



## 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

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### 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. <sup>[1]</sup> |
|-----------------|---|

#### 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 |
|----------------|-----------|

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End point timeframe:  
approximately 2 months

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|                             |                                |  |  |  |
|-----------------------------|--------------------------------|--|--|--|
| <b>End point values</b>     | Hormone<br>receptor<br>imaging |  |  |  |
| Subject group type          | Reporting group                |  |  |  |
| Number of subjects analysed | 13                             |  |  |  |
| Units: SUV                  | 13                             |  |  |  |

### Statistical analyses

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No statistical analyses for this end point



## Adverse events

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### Adverse events information<sup>[1]</sup>

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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 %

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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:

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### 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: