



## Clinical trial results:

### An Open Label Multi-Centre Preoperative Window of Opportunity Study of Afatinib in Stage Ia to IIb Non-Small Cell Lung Cancer

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-004537-16 |
| Trial protocol           | GB             |
| Global end of trial date | 01 August 2016 |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 28 December 2019   |
| First version publication date    | 28 December 2019   |
| Summary attachment (see zip file) | ABLE Termination Documentation (ABLE Endo of Trial Documentation MHRA 15Aug16.pdf) |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | MO11/10085 |
|-----------------------|------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | University of Leeds   |
| Sponsor organisation address | Worsley Building, Leeds, United Kingdom, LS2 9JT                                    |
| Public contact               | Dr Clive Mulatero, University of Leeds, 0113 2068650, clive.mulatero@leedsth.nhs.uk |
| Scientific contact           | Dr Clive Mulatero, University of Leeds, 0113 2068650, clive.mulatero@leedsth.nhs.uk |

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 August 2016 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 01 August 2016 |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 01 August 2016 |
| Was the trial ended prematurely?                     | Yes            |

Notes:

## General information about the trial

Main objective of the trial:

The principal research question is whether a reduction in the amount of energy the cancer uses can be seen when a short course of afatinib is given to early stage lung cancer patients before surgery?

Protection of trial subjects:

To assess safety and tolerability of preoperative afatinib was a secondary objective of the trial. The Trial was overseen by a Independent Data Monitoring committee and trial steering committee, was monitored by the Sponsor twice over it's life cycle, and was conducted in accordance with GCP. Each PI retains overall responsibility for the informed consent of participants at their site and must ensure that any person delegated responsibility to participate in the informed consent process is duly authorised, trained and competent to participate according to the ethically approved protocol, principles of Good Clinical Practice (GCP) and Declaration of Helsinki 1996.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 01 January 2013 |
| 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 | United Kingdom: 7 |
| Worldwide total number of subjects   | 7                 |
| EEA total number of subjects         | 7                 |

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)                      | 4 |
| From 65 to 84 years                       | 3 |

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

## Subject disposition

### Recruitment

Recruitment details:

Participants will be recruited from NHS hospitals in the UK. The annual recruitment target is 40 participants per year. Recruitment will be competitive between participating centres. Up to 69 eligible patients may be recruited in order that a total of 59 patients will complete the protocol specified treatment.

### Pre-assignment

Screening details:

Once written informed consent has been obtained and the participant has been registered, they must then be formally assessed for eligibility prior to commencing treatment. Patients identified as not eligible for trial treatment through eligibility screening will not be considered enrolled in the trial and will return to standard clinical care.

### Period 1

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

### Arms

|                              |              |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes          |
| <b>Arm title</b>             | Baseline Arm |

Arm description: -

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Afatinib     |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Afatinib (BIBW2992) at a dose of 50mg orally will be administered daily for at least two weeks prior to surgery and for a maximum of thirty days.

|                  |          |
|------------------|----------|
| <b>Arm title</b> | End Data |
|------------------|----------|

Arm description: -

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Afatinib     |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Afatinib (BIBW2992) at a dose of 50mg orally will be administered daily for at least two weeks prior to surgery and for a maximum of thirty days.

| <b>Number of subjects in period 1</b> | Baseline Arm | End Data |
|---------------------------------------|--------------|----------|
| Started                               | 1            | 6        |
| Completed                             | 1            | 6        |

## Baseline characteristics

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Main Trial Period |
|-----------------------|-------------------|

Reporting group description: -

| Reporting group values                                | Main Trial Period | Total |  |
|---|-------------------|-------|--|
| Number of subjects                                    | 7                 | 7     |  |
| Age categorical                                       |                   |       |  |
| Units: Subjects                                       |                   |       |  |
| In utero  | 0                 | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                 | 0     |  |
| Newborns (0-27 days)                                  | 0                 | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0                 | 0     |  |
| Children (2-11 years)                                 | 0                 | 0     |  |
| Adolescents (12-17 years)                             | 0                 | 0     |  |
| Adults (18-64 years)                                  | 4                 | 4     |  |
| From 65-84 years                                      | 3                 | 3     |  |
| 85 years and over                                     | 0                 | 0     |  |
| Gender categorical                                    |                   |       |  |
| Units: Subjects                                       |                   |       |  |
| Female  | 2                 | 2     |  |
| Male  | 5                 | 5     |  |

