



Clinical trial results:

Androgen receptor and estrogen receptor imaging in metastatic breast cancer patients (FDHT FESPET / ARER)

Summary

EudraCT number	2012-003981-42
Trial protocol	NL
Global end of trial date	10 September 2015

Results information

Result version number	v1 (current)
This version publication date	14 July 2022
First version publication date	14 July 2022

Trial information

Trial identification

Sponsor protocol code	2012.2708
-----------------------	-----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01988324
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Groningen
Sponsor organisation address	Hanzeplein 1, Groningen, Netherlands,
Public contact	Department of Medical Oncology, University Medical Center Groningen, +31 503616161, g.a.p.hospers@umcg.nl
Scientific contact	Department of Medical Oncology, University Medical Center Groningen, +31 503616161, g.a.p.hospers@umcg.nl
Sponsor organisation name	VUMC
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands,
Public contact	Department of Medical Oncology, VUMC, +31 2044444444, e.boven@vumc.nl
Scientific contact	Department of Medical Oncology, VUMC, +31 2044444444, e.boven@vumc.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	01 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 September 2015
Global end of trial reached?	Yes
Global end of trial date	10 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To visualize and quantify androgen receptor and estrogen receptor expression by PET imaging with the tracers 18F-FDHT and 18F-FES respectively.

Protection of trial subjects:

Other than infrequent transient intravenous site discomfort, no adverse events have been noted in current published - FES PET and FDHT PET studies. Radiation exposure by the two PET imaging studies is 11.0 mSv. According to the investigators this radiation burden is justifiable, in this patient group with metastatic disease, by the information that can be obtained in this study. Tumor biopsy will be performed from an easy accessible lesion, and location will be determined based on safety aspects. The risk for significant complications and mortality from tumor biopsy is low: 0.24-1.6% and 0.11-0.48% for major complications and mortality respectively. The combined imaging techniques may show lesions that were previously unknown or may show changes in ER-expression. When biopsy confirms the presence of the metastasis and/ or confirms altered ER-expression, this may have therapeutic consequences (e.g. radiotherapy, bisphosphonates for previously unknown bone metastases, or altered systemic therapy). Therefore information obtained during this study may have beneficial effects for the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 September 2014
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: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	9
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

21 patients were included between September 2014 and August 2015
13 were evaluable for the primary endpoint

Pre-assignment

Screening details:

21 patients were included between September 2014 and August 2015
13 were evaluable for the primary endpoint

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	Hormone receptor imaging
-----------	--------------------------

Arm description:

Hormone receptor imaging

Arm type	Experimental
Investigational medicinal product name	16-alpha-[18F]fluoro-17-beta-estradiol
Investigational medicinal product code	18F-FES
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

222 MBq per day

Number of subjects in period 1	Hormone receptor imaging
Started	13
Completed	13

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
-----------------------	---------------

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	13	13	
Age categorical			
Units: Subjects			
Adults (18-64 years)	9	9	
From 65-84 years	4	4	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	2	2	

End points

End points reporting groups

Reporting group title	Hormone receptor imaging
Reporting group description:	
Hormone receptor imaging	

Primary: The concordance between PET (with 18F-FDHT and 18F-FES), and immunohistochemistry (for AR and ER) on concurrent (within 8 weeks) tumor biopsy will be evaluated.

End point title	The concordance between PET (with 18F-FDHT and 18F-FES), and immunohistochemistry (for AR and ER) on concurrent (within 8 weeks) tumor biopsy will be evaluated. ^[1]
-----------------	---

End point description:

FDHT PET and FES PET will be qualitatively assessed. The nuclear medicine physician visually identifies lesions with increased tracer uptake, above background signal, which cannot be attributed to an artefact or physiological uptake.

Next, 18F-FDHT, and 18F-FES-uptake will be quantified for all individual tumor lesions observed according to the European Association of Nuclear Medicine (EANM) guidelines and recorded as standardized uptake value. CT-scan and bone scan will be used to identify metastases >10 mm that were not detected on PET. The uptake of these lesions will also be quantified.

The sensitivity and specificity of qualitatively scored FDHT PET will be calculated using immunohistochemistry of a biopsied lesion as golden standard. Receiver operating characteristic (ROC) analysis will be used to determine the quantitative threshold (SUVmax/mean) that optimally differentiates between AR-positive and AR-negative lesions.

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

End point timeframe:

within 2 months

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: See enclosed publication

End point values	Hormone receptor imaging			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: SUV	13			

Statistical analyses

No statistical analyses for this end point

Secondary: The number of lesions detected on PET imaging compared to CT-scan and bone scintigraphy.

End point title	The number of lesions detected on PET imaging compared to CT-scan and bone scintigraphy.
-----------------	--

End point description:

278 lesions could be used for ER imaging

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

End point timeframe:
within 6 weeks

End point values	Hormone receptor imaging			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: suv	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Inter- and intra-patient variation in tumor FDHT and FES-uptake will be calculated.

End point title	Inter- and intra-patient variation in tumor FDHT and FES-uptake will be calculated.
-----------------	---

End point description:

in total 278 lesions could be used for ER analysis

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

End point timeframe:

within 6 weeks

End point values	Hormone receptor imaging			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: SUV	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Inter-observer variation in FES PET and FDHT PET results in two independent observers.

End point title	Inter-observer variation in FES PET and FDHT PET results in two independent observers.
-----------------	--

End point description:

in total 278 lesions could be used for ER analysis

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

End point timeframe:
approximately 2 months

End point values	Hormone receptor imaging			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: SUV	13			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

All (serious) adverse events occurring during the study or which comes to the attention of the investigator within 28 days after the study, whether considered treatment-related or not, must be reported.

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

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Frequency threshold for reporting non-serious adverse events: 2 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: See enclosed publication

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 August 2014	PI change in participating center

Notes:

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.

n.a.

Notes: