



## Clinical trial results:

### The effects of allergen immunotherapy on anti-viral immunity in patients with allergic asthma

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2019-003261-18  |
| Trial protocol           | DK              |
| Global end of trial date | 31 October 2022 |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1 (current)      |
| This version publication date  | 27 September 2023 |
| First version publication date | 27 September 2023 |

#### Trial information

##### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | VITAL |
|-----------------------|-------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04100902 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                                                                                                                                    |
|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Respiratory Research Unit, Department of Respiratory Medicine, Bispebjerg University Hospital                                                                                                                      |
| Sponsor organisation address | Ebba Lunds Vej 48, Entr. 66, Copenhagen NV, Denmark, 2400                                                                                                                                                          |
| Public contact               | Christian Woehlk, Dept. Respiratory and Infectious Diseases, Bispebjerg Hospital, Respiratory Research Unit, Dept. Respiratory and Infectious Diseases, Bispebjerg Hospital, DK, +45 53644292, cwoe0007@regionh.dk |
| Scientific contact           | Christian Woehlk, Dept. Respiratory and Infectious Diseases, Bispebjerg Hospital, Respiratory Research Unit, Dept. Respiratory and Infectious Diseases, Bispebjerg Hospital, DK, +45 53644292, cwoe0007@regionh.dk |

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                       | 31 October 2022 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 03 March 2022   |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 31 October 2022 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the effects of allergen immunotherapy on anti-viral immunity in patients with allergic asthma. Main outcome is to investigate potential change in bronchial epithelial cells interferon secretion before and after 6 month of treatment with ACARIZAX or placebo.

Protection of trial subjects:

Pseudoanonymised

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 03 February 2020 |
| 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 | Denmark: 39 |
| Worldwide total number of subjects   | 39          |
| EEA total number of subjects         | 39          |

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)                      | 39 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Patients recruited via the respiratory outpatient clinic at Bispebjerg Hospital, Copenhagen, Denmark and via social media.

### Pre-assignment

Screening details:

As per investigators judgement

### Period 1

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

Blinding implementation details:

Since both Acarizax and placebo are relabelled at the central pharmacy according to a randomization code, the investigational product will be received blinded to the study site.

### Arms

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

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

Arm description:

SQ HDM-SLIT

|                                        |                                   |
|----------------------------------------|-----------------------------------|
| Arm type                               | Active comparator                 |
| Investigational medicinal product name | ACARIZAX® 12 SQ oral lyophilisate |
| Investigational medicinal product code |                                   |
| Other name                             | ODACTRA®, MITICURE (TM)           |
| Pharmaceutical forms                   | Chewable/dispersible tablet       |
| Routes of administration               | Sublingual use                    |

Dosage and administration details:

12-SQ, QD

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

Arm description:

Placebo

|                                        |                    |
|----------------------------------------|--------------------|
| Arm type                               | Placebo            |
| Investigational medicinal product name | Placebo            |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Dispersible tablet |
| Routes of administration               | Sublingual use     |

Dosage and administration details:

No active ingredient, QD

| <b>Number of subjects in period 1</b> | Active | Placebo |
|---------------------------------------|--------|---------|
| Started                               | 20     | 19      |
| Completed                             | 18     | 18      |
| Not completed                         | 2      | 1       |
| Consent withdrawn by subject          | 1      | -       |
| Suspected pregnancy                   | -      | 1       |
| Adverse event, non-fatal              | 1      | -       |

## Baseline characteristics

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | Active |
|-----------------------|--------|

Reporting group description:

SQ HDM-SLIT

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

Reporting group description:

Placebo

| Reporting group values | Active | Placebo | Total |
|------------------------|--------|---------|-------|
| Number of subjects     | 20     | 19      | 39    |
| Age categorical        |        |         |       |
| Units: Subjects        |        |         |       |
| Adults (18-64 years)   | 20     | 19      | 39    |
| Age continuous         |        |         |       |
| Units: years           |        |         |       |
| arithmetic mean        | 28     | 28      |       |
| standard deviation     | ± 7.3  | ± 8.8   | -     |
| Gender categorical     |        |         |       |
| Units: Subjects        |        |         |       |
| Female                 | 13     | 12      | 25    |
| Male                   | 7      | 7       | 14    |
| FEV1                   |        |         |       |
| L/s                    |        |         |       |
| Units: L/s             |        |         |       |
| arithmetic mean        | 3.6    | 3.7     |       |
| standard deviation     | ± 0.82 | ± 0.71  | -     |
| FEV1/FVC               |        |         |       |
| Units: ratio           |        |         |       |
| arithmetic mean        | 0.77   | 80      |       |
| standard deviation     | ± .078 | ± .077  | -     |
| FEV1 pct               |        |         |       |
| Units: percentage      |        |         |       |
| arithmetic mean        | 90     | 95      |       |
| standard deviation     | ± 13   | ± 12    | -     |

## End points

### End points reporting groups

|                              |         |
|------------------------------|---------|
| Reporting group title        | Active  |
| Reporting group description: |         |
| SQ HDM-SLIT                  |         |
| Reporting group title        | Placebo |
| Reporting group description: |         |
| Placebo                      |         |

### Primary: Delta IFN-B mRNA rel. to UBC/GADPH

|                                                                              |                                    |
|------------------------------------------------------------------------------|------------------------------------|
| End point title                                                              | Delta IFN-B mRNA rel. to UBC/GADPH |
| End point description:                                                       |                                    |
| Delta IFN-B is calculated within groups from baseline to week-24 (follow-up) |                                    |
| End point type                                                               | Primary                            |
| End point timeframe:                                                         |                                    |
| Baseline and Week-24                                                         |                                    |

| End point values                     | Active             | Placebo            |  |  |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed          | 17                 | 17                 |  |  |
| Units: IFN-B mRNA rel. to UBC/GADPH  |                    |                    |  |  |
| arithmetic mean (standard deviation) | 1.50 ( $\pm$ 2.84) | 1.11 ( $\pm$ 2.16) |  |  |

|                            |                 |
|----------------------------|-----------------|
| Attachments (see zip file) | Eudract IFN.png |
|----------------------------|-----------------|

### Statistical analyses

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                              |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Statistical analysis title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Delta IFN-B mRNA expression rel to UBC/GADPH |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                              |
| Total RNA was extracted from HBECs using a RNeasy Plus Mini Kit (Qiagen) and 1 µg of RNA was reverse transcribed to cDNA (High-Capacity cDNA Reverse Transcription Kit, applied biosystems, Thermo Fisher Scientific). Amplification was performed by AriaMX realtime PCR system (Agilent Technologies, Glostrup, Denmark) as previously described. Target genes are listed in the Online Supplementary. The $-\Delta\Delta C_t$ method was then applied for relative quantification using UBC/GAPDH as housekeeping genes |                                              |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Active v Placebo                             |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 34                                           |
| Analysis specification                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Pre-specified                                |
| Analysis type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | equivalence                                  |
| P-value                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | = 0.41                                       |
| Method                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | t-test, 2-sided                              |
| Parameter estimate                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Mean difference (final values)               |



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Full study

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | RedCap |
|-----------------|--------|

|                    |   |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | Active |
|-----------------------|--------|

Reporting group description:

SQ HDM-SLIT

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

Reporting group description:

Placebo

| Serious adverse events                            | Active                                                   | Placebo        |  |
|---------------------------------------------------|----------------------------------------------------------|----------------|--|
| Total subjects affected by serious adverse events |                                                          |                |  |
| subjects affected / exposed                       | 2 / 20 (10.00%)                                          | 1 / 19 (5.26%) |  |
| number of deaths (all causes)                     | 0                                                        | 0              |  |
| number of deaths resulting from adverse events    | 0                                                        | 0              |  |
| Immune system disorders                           |                                                          |                |  |
| Angioedema                                        |                                                          |                |  |
| subjects affected / exposed                       | 1 / 20 (5.00%)                                           | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all   | 1 / 1                                                    | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0                                                    | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders   |                                                          |                |  |
| Pleuritis                                         | Additional description: Pleuritis following bronchoscopy |                |  |
| subjects affected / exposed                       | 1 / 20 (5.00%)                                           | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1                                                    | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0                                                    | 0 / 0          |  |
| Renal and urinary disorders                       |                                                          |                |  |
| Pyelonephritis acute                              |                                                          |                |  |
| subjects affected / exposed                       | 0 / 20 (0.00%)                                           | 1 / 19 (5.26%) |  |
| 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 %

| <b>Non-serious adverse events</b>                     | Active          | Placebo         |  |
|-------------------------------------------------------|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                 |                 |  |
| subjects affected / exposed                           | 8 / 20 (40.00%) | 8 / 19 (42.11%) |  |
| General disorders and administration site conditions  |                 |                 |  |
| Throat irritation                                     |                 |                 |  |
| subjects affected / exposed                           | 8 / 20 (40.00%) | 6 / 19 (31.58%) |  |
| occurrences (all)                                     | 17              | 17              |  |
| Respiratory, thoracic and mediastinal disorders       |                 |                 |  |
| Cough                                                 |                 |                 |  |
| subjects affected / exposed                           | 5 / 20 (25.00%) | 6 / 19 (31.58%) |  |
| occurrences (all)                                     | 17              | 17              |  |
| Infections and infestations                           |                 |                 |  |
| Fever                                                 |                 |                 |  |
| subjects affected / exposed                           | 2 / 20 (10.00%) | 2 / 19 (10.53%) |  |
| occurrences (all)                                     | 17              | 17              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment                                                                                                                                                                                                                                                                                                         |
|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 03 June 2020 | Amendment v.2.2.<br>Deletion of exclusion criteria: Birch sensitisation<br>Change GINA 3-5 to 2-4<br>Add inclusion criteria Dose of ICS budesonide equivalent $\geq 400$ $\mu\text{g}$<br>Change inclusion criteria: Moderate to severe rhinitis to HDM induced mild-severe allergic rhinitis for at least 1 year |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/36701676>