## End points

### End points reporting groups

|                                |              |
|--------------------------------|--------------|
| Reporting group title          | Baseline Arm |
| Reporting group description: - |              |
| Reporting group title          | End Data     |
| Reporting group description: - |              |

### Primary: prospectively evaluate whether changes in SUVmax can be observed with 18F-FDG PET/CT imaging after only two weeks of afatinib (BIBW2992) therapy.

|   |   |
|---|---|
| End point title                                 | prospectively evaluate whether changes in SUVmax can be observed with 18F-FDG PET/CT imaging after only two weeks of afatinib (BIBW2992) therapy. <sup>[1][2]</sup> |
| End point description:                          |   |
| End point type                                  | Primary   |
| End point timeframe:                            |   |
| after two weeks of afatinib (BIBW2992) therapy. |   |

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: The trial was terminated early and no data was collected on participants.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The trial was terminated early and no data was collected on participants.

| End point values            | End Data         |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[3]</sup> |  |  |  |
| Units: SUVmax               |                  |  |  |  |
| number (not applicable)     |                  |  |  |  |

Notes:

[3] - The trial was terminated early and no data was collected on participants.

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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

Timeframe for reporting adverse events:

Adverse events will be collected for all participants from the time of written informed consent until 30 days post cessation of trial therapy. All AEs will be monitored until resolution, or if the AE is determined to be chronic, until a cause is identified

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

### Dictionary used

|                    |       |
|--------------------|-------|
| Dictionary name    | CTCAE |
| Dictionary version | 4.0   |

### Reporting groups

|                                |              |
|--------------------------------|--------------|
| Reporting group title          | Baseline Arm |
| Reporting group description: - |              |
| Reporting group title          | End Data     |
| Reporting group description: - |              |

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: The trial was terminated early and no data was collected on participants.

| Serious adverse events                            | Baseline Arm  | End Data       |  |
|---|---|----------------|--|
| Total subjects affected by serious adverse events |   |                |  |
| subjects affected / exposed                       | 0 / 1 (0.00%)   | 1 / 6 (16.67%) |  |
| number of deaths (all causes)                     | 0   | 0              |  |
| number of deaths resulting from adverse events    | 0   | 0              |  |
| Blood and lymphatic system disorders              |   |                |  |
| Chyle Leak  | Additional description: Event was reported as a SUSAR |                |  |
| subjects affected / exposed                       | 0 / 1 (0.00%)   | 1 / 6 (16.67%) |  |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 1          |  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0          |  |

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

| Non-serious adverse events                            | Baseline Arm  | End Data      |  |
|---|---------------|---------------|--|
| Total subjects affected by non-serious adverse events |               |               |  |
| subjects affected / exposed                           | 0 / 1 (0.00%) | 0 / 6 (0.00%) |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 04 March 2013    | Protocol version 4.0 dated 1st March 2013<br>Main PIS and consent version 4.0 dated 1st March 2013<br>GP letter version 4.0 dated 1st March 2013<br>Revised label version 4.0<br>Investigator Brochure version 13 dated 11 July 2012   |
| 16 April 2013    | Protocol version 5.0 dated 11 April 2013   |
| 29 November 2013 | Protocol version 6.2 dated 25 November 2013<br>Main patient information sheet and consent version 6.0 dated 25 November 2013<br>Patient information sheet and consent version 3.0 dated 9 May 2013<br>GP letter version 5.1 dated 25 November 2013<br>Diary card version 3.0 dated 27 September 2013 |
| 18 December 2014 | Protocol v 7.0   |
| 16 March 2016    | Protocol version 8.0, Amendment 6, 27 January 2016<br>PIS version 7.0, 27 January 2016<br>GP Letter version 6.0, 27 January 2016   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported