Clinical trial results:
PHASE II STUDY OF LUTETIUM-177 LABELED CHIMERIC MONOCLONAL ANTIBODY cG250 (177Lu-DOTA-cG250) TREATMENT IN PATIENTS WITH ADVANCED RENAL CANCER

Summary

EudraCT number	2008-004548-35
Trial protocol	NL
Global end of trial date	03 August 2015

Results information

Result version number	v1 (current)
This version publication date	23 August 2024
First version publication date	23 August 2024
Summary attachment (see zip file)	Synopsis acc ICH e3 177Lutetium_cG250 in RCC Phase II clinical trial (Synopsis acc ICH e3 177Lutetium_cG250 in RCC Phase II clinical trial.pdf)

Trial information

Trial identification

Sponsor protocol code	15081982

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02002312
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Radboud University Medical Centre
Sponsor organisation address	Geert Groote plein Zuid 10, Nijmegen, Nijmegen, Netherlands, 6525GA
Public contact	RadboudUMC, RadboudUMC, +31 243613735, secretariaat.uro@radboudumc.nl
Scientific contact	RadboudUMC, RadboudUMC, +31 243613735, secretariaat.uro@radboudumc.nl

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	03 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 August 2015
Global end of trial reached?	Yes
Global end of trial date	03 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the clinical efficacy of multiple doses of 177Lutetium-girentuximab (177Lu-cG250) at MTD in patients with advanced renal cancer using RECIST criteria.

Protection of trial subjects:

Patients who fulfilled the selection criteria:
Inclusion Criteria:
- Patients with proven advanced and progressive renal cell carcinoma of the clear cell type
- At least one evaluable lesion less than 5 cm
- Performance status: Karnofsky > 70 %
- Laboratory values obtained less than 14 days prior to registration:
- White blood cells (WBC) > 3.5 x 109/l
- Platelet count > 100 x 109/l
- Hemoglobin > 6 mmol/l
- Total bilirubin < 2 x upper limit of normal (ULN)
- ASAT, ALAT < 3 x ULN (< 5 x ULN if liver metastases present)
- Serum creatinine < 2 x ULN
- Negative pregnancy test for women of child¬bearing potential (urine or serum)
- Age over 18 years
- Ability to provide written informed consent

Exclusion Criteria:
- Known metastases to the brain
- Untreated hypercalcemia
- Metastatic disease limited to the bone
- Pre-exposure to murine/chimeric antibody
- Chemotherapy, external beam radiation, immunotherapy or angiogenesis inhibitors within 4 weeks prior to study. Limited field external beam radiotherapy to prevent pathological fractures is allowed, when unirradiated, evaluable lesions elsewhere are present.
- Cardiac disease with New York Heart Association classification of III or IV
- Patients who are pregnant, nursing or of reproductive potential and are not practicing an effective method of contraception
- Any unrelated illness, e.g. active infection, inflammation, medical condition or laboratory abnormalities, which in the judgment of the investigator will significantly affect patients' clinical status
- Life expectancy shorter than 6 months.

Patients were controlled as follows:
- Wk 1: screening and injection 111In-cG250 (day 1) and 2 scans (day 2-4 and 5-7)
- Wk 2: injection 177Lu-cG250 and subsequent hospital admission for 1 night only
- Wk 3 until 8: Weekly visit UMCN for blood draw and physical exam.
- W 3 - 6: during fulminant hematological toxicity increased checks laboratory values
- Wk 12: CT-scan and Wk 13: blood draw

Background therapy:

not applicable

Evidence for comparator:

not applicable

Actual start date of recruitment	01 August 2011
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	Netherlands: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total, 16 adult patients with metastatic clear cell renal cell carcinoma (ccRCC) were enrolled between August 2011 and April 2014 to participate in this Study if metastasis showed targeting of diagnostic imaging.

Pre-assignment

Screening details:

After screening 2 patients were excluded from the study because known ccRCC lesions did not show any targeting at diagnostic imaging postinjection of indium 111 (111In)–girentuximab. 14 patients who showed
targeting at scans postinjection of indium 111 (111In)–girentuximab were eligible for treatment with 177Lutetium-girentuximab.

Period 1

Period 1 title	Cycle 1
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

No blinding was chosen in this first pilot study of treatment with 177Lutetium-girentuximab.

Arms

Arm title	Cycle 1

Arm description:

In Cycle 1, 14 patients started treatment with 177Lutetium-cG250 at a dose level of 2405 MBq/m2.

Arm type	Experimental
Investigational medicinal product name	cG250
Investigational medicinal product code	
Other name	LUTETIUM-177 LABELED CHIMERIC MONOCLONAL ANTIBODY cG250; 177Lu-DOTA-cG250; 177Lutetium-girentuximab
Pharmaceutical forms	Solution for injection in administration system
Routes of administration	Intravenous use

Dosage and administration details:

In Cycle 1, 14 patients received 177Lutetium cG2502 at a dose of 2405 MBq/m2.

Number of subjects in period 1	Cycle 1
Started	14
completed Cycle 1	14
Completed	14

Period 2	
Period 2 title	Evaluation results Cycle 1
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Eligible to start in Cycle 2

Arm description:

To evaluate if patients were eligible for treatment in Cycle 2

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Eligible to start in Cycle 2
Started	14
Evaluation of Cycle 1	14
Completed	6
Not completed	8
Adverse event, non-fatal	3
Lack of efficacy	5

Period 3	
Period 3 title	Cycle 2
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

In Cycle 2, 6 patients started treatment with 177Lutetium-cG250 at a dose level of 1805 MBq/m2.

Arms

Arm title	Cycle 2

Arm description:

In Cycle 2, 6 patients started treatment with 177Lutetium-cG250 at a dose level of 1805 MBq/m2.

Arm type	Experimental
Investigational medicinal product name	cG250
Investigational medicinal product code	
Other name	LUTETIUM-177 LABELED CHIMERIC MONOCLONAL ANTIBODY cG250; 177Lu-DOTA-cG250; 177Lutetium-girentuximab
Pharmaceutical forms	Solution for injection in administration system
Routes of administration	Intravenous use

Dosage and administration details:

In Cycle 2, 14 patients received 177Lutetium cG2502 at a dose of 1805 MBq/m2.

Number of subjects in period 3	Cycle 2
Started	6
completed Cycle 2	6
Completed	6

Period 4	
Period 4 title	Evaluation results Cycle 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Eligible to start in Cycle 3

Arm description:

To evaluate if patients were eligible for treatment in Cycle 3

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 4	Eligible to start in Cycle 3
Started	6
Completed	0
Not completed	6
Adverse event, non-fatal	5
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Cycle 1
Reporting group description:	
In Cycle 1, 14 patients started treatment with 177Lutetium-cG250 at a dose level of 2405 MBq/m2.	

Reporting group values	Cycle 1	Total	
Number of subjects	14	14	
Age categorical			
14 patients were treated according to protocol with a median age of 68 years; range: 56-75 years.			
Units: Subjects			
Adults (18-64 years)	6	6	
From 65-84 years	8	8	
Gender categorical			
Gender			
Units: Subjects			
Female	5	5	
Male	9	9	

End points

End points reporting groups

Reporting group title	Cycle 1
Reporting group description:	
In Cycle 1, 14 patients started treatment with 177Lutetium-cG250 at a dose level of 2405 MBq/m2.	
Reporting group title	Eligible to start in Cycle 2
Reporting group description:	
To evaluate if patients were eligible for treatment in Cycle 2	
Reporting group title	Cycle 2
Reporting group description:	
In Cycle 2, 6 patients started treatment with 177Lutetium-cG250 at a dose level of 1805 MBq/m2.	
Reporting group title	Eligible to start in Cycle 3
Reporting group description:	
To evaluate if patients were eligible for treatment in Cycle 3	

Primary: Clinical response 3 months after treatment

End point title	Clinical response 3 months after treatment[1]
End point description:	
End point type	Primary
End point timeframe:	
Clinical response was evaluated 3 months after treatment by using CT scanning and evaluation according to RECIST v1.1.	

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: A Simon two-stage minimax design was used to calculate the no. of patients needed to reach a desirable response rate (RR) defined as at least Stable Disease (RECIST v1.1). If RR >0.25 after the first cycle of treatment in the first 6 patients after 3 months, 14 patients had to be included. Desirable RR was set at 0.65 with alpha of 0.05 and beta of 0.10. Response was defined as at least SD on RECIST v1.1 evaluation after 3 months. After 6 patients RR was 0.5 so 14 patients were included.

End point values	Eligible to start in Cycle 2	Eligible to start in Cycle 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	6		
Units: 14				
PR	1	1		
SD	8	4		
PD	5	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity of treatment 12 weeks after treatment

End point title	Toxicity of treatment 12 weeks after treatment

End point description:

End point type	Secondary

End point timeframe:

Patients were monitored at least once a week for 12 weeks for hematological toxicity (using Common Toxicity Criteria for Adverse Events v.3.0)

End point values	Eligible to start in Cycle 2	Eligible to start in Cycle 3		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[2]	6[3]		
Units: 14				
CTC hematological toxicity Grade 0,1 or 2	1	1		
CTC hematological toxicity Grade 3 or 4	13	5		

Notes:

[2] - 14 patients received Cycle 1

[3] - 6 patients received Cycle 2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were evaluated the whole study period.

Adverse event reporting additional description:

Adverse events were evaluated using the Common Toxicity Criteria V3.0

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	v3

Reporting groups

Reporting group title	Per Protocol reporting group

Reporting group description:

All 14 patients who received treatment according to the protocol were in the intention to treat reporting group for adverse event reporting.

Serious adverse events	Per Protocol reporting group		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 14 (50.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Investigations			
prolonged hospital stay	Additional description: Prolonged hospital stay without clear system organ class		
subjects affected / exposed	2 / 14 (14.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cell carcinoma	Additional description: One patient died due to progression of Renal cell carcinoma.		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
facialis paresis	Additional description: One patient developed a one-sided facialis parese. This patient also had a thrombocytopenia and leucopenia. This event was considered unexpected.		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Neutropenia	Additional description: A total of 2 patients were hospitalised with fever and shivers due to neutropenia. Treated with antibiotics. One patient was hospitalised with severe neutropenia for observation only.		
subjects affected / exposed	3 / 14 (21.43%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
thrombocytopenia	Additional description: One patient was hospitalised for thrombocytopenia and received thrombocytes suppletion. Another patient prolonged hospitalisation for 2 days due to thrombocytopenia.		
subjects affected / exposed	2 / 14 (14.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Confusional state	Additional description: One patient was hospitalised in a confusional state, possibly due to cerebral vascular infarction. This event was considered unexpected.		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism	Additional description: One patient was hosptitalised due to a pulmonary embolism. This event was considered as unexpected.		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypercalcaemia of malignancy	Additional description: prolonged hospital stay for observation hypercalcaemia possibly due to progressive disease		
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Per Protocol reporting group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
General disorders and administration site conditions			

Fatigue	Additional description: A total of 13 patients experienced mild (grade 1-2) general adverse events such as fatigue, anorexia, nausea, and diarrhea. Only two patients had grade 3 general adverse events, 1 with fatigue and 1 with anorexia.		
subjects affected / exposed	14 / 14 (100.00%)		
occurrences (all)	14		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26706103