



## Clinical trial results:

### Early identification of patients who benefit from palbociclib in addition to letrozole

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2015-004231-12    |
| Trial protocol           | NL                |
| Global end of trial date | 28 September 2022 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 08 February 2023 |
| First version publication date | 08 February 2023 |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | NL20151001 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02806050 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | University Medical Center Groningen   |
| Sponsor organisation address | Hanzeplein 1, Groningen, Netherlands, 9713 GZ   |
| Public contact               | CP Schröder, University Medical Center Groningen, +31 503616161, c.p.schroder@umcg.nl |
| Scientific contact           | CP Schröder, University Medical Center Groningen, +31 503616161, c.p.schroder@umcg.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                       | 28 September 2022 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 28 September 2022 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 28 September 2022 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate in a feasibility study whether low uptake on FES-PET at baseline is related to non response to letrozole plus palbociclib treatment.

Protection of trial subjects:

All patients will receive an effective treatment combination. In addition to the standard control visits to the clinic, three extra visits will be performed as part of the study: for screening, for the FES-PET scan and for the early FDG-PET. The FESPET scan will induce an extra radiation burden of 6.1 mSv and the early FDG-PET 5 mSv. In the future, this study may potentially contribute to improved selection of patients for this combination treatment. This is of relevance in view of optimal treatment for individual patients, avoiding unnecessary toxicity and financial burden.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 16 September 2016 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                 |
|--------------------------------------|-----------------|
| Country: Number of subjects enrolled | Netherlands: 29 |
| Worldwide total number of subjects   | 29              |
| EEA total number of subjects         | 29              |

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)                      | 20 |
| From 65 to 84 years                       | 9  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

31 patients were included in the study, 29 patients completed the study.

2 patients discontinued the study prematurely:

- 1 patient had dural metastases therefore no response PET/CT scan was performed
- 1 patient had elevated liver enzymes, therefore a response PET/CT was performed after 1 cycle (instead of after 2 cycles), progressive disease

### Pre-assignment

Screening details:

See enclosed paper

### Period 1

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

### Arms

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Palbociclib and FES PET |
|------------------|-------------------------|

Arm description:

To evaluate whether low uptake on FES-PET at baseline is related to non-response to letrozole plus palbociclib treatment.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | 18F-FES                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

total 200 MBq

|  |               |
|--|---------------|
| Investigational medicinal product name | Palbociclib   |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

per day 125 mg

|                                       |                         |
|---------------------------------------|-------------------------|
| <b>Number of subjects in period 1</b> | Palbociclib and FES PET |
| Started                               | 29                      |
| Completed                             | 29                      |



## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values | overall trial | Total |  |
|------------------------|---------------|-------|--|
| Number of subjects     | 29            | 29    |  |
| Age categorical        |               |       |  |
| Units: Subjects        |               |       |  |
| Adults (18-64 years)   | 20            | 20    |  |
| From 65-84 years       | 9             | 9     |  |
| Gender categorical     |               |       |  |
| Units: Subjects        |               |       |  |
| Female                 | 29            | 29    |  |
| Male                   | 0             | 0     |  |

### Subject analysis sets

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Palbociclib and FES PET |
|----------------------------|-------------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:  
study population

| Reporting group values | Palbociclib and FES PET |  |  |
|------------------------|-------------------------|--|--|
| Number of subjects     | 29                      |  |  |
| Age categorical        |                         |  |  |
| Units: Subjects        |                         |  |  |
| Adults (18-64 years)   | 20                      |  |  |
| From 65-84 years       | 9                       |  |  |
| Gender categorical     |                         |  |  |
| Units: Subjects        |                         |  |  |
| Female                 | 29                      |  |  |
| Male                   | 0                       |  |  |

## End points

### End points reporting groups

|   |                         |
|---|-------------------------|
| Reporting group title   | Palbociclib and FES PET |
| Reporting group description:<br>To evaluate whether low uptake on FES-PET at baseline is related to non-response to letrozole plus palbociclib treatment. |                         |
| Subject analysis set title  | Palbociclib and FES PET |
| Subject analysis set type   | Full analysis           |
| Subject analysis set description:<br>study population   |                         |

### Primary: The relation between low uptake on FES-PET to response per lesion

|  |  |
|--|--|
| End point title  | The relation between low uptake on FES-PET to response per lesion <sup>[1]</sup> |
| End point description:   |  |
| End point type   | Primary  |
| End point timeframe:<br>8 weeks after start of treatment   |  |
| Notes:<br>[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.<br>Justification: See enclosed paper |  |

| End point values            | Palbociclib and FES PET | Palbociclib and FES PET |  |  |
|-----------------------------|-------------------------|-------------------------|--|--|
| Subject group type          | Reporting group         | Subject analysis set    |  |  |
| Number of subjects analysed | 29                      | 29                      |  |  |
| Units: SUV                  | 29                      | 29                      |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: quantitative FES-uptake and correlation with progression free survival

|                                  |  |
|----------------------------------|--|
| End point title                  | quantitative FES-uptake and correlation with progression free survival |
| End point description:           |  |
| End point type                   | Secondary  |
| End point timeframe:<br>6 months |  |

| End point values            | Palbociclib and FES PET | Palbociclib and FES PET |  |  |
|-----------------------------|-------------------------|-------------------------|--|--|
| Subject group type          | Reporting group         | Subject analysis set    |  |  |
| Number of subjects analysed | 29                      | 29                      |  |  |
| Units: SUV                  | 29                      | 29                      |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: analysis of circulating tumor DNA and correlation with FES-PET results and progression free survival

|                 |  |
|-----------------|--|
| End point title | analysis of circulating tumor DNA and correlation with FES-PET results and progression free survival |
|-----------------|--|

End point description:

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

End point timeframe:

6 months

| End point values            | Palbociclib and FES PET | Palbociclib and FES PET |  |  |
|-----------------------------|-------------------------|-------------------------|--|--|
| Subject group type          | Reporting group         | Subject analysis set    |  |  |
| Number of subjects analysed | 29                      | 29                      |  |  |
| Units: SUV                  | 29                      | 29                      |  |  |

### Statistical analyses

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:

During the study

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

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### Dictionary used

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|                 |       |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

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|                    |     |
|--------------------|-----|
| Dictionary version | 4.0 |
|--------------------|-----|

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Frequency threshold for reporting non-serious adverse events: 3 %

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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 paper

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 19 June 2017      | 1. Moving the FDG PET scan from 8 weeks to 2 weeks after the start of treatment.<br>2. Expand the number of patients from n=15 to n=30 for the implementation of point 1. Expanding the number of patients also enables further refinement of the FES-PET analysis: namely by adding a per-patient analysis with regard to response, in addition to the per-lesion analysis (the primary endpoint). |
| 14 August 2017    | update IMPD   |
| 12 February 2018  | 1. Expand inclusion of exclusively postmenopausal patients with also premenopausal patients, provided they are undergoing ovarian suppression with an LHRH analog<br>2. Textual adjustment in PIF and protocol that the combination treatment in The Netherlands is registered  |
| 21 August 2018    | Diagnostic change in follow-up, in which the CT scan every 3 months for measurable disease according to RECIST criteria 1.1 is cancelled  |
| 18 September 2018 | Update investigator's brochure palbociclib  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31891878>