

**Clinical trial results:****A Multicentre, Randomized, Double-blind, Parallel Group, Placebo-controlled, Phase III Efficacy and Safety Study of Benralizumab (MEDI-563) Added to Medium-dose Inhaled Corticosteroid Plus Long-acting 2 Agonist in Patients with Uncontrolled Asthma (PAMPERO)****Summary**

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-002352-32 |
| Trial protocol           | DE PL SE BG    |
| Global end of trial date | 22 July 2014   |

**Results information**

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 01 February 2017 |
| First version publication date | 06 August 2015   |

**Trial information****Trial identification**

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | D3250C00016 |
|-----------------------|-------------|

**Additional study identifiers**

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

Notes:

**Sponsors**

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AZ-PPD  |
| Sponsor organisation address | Granta Park, Great Ablington, Cambridge, United Kingdom, CB21 6GQ       |
| Public contact               | Peggy Snowden, Astrazeneca, 1 3013980466, Peggy.snoden@astrazeneca.com  |
| Scientific contact           | Steven Fox, AZ-PPD, 44 1480716682, steven.fox@ppdi.com                  |
| Sponsor organisation name    | Astrazeneca   |
| Sponsor organisation address | 1 MedImmune Way, Gaithersburg, MD, United States, 20878                 |
| Public contact               | Peggy Snowden, Astrazeneca, 1 3013980466, peggy.snowden@astrazeneca.com |
| Scientific contact           | Curt Johnson, Astrazeneca, 1 3013980466, Curt.johnson@astrazeneca.com   |

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                       | 12 June 2015 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 22 July 2014 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 22 July 2014 |
| Was the trial ended prematurely?                     | Yes          |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effect of two dosing regimens of benralizumab on asthma exacerbations in adult patients with uncontrolled asthma.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference on Harmonisation/Good Clinical Practice (GCP) and applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples. The investigator at each center ensured that the patient, parent, guardian, or legal representative (as appropriate) was given full and adequate oral and written information about the nature, purpose, possible risk, and benefit of the study. The patient, parent, guardian, or legal representative (as appropriate) were notified that they were free to discontinue from the study at any time and were given the opportunity to ask questions and allowed time to consider the information provided.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 20 November 2013 |
| 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 | United States: 13 |
| Worldwide total number of subjects   | 13                |
| EEA total number of subjects         | 0                 |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 11 |
| From 65 to 84 years       | 2  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The study was stopped with 13 patients randomised

### Pre-assignment

Screening details:

13 patients were enrolled and 13 were randomised

### Pre-assignment period milestones

|                              |                    |
|------------------------------|--------------------|
| Number of subjects started   | 130 <sup>[1]</sup> |
| Number of subjects completed | 13                 |

### Pre-assignment subject non-completion reasons

|                            |  |
|----------------------------|--|
| Reason: Number of subjects | Sponsor decision to terminate study: 117 |
|----------------------------|--|

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of subjects enrolled is smaller because the study was terminated.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Overall Study (overall period)                                |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Benra 30 mg q.4 weeks |
|------------------|-----------------------|

Arm description:

Fixed 30 mg dose of benralizumab (every 4 weeks)

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Benralizumab  |
| Investigational medicinal product code | MEDI-563  |
| Other name                             | aa  |
| Pharmaceutical forms                   | Concentrate and solvent for solution for injection/infusion |
| Routes of administration               | Subcutaneous use  |

Dosage and administration details:

30 mg q.4

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | Benra 30 mg-Placebo q.8 weeks |
|------------------|-------------------------------|

Arm description:

Fixed 30 mg dose of belralizumab (every 4 weeks for the first 3 doses and then every 8 weeks thereafter)

|  |   |
|--|---|
| Arm type                               | Experimental                                      |
| Investigational medicinal product name | Benralizumab                                      |
| Investigational medicinal product code | MEDI-563  |
| Other name                             | aa  |
| Pharmaceutical forms                   | Concentrate and solvent for solution for infusion |
| Routes of administration               | Subcutaneous use                                  |

Dosage and administration details:

30 mg q.8

|  |   |
|--|---|
| <b>Arm title</b>                       | Placebo   |
| Arm description:                       |   |
| A (Dummy) injection                    |   |
| Arm type                               | Placebo   |
| Investigational medicinal product name | placebo   |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Concentrate for solution for injection/infusion |
| Routes of administration               | Subcutaneous use                                |
| Dosage and administration details:     |   |
| 30 mg                                  |   |

| <b>Number of subjects in period 1</b> | Benra 30 mg q.4 weeks | Benra 30 mg-Placebo q.8 weeks | Placebo |
|---------------------------------------|-----------------------|-------------------------------|---------|
| Started                               | 3                     | 5                             | 5       |
| Completed                             | 3                     | 5                             | 5       |

## Baseline characteristics

### Reporting groups

|  |                               |
|--|-------------------------------|
| Reporting group title  | Benra 30 mg q.4 weeks         |
| Reporting group description:<br>Fixed 30 mg dose of benralizumab (every 4 weeks)   |                               |
| Reporting group title  | Benra 30 mg-Placebo q.8 weeks |
| Reporting group description:<br>Fixed 30 mg dose of belralizumab (every 4 weeks for the first 3 doses and then every 8 weeks thereafter) |                               |
| Reporting group title  | Placebo                       |
| Reporting group description:<br>A (Dummy) injection  |                               |

| Reporting group values                             | Benra 30 mg q.4 weeks | Benra 30 mg-Placebo q.8 weeks | Placebo |
|--|-----------------------|-------------------------------|---------|
| Number of subjects                                 | 3                     | 5                             | 5       |
| Age categorical<br>Units: Subjects                 |                       |                               |         |
| In utero   | 0                     | 0                             | 0       |
| Preterm newborn infants (gestational age < 37 wks) | 0                     | 0                             | 0       |
| Newborns (0-27 days)                               | 0                     | 0                             | 0       |
| Infants and toddlers (28 days-23 months)           | 0                     | 0                             | 0       |
| Children (2-11 years)                              | 0                     | 0                             | 0       |
| Adolescents (12-17 years)                          | 0                     | 0                             | 0       |
| Adults (18-64 years)                               | 2                     | 4                             | 5       |
| From 65-84 years                                   | 1                     | 1                             | 0       |
| 85 years and over                                  | 0                     | 0                             | 0       |
| Age Continuous  <br>Units: years                   |                       |                               |         |
| arithmetic mean                                    | 58.7                  | 57.8                          | 49.6    |
| standard deviation                                 | ± 15.7                | ± 6.38                        | ± 6.35  |
| Gender, Male/Female<br>Units: Male/Female          |                       |                               |         |
| Female   | 2                     | 4                             | 5       |
| Male   | 1                     | 1                             | 0       |

| Reporting group values                             | Total |  |  |
|--|-------|--|--|
| Number of subjects                                 | 13    |  |  |
| 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)  | 11 |  |  |
| From 65-84 years  | 2  |  |  |
| 85 years and over   | 0  |  |  |
| Age Continuous  <br>Units: years<br>arithmetic mean<br>standard deviation | -  |  |  |
| Gender, Male/Female<br>Units: Male/Female                                 |    |  |  |
| Female  | 11 |  |  |
| Male  | 2  |  |  |

## End points

### End points reporting groups

|  |                               |
|--|-------------------------------|
| Reporting group title  | Benra 30 mg q.4 weeks         |
| Reporting group description:<br>Fixed 30 mg dose of benralizumab (every 4 weeks)   |                               |
| Reporting group title  | Benra 30 mg-Placebo q.8 weeks |
| Reporting group description:<br>Fixed 30 mg dose of belralizumab (every 4 weeks for the first 3 doses and then every 8 weeks thereafter) |                               |
| Reporting group title  | Placebo                       |
| Reporting group description:<br>A (Dummy) injection  |                               |

### Primary: Asthma exacerbations over 48 weeks treatment

|  |   |
|--|---|
| End point title  | Asthma exacerbations over 48 weeks treatment <sup>[1]</sup> |
| End point description:   |   |
| End point type   | Primary   |
| End point timeframe:<br>48 weeks 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: Owing to the insufficient sample size no statistical analyses were performed . |   |

| End point values            | Benra 30 mg q.4 weeks | Benra 30 mg-Placebo q.8 weeks | Placebo         |  |
|-----------------------------|-----------------------|-------------------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group               | Reporting group |  |
| Number of subjects analysed | 3                     | 5                             | 5               |  |
| Units: Number of events     | 0                     | 0                             | 0               |  |

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

57 days was the maximum duration experienced by a patient, since the study was stopped early.

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Benra 30 mg q.4 weeks |
|-----------------------|-----------------------|

Reporting group description:

Fixed 30 mg dose of benralizumab (every 4 weeks)

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

A (Dummy) injection

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Benra 30 mg-Placebo q.8 weeks |
|-----------------------|-------------------------------|

Reporting group description:

Fixed 30 mg dose of belralizumab (every 4 weeks for the first 3 doses and then every 8 weeks thereafter)

| Serious adverse events                            | Benra 30 mg q.4 weeks | Placebo       | Benra 30 mg-Placebo q.8 weeks |
|---|-----------------------|---------------|-------------------------------|
| Total subjects affected by serious adverse events |                       |               |                               |
| subjects affected / exposed                       | 0 / 3 (0.00%)         | 0 / 5 (0.00%) | 0 / 5 (0.00%)                 |
| number of deaths (all causes)                     | 0                     | 0             | 0                             |
| number of deaths resulting from adverse events    | 0                     | 0             | 0                             |

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

| Non-serious adverse events                            | Benra 30 mg q.4 weeks | Placebo        | Benra 30 mg-Placebo q.8 weeks |
|---|-----------------------|----------------|-------------------------------|
| Total subjects affected by non-serious adverse events |                       |                |                               |
| subjects affected / exposed                           | 0 / 3 (0.00%)         | 1 / 5 (20.00%) | 0 / 5 (0.00%)                 |
| Respiratory, thoracic and mediastinal disorders       |                       |                |                               |
| Prolonged expiration                                  |                       |                |                               |
| alternative assessment type: Non-systematic           |                       |                |                               |
| subjects affected / exposed                           | 0 / 3 (0.00%)         | 1 / 5 (20.00%) | 0 / 5 (0.00%)                 |
| occurrences (all)                                     | 0                     | 1              | 0                             |



## 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? Yes

| Date         | Interruption                  | Restart date |
|--------------|-------------------------------|--------------|
| 22 July 2014 | Sponsor decision to terminate | -            |

Notes:

### Limitations and caveats

None reported