



## Clinical trial results:

### The influence of UGT inhibition on endoxifen exposure in cancer patients treated with tamoxifen: A proof of concept study. "The PROTAM study"

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2019-004854-27 |
| Trial protocol           | NL             |
| Global end of trial date | 01 July 2021   |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 21 May 2022  |
| First version publication date    | 21 May 2022  |
| Summary attachment (see zip file) | Summary results (Buck et al. Influence of probenecid on endoxifen systemic exposure in breast cancer patients on adjuvant tamoxifen treatment.pdf) |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | PROTAM |
|-----------------------|--------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Erasmus MC  |
| Sponsor organisation address | Dr Molewaterplein 40, Rotterdam, Netherlands, 3015GD                      |
| Public contact               | R.H.J. Mathijssen, Erasmus MC Cancer Institute, a.mathijssen@erasmusmc.nl |
| Scientific contact           | R.H.J. Mathijssen, Erasmus MC Cancer Institute, a.mathijssen@erasmusmc.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                       | 05 May 2022  |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 01 July 2021 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 01 July 2021 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

To compare the Area under the curve (AUC) of endoxifen in patients with breast cancer treated with tamoxifen with and without probenecid.

Protection of trial subjects:

Interim analysis, monitoring and follow up by medical oncologists

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 01 March 2020 |
| 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: 11 |
| Worldwide total number of subjects   | 11              |
| EEA total number of subjects         | 11              |

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)                      | 11 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Metastatic breast cancer treated with tamoxifen

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 11 |
| Number of subjects completed | 11 |

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Tamoxifen (overall period)  |
| Is this the baseline period? | Yes                         |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

### Arms

|  |                        |
|--|------------------------|
| Arm title                              | tamoxifen + probenecid |
| Arm description: -                     |                        |
| Arm type                               | Experimental           |
| Investigational medicinal product name | tamoxifen + probenecid |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Tablet                 |
| Routes of administration               | Oral use               |

Dosage and administration details:

tamoxifen: 20mg qd

Probenecid: 1000mg bid

| Number of subjects in period 1 | tamoxifen + probenecid |
|--------------------------------|------------------------|
| Started                        | 11                     |
| Completed                      | 11                     |

## Baseline characteristics

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | Tamoxifen |
|-----------------------|-----------|

Reporting group description: -

| Reporting group values                             | Tamoxifen | Total |  |
|--|-----------|-------|--|
| Number of subjects                                 | 11        | 11    |  |
| 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)                               | 11        | 11    |  |
| From 65-84 years                                   | 0         | 0     |  |
| 85 years and over                                  | 0         | 0     |  |
| Adults   | 0         | 0     |  |
| Gender categorical                                 |           |       |  |
| Units: Subjects                                    |           |       |  |
| Female   | 11        | 11    |  |
| Male   | 0         | 0     |  |

### Subject analysis sets

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Endoxifen AUC0-24h |
|----------------------------|--------------------|

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

Subject analysis set description:

Endoxifen AUC0-24h with and without probenecid

| Reporting group values                             | Endoxifen AUC0-24h |  |  |
|--|--------------------|--|--|
| Number of subjects                                 | 11                 |  |  |
| 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)                               | 11                 |  |  |
| From 65-84 years                                   | 0                  |  |  |
| 85 years and over                                  | 0                  |  |  |
| Adults   | 0                  |  |  |

|                    |    |  |  |
|--------------------|----|--|--|
| Gender categorical |    |  |  |
| Units: Subjects    |    |  |  |
| Female             | 11 |  |  |
| Male               | 0  |  |  |

## End points

### End points reporting groups

|  |                        |
|--|------------------------|
| Reporting group title                          | tamoxifen + probenecid |
| Reporting group description: -                 |                        |
| Subject analysis set title                     | Endoxifen AUC0-24h     |
| Subject analysis set type                      | Full analysis          |
| Subject analysis set description:              |                        |
| Endoxifen AUC0-24h with and without probenecid |                        |

### Primary: Endoxifen AUC0-24h

|                        |                                   |
|------------------------|-----------------------------------|
| End point title        | Endoxifen AUC0-24h <sup>[1]</sup> |
| End point description: |                                   |

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| 0-24 hours           |         |

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: Commented on in attachment

| End point values                                       | tamoxifen +<br>probenecid | Endoxifen<br>AUC0-24h |  |  |
|--|---------------------------|-----------------------|--|--|
| Subject group type                                     | Reporting group           | Subject analysis set  |  |  |
| Number of subjects analysed                            | 11                        |                       |  |  |
| Units: ng*h/mL   |                           |                       |  |  |
| geometric mean (geometric coefficient<br>of variation) |                           |                       |  |  |
| tamoxifen  | 402 (± 43)                | 402 (± 43)            |  |  |
| tamoxifen + probenecid                                 | 505 (± 41)                | 505 (± 41)            |  |  |

### 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 probenecid treatment

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

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### Dictionary used

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

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|                    |   |
|--------------------|---|
| Dictionary version | 5 |
|--------------------|---|

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

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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: Commented on in attachment

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported