# Clinical trial results:
# MIMEB - Molecular Imaging with erlotinib and bevacizumab. A Phase II Clinical Trial to Evaluate the Accuracy of FDG-/FLT-PET and DCE-MRI for Early Prediction of Non-Progression in Patients with Advanced Non Squamous Cell Non Small Cell Lung Cancer (NSCLC) treated with Erlotinib and Bevacizumab and to Associate Imaging Findings with Molecular Markers

## Summary

| | |
|---|---|
| EudraCT number | 2009-012607-26 |
| Trial protocol | DE |
| Global end of trial date | 23 November 2013 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 15 May 2021 |
| First version publication date | 15 May 2021 |
| Summary attachment (see zip file) | Final_Report_MIMEB (MIMEB_Final_report_23.06.2020_F.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | MIMEB |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01047059 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | University of Cologne |
| Sponsor organisation address | Albertus-Magnus-Platz, Cologne, Germany, 50923 |
| Public contact | Jürgen Wolf, Lung Cancer Group Cologne, juergen.wolf@uk-koeln.de |
| Scientific contact | Matthias Scheffler, University of Cologne, matthias.scheffler@uk-koeln.de |

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 | 23 November 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 23 November 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 November 2013 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the accuracy of imaging findings in FDG-/FLT-PET and DCE-MRI after one week of treatment for early prediction of RECIST-based non-progression (CR+PR+SD) after 6 weeks of therapy in patients with NSCLC stage IIIb/IV treated first line with erlotinib and bevacizumab.

To evaluate the accuracy of imaging findings in FDG-/FLT-PET and DCE-MRI after one week of treatment for early prediction of PFS in patients with NSCLC stage IIIb/IV treated first line with erlotinib and bevacizumab.

Protection of trial subjects:

All patients had trial insurance as demanded by the Arzneimittelgesetz (AMG).

Background therapy:

n/a

Evidence for comparator:

n/a

| | |
|---|---|
| Actual start date of recruitment | 18 January 2010 |
| 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 | Germany: 40 |
| Worldwide total number of subjects | 40 |
| EEA total number of subjects | 40 |

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) | 25 |
| From 65 to 84 years | 15 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Monocentric recruitment in Cologne, Germany.

### Pre-assignment

Screening details:

18.01.2010 - 23.11.2013 in Cologne.

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | Treatment arm |

Arm description:

Erlotinib and Bevacizumab in St. IV NSCLC; early and late FLT-, FDG-PET and DCE-MRI

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

Dosage and administration details:

Tablets administrated once per day.

| | |
|---|---|
| Investigational medicinal product name | Bevacizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Infusions q3 weeks.

| **Number of subjects in period 1** | Treatment arm |
|---|---|
| Started | 40 |
| Completed | 40 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Overall period |
|---|---|

Reporting group description: -

| Reporting group values | Overall period | Total | |
|---|---|---|---|
| Number of subjects | 40 | 40 | |
| Age categorical<br>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) | 25 | 25 | |
| From 65-84 years | 15 | 15 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| median | 60 | | |
| full range (min-max) | 30 to 76 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 16 | 16 | |
| Male | 24 | 24 | |

### Subject analysis sets

| Subject analysis set title | Intention-to-treat |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

All pateints that were included into the study

| Reporting group values | Intention-to-treat | | |
|---|---|---|---|
| Number of subjects | 40 | | |
| Age categorical<br>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) | 25 | | |

| | | | |
|---|---|---|---|
| From 65-84 years | 15 | | |
| 85 years and over | 0 | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years | | | |
| median | 60 | | |
| full range (min-max) | 30 to 76 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 16 | | |
| Male | 24 | | |

## End points

### End points reporting groups

| Reporting group title | Treatment arm |
|---|---|
| Reporting group description: | |
| Erlotinib and Bevacizumab in St. IV NSCLC; early and late FLT-, FDG-PET and DCE-MRI | |
| Subject analysis set title | Intention-to-treat |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All pateints that were included into the study | |

### Primary: Changes in SUV

| End point title | Changes in SUV |
|---|---|

End point description:

Percentaged changes (proposed reductions) in the SUVs of PET images after one week of therapy as compared with the baseline assessment were compared with the response outcome (i. e., PD vs non-PD) in the first restaging procedure after six weeks of com-bined therapy. The related changes were analyzed using a responder-operator-characteristics (ROC) curve and the corresponding area under the curve (AUC).
The maximal Youden-indices found in these analyses were then taken as cut-off values for Kaplan Meier analyses regarding PFS. Further, we tested predefined cut-off values (20%, 30% reductions in PET activities) regarding their potential role in discriminating patients with benefit from therapy as seen in prolonged PFS.

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

End point timeframe:

18.01.2010 - 23.11.2013

| End point values | Treatment arm | Intention-to-treat | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 40 | 40 | | |
| Units: n/a | | | | |
| number (not applicable) | | | | |
| Response | 40 | 40 | | |

### Statistical analyses

| Statistical analysis title | Sample size calculation |
|---|---|

Statistical analysis description:

Assumptions:
(1) 20% responder, 40% progressers; thus 60% non-progressers
(2) Primary variable is the ‘area under the ROC curve (AUC, )’
(3) Type-I-error 0.043; type-II-error 0.20
(4) True accuracy (AUC) is at least 0.70 (alternative hypothesis; some common diagnostic tests have an AUC greater than 0.70)
The sample size in the following table was calculated using formulae (6.3) and (6.6) in [118]. Thus, assuming Sigma1 = 0.75, about 40 patients are needed to reject the null hypothesis.

| Comparison groups | Treatment arm v Intention-to-treat |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.05 |
| Method | Responser Operator Characteristics (ROC) |
| Parameter estimate | Youden-Index |

## Adverse events

| Adverse events information[1] | |
|---|---|
| Timeframe for reporting adverse events: 18.01.2010 - 23.11.2013 | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 16 |

Frequency threshold for reporting non-serious adverse events: 0 %

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: AE analysis is provided in summary.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported