



## Clinical trial results:

### The impact of proton-pump inhibitors (antacids) on threshold dose distributions

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-001863-38 |
| Trial protocol           | ES             |
| Global end of trial date | 30 June 2018   |

#### Results information

|                                   |                                    |
|-----------------------------------|------------------------------------|
| Result version number             | v1 (current)                       |
| This version publication date     | 12 April 2021                      |
| First version publication date    | 12 April 2021                      |
| Summary attachment (see zip file) | Summary (201500186338_SUMMARY.pdf) |

#### Trial information

##### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | iFAAM-PPIwalnut |
|-----------------------|-----------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Fundación Investigación Biomédica Hospital Clínico San Carlos  |
| Sponsor organisation address | Profesor Martín Lagos s/n, Madrid, Spain, 28040  |
| Public contact               | UICEC, Fundación para la investigación biomédica Hospital Clínico San Carlos, +34 9133030007360, fibucicec.hcsc@salud.madrid.org |
| Scientific contact           | UICEC, Fundación para la investigación biomédica Hospital Clínico San Carlos, +34 9133030007360, fibucicec.hcsc@salud.madrid.org |

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                       | 25 May 2020  |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 30 June 2018 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 30 June 2018 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

Investigation of effect of Omeprazole on the threshold dose-distribution curve and the severity of the clinical manifestation of walnut allergic patients

Protection of trial subjects:

No needed to take any special measures aside from performin the trial in a controlled enviroment, according to the actual clinical trials regulation.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 01 July 2015 |
| 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 | Spain: 52 |
| Worldwide total number of subjects   | 52        |
| EEA total number of subjects         | 52        |

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)                      | 52 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment started on April 2016 and ended on June 2018

### Pre-assignment

Screening details:

- Positive case history of immediate allergic reaction(s) to walnut.
- Age  $\geq$  18 years.
- Presence of specific IgE to walnut defined as a positive ( $\geq$  3 mm wheal diameter) skin prick test and/or a serum IgE to walnut  $\geq$  0.35 kU/L (ImmunoCAP).

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Overall treatment (crossover design) (overall period) |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                               |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator                                 |

### Arms

|                              |            |
|------------------------------|------------|
| Are arms mutually exclusive? | No         |
| <b>Arm title</b>             | Omeprazole |

Arm description: -

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Omeprazole Sandoz |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Capsule           |
| Routes of administration               | Oral use          |

Dosage and administration details:

40mg qd

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Mannitol |
|------------------|----------|

Arm description: -

|  |          |
|--|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Mannitol |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Capsule  |
| Routes of administration               | Oral use |

Dosage and administration details:

Mannitol opaque capsule

| <b>Number of subjects in period 1</b> | Omeprazole | Mannitol |
|---------------------------------------|------------|----------|
| Started                               | 40         | 41       |
| Completed                             | 38         | 38       |
| Not completed                         | 2          | 3        |
| Consent withdrawn by subject          | 2          | 2        |
| Lack of compliance                    | -          | 1        |

## Baseline characteristics

### Reporting groups

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Overall treatment (crossover design) |
|-----------------------|--------------------------------------|

Reporting group description: -

| Reporting group values | Overall treatment (crossover design) | Total |  |
|------------------------|--------------------------------------|-------|--|
| Number of subjects     | 52                                   | 52    |  |
| Age categorical        |                                      |       |  |
| Adults 18-64           |                                      |       |  |
| Units: Subjects        |                                      |       |  |
| Adults 18-64           | 52                                   | 52    |  |
| Age continuous         |                                      |       |  |
| 18-64                  |                                      |       |  |
| Units: years           |                                      |       |  |
| median                 | 31.04                                |       |  |
| standard deviation     | ± 10.17                              | -     |  |
| Gender categorical     |                                      |       |  |
| Units: Subjects        |                                      |       |  |
| Female                 | 32                                   | 32    |  |
| Male                   | 20                                   | 20    |  |

## End points

### End points reporting groups

|                                |            |
|--------------------------------|------------|
| Reporting group title          | Omeprazole |
| Reporting group description: - |            |
| Reporting group title          | Mannitol   |
| Reporting group description: - |            |

### Primary: Change on the minimal eliciting dose of walnut protein in walnut allergic patients

|                        |  |
|------------------------|--|
| End point title        | Change on the minimal eliciting dose of walnut protein in walnut allergic patients |
| End point description: |  |
| End point type         | Primary  |
| End point timeframe:   | At the moment of food challenge (after 5 days taking the drug)                     |

| End point values            | Omeprazole      | Mannitol        |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 24              | 24              |  |  |
| Units: grams                | 40              | 41              |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | The effect of omeprazole on walnut threshold |
| Comparison groups                       | Omeprazole v Mannitol                        |
| Number of subjects included in analysis | 48   |
| Analysis specification                  | Pre-specified                                |
| Analysis type                           | superiority                                  |
| P-value                                 | ≤ 0.05                                       |
| Method                                  | Regression, Cox                              |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

5th day after taking the drug (during each food challenge)

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

### Dictionary used

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

|                    |   |
|--------------------|---|
| Dictionary version | 1 |
|--------------------|---|

### Reporting groups

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

Reporting group description: -

|                       |           |
|-----------------------|-----------|
| Reporting group title | Omeprazol |
|-----------------------|-----------|

Reporting group description: -

| Serious adverse events                            | Placebo        | Omeprazol      |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 41 (0.00%) | 0 / 40 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events                            | Placebo          | Omeprazol        |  |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 30 / 41 (73.17%) | 18 / 40 (45.00%) |  |
| Nervous system disorders                              |                  |                  |  |
| Any nervous system disorder                           |                  |                  |  |
| subjects affected / exposed                           | 10 / 41 (24.39%) | 6 / 40 (15.00%)  |  |
| occurrences (all)                                     | 30               | 18               |  |
| Gastrointestinal disorders                            |                  |                  |  |
| Any gastrointestinal disorder                         |                  |                  |  |
| subjects affected / exposed                           | 10 / 41 (24.39%) | 4 / 40 (10.00%)  |  |
| occurrences (all)                                     | 30               | 18               |  |
| Respiratory, thoracic and mediastinal disorders       |                  |                  |  |
| Any respiratory tract disorder                        |                  |                  |  |

|   |                       |                      |  |
|---|-----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 7 / 41 (17.07%)<br>30 | 3 / 40 (7.50%)<br>18 |  |
| Skin and subcutaneous tissue disorders<br>Any skin-eye disorder<br>subjects affected / exposed<br>occurrences (all)         | 1 / 41 (2.44%)<br>30  | 2 / 40 (5.00%)<br>18 |  |
| Musculoskeletal and connective tissue disorders<br>Any musculo-skeletal<br>subjects affected / exposed<br>occurrences (all) | 2 / 41 (4.88%)<br>30  | 3 / 40 (7.50%)<br>18 |  |



## **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