or discontinuation due to AE or death (from any cause).

Reporting group values	Overall trial	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	2	
From 65-84 years	6	6	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	67.4		
full range (min-max)	49 to 76	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	1	1	
Primary tumor Units: Subjects			
NSCLC	3	3	
SCLC	4	4	
Breast cancer	1	1	

Subject analysis sets

Subject analysis set title	Overall trial
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects enrolled in the study

Reporting group values	Overall trial		
Number of subjects	8		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	2		
From 65-84 years	6		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
full range (min-max)			
Gender categorical			
Units: Subjects			
Female	7		
Male	1		
Primary tumor			
Units: Subjects			
NSCLC	3		
SCLC	4		
Breast cancer	1		

End points

End points reporting groups

Reporting group title	Overall trial
Reporting group description:	
Cabazitaxel 25 mg/m^2 intravenous (IV) infusion on Day 1 of each 21-day cycle until disease progression (PD) or discontinuation due to AE or death (from any cause).	
Subject analysis set title	Overall trial
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects enrolled in the study	

Primary: Objective tumor response of brain metastases

End point title	Objective tumor response of brain metastases[1]

End point description:

Objective tumor response of brain metastases was defined as complete response [CR] or partial response [PR] or at least a minor response [MR; 25-50% reduction] according to WHO criteria and Iwamoto et al. [2008] confirmed by magnetic resonance imaging [MRI].

No objective response of brain metastases was documented in any of the eight patients. Two patients had stable diseases (SD) as best overall response, and two patients had progressive disease (PD). For four patients, no post-baseline tumor assessment could be conducted as they died before assessment. Thus, response rate is 0.0%.

End point type	Primary

End point timeframe:

From baseline until disease progression (PD, assessment Q6W) or death from any cause

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 trial was ended prematurely due to low recruitment, and the sample size is too small for any meaningful statistical analysis.

End point values	Overall trial			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Subjects				
CR	0			
PR	0			
SD	2			
PD	2			
not evaluated	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival for brain metastases

End point title	Progression-free survival for brain metastases

End point description:

End point type	Secondary

End point timeframe:

From first day of first treatment cycle until disease progression (PD, assessment Q6W) or death from any cause

End point values	Overall trial			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: days				
median (confidence interval 95%)	43.5 (10.0 to 75.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival for extracerebral tumor disease

End point title	Progression-free survival for extracerebral tumor disease

End point description:

End point type	Secondary

End point timeframe:

From first day of first treatment cycle until disease progression (PD, assessment Q6W) or death from any cause

End point values	Overall trial			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: days				
median (confidence interval 95%)	50.0 (10.0 to 142.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

From first day of first treatment cycle until death from any cause

End point values	Overall trial			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: days				
median (confidence interval 95%)	59.0 (10.0 to 142.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Failure

End point title	Time to Treatment Failure

End point description:

End point type	Secondary

End point timeframe:

From first day of first treatment cycle until discontinuation of cabazitaxel for any reason

End point values	Overall trial			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: days				
median (confidence interval 95%)	22 (1.0 to 60.0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of informed consent until death (7 patients) or lost-to-follow-up (1 patient).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Overall study

Reporting group description: -

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	3		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Leucopenia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Disease progression			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Performance status decreased				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Infections and infestations				
Lung infection				
subjects affected / exposed	1 / 8 (12.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 8 (12.50%)			
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	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Condition aggravated			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Gait disturbance			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Candida infection			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

Investigations C-reactive protein increased subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Nervous system disorders Ataxia subjects affected / exposed occurrences (all) Burning sensation subjects affected / exposed occurrences (all) Cerebral haemorrhage subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Granulocytopenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 2 / 8 (25.00%) 2 4 / 8 (50.00%) 4		

Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 2 / 8 (25.00%) 2		
Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 2 / 8 (25.00%) 2		
Infections and infestations Bronchopneumonia subjects affected / exposed occurrences (all) Moraxella infection subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Metabolism and nutrition disorders			

Cachexia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Decreased appetite subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Dehydration subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2		

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.

The trial was terminated prematurely with only 8 subjects recruited. Planned sample size, using a two-stage trial desing, was 29 or 63 subjects.

Notes